SYNTHESES OF NOVEL β-DIKETONE DERIVATIVES OF PYRAZOLE

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Abstract: Condensation of pyrazole-1-acetyl chloride **1** with acetophenone derivatives **2** in the presence of sodium methoxide in dry methanol led to the formation of various substituted β-diketones **3** (a-l). The structures of these newly synthesized compounds have been established by elemental analysis and spectral studies *viz.* IR, ^{1}H NMR.

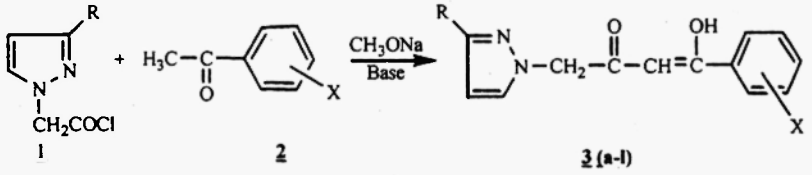
Introduction

Pyrazoles are an important class of heteroaroamtic ring systems that find extensive use in pharmaceutical industry[1-4]. The selection of pyrazole derivatives in the field of clinical medicine is undoubtedly principal as such compounds are used as antitumor[5], antiviral[6], antibacterial[7] and anti-inflammatary agents[8]. Pyrazole derivatives are also effective against the metabolism schistosomiasis in snails[9,10].Their derivatives have got significant biological properties as antiproliferative agents[11], antidiabetes and also useful in Alzheimer's disease[12]. They are useful intermediates for many industrial products[13,14].

β-Dicarbonyl compounds have been widely used in organic synthesis because of their ready access, predictable reactivity, and expanded reaction repertoire. They serve as precursors for the synthesis of pharmacologically active heterocylic compounds such as diazepines[15], benzodiazepines[16], benzothiazepines[17], pyrazoles[18] and isoxazoles[18].

Experimental

All melting points are uncorrected. The IR spectra were recorded on a Nicolet-megna-FT-IR-550 spectrometer in KBr pellets. ^{1}H NMR spectra were recorded on model DRX 300 at 300.13 MHz in $CDCl_3$ using TMS as an internal standard. The purity of the newly synthesized compounds were checked by TLC using silica gel 'G' as stationary phase and benzene : ethanol : ammonia (7:2:1) upper layer as mobile phase.



(a) X = H, R = H (b) X = CH_3, R = H (c) X = OCH_3, R = H
(d) X = Cl, R = H (e) X = Br, R = H (f) X = NO_2, R = H
(g) X = H, R = CH_3 (h) X = CH_3, R = CH_3 (i) X = OCH_3, R = CH_3
(j) X = Cl, R = CH_3 (k) X = Br, R = CH_3 (l) X = NO_2, R = CH_3

General preparation of β-diketones

A mixture of sodium methoxide (0.5 gm, 0.01 M) and acetophenone derivatives (0.01M) and dry toluene (15 ml) was stirred for an hour on a magnetic stirrer. The reaction mixture was heated for about twenty to twenty two hours at 80°C with proper

stirring. The progress of reaction was monitored through TLC using benzene : ethanol : ammonia (7:2:1) upper layer as mobile phase. After completion of the reaction, the reaction mixture was cooled overnight in refrigerator and toluene was removed under reduced pressure. The solid residue so obtained was extracted with $CHCl_3$ and washed several times with water. The chloroform layer was dried over anhydrous sodium sulphate, filtered and chloroform was removed under vaccuo. The solid was crystallized with a mixture of different solvents.

Analytical data of synthesized compounds are tabulated in Table 1. IR and ^1H NMR data of synthesized heterocyclic compounds are included in Table 2 and 3 respectively.

Table-1: Elemental analysis

Compounds 3	Molecular formula	M.P. (in °C)	Yield in (%)	Found (Calcd.) %		
				C	H	O
a	$C_{13}H_{12}N_2O_2$	160	45	68.42 (68.40)	5.26 (5.23)	14.03 (14.05)
b	$C_{14}H_{14}N_2O_2$	184	40	69.42 (69.39)	5.78 (5.81)	13.22 (13.23)
c	$C_{14}H_{14}N_2O_3$	190	48	65.11 (65.09)	5.42 (5.45)	18.60 (18.58)
d	$C_{13}H_{11}N_2O_2Cl$	178	42	59.42 (59.41)	4.19 (4.18)	12.19 (12.17)
e	$C_{13}H_{11}N_2O_2Br$	170	51	51.48 (51.51)	3.63 (3.66)	10.56 (10.55)
f	$C_{13}H_{11}N_3O_4$	178	49	57.14 (57.10)	4.02 (4.04)	23.44 (23.41)
g	$C_{14}H_{14}N_2O_2$	176	52	69.42 (59.38)	5.78 (5.80)	13.22 (13.19)
h	$C_{15}H_{16}N_2O_2$	185	56	70.31 (70.33)	10.93 (10.95)	12. (12.2)
i	$C_{15}H_{16}N_2O_3$	210	50	66.17 (66.16)	5.88 (5.91)	17.64 (17.62)
j	$C_{14}H_{13}N_2O_2Cl$	174	48	60.75 (60.73)	4.70 (4.73)	11.57 (11.55)
k	$C_{14}H_{13}N_3O_2Br$	182	47	52.50 (52.51)	4.06 (4.08)	10.00 (9.89)
l	$C_{14}H_{13}N_3O_4$	164	43	58.53 (58.55)	4.52 (4.49)	22.29 (22.57)

