Reaction of Isocyanates with 2-Phenyliminotetrahydro-1,3-thiazines and Oxazines

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It has been found that the reaction of isocyanates with 2-phenyliminotetrahydro-1,3-thiazines and oxazines **3-8** occurs at the ring nitrogen to give the endo carbamoylated compound first, and then the carbamoyl group migrates to the exo nitrogen with differing rates depending upon the structure of the thiazines or the oxazines. Though the carbamoylated thiazines (both endo and exo) were found to exist in equilibrium with the isocyanate and the thiazine in solution, crossover experiments showed that the rearrangement proceeded by an intramolecular mechanism.

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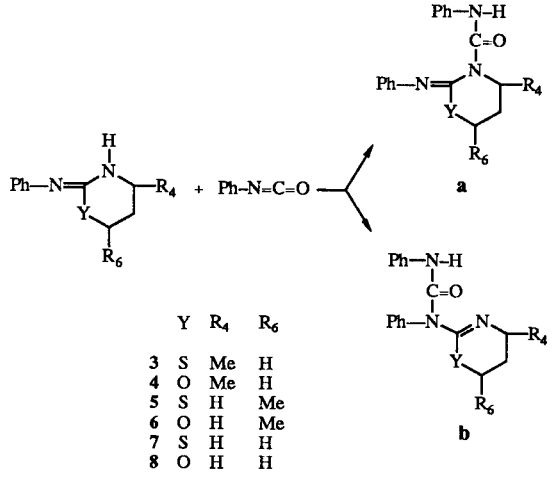
In the cyclic isothioureas of the tautomeric structures **1a** and **1b**, there are always two possibilities in the acylation site, one at the ring nitrogen (endo acylation) and the other at the exo nitrogen (exo acylation). Toldy, Sohár

1a **1b**

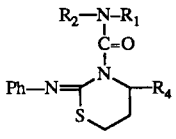
and Faragó found, in their extensive investigation on the acylation of such isothioureas [1], that the endo/exo ratios of the acylation were influenced by the nature of the acylation reagents and also by the electronic and the steric factors of the Ar groups. They concluded further that the ratios of the endo acylation were larger in the six-membered ring compounds **1** (n = 3) than in the five-membered ones **1** (n = 2) owing to the greater flexibility of the six-membered ring than that of the five-membered ring. In their study on the mesylation of the same systems [2], they found that the mesylation took place at N-3, and on heating of the endo mesylated compounds in bromoform at 110°, the mesyl group migrated to the exo nitrogen. More recently, work on the reaction of phenyl isothiocyanate and phenyl isocyanate with 4,5-dihydro-2-thiazolamine (**2**) was published by Rasmussen, Vilani, Mutter and Griffin [3]. They have suggested that the initial reactions of **2** occur at the endocyclic nitrogen, and these adducts may then rearrange to the thermodynamically more stable exo derivatives intramolecularly and/or by a mechanism involving dissociation to the reactants and recombination. In our earlier study to determine the enantiomeric composition of optically active thiazines and oxazines **3-6** [4] with α-methoxy-α-trifluoromethylbenzyl isocyanate [5], we found that the site of the carbamoylation largely depended on the structure of the thiazines or the oxazines, and that the ratio of the isomers changed when the solution of the mixture was left standing at room temperature. This work was undertaken to establish the structure of the endo or the exo carbamoylated compound, and further to elucidate the mechanism of the transformation of one isomer to the other.



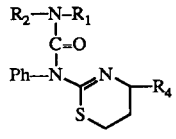
	Y	R_4	R_6
3	S	Me	H
4	O	Me	H
5	S	H	Me
6	O	H	Me
7	S	H	H
8	O	H	H

