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## SOME REACTIONS OF NITROGEN NUCLEOPHILES WITH 6-BROMO-2,4-DICHLOROQUINAZOLINE, 6-BROMO-2-CHLORO-3-METHYL-4(3H)- QUINAZOLINONE AND 6-BROMO-4-CHLORO- OR (6-BROMO-4-CHLORO-1-PHENYL)-1-H- QUINAZOLIN-2-THIONE

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6-Bromo-2,4-dichloroquinazoline (1) and 6-bromo-2-chloro-3-methyl-4 (3H)-quinazolinone (2) have been prepared by the reaction of 6-bromo- or 6-bromo-3-methyl-2,4 (1H, 3H)-quinazolinone with phosphorous oxychloride. The reaction of (1 and 2) with hydrazine and various amines to give amino derivatives (3) and (4) respectively have been described. Also 6-bromo-4-chloro- or 6-bromo-4-chloro-1-phenyl-1H-quinazolin-2-thione (5 and 6) respectively were prepared by treating 6-bromo- or 6-bromo-1-phenyl-4 (1H, 3H)-quinazolinone-2-thione with phosphorous oxychloride and their reaction with hydrazine and various amines gave the corresponding substituted amino derivatives (7) and (8) respectively.

### INTRODUCTION

Certain 4-quinazolinones have been shown to possess diuretic [1], antihistaminic [2], antiinflammatory [3], bronchodilator [4, 5], antihypertensive [6], hypnotic [7], anticonvulsant [8], tuberculostatic [9] and blood sugar lowering activity [10]. This stimulated us to extend the chemistry of quinazolinone derivatives by preparing some new ones and studying their behaviour towards different nucleophiles. Thus, in the present work 6-bromo-2, 4-dichloroquinazoline (1) and 6-bromo-2-chloro-3-methyl-3 (3H)-quinazolinone (2) have been prepared by the interaction of 6-bromo- or 6-bromo-3-methyl-2,4 (1H, 3H)-quinazolinone with phosphorous oxychloride respectively. The structures of compounds (1) and (2) were confirmed from IR spectra which showed absorption bands at 1630  $\text{cm}^{-1}$  in the case of (1) and at 1685  $\text{cm}^{-1}$   $\nu$  CO and 1635  $\text{cm}^{-1}$   $\nu$  C=N in the case of (2).

The reaction of (1) with various amines, viz., benzylamine, aniline, *n*-butylamine, piperidine and/or hydrazine hydrate in boiling alcohol led to the formation of the substituted products 6-bromo-2, 4-(dibenzylamino, dianilino, dibutylamino, dipiperidino and dihydrazino) quinazolinone (3a-e) respectively. The IR spectra of compounds (3) exhibited bands at 3420  $\text{cm}^{-1}$  attributable for  $\nu$ NH, and at 1630  $\text{cm}^{-1}$  for  $\nu$  C=N, for compound (3d) no band at 3420  $\text{cm}^{-1}$  for  $\nu$  NH, and for compound (3e) there are other bands at 3350 and 3260  $\text{cm}^{-1}$  due to  $\nu$  NH<sub>2</sub>. The

appearance of these bands are consistent with the proposed structures.

The <sup>1</sup>HNMR of compound (3a) showed signals at  $\delta$  3.4 (s, 4H, 2-N-CH<sub>2</sub>-Ar) at  $\delta$  2.1 (s, 2H, 2NH protons) and at 7-7.5 (m, 13H, aromatic protons).

Similarly, it has been found that compound (2) reacted with the same nitrogen nucleophiles (benzylamine, aniline, *n*-butylamine, piperidine and/or hydrazine) in boiling alcohol and yielded the corresponding 6-bromo-3-methyl-2-(benzylamino, anilino, *n*-butylamino, piperidino and/or hydrazino) 4-(3H)-quinazolinone (4a-e) respectively. The assigned structures for compounds (4) were supported from IR spectra which showed absorption bands attributable for  $\nu$  C=N at 1640  $\text{cm}^{-1}$ , at 3400  $\text{cm}^{-1}$  for  $\nu$  NH and at 1680 for  $\nu$  CO for compound (4d) no band at 3420  $\text{cm}^{-1}$  for  $\nu$  NH, and for compound (4e) there are other bands at 3360 and 3280  $\text{cm}^{-1}$  due to  $\nu$  NH<sub>2</sub>.

