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# Structure and solid–liquid phase transition thermodynamics of *N*-(diethylaminothiocarbonyl)benzimido derivatives

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Dedicated to Professor Eberhard Hoyer on the occasion of his 80th birthday.

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#### 1. Introduction

#### ABSTRACT

A set of three *N*-(diethylaminothiocarbonyl)benzimido derivatives was structurally characterized by solid state single crystal X-ray diffractometry. The temperature, standard molar enthalpies, and entropies of fusion were measured and derived using differential scanning calorimetry, including two more derivatives, whose structures have been published before. The compounds were further analysed by solid state FTIR spectroscopy and the experimental FTIR spectra were compared with the calculated gas phase spectra at the B3LYP/6-311+G(d) level of theory. The structural results for the set were further used in the interpretation of thermophysical phase transition properties of the title compounds. A detailed molecular picture of *N*-(diethylaminothiocarbonyl)benzimido derivatives was obtained from Natural Bond Order (NBO) analysis. The combination of the applied methods reveals a deeper insight into the structures of this type of compound.

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*N*-(diethylaminothiocarbonyl)benzimido derivatives are relatively stable substances; many members of this family may act as bidentate ligands with the potential of forming complexes with transition metal ions [1,2]. These compounds have been investigated because of their application as radio pharmaceuticals ( $^{99m}$ Tc) [3]. A large number of serine proteinase inhibitors has been developed, starting from benzamidine and its derivatives [4–6]. Reports on the thermochemistry of *N*-(diethylaminothiocarbonyl)benzimido derivatives [7,8] and some of their Ni-complexes [9] are available. Generally, we can state that understanding structure-energy relations of thiourea derivatives may help our understanding of the binding process in biologically relevant materials.

Here we report on structural and thermophysical properties of the following compounds: *N*-(diethylaminothiocarbonyl)benzamidine, PhCNH<sub>2</sub>NCSNEt<sub>2</sub> (**1**), *N*-(diethylaminothiocarbonyl)-*N*'-phenylbenzamidine, PhCNHPhNCSNEt<sub>2</sub> (**2**), *N*-(diethylaminothiocarbonyl)-*N*'-monoethylbenzamidine, PhCNHEtNCSNEt<sub>2</sub> (**3**), *N*-(diethylamino-

thiocarbonyl)-*N*,*N*-diethylbenzamidine, PhCNEt<sub>2</sub>NCSNEt<sub>2</sub> (**4**), and *N*-(diethylaminothiocarbonyl)benzimido ethylester, PhCOEtNCSNEt<sub>2</sub> (**5**), as shown in Fig. 1. The solid state structures of compounds **3–5** have been resolved by single crystal X-ray diffractometry and are published here. The crystal structures of compounds **1** [10] and **2** [11] have been published elsewhere.

This work is part of our research on structure-energy relationships of thiourea derivative based ligand systems [12,13] as well as their related transition metal complexes [14].

### 2. Experimental

#### 2.1. Synthesis

The synthesis was performed as described in detail elsewhere [1]: Pure *N*-(diethylaminothiocarbonyl)benzimide chloride (available through the reaction of equimolar amounts of bis(*N*', *N*'-diethyl-*N*-benzoylthioureato)nickel(II) and thionyl chloride in dried THF) reacts with ammonia or primary or secondary amines, in acetone. In the presence of proton trapping reagents (excess of ammonia or an equimolar amount on triethylamine) and after removal of the precipitated triethylamine hydrochloride and

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Selection of N-(diethylaminothiocarbonyl)benzimido derivatives



Fig. 1. Selection of N-(diethylaminothiocarbonyl)benzimido derivatives.

successive recrystallisation from ethanol, the respective *N*-thiocarbamoylbenzamidines (**1–4**) were yielded as pale, yellow crystals. *N*-(diethylaminothiocarbonyl)benzimidoethylester (**5**): equimolar amounts of sodium ethanoate (readily available from refluxing ethanol over sodium under a nitrogen atmosphere) and *N*-(diethylaminothiocarbonyl)benzimide chloride were dissolved in ethanol. After refluxing and removing the solvent in vacuo, the residue is taken over with 20 cm<sup>3</sup> of H<sub>2</sub>O; the precipitating oil crystallizes after applying some friction. Pale yellow crystals of **5** were washed with water and recrystallized from *n*-hexane.

