# A Correlation of Substituent Effects with the Acidity of Aromatic Tetrazolic Acids

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The values of thermodynamic dissociation constants, $K_a$, have been determined for *ortho*-, *meta*-, and *para*-substituted 5-phenyltetrazoles (referred to as tetrazolic acids) and the effect of the nature of the substituent on the strength of the acids are discussed. The p$K_a$ values, determined in 50% (v/v) ethanol–water and in 75% (v/v) dimethyl sulphoxide–water are correlated with the substituent constants $\sigma_m$ and $\sigma_p$, which are equal to 0.64 and 0.56 respectively for the tetrazolyl substituent. To evaluate the contribution of the field and resonance effects, the $K_a$ values were correlated with the $\mathscr{F}$ and $\mathscr{R}$ constants based on the Swain–Lupton equation. The correlation, accomplished by using a two-parameter linear regression, gave $\mathscr{F} = 1.17$ and $\mathscr{R} = -0.13$.

TETRAZOLE, $HCN_4H$, is the simplest compound in the series of five-membered heterocycles containing four nitrogen atoms in the ring. A linear dependence was reported[1] between the acidity and the number of ring-nitrogen atoms in a series of unsubstituted nitrogen-containing azoles, tetrazole itself being characterized by having the highest dissociation constant ($K_a = 1.62 \times 10^{-5}$).

The acidity of substituted tetrazoles has, however, been investigated only fragmentarily,[1–5] although a survey and a comprehensive discussion of the acid–base properties of substituted 5-phenyltetrazoles have been given by Herbst;[3] only a limited number of substituents (including $Me_3$, Cl, Br, and OMe), were, however, considered by the author. Consequently, we undertook a more comprehensive investigation of the effect of *ortho*-, *meta*-, and *para*-substituents on the acidity of 5-phenyltetrazoles.

In this work the acid dissociation constants of 5-phenyltetrazoles have been determined in 50% ethanol–

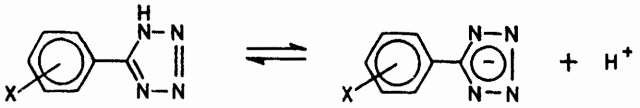
TABLE 1

Data of *ortho*-, *meta*-, and *para*-substituted 5-phenyltetrazoles ($XC_6H_4CH_4H$)

