

**SOME REACTIONS OF 2-(*p*-CHLOROPHENYL)-4H-1,3-BENZOXAZIN-4-ONE AND
2-(*p*-CHLOROPHENYL)-4H-1, 3-BENZOTHIAZIN-4-THIONE COMPARED WITH THAT OF
4H-3,1-BENZOXAZIN-4-ONE AND 4H-3,1-BENZOTHIAZIN-4-THIONE**

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The reaction of 1,3-benzoxazin-4-one (1) and 1,3-benzothiazin-4-thione (5) with alkyl, aralkyl and or aralkyl magnesium halides has been described. P_2S_5 reacted with (1) and yielded the corresponding benzothiazin-4-one (5). Primary amines condensed with (1) and (5) giving the corresponding Schiff's bases (7 a-d) or (8a-d) respectively. Also 1 reacted with hydrazine hydrate and gave the triazole derivative (9). But (1) condensed with *p*-nitrophenyl hydrazine and hydroxyl amine and yielded the corresponding hydrazone and oxime derivatives (10a-b). On the other hand, compound (5) reacted with ammonia derivatives and gave the condensation products (11a-d).

INTRODUCTION

2-(*p*-chlorophenyl)-4H-1, 3-benzoxazin-4-one (1) bears a structural resemblance with 4H-3,1-benzoxazine-4-one-2, the former having in the hetero ring the system-O-C = N. in place of -N=C-O in the latter. This has stimulated us to investigate the analogy between 1 and 2 in their chemical reactions.

In the present work, we have shown that in contrast to 4H-3,1-benzoxazine-4-one which underwent hetero ring opening with ethyl and/or phenyl magnesium bromides, [1] 2-(*p*-chlorophenyl)-4H-1,3-benzoxazine-4-one reacts with the same reagents under the same reaction conditions to yield 2-(*p*-chlorophenyl)-4-(ethyl, or phenyl)-4-hydroxy-4H-1,3-benzoxazine (3a-b) respectively.

The ir spectra of (3a-b) exhibit a broad band at 3440 cm^{-1} attributable to νOH and another band at 1630 cm^{-1} due to $\nu\text{C}=\text{N}$. On the other hand, 2-(*p*-chlorophenyl)-4-benzylidene 1,3-benzoxazine (4) was obtained by treating (1) with benzyl magnesium chloride, while (2) when treated with benzyl magnesium chloride under the same reaction conditions, gave desoxybenzoin derivatives [2].

The structure of compound 4 was confirmed from the following:-

- (1) Ir spectrum which showed absorption bands at 1610 cm^{-1} ($\nu\text{C}=\text{C}$) and 1630 cm^{-1} ($\nu\text{C}=\text{N}$).
- (2) ^1H NMR spectrum showed signals at δ ppm 5.3 (s, 1H, C=CH), and at 7.1 - 7.5 (m, 13 H aromatic protons).
- (3) Compound (4) was also obtained via an unambiguous

synthesis by fusion of compound (1) with phenyl acetic acid at 160°

- (4) Compounds (3a-b) are colourless, while compound (4) is yellow and does not contain a hydroxyl group.

By analogy with the reaction of compound (2) with P_2S_5 in dry xylene [1, 3] compound (1) reacted readily with P_2S_5 under the same conditions to produce 2-(*p*-chlorophenyl)-4H-1,3-benzothiazine-4-thione.

- (5) The assigned structure for the thione (5) is supported from ir spectrum which showed bands attributable to $\nu\text{C}=\text{N}$ at 1640 cm^{-1} and $\nu\text{C}=\text{S}$ at 1325 [1].

It has been shown that the reaction of 4H-3,1-benzothiazin-4-thione with Grignard reagents resulted in the cleavage of C-S bond [4]. But we have investigated the reaction of the thione (5) with ethyl magnesium iodide and with phenyl magnesium bromide under the same reaction conditions that resulted in addition to the thio carbonyl group without ring opening and yielded 2-(*p*-chlorophenyl)-4-(ethyl or phenyl)-1,3-benzothiazine-4-thiol (6a and 6b) respectively.

