Cyclization of the Substituted *N*-(*Ortho*-Cyclopropylphenyl)-*N*′-Aryl Ureas and Thioureas in the Gas Phase and Solution

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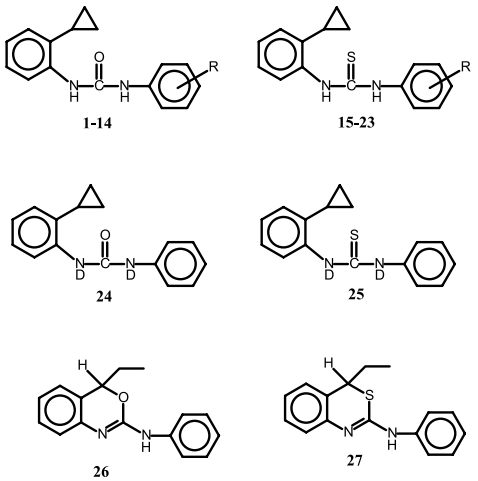
Electron ionization (EI), chemical ionization (CI), tandem mass spectrometry, high-resolution measurements, and labeling studies as well as quantum chemical calculations were used to understand the behavior of the molecular radical cations (EI) and protonated molecules (CI) of substituted *N*-(*ortho*-cyclopropylphenyl)-*N*′-aryl ureas and *N*-(*ortho*-cyclopropylphenyl)-*N*′-aryl thioureas in a mass spectrometer. Fragmentation schemes and possible mechanisms of primary isomerization were proposed. According to the fragmentation pattern, formation of the corresponding benzoxazines and benzothiazines was considered as the major process of isomerization of the original $M^{+\cdot}$ and MH^+, although some portions of these ions definitely transformed into other structures. The treatment of *N*-(*ortho*-cyclopropylphenyl)-*N*′-phenyl urea and *N*-(ortho-cyclopropylphenyl)-*N*′-phenylthiourea in solution with strong acids formed predicted 4-ethyl-*N*-phenyl-4*H*-3,1-benzoxazin-2-amin and 4-ethyl-*N*-phenyl-4*H*-3,1-benzothiazin-2-amine as principal products. (J Am Soc Mass Spectrom 2005, 16, 1739–1749)

Mass spectrometry has been proven to be a powerful, rapid method for the prediction of the direction and yields of monomolecular reactions of organic compounds in solution [1]. Previously, we successfully used mass spectrometry to study cyclization of various diazo compounds [2] and *ortho*-substituted phenylcyclopropanes [3]. The spectral conclusions for a representative series of *N*-(*ortho*-cyclopropylphenyl)benzamides were used to confirm the presence of the predicted heterocycles in solution. The cyclization products of the molecular ions for these benzamides were identical to those synthesized in the condensed phase [4, 5]. In the present study, we continue research in this area, investigating the possibility of rearrangements of substituted *N*-(*ortho*-cyclopropylphenyl)-*N*′-aryl ureas (**1**–**14**).) and *N*-(*ortho*-cyclopropylphenyl)-*N*′-aryl thioureas (**15**–**23**), structurally related to the earlier studied acetamides [6] and benzamides [4, 5]. These compounds were expected to undergo EI induced and acid catalyzed cyclization in a similar manner.



Substituted *N*-(*ortho*-cyclopropylphenyl)-*N*′-aryl ureas (**1**–**14**) and *N*-(*ortho*-cyclopropylphenyl)-*N*′-aryl thioureas (**15**–**23**) possess four nucleophilic sites [*N*, *N*′, O (**1**–**14**) or S (**15**–**23**), and the *ortho*-position of the aromatic ring attached to *N*′], which are able to attack the charged cyclopropyl moiety. Therefore, at least four heterocycles ($\mathbf{P_1}$–$\mathbf{P_4}$) can be formed in the intramolecular cyclization reaction.

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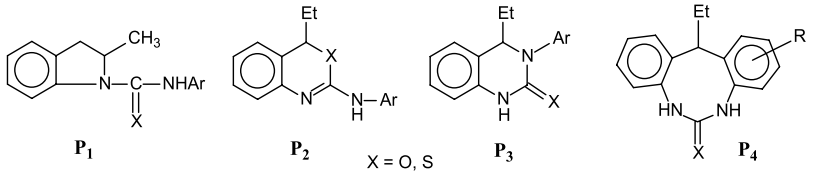


Experimental

The purity of all compounds, **1–23**, obtained by the interaction of the corresponding arylisocyanates or arylisothiocyanates with *ortho*-aminophenylcyclopropane [7, 8], was checked by TLC and NMR. Electron ionization mass spectra of ureas **1–14** and thioureas **15–23** were recorded with Finnigan SSQ 7000 (San Jose, CA) mass spectrometer in direct insertion mode. Source temperature was held at 180 °C, and ionization energy at 70 eV. EI mass spectra of benzoxazine **26** and benzothiazine **27** were recorded with the same instrument in GC-MS mode. An SGE fused silica capillary column (30 m, 0.25 mm i.d., ID-BPX5 0.25 μm) with helium as a carrier gas was used for chromatographic separation. The oven temperature was increased from 70 to 290 °C (10 °C/min). Source temperature was held at 180 °C, and ionization energy at 70 eV.

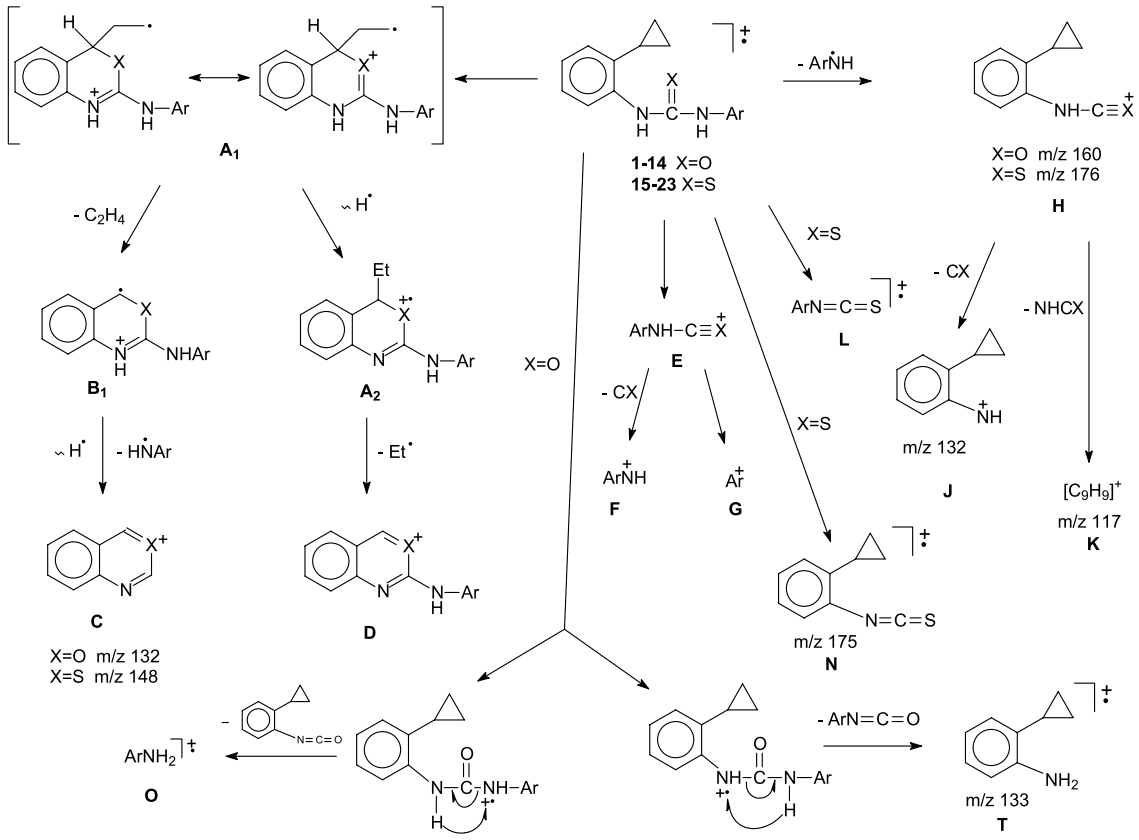
High-resolution measurements, chemical ionization spectra (gas-reagent–isobutane) and MS/MS experiments were performed with a ZABSpec-oaTOF instrument (Micromass, Manchester, UK). Source temperature was held at 160 °C, the ionization energy at 70 eV, and the accelerating voltage at 8 kV. Samples were introduced by direct probe.

