Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2013, 5(9):130-134

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis and antimicrobial activity of some new 3,5-dimethyl azopyrazole derivatives

Pranali D. Kale

Postgraduate Department of Chemistry, Shri Shivaji Science College, Sant Gadge Baba Amravati University, Amravati

---

ABSTRACT

The required starting material 3-(2-(4-substitutedphenyl)-hydrazono)-pentane-2, 4-dione (2a-b) was synthesized from 4-substitutedaniline reacted with acetyl acetone. The 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-substituted phenyl)-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. The newly synthesized compounds were characterized by analytical and spectral studies. All the synthesized compounds were evaluated for antimicrobial activity. Some of these compounds show moderate antimicrobial activity as compared to the known reference drug ciprofloxacin.

Keywords: 4-substitutedaniline, acetyl acetone, hydrazine hydrate, phenyl hydrazine, acetyl chloride, antimicrobial activity, ciprofloxacin.

INTRODUCTION

Pyrazoles 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 pyrazoles 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 anaesthetics.

Keeping in view their biological activities, synthesis of some new 3, 5-dimethyl azopyrazole derivatives have been carried out.

The starting material 3-(2-(4-substituedphenyl)-hydrazono)-pentane-2, 4-dione (2a-b) was synthesized by the reaction of 4-substituedaniline with acetyl acetone in the presence of sodium nitrite and sodium acetate. The compound 4-((4-Chlorophenyl)-diazenyl)-3, 5-dimethyl-1H-pyrazole (3a-b) and 4-((4-substituedphenyl)-diazenyl)-3, 5-dimethyl-1-phenyl-1H-pyrazole (4a-b) was prepared by the reaction of 3-(2-(4-substituedphenyl)-hydrazono)-pentane-2, 4-dione (2a-b) (0.01 mole) with hydrazine hydrate and phenyl hydrazine 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.

EXPERIMENTAL SECTION

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

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}. ^{1}H-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: 71%, M.P.: 230-233 ^oC, M.W.: 238.67, Anal. Calculation for $C_{12}H_{14}ClN_2O_2$: Found: C: 55.36, H: 4.65, N: 11.74, Calcd. C: 68.55, H: 5.18, N: 7.99. 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.

