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On the search of cumulative effect of fluoro-substituents in the structural and vibrational properties of sulfinylanilines: Study of 3,4-difluorosulfinylaniline and 2,3,4-trifluorosulfinylaniline

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ABSTRACT

The study of substitution effects on the structural and vibrational properties of a series of recently reported mono fluoro-substituted sulfinylanilines proceeds a step forward with the present study of 3,4-difluorosulfinylaniline and 2,3,4-trifluorosulfinylaniline. These substances were synthesized and characterized by FTIR, Raman and NMR spectra, which were subsequently compared with theoretical spectra, obtained by quantum chemical calculations at different levels of theory. The number of signals in the vibrational spectra, together with the analysis of the potential energy surface of both compounds reveal the presence of stable conformers possessing the angular N═S→O group in a *syn* conformation of the C−N and S→O bonds and coplanar with the ring plane. According to the Natural Bond Orbital analysis performed, the prevalence of a given structure of the stable *syn* conformer over other local minima of the potential energy surface obtained upon rotation around the N═S and C−N bonds is a consequence of different orbital interactions. The planar conformation predicted for stable minima are stabilized by conjugation between the π-systems of the N═S→O group and the ring and by a weak orbital interaction between oxygen and the *ortho* hydrogen closest to it.

1. Introduction

As a substituent, fluorine is rarely ineffective and producesinteresting effects not only on chemical properties but also on biological activities of fluorinated compounds. A recent review deals with the significant fluorine effects in nucleophilic, electrophilic, radical and transition metal-mediated fluoroalkylation reactions in comparison with either non-fluorinated or fluorinated counterparts with different numbers of fluorine atoms [1]. Wiberg and Rablen determined that the effect of fluorine on the structural parameters of benzene ring is mainly related to polarization. The only cases in which fluorine was found to be a π-donor were those where a full positive charge may be stabilized. They observed that an increase in electronegativity of X leads to a decreased C−X bond length (X: substituent), an increase in the C−C−C bond angle and a decrease in the C−C bond lengths adjacent to the substituent [2]. Chambers et al. discussed the effect of fluorine as a substituent on nucleophilic aromatic substitution. They found that a fluorine atom located in the *ortho* and *meta* positions with respect to a given functional group may be of variable activating influence, whereas a fluorine located in *para* position is slightly deactivating [3]. In addition, Siodla et al. introduced a few quantum-chemical models for the interpretation of the substituent effect acting on fluorine atom or a CF_3 group attached to ethene or benzene [4]. Leyva et al. investigated the effects of fluorine substituent on naphthoquinones by NMR spectroscopy; since fluorine is both electron-attracting (σ acceptor) and electron-donating (π donor), the effect of fluorine substituent will depend on its position in the ring. According to ^{1}H chemical shifts, they observed that a fluoro substituent in *meta* or *para* position behaves as a σ acceptor, while a fluoro substituent in *ortho* position actually acts as a π donor [5].

On the search of the influence of fluorine on structural and vibrational properties of substituted sulfinylanilines, our group recently reported the results for a series of monosubstituted derivatives of parent *N*-sulfinylaniline, *i.e.* *o*-, *m*- and *p*- isomers of fluorosulfinylaniline (FArNSO) [6–8]. This family of fluorine substituted compounds is supplemented in the present article by the joint study of the di- and trisubstituted derivatives 3,4-difluorosulfinylaniline (3,4-diFArNSO) and 2,3,4-trifluorosulfinylaniline (2,3,4-triFArNSO), respectively. As members of the sulfinyl compounds family, they possess the NSO functional group. The non-linear configuration of this group can possess *syn* and *anti* forms (*syn* or *anti* of the SO bond relative to the CN bond). All studies performed up to date demonstrated that the *syn* form is the most

