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One pot Multicomponent Synthesis of 1, 3-oxazine derivatives.

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ABSTRACT:

In the present work entitled 1, 3-oxazine derivative is prepared by using greener approaches. Amberlyst IR-120 has been used as catalyst for synthesis of few of these derivatives. Attempt has been made to develop a new one pot multicomponent methodology to synthesize these oxazine derivatives. Purity has been checked by using TLC method & formation of derivative is confirmed by spectral analysis.

KEY WORDS: 1, 3-oxazine, Amberlyst IR-120, p-bromoaniline, formaldehyde.

1.0] INTRODUCTION:

Heterocyclic compounds are those compounds which possess one or more hetero atoms in its structure (Greek word "heteros" means different). More than half of the organic compounds are heterocyclic. There is a vast number of pharmacologically active compounds which are regularly used in medicine and are widely distributed in nature and many of them are of fundamental importance for life processes e.g. Nucleic acid contains purine and pyrimidine, essential dietary ingredients containing vitamin B1, B2,B3,B6 and ascorbic acid etc. The 1, 3-oxazine nucleus features prominently in many biologically important natural products and other bioactive molecules1-4. 1, 3-O, N heterocyclic having a great number of synthetic possibilities, e.g., they can be used as intermediates in the synthesis of N-substituted amino alcohols or nitrogen-bridged heterocyclic systems and they serve as aldehyde sources in carbon transfer reactions[5]. 1, 3-oxazine ring system exhibited a wide spectrum of pharmacological activities such as anti-tumor[6], anti-bacterial[7], anti-HIV8 and anti malarial[9] agents. In addition, 6-arylbenzoxazines are reported as potent non-steroidal progesterone receptor agonists[10]. In addition, naphthoxazine derivatives have therapeutic potential in the treatment of Parkinson's diseases[11-12].

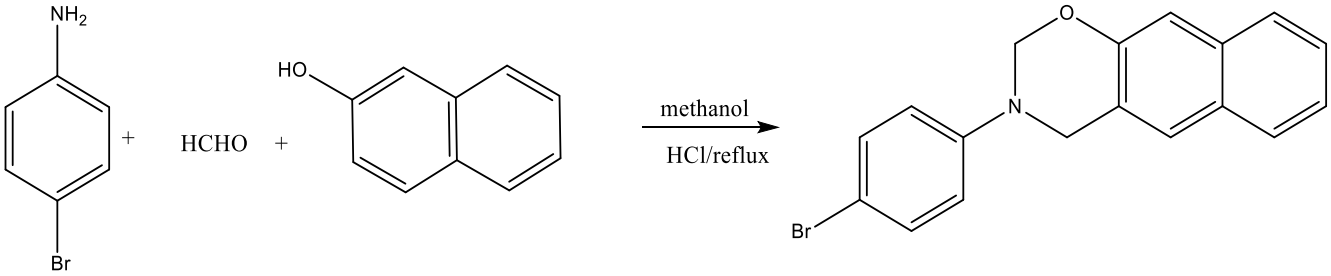
The present investigation includes synthesis of 1, 3-oxazine derivatives. This is in relation to the reaction of representative substituted aromatic amines with formaldehyde and β-naphthol as well as α-naphthol. The primary aromatic amines are of particular interest in such studies since their chemical behaviour can be modified significantly by ring substitution and they can undergo nuclear condensation with formaldehyde. Literature research for the synthesis of 2,3-dihydro-2-phenyl-1H-naphtho[1,2-e] [1,3]-oxazine provides only few previous reports on such moiety where the synthesis of above-mentioned compound was performed using formaldehyde, a primary aromatic amine, and β-naphthol 13-16. Therefore, we have further investigated this molecule of interest using greener approaches and in search of better alternatives over reported methods. We report the use of amberlyst IR-120 as a catalyst for the synthesis of 2,3-dihydro-2-phenyl-1H-naphtho[1,2-e] [1,3]-oxazine and 3,4-dihydro-3-phenyl-2H-naphtho [2,1-e][1,3]oxazine.

2.0] RESEARCH METHODOLOGY:

2.1 Experimental section:

All chemicals and solvent used in laboratory are grade purified prior use. The reactions are monitored and their purity was checked by TLC. Those reaction components were visualized in iodine chamber.