Reaction of phenyl isocyanate with **3** gave a mixture of two compounds, **3a** and **3b**. The ^{1}H nmr spectrum of the mixture showed that one of the isomers had a signal at 5.4 ppm attributable to 4-C*H*, while the other had a signal for 4-C*H* at 3.7 ppm. With other carbamoylated derivatives of **3** and **4** also, the 4-C*H* signal was always found downfield (4.9-5.4 ppm) in one isomer in contrast to the other in which the position of the signal was not changed appreciably (3.5-3.7 ppm) from that of **3** or **4** (3.5 ppm in both compounds) (Table I). A ball-and-stick model of **3b**, in which the N-*H* is hydrogen-bonded to N-3 shows that the benzene ring (in the anilino group at C-2) can be placed in the same plane as the 4-C*H* (should be axial), and in the conformation the distance between the 4-C*H* and the

center of the benzene ring can be as short as 3.5 Å. Thus, the strong deshielding of the 4-C*H* is attributable to the paramagnetic anisotropy of the benzene ring in **3b**. In **3a**, the 4-C*H* can not be in the same plane as the benzene ring since the Ph-N=C< moiety should be planar. The fact that the chemical shift of 4-C*H* in **9b** (4.3 ppm, entry 5 in Table I) is smaller than those in other exo derivatives with NH group might be due to the lack of the hydrogen-bonding so that the benzene ring would not be confined in a conformation mentioned above for **3b**. Further support



a



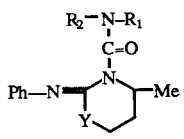
b

	R_1	R_2	R_4
9a,b	Me	Ph	Me
10a,b	Me	Ph	H
11a,b	Ph	Ph	H
12a,b	H	$PhCH_2$	Me

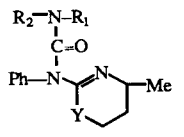
for the endo or exo assignment was obtained by the comparison of the nmr spectra of **9a** and **9b**: in the latter a doublet was found at 6.5 ppm assignable to the ortho hydrogens of the phenyl group, while in the former, the signals for the phenyl hydrogens (of Ph-N= at C-2) were found in the range of 7.0-7.3 ppm (by analogy to the case in **10a** and **10b** mentioned in the Experimental). Such a shift of the *ortho* hydrogens is considered to be due to the diamagnetic anisotropy of the neighboring carbonyl group, and similar shielding by acyl carbonyl [1] or sulfonyl group [2] was reported by Toldy et al and used as a support for the exo acylated structure.

Table I

Chemical Shifts of 4-C*H* of Endo or Exo Carbamoylated Derivatives of **3** and **4** [a]



a



b

Entry		Y	R_1	R_2	**a**	**b**
1	**3a,b**	S	H	Ph	3.7	5.4
2		S	H	2,6-dimethyl-phenyl	3.7	5.4
3	**12a,b**	S	H	$PhCH_2$	3.6	5.4
4		S	H	*t*-Bu	3.6	5.3
5	**9a,b**	S	Me	Ph	3.5	4.3
6	**4a,b**	O	H	Ph	3.7	5.1
7		O	H	2,6-dimethyl-phenyl	3.7	5.0
8		O	H	$PhCH_2$	3.6	5.0
9		O	H	*t*-Bu	3.6	4.9

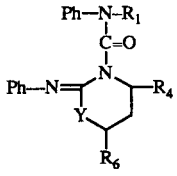
[a] Measured in chloroform-d.

In a previous paper [5], we reported that the isocyanate reaction occurred only at one place in **5** and **6**, and assigned the endo carbamoylated structure to the reaction product [6]. However, further study showed that the assignment was not true. Reaction of phenyl isocyanate with **7** at a low temperature (Dry-Ice) and measurement of the ^1H nmr spectra at -40° disclosed the existence of an isomer, **7a**. With other thiazines and oxazines, **5**, **6** and **8**, each pair of isomers was found in the ^1H nmr spectra by the low temperature experiment (Table II). Assignment of the endo or exo was done based on the chemical shifts of 4-CH_2 for each pair of isomers: to the isomer with a higher 4-CH_2 signal was assigned the endo, and to the one with a lower 4-CH_2 signal the exo carbamoylated structure. In these cases however, the shifts differences are not so large as in the case of **3a,b** and **4a,b**. In the former, the chemical shifts for the 4-CH_2 should be the time average of the axial and the equatorial hydrogens due to the fast inversion of the six-membered ring. Here again, the validity of the assignment for the exo adduct was obtained by the existence of the high field signal (at 6.5 ppm) for the *ortho* hydrogens of the phenyl group in **10b**. Such a high field signal was also found in **11b** (at 6.6 ppm).

