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Journal of Molecular Structure 743 (2005) 29–48

Journal of MOLECULAR STRUCTURE

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Furan derivatives of substituted phenylthiourea: spectral studies, semi-empirical quantum-chemical calculations and X-ray structure analyses

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Received 24 January 2005; accepted 16 February 2005
Available online 6 April 2005

Abstract

Fifty new derivatives of 1-(furan-2-carbonyl)- and 1-(furan-3-carbonyl)-3-phenyl substituted thiourea have been synthesised and identified. Intramolecular hydrogen bonds were investigated in detail, using IR spectroscopy. The three-level Fermi resonance effect in the IR spectra was analysed after deconvolution and band separation. Semi-empirical quantum-chemical calculations (AM1 and PM3) support the results of the IR spectroscopic studies. X-ray single crystal diffraction analyses of four selected compounds, namely 1-(furan-3-carbonyl)-3-(2-trifluoromethyl-phenyl)-thiourea (**1e**), 1-(2-methyl-furan-3-carbonyl)-3-(2-trifluoromethyl-phenyl)-thiourea (**2e**), 1-(2,6-dichloro-phenyl)-3-(2-methyl-furan-3-carbonyl)-thiourea (**2n**) and 1-(4-methoxyphenyl)-3-(3-methyl-2-furan-carbonyl)-thiourea (**3e**), corroborated the molecular and crystal structure of these compounds. Relatively strong intramolecular hydrogen bonds of the N–H···O=C type as well as intermolecular two-centred and bifurcated three-centred hydrogen bonds were observed, confirming the results of the IR spectral study and the semi-empirical quantum-chemical calculations. A variety of intermolecular interactions, yielding the supramolecular architectures in the four crystalline compounds, are discussed in detail.

Keywords: Thiourea; Hydrogen bonds; Fermi resonance; AM1; PM3; X-ray structure analysis

1. Introduction

Their interesting biological properties, potential for practical application and availability have considerably stimulated structure investigation of derivatives of thiourea [1–3], especially, with respect to their capability of hydrogen bond formation [4]. Besides an interest in preparation and properties of individual molecules, an increasingly significant portion of up-to-date research in organic chemistry concerns interactions among molecules. Such interactions are governed by intermolecular forces whose energetic and geometric properties are less well understood than those of covalent bonds. Conventional hydrogen bonds (i.e. O–H···O, N–H···O) play a dominating role among intermolecular interactions due to their strength and directionality. They are also known to influence properties and functions of biologically significant substances, e.g. saccharides, proteins and nucleic acids [5]; hence information about hydrogen bond interactions involving these molecules has proved to be essential for the understanding of biochemical processes of vital importance, such as enzyme–substrate, drug–receptor, and protein–ligand interactions, among others. Nevertheless, because recognition as well as packing of molecules is determined by a sensitive balance of many different intermolecular

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doi:10.1016/j.molstruc.2005.02.014

forces, a substantial amount of chemical research today is directed toward increasing the understanding of the nature and character of weaker interaction forces than those of classical hydrogen bonds [6,7]. Interactions involving organic halogens have been discussed in the literature for some considerable time [8,9]. However, hydrogen bonds, differing from the conventional X–H···X (X = O, N) case, such as C–H···O and X–H···π interactions (X = O, N, C) [10–15], anti-hydrogen bonds [16–18] and the 'dihydrogen bond' X–H···H–M (X = O, N; M = Ir, Re) [10] have been recognized as interactions of chemical relevance only during the last decade. Moreover, although sulphur, an important element in biochemistry, can be regarded as a conventional H-bond acceptor [19], the X–H···S bonds (X = O, N) are only of moderate strength [20] and together with the considerably weaker C–H···S interactions are demanding further evidence. In this connection, investigation of the conditions and requirements of formation of hydrogen bonds and related intermolecular interactions by various thiourea derivatives in the solid state may lead to valuable information about interaction modes between selected functional groups, on the one hand, and about the characteristics of this compound family, on the other.

Conventional hydrogen bonds can be detected by vibrational spectroscopy. In addition, very specific so-called resonance phenomena can also be observed in vibrational spectra, mainly Fermi resonance, which is very important for analysis of rotation–vibration spectra and correct interpretation of hydrogen bonds. We encounter it mainly in polyatomic molecules, if two or three vibrational levels exhibit the same symmetry and similar energies.

