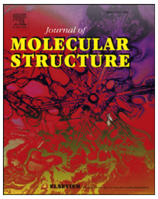
Journal of Molecular Structure 1151 (2018) 301–314

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: http://www.elsevier.com/locate/molstruc



Spectroscopic and theoretical studies of some 2-(2′-haloacetyl)-5-substituted: 1-Methylpyrrole, furan and thiophene

Jéssica Valença [a, **], Daniel N.S. Rodrigues [a, *], Paulo R. Olivato [a], Maurizio Dal Colle [b]

[a] Conformational Analysis and Electronic Interactions Laboratory, Instituto de Química, USP, CP 26077, 05513-970, São Paulo, SP, Brazil
[b] Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Ferrara, 44121, Ferrara, Italy

ARTICLE INFO

Article history:
Received 2 August 2017
Received in revised form
16 September 2017
Accepted 18 September 2017
Available online 20 September 2017

keywords:
Infrared spectroscopy
Theoretical calculations
Solvent effect
Conformational analysis
2-(2′-haloacetyl)-5-substituted
heteroaromatic compounds

ABSTRACT

The conformational study of some 2-(2′-haloacetyl)-5-substituted five-membered heteroaromatic compounds Z-CH$_2$C(O)(C$_4$H$_2$X)−Y bearing a halogen (Z = Cl or Br) at the 2′-position and (Y = NO$_2$, H, Me or Cl) substituents at the 5-position of the heteroaromatic ring for X = NMe, O and S was performed by IR carbonyl stretching band (ν_{CO}) analysis supported by the harmonic frequency, NBO and PCM calculations on the minima and saddle-point structures obtained at the M05-2X/aug-cc-pVTZ level. The computational results predicted the presence of four stable conformers, classified by the orientation of the X$_{ring}$−C−C=O (*syn*/*anti*) and the O=C−C−Z (*anticlinal*/ *synperiplanar*) moieties as *ac*(*syn*), *sp*(*syn*), *ac*(*anti*) and *sp*(*anti*). The *anti*/*syn* equilibrium controls the relative stabilities of the conformers to a large extent while the *anticlinal*/*synperiplanar* accounts for the observed trend of the IR carbonyl band components. The computed ν_{CO} frequencies and the PCM trend of the relative abundance in solvents of increasing permittivity allowed the pairs of *ac*(*syn*)/*ac*(*anti*) and *sp*(*syn*)/*sp*(*anti*) conformers to be assigned to the lower and higher ν_{CO} frequency IR carbonyl doublet components, respectively. The PCM data failed to reproduce the experimental carbonyl triplet found in chloroform. However, the additional component could be justified by assuming the formation of complexes constituted by one chloroform molecule hydrogen bonded to the conformers in a PCM chloroform continuum.

The NBO and short contact analysis suggested that the *syn*/*anti* conformational equilibrium is governed mainly by electrostatic interactions, while the *anticlinal*/*synperiplanar* depends to different extents on both orbital and electrostatic interactions.

1. Introduction

Aromatic heterocyclic compounds are widely studied from a synthetic point of view as building blocks [1,2], due to their applicability in the polymer [3,4] and food industries [5,6] and to their potential biological activity [7].

In 2-formylthiophene and some thiophene-2-carbonyl halides [8,9], the higher relative abundance of the *cis* conformer was ascribed to the coulombic interaction between the oppositely charged $O^{\delta-}_{(CO)}$ and $S^{\delta+}$ atoms. The same stability order for 2-acetylthiophene in *n*-hexane and benzene was determined through Kerr constants and dipole moments [10] and was confirmed by DFT calculations and infrared spectra in carbon tetrachloride and chloroform [11]. These findings are also supported by Photoelectron (PE) and Electron Transmission (ET) spectral analysis [12], as well as by *ab-initio* HF/6-31G** and MP2/6-31G** calculations [13]. Therefore, all these studies indicate that the *cis* conformer (relative to the O=C−C−S moiety) is more stable than the *trans*.