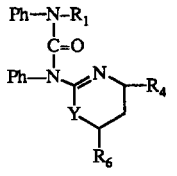
All the endo derivatives with NH group in Table II were found to isomerize to the exo with differing rates. The composition of **7a** and **7b** in a mixture at -40° (77/23) did not change after standing of the sample for 1 hour at 0°. In the corresponding oxazine by contrast, the endo adduct **8a** was very difficult to detect under the same conditions and rapidly rearranged to the exo derivative **8b**: composition of endo/exo = 7/93 measured at -40° changed to 4/96 after 1 hour at 0°. Similarly, the endo adduct **6a** was found to be very unstable. All the endo adducts from **5**, **6**, **7** and **8** disappeared after 1 hour standing at room temperature. Introduction of a methyl group at C-4 in the six-membered ring was found to increase the stability of the endo adducts and greatly decrease the rate of endo → exo conversion. In the reaction of **3** with phenyl isocyanate, only **3a** was obtained under the conditions mentioned above, and the nmr spectrum did not change at all after 1 hour standing at 0°. In the corresponding oxazine, composition of **4a**/**4b** = 67/33 observed at -40° changed to 44/56 after 1 hour at 0°. These endo adducts from **3** and **4** were found to isomerize to exo gradually at room temperature until the endo/exo ratio leveled off at some final value in each case. The reason for the stabilizing effect of 4-Me for the endo derivatives is not clear now. Other endo carbamoylated 4-methylthiazines and oxazines showed similar behavior, and the endo/exo ratios at equilibrium are summarized in Table III. It is noted from Table III that the steric factor of the isocyanates has some influence

Table II

Proton NMR Chemical Shifts of Thiazines and Oxazines **3-8** and the Carbamoylated Derivatives [a]



a



b

Entry	Compd	Y	R_1	R_4	R_6	4-CH_2 or 4-CH	5-CH_2	6-CH_2 or 6-CH	4-CH_2 or 4-CH	5-CH_2	6-CH_2 or 6-CH
1	**3**	S	–	Me	H	3.53 (m)	1.68 (m) 2.10 (m)	3.0 (m)			
2	**3a,b**	S	H	Me	H	3.71 (m)	1.4 (m) 2.02 (m)	2.9 (m) 3.1 (m)	5.39 (m)	2.0 (m) 2.2 (m)	2.9 (m) 3.1 (m)
3	**9a,b** [b]	S	Me	Me	H	3.51 (m)	1.28 (m) 1.71 (m)	2.83 (t)	4.32 (m)	1.86 (m) 2.30 (m)	2.69 (m)
4	**4**	O	–	Me	H	3.54 (m)	1.6 (m) 1.96 (m)	4.1– 4.3 (m)			
5	**4a,b**	O	H	Me	H	3.72 (m)	1.6 (m) 2.0 (m)	4.2 (m)	4.98 (m)	2.0 (m) 2.3 (m)	4.2– 4.4 (m)
6	**5**	S	–	H	Me	3.4– 3.5 (m)	1.65 (m) 2.07 (m)	3.4 (m)			
7	**5a,b**	S	H	H	Me	3.72 (m) 4.10 (m)	1.46 (m) 2.00 (m)	3.25 (m)	3.87 (m) 4.35 (m)	1.75 (m) 2.36 (m)	3.48 (m)
8	**6**	O	–	H	Me	3.40 (m)	1.64 (m) 1.90 (m)	4.30 (m)			4.43 (m)
9	**6a,b**	O	H	H	Me	[c]	[c]	[c]	3.67 (m) 4.20 (m)	1.89 (m) 2.20 (m)	
10	**7**	S	–	H	H	3.46 (t)	1.99 (qui)	3.00 (t)			
11	**7a,b**	S	H	H	H	3.85(t)	1.86 (qui)	2.99 (t)	4.12 (t)	2.19 (qui)	3.00 (t)
12	**10a,b** [b]	S	Me	H	H	3.61(t)	1.59 (qui)	2.81 (t)	3.74 (t)	2.12 (qui)	2.69 (t)
13	**11a,b** [b]	S	Ph	H	H	3.64 (t)	1.64 (qui)	2.85 (t)	3.85 (t)	2.18 (qui)	2.68 (t)
14	**8**	O	–	H	H	3.40 (t)	1.92 (qui)	4.23 (t)			
15	**8a,b**	O	H	H	H	3.60 (t)	1.92 (b.s)	4.18 (t)	3.93 (t)	2.17 (qui)	4.27 (t)

