Asian Journal of Chemistry Vol. 19, No. 5 (2007), 4129-4131

NOTE

Synthesis and Biological Activities of Some Arylazopyrazoles

K.P. SHARMA* and HARENDRA K. SHARMA
Chemical Laboratories, Government Model Science College, Gwalior-474009, India

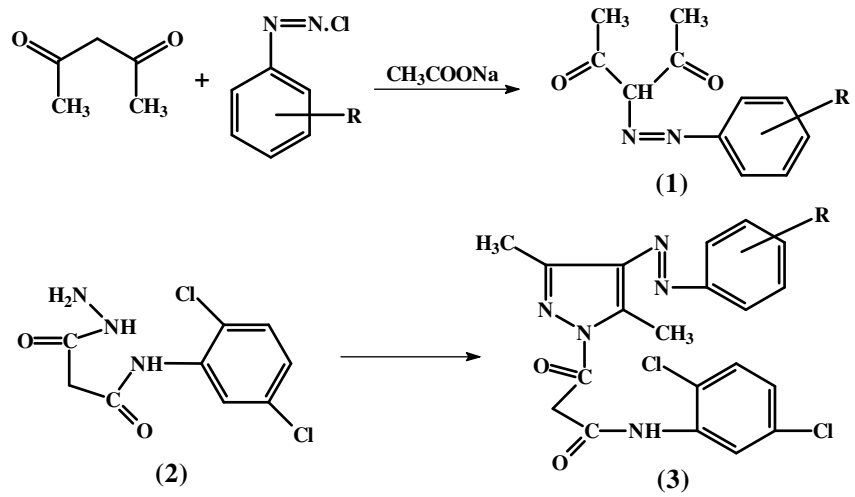
Reaction of different diazonium chlorides with acetylace-tone afford 2,4-diketo-3-(unsubstituted/substituted phenylazo) pentanes (**1**), which on treatment with 2-(2,5-dichloroanilido) aceto hydrazide (**2**) in acetic acid medium resulted in the formation of 1-(2,5-dichloro-anilinomalonyl)-3,5-dimethyl-4-(unsubstituted/substituted phenylazo) pyrazoles (**3**). Antibacterial and antifungal activities of **3** were also determined.

Key Words: Arylazopyrazoles, Synthesis, Biological activities.

Arylazopyrazoles constitutes an important class of compounds possessing diverse pharmacological activities[1-4] including antibacterial, antidiuretic, antifungal and anti-HIV. Herein, the synthesis of some new arylazopyrazoles is reported for assessing their biological activities. Reaction of acetylacetone with different diazonium salts in the presence of sodium acetate furnished 2,4-diketo-3-(unsubstituted/substituted phenylazo) pentanes (**1**), which on treatment with 2-(2,5-dichloroanilido)acetohydrazide (**2**) in acetic acid resulted in the formation of 1-(2,5-dichloroanilinomalonyl)-3,5-dimethyl-4-(unsubstituted/substituted phenylazo)pyrazoles (**3a-k**). (**Scheme-I**) in varying yields 42-65 % (Table-1). Antibacterial and antifungal activities of new pyrazole derivatives were determined.

Melting points were taken in open capillaries and are uncorrected. Purity and homogeneity of the compounds was checked with TLC. IR spectra (KBr) was recorded on a Perkin-Elmer-577 spectrophotometer and PMR spectra on a Jeol-Ex-90 FT-NMR spectrometer, 2-(2,5-dichloroanilido) acetohydrazide (**2**) was prepared by an adoptation of the procedure[8] given by Rathore and Ittyerah[5].

2,4-Diketo-3-(phenylazo) pentane (1, R = H): Aniline (9.3 mL, 0.1 mol) was dissolved in aqueous hydrochloric acid (80 mL, 1:1). The contents were stirred, cooled (0-2°C) and cold solution of sodium nitrite (12.0 g in 30 mL water) was slowly added maintaining the temperature between 0-2°C. The cold diazotized solution was added dropwise with stirring to a well cooled mixture of acetylacetone (0.1 mol, 10 mL) and sodium acetate (12 g dissolved in 10 mL of 50 % aqueous ethanol). Stirring was further



Scheme-I

continued for 45 min, when yellow crystals separated out. The product was filtered under suction, washed with water and recrystallized from aqueous ethanol. Yield 59 %, m.p. 61°C. IR (KBr, ν_{max}, cm^{-1}): 1740 (C=O Diketone), 1560 (-N=N-Azo), 1500 (C-N). Other 2,4-diketo-3-(substituted phenylazo)pentanes were prepared by aforementioned procedure[7].

2-(2,5-Dichloroanilido) acetohydrazide (2): A mixture of 2,5-dichloroaniline (5 mL) and diethylmalonate (10 mL) was refluxed for 45 min in a round bottomed flask fitted with an air condenser of such a length (14") that ethanol formed escaped and diethylmalonate flowed back into the flask. Contents were cooled, ethanol (30 mL) was added, when malon-2,5-dichlorodianilide separated out. It was filtered under suction. The filtrate was poured on to crushed ice (*ca.* 160 g) and stirred when ethyl-2-(2,5-dichloroanilido)ethanoate precipitated as green mass. On crystallization from aqueous ethanol (50 %) ester was obtained as white crystals. Yield 64 %, m.p. 53°C. Anal. Calcd. (Found) % $C_{11}H_{11}O_3NCl_2$: N 5.07 (4.92) , Cl 25.72 (25.45).

