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SYNTHESIS OF 2-AMINO-4H-3,1-BENZOXAZINES AND 2-AMINO-4H-3,1-BENZOTHIAZINES BY THE REARRANGEMENT OF *o*-CYCLOPROPYLPHENYL-UREAS AND *o*-CYCLOPROPYLPHENYLTHIOUREAS

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Syntheses are reported for 2-cyclopropylphenylureas and 2-cyclopropylphenylthioureas and the behavior of these compounds was studied under conditions for the acid-catalyzed opening of the cyclopropyl ring. Upon the action of concentrated sulfuric acid or trifluoroacetic acid, these ureas and thioureas can undergo rearrangement to the corresponding 3,1-benzoxazines and 3,1-benzothiazines.

Keywords: 2-arylamino-3,1-benzoxazines, 2-arylamino-3,1-benzothiazines, tautomers, N-(2-cyclopropyl)phenylureas, N-(2-cyclopropyl)phenylthioureas, intramolecular rearrangements.

Functionally-substituted cyclopropanes, which have now become readily available, are finding increasing use as starting compounds in the synthesis of various organic compounds produced by the transformation of the three-membered ring upon the action of specific reagents. These transformations may yield either saturated or unsaturated acyclic products of opening of the cyclopropyl ring [1-4] or carbo- and heterocycles [5-11]. An especially large number of studies have been devoted to donor-acceptor functionally-substituted cyclopropanes [11]. The reactions in this case proceed predominantly with the participation or effect of the substituents directly bound to the three-carbon ring. There has been considerably less work on the transformations of cyclopropane compounds, in which the substituents, not directly bound to the cyclopropane ring, participate in the reaction. Nevertheless, examples of such transformations [9, 12-14] show that the synthetic scope of functionally-substituted cyclopropanes may be considerably expanded. Here, definite promise is found in intramolecular acid-catalyzed *ortho*-substituted arylcyclopropanes due to the unique *ortho*-orienting effect of the cyclopropane substituent in electrophilic nitration reactions [15-17]. These reagents are now readily available.

In a search for new examples of the intramolecular rearrangement of *ortho*-functionally-substituted arylcyclopropanes, we synthesized 2-cyclopropylphenylureas and 2-cyclopropylphenylthioureas and studied their transformations in trifluoroacetic and concentrated sulfuric acids. We assumed that the acid-catalyzed opening of the cyclopropane ring in suitable cyclopropylureas and cyclopropylthioureas would initiate reaction of the resultant benzylic carbenium ion with the internal nucleophile (urea or thiourea fragment) to form 2-amino-3,1-benzoxazines and 3,1-benzothiazines or isomeric compounds.

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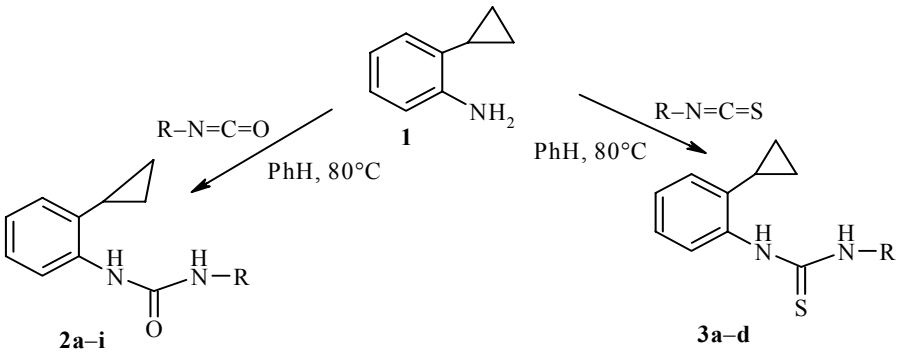
The required cyclopropylureas **2a-i** and cyclopropylthioureas **3a-d** (Table 1) were synthesized by the reaction of 2-cyclopropylaniline (**1**) with aryl isocyanates* and with aryl isothiocyanates.



2 a R = H, **b** R = Ph, **c** R = *p*-$Me_2CHC_6H_4$, **d** R = *p*-MeC_6H_4, **e** R = *p*-$MeOC_6H_4$, **f** R = *p*-ClC_6H_4, **g** R = $C_6H_4CO_2Et$-*p*, **h** R = *p*-$O_2NC_6H_4$, **i** R = *p*-$MeC_6H_4SO_2$; **3 a** R = Ph, **b** R = *o*-EtC_6H_4, **c** R = *o*-$MeOC_6H_4$, **d** R = *p*-$EtOC_6H_4$

We should note that in interpreting the mass spectra of cyclopropylureas **2a-i** and cyclopropylthioureas **3a-d**, we not only confirmed the structures of these compounds but also obtained results supporting the high probability of the conversion of cyclopropanes **2a-i** and **3a-d** into the corresponding heterocycles by the action of acid. This conclusion was indicated by the finding that the formation of heterocyclic ions such as $\mathbf{A_1}$ occurs immediately upon electron impact in the dissociative ionization of these 2-cyclopropylureas and 2-cyclopropylthioureas (see Scheme). The formation of such ions is necessary under conditions for the acidic rearrangement to the corresponding heterocyclic compounds.

