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# Hydrogen bonds in "push-pull" enamines†

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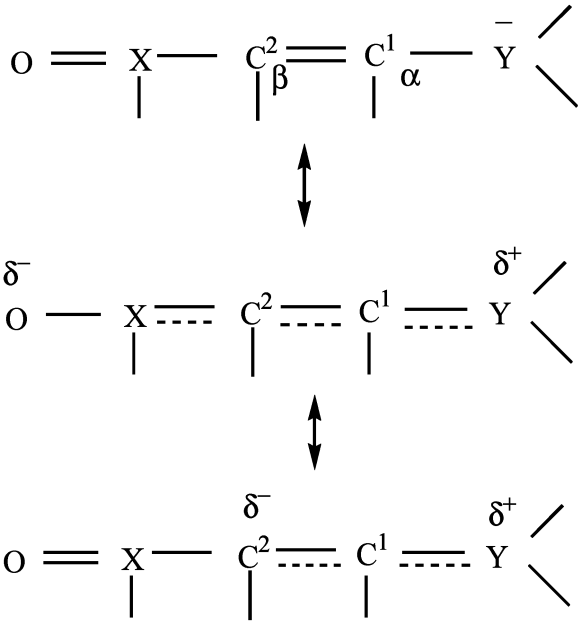
A comparison of hydrogen bond strengths in various enamines was made by monitoring the differential shifts $\Delta\delta$(X) as the difference of NMR chemical shifts between *E* and *Z* forms of the nuclei directly involved in hydrogen bonding, *i.e.*, X = $^{15}$N, $^{1}$H, $^{17}$O atoms. The interpretation of these differential values was aided by *ab initio* calculations and X-ray derived geometric parameters for selected compounds. It is shown that $\Delta\delta(N^1H)$ and $\Delta\delta(^{15}N)$ give conclusive results and their changes are rationally interpreted by invoking established contributing effects that influence the values of chemical shifts. The $\Delta\delta(^{17}O)$ parameter is sensitive to intramolecular geometry, mainly bond angles around oxygen and co-planarity of the atoms forming the hydrogen bonds. The latter factor is important in determining the strength of hydrogen bonds. Even a weak acceptor such as the lactone function gives a relatively strong hydrogen bond as compared with sp$^3$-hybridized sulfonyl or sulfinyl acceptors. The hybridization of the penultimate atom of an acceptor plays a crucial role in determining the strength of hydrogen bonding.

## Introduction

There is a vast amount of literature data concerning hydrogen bonding in "push-pull" ethylene derivatives,[1] containing X=O groups (X = C, COR, NO, S, SO) and Y substituents (Y = $NH_2$, NHR, $NR_2$, OH, OR), in the α and β positions, respectively. These compounds are often involved in prototropic equilibria and show stereochemical variations around the formally double C=C bonds, which is caused by the specific electron distribution along the aliphatic skeleton (see Scheme 1).

The above species can be divided into two classes, differing in the type of the Y substituent: enamines (Y = $NH_2$, NHR, $NR_2$) and enoles or their alkyl derivatives (Y = OH, OR). During the present work we have focused on the former category, which also consists of two subgroups, dependently on the character of the X central atom. The first one involves enamines in which X is sp$^2$-hybridized (C, C–O, N=O), resulting in an extended π-conjugation over the whole skeleton, whereas within the second set of species the sp$^3$-hybridization of X (S, S=O) causes a less effective π-conjugation but a strong σ-delocalization in the system.

In the past, various techniques were used to evidence the presence of and evaluate the strength of hydrogen bonds for the sp$^2$-hybridized systems. These studies included multinuclear NMR[2,3] techniques coupled with isotope labelling[4] as well as other spectroscopic techniques.[5,6] In contrast, the data concerning the "push-pull" enamines with sp$^3$ hybridization




**Scheme 1**

† Electronic supplementary information (ESI) available: crystal packing of **8** and X-ray geometry of **15**. See http://www.rsc.org/suppdata/nj/b4/b409254f/

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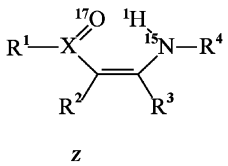
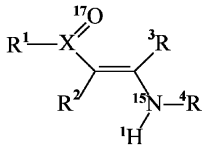