The purity of the samples was checked by IR spectroscopy and by elemental analysis; the mass fraction w of C, H, N and S were as follows: for **1**,  $C_{12}H_{17}N_3S$ , found  $10^2 w(C) = 61.60$ ,  $10^2 w(H) = 7.18$ ,  $10^2$  $w(N) = 17.50, \ 10^2 \ w(S) = 13.60, \ calculated \ 10^2 \ w(C) = 61.24, \ 10^2$  $w(H) = 7.28, 10^2 w(N) = 17.85, 10^2 w(S) = 13.62;$  for **2**,  $C_{18}H_{21}N_3S$ , found  $10^2 w(C) = 69.24$ ,  $10^2 w(H) = 6.56$ ,  $10^2 w(N) = 13.60$ ,  $10^2$ w(S) = 10.58, calculated  $10^2 w(C) = 69.42$ ,  $10^2 w(H) = 6.80$ ,  $10^2$ w(N) = 13.49,  $10^2 w(S) = 10.29$ ; for **3**,  $C_{14}H_{21}N_3S$ , found  $10^2 w(C) = 63.6$ ,  $10^2 w(H) = 8.9$ ,  $10^2 w(N) = 15.9$ ,  $10^2 w(S) = 12.0$ , calculated  $10^2 w(C) = 63.84$  $10^2 w(H) = 8.04$ ,  $10^2 w(N) = 15.95$ ,  $10^2 w(S) = 12.17$ ; for **4**,  $C_{16}H_{25}N_3S$ , found  $10^2 w(C) = 65.30$ ,  $10^2$  $w(H) = 8.53, 10^2 w(N) = 13.80, 10^2 w(S) = 11.49$ , calculated  $10^2$  $w(C) = 65.94, 10^2 w(H) = 8.65, 10^2 w(N) = 14.42, 10^2 w(S) = 11.00;$ for **5**,  $C_{14}H_{20}N_2OS$ , found  $10^2w(C) = 63.5$ ,  $10^2w(H) = 7.8$ ,  $10^2 w(N) = 10.3$ ,  $10^2 w(0) = 6.0$  $10^2 w(S) = 12.0$ , calculated  $10^2 w(C) = 63.60, \ 10^2 w(H) = 7.62, \ 10^2 w(N) = 10.60, \ 10^2 w(O) = 6.05,$  $10^2 w(S) = 12.13.$ 

The relative atomic masses used were those recommended by the IUPAC Commission in 2007 [15].

#### 2.2. Structural characterization

X-ray quality single crystals for compounds **3–4** were obtained by slow evaporation of a ethanolic solution. Crystals of **5** were obtained from the re-crystallization process in *n*-hexane. The intensity data were collected by a Bruker-Nonius CCD diffractometer. Data collection, cell refinement and data reduction were made with the software package of the diffractometer: *COLLECT* [16] for data collection; *SMART* and *SAINT* [16] for cell refinement and for data reduction. Absorption correction was performed with *SADABS* [17]. The structure was solved and refined using the software: *OSC-AIL* [18] and *SHELXL97* [19]. H atoms were treated as riding atoms with C—H(aromatic), 0.95 Å, C—H(CH<sub>2</sub>), 0.99 Å, with Uiso (H) = 1.2Ueq(C), C—H(methyl), 0.98 Å, with Uiso(H) = 1.5Ueq(C). The hydrogen atom H1 of **3** was located on a difference map and refined as riding atom with Uiso(H) = 1.2Ueq(N).

Molecular graphics were produced by *ORTEPIII* [20] and *PLATON* [21]. The complete set of structural parameters in CIF format is available as an Electronic Supplementary Publication from the Cambridge Crystallographic Data Centre (CCDC 805625, 805314 and 804439, for **3**, **4** and **5**, respectively). Crystal data, data acquisition conditions and refinement parameters for the compounds are listed in Table 1.