Indeed, as we subsequently learned, *o*-cyclopropylureas **2a-i** and *o*-cyclopropylthioureas **3a-d** are converted by the action of acids into 2-amino-3,1-benzoxazines **4a-i***[2] and 2-amino-3,1-benzothiazines **5a-d***[3] in high yield. While cyclopropylureas **2a-i** are capable of conversion to 2-amino-4H-3,1-benzoxazines **4a-i** both in trifluoroacetic and concentrated sulfuric acids, cyclopropylthioureas **3a-d** form the corresponding 2-amino-4H-3,1-benzothiazines **5a-d** only by the action of sulfuric acid; these thioureas remain virtually unchanged in trifluoroacetic acid.

The observed difference in the behavior of *o*-cyclopropylureas **2a-i** and *o*-cyclopropylthioureas **3a-d** in the reaction with trifluoroacetic acid is probably a consequence of the greater capacity of the thiourea fragment to undergo protonation under the conditions employed relative to the urea fragment, which imparts the properties of a strong electron-withdrawing substituent, thereby inhibiting opening of the cyclopropane ring of thioureas **3a-d** by the action of the weaker trifluoroacetic acid. This hypothesis is supported, for example, by the finding that neither *o*-nitrophenylcyclopropanes nor *o*-cyanophenylcyclopropanes rearrange by the action of trifluoroacetic acid, while these compounds are converted quantitatively to the corresponding products of transformation of the three-membered carbocycle by the action of concentrated sulfuric acid [12, 18]. It is interesting that phenylcyclopropane lacking electron-withdrawing substituents or phenylcyclopropanes with weak electron-withdrawing substituents in the *ortho* position [5, 14, 19] are converted by the action of trifluoroacetic acid, similarly to cyclopropylureas **2a-i**, into the corresponding cyclopropane ring transformation products.

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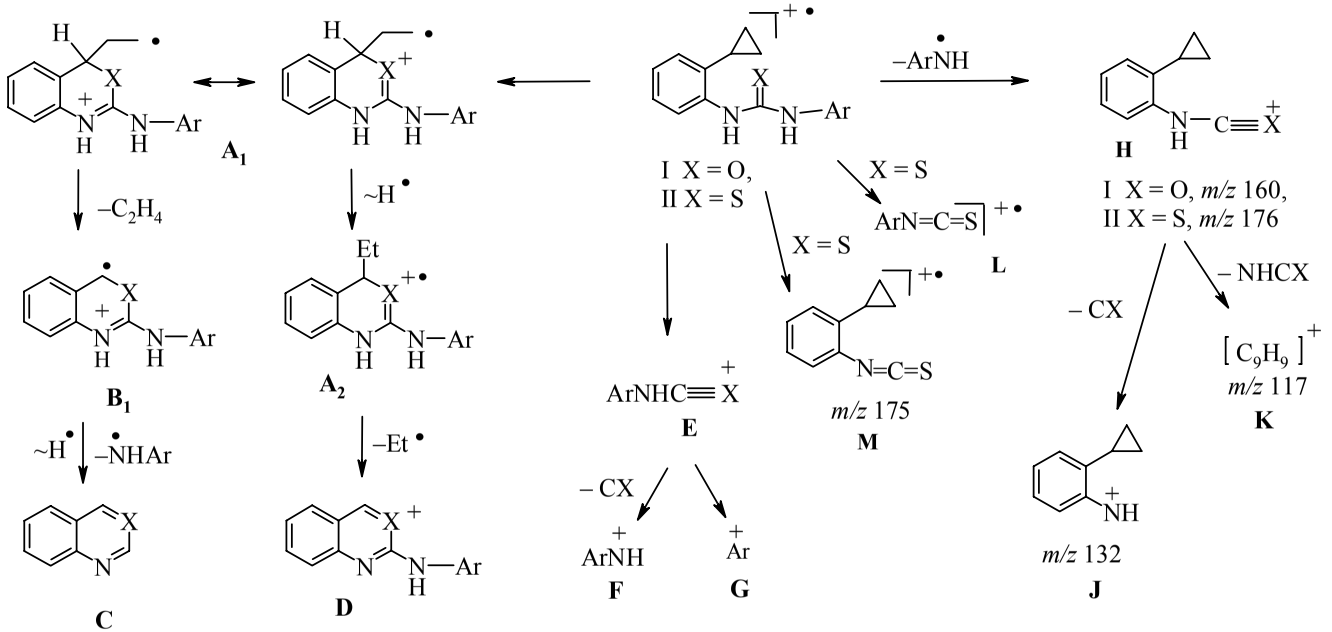
* Cyclopropane **2a** was obtained by the reaction of 2-cyclopropylaniline (**1**) with potassium cyanate (see Experimental).

*[2] The designations R for **4a-i** are the same as for **2a-i**.

*[3] The designations R for **5a-d** are the same as for **3a-d**.