Accurate masses were measured for all significant peaks formed under EI (70 eV) using peak matching technique. The resolving power was 10,000 (10% valley definition) while perfluorokerosene was used as a reference.

CID spectra were obtained using helium as a collision gas. The pressure in the first collision cell (1 FFR) was set to decrease the abundance of the precursor ion by 50%.

Calculations

All calculation were performed with the Gaussian 98 program package [9] using the B3LYP hybrid functional, which is a combination of Becke's three-parameter hybrid functional [10] and the correlation functional of Lee et al. [11]. The frequencies and zero-point energies (ZPE) were calculated at the B3LYP/6-



Scheme 1. Fragmentation pathways of Compounds **1–23** in EI conditions.

Table 1. Relative intensities (% in the total ion current) of the key ions formed at EI of Compounds **1–23**

No	A	B	C	D	E	F	G	H	J	K	L	N	O	R	T
1	3.2	11.4	7.8	1.0	0.4	1.4	4.2	2.3	J=C	3.8	0.5	0.7	24.4	3.1	4.0
2	4.2	9.0	6.6	1.2	—	6.7	3.0	1.1	J=C	3.2	4.5	0.5	14.1	2.5	T=L
3	6.0	6.6	5.8	0.6	—	4.6	—	0.5	J=C	2.7	1.1	0.2	14.6	1.1	1.8
4	4.7	8.9	8.4	1.1	—	2.0	1.0	4.3	J=C	3.7	0.5	1.0	26.3	1.7	3.2
5	10.7	12.7	6.1	1.4	0.3	3.0	1.0	4.6	J=C	3.7	0.4	1.2	2.9	2.9	3.7
6	3.9	6.8	9.3	1.0	—	6.6	1.8	6.8	J=C	K=F	1.7	3.2	13.6	1.9	3.6
7	2.4	6.3	7.6	0.7	—	0.6	—	2.8	J=C	3.7	0.4	1.2	9.0	1.7	4.4
8	5.1	9.5	6.4	1.0	—	1.1	1.6	1.1	J=C	2.7	0.1	0.4	8.0	1.4	3.5
9	1.9	4.4	9.4	0.4	0.2	0.0	0.1	4.8	J=C	5.9	0.6	2.7	5.0	1.3	3.3
10	7.6	5.2	5.3	0.4	—	4.2	—	0.6	J=C	2.4	1.9	—	21.9	0.6	1.4
11	9.0	8.4	5.4	0.8	—	2.2	0.1	0.5	J=C	2.8	1.5	0.2	11.1	1.0	2.3
12	8.1	14.5	7.6	1.4	—	6.5	3.2	1.4	J=C	3.1	L=T	—	16.4	3.0	3.8
13	7.8	14.1	6.8	1.0	—	1.2	—	1.2	J=C	3.0	1.1	0.4	15.5	2.4	4.0
14	2.9	9.8	8.3	0.6	0.5	1.1	2.2	4.0	J=C	4.7	0.3	2.9	18.6	2.3	2.8
15	3.6	18.6	1.2	1.9	1.4	0.5	5.0	0.5	2.3	2.2	1.6	1.6	5.0	—	1.1
16	1.4	3.9	2.8	0.6	0.3	13.2	4.4	0.7	2.9	2.7	3.7	4.8	7.9	—	2.5
17	1.5	4.6	5.6	0.6	—	1.0	1.2	—	2.3	2.5	3.4	4.4	5.7	—	2.0
18	7.4	14.2	0.7	0.5	—	0.5	0.5	—	2.0	1.4	2.3	2.7	4.4	—	1.6
19	2.3	8.2	1.6	1.4	1.5	1.3	4.5	0.7	3.5	2.5	3.5	1.2	9.7	—	2.0
20	2.9	12.4	1.5	0.2	0.9	5.0	4.2	0.5	3.1	2.5	1.2	1.3	5.5	—	1.2
21	5.1	11.3	1.1	0.5	0.4	3.3	—	H=E	J=F	2.5	2.6	N=L	1.5	—	T=O
22	3.7	18.7	1.6	1.1	0.3	0.9	0.4	0.3	3.0	2.0	1.6	0.9	1.8	—	1.7
23	5.2	10.5	0.4	0.3	0.1	—	0.4	—	1.9	1.3	1.1	4.3	0.1	—	1.7

31G(d) level. The ZPE were scaled by 0.9806 [12]. B3LYP single point energy calculations were carried out using the 6-311 + G(d,p) basis set.

Results and Discussion

The most important fragmentation pathways of molecular ions of Compounds **1–23** are summarized in Scheme **1**. Table 1 demonstrates the relative abundances of the peaks of the selected ions. According to the data presented and on the basis of our previous observations [3–5], it is possible to assume that the *ortho*-effect plays an important role with heterocycles $\mathbf{A_1}$ and $\mathbf{A_2}$ (represented in Scheme **1**) being the main products of transformation of the original molecular ions. The influence of substituents on the aromatic ring is often unpredictable. Consequently, besides formation of oxazine and thiazine structures ($\mathbf{A_1}$ and $\mathbf{A_2}$), other mechanisms of rearrangement of $M^{+\cdot}$ should be taken into account (see below). As a rule the most abundant peak in EI mass spectra of substituted *N*-(*ortho*-cyclopropylphenyl)-*N*′-arylureas and thioureas corresponds to the $[M - 28]^{+\cdot}$ ion (Table 1, Figure 1b). Formation of $ArNH_2^{+\cdot}$ ions is another important process (Figure 1a) in the case of ureas **1–15** [13].

