Research Article

Synthesis and Characterization of Some Di Five and Six Heterocyclic Rings

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ABSTRACT

The synthesis of phthalazine, pyridazindione, pyrazole and pyrazol-5-one compounds (4-8) starting from *p*-phenylenediamine by the reaction of compound (3) with phthalic anhydride, maleic anhydride, succinic anhydride, acetyl acetone and ethyl acetoacetate in presence of acetic acid as solvent and catalyst in compounds (4-6) and catalyst in compounds (7 and 8). The synthesized compounds were characterized by FTIR spectrum and some of them were characterized by CHNS, ^{1}H-NMR and ^{13}C-NMR spectral data.

Keywords: phthalazine, pyridazindione, pyrazole and pyrazol-5-one.

INTRODUCTION

Nitrogen heterocycles containing the pyrazole, phthalazine moieties are important targets in synthetic and medicinal chemistry because this fragment is a key moiety in numerous biologically active compounds[1-3], because they show some pharmacological and biological activities[4-6]. In particular, they are used as antitumor[7-8], antibacterial and antifungal, antiviral, antiphrastic, antitubercular and insecticidal agents[9-12].

Experimental

Melting points were determined on Gallenkamp melting point apparatus and were uncorrected, elemental analysis (CHNS) were carried out using a Perkin-Elmer model 2400 instrument, FTIR measurements were recorded on Shimadzu model FTIR-8400S. ^{1}H-NMR and ^{13}C-NMR spectra were obtained with Bruker spectrophotometer model ultra shield at 300 MHz in DMSO-d_6 solution with the TMS as internal standard.

Synthesis of N,N'-Bis-(carbethoxy methyl)-*p*-phenylenediamine[2]

Ethyl chloro acetate (22.64 g., 0.1848 mol.)was added drop wise to a stirred cold solution of *p*-phenylenediamine (10 g., 0.0924 mol.), after that anhydrous potassium carbonate (25.54 g., 0.1848 mol.) in absolute ethanol (75 ml.) was added. The reaction mixture was refluxed for (12 hours), the resulting precipitate from KCl was filtered, the solvent was evaporated and the crude product was obtained as a gum, yield (76%). FTIR: 3381 (NH), 3375 (NH_2), 2923 (CH), 1733 (C=O). ^{1}H-NMR (DMSO-d_6) δ: 1.080-1.297 (t, 3H, CH_3), 3.771 (s, 1H, NH) (exchangeable with D_2O), 4.261 (s, 2H, CH_2), 4.878-4.963 (q, 2H, CH_2) for ethyl group , 6.484 (s, 5H, benzene ring). ^{13}C-NMR (DMSO-d_6) δ: 12.30 (2C, CH_3), 48.89 (2C, $\underline{C}H_2$-NH), 63.07 (2C, $\underline{C}H_2$-CH_3), 120.76 (4C, benzene ring), 142.45 (2C, $\underline{C}$-NH benzene ring), 172.60 (2C, C=O).

Synthesis of N,N'-Bis-(acetic hydrazide)-*p*-phenylenediamine[2]

Compound (3) was synthesized by addition of hydrazine hydrate (10 ml.) to (5 g., 0.0178 mol.) of compound (2), the mixture was refluxed for (2 hours). Then (25 ml.) of ethanol was added and refluxed for (1 hour). After cooling, the product was filtered off and recrystallized from ethanol, m.p. (220-222) °C, yield (85%). FTIR: 3346-3300 (NH_2), 1658,1608 (C=O) amid I and II. ^{13}C-NMR (DMSO-d_6) δ: 60.13 (2C, CH_2), 119.87 (4C, benzene ring), 130.54 (2C, $\underline{C}$-NH), 167.26 (2C, C=O).

Synthesis of N,N'-Bis-[1-(acetyl)-2-hydrophthalazin-3,8-dione]-*p*-phenylenediamine (4), N,N'-Bis-[1-acetyl-2-hydropyridazin-3,6-dione]-*p*-phenylenediamine (5), N,N'-Bis-[1-acetyl-2,4,5-trihydropyridazin-3,6-dione]-*p*-phenylenediamine (6)
General procedure

Compound (3) (1 g., 0.0039 mol.), was mixed with appropriate acid anhydride, in acetic acid (5 ml.), the mixture was refluxed for (7 hours) then cooled and added to crushed ice. The precipitate was filtered off, washed with water to give the final product. The physical properties for the synthesized compounds are showed in Table (1).

