STERIC HINDRANCE IN THE SOLUTE–SOLVENT INTERACTIONS OF 2-SUBSTITUTED 4,5-DIMETHOXYPYRIDAZIN-3(2*H*)-ONES: AN INFRARED SPECTRAL AND THEORETICAL STUDY

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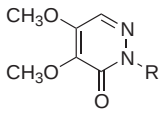
Infrared spectra for a series of 2-substituted 4,5-dimethoxypyridazin-3(2*H*)-ones (**1**) were measured in hexane (n-C_6H_{14})–$CHCl_3$ and CH_3CN–D_2O binary mixtures. The solute–solvent interactions of pyridazinones **1** were studied by correlation of $\tilde{\nu}$(C=O) values with mole fractions of the less polar components of binary mixtures. The different solute–solvent interacting species were distinguished and compared with those for 3-methyl-4-phenylthiazol-2(3*H*)-one (**2**) and previously investigated 1-methylpyrrolidin-2-one (**3**). The steric effects of the substituents adjacent to the C=O group amplified by the geometrical requirements of the six-membered pyridazin-3(2*H*)-one ring appeared to be the main factor governing the existence of individual hydrogen-bonded species. The solute–solvent interactions are sterically most restricted in pyridazinones **1**, while in thiazolones **2** they are freer and almost comparable to those in the sterically least hindered 1-methylpyrrolidin-2-ones **3**. The above results were confirmed by inspection of calculated semiempirical AM1 and PM3 and *ab initio* 6-31G* geometrical data for methyl derivatives **1h**, **2** and **3**.

Keywords: Pyridazin-3(2*H*)-ones; IR spectroscopy; Solute–solvent interactions; Interacting molecular species; Steric effects; Solvent effects; Semiempirical and *ab initio* calculations.

The solute–solvent interactions of 1-substituted pyrrolidin-2-one derivatives of type **3** in both organic and aqueous solvent mixtures were studied in a series of our earlier works[1–5]. It was shown that in the interactions of various carbonyl compounds with proton donor components of binary

mixtures it is possible to reliably distinguish the free and different interacting molecular species using the very sensitive response of the infrared C=O stretching vibrational wavenumbers ($\tilde{\nu}$(C=O))[2,4]. Such a distinction was originally discussed by Laurence *et al.*[6] on the basis of splitting of $\tilde{\nu}$(X–H) or $\tilde{\nu}$(X–D) bands of proton donors forming hydrogen bonds with carbonyl groups. Two stereochemically different types of intermolecular hydrogen bonds were found to operate between the C=O group and the proton donor: (i) the conventional angular hydrogen bond (ANG) formed by a favoured contribution of a covalent interaction between the hydrogen atom and the lone electron pairs on the oxygen atom and (ii) the linear hydrogen bond (LIN) resulting from an electrostatic attraction between the π-electrons of the C=O group and the hydrogen atom. In the cases of sterically hindered carbonyl groups, the angular interaction destabilizes and the linear hydrogen bond is favored. The above types of hydrogen bonds were later investigated also by Massat *et al.*[7] and used in a supramolecular study of binding features of molecular clip derivatives of diphenylglycoluril[8]. The importance of distinguishing angular and linear hydrogen-bonded species has been stressed in study of enzymatically catalyzed acetylation of chloramphenicol[9], where the substrate held in place by both mentioned types of hydrogen bonds.

Pyridazin-3(2*H*)-ones **1** belong to compounds possessing significant pesticidal activities[10–14]. For example, 5-amino-4-chloro-2-phenyl derivative (Pyramin) well known under the commercial name Burex is one of the most used herbicides in cultivation of the sugar beet[15]. Some pyridazin-3(2*H*)-ones were employed as starting materials for the synthesis of organophosphate pesticides[16]. The preparation of 2-substituted 4,5-dimethoxypyridazin-3(2*H*)-ones (**1a**–**1k**) was reported and their inhibition effect on the Hill reaction was studied in comparison with Pyrazone standard[17].