Loss of a neutral species of 28 Da (C_2H_4 confirmed by high-resolution measurements) occurs directly from $M^{+\cdot}$ of **1–23** and is consistent with an *ortho*-interaction of the substituents accompanied by the preliminary opening of the cyclopropane ring ($\mathbf{A_1}$) (Scheme **1**). The spectra of labeled Compounds **24** and **25** indicated that amido hydrogens were not involved in the loss of this ethylene molecule.

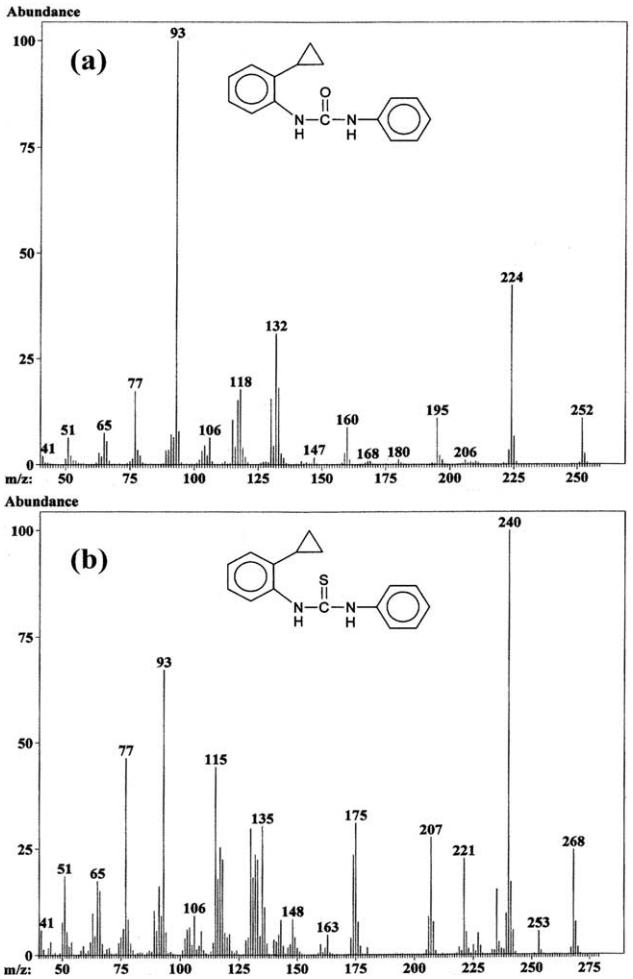


Figure 1. EI mass spectra of Compounds **1** (**a**) and **15** (**b**).

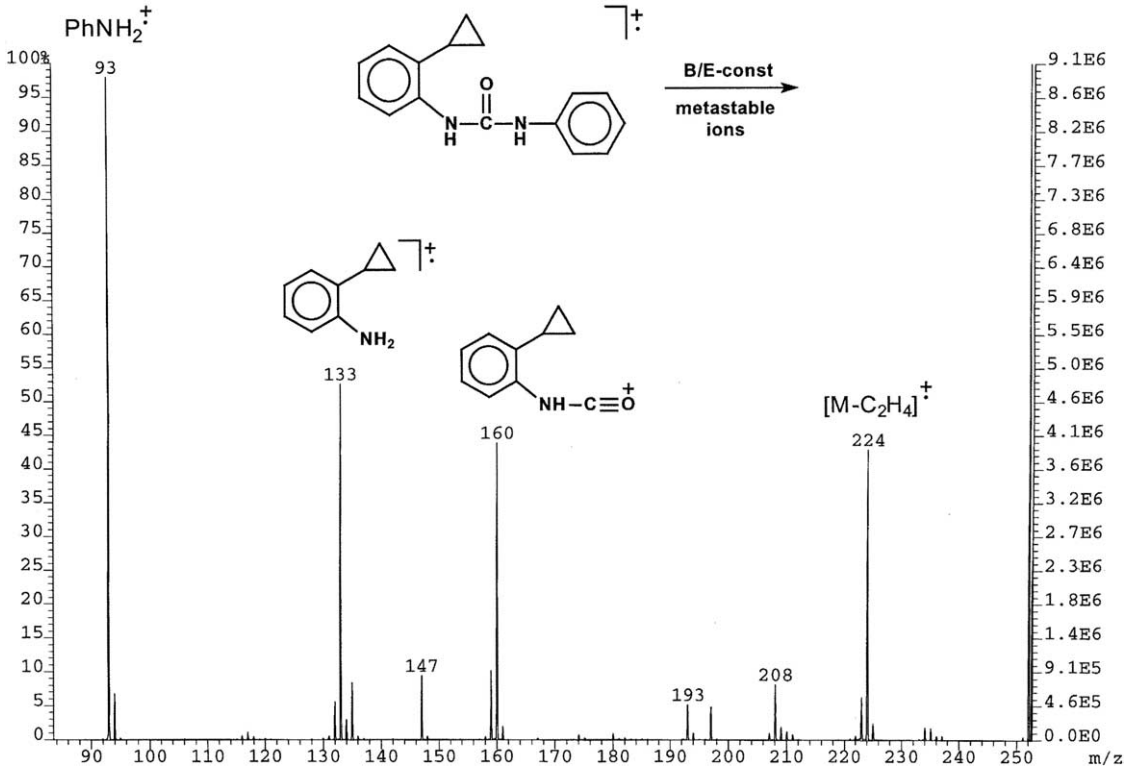


Figure 2. B/E-linked scan spectra of $M^{+\cdot}$ of Compound **1**.

A less abundant peak corresponds to the loss of a neutral species of 29 Da from $M^{+\cdot}$. High-resolution measurements confirmed this loss to be attributable to an ethyl radical. This process can be explained by migration of a hydrogen atom in $\mathbf{A_1}$ to form ion $\mathbf{A_2}$, followed by the loss of an ethyl radical to afford ion **D**.

