CORRELATION BETWEEN THE STRUCTURE OF AROMATIC COMPOUNDS AND THE RATE OF THEIR BIOLOGICAL DEGRADATION

Pavel PITTER

Department of Water Technology and Environmental Engineering, Prague Institute of Chemical Technology, 166 28 Prague 6

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Linear relations have been obtained between the logarithms of the biological degradation rate of phenol and aniline derivatives and the substituent constants σ accounting for their electronic effects. The reaction constant in the Hammett equation is negative; the biological degradation rate is negatively affected by electron-withdrawing substituents. Of the OH, CH_3, Cl, NO_2, and NH_2 substituents tested, only the amino group led to deviations from the linear correlations for monosubstituted phenols. The rate of degradation of the aromatic system seems to be controlled by electronic effects, the limiting stage being the electrophilic substitution; correlations using the steric or lipophilic constants failed.

Biological degradability together with the toxicity is a fundamental characteristics of substances from the environmental point of view. Recently, effort has been made to treat the experimental biological degradability data by correlation analysis, in order to make it possible for the degradability of nontested substances to be predicted. In spite of the complexity of the biochemical processes, relations are believed to exist between these processes and the chemical reaction mechanism and reactivity, and so the methods of correlations in organic chemistry are applied making allowance for some particular aspects of biological systems[1-4]. Data on the relation between the structure and the biological degradability, without a quantitative evaluation, have been reviewed recently[5-7]. Correlation treatment of biological degradability is only at its outset[8-11]; molecular parameters accounting for the electronic, steric, and lipophilic physico-chemical properties are tried for this purpose[3,4,8,11]. For such investigations, the reaction centre on the one hand and the substituent left intact during the reaction, on the other hand, must be recognized. The operation of the same reaction mechanism within the entire reaction series examined is also prerequisite for a successful correlation[1,3].

The mechanism of the biological degradation of aromatic ring systems has been studied extensively[12-15]. The process comprises two stages, *viz.* hydroxylation followed by oxidative ring opening. The hydroxy group is supposed to be the reaction centre. The biological hydroxylation and the following oxidative ring cleavage

are decisive for the facility of the system degradation, the aliphatic compounds formed undergoing biological degradation quite readily[6,7].

In the present work, correlation analysis is performed for the biological degradation of 32 monosubstituted and disubstituted phenols and anilines carrying OH, NH_2, COOH, Cl, NO_2, and SO_3H groups in various positions (hence, aminophenols, cresols, chlorophenols, nitrophenols, toluidines, chloroanilines, hydroxybenzoic acids, aminobenzoic acids and 4-aminobenzenesulphonic acid).

Method

The biological degradation rates of the substances tested were determined under identical conditions using an adapted heterogeneous microbiological culture[16]. The rate is expressed as mg of substrate decomposed in an hour by one g of dry initial microbiological inocculum. The substrate concentration was converted to oxygen equivalents, *i.e.* oxygen used up for the substrate oxidation as far as CO_2 and H_2O (chemical oxygen demand).

The electronic effects were evaluated in terms of the Hammett σ constants[1,3], using values verified for anilines and phenols, where conjugation of substituent with the reaction centre can occur in some positions[17,18].

RESULTS AND DISCUSSION

For monosubstituted phenols, the logarithms of the rate of biological degradation v are plotted *vs* the substituent σ constants in Fig. 1. Only the amino derivatives deviate from linear dependences for *ortho*, *meta*, and *para* substituted phenols, respectively. Aminophenols were therefore omitted from the regression straight line equation calculations. For *ortho*-substituted phenols (number of substances tested $n = 5$),

$$\log v = -0{\cdot}43\sigma_0 + 1{\cdot}7\,,$$

with the standard deviation $s = 0{\cdot}040$ and the correlation coefficient $r = 0{\cdot}98$ as compared with the critical value at the 5% significance level $r_{0.05} = 0{\cdot}878$.