Table 1: Physical data for compounds (4-6)

Comp. No.	m.p. °C	Yield %
(4)	170-171dec.	50
(5)	133-135	60
(6)	239-240	65

Table 2: FTIR data of compounds(4-6)

Comp. No.	υN–H str.	υC–H Aromatic	υC=O str. Pyridazine	υC=O Amide	C=C str.	N–H Bending
(4)	3199	3032 - 3024	1708	1685	1589	1516
(5)	3215	3045	1710	1610	1589	1519
(6)	3264	3040	1701	1674	1592	1519

^{1}H-NMR of compound (6) (DMSO-d_6) δ: 2.798-2.897 (t, 2H, CH_2 pyridazine ring), 3.701 (s, 2H, CH_2), 3.908 (s, 1H, NH) (exchangeable with D_2O), 7.381 (s, 4H, benzene ring), 9.244 (s, 1H, NH pyridazine ring) (exchangeable with D_2O).

Synthesis of N,N'-Bis-[1-(acetyl)-5-methyl-pyrazol-5-one]-*p*-phenylenedi-amine (7), N,N'-Bis-[1-(acetyl)-3,5-dimethylpyrazole]-*p*-phenylenediamine (8)
General procedure

Compound (3) (1 g., 0.0039 mole.) was treated with (ethyl acetoacetate or acetyl acetone) respectively, acetic acid (0.5 ml.) in absolute ethanol (10 ml.) was heated under reflux for (7 hours). The reaction mixture was cooled and the formed precipitate was filtered off to give the final product. The physical properties for the synthesized compounds are showed in Table (3).

Table 3: Physical data of compounds7,8

Comp. No.	m.p. °C	Yield %
(7)	197-199	52
(8)	112-114	59

Table 4: FTIR data of compounds[7,8]

Comp. No.	υN–H str.	υC–H Aromatic	υC–H Alephatic	υC=O Amide	υC=N str.	C=C str.	N–H bending	Other bands
(7)	3292	3076-3066	2981-2930	1683	1610	1577	1521	C=O Pyrazole 1734
(8)	3329	3032 -3024	2981 - 2926	1662	1658 overlape	1610	1516	-

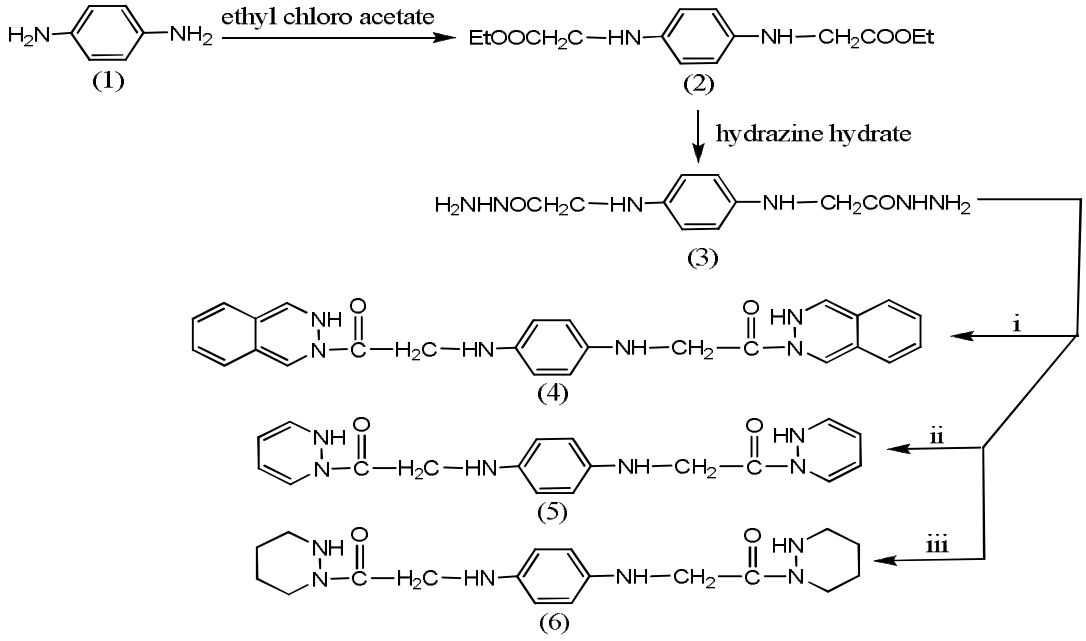
^{1}H-NMR of compound (8), (DMSO-d_6) δ: 1.391 (s, 3H, CH_3), the singlet signal at δ 2.410 (s, 2H, CH_2 pyrazolone ring), the singlet signal at 3.572 (s, 2H, CH_2), 4.066 (s, 1H, NH), 6.073 (s,4H, benzene ring).