A1
A2
B1
C
I X = O, m/z 132,
II X = S, m/z 148
D
I X = O,
II X = S
E
F
G
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M
m/z 175
L
H
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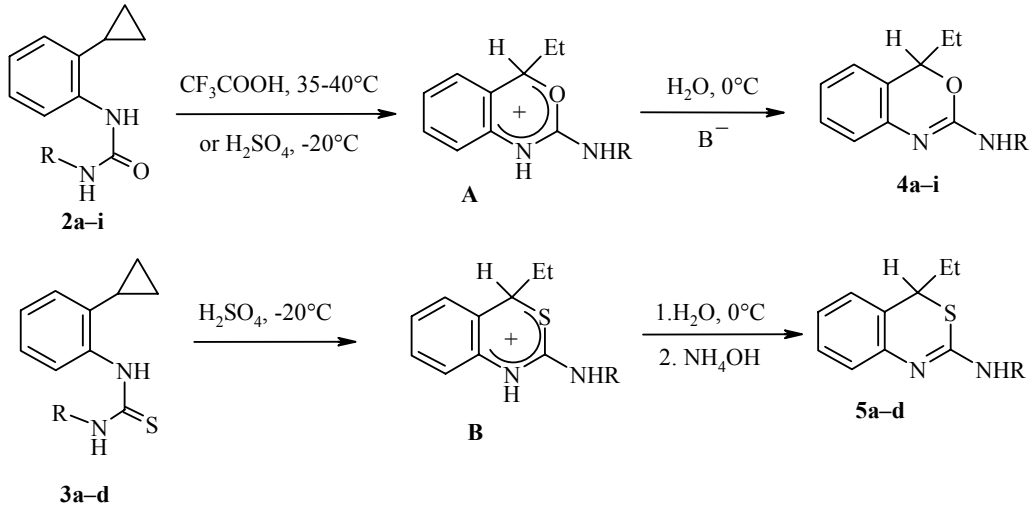
II X = S, m/z 176
J
K
m/z 117



2a–i **A** **4a–i**

3a–d **B** **5a–d**

TABLE 1. Characteristics of Products **2-5**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C (solvent for recristallization)	Yield, %
		C	H	N		
1	2	3	4	5	6	7
2a	$C_{10}H_{12}N_2O$	68.33 / 68.16	7.03 / 6.86	15.62 / 15.89	193-194 (ethanol–water)	91
2b	$C_{16}H_{16}N_2O$	76.36 / 76.16	6.55 / 6.39	10.81 / 11.10	176-177 (ether–petr. ether)	92
2c	$C_{19}H_{22}N_2O$	77.68 / 77.52	7.67 / 7.53	9.70 / 9.52	140-141 (benzene)	81
2d	$C_{17}H_{18}N_2O$	76.26 / 76.66	6.65 / 6.81	10.34 / 10.52	134-135 (benzene)	85
2e	$C_{17}H_{18}N_2O_2$	72.63 / 72.32	6.55 / 6.43	9.82 / 9.92	167-168 (benzene)	75
2f	$C_{16}H_{15}ClN_2O$	67.45 / 67.02	5.38 / 5.27	6.46 / 6.77	185-186 (ethanol)	91
2g	$C_{19}H_{20}N_2O_3$	70.61 / 70.35	6.41 / 6.21	8.45 / 8.63	145-146 (ethanol)	65
2h	$C_{16}H_{15}N_3O_3$	64.93 / 64.64	5.35 / 5.09	13.83 / 14.13	162-163 (ethanol)	92
2i	$C_{17}H_{18}N_2O_3S$	61.97 / 61.80	5.65 / 5.49	8.27 / 8.48	148–149 (ethanol)	95
3a	$C_{16}H_{16}N_2S$	71.85 / 71.61	6.12 / 6.01	10.09 / 10.44	133-134 (ether–petr. ether)	90
3b	$C_{18}H_{20}N_2S$	72.75 / 72.93	6.91 / 6.80	9.12 / 9.45	142-143 (chloroform–petr. ether)	91
3c	$C_{17}H_{18}N_2OS$	68.50 / 68.43	6.12 / 6.08	6.15 / 6.39	127-128 (chloroform–petr. ether)	85
3d	$C_{18}H_{20}N_2OS$	69.45 / 69.20	6.32 / 6.45	8.71 / 8.97	166-167 (chloroform–petr. ether)	75
4a	$C_{10}H_{12}N_2O$	68.45 / 68.16	6.98 / 6.86	15.73 / 15.89	Oil	75
4b	$C_{16}H_{16}N_2O$	76.47 / 76.16	6.45 / 6.39	10.91 / 11.10	89-91 (ether)	67
4c	$C_{19}H_{22}N_2O$	77.66 / 77.52	7.70 / 7.53	9.68 / 9.52	Oil	72
4d	$C_{17}H_{18}N_2O$	76.31 / 76.66	6.55 / 6.81	10.23 / 10.52	86-88 (ethanol)	86
4e	$C_{17}H_{18}N_2O_2$	72.56 / 72.32	6.68 / 6.42	9.75 / 9.92	95-96 (chloroform–hexane)	45
4f	$C_{16}H_{15}ClCN_2O$	67.33 / 67.02	5.44 / 5.27	9.55 / 9.77	120-121 (ether–petr. ether [40-70°C])	86

TABLE 1. (continued)

1	2	3	4	5	6	7
4g	$C_{19}H_{20}N_2O_3$	70.78 / 70.35	6.48 / 6.21	8.32 / 8.63	138-139 (chloroform–petr. ether [40-70°C])	65
4h	$C_{16}H_{15}N_3O_3$	64.81 / 64.64	5.26 / 5.09	13.87 / 14.13	155-156 (ethanol)	90
4i	$C_{17}H_{18}N_2O_3S$	62.22 / 61.80	5.76 / 5.49	8.31 / 8.48	106-107 (ether)	84
5a	$C_{16}H_{16}N_2S$	71.96 / 71.60	6.18 / 6.01	10.25 / 10.44	194-195 (ether–petr. ether [40-70°C])	89
5b	$C_{18}H_{20}N_2S$	72.67 / 72.93	7.02 / 6.80	9.60 / 9.45	123-124 (chloroform–petr. ether [40-70 °C])	81
5c	$C_{17}H_{18}N_2OS$	68.69 / 68.43	6.18 / 6.08	9.46 / 9.39	109-110 (chloroform–hexane)	55
5d	$C_{18}H_{20}N_2OS$	69.66 / 69.20	6.52 / 6.45	9.07 / 8.96	123-125 (chloroform–petr. ether [40-70 °C])	83

An additional finding confirming the correct identification of the transformation products of cyclopropanes **2a-i** and **3a-d** was the total correlation of the spectral characteristics of heterocycles **4a-i** and **5a-c** (Table 2) with the corresponding characteristics of numerous analogs (see, for example, the work of various authors [20-23]).

