added slowly with stirring. After filtering, the layers were separated and the aqueous layer was extracted with diethyl ether. The organic layers were combined, dried over $MgSO_4$, and filtered, and the diethyl ether was removed by rotary evaporation. The physical properties of the 4-substituted benzeneselenols are listed in Table V.

Bis(4-substituted-benzene) Diselenide. To 0.30 mol of 4-substituted benzeneselenol in 500 mL water was added 12.0 g (0.30 mol) of NaOH. To the mixture was added 225 mL of 3% hydrogen peroxide at such a rate that the temperature of the reaction mixture did not exceed 30 °C. After the addition of hydrogen peroxide, the reaction mixture was stirred overnight at room temperature. The crystals of diselenide were filtered and washed with warm water and then by distilled water until the filtrate was alkaline free. The physical properties of the bis(4-substituted-benzene) diselenides are listed in Table V.

4-Substituted Benzeneselenenyl Chlorides. To a solution of 0.25 mol of bis(4-substituted-benzene) diselenide in 400 mL of CCl_4 was added dropwise a solution of 0.25 mol of SO_2Cl_2 in 250 mL of CCl_4. The reaction mixture was allowed to stand for 30 min at room temperature after addition of SO_2Cl_2. The solvent was removed by rotatory evaporation. The resulting oil or solid was recrystallized from pentane. The physical properties of the 4-substituted benzeneselenenyl chlorides are given in Table V and the elemental analyses for all the new compounds were satisfactory.

Preparation of Areneselenenyl Chlorides via Arene Selenocyanates: General Procedure. 4-Substituted-benzene Selenocyanates. To a solution of 0.10 mol of the appropriately substituted aniline in 85 mL of 20% H_2SO_4 cooled to 4 °C was added in portions with stirring 8.0 g of $NaNO_2$. Sodium acetate was added until the pH of the reaction mixture was 6.0 and then a solution of 14.0 g (0.10 mol) of KSeCN in 150 mL of cold water was added slowly. The reaction mixture was stirred at room temperature for 48 h, filtered, and extracted with CH_2Cl_2. The CH_2Cl_2 layer was dried over $MgSO_4$ and the solvent removed by rotary evaporation leaving the solid selenocyanate. The melting points of the 4-substituted-benzene selenocyanates prepared in this study are given in Table V.

4-Substituted Benzeneselenenyl Chlorides. The 4-substituted-benzene selenocyanates were chlorinated with SO_2Cl_2 in CCl_4 by the same procedure used for bis(4-substituted benzene) diselenides. Attempts to isolate 4-fluorobenzeneselenenyl and 4-nitrobenzeneselenenyl chlorides were unsuccessful. Solutions of these areneselenyl chlorides in CH_2Cl_2 for kinetic runs were prepared immediately after the chlorination reaction. The CCl_4 was removed from the reaction mixture under high vacuum to constant weight. A known volume of anhydrous CH_2Cl_2 was added, and the amount of areneselenenyl chloride was determined by titrating an alloquot with (*E*)-3-hexene.

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Registry No. **1a**, 57878-19-0; **1b**, 52178-47-9; **1c**, 5707-04-0; **1d**, 57878-20-3; **1e**, 71912-36-2; **1f**, 57878-21-4; **1g**, 71912-37-3; **1h**, 57878-23-6; (*Z*)-4-$C_6H_5OC_6H_4CH$=$CHCH_3$, 60319-64-4; (*Z*)-4-$CH_3OC_6H_4CH$=$CHCH_3$, 25679-28-1; (*Z*)-4-$CH_3C_6H_4CH$=$CHCH_3$, 2077-29-4; (*Z*)-4-ClC_6H_4CH=$CHCH_3$, 1879-52-3; (*Z*)-4-$NO_2C_6H_4CH$=$CHCH_3$, 1879-54-5; (*Z*)-3-$NO_2C_6H_4CH$=$CHCH_3$, 23281-57-4; (*E*)-4-$C_6H_5OC_6H_4CH$=$CHCH_3$, 60319-66-6; (*E*)-4-$CH_3OC_6H_4CH$=$CHCH_3$, 4180-23-8; (*E*)-4-$CH_3C_6H_4CH$=$CHCH_3$, 2077-30-7; (*E*)-4-ClC_6H_4CH=$CHCH_3$, 1879-53-4; (*E*)-4-$NO_2C_6H_4CH$=$CHCH_3$, 1879-55-6; (*E*)-3-$NO_2C_6H_4CH$=$CHCH_3$, 23204-79-7; (*Z*)-1-phenylpropene, 766-90-5; (*E*)-1-phenylpropene, 873-66-5.