In accordance with the ideas mentioned above, the aim of the present investigation has been to contribute to the study of hydrogen bonds in four series of, mostly novel, 1-(furan-2-carbonyl)- and 1-(furan-3-carbonyl)-3-phenyl-substituted thiourea derivatives. These compounds seem to us to be good model compounds for such a study, because they contain various heteroatoms and functional groups accessible to formation of hydrogen bonds. We have therefore studied hydrogen bonding in this class of compounds, using IR spectroscopy, semi-empirical calculations and X-ray diffraction analysis.

2. Results and discussion

2.1. Syntheses

The derivatives of 1-(furan-2-carbonyl)- and 1-(furan-3-carbonyl)-3-phenyl-substituted thiourea (**1a**–**1n**, **2a**–**2p**, **3a**–**3n**, **4a**–**4f**) (Scheme 1) were prepared by reaction of corresponding furoylisothiocyanates with amines. The molecular structures of the newly synthesized compounds were established by IR and NMR spectral methods. The details are gathered in the experimental part.

2.2. IR spectroscopy

IR spectra of 1-(furan-2-carbonyl)- and 1-(furan-3-carbonyl)-3-phenyl thiourea derivatives are shown in Table 1.

In a detailed study of the IR spectra of these substances, we observed the absorption bands belonging to the free amidic NH group, which appear in the 3423–3385.1 cm^{-1} region (Table 1). The spectra of all studied compounds exhibit absorption bands also in the 3238.3–3208.8 cm^{-1} region, which we attribute to intramolecular hydrogen bonding between the hydrogen atom of the thioamidic NH group and the oxygen atom of the carbonyl group [4,21,22]. The concentration independence of the intensity ratio of those bands as well as the absence of another band of the free NH group at low concentrations also indicate that the compounds occur mostly in the conformation containing the closed, H-bonded six-membered ring. In addition to the hydrogen bond indication, we also observed anomalous splitting of the absorption bands of the thioamidic NH bond due to Fermi resonance [23,24], with the $\nu(C{=}C)_{ar}$ overtone and the $\nu(C{=}C)_{ar}+\delta(NH)$ combination vibration, so it gives the interaction for three vibrational levels (Table 1). It is also well known that Fermi resonance can play a major role not only in strong hydrogen bonds, but also in relatively weak hydrogen bonds [25,26]. This implies that, if we want to assess the hydrogen bond strength, we have to obtain the wave number of the absorption bands without the influence of Fermi resonance, because only such wave numbers will be dependent solely on the force constant [27]. For this reason, the relations based on the method of Langseth and Lord and improved by Nyquist et al. [28] have been applied in cases involving three-level interactions to enable the calculation of the wave numbers of the bands, corrected for Fermi resonance (Table 1). We found that the first band in the Fermi triplet is associated with the branch that, after elimination of the resonance, belongs to the bonded $\nu(NH)$ stretching vibration. The middle branch of the triplet can be assigned to the first overtone $\nu(C{=}C)_{ar}$ of the phenyl ring, and the other side branch of the triplet is connected with the $\nu(C{=}C)_{ar}+\delta(NH)$ combination vibration. From the unperturbed wave number values we calculated the extent of interaction [28,29] between the absorption band pairs W_{AB}, W_{BC}, W_{AC} (Table 1), and found that the $\nu(NH\cdots O{=}C)$ ground stretching vibration interacts more with the $\nu(C{=}C)_{ar}+\delta(NH)$ combination vibration than with the $\nu(C{=}C)_{ar}$ overtone in almost all of the compounds. The very strong absorption bands of the carbonyl stretching vibrations lie within the 1699.6–1670 cm^{-1} range for all the compounds, but the wave numbers are also affected by the intramolecular NH···O=C hydrogen bonds. The strength of those hydrogen bonds can be demonstrated by calculating their force constants [30] from the band positions corrected for Fermi resonance. For the NH···O=C hydrogen bonds, the force constants lie within the $(5.749–5.654)\times 10^{2}$ $N\,m^{-1}$ range. These results could be compared with previous data