Z



E

| No | X | $R^1$; $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| **1** | C | $CH_3$; $CH_3CO$ | H | H |
| **2** | C | $C_2H_5$; $CH_3$ | H | $CH_3$ |
| **3** | C | -$(CH_2)_3$- | H | $CH_3$ |
| **4** | C | -O-$(CH_2)_2$- | H | $CH_3$ |
| **5** | SO | *p*-$CH_3C_6H_4$; H | $CH_3$ | *t*-$C_4H_9$ |
| **6** | SO | $CH_3$; H | $CH_3$ | $CH_2C_6H_5$ |
| **7** | SO | $CH_3$; H | $CH_3$ | $CH(CH_3)C_6H_5$ |
| **8** | SO | $CH_3$; H | $CH_3$ | *i*-$C_3H_7$ |
| **9** | SO | $CH_3$; H | H | *i*-$C_3H_7$ |
| **10** | SO | $CH_3$; H | H | *t*-$C_4H_9$ |
| **11** | SO | *p*-$ClC_6H_4$; H | H | *t*-$C_4H_9$ |
| **12** | S | *t*-$C_4H_9$; H | H | *t*-$C_4H_9$ |
| **13** | SO | $C_2H_5$; $CH_3$ | H | $CH_3$ |
| **14** | SO | $C_2H_5$; $CH_3$ | H | *t*-$C_4H_9$ |
| **15** | SO | -$(CH_2)_3$- | H | *t*-$C_4H_9$ |
| **16** | SO | -$(CH_2)_3$- | H | $CH_2C_6H_5$ |

**Scheme 2**



of X are rather scarce.[7] Recently, some experimental and theoretical works have dealt with the cycloconjugation effects of second-row elements on the β-sulfonylenamine moiety.[8]

The aim of the present work was to study the differences between the two types of enamines as regards the influence of hydrogen bond formation on the measured and calculated NMR parameters. The experimental values and their variation were then used to monitor the presence and strength of intramolecular hydrogen bonds in the studied compounds, which are presented in Scheme 2. The tautomeric equilibrium and stereochemistry of most of these compounds were studied by us previously.[9,10]

## Experimental

The detailed syntheses of all compounds will be published elsewhere.[11] The compounds studied were characterized using IR, elemental analyses and MS spectroscopy.

### Crystal structure determination

Colourless crystals of **8** and **15** were mounted on a Nonius B.V. MACH 3 and a Kuma KM-4 κ-axis diffractometer, respectively. Fifteen and twenty-five centred reflections were used in the least-squares procedure to obtain the unit cell parameters for **8** and **15**, respectively. Monoclinic $P2_1/c$ and $P2_1$ space groups were chosen according to the established cell dimensions and systematic absences. To collect the data for **8** monochromatic copper radiation was used, whereas the molybdenum characteristic Kα line was applied for **15**. The stability of the crystals of **8** and **15** during the period of data collection was checked every 100 and 200 reflections, respectively. A total of 1812 and 1736 reflections were collected to $2\Theta$ of 147° and 48°, respectively. The data were corrected for Lorentz and polarization effects and in the case of **8** also for absorption and extinction. The structures were solved using direct methods from SHELXS97[12] software and refined by application of full-matrix least-squares procedure from the SHELXL97[13] program. All non-hydrogen atoms were found from the E-maps. After isotropic refinement of the models a consecutive anisotropic refinement revealed, in the case of **15**, a partial disorder in both the *t*-butyl and sulfonyl group regions. Finally, the hydrogen atoms were added to both models using standard geometrical constraints. In the last cycles of refinement of the structures all ordered non-hydrogen atom positions were refined together with their anisotropic displacement parameters, whereas the disordered carbon and oxygen atom positions were refined with their isotropic thermal parameters. Also positions of amine and those hydrogens connected to the planar $sp^2$ carbon atoms were refined isotropically. The remaining hydrogen atoms of **15** were included into the model as fixed contributors with the isotropic thermal coefficients being 1.2 and 1.5 times the corresponding isotropic parameter of the heavy atom for the ring and methyl group hydrogens, respectively. In the case of **8**, however, the isotropic displacement parameters of the hydrogens were also unconstrained and refined. Selected data for **8** and **15** are given in Table 1.‡

### NMR measurements

The NMR spectra were run on a Varian INOVA 500 NMR spectrometer, operating at 499 806 MHz for $^1$H observation, in 5 mm sample tubes using 25–45 mg of the solute in 0.7 ml of $CDCl_3$. The $^{13}$C, $^{15}$N and $^{17}$O NMR parameters were acquired from the same samples; the $\delta$ values were calibrated *vs.* internal TMS, and the external $CH_3NO_2$ and $H_2O$ for their respective resonances.

