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Eco-friendly Synthesis and characterization of some (2-pyrazoline) and (2-isoxazoline) containing anthracene moiety by using PEG(400) as a Catalyst

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ABSTRACT

A series of substituted chalcones (2 a-d) were synthesized and used to prepare some new five membered heterocyclic compounds (pyrazoline) (3 a-d) by their condensation with hydrazine hydrate and (Isoxazolines) (4 a-d) by their condensation with hydroxylamine hydrochloride .The synthesized compounds were characterized by using FTIR ,^{1}H NMR and mass spectra, C.H.N. analysis. The validity of the expected chemical compounds to the prepared compounds in this search was obvious from FTIR spectra and C.H.N. results.

Keywords: Chalcones, Pyrazoline, Isoxazoline, 9-acetyl anthracene, Aromatic aldehydes, Aqueous NaOH, PEG (400).

INTRODUCTION

Chalcones are natural substances found in a number of plants or synthetically prepared. These compounds are of a high interest due to their use as starting material in the synthesis of a series of heterocyclic compounds [1-2]. Nitrogen and oxygen containing five membered heterocyclic compounds, natural as well as synthetic, have received considerable attention due to the wide range of pharmacological activities.

Isoxazoline represent one of the active classes of compounds possessing a wide spectrum of biological activities. Isoxazolines posses medicinal activities such as anti-inflammatory1[3], antibacterial, anticonvulsant [4],antibiotic [5], antitubercular [6], antifungal [7] and anxiolytic activity [8].antiproliferative and apoptotic activities in the micro molar concentration range [9]. Various substituted pyrazolines and their derivatives are important biological agents and a significant amount of research activity has been directed towards this class of compounds. In particular, they show antimicrobial [10] antimicrobacterial [11] anti-inflammatory and analgesic [12] and antidepressant activities [13].

In view of these observation and in continuation of the research work on bio active heterocycles [14]. It was intended to design and synthesize some new chalcones, pyrazolines and isoxazolines and evaluate their spectral data.

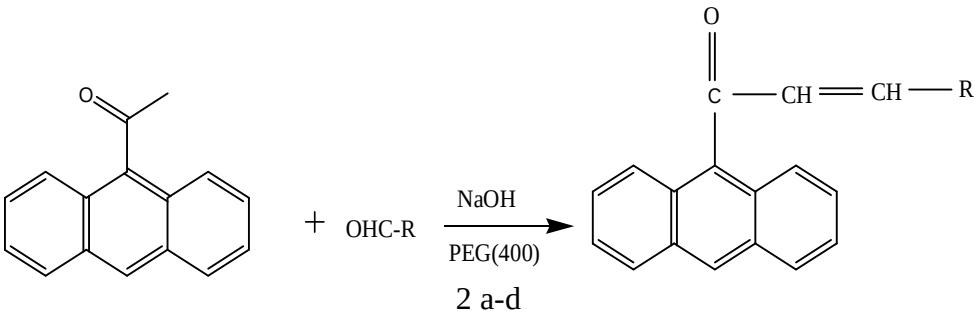
MATERIALS AND METHODS

9-acetyl anthracene , all aromatic aldehydes, hydrazine hydrate and hydroxyl amine hydrochloride were purchased from Sigma Aldrich. PEG used was of Thomas baker. Ethanol and other chemicals of A.R. grade were used as received.

General procedure for the synthesis of chalcones(2a-h): A mixture (0.01 mol) and appropriate aldehyde (R) (0.01 mol) was stirred in ethanol and then aqueous solution of NaOH (40%,9- 10 ml) was added to it and in this solution 2 ml PEG (400) was added as a catalyst with continuous stirring. The mixture was kept at room temperature for 2 h. The sodium salt of chalcone separated was decomposed by ice-cold HCl (30%). The separated chalcone was filtered, washed with water (50 ml) , dried and recrystallized from absolute ethanol. Compounds 2b-d were also prepared in a similar manner.

