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Note

Synthesis of pyrazole and isoxazole in triethanolamine medium.

Nitin N Agrawal* & P A Soni

Department of Chemistry, Government Vidharbha Institute of Science and Humanities, Amravati 444 604, India.

E-mail nitinnagrawal@rediffmail.com

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Reactions of 2′-hydroxy chalcone dibromides **2a-l** with phenyl hydrazine and hydrazine hydrate afford pyrazoles **1a-l** and with hydroxylamine hydrochloride give isoxazoles **5a-f** in triethanolamine medium. Similarly reaction of β-diketone **3b-e** with phenyl hydrazine and hydrazine hydrate in TEA gives pyrazoles **4a-l** in high yield in shorter time. The products are confirmed by their m.p., m.m.p., chemical analysis and IR, ^{1}H NMR spectral data.

Keywords: Chalcone, pyrazole, isoxazole, β-diketone, triethanolamine

IPC: Int.Cl.[8] C07D

Pyrazole derivatives are well known as analgesic, antipyretic, anti-inflammatory, antidiabetics, antifedant[1-3]. Insecticidal, miticidal and hypoglycemic activities of pyrazole have been reported[4-6]. Pinto[7] has also reported medicinal importances of pyrazole derivatives. On the other hand isoxazole derivatives controlled botrytis cinera on cucumbers[8] has been found to have antiviral properties against herpes type 2 virus[9]. Penicillin derivatives containing isoxazole ring are found to be antibacterial[10]. Isoxazole derivatives are used as corrosion inhibitors for fuels and lubricants[11]. Its derivatives also show a good potency in animal models of thrombosis[7].

Hence the syntheses of these derivatives are largely on account of their biological activities. In our earlier communication we have reported the use of TEA in the synthesis of pyrazoline and isoxazoline[12] and hence it was thought interesting to use TEA for the synthesis of title compounds.

Experimental Section

Chalcones, chalcone dibromides and β-diketones were prepared according to the general procedures[13]. Authentic samples of pyrazoles **4a-b** and isoxazoles **5a-b** were prepared by known procedures[14,15]. The compounds were purified by recrystallization using glacial acetic acid or rectified spirit. The IR and ^{1}H NMR spectra were recorded on a Perkin Elmer 1800 and Bruker AC 300 F spectrometer.

Synthesis of pyrazoles 4a-l from chalcone dibromide 2a-l. Chalcone dibromide 2a-l (0.005 mole) and phenylhydrazine or hydrazine hydrate (0.01 mole) were heated in TEA (15 mL) when solution starts bumping (10-15 mins) heating was stopped. The reaction mixture was cooled, poured on ice-cold water and crystallized from AcOH to give 4a-l (Scheme I). Yield 65 to 80%. The compounds prepared are listed in **Table I**.

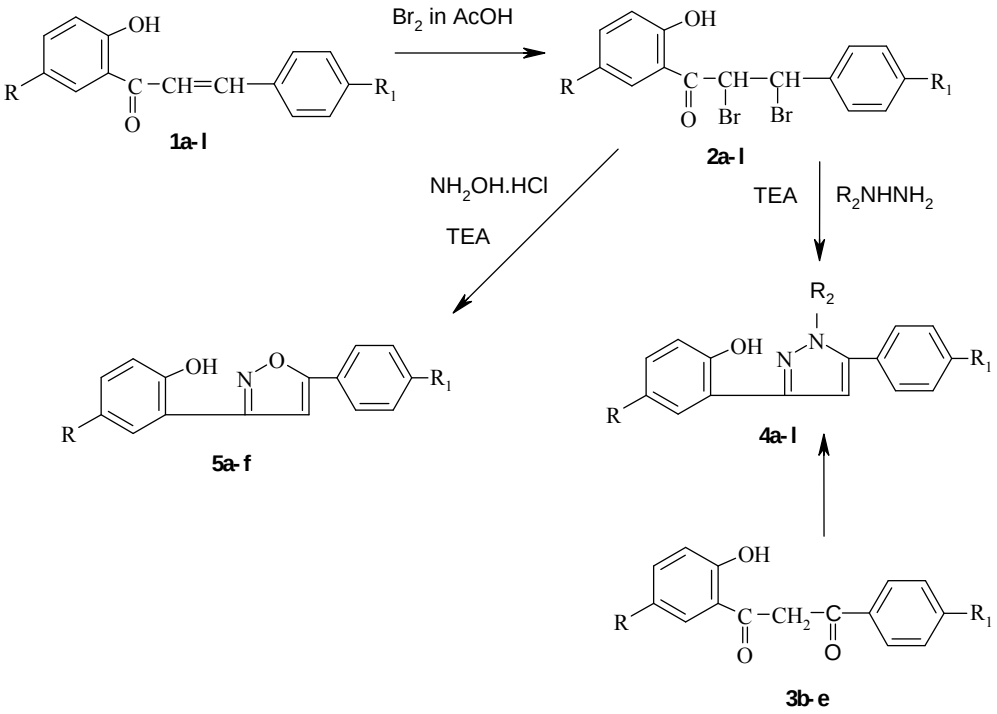
4a: IR: 1610 (-C=N-), 1511 (N-C_6H_5), 3224 (-OH). ^{1}H NMR: δ 8.02 (s, 1H, Ar-OH), δ 2.48 (s, 3H, Ar-CH_3), δ 3.90 (s, 3H, -OCH_3), δ 6.90 (s, 1H, heteroaromatic H), δ 7.02 to 8.02 (m, 12H, Ar-H).