Table 2: IR data of compounds 3 (a-*l*) (cm^{-1})

Compd. 3	C=O	Ar-H	-CH	C=C	C-O-C
a	1725	3040	2925	1467-1630	-
b	1710	3036	2920	1460-1690	-
c	1690	3032	2917	1450-1660	1090
d	1735	3036	2920	1460-1630	-
e	1732	3035	2918	1456-1630	-
f	1730	3032	2915	1555-1628	-
g	1732	3045	2945	1490-1680	-
h	1725	3049	2941	1450-1690	1085
i	1718	3043	2934	1430-1670	-
j	1735	3035	2920	1460-1632	-
k	1733	3032	2918	1455-1628	-
l	1728	3035	2917	1450-1625	-

Table 3: ^{1}H NMR data of compounds (δ ppm, $CDCl_3$)

Compd. 3	Ar-H	N-CH_2	=CH (enol)	-OH (enol)	C-CH_3	-OCH$_3$
a	6.51-7.80 (m)	3.86 (s)	6.65 (s)	17.05 (s)	-	-
b	6.35-7.74 (m)	3.82 (s)	6.63 (s)	16.94 (s)	2.12 (s)	-
c	6.50-7.75 (m)	3.84 (s)	6.76 (s)	17.13 (s)	-	3.68 (s)
d	6.52-7.81 (m)	3.89 (s)	6.72 (s)	16.95 (s)	-	-
e	6.54-7.82 (m)	3.87 (s)	6.80 (s)	16.94 (s)	-	-
f	6.52-7.84 (m)	3.40 (s)	6.79 (s)	16.93 (s)	-	-
g	6.57-7.70 (m)	3.84 (s)	6.80 (s)	17.03 (s)	-	-
h	6.62-7.80 (m)	3.79 (s)	6.64 (s)	16.96 (s)	1.82 (s)	-
i	6.65-7.78 (m)	3.81 (s)	6.61 (s)	17.15 (s)	-	3.85 (s)
j	6.51-7.80 (m)	4.02 (s)	6.63 (s)	16.97 (s)	-	-
k	6.50-7.82 (m)	3.89 (s)	6.80 (s)	16.96 (s)	-	-
l	6.50-7.78 (m)	4.01 (s)	6.79 (s)	17.10 (s)	-	-

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References

1. L.V.G. Nargurid, G.R.N. Reddy and V. Hariprasad, Indian J. Chem., 35B, 1996, 499.
2. A.S. Bascif, H.M. Faidallah and Y.S. Hassam, Indian J. Heterocyclic Chem., 6, 1996, 53.
3. M.B. Deshmukh and B.S. Shinde, Indian J. Heterocyclic Chem., 4, 1995, ???.
4. Elguero, A.R. Katritzky, C.W. Rees and E.F.V. Scriven, Eds; Pergamon. Oxford, J. Comprehensive Heterocyclic Chemistry; 1996, 5.
5. M.I. Younes, H.H. Abas and S.A.M. Metwally, Pharmazie, 46, 1991, 98.
6. B.K. Bhattacharya, R.K. Robins, G.R. Revankar and R. Ganapathi, J. Heterocyclic Chemistry, 27(3), 1990, 795.
7. D.S. Fernandes, S. Desai, N. Gauri, S. Pandey and H. Patel, J. Indian Chem. Soc., 61, 1984, 818.
8. H.C.V. Patel and P.S. Fernandes, J. Indian Chem. Soc., 67, 1990, 321.
9. H.E. Skipper, R.K Robins, J.R. Thomson, C.C. Ching, R.W. Brockman and R.W. Schabel and F.M. Schabel, Cancer Res. 17, 1957, 579.
10. H.E. Skipper, R.K. Robins and J.R. Thomson, Proc. Soc. Expt. Biol. Med. 89, 1955, 594 .
11. E.W. Yue, Chem. Abstr. 147, 2002, 20374.
12. D. Bebbington, J.D. Charrier, R. Davies, S. Eveitt, D. Kay, R. Knegtal and S. Patel, Chem. Abstr., 137, 2002, 47221.
13. C. Cativiela, J.L. Serrano and M.M. Zurbano, J. Org. Chem., 60, 1995, 3074.
14. S. Sugiura, S. Ohno, O. Ohtani, K. Izuni, T. Kitamikado, H. Asai, K. Kato, M. Hori, and H. Fujimura, J. Med. Chem., 20, 1977, 80.
15. R. Unny, P. Joshi, M.P. Dobhal and Y. Joshi, Heterocyclic Commun., 9(2), 2003, 171-174.
16. M. ZIA-UL-HAQ, Shahid Hameed, Turk J. Chem., 26, 2002, 807-813.
17. S. Nigam and Y.C. Joshi, Phosphorus, Sulfur and Silicon, 178, 2003, 1583-1586.
18. M.K. Uladzimir and M.K. Mikalai, Liquid Crystals, 33 (11), 2006, 121-127.

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