TABLE 2. Spectral Characteristics of Compounds **2-5**

Com-pound	IR spectrum, ν, cm^{-1}	^1H NMR spectrum, δ, ppm (*J*, Hz)*	Mass psectrum *m*/*z*, (I_{rel}, %)
1	2	3	4
2a	3200, 3295 (NH), 3330, 3430, 1680 (C=O)	0.67 (2H, m), 1.01 (2H, m) and 1.94 (1H, m) – cyclopropane; 6.48 (2H, br. s, NH_2); 7.07 (1H, d, *J* = 8.2, H-3); 7.14 (1H, t, *J* = 8.2, H-5); 7.22 (1H, t, *J* = 8.2, H-4); 7.28 (1H, s, NH); 7.52 (1H, d, *J* = 8.2, H-6)	176 $[M]^+$ (37.5)
2b	3100, 3315 (NH), 1680 (C=O)	0.65 (2H, m), 1.05 (2H, m) and 1.89 (1H, m) – cyclopropane; 6.85 (1H, d, *J* = 7.8, H-3); 6.90 (1H, t, *J* = 7.8, H-5); 6.97 (1H, t, *J* = 7.8, H-4); 7.11 (1H, t, *J* = 8.0, H-4); 7.23 (2H, t, *J* = 8.0, H-3',5')*[2]; 7.48 (2H, d, *J* = 8.0, H-2',6'); 7.81 (1H, s, NH); 7.96 (1H, d, *J* = 7.8, H-6); 8.91 (1H, s, NH)	252 $[M]^+$ (11.4)
2c	3100, 3300 (NH); 1680 (C=O)	0.62 (2H, m), 0.99 (2H, m), 1.87 (1H, m) – cyclopropane; 1.21 (6H, d, *J* = 6.4, $CH(C\underline{H}_3)_2$); 2.85 (1H, сп, $C\underline{H}(CH_3)_2$); 6.94 (1H, t, *J* = 8.1, H-5); 7.02 (1H, d, *J* = 8.1, H-3); 7.15 (1H, t, *J* = 8.1, H-4); 7.17 (2H, d, *J* = 8.2, H-3',5'); 7.41 (2H, d, *J* = 8.2, H-2',6'); 7.91 (1H, d, *J* = 8.1, H-6); 8.01(1H, s, NH); 9.14 (1H, s, NH)	294 $[M]^+$ (20.8)
2d	3100, 3300 (NH); 1680 (C=O)	0.61 (2H, m), 0.99 (2H, m) and 1.85 (1H, m) – cyclopropane; 2.24 (3H, s, CH_3); 6.93 (1H, t, *J* = 7.8, H-5); 7.01 (1H, d, *J* = 7.8, H-3); 7.09 (2H, d, *J* = 8.2, H-3',5'); 7.13 (1H, t, *J* = 7.8, H-4); 7.36 (2H, d, *J* = 8.2, H-2',6'); 7.89 (1H, d, *J* = 7.8, H-6); 8.03 (1H, s, NH); 9.15 (1H, s, NH)	266 $[M]^+$ (25.5)
2e	3085, 3300 (NH), 1675 (C=O)	0.68 (2H, m), 1.02 (2H, m) and 1.90 (1H, m) – cyclopropane; 3.82 (3H, s, OCH_3); 6.88 (2H, d, *J* = 8.2, H-3',5'); 6.91 (1H, d, *J* = 7.8, H-3); 7.02 (1H, t, *J* = 7.8, H-5); 7.16 (1H, t, *J* = 7.8, H-4); 7.39 (2H, d, *J* = 8.2, H-2',6'); 7.91 (1H, d, *J* = 7.8, H-6); 8.01 (1H, s, NH); 9.02 (1H, s, NH)	282 $[M]^+$ (34.5)

TABLE 2. (continued)

