HYDROGEN BONDS IN DERIVATIVES OF N-SUBSTITUTED N′-BENZOYL- AND N′-(2-CHLOROBENZOYL)THIOUREA

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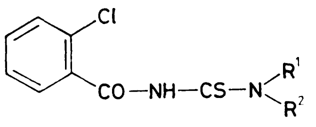
Received July 25, 1990
Accepted October 10, 1990

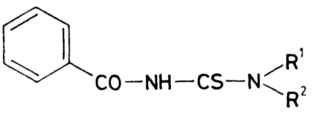
Intramolecular hydrogen bonds of the N—H···O=C type have been detected in the derivatives of N-substituted N′-benzoyl- and N′-(2-chlorobenzoyl)thiourea on the basis of IR spectral studies. The title compounds can exist in two tautomeric forms.

From literature[1] it is known that hydrogen bonds can affect a number of various properties of organic compounds, and the knowledge of nature of hydrogen bond can be utilized for prediction and interpretation of reactivity, structure, and stereochemistry of both simple and complex organic substances.

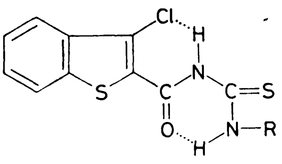
In our previous paper[2] an attempt was made to explain the different course of photochemical reaction of derivatives of N-(3-chloro-2-benzo[*b*]thienocarbonyl)- and N-(2-benzo[*b*]thienocarbonyl)-N′-monosubstituted thiourea as compared with that of its analogous N′,N′-disubstituted derivatives. We found that the differences in reactivity are due to different stereochemistry caused by formation of intramolecular hydrogen bonds. The aim of the present communication was to find whether or not there exist analogies of formation of the intramolecular hydrogen bonds and occurrence of certain conformers between the compounds mentioned and derivatives of N-substituted N′-benzoyl- and N′-(2-chlorobenzoyl)thiourea. In the IR spectra of all the compounds *I – VIII* studied we observed – in the region of 3 432 – 3 392 cm^{-1} – only the absorption bands due to free amidic NH group (Table I). The presence of these bands in compounds *I – IV* disproved our presumptions about the existence of intramolecular hydrogen bond of the N—H···Cl type such as in the analogous derivatives of the thiourea *IX* (ref.[2]). The formation of the N—H···Cl hydrogen bonds observed in the region of 3 371 – 3 360 cm^{-1} of IR spectra of these compounds can be explained by the probably higher electron density at the chlorine atom due to the electron-donor effect of the sulfur atom in the thiophene ring and by decreased possibility of rotation of the thiourea residue around the Ar—C single bond. In addition the spectra of compounds *I – III*, *V – VII* exhibit absorption bands in the region of 3 299 – 3 173 cm^{-1} (Table I) which were assigned to the intramolecular hydrogen bond formed between the hydrogen atom of the thioamide NH group and the oxygen atom of carbonyl group$^{2-5}$. The fact that the intensity ratio of these bands is independent of concentration and that no additional band of free NH group is present at low concentrations confirms the predominant six-membered cyclic form of the given compounds. The derivatives of N-substituted N'-benzoylthiourea form a stronger hydrogen bond of the type N—H···O=C as compared with the corresponding compounds with a chlorine substituent at 2-position of the aromatic nucleus. This is explained by the strong $-I$ effect of chlorine atom which decreases the electron density in the aromatic nucleus as well as the partial negative charge on the oxygen atom involved in the hydrogen bond formation. The strength of hydrogen bonds is also affected by the substituents bound to the thioamide group. The alkylsubstituted thiourea derivatives *II*, *VI* form weaker intramolecular hydrogen bonds due to the $+I$ effect of the alkyl groups which lower the acidity of hydrogen atom in thioamide group. On the other hand, the aryl substituents in compounds *III*, *VII* increase the said acidity and, hence, also the strength of hydrogen bond. The shifts in wavenumbers of the valence vibrations involved in the intramolecular hydrogen bond N—H···O=C in the compounds *I*–*III*, *V*–*VII* stand in accordance also with the respective ^{1}H NMR spectra in which the corresponding proton signal exhibits a downfield shift (10·1 – 12·6 ppm) (Table I). All the compounds studied show very strong absorption bands of the valence vibrations ν(C=O) in the region of 1 717 – 1 665 cm^{-1}. The IR spectra of the compounds mentioned show – in the region of 3 191 – 3 139 cm^{-1} – additional absorption bands due to the Fermi resonance of the first overtone of the valence vibrations ν(CO) with the valence vibrations of NH bond, which is a similar situation to that of secondary amides^{6,7}.