The $^1$H NMR spectra were usually acquired using a 5000 Hz spectral window, 30° pulse, 32K data points, 3.3 s acquisition and no pulse delay. The $^{13}$C NMR spectra were run by using a 25 kHz spectral range, a 30° tip angle, 64K data points, a 1.3 s acquisition time, a 1.0 s relaxation delay and 512 transients.

The $^1$H-$^{15}$N HMQC[14] spectra were recorded with an acquisition time of 0.2 s, a spectral width of 5000 Hz, 2048 points in the $^1$H dimension and 20 kHz in the $^{15}$N dimension, 256 increments, $^nJ$(N,H) = 4.5 Hz; 96 transients were recorded for each increment, with a relaxation delay of 1 s. The $^1$H-$^{15}$N HSQC[15] were run under the same conditions, using $^1J$(N,H) = 90 Hz and 4096 data points in the $^1$H dimension to afford better resolution when reading off the $^nJ$(N, H) coupling constants in $F_2$.

The $^{17}$O NMR data in direct detection mode were acquired usually from 45 mg of solute in 0.7 ml of $CDCl_3$ or $CD_3CN$ in a 5 mm sample tube or from solutions of 100–200 mg of a solute in 3 ml of solvent in 10 mm sample tube at a resonance frequency of 67.7 MHz on a Varian INOVA. Spectral width was usually 27 kHz; 4096 data points were acquired with a 0.076 s acquisition time delayed 40 μs. Usually 30 000–100 000 FID's were acquired, in blocks of 1024, and processed with the weighting function lb = 10–20 Hz. The halfwidth of signals

‡ CCDC reference numbers 233419 and 233420 for **8** and **15**, respectively. See http://www.rsc.org/suppdata/nj/b4/b409254f/ for crystallographic data in .cif or other electronic format.

**Table 1** Crystal data and structure refinement for **8** and **15**

| | **8** | **15** |
|---|---|---|
| Empirical formula | $C_7H_{15}NO_2S$ | $C_9H_{17}NO_2S$ |
| Formula weight | 177.26 | 203.30 |
| $T$/K | 293(2) | 293(2) |
| Crystal system | Monoclinic | Monoclinic |
| Space group | $P2_1/c$ | $P2_1$ |
| $a$/Å | 5.3858(3) | 5.764(5) |
| $b$/Å | 13.3905(9) | 16.888(12) |
| $c$/Å | 13.4835(6) | 6.447(4) |
| $\alpha$/° | 90 | 90 |
| $\beta$/° | 96.434(9) | 115.20(7) |
| $\gamma$/° | 90 | 90 |
| $U$/Å$^3$ | 966.29(9) | 567.8(7) |
| $Z$ | 4 | 2 |
| $\mu$/mm$^{-1}$ | 2.645 | 0.257 |
| Total reflections | 1812 | 1736 |
| Independent reflections | 1614 | 935 |
| $R_{int}$ | 0.0491 | 0.0862 |
| $R_1$ [$I > 2\sigma(I)$] | 0.0634 | 0.0531 |
| $wR_2$ [$I > 2\sigma(I)$] | 0.1447 | 0.1334 |

was 200–500 Hz. In the case of closely lying signals a deconvolution procedure was applied.

### Quantum-chemical calculations

The quantum-mechanical calculations of studied compounds were performed to estimate the geometry and energies for the most stable conformers using the GAUSSIAN98 program.[16] Geometry optimizations were performed using density functional theory (DFT) with the B3LYP exchange functional and the split-valence 6-31G** basis set.[17] The geometry of **8** was also calculated using MP2 theory, for comparison with DFT results (see table to Scheme 3 below).

## Results and discussion

### X-Ray structure of 8

The X-ray structure of compound **8** is shown in Fig. 1. It shows the intermolecular hydrogen bonding of two molecules. Fig. S1 in the Electronic supplementary information (ESI) shows the packing in a unit cell.

### NMR parameters

The NMR data of the studied compounds are gathered in Table 2.

