

HYDROGEN BONDS IN N-(3-CHLORO-2-BENZO[*b*]THIENOCARBONYL)- AND N-(2-BENZO[*b*]THIENOCARBONYL)-N'-MONOSUBSTITUTED THIOUREAS

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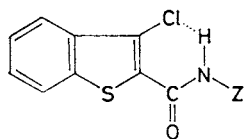
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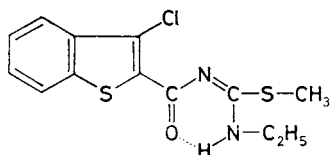
N-(3-Chloro-2-benzo[*b*]thienocarbonyl)-N'-monosubstituted thiourea derivatives undergo photocyclizations with lower yields than those obtained from analogous N',N'-disubstituted derivatives. This decreased reactivity is caused by the existence of a six-membered cyclic form with the very strong hydrogen bond $\text{NH}\cdots\text{O}=\text{C}$. The possibility of formation of various conformers has been found with N-(2-benzo[*b*]thienocarbonyl)-N'-monosubstituted thiourea derivatives as a consequence of the rotation around the $\text{C}_{(2)}-\text{C}(\text{O})$ connecting line.

Our previous report¹ dealt with the photocyclization of N-(3-chloro-2-benzo[*b*]thienocarbonyl)-N'-monosubstituted thiourea derivatives. These derivatives were found to give, on irradiation with a high-pressure mercury discharge lamp through a pyrex or quartz filter, lower yields of benzothienothiazine derivatives as compared with analogous N',N'-disubstituted thioureas².

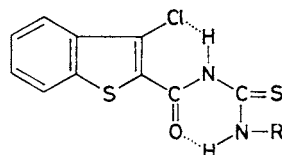
In the present paper we have tried to explain another course of the photochemical reaction of N'-monosubstituted thioureas on the basis of results of a more detailed study of the IR spectra. We presume the different reactivity to be due to differences in spatial structure caused by intramolecular hydrogen bonds. In order to solve this problem, we compared the IR spectra of N-(3-chloro-2-benzo[*b*]thienocarbonyl)-N'-ethylthiourea (*III*) with the model compounds N-(3-chloro-2-benzo[*b*]thienocarbonyl)-N',N'-diethylthiourea (*I*) and N-(3-chloro-2-benzo[*b*]thienocarbonyl)-N'-ethyl-S-methylisothiourea (*II*) which contain in their molecules only amidic and isothioamidic NH groups, respectively.



I, $\text{Z} = -\text{N}(\text{C}_2\text{H}_5)_2$

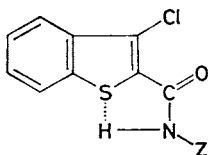


II



III, $\text{R} = \text{C}_2\text{H}_5$
IV, $\text{R} = \text{C}_6\text{H}_5$

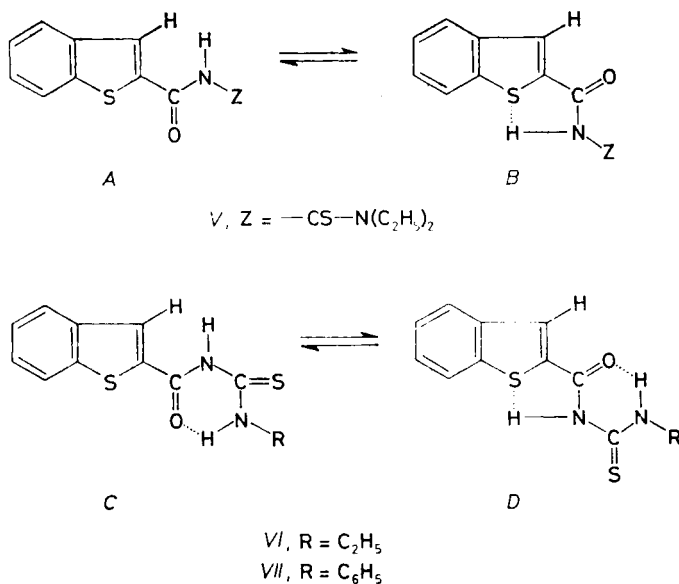
The IR spectrum of compound *I* exhibits, in the region of the valence vibrations $\nu(\text{N—H})$, a single absorption band of medium intensity at $3\,360\text{ cm}^{-1}$ which was assigned to the NH group forming a weak hydrogen bond with the chlorine atom at position 3 of the thiophene nucleus^{3,4}. For this compound it is also possible to consider the conformation *Ia* with the intramolecular hydrogen bond of $\text{NH}\cdots\text{S}$ type⁵.