Scheme 1: Synthesis of 3-(4-bromophenyl)-3, 4-dihydro-2H-naptho [2, 1-e] [1, 3] oxazine derivative.

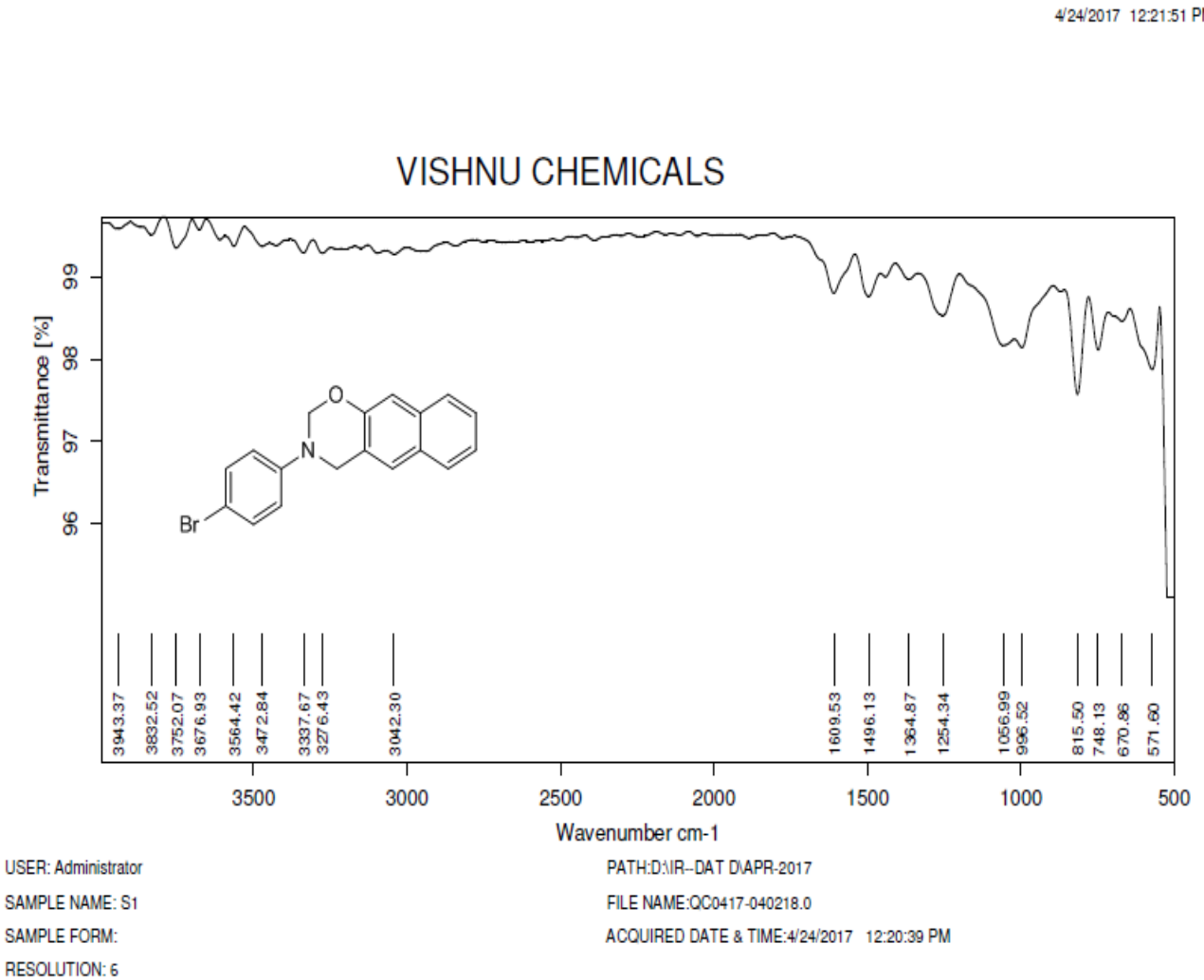


1 (a-e) 2 3 4 (a-e)

2.2 General procedure:

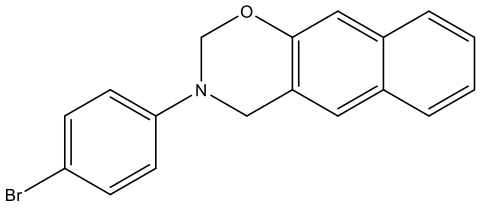
A mixture of formaldehyde (2mmol) and the p-bromoaniline (1mmol), β-napthol (1mmol) were stirred in methanol (20ml) at 80-90^{0}C for three hours, in the presence of catalytic amount of hydrochloric acid. After completion, the reaction was monitored by TLC. The reaction mixture was diluted with water and extracted with diethyl ether (2×20 ml). The combined organic layers were dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The crude product was recrystallized from ethanol. The reaming derivatives were also prepared by same method.