1	R
a	*t*-C_4H_9
b	cyclohexyl
c	*n*-C_6H_{13}
d	*n*-C_5H_{11}
e	i-C_3H_7
f	*n*-C_4H_9
g	C_2H_5
h	CH_3
i	$CH_2C_6H_5$
j	C_6H_5
k	3-$CF_3C_6H_4$

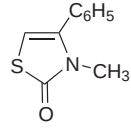


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CHART 1

Since the biological activity of a solute can be better explained by its interactions with the solvent, the aim of the present work was to study the infrared spectra of compounds **1a**–**1k** in organic *n*-C_6H_{14}–$CHCl_3$ and aqueous CH_3CN–D_2O binary solvent mixtures to distinguish the individual interacting species and compare them with 3-methyl-4-phenylthiazol-2(3*H*)-one (**2**) and the previously investigated biologically important pyrrolidin-2-ones[1–5], in particular 1-methylpyrrolidin-2-one (**3**) (Chart 1).

EXPERIMENTAL

Materials

2-Substituted 4,5-dimethoxypyridazin-3(2*H*)-ones (**1a**–**1k**) were synthesized using the previously described procedure[17]. The compounds were carefully purified by crystallization or distillation prior to use for spectral measurements. Their physical constants were in a good agreement with the reported data[17].

3-Methyl-4-phenylthiazol-2(3*H*)-one (**2**) was prepared according to the published procedures[18,19] and its physical characteristics were in a good accordance with those reported[19].

The solvents for spectral investigation – hexane, chloroform, acetonitrile and D_2O (99.8 atom %) were of spectroscopic purity (Uvasol, Merck).

Spectroscopy

Infrared spectra were recorded at room temperature using a Zeiss Specord M80 spectrophotometer. For solutions in organic *n*-C_6H_{14}–$CHCl_3$ solvent mixtures, NaCl cells with 0.1- or 0.5-mm path lengths were used and the concentrations of solutes were between 1×10^{-1} and 3×10^{-3} mol dm^{-3}. For solutions in aqueous CH_3CN–D_2O mixtures, CaF_2 cells having 0.02-mm path lengths were employed and the concentrations of solutes in the mixtures were $3–6 \times 10^{-2}$ mol dm^{-3}. The solvent mixtures were prepared in volume concentrations using Exmire microsyringes. Similarly to previous cases[1–4] no measurements under nitrogen atmosphere were needed to eliminate the effect of water-vapour bending vibrational band on the measured spectra. The maxima of the $\tilde{\nu}$(C=O) absorption bands were measured within ± 0.1 cm^{-1}.

CALCULATIONS

The computations of the C=O bond orders of pyridazinones **1** (*p*(C=O)) were performed using the semiempirical AM1 and PM3 Hamiltonians[20,21] with the program package AMPAC [22]. Geometries were completely optimized. For 2-methyl derivatives **1h**, **2** and **3** also the *ab initio* modeling was carried out at the SCF/6-31G* level[23]. The interatomic *r*(O···C) distances between the C=O oxygen atom and the methyl carbon atom, and the angles γ between the bond vectors of the C=O group and the adjacent single bond connecting the ring-nitrogen atom and the methyl group in pyridazinone **1h**,

thiazolone **2** and pyrrolidinone **3** were determined from the results of all employed quantum chemical methods.