Reactions with 3,1-Benzoxazin-4-ones. 3.[1] Reactions of 6,8-Dibromo-2-methyl-3,1-benzoxazin-4-ones with Amines

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We observed that the reaction of 6,8-dibromo-2-methyl-3,1-benzoxazin-4-one, **5**, with primary amines occurs very slowly in ethanol solution at room temperature and that the product is usually the corresponding 2-acetamido-3,5-dibromobenzamide, **6**. These results are in sharp contrast to the results reported for the corresponding reactions with 6-bromo-2-methyl-3,1-benzoxazin-4-one, **5'**. The latter occur very rapidly to give the corresponding *N*-(2-carboxy-4-bromophenyl)-*N'*-substituted-acetamidine intermediate, **4**, which undergoes cyclodehydration in solution (sometimes spontaneously) to give the corresponding *N*-substituted-2-methyl-6-bromoquinazolin-4-ones, **7'**. It was inferred from these observations that the qualititive difference in chemistry exhibited by **5** and **5'** is somehow attributable to the presence of the substituent in the 8-position of compound **5**.

In a recent series of publications,[2-6] Errede et al. reinvestigated the reactions of 3,1-benzoxazin-4-ones **1** with amines. They reported that the products, ortho-substituted benzamides (**2**) and/or quinazolin-4-ones (**3**), were not formed sequentially (**3** from **2**) as was assumed by early investigators but rather were formed competitively via alternative pathways A and B as shown in Scheme I.

These authors showed that the precursors of **3** are the amidine salt intermediates **4**. These intermediates were isolated in >90% yield when R'' is aromatic (Table IV of ref 4 and Table I of ref 3) and when R'' is nonsterically hindered aliphatic amines (Table I of ref 5). They undergo cyclodehydration quantitatively even in aqueous solution at room temperature within a few minutes to a few hours. In contrast, the *o*-acetamidobenzamides, **2**, need temper-

(1) Part 2, M. F. Ismail, N. A. Shams, M. R. Salem, and S. A. Emara, *J. Prakt. Chem.*, in press.
(2) L. A. Errede, *J. Org. Chem.*, **41**, 1763 (1976).
(3) L. A. Errede, J. J. McBrady, and H. T. Oien, *J. Org. Chem.*, **41**, 1765 (1976).
(4) L. A. Errede, H. T. Oien, and D. R. Yarian, *J. Org. Chem.*, **42**, 12 (1977).
(5) L. A. Errede, J. J. McBrady, and H. T. Oien, *J. Org. Chem.*, **42**, 656 (1977).
(6) L. A. Errede and J. J. McBrady, *J. Org. Chem.*, **43**, 1884 (1978).

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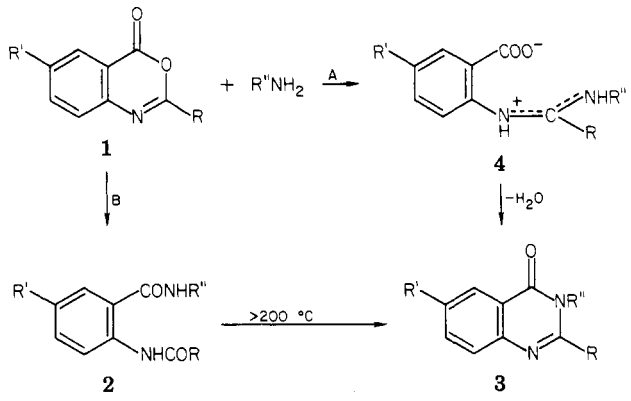
Scheme I[a]



[a] R' = H, Br, NO_2.