The <sup>1</sup>HNMR of compound (4a) showed the following signals at  $\delta$  3.5 (s, 2H, N-CH<sub>2</sub>-Ar), at  $\delta$  2.3, (s, 3H, N-CH<sub>3</sub>), at  $\delta$  2 (s, 1H, NH proton) and at  $\delta$  7 - 7.5 (m, 8H, aromatic protons).

On the other hand, 6-bromo-4-chloro- or 6-bromo-4-bromo-4-chloro-1-phenyl-1H-quinazolin-2-thione (5) and (6) respectively were prepared by treating 6-bromo or 6-bromo-1-phenyl-4 (1H, 3H) quinazolinone-2-thione with phosphorous oxychloride. The structure of compounds (5) and (6) were supported from IR spectra which showed absorption bands at 3350  $\text{cm}^{-1}$  for  $\nu$  NH, 1630  $\text{cm}^{-1}$  for  $\nu$

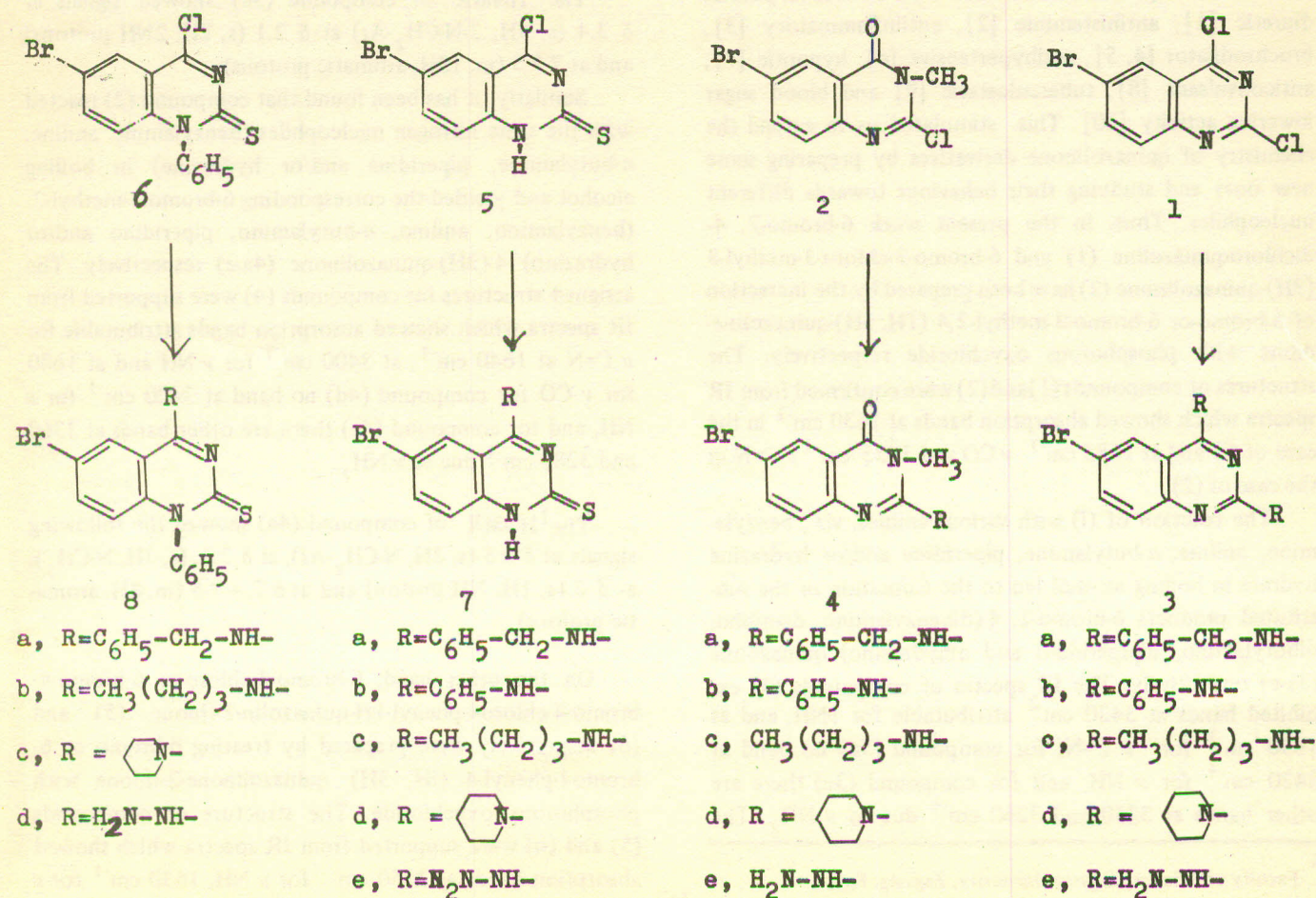
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C=N and at 1220 for  $\nu$  C=S and the absence of  $\nu$  NH at 3350  $\text{cm}^{-1}$  in the case of compound (6).