[a] Measured in dichloromethane-d_2 unless otherwise noted. [b] Measured in chloroform-d. [c] Unable to observe. Only the signal for CH_3 was seen at 1.10 ppm (d).

upon the ratio. However, the electronic nature of the isocyanates does not seem to have any effect (compare entry 1, 5 and 6 in Table III) in contrast to the results reported by Toldy et al for the acylation of **1** [1].

Table III

Ratios of Endo/Exo in the Reaction of R_2–N=C=O with **3** and **4** at Equilibrium [a]

Entry	R_2	**3** Endo	**3** Exo	**4** Endo	**4** Exo
1	Ph	48	52	25	75
2	$PhCH_2$	35	65	31	69
3	2,6-Dimethylphenyl	29	71	15	85
4	*t*-Bu	[b]	[b]	36	64
5	*p*-Methoxyphenyl	49	51		
6	*p*-Chlorophenyl	50	50		

[a] Measured in chloroform-d. [b] Reaction was not complete after 20 days.

Finally, the mechanism of the isomerization was investigated. First, the possibility of the carbamoylated products to dissociate to the reactants was tested. When **7** (5 mg) was added to a mixture of **3a** and **3b** (5 mg) in chloroform (Table III) at room temperature, formation of **7b** was observed with simultaneous decrease in the ratio of **3a/3b**, and after standing the solution for a day, neither **3a** nor **3b** was observed in the nmr. Addition of **3** (5 mg) to a solution of **7b** (5 mg) in chloroform, on the other hand, gave a mixture of **3a** and **3b** in a ratio of 70/30 after 30 minutes and after a day, the ratio changed to 50/50 and still 81% of **3** was found unchanged. These facts suggest that in solution the isocyanate adducts of thiazines (both endo and exo) exist in equilibrium with the isocyanate and the original thiazine. The fact that the ratio of **3a/3b** decreased at an early stage of the reaction of **7** with a mixture of **3a** and **3b** shows that the dissociation is taking place more extensively in the endo than in the exo derivative. That only a part of **7b** was consumed by **3** on mixing the two compounds will be explained by the relative stabilities of the adducts **3a**, **3b** and **7b**, **7b** being the most stable. Next, our attention was focused on whether the isomerization proceeded by an intermolecular or an intramolecular mechanism. The presence of excess isocyanate did not affect the endo/exo ratio at equilibrium: addition of phenyl isocyanate to a mixture of **3a** and **3b** did not change the ratio. However, addition of

benzyl isocyanate to the same mixture gave **12a** first. After 3 hours, the formation of **12b** was discernible, and after 4 days standing, the reaction mixture consisted of two isomer pairs with endo/exo ratio at equilibrium in each of **12a/12b** = 31/69 and **3a/3b** = 47/53. This means that the reaction of benzyl isocyanate does not occur at the exo nitrogen even in abundant presence of the isocyanate and despite that the exo adduct also exists in equilibrium with the isocyanate and the thiazine. With these facts, we would suggest an intramolecular mechanism in which the exo nitrogen should attack the carbonyl carbon before the -R_2N-CO- moiety is split off as an isocyanate. The presence of the N*H* seems to be important for the facile rearrangement of the endo derivative since **10a** isomerized to **10b** only at a higher temperature. The reaction scheme may be depicted as follows:

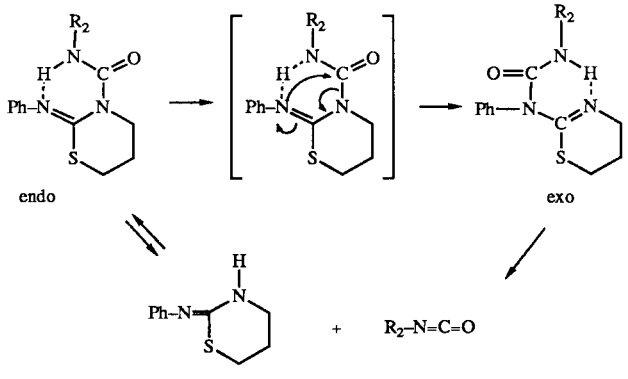


Table IV
Carbon-13 NMR shifts of 2-Phenyliminotetrahydro-1,3-thiazines and the Carbamoylated Derivatives [a]