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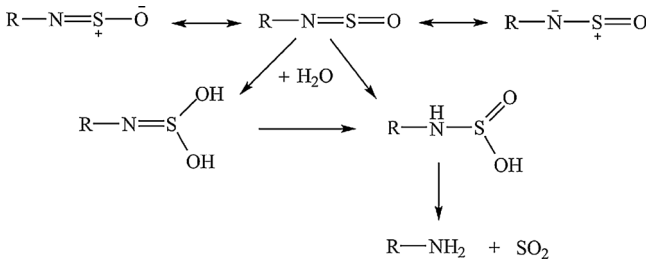

Scheme 1. Hydrolysis of *N*-sulfinylamines.

stable isomer [9,10]. These compounds are generally liquids or low-melting solids and are extremely reactive. Due to their extreme sensitivity towards water these compounds are very prone to decomposition through hydrolysis reactions with the formation of amine derivatives and sulfur dioxide [11] (see Scheme 1).

The outstanding reactivity of the sulfinyl group makes them also suitable for several chemical processes of synthetic utility, particularly cycloaddition reactions, producing four-membered heterocycles with interesting biological activities [12]. Within this context, Veremeichik reported the synthesis of fluorinated sulfonamides *via* heteroatomic Diels-Alder reaction of 4-fluoro-*N*-sulfinylaniline with bicyclic [2.2.1] heptanes [13] and Makarov et al. performed a detailed structural study of a number of new fluorinated derivatives of benzodithiadiazine obtained by a general method starting from 3,5- and 3,4-difluorosulfinylanilines and 2,3,4-trifluorosulfinylaniline through electrophilic cyclisation reactions [14]. In general, the reactivity of *N*-sulfinylanilines depends on the substituent R attached to the NSO group. It has been demonstrated that electron-withdrawing substituents, such as fluorine and the trifluoromethyl group, increase the reactivity of *N*-sulfinylanilines since the electrophilicity of sulfur atom increases and the majority of the reactions proceeds across the N=S bond [15].

In addition to the structural, conformational and vibrational studies of *o*-, *m*- and *p*- isomers of fluorosulfinylaniline mentioned before, similar studies were performed by our group for *m*- [16] and *p*-chlorosulfinylaniline (ClArNSO) [17] and recently, *p*-trifluoromethylsulfinylaniline (*p*-CF_3ArNSO) [18]. Since the NSO group constitutes the key functional group in several reaction paths [11–15], these studies were devoted to the analysis of the influence of substituents attached to the aromatic ring on the structural and vibrational properties of this functional group. From our findings we concluded that although the vibrational stretches involving the NSO group are coupled in symmetric and antisymmetric modes, the former shows a higher character of SO stretching while the stretching of the NS bond is dominant in the antisymmetric vibration. From these studies it was clear that the effect exerted by the substituent was stronger in the NS bond of the NSO group than in the SO bond. The present work allows us to rationalize similarities and differences among the different fluoro-substituted compounds considering now the increase in the number of fluorine atoms, with the consequent better understanding of the effects involved. Despite the difference in the electron donor-acceptor properties of the NH_2 and NSO groups, it is worth mentioning that for the 2,3- and 2,4-difluoroaniline isomers as well as for the 2,3,4- and 2,3,6-trifluoroanilines an elaborated study of the effect of fluorine atoms on the geometries and normal modes of the aniline derivatives were reported [19,20]. The analysis of the vibrational spectra of these compounds reveals that the presence of the fluorine atoms modifies the wavenumbers of different vibrational fundamental modes and these changes depend on their position in the aromatic ring.

