Ultrasound Assisted Synthesis Of Pyrazolone Derivatives

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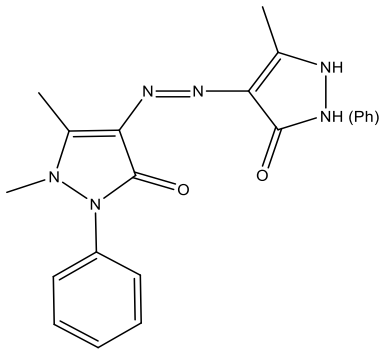
الخلاصة

تم ازدواج ملح الديازونيوم ل4-أمينو-5,1- ثنائي مثيل-2- فنيل-H1- بايرازول -5-اون (4-أمينوأنتي بايرين) مع أسيتوخلات الأثيل وبنزويل خلات الأثيل في الوسط القاعدي ليعطي مركبات الديازو المقابلة. تلك النواتج تمت مفاعلتها مع الهيدرازين المائي والفنيل هيدرازين بطريقة الموجات فوق الصوتية لتعطي مشتقات البايرازولون(I) بنسبة عالية.

ABSTRACT

The diazonium salt of 4-amino-1,5-dimethyl-2-phenyl-1H-pyrazol-2-one (4-aminoantipyrine) was coupled with ethylacetoacetate and ethyl benzoylacetate to give the corresponding diazo compounds under basic media. These products were allowed to react with hydrazine hydrate and phenylhydrazine under Ultrasound method to give pyrazolone derivatives (I) in high yields.

Keywords: Ultrasound, Pyrazolone, Ethylaceto and/or Ethylbenzoylacetate



(I)

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INTRODUCTION:

Heterocyclic compounds are acquiring more importance in recent years because of broad pharmacological activities. Pyrazolone have a particular value due to both their broad spectrum of biological activity and their wide ranging utility as synthetic tools in the design of various bioactive molecules. Pyrazolone is a five-membered lactam ring which contains two nitrogens and a ketone in the same molecule[1,2] . The chemistry of pyrazolone was started by knorr in 1883 and reported the first pyrazolone derivative[3] . The pronounced synthetic utility of heterocycles in the area of pharmaceuticals[4-6], dyes and pigment[7], technology[8,9] and natural products[10] Pyrazolone or 4-aminoantipyrine derivatives are interesting series of heterocyclic compounds, which have been shown to be diverse biological properties such as cytotoxic, anti-inflammatory[11], antimicrobial[12], antioxidant, antifungal[13], antiviral, antitumor[14], analgesic[15,16]. The approach reported here deals with the synthetic of some new pyrazolones start in 1,3-dicarbonyl compound such as ethylacetoacetate and ethylbenzoylacetate after coupled with 4-amino-1,5-dimethyl-2-phenyl-1H-pyrazol-2-one (4-aminoantipyrine) and then reacted with hydrazine or phenylhydrazine to give pyrazolone derivatives using simple methodology, i.e Ultrasound and benign multicompenent procedure. Furthermore conventional methods.

EXPEREMENTAL:

Melting point were determined on a Stuat melting apparatus SMP30 Infrared spectra were recorded on a Bruker, FT-IR Spectrophotometer Tensor 27, Germany, and a biotech Engineering, FT-IR-600, U.K., using KBr discs. Ultra-Violet spectra were recorded on Shimadzu UV – 1650 pc, UV-Visible spectrophotometer, Japan, using chloroform as a solvent.

Synthesis of ethyl 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)diazenyl)-3-oxobutanoate(3) and ethyl 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)diazenyl)-3-oxo-3-phenylpropanoate(4)[17].

