Heteroatom and solvent effects on molecular properties of formaldehyde and thioformaldehyde symmetrically disubstituted with heterocyclic groups $C_4H_3Y$ (where $Y = O–Po$)

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**Abstract** In this work several molecular properties of symmetrically disubstituted formaldehyde and thioformaldehyde have been studied using a quantum chemistry approach based on density functional theory. Five-membered heteroaromatic rings containing a single group 16 heteroatom were taken into account as the substituents (i.e., furan-2-yl, thiophen-2-yl, selenophen-2-yl, tellurophen-2-yl, and the experimentally as yet unknown polonophen-2-yl). For the resulting ten formaldehyde and thioformaldehyde derivatives, the geometry, energetics, frontier molecular orbitals, dipole moment and polarizability of their molecules were examined in order to establish the effect of ring heteroatom on these properties. Furthermore, these properties were also determined for the molecules in three solvents of low polarity (benzene, chloroform, and dichloromethane) in order to expand our study to include solvent effects. The dipole moment and polarizability of the investigated molecules show regular variations when the ring heteroatom descends through group 16 and the solvent polarity grows. The heteroatom and/or solvent effects on the part of the studied properties are, however, more complex. An attempt is made to rationalize the observed variations in the molecular properties. The conformational behavior of the investigated molecules was also explored and the conformationally weighted values of dipole moment and polarizability are presented.

**Keywords** Quantum chemical calculations · Molecular properties · Five-membered heterocyclic substituents · Group 16 heteroatoms

**Introduction**

Organic molecules containing heterocyclic fragments constitute one of the most important research areas in modern organic, bioorganic and medicinal chemistry [1–3]. The importance of such molecules is reflected in their innumerable applications, at both laboratory and industrial scale. A reason for this importance arises from the possibility of modifying existing functions or imparting new desired features to organic molecules through the introduction of one or more heteroatoms into their cyclic fragments. The presence of heteroatoms in the resulting heterocyclic fragments leads to the redistribution of electron density and changes in possible aromatic character [4], which allows for the manipulation of various molecular properties, such as reactivity, optoelectronic properties, chelating ability and many others. These properties may be strongly affected by the occurrence of a heteroatom in a heterocyclic fragment, and by the kind of heteroatom introduced. This is usually referred to as the heteroatom effect. In the case of molecules with substituents being five-membered aromatic monocycles with a single group 16 heteroatom (furan, thiophene, selenophene, tellurophene), it is known that the heteroatom effect is responsible for changes in their properties that respond to many demands relevant to organic synthesis [5–7], optics [8–10], electronics [11], material science [12], pharmacology [13] and biology [14]. If such molecules are in solution, the surrounding solvent usually exerts an
additional influence on their properties. For instance, the dependence of their reactivity [6, 15], conformational preference [16–18], reaction kinetics [19] or spectroscopic properties [20, 21] on the presence of a solvent and its polarity has been detected.

In this work, a set of ten molecules representing symmetrically disubstituted formaldehyde and thioglycolaldehyde is the subject of a quantum chemical investigation of their molecular properties. Five-membered heterocyclic substituents C₄H₃Y containing a single group 16 heteroatom Y (furan-2-yl for Y = O, thiophen-2-yl for Y = S, selenophen-2-yl for Y = Se, tellurophen-2-yl for Y = Te, and the experimentally as yet unknown polonophen-2-yl for Y = Po) are taken into account. The resulting two series of formaldehyde and thioglycolaldehyde derivatives, also termed here symmetrical diheteroaryl ketones and thioformaldehydes, are interesting from both theoretical and experimental points of view. In general, they are useful for the synthesis of other important organic compounds [7, 22, 23]. The preparative perspective also reveals their mutual connection. Such thioketones can be prepared from corresponding ketones via oxygen/sulfur exchange, as has very recently been carried out using Lawesson’s reagent [24]. Here, the geometry, energetics, frontier molecular orbitals, dipole moment and polarizability in vacuum and in solvents, were obtained for the aforementioned two series of molecules, using a density functional theory method and an implicit solvation model. Tracking variations in these properties along the two series of molecules allowed us to establish how strongly these properties are linked with the kind of ring heteroatom and the presence of solvent. To the best of our knowledge, there are only sparse computational studies that include an analysis of heteroatom and/or solvent effects for some symmetrical diheteroaryl ketones and thioformaldehydes [17, 25, 26]. In the case of the title compounds, only molecules with light ring heteroatoms (most often with sulfur) have been studied using quantum chemical methods so far [17, 20, 21, 26–28]. This work extends our previous computational study of symmetrical diheteroaryl ketones and thioformaldehydes [26] to the full range of group 16 ring heteroatoms, and, additionally, it includes the effect of solvent.

**Computational details**

The molecular geometries of five symmetrical diheteroaryl ketones (1a–5a, see Scheme 1) and their thioformaldehyde analogs (1b–5b) were optimized in vacuum at the RI-B3LYP/def2-QZVPP level of theory [29–33]. The obtained geometries of isolated molecules were subsequently optimized in the presence of a solvent, using RI-B3LYP/def2-QZVPP and the COSMO implicit solvation model [34]. Three solvents of low polarity, in terms of both their dipole moment and dielectric constant, were considered. In order of increasing polarity, these solvents are benzene, chloroform, and dichloromethane. Our interest in solvents of low polarity arises from their frequent use in the synthesis and reactions of diheteroaryl ketones and thioformaldehydes [24]. Harmonic vibrational frequency calculations yield no imaginary frequencies for all the optimized molecular geometries. For the molecules containing heavy atoms, such as Te in 4a and 4b, and Po in 5a and 5b, the inner electrons of these atoms are modeled by the Stuttgart effective core potentials [35, 36] provided with the def2-QZVPP basis set. The [Ar]3d¹⁰ inner electrons of Te and the [Kr]4d⁴f⁴ inner electrons of Po are replaced with the Stuttgart effective potentials. The application of these effective core potentials allows for the inclusion of scalar relativistic effects in the geometry optimizations of 4a, 4b, 5a, and 5b. Such a one-component treatment of relativity should be sufficient for obtaining molecular geometries with reasonable accuracy, because scalar relativistic effects are usually much more important for geometries than spin-orbit relativistic effects [37, 38]. However, an accurate determination of energetics for molecules with heavy atoms requires a computational treatment accounting for spin-orbit coupling. Therefore, the final total energies of 4a, 4b, 5a, and 5b have been recalculated at the two-component relativistic RI-B3LYP/def2-QZVPP-2c level of theory [39, 40]. The sizes of Te and Po cores described by the def2-QZVPP-2c effective potentials are the same as those defined by def2-QZVPP. The calculations of molecular dipole moments, average static dipole polarizabilities, and polarizability anisotropies were carried out using the aforementioned levels of theory. In addition, the def2-QZVPP and def2-QZVPP-2c basis sets were augmented with a small number of moderately diffuse functions recommended for efficient computations of electronic response properties [41]. Test calculations performed for a set of small molecules with structural features occurring in 1a–5a and 1b–5b confirm that the use of these diffuse functions does improve the accuracy of the predicted molecular dipole moments and polarizabilities (see sections S1 and S2 in the Electronic Supplementary Material).