Also, it was our purpose to see whether compounds (5) and (6) would behave similarly or not towards the action of nitrogen nucleophiles.

Thus, when compounds (5) and/or (6) were allowed to react with benzylamine, aniline, *n*-butylamine, piperidine and/or hydrazine hydrate in boiling alcohol they gave the corresponding 6-bromo-4-(benzylamino, anilino, *n*-butylamino, piperidino and/or hydrazino)-1H-quinazolin-2-thione (7a-e) respectively and 6-bromo-1-phenyl-4-(benzylamino, *n*-butylamino, piperidino and/or hydrazino)-1H-quinazolin-2-thione (8a-d) respectively. The IR spectra of compounds (7) and (8) exhibited the absorption bands at 1640  $\text{cm}^{-1}$  due to  $\nu$  C=N, at 1225  $\text{cm}^{-1}$  due to  $\nu$  C=S and 3380  $\text{cm}^{-1}$  due to  $\nu$  NH, for compound (8c) no band at 3380  $\text{cm}^{-1}$  for  $\nu$  NH, and for compounds (7c and 8d) there are other bands at 3350 and 3260  $\text{cm}^{-1}$  due to  $\nu$  NH<sub>2</sub>.

The <sup>1</sup>HNMR of compound (7a) exhibited signals at  $\delta$  3.2 (s, 2H, N-CH<sub>2</sub>-Ar) at  $\delta$  2 (s, 2H, 2NH) and at  $\delta$  7-7.5 (m, 8H aromatic protons).



## EXPERIMENTAL

The infrared absorption spectra were determined with a Unicam SP 1200 Spectrophotometer using KBr wafer technique. The NMR spectra were determined by a Varian analytical instrument division chart S-60T using TMS as internal standard.

*Preparation of the chloro derivatives (1,2,5 and 6):* A mixture of (0.1 mol.) of 6-bromo- or 6-bromo-3-methyl-2,4(1H, 3H) quinazolinone-2-thione and/or 6-bromo- or 6-bromo-1-phenyl-4-(1H, 3H) quinazolinone-2-thione and (0.25 mol.) of phosphorous oxychloride was heated under reflux for 10 hr. The solvent was distilled off to give a semi-solid paste which was washed with dry ether and recrystallised from the suitable solvent to give (1,2,5 and 6) respectively.

*Reaction of the chloro compounds (1,2,5 and 6) with amines:* Compounds (1,2,5 and/or 6) (0.01 mol.) and excess of the amine, viz., benzylamine, aniline, *n*-butylamine and/or piperidine in ethanol were heated under reflux for 8 hr. The solid obtained after concentration of the solvent, was recrystallised from the suitable solvent to give (1, 2, 5 and 6) respectively.

## Physical data of compounds prepared

Compound	mp <sup>o</sup> C colour	Solvent yield %	Formula (Mol. wt.)	Analysis		
					Required	Found
1	288 yellow	A 70	C <sub>8</sub> H <sub>3</sub> BrCl <sub>2</sub> N <sub>2</sub> 276.92	C	34.67	34.35
				H	1.08	1.06
				N	10.11	10.00
2	260 yellow	A 65	C <sub>9</sub> H <sub>6</sub> BrClN <sub>2</sub> O 273.42	C	39.50	39.43
				H	2.19	2.17
				N	10.24	10.20
3a	250 colourless	B 75	C <sub>22</sub> H <sub>19</sub> BrN <sub>4</sub> 418.92	C	63.02	63.09
				H	4.54	4.50
				N	13.37	13.33
3b	254 yellow	A 60	C <sub>20</sub> H <sub>15</sub> BrN <sub>4</sub> 390.92	C	61.39	61.32
				H	3.84	3.80
				N	14.33	14.30
3c	220 brown	B 70	C <sub>16</sub> H <sub>23</sub> BrN <sub>4</sub> 350.92	C	54.71	54.69
				H	6.55	6.57
				N	15.96	15.99
3d	265 brown	B 67	C <sub>18</sub> H <sub>23</sub> BrN <sub>4</sub> 374.92	C	57.62	57.64
				H	6.13	6.20
				N	14.94	14.96
3e	215 brown	E 70	C <sub>8</sub> H <sub>9</sub> BrN <sub>6</sub> 268.92	C	35.70	35.69
				H	3.35	3.33
				N	31.24	31.22
4a	251 yellowish	E 75	C <sub>16</sub> H <sub>14</sub> BrN <sub>3</sub> O 343.92	C	55.83	55.80
				H	4.07	4.10
				N	12.21	12.23
4b	290 yellowish brown	A 60	C <sub>15</sub> H <sub>12</sub> BrN <sub>3</sub> O 329.92	C	54.56	54.58
				H	3.64	3.61
				N	12.73	12.69
4c	286 yellow	A 65	C <sub>13</sub> H <sub>16</sub> BrN <sub>3</sub> O 309.92	C	50.34	50.40
				H	5.16	5.2
				N	13.55	13.56
4d	280 yellowish	A 62	C <sub>14</sub> H <sub>16</sub> BrN <sub>3</sub> O 321.92	C	52.19	52.18
				H	4.97	4.95
				N	13.05	13.00
4e	215 brown	E 68	C <sub>9</sub> H <sub>9</sub> BrN <sub>4</sub> O 268.92	C	40.16	40.20
				H	3.35	3.40
				N	20.82	20.83