A well stirred solution of 4-aminoantipyrine(1) (2.03g, 0.01 mol) in conc. HCl (3 mL) and 2 mL H_2O was cooled in ice-bath and diazotized with the solution of $NaNO_2$ (0.35g, 5.1 mmol in 5mL H_2O). The cold diazonium solution was added slowly to a well stirred of ethylacetoacetate (1.3g, 0.01 mol) or ethylbenzoylacetate (1.92g, 0.01 mol) in absolute ethanol (25 mL) containing sodium acetate (0.82g, 0.01 mol). The reaction mixture was stirred for another 2 h. The crude product was filtered off, dried well and recrystallized from ethanol to give corresponding compounds (3 or 4), that yield (84%).

Synthesis of 1,5-dimethyl-4-((5-methyl-3-oxo-2,3-dihydro-1*H*-pyrazol -4-yl)diazenyl)-2-phenyl-1*H*-pyrazol-3(2*H*)-one(5) and 1,5-dimethyl-4-((3-oxo-5-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)diazenyl)-2-phenyl-1*H*-pyrazol-3(2*H*)-one(6)[18].

A solution of hydrazine hydrate (0.05g, 0.001mol) in ethanol (0.8 mL) was added dropwise to the corresponding β–ketoester compounds (3)(0.344g, 0.001 mol) or (4)(0.406g, 0.001 mol)in a 25mL,round bottom flask. The mixture was irradiated in the water bath of an ultrasonic cleaner for 30 min. The cold reaction mixture was treated with ethanol, ether, or pet. ether (80-100). The solid product was filtered and dried. The solid obtained was pure and did not need recrystallization, that yield (90%) for (5) and (95%) for (6), Tables(1,2).

Synthesis of 1,5-dimethyl-4-((5-methyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl)diazenyl)-2-phenyl-1*H*-pyrazol-3(2*H*)-one(7) and 1,5-dimethyl-4-((3-oxo-2,5-diphenyl-2,3-dihydro-1*H*-pyrazol-4-yl)diazenyl)-2-phenyl-1*H*-pyrazol-3(2*H*)-one(8)[18].

Follow the same procedure for preparation of compound(5) and (6). A solution of phenylhydrazine (0.108g, 0.001mol) in ethanol (0.8 mL) was added dropwise to the corresponding β – keto ester compounds(3) (0.344g, 0.001 mol) or (4) (0.406g, 0.001 mol) in a 25mL, round bottom flask. The mixture was irradiated in the water bath of an ultrasonic cleaner for 30 min. The cold reaction mixture was treated with ethanol, ether, or pet. ether (80-100). The solid product was filtered and dried. The solid obtained was pure and did not need recrystallization, that yield (86%) for (7) and (88%) for (8), Tables(1,2).

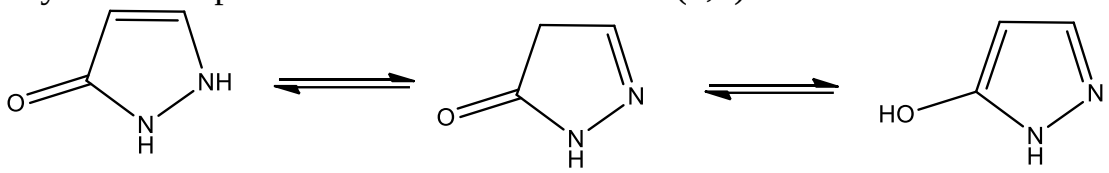
RESULTS AND DISCUSSION

In this paper the intermediate 1,3-dicarbonyl compounds, ethyl 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)diazenyl)-3-oxobutanonoate(3)and ethyl 2-((1,5-dimethyl-3-oxo-2-phenyl-2,3dihydro -1H-pyrazol-4-yl)diazenyl)-3-oxo-3-phenylpropanoate(4) used for synthesis of pyrazolone diazines derivatives(5-8) were prepared by the coupling of diazonium salt(2) with ethylacetoacetate and ethylbenzoyl acetate in an alkaline medium to get yellow and orange coloured compounds. The diazonium salt of 4-aminoantipyrine have been found to be easy to couple with 1,3-diketone. Since, 4-aminoantipyrine possessing electron-donating group give excellent yields[18]. The compound(3), which show absorptions ν cm^{-1} at 1707 (C=O), (C=O) (ester), and 1655 (C=O) conjugated amide and (C=C),1484 (N=N),2929, 2987 (C-H) aliph. 3153,3187(Ar-H), λmax 332 nm n- π* transition. Compound (4) show absorption νcm^{-1} at 1710 (C=O) and (C=O) ester, 1676 (C=O) conjugated amide and (C=C),1486 (N=N), 3178,3284(Ar-H), λmax 322 nm n- π*