2. Results and discussion

Figs. 1 and 2 show the FTIR and Raman spectra in the 1800–400 cm^{-1} (or 100 cm^{-1}) spectral ranges, for the liquid samples of

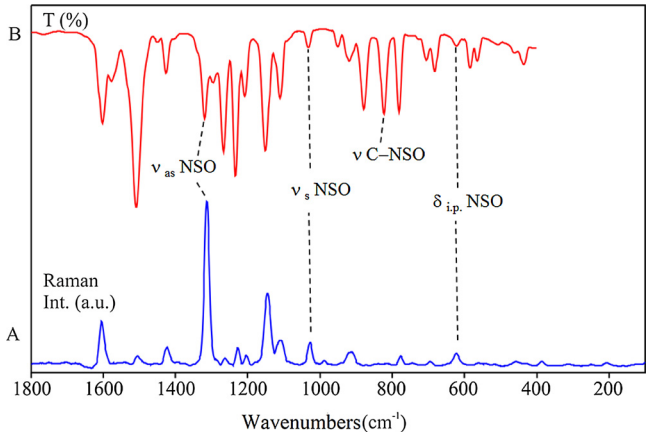

Fig. 1. Experimental spectra of 3,4-difluorosulfinylaniline (3,4-diFArNSO). A) Raman spectrum of the liquid sample recorded in the region of 1800-100 cm^{-1} at room temperature. B) Infrared spectrum of the liquid sample held between KRS-5 windows recorded in the region of 1800-400 cm^{-1} at room temperature.

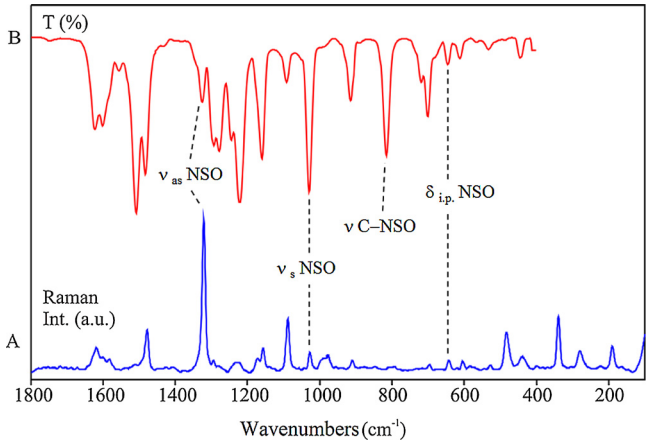

Fig. 2. Experimental spectra of 2,3,4-trifluorosulfinylaniline (2,3,4-triFArNSO). A) Raman spectrum of the liquid sample recorded in the region of 1800-100 cm^{-1} at room temperature. B) Infrared spectrum of the liquid sample held between KRS-5 windows recorded in the region of 1800-400 cm^{-1} at room temperature.

3,4-diFArNSO and 2,3,4-triFArNSO, respectively, obtained after purification. The absence of bands attributable to the NH_2 group (between 3500 and 3400 cm^{-1}, region not shown) indicates that the amine precursor has been completely eliminated.

2.1. Conformational analysis and structural characterization

As it was reported for all R–NSO compounds studied so far, the potential energy function for rotation around the NS bond determined by structure optimizations at fixed CNSO dihedral angles for the di- and tri-fluoro-substituted *N*-sulfinylanilines under investigation demonstrated that the most stable conformers possess *syn* configuration of the carbon nitrogen and sulfur oxygen bonds. Theoretical calculations for the studied molecules with the B3LYP/6-311 + G(df) approximation predict a local minimum for the *anti* conformation of these bonds and ΔE° (*anti–syn*) = 8.00 kcal mol^{-1} (ΔG° (*anti–syn*) = 7.42 kcal mol^{-1}) and ΔE° (*anti–syn*) = 6.37 kcal mol^{-1} (ΔG° (*anti–syn*) = 5.25 kcal mol^{-1}) for 3,4-diFArNSO and 2,3,4-triFArNSO, respectively. These large energy differences indicate that only the *syn* form of both studied molecules would be observed in the experimental spectra. In this context, Lee et al. studied Diels-Alder reactions involving sulfinyl dienophiles and observed that the *syn* forms of X-substituted sulfinyl dienophiles $O^{-}-S^{+}=N-X$ are more stable than the *anti* ones, and even though the