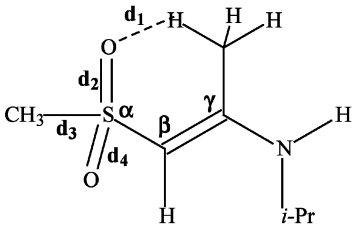
**Differential parameters $\Delta\delta(^1H, ^{15}N, ^{17}O)$.** In the majority of studied enamines, it is relatively easy to conclude that an intramolecular hydrogen bond is formed due to observation of both the *Z* and *E* forms. In principle, the parameters in the *E* form can be treated as reference values for the $\Delta\delta(^1H, ^{15}N, ^{17}O)$ parameters, which denote the difference between the *Z* and *E* values in a given resonance. It should be noted however, that the $\delta(^1H)$ values in the *E* form can be affected by factors other than intramolecular ones, such as concentration, solvent and temperature of the sample.

The hydrogen bond in "push-pull" enamines can be studied effectively by $^{15}N$ and $^{17}O$ NMR[18,19] but also by means of the isotope effect $^2\Delta\delta C$ on $C^1$ in $^{13}C$ NMR upon NH deuteriation.[20–22] Existing data can serve as a base for interpretation of spectral parameters in related compounds. Based on this information we have tried to evaluate the relative strength of the hydrogen bond in the studied β-sulfonylenamines with respect to other "push-pull" enamines and rationalize the origins of the observed differences in magnitude and sign of the differential parameter $\Delta\delta$ in $^1H$, $^{15}N$ and $^{17}O$ NMR.

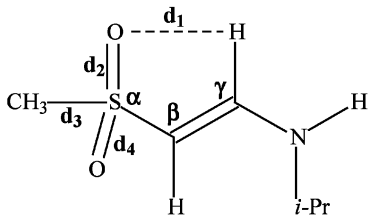
***Δδ(¹H).*** Direct probes for an intramolecular hydrogen bond are the values of $\delta(^1H)$ and $\delta(^{17}O)$. The values of $\Delta\delta(N^1H)$ of enamines are cited in Table 2. This difference seems to be the simplest indicator of the hydrogen bond strength. Based on this parameter one can predict observation of the strongest hydrogen bonds for compounds listed at the beginning of Table 2 [$\Delta\delta(N^1H)$ 3.9–5.2 ppm] and the weakest ones for those at the end [$\Delta\delta(N^1H) \approx 1.3$ ppm].

The studied sulfones have distinct values of the differential parameter $\Delta\delta(N^1H)$, comprising three different groups of compounds, ranging from *ca.* 3 ppm for α-substituted compounds, to 2 ppm for unsubstituted and an acyclic β-alkyl substituted compounds, to 1.5 ppm for cyclic β-substituted compounds. These values classify the strength of the hydrogen bonds in these β-sulfonylenamines in the order of appearance in Table 2. They are much weaker than in enaminones. Even the weak acceptor in **4** (COO) forms a relatively strong hydrogen bond as compared with $sp^3$-hybridized sulfonyl or sulfinyl acceptors.

***Δδ(¹⁷O).*** The direct partner in the hydrogen bond, the oxygen atom, shows a much larger chemical shift dispersion, as seen in the $\Delta\delta(^{17}O)$ values. The strong hydrogen bond in enaminones gives characteristically, for the carbonyl moiety, a $\Delta\delta(^{17}O)$ value of −34 ppm, which is smaller for an acyclic ketone, being −25 ppm. For a cyclic 5-membered ring enaminone or lactone, of similar hydrogen bond strength, as judged from the $\Delta\delta(N^1H)$ value, the reversal of the sign of this




**9**




**8**

| No | | | $d_1$[Å] | $d_2$[Å] | $d_3$[Å] | $d_4$[Å] | α[°] | [°] | γ[°] |
|---|---|---|---|---|---|---|---|---|---|
| **8** | **calculated** | **DFT** | 2.175 | 1.498 | 1.844 | 1.493 | 111.7 | 128.0 | 125.2 |
| | | **MP2** | 2.215 | 1.475 | 1.788 | 1.471 | 111.3 | 126.5 | 125.2 |
| | **X-ray geometry** | | 2.357 | 1.446 | 1.761 | 1.441 | 111.9 | 125.3 | 123.4 |
| **9** | **Calculated** | **DFT** | 2.399 | 1.497 | 1.842 | 1.494 | 108.53 | 118.45 | 117.5 |

**Scheme 3**

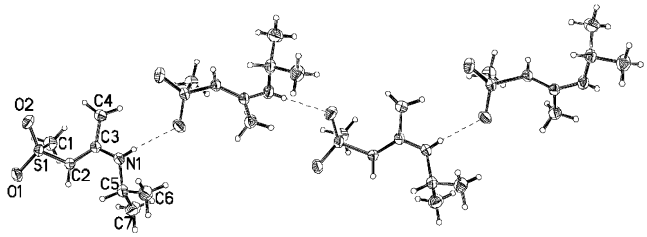



**Fig. 1** Structural motif of the X-ray structure of sulfone **8**. Molecules form infinitive hydrogen-bonded chains in the *c* direction. The numbering scheme is shown for one molecule.