I, $R^1 = R^2 = H$
II, $R^1 = H$; $R^2 = C_2H_5$
III, $R^1 = H$; $R^2 = C_6H_5$
IV, $R^1 = R^2 = C_2H_5$



V, $R^1 = R^2 = H$
VI, $R^1 = H$; $R^2 = C_2H_5$
VII, $R^1 = H$; $R^2 = C_6H_5$
VIII, $R^1 = R^2 = C_2H_5$



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According to literature data[4,5,8], thiourea derivatives can exist in two tautomeric forms: thione and thiol form. This is in accordance with the IR spectra of compounds *II*, *III*, *VI*, *VII* which exhibit always two absorption bands due to the valence vibrations of the bonded NH groups in the two forms *A* and *B* (Table I). The IR spectra of compounds *I*, *IV*, *V*, *VIII* always exhibit only one absorption band in the region of 3 299 – 3 232 cm^{-1} which was assigned to the thione form. As with N-(3-

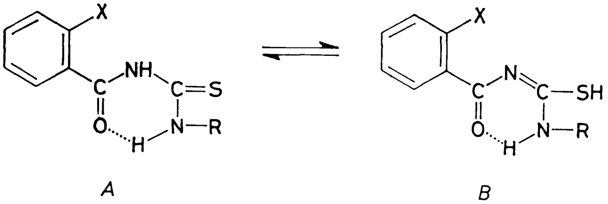


TABLE I

IR and ^{1}H NMR spectral parameters of the thiourea derivatives *I*– *VIII*

Compound	IR, ν(cm^{-1}), tetrachloroethylene $(C{=}O)_{free}$	$(C{=}O)_{bonded}$	$(NH_2)_{as}$	NH	NH···O=C thione form	NH···O=C thiol form	Fermi resonance	^{1}H NMR, δ(ppm) NH
I	—	1 674	3 489	3 404	3 299	—	—	9·30 9·80
II	—	1 667 1 683	—	3 406	3 264	3 231	3 191	9·25 10·45
III	—	1 665 1 680	—	3 400	3 233	3 181	3 142	9·30 12·40
IV	1 701 1 717	—	—	3 392	—	—	—	8·50
V	—	1 682	3 489	3 432	3 292	—	—	9·20 10·10
VI	—	1 677 1 683	—	3 427	3 253	3 220	3 187	9·10 10·70
VII	—	1 671 1 684	—	3 425	3 232	3 173	3 139	9·10 12·60
VIII	1 696 1 705	—	—	3 392	—	—	—	8·50

-chloro-2-benzo[*b*]thienocarbonyl)-N'-ethyl-S-methylisothiourea[2] the vibrations ν(NH) of bonded isothioamidic group at 3 178 cm^{-1} are only observed, we ascribed the absorption bands in the region of 3 231 – 3 173 cm^{-1} to the thiol form. The thione–thiol tautomerism of compounds *II*, *III*, *VI*, *VII* is also confirmed by the split bands of valence vibrations ν(C=O) which correspond to both the bonded forms of carbonyl group. An attempt was also made at quantitative evaluation of strength of hydrogen bond of the compounds investigated. The thermodynamic quantities ΔH^0, ΔS^0 were calculated from the graphically differentiated IR absorption bands of the derivatives *II*, *III*, *VI*, *VII* measured at various temperatures (Table *II*). These spectra could not be evaluated with derivative *III* (N-phenyl-N'-(2-chlorobenzoyl)thiourea) because of the coalescence of the thione and thiol forms with increasing temperature. In a certain way this fact confirms the equilibrium between the thione and thiol forms. The strongest intramolecular hydrogen bond of the N—H···O=C type is formed in N-phenyl-N'-benzoylthiourea (*VII*). The approximately equal values of its energy for the thione and thiol forms (Table II) show that the substance can exist in the tautomeric equilibrium. On the other hand, the energy values of the hydrogen bonds in compound *VI* indicate the predominance of the thione form. In the IR spectrum of compound *II* the thiol form is only perceptible in the form of a small shoulder whose temperature dependence could not be evaluated.