RESULTS AND DISCUSSION

The values of the C=O stretching wavenumbers for free and differently hydrogen-bonded molecular species of pyridazinones **1** and thiazolone **2** at various compositions of organic (n-C_6H_{14}–$CHCl_3$) and aqueous (CH_3CN–D_2O) solvent mixtures are listed in Tables I and II, respectively. The assignment and names of the individual molecular species were based on the analogy with the original idea of Laurence *et al.*[6] and its application to further reports[1–5,7,8], and is illustrated in Chart 2. The highest set of $\tilde{\nu}$(C=O) values of compounds measured in the neat less polar component of the mixture, or in its mixtures with a very small amount of the more polar component belongs to the free (*i.e.* non-hydrogen-bonded) species. The lower set of the $\tilde{\nu}$(C=O) values measured in binary mixtures reflects the electrostatic attraction of the hydrogen atom of the proton donor component in the solvent mixture directed toward the π-electrons of the C=O group of solute (linear hydrogen bond). The next lower set of C=O stretching wavenumbers represents the conventional covalently hydrogen-bonded complex in which the X–H group is oriented in the direction of the n-electrons on the oxygen atom of C=O group (angular hydrogen bond). Finally, the lowest set of $\tilde{\nu}$(C=O) values can be related to the hydrogen-bonded system involving both pairs of n-electrons on the carbonyl group and complexing in the primary interaction two molecules of proton donor component of the solvent mixture (bi-angular hydrogen bond, BI-ANG). The highest $\tilde{\nu}$(C=O) values in each individual set characterizing the differently hydrogen-bonded species correspond to the primary solute–solvent interactions (with the first mole-

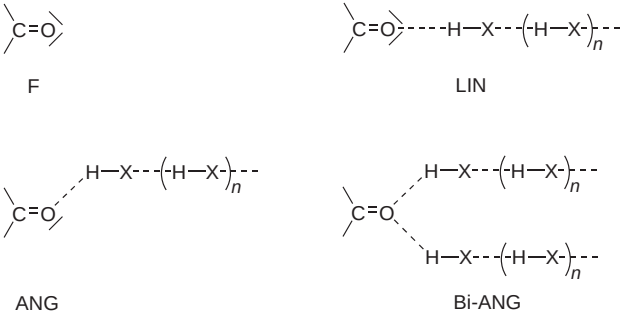

CHART 2

TABLE I

Wavenumbers of C=O stretching vibrational modes (in cm^{-1}) of molecular species of 2-R-4,5-dimethoxypyridazin-3(2*H*)-ones (**1**) and 3-methyl-4-phenylthiazol-2(3*H*)-one (**2**) in *n*-C_6H_{14}, $CHCl_3$ and in their binary mixtures

Solvent composition[a]	F	LIN	ANG	F	LIN	ANG	F	LIN	ANG	F	LIN	ANG
		1a			**1b**			**1c**			**1d**	
A	–	1638.4		–	–	1632.0	–	–	1632.0	–	–	1633.2
B	–	1638.4		–	–	1632.0	–	–	1635.2	–	–	1635.2
C	–	1638.4		–	–	1632.4	–	–	1635.2	–	–	1635.2
D	–	1638.4		–	–	1632.0	–	1638.4	–	–	1638.4	–
E	–	1638.4		–	–	1632.0	–	1638.4	–	–	1638.4	–
F	–	1638.4		–	–	1632.0	–	1638.4	–	–	1638.4	–
G	–	1641.6		–	1638.4	1632.0	–	1638.4	–	–	1638.4	–
H	–	1641.6		–	1638.4	1632.0	–	1638.4	–	–	1638.4	–
I	–	1641.6		–	1638.4	–	–	1638.4	–	–	1638.4	–
J	–	1641.6		–	1638.4	–	–	1638.4	–	–	1641.6	–
K	1650.0	1641.6		–	1638.4	–	–	1641.6	–	–	1641.6	–
L	1650.0	1641.6		1649.0	1638.4	–	1650.2	1641.6	–	1651.2	1641.6	–
M	1651.2	–		1650.0	1638.4	–	1651.2	1641.6	–	1651.2	1641.6	–
N	1651.2	–		1651.2	–	–	1651.2	–	–	1652.0	–	–
		1e			**1f**			**1g**			**1h**	
A	–	–	1633.2	–	–	1632.0	–	–	1632.0	–	–	1635.2
B	–	–	1633.2	–	–	1632.0	–	–	1632.0	–	–	1635.2
C	–	–	1635.2	–	1638.4	1632.0	–	1638.4	1632.0	–	–	1635.2
D	–	–	1635.2	–	1638.4	1632.0	–	1638.4	1632.0	–	1638.4	–
E	–	1638.4	–	–	1641.0	1632.0	–	1638.4	1632.0	–	1638.4	–
F	–	1638.4	–	–	1638.4	1632.0	–	1638.4	–	–	1638.4	–
G	–	1638.4	–	–	1638.4	1632.0	–	1638.4	–	–	1641.6	–