# 2.3. Differential scanning calorimetry

The temperatures and the standard molar enthalpies of fusion for all compounds were measured in a power compensation differential scanning calorimeter, Perkin Elmer Model Diamond DSC,



# Table 1

Crystal data, data acquisition conditions and re	finement parameters for compounds 3, 4 and 5.
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	3	4	5
Empirical formula	C <sub>14</sub> H <sub>21</sub> N <sub>3</sub> S	C <sub>16</sub> H <sub>25</sub> N <sub>3</sub> S	C <sub>14</sub> H <sub>20</sub> N <sub>2</sub> OS
Formula weight (g mol <sup>-1</sup> )	$M_r = 263.40$	$M_r = 291.45$	$M_r = 246.38$
Temperature (K)	T = 150(2)	T = 150(2)	T = 150(2)
Wavelength (Mo Kα) (Å)	0.71073	0.71073	0.71073
Crystal system, space group	Orthorhombic, Pbca	Monoclinic, $P2_1/n$	Orthorhombic, Pbca
Unit cell dimensions			
a (Å)	13.5971(8)	10.9448(6)	10.2793(3)
b (Å)	13.7243(8)	14.1110(7)	14.5792(5)
c (Å)	16.2103(8)	11.4365(6)	19.0324(5)
β (°)		105.386(3)	
Volume (Å <sup>3</sup> )	3025.0(3)	1702.97 (15)	2852.27 (15)
Z, calc. density, $ ho$ (Mg m <sup>-3</sup> )	8, 1.157	4, 1.137	8, 1.231
Absorpt. coeff., $\mu$ (mm <sup>-1</sup> )	0.20	0.19	0.22
T <sub>max</sub> and T <sub>min</sub>	0.992, 0.942	0.996, 0.957	0.994, 0.938
Crystal size (mm)	$0.30 \times 0.16 \times 0.04$	$0.24 \times 0.20 \times 0.02$	$0.30 \times 0.20 \times 0.03$
F(0 0 0)	1136	632	1136
$\theta$ range for data collection (°)	3.0-29.1	3.0-27.2	2.7-29.1
Index ranges	$-17 \le h \le 18$	$-14 \le h \le 13$	$-14 \le h \le 14$
	$-18 \le k \le 18$	$-14 \le k \le 18$	$-19 \le k \le 19$
	$-22 \le l \le 20$	$-14 \le l \le 14$	$-25 \le l \le 26$
Reflections collected/Independent reflections	4066/3148	3755/2996	3834/3080
Reflections with $l > 2\sigma(l)$ ;	$(R_{\rm int} = 0.049)$	$(R_{\rm int} = 0.039)$	$R_{\rm int} = 0.049$
Completeness to $\theta$ = 27.5°	99.9%	99.3%	99.8%
Absorption correction	Multi-scan	Multi-scan	Multi-scan
Refinement method	Full-matrix least squares on $F^2$	Full-matrix least squares on $F^2$	Full-matrix least squares on $F^2$
GooF	S = 1.02	<i>S</i> = 1.03	S = 1.03
Data/parameters/restrains	4066/166/0	3755/185/0	3834/163/0
Final R indices $(I > 2\sigma(I))$	<i>R</i> = 0.037, <i>wR</i> = 0.095	R = 0.035, wR = 0.089	<i>R</i> = 0.036, <i>wR</i> = 0.097
Maximum and minimum difference peaks (e Å <sup>-3</sup> )	$\Delta  ho_{ m max}$ = 0.30	$\Delta  ho_{ m max}$ = 0.27	$\Delta  ho_{ m max}$ = 0.30
	$\Delta  ho_{ m min}$ = $-0.23$	$\Delta  ho_{ m min}$ = $-0.25$	$\Delta  ho_{\min}$ = -0.23
CCDC	805625	805314	804439

using a heating rate of  $3.33 \times 10^{-2}$  K s<sup>-1</sup>, and aluminium crucibles, with five measurements per individual compound. The temperature and heat flux scales were calibrated by measuring the temperature and the heat of fusion of recommended calibration substances. From the experimental values of temperatures and the standard molar enthalpies of fusion, the standard molar entropies of fusion of each compound were derived.