Ethyl-2-(2,5-dichloroanilido)ethanoate (2 g) was dissolved in ethanol (6 mL) in a small beaker kept in ice bath. Hydrazine hydrate (12 mL, 80 %) was added and the contents were stirred for ten min. The solid obtained was filtered under suction and recrystallized from ethanol in white crystals. Yield 85 %, m.p. 173°C. Anal. Calcd. (Found) % $C_9H_9O_2N_3Cl_2$: N 16.03 (15.94), Cl 27.09 (26.85). IR (KBr, ν_{max}, cm^{-1}): 3205 (N-H stretching), 1688 (C=O), 1094 (C-Cl), 773 (C-H).

1-(2,5-Dichloroanilinomalonyl)-3,5-dimethyl-4-(phenylazo) pyrazole (3a): 2,4-Diketo-3-(phenylazo)pentane (0.430 g, 0.001 mol) and malonanilic acid hydrazide (0.262 g, 0.001 mol) were dissolved in glacial

aceticacid (5 mL) and the solution was refluxed for 10 h. The resulting solid was purified by repeated washing with acetic acid and crystallized from aceticacid as light yellow crystals. Yield 42 %, m.p. 224°C. Anal. Calcd. (Found) % $C_{20}H_{17}O_2N_5Cl_2$: N 16.27 (16.18), Cl 16.51 (16.48).
IR (KBr, ν_{max}, cm^{-1}): 1670 (C=O Diketone), 1630 (C=N Pyrazole), 1510, 1450 (C=C), 1565 (N=N). PMR (DMSO-d_6): δ 2.23 (2H, s, CH_2); 4.22 (1H, s, NH), 6.80-7.02 (17H, m, Ar-H).

Other pyrazole derivatives were obtained by the aforementioned procedure. The characterization data are given in Table-1.

TABLE 1
PHYSICAL DATA OF ARYLAZOPYRAZOLES*(3)

S.No.	R	Colour	m.p. (ºC)	Yield (%)	m.f.
3a.	H	L.Y.	224	42	$C_{20}H_{17}N_5O_2Cl_2$
3b.	CH_3 (*o*)	Y.	264	55	$C_{21}H_{19}N_5O_2Cl_2$
3c.	CH_3 (*m*)	L.Y.	206	52	$C_{21}H_{19}N_5O_2Cl_2$
3d.	CH_3 (*p*)	L.Y.	269	54.5	$C_{21}H_{19}N_5O_2Cl_2$
3e.	Cl (*o*)	Y.	265	60	$C_{20}H_{16}N_5O_2Cl_3$
3f.	Cl (*m*)	Y.	253	59	$C_{20}H_{16}N_5O_2Cl_3$
3g.	Cl (*p*)	Y.	275	56	$C_{20}H_{16}N_5O_2Cl_3$
3h.	OCH_3 (*o*)	L.Y.	260	55	$C_{21}H_{19}N_5O_3Cl_2$
3i.	OCH_3 (*m*)	Y.	258	46	$C_{21}H_{19}N_5O_3Cl_2$
3j	OCH_3 (*p*)	Y.	270	49	$C_{21}H_{19}N_5O_3Cl_2$
3k.	F (*p*)	L.Y.	262	51	$C_{20}H_{16}N_5O_2Cl_2F$

Y = Yellow, LY = Light Yellow, PY = Pale Yellow
*All compounds gave satisfactory elemental analysis

Biological evaluation: All the compounds were screened for their antibacterial activity by agar plate diffusion method. The activity was seen against gram-positive bacteria *S. albus* and the gram-negative bacteria *E. coli*. Ampicillin and tetracycline were used as the standard drugs. The compounds were also screened for antifungal activity against *Aspergillus niger* and *Alternaria alternata* at a concentration of 50 µg/mL using Sabouraud and dextrose agar media. Compounds **3g**, **3h**, **3i** and **3k** showed moderate antibacterial activity. All these compounds did not show significant antifungal activity.

REFERENCES

1. V.K. Ahluwalia and B. Mittal, *Indian J. Chem.*, **28B**, 150 (1989).
2. V. Dhingra and S. Pendse, *Indian J. Heterocycl. Chem.*, **2**, 65 (1992).
3. V.S. Jolly, M. Pathak and R. Jain, *Indian J. Chem.*, **32B**, 505 (1993).
4. V. Dhingra, R. Bhatwadekar and S. Pendse, *Indian J. Chem.*, **32B**, 515 (1993).
5. B.S. Rathore and P.I. Ittyerah, *J. Indian Chem. Soc.*, **37**, 591 (1960).

(*Received*: 12 May 2006; *Accepted*: 14 March 2007) AJC-5531