Table I. 2-(Acetylamino)-3,5-dibromobenzamide Derivatives 6[a]

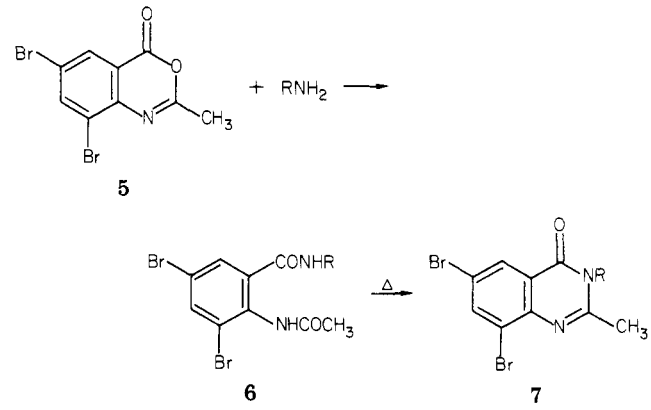
compd	mp, °C	yield, %	IR, cm^{-1} ν_{NH}	IR, cm^{-1} $\nu_{C=O}$
6a[b]	219-220	60	3280	1645, 1680
6b[b]	206-207	70	3280	1640, 1670
6c[c]	205-206	72	3280	1635, 1660
6d[b]	239-240	58	3260	1638, 1665
6f[c]	235-236	20	3260	1650, 1670
8i[d]	165-166	60	3230	1640, 1680
8j[d]	170-171	62	3240	1634, 1690

[a] Combustion analytical data were reported for these compounds. Solvents of crystallization: [b] Benzene-ethanol mixture. [c] Ethanol. [d] Light petroleum (bp 100-120 °C).

atures above 200 °C to affect cyclodehydration to 3 (Table I, ref 2). The authors postulated that the electronic and steric effects associated with the substituent R at the 2-position and also the steric hindrance on the part of the coreactant amine are the significant factors that determine selectivity via either pathways. Thus, they observed that the selectivity ratio for reaction via pathway A to pathway B as well as the rate of conversion to products decrease with increase in the bulk of R. Since the above chemistry was shown to be valid for 1 with R = H, Br, NO_2 and was consistent with the substituents in the 5-, 6-, and 7-positions, it was suggested that the reaction via pathway A might be general for all 2-methyl-3,1-benzoxazin-4-ones (1, R = CH_3). They also observed that the reactions with simple primary amines such as methylamine and aniline occur rapidly and follow pathway A, whereas reactions with secondary amines and bulky primary amines occur slowly and follow pathway B.

When we extend the above chemistry to the reactions of 6,8-dibromo-2-methyl-3,1-benzoxazin-4-one (**5**) with primary amines RNH_2 [where R is (a) methyl, (b) *n*-butyl, (c) benzyl, (d) *p*-tolyl, (e) *m*-tolyl, (f) *p*-anisyl, and (h) phenyl], we did not observe *rapid* formation of the corresponding acetamidine salt intermediate **4**; we observed instead *slow* formation of the corresponding stable 2-acetamidobenzamides **6**, Scheme II), which were isolated in good yields (Table I), with the exception of the reaction with *p*-anisidine (f). In this exception 2-methyl-3-(*p*-methoxyphenyl)-6,8-dibromoquinazolin-4-one (**7f**) was isolated as the major product (70% yield), and 2-acetamido-3,5-dibromo-*N*-(*p*-methoxyphenyl)benzamide (**6f**) was isolated as the minor product. The times required to effect completion of these reactions in ethanol at room temperature (i.e., about 24 h) were comparable to those for the corresponding reactions of **5** with the secondary

Scheme II



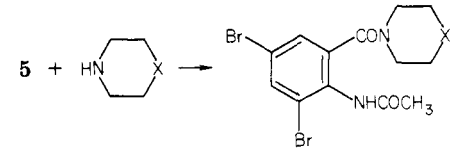
a, R = CH_3
b, R = n-C_4H_9
c, R = $C_6H_5CH_2$
d, R = C_6H_4-p-CH_3
e, R = C_6H_4-m-CH_3
f, R = C_6H_4-p-OCH_3
g, R = C_6H_4-o-OCH_3
h, R = C_6H_5

Table II. 3-Substituted-6,8-dibromo-2-methylquinazolin-4-ones 7[a]

compd	mp, °C	yield, %	$\nu_{C=O}$, cm^{-1}
7a[b]	148-149	70	1680
7b[c]	79-80	71	1670
7c[b]	134-135	79	1685
7d[b]	172-173	51	1682
7e[b]	199-200	61	1675
7f[b]	159-160	70	1680
7g[d]	201-202	66	1690