Synthesis of pyrazoles 4a-d from β-diketone 3b-e. β-diketone **3b-e** (0.005 mole) and phenylhydrazine or hydrazine hydrate (0.01 mole) was heated in TEA (15 mL). When solution starts bumping (10-15 mins) heating was stopped. The reaction mixture was cooled, poured on ice-cold water and crystallized from AcOH to give **4b-e**. The compounds prepared are listed in **Table II**.

4b: IR:1596 (-C=N-), 1549 (N-C_6H_5-), 3430 (-OH), 766 (=CH), 1064 (-O-CH_3). ^{1}H NMR: δ 10.5-10.7 (s 1H, Ar-OH), 2.34 (s, 3H, Ar - CH_3), 6.97 (s, 1H, heteroaromatic H), 7.03 to 7.47 (m, 13H, Ar-H).

Synthesis of isoxazoles 5a-f from chalcone dibromide 2a-f. Chalcone dibromide **2a-f** (0.005 mole) and hydroxyl ammine hydrochloride (0.01 mole) were heated in TEA (15 mL). When solution starts bumping (10-15 mins) heating was stopped. The reaction mixture was cooled, poured on ice-cold water and crystallized from AcOH to give **5a-f** (**Scheme I**).

The compound obtained did not give colouration with ferric chloride but gave yellow colouration with conc. H_2SO_4 indicating the product to be isoxazole **5a-f** Yield 70-80%. The compounds prepared are listed in **Table II**.



Pyrazoles 4a -l and β-diketones 3b-e.

Compounds	R	R_1	R_2
4a	CH_3	OCH_3	Ph
4b	CH_3	H	Ph
4c	CH_3	H	H
4d	H	H	Ph
4e	H	H	H
4f	CH_3	Cl	Ph
4g	H	Cl	H
4h	CH_3	Cl	H
4i	CH_3	OCH_3	H
4j	H	OCH_3	Ph
4k	H	OCH_3	H
4l	H	Cl	Ph

Isoxazoles 5a -f

Compounds	R	R_1
5a	CH_3	OCH_3
5b	CH_3	H
5c	CH_3	Cl
5d	H	OCH_3
5e	H	H
5f	H	Cl

Scheme I

Table I — Physical characteristics of pyrazoles **4a-l** From chalcone dibromides **2a-l**

Compd	m.p. °C	N (%) Calcd	Found
4a	168-69	7.86	7.80
4b	117	8.58	8.51
4c	153-54	11.2	10.95
4d	181	8.97	8.88
4e	145	11.86	11.75
4f	212	7.76	7.67
4g	206	10.35	10.25
4h	257	9.84	9.71
4i	162	10.44	10.40
4j	187	8.18	8.11
4k	138	10.52	10.43
4l	202	8.08	8.00
From β-diketone **3b-e**			
4b	115-16	8.58	8.48
4c	152	11.2	10.97
4d	182	8.97	8.85
4e	143	11.86	11.73

5a: IR :1646 (-C=N), 1605 (-C=C), 1267 (Ar-O-ether), 3428 (-OH).^{1}H NMR: δ 8.07 (s, 1H, Ar-OH), 2.46 (s, 3H, Ar-CH_3), 3.89 (s, 3H, OCH_3), 6.99(s, 1H, heteroaromatic H), 7 to 7.9 (m, 3H, Ar-H).

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Table II — Physical characteristics of isoxazoles **5a-f**

Compd	m.p. °C	N (%) Calcd	Found
5a	229-30	4.98	4.90
5b	185-86	5.57	5.50
5c	214-15	4.90	4.81
5d	gummy mass not isolated	-	-
5e	gummy mass not isolated	-	-
5f	209-10	5.15	5.05

* Satisfactory C, H analysis were found in all the compounds.

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