| Substituent X | Yield (%) | M.p. ($t$/°C) | Recrystn. solvent[a] | Found (%) | | | Formula | Required (%) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | C | H | N | | C | H | N |
| H | 95 | 217[b] | W | | | | | | | |
| *o*-Me | 46 | 155—156[c] | M–W | | | | | | | |
| *m*-Me | 66 | 152—153[d] | M–W | | | | | | | |
| *p*-Me | 78 | 250—251[e] | M–W | | | | | | | |
| *p*-$Me_2N$ | 41 | 225—226[f] | W | | | | | | | |
| *m*-$H_2N$ | 40 | 195—197[g] | M–W | | | | | | | |
| *p*-$H_2N$ | 56 | 268—271[h] | M–W | | | | | | | |
| *m*-MeO | 43 | 158—160 | W | 54.3 | 4.6 | 32.1 | $C_8H_8N_4O$ | 54.5 | 4.6 | 31.8 |
| *p*-MeO | 82 | 232—233 | A | | | | | | | |
| *m*-MeCONH | 46 | 264[j] | W | | | | | | | |
| *p*-MeCONH | 89 | 278[k] | W | | | | | | | |
| *o*-HO | 52 | 221—222 | B | 51.6 | 3.9 | 35.0 | $C_7H_6N_4O$ | 51.85 | 3.75 | 34.55 |
| *p*-HO | 40 | 239—241 | M–W | 51.6 | 3.7 | 34.7 | $C_7H_6N_4O$ | 51.85 | 3.75 | 34.55 |
| *o*-$HO_2C$ | 56 | 212—214 | W | 50.8 | 3.1 | 29.8 | $C_8H_6N_4O_2$ | 50.5 | 3.2 | 29.5 |
| *m*-$HO_2C$ | 81 | 275—277 | W | 50.6 | 3.05 | 29.6 | $C_8H_6N_4O_2$ | 50.5 | 3.2 | 29.5 |
| *p*-$HO_2C$ | 88 | 300—302[l] | E | | | | | | | |
| *o*-I | 62 | 176—178 | M–W | 30.85 | 1.95 | 20.5 | $C_7H_5N_4I$ | 30.9 | 1.85 | 20.6 |
| *m*-I | 56 | 172—174 | M–W | 30.8 | 2.0 | 20.6 | $C_7H_5N_4I$ | 30.9 | 1.85 | 20.6 |
| *p*-I | 79 | 270—271 | M–W | 31.2 | 1.9 | 20.9 | $C_7H_5N_4I$ | 30.9 | 1.85 | 20.6 |
| *o*-Br | 52 | 183—184[m] | A | | | | | | | |
| *m*-Br | 64 | 154—155[n] | T | | | | | | | |
| *p*-Br | 54 | 267—269[o] | A | | | | | | | |
| *o*-Cl | 76 | 179—180[p] | A | | | | | | | |
| *m*-Cl | 79 | 139—140[q] | W | | | | | | | |
| *p*-Cl | 85 | 252—253[r] | A | | | | | | | |
| *o*-NC | 66 | 227—228 | E | 56.5 | 3.0 | 41.0 | $C_8H_5N_5$ | 56.15 | 2.95 | 40.9 |
| *m*-NC | 71 | 138—140 | M–W | 55.9 | 3.1 | 40.55 | $C_8H_5N_5$ | 56.15 | 2.95 | 40.9 |
| *p*-NC | 89 | 188—189[s] | M–W | 56.2 | 2.95 | 41.1 | $C_8H_5N_5$ | 56.15 | 2.95 | 40.9 |
| *o*-$O_2N$ | 50 | 160—161[t] | W | | | | | | | |
| *m*-$O_2N$ | 78 | 150—151[u] | W | | | | | | | |
| *p*-$O_2N$ | 72 | 223[v] | W | | | | | | | |
| *o*-$HN_4C$ | 36 | 218—219 | M–W | 44.7 | 2.8 | 51.95 | $C_8H_6N_8$ | 44.85 | 2.8 | 52.3 |
| *m*-$HN_4C$ | 62 | 276 | M | 44.5 | 2.9 | 52.5 | $C_8H_6N_8$ | 44.85 | 2.8 | 52.3 |
| *p*-$HN_4C$ | 75 | 301[w] | M | | | | | | | |

[a] W = water; M = methanol; A = acetic acid; B = benzene; E = ethanol; T = toluene. [b] M.p. 217—218 °C; ref. 4. [c] M.p. 157—158 °C. [d] M.p. 152—152.5 °C. [e] M.p. 250—250.5 °C; J. S. Mihina and R. M. Herbst, *J. Org. Chem.*, 1950, **15**, 1082. [f] M.p. 225—226 °C; R. Huisgen, J. Sauer, H. J. Sturm, and J. H. Markgraf, *Chem. Ber.*, 1960, **92**, 2106. [g] M.p. 199—200 °C; J. M. McManus and R. M. Herbst, *J. Org. Chem.*, 1959, **24**, 1044. [h] M.p. 268—270 °C; ref. 8. [i] M.p. 238—239 °C; ref. 4. [j] M.p. 254—255 °C. [k] M.p. 278 °C; ref. see footnote *g*. [l] M.p. 300—303 °C; ref. see footnote *f*. [m] M.p. 183—184 °C. [n] M.p. 154—155 °C. [o] M.p. 278—279 °C; ref. 4. [p] M.p. 179—180 °C. [q] M.p. 139—140 °C. [r] M.p. 262—263 °C; ref. 4. [s] Ref. 8 gives m.p. 300 °C. [t] M.p. 159.5—161 °C. [u] M.p. 150.5—151.5 °C. [v] M.p. 218.5—219 °C; ref. see footnote *g*. [w] M.p. 304 °C; ref. 8.

water and in 75% $Me_2SO$–water mixtures and the values correlated with the substituent constants.



EXPERIMENTAL

*Preparation of 5-Phenyltetrazoles.*—*ortho*-, *meta*-, and *para*-Substituted 5-phenyltetrazoles were obtained from the appropriate benzonitriles (commercially available products or compounds synthesized by known methods[6,7]) and ammonium azide in DMF, at *ca.* 100 °C.[8] Tetrazolic acids were purified by crystallization until a constant melting point was achieved. The acids were identified on the basis of their i.r., u.v., and n.m.r. spectra and elemental analyses. The aromatic tetrazolic acids are shown in Table 1.