[a] Combustion analytical data were reported for these compounds. Solvents of crystallization: [b] Light petroleum (bp 100-120 °C). [c] Light petroleum (bp 60-80 °C). [d] Acetic acid.

amines, piperidine (i) and morpholine (j), which also gave the corresponding 2-acetamidobenzamides (**8i** and **8j**) in good yields (Table I). Samples of the benzamides (**6a–h**)

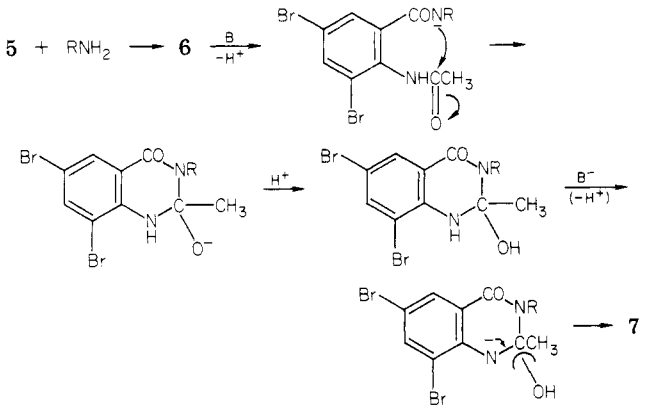


8i, X = CH_2
j, X = O

were converted to the corresponding 2-methylquinazolin-4-ones (**7a–h**) by thermal cyclodehydration of the melt at about 250 °C (Table II). These products of cyclodehydration were also obtained as expected by fusion of **5** with an equivalent amount of the appropriate amine at about 250 °C.

The above chemistry is characteristic of the reactions of primary amines with 3,1-benzoxazin-4-ones that have a bulky substituent such as a phenyl or an isopropyl group in the 2-position, which imparts steric hindrance to nucleophilic attack at this site by the coreactant amine[6]. These results contrast sharply with the chemistry reported[4] for 6-bromo-2-methyl-3,1-benzoxazin-4-one, which requires only minutes for reaction with amines a and c–h, under the same condition to give the corresponding acetamidine salt intermediate 4 via pathway A (Scheme I). One would expect that the added electron-withdrawing effect on the

Scheme III[a]



[a] B^- = base.

2-position caused by the second bromine atom in the 8-position of **5** would enhance nucleophilic attack at this site by the coreactant amine. That the opposite result was obtained is therefore interesting. It is now necessary to show whether or not this is unique to 8-bromo or general for all such compounds with a substituent in the 8-position and then to determine why.

When the reactions of **5** with an equivalent amount of a primary amine (a–g) in ethanol were made to occur at reflux temperatures, the product isolated in good yield was always the corresponding quinazolin-4-one (**7a–g**, Table II). This implies that pathway A (Scheme I) is favored over pathway B at reflux temperature, whereas pathway B is favored at room temperature. This conclusion, however, may not be completely justified, since we observed in another experiment that 2-acetamido-3,5-dibromo-*N*-methylbenzamide (**6a**) in ethanol solution made basic with methylamine will undergo cyclodehydration at room temperature over a period of 7 days to give **7a** in 72% yield. Although the rate of this conversion is considerably slower than the rate of cyclodehydration of *N*-(2-carboxyphenyl)-*N'*-methylacetamidine (**4a**) under the same conditions to give **7a**, which was reported to occur in a matter of minutes,[6] it does suggest that some of the **7a** isolated in the above reaction at reflux temperature may have been formed via catalytic interaction of product **6a** with as yet unreacted methylamine, perhaps as suggested in Scheme III.

Experimental Section

All melting points are uncorrected. Elemental anslyses were carried out at the Microanalytical Units, Cairo University and El-Nasr Co. for Pharmaceutical Chemicals. IR spectra in KBr were recorded on a Pye-Unicam SP 1200 spectrophotometer.

The structures of **6** and **8** were inferred from the following: (i) analytical data, (ii) their infrared spectra, which show the characteristic carbonyl and NH stretching frequencies of amides (Table I), (iii) formation of **2** from **6** via thermal cyclohydration above their melting points (i.e., ~200 °C, Table I) for short periods.