Table 5: Elemental analysis for some of the synthesized compounds

Comp. No.	Elemental analysis Calc. (Found)			
	%C	%H	%N	%S
(3)	47.61 (47.33)	6.39 (6.01)	33.31 (33.49)	_ _
(6)	51.92 (52.03)	4.84 (4.76)	20.19 (20.15)	_ _
(7)	63.14 (62.92)	6.36 (5.97)	22.09 (22.15)	_ _

RESULTS AND DISCUSSION

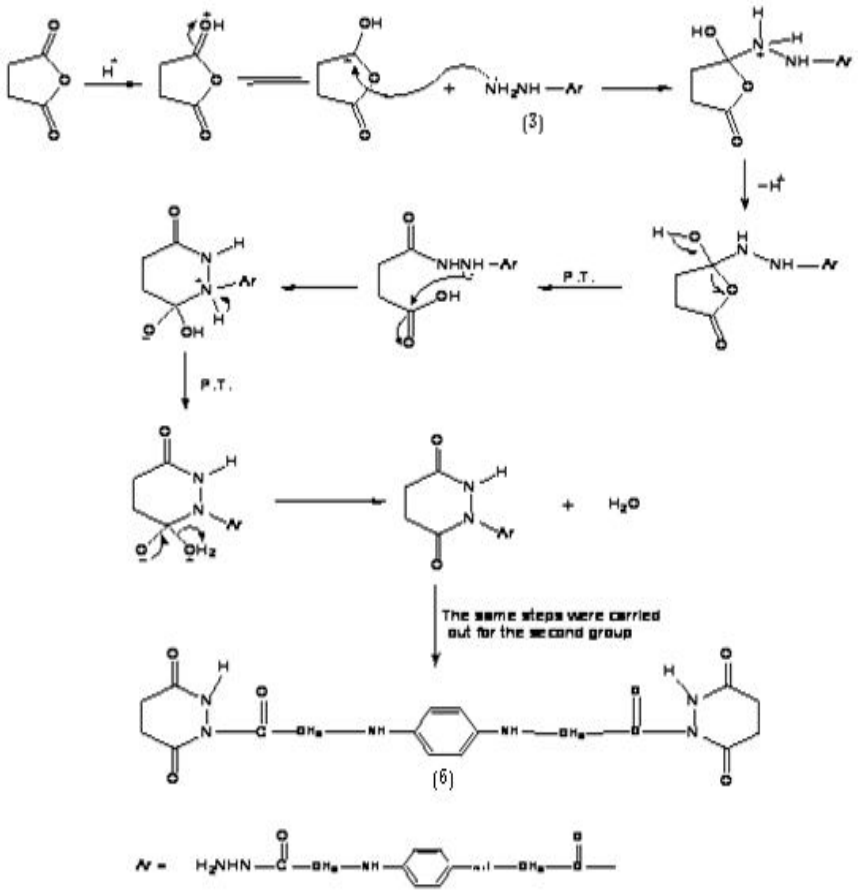
To synthesis of phthalazine and pyridazindione derivatives (4), (5) and (6), Scheme (1).