1	2	3	4
2f	3100, 3310 (NH), 1675 (C=O)	0.62 (2H, m), 0.99 (2H, m) and 1.89 (1H, m) – cyclopropane; 6.92 (1H, d, *J* = 7.8, H-3); 6.97 (1H, t, *J* = 7.8, H-5); 7.12 (1H, t, *J* = 7.8, H-4); 7.32 (2H, d, *J* = 8.3, H-2',6'); 7.52 (2H, d, *J* = 8.3, H-3',5'); 7.88 (1H, d, *J* = 7.8, H-6); 8.11 (1H, s, NH); 9.38 (1H, s, NH)	286 $[M]^+$ (17.2)
2g	3100, 3310 (NH), 1680, 1730 (C=O)	0.64 (2H, m), 1.02 (2H, m) and 1.91 (1H, m) – cyclopropane; 1.35 (3H, t, *J* = 6.3, $OCH_2C\underline{H}_3$); 4.31 (2H, q, *J* = 6.3, $OC\underline{H}_2CH_3$); 7.01 (1H, d, *J* = 7.8, H-3); 7.04 (1H, t, *J* = 7.8, H-5); 7.19 (1H, t, *J* = 7.8, H-4); 7.66 (2H, d, *J* = 8.2, H-2',6'); 7.91 (1H, d, *J* = 7.8, H-6); 7. 94 (2H, d, *J* = 8.2, H-3',5'); 8.25 (1H, s, NH); 9.62 (1H, s, NH)	324 $[M]^+$ (22.5)
2h	3310, 3500 (NH), 1675 (C=O)	0.61 (2H, m), 0.98 (2H, m) and 1.86 (1H, m) – cyclopropane; 6.98 (1H, d, *J* = 7.8, H-3); 7.01 (1H, t, *J* = 7.8, H-5); 7.18 (1H, t, *J* = 7.8, H-4); 7.71 (2H, d, *J* = 8.4, H-2',6'); 7.84 (1H, d, *J* = 7.8, H-6); 8.19 (2H, d, *J* = 8.4, H-3',5'); 8.28 (1H, s, NH)	297 $[M]^+$ (18.3)
2i	3100, 3350 (NH), 1660 (C=O)	0.59 (2H, m), 0.93 (2H, m) and 1.74 (1H, m) – cyclopropane; 2.38 (3H, s, CH_3); 7.01 (1H, d, *J* = 7.8, H-3); 7.02 (1H, t, *J* = 7.8, H-5); 7.14 (1H, t, *J* = 7.8, H-4); 7.41 (1H, s, NH); 7.43 (2H, d, *J* = 8.3, H-3',5'); 7.68 (1H, d, *J* = 7.8, H-6); 7.92 (2H, d, *J* = 8.3, H-2',6'); 8.29 (1H, s, NH)	330 $[M]^+$ (5.6)
3a	3160, 3340 (NH), 1470 (C=S)	0.65 (2H, m), 0.93 (2H, m) and 2.01 (1H, m) – cyclopropane; 6.95 (1H, d, *J* = 7.8, H-3); 7.21 (3H, m, H-3',4',5'); 7.31 (2H, t, *J* = 7.8, H-4,5); 7.50 (1H, d, *J* = 7.8, H-6); 7.57 (2H, d, *J* = 7.8, H-2',6'); 8.98 (1H, s, NH); 9.45 (1H, s, NH)	268 $[M]^+$ (24.3)
3b	3130, 3350 (NH), 1460 (C=S)	0.66 (2H, m), 0.92 (2H, m) and 1.98 (1H, m) – cyclopropane; 1.19 (3H, t, *J* = 6.6, $CH_2C\underline{H}_3$); 2.61 (2H, q, *J* = 6.6, $C\underline{H}_2CH_3$); 6.96 (1H, d, *J* = 7.8, H-3); 7.16 (4H, m, H-4,5,3',5'); 7.39 (3H, m, H-6,4',6'); 9.25 (1H, s, NH); 9.61 (1H, s, NH)	296 $[M]^+$ (19.5)
3c	3135, 3345 (NH), 1460 (C=S)	0.61 (2H, m), 0.91 (2H, m) and 1.99 (1H, m) – cyclopropane; 3.84 (3H, s, OCH_3); 6.94 (1H, d, *J* = 7.8, H-3); 7.06 (1H, t, *J* = 7.8, H-5); 7.21 (4H, m, H-4,3',4',5'); 7.43 (1H, t, *J* = 8.1, H-6'); 8.21 (1H, d, *J* = 7.8, H-6); 9.11 (1H, s, NH); 9.63 (1H, s, NH)	298 $[M]^+$ (38.5)
3d	3140, 3350 (NH), 1465 (C=S)	0.64 (2H, m), 0.94 (2H, m) and 1.97 (1H, m) – cyclopropane, 1.39 (3H, t, *J* = 6.4, $OCH_2C\underline{H}_3$); 4.02 (2H, q, *J* = 6.4, $OC\underline{H}_2CH_3$); 6.84 (2H, d, *J* = 8.0, H-3',5'); 6.93 (1H, d, *J* = 7.8, H-3); 7.12 (2H, m, H-4,5); 7.35 (2H, d, *J* = 8.0, H-2',6'); 7.47 (1H, d, *J* = 7.8, H-6); 8.95 (1H, s, NH); 9.36 (1H, s, NH)	312 $[M]^+$ (43.9)
4a	2700-3320 (salts NH), 1655 (N=C)	0.96 (3H, t, *J* = 6.5, $CH_2C\underline{H}_3$); 1.81 (2H, m, $C\underline{H}_2CH_3$); 5.25 (1H, m, CH-benzylic); 5.91 (2H, s, NH_2); 6.84 (1H, d, *J* = 7.8, H-5); 6.95 (1H, t, *J* = 7.8, H-7); 7.05 (1H, d, *J* = 7.8, H-8); 7.18 (1H, t, *J* = 7.8, H-6)	176 $[M]^+$ (21.3)
4b	2800-3200 (salts NH), 1650 (N=C)	1.01 (3H, t, *J* = 6.4, $CH_2C\underline{H}_3$); 1.92 (2H, m, $C\underline{H}_2CH_3$); 5.21 (1H, m, CH-benzylic); 6.91 (4H, m, H-5–8); 7.16 (1H, t, *J* = 8.0, H-4'); 7.25 (2H, t, *J* = 8.0, H-3',5'); 7.37 (2H, d, *J* = 8.0, H-2',6'); 9.18 (1H, br. s, NH)	252 $[M]^+$ (3.1)
4c	2820-3200 (salt NH), 1655 (N=C)	0.99 (3H, t, *J* = 6.4, $CH_2C\underline{H}_3$); 1.21 (6H, d, *J* = 6.2, $CH(C\underline{H}_3)_2$); 1.99 (2H, m, $C\underline{H}_2CH_3$); 2.89 (1H, m, $C\underline{H}(CH_3)_2$); 5.67 (1H, m, CH-benzylic); 7.11 (1H, d, *J* = 7.8, H-5); 7.17 (1H, t, *J* = 7.8, H-7); 7.25 (1H, d, *J* = 7.8, H-8); 7.28*[3] (2H, d, *J* = 8.2, H-3',5'); 7.34 (1H, t, *J* = 7.8, H-6); 7.45 (2H, d, *J* = 8.2, H-2',6')	294 $[M]^+$ (31.1)

