SYNTHESIS OF NOVEL PYRAZOLE DERIVATIVES FROM DIARYL 1,3-DIKETONES (PART-I)

Sandeep Nigam, Y.C. Joshi* and P. Joshi**

**Department of Chemistry, University of Rajasthan, Jaipur-302 004, India*

***S.S. Jain, Subodh P.G. College, Jaipur, Rajasthan*

Abstract : Reactions of various, diaryl 1,3-diketones (1a-1i) with hydrazine hydrate in absolute ethanol led to the formation of corresponding pyrazole derivatives (2a-2i). Structures of these compounds were established on the basis of spectral studies viz. elemental analysis, IR, ^{1}H NMR, MS etc. The ^{13}C NMR data of these derivatives has also been presented.

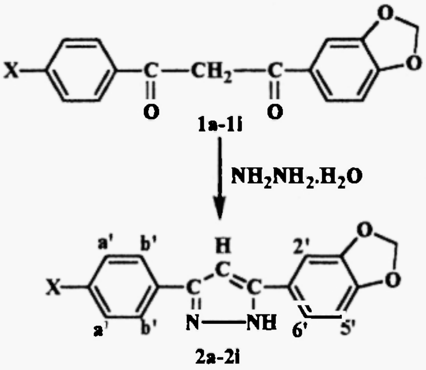
Introduction

The attachment of pyrazole ring in an organic structure is of significant interest because of its easy accessibility and diverse properties that are associated with it[1-4]. It is interest to note that pyrazoles are reported as well known pharmaceuticals[5-7]. The selection of pyrazole derivative in the field of clinical medicine, is undoubtedly the principal practical application that one can come across because of their considerable antitumor[8], antiviral[9], pesticidal[10] action. The pharmacological importance of various pyrazole derivative prompted our interest in exploring some new pyrazole derivatives with the attempts to discover some potential compound of medicinal importance.

Result and discussion

Condensation reaction of propane-1-(1,3-benzodioxol-5-yl)-3-phenyl-1,3-dione (1a) or other compounds (1b-1i) having various substituent in the phenyl ring, in absolute ethanol with hydrazine hydrate gives schiff bases type compound having pyrazole nucleus. Hydrazine hydrate beside being reactant also make the media basic, to promote the enol form of mentioned diketone. The structure of the synthesized compounds are well supported by spectroscopic data (Scheme 1, Table 1)

	X
a	-H
b	$-CH_3$
c	-Cl
d	-Br
e	$-OCH_3$
f	-OH
g	$-NH_2$
h	$-NO_2$
i	$-OC_2H_5$



Scheme 1

Spectral studies

The IR spectra, showed a characterstic –NH stretching vibration around 3250 cm^{-1}, –CN stretching band around 1420 cm^{-1}, asymmetrical C-O-C stretching band around 1200-1275 cm^{-1} and symmetrical stretching near 1020-1075 cm^{-1}. In ^1H NMR, a peak is observed at δ 6.6-6.7, which is assigned to methine proton of pyrazole ring. A singlet at δ 5.98-6.01 is due to dioxymethylene group. Proton attach to nitrogen give a singlet around δ 7.26-7.37. A complicated pattern in the aromatic region at δ 6.9-8.2 indicates the presence of seven aromatic protons. ^1H NMR data of the title compounds are given in table 2.

In the mass spectra all the compounds shows molecular ion peak. The mass spectrum of the compound 2d shows a cluster of peaks at m/z 343 and

Table-2

^{1}H NMR Data of Title Compounds (in δ, ppm)