TABLE I
(*Continued*)

Solvent composition[a]	F	LIN	ANG	F	LIN	ANG	F	LIN	ANG	F	LIN	ANG	BI-ANG
	1e			**1f**			**1g**			**1h**			
H	–	1638.4	–	–	1638.4	–	–	1638.4	–	–	1641.6	–	
I	–	1638.4	–	–	1641.6	–	–	1638.4	–	–	1641.6	–	
J	–	1638.4	–	–	1638.4	–	–	1638.4	–	–	1641.6	–	
K	–	1641.6	–	–	1641.6	–	–	1641.6	–	–	1641.6	–	
L	1651.2	1641.6	–	1651.2	1638.4	–	1651.2	1641.6	–	1652.0	1641.6	–	
M	1651.2	1641.6	–	1651.2	1641.6	–	1651.2	1641.6	–	1653.0	1641.6	–	
N	1651.2	–	–	1651.6	–	–	1651.9	–	–	1654.7		–	
	1i			**1j**			**1k**			**2**			
A	–	1638.4		–	–	1648.0	–	–	1651.2	–	–	–	1651.2
B	–	1638.4		–	–	1648.0	–	1657.6	1651.2	–	–	–	1651.2
C	–	1638.4		–	–	1648.0	–	1657.6	1651.2	–	–	1663.0	1651.2
D	–	1638.4		–	1651.2	–	–	1657.6	1651.2	–	–	1664.0	1651.2
E	–	1641.6		–	1651.2	–	–	1657.6	1651.2	–	–	1665.2	1651.2
F	–	1641.6		–	1651.2	–	–	1657.6	1651.2	–	–	1665.2	1651.5
G	–	1641.6		–	1651.2	–	–	1657.6	1651.2	–	–	1667.2	1651.0
H	–	1641.6		–	1651.2	–	–	1657.6	1651.2	–	–	1667.2	1652.0
I	–	1641.6		–	1651.2	–	–	1657.6	1651.2	–	1672.0	1668.4	–
J	–	1641.6		–	1651.2	–	–	1657.6	1651.2	1687.0	1672.0	1668.0	–
K	–	1641.6		–	1651.2	–	1667.2	1657.6	1651.2	1687.0	1672.0	–	–
L	1657.0	1641.6		–	1651.2	–	1667.2	1657.6	–	1687.4	1672.4	–	–
M	1657.6	–		1667.2	–	–	1667.2	–	–	1687.2	1672.8	–	–
N	1657.6	–		1667.2	–	–	1670.0	–	–	1688.0	–	–	–

[a] Mole fraction of n-C_6H_{14} in n-C_6H_{14}–$CHCl_3$ mixture: A, 0.000; B, 0.064; C, 0.133; D, 0.208; E, 0.290; F, 0.388; G, 0.479; H, 0.588; I, 0.647; J, 0.710; K, 0.776; L, 0.846; M, 0.921; N, 1.000.

TABLE II

Wavenumbers of C=O stretching vibrational modes (in cm^{-1}) of molecular species of 2-R-4,5-dimethoxypyridazin-3(2*H*)-ones (**1**) and 3-methyl-4-phenylthiazol-2(3*H*)-one (**2**) in CH_3CN, D_2O and in their binary mixtures