#### 2.4. Gaseous phase quantum chemical calculations

After prior conformational analysis at a less demanding level of theory, ab initio geometry optimisation for the energetically most favoured gas-phase conformers was performed using density functional theory. The quantum chemical calculations were performed at the B3LYP exchange correlation functional, which combines the hybrid exchange functional of Becke [22] with the gradient-correlation functional of Lee et al. [23] and the split-valence polarised 6-311+G(g) basis set [24] level of theory. The GaussView 3.0 [25] program was used to get visual animation and the normal vibrational modes descriptions. At the same theoretical level, analytical frequency calculations were performed to ensure true minima ( $N_{\rm img} = 0$ ). All theoretical calculations were performed with the GAUSSIAN 03 program package [26].

The bonding characteristics of the compounds studied were investigated using natural bond orbital (NBO) analysis of Reed and Weinhold [27,28]. Values for the atomic natural total charges and information on natural bond orbitals have been retrieved. The NBO analysis was performed using the NBO 3.1 program [29] as implemented in Gaussian03.

# 2.5. FTIR analysis

FTIR spectra were obtained, at room temperature, in the range of [4000–400] cm<sup>-1</sup>, using KBr pellets in a FTIR Mattson 7000 galaxy series spectrometer, with a resolution of  $2 \text{ cm}^{-1}$ . Density

functional theory gas phase vibrational spectra have been calculated at B3LYP/6-311+G(d) level of theory.

# 3. Results and discussion

#### 3.1. Crystal structures for 3, 4 and 5

ORTEP diagrams for compounds **3–5** are shown in Figs. 2–4. Compound **4** crystallises in the monoclinic  $P2_1/n$  while **3** and **5** 



**Fig. 2.** ORTEP view of **3** [*N*-(diethylaminothiocarbonyl)-*N*<sup>-</sup>-monoethylbenzamidine] showing the atom labelling. Ellipsoids represent 30% probability level.



**Fig. 3.** ORTEP view of **4** [*N*-(diethylaminothiocarbonyl)-*N*-*N*-diethylbenzamidine] showing the atom labelling. Ellipsoids represent 30% probability level.



**Fig. 4.** ORTEP view of **5** [*N*-(diethylaminothiocarbonyl)benzimido ethylester] showing the atom labelling. Ellipsoids represent 30% probability level.

crystallises in the orthorhombic Pbca space groups. The main bond lengths and angles between atoms of the aminothiocarbonyl, benzamidine and benzimido-alkylester moieties are within the expected values for similar compounds [10,11,30]. Bond lengths and angles indicate the electronic conjugation character of the aminothiocarbonyl residue (N5C4S4) and of the benzimidine (N3C2N1). The C4–N3 bond distance is significantly higher  $(3\sigma)$ than the other C—N bonds and may be attributed to a single C<sub>sp2</sub>—N type. In fact a rotation is allowed around this bond which gives rise to differences in conformation for those molecules. For compound 3 and 4, the mostly planar aminothiocarbonyl residue forms dihedral angles with the N3-C2-N1-C11 amidine residue of 72.85(7)° and  $67.17(7)^\circ$ , respectively, while in **5** the corresponding dihedral angle is of 82.02(6). The aromatic phenyl group plane makes a dihedral angle of 35.73(6)° with N3-C2-N1-C11 amidine in 3 and of 51.97(6) in 4, probably reflecting the steric hindrance of the ethyl substituent in molecule 4. Interestingly, the phenyl ring in **5** is less affected; its dihedral angle with the benzimido-alkylester moiety plane is 16.03(4).