Entry		4-*C*	5-*C*	6-*C*	4-CH_3	N-CH_3
1	**3**	48.60	26.11	30.29	22.67	
2	**3a**	50.95	26.09	27.87	23.77	
3	**3b**	45.80	25.14	28.86	17.90	
4	**9a**	51.59	25.45	26.04	22.34	38.75
5	**9b**	50.82	24.56	30.86	20.58	38.78
6	**7**	42.82	22.56	26.94		
7	**7b**	42.46	23.72	28.42		
8	**10a**	47.14	19.62	26.93		38.85
9	**10b**	45.35	23.92	26.76		38.63
10	**11a**	47.37	19.47	26.93		
11	**11b**	44.92	23.92	26.65		

[a] Measured in chlorofrm-d.

EXPERIMENTAL

Melting points (taken on a Laboratory Device MEL-TEMP) and boiling points are uncorrected. Infrared spectra were obtained on a Shimazu IR-400 spectrometer. The nmr spectra (^{1}H and ^{13}C) were recorded on a JEOL GSX-270 (270 MHz) spectrometer. Mass spectra were obtained on a JEOL DX-300 spectrometer (electron impact method). Compounds **3-8** were prepared according to the method reported in a previous paper [7]. Isocyanates, carbamoyl chlorides and aniline-d_5 were obtained commercially (Aldrich).

Reaction of 2-Phenylimino-4-methyltetrahydro-1,3-thiazine (**3**) with Phenyl Isocyanate.

An ethereal solution of phenyl isocyanate (130 mg, 1.1 mmoles) was added to a cooled (ice) solution of **3** (206 mg, 1 mmole) in ether, and the solution was concentrated to give white crystals. They were collected on a filter and recrystallized from benzene and petroleum ether (bp 35-70°) to give a mixture of **3a** and **3b** (**3a/3b** = 66/34 measured in chloroform-d right after dissolution). On tlc (ethyl acetate/benzene = 50/50), the mixture gave two spots (Rf values 0.78 and 0.67) along with a spot at the bottom (presumably of **3** owing to the decomposition of the adducts on the tlc plate) with extensive tailing. From the ^{13}C nmr spectra (Table IV) the mixture consisted of **3a** and **3b** only.

Reactions of **3** and **4** with other isocyanates were done in nmr tubes using chloroform-d as a solvent, and the nmr spectra were observed right after dissolution, and after 20 days to obtain the values of endo/exo at equilibrium (Table III). The value of **3a/3b** obtained in this way was identical to that obtained by dissolving the crystalline mixture and standing the solution for 20 days afterwards. The rate of isomerization of **12a** was found to be very slow compared to those of other endo derivatives. Right after reaction, the ratio of **12a/12b** was 93/7, and after standing the mixture for a day, it changed to 41/59, and still it took several days until the value leveled off at 35/65.

Reactions of **5**, **6**, **7** and **8** with Phenyl Isocyanate at an Ambient Temperature.

These reactions were carried out in similar manners as in the case with **3**, and the products **5b-8b** were recrystallized from benzene and petroleum ether. The melting points and the analytical data are listed below:

		Analyses					
		C		H		N	
Compound	mp (°)	Calcd.	Found	Calcd.	Found	Calcd.	Found
5b	157-160	66.44	66.52	5.89	5.92	12.92	12.56
			66.59		5.93		12.56
6b	154-157	69.88	70.00	6.19	6.28	13.58	13.18
			69.95		6.27		13.15
7b	119-121	65.58	65.64	5.50	5.50	13.50	13.46
8b	126-128	69.13	69.03	5.80	5.81	14.23	14.22

Reaction of 2-Phenyliminotetrahydro-1,3-thiazine (**7**) with Phenyl Isocyanate at a lower Temperature.