*Materials.*—Ethanol (96%) was purified by distillation using a Widmer column and dimethyl sulphoxide (DMSO) by distillation under reduced pressure at 59—60 °C. Aqueous solutions of ethanol (50%) and DMSO (75%) were prepared by mixing together appropriate volumes of each of the solvents with $CO_2$-free redistilled water. Picric acid and tetramethylammonium picrate were purified by crystallization from ethanol. Potassium salts of *ortho*-, *meta*-, and *para*-substituted 5-phenyltetrazoles were prepared by potentiometric titration of the parent acid (*ca.* 2.8 mmol) dissolved in aqueous ethanol or aqueous DMSO against 0.1N-KOH. After removing the solvent by distillation, the salts were dried *in vacuo* at 60 °C over $P_2O_5$.

*Measurements.*—Measurements were carried out by using an N5122 pH-meter Mera–Elmat, Poland with a reading accuracy of $\pm 1$ mV. The system of an S–60 glass electrode and a calomel electrode was used. The latter was modified by replacing aqueous KCl with a KCl solution in 50% ethanol–water or 75% DMSO–water.

The response of the glass electrode in 50% ethanol–water was determined by measuring the e.m.f. of the glass electrode–calomel electrode system in a series of buffer solutions in 50% ethanol–water containing benzoic acid and sodium benzoate. A plot of the function $E = f(\log c_a/c_s)$ had a slope $S = 59.1$ mV/log $c_a/c_s$. Then, based on the literature $K_a$ value for benzoic acid in the given medium ($K_a = 1.78 \times 10^{-6}$),[9] the standard potential of the glass electrode, $E_0^{\mathrm{EtOH}}$, was calculated from the relations (1) and (2). The $E_0^{\mathrm{EtOH}}$ value found in this way was 0.4384 V.

For calibration of the electrode in 75% DMSO–water solutions containing a mixture of picric acid and tetramethylammonium picrate were used. On the assumption that both the acid and salt are completely ionized in this solvent,[10] e.m.f. *vs.* log $a_{\mathrm{H}^+}$ was plotted to give $E_0^{\mathrm{DMSO}} = 0.3777$ V, and $S = 59.1$ mV/pa$_{\mathrm{H}^+}$.

The stability and reproducibility of the electrode potentials were occasionally checked by carrying out e.m.f. measurements with a saturated solution of potassium hydrogen phthalate either in 50% ethanol–water or 75% DMSO–water. The electrode potential, measured prior to and after carrying out a series of measurements, varied less than 2 mV during 8 h.

Between measurements, the glass electrode was kept in distilled water and the calomel one in a saturated KCl solution in 50% ethanol–water or 75% DMSO–water.

*Determination of Dissociation Constants.*—To a solution of tetrazolic acid of known concentration in a given solvent, a solution of its salt in this solvent was added from a burette, in such a quantity as to obtain a series of solutions in which the ratio of the acid ($c_a$) to salt ($c_s$) concentrations covered the range 0.1 to 10. In each solution, the hydrogen ion activity, $pa_{\mathrm{H}^+}$ was determined by measuring the e.m.f. of a cell with a glass electrode. The dissociation constant of a tetrazolic acid belonging to a given series was calculated as a mean of 10—13 values obtained for solutions of variable $c_a/c_s$ ratio. The constants were calculated from relations (1) and (2) where: $K_a$ is the thermodynamic dissociation constant of the acid, $a_{\mathrm{H}^+}$ is the activity of hydrogen ions, $E$ is the potential of the glass electrode measured in a solution of a given $c_a/c_s$ ratio, $E_0$ is the standard potential of the glass

$$\log K_a = \log a_{\mathrm{H}^+} - \log c_a/c_s + \log f_\pm \qquad (1)$$

$$\text{and } \log a_{\mathrm{H}^+} = \frac{E - E_0}{S} \qquad (2)$$

electrode in a given medium, $S$ is the slope of response of the glass electrode, $c_a$ is the total acid concentration (mol/dm$^3$), $c_s$ is the total salt concentration (mol/dm$^3$), and $f_\pm$ is the mean ionic activity coefficient of the electrolyte ($\log f_\pm = -1.0258\sqrt{\mu}$ and $\log f_+ = -0.6756\sqrt{\mu}$, for 50% ethanol–water and DMSO–water, respectively, in denoting ionic strength).

