# AROMATICITY OF THIAZOLE III.
## THE TRANSMISSION OF SUBSTITUENT EFFECTS AND THE POLARIZABILITY OF THE ELECTRONIC SYSTEM OF THIAZOLE

Ioan A. Silberg[a]*, Simona Silberg[b] and Adina Ghirisan[a]

[a]Babes-Bolyai" University, Dept. of Organic Chemistry
Arany Janos 11, RO-3400 Cluj-Napoca, Roumania
[b]Pharmaceutical Faculty, Dept. of Organic Chemistry
Victor Babes 41, RO-3400 Cluj-Napoca, Roumania

## ABSTRACT

A comparative discussion is given of the transmission of substituent effects through the 2,4- and 2,5-thiazolylene bridges and of the solvent effects on the transmission factors. The value of the transmission coefficient of *meta*-phenylene bridge is calculated and compared to that of the *para*-phenylene. An estimation of the delocalization energy of thiazole is made on the basis of the transmission factors.

## INTRODUCTION

In the previous papers of this series (1, 2) we reported the determination, by IR- and $^1$H-NMR spectroscopy, of the transmission factors of the 2,4- and 2,5-thiazolylene bridges. This first parallel estimation of the attenuation of substituent electronic effects on propagation along the two major directions of a five-membered heterocyclic ring provides the opportunity of obtaining a deeper insight into the response of the electronic system of thiazole to perturbations by substituents and solvents.

## DISCUSSION

A comparative survey of the transmission factors of the two thiazolylene bridges points out to the somewhat unexpected similitude of their values:

$$\pi'_{2,4-thz}=0.42\pm0.02 \quad \text{and} \quad \pi'_{2,5-thz}=0.38\pm0.02$$
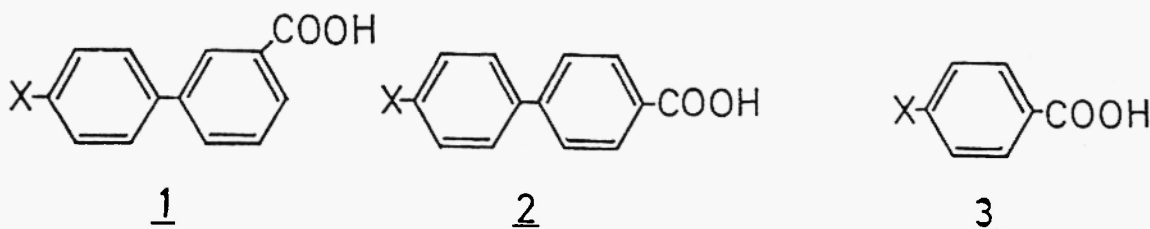
both referring to $CCl_4$, a non-polar solvent, in which the intrinsic features of the phenomenon under investigation are clearly prevailing over external perturbations.

Since the 2,5-disubstituted thiazoles are assimilated to *para*-disubstituted benzene, whereas the 2,4-relationship represents a "pseudo-*meta*" disposition of the interacting groups, one would expect, on the basis of currently used concepts (3), that the influence of the substituents would be felt with

greater intensity in the first series. This does not appear to be the case, and within experimental errors, the 2,4-thiazolylene bridge seems to be a slightly better transmitter of electronic perturbations.

The only difference to be noted is the one revealed by Swain-Lupton analysis (4), which constantly shows that the weight of mesomeric effects is higher in the 2,5- than in the 2,4-interactions, as long as the interference of the solvents does not affect the electron distribution in the molecule.

It is a fact that such rather surprising observations have already been made (5, 6) in comparisons of transmission factors, e. *g.* the close values of $\pi'$ for $-CH_2-$ ( $0.43 \pm 0.06$ ) and for $-CH=CH-$ groups ( $0.48 \pm 0.03$ ) in spite of the current opinion that vinyl is a much better conveyer of electronic perturbations that methylene; however, we felt it was necessary to confront our findings with those in other series. A search of the literature revealed that, in contrast to the 1,4-phenylene bridge, for which several values of $\pi'$ have been advanced : $0.24 \pm 0.01$ (6); 0.37 (7); 0.45 and 0.30 (8); 0.27 (9); 0.32 (10), 0.30 (11); little or no attention has been paid to the determination of the transmission factor of the 1,3-phenylene bridge. We found only one series of physical constants which can be used for this purpose, namely the pKa values of 4-substituted-biphenyl-3'- **1** and 4'-carboxylic acids **2**, reported by Drapala and Malawski (12).



greater intensity... 
$$\underline{1} \qquad\qquad \underline{2} \qquad\qquad \underline{3}$$