A solution of **7** (6 mg) in dichloromethane-d_2 in an nmr tube was cooled in a Dewar flask containing dry ice, and to the solution was added phenyl isocyanate (6 mg *ca*). The sample tube was quickly placed in the nmr probe and the spectrum was obtained at -40°. Spectra were observed after 1 hour at 0°, and after additional 1 hour at room temperature. Spectra of other samples were obtained in similar manners.

Preparation of 2-Phenylimino-3-(*N*-methyl-*N*-phenylcarbamoyl)-tetrahydro-1,3-thiazine (**10a**) and 2-*N*-(*N'*-Methyl-*N'*-phenylcarbamoyl)anilino-5,6-dihydro-4*H*-1,3-thiazine (**10b**).

A solution of **7** (192 mg, 1 mmole), *N*-methyl-*N*-phenylcarbamoyl chloride (186 mg, 1.1 mmoles) and triethylamine (200 mg) in benzene was heated for 10 hours under reflux. After removing

triethylamine hydrochloride by filtration, the filtrate was washed with water and dried with sodium sulphate. Concentration of the solution gave 350 mg of a mixture of **10a** and **10b**. Column chromatography (benzene-ethyl acetate) of the mixture gave 90 mg of **10b** and 250 mg of **10a**. Crude **10a** or **10b** was recrystallized from benzene and petroleum ether. Compound **10a** melted at 116-118°; ms: m/e 325 (M^+, 26), 233 ((M-H-C_6H_5N)$^+$, 61), 219 (34), 191 (32), 134 (PhNMeCO$^+$, 100), 106 (48), 77 (67).

Anal. Calcd. for $C_{18}H_{19}N_3OS$: C, 66.44; H, 5.89; N, 12.92. Found: C, 66.43; H, 5.90; N, 12.72.

Compound **10b** melted at 94-96°; ms: m/e 325 (M^+, 24) 233 ((M-H-C_6H_5N)$^+$, 61), 219 (34), 191 (32), 134 (PhNMeCO$^+$, 100), 106 (51), 77 (71).

Anal. Calcd. for $C_{18}H_{19}N_3OS$: C, 66.44; H, 5.89; N, 12.92. Found: C, 66.33; H, 5.89; N, 12.63.

Compounds **9a** and **b** and **11a** and **b** were prepared similarly from **3** and *N*-methyl-*N*-phenylcarbamoyl chloride in the former, and from **7** and *N,N*-diphenylcarbamoyl chloride in the latter. Compound **9a** melted at 121-124°.

Anal. Calcd. for $C_{19}H_{21}N_3OS$: C, 67.24; H, 6.24; N, 12.38. Found: C, 67.43; H, 6.26; N, 12.19.

Compound **9b** melted at 102-105°.

Anal. Calcd. for $C_{19}H_{21}N_3OS$: C, 67.24; H, 6.24; N, 12.38. Found: C, 67.30; H, 6.24; N, 12.21.

Compound **11a** melted at 163-166°; ms: m/e 387 (M^+, 9), 267 ((M-H-PhNCO)$^+$, 100), 219 (45), 196 (34), 168 (35), 77 (40).

Anal. Calcd. for $C_{23}H_{21}N_3OS$: C, 71.30; H, 5.46; N, 10.85. Found: C, 71.12; H, 5.41; N, 10.69.

Compound **11b** melted at 157-159°; ms: m/e 387 (M^+, 7), 267 ((M-H-PhNCO)$^+$, 100), 219 (44), 196 (34), 168 (37), 77 (41).

Anal. Calcd. for $C_{23}H_{21}N_3OS$: C, 71.30; H, 5.46; N, 10.85. Found: C, 70.88; H, 4.93; N, 10.66.

Methylation of **7b**.

Sodium hydride dispersion (50 mg, 50% in oil) was treated with dry benzene, and to this was added 1 ml of THF and 0.2 ml of HMPA. After cooling the mixture (ice-salt), a solution of 104 mg (0.33 mmole) of **7** in 1 ml of THF was added dropwise with stirring, and then 0.2 ml of methyl iodide was added slowly and the mixture was stirred overnight under nitrogen. The reaction mixture was poured into ice-water and extracted with benzene. Evaporation of benzene and column chromatography (benzene-ethyl acetate) of the residue gave 50 mg of almost pure **10b**.