parameter is observed, that is a shift of the *Z* resonance to higher values of $\delta(^{17}O)$ upon hydrogen bonding. The effect can be, in general, linked to changes in geometry affecting the hydrogen bond, coupling of the exocyclic double bond with a 5-membered ring. It is noteworthy that the changes in intramolecular geometry may affect to a large extent the sign of the observed differential parameters.

Due to experimental difficulties, inherent to $^{17}O$ NMR measurements in this class of compounds (broad lines, ambiguous intensity measurements, signal overlap), values of $\Delta\delta(^{17}O)$ could not be reported for all studied β-sulfonylenamines.

In β-substituted β-sulfonyloenamines only one signal was observed, which in the case of **16** and **14** was assigned to the *E* form, due to the very small content of the *Z* form in the studied solutions, 2% and 7%, respectively. Adopting a more conservative approach we do not discuss the signal positions of the *Z* forms in **15** and **13**, although the respective *Z* abundances were 21% and 10%, though only one signal was observed. This was also assigned to the major *E* form.

In α-substituted β-sulfonylenamines **6**, **7** and **8**, present in $CDCl_3$ on average as 20% *E* and 60% *Z* (the rest being an imine form), again one signal was observed, although the coincidental overlap of signals due to *E* and *Z* forms cannot be rejected unambiguously, as unsymmetrical signals were observed in a few cases. This is also confirmed by the observation of three separate signals due to *E*, *Z* and imine for **6** ($\delta$ = 165.7; 164.0; 160.9 ppm) and **8** ($\delta$ = 166.1; 164.0; 160.3 ppm) dissolved in $CD_3CN$ (Fig. 2).[7]

In double bond unsubstituted β-sulfonylenamines **9**, **10** and **11** two signals are observed. The assignment of individual forms was based on **9**, which showed 87% of the *E* form and 10% of *Z* and therefore the assignment of the *E* form was unambiguous. In other cases the signals had comparable half-widths and intensities. Observed $\Delta\delta(^{17}O)$ effects are comparable in this group of compounds (+9.2, +9.4, +9.9 ppm for **9**,