The selection of B3LYP for this work was originally based on the well-known good performance of this density functional in predicting geometries and energies [42]. The accurate prediction of electric properties is generally a more difficult
challenge for B3LYP, with its performance then depending on which electric property is calculated and what class of molecules is considered [43, 44]. There are several benchmark studies that report a relatively good performance of B3LYP for calculating low-order ground-state electric properties such as dipole moment and polarizability [45–47]. The results of our test calculations from section S2 also indicate the satisfactory performance of B3LYP for molecular dipole moments and polarizabilities in a set of small molecules with structural features occurring in 1a–5a and 1b–5b.

All calculations were carried out using TURBOMOLE (versions 6.5 and 7.0.1) [48]. Contours of frontier molecular orbitals were visualized using TmoleX 4.1 [49].

Results and discussion

Molecular geometry and stability

The molecules of the investigated compounds can adopt three conformations, differing in the orientation of ring heteroatoms (Y = O–Po) relative to the carbonyl oxygen atom (X = O) in 1a–5a or the thio carbonyl sulfur atom (X = S) in 1b–5b. The first type of conformation exists if X and both Y atoms are on the same side of the C–C bonds linking the heteroaryl substituents with the C=X group. In other words, both Y atoms display a cis-like orientation with respect to the X atom. The resulting conformer will be denoted here by the prefix cc. The trans-like orientation of X relative to Y of both heteroaryl rings leads to the tt-conformer. Finally, the third type of conformation combines a X,Y-cis-like orientation for one heteroaryl ring and a X,Y-trans-like orientation for another ring. The ct- and tc-conformers are regarded to be identical due to dissubstitution with the same heteroaryl group. In other words, the third type of conformation refers to two degenerate structures (a schematic visualization of possible conformations is presented in Scheme 2). Torsion angles τ formed by three consecutive bonds in the X=C–C–Y fragments are suitable geometrical parameters for characterizing the three conformations. Due to its symmetrical molecular geometry, each cc- and tt-conformer possesses a pair of identical τ twist angles. The values of τ for all conformers of 1a–5a and 1b–5b are shown in Tables 1 and 2.

The replacement of Y = O by a heavier group 16 heteroatom leads to a gradual increase in the twist angle of heteroaryl substituents relative to the C=X group for the tt-conformers in vacuum. Their τ values become smaller with the growing atomic radius of Y, which means that the substituents are more and more distorted from coplanarity with the C=X group. The same trend in τ is observed for the trans-like heteroaryl ring of ct-conformers. The cis-like heteroaryl ring displays less regular changes in τ but the total inclination between the planes of both heteroaryl rings still grows while Y descends through group 16. For the cc-conformers, the replacement of oxygen by a heavier Y heteroatom results in irregular changes of τ. In this case, keeping balance between some additional subtle effects, such as intramolecular X⋯Y and H⋯H interactions [28], may be decisive.

The presence of a solvent essentially strengthens the effect of Y on τ, if compared to the corresponding τ values detected for the ct- and tt-conformers in vacuum. The resulting solvent effect is, however, rather minor: the inclination between the planes of heteroaryl rings in the solvated ct- and tt-conformers grows by merely several degrees. The solvent effect does not hold for ct-1a and tt-1a, which retain their planar geometry in solvents. The inclination between the planes of heteroaryl rings is usually augmented by the increase of solvent polarity. 1a, 1b, 2a, and 2b in the cc-conformation show, however, the reverse relationship between the inclination of heteroaryl rings and the solvent dielectric constant ε.

The relative stability of individual conformers of the investigated compounds was established using the differences ΔG in the Gibbs free energies of the conformers at 298.15 K. For each compound, its most stable conformer is characterized by ΔG = 0, whereas those possessing higher (i.e., less negative) Gibbs free energies than the preferred conformer demonstrate ΔG > 0. An inspection of the ΔG values presented for the isolated molecules in Tables 1 and 2 reveals that the ct-conformation is the most energetically favorable if Y = O. Unlike 1a and 1b, all the remaining compounds prefer the cc-conformation, while their tt-conformers are least stable. The growing atomic radius of Y along the series 2a–5a and 2b–5b results in increases of ΔG for the ct- and tt-conformers. For that reason, the compounds with Y = Te, Po exhibit negligible percentage abundances of their tt-conformers relative to the cc-conformers (the conformer abundances are based on the Boltzmann distribution of conformers in their equilibrium mixture at 298.15 K; see section S1). The preferred conformers of the investigated compounds usually make dominant contributions to the corresponding equilibrium mixtures.
Table 1  Twist angles between the X and Y atoms of the X=C–C–Y fragments (τ in °) and relative Gibbs free energies (ΔG in kcal mol⁻¹) for the conformers of 1a–5a in vacuum and solvents