The structure of (6a and 6b) was proved from the ir spectra which showed absorptions characteristic of νSH at 2550 cm^{-1} and $\nu\text{C}=\text{N}$ at 1635 cm^{-1}

^1H NMR spectrum of 6a shows signals at δ ppm 1.1 (q, 2H, methylene protons), at 0.9 (t, 3H, methyl proton), at 7.2-7.6 (m, 8H aromatic protons) and at 4.1 (broad signal, 1H, SH proton).

Also, whereas 4H-3,1-benzothiazine-4-thione or 4H-3,1-benzoxazine-4-one underwent ring opening by treatment with amines in boiling alcohol [5, 6], compound (1) con-

densed with primary amines, namely, ethyl amine, benzyl amine, *p*-toluidine and/or *o*-chloroaniline in boiling alcohol to yield the corresponding Schiff's bases N-2 (*p*-chlorophenyl)-1,3-benzoxazine-5-ylidene (ethylamine, benzylamine *p*-toluidine and *o*-chloroaniline) (7a-d) respectively.

The structure of compounds (7a-d) was based on the following evidences:

(1) The ir spectra which showed a band at 1640 cm^{-1} due to $\nu\text{C}=\text{N}$.

(2) ^1H NMR spectrum of compound 7b shows signals at δ ppm 3.3 (s, 2H; N-CH₂-Ph), and at 7.2-7.5 (m, 13H aromatic protons).

Similarly compound (5) condensed with the same primary amines under the same conditions and gave N-2(*p*-chlorophenyl)-1,3-benzothiazin-4-ylidene (ethylamine, benzylamine, *p*-toluidine and/or *o*-chloroaniline) (8a-d) respectively.