General procedure for the synthesis of pyrazolines: Compound 2a (0.01mol) was dissolved in 10 ml of ethanol. To this hydrazine hydrate (0.03 mol) was added. The reaction mixture was heated at reflux for 2 h and then 1ml glacial acetic acid and 1ml PEG (400) was added and then heating was continuous for further 2 h. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to RT. At the end 50 ml cold water was slowly added in to the flask and separated product was filtered off and washed with cold water several times. The crude product was purified by recrystallisation from ethanol to obtain pyrazoline 3a. Compounds 3b-d were also prepared in a similar manner.

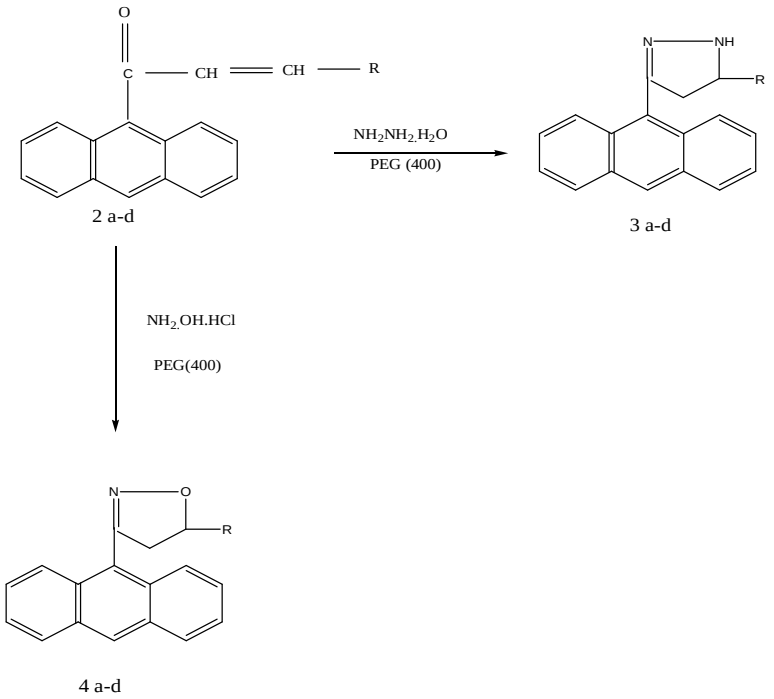
General procedure for the synthesis of Isoxazolines: Compound 2a (0.01 mol), hydroxyl amine hydrochloride (0.01 mol) and 0.5 g NaOH were taken in 15 ml ethanol. The reaction mixture was heated at reflux for 2 h and then 1 ml PEG (400) was added and then heating was continuous for further 2h.The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was poured over crushed ice and neutralized with acetic acid. The precipitates were separated by filtration, washed with water and purified by recrystallisation from ethanol to obtain the isoxazoline 4a. Compounds 4b-d were also prepared in a similar manner.



2 a-d

Where R= 4-Cl, 4-NO_2, 4-Br , 4-OCH_3

Scheme 1



Where R= 4-Cl, 4-NO_2, 4-Br , 4-OCH_3

Scheme 2

Physical measurements and analytical data: The melting points were determined in open capillaries on Electro thermal apparatus and are uncorrected. The purity of all compounds were checked by thin layer chromatography using percolated silica 60 F 254 plate using hexane, ethyl acetate, chloroform (6:2:2) as mobile phase. Micro analysis of carbon, hydrogen, oxygen and nitrogen of the compounds were carried on a Heraeus Carlo Erba 1108 elemental analyzer. IR spectra were recorded on a Perkin-Elmer RX-1 infrared spectrophotometer in the range 4000–400 cm^{-1}. 1HNMR spectra of the compounds were recorded on a Bruker Avance 400 MHz The ESI mass spectra were recorded on a JEOL-Accu TOF JMS-100LC Mass spectrometer.