| Conformer | Medium | Vacuum | | Benze | Chloroform | Dichloromethane |
|-----------|--------|--------|---|--------|--------|---------------|
|           |        | τ      | ΔG a | τ      | ΔG a | τ      | ΔG a |
| ce-1a     |        | −17.7  | 2.84 [0.3] | −17.0 | 2.17 [1.1] | −16.5 | 1.76 [2.3] |
| ct-1a     |        | 0.0 (179.9) | 0.0 [80.7] | 0.0 (179.9) | 0.0 [87.8] | 0.0 (179.9) | 0.0 [88.8] |
| tc-1a     |        | 180.0  | 0.45 [19.0] | 180.0 | 0.81 [11.1] | 180.0 | 0.95 [9.0] |
| ce-2a     |        | −18.6  | 0.00 [38.8] | −18.5 | 0.00 [44.1] | −18.4 | 0.00 [49.7] |
| ct-2a     |        | −15.9 (157.9) | 0.17 [58.4] | −16.6 (157.2) | 0.30 [53.3] | −16.9 (156.9) | 0.43 [48.2] |
| tc-2a     |        | 159.2  | 1.56 [2.8] | 158.0 | 1.67 [2.6] | 157.4 | 1.85 [2.2] |
| ce-3a     |        | −18.1  | 0.00 [66.7] | −18.7 | 0.00 [68.8] | −19.0 | 0.00 [68.8] |
| ct-3a     |        | −16.1 (154.6) | 0.84 [32.6] | −16.8 (154.0) | 0.89 [30.5] | −17.2 (153.7) | 0.89 [30.5] |
| tc-3a     |        | 155.9  | 2.73 [0.7] | 154.9 | 2.70 [0.7] | 154.3 | 2.73 [0.7] |
| ce-4a     |        | −17.0  | 0.00 [90.3] | −17.5 | 0.00 [87.7] | −17.8 | 0.00 [86.3] |
| ct-4a     |        | −15.3 (150.4) | 1.74 [9.6] | −16.3 (149.8) | 1.58 [12.1] | −16.9 (149.5) | 1.51 [13.5] |
| tc-4a     |        | 152.4  | 4.16 [0.1] | 151.1 | 3.82 [0.1] | 150.5 | 3.58 [0.2] |
| ce-5a     |        | −16.7  | 0.00 [95.2] | −17.8 | 0.00 [93.9] | −18.5 | 0.00 [92.3] |
| ct-5a     |        | −14.8 (148.6) | 2.19 [4.7] | −15.7 (147.8) | 2.03 [6.1] | −16.4 (147.4) | 1.89 [7.6] |
| tc-5a     |        | 151.1  | 4.80 [0.0] | 149.7 | 4.34 [0.1] | 149.2 | 4.01 [0.1] |

ΔG a The percentage abundances of individual conformers in the equilibrium mixture of three conformers of each compound are shown in square brackets of three conformers. The lowest percentage abundances of the preferred conformer are found for 2a and 2b (38.8% and 48.8%, respectively), which results from the small ΔG values of their ct-conformers.

Table 2  Twist angles between the X and Y atoms of the X=C–C–Y fragments (τ in °) and relative Gibbs free energies (ΔG in kcal mol⁻¹) for the conformers of 1b–5b in vacuum and solvents

| Conformer | Medium | Vacuum | | Benze | Chloroform | Dichloromethane |
|-----------|--------|--------|---|--------|--------|---------------|
|           |        | τ      | ΔG a | τ      | ΔG a | τ      | ΔG a |
| ce-1b     |        | −21.4  | 2.58 [0.6] | −21.0 | 1.70 [2.5] | −20.6 | 1.27 [5.2] |
| ct-1b     |        | −6.4 (172.5) | 0.00 [89.9] | −7.8 (170.4) | 0.00 [87.2] | −8.4 (169.5) | 0.00 [88.0] |
| tc-1b     |        | 164.5  | 0.92 [9.5] | 164.5 | 0.85 [10.3] | 164.8 | 1.10 [6.9] |
| ce-2b     |        | −22.8  | 0.00 [49.3] | −22.8 | 0.00 [53.1] | −22.7 | 0.00 [56.3] |
| ct-2b     |        | −21.5 (149.7) | 0.42 [48.8] | −21.9 (149.6) | 0.51 [45.1] | −22.2 (149.7) | 0.58 [42.1] |
| tc-2b     |        | 150.6  | 1.92 [1.9] | 150.2 | 2.00 [1.8] | 150.1 | 2.11 [1.6] |
| ce-3b     |        | −22.2  | 0.00 [67.4] | −22.5 | 0.00 [67.6] | −22.6 | 0.00 [68.4] |
| ct-3b     |        | −19.9 (146.3) | 0.85 [31.9] | −20.7 (146.5) | 0.86 [31.5] | −21.2 (146.7) | 0.88 [30.7] |
| tc-3b     |        | 148.9  | 2.71 [0.7] | 148.2 | 2.62 [0.8] | 147.9 | 2.61 [0.8] |
| ce-4b     |        | −20.6  | 0.00 [89.2] | −21.0 | 0.00 [87.2] | −21.3 | 0.00 [85.7] |
| ct-4b     |        | −16.2 (141.2) | 1.67 [10.7] | −17.3 (141.6) | 1.55 [12.7] | −18.2 (142.2) | 1.48 [14.1] |
| tc-4b     |        | 146.9  | 4.24 [0.1] | 146.1 | 3.87 [0.1] | 145.9 | 3.62 [0.2] |
| ce-5b     |        | −20.3  | 0.00 [92.9] | −21.0 | 0.00 [91.5] | −21.8 | 0.00 [88.8] |
| ct-5b     |        | −15.0 (139.2) | 1.93 [7.1] | −16.1 (139.5) | 1.82 [8.4] | −17.1 (140.1) | 1.65 [11.0] |
| tc-5b     |        | 146.6  | 4.64 [0.0] | 146.4 | 4.18 [0.1] | 146.4 | 3.79 [0.1] |

ΔG a The percentage abundances of individual conformers in the equilibrium mixture of three conformers of each compound are shown in square brackets of three conformers. The lowest percentage abundances of the preferred conformer are found for 2a and 2b (38.8% and 48.8%, respectively), which results from the small ΔG values of their ct-conformers.
The presence of a solvent essentially does not change the sequences of conformers ordered relative to their stability. Such a solvent effect occurs for all the investigated compounds with one exception. For 1b solvated in dichloromethane, the sequence of higher-energy conformers is swapped, compared to the ordering of such conformers in vacuum and in two solvents of lower polarity. The solvent effect on the percentage abundances of preferred conformers is non-uniform, with both increases and decreases in abundance observed while the solvent polarity is growing. For instance, the percentage abundance of ct-1a is enhanced in polar solvents, whereas the opposite situation is observed for ct-1b. Nevertheless, a general finding can be made that an increase in the solvent polarity leads to an additional stabilization of cc-conformation for 1a-3a and 1b-3b. In consequence, the percentage abundances of these cc-conformers go up while the solvent varies from benzene to chloroform and then to dichloromethane. The solvents produce the reverse effect on the cc-conformation of 4a, 4b, 5a, and 5b. For these compounds, their ct-conformers experience an effective stabilization by the solvents with higher ε. This is accompanied by the corresponding increases in the percentage abundances of ct-conformers at the expense of cc-conformer abundances.