Supramolecular structures of **3** and **4** are stabilised by N–H···S and C–H···S, interactions respectively. In **5**, a weak C–H··· $\pi$  interaction (see Table 2 for details) stabilises its supramolecular structure. In 3, the molecules are linked into sheets by the weak hydrogen bonds N1—H1...S4 (-0.5 + x, 0.5 - y, 1 - z), in C6 chains, C51—H51B···S4 (1.5 - x, 0.5 + y, z), in C5 chains. These sheets lie perpendicular to the *c*-axis and there are two anti-parallel sheets in each unit cell (Fig. 5). In 4, the molecules are linked into centrosymmetric dimers by the C24–H24···S4 (1 - x, 1 - y, -z) hydrogen bond (Fig. 6). This results in a short  $\pi \cdots \pi$  contact between the phenyl ring in the molecule at (x, y, z) and that in the centrosymmetrically related molecule at (1 - x, 1 - y, z), Fig. 7. The distance between the centres-of-gravity of the rings is 4.4486(10) Å, the perpendicular distances is 3.4428(6)Å and the slippage is 2.817 Å. In **5**, there is a short C–H $\cdots$  $\pi$  intermolecular contact. C11–H11··· $\pi_1$  (1 – x, 1 – y, 1 – z), forming a centrosymmetric dimer.  $\pi_1$  lies on the centre-of-gravity of the phenyl ring containing C21 (Fig. 8).

#### 3.2. Solid-liquid phase transition

In the temperature range (273.15 K – ( $T_{onset}$  + 10 K)), no higher order phase transitions or signs of decomposition were detected. The experimental fusion temperatures, standard molar enthalpies, and entropies of fusion, measured in a power compensation differential scanning calorimeter, Perkin Elmer Model Diamond DSC, for all compounds, are presented in Table 3.

The experimental results obtained in a crystal-liquid equilibrium study of all compounds show that **4** exhibits the lowest enthalpy of fusion, followed by **1**. Additionally, **4** shows a remarkably low fusion temperature when compared with the other *N*-(diethylaminothiocarbonyl)benzimido derivatives. These results are in agreement with the existing crystal packing constraints due to the non-existing intermolecular N—H···S hydrogen-bond interactions in **4** and **1** [10].

Starting from **1**, substances **3** and **4** can be obtained by successively substituting the hydrogen atom bond to the enamine nitrogen with ethyl groups. From the standard molar enthalpies of sublimation [7,8], derived for T = 298.15 K, as compiled in Table 4, the hydrogen bond enthalpy for the intermolecular (N–H···S) bond in **3** seems to be deducable in a similar manner as reported by Almeida and Monte for the intermolecular (NH···O) hydrogen bond in *N*-methylbenzamide [31], given the fact that crystallographic studies revealed the presence of the intermolecular (N–H···S) bond in **3**, only. But the fore mentioned procedure cannot be applied in the case of the *N*-(diethylaminothiocarbonyl)benzimido derivatives, since in **3** and **4**, the additionally detected (CH···S) interactions impede the extraction of a numerical value for the enthalpy of the intermolecular (N–H···S) bond.

Table 2

Intermolecular interactions (Å, °) in the supramolecular structures of 3, 4 and 5.  $\pi_1$  is the centroid of the C21–C26 ring.

Compound	H-bond	D—H	$H{\cdots}A$	D···A	Angle at H
3	N1– $H1$ ···S4 <sup>i</sup>	0.90	2.49	3.3393(11)	157
	C51−H51…S4 <sup>ii</sup>	0.99	2.72	3.5795(13)	145
4	C24—H24…S4 <sup>iii</sup>	0.95	2.81	3.7540(18)	172
5	C11—H11B··· $\pi_1^{iv}$	0.99	2.67	3.5518(14)	147

<sup>i</sup> (-0.5 + x, 0.5 - y, 1 - z).

<sup>ii</sup> (1.5 - x, 0.5 + y, z).

<sup>iii</sup> (1 - x, 1 - y, -z).

<sup>iv</sup> (1-x, 1-y, 1-z).



**Fig. 5.** Stereographic diagram showing the supramolecular structure for **3** [*N*-(diethylaminothiocarbonyl)-*N*-monoethylbenzamidine]. In **3**, the molecules are linked into sheets by the weak hydrogen bonds N1-H1 $\cdots$ S4 (-0.5 + *x*, 0.5 - *y*, 1 - *z*), in C6 chains, C51-H51B $\cdots$ S4 (1.5 - *x*, 0.5 + *y*, *z*), in C5 chains.



