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NOTE

Synthesis and Antibacterial Activity of 1-Hydro-5-methyl-6 (Substituted Phenylhydrazono)-4-Pyrazolin-7-ones

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Various 1-hydro-5-methyl-6 (substituted phenylhydrazono)-4-pyrazolin-7-ones were synthesized in two steps using moderate conditions and evaluated for their antibacterial activity.

Key Words: Substituted phenylhydrazono, Pyrazolin-7-ones.

Pyrazoles[1,2] represent one of the most active classes of heterocyclic compounds possessing a wide spectrum of biological activities[3-5]. Incorporation of hydrazono[6]/azo[7,8] group imparts biological activities. The anti-inflammatory activity is also shown by some pyrazolones[9]. Hence it was considered worthwhile to prepare 1-hydro-5-methyl-6 (substituted phenylhydra-zono)-4-pyrazolin-7-ones. 7 Members rings are rather difficult to synthesize because strain and distance factors becomes worse[10,11]. But such rings can be obtained by using drastic reaction conditions.

The synthesis involves treatment of ethyl acetoacetate (EAA) with different diazonium salts in the presence of sodium acetate to yield ethyl-2-aryl hydrazono-3-oxo butyrats. The latter compounds on treatment with *o*-phenylenediamine furnished 1-hydro-5-methyl-6 (substituted phenylhydra-zono)-4-pyrazolin-7-ones (**Scheme-I**). The yield of the compounds **IIf** and **IIg** was in the range 13-14 %. Various attempts were made to improve the yield of the reaction such as increase in reaction time from 2-6 h and change in solvents. Even then the yield of the products remained in the range from 13-14 %.

The spectral data indicates that these compounds exist in hydrazono form. The structure requires that the >C=O group in position 7 should be conjugation with >C=N group. A strong band appears at 1564 and 1650 cm^{-1}. The presence of low frequency band may be attributed to the conjugation of cyclic >C=O group at position 7 with >C=N group. The lower frequency of >C=O group may also be due to participation of >C=O group at position 7 in hydrogen bonding with N-H group as shown in structure. Hydrazono structure is further supported by NMR spectral studies. The NMR spectra exhibit signal at δ 13.52 which could be assigned due to N-H grouping.

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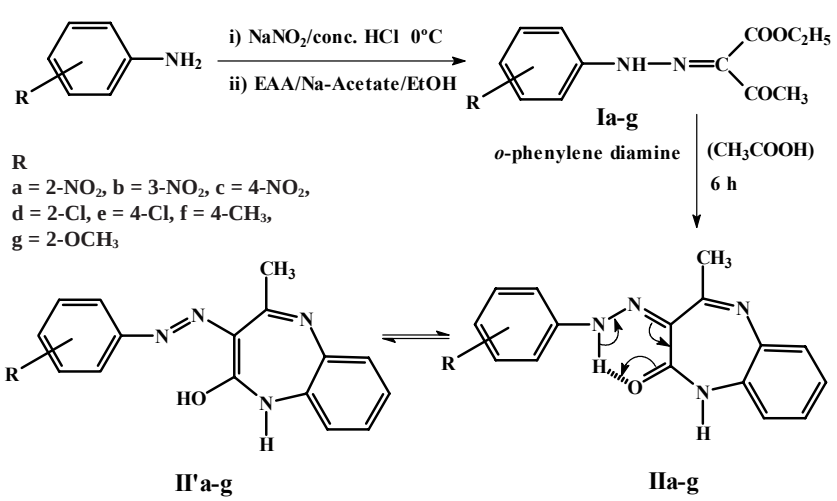

Scheme-I

Melting points were determined by open capillary method and are uncorrected. IR Spectra (cm^{-1}) were recorded on Perkin Elmer spectrophotometer in KBr pellets. ^1H NMR spectra were recorded on Bruker-400 MHz FT-NMR using TMS as internal referance. The elemental analysis was found satisfactory. Purity of compounds was checked by TLC on silica gel plates.