**Frontier molecular orbitals**

Among frontier molecular orbitals, the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) are particularly important in describing intrinsic molecular properties. Therefore, it is interesting to inspect the heteroatom and solvent effects on the HOMO and LUMO of 1a-5a and 1b-5b.

Figure 1 presents the plots of HOMO and LUMO contours for a part of the investigated molecules. The molecules shown in this figure are selected in a way that allows us to detect trends in the heteroatom effect. For 1a-3a, their HOMO shows a purely π character and it is delocalized over the heteroaryl substituents. The HOMO of the ketones with heavier ring heteroatoms (Y = Te, Po) possesses substantial contributions from the σ-based orbitals belonging to these heteroatoms, and a minor share of X-atom lone pair orbital. The LUMOs of all ketones demonstrate common features. The contribution of the π* orbital of carbonyl group predominates and the LUMOs also spread over the π*-type orbitals of heteroaryl substituents. In the case of the thioketones, their HOMO is centered mainly on the S atom of the thiocarbonyl group. In addition to the lone pair orbital of this S atom, the heavier ring heteroatoms (Y = Te, Po) also provide notable contributions to the HOMO. The LUMO of 1b-5b is fairly similar to that of the ketones.

Figure 2 presents the HOMO and LUMO levels of the isolated cc-conformers. The difference between the HOMO and LUMO levels, i.e., the HOMO–LUMO energy gap, is

![Fig. 1 Frontier molecular orbitals of 1a, 1b, 4a, and 4b adopting the cc-conformation. Contours of these orbitals are plotted with an isovalue of 0.05 a.u.](image-url)

![Fig. 2 Diagrams illustrating the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) levels of the cc-conformers of 1a-5a and 1b-5b in vacuum. The energy gaps between these levels are also shown. All energies are given in eV](image-url)
also shown for each cc-conformer. It is apparent that the growing size of Y progressively narrows the HOMO–LUMO energy gap of both the ketones and thiketones adopting the cc-conformation. Such a finding is essentially valid for the other conformations of the investigated molecules (see Figs. S1 and S2). The impact of the kind of Y on the HOMO–LUMO energy gap of the cc-conformers of 1a–5a and 1b–5b mimics the corresponding heteroatom effect observed for a series of chalcophenes C4H4Y (Y = O, S, Se, Te) [50]. The narrowing corresponding heteroatom effect observed for a series of their HOMO levels, which are shifted to lower (that is, more negative) energies upon solvation (see Fig. S4). The HOMO contours presented in Fig. 1 can serve as a rough rationalization for this shift. The HOMO of cc-1b and cc-4b resides mainly on the thiocarbonyl S atom, and the resulting polarization of the HOMO toward the S atom suggests a greater stabilization by more polar solvents. In the case of the LUMO levels of 1b–5b, their stabilization is triggered by the solvents. Unsurprising, this effect is common to both the ketones and thiketones, which is due to the striking similarity of their LUMOs. The aforementioned trends in the solvent effects on the HOMO–LUMO energy gap of the

A non-uniform behavior of 1a–5a versus 1b–5b can be seen while analyzing the solvent effect in Fig. 3. For the cc-conformers of the ketones, the presence of the solvents provokes a reduction in their HOMO–LUMO energy gap. Moreover, the HOMO–LUMO energy gap narrows gradually upon increasing the polarity of the solvents. This narrowing is predominantly caused by the stabilization of LUMO levels in the solvated cc-conformers (see Fig. S3). The HOMO levels are only marginally affected by solvation. The solvents usually have a slight destabilizing influence on these levels. Unlike the ketones, their thiocarbonyl analogs exhibit a broadening in their HOMO–LUMO energy gap upon solvation. The values of the HOMO–LUMO energy gap become larger when the solvent polarity increases. An exception to such a solvent effect occurs for 5b, whose energy gap remains practically constant in vacuum and three solvents. The broadening of the HOMO–LUMO energy gap of 1b–4b is mainly associated with their HOMO levels, which are shifted to lower (that is, more negative) energies upon solvation (see Fig. S4). The HOMO contours presented in Fig. 1 can serve as a rough rationalization for this shift. The HOMO of cc-1b and cc-4b resides mainly on the thiocarbonyl S atom, and the resulting polarization of the HOMO toward the S atom suggests a greater stabilization by more polar solvents. In the case of the LUMO levels of 1b–5b, their stabilization is triggered by the solvents. Unsurprising, this effect is common to both the ketones and thiketones, which is due to the striking similarity of their LUMOs. The aforementioned trends in the solvent effects on the HOMO–LUMO energy gap of the

Fig. 3 Plots of the HOMO–LUMO energy gap (in eV) against the COSMO correction factor f(ε) for the cc-conformers of 1a–5a and 1b–5b in vacuum and three solvents. The f(ε) values of vacuum, benzene, chloroform, and dichloromethane amount to 0.00, 0.46, 0.71, and 0.84, respectively.

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cc-conformers of 1a–5a and 1b–5b are also valid for the ct- and tct-conformers of these compounds.