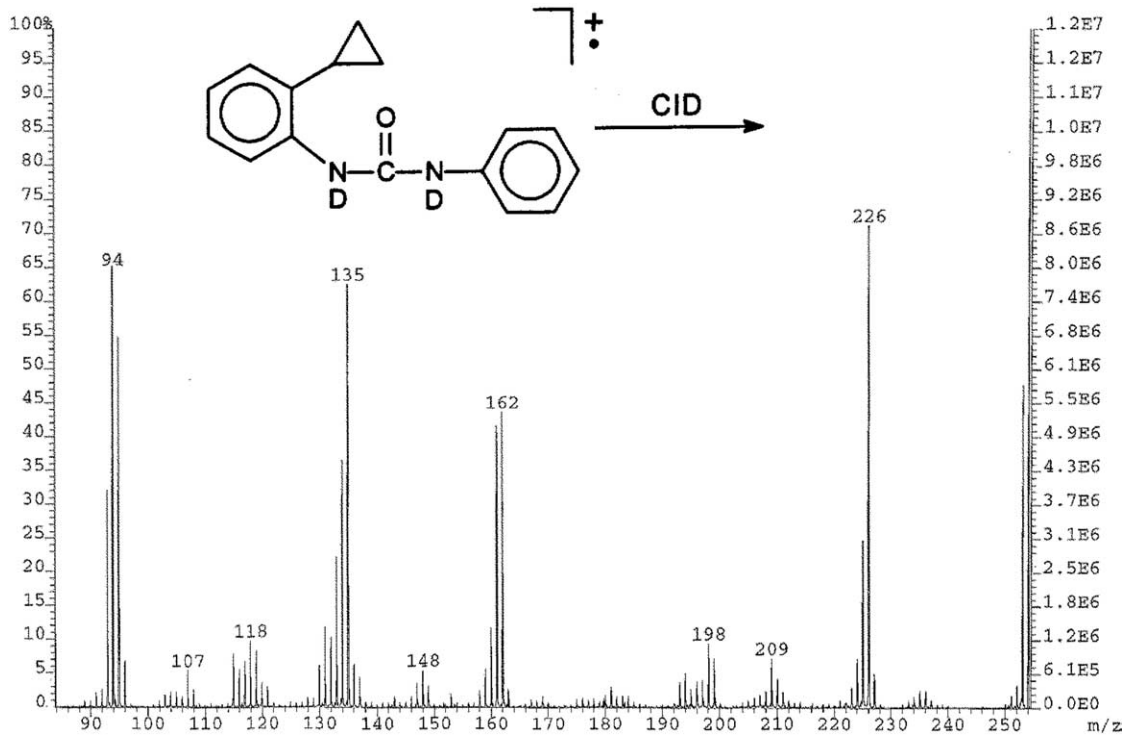
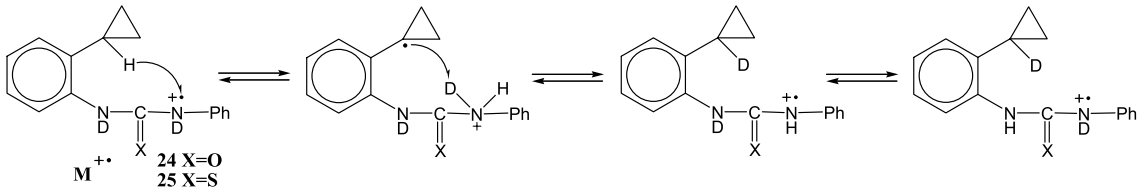
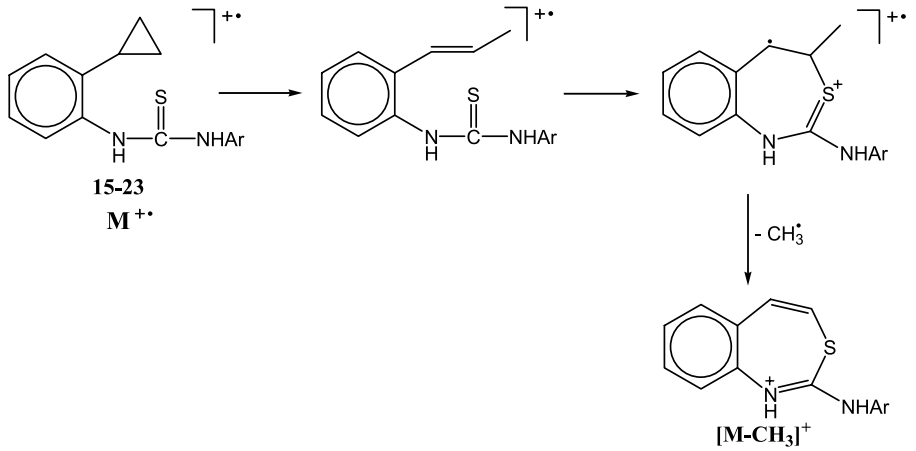


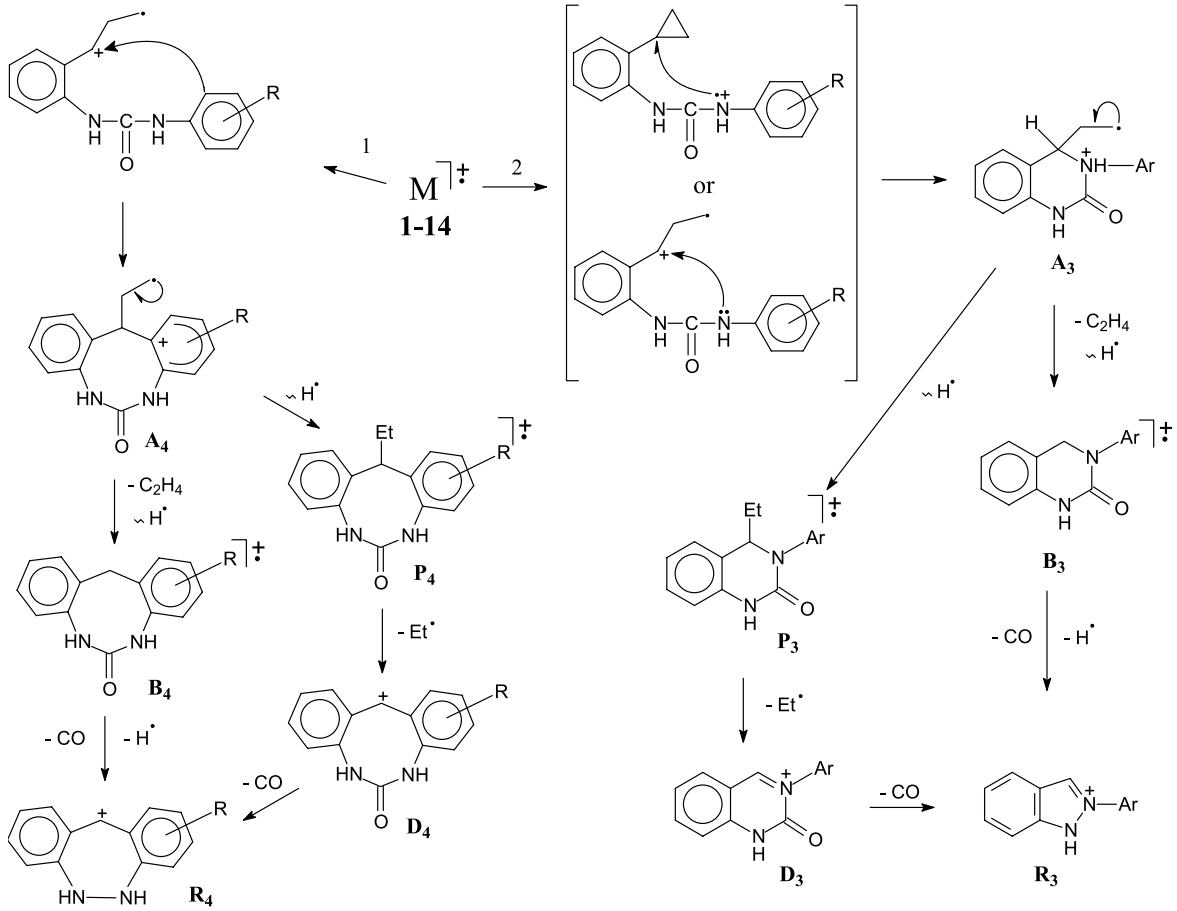
Figure 3. B/E-linked scan spectra of $M^{+\cdot}$ of Compound **24**.