TABLE 2. (continued)

1	2	3	4
4d	2820-3230 (salt NH), 1650 (N=C)	0.95 (3H, t, *J* = 6.3, $CH_2C\underline{H}_3$); 1.95 (2H, m, $C\underline{H}_2CH_3$); 2.27 (3H, s, CH_3); 5.64 (1H, m, CH-benzylic); 7.11 (1H, d, *J* = 7.8, H-5); 7.17 (1H, t, *J* = 7.8, H-7); 7.21 (2H, d, *J* = 8.1, H-3',5'); 7.22 (1H, d, *J* = 7.8, H-8); 7.23 (1H, s, NH); 7.32 (1H, t, *J* = 7.8, H-6); 7.43 (2H, d, *J* = 8.1, H-2',6')	266 $[M]^+$ (375)
4e	2750-3320 (salt NH), 1660 (N=C)	1.05 (3H, t, *J* = 6.5, $CH_2C\underline{H}_3$); 2.23 (2H, m, $C\underline{H}_2CH_3$); 3.85 (3H, s, OCH_3); 5.90 (1H, m, CH-benzylic); 7.22-7.53 (9H, m, 8ArH, NH)	282 $[M]^+$ (8.3)
4f	2750-3300 (salt NH), 1655 (N=C)	1.09 (3H, t, *J* = 6.5, $CH_2C\underline{H}_3$); 2.11 (2H, m, $C\underline{H}_2CH_3$); 5.62 (1H, m, CH-benzylic); 7.07 (1H, d, *J* =7.8, H-5); 7.17 (1H, t, *J* =7.8, H-7); 7.23 (1H, d, *J* =7.8, H-8); 7.32 (1H, t, *J* =7.8, H-6); 7.48*[3] (2H, d, *J* = 8.1, H-2',6'); 7.54 (2H, d, *J*=8.1, H-3',5')	286 (91.0)
4g	2820-3230 (salt NH), 1655 (N=C), 1728 (COOEt)	1.02 (3H, t, *J* = 6.5, $CH_2C\underline{H}_3$); 1.41 (3H, t, *J* = 6.4, $OCH_2C\underline{H}_3$). 2.10 (2H, m, $C\underline{H}_2CH_3$); 4.38 (2H, q, *J* = 6.4, $OC\underline{H}_2CH_3$); 5.63 (1H, m, CH-benzylic); 7.08 (1H, d, *J* =7.8, H-5); 7.18 (1H, t, *J* = 8.2, H-7); 7.26 (1H, d, *J* = 7.8, H-8); 7.36 (1H, t, *J* = 7.8, H-6); 7.48 (2H, d, *J* = 8.2, H-2',6'); 7.65 (1H, s, NH); 8.03 (2H, d, *J* = 8.2, H-3',5')	324 (2.4)
4h	2750-3300 (salt NH), 1655 (N=C)	1.03 (3H, t, *J* = 6.5, $CH_2C\underline{H}_3$); 1.98 (2H, m, $C\underline{H}_2CH_3$); 5.59 (1H, m, CH-benzylic); 7.11 (1H, br. s, NH); 7.12 (1H, d, *J* = 7.8, H-5); 7.16 (1H, t, *J* = 7.8, H-7); 7.21 (1H, d, *J* = 7.8, H-8); 7.33 (1H, t, *J* = 7.8, H-6); 7.69 (2H, d, *J* = 8.3, H-2',6'); 8.26 (2H, d, *J* = 8.3, H-3',5')	—
4i	2700-3200 (salt NH), 1650 (N=C)	0.91 (3H, t, *J* = 6.5, $CH_2C\underline{H}_3$); 1.77 (2H, m, $C\underline{H}_2CH_3$); 2.32 (3H, s, CH_3); 4.82 (1H, m, CH-benzylic); 7.24*[3] (6H, m, H-5,7,8,3',5'); 7.33 (1H, t, *J* = 7.8, H-6); 7.49 (2H, d, *J* = 8.2, H-2',6')	-48 $[M^+]$ (11.4) -49 $[M^+]$ (55.2)
5a	2600-3300 (salt NH), 1640 (N=C)	0.95 (3H, t, *J* = 6.6, $CH_2C\underline{H}_3$); 1.79 (2H, m, $C\underline{H}_2CH_3$); 4.18 (1H, m, CH-benzylic); 4.88 (1H, br. s, NH); 7.19-7.42 (7H, m, H-5–8,3'–5'); 7.61 (2H, d, *J* = 8.0, H-2',6')	268 (44.2)
5b	2730-3220 (salt NH), 1635 (N=C)	0.87 (3H, t, *J* = 6.5, $CH_2C\underline{H}_3$); 1,16 (3H, t, *J* = 6.3, $CH_2C\underline{H}_3$); 1.75 (2H, m, $CHC\underline{H}_2CH_3$); 2.61 (2H, q, *J* = 6.3, $C\underline{H}_2CH_3$); 4.23 (1H, m, $C\underline{H}CH_2CH_3$); 7.12-7.24 (3H, m), 7.25-7.31 (3H, m), 7.33-7.39 (3H, m) – 8ArH, NH	296 (83.7)
5c	2800-3310 (salt NH), 1630 (N=C)	0.93 (3H, t, *J* = 6.5, $CH_2C\underline{H}_3$); 1.81 (2H, m, $C\underline{H}_2CH_3$); 4.11 (3H, s, OCH_3); 4.35 (1H, m, CH-benzylic); 7.12-7.41 (9H, m, 8ArH, NH)	298 (25.2)
5d	3140-3350 (salt NH), 1655 (N=C)	0.89 (3H, t, *J* = 6.5, $CHCH_2C\underline{H}_3$); 1.35 (3H, t, *J* = 6.4, $OCH_2C\underline{H}_3$); 1.73 (2H, m, $CHC\underline{H}_2CH_3$); 4.01 (2H, q, *J* = 6.4, $OC\underline{H}_2CH_3$); 4.29 (1H, m, $C\underline{H}CH_2CH_3$); 6.72 (2H, d, *J* = 8.1, H-3',5'); 7.05 (1H, t, *J* = 7.8, H-7); 7.09 (2H, d, *J* = 8.1, H-2',6'); 7.15 (1H, d, *J* = 7.8, H-5); 7.18 (1H, t, *J* = 7.8, H-6); 7.35 (1H, s, NH); 7.56 (1H, d, *J* = 7.8, H-8)	312 (71.2)

