Pak. j. sci. ind. res., vol. 38, nos. 5-6, May-June 1995

SYNTHESIS OF SOME HYDRAZONE AND PYRAZOLINE DERIVATIVES

HASSAN M. FAIDALLAH, HASSAN M. MOKHTAR, AHMED NASSAR AND MOHAMED M. AHMED

Department of Chemistry, Faculty of Science, University of Alexandria, Alexandria, Egypt

(Received October 1992 ; revised February 20, 1995)

Condensation of chalcones (1) with aroyl- and arylhydrazines afforded the corresponding hydrazones (2 and 3), cyclization of the hydrazones (3) with HCl gave the pyrazoline derivatives (4) which on oxidation with bromine water yielded the corresponding pyrazoles (5). Addition of 5-p-bromophenyl-3-methyl-1-p- sulphamylphenylpyrazole (5c) to allylisothiocyanate afforded the thiourea derivative (6) which was readily cyclized with ethyl bromoacetate to the corresponding oxothiazolidine (7).

Key words: Hydrazones, Pyrazolines, Preparation.

Introduction

Chalcones [1] as well as hydrazones [2] are useful intermediates in the synthesis of certain pyrazolines which is then used in the preparation of many other compounds such as pyrazoles [3]. 2H-pyran-2-ones [4] cyclopropanes [5].

Experimental

1-p-bromophenylbut-1-en-2-one (1a). A solution of 10% NaOH (2.2 ml) in H_2O) was added to a solution of p-bromobenzaldehyde (10 g) in acetone (3.1 ml). The temperature was kept at 20°C and stirring was continued for 4 hr. The deposited chalcone was filtered off, washed repeatedly with water until free alkalinity and dried. It was recrystallized from light petroleum (b.p.40-60°C) as pale yellow needles, m.p. 84°C, yield (8 g) (lit[6].m.p. 78-80°C).

1,5-Di(p-bromophenyl) pent-1,4-dien-3-one (1b). A solution of 10% NaOH (2.2ml) was added to a solution of p-bromobenzaldehyde (10 g) in acetone (1.5 ml).The temperature of the reaction mixture was kept at 25°C and stirring was continued for 4 hr, then worked up as previously. It was recrystallized from ethanol in yellow needles, m.p. 224°C, yield (8.2 g) (lit [6] .m.p. 225-7°C).

Aroylhydrazone derivatives (2; Table 1). A solution of the appropriate chalcone (1; 0.01 mol) in ethanol 30 ml) was refluxed with the corresponding aroylhydrazine (0.011 mol) in presence of few drops of glacial acetic acid for 1 hr. Ethanol was remove under reduced pressure and the residue was treated with methanol to give the product which was recrystallized from methanol.

Arylhydrazone derivatives (3; Table 1). A solution of (1; 0.01 mol) in ethanol (30 ml) was refluxed with a mixture of the appropriate arylhydrazine hydrochloride (0.011 mol) and sodium acetate (0.012 mol) in water (5 ml) for 1 hr. The reaction mixture was poured into water, the precipitated product was filtered off and recrystallized from alcohol.

1,3,5-Trisubstituted-2-pyrazolines (4; Table 3): A solution of the appropriate chalcone (1; 0.01 mol) in ethanol (50 ml) was refluxed with the proper arylhydrazine hydrochloride (0.011 mol) for 4 hr, cooled and diluted with water. The precipitated crude product was filtered off and recrystallized from ethanol in the form of needles.

The pyrazolines (4) were also obtained (65% yield) by refluxing the appropriate hydrazone in ethanol with few drops of hydrochloric acid for 3 hr.

1,3,5-Trisubstituted pyrazoles (5; Table 3). A suspension of 4 (0.01 mol) in water (10 ml) was treated with excess 5% bromine water with stirring until a faint yellow colour was developed. After stirring for 4 hr, the crude pyrazole was filtered off, washed with water and recrystallized from methanol in needles.