**Dipole moment**

The molecular dipole moment, $\mu$, is an essential quantity describing the spatial distribution of electron charge within a molecule. It is known that the magnitude and direction of $\mu$ is sensitive to molecular size and shape, and, in consequence, different conformers of a molecule can have very different dipole moments. This happens to the molecules of 1a–5a and 1b–5b, which can adopt three conformations, each exhibiting its own abundance at 298.15 K. Therefore, it is reasonable to characterize the dipole moment of every single compound of interest by using its conformationally weighted dipole moment $\mu_{cw}$ (a methodology for calculating $\mu_{cw}$ is proposed in section S1). The calculated values of $\mu_{cw}$ for 1a–5a and 1b–5b are shown in Table 3.

We begin by discussing the calculated $\mu_{cw}$ values for the molecules of 1a–5a and 1b–5b in vacuum. The $\mu_{cw}$ values of the ketones range between 1.98 D and 3.72 D. The effect of the type of ring heteroatom on these values is clearly evident; there is a gradual decrease in $\mu_{cw}$ while Y descends through group 16. The same effect occurs for the thietiones. Their range of $\mu_{cw}$ is shifted toward higher values, but it is still of similar width to that found for the ketones. The effect of Y on $\mu_{cw}$ can be rationalized in terms of variations in the electronegativity of Y, and in the resultant local dipole moment of a heteroaryl substituent. The decrease of Y electronegativity along the series from Y = O to Y = Te is associated with a decrease in the local dipole moment of the corresponding heteroaryl substituent. The local dipole moment of a heteroaryl ring with Y = O-Se acts from the Y heteroatom toward the ring center (assuming that the dipole vector is directed toward the center of positive partial charge). Two such oriented dipole moments added to the local dipole vector of the C=X group generate a large molecular dipole moment for the cc-conformers of 1a–3a and 1b–3b. Our calculations of $\mu$ for tellurophene predict a negligible value of 0.04 D, while polonophene possesses larger $\mu$ (0.44 D) yet its orientation is reversed. The local dipole moments of the polonophen-2-yl rings compensate to a certain degree the local dipole moment of the C=X group for the cc-conformers of 5a and 5b. The high abundance of these conformers has, in turn, a direct effect on $\mu_{cw}$ and, therefore, the values of $\mu_{cw}$ for 5a and 5b are smallest in both series of compounds.

The comparison of $\mu_{cw}$ for every 1a–5a in vacuum with $\mu_{cw}$ for the corresponding thiocarbonyl analog reveals that the former is generally smaller in magnitude than the latter. This indicates that the distribution of electron charge is less polarized within the molecules of the ketones than within the molecules of the corresponding thietones. The $\mu_{cw}$ values of 1a–5a turn out to be smaller despite the fact that the electronegativity of oxygen is larger than that of sulfur and, in principle, the C=O group as such is more polarized than the C=S group [51]. In this case, the electron donor–acceptor properties of heteroaryl rings become a factor reinforcing the charge separation within the molecules of 1b–5b. An increase in the magnitude of molecular dipole moment upon replacing C=O by C=S was previously observed for diaryl ketones [52] and for uracil and its thio-analogs [53].

Having analyzed the $\mu_{cw}$ values in vacuum, we turn our attention to the solvent effect on $\mu_{cw}$. It is evident from Table 3 that the $\mu_{cw}$ values of the investigated compounds in three solvents are always larger than those characterizing these compounds in vacuum. This indicates a stronger charge separation within the solvated molecules of 1a–5a and 1b–5b than within the corresponding isolated molecules. This is because the charge distribution of each solute molecule polarizes the solvent, which, in turn, acts back on the solute molecule, enhancing its intramolecular interaction.

### Table 3

Conformationally weighted dipole moments ($\mu_{cw}$ in Debye), polarizabilities ($\alpha_{cw}$ in Å³) and polarizability anisotropies ($\Delta \alpha_{cw}$ in Å³) for 1a–5a and 1b–5b in vacuum and solvents

| Compound | Medium       | Vacuum       | Benzene         | Chloroform         | Dichloromethane        |
|----------|--------------|--------------|-----------------|--------------------|-------------------------|
|          | $\mu_{cw}$  | $\alpha_{cw}$ | $\Delta \alpha_{cw}$ | $\mu_{cw}$  | $\alpha_{cw}$ | $\Delta \alpha_{cw}$ | $\mu_{cw}$  | $\alpha_{cw}$ | $\Delta \alpha_{cw}$ |
| 1a       | 3.72         | 18.2         | 14.5            | 3.81               | 21.2               | 16.7               | 3.84               | 23.5               | 18.4               | 3.87                   | 24.9               | 19.5               |
| 2a       | 3.60         | 22.4         | 15.8            | 3.64               | 26.5               | 17.9               | 3.68               | 29.5               | 19.5               | 3.71                   | 31.4               | 20.5               |
| 3a       | 3.50         | 24.7         | 16.8            | 3.51               | 29.3               | 19.0               | 3.51               | 32.9               | 20.6               | 3.52                   | 35.0               | 21.6               |
| 4a       | 2.78         | 29.1         | 18.9            | 2.79               | 34.8               | 21.3               | 2.79               | 39.2               | 23.0               | 2.79                   | 42.0               | 24.0               |
| 5a       | 1.98         | 31.5         | 20.0            | 1.99               | 38.2               | 22.4               | 2.01               | 43.4               | 24.0               | 2.02                   | 46.7               | 25.0               |
| 1b       | 4.03         | 22.7         | 17.2            | 4.04               | 27.3               | 20.7               | 4.08               | 30.9               | 23.6               | 4.11                   | 33.2               | 25.5               |
| 2b       | 3.86         | 26.7         | 17.9            | 3.88               | 32.2               | 21.4               | 3.90               | 36.5               | 24.2               | 3.91                   | 39.3               | 26.1               |
| 3b       | 3.69         | 29.0         | 19.4            | 3.69               | 35.2               | 23.1               | 3.69               | 40.1               | 26.1               | 3.70                   | 43.2               | 28.1               |
| 4b       | 3.02         | 33.4         | 22.9            | 3.03               | 40.8               | 27.0               | 3.03               | 46.7               | 30.2               | 3.03                   | 50.5               | 32.3               |
| 5b       | 2.34         | 35.9         | 24.4            | 2.35               | 44.3               | 28.7               | 2.37               | 51.1               | 32.0               | 2.39                   | 55.5               | 34.1               |
charge separation and magnitude of molecular dipole moment. As states above, $\mu_{cw}$ grows if the phase of each compound has been altered from vacuum to solution, and additionally, the resulting growth of $\mu_{cw}$ is enhanced by the increasing polarity of the solvents. Thus, the largest $\mu_{cw}$ values are observed for the investigated compounds solvated by dichloromethane. The growth of $\mu_{cw}$ is, however, rather minor and does not exceed several percent, compared to $\mu_{cw}$ in vacuum (the maximal $\mu_{cw}$ growth amounting to 4.1% is observed for 1a in dichloromethane). This also suggests that there will be a modest increase in the intermolecular solute–solute interaction if the solvent is changed from benzene to dichloromethane.