* The ^{1}H NMR spectra were taken in $CDCl_3$ for **2a-e,g,h,** and **3a-c** and in DMSO-d_6 for **2f, i, 4a-i,** and **5a-d.**

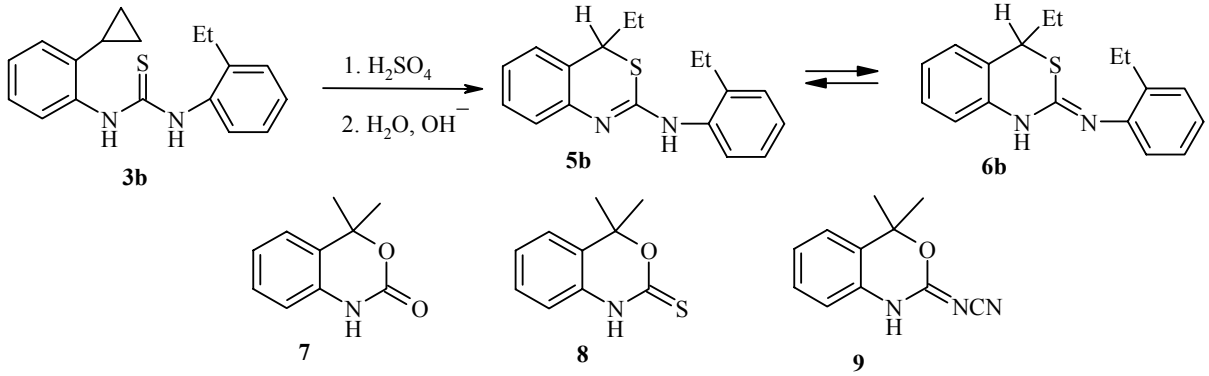
*[2] Here and subsequently, the atoms in the aryl substituent R are indicated with a prime sign.

**[3] The signal for the NH group proton is in the aromatic proton multiplet.

Thus, the acid-catalyzed rearrangement of arylcyclopropanes containing a urea or thiourea fragment in the *ortho* position relative to the cyclopropane substituent may be used for the synthesis of 2-amino-4H-3,1-benzoxazines and 2-amino-4H-3,1-benzothiazines.

The following discussion is of interest in the framework of the present investigation. In virtually all the studies on the synthesis of 2-amino-4H-3,1-benzoxazines or 2-amino-4H-3,1-benzothiazines, the question of alternative structures for these heterocyclic compounds, namely, the corresponding imino-3,1-benzoxazin-2-ones (**6b**) and imino-3,1-benzothiazin-2-ones (**9**) is completely ignored. We should note that despite the large number of 2-amino-4H-3,1-benzoxazines and 2-amino-4H-3,1-benzothiazines synthesized, there have hardly been any X-ray diffraction structural analyses of these compounds.

It was only in 2005 that we were the first to publish the results of our X-ray diffraction study of the structure of the heterocyclic compound formed by the action of sulfuric acid on $N_{(1)}$-(2-cyclopropylphenyl)-$N_{(2)}$-(2-ethylphenyl)thiourea **3b** [24]. The ^{1}H NMR spectrum of the heterocyclic compound formed in this reaction taken in DMSO-d_6 was used to identify it as 4-ethyl-2-(2'-ethylphenyl)amino-4H-3,1-benzothiazine (**5b**), while the results of an X-ray diffraction structural study of the crystal structure corresponded to 4-ethyl-2-(2'-ethylphenyl)imino-4H-3,1-benzothiazine (**6b**). This finding suggests that 2-aminobenzoxazines and 2-aminobenzothiazines may exist in different tautomeric forms in solution and crystalline state. Actually, if the compound obtained from thiourea **3b** in solution retained the iminobenzothiazine structure **6b** found by X-ray diffraction structural analysis, we would have expected the ^{1}H NMR spectrum to show a downfield signal for the proton of the endocyclic NH group, whose chemical shift would have to correlate with the corresponding values of the protons of similar groups found for analogs **7-9** [22, 25].