*Ia*

We presume this possibility to be insignificant in our case because of the repulsive forces between electronegative chlorine atom and carbonyl group similar as in 3-chloromethyl-2-oxabenzothiazole⁶. Derivative *II* only exhibits the $\nu(\text{NH})$ vibrations of bonded isothioamide group at $3\,178\text{ cm}^{-1}$, which indicates the existence of six-membered cyclic form of this compound. Similarly, the spectrum of derivative *III* shows the absorption bands of bonded amide group NH at $3\,371\text{ cm}^{-1}$ and bonded thioamidic NH group at $3\,254\text{ cm}^{-1}$. The concentration independence of the intensity ratio of these bands and the absence of any further band of free NH group at low concentrations confirm the fact that the *N'*-monosubstituted thiourea derivatives in their ground states exist as six-membered cyclic conformers unfavourable for the cyclization. This form is also stabilized by the possibility of formation of a weaker hydrogen bond between the chlorine atom in the thiophene nucleus and hydrogen atom of amidic NH group.

These findings also agree with the IR spectrum of *N*-(3-chloro-2-benzo[*b*]thienocarbonyl)-*N'*-phenylthiourea (*IV*), its respective proton exhibiting an enhanced acidity due to delocalization of free electron pair of nitrogen atom of the phenylamine residue to the aromatic nucleus. The shift of the absorption band of the bonded thioamidic NH group to lower wavenumbers (Table I) indicates a stronger intramolecular $\text{NH}\cdots\text{O}=\text{C}$ hydrogen bond in this compound as compared with the derivative *III*. This is also confirmed by the ¹H NMR spectrum of compound *IV* (Table I) in which the signal of this proton is shifted downfield by 1.84 ppm. The existence of a stronger hydrogen bond in compound *IV* probably also causes the change in photoreactivity. Its irradiation does not produce the benzothienothiazine derivative but produces two other products, *viz.* 3-chlorobenzo[*b*]thiophene-2-carboxylic acid amide and phenyl isothiocyanate¹.

In the context of the given studies we also dealt with the IR spectra of N-(2-benzo[*b*]thienocarbonyl)-N',N'-diethylthiourea (*V*), N-(2-benzo[*b*]thienocarbonyl)-N'-ethylthiourea (*VI*), and N-(2-benzo[*b*]thienocarbonyl)-N'-phenylthiourea (*VII*) which, in contrast to the previous derivatives, have a hydrogen atom instead of chlorine at the position 3 of thiophene nucleus, *i.e.* these compounds contain no hydrogen bond of the NH···Cl type. According to literature data⁷ it is possible here to presume the existence of the *s-trans* and *s-cis* conformers formed by rotation around the C₍₂₎—C(O) connecting line. This presumption was confirmed by the IR spectra exhibiting two absorption bands (at 3 396 and 3 373 cm⁻¹) for compound *V*. They are assigned to the valence vibrations of NH groups in the *A* and *B* conformers. In the case of the compound *VI* it can be presumed that, due to the intramolecular hydrogen bond NH···O=C, the conformations *C*, *D* (in which the acylthiourea residue is present in the form of a six-membered cyclic structure) are preferred.



In accordance with the above-mentioned presumption, the IR spectrum of this compound exhibits two absorption bands of the amidic NH groups of the *C*, *D* conformers at 3 402 and 3 375 cm⁻¹ and the absorption bands at 3 241 and 3 197 cm⁻¹ due to the bonded thioamidic NH group. The lower position of absorption bands at 3 373 and 3 375 cm⁻¹ of compounds *V* and *VI* — as compared with the 3-chloro derivatives *I* and *III* (Table I) — indicates the existence of a weaker hydrogen bond of the amidic NH group with the sulphur atom of thiophene ring (the *B*, *D* conformers), which is a consequence of the electron-donor effect of the

sulphur atom interacting with the NH group. The presence of the *C*, *D* conformers is presumed in compound *VII*, too. The presumption is supported by the IR spectra of compound *VII* which show 4 absorption bands in the region of the valence vibrations $\nu(\text{NH})$. The absorption bands at 3 420 and 3 388 cm^{-1} are ascribed to the valence vibrations of the free amidic NH group and to the weaker hydrogen bond of this NH group to the sulphur atom of thiophene ring (similar to the conformers *B*, *D*). The broad absorption bands at 3 231 and 3 178 cm^{-1} belong to the bonded thioamidic NH group of the *C*, *D* conformers (Table I). In analogy to compound *IV*, also the ^1H NMR spectrum of compound *VII* (Table I) contains the signal of the NH proton (which is involved in the hydrogen bond $\text{NH}\cdots\text{O}=\text{C}$) shifted downfield by 2.18 ppm, which indicates the existence of a stronger intramolecular hydrogen bond than that in compound *VI*. From the difference of the chemical shifts of the NH proton in the compounds containing chlorine atom at position 3 of the thiophene ring (*III*, *IV*, $\Delta\delta = 1.84$ ppm) and in those without the chlorine atom (*VI*, *VII*, $\Delta\delta = 2.18$ ppm) it follows that these compounds exist in a six-membered cyclic form involving the stronger hydrogen bond of the $\text{NH}\cdots\text{O}=\text{C}$ type, which probably also causes the change in their photoreactivity.