Solvent composition[a]	F	LIN	F	LIN	F	LIN	F	LIN	ANG
	1a		**1b**		**1c**		**1d**		
A	–	*b*	–	*b*	–	*b*	–	*b*	
B	–	*b*	–	*b*	–	*b*	–	*b*	
C	–	*b*	–	1626.0	–	*b*	–	*b*	
D	–	*b*	–	1626.0	–	*b*	–	*b*	
E	–	*b*	–	1626.0	–	–	–	1626.4	
F	–	1630.0	–	1628.0	–	1626.0	–	1627.2	
G	–	1631.5	–	1628.0	–	1628.0	–	1628.0	
H	–	1632.0	–	1629.0	–	1629.0	–	1628.8	
I	–	1632.0	–	1630.0	–	1630.0	–	1630.4	
J	–	1632.0	–	1630.0	–	1630.0	–	1629.6	
K	–	1632.0	–	1630.0	–	1630.0	–	1630.4	
L	–	1633.0	1635.0	–	–	1631.0	–	1632.0	
M	1638.0	–	1636.0	–	1639.0	–	–	1633.6	
N	1641.0	–	1641.0	–	1640.8	–	1640.0	–	
	1e		**1f**		**1g**		**1h**		
A	–	1625.6	–	1626.0	–	1626.0	–	1626.4	–
B	–	1625.6	–	1626.0	–	1626.0	–	1626.4	–
C	–	1625.6	–	1626.0	–	1626.0	–	1626.0	–
D	–	1625.6	–	1626.0	–	1626.0	–	1625.6	–
E	–	1625.6	–	1626.8	–	1626.0	–	1626.0	–
F	–	1625.6	–	1626.8	–	1626.4	–	1626.8	–
G	–	1625.6	–	1628.0	–	1626.4	–	1626.8	–

TABLE II
(*Continued*)

Solvent composition[a]	F	LIN	F	LIN	ANG	F	LIN	F	LIN	ANG
	1e		**1f**			**1g**		**1h**		
H	–	1625.6	–	1628.0		–	1627.6	–	1628.0	1618.0
I	–	1625.6	–	1628.8		–	1628.8	–	1628.0	1616.1
J	–	1626.8	–	1629.2		–	1629.2	–	1629.6	1618.2
K	1635.0	–	–	1630.4		–	1629.2	–	1630.4	1619.5
L	1637.0	–	–	1631.2		–	1631.2	–	1633.0	1620.0
M	1638.8	–	–	1632.0		–	1632.0	–	1634.8	1623.0
N	1640.4	–	1640.4	–		1640.4	–	1643.4	–	1622.0
	1i		**1j**			**1k**		**2**		
A	–	*b*	–	*b*	–	–	*b*	–	*b*	
B	–	*b*	–	*b*	–	–	*b*	–	*b*	
C	–	*b*	–	*b*	–	–	*b*	–	*b*	
D	–	1628.0	–	*b*	–	–	*b*	–	*b*	
E	–	1627.0	–	*b*	–	–	*b*	–	*b*	
F	–	1630.0	–	1641.6	–	–	1641.0	–	1638.4	
G	–	1630.0	–	1641.2	–	–	1642.0	–	1638.8	
H	–	1631.0	–	1641.2	1621.0	–	1643.0	–	1640.8	
I	–	1632.0	–	1641.6	1622.0	–	1645.0	–	1640.8	
J	–	1632.0	–	1643.2	1623.0	–	1646.0	–	1642.8	
K	–	1633.0	–	1643.6	1624.0	–	1647.0	1660.0	1644.8	
L	–	1634.0	–	1644.0	1624.5	–	1649.0	1661.0	1646.0	
M	–	1634.0	1650.0	–	1627.0	–	1651.0	1662.8	–	
N	1642.0	–	1652.0	–	1630.0	1656.0	–	1664.8	–	

[a] Mole fraction of CH_3CN in CH_3CN–D_2O mixture: A, 0.000; B, 0.037; C, 0.079; D, 0.128; E, 0.185; F, 0.255; G, 0.339; H, 0.444; I, 0.506; J, 0.577; K, 0.659; L, 0.765; M, 0.866; N, 1.000. [b] Insoluble.

cule of the proton donor), while the lower belong to the secondary solute–solvent interactions extending the hydrogen bonded chains by further proton donor molecules (see Chart 2). A typical separation and distinction of interacting molecular species can be illustrated when plotting the $\tilde{\nu}$(C=O) values of solute against the mole fractions of the less polar component of a solvent mixture. Such dependences are shown for organic solutions of pyridazinones **1a**, **1b** and thiazolone **2** in Figs 1, 2 and 3, respectively. In most cases large differences were not observed between the highest and lowest $\tilde{\nu}$(C=O) values in the sets characterizing individual interacting molecular species of pyridazinones **1**, which indicates that in the six-membered ring system the secondary solute–solvent interactions are more or less hindered. This is substantially different from thiazolone **2** and the previously studied pyrrolidinones of type **3** [2,4], where the secondary solute–solvent interactions play also a significant role.