RESULTS AND DISCUSSION

Anthracene chalcones (a-d) were prepared by carrying out the reactions of 9-acetyl anthracene with 4-chloro benzaldehyde, 4-nitro benzaldehyde, 4-bromo benzaldehyde, 4- methoxy benzaldehyde and ethanol using aqueous sodium hydroxide and PEG(400) as a catalyst. Synthesis of chalcone is a single step method. The synthesized chalcones were condensed with hydrazine hydrate to form pyrazoline (3a-d) and hydroxyl amine hydrochloride to form isoxazoline(4 a-d). All the synthesized compounds were undergone physiochemical characterization and the obtained results are given. The yield of the synthesized compounds was found to be significant because of PEG (400)use as a catalyst. Elemental analysis showed that the percentage of carbon, hydrogen, oxygen and nitrogen was found experimentally is equivalent to the calculated values in all compounds.

The data obtained of the synthesized compounds -

1. 1(anthracene-9-yl)-3-(4-chloro phenyl) prop-2ene-1-one: yellow crystals ,yield: 81%; m.p. 205˚C; Anal. Calcd. for $C_{32}H_{39}ClO$; C: 80.90; H: 8.27; O: 3.37 (%); Found: C: 80.98; H: 8.50; O:4.45 (%); IR (cm^{-1}):-1640 (C=O), 1601 (C=C), 1273 (C-O-C); , ^{1}HNMR-(400 MHz, DMSO-d6): ∂ (in ppm) , ∂=8.18-8.17

(m, 1H), 7.76 (d, 1H, Ar -H), 7.67 (d, 1H, Ar-H), 7.56 (d, 2H, Ar-H), 7.40-7.36 (m, 4H); MS m/z 475 (M+).

2. 1(anthracene-9-yl)-3-(4-nitro phenyl) prop-2ene-1-one: yellow crystals ,yield: 80%; m.p. 230˚C; Anal. Calcd. for $C_{32}H_{39}NO_3$; C: 79.14; H: 8.09; O: 9.88 (%); Found: C: 79.49; H: 8.50; O:9.95 (%) IR (cm-1):- 1650 (C=O), 1585, 1560 (C=C), 1305 (C-O-C), ^{1}HNMR-(400 MHz,DMSO-d6) ∂ (in ppm) , ∂=7.81-7.47 (m, 1H), 8.31 (d, IH, Ar- H), 8.11 (d, 1H, Ar-H), 7.64-7.63 (m, 2H, Ar-H), 7.44-7.43 (m, 3H) ; MS m/z 520 (M+).

3. 1(anthracene-9-yl)-3-(4-bromo phenyl) prop-2ene-1-one: yellow crystals yield: 82%; m.p. 220˚C; Anal. Calcd. for $C_{32}H_{39}BrO$; C: 73.98; H: 7.57; O: 3.08 (%); Found: C: 73.49; H: 7.60; O:3.95 (%) IR (cm-1):- 1617 (C=O), 1561, 1550 (C=C), 1325 (C-O-C), ^{1}HNMR-(400 MHz,DMSO-d6) ∂ (in ppm) , ∂=8.18-8.17 (m, 1H), 7.74 (d, 1H, Ar-H), 7.65-7.63(m,1H, Ar-H), 7.54 (d, 2H, Ar-H), 7.48 (d, 2H, Ar-H), 7.41-7.36 (m, 2H) ; MS m/z 486 (M+).

4. 1(anthracene-9-yl)-3-(4-methoxy phenyl) prop-2ene-1-one: yellow crystals yield: 85%; m.p. 210˚C; Anal. Calcd. for $C_{33}H_{42}O_2$; C: 84.21; H: 8.99; O: 6.80 (%); Found: C: 84.45; H: 9.10; O:6.95 (%) IR (cm-1):- 1654 (C=O), 1462, 1460 (C=C), 1350 (C-O-C), ^{1}HNMR-(400 MHz,DMSO-d6) ∂ (in ppm) , ∂=8.17-8.15 (m, 1H,Ar-H), 7.81 (d, 1H, Ar-H),7.67(d 1H,Ar-H), 7.60 (d, 2H,Ar-H),7.37-7.35(m,1H Ar-H),7.31 (d 1H,Ar,-H), 6.94 (d,2H, Ar-H), 3.85 (s, 3H-OCH_3) ; MS m/z 471 (M+).