Ethyl-2-substituted phenyl hydrazono-3-oxo butyrates (Ia-g): Substituted aniline (0.01 mol) was dissolved in a mixture of conc. HCl (5 mL) and water (8 mL) and cooled to 0ºC in an ice bath. To it a cold aqueous solution of sodium nitrate (1 g) was added. The diazonium salt solution was filtered into a cooled solution of ethyl acetoacetate (0.01 mol) and sodium acetate (0.12 mol) in 25 mL of ethanol and the resulting yellow solid washed with water and then recrystallized from alcohol to furnished **Ia-g: Ia** m.p. 88ºC (85 %), **Ib** 115ºC (74 %), **Ic** 120ºC (80 %), **Id** 68ºC (87 %), **Ie** 118ºC (76 %), **If** 64ºC (84 %), **Ig** 85ºC (76 %). **Ia**, IR (KBr, cm^{-1}): 3450 ν(N-H), 2910 ν(C-H), 1690 ν(C=O), 1520 ν(NH-N=C).

1-Hydro-5-methyl-6 (substituted phenylhydrazono)-4-pyrazolin-7-ones (IIa-g): To compound **Ia-g** (0.001 mol) dissolved in glacial acetic acid (20 mL), *o*-phenylenediamine (0.001 mol) in glacial acetic acid was added and the mixture was heated on water bath for 6 h. Cooled and then allowed to stand overnight. The resulting solid was dried and then recrystallized from acetic acid to furnish **IIa-g**. **IIa** m.p. 260ºC (19.95 %), **IIb** 230ºC (26.86 %), **IIc** 185ºC (33 %), **IId** 220ºC (28.26 %), **IIe** 225ºC (40.45 %), **IIf** 215ºC (13 %), **IIg** 218ºC (13 %).

IIa: IR (KBr, cm^{-1}): 3103 ν(N-H), 3301 ν(OH), 1650 ν(C=O), 1564 ν(NHN=C), ^1H NMR ($CDCl_3$): 2.36 δ (s, 3H, CH_3), 7.50-7.55 δ (m, 4H),

8.30-8.35 δ (m, 4H), 13.52 δ (s, 1H, NH). **IId:** IR (KBr, cm^{-1}): 3178 ν(N-H), 3309 ν(OH) 1652 ν(C=O), 1558 ν(NHN=C), ^{1}H NMR (DMSO-d_6): 2.65 δ (s, 3H, CH_3), 7.63-7.65 δ (m, 4H), 7.87-7.88 δ (m, 4H), 12.99 δ (s, 1H, NH), 10.7d (S,1H,OH). **IIe:** IR (KBr, cm^{-1}): 3101 ν(N-H), 1650 ν(C=O), 1555 ν(NHN=C), ^{1}H NMR ($CDCl_3$): 2.35 δ (s, 3H, CH_3), 7.37-7.39 δ (m, 4H), 7.91-7.96 δ (m, 4H), 13.52 δ (s, 1H, NH). **IIf:** IR (KBr, cm^{-1}): 3400 ν(OH), 3100 ν(N-H), 1651 ν(C=O), 1556 ν(NHN=C), ^{1}H NMR ($CDCl_3$): 2.50 δ (s, 3H, CH_3), 7.26-7.28 δ (m, 4H), 7.51-7.53 δ (m, 4H), 12.65 δ (s, 1H, NH), 10.7 δ (s, 1H,OH). **IIg:** IR (KBr, cm^{-1}): 3100 ν(N-H), 1651 ν(C=O), 1264 ν(C-O-C), 1556 ν(NHN=C), ^{1}H NMR ($CDCl_3$): 3.36 δ (s, 3H, OCH_3), 7.23-7.26 δ (m, 4H), 7.77-7.79 δ (m, 4H), 12.78 δ (S, 1H, NH).

Biological activity: All the parazole derivatives were screened for *in vitro* antibacterial activity against *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginasa* using paper disc diffusion method using DMF as solvent. All compounds showed mild antibacterial activity against the three strains.

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