**Fig. 6.** Diagram showing the supramolecular structure for **4** [*N*-(diethylaminothio-carbonyl)-*N*'-*N*'-diethylbenzamidine]. The molecules are linked into centrosymmetric dimers by the C24–H24…S4 (1 - x, 1 - y, -z) hydrogen bond.

#### 3.3. Gaseous phase quantum chemical calculations

The total electronic energies of all *N*-(diethylaminothiocarbonyl)benzimido derivatives, as obtained from geometry optimisations of the most stable gas phase conformers, at the B3LYP/6-311+G(d) level of theory, are given in Supporting information S1. The zero-point energy correction was scaled using a 0.9887 scaling factor and the enthalpy correction using a 0.9688 scaling factor [32]. The characteristic bond distances, as obtained from quantum chemical gas phase geometry optimisations, at the B3LYP/6-311+G(d) level of theory, are given in Table 5, the atom-labelling scheme of Fig. 9 is used.

Furthermore, in order to obtain the natural atomic charges, a population analysis was performed, using the natural bond orbital (NBO) analysis [27–29]. Natural atomic charges represent nuclear charges minus the summed natural populations of the natural atomic orbitals on the atoms and characterize the ground electronic state of the molecule. The calculated charges located at the heavy atoms for both compounds are reported in Fig. 10.

For the *N*-(diethylaminothiocarbonyl)benzamidines 1-4, the negative charge is located at the three N atoms, at the S atom



**Fig. 7.** Stereographic diagram showing a short  $\pi \cdots \pi$  contact between the phenyl ring in the molecule at (x, y, z) and that in the centrosymmetrically related molecule at (1 - x, 1 - y, z) in **5** [*N*-(diethylaminothiocarbonyl)benzimido ethylester].

and at the C atoms of the ethyl groups, while the positive charges reside at the imine carbon as well as at the hydrogen atoms on the enamine nitrogen and the remaining hydrocarbon. In **1**, **3** and **4**, the incremental influence of ethyl group substitution on the enamine nitrogen leads to an increase of negative charge on the terminal N-C(S) nitrogen, while the enamine nitrogen atom suffers from a decrease in their respective negative charge; at the same time, the positive charge at the imine carbon increases. Both the sulphur and imine nitrogen atom show a qualitatively similar trend, inverse to the thiocarbonyl carbon atom; in the benzimidoester **5**, they reach their lowest values. The charge distribution is



**Fig. 8.** Diagram of **5** [*N*-(diethylaminothiocarbonyl)benzimido ethylester], showing a short C—H··· $\pi$  intermolecular contact, C11—H11··· $\pi_1$  (1 – *x*, 1 – *y*, 1 – *z*) forming a centrosymmmetric dimer.  $\pi_1$  lies on the centre-of-gravity of the phenyl ring containing C21.

#### Table 3

Fusion temperatures,  $T_{onset}$ , standard molar enthalpies of fusion,  $\Delta_{cr}^{l}H_{m}^{0}(T_{onset})$ , and standard molar entropies of fusion,  $\Delta_{cr}^{l}S_{m}^{0}(T_{onset})$ , of *N*-(diethylaminothiocarbonyl)ben-zimido derivatives.

Compound	$T_{\text{onset}}\left(\mathbf{K}\right)$	$\Delta_{cr}^{l}H_{m}^{0}(T_{onset})/kJ\ mol^{-1}$	$\Delta_{cr}^{l}S_{m}^{0}(T_{onset})/J~\mathrm{K}^{-1}~\mathrm{mol}^{-1}$
1 2 3 4	$371.42 \pm 0.26$ $374.88 \pm 0.17$ $383.36 \pm 0.30$ $334.77 \pm 0.12$	$27.18 \pm 0.28$ $29.37 \pm 0.32$ $32.74 \pm 0.40$ $25.58 \pm 0.27$ $24.20 \pm 0.20$	$73.2 \pm 0.8 78.4 \pm 0.9 85.3 \pm 1.0 76.4 \pm 0.8 92.2 \pm 1.1 1$
Э	330.34 ± 0.26	34.39 ± 0.39	98.2 ± 1.1

#### Table 4

Standard Molar Enthalpies of Sublimation,  $\Delta_{cr}^{g}H_{m}^{0}(298.15 \text{ K})$  of *N*-(diethylaminothiocarbonyl)benzimido derivatives.