The ir spectrum of compound (8) exhibit bands attri-

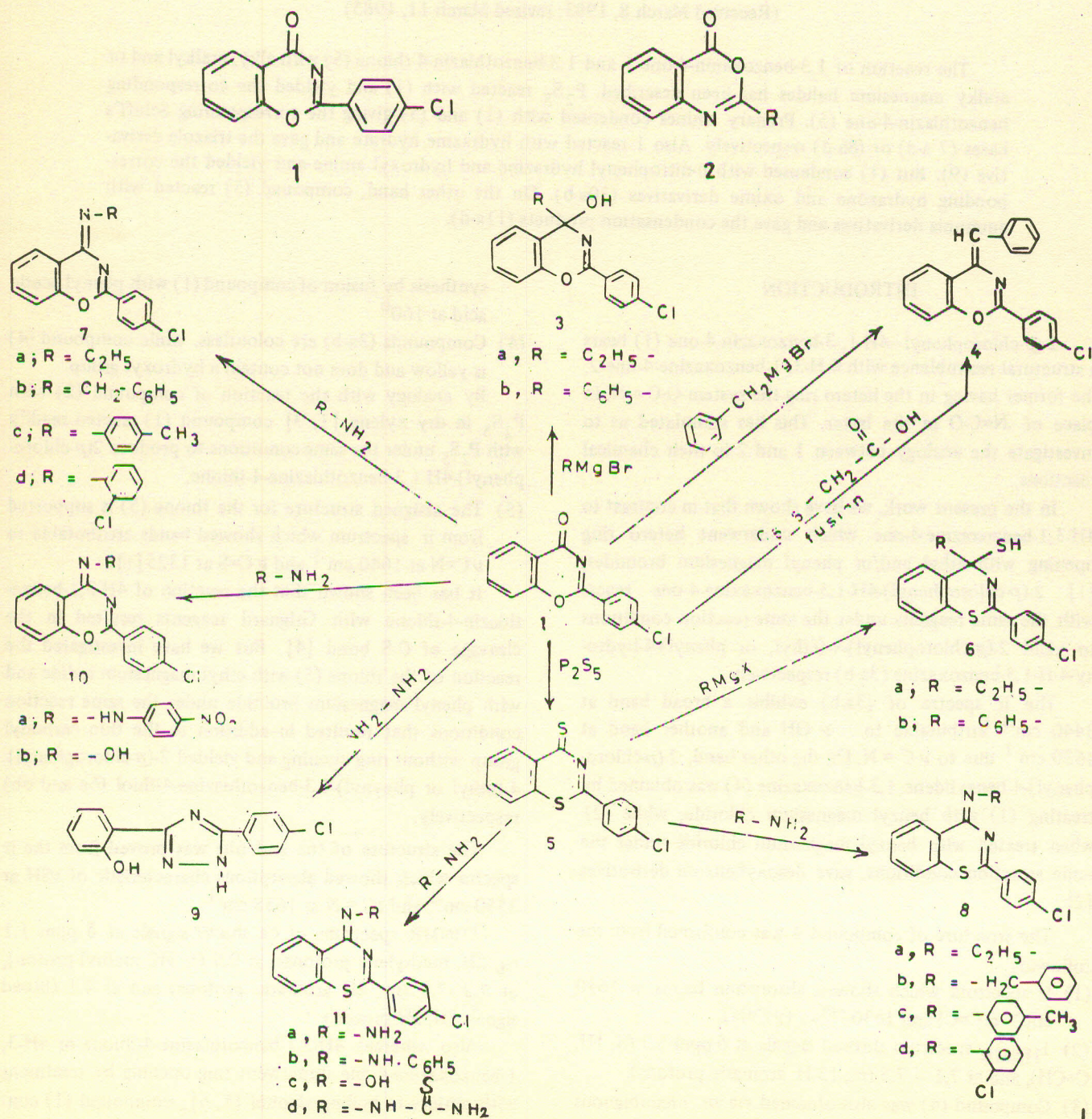


Table. Physical data of the compounds prepared.

Compound	m.p., °C. Colour	Solvent yield %	Formula (mol. wt.)	Analysis		
					Required	Found
3a	190 colourless	M 50	$C_{16}H_{14}ClNO_2$ 287.5	C	66.90	66.89
				H	4.88	4.87
				N	4.88	4.88
3b	180 colourless	B 40	$C_{20}H_{14}ClNO_2$ 335.5	C	71.54	71.52
				H	4.17	4.09
				N	4.14	4.11
4	90 yellow	M 40	$C_{21}H_{14}ClNO$ 331.5	C	76.02	76.01
				H	4.22	4.21
				N	4.22	4.22
5	150 orange	B/P(40-60) 60	$C_{14}H_8ClNS_2$ 289.5	C	58.03	58.01
				H	2.76	2.73
				N	4.84	4.81
				S	22.11	22.10
6a	130 orange	P(60-80) 40	$C_{16}H_{14}ClNS_2$ 319.5	C	60.09	60.07
				H	4.38	4.36
				N	4.38	4.37
				S	20.03	20.01
6b	210 red	B/P(40-60) 50	$C_{20}H_{14}ClNS_2$ 367.5	C	65.34	65.32
				H	3.81	3.79
				N	3.81	3.78
				S	17.41	17.39
7a	218 colourless	B 60	$C_{16}H_{13}ClN_2O$ 284.5	C	67.49	67.45
				H	4.57	4.54
				N	9.84	9.81
7b	165 colourless	E 55	$C_{21}H_{15}ClN_2O$ 346.5	C	72.73	72.70
				H	4.33	4.31
				N	8.08	8.07
7c	205 colourless	B 65	$C_{21}H_{15}ClN_2O$ 346.5	C	72.73	72.70
				H	4.33	4.31
				N	8.08	8.08

