TETRAZOLE DERIVATIVES.

28.† σ CONSTANTS OF 5-TETRAZOLYL GROUPS

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A number of σ constants of 5-tetrazolyl (σ_I, σ*, σ_m, σ_p), its anion (σ_I, σ*, σ_m), protonated 5-tetrazolyl (σ_p), and 1- and 2-methyl-5-tetrazolyls (σ_I, σ*) were found by means of correlation analysis of the acid–base properties of substituted tetrazoles.

A significant amount of data that show that the introduction of a tetrazole residue into certain compounds can substantially change their characteristics and often leads to the development of new properties that have important practical applications [2] has been accumulated. Thus the replacement of an N-aryl residue by a tetrazole residue in compounds such as formazans, tetrazolium salts, verdazyls, and leucoverdazyls leads to the following changes in their properties. Formazans markedly increase the selectivity of complexing with metals [3, 4], leucoverdazyls become resistant to autooxidation and display the properties of effective antioxidants [5], tetrazolium salts become nontoxic and display high inhibiting activity with respect to monoamine oxidase [6], and formazans and verdazyls that contain a 2-methyl-5-tetrazolyl residue markedly inhibit radical polymerization [7, 8].

Criteria of the donor-acceptor properties (σ constants) of 5-tetrazolyl groups that make it possible to compare them with one another, as well as with other substituents, particularly aryl and hetaryl substituents, are necessary to ascertain the role of the tetrazolyl residue in the change in the structures and reactivities of various substrates. The Taft inductive σ* constants [9] are of the greatest value for these ends.

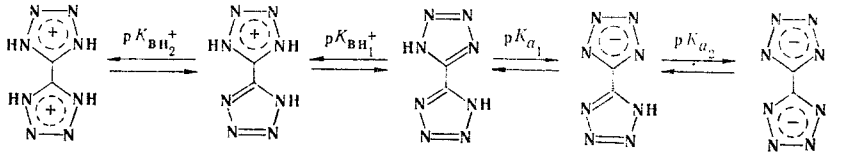
The σ_p, σ_m, and σ_I constants in the tetrazole series are known for 5-tetrazolyl [10, 11], 1- and 2-tetrazolyls [11-14], and some 5-substituted 1- and 2-tetrazolyls [12]. In the present communication, on the basis of data obtained in a study of the acid–base properties of tetrazoles [11, 15-20], we calculated the σ constants of a number of 5-tetrazolyl groups.

Using the pK_a‡ values of 1- and 2-methyl-5-tetrazolylacetic acids [11] and Charton equation (1) for substituted acetic acids [21].

$$\sigma_I = -0.251pK_a + 1.186, \quad (1)$$

we calculated the σ_I constants of 1- and 2-methyl-5-tetrazolyl groups: 0.48 and 0.32, respectively.

A number of σ constants of 5-tetrazolyls were obtained by using the acidity and basicity constants of 5,5'-ditetrazolyl (I) [15] and correlation ratios that link the acid–base properties of 5-substituted tetrazoles with the σ substituent constants.



I

†See [1] for communication 27.

‡Here and subsequently, in the entire research we used the pK_a and pK_{BH^+} values determined in aqueous solutions at 25°C.

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The introduction of ditetrazolyl I into the reaction series of 5-substituted tetrazoles for the determination of the σ constants of 5-tetrazolyls is possible on the basis of the fact that one of the tetrazole rings in this compound does not exert steric hindrance to protonation or deprotonation of the other tetrazole ring. This is indicated by the following information. A substituent such as the phenyl group, being more bulky than 5-tetrazolyl, attached to the $C_{(5)}$ atom of the tetrazole does not exert appreciable steric hindrance to protonation of the tetrazole. This follows from the fact that in series of 5-substituted 1- and 2- methyltetrazoles (II, III) the 5-phenyl derivatives do not deviate from the linear relationship that links the pK_{BH^+} values [16, 17, 22, 23] and the σ_p constants of the substituents. One observes excellent correlation:

5-substituted 1-methyltetrazoles (II)

$$pK_{BH^+} = -7{,}78\sigma_p - 3{,}03,\ r = 0{,}997,\ s = 0{,}33,\ n = 5 \quad (2)$$