For 2-acetylfuran, the observed trend is reversed. The Kerr constants and dipole moments in *n*-hexane and benzene [10] indicate the *trans* conformer to be the more stable. An NMR, infrared and DTF study [14] also reported preference for the *trans* conformer in vacuum, dichloromethane and acetone. Semi-empirical calculations suggest that electronic delocalisation should favour the *cis* conformer, indicating that the *trans* preference is mainly a consequence of the strong Repulsive Field Effect

---

* Corresponding author. Conformational Analysis and Electronic Interactions Laboratory, Instituto de Química, Universidade de São Paulo, P. O. Box 26077, 05513-970, São Paulo, SP, Brazil.

** Corresponding author. Conformational Analysis and Electronic Interactions Laboratory, Instituto de Química, Universidade de São Paulo, P. O. Box 26077, 05513-970, São Paulo, SP, Brazil.

E-mail addresses: dannopper@gmail.com (J. Valença), jvalenca@iq.usp.br (D.N.S. Rodrigues).

https://doi.org/10.1016/j.molstruc.2017.09.055
0022-2860/© 2017 Published by Elsevier B.V.

(RFE) that acts on the $O^{\delta-}{}_{(CO)} \ldots O^{\delta-}$ short contact [15].

For 2-acetylpyrrole, the *cis* conformer is highly stabilised in CS_2/CD_2Cl, CCl_4, $CHCl_3$, CH_3CN and acetone-d6 by the intramolecular hydrogen bond $N{-}H^{\delta+} \ldots O^{\delta-}{}_{(CO)}$ [16]. In the same study, only this conformer was evidenced in *N*-methyl-2-acetylpyrrole.

In the solid state, *N*-methyl-2-trichloroacetylpyrrole assumes an *s-cis* conformation, which is stabilised by a network of intermolecular halogen and hydrogen bonding interactions [17]. DFT calculations assigned the singlet ν_{CO} IR symmetric band at 1681 cm^{-1} to this structure [18]. Similarly, the *s-cis* conformer was ascribed to the most intense doublet ν_{CO} component at a lower frequency (1662 cm^{-1}) for *N*-methyl-2-(2-chloroacetyl)pyrrole [19].

The present paper reports infrared and theoretical studies of some 2-(2′-haloacetyl)-5-substituted five-membered heteroaromatic compounds $Z{-}CH_2C(O)(C_4H_2X){-}Y$ (**1**–**7**) bearing halogen (Z = Cl or Br) at the 2′-position and the substituent (Y = NO_2, H, Me or Cl) at the 5-position of the heteroaromatic ring, for X = NMe, O and S (See Scheme 1). These compounds were chosen taking into account that both the X and Y substituents may affect the *syn/anti* and the *synperiplanar/anticlinal* conformational equilibrium with respect to the X–C–C=O and O=C–C–Z moieties, respectively.

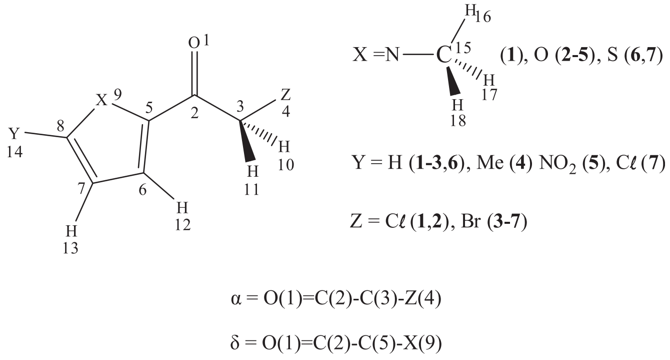
2. Experimental

2.1. Materials

All solvents for IR measurements were spectrograde and were used without further purification. The title compounds **1**–**7** were commercially available (**1**–**3** from Ablock Pharmatech and **4**–**7** from Sigma-Aldrich).