Scheme 2. Intramolecular D/H-exchange in $M^{+\cdot}$ of Compounds **24** and **25**.



Scheme 3. The loss of methyl radical from $M^{+\cdot}$ of Compounds **15–23**.



Scheme 4. Formation of $[M - C_3H_5O]^+$ ions in EI mass spectra of ureas (**1–14**).

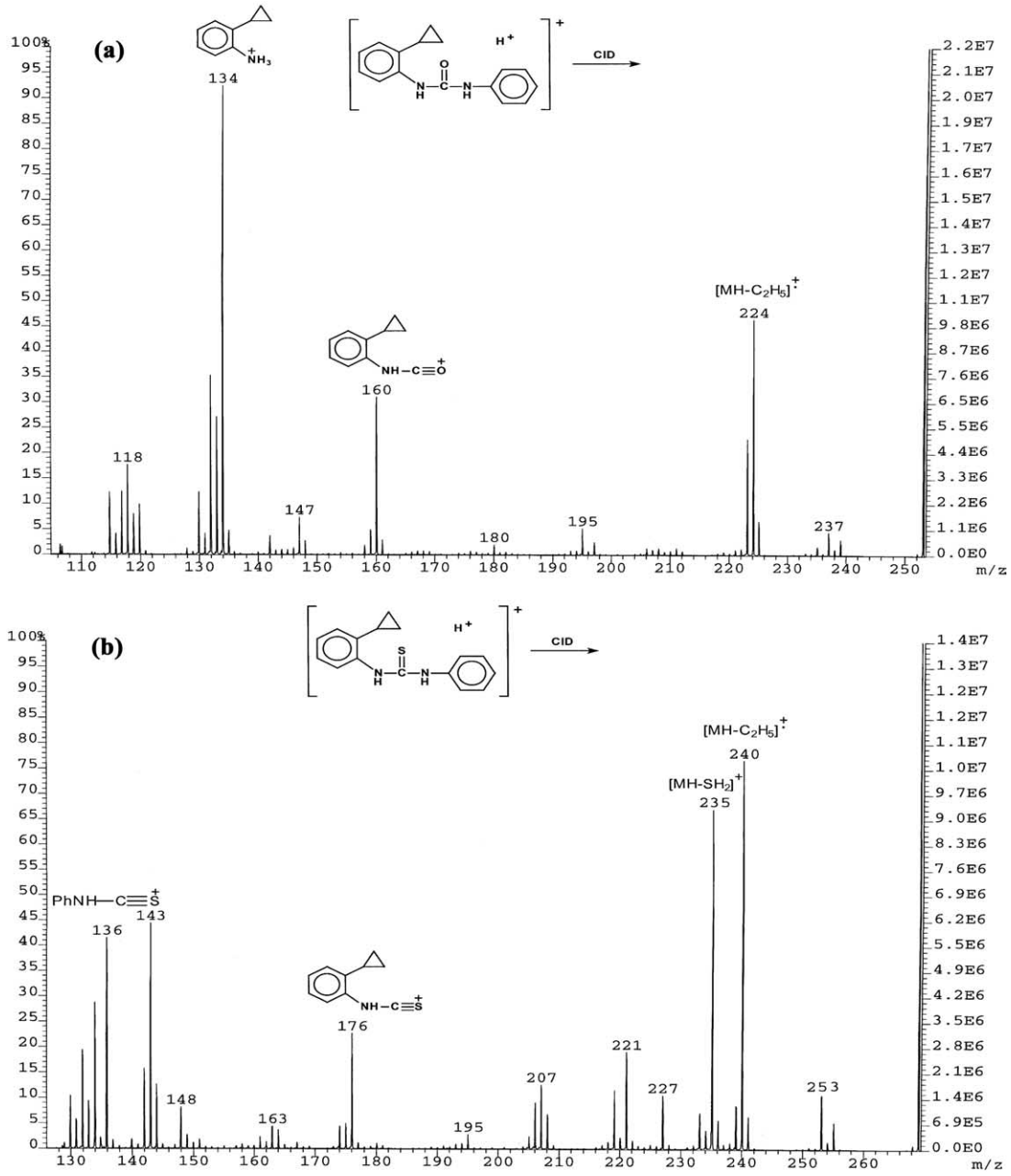


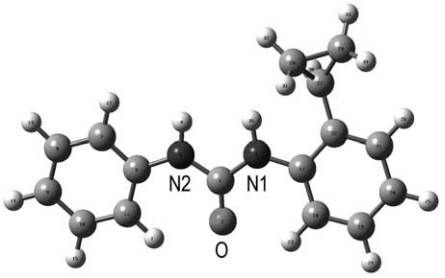
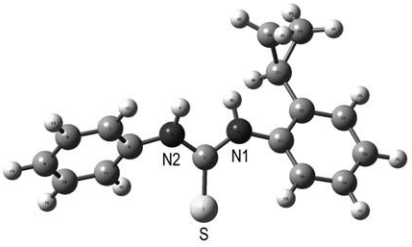
Figure 4. B/E-linked scan spectra of MH^+ ions of Compounds **1** (**a**) and **15** (**b**).

The higher abundance of ions $[M - C_2H_4]^{+\cdot}$ relative to $[M - C_2H_5]^+$ results from the fact that the majority of $M^{+\cdot}$ starts dissociating at the stage of the cyclic intermediate $\mathbf{A_1}$. A similar situation was observed with the analogous cyclopropanes studied earlier [4, 6]. The loss of ethylene from $\mathbf{A_1}$ leads to ion $\mathbf{B_1}$, which in turn fragments to furnish the even-electron ion **C**.

Baldwin et al. [14, 15] demonstrated that $M^{+\cdot}$ of arylureas and arylthioureas readily eliminated the *ortho*-substituent of a benzene ring during a cyclization process. Thus, we would expect elimination of the cyclopropyl radical, since it is an *ortho*-substituent in Compounds **1**–**23**. However the corresponding $[M - 41]^+$ ion was observed only in the spectra of thioureas **15**–**23** with an abundance of about 0.5% of the TIC. This fact indicates that other fragmentation processes (e.g., heterocyclization with the cleavage of the small ring) appear to be more favorable.