5-substituted 2-methyltetrazoles (III)

$$pK_{BH^+} = -7{,}51\sigma_p - 3{,}25,\ r = 0{,}999,\ s = 0{,}08,\ n = 4 \quad (3)$$

The following correlation ratio is satisfied for the acidic properties of substituted 5-phenyltetrazoles (IV) [18], which contain a substituent in the para or meta position of the phenyl ring:

$$pK_a = -1{,}38\sigma^0 + 4{,}47,\ r = 0{,}982,\ s = 0{,}13,\ n = 4 \quad (4)$$

In order to arrive at a scale of inductive effects that is unique for tetrazoles and substituted phenyl rings let us express σ^0 in terms of the Taft σ^* constant using the relationship [9]

$$\sigma^*(X—C_6H_4) = \sigma^0(X) + 0{,}6 \quad (5)$$

From Eqs. (4) and (5) we obtain an expression for the determination of the σ^* constant:

$$\sigma^* = [(4{,}47 - pK_a)/1{,}38] + 0{,}6 \quad (6)$$

Using the pK_{a_1} and pK_{a_2} values of ditetrazolyl I we find from Eq. (6) the σ^* constants of 5-tetrazolyl (2.82) and its anion (0.76).

From the expression [24]

$$\sigma_I = \sigma^*/6{,}23 \quad (7)$$

we determine the inductive σ_I constants of 5-tetrazolyl (0.45) and its anion (0.12). The close correspondence of the σ_I value of 5-tetrazolyl obtained by us and found in [11] (0.41) by means of Eq. (1) and the pK_a value of 5-tetrazolylacetic acid once again provides evidence for the correctness of the inclusion of ditetrazolyl I in the reaction series of 5-substituted tetrazoles for the determination of the σ constants of 5-tetrazolyl groups.

The pK_a values of 5-substituted tetrazoles (V) [16, 25] correlate with the σ_m constants:

$$pK_a = -7{,}64\sigma_m + 4{,}97,\ r = 0{,}992,\ s = 0{,}32,\ n = 7 \quad (8)$$

Using the pK_{a_1} and pK_{a_2} values of 5,5'-ditetrazolyl and Eq. (8) we find the σ_m constants of 5-tetrazolyl (0.46) and its anion (0.09).

The pK_{BH^+} values of tetrazoles [16, 22] correlate with the σ_p constants;

$$pK_{BH^+} = -7{,}66\sigma_p - 3{,}09,\ r = 0{,}997,\ s = 0{,}28,\ n = 7 \quad (9)$$

By means of Eq. (9) and the $pK_{BH_1^+}$ and $pK_{BH_2^+}$ values of ditetrazolyl I we determined the σ_p constants of 5-tetrazolyl (0.31) and protonated 5-tetrazolyl (1.02).

A number of conclusions that are of importance for the chemistry of tetrazole follow from the results of our correlation analysis.

The fact that the pK_{BH^+} values of aminotetrazoles that enter into the II, III, and V reaction series do not deviate from the linear relationship constitutes evidence for their protonation, just as in the case of other tetrazoles [19], at the $N_{(4)}$ atom rather than at the amino group.

Extremely close agreement between the ρ values in the Eqs. (2), (3), (8), and (9), which describe both splitting out of a proton in the series of 5-substituted tetrazoles (ρ = −7.64) and the protonation of these compounds, as well as their 1- and 2-methyl derivatives (ρ =

−7.66, −7.78, and −7.51, respectively) is observed. This constitutes evidence for the similarity in the reaction centers in the given series [26]. Protonation of tetrazoles take place at the α-nitrogen atom $N_{(4)}$ [19]. Consequently, when acidic properties are displayed by 5-substituted tetrazoles, the reaction center in them is also found at the α-nitrogen atom, and this means that within the limits of the entire series V, when the most diverse substituents — from the amino to the nitro group — are present, they exist in the form of 1H rather than 2H tautomers.

