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Research Article

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Synthesis, characterization of some new 3, 5-dimethyl azopyrazoles and its derivatives

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ABSTRACT

In our present study 4-substitutedaniline (1a) has been reacted with acetyl acetone (1b) in presence of sodium nitrite and sodium acetate yielded 3-[2-(4-substitutedphenyl)-hydrazono]-pentane-2, 4-dione (2a-b). Compound (2a-b) react with hydrazine hydrate and phenyl hydrazine to give 4-[(4-substitutedphenyl)-diazenyl]-3, 5-dimethyl-1H-pyrazole (3a-b) and 4-[(4-substitutedphenyl)-diazenyl]-3, 5-dimethyl-1-phenyl-1H-pyrazole (4a-b) respectively. 1-[4-((4-substitutedphenyl)-diazenyl)-3, 5-dimethyl-1H-pyrazol-1-yl]-ethanone (5a-b) has been synthesized by the treatment of 4-[(4-substitutedphenyl)-diazenyl]-3, 5-dimethyl-1H-pyrazole (3a-b) with acetyl chloride in pyridine. All the synthesized compounds were characterized on the basis of melting point, IR spectra and NMR spectra.

Keywords: 4-substituted aniline, sodium nitrite, sodium acetate, hydrazine hydrate, phenyl hydrazine, acetyl chloride, pyridine.

INTRODUCTION

Pyrazole and their substituted derivatives are interesting as potential pharmaceuticals and intermediates in dye industry. Azopyrazoles [1] exhibited a wide variety of biological and pharmaceutical activities and therefore they play important role in medicinal chemistry. An exciting development in the synthesis of nitrogen heterocycles like azopyrazoles has commenced in last few years.

The pyrazole nucleus has been reported to possess a wide spectrum of biological properties such as anti-inflammatory [2], antibacterial [3], analgesic [4], antifungal [5] and antiviral [6]. Pyrazoles having azo group have been found to exhibit a wide range of biological activities like antibacterial, CNS depressant, antitumor, potent local anesthetics.

Keeping in view their biological activities, synthesis of some new azopyrazoles and their acetyl derivatives have been carried out.

The starting compounds were 4-substitutedanilines. These 4-substitutedaniline on treatment with acetyl acetone in presence of sodium nitrite, sodium acetate, hydrochloric acid and ethanol yielded 3-(2-(4-substitutedphenyl)-hydrazono)-pentane-2, 4-dione (2a-b). The reaction of 3-(2-(4-substitutedphenyl)-hydrazono)-pentane-2, 4-dione (2a-b) with hydrazine hydrate and phenyl hydrazine in acetic acid yielded 4-((4-substitutedphenyl)-diazenyl)-3, 5-

dimethyl-1H-pyrazole (3a-b) and 4-((4-substitutedphenyl)-diazenyl)-3, 5-dimethyl-1-phenyl-1H-pyrazole (4a-b) respectively. The reaction of acetyl chloride with 4-((4-substitutedphenyl)-diazenyl)-3, 5-dimethyl-1H-pyrazole (3a-b) yielded 1-((4-(4-substitutedphenyl)-diazenyl)-3, 5-dimethyl-1H-pyrazol-1-yl)-ethanone (5a-b).

EXPERIMENTAL SECTION

Materials: 4-Chloroaniline, 4-methylaniline, acetyl acetone, sodium nitrite, sodium acetate, hydrazine hydrate, phenyl hydrazine, acetyl chloride, ethanol, glacial acetic acid, pyridine.

All the melting points were determined in open capillaries and are uncorrected. IR spectra were recorded in KBr using Perkin Elmer model 2000 spectrophotometer and reported wave numbers are given in cm^{-1}. ^1H NMR spectra were recorded in $CDCl_3$ on a Brucker Advance II 400 MHz spectrophotometer using TMS as an internal standard. Chemical shift values are shown in δ ppm. Mass spectra were recorded on Agilent 6320 Ion Trap mass spectrometer. The purity of all the synthesized compounds was checked by TLC on silica gel plates by using appropriate solvents.

Synthesis of 3-(2-(4-Chlorophenyl)-hydrazono)-pentane-2, 4-dione (2a):
4-Chloroaniline (0.01 mole) was dissolved in a mixture of concentrated HCl (8 mL) and water (6 mL) and cooled to 0 ^oC on ice bath. A cold aqueous solution of sodium nitrite (0.02 mole) was added. The cold diazonium salt solution was filtered into a cooled solution of acetyl acetone in presence of sodium nitrite (0.01 mole) and sodium acetate (0.05 mole) in ethanol (20 mL) and stirred for 2 hours and resulting solid was filtered, dried and purified by recrystallization from ethanol to afford compound (2a).