Compound	$\Delta^g_{cr} H^0_m(298.15 \mathrm{K})/\mathrm{kJ} \ \mathrm{mol}^{-1}$
1	126.0 ± 1.5 [7]
2	159.4 ± 3.3 [7]
3	141.2 ± 1.2 [8]
4	122.2 ± 2.0 [7]
5	135.6 ± 2.6 [8]



Fig. 9. Atom-labelling scheme of heavy atoms.

counterbalanced with a higher positive charge at the imine carbon as well as the lower negative charge at the methylene group of the ester.

#### 3.3.1. The terminal N-C(S) bond

The two types of C–N bonds as found by X-ray crystal structure analysis are reproduced in the course of the ab initio calculations. The terminal N–C(S) bond reveals a considerable  $\pi$  overlap between the lone pair on thioamide nitrogen and the thiocarbonyl carbon, with the lone pair of nitrogen residing in a p orbital, permitting  $\pi$  overlap with the p orbital on the thiocarbonyl carbon, resulting in a trigonal planar geometry with sp<sup>2</sup> hybridization of the thioamide nitrogen; additionally a p lone pair that may delocalize into the vicinal antibonding orbitals, as well. In more detail, the nitrogen of the terminal N-C(S) bond shows sp<sup>*n*</sup> hybridization (with n = 1.60-1.73), while the occupancy of the 2 p<sub>Z</sub> orbital ranges from 1.37-1.61, indicating delocalization and a partial double bond. The terminal N–C(S) bond can be represented as a 2-centre bond, for each compound 1-5, with the equations (1-5, in Supporting information S2) describing the participating natural atomic hybrids and finally, the composition of the natural bond orbitals.

To assess the energy barrier of the resulting hindered rotation around the terminal N—C(S) bond, one-dimensional potential energy scans were performed, starting from the respective gaseous phase conformational energy minimum, using Turbomole V6.2 [33]. Relaxed scans around the terminal N—C(S) bond have been accomplished at the RI-DFT BP level using the def-TZVP basis set [34]; the calculated energy barriers of the hindered rotation are given as Supporting information S3. For the *N*-(diethylaminothiocarbonyl)benzamidines **1–4**, the barrier corresponds to an average value of ( $\Delta H^{\#} = (75.6 \pm 1.8)$  kJ mol<sup>-1</sup>). The benzimidoester **5** shows a barrier which is around 10 kJ mol<sup>-1</sup> (distinctively) higher. These

#### Table 5

Bond distances as obtained from quantum chemical gas phase geometry optimisations, at the B3LYP/6-311+G(d) level of theory (all in Å).



Compound	$R_1$	$R_2$	C2—N3	C2-N1	C4—N3	C4—N5	C4—S4
1	Н	Н	1.30392	1.35139	1.3757	1.35838	1.71298
2	Ph	Н	1.30837	1.35513	1.36952	1.36029	1.71542
3	Et	Н	1.31642	1.34033	1.36882	1.36273	1.72045
4	Et	Et	1.29744	1.36411	1.37772	1.36131	1.69431
5	-	-	1.27624	1.34642 <sup>a</sup>	1.38456	1.35880	1.68541

<sup>a</sup> Refers to the bond distance C2–O1.