These determinations had been carried out in 50% aq. ethanol, so that the corresponding reference series consisted of the pKa values of 4-substituted benzoic acids **3** measured in the same medium by Roberts *et al.* (13). We plotted these values against the $\sigma_p$ substituent constants and found a correlation coefficient of 0.999, with a slope of -1.484, very close to the one found by the original authors (13) : -1.464, who included two points corresponding to *meta*-substituted benzoic acids. The values of pKa for **1** and **2** also give very high correlation coefficients with $\sigma_p$ constants of X ( 0.996 and 0.998, respectively ), the slopes being -0.459 and -0.447. The ratio of the slopes $\rho_1 / \rho_3$ and $\rho_2 / \rho_3$ will give, as already mentioned (1, 2), the measure of the attenuation of the influence exerted by X on the -COOH group when the 1,3-, respectively the 1,4-phenylene bridge is introduced in between. In the case of **2**, the value $\pi'_{1,4} = 0.301$ represents another determination of the transmission coefficient of the *para*-phenylene bridge, and it is in quite good agreement with other literature data(*vide supra;* the mean value of the given coefficients, assuming equal statistical weights, is 0.32). This is reinforcing confidence in the validity of value $\pi'_{1,3} = 0.309$ which can be deduced in exactly the same way from data referring to **1** and **3** , and represents the transmission coefficient of the *meta*
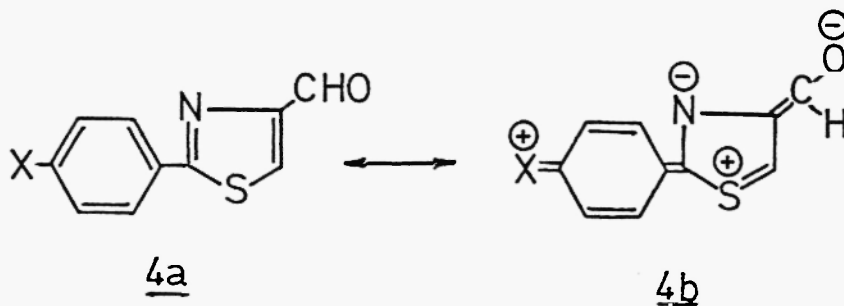
bridge. It is rewarding to conclude that the 1,4- and the 1,3-phenylene bridges have almost identical abilities of transmitting substituent effects, the latter being even slightly better, exactly as in the case of our thiazolylene bridges.

These data deserve a more detailed discussion, in terms of Kirkwood-Westheimer (14), Branch-Calvin (15), Dewar-Grisdale (16) or other new models (17), which is beyond the scope of this paper and will be reported elsewhere.

The influence of the solvents on the intensity of propagation of substituent effects across the thiazole ring can be best followed in the case of the transmission coefficients of the 2,4-thiazolylene bridge. The reader be reminded that the values were (2) 0.42 in $CCl_4$, 0.312 in DMSO, and 0.308 in $CHCl_3$, showing a clear trend to decrease in passing from the non-polar solvent to the polar ones. In fact, solvation is the determining factor, rather than polarity, as shown by the important effect of $CHCl_3$, which can act by hydrogen bonding, too.

In agreement with literature data (18-20) a better solvation leads to a decreased sensitivity towards substituent effects, the transmission coefficients becoming lower.

As already mentioned (2), these observations are easily explained in the case of our 2-aryl-4-thiazolecarboxaldehydes by taking into account the differential solvation of "normal" 4a and "zwitterionic" 4b forms.



4a                    4b

The dipoles of the solvent favor a more rigid localization of charges within the ( already internally polarized ) thiazole ring, and the perturbations produced by the substituents are "buffered" more effectively in polar than in non-polar solvents. The important solvent-induced shifts in $^1$H-NMR spectra clearly show that these interactions are indeed very strong (1, 2).

The influence of the solvents on the ability of the thiazole electronic system to relay substituent effects from position 2 to 4 can also be followed by reinterpreting the data in the literature, concerning some 2-aryl-4-thiazolecarboxylic acids. Experimental (21) and quantum-mechanical (22) investigations led to results from which the value 0.46 can be derived for $\pi'_{2,4-thz}$ in pure ethanol and 0.17 in water.

Although the values, as such, are most questionable ( due to the fact that the application of

classical Hammett techniques are fraught with principial difficulties in the azaaromatic series, where betainic, "zwitterionic" forms and corresponding equilibria can overshadow the basic substituent effects) it is obvious that an increased polarity of solvent ( water ) led to a smaller value of $\pi'$. It is interesting to note that the theoretically calculated value 0.36 (22) is in rather good agreement with our experimental data.

The obvious connection between the propagation of substituent effects and the stability of the electronic system prompted several workers (23, 24) to postulate that a parallel evolution should be expected for the values of transmission factors and of delocalization energies in cyclic systems. Perjessy and co-workers (24) advanced the idea that these two parameters might obey a linear relationship. If this is the case ( and the values of $\pi'$ so far available support such an assumption ) the transmission factor of the 2,5-thiazolylene bridge can be used for an estimation of resonance energy of thiazole, a value which is very difficult to obtain both by experimental and by theoretical procedures, owing to the complications generated by the heteroatoms.