Compd.	Ar-X	-NH 1H, (s)	Methine 1H, (s)	OCH_2O 2H, (s)	Aromatic Protons				
					H_3' (2H,d)	H_5' (2H,d)	H_2' (1H,d)	H_5' (1H,d)	H_6' (1H,m)
2a	-	7.37	6.70	6.00	(5H-m)		7.25	6.87	7.31-7.37
2b	2.37, 3H, s	7.36	6.69	5.98	7.22	7.66	7.26	6.86	7.29-7.33
2c	-	7.27	6.63	6.00	7.27	7.67	7.25	6.87	7.28-7.29
2d	-	7.35	6.71	6.00	7.55	7.69	7.24	6.88	7.28-7.29
2e	3.85, 3H, s	7.26	6.66	6.01	6.96	7.62	7.21	6.88	7.22-7.23
2f	4.05, 1H, s	7.35	6.67	6.00	6.93	7.96	7.22	6.86	7.24-7.26
2g	4.81 (b), 2H, s	7.29	6.66	6.01	6.69	7.90	7.21	6.88	7.23-7.25
2h	-	7.31	6.68	6.00	8.11	8.36	7.26	6.88	7.28-7.31
2i	1.76 (3H, t, J = 7 Hz) 3.92 (2H, q, J = 7 Hz)	7.28	6.66	5.98	6.99	7.66	7.24	6.87	7.22-7.23

345 corresponding to M^+ and $[M+2]^+$ respectively. M^+ and $[M+2]^+$ peaks have same intensity, showing the presence of bromine.

The ^{13}C NMR data for the compounds 2a-2i are presented in table 3 and these data are in reasonable agreement with their structures.

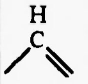
Table – 1

Elemental analysis data of title compounds.

Compd.	**M.F.**	**M.W.**	**Elemental Analysis Calcd. and (Found)**				**M.P. (°C)**
			C%	**H%**	**N%**	**X%**	
2a	$C_{16}H_{12}O_2N_2$	264	72.72 (72.38)	4.55 (4.21)	10.61 (9.81)	-	122
2b	$C_{17}H_{14}N_2O_2$	278	73.38 (72.89)	5.04 (4.91)	10.07 (9.88)	-	173
2c	$C_{16}H_{11}N_2O_2Cl$	298.5	64.32 (63.89)	3.69 (3.45)	9.38 (9.02)	11.89 (10.47)	116
2d	$C_{16}H_{11}N_2O_2Br$	343	55.98 (54.61)	3.21 (3.08)	8.16 (8.01)	23.32 (22.96)	128
2e	$C_{17}H_{14}N_2O_3$	294	69.39 (68.27)	4.76 (4.54)	9.52 (9.16)	-	149
2f	$C_{16}H_{12}N_2O_3$	280	68.57 (68.02)	3.51 (3.32)	10.00 (9.66)	-	157
2g	$C_{16}H_{13}N_3O_2$	279	68.82 (68.36)	4.66 (4.42)	15.05 (14.92)	-	101
2h	$C_{16}H_{11}N_3O_4$	309	62.14 (61.86)	3.56 (3.22)	13.59 (13.07)	-	123
2i	$C_{18}H_{16}N_2O_3$	308	70.13 (69.88)	5.19 (4.96)	9.09 (8.84)	-	152

Table – 3

^{13}C NMR data of title compounds. (in δ ppm)

Cpd.	Ar-X	O(C)O	$>C=N$	$>C-NH$		Ar at C_3	Ar at C_5
2a	-	100.2	149.9	135.0	98.4	132.0-124.6	147.4-105.5
2b	CH_3–20.6	100.5	150.0	135.4	98.1	137.0-118.6	147.3-105.5
2c	-	100.6	150.0	134.9	98.3	130.6-116.7	147.3-105.3
2d	-	100.6	149.8	134.2	98.6	131.2-118.9	147.2-105.3
2e	OCH_3-54.8	100.4	149.8	135.1	97.9	158.9-113.6	147.4-105.7
2f	-	100.2	150.1	134.7	98.4	161.8-115.2	147.4-105.4
2g		100.5	149.9	135.0	98.4	151.5-113.5	147.3-105.4
2h	-	100.6	151.6	134.8	97.8	152.3-116.4	147.4-105.5
2i	OCH_2-63.2, CH_3-14.7	100.3	149.9	134.8	98.2	162.3-114.4	147.4-105.7

Experimental

Melting points are uncorrected. The IR spectra were recorded in KBr disk on a Nicolet Megna-FT-IR 550 spectrometer. ^1H NMR and ^{13}C NMR were recorded on model DRX300 at 300.13 and 75.48 MHz, respectively, in $CDCl_3$/DMSO-d_6 using TMS as internal standard. Mass spectra were recorded on Jeol D-300 spectrometer. The purity of the newly synthesized compounds were checked by TLC.