A comparison of data in Tables I and II shows that the sterically most demanding 2-*tert*-butyl derivative **1a**, but also the rotationally staggered 2-benzyl derivative **1i** exhibit in both organic and aqueous media only two interacting molecular species: the free (F) and the linear hydrogen-bonded. The behavior of the remaining pyridazinones **1** is similar. They exhibit in organic media all three, free, linear hydrogen-bonded and angular hydrogen-bonded species, while in aqueous media they show only the combination of F and LIN species. The only exception is the sterically least

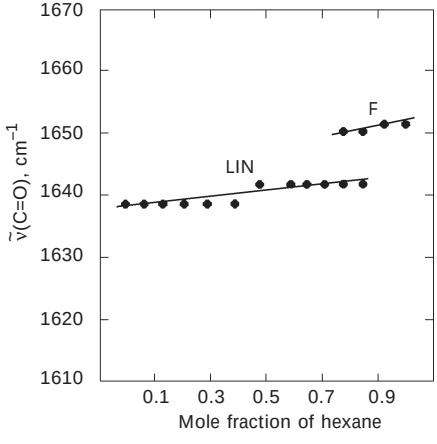

FIG. 1
Dependence of the $\tilde{\nu}$(C=O) values of molecular species for 2-*tert*-butyl-4,5-dimethoxypyridazin-3(2*H*)-one (**1a**) on the mole fraction of hexane in the mixtures of hexane and chloroform

hindered 2-methyl derivative (**1h**), which forms also in aqueous mixtures all the three interacting species: F, LIN and ANG. The comparison between the solute–solvent interactions of pyridazinones **1** in aqueous and organic media indicates that in CH_3CN–D_2O mixtures the conventional angular hydrogen bond is destabilized. This is in a contradiction with the smaller dimension

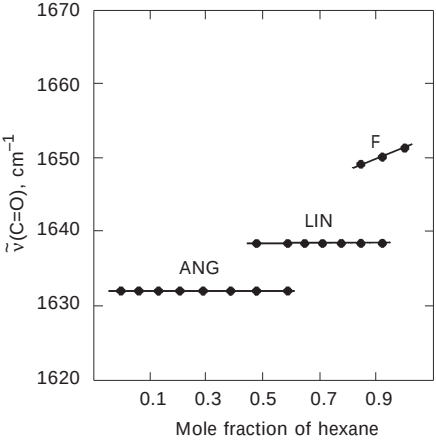

FIG. 2
Dependence of the $\tilde{\nu}$(C=O) values of molecular species for 2-cyclohexyl-4,5-dimethoxypyridazin-3(2*H*)-one (**1b**) on the mole fraction of hexane in the mixtures of hexane and chlorofom

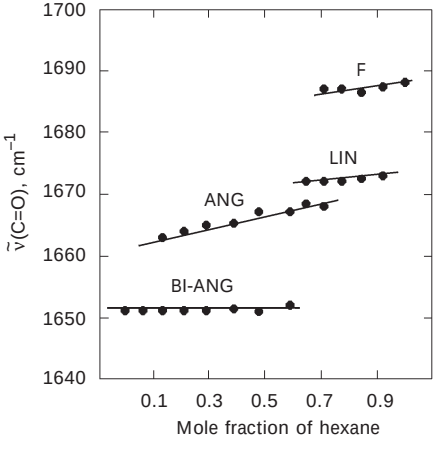

FIG. 3
Dependence of the $\tilde{\nu}$(C=O) values of molecular species for 3-methyl-4-phenylthiazol-2(3*H*)-one (**2**) on the mole fraction of hexane in the mixtures of hexane and chloroform