A similar procedure was employed for the determination of the acidity constants of selected benzoic acids in 75% DMSO–water.

RESULTS

A few dissociation constants for aromatic tetrazolic acids reported in the literature were determined in water–

TABLE 2

Values of dissociation constants and standard deviations of *ortho*-, *meta*-, and *para*-substituted aromatic tetrazolic acids ($XC_6H_4$–$CN_4H$) in 50% ethanol–water and 75% DMSO–water at 25 °C

| Substituent X | $K_a \times 10^5$ in 50% ethanol | $K_a \times 10^5$ in 75% DMSO | $\frac{K_a^{75}\ \%\ \mathrm{DMSO}}{K_a^{50}\ \%\ \mathrm{ethanol}}$ |
|---|---|---|---|
| H | 1.05 ± 0.02 | 1.23 ± 0.01 | 1.17 |
| *o*-Me | 0.61 ± 0.01 | | |
| *m*-Me | 0.81 ± 0.02 | 0.96 ± 0.02 | 1.18 |
| *p*-Me | 0.67 ± 0.01 | | |
| *p*-$Me_2N$ | 0.12 ± 0.01 | | |
| *p*-$H_2N$ | 0.16 ± 0.01 | | |
| *m*-MeO | 1.46 ± 0.02 | 1.58 ± 0.03 | 1.08 |
| *p*-MeO | 0.56 ± 0.01 | | |
| *m*-MeCONH | 1.92 ± 0.05 | | |
| *p*-MeCONH | 0.55 ± 0.03 | | |
| *o*-HO | 0.67 ± 0.01 | | |
| *p*-HO | 0.28 ± 0.01 | | |
| *m*-$HO_2C$ | 4.97 ± 0.02 | 4.32 ± 0.07 | 0.87 |
| *p*-$HO_2C$ | 5.31 ± 0.22 | 4.90 ± 0.10 | 0.92 |
| *o*-I | 2.09 ± 0.05 | | |
| *m*-I | 3.65 ± 0.11 | 4.73 ± 0.10 | 1.30 |
| *o*-Br | 2.09 ± 0.01 | | |
| *m*-Br | 4.13 ± 0.10 | 5.91 ± 0.12 | 1.43 |
| *p*-Br | 2.06 ± 0.10 | 3.28 ± 0.05 | 1.59 |
| *o*-Cl | 1.99 ± 0.04 | | |
| *m*-Cl | 4.04 ± 0.10 | 5.22 ± 0.09 | 1.29 |
| *p*-Cl | 3.23 ± 0.02 | 3.27 ± 0.09 | 1.01 |
| *o*-NC | 17.3 ± 0.29 | | |
| *m*-NC | | 11.2 ± 0.27 | |
| *p*-NC | 12.2 ± 0.46 | 12.7 ± 0.22 | 1.04 |
| *o*-$O_2N$ | 9.42 ± 0.02 | | |
| *m*-$O_2N$ | 12.3 ± 0.20 | 17.4 ± 0.35 | 1.41 |
| *p*-$O_2N$ | 20.2 ± 0.40 | 21.9 ± 0.22 | 1.08 |
| *o*-$HN_4C$ | 8.62 ± 0.29 | | |
| *m*-$HN_4C$ | | 15.4 ± 0.22 | |
| *p*-$HN_4C$ | | 12.8 ± 0.14 | |

alcohol mixtures.[3,4] To correlate the literature values with the $K_a$ values determined in this work, the 50% ethanol–water mixture was chosen. Because of the difficulty in dissolving some substituted 5-phenyltetrazoles and their salts in ethanol–water mixtures, the 75% (v/v) DMSO–water was also employed. DMSO was found to be particularly suitable for these studies because of its high dielectric constants and excellent capacity to solvate ions.[11] Anhydrous DMSO proved unsuitable because of the difficulty of dissolving potassium tetrazolates in it. Moreover, the use of aqueous DMSO facilitated its storage and purification, the latter operation consisting in distillation of DMSO under reduced pressure. The values of the dissociation constants and standard deviation of the mean for various aromatic tetrazolic acids are listed in Table 2.