transition. The compound (3) and (4) was converted to pyrazlone diazine derivatives(5-8) by reacted compounds (3) and (4) with hydrazine hydrate and phenylhydrazine via.

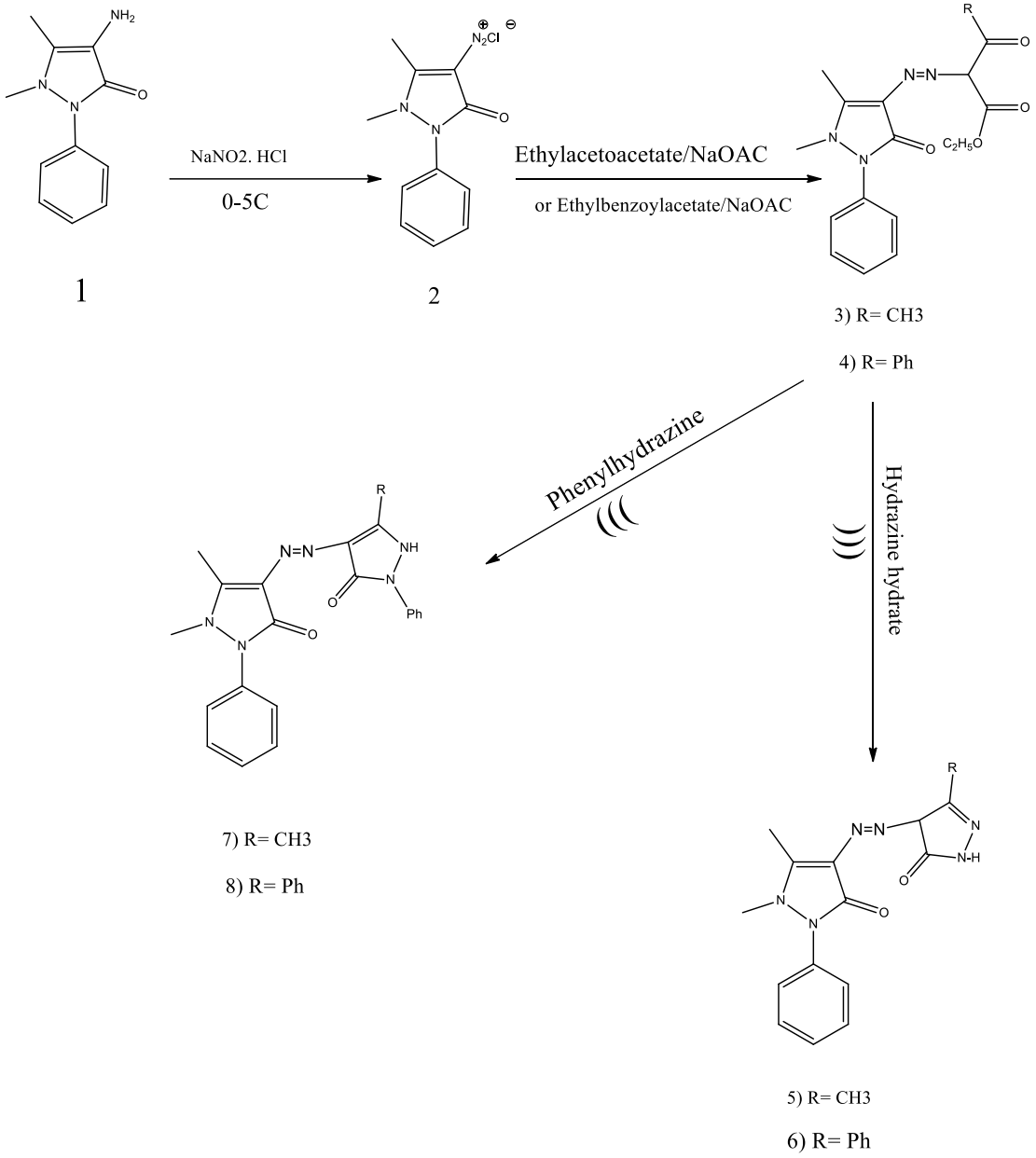
ultrasound irradiation compounds (5 and 6) get from compounds (3) and (4) were reacted with hydrazine hydrate under ultrasound irradiation. Compound(5), which show absorption *v* cm^{-1} at 1697 (C=O) unconjugated amide, 1647(C=O) conjugated amide, (C=N) and (C=C), 1494(N=N), 2925,2979 (C-H) 3055,3178 (Ar-H) and 3462 (N-H), λmax 343 nm n- π* transition[19]. The compound(6) show absorption *v* cm^{-1} at 1701 (C=O) uncojugated amide, 1662 (C=O) conjugated amide, (C=N) and (C=C), 1497(N=N), 2866,2927 (C-H), 3057,3178 (Ar-H) and 3431 (N-H), λmax 346 nm n- π* transition. While (C=N) Peaks disappeared in compounds (7 and 8) because that, found tautomarism in the pyrazolone scheme(1) Compounds (7 and 8) was prepared from compounds (3 and 4) when treated with phenylhydrazine . Compound (7) show absorption *v* cm^{-1} at 1668 (C=O) conjugated amide, 1580 (C=C), 1506(N=N), 3452 (N-H) 2858,2927 (C-H), and 3024,3078 (Ar-H). λmax 352 nm n- π* transition. Compound (8) show absorption *v* cm^{-1} at 1664 (C=O) conjugated amide, 1582 (C=C), 1513(N=N), 3443 (N-H), 2841, 2922 (C-H), 3025, 3183 (Ar-H) λmax 354 nm n- π* transition.