2.3 Spectral analysis:



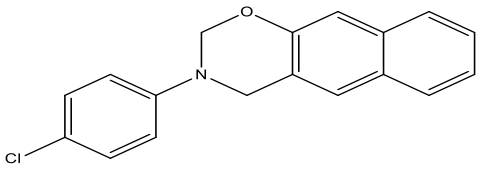
Possible spectroscopic data of some selected compounds:

4a: 3-(4-bromophenyl)-3, 4-dihydro-2H-naphthol [2, 3-e] [1, 3] oxazine.



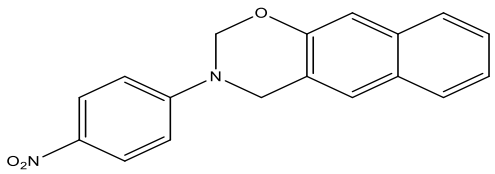
MP 118-120^0 C.; Yield (87%).; IR (KBr, cm^{-1}): vmax 3032 (Ar C-H), 2927 (C-H), 1414 (C=C),1221 (C-O-C).550 (C-Br); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 4.69 (s, 2H-N-CH_2-), 5.39 (s, 2H -O-CH_2-N), 6.82 (d, 1H, J=6 Hz Ar-H), 6.89 (t, 1H, J=7.4 Hz Ar-H), 7.03. (d, 1H, J=5.8 Hz Ar-H), 7.11 (t 1H, J= 6.00 Hz Ar-H), 7.38 (d, 2H, J=5.7 Hz Ar-H), 7.73 (s,1H, Ar-H), 7.75 (s, 1H, Ar-H); ^{13}CNMR ($CDCl_3$,75 MHz) δ ppm; 50.4, 79.3, 112.1, 115.6, 117.1, 120.0, 121.1, 123.1, 126.7, 128.2, 129.9, 149.2, 154.0; ESI-MS m/z 339[M+].

4b: 3-(4-chlorophenyl)-3, 4-dihydro-2H-naphtho [2, 3-e] [1, 3] oxazine.



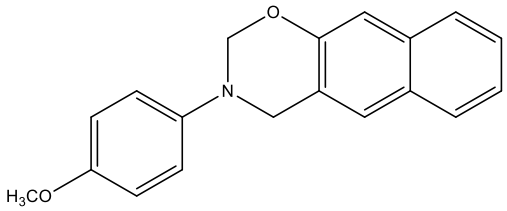
MP 128-130^0 C.; Yield (85%).; IR (KBr, cm^{-1}): vmax 3032 (Ar C-H), 2927 (C-H), 1414 (C=C),1221 (C-O-C), 751 (C-Cl),; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 4.69 (s, 2H-N-CH_2-), 5.39 (s, 2H -O-CH_2-N), 6.82 (d, 1H, J=6 Hz Ar-H), 6.89 (t, 1H, J=7.4 Hz Ar-H), 7.04. (d, 1H, J=5.8 Hz Ar-H), 7.12 (t 1H, J= 6.00 Hz Ar-H), 7.39 (d, 2H, J=5.7 Hz Ar-H), 7.74 (s,1H, Ar-H), 7.76 (s, 1H, Ar-H); ^{13}CNMR ($CDCl_3$,75 MHz) δ ppm; 50.4, 79.3, 112.1, 115.6, 117.1, 120.0, 121.1, 123.1, 126.7, 128.2, 129.9, 149.2, 154.0; ESI-MS m/z 295[M+].

4c: 3-(4-nitrophenyl)-3, 4-dihydro-2H-naphtho [2, 3-e] [1, 3] oxazine.