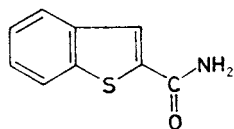
With the aim of verification of the presumptions about the effect of hydrogen bonds on the photoreactivity of the compounds investigated, we also examined the

TABLE I
The IR and ^1H NMR spectra

Compound	IR, ν , cm^{-1}					^1H NMR, δ , ppm NH
	C=O	NH \cdots O=C	NH \cdots Cl	NH \cdots S	NH	
<i>I</i>	1 675	—	3 360	—	—	8.99
<i>II</i>	1 560	3 178	—	—	—	10.81
<i>III</i>	1 653	3 254	3 371	—	—	9.93 10.38
<i>IV</i>	1 653	3 218	3 362	—	—	10.07 12.22
<i>V</i>	1 692	—	—	3 373	3 396	<i>a</i>
<i>VI</i>	1 660	3 197 3 241	—	3 375	3 402	8.75 10.45
<i>VII</i>	1 664	3 178 3 231	—	3 388	3 420	11.06 12.63

^a The NH signal is in the region of aromatic protons.

photolyses of compounds *V–VII*. The compounds *V* and *VI* are unreactive, which agrees with the fact that the photocyclization of the corresponding 3-chloro derivatives does not proceed by the electrocyclic mechanism as it was confirmed in the case of analogous esters of monothiocarbamic acid⁴. On the other hand, compound *VII* gives, as gives compound *IV* at the same conditions, analogous products, *viz.* benzo[*b*]thiophene-2-carboxylic acid amide (*VIII*) and phenyl isothiocyanate which

*VIII*

was proved by transformation into *N,N'*-diphenylthiourea (*X*) by the reaction with aniline. The reaction of compound *VII* lasts only 1 h, whereas the photolysis of compound *IV* lasts 3 h (ref.¹). The results obtained agree with the presumption that the reaction is the easier the stronger is the $\text{NH}\cdots\text{O}=\text{C}$ hydrogen bond.

Very strong absorption bands of the valence vibrations $\nu(\text{C}=\text{O})$ are found in the region from 1 653 to 1 692 cm^{-1} with all the compounds studied. The wavenumbers of the bands are affected mainly by the existence of the intramolecular hydrogen bond of the $\text{NH}\cdots\text{O}=\text{C}$ type. The decrease of the value of $\text{C}=\text{O}$ valence vibration of compound *II* is caused by enhanced conjugation of this group with the $\text{C}=\text{N}$ bond as well as by the strong hydrogen bond in evidently planar six-membered arrangement. The region from 3 060 to 3 120 cm^{-1} also contains the absorption bands due to the Fermi resonance of the first overtone of the valence vibrations $\nu(\text{C}=\text{O})$ with the valence vibration of NH bond, which is similar to secondary amides^{8,9}.

EXPERIMENTAL

The infrared absorption spectra were measured with a Specord IR 75 (Zeiss Jena) apparatus in the region from 3 600 to 800 cm^{-1} . The measurements were carried out at room temperature in adjustable cells (0.03–0.5 cm) with the concentrations from 0.004 to 0.1 mol l^{-1} , the maximum absorption being from 70 to 80%. Tetrachloroethylene was used as the solvent, the wavenumber values are given in cm^{-1} . The wavenumbers of bands were determined as average values from three measurements each, with the accuracy of $\pm 2 \text{ cm}^{-1}$. The ¹H and ¹³C NMR spectra were measured in deuteriochloroform (*V, VI*) and hexadeuteriodimethyl sulphoxide (*VII*) with a Tesla BS 487 A (80 MHz) and a Tesla BS 567 (25.15 MHz) apparatus using tetramethylsilane as the internal standard; the values of chemical shift δ are given in ppm. The UV spectra were measured with a Perkin-Elmer 402 apparatus in ethanol (concentrations from $1 \cdot 10^{-4}$ to $3 \cdot 10^{-5}$ mol l^{-1}). The positions of absorption maxima λ are given in nm and those of molar absorption coefficients $\log \epsilon$ in $\text{m}^2 \text{mol}^{-1}$. Preparation and spectral properties of compound *I* (ref.²) and *II–IV* (ref.¹) are described in literature.