Allyl p-(5-p-bromophenyl-3-methylpyrazol-1-yl) benzenesulphonyl-thiourea (6). A mixture of 5c (0.01 mol) and anhydrous potassium (0.02 mol) in dry acetone (25 ml) was stirred and refluxed for 1 hr. At this temperature, a solution of allylisothiocyanate (0.015 mol) in dry acetone (5 ml) was added dropwise. After the mixture was stirred and refluxed overnight, acetone was removed under reduced pressure, and the solid residue was dissolved in water. The crude product was isolated by acidification with 2N HCl and purified by crystallization from ethanol in needles (68% yield), m.p. 118°C. IR (KBr); 1336, 1168 (SO_2N); 3089 3255 (NH); 1100 (CS), and it gave satisfactory analysis.

3-Allyl-2-[p-(5-p-bromophenyl-3-methylpyrazol-1-yl) benzenesulphonylimino]-4-oxothiazolidine (7). A mixture of(6) (0.01 mol) and ethyl bromoacetate (0.011 mol) in absolute ethanol (50 ml) was refluxed with stirring for 6 hr, concentrated and allowed to cool. The product obtained was recrystallized from ethanol in needles (62% yield). m.p. 172°C. IR (KBr); 1330, 1155 (SO_2N);1620 (CN); 1740 (CO), and it gave satisfactory analysis.

TABLE 1. CHARACTERISTIC DATA OF AROYL-(2) AND ARYLHYDRAZONE (3) DERIVATIVES.

Compd. No.	R	X	Yield (%)	M.P. (°C)	Me and/or OMe (s, 3H)	^{1}H-NMR (/ppm) Ar and Olefinic H	NH (s, 1H)	IR υ_{max}(cm^{-1}) C=O,	C=N	NH
2a	Me	H	87	206	2.2	6.8-7.6 (11H)	9.1	1657,	1602	3221
2b	Me	Me	85	226	2.1, 2.4	6.8-7.9 (10H)	8.9	1652,	1585	3198
2c	Me	MeO	86	210				1662.	1595	3203
2d	Me	Cl	85	222	2.2	6.9-7.9 (10H)	8.9	1656,	1592	3202
2e	Me	Br	86	238				1656,	1588	3165
2f	Me	NO_2	83	220	2.2	6.8-7.7 (10H)	9.3	1660,	1600	3180
2g	p-bromostyryl	H	80	223		6.8-7.9 (17H)	8.8	1652,	1598	3108
2h	p-bromostyryl	Me	79	217	2.1	6.9-7.8 (16H)	8.9	1660,	1595	3120
2i	p-bromostyryl	MeO	82	226				1665,	1596	3160
2j	p-bromostyryl	Br	80	230				1667,	1588	3125
3a	Me	H	78	225	2.1	6.7-7.7 (11H)	8.9	1599		3085
3b	Me	Cl	75	185				1595		3080
3c	Me	Br	76	175	2.1	6.8-7.8 (10H)	9.0	1600		3110
3d	p-bromostyryl	H	78	213				1607		3115
3e	p-bromostyryl	Cl	75	184		6.6-7.8 (16H)	8.9	1595		3080
3f	p-bromostyryl	Br	78	176		6.5-7.7 (16H)	9.1	1588		3120

TABLE 2. MASS SPECTRAL DATA FOR COMPOUNDS (2a, 4d, 4e AND 5d).

