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SYNTHESIS OF 2/3/4- NITRO-1-THIOCARBAMOYL /SEMICARBAMOYL-3,5-DIETHOXY-4-(PHENYLAZO) PYRAZOLES AND 2/3/4-NITRO-3,5-DIETHOXY-4-(PHENYLAZO) ISOXAZOLES

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Abstract
Various 1-thiocarbamoyl (**2a-c**)/ semicarbamoyl -3,5- diethoxy-4- (2-nitro/3-nitro/4-nitro) pyrazoles(**3a-c**) and 3,5- diethoxy-4- (2-nitro/3-nitro/4-nitro) isoxazoles (**4a-c**) have been synthesized and characterized by elemental analysis, IR, ^{1}H NMR and Mass Spectral studies.

Keywords: Thiocarbamoyl; Semicarbamoyl; Pyrazoles; Isoxazoles

Introduction

Isoxazole is a five membered heterocyclic compound having various pharmacological activities[1]. Oxazoles are attractive heterocycles not only because of their unique structures and varied applications but also they serve as structural elements for a variety of natural products, pharmaceuticals and bioactive compounds[2]. They are also found to display a variety of activities such as antihelmintic, anticonvulsant[3], antipsychotic, antihistaminic, anticancer[4], antiviral, antiproliferative, antioxidant, antidepressant, hypertensive, and antifungal properties[5]. Pyrazoles and their substituted derivatives are potential pharmaceuticals and intermediates in dye industry[6], are synthesized and screened for various pharmacological activities like antimicrobial, antiviral, antitumor, antihistaminic, antidepressant, insecticides , fungicides[7], antibacterial, anti-inflammatory and anticonvulsant activity.[8] We have synthesised some new nitro group containing azo derivatives of pyrazoles and isoxazoles. Herein we report the synthesis of few substituted pyrazoles and isoxazoles that contain N-aryl substituted azo group.

Experimental

All the melting points were determined in open capillaries and are uncorrected. IR spectra (cm-^{1}) were recorded on a SHIMADZU 8400S FT-IR spectrometer in KBr pellets. ^{1}H NMR spectra were recorded in $CDCl_3$ solvent on a JEOL RESONANCE 400 MHz spectrophotometer using TMS as an internal standard. Chemical shift values are shown in δ ppm. Mass spectral studies were done on XEVO G-25 QTOF. Elemental analysis were performed by Perkin Elmer series C,H,N and S analyser-2400.The purity of all the

synthesized compounds were checked by TLC. Compounds 1a-c were prepared by reported method[9].

3,5-Diethoxy-4-(2/3/4-nitro-phenylazo)-pyrazole-1-carbothionicacid amide(2a-c)

A mixture of **1a-c** (0.01 mol) and thiosemicarbazide (0.01 mol) in acetic acid (20 ml) was refluxed on a water bath for 5-8 hrs and then allowed to cool over night and then separated solid was crystallised from ethanol (**2a-c**).

3,5-Diethoxy-4-(2/3/4-nitro-phenylazo)-pyrazole-1-carboxylicacid amide (3a-c)

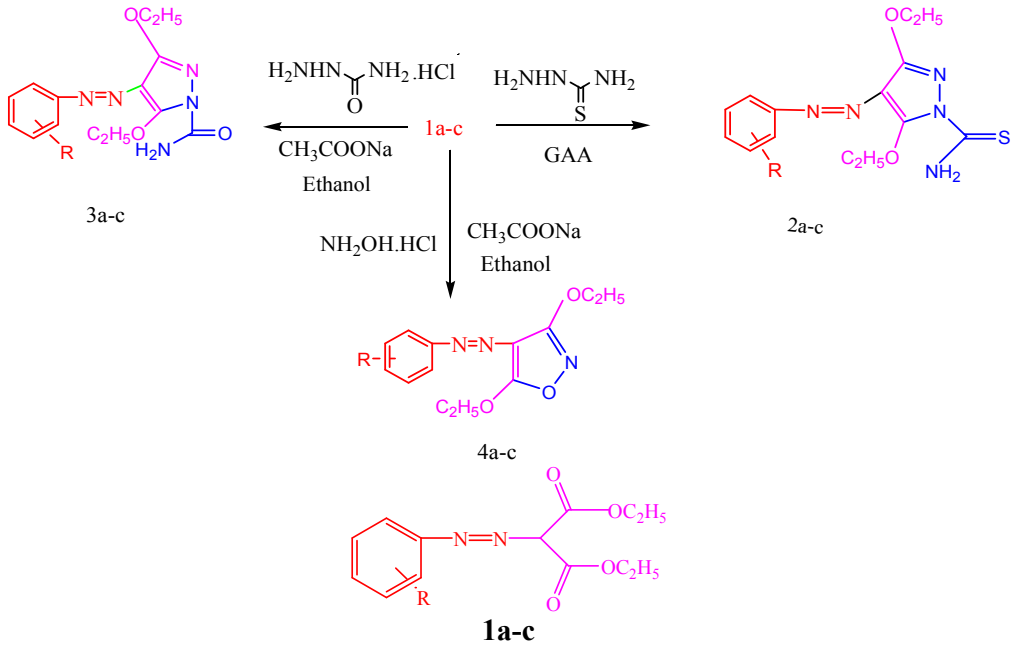
A mixture of **1a-c** (0.01 mol) in ethanol (20 ml), a solution of sodium acetate (1gm) and semicarbazide hydrochloride (0.01 mol) in water was added and the solution was refluxed on a water bath for 4-7hrs. The reaction mixture was cooled and resulting solid was crystallised from ethanol (**3a-c**).