Thiourea Derivatives V—VII

A solution of 13.7 mmol 2-isothiocyanatocarbonylbenzo[*b*]thiophene in 200 ml hexane was stirred and treated with a solution of 14 mmol respective amine in 10 ml benzene. The immediately separated precipitate was left to stand 1 h and collected by suction, washed with hexane, dried, and recrystallized from a suitable solvent.

N-(2-Benzo[*b*]thienocarbonyl)-*N'*,*N'*-diethylthiourea (V): Yield 80%, m.p. 103–105°C (tetrachloromethane–petroleum ether). For $C_{14}H_{16}N_2OS_2$ (292.4) calculated: 57.51% C, 5.52% H, 9.58% N; found: 57.42% C, 5.68% H, 9.34% N. IR spectrum: 3396 (N—H)_{free}, 3373 (N—H)_{bonded}, 1692 (C=O), 1515 (NHCS). ¹H NMR spectrum: 1.30 t, 6 H, (CH₃, $J_{AB} = 7$ Hz); 3.80 m, 4 H (CH₂); 7.38 m, 2 H, 7.83 m, 2 H and 7.94 s, 1 H (2-substituted benzo[*b*]thiophene). ¹³C NMR spectrum: 179.84 s (C=S), 160.06 s (C=O). UV spectrum: 208 (3.42), 230 (3.30), 250 (3.30), 289 (3.43).

N-(2-Benzo[*b*]thienocarbonyl)-*N'*-ethylthiourea (VI): Yield 89%, m.p. 115–117°C (cyclohexane). For $C_{12}H_{12}N_2OS_2$ (264.4) calculated: 54.51% C, 4.57% H, 10.59% N; found: 54.69% C, 4.40% H, 10.78% N. IR spectrum: 3402 (N—H)_{free}, 3375, 3241, and 3197 (N—H)_{bonded}, 1660 (C=O), 1500 (NHCS). ¹H NMR spectrum: 1.31 t, 3 H, (CH₃, $J_{AB} = 7$ Hz); 3.73 m, 2 H (CH₂); 7.45 m, 2 H, 7.85 m, 2 H, and 7.92 s, 1 H (2-substituted benzo[*b*]thiophene); 8.75 s, 1 H (NH); 10.45 s, 1 H (NH). ¹³C NMR spectrum: 179.10 s (C=S); 161.70 s (C=O). UV spectrum: 214 (3.98), 242 (4.05), 306 (4.11).

N-(2-Benzo[*b*]thienocarbonyl)-*N'*-phenylthiourea (VII): Yield 83%, m.p. 189–191°C (acetone–water). For $C_{16}H_{12}N_2OS_2$ (312.4) calculated: 61.52% C, 3.87% H, 8.97% N; found: 61.73% C, 3.66% H, 9.18% N. IR spectrum: 3420 (N—H)_{free}, 3388, 3231, and 3178 (N—H)_{bonded}, 1664 (C=O), 1508 (NHCS). ¹H NMR spectrum: 7.24–7.95 m, 9 H and 8.54 s, 1 H (2-substituted benzo[*b*]thiophene and aromatics); 11.06 s, 1 H (NH); 12.63 s, 1 H (NH). ¹³C NMR spectrum: 178.10 s (C=S); 162.13 s (C=O). UV spectrum: 211 (3.64), 230 (3.49), 258 (3.39), 311 (3.66).

Photolysis of Compound VII

A solution of 0.91 g (2.9 mmol) thiourea VII in acetone (250 ml) was irradiated with a high-pressure mercury discharge lamp (TQ 150 Original Hanau) through a pyrex filter for 1 h in an immersion apparatus equipped with a magnetic stirrer with the discharge lamp placed in a quartz, water-cooled jacket. Nitrogen gas was passed through the mixture during the photolysis and 15 min before its beginning. Thereafter, the acetone was evaporated and the residue was mixed twice with 50 ml hot hexane, thoroughly shaken, and filtered. The filtrate containing phenyl isothiocyanate was concentrated to the volume of 40 ml and treated with 0.28 g (3 mmol) aniline. After one day standing a precipitate was obtained: yield 0.33 g (50%) *N,N'*-diphenylthiourea (X), m.p. 154–155°C (ethanol–water); ref.¹⁰ gives m.p. 155°C. The precipitate of benzo[*b*]thiophene-2-carboxylic acid amide (VIII) which remained after the mixing with hexane was dried and recrystallized from an ethanol–water mixture. Yield 0.50 g (98%), m.p. 174–175°C; ref.¹¹ gives m.p. 177°C.

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