For *meta*-substituted phenols ($n = 4$),

$$\log v = -0{\cdot}616\sigma_m + 1{\cdot}72\,,$$

$s = 0{\cdot}102$, $r = 0{\cdot}94$, $r_{0.05} = 0{\cdot}95$, and for *para*-substituted phenols ($n = 4$),

$$\log v = -0{\cdot}323\sigma_p + 1{\cdot}65,$$

$s = 0{\cdot}083$, $r = 0{\cdot}99$, $r_{0.05} = 0{\cdot}95$.

Of disubstituted phenols, 2,5-dihydroxybenzoic acids, xylenols, phloroglucinol, 2,4-dichlorophenol, 2-chloro-4-nitrophenol, and 2,4-dinitrophenol were tested. The substituent constant additivity rule[3] was applied; the dependence of logarithms

of the degradation rate on the $\sum\sigma$ value is shown in Fig. 2. The regression straight line equation obtained ($n = 7$) is

$$\log v = -0{\cdot}32\sum\sigma + 1{\cdot}43$$

($s = 0{\cdot}118$, $r = 0{\cdot}95$, $r_{0.05} = 0{\cdot}75$).

All the above equations are one-parameter equations in the general form $\log v = \varrho\sigma + \log v_0$, where ϱ is the reaction constant and v_0 is the reaction rate of degradation for unsubstituted phenol. The reaction rate ϱ is invariably negative, thus indicating an electrophilic attack on the reaction centre of the system[3]. This suggests that the limiting stage in the biological degradation of aromatic compounds is the electrophilic substitution. In such instances the reaction is slowed down on electron withdrawal from the reaction centre by substituents possessing high positive values of the substituent constant. This is why the reaction is slowed down by halogens and, in particular, by the nitro group, and conversely, it is promoted by substituents possessing high negative values of the substituent constant.

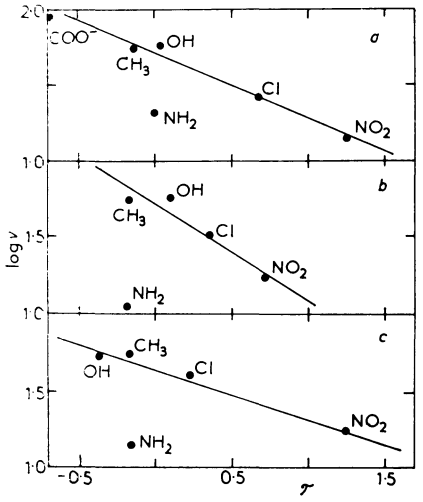

FIG. 1

Correlation of the biological degradation rate v with substituent constants σ for monosubstituted phenols. *a* *ortho*-substituted phenols, *b* *meta*-substituted phenols, *c* *para*-substituted phenols

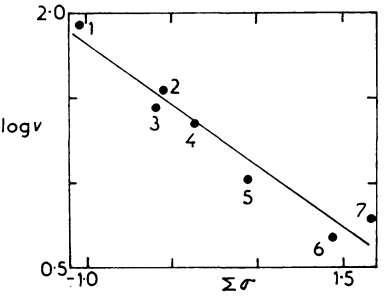

FIG. 2

Correlation of the biological degradation rate v with sum of substituent constants $\sum\sigma$ for disubstituted phenols. Substituents: *1* 2-COOH, 4-OH; *2* 2-CH_3, 4-CH_3; *3* 2-CH_3 4-CH_3; *4* 3-OH, 5-OH; *5* 2-Cl, 3-Cl; *6* 2-Cl, 4-NO_2; *7* 2-NO_2, 4-NO_2

The log v values do not correlate with the steric constants E_s or the lipophilic constants π (taken from refs[17,18-21]), as is demonstrated for *ortho*-substituted phenols in Figs 3 and 4, respectively. Thus the rate of biological degradation of substituted phenols seems to be governed primarily by electronic effects of substituents. The statistical significance of the correlation with the σ constants also bears out the assumption that the reaction centre is the hydroxy group[12-15].