There are available experimental values of molecular dipole moment for three out of ten investigated compounds. Experimental measurements were made for 1a (3.65 D), 2a (3.71 D), and 2b (3.75 D), all in benzene solution [54]. The $\mu_{cw}$ values calculated for 1a, 1b, and 2b in benzene reproduce the corresponding experimental dipole moments with an accuracy of 0.16 D or better. The agreement of the trend in the $\mu_{cw}$ values with the experimental results was, however, successful only in part. The $\mu_{cw}$ values of 2a and 2b mimic the experimentally measured growth of molecular dipole moment. The $\mu_{cw}$ values of 1a and 2a, by contrast, do not follow the experimental trend. One should bear in mind that both the experimental dipole moments and $\mu_{cw}$ characterize the equilibrium mixtures of conformers, so the aforementioned disagreement may result even from a minor difference in the abundance of individual conformers.

Next, the analysis of the molecular dipole moments of 1a–5a and 1b–5b will be deepened by inspecting the $\mu$ values of individual conformers. The $\mu$ values of all investigated conformers are collected in Table 4. It is apparent that there are noticeable differences in $\mu$ between individual conformers of every compound. For 1a–3a and their thiocarbonyl counterparts, the cc-conformation exhibits the largest values of $\mu$, whereas the tt-conformers possess the smallest $\mu$ values. The molecular dipole moments of 4a, 4b, 5a, and 5b are also sensitive to conformational changes, but these compounds show an increase in their $\mu$ values while passing from the cc-conformation to the ct-conformation and further to the tt-conformation. For all conformers, the spatial orientation of their $\mu$ vectors is determined, to a great extent, by the orientation of the local dipole moment of their C=O or C=S group (this local dipole moment is directed from the O or S atom toward the C atom). The relation between the increment of $\mu$ and the kind of conformation can be understood in terms of the local dipole moments ascribed to the heteroaryl fragments and the C=O and C=S groups. The orientations of these local dipole moments for the cc-conformers of 1a–5a and 1b–5b have been discussed earlier in this subsection. The tt-conformers of 1a–3a and 1b–3b possess the smallest $\mu$ values because the local dipole moments of their heteroaryl fragments and of their C=O and C=S groups are directed oppositely. These local dipole moments demonstrate an approximately concordant direction for the tt-conformers of 5a and 5b, and, therefore, their tt-conformation exhibits the largest $\mu$ values.

The effect on $\mu$ exerted by the solvents is not of identical magnitude for all conformers. For each compound, the difference between the $\mu$ values of its most polar and least polar conformers increases upon solvation, and such a difference keeps growing with increasing solvent polarity. The conformers of 1b–5b exhibit higher growth of $\mu$ upon solvation than the corresponding ketone conformers. This is in agreement with previous findings reported for formaldehyde and thioformaldehyde solvated in water [55]. The polarity of the C–S π bond in thioformaldehyde is increased to a greater extent than that observed for the C–O π bond in formaldehyde.

Finally, it is instructive to relate the abundances of solvated conformers in their equilibrium mixtures to the changes of their $\mu$ values upon solvation. In principle, it can be expected that a conformer possessing a high $\mu$ value becomes more favorable in solvents of high polarity [56]. Such a relationship exists for the solvated conformers of 1a–5a and 1b–5b, and their percentage abundances shown in Tables 1 and 2 provide evidence confirming this. Among the three conformations of 1a–3a and 1b–3b in vacuum, the cc-conformers exhibit the highest $\mu$ values; hence, these conformers become more and more abundant in the solvents of increasing polarity. The same concerns the tt-conformers of 4a, 4b, 5a, and 5b, although these conformers are still much higher in energy than the preferred conformers, and, therefore, the abundances of the tt-conformers rise extremely slowly (their tabulated percentage abundances sometimes seem not to grow, but this is because the percentage abundances have been rounded to one digit after the decimal point).

| Conformer | $\mu$ | Conformer | $\mu$
|-----------|-------|-----------|-------|
| cc-1a | 4.75/5.67/6.38/6.82 | cc-1b | 4.72/5.86/6.79/7.39 |
| cr-1a | 3.91/4.69/5.27/5.64 | cr-1b | 4.10/5.10/5.92/6.44 |
| tt-1a | 2.90/3.45/3.87/4.12 | tt-1b | 3.35/4.14/4.77/5.19 |
| cc-2a | 4.03/4.89/5.55/5.97 | cc-2b | 4.14/5.17/6.02/6.57 |
| cr-2a | 3.36/4.09/4.66/5.01 | cr-2b | 3.62/4.52/5.26/5.74 |
| tt-2a | 2.69/3.27/3.72/4.00 | tt-2b | 3.09/3.84/4.45/4.85 |
| cc-3a | 3.65/4.47/5.11/5.52 | cc-3b | 3.81/4.79/5.60/6.13 |
| cr-3a | 3.20/3.93/4.50/4.87 | cr-3b | 3.46/4.36/5.10/5.59 |
| tt-3a | 2.80/3.44/3.94/4.26 | tt-3b | 3.17/3.98/4.64/5.08 |
| cc-4a | 2.76/3.42/3.96/4.30 | cc-4b | 3.00/3.83/4.52/4.98 |
| cr-4a | 2.94/3.67/4.26/4.63 | cr-4b | 3.19/4.08/4.83/5.33 |
| tt-4a | 3.24/4.02/4.63/5.03 | tt-4b | 3.60/4.58/5.40/5.94 |
| cc-5a | 1.93/2.32/2.66/2.89 | cc-5b | 2.28/2.87/3.39/3.74 |
| cr-5a | 2.85/3.62/2.64/6.68 | cr-5b | 3.10/4.06/4.90/5.47 |
| tt-5a | 3.82/4.89/5.77/6.35 | tt-5b | 4.17/5.50/6.64/7.43 |