Physical and spectral data are listed in Table (1,2).



NH-form CH-form OH-form

Scheme (1)


NaNO2. HCl
0-5C
Ethylacetoacetate/NaOAC
or Ethylbenzoylacetate/NaOAC
1
2
3) R= CH3
4) R= Ph
Phenylhydrazine
Hydrazine hydrate
7) R= CH3
8) R= Ph
5) R= CH3
6) R= Ph

Scheme(2)

Table (1): Physical data of compounds(3-8).

Comp. No.	Molecular formula	Yield %	m.p. (^{0}C)
3	$C_{17}H_{20}N_4O_4$	84	174-177
4	$C_{22}H_{22}N_4O_4$	84	126-129
5	$C_{15}H_{16}N_6O_2$	90	191-193
6	$C_{20}H_{18}N_6O_2$	95	182-185
7	$C_{21}H_{20}N_6O_2$	86	198-200
8	$C_{26}H_{22}N_6O_2$	88	238-240

Table (2): Spectral data of compounds (3-8)

Comp. No.	IR *V* cm^{-1}, KBr									U.V. $CHCl_3$ λmax
	C=O unco. ami	C=O conj. amid	C=O, C=O est.	C=N	N=N	C=C	C-H ali.	Ar-H	N-H	
3	–––––	1655	1707	––––––	1484	1655	2929, 2987	3153, 3187	–––––––	332
4		1676	1710	––––––	1486	1676	––––––	3178, 3284	–––––––	322
5	1697	1647	–––––	1647	1494	1647	2925, 2979	3055, 3178	3462	343
6	1701	1662	––––––	1662	1497	1662	2866, 2927	3057, 3178	3431	346
7	------	1668	––––––	–––––	1506	1580	2858, 2927	3024, 3078	3452	352
8	–––––	1664	––––––	––––––	1513	1582	2841, 2922	3025, 3183	3443	354

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