Compound	m/z values of principle fragments (relative intensity, %)
4-(p-Bromophenyl)but-3-en-2-one benzoylhydrazone (2a)	342(M^+, 22), 237 ($C_{10}H_{10}N_2Br$, 48), 222 ($C_{10}H_9NBr$, 13), 128 (C_9H_6N, 13), 105 (C_7H_5O, 100), 77 (C_6H_5, 74), 51 (C_4H_3,35).
5-(p-Bromophenyl)-3-methyl-1-p-sulphamylphenylpyrazoline (4d)	393 (M^+,96), 238 ($C_{10}H_{12}N_3O_2S$, 88), 182 (C_8H_7Br, 24), 170 ($C_6H_6N_2O_2S$, 32), 128 ($C_{10}H_8$, 24), 106 ($C_6H_6N_2$, 100), 90 (C_6H_4N, 60), 76 (C_6H_4 40), 63 (C_5H_3, 92), 50 (C_4H_2, 40).
5-(p-Bromophenyl)-3-p-bromostyryl-1-phenylpyrazoline (4e)	480 (M^+, 2), 392 ($C_{16}H_{14}N_2Br_2$, 42), 311 ($C_{16}H_{12}N_2Br$,42), 204($C_{15}H_{10}N$, 54), 181 (C_8H_6Br, 17), 102 (C_8H_6, 100), 76 (C_6H_4, 46), 51 (C_4H_3, 33).
5-(p-Bromophenyl)-3-methyl-1-p-sulphamylphenylpyrazole (5c)	391 (M^+, 92), 389 ($C_{16}H_{12}N_3O_2BrS$, 100), 312 ($C_{16}H_{13}N_3O_2S$,28), 184($C_6H_6N_3O_2S$,48), 155 (C_6H_4Br, 40), 127 ($C_{10}H_7$, 32), 115 (C_8H_5N, 16), 105 ($C_6H_5N_2$, 56), 90 (C_6H_4N, 32), 76 (C_6H_4, 88), 63 (C_5H_3, 60), 51 (C_4H_3, 80).

Results and Discussion

Reaction of 4-p-bromophenylbut-3-en-2-one [6] (1a) and 1,5-di-p-bromophenylpent-1, 4-dien-3-one [6] (1b) with acylhydrazines in presence of acid catalyst afforded the corresponding aroylhydrazones (2, Table 1). The structure of these hydrazones (2) was further confirmed by measuring the mass spectra of compound (2a) (Table 2), where it gave a small molecular ion peak at m/z 342 (Br^{79}). The base peak appeared at m/z 105 and was due to the (C_7H_5O)+ ion, followed by all expected fragments produce from its structure.

On the other hand, condensation of arylhydrazine hydrochlorides with chalcones (1) afforded 1,3,5-trisubstituted-2-pyrazolines (4; Table 3), while with chalcones (1) in the presence of sodium acetate yielded the corresponding arylhydrazones (3, Table 1) which were easily cyclized to the pyrazolines (4) when boiled with a few drops of HCl. The mass spectra of compounds (4d)and (4e) supported the structure of the prepared pyrazolines (4). Compound (4d) gave a large molecular ion peak at m/z 393 (Br^{79}), whereas, (4e) revealed a smaller one at m/z 480 (Br^{79}). The base peak for (4d) appeared at m/z 106 and was due to $(C_6H_6N_2)$+ ion, whereas, that for (4e) was observed at m/z 102 and was attributed to the (C_8H_6)+ ion; followed by all expected fragments produced form their structures (Table 2).

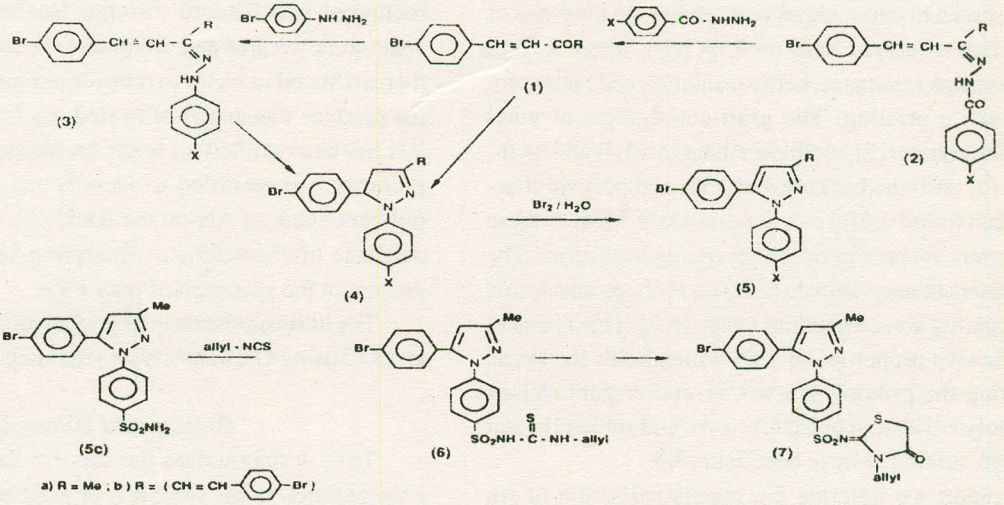
Mild oxidation of pyrazolines (4) with bromine water afforded the corresponding pyrazoles (5; Table 3). The structure of these pyrazoles was further confirmed from the mass spectra of compound (5d) (Table 2). It revealed a large molecular ion peak at m/z 391 (Br^{79}), and the base peak appeared at m/z 389 was attributed to the $(C_{16}H_{12}N_3O_2BrS)$+ ion, followed by all fragments expected from its structure.