One's attention is directed to the difference in the correlation of the acidic and basic properties of 5-substituted tetrazoles: Whereas the pK_a values correlate with the σ_m constants, the σ_p constants are necessary for correlation of the pK_{BH^+} values. This is due to the differences in the transmission of the effect of the substituent to the reaction center. In fact, in the manifestation of basic properties of 5-substituted tetrazoles and their methylated analogs the $C_{(5)}$—$N_{(4)}$ bond through which transmission of the effect of the substituent occurs evidently has a significant degree of double-bond character, whereas the $C_{(5)}$—$N_{(1)}$ bond in 5-substituted tetrazoles is close to a single bond in the case of manifestation of acidic properties by them. Thus, according to the results of quantum-chemical calculations made by the CNDO (complete neglect of differential overlap) method, the orders of the $C_{(5)}$—$C_{(1)}$ bond in 1H-tetrazole and its conjugate anion are 1.27 and 1.43, respectively, whereas the orders of the $C_{(5)}$—$N_{(4)}$ bonds in $N_{(4)}$-protonated tetrazole and in tetrazole itself are 1.40 and 1.54 [20]. The transmission of the effect of the substituent along the $C_{(5)}$—$N_{(1)}$ bond of the tetrazole ring therefore takes place via an inductive and mesomeric mechanism; this is reflected in correlation of the pK_a values by means of the σ_m constants, whereas the σ_p constants reflect an increase in the polar conjugation in transmission of the effect of the substituent to the $N_{(4)}$ atom in protonated 5-substituted tetrazoles.

The deviation in the σ_m and σ_p constants of 5-tetrazolyl that we determined (0.46 and 0.56) from the correlation of the pK_a values of substituted 5-phenyltetrazoles is not surprising, since the pK_a and pK_{BH^+} values that we used to find these constants were determined in water, whereas the data in [10] were obtained in aqueous dimethyl sulfoxide (DMSO). Inasmuch as 5-tetrazolyl, as substituent, should be classified as "chemically active" due to its ability to form hydrogen bonds with the solvent, different scales of σ constants that depend on the type of solvent are required for it [9].

In order to evaluate the ability of tetrazole and its anion to undergo conjugation we used the expression [42]

$$\sigma_C = \sigma - \sigma_I \qquad (10)$$

to calculate the $\sigma_{C(meta)}$ and $\sigma_{C(para)}$ constants of 5-tetrazolyl (0.01 and −0.14) and the $\sigma_{C(meta)}^{-}$ constant of its anion (−0.03). Let us note that these constants are close to the σ_C constants of phenyl [$\sigma_{C(meta)} = -0.02$, $\sigma_{C(para)} = -0.09$]. This makes it possible to conclude that 5-tetrazolyl and its anion resemble phenyl with respect to conjugation when they act as substituents. The negative value of the $\sigma_{C(para)}$ constant of 5-tetrazolyl, which indicates its ability to display +M and +C effects, in agreement with the negative $\mathfrak{R}$ value of the resonance constant (−0.13) found for 5-tetrazolyl from the Swain—Lupton equation [10].

From expression (7) we find the σ* constants of 1- and 2-methyl-5-tetrazolines (2.99 and 1.99). The greater acceptor character of the 1-methyl-5-tetrazolyl residue as compared with its isomer, viz., the 2-methyl-5-tetrazolyl residue, is in agreement with the results of quantum-chemical calculations (by the CNDO method) of 5-substituted 1- and 2-methyltetrazoles, which show that the effective positive charge on the $C_{(5)}$ atom of the tetrazole ring has a greater value precisely in 1-methyltetrazoles [20].

With respect to their electron-acceptor abilities, 5-tetrazolyl and 1-methyl-5-tetrazolyl (σ* 2.82 and 2.99) are comparable with most electron-acceptor residues of substituted phenyl rings as the picryl residue (σ* 3.24).† However the tetrazolyl residues differ with respect to their high degree of compact character and, in the case of 5-tetrazolyl and 2-methyl-5-tetrazolyl, with respect to the complete absence of steric hindrance in the α position. Tetrazole residues can therefore be successfully introduced into various compounds, thereby ensuring extremal changes in their properties.

†Calculated by the additivity rule from Eq. (5).

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