7d	200 colourless	M 80	$C_{20}H_{12}Cl_2N_2O$ 367	C	65.40	65.39
				H	3.27	3.26
				N	7.63	7.60
8a	180 yellow	E 30	$C_{16}H_{13}ClN_2S$ 300.5	C	63.89	63.86
				H	4.33	4.30
				N	9.32	9.30
				S	10.65	10.63
8b	135 reddish brown	B 35	$C_{21}H_{15}ClN_2S$ 362.5	C	69.52	69.50
				H	4.14	4.12
				N	7.72	7.70
				S	8.83	8.81
8c	130 pale yellow	B/P (40-60)	$C_{21}H_{15}ClN_2S$ 362.5	C	69.52	69.51
				H	4.14	4.13
				N	7.72	7.70
				S	8.83	8.82
8d	165 orange	M 40	$C_{20}H_{12}Cl_2N_2S$ 383	C	62.66	62.65
				H	3.13	3.12
				N	7.31	7.31
				S	8.36	8.35
9	155 colourless	M 50	$C_{14}H_{10}ClN_3O$ 271.5	C	61.88	61.86
				H	3.68	3.65
				N	15.47	15.46
10a	210 orange	E 60	$C_{20}H_{13}ClN_4O_3$	C	61.15	61.13
				H	3.31	3.30
				N	14.27	14.26
10b	200 colourless	E 75	$C_{14}H_9ClN_2O_2$ 272.5	C	61.65	61.64
				H	3.30	3.29
				N	10.28	10.26
11a	240 pale yellow	M 50	$C_{14}H_{10}ClN_3S$ 287.5	C	58.43	58.40
				H	3.48	3.46
				N	14.61	14.60
				S	11.13	11.12

11b	120	P(40-60)	$C_{20}H_{14}ClN_3S$	C	66.02	66.00
	brown	30	363.5	H	3.85	3.83
				N	11.55	11.54
				S	8.80	8.80
11c	120	B	$C_{14}H_9ClN_2SO$	C	58.23	58.22
	colourless	50	288.5	H	3.12	3.11
				N	9.71	9.70
				S	11.09	11.08
11d	170	M	$C_{15}H_{11}ClN_4S_2$	C	51.95	51.93
	orange	70	346.5	H	3.17	3.16
				N	16.16	16.15
				S	18.47	18.46

B = benzene, E = ethanol, M = methanol, P = light petrol.

butable to $\nu C=N$ at 1635cm^{-1}

It has been established that the action of hydrazines or hydroxyamine on compound (2) leads to the formation of quinazolinones via ring opening followed by cyclization [7, 8]. But we have investigated the action of hydrazine hydrate on compound (1) that gave the 1,2,4-triazole derivative (9), which was a colourless compound, soluble in aqueous sodium hydroxide solution and gave a violet colour with $FeCl_3$. The ir spectrum of compound (9) shows strong absorption bands at 3350cm^{-1} , 3260cm^{-1} and 1635cm^{-1} attributable to νOH , νNH and $\nu C=N$ respectively which agree well with the proposed structure. On the other hand, the action of *p*-nitrophenyl hydrazine and/or hydroxylamine on compound (1) led to the formation of *p*-nitrophenyl hydrazone and the oxime derivatives (10 a-b) respectively.

The ir spectra of compound (10) exhibit absorption bands at 1632cm^{-1} and 1620cm^{-1} attributable to ν_{\max} of two $C=N$ groups, with an additional bands at 3340cm^{-1} , 3250cm^{-1} due to νOH in the case of (10b) and νNH in the case of (10a). These ir data were consistent with the suggested structures.

Similarly, the thione (5) condensed with hydrazine, phenyl hydrazine, hydroxylamine and/or thiosemicarbazide to give the corresponding hydrazone derivatives (11a 11b), the oxime and thiosemicarbazone derivatives (11c and 11d) respectively.

The structure of compound (11) was confirmed from its ir. spectra which show absorption bands at 1637cm^{-1} , 1625cm^{-1} attributable to *exo* and *endo* $\nu C=N$ groups with additional bands at 3290cm^{-1} due to νNH for 11a, ν_{\max}

of two NH groups at 3250cm^{-1} and at 1340cm^{-1} attributable to $\nu C=S$ for (11d).

EXPERIMENTAL

The ir absorption spectra were determined with Unicam SP 1200 spectrophotometer using the KBr wafer technique. The NMR spectra were determined with VN s-60T.

(i) *Action of Grignard reagents on the benzoxazone 1: Formation of 3a, 3b and 4.* A solution of (1) (0.01 mole) in dry benzene was treated with an ethereal solution of ethyl magnesium bromide or phenyl magnesium bromide or benzyl magnesium chloride (0.03 mole) for 30 min. The reaction mixture was heated under reflux for 5 hr, left overnight at room temperature and then decomposed in the usual way. The oil obtained was triturated with light petrol and the products were crystallized from the proper solvent.