Addition of 5-p-bromophenyl-3-methyl-1-p-sulphamyphenylpyra zole (5c) to allylisothiocyanate in dry acetone afforded the corresponding thiourea derivative (6) which readily cyclized with ethyl bromoacetate to give the oxothiazolidine derivative (7) in 70% yield.

TABLE 3. CHARACTERISTIC DATA OF PYRAZOLINE (4) AND PYRAZOLE (5) DERIVATIVES.

Compd. No.	R	X	Yield %	M.P. °C	^{1}H-NMR(/ppm) H-4 (m, 2H)	H-5 (m, 1H)	Ar-H (m)	NH_2 (sb, 1H)	Me (s, 3H)
4a	Me	H	70	192	3.7	5.1	6.8-7.8 (10H)	-	2.2
4b	Me	Cl	68	152	3.1	5.0	6.8-7.7 (9H)	-	2.2
4c	Me	Br	69	159	3.1	4.9	6.7-7.8 (9H)	-	2.1
4d	Me	SO_2NH_2	68	238	3.5	5.4	7.0-7.9 (9H)	6.5	2.3
4e	p-bromostyryl	H	67	226	3.2	5.1	6.8-7.5 (16H)	-	-
4f	p-bromostyryl	Cl	66	225	3.5	4.9	6.8-7.8 (15H)	-	-
4g	p-bromostyryl	Br	65	135	-	-	-	-	-
4h	p-bromostyryl	SO_2NH_2	65	208	3.6	5.5	7.0-7.9 (15H)	6.9	
5a	Me	Cl	80	105	-	-	6.9-7.8 (8H)	-	2.3
5b	Me	Br	82	132	-	-	6.8-7.8 (8H)	-	2.3
5c	Me	SO_2NH_2	80	147	-	-	6.8-7.9 (8H)	6.8	2.5
5d	p-bromostyryl	Cl	75	205	-	-	-	-	-
5e	p-bromostyryl	Br	78	150	-	-	-	-	-
5f	p-bromostyryl	SO_2NH_2	75	212	-	-	7.1-8.2 (14H)	6.7	-

All Compounds gave correct elemental analysis. Melting points are uncorrected. ^{1}H-nmr spectra were recorded on a Varian EM 360L using TMS as internal standard and the ir spectra were measured on a Unicam Sp 1025 spectrophotometer using KBr pellets.



References

1. A.A. Bilgin, N. Yulg. Serac and A. Tayhan, FABAD, Farm. Bilimler Derg., **14**, 135 (1987), C.A., 112, 135856 (1990).
2. H.M. Faidallah and H.M. Mokhtar, Indian, J. Chem., **27B**, 245 (1988).
3. F. Pragst, Z. Chem., **14**, 236 (1974), C.A., 81, 85204 (1974).
4. I.S. El-Kholy, M.M. Mishrikey and H.M. Faidallah, J. Heterocyclic Chem., **18**, 105 (1981).
5. I.S. El-Kholy, H.M. Faidallah and M.M. Mishrikey, J.Heterocyclic Chem., **17**, 541 (1980).
6. E. Jose, J. Robbert and M. Claude, Bull. Soc. Chim. Fr., **4**, 1367 (1969), C.A. 71, 80867 (1969).