**Table 2** Comparison of the NMR parameters of atoms engaged in hydrogen bonding in *E*/*Z* enamines[ab]

| No. | *E*/*Z*[c] | $\delta^{17}O$ | $\Delta\delta(^{17}O)$ | $\delta^{15}N$ | $\Delta\delta(^{15}N)$ | $\delta(N^1H)$ | $\Delta\delta(N^1H)$ | $^1J(N,H)$ | $\delta_I$ $^{15}N$ |
|---|---|---|---|---|---|---|---|---|---|
| **1** | *E* | 491 | −34 | −273 | | 6.4 | 3.9 | 92.7 | — |
| | *Z* | 457 | | | | 10.3 | | | |
| **2** | *E* | 446 | −25 | −303.1 | +11.6 | 4.3 | 5.2 | 91.6 | — |
| | *Z* | 421 | | −291.5 | | 9.5 | | 92.4 | |
| **3** | *E* | 397 | +17 | | | 5.2 | 3.3 | | — |
| | *Z* | 414 | | | | 8.5 | | | |
| **4** | *E* | 265 | +23 | −303.5 | +1.7 | 4.9 | 3.3 | | — |
| | *Z* | 288 | | −301.8 | | 8.2 | | | |
| **5** | *E* 0.29 | — | — | −259.5 | −5.4 | 4.2 | 3.3 | 89.9 | −12.3 |
| | *Z* 0.61 | — | | −264.9 | | 7.5 | | 86.3 | |
| **6** | *E* 0.22 | 165.6 | 0.0 | −283.2 | −8.1 | 4.8 | 2.8 | 91.3 | −43.9 |
| | *Z* 0.63 | 165.6 | | −291.3 | | 7.6 | | 91.6 | |
| **7** | *E* 0.19 | 164.7 | 0.0 | −272.0 | −5.3 | 4.7 | 3.0 | | −30.3 |
| | *Z* 0.66 | 164.7 | | −277.3 | | 7.7 | | | |
| **8** | *E* 0.20 | 165.1 | 0.0 | −267.8 | −4.0 | 4.2 | 2.8 | 92.5 | −27.5 |
| | *Z* 0.65 | 165.1 | | −271.8 | | 7.0 | | 90.0 | |
| **9** | *E* 0.87 | 156.6 | +9.2 | −275.9 | +1.1 | 4.8 | 1.8 | | −12.0 |
| | *Z* 0.10 | 165.8 | | −274.8 | | 6.6 | | | |
| **10** | *E* 0.60 | 157.2 | +9.4 | −269.6 | +2.8 | 4.7 | 2.2 | 87.8 | −4.7 |
| | *Z* 0.32 | 166.6 | | −266.8 | | 6.9 | | 89.7 | |
| **11** | *E* 0.60 | 147.4 | +9.9 | −267.5 | +2.7 | 4.9 | 2.2 | 88.8 | −3.9 |
| | *Z* 0.37 | 157.3 | | −264.8 | | 7.1 | | 91.0 | |
| **12** | *E* | — | — | −272.3 | −4.3 | 4.5 | 1.7 | 90.1 | |
| | *Z* | — | | −276.6 | | 6.2 | | 89.0 | |
| **13** | *E* 0.84 | 135.6 | — | −314.0 | +1.0 | 4.1 | 2.2 | | |
| | *Z* 0.10 | — | | −313.0 | | 6.3 | | | |
| **14** | *E* 0.91 | 136.0 | — | −273.8 | 0 | 4.1 | 2.0 | | −11.3 |
| | *Z* 0.07 | — | | −273.8 | | 6.1 | | | |
| **15** | *E* 0.58 | 154.5 | — | −276.0 | −1.6 | 3.9 | 1.5 | 87.1 | −12.9 |
| | *Z* 0.21 | — | | −277.6 | | 5.4 | | 87.9 | |
| **16** | *E* 0.66 | 154.7 | — | −301.05 | — | 4.2 | 1.3 | | −37.6 |
| | *Z* 0.02 | — | | — | | 5.5 | | | |

[a] $^{17}O$ NMR chemical shifts for **1–4** and **12** are taken from ref. 7, $^{15}N$ NMR chemical shifts for **1** and **2**are taken from ref. 23 and for **12** from ref. 24. Imine chemical shift values are given in the last column. [b] The lack of the second $\Delta\delta^{17}O$ value is due to the low abundance of the isomer or poor signal dispersion of broad signals. [c] Mole fraction of isomers.

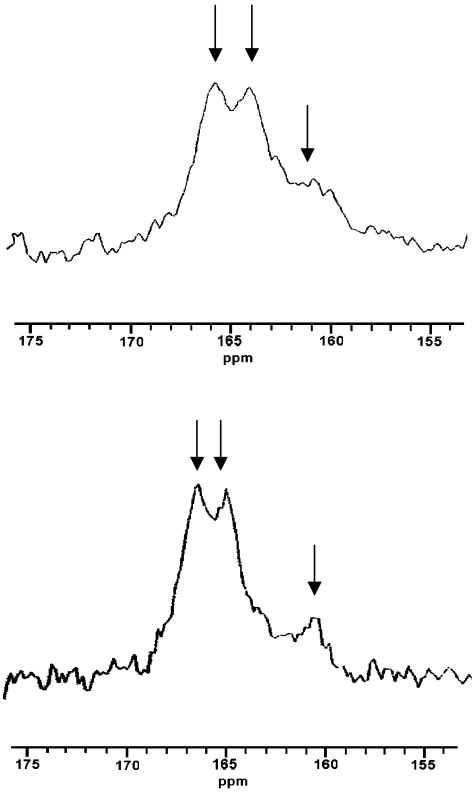
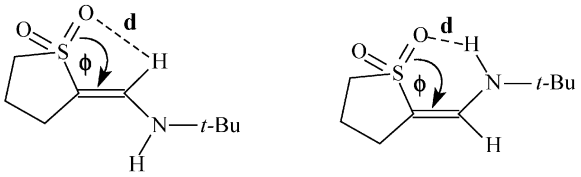



**Fig. 2** $^{17}O$ NMR spectra of (a) **6** and (b) **8** in $CD_3CN$ solution showing distinct chemical shifts for three isomers.