The structure of the quinazolinones **7** was inferred from microanalytical and infrared spectral data, which show strong absorptions at 1670–1690 cm^{-1} characteristic of the carbonyl stretching frequencies of quinazolin-4-ones (Table II).

2-(Acetylamino)-3,5-dibromo-*N*-substituted-benzamides (6 and 8). The solution of (0.01 mol) of 6,8-dibromo-2-methyl-3,1-benzoxazin-4-one (**5**) in ethanol (20 mL) was treated with the appropriate primary or secondary amine (0.01 mol), and the reaction mixture was left overnight at room temperature with occasional shaking. The solid that formed was filtered off and crystallized from the suitable solvent to give **6** and **8** (Table I). In the case of the reaction of **5** with *p*-toluidine and *p*-anisidine, the reaction mixture was left at room temperature for several days. In the latter case, a mixture of **6** and **7** was formed with the latter predominating.

3-Substituted-6,8-dibromo-2-methylquinazolin-4-ones (7). Method A. A mixture of **5** (0.01 mol) in ethanol (20 mL) and the appropriate primary amines (0.01 mol) was heated under reflux for 5 h, and then left overnight. The solid that separated, in each case, was filtered off and crystallized from a suitable solvent to give **7a–g** as colorless crystals (Table II).

Method B. A mixture of **5** (0.01 mol) and the appropriate primary amine (0.01 mol) was heated for 1 h at 250 °C and left to cool. Trituration of the fused mixture with ethanol and concentration of the triturant yielded **7**, yield 55–65%.

Method C. 2-(Acetylamino)-3,5-dibromo-*N*-substituted-benzamide **6** was heated for 1 h at 250–260 °C and left to cool. The melt that formed was triturated with cold ethanol and the solid that formed was filtered and crystallized from the appropriate solvent, yield 75–80%.

Alternative Methods for the Synthesis of 6,8-Dibromo-2,3-dimethylquinazolin-4-one (5a). (i) A mixture of **5** (0.01 mol) in ethanol (20 mL) and methylamine (0.01 mol) was left for 7 days at room temperature with occasional shaking. The solid that separated was filtered off and recrystallized from light petroleum (bp 100–120 °C) to give **7a**, yield 71%.

(ii) 2-(Acetylamino)-3,5-dibromo-*N*-methylbenzamide (**6a**; 0.01 mol) in methanol (20 mL) was treated with few drops of methylamine and left for 7 days at room temperature. The solid that separated was identified as **7a**, yield 72%.

Cyclization of 6c to 7c in the Presence of Benzylamine. A mixture of **6c** (0.01 mol) and benzylamine (0.01 mol) was heated at 150 °C for 1 h, cooled, and triturated with ethanol. The solid that formed was identified as **7c**, yield 70%.

Reaction of Aniline with 5 in Benzene. To the clear solution of **5** (0.01 mol) in benzene (20 mL) was added aniline (0.01 mol), and the reaction mixture was left overnight at room temperature. The solid that separated was filtered off and recrystallized from benzene to give **6h** as colorless crystals, mp 231–232 °C, yield 80%. The product showed no depression when admixed with authentic sample prepared according to Ismail et al.[7]

Registry No. **5**, 40889-42-7; **6a**, 86993-54-6; **6b**, 86993-55-7; **6c**, 86993-56-8; **6d**, 86993-57-9; **6f**, 86993-58-0; **7a**, 86993-61-5; **7b**, 86993-62-6; **7c**, 86993-63-7; **7d**, 86993-64-8; **7e**, 86993-65-9; **7f**, 31385-80-5; **7g**, 86993-66-0; **8i**, 86993-59-1; **8j**, 86993-60-4; RNH_2 (R = CH_3), 74-89-5; RNH_2 (R = *n*-C_4H_9), 109-73-9; RNH_2 (R = $C_6H_5CH_2$), 100-46-9; RNH_2 (R = C_6H_4-*p*-CH_3, 106-49-0; RNH_2 (R = C_6H_4-*m*-CH_3), 108-44-1; RNH_2 (R = C_6H_4-*p*-OCH_3), 104-94-9; RNH_2 (R = C_6H_4-*o*-OCH_3), 90-04-0; RNH_2 (R = C_6H_5), 62-53-3; piperidine, 110-89-4; morpholine, 110-91-8.

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