of the interacting D_2O molecules compared to bulky CH_3CN species. However, it can be reasonably comprehended as a result of a stronger competitive solvation interaction between the solute, CH_3CN and D_2O molecules. The behavior of the thiazolone derivative **2** is in the straight expectation with its lower steric requirements compared to pyridazinones **1**. Namely, in organic mixtures this compound exhibits all possible interacting molecular species: F, LIN, ANG and BI-ANG. In Table III there is compared the occurrence of the free and interacting molecular species formed by primary solute–solvent interactions and reflected by their characteristic $\tilde{\nu}$(C=O) values for methyl substituted pyridazinone **1h**, thiazolone **2** and pyrrolidinone **3**. The steric requirements of above heterocyclic systems are characterized by interatomic distances *r*(O···C) and angles γ in Table IV. It follows from this

TABLE III
Wavenumbers of C=O stretching vibrational modes (in cm^{-1}) of free and interacting molecular species formed by primary solute–solvent interactions for pyridazinone **1h**, thiazolone **2** and 1-methylpyrrolidin-2-one (**3**)

Compound	*n*-C_6H_{14}–$CHCl_3$ mixture				CH_3CN–D_2O mixture			
	F	LIN	ANG	BI-ANG	F	LIN	ANG	BI-ANG
1h	1654.7	1641.6	1638.4	–	1643.4	1634.8	1622.0	–
2	1688.0	1672.8	1668.0	1652.0	1664.8	1646.0	–	–
3	1712.2[a]	1697.4[a]	1683.0[a]	–	1684.6[a]	1667.4[a]	1657.0[a]	11641.0[a]

[a] Taken from ref.[4]

TABLE IV
Geometrical parameters[a] for pyridazinone **1h**, thiazolone **2** and 1-methylpyrrolidin-2-one (**3**)

Compound	*r*(O···C), nm			γ, °		
	AM1	PM3	6-31G*	AM1	PM3	6-31G*
1h	2.702	2.768	2.690	55.8	57.9	59.1
2	2.866	2.872	2.744	65.9	62.3	65.6
3	2.900	2.913	2.851	67.7	63.2	68.9

[a] See Chart 3.

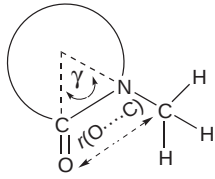

CHART 3

comparison that thiazolones and pyrrolidinones of type **2** and **3**, respectively, can exhibit molecular species involving two proton donor molecules (BI-ANG), while pyridazinones **1** form always species only with single molecules of proton donor (*i.e.* maximally ANG species). This is in a good harmony with a substantially shorter r(O···C) interatomic distance and a smaller angle γ in **1h** compared to **2** and **3**.

To investigate the substituent effect on the spectral characteristics of the free molecules and some interacting molecular species of pyridazinones **1** the $\tilde{\nu}$(C=O) values were correlated with Taft σ* substituent constants and AM1 p(C=O) values *i.e.* C=O bond orders collected in Table V. In all correlations with σ* constants, the point for compound **1i** was omitted because of its remarkable deviation from the straight lines. Neglecting of the steric effect of the bulky and conformational staggered benzylidene substituent in the Taft equation could reasonably explain this. It follows from Table VI that there are satisfactory linear correlations of between the wavenumbers of the C=O stretching vibration of free molecular species (in n-C_6H_{14} and CH_3CN) and empirical σ* constants, as well as theoretical p(C=O) values. In the case of $\tilde{\nu}$(C=O) *vs* σ* and $\tilde{\nu}$(C=O) *vs* p(C=O) correlation for data measured in D_2O–CH_3CN (1:1, v/v) mixtures all points fit the same straight line, which indicates that all molecular species have the same configuration, *i.e.* LIN. The composition 1:1 was chosen for correlation analysis as such a mixture contained the highest possible portion of D_2O for all compounds, since the solubility of pyridazinones **1** in aqueous media was limited (see Table II). On the other hand, in $\tilde{\nu}$(C=O) *vs* σ* and $\tilde{\nu}$(C=O) *vs* p(C=O) correla-

TABLE V
Calculated AM1 C=O bond orders 2-R-4,5-dimethoxypyridazin-3(2*H*)-ones (**1**)