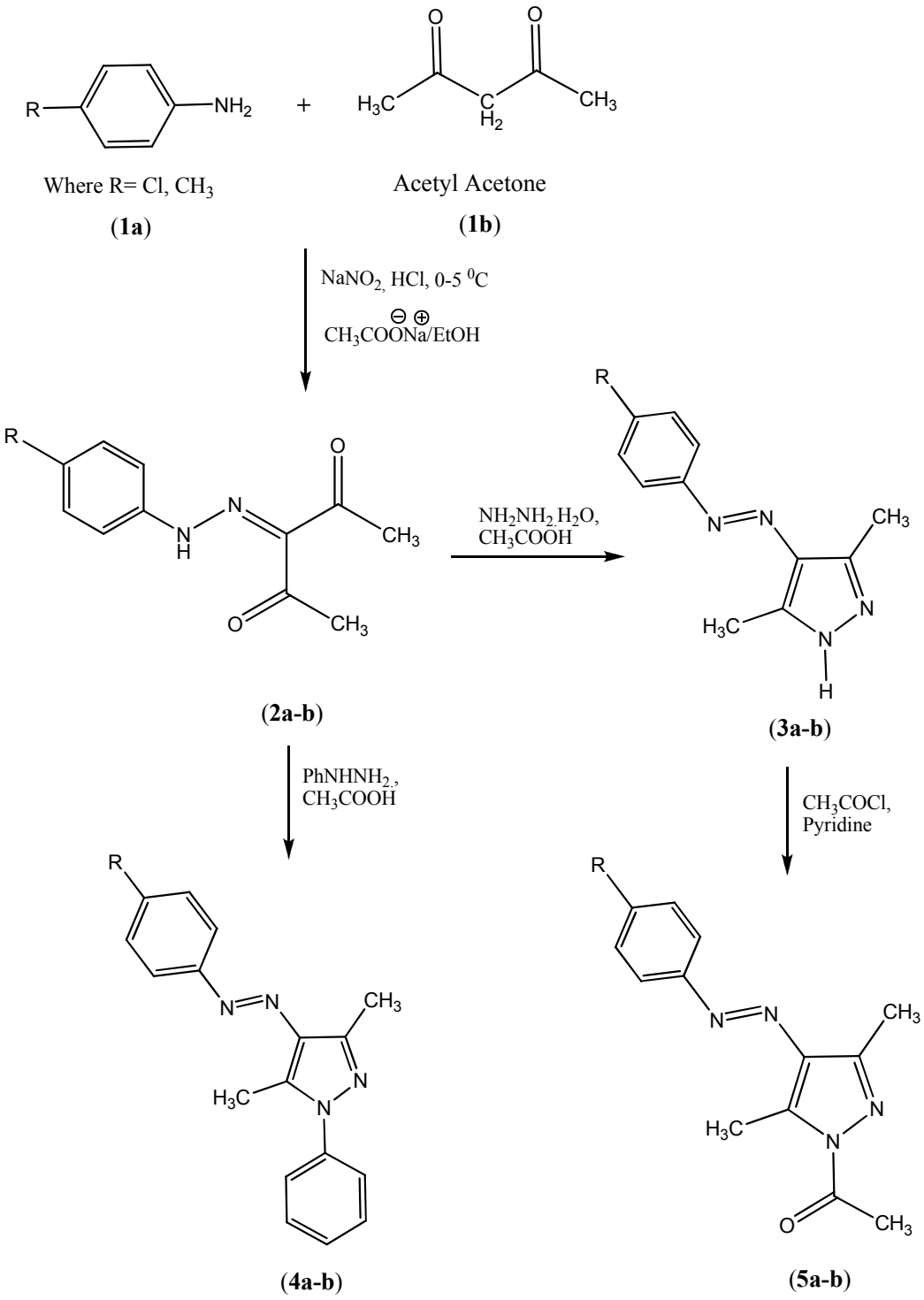
Synthesis of 4-((4-Chlorophenyl)-diazenyl)-3, 5-dimethyl-1H-pyrazole (3a):
A mixture of 3-(2-(4-chlorophenyl)-hydrazono)-pentane-2, 4-dione (2a) (0.01 mole) and hydrazine hydrate (0.015 mole) in glacial acetic acid (15 mL) is refluxed for 4-5 hours. The resulting mixture was concentrated and allowed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

Yield: 71%, M.P.: 180-183 ^oC, M.W.: 234.68, Anal. Calculation for $C_{11}H_{11}ClN_4$: Found: C: 68.49, H: 5.23, N: 8.02, Calcd. C: 68.55, H: 5.18, N: 7.99. 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, Anal. Calculation for $C_{17}H_{15}ClN_4$: 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 ^0C. Acetyl chloride (0.01 mole) was added slowly in a dropwise fashion to the reaction mixture to maintain temperature below 10 ^0C 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).


R
NH2
+
O
O
H3C
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

Yield: 68%, M.P.: 250-253°C, 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.

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	68	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	180-182	64	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	118-120	63	310.18	$C_{17}H_{15}ClN_4$
6	4b	CH_3	140-142	67	290.36	$C_{18}H_{18}N_4$
7	5a	Cl	250-252	65	276.72	$C_{13}H_{13}ClN_4O$
8	5b	CH_3	115-117	71	256.30	$C_{14}H_{16}N_4O$

ANTIMICROBIAL ACTIVITY

All the synthesized compounds were evaluate for their antimicrobial activity by using agar diffusion method[7] against different strains of bacteria such as S. aureus and B. subtilis a gram positive bacteria and E. coli and S. paratyphi a gram negative bacteria in nutrient agar medium. Ciprofloxacin was used as reference drugs. By visualizing inhibition zone, it was found that the compounds with chlorosubtituents 3, 5-dimethyl azopyrazole derivatives have shown remarkable inhibition against *E. coli* and *S. aureus.*

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 showed absorption band at 1680 cm^{-1} due to the –C=O group and 1600 cm^{-1} due to the –C=N group. The IR spectrum of compounds 3a, 4a and 7a shows the characteristic band at 1500-1650 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 IR spectrum of compound 5a shows the characteristic band at 1685 cm^{-1} indicating the presence of –C=O group.