For all the amino derivatives, significant deviations from the general trend are found (Fig. 1). This may be due to other effects not accounted for by the substituent con-

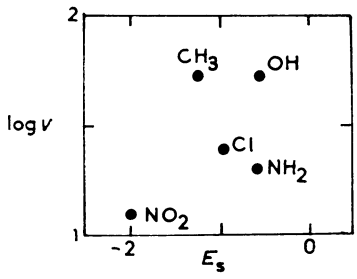

FIG. 3

Correlation of the biological degradation rate v with steric constants E_s for *ortho*-substituted phenols

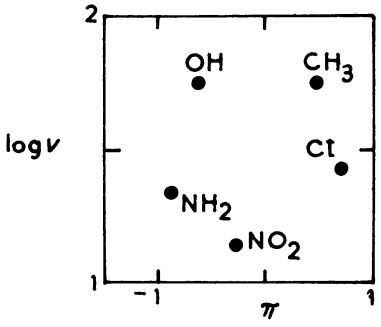

FIG. 4

Correlation of the biological degradation rate v with lipophilic constants π for *ortho*-substituted phenols

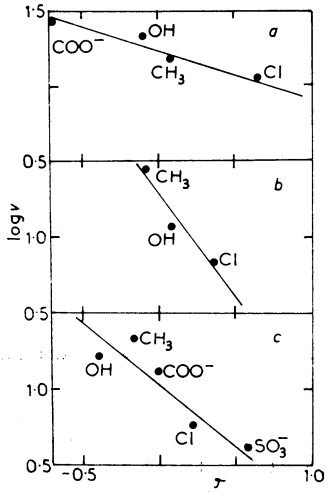

FIG. 5

Correlation of the biological degradation rate v with substituent constants σ for monosubstituted anilines. *a* *ortho*-substituted anilines, *b* *meta*-substituted anilines, *c* *para*-substituted anilines

stants used, to a change in the substituent nature by side reactions preceding the attack on the assumed reaction centre, to a change in the position of the assumed reaction centre, or to a different reaction mechanism[3]. Steric or lipophilic effects do not seem to be responsible for the deviations. Alterations in the reaction mechanism are not likely either, no deviations from the mechanism assumed (*i.e.*, hydroxylation and oxidative ring opening) having been observed[11–15]. However, biological hydroxylation in the amino group position, where the oxidative deamination takes place prior to the aromatic ring cleavage, is conceivable[12,13,15]. As the amino group is transformed into a hydroxy group, this site becomes the reaction centre, and the remaining functional groups (including the initial hydroxy group if present) then act as substituents. In order to test this hypothesis, the correlation was tried assuming that the primary reaction centre is the amino group, the remaining functional groups being substituents. Published σ constants for anilines[17,18] were used.

The plot of the logarithms of the decomposition rate v *vs* the substituent constants σ for monosubstituted anilines is shown in Fig. 5. Linear dependences were obtained for OH, CH_3, Cl, SO_3H,and COOH groups as substituents in the three positions. The regression straight line equations calculated are

$$\log v = -0{\cdot}30\sigma_0 + 1{\cdot}24 ,$$

$s = 0{\cdot}048$, $r = 0{\cdot}975$, $r_{0.05} = 0{\cdot}95$ for *ortho*-substituted anilines ($n = 4$),

$$\log v = -1{\cdot}53\sigma_m + 1{\cdot}31 ,$$

$s = 0{\cdot}127$, $r = 0{\cdot}97$, $r_{0.05} = 0{\cdot}997$ for *meta*-substituted anilines ($n = 3$), and

$$\log v = -0{\cdot}78\sigma_p + 1{\cdot}04 ,$$

$s = 0{\cdot}117$, $r = 0{\cdot}942$, $r_{0.05} = 0{\cdot}878$ for *para*-substituted anilines ($n = 5$).

The results can be interpreted similarly as above inasmuch as the reaction constants ϱ are also negative. For the chloro and sulpho derivatives a significant deactivation effect of substituent is observed as expected. A similar negative effect can be predicted for the nitro group with high positive substituent constant values in the three positions; really, nitroanilines have been found to undergo biological degradation reluctantly[16,19,20].

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