## DISCUSSION

Table 2 lists the acidity of most of the *ortho-*, *meta-*, and *para*-substituted 5-phenyltetrazoles in 50% ethanol–water. A characteristic feature of this compilation is that the *meta*-isomers of variously substituted 5-phenyltetrazoles have the highest $K_a$ values. According to Herbst,[3] in each group of isomers the $K_a$ values decrease in the order *meta* > *ortho* > *para*. In Table 2 this conclusion is not completely corroborated. With some tetrazoles the sequence of the $K_a$ values for the *ortho*- and *para*-isomers is the reverse of that claimed by Herbst (*cf.* those with the Me, CN, and $NO_2$ substituents). Probably it arises from the deviation of the planarity of phenyl and tetrazolyl rings in some *ortho*-compounds, and also from the influence of intramolecular hydrogen bonds.

TABLE 3

Comparison of dissocation constants ($K_a \times 10^5$) of substituted aromatic tetrazolic acids (TA) and benzoic acids (BA) in different solvents

| Substituent X | 50% Methanol–water [a] $K_a^{TA}$ | 50% Ethanol–water $K_a^{BA}$ [b] | 50% Ethanol–water $\frac{K_a^{TA}}{K_a^{BA}}$ | 75% DMSO–water $K_a^{BA}$ | 75% DMSO–water $\frac{K_a^{TA}}{K_a^{BA}}$ | $\frac{K_a^{TA} \text{ in 50\% aqueous methanol}}{K_a^{TA} \text{ in 50\% aqueous ethanol}}$ |
|---|---|---|---|---|---|---|
| H | 2.90 (1.3) [c] | 0.178 | 5.90 | 0.0145 | 85 | 2.76 |
| *o*-Me | 1.52 | | | | | 2.49 |
| *m*-Me | 2.0 | | | | | 2.47 |
| *p*-Me | 1.52 | 0.115 | 5.83 | | | 2.27 |
| *o*-MeO | 0.12 | | | | | 2.5 |
| *p*-MeO | 1.40 | 0.085 | 6.59 | | | |
| *o*-Br | 6.0 | | | | | 2.87 |
| *m*-Br | 9.2 (4.2) [c] | 0.603 | 6.85 | | | 2.23 |
| *p*-Br | (3.0) [c] | 0.447 | 4.61 | 0.042 | 78 | |
| *o*-Cl | 5.7 (2.5) [c] | | | | | 2.86 |
| *m*-Cl | 8.7 | | | | | 2.15 |
| *p*-Cl | (3.2) | | | 0.037 | 88 | |
| *m*-$O_2N$ | | 2.19 | 5.62 | | | |
| *p*-$O_2N$ | | 2.95 | 6.85 | 0.32 | 68 | |

[a] Data from ref. 3. [b] Data from ref. 10. [c] In 75% methanol–water.

The $K_a$ value of the unsubstituted 5-phenyltetrazole is almost four times higher than that of benzoic acid in 50% methanol–water[3] and *ca.* six times higher in 50% ethanol–water (Table 3). The difference in the acidity constants can be explained in terms of an enhanced resonance stabilization of the 5-phenyltetrazolate anion as compared with that of the benzoate, on the one hand, and to differences in solvation of the two ions, on the other.

A comparison of the dielectric constants for water, methanol, and ethanol (78.5, 32.6, and 24.3, respectively, at 25 °C)[12] suggests that the p$K_a$ values in the methanol–water mixture should be higher than in the ethanol–water mixture. The results shown in Table 3 confirm this suggestion. The literature $K_a$ values[3,4] reported for several substituted 5-phenyltetrazoles in 50% methanol–water are *ca.* 2.5 times higher than in the latter (Table 3). It is worth noting that the $K_a$ values of 5-phenyltetrazoles in 75% methanol–water[3,4] are very close to those determined in 50% ethanol–water owing to the close values of dielectric constants of the two solvents.