2.2. IR measurements

The IR spectra were recorded with a Michelson Bomem MB100 FTIR spectrometer, with 1.0 cm^{-1} resolution at a concentration of 1.0×10^{-2} mol dm^{-3} in *n*-hexane, carbon tetrachloride, chloroform, dichloromethane and acetonitrile using a 0.519 mm sodium chloride cell, for the fundamental carbonyl region (1800–1600 cm^{-1}). The spectra of the carbonyl first overtone (3600–3100 cm^{-1}) were recorded in carbon tetrachloride solution (1.0×10^{-2} mol dm^{-3}), using a 1.00 cm quartz cell. The overlapping carbonyl bands (fundamental and first overtone) were resolved by means of the Grams/32 curve-fitting software, version 4.04, Level II [20]. This software detects, through the second derivative of the actual carbonyl band, the number of components that composes it and then, statistically, adjusts them to the original band using a Gaussian/Lorentzian profile. The conformer populations for compounds **1**–**7** in the referred solvents were expressed as percentages of the integrated intensity estimated from the integrated absorbance $B = \int_{band} \ln(I_o/I)_\nu \, d\nu$ (ν in cm^{-1}) for each resolved carbonyl multiplet (doublet, triplet or quartet) component, on the assumption of equal integrated molar absorption coefficient $\overline{A}$ [21] for all the conformers (for details see Table S1 and Note S1).



Scheme 1. Atom labelling of 2-(2′-haloacetyl)-5-substituted five-membered heteroaromatic compounds $Z{-}CH_2C(O)(C_4H_2X){-}Y$ (**1**–**7**) and definition of the relevant dihedral angles.

2.3. Theoretical calculations

The local and global minima, as well as the first order saddle point geometries, were found by rotating the α (O=C–C–Z) and δ (X–C–C=O) dihedral angles, from 0° to 180° with steps of 10°, through the relaxed SCAN method (Mod Redundant) implemented in the Gaussian 09 package [22] at the M05-2X/aug-cc-pVDZ [23,24] level of theory. The final geometries, harmonic vibrational modes and orbital interaction at 298 K were refined at the same M05-2X/aug-cc-pVTZ [25] level. Condensed phase Polarisable Continuum Model (PCM) [26] calculations were carried out at the M05-2X/aug-cc-pVTZ level, as implemented in Gaussian 09, in order to obtain the Gibbs free energies of solvation. Relative energies were estimated using the harmonic zero point energy (ZPE) correction. Due to the symmetry of the conformers, either C_1 or C_S point groups, in order to obtain accurate molar fractions, the thermodynamic probability factor ($\omega = e^{(S/R)}$) was applied as a weighting factor of 2 or 1, respectively. The NBO 3.1 program [27] implemented in the Gaussian 09 package was used to estimate delocalisation energies (E2) by means of second-order perturbation theory. The partial atomic charges were calculated using Natural Population Analysis (NPA) [27].

3. Results and discussion

Table 1 collects the frequencies and relative intensities of the resolved components of the carbonyl stretching (ν_{CO}) band for compounds **1**–**7** in solvents of increasing relative permittivity, from *n*-hexane to acetonitrile [28]. In general, a doublet is observed, with a less intense component at higher ν_{CO} frequency (*ca.* 18 cm^{-1}). For all compounds, the relative intensity of this component increases as the dielectric constant of the medium increases. In chloroform, an additional ν_{CO} component at the lowest frequency is detected for compounds **1**, **3** and **5**. This triplet component is the most intense for compound **3** and least intense for compounds **1** and **5**.

In contrast, for compound **7** in *n*-hexane, the doublet is split into a quartet with a difference of *ca.* 20 cm^{-1} between the highest frequency (1702 cm^{-1}) and the third component (1683 cm^{-1}) and between the second component (1694 cm^{-1}) and that at the lowest frequency (1673 cm^{-1}). The solvent effect on the carbonyl band components is illustrated in Figs. 1–3 for compounds **1**, **2** and **7**, taken as representatives of the 2-(2′-haloacetyl)-5-substituted 1-methylpyrrole (**1**), furans (**2**–**5**) and thiophenes (**6** and **7**). The carbonyl first overtone band profiles match those of the fundamentals. The resolved components, in carbon tetrachloride, appear at frequencies twice those of the fundamental minus two times the mechanical anharmonicity [21] of *ca.* 20 cm^{-1}. These features indicate the existence of at least two conformers in solution for the studied compounds **1**–**7** [29,30], ruling out the existence of any vibrational effect in the fundamental transition of the ν_{CO} mode.

In Table 2, the relative energies and populations, dipole moments, carbonyl stretching frequencies and dihedral angles of the global and local minima at the M05-2X/aug-cc-pVTZ level of theory for compounds **1**–**7** are reported.

The calculation results suggest the presence in vacuum of four conformers, which may assume either an *anticlinal* or *synperiplanar* geometry on the α dihedral angle and either a *synperiplanar* or