From the IR spectral results given it can be concluded that the existence of two tautomeric forms also affects the reactivity of these compounds. The N'-(2-chlorobenzoyl)thioureas prepared from primary alkyl and aryl amines give derivatives of quinazolines on heating in dimethylformamide in the presence of lithium hydride. The benzoyl- and 2-chlorobenzoylthioureas obtained from arylamines give benzothiazole products on treatment with bromine[9]. As the N-alkyl-N'-(2-chlorobenzoyl)thioureas *I* and *II* predominantly exist in their thione form *A*, this form will probably

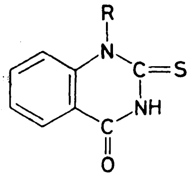
TABLE II

Thermodynamic parameters of the derivatives *II*, *VI*, *VII*

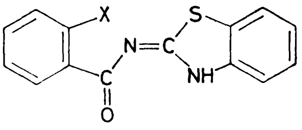
Compound	N—H···O=C (thione form)		N—H···O=C (thiol form)	
	ΔH^0 kJ mol^{-1}	ΔS^0 J K^{-1} mol^{-1}	ΔH^0 kJ mol^{-1}	ΔS^0 J K^{-1} mol^{-1}
II	−1·10 ± 0·48	5·60 ± 1·44	[a]	[a]
VI	−1·91 ± 0·17	9·38 ± 0·5	−5·33 ± 0·3	−4·29 ± 0·89
VII	8·32 ± 1·57	18·00 ± 4·5	6·08 ± 2·68	22·67 ± 5·7

[a] The value cannot be estimated.

favour the formation of quinazoline products *C*. On the other hand, in the case of



C



D, X = H,Cl

N-phenyl-N′-(2-chlorobenzoyl)thiourea (*III*) the thione and thiol forms are in equilibrium. It is presumed that the thione form of this compound supports the formation of quinazoline derivatives *C* and its thiol form favours the reaction producing 1,3-benzothiazole compounds *D*. Similarly, the thiol form of N-phenyl-N′-benzoylthiourea (*VII*) gives the corresponding derivative *D*.

EXPERIMENTAL

The IR absorption spectra were measured with a Specord IR 75 (Zeiss Jena) apparatus in the region of 3 600—800 cm^{-1}. The measurements were carried out at room temperature using a cell of adjustable thickness (0·1—0·5 cm) and the concentration range of 0·002 2—0·06 mol l^{-1} with tetrachloroethylene and chloroform as the solvents. The wavenumbers ν are given in cm^{-1}. The wavenumber values of bands of the functional groups were obtained as mean values from three measurements with the accuracy of ± 2 cm^{-1}. The ^{1}H NMR spectra were measured in deuteriochloroform at 80 MHz using a Tesla BS 487 A apparatus with tetramethylsilane as the internal standard; the values of chemical shifts are given in ppm (δ scale). The temperature-dependent spectra were measured with a Specord IR 75 (Zeiss Jena) apparatus within the range of 3 600—2 500 cm^{-1}. The measurements were carried out in thermostated cells with a heating jacket, the cell thickness of 0·06 cm, the temperature range of 21—110°C. The temperature of solutions in the cells (concentrations of 0·025—0·06 mol l^{-1}) was measured by means of a millivoltmeter and thermocouple (Fe-const., 15·5 mV—300°C 290 ohm) with the accuracy of ±0·5°C. Tetrachloroethylene was used as the solvent, and the values of ΔH^0 and ΔS^0 are presented. The equilibrium constants were calculated from the relation $K = A_b a_b / A_f a_f$, where A_b, A_f are the integrated absorption intensities of the bands of the bonded thioamidic and free amidic NH groups, respectively, and a_b, a_f are the band intensities related to one molecule. The calculation starts from the presumption that the a_b/a_f ratio is temperature independent within a reasonably narrow temperature interval. The thermodynamic quantities ΔH^0 and ΔS^0 were calculated from the dependence of log K on T^{-1}. The preparation methods and spectral properties of compounds *I*—*IV* (ref.[9]), *V* (refs[10,11]), *VI*, *VIII* (ref.[12]), *VII* (refs[13,14]) are given in literature.

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Translated by J. Panchartek.