The results shown in Table 2 support the general rule that the introduction of electron-withdrawing groups to the phenyl ring (Cl, Br, $CO_2H$, CN, and $NO_2$) increases the $K_a$ values as compared with those of the unsubstituted 5-phenyltetrazole. As opposed to this electron-donating substituents ($NH_2$, $NMe_2$, NHAc, OH, OMe, and Me) decrease the acidity of the compounds.

A correlation of the substituent constants $\sigma_m$ and $\sigma_p$ with the log $K_a/K_a^0$ values in 50% ethanol–water is shown in Figure 2. In this expression $K_a$ is the dissociation constant of a substituted 5-phenyltetrazole and $K_a^0$ is the dissociation constant of the unsubstituted one. The equation for the plot shown in Figure 1 is given by log $K_a/K_a^0 = 1.52\ \sigma$, the correlation coefficient being 0.976.

Because of the very poor solubility of *m*- and *p*-ditetrazolylbenzenes, their acidity constants could not be determined. Consequently, it was impossible to determine substituent constants for the tetrazolyl group in this medium.

To be able to determine these constants, the $K_a$ values of a variety of *meta*- and *para*-substituted 5-phenyltetrazoles in 75% DMSO–water were utilized. The $K_a$ values in this solvent are generally higher than in 50% ethanol–water. On the other hand it is worth noting that in 75% DMSO–water, the 5-phenyltetrazoles were found to be *ca.* 80 times stronger acids than the benzoic acids (*cf.* Table 3).

Such behaviour of the tetrazolic acids is indicative of a stronger solvation of the tetrazolate anion as compared with the benzoate.

A variety of expansions of the Hammett [13] equation (3)

$$\log K/K^0 = \rho\sigma \qquad (3)$$

have been suggested for correlating substituent effects with the properties of molecules. In Figure 2, $\log K/K^0$ in 75% DMSO–water *vs.* substituent constants $\sigma_m$ and $\sigma_p$ has been shown for the *meta-* and *para*-substituted 5-phenyltetrazoles. The values of the constants determined from Figure 2 for the tetrazolyl substituent are $\sigma_m = 0.64$ and $\sigma_p = 0.57$ ($\rho = 1.67$).

The $\rho$ values for dissociation of benzoic and tetrazolic acids increases from 50% ethanol ($\rho_{BA} = 1.41$, and $\rho_{TA} = 1.52$) to 75% DMSO ($\rho_{BA} = 1.84$ and $\rho_{TA} = 1.67$) solutions. The small difference in the $\rho$ value for tetrazolic acids in both solvents in comparison to benzoic acids can be explained in the term of greater delocalization of negative charge in 5-phenyltetrazolate anion. Therefore, the dissociation of aromatic tetrazolic acids is less sensitive to changes in solvent.

To evaluate the field effect and the resonance effect of the 5-tetrazolyl substituent use was made of the Swain and Lupton [14] equation (4). By the linear regression

$$\sigma = f\mathcal{F} + r\mathcal{R} \qquad (4)$$

method, the $\Delta pK_a$ values of the *meta-* and *para*-substituted 5-phenyltetrazoles were correlated with the substituent constants $\mathcal{F}$ (field effect) and $\mathcal{R}$ (resonance effect). The *m-* and *p*-ditetrazolylbenzenes were assumed to belong to the population of the *meta-* and *para*-substituted 5-phenyltetrazoles. Hence, the effect of the tetrazolyl substituent on the $\Delta pK_a$ values was correlated with the $\mathcal{F}$ and $\mathcal{R}$ constants by means of the same regression equations as those used with the remaining *meta-* and *para*-substituted 5-phenyltetrazoles. In this way, the following $f$ and $r$ values were obtained (standard deviation given):

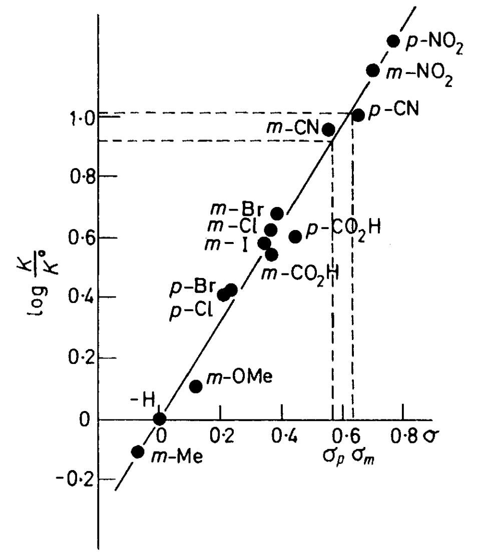


FIGURE 1 Dependence of $\log K_a/K_a^0$ on $\sigma$ (where $K_a$ is the dissociation constant of *meta-* and *para*-substituted 5-phenyltetrazoles and $K_a^0$ is the dissociation constant of the unsubstituted 5-phenyltetrazole) in 50% ethanol–water, at 25 °C