Formation of odd-electron ions **O** and **T** corresponding to the molecular ions of substituted anilines occurs directly from $M^{+\cdot}$ through a four member transition-state [15, 16]. The corresponding peaks are very abundant in the EI spectra of ureas (Figure 1a), however, they are rather low in the case of thioureas (Figure 1b). Comparison of CID spectra of unlabeled (**1**, **15**) and d2-labeled analogues (**24**, **25**) shows that 0-2 deuterium atoms remain in ions **O** and **T** (Figures 2 and 3). This fact suggests that, besides the 4-membered intermediate

Table 2. Calculated gas phase proton affinities (PA) in kcal/mol [B3LYP/6–311 + G(d,p)//B3LYP/6–31G(d,p)]

N-(ortho-cyclopropylphenyl)-N′-phenylurea **1**	N-(ortho-cyclopropylphenyl)-N′-phenylthiourea **15**
	
PA(Cp) 223.1 kcal/mol PA(O) 222.2 kcal/mol PA(N1) 210.5 kcal/mol PA(N2) 207.5 kcal/mol	PA(S) 231.4 kcal/mol PA(Cp) 223.5 kcal/mol PA(N1) 213.5 kcal/mol PA(N2) 210.1 kcal/mol

state (forming $ArND_2$ ions in the case of labeled compounds), other mechanisms of formation of these ions are possible. Protium atoms may come from the cyclopropyl moiety or from the *ortho*-positions of the aromatic rings. The most probable process can be rationalized by Scheme 2. In this case, migrations involve both amide hydrogens and hydrogens from the small ring. Ortho positions of the aromatic rings should also be considered as possible sites of hydrogen migration.

Ions **E** and **H** are formed by α-cleavage, induced by a radical center located at the heteroatom (O or S). The loss of CX and NHCX (X = O, S) from these ions leads to the formation of **F**, **G**, **J**, and **K** ions. For each pair of these ions, the abundance of the fragment containing a cyclopropane ring is considerably higher than that of the alternative. This results from a decrease in ionization energy due to introduction of the cyclopropyl moiety (IE = 8.0 eV [17]. The shift of this ion of 1 or 2 units along the mass scale in the spectra of d2-labeled compounds suggests some sort of hydrogen exchange and supports the equilibrium in Scheme 2.

Other principal processes for Compounds **15–23** are the loss of a methyl radical and SH· from $M^{+\cdot}$ (Figure 1b) as well as expulsion of SH· from the $[M - C_2H_4]^{+\cdot}$

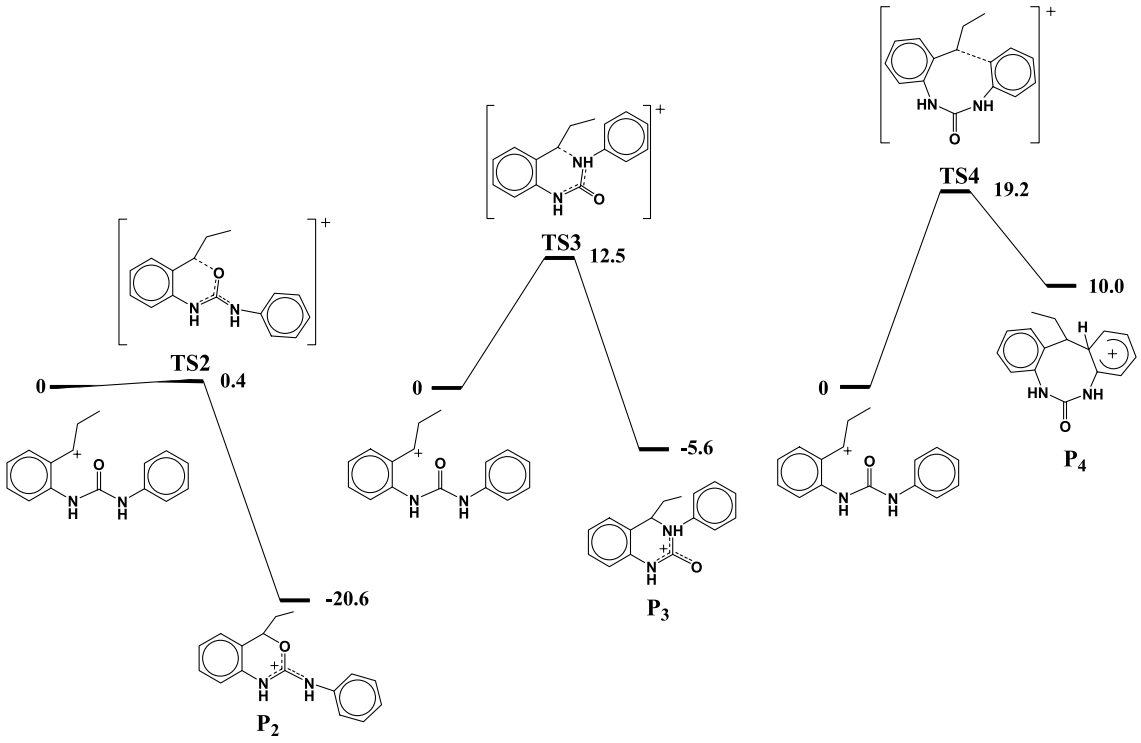


Figure 5. Transformation of the MH^+ ion of **1** protonated at the cyclopropyl group into protonated P_2-P_4. Relative energies (in kcal mol^{-1}) at B3LYP/6-311 + G(d,p)//B3LYP/6-31G(d,p) level of theory.