Yield: 69%, M.P.: 230-233 ^oC, M.W.: 238.67, IR (KBr, cm^{-1}): 3200 (N-H), 3000 (Ar C-H), 1680 (C=O), 1600 (C=N), 1500 (C=C), 1169 (C-O). ^{1}NMR: ($CDCl_3$, 400 MHz): 2.58 (s, 6H, CH_3), 7.49-7.45 (d, 2H, Ar-H), 7.90-7.74 (m, 2H, Ar-H), 8.11 (s, 1H, -NH). Other compound of this type (2b) was prepared similarly and is recorded in Table-1.

Synthesis of 4-((4-Chlorophenyl)-diazenyl)-3, 5-dimethyl-1H-pyrazole (3a):
A mixture of 3-(2-(4-Chlorophenyl)-hydrazono)-pentane-2, 4-dione (2a) (0.01 mole) and hydrazine hydrate (0.015 mole) in glacial acetic acid (15 mL) is refluxed for 4-5 hours. The resulting mixture was concentrated and allowed to cool. The resulting solid was filtered, washed, dried & recrystallized from ethanol to afford compound (3a).

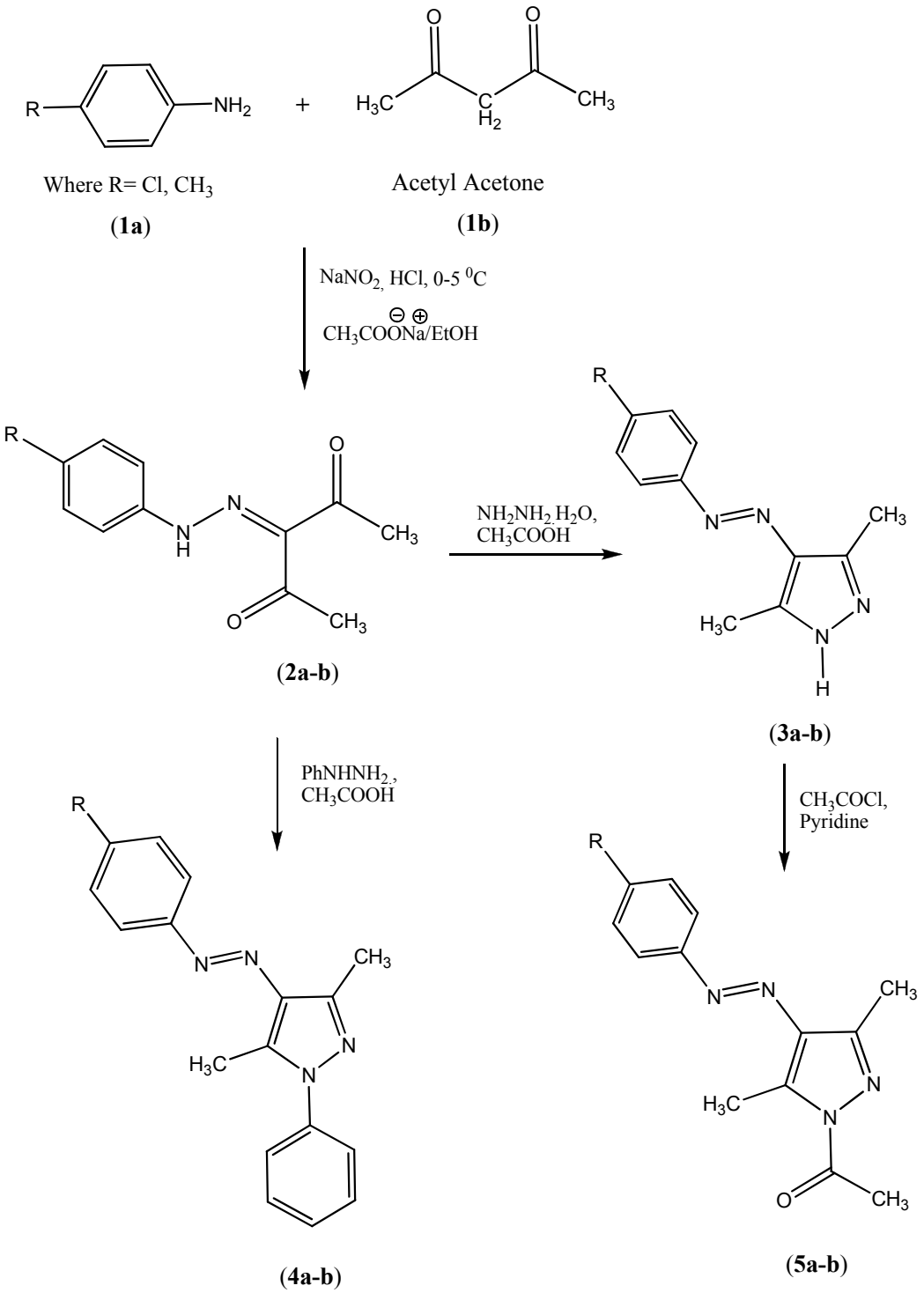
Yield: 66%, M.P.: 180-183 ^oC, M.W.: 234.68, IR (KBr, cm^{-1}): 3250 (-NH), 1650 (C=N), 1600 (C=C), 1140 (C-O). ^{1}NMR: ($CDCl_3$, 400 MHz): 2.66 (s, 6H, CH_3), 7.45-7.43 (d, 2H, Ar-H), 7.61 (s, 1H, NH), 7.79 - 7.78 (d, 2H, Ar-H). Other compound of this type (3b) was prepared similarly and is recorded in Table-1.