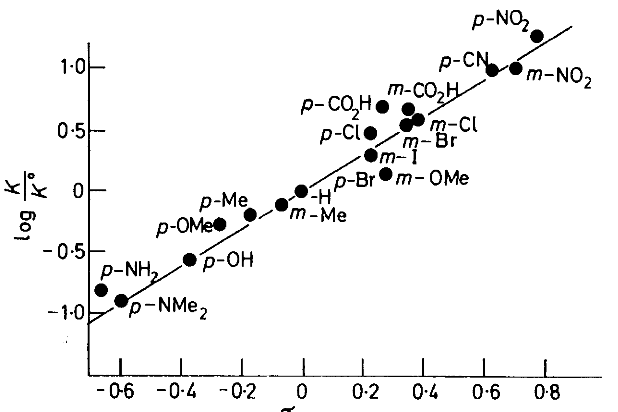


FIGURE 2 Dependence of $\log K_a/K_a^0$ on $\sigma$ ($K_a$ is the dissociation constant of selected *meta-* and *para*-substituted 5-phenyltetrazoles, $K_a^0$ is the dissociation constant of the unsubstituted 5-phenyltetrazole) in 75% DMSO–water, at 25 °C. The value of the substituent constants of the tetrazolyl group taken from the plot are: $\sigma_m = 0.64$ and $\sigma_p = 0.56$

for *meta*-compounds, $f = 0.998 \pm 0.05$; $r = 0.489 \pm 0.08$,
for *para*-compounds, $f = 0.954 \pm 0.07$; $r = 1.246 \pm 0.17$.

The correlation coefficients for the *meta-* and *para*-sets are 0.997 and 0.996 respectively. The $\mathcal{F}$ and $\mathcal{R}$ values for the tetrazolyl ring were obtained by inserting the $\Delta pK_a$ (*meta*) value of 1.09 and of the $\Delta pK_a$ (*para*) value of 0.98 to equation (4). Hence, $\mathcal{F} = 1.17$ and $\mathcal{R} = -0.13$. Close $\mathcal{F}$ and $\mathcal{R}$ values ($\mathcal{F} = 1.02$ and $\mathcal{R} = -0.004$) for the substituent were obtained in the preceding work [15] from proton chemical shifts of the benzene ring protons in the n.m.r. spectra of *meta-* and *para*-substituted 5-phenyltetrazoles.

The $\mathcal{F}$ and $\mathcal{R}$ values defining unequivocally the electronic effect for a substituent, indicate that for the tetrazolyl ring the field effect is very high, being comparable with that of the nitro-group, *i.e.* it is characterized by a negative inductive effect. The value of the resonance constant, $\mathcal{R}$, of the tetrazolyl substituent is close to those of such substituents as Me and Cl.[14] Accordingly, the substituent exerts a moderate, positive resonance effect. The balance between these effects results in typical electron-withdrawing behaviour for the tetrazolyl group.

This small but significant resonance effect of the 5-tetrazolyl group can be observed by comparison of the acidity of 5-phenyltetrazoles with $NO_2$ ($-I$, $-M$) and tetrazolyl ($-I$, $+M$) substituents in the *meta-* and *para*-positions (Table 2). In the case of $NO_2$ substituent the *para*-isomer is more acidic than the *meta*-compound. This is the reverse acidity of ditetrazolylbenzenes. The difference arises from the $+M$ effect of the tetrazolyl substituent which is clearly more important in the *para-* than in the *meta*-position. This interesting and rather unexpected resonance effect of the 5-tetrazolyl group, which is electron-realising in character, probably arises from accumulation in tetrazole ring of as many as 12 $\pi$ and $\eta$ electrons.

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