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5	112 yellowish	A 55	$C_8H_4BrClN_2S$ 275.42	C	34.86	34.87
				H	1.45	1.46
				N	10.17	10.16
				S	11.62	11.59
6	284 yellow	A 60	$C_{14}H_8BrClN_2S$ 351.42	C	47.81	47.53
				H	2.28	2.27
				N	7.97	7.99
				S	9.12	9.11
7a	165 brown	E 67	$C_{15}H_{12}BrN_3S$ 345.92	C	52.04	52.03
				H	3.47	3.46
				N	12.14	12.15
				S	9.25	9.24
7b	182 yellow	E 68	$C_{14}H_{10}BrN_3S$ 331.92	C	50.61	50.60
				H	3.01	3.20
				N	12.65	12.66
				S	9.64	9.63
7c	255 brown	T 65	$C_{12}H_{14}BrN_3S$ 311.92	C	46.17	46.20
				H	4.49	4.44
				N	13.46	13.40
				S	10.26	10.30
7d	260 yellow	E 75	$C_{13}H_{14}BrN_3S$ 323.92	C	48.16	48.15
				H	4.32	4.34
				N	12.97	12.93
				S	9.88	9.85
7e	216 brown	B 70	$C_8H_7BrN_4S$ 270.92	C	35.43	35.46
				H	2.58	2.56
				N	20.67	20.69
				S	11.81	11.78
8a	265 yellow	E 72	$C_{21}H_{16}BrN_3S$ 421.92	C	59.73	59.75
				H	3.79	3.76
				N	9.95	9.93
				S	7.58	7.60
8b	240 pale yellow	E 65	$C_{18}H_{18}BrN_3S$ 387.92	C	55.68	55.69
				H	4.64	4.63
				N	10.83	10.88
				S	8.25	8.23
8c	236 yellow	E 58	$C_{19}H_{18}BrN_3S$ 399.92	C	57.01	57.11
				H	4.50	4.60
				N	10.50	10.48
				S	8.00	8.11
8d	215 brown	E 62	$C_{14}H_{11}BrN_4S$ 346.92	C	48.43	48.39
				H	3.17	3.20
				N	16.14	16.16
				S	9.22	9.24

A - acetic acid, E - ethanol, T - toluene and B - butanol.

*Reaction of the chloro compounds (1, 2, 5 and 6) with amines.* Compounds (1, 2, 5 and/or 6) (0.01 mol.) and excess of the amine, viz., benzylamine, aniline, *n*-butylamine and/or piperidine in ethanol were heated under reflux for 8 hr. The solid obtained after concentration of the solvent, was recrystallised from the proper solvent to yield compounds (3*a-d*, 4*a-d*, 7*a-d* and 8*a-c*) respectively.

*Reaction of chloro compounds (1,2,5 and 6) with hydrazine hydrate:* Compounds (1,2,5 and/or 6) (0.01 mol.) and excess of hydrazine hydrate (0.025 mole in case of reaction with compound (2) or 0.012 mole) in case of compounds (1, 5 and 6) in ethanol were heated under reflux for 5h. The solid obtained after concentration of the solvent was crystallised from the suitable solvent to give compounds (3*e*, 4*e*, 7*e*, 8*d*) respectively.

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