Available online at www.sciencedirect.com

SCIENCE DIRECT®

Tetrahedron Letters 45 (2004) 4127–4129

Tetrahedron Letters

Classical versus redox tautomerism: substituent effects on the keto/enol and sulfoxide/sulfenic acid equilibria

Ibon Alkorta* and José Elguero

Instituto de Química Médica (CSIC), Juan de la Cierva 3, E-28006 Madrid, Spain

Received 28 January 2004; revised 22 March 2004; accepted 24 March 2004

Abstract—MP2/6-311+G** ab initio calculations have been carried out for a classical example of tautomerism, the keto/enol [$RCOCH_3/RC(OH)CH_2$] and an example of redox tautomerism, the sulfoxide/sulfenic acid [RS(O)H/RSOH]. Eleven R substituents have been examined. Both equilibria show proportional energies and similar dependence on the Swain–Lupton *F* and *R* parameters.

The present paradigm of organic chemistry rests heavily on a few simple principles. For instance, in the case of conjugated systems these are aromaticity, the Diels–Alder reaction and tautomerism. Thousands of papers have been devoted to these three topics, both experimental and theoretical and continue to be the subject of intense research. Prototropic tautomerism concerns the equilibrium between triads (Scheme 1) or their vinylogs.

The external groups, X and Z, can be CH_2 (CRR′), NH (NR), S or O, whereas the central one can be CR, N or SR (other elements are possible but these are the most relevant). In total, 30 combinations are possible, most examples concerning the case where Y = CR. Using semi-empirical methods (CNDO/2, PCILO), we studied the cases Y = CH, Z = NH and X = CH_2, NH, O and S,[1] as well as Y = N, Z = CH_2 and X = CH_2, NH and O.[2] As a representative of Scheme 1 triad, we have now selected the keto/enol tautomerism **1a/1b** (X = CH_2, Y = CR, Z = O, Scheme 2).

$$XH-Y=Z \rightleftharpoons X=Y-ZH$$

Scheme 1.

There is another class of tautomerism that we propose to name redox tautomerism, in which the central atom Y changes its degree of oxidation (its valency). The central atom can be sulfur or phosphorus, one of the most interesting cases being that of sulfoxide/sulfenic (thioperoxide) equilibrium. Sulfoxides present also a classical tautomeric equilibrium with the aci-form **2a/2b** (X = CH_2, Y = SR, Z = O, Scheme 2).

Redox tautomerism requires that the sulfur atom bears at least a hydrogen atom: **3a/3b** (Scheme 3), with the sulfoxide being the oxidized form and the sulfenic acid (a thioperoxide) the reduced one.

The aim of the present work is double: (i) using ab initio (MP2/6-311+G**) calculations to determine the effect of

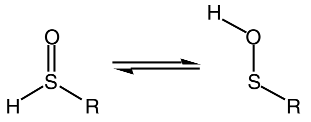
1a **1b** **2a** **2b**

Scheme 2.

Keywords: Tautomerism; Ab initio calculations; Redox tautomerism.

* Corresponding author. Tel.: +34-91-562-29-00; fax: +34-91-564-48-53; e-mail: ibon@iqm.csic.es

doi:10.1016/j.tetlet.2004.03.141



3a **3b**

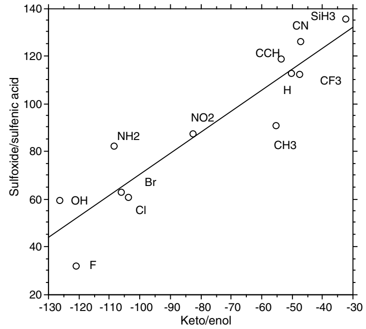
Scheme 3.

the substituent R on the equilibria **1a/1b** and **3a/3b**; (ii) to try to model these differences in energy using linear free-energy relationships (LFER). Concerning the keto/enol tautomerism, the work of Lien and co-workers is the most relevant.[3] These authors studied at the MP2/6-31G** level the effect of eight different R substituents (BH_2, CN, NH_2, OH, F, CN, H and Cl), and their results will be subsequently compared with ours. Concerning the redox equilibrium of sulfoxides, Wolfe and Schleger studied the case R = H or CH_3, pointing out the anomaly that, in these systems, **3b** is more stable than **3a**.[4] They described the **3a**,**b** compounds as tautomers. The isomerization of dimethylsulfoxide radical cation into methyl methanesulfenate (CH_3–S–O–CH_3) radical cation $\mathbf{5}^{+\cdot}$ has been studied by mass spectrometry.[5] According to our calculations, neutral dimethylsulfoxide **4** is less stable than neutral methyl methanesulfenate **5** by 15.1 kJ mol^{-1}. Other authors have studied by mass spectrometry and ab initio calculations the **2a/2b** equilibrium (R = CH_3).[6] The equilibrium **3a/3b** for R = H has been studied experimentally in the gas phase (existence of hydrogen thioperoxide **3b**)[7,8] and theoretically (G2/MP2/6-31G*), the conclusion being that **3b** is more stable than **3a** by 72.2 kJ mol^{-1}.[8]

Our results are reported in Table 1 together with those of Lien and co-workers[3] (we have not calculated the BH_2 substituent because its empirical parameters are not known).