5. 3-(anthracene-9-yl)-5-(4-chloro phenyl)-2- pyrazoline- : Light yellow Crystals yield: 88%; m.p. 168˚C; Anal. Calcd. for $C_{23}H_{17}ClN_2$; C: 77.41; H: 4.80; N:7.85 (%); Found: C: 77.45; H: 5.10; N:7.95 (%) IR (cm $^{-1}$):- 3290 (-NH), 3120(C-H), 1630 (C=N), 1580 (C=C), ^{1}H NMR-(400 MHz ,DMSO-d6) ∂ (in ppm): 3.01(dd, 1 H, CH_2), 6.85-7.85(11H, m, Ar-H), 6.09 (1H, s- NH), 5.18(1H, dd, -CH), 3.58 (1H, dd- CH_2), 3.20 (1H, dd, -CH_2); MS m/z 358 (M+).

6. 3-(anthracene-9-yl)-5-(4-nitro phenyl)-2- pyrazoline- :.Light yellow Crystals yield: 84%; m.p. 155˚C; Anal. Calcd. for $C_{23}H_{17}N_3O_2$; C: 75.19; H: 4.66; N:11.44 (%); Found: C: 76.35; H: 4.88; N:11.45 (%) IR (cm $^{-1}$):- 3350 (-NH), 3131(C-H), 1625 (C=N), 1570 (C=C), ^{1}H NMR-(400 MHz ,DMSO-d6) ∂ (in ppm): 3.20(dd, 1 H, CH_2), 7.63-7.94(10H, m, Ar-H), 6.08 (1H, s- NH), 5.21(1H, dd, -CH), 3.45(1H, dd- CH_2), 3.25 (1H, dd, -CH_2); MS m/z 401(M+).

7. 3-(anthracene-9-yl)-5-(4-bromo phenyl)-2- pyrazoline*.:* Light yellow Crystals yield: 81%; m.p. 180˚C; Anal. Calcd. for $C_{23}H_{19}BrN_2$; C: 68.84; H: 4.27; N: 6.98 (%); Found: C: 68.90; H: 4.88; N:7.15 (%) IR (cm $^{-1}$):- 3280 (-NH), 3135(C-H), 1636 (C=N), 1642 (C=C), ^{1}H NMR-(400 MHz ,DMSO-d6) ∂ (in ppm): 3.22(dd, 1 H, CH_2), 7.69-7.94 (9H, m, Ar-H), 6.04 (1H, s- NH), 5.20(1H, dd, -CH,), 3.49(1H, dd- CH_2), 3.10(1H, dd, -CH_2) ; MS m/z 368(M+).

8. 3-(anthracene-9-yl)-5-(4-methoxy phenyl)-2- pyrazoline.: Light yellow Crystals yield: 82%; m.p. 175˚C; Anal. Calcd. for $C_{24}H_{20}N_2$; C: 81.79; H: 5.72; N: 7.95 (%); Found: C: 81.85; H: 5.85; N:7.98 (%) IR (cm $^{-1}$):- 3245 (-NH), 3120(C-H), 1648 (C=N), 1630 (C=C), ^{1}H NMR-(400 MHz ,DMSO-d6) ∂ (in ppm): 3.25(dd, 1 H, CH_2), 6.70-7.72 (9H, m, Ar-H), 6.19 (1H, s- NH), 5.18(1H, dd, -CH), 3.15(1H, dd- CH_2), 2.30 (3H, s, -OCH_3) ; MS m/z 353(M+).