*a The $\mu$ values are listed in the following media: vacuum/benzene/chloroform/dichloromethane.
Polarizability

The molecular average dipole polarizability $\alpha$ and the polarizability anisotropy $\Delta \alpha$ measure the deformation of charge distribution within a molecule under an applied external electric field. Here, the importance of $\alpha$ and $\Delta \alpha$ is attributed to the fact that these quantities may be good indicators of how the deformation of charge distribution within the investigated molecules is affected by the kind of Y and the presence of solvent. Similarly to $\mu_{cw}$, the $\alpha$ and $\Delta \alpha$ values of three conformers of each compound are subjected to conformational weighting in order to obtain $\alpha_{cw}$ and $\Delta \alpha_{cw}$. The $\alpha_{cw}$ and $\Delta \alpha_{cw}$ values calculated for 1a–5a and 1b–5b are appended to Table 3.

The Y heteroatom effect on $\alpha_{cw}$ and $\Delta \alpha_{cw}$ is the opposite of that detected for $\mu_{cw}$. For each series of compounds, the replacement of oxygen by a heavier group 16 element at the Y position increases the values of $\alpha_{cw}$ and $\Delta \alpha_{cw}$ gradually. The distribution of electron charge in 5a and 5b undergoes the greatest distortion caused by an external electric field. The trend in $\alpha_{cw}$ can be interpreted in terms of changes in the molecular polarizabilities of five-membered heterocycles C$_4$H$_4$Y. Figure 4 proves that the $\alpha_{cw}$ values of 1a–5a in vacuum are linearly correlated with the polarizabilities of isolated chalcophenes. The same applies to the thioketones. The $\alpha_{cw}$ values of 1b–5b are shifted toward more positive values due to the higher atomic polarizability of the thiocarbonyl S atom compared to the O atom of the C=O group. The molecular polarizabilities of C$_4$H$_4$Y heterocycles are, in turn, in excellent linear correlation with the atomic polarizabilities of the corresponding Y atoms [57]. This indicates that the evolution of $\alpha_{cw}$ along the series of the ketones or thioketones investigated here is determined mainly by the kind of Y heteroatom.

The heteroatom effect on polarizability can also be rationalized in terms of HOMO–LUMO energy gap and molecular size for a fixed type of molecular conformation. In principle, the polarizability of a molecule is expected to be enhanced with the decreasing HOMO–LUMO energy gap and growing size of the molecule [58]. As noted earlier in this work, replacing Y with a heavier and heavier group 16 element leads to reduction of the HOMO–LUMO energy gap. This reduction is indeed inversely related with $\alpha$ for the isolated cc-conformers of 1a–5a and 1b–5b (see Fig. S5). Additionally, there is an approximately linear relationship between $\alpha$ and the molecular volume of the isolated cc-conformers of the investigated compounds (Fig. S5). This reflects the well-known proportionality between molecular polarizability and molecular size [58]. The use of the molecular volume of the cc-conformers to estimate their molecular size turns out to be successful for providing a clear correlation with $\alpha$. On the one hand, this may be a consequence of the structural similarity of the cc-conformers. On the other hand, the existence of a general relationship between polarizability and volume was previously postulated, although such a relationship did not fulfill an ideal linear correlation [59].

The $\alpha_{cw}$ and $\Delta \alpha_{cw}$ values of 1a–5a and 1b–5b in three solvents are reported in Table 3. An inspection of these values reveals that they are affected by the presence and kind of solvents. Compared to $\alpha_{cw}$ and $\Delta \alpha_{cw}$ of 1a–5a and 1b–5b in vacuum, the $\alpha_{cw}$ and $\Delta \alpha_{cw}$ values of solvated molecules are noticeably larger, and they increase further with the growing polarity of solvents. The growth of $\alpha_{cw}$ and $\Delta \alpha_{cw}$ for the molecules solvated in dichloromethane can reach even 50% of the $\alpha_{cw}$ and $\Delta \alpha_{cw}$ values for the corresponding isolated molecules. The growing solvent polarity facilitates the charge separation within the molecules of 1a–5a and 1b–5b, which, in turn, enhances the deformation of their charge distribution under an external electric field. For 1a–5a, the solvent effect may also be explained by the continuous decrease of the HOMO–LUMO energy gap (see Fig. 2). Such an explanation does not apply to the thioketones, for which the growth of their molecular volume upon solvation determines the increase of $\alpha$ (for details, consult Figs. S6 and S7).

The molecular polarizability is only very slightly sensitive to the conformation adopted by the molecules of 1a–5a and 1b–5b. Therefore, the $\alpha$ values of three conformers of each compound show much lower variability than the $\mu$ values. From an experimental perspective, the $\alpha$ values seem of little use to unambiguously distinguish the conformers from each other.

**Summary**

Density functional theory calculations of geometry, energetics, frontier molecular orbitals, dipole moment and polarizability for formaldehyde and thioformaldehyde symmetrically disubstituted with five-membered heteroaromatic rings containing a single group 16 heteroatom have yielded a detailed picture of variations in these molecular properties as a result of
replacing the ring heteroatom (i.e., oxygen) by a heavier element, up to polonium. Furthermore, embedding the molecules of the investigated compounds in a continuum with a small dielectric constant of benzene, chloroform, or dichloromethane has served as a computational tool for establishing to what extent the presence of these low polarity solvents affects the aforementioned properties.