Synthesis of 4-((4-Chlorophenyl)-diazenyl)-3, 5-dimethyl-1-phenyl-1H-pyrazole (4a):
A mixture of 3-(2-(4-chlorodphenyl)-hydrazono)-pentane-2, 4-dione (2a) (0.01 mole) and phenyl hydrazine (0.015 mole) in glacial acetic acid (15 mL) is refluxed for 4-5 hours. The resulting mixture was concentrated and allowed to cool. The resulting solid was filtered, washed, dried & recrystallized from ethanol to afford compound (4a).

Yield: 71%, M.P.: 118-121^oC, M.W.: 310.78, IR (KBr, cm^{-1}): 3000 (Ar-H), 1500 (C=N), 1420 (C=C), 810 (C-Cl). ^{1}NMR: ($CDCl_3$, 400 MHz): 2.58 (s, 3H, CH_3), 2.68 (s, 3H, CH_3), 7.36-7.33 (m, 2H, Ar-H), 7.45-7.41 (m, 5H, Ar-H), 7.53–7.50 (m, 2H, Ar-H). Other compound of this type (4b) was prepared similarly and is recorded in Table-1.

Synthesis of 1-[(4-(4-Chlorophenyl)-diazenyl)-3, 5-dimethyl-1H-pyrazol-1-yl]-ethanone (5a):
4-((4-Chlorophenyl)-diazenyl)-3, 5-dimethyl-1H-pyrazole (3a) (0.01 mole) was dissolved and in pyridine (10 mL). The reaction mixture was cooled to 0-5 ^oC. Acetyl chloride (0.01 mole) was added slowly in a dropwise fashion to the reaction mixture to maintain temperature below 10 ^oC with constant stirring. After complete the addition keep the reaction mixture at room temperature for 1-2 hours. The reaction mixture was poured into crushed ice. The resulting mixture was treated with cold HCl (2N). The resulting solid was filtered and washed successively with water, dried & crystallized from ethanol to afford compound (5a).

Yield: 68%, M.P.: 250-253^oC, M.W.: 276.72, IR (KBr, cm^{-1}): 1685 (C=O), 1500 (C=N), 1420 (C=C), 810 (C-Cl). ^{1}NMR: ($CDCl_3$, 400 MHz): 2.41 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 2.78 (s, 3H, CH_3), 7.36-7.33 (m, 2H, Ar-H), 7.48-7.44 (m, 2H, Ar-H). Other compound of this type (5b) was prepared similarly and is recorded in Table-1.


R
NH2
+
H3C
O
O
C
H2
CH3
Where R= Cl, CH3
(1a)
Acetyl Acetone
(1b)
NaNO2, HCl, 0-5 0C
CH3COONa/EtOH
(2a-b)
NH2NH2.H2O,
CH3COOH
(3a-b)
PhNHNH2.,
CH3COOH
(4a-b)
CH3COCl,
Pyridine
(5a-b)

SCHEME

Table-1: Physicochemical data of the synthesized compounds

Sr. No.	Compds	R	M.P. (°C)	Yield (%)	Molecular Weight	Molecular Formula
1	2a	Cl	230-232	69	238.67	$C_{11}H_{11}ClN_2O_2$
2	2b	CH_3	90-93	66	218.25	$C_{12}H_{14}N_2O_2$
3	3a	Cl	180-183	66	234.68	$C_{11}H_{11}ClN_4$
4	3b	CH_3	102-105	65	214.27	$C_{12}H_{14}N_4$
5	4a	Cl	118-121	71	310.18	$C_{17}H_{15}ClN_4$
6	4b	CH_3	140-143	67	290.36	$C_{18}H_{18}N_4$
7	5a	Cl	250-252	68	276.72	$C_{13}H_{13}ClN_4O$
8	5b	CH_3	115-117	71	256.30	$C_{14}H_{16}N_4O$

RESULTS AND DISCUSSION

The structures of the synthesized compounds were characterized with the help of TLC, IR and NMR. The IR spectrum of compound 2a and 5a shows the characteristic band at 1600-1700 cm^{-1} due to the –C=O group. The IR spectrum of compounds 3a, 4a and 5a shows the characteristic band at 1500-1600 cm^{-1} due to the –C=N group. There are no absorptions in the region of 1600-1700 cm^{-1} indicating the absence of –C=O group in 3a and 4a compounds.

The ^{1}H NMR spectrum of compound 2a showed singlet of –NH at δ 8.11 ppm and multiple of Ar-CH at δ 7.90-7.45 ppm. The ^{1}H NMR spectrum of compound 3a and 4a showed there are no absorptions peaks in the region δ 8.11 ppm due to –NH confirmed the cyclisation in azopyrazoles.

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