Natural atomic charges from population analysis (NBO), at the B3LYP/6-311+G(d) level of theory



Fig. 10. Natural atomic charges from population analysis (NBO), at the B3LYP/6-311+G(d) level of theory.

data compare with experimental free energies of activation,  $\Delta G^{\#}$ , for hindered rotation in *N'-benzoyl-N*,*N*-diethylthiourea ((64.4 ± 0.5) kJ mol<sup>-1</sup>) [35], and *N*,*N*-diethylbenzamide (62.6 kJ mol<sup>-1</sup>) [36], as measured in solution. For the latter,  $\Delta H^{\#}$  was given with 40.92 kJ mol<sup>-1</sup> [37], indicating that the entropic contribution is not negligible, while the gas-phase calculation at the RI-DFT BP level using the def-TZVP basis set yields  $\Delta H^{\#} = 56.7$  kJ mol<sup>-1</sup>.

# 3.4. FTIR analysis

The frequencies obtained from theoretical predictions were examined and assigned using the graphical user interface Gauss-View 3.0 and compared with the experimental frequencies. The FTIR experimental data and the corresponding attempt of theoretical frequencies assignments for **1** are given as Supporting information S4. In Fig. 11, the experimental solid state vibrational frequencies are plotted against the DFT gas phase unscaled vibrational frequencies, with **1** given as an example. Its global energy minimum gas-phase conformer coincides closely with the solidstate crystal structure. A reasonably good linear correlation is obtained, when DFT gas phase and experimental solid state vibrational frequencies are directly compared. The simple scaling factor (k) correlation between the experimental wavelengths,  $v_{exp}$ , and the theoretical predictions,  $v_{\text{theo}}$ , in the form  $v_{\text{exp}} = k \cdot v_{\text{theo}}$ (k = 0.96) is in agreement with the typical recommendation for the vibrational frequency scaling factor (0.96-0.97) for the B3LYP with a Gaussian triple zeta basis set [25]. In Supporting information S5, wave numbers of characteristic valence vibrations are given for all compounds, as obtained experimentally and based on the quantum chemical calculations. The experimental IR spectra of the studied N-(diethylaminothiocarbonyl)benzimido derivatives show four valence vibrations of special interest, given the fact that all necessary structural features are available in the individual case:  $v_{NH}$  (3424–3265 cm<sup>-1</sup>),  $v_{CN(terminal N-C(S))}$  (1411–1425 cm<sup>-1</sup>),  $v_{CN(imine)}$  (1497–1692 cm<sup>-1</sup>) and  $v_{C=S}$  (1245–1253 cm<sup>-1</sup>). The observed frequencies show vibronic coupling, at times, to a considerable extent; e.g., the frequency corresponding to  $v_{CN(imine)}$ is coupled to symmetrical stretching of the benzene ring; except for 1, no simple vibrational stretch mode can be assigned to the enamine nitrogen.



**Fig. 11.** Plot of the experimental solid state vibrational frequencies y(exp) as function of the calculated (B3LYP/6-311+G(d) level of theory) gas phase unscaled vibrational frequencies, v(theo) of 1. v(exp) = .96 v(theo).

While in **1** two bands can be attributed to  $v_{\rm NH}$ , in **2** and **3** only a single signal appears, whereas it is completely missing in 4, as it is expected for the consecutive substitution of a primary amino The appearance of  $v_{CN(amine)}$  in the spectrum depends on the substituent it carries. The lone pairs at the terminal N–C(S) nitrogen and the enamine nitrogen interact with vicinal groups influencing their vibrational modes, as can be seen by applying NBO.

#### 4. Conclusion

A set of *N*-(diethylaminothiocarbonyl)benzimido derivatives has been structurally examined by solid state by single crystal X-ray diffractometry. For substance 3, an intermolecular NH···S interaction has been found, similar to the earlier reported substance 2 [11], for which recently a polymorph has been reported [38]. The temperature, standard molar enthalpies, and entropies of fusion were measured and derived using differential scanning calorimetry. The structural results for the set were further used in the interpretation of thermophysical phase transition properties of the title compounds. All compounds were further analysed by FTIR spectroscopy and the experimental FTIR spectra were compared with the calculated ones at B3LYP/6-311+G(d) level of theory. A detailed molecular picture of N-(diethylaminothiocarbonyl)benzimido derivatives was obtained from Natural Bond Order (NBO) analysis. The combination of the applied methods reveals a deeper insight into the structures of this type of compound.

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#### Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/i.molstruc.2011.08.014.

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