In Figure 1, the linear plot of $\pi'$ values *vs.* $E_d$ ( kcal/mole) is shown together with the values of $\pi'_{2,5\text{-thz.}}$

The conclusion can be drawn that the delocalization energy of thiazole is of the order of 29-31 kcal/mole, that is, slightly higher than the one of thiophene. This finding would parallel views in the literature concerning another pair of azalogs, namely benzene and pyridine (25), values a few kcal/mole higher being advanced for the latter.
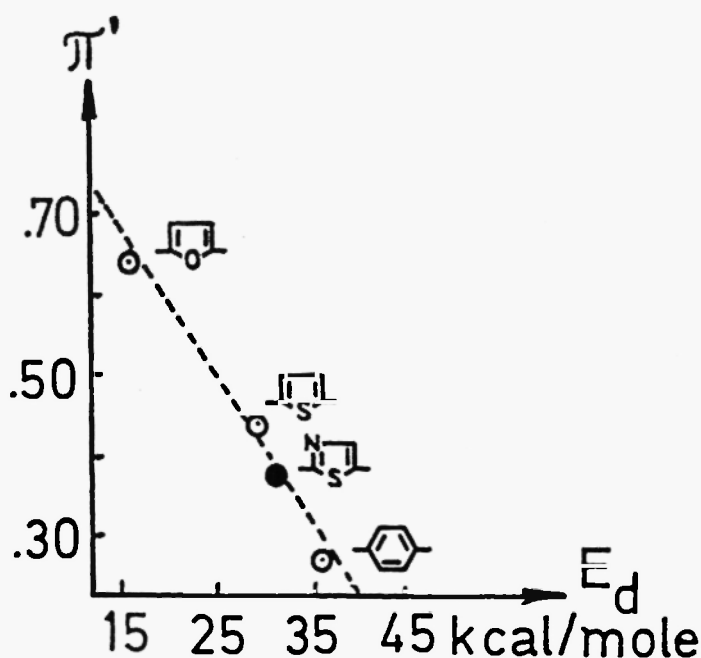


Fig.1. The dependence of the transmission factor on the delocalization energy.

# REFERENCES

(1) S. Silberg, I. A. Silberg and A. Ghirisan, *Studia, Univ. "Babes-Bolyai" Ser. Chem.*, in press

(2) I. A. Silberg, S. Silberg and A. Ghirisan, *Studia, Univ. "Babes-Bolyai" Ser. Chem.*, in press

(3) M. Charton, *Correlation Analysis in Chemistry, Recent Advances,* edited by N. B. Chapman and J. Shorter, Plenum Press, New York, 5, 175 (1978)

(4) C. G. Swain and E. C. Lupton, *J. Amer. Chem. Soc.*, 90, 4328 (1968)

(5) H. H. Jaffe, *Chem. Rev.* , 53, 191 (1953)

(6) L. P. Hammett, *Physical Organic Chemistry*, 2nd edition, McGraw-Hill, New York, 355 (1970)

(7) E. Berliner and E. A. Blommers, *J. Amer. Chem. Soc.*, 73, 2479 (1951)

(8) D. J. Byron, G. W. Gray and R. C. Wilson, *J. Chem. Soc. C*, 831 (1966)

(9) Yu. A. Zhdanov and V. I. Minkin, *Korrelacionnyj Analiz v Organicheskoi Khimii*, Izd. Rostovskogo Univ., Rostov, 1966

(10) A. Morton, A. Beno and M. Uher, *Chem. Zvesti*, 26, 163 (1972)

(11) D. Cristoforou and A. R. D. Happer, *Austr. J. Chem.*, 35, 729 (1982)

(12) T. Drapala and M. J. Malawski, *Rocz. Chem.*, 38, 1593 (1964)

(13) J. D. Roberts, E. A. McElhill and R. Armstrong, *J.Amer. Chem. Soc.*, 71, 2923 (1949)

(14) J. G. Kirkwood and F. H. Weistheimer, *J.Chem. Phys.*, 6, 506 (1938)

(15) G. E. K. Branch and M. Calvin, *The Theory of Organic Chemistry*, Prentice Hall, New York, 1941

(16) M. J. S. Dewar and P. J. Grisdale, *J. Amer. Chem. Soc.*, 84, 3539 and 3548 (1962)

(17) O. Exner and Z. Friedl, *Phys. Org. Chem.*, 19, 259 (1992)

(18) K. Bowden and D. C. Parkin, *Can. J. Chem.*, 47, 185 (1969)

(19) L. W. Deady and R. A. Shanks, *Austr. J. Chem.*, 25, 2363 (1972)

(20) J. Shorter in "*Similarity Models in Organic Chemistry, Biochemistry and Related Fields*"; *Studies in Organic Chemistry*, edited by R. I. Zalewski, T. M. Krygowsky and J. Shorter, Elsevier Science Publishers B. V., Amsterdam, 42, 129 (1991)

(21) A. Benko, I. Zsako and P. Nagy, *Chem. Ber.*, 100, 2178 (1967)

(22) O. Horowitz and I.Zsako, *Studia, Univ. "Babes-Bolyai" Ser.Chem.*, 13, 79 (1968)

(23) O. Exner and W. Simon, *Coll. Czech. Chem.Commun.*,29, 2016 (1964)

(24) A. Perjessy, P. Hrnciar, R. Frimm and L. Fisera, *Tetrahedron*, 28, 3781 (1972)

(25) M. H. Palmer, "*The Structure and Reactions of Heterocyclic Compounds*", Arnold Publ. House, London, 1967