Generalized Preparation of pyrazole derivatives

A mixture of diketone (0.0625 M) and hydrazine hydrate (4.9g, 0.1 M) was refluxed in absolute ethanol (80 ml) for approx. four hours on steam bath. The mixture is cooled and filtered. Crystallization with ethanol yields the crystalline product. Purity of compounds is checked by TLC using ($CHCl_3$: CH_3OH, 9:1) as mobile phase.

Acknowledgment

Authors are thankful to Head, Department of Chemistry, University of Rajasthan, Jaipur for providing laboratory facilities. Authors are also thankful to Central Drug Research Institute, Lucknow for providing spectral data. One of them (SN) is thankful to the CSIR, New Delhi for the award of Junior research fellowship.

References

1. Nagpal, A.; Unny, R.; Joshi, P. and Joshi, Y.C., *Heterocycl. Commu.*, 7, 589-592 (2001)
2. Becher, J.; Jorgensen, P.L.; Pluta, K.; Krake, N.J. and Hansen, B.F., *J. Org. Chem.*, **57**, 2127 (1992)
3. Niley, R.H. and Niley, P., "Pyrazoles, Pyrazolidones and derivative" Intersceince Publishers, London (1964)
4. Panca, I.; Ghirisan, A.; Cristea, I.; Gropeanu R. and Silbery, I.A., *Heterocycl. Commu.*, **7**, 563 (2001)
5. A. Steinmetz, L.F. Tietze, Ger Offen. DE 19, 627, 002 (CL. CO7D231/22) 8 Jan. 1998, Appl. 19, 627, 002, 5 Jul 1996, 14 pp; *Chem. Abstr.*, **128**, 114946e (1998)
6. Suzuki, Y.; Takemura, Y.; Iwamoto, K.; Higashino, T. and Miyashito, A.; *Chem. Pharm. Bull.*, **46**, 199 (1998)
7. S.S. Bhagwat, C. Lee, M.D. Cowart, J. Mckie, A.L. Grillot, PCT Int. Appl. WO 9846, 605 (CL. CO7D47104) 22 Oct. 1998, US Appl. 818, 216, 16 Apr. 1997, 172 pp, *Chem. Abstr.*, **129**, 316240b (1998)
8. Spasova, M.K., Zkharieva, R.D. (Inst. Mol. Biol. Acad. Sci. 1113 Sofia, Bulg) F.E. C.S. Int. Conf. Chem. Biotechnol Biol. Act. Nat. Prod. (Proc.) 3rd 1985 (Pub. 1987), 5, 410-13 (Eng.) VcH : Winheim, Fed, Rep. Ger, *Chem. Abstr.*, **110**, 135140f (1989)
9. Bhattacharya, Birendra K., Robins, Roland K., Revankar and Ganapathi R., *J. Heterocycl. Chem.*, **1990**, *27(3)*, 795-801; *Chem. Abstr.*, **113**, 78887r (1990).
10. Neubauer, Hans Juergen, Kardorff, Uwe, Leyendecker, Joachim, Kuenast, Christoph, Hofmeister, Peter, Krieg, Wolfgang (BASF A.G.) Ger. Offen, DE 3, 825, 822 (Cl. Co 7D 261/08), 01 Feb. 1990, Appl. 29 Jul. 1988, 28 pp. *Chem. Abstr.*, **113**, 6353r (1990)

Received on May 12, 2003