The effect of ring heteroatom on the preferred geometrical orientation of heteroaryl rings is non-uniform for 1a–5a and 1b–5b. The furan-2-yl substituents of 1a and 1b favor the \( \sigma \) -conformation, whereas the heavier Y heteroatoms tend to prefer the \( \pi \)-conformation. The presence of a solvent further diversifies the conformational behavior of the investigated molecules. The three solvents stabilize the \( \pi \)-conformation of the heteroaryl rings containing \( Y = O, S, Se \) and destabilize this conformation if \( Y = Te, Po, Po \). Such a solvent effect may be rationalized by the analysis of molecular dipole moment for individual conformers. Even if the solvents display low polarity, they have a noticeable influence on the percentage abundances of three conformers in their equilibrium mixture at 298.15 K. The HOMO–LUMO energy gap of 1a–5a and 1b–5b gradually decreases while Y descends through group 16. Two opposite trends in this property are detected for the solvated molecules (1a–5a versus 1b–5b), which is attributed to different stabilization/destabilization patterns of frontier molecular orbitals in the two series of molecules. The growing size of Y is associated with the decrease of \( \mu_{\text{cw}} \) and, simultaneously, with the increases of \( \alpha_{\text{cw}} \) and \( \Delta\alpha_{\text{cw}} \). These changes correlate with the electronegativity and polarizability of Y. Both \( \mu_{\text{cw}} \) and \( \alpha_{\text{cw}} \) increase when the solvents have been introduced. However, \( \alpha_{\text{cw}} \) is much more sensitive to the growing polarity of the solvents than is \( \mu_{\text{cw}} \).

We believe that this work may contribute to a better understanding of the role of heteroatom and solvent in establishing structure–property patterns for organic molecules containing \( \text{C}_n\text{H}_m\text{Y} \) groups.

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References

1. Joule JA, Mills K (2010) Heterocyclic chemistry, 5th edn. Wiley, Chichester
2. Nylund K, Johansson P, Puterova Z, Krutosikova A (2010) Heterocyclic compounds: synthesis, properties and applications. Nova Science, Hauppauge
3. Quin LD, Tyrell J (2010) Fundamentals of heterocyclic chemistry: importance in nature and in the synthesis of pharmaceuticals. Wiley, Hoboken
4. Balaban AT, Oniucu DC, Katritzky AR (2004) Aromaticity as a cornerstone of heterocyclic chemistry. Chem Rev 104:2777–2812
5. Belenkii LI, Suslov IA, Chuyylkin ND (2003) Substrate and positional selectivity in electrochemical substitution reactions of pyrrole, furan, thiophene, and selenophene derivatives. Chem Heterocycl Compd 39:36–48
6. Ortiz P, del Hoyo AM, Harutyunyan SR (2015) Catalytic asymmetric allylation of aryl heteroaryl ketones. Eur J Org Chem 2015:72–76
7. Milstof G, Grzelak P, Mikina M, Linden A, Heimgartner H (2015) Hetero-Diels–Alder reactions of hetaryl and aryl thioketones with acetylenic dienophiles. Beilstein J Org Chem 11:576–582
8. Zhang G, Ma J, Wen J (2007) Interchain impacts on electronic structures of heterocyclic oligomers and polymers containing group 14, 15, and 16 heteroatoms: quantum chemical calculations in combination with molecular dynamics simulations. J Phys Chem B 111:11670–11679
9. Zajac M, Hrobarik P, Majdole P, Foltova P, Zahradnik P (2008) Donor–π-acceptor benzothiazole-derived dyes with an extended heteroaryl-containing conjugated system: synthesis, DFT study and antimicrobial activity. Tetrahedron 64:10605–10618
10. Acharya R, Cekli S, Zeman CJ, Althamimi RM, Schanze KS (2016) Effect of selenium substitution on intersystem crossing in π-conjugated donor–acceptor–donor chromophores: the LUMO matters the most. J Phys Chem Lett. 7:693–697
11. Kobilka BM, Hale BJ, Ewan MD, Dubrovskiy AV, Nelson TL, Dzhokoe V, Jeffries-EL M (2013) Influence of heteroatoms on photovoltaic performance of donor-acceptor copolymers based on 2,6-di(thiophen-2-yl)benzo[1,2-b:4,5-b’]difurans and diketopyrrolopyrrole. Polym Chem 4:5329–5336
12. Raychev D, Gusikova O, Seifert G, Sommer J-U (2017) Conformational and electronic properties of small benzothiazolocore oligomers with aryl flanking units: thiophene versus furan. Comput Mater Sci 126:287–298
13. Sperry JB, Wright DL (2005) Furan, thiophenes and related heterocycles in drug discovery. Curr Opin Drug Discov Devel 8:723–740
14. Pitucha M, Pachuta-Stec A, Kacoor AA (2013) New five-membered ring heterocyclic compounds with antibacterial and antifungal activity. In: Méndez-Vilas A (ed) Microbial pathogens and strategies for combating them: science, technology and education, vol 1. Microbiology Book Series #4. Formatex Research Center, Badajoz, pp 562–573
15. Ruengsangtongkul S, Taprasert P, Sirion U, Jaratjaroonphong J (2016) Facile synthesis of nonsymmetrical heteroarylsubstituted triarylmethanes via the FeCl3·6H2O-catalyzed two-step Friedel–crafts-type reaction. Org Biomol Chem 14:8493–8502
16. Guerra M, Pedulli GF, Tiecco M, Martelli G (1974) Conformational isomers and rotational barriers in the ketyl radicals of thiophen and thienothiophens. J Chem Soc Perkin Trans 2 1974:562–567
17. Benassi R, Folli U, Iarossi D, Schenetti L, Teddi F, Musatti A, Nardelli M (1989) Conformational analysis of organic carbonyl compounds. Part 11. Conformational properties of difuryl, dithienyl, and fural thiienyl ketones studied by X-ray crystallography, N.M.R. lanthanide-induced shifts and ab-initio MO calculations. J Chem Soc Perkin Trans 2 1989:1741–1751
18. Ryhmä L, Abdallah HH, Ranasami P (2011) Quantum mechanical study of the syn-anti isomerisation of 2-tellurophenecarboaldehyde: vive la différence. Spectrochim Acta A 78:258
19. Taylor R (1968) Measurement of electrophilic aromatic reactivities via pyrolysis of 1-arylethyl acetates. Part 11. The 2- and 3-positions of furan and thiophen. J Chem Soc B 1968:1397–1401
20. Becker RS, Favaro G, Poggi G, Romani A (1995) Photophysical properties of some thienyl ketones: an experimental and theoretical study. J Phys Chem 99:1410–1417