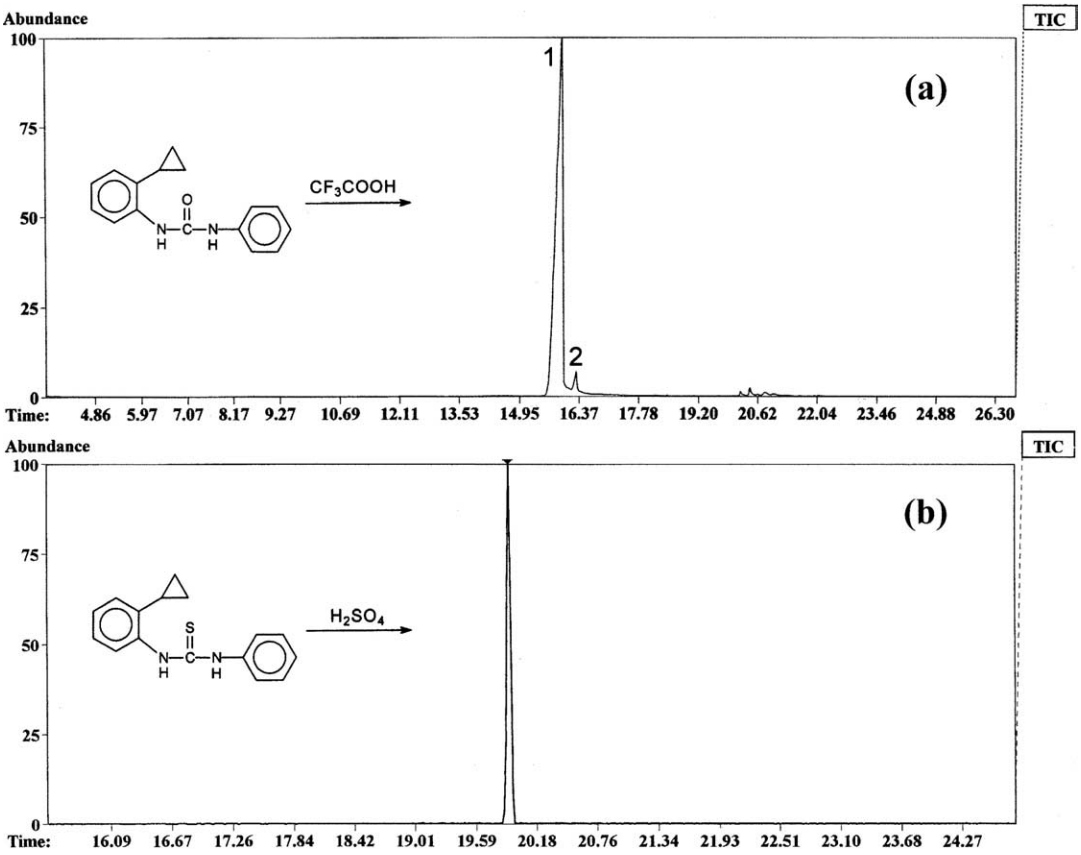


Figure 6. GC/MS analysis of reaction mixtures of Compounds **1** (**a**) and **15** (**b**).

ion. Earlier it was shown that $M^{+\cdot}$ of arylthioureas eliminate an $SH^{\cdot}$ radical. Hydrogen atoms in this process come from the *ortho*-position of the aromatic ring, or from the α-position of an *ortho*-substituent [16, 18]. Since, in the case of d2-labeled Compound **25**, $SD^{\cdot}$ is lost in addition to $SH^{\cdot}$, either the amine hydrogen participates in this process to some extent, or the α-hydrogen of the small ring is involved (Scheme 2).

The loss of the methyl radical may be rationalized by a rearrangement process presented in Scheme 3. If the phenylcyclopropane moiety initially rearranges to β-methylstyrene [19] or allylbenzene [20], the sulphur atom can attack the β-carbon atom. In our earlier publications this process was discussed and used to predict the ratio of heterocycles forming in solution in the case of *ortho*-carboxy and *ortho*-carboxamidocyclopropylbenzenes [21]. However, considering that in the spectra of d2-labeled thiourea **25** the abundance of the $[M - CH_2D]^+$ peak (*m/z* 254) constitutes 60% of the abundance of the $[M - CH_3]^+$ peak (*m/z* 255), this process may involve other mechanisms.

A feature characteristic only for ureas **1**–**14** involves formation of a $[M - C_3H_5O]^+$ ion (confirmed by high-resolution measurements). This is a sequential process occurring in two different ways. The first involves both successive and simultaneous losses of CO and H· from the $[M - C_2H_4]^{+\cdot}$ ion, the other, the loss of CO from the $[M - C_2H_5]^+$ ion (confirmed by B^2/E-linked scan spectra of the $[M - C_3H_5O]^{+\cdot}$ ion of *m/z* 195 and B/E-linked scan spectra of the $[M - C_2H_5]^+$ ion of *m/z* 223 of Compound **1**). These processes cannot be explained by expulsion of neutral particles from ions with structures $\mathbf{A_2}$ and $\mathbf{B_1}$. Therefore, some other structures of these precursors should be taken into account.

Since *N*-(*ortho*-cyclopropylphenyl)-*N*′-arylureas (**1**–**14**) possess four nucleophilic sites, cyclization with participation of multiple sites might be involved. A nucleophilic attack of the *N*′-attached aromatic ring on the site of the positive charge in the distonic ion to form ion $\mathbf{A_4}$ is quite possible (Direction 1, Scheme 4). An alternative process involves attack of the second nitrogen atom on the same distonic ion, or attack of the cyclopropyl ring by the charged nitrogen atom (Direction 2, $\mathbf{A_3}$, Scheme 4).

The spectrum of labeled Compound **24** demonstrates that ion $[M - C_2H_4]^{+\cdot}$ of *m/z* 226 loses a hydrogen atom and CO molecule to form ion **R**. The B/E linked scan spectrum of the $[M - C_2H_4]^{+\cdot}$ ion shows that 70% of the deuterium label remains in the charged fragments. Therefore, the $\mathbf{R_4}$ structure is more favored, as in this case the *ortho*-hydrogen atom from the aryl moiety is eliminated. To form the $\mathbf{R_3}$ ion D· should be lost.

It is most likely that the loss of CO proceeds from cyclic structures $\mathbf{B_3}$ and $\mathbf{B_4}$, formed by elimination of ethylene from cyclic structures $\mathbf{A_3}$ and $\mathbf{A_4}$ respectively (Scheme 4). Both $\mathbf{B_3}$ and $\mathbf{B_4}$ structures also allow the loss

of a hydroxyl radical from their enol tautomers to give an ion of *m/z* 206. In the case of thioureas **15–23** the $[M - C_2H_4]^+$ ion does not eliminate CS, HCS, or NHCS moieties. This fact may support the hypothesis that only 1,3-thiasines ($\mathbf{P_2}$ structures) and, perhaps, benzothiazepines (Scheme 3) are formed after ionization.

Similar transformation processes take place during chemical ionization (isobutane) of cyclopropanes **1** and **15** (Figure 4). Fragmentation pathways in CI mass spectra may be accounted for by formation of various MH^+ ions protonated at different sites. For example, the presence of a $[MH - C_2H_5]^{+\cdot}$ ion is caused by protonation of the cyclopropyl group, followed by *ortho*-interaction of the substituents. Fragmentation of MH^+ ions protonated at nitrogen atoms afford the charged fragments of *m/z* 132, 134, and 160 for urea **1** and *m/z* 134, 136, and 176 for urea **15**.

Calculated gas-phase proton affinities showed that in the case of *N*-(ortho-cyclopropylphenyl)-*N*′-phenylthiourea **15** the sulfur atom is the most probable site of protonation, while cyclopropyl group protonation is the most favorable process for *N*-(ortho-cyclopropylphenyl)-*N*′-phenylurea **1** (Table 2). It is worth mentioning that if protonation of N, S, or O is a reversible process, protonation of the cyclopropane ring leads to cleavage with formation of a corresponding benzylic cation,