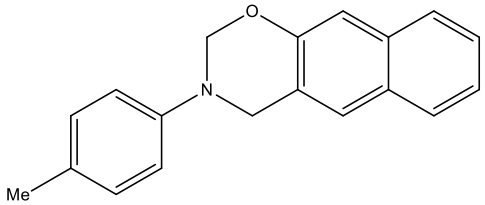
MP 168-170^0 C. Yield (88%).; IR (KBr, cm^{-1}): vmax 3018(Ar C-H), 2916 (C-H), 1533(NO_2),1409(C=C),1233(C-O-C).; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 4.73 (s, 2H-N-CH_2-), 5.40 (s, 2H -O-CH_2-N), 6.85 (d, 1H, J= 7.4 Hz), 6.93 (t, 1H, J=7.4Hz), 6.97 (d, 1H, J=7.6Hz), 7.05 (t 3H, J=7.6 Hz), 7.15 (d, 1H, J=7.4 Hz), 7.18 (d, 1H, J=8.0 Hz); ^{13}CNMR ($CDCl_3$,75 MHz) δ ppm; 49.4, 79.8, 114.9, 117.2,120.0, 121.5, 125.7, 126.7, 128.3, 140.3, 152.8, 153.9; ESI-MS m/z 306 [M+].

4d: 3-(4-methoxyphenyl)-3, 4-dihydro-2H-naphtho [2, 3-e] [1, 3] oxazine.



MP 76-78^0 C.; Yield (84%).; IR (KBr, cm^{-1}): vmax 3018(Ar C-H), 2916 (C-H), 1409(C=C),1233(C-O-C).; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 4.73 (s, 2H-N-CH_2-), 5.40 (s, 2H -O-CH_2-N), 6.85 (d, 1H, J= 7.4 Hz), 6.93 (t, 1H, J=7.4Hz), 6.97 (d, 1H, J=7.6Hz), 7.06 (t 3H, J=7.6 Hz), 7.16 (d, 1H, J=7.4 Hz), 7.19 (d, 1H, J=8.0 Hz); ^{13}CNMR ($CDCl_3$,75 MHz) δ ppm; 49.4, 79.8, 114.9, 117.2,120.0, 121.5, 125.7, 126.7, 128.3, 140.3, 152.8, 153.9; ESI-MS m/z 291 [M+].

4e 3-(p-tolyl)-3, 4-dihydro-2H-naphtho [2, 3-e] [1, 3] oxazine.



MP 69-71^0 C.; Yield (80 %).; IR (KBr, cm^{-1}): vmax 3011(Ar C-H), 2911 (C-H), 1409(C=C), 1233(C-O-C).; ^{1}H NMR (400MHz, $CDCl_3$) δ ppm: 4.73 (s, 2H-N-CH_2-), 5.40 (s, 2H –O-CH_2-N), 6.85 (d, 1H, J=7.4Hz), 6.93 (t, 1H, J=7.4Hz), 6.97(d, 1H, J=7.6 Hz), 7.07 (t, 3H, J=7.6 Hz), 7.17 (d, 1H, J=7.4 Hz), 7.21 (d, 1H, J=8.0 Hz); ^{13}CNMR ($CDCl_3$,75 MHz) δ ppm; 49.4, 79.8, 114.9, 117.2,120.0, 121.5, 125.7, 126.7, 128.3, 140.3, 152.8, 152.9; ESI-MS m/z276 [M$^+$]

3.0] RESULT AND DISCUSSION:

The synthetic protocol for the synthesis of titled compound is outlined in scheme1. In continuation and encouraged from our previous work an attempt has been done to develop a new one-pot methodology for the synthesis of 3-(4-bromophenyl)-3,4-dihydro-2H-naptho [2, 3-e] [1,3] oxazine derivatives.

The synthesis of 3-(4-bromophenyl)-3, 4-dihydro-2H-naptho [2, 3-e] [1, 3] oxazine derivatives involve condensation reaction intermediate formed, substituted aniline and formaldehyde.

All the synthesized compounds were characterized by means of IR analysis. The formation of these derivatives is confirmed by spectral analysis.

4.0] CONCLUSION:

Synthesis of 3-(4-bromophenyl)-3, 4-dihydro-2H-naphtho [2, 3-e] [1, 3] oxazine from various aryl amines and napthol. The remarkable advantages offered by this method are short reaction times, ease of product isolation, and high yields. We believe that this method is a useful in addition to the present methodology for the synthesis of 3-(4-bromophenyl)-3, 4-dihydro-2H-naptho [2, 3-e] [1, 3] oxazine derivative.

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