Chemical shift for the NH group proton, δ, ppm: 9.43 (for **7**), 9.49 (for **8**), and 11.5 (for **9**).

Since the signal of the NH group in the ^{1}H NMR spectrum of the solution of the compound obtained from thiourea **3b** appears at 7.25-7.33 ppm (see Table 2 and our previous work [24]), which is in accord with the chemical shifts of the corresponding protons of the compounds **4a-i,** and **5a,c,d** (Table 2) and with the chemical shifts of the corresponding protons described in the literature for this type of heterocyclic compounds [20-23], it is quite likely that the heterocyclic product, which is formed upon the rearrangement of **3b**, is present in solution as 2-amino-4H-3,1-benzothiazine **5b**, though that this product exists in the crystal as tautomer **6b**.

EXPERIMENTAL

The ^{1}H NMR spectra were taken on a Varian VXR-400 spectrometer at 400 MHz. The chemical shifts were measured relative to the residual protons of the deuterated solvents ($CDCl_3$ or DMSO-d_6). The IR spectra were taken on a UR-20 spectrometer neat, in vaseline mull or in hexachlorobutadiene. The mass spectra

were taken on a Finnigan SSQ-7000 GC/MS using a 30-m capillary column placed with DV-1 as the stationary phase, helium as the gas carrier, and temperature programming from 50 to 300°C (10 deg/min). The ionization energy was 70 eV. The purity of the products was monitored on Silufol plates and Brockmann grade-II activity alumina using 1:1:3 ether–chloroform–petroleum ether (40-70°C) as the eluent.

N-(2-Cyclopropyl)phenylurea (2a). 2-Aminophenylcyclopropane (6 g, 0.045 mol) (bp 103-104°C (9 mm Hg), n_D^{20} 1.5812 [16]) was added to of 1:2 acetic acid–water (75 ml) and heated to 35°C. Then, a solution of potassium cyanate (13 g, 0.1 mol) was added gradually at this temperature with vigorous stirring. The suspension formed was stirred for 10 min and maintained for 3 h at 20°C. Then, water (30 ml) was added and the mixture was cooled to 0°C. The crystalline precipitate was filtered off, washed with water, thoroughly pressed, and recrystallized from aqueous ethanol (12 ml ethanol and 3 ml water per 1 g crude **2a**). The yield of **2a** was 91%.

N-(2-Cyclopropyl)phenylureas 2b-i and N-(2-Cyclopropyl)phenylthioureas 3a-d (General Method). Corresponding aryl isocyanate or aryl isothiocyanate (0.01 mol) was added with stirring to a solution of 2-aminophenylcyclopropane (0.01 mol) in benzene (20 ml) and heated at reflux for 3 h. In the case of cyclopropylphenylureas **2b-i**, the crystalline precipitate formed upon cooling to 20°C was filtered off, washed with cold benzene, and dried in the air. In the case of 2-cyclopropylphenylthioureas **3a-d**, benzene was distilled off and the residue was recrystallized from a suitable solvent.

Rearrangement of N-(2-Cyclopropyl)phenylureas 2a-i by the Action of Trifluoroacetic Acid (General Method). Corresponding cyclopropylphenylurea **2a-i** (0.01 mol) was added gradually to trifluoroacetic acid (30 ml) with stirring, heated to 40-45°C, and stirred at this temperature for 3 h. The reaction mixture was cooled to 20°C, then poured with stirring into 150 g of a 1:1 mixture of ice and water, and neutralized by adding aqueous ammonium hydroxide. The organic compounds were extracted with methylene chloride (2×50 ml). The extract was washed with water and dried over calcium chloride. The solvent was evaporated off and the residue was recrystallized from a suitable solvent.

Rearrangement of N-(2-Cyclopropyl)phenylthioureas 3a-d by the Action of Concentrated Sulfuric Acid (General Method). Corresponding thiourea **3a-d** (0.01 mol) was added in portions to concentrated sulfuric acid (20 ml) (*d* 1.84) cooled to -20°C and stirred at this temperature for an additional 1 h. The clear solution formed was poured into a mixture of ice (100 g) and water (100 ml), carefully neutralized by adding $NaHCO_3$, and extracted with methylene chloride (2×50 ml). The extract was washed with water, and dried over calcium chloride. The residue was recrystallized from a suitable solvent or mixture of solvents.

The procedure described above gave 4-ethyl-2-(*p*-tolyl)amino-4H-3,1-benzoxazine (**4d**) 1.01 g (75%) from $N_{(2)}$-(4-methylphenyl)-$N_{(1)}$-(2-cyclopropylphenyl)urea (**2d**) (1.35 g), 4-ethyl-2-(*p*-nitrophenyl)amino-4H-3,1-benzoxazine (**4h**) 1.21 g (81%) from $N_{(2)}$-(4-nitrophenyl)-$N_{(1)}$-(2-cyclopropylphenyl)urea (**2h**) (1.5 g). The ^{1}H NMR spectra of **4d** and **4h** obtained using this procedure are identical to the spectra of the corresponding compounds obtained by rearrangement of ureas **2d** and **2h** by the action of trifluoroacetic acid. No melting point depression was noted for mixed samples.

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