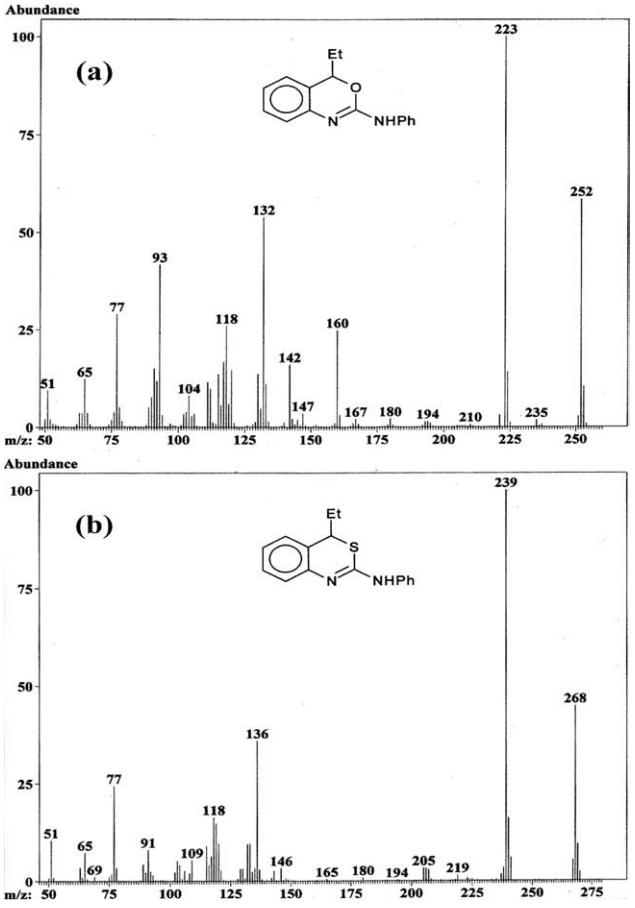
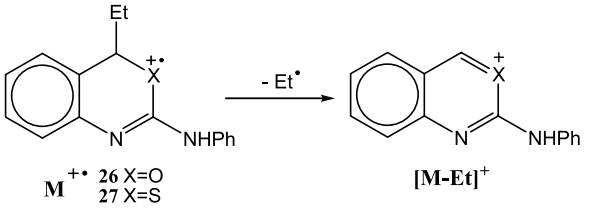


Figure 7. EI mass spectra of Compounds **26** (**a**) and **27** (**b**).



Scheme 5

followed by nucleophilic attack of an *ortho*-substituent and subsequent cyclization.

One should note that the difference in nucleophilicity between the sulfur atom and other sites in thiourea **15** is bigger than that between the oxygen atom and other sites in urea **1**. Therefore thiazine should be a major product of thioureas **15–23** upon interaction with acids$_2$ (the 7-membered heterocycle in Scheme **3** must also be taken into account), while ureas **1–14** should react with possible formation of other heterocycles ($\mathbf{P_2}$ and $\mathbf{P_4}$) besides the oxazines $\mathbf{P_2}$.

Quantum chemical calculations performed for urea **1** protonated at the cyclopropyl group demonstrate that formation of benzoxazine $\mathbf{P_2}$ is the most preferable process of the three possibilities (Figure 5). The formation of benzoxazine $\mathbf{P_2}$ and benzodiazinone $\mathbf{P_3}$ are exothermic processes (−20.6 and −5.6 kcal·mol^{-1}, respectively) while the formation of $\mathbf{P_4}$ is endothermic (10 kcal·mol^{-1}). As the activation barrier is very low in the case of $\mathbf{P_2}$ (0.4 kcal mol^{-1}, **TS2**), its formation is preferable both thermodynamically and kinetically.

In the conditions of the gas-phase experiment (CI, isobutane, PA = 193.6 kcal mol^{-1} [22], the internal energy of the MH^+ ion of **1** protonated at the cyclopropyl group calculated by the formula: E_{in} = PA[urea **1** (Cp)] − PA(gas reagent) is 29.5 kcal·mol^{-1}. This is sufficient to surmount the activation barrier of any of the three reaction pathways. However, taking into account the stability of the cyclic species as well as the entropy factor, formation of benzoxazine $\mathbf{P_2}$ and benzodiazine $\mathbf{P_3}$ are the preferable processes.

To confirm the mass spectral conclusions, two model compounds, [*N*-(ortho-cyclopropylphenyl)-*N*′-phenylurea **1** and *N*-(ortho-cyclopropylphenyl)-*N*′-phenylthiourea **15**], were subjected to interaction with sulphuric and trifluoroacetic acids. In each case, the reaction mixtures were poured into water, neutralized, and the organic matter was extracted with dichloromethane. The extracts were then injected into the GC-MS instrument (Figure 6).

In the case of thiourea **15** (Figure 6b) the resulting chromatogram contains only one peak corresponding to 4-ethyl-*N*-phenyl-4*H*-3,1-benzothiazin-2-amine **27** (proved by ^{1}H and ^{13}C NMR), whereas in the case of urea **1** there are two peaks which correspond to isomers with *m/z* 252 (Figure 6a). The most abundant peak (Peak 1, Figure 6a) is 4-ethyl-*N*-phenyl-4*H*-3,1-benzoxazin-2-amine **26**. Unfortunately, the quantity of the second isomer (Peak 2; Figure 6a) was insufficient for isolation

and proof of its structure. Our attempts to vary the acidic nature or temperature of the reaction did not increase the yield of this compound. It is worth mentioning that the loss of 29 Da (most likely an ethyl radical) is a dominant process in the mass spectral fragmentation of this compound. Presumably, it should represent an alternative isomeric heterocyclic structure of 4-ethyl-3-phenyl-3,4-dihydroquinazolin-2(1*H*)-one (**P_3**), since the two other possible isomeric structures [linear (**1**) and cyclic (**P_4**) ureas] do not pass through a chromatographic column.

Finally, 4-ethyl-*N*-phenyl-4*H*-3,1-benzoxazine-2-amine (**26**) and 4-ethyl-*N*-phenyl-4*H*-3,1-benzothiazin-2-amine (**27**) were isolated from the extracts and characterized by mass spectrometry, NMR, IR, and X-ray analysis, while their spectral data were compared with those of similar 4*H*-3,1-benzoxazin-2-amines [23] and 4*H*-3,1-benzothiazin-2-amines [24]. EI mass spectra of these compounds are characterized by the loss of a neutral species of 29 Da from $M^{+\cdot}$ (Figure 7).

This process is dominant and corresponds to the elimination of an ethyl radical (confirmed by high resolution measurements) with formation of stable aromatic ions (Scheme **5**).

Conclusions

1. Mass spectrometry allows for the prediction of monomolecular reactions of the substituted *N*-(*ortho*-cyclopropylphenyl)-*N*′-aryl ureas (**1–14**) and *N*-(*ortho*-cyclopropylphenyl)-*N*′-arylthioureas (**15–23**) catalyzed by acids in solution. Two model compounds, (**1** and **15**), were subjected to the acid catalyzed cyclization. In solution, the observed 4-ethyl-*N*-phenyl-4*H*-3,1-benzoxazine-2-amine (**26**) and 4-ethyl-*N*-phenyl-4*H*-3,1-benzothiazin-2-amine (**27**) were identical to that predicted on the basis of mass spectral experiments.
2. Interaction of the substituted *N*-(*ortho*-cyclopropylphenyl)-*N*′-aryl ureas (**1–14**)) and *N*-(*ortho*-cyclopropylphenyl)-*N*′-aryl thioureas (**15–23**)) with strong acids is a convenient method for synthesis of substituted benzoxazines and benzothiazines.

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