The ^{1}H NMR spectrum of compound 2a showed singlet at δ 8.11 ppm, due to –NH group. The ^{1}H NMR spectrum of compound 3a, 4a and 5a showed multiplet in the region about δ 7.36-7.78 ppm due to aromatic group.

All the newly synthesized compounds were evaluated for their antibacterial activity. It has been observed that compounds 3a and 5a indicated better activity than reference drug. The remaining compounds were less active than the reference drug.

CONCLUSION

In summary, we have synthesized some new 3, 5-dimethyl azopyrazole derivatives. The antibacterial study show that compounds 3a and 5a showed better zone of inhibition than the reference drug.

Acknowledgment

The authors are grateful to the authorities of Shri Shivaji Science College, Amravati for providing necessary facilities. RSIC, Chandigarh for spectral analyses.

REFERENCES

[1] U Garg, V Sareen, V Khatri and S. Chaugh, *Indian J. Heterocyclic Chem*., **2002**,12,139.
[2] A A Bekhit and T Abdel-Aziem, *Bioorg Med Chem*., **2004**, 12, 1935.
[3] A Mohammed, SM Hassan and A Wadood, *Oriental Journal of Chemistry*, **2002**, 18, 351.
[4]Z Tabarelli, M A Rubin, DB Berlese, PD Sauzem, TP Missio, MV Teixeira, AP Sinhorin, MA Martins, N Zanatta., HG Bonacorso and CF Mello, *Brag J. Med Biol Res*, **2004**, 37, 1531.
[5] SK Sahu, M Banerjee, A Samantray, C Behara and MA Azam, *Trop J. Pharm Res*., **2008**, 7, 961.

[6] AE Rashad, MI Hegab, RE Abdel-Megeid, JA Micky and FME Abdel-Megeid, *Bioorganic Med. Chem*., **2008**, 16, 7102.
[7] B.S. Holla, M. Mahalinga, B. Poojary, A. Mithun and M.A. Kberali, *Indian J. Chem*., **45B (2)** (**2006**), 568.
[8] CH Collins, Microbiological Methods, Butterworths London. **1947**, 364.
[9] NB Sorolove, LP Kovzhina, NM Mitrieva and NV Potinna, *Russian Journal of Appl. Chem*., **2002**, 75, 254.
[10] H Usui, *Jpn. Kokai Tokko Koho* JP 04,189,183 [92, 189, 183]; C.A., 118, 30112k (**1993**).
[11] Shankaralah Konda, Vishnu Khedkar and Bhaskar Dawane, *Journal of Chemical and Pharmaceutical Research*, **2010**, 2(1), 187-191.
[12] D Ishibashi, H Ohya and A Onodera, *Jpn. Kokai Tokko Koho* JP 11,106, 694 [99, 106, 694]; C.A., 130, 298109e (**1999**).
[13] BP Patel, HS Patel and PJ Shah, *Orbital Elec. J. Chem*., **2010**, 2 (3), 303-310.
[14] SB Zangade, JD Jadhav, Lalpod, YB Vibhute and BS Dawane, *Journal of Chemical and Pharmaceutical Research*, **2010**, 2(1), 310-314.
[15] CP Singh and AC Ojha, *Journal of Chinese Chem. Soc*., **1981**, 28, 51-57.
[16] MF Abo El-Ghar, NT Abdel-Ghani, Y Badr and OM El-Borady, *ISESCO Science and Technology Vision*, **2007**, 3 (3), 58-63.
[17] Chirag Patel, CS Rami, B Panigrahi and CN Patel, *Journal of Chemical and Pharmaceutical Research*, **2010**, 2(1), 73-78.
[18] AM Amer, EK Mohamed, S Raslan and H El-Tahawe, *Journal of American Science*, **2010**, 6 (9), 889-892.
[19] S. B. Zangade, J. D. Jadhav, Lalpod, Y. B. Vibhute, B. S. Dawane. *J. Chem. Pharm. Res*., 2010, 2(1): 310-314
[20] M. R. Jayapa, K. Sreenivasa Prasad and N. Y. Sreedhar *J. Chem. Pharm. Res*., 2010, 2(3):127-132
[21] Biswajit Chandra Das, G. Mariappan+, Sudip Saha, Debjit Bhowmik, *Chiranjib J. Chem. Pharm. Res*., 2010