(3, 5-Diethoxy-isoxazol-4-yl)-(2/3/4-nitro-phenyl)-diazene (4a-c)

A mixture of **1a-c** (0.01 mol) in ethanol (20 ml), a solution of sodium acetate (1gm) and hydroxylamine hydrochloride (0.01 mol) in water was added and the solution was refluxed on a water bath for 4-7hrs. The reaction mixture was cooled and resulting solid was crystallised from ethanol.

Results and discussion

Different substituted amines react with sodium nitrite and conc. HCl to form aryl diazonium salts which react with malonic ester in the presence of sodium acetate (CH_3COONa) in EtOH to give 2- [(substituted phenyl)]-hydrazono] substituted ethyl ester (**1a-c**).The hydrazono compounds were then treated with thiosemicarbazide in glacial acetic acid to obtain (substituted phenyl azo)pyrazole-1-carbothionic acid amide(**2a-c**). When the hydrazono compounds were treated with semicarbazide hydrochloride in ethanol in the presence of sodium acetate (substituted pyrazole) -1-carboxylic acid amides (**3a-c**) were obtained. Similarly when the hydrazono compounds were treated with hydroxyl amine hydrochloride in ethanol in the presence of sodium acetate produced substituted isoxazoles



GAA=Glacial Acetic acid , R=2-NO_2,3-NO_2,4-NO_2

(**4a-c**).The structures of all these newly synthesized compounds have been confirmed by elemental analysis, IR, ^{1}H NMR, and Mass Spectral studies.

2a-c compounds were confirmed by IR spectra: 1560-1570 (**>C=N**), 1600-1650 (C=C), 1510-1550 (N=N), 3400-3500 (NH_2), 1140-1145 (C=S), 1160-1200 (C-O) cm^{-1} , ^{1}H NMR spectra (δ,ppm): 8.21 (dd, 1H, ArH), 7.6 (dd, 2H, ArH), 7.1 (m, 1H, ArH), 4.38 (q, 4H, CH_2), 1.38 (t, 6H, CH_3);

3a-c compounds were confirmed by IR spectra 1500-1600 **(>C=N**), 1600- 1650 (C=C), 1510-1560 (N=N), 1690- 1720 (C=O),1100-1200(C-O) cm^{-1}; ^{1}H NMR spectra in (δ,ppm): 7.2 (1, 1H, ArH), 7.8 (dd, 2H, ArH), 7.5 (m, 1H, ArH) ,3.58 (q, 4H, CH_2), 1.53 (t, 6H, CH_3);

4a-c compounds were confirmed by IR spectra 1500- 1600 (**>C=N**), 1600- 1650 (C=C), 1510- 1560 (N=N), 1100-1200 (C-O) cm^{-1} ,^{1}H NMR spectra in (δ,ppm): 8.0 (d, 2H, ArH), 7.2 (d, 2H, ArH), 3.58 (q, 4H, CH_2), 1.13 (t, 6H, CH_3);

Table-1 Physical and analytical data of the compounds prepared

S.No.	Compound	R	R'	Molecular Formula	M.p. (^oC)	Yield (%)	Elemental Analysis (Calculated) % Found C H N S
1	2a	2-NO_2	OC_2H_5	$C_{14}H_{16}N_6O_4S$	77	53	46.09 4.41 23.01 8.76 (46.15) (4.43) (23.06) (8.80)
2	2b	3-NO_2	OC_2H_5	$C_{14}H_{16}N_6O_4S$	98	42	46.11 4.39 s 23.03 8.77 (46.15) (4.43) (23.06) (8.80)
3	2c	4-NO_2	OC_2H_5	$C_{14}H_{16}N_6O_4S$	110	60	46.12 4.38 23.05 8.78 (46.15) (4.43) (23.06) (8.80)
4	3a	2-NO_2	OC_2H_5	$C_{14}H_{16}N_6O_5$	82 82	75	48.23 4.61 24.10 (48.28) (4.63) (24.13) -
5	3b	3-NO_2	OC_2H_5	$C_{14}H_{16}N_6O_5$	89	41	48.26 4.59 24.08 (48.28) (4.63) (24.13) -
6	3c	4-NO_2	OC_2H_5	$C_{14}H_{16}N_6O_5$	104	52	48.21 4.60 24.11 (48.28) (4.63) (24.13) -
7	4a	2-NO_2	OC_2H_5	$C_{13}H_{14}N_4O_5$	86	74	50.91 4.54 18.26 (50.98) (4.61) (18.29) -
8	4b	3-NO_2	OC_2H_5	$C_{13}H_{14}N_4O_5$	96	40	50.96 4.59 18.27 (50.98) (4.61) (18.29) -
9	4c	4-NO_2	OC_2H_5	$C_{13}H_{14}N_4O_5$	111	65	50.94 4.57 18.24 (50.98) (4.61) (18.29) -

Conclusion

A series of novel pyrazoles and isoxazoles containing N -aryl substituted azo group have been synthesized by refluxing in ethanol and glacial acetic acid.

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