**10** and **11**, respectively), although the compounds differ in the substituent character on the sulfur ($CH_3$ or *p*-$ClC_6H_4$) and nitrogen (*i*-$C_3H_7$ or *t*-$C_4H_9$) atoms. Therefore, it seems reasonable to suggest that in β-sulfonylenamines the strength of an intramolecular hydrogen bond is strongly related to intramolecular geometry parameters that are altered by double bond substitution; however, other intramolecular effects may play a role as well. A relevant example aiding this hypothesis is furnished by a comparison of **9** and **8**. These compounds differ only by the methyl substitution at the α carbon atom but their $\Delta\delta(^{17}O)$ values are +9.2 and 0.0 ppm, respectively. In both compounds the *Z* forms have the same chemical shifts, although, judging from the NH chemical shifts, the stronger hydrogen bonding is expected for α-substituted compounds. On the other hand, the $\delta(^{17}O)$ values for the *E* form differ substantially. Here, the influence of intermolecular hydrogen bonding, conformations of both forms and intramolecular geometry can be invoked. It was established that the *E* tautomer of **9** exists as an *E*–*Z*/*E*–*E* mixture and the sulfone **8** as an *E*–*Z* form. For the *E*–*Z* forms of both compounds the intramolecular geometry is visualized in Scheme 3. The X-ray geometry of the relevant conformation of **8** is also shown, to assess the confidence in the comparison of calculated values. The comparison of the *E*–*Z* forms in Scheme 3 suggests simultaneous expansion of all labelled angles, including the O=S–$C^2$ angle (α), which directly influences the $^{17}O$ chemical shift. The S=O···H–$C^1$ interaction in **9** *vs.* the S=O···$H_3C$–$C^1$ interaction in **8** may also be important, which as also shown in Scheme 3 are quite different.

***Δδ(^15N).*** Discussion of the $\Delta\delta(^{15}N)$ values leads to the same conclusions as those obtained by considering the $\Delta\delta(^1H)$ parameters. In this instance one has to consider the contribution of two contradictory effects: the large high-frequency shift due to hydrogen bonding and a low-frequency shift due to steric crowding around the nitrogen atom and $C^1$. Thus, the groups $R^1$–X=O and HN–$R^4$, being in a sterically compressed situation in the *Z* form, generate this effect intrinsically whereas the hydrogen bonding counterbalances it. Strong hydrogen bonding in enaminones leads to large values of the $\Delta\delta(^{15}N)$ parameter of *ca.* +10 ppm. It can also be suggested that negative values of this parameter, *ca.* −4 to −8 ppm, in α-substituted sulfones reflects the dominance of the buttressing effect of the $C^1$–$CH_3$ and N–$R^4$ groups over relatively weak hydrogen bonding. In double bond unsubstituted sulfones, $\Delta\delta(^{15}N)$ values of *ca.* 1–2.8 ppm are observed, hinting at weak hydrogen bonding, as in α-substituted sulfones, which not counterbalanced by the buttressing effect of a substituent at $C^1$.




**15** ***E*-*E*** **15** ***Z*-*E***

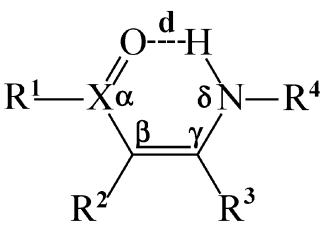
| | | d[ ] | ϕ[°] |
|---|---|---|---|
| **15** ***E*-*E*** | **Calculated DFT** | 2.773 | 38.67 |
| | **X-ray geometry** | 2.555 | -8.02 |
| **15** ***Z*-*E*** | **Calculated DFT** | 2.150 | 34.49 |

**Scheme 4**

The weakest hydrogen bonds, $\Delta\delta(N^1H)$ ~1.5 ppm, are observed in β-substituted β-sulfonyloenamine **15** (see the overview of the X-ray derived structure in the ESI) and in sulfoxide **12**. The $\Delta\delta(^{15}N)$ values in these compounds are −1.6 and −4.3 ppm, respectively, suggesting the dominance of steric compression in the *Z* form. Scheme 4 illustrates this situation with a comparison of the calculated and X-ray geometry of an *E*–*E vs.* calculated geometry in the *Z*–*E* form of **15**. It is clearly seen that the *Z* form has the sulfonyl oxygen nonplanar with the double bond, which is expected to weaken the hydrogen bond.

Our confidence in the above discussion is strengthened by the fact that the experimental results of $\Delta\delta(N^1H)$ are supported by the *ab initio* calculations. The calculated O···H distances *d* in *Z*–*E* isomers of **2**, **3**, **8**, **9** and **15** are 1.779, 1.896, 1.902, 1.974 and 2.150 Å, respectively, correlating well with the experimental $\Delta\delta(N^1H)$ values (Table 2 and Scheme 5).