9. 3 -(anthracene-9-yl)-5-(4-chloro phenyl)-2-isoxazoline.*:* Shiny yellow Crystals yield: 83%; m.p. 140˚C; Anal. Calcd. for $C_{23}H_{16}ClNO$; C: 77.20; H: 4.51; N: 3.91 (%); Found: C: 77.35; H: 4.65; N:3.98 (%) IR (cm $^{-1}$):- 1682 (C= N), 1593,1568(C=C), 1348 (C-O), 851, 680 (C-H .), 735 (C-Cl Str) ^{1}H NMR-(400 MHz ,DMSO-d6) ∂ (in ppm): 7.61-8.51 (r, 4H,),7.31-7.20 (s, 4H,), 4.5 (m,1H, CH), 3.39-3.52 (s,2H, CH_2) ; MS m/z 359(M+).

10. 3 -(anthracene-9-yl)-5-(4-nitro phenyl)-2-isoxazoline: Shiny yellow Crystals yield: 81%; m.p. 132˚C; Anal. Calcd. for $C_{23}H_{16}N_2O_3$; C: 74.99; H: 4.38; N: 7.60 (%); Found: C: 7505; H: 4.65; N:7.78 (%) IR (cm $^{-1}$):- 1640 (C= N), 1520,1548(C=C), 1360 (C-O-N), 835, 630 (C-H), ^{1}H NMR,(400 MHz ,DMSO-d6) ∂ (in ppm): 7.80-8.19 (r, 4H,),5.09-5.61 (s, 4H,), 3.5 (m,1H, CH), 3.87-3.95 (s,2H, CH_2) ; MS m/z 370(M+).

11. 3 -(anthracene-9-yl)-5-(4-bromo phenyl)-2-isoxazoline*:* Shiny yellow Crystals yield: 81%; m.p. 121˚C; Anal. Calcd. for $C_{23}H_{16}$ BrNO; C: 68.67; H: 4.01; N: 3.48 (%); Found: C: 68.75; H: 4.25; N:3.68 (%) IR (cm $^{-1}$):- 1660 (C= N), 1612,1599(C=C), 1348 (C-O-N), 851, 680 (C-H), 640 (C-Br) ^{1}H NMR-(400 MHz ,DMSO-d6) ∂ (in ppm): 7.61-8.51 (r, 4H),7.08-7.36 (s, 4H), 4.5 (m,1H, CH), 3.39-3.52 (s,2H, CH_2) ; MS m/z 403(M+).

12. 3 -(anthracene-9-yl)-5-(4-methoxy phenyl)-2-isoxazoline*:* Shiny yellow Crystals yield: 85%; m.p. 148˚C; Anal. Calcd. for $C_{24}H_{19}NO_2$; C: 81.56; H: 5.42; N: 3.96 (%); Found: C: 8165; H: 5.65; N:3.99 (%) IR (cm $^{-1}$):- 1655 (C= N), 1587,1566(C=C), 1340 (C-O-N), 1252(Ar C-O , OCH_3),820,695 (Ar, C-H), ^{1}H NMR-(400 MHz ,DMSO-d6) ∂ (in ppm): 7.62-8.42 (r, 4H) ,6.77-7.10 (s, 4H,), 3.75 (s,3H, CH_3)) ; MS m/z 354 (M+).

APPLICATIONS

This is an environmentally benign procedure and reduces the total reaction time and good to excellent yields of chalcones, pyrazoline and isoxazoline.

CONCLUSIONS

In summary, we have synthesized a new series of 2-pyrazoline and 2-isoxazoline derivatives containing anthracene moiety by the treatment of 1-(anthracene-9-yl)-3-aryl-2-propene-1- ones with hydrazine hydrate and hydroxyl amine hydrochloride respectively, in ethanol under reflux condition. The synthesis of following compounds using PEG (400) as a catalyst results enhancements in the rate of reaction. The proposed method for the synthesis reduces the total reaction time and good to excellent yields, also allows easy separation of the product.

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