In general, our values are 21 kJ mol^{-1} above those of Lien. Note that for R = H exclusively, Lien and co-workers[3] have calculated the difference of energy at higher levels; at MP2/6-31G** it amounts to 61.5 and at G2 to 49.4, not far from our value of 50.1 kJ mol^{-1}.

(1) Both equilibrium constants (i.e., energy differences) are roughly proportional [$\Delta E_{\mathbf{3a/3b}} = (159 \pm 9) + (0.88 \pm 0.11)\Delta E_{\mathbf{1a/1b}}$]. The sign of the slope indicates that the substituents produce the same effects: the OH and F substituents stabilize the X = Z forms **a** (keto and sulfoxide) while SiH_3 one stabilizes the XZH ones **b** (enol and sulfenic acid).



(2) In order to study the adequacy of biparametric LFER models to describe these equilibria, we have first calculated the relative (to H as substituent) energies ($\Delta RE_i - \Delta RE_H$). Amongst the multitude of available parameters,[9] we have selected Swain and Lupton's F and R, because they are unique in contrast to Taft's σ_R and σ_I for which many values are available. The correlations (11 points, Table 1) are moderately good:

$$\Delta RE_{\mathbf{1a/1b}} = -(67 \pm 10)F + (82 \pm 10)R, \quad r^2 = 0.95$$

$$\Delta RE_{\mathbf{3a/3b}} = -(65 \pm 17)F + (60 \pm 17)R, \quad r^2 = 0.83$$

Nevertheless they allow to predict the behaviour of other tautomeric pairs. Besides, they show that the sensitivity to field and resonance effects is similar in both cases.

In conclusion this study has shown the analogies and differences of two kinds of tautomerism concerning the influence of substituents. Other tautomerisms probably will behave similarly and the establishment of a general theory of substituent effects on tautomerism should be possible.

Table 1. Energy differences (kJ mol^{-1}, MP2/6-311+G**) corresponding to equilibria **1a/1b** (**1a** being always more stable) and **3a/3b** (**3b** being always more stable)

Substituent	**1a/1b** from Ref. 3	**1a/1b** this work	**3a/3b** this work	F	R
H	−71.5	−50.1	112.9	0.00	0.00
F	−140.6	−121.0	32.0	0.45	−0.39
Cl	−121.3	103.6	60.7	0.42	0.19
Br	—	−106.2	63.2	0.45	−0.22
CH_3	−77.8	−55.2	90	0.01	−0.18
CF_3	—	−47.6	112.3	0.38	0.16
C≡CH	—	−53.6	119.0	0.22	0.01
CN	−66.9	−47.3	126.4	0.51	0.15
NH_2	−132.6	−108.4	82.5	0.08	−0.74
NO_2	—	−82.5	87.3	0.65	0.13
OH	−144.7	−126.4	59.6	0.33	−0.70
SiH_3	—	−32.5	135.6	0.06	0.04

Acknowledgements

Financial support was provided by the Spanish DGI/MCYT (Projects no BQU-2003-01251 and SAF-2003-08003-C02-02).

References and notes

1. Teysseyre, J.; Arriau, J.; Elguero, J.; Katritzky, A. R. *Bull. Soc. Chim. Belg.* **1976**, *85*, 39.
2. Lhamyani-Chraibi, M.; Gélizé-Duvigneau, M.; Arriau, J.; Elguero, J. *Bull. Soc. Chim. Belg.* **1980**, *89*, 71.
3. Su, C.-C.; Lin, C.-K.; Wu, C.-C.; Lien, M.-H. *J. Phys. Chem. A* **1999**, *103*, 3289.
4. Wolfe, S.; Schlegel, H. B. *Gazz. Chim. Ital.* **1990**, *120*, 285.
5. Carlsen, L.; Egsgaard, H. *J. Am. Chem. Soc.* **1988**, *110*, 6701.
6. Bouchoux, G.; Le, H. T.; Nguyen, N. T. *J. Phys. Chem. A* **2001**, *105*, 11128.
7. Iraqi, M.; Schwarz, H. *Chem. Phys. Lett.* **1994**, *221*, 359.
8. Goumri, A.; Rocha, J.-D. R.; Laakso, D.; Smith, C. E.; Marshall, P. *J. Chem. Phys.* **1994**, *101*, 9405.
9. Hansch, C.; Leo, A.; Hoekman, D. *Exploring QSAR*; American Chemical Society: Washington, 1995.