i) phthalic anhydride ii) maleic anhydride iii) sccinic anhydride

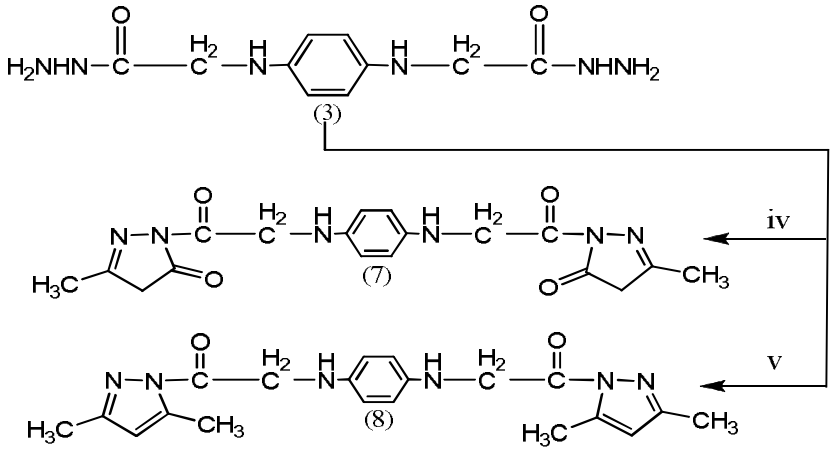
Scheme (1) Synthesis rout of compounds (4-6)

Compounds (4), (5) and (6) were synthesized from the reaction of compound [3] with phthalic anhydride, maleic anhydride and succinic anhydride respectively, in the presence of acetic acid as a solvent and catalyst. The suggested mechanism for the synthesis of the compound (6) is shown in scheme (2), the synthesis of compounds (4) and (5) were followed the same mechanism as in compound (6). In the first step of the reaction, a protonation process takes place by the acid, followed by a nucleophilic attack by the hydrazide on the carbon atom bearing the positive charge. Losing a proton and rearrangement lead to cyclization with losing a water molecule. The suggested mechanism of the reaction is shown in Scheme (2).



Scheme (2) suggested mechanism for synthesis of compound (6)

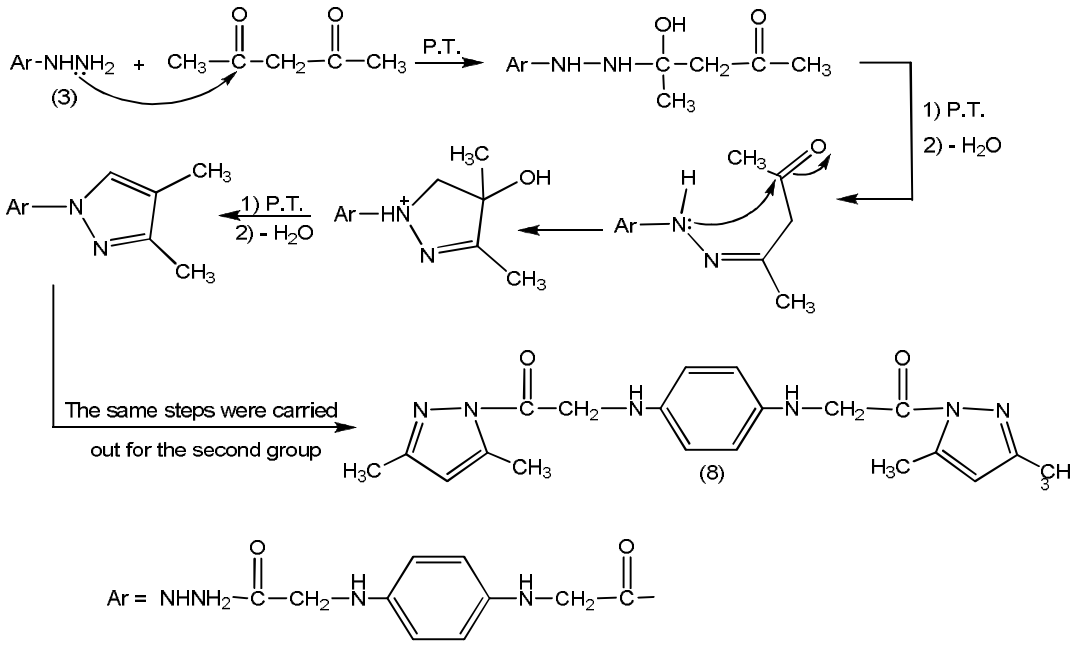
Compounds [7] and [8] were synthesized from the reaction of compound [64] with acetyl acetone and ethyl aceto acetate, respectively in the presence of acetic acid using absolute ethanol as a solvent, Scheme (3).



Scheme (3) Synthesis rout of compounds (7,8)

iv) ethyl acetoacetate v) acetyl acetone

The suggested mechanism of the reaction is shown in Scheme (4).



Scheme (4) suggested mechanism for synthesis of compound (8)

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