**Isotope effect of $^2H$ on $^{13}C$ chemical shifts.** As established earlier,[20–22] the hydrogen bond strength is clearly reflected in the secondary isotope effect on $^{13}C$ chemical shifts induced by the NH → ND substitution. The effect is mainly seen for the $C^1$ carbon atom of the *Z* forms as compared with the *E* form.




| | α [°] | β[°] | γ [°] | δ[°] | d [ ] |
|---|---|---|---|---|---|
| **2** | 122.74 | 119.16 | 125.28 | 112.26 | 1.779 |
| **3** | 126.68 | 121.67 | 123.10 | 113.19 | 1.896 |
| **8** | 108.70 | 125.90 | 124.20 | 113.90 | 1.902 |
| **9** | 108.06 | 124.17 | 128.90 | 114.95 | 1.974 |

**Scheme 5**

**Table 3** Comparison of the deuterium isotope effect (NH → ND) at carbon atom $C^1$, $^2\Delta\delta C^1$, in various enamines[ab]

| | | $\delta$NH | | $^2\Delta\delta C^1$ | |
|---|---|---|---|---|---|
| | Solvent | *Z* | *E* | *Z* | *E* |
| **2** | $CDCl_3$ | 9.5 | 4.3 | 0.280 | 0.100 |
| **12** | $CDCl_3$ | 6.2 | 4.5 | 0.111 | 0.091 |
| **6** | $CDCl_3$ | 7.7 | 5.7 | 0.110 | 0.090 |
| **8** | $CD_3CN$ | 7.7 | 5.2 | 0.100 | 0.070 |

[a] Isotope effect $^2\Delta\delta$ $C^1$ is calculated as $\delta(C^1\text{-ND})\text{-}\delta(C^1\text{-NH})$. [b] $^2\Delta\delta$ $C^1$ for **12** are taken from ref. 22.

Table 3 gives such a comparison for selected enamines. The strongest hydrogen effect is observed in the situation where the $C^1$ carbon atom is embedded in a planar six-membered ring closed by a hydrogen bond. This is observed in enaminones. Data shown in Table 3 are complementary to the $\Delta\delta(N^1H)$ and other differential parameter values discussed above. In *Z* enaminones a very strong hydrogen bond yields the largest isotope effect, nearly threefold larger than in the *E* form. Sulfones and sulfoxides form weak, comparable in strength, hydrogen bonds and the isotope effect is of the same order in the *Z* and *E* forms.

Fig. 1 shows the X-ray structure of sulfone **8**. It evidences the presence of the intermolecular hydrogen bond in the solid state between two molecules of *E*–*Z* isomers. It cannot be established from the present experiments to what extent this type of hydrogen bonding persists in chloroform or acetonitrile solution. The sulfone **8** exists in solution as a mixture of 60% *Z* and 30% *E* forms (with 10% imine form). It seems reasonable to assume that the driving force for the predominance of the *Z* isomer in solution is the strength of the intramolecular hydrogen bond. The isotope effects cited in Table 3 suggest a comparable strength of hydrogen bonding in both the *E* and *Z* forms. Therefore, it can be concluded that the intramolecular hydrogen bond is at least as strong as the intermolecular hydrogen bond in the *E* form, possibly due to the buttressing effect of the methyl substituent at the $C^1$ carbon atom, leading to geometry changes such as shown in Scheme 3.

## Conclusions

We have established a way to compare the strength of hydrogen bonds in various enamines by monitoring differential shifts of the type $\Delta\delta(X)$, which are the difference of chemical shifts between the *E* and *Z* forms of nuclei directly involved in hydrogen bonding (*i.e.*, N, H, O atoms). It is shown that $\Delta\delta(N^1H)$ and $\Delta\delta(^{15}N)$ give conclusive results and their changes are rationally interpreted invoking established contributing effects that influence the values of chemical shifts. The $\Delta\delta(^{17}O)$ parameter is sensitive to the intramolecular geometry, mainly the bond angles around oxygen and the co-planarity of atoms forming hydrogen bonds.

The results show also that the latter situation is important in defining the strength of hydrogen bonds. Even a weak acceptor such as COO in **4** gives a relatively strong hydrogen bond as compared with $sp^3$-hybridized sulfonyl or sulfinyl acceptors.

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