Compound	**1a**	**1b**	**1c**	**1d**	**1e**	**1f**	**1g**	**1h**	**1i**	**1j**	**1k**
p(C=O)	1.7431	1.7495	1.7475	1.7475	1.7462	1.7459	1.7499	1.7511	1.7457	1.7703	1.7720

tions for data measured in neat $CHCl_3$ the points for compounds **1a** and **1i** were omitted, because the corresponding interacting species have a different configuration, namely LIN, while other compounds form angular hydrogen-bonded species. For example, the deviation of the point for **1a** from the straight line is 8.3 cm^{-1}. The above example shows that in particular cases the correlation analysis can be also regarded as a satisfactory method to confirm the assignment of interacting molecular species formed by solute–solvent interactions. The values for compound **1i** were omitted in all correlations, since the used Taft equation is neglecting the steric effect of the bulky and conformationally staggered benzylidene substituent.

Since the Taft σ* constant for 3-(trifluoromethyl)phenyl group has been so far unreported, we estimated it from two $\tilde{\nu}$(C=O) *vs* σ* correlations in Table V (having the highest values of correlation coefficients) and the corresponding $\tilde{\nu}$(C=O) values for compound **1k**. The average value obtained from these estimates is σ*(3-$CF_3C_6H_4$) ≅ 0.82, which means that the 3-$CF_3C_6H_4$ group is a stronger electron withdrawing substituent than the phenyl group (σ*(C_6H_5) = 0.60).

TABLE VI
Statistical results of linear correlations for 2-R-4,5-dimethoxypyridazin-3(2*H*)-ones (**1**)

$$\tilde{\nu}(C{=}O) = \rho x + \tilde{\nu}(C{=}O)^{\circ}$$

x[a]	Solvent (Solvent mixture)	Molecular species	*n*[b]	*r*[c]	*s*[d]	ρ	$\tilde{\nu}$(C=O)°	*F*[e]
σ*	*n*-C_6H_{14}	F	9[f]	0.980	1.11	18.44±1.42	1655.4	169
σ*	CH_3CN	F	9[f]	0.953	1.24	13.27±1.59	1643.4	70
σ*	$CHCl_3$	ANG	8[g]	0.970	1.43	18.72±1.90	1636.0	97
σ*	(D_2O–CH_3CN)[g]	LIN	9[f]	0.856	2.71	15.18±3.46	1630.4	19
p(C=O)	C_6H_{14}	F	11	0.936	2.53	647.20±81.16	521.8	64
p(C=O)	CH_3CN	F	11	0.961	1.59	528.16±50.36	718.2	110
p(C=O)	CH_3Cl	ANG	9[f]	0.984	1.43	722.38±49.46	370.0	213
p(C=O)	(D_2O–CH_3CN)[h]	LIN	11	0.915	2.42	527.54±77.57	706.0	48

[a] The σ* values were taken from ref.[24] [b] The number of points used in the correlation. [c] Correlation coefficient. [d] Standard deviation. [e] Fisher–Snedecor test for parameters significant at 95% level. [f] Point **1i** was omitted. [g] Points for **1a** and **1i** were omitted. [h] D_2O–CH_3CN mixture (1:1, v/v) of the mole fraction 0.255 of CH_3CN.

The conclusion can be drawn on the basis of above discussed results that in 2-substituted 4,5-dimethoxypyridazin-3(2*H*)-ones (**1**) the molecular species formed by solute–solvent interactions can by easily distinguished by the measurement of C=O stretching wavenumbers and the study of their solvent-mixture and substituent dependences. The steric hindrance in the solute–solvent interactions is dependent on the substituents in position 2 adjacent to the C=O group, but basically, the overall steric effect determined by the geometry of the heterocyclic system plays a decisive role in appearance of individual molecular species. Consequently, the six-membred pyridazin-3(2*H*)-ones **1** appeared as the sterically most hindered compounds in comparison with the five-membered thiazol-2(3*H*)-ones **2** and pyrrolidin-2-ones **3**.

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