(ii) *Action of phenylacetic acid on benzoxazone (1): Formation of (4).* 0.01 mole of (1) was fused with 0.01 mole of phenylacetic acid on an oil bath at 160° for 3 hr. The product obtained was crystallized from alcohol to give (4).

(iii) *Action of phosphorous pentasulphide on benzoxazone (1): Formation of (5).* A solution of 0.01 mole) and P_2S_5 (0.02 mole) in 100 ml of dry xylene was heated under reflux for 6 hr. The reaction mixture was filtered while hot, and concentrated. The product separated on cooling was crystallized from the proper solvent to give (5).

(iv) *Action of amines on benzoxazone (1): Formation of 7a-d.* A solution of (1) (0.01 mole) and primary amines, namely, ethylamine, benzylamine, *p*-methyl aniline and *o*-

chloroaniline (0.01 mole) in (50 ml) ethanol was heated under reflux for 5 hr. The products that separated on cooling were crystallized from a suitable solvent to give (7a-d).

(v) *Action of amines on thione (5): Formation of (8a-d).* A solution of thione 5 (0.01 mole) and primary amines, namely, ethylamine, benzylamine, *p*-methyl aniline and *o*-chloroaniline was heated under reflux for 8 hr. The product that separated on cooling was crystallized from a proper solvent to yield 8a-d.

(vi) *Action of Grignard reagent on thione (5): Formation of (6a and 6b).* A solution of thione 5 (0.01 mole) in dry ether was treated with ethyl magnesium iodide or phenyl magnesium bromide (0.03 mole) in ether in the course of 30 min. The reaction mixture was heated under reflux for 4 hr., left overnight at room temperature and then decomposed in the usual way. The oil obtained was triturated with light petrol and the products were crystallized from proper solvents to produce 6a and 6b.

(vii) *Action of hydrazines on benzoxazone (1) or thione (5): Formation of (9), (10 a) and (11 a and 11b).* A solution of (1) or (5) (0.01 mole) and hydrazines, namely, hydrazine hydrate, *p*-nitrophenyl hydrazine and phenyl hydrazine (0.03 mole) in ethanol (50 ml) was refluxed for 8 hr. The solid that separated on cooling was crystallised from a proper solvent to yield (9), (10a) and (11 a) and (11b).

(ix) *Condensation of benzoxazone (1) or thione (5) with hydroxyl amine hydrochloride or thiosemicarbazide formation of (10b), (11c and 11d).* A mixture of 1 or 5 (0.01 mole) and hydroxylamine hydrochloride or thiosemicarbazide (0.03 mole) in dry pyridine (50 ml) was heated under reflux for 10 hr. The reaction mixture was poured into cold dilute 11Cl to give solids which were crystallized from a proper solvent to give (10a) and (11c) and (11d).

REFERENCES

1. M.A.El-Hashash, M.A. Hassan and M.A. Sayed., *Pakistan J. Sci. Ind. Res.*, **20**, 336 (1977).
2. A.F.M. Fahmy, M.A. El-Hashash, M.M. Habashy and S. A. El-Wannise, *Rev. Roum. Chim.* **23**, 1597 (1978).
3. A. Essawy, M.A.El-Hashash and M.M. Mohamed., *Indian J. Chem.* **19B**, 663 (1980).
4. M.A.El-Hashash and M.A. Sayed., *Egypt. J. Chem.* **21**, 115 (1978).
5. M.A. El-Hashash, M.M. Mohamed, A.El-Naggar and O.A. El-Sayed, *Rev. Roum. Chim.* **24**, 10, 1343 (1979).
6. M. M. Mohamed, M.A. El-Hashash, A. Essawy and M. E. Shaban, *Indian. J. Chem.*, **20B**, 718 (1981).
7. M.A.El-Hashash, M.M. Mohamed and M.A. Sayed., *Rev., Roum. Chim.* **24** 1509 (1979).
8. M.M. Mohamed and M.A. El-Hashash., *Rev. Roum. Chim.* **24** 849 (1979).