Confirmation of the Assignment of the Doublet at 6.5 ppm in **10b**.

In order to distinguish the signals of aromatic hydrogens of the 2-anilino group from those of *N*-carbamoyl moiety in **10b**, aromatic ring deuteriated **7** was prepared. Phenyl isothiocyanate-d_5 was prepared from aniline-d_5 according to a reported procedure [8], and was distilled at 95°/13 mm. It had a band of N=C=S at 2100 cm^{-1} in the ir (neat). Reaction of the isothiocyanate with 3-aminopropanol and the cyclization of the addition product gave **7**-d_5 melting at 120-122°; ms: m/e 197 (M^+, 40), 195 ((M-D)$^+$, 100), 167 ((M-D-C_2H_4)$^+$, 15), 141 (25), 123 (29), 82 (37). Compound 7-d_5 was then converted to **10a**-d_5 and **10b**-d_5 in a similar way as for **10a** and **10b**. Compound **10a**-d_5 melted at 116-123°; ms: m/e 330 (M^+, 13), 272 ((M-D-C_3H_6N)$^+$, 5), 233 ((M-H-C_6D_5N)$^+$, 66), 224 (27), 195 (24), 188 (18), 134 (100), 106 (64), 77 (63). Compound **10b**-d_5 melted at 95-97°; ms: m/e 330 (M^+, 16), 272 ((M-D-C_3H_6N)$^+$, 6), 233 ((M-H-C_6H_5N)$^+$, 70), 224 (28), 195 (23), 188 (18), 134 (100), 106 (63), 77 (63).

In the nmr spectrum of **10b**-d_5, no doublet was found at 6.5 ppm but only a very small singlet (presumably arising from the residual *ortho* hydrogens in aniline-d_5 used as the starting material) was seen instead. Comparison of the nmr spectra of **7**-d_5 and **7**, and **10b**-d_5 and **10b** showed that the signal for the *ortho* hydrogens moved from 7.1 to 6.5 ppm when the carbamoyl group was introduced, while those of the *meta* and *para* hydrogens remained at the same place.

Conversion of **10a** to **10b**.

Compound **10a** was heated at 100° in benzene-d_6 in an nmr tube for 6 hours. The nmr spectrum showed that 30% of **10a** had been converted to **10b** and 70% of **10a** still remained unchanged.

REFERENCES AND NOTES

[1] L. Toldy, P. Sohár, and K. Faragó, *Tetrahedron Letters*, **25**, 2183 (1970).

[2a] L. Toldy, P. Sohár, K. Faragó, I. Tóth, and L. Bartalits, *Tetrahedron Letters*, **25**, 2177 (1970); [b] G. Tóth and L. Toldy, *Tetrahedron*, **27**, 5025 (1971); [c] G. Tóth, L. Toldy, J. Tamás and G. Zólyomi, *Tetrahedron*, **28**, 167 (1972).

[3] C. R. Rasmussen, F. J. Vilani, Jr., M. S. Mutter and E. A. Griffin, *J. Org. Chem.*, **51**, 1910 (1986).

[4] Though there has been a lot of controversy about the exocyclic **1a** or the endocyclic double bond structure **1b** in these compounds, the conclusion claiming the predominance of the structure **1a** by Jackman and Jen seems most convincing. We are now working on the subject; L. M. Jackman and T. Jen, *J. Am. Chem. Soc.*, **97**, 2811 (1975).

[5] A. Nabeya and T. Endo, *J. Org. Chem.*, **53**, 3358 (1988).

[6] The same assignment has been done by Rabinowitz and the coworkers for the addition product of **7** with phenyl isocyanate; E. Cherbuliez, B. Baeler, O. Espejo, H. Jindra, B. Willhalm and J. Rabinowitz, *Helv. Chim. Acta*, **50**, 331 (1967).

[7] Y. Iwakura, A. Nabeya, T. Nishiguchi and K. Ohkawa, *J. Org. Chem.*, **31**, 3352 (1966).

[8] J. E. Hodgkins and M. G. Ettinger, *J. Org. Chem.*, **21**, 404 (1956).