Resonance in the Chloracetic Acids

IN a letter in NATURE, H. O. Jenkins[1] has discussed the dissociation constants of the chloracetic acids, and concluded that the electrostatic inductive effect cannot account for the strength of the di- and trichloracids, although that of the mono-acid is quantitatively explicable on this basis[2], since "no functional relationship can be traced between μ_R (resultant moment of the C-Cl links) and K (dissociation constant)". This conclusion is, however, incorrect; for, if the bonds are tetrahedrally arranged around their carbon atom, the change in the electrostatic potential ψ ($= \mu\cos\theta/r^2$) at the carboxyl group (which is the inductive effect), should be proportional to the number of C-Cl links present, if μ, θ and r remain unchained for each link. That is, we should have

$$pK = pK_0 - qx, \quad . \quad . \quad (1)$$

where pK is the negative logarithm of K, for x chlorine atoms, pK_0 that of acetic acid, and q a constant; that is, the Ostwald-Wegscheider rule, although the resultant moments of the corresponding chlormethanes are not as 1 : 2 : 3.

The results given below show that the factor q decreases with x; hence the di- and tri-acids are weaker than they should be on this simple hypothesis, while Jenkins represents them as abnormally strong. This diminution in q can easily be explained. Smyth and McAlpine[3,4] pointed out that the dipole moments of the C-Cl links in CH_2Cl_2 are less than that of this link in CH_3Cl because of the mutual effect of the dipoles, and that this effect would probably be linear in the number of C-Cl links present. Hence we might expect

$$pK = pK_0 - sx + t\,(x - 1). \quad . \quad (2)$$

The available data on these acids are given in the accompanying table ($pK_r = pK - pK_0$):

	pK			pK_r		
	H_2O	MeOH	EtOH	H_2O	MeOH	EtOH
CH_3COOH	4·757[5]	9·762[7]	10·44[7]	0	0	0
$CH_2ClCOOH$	2·861[6]	7·838[7]	8·51[7]	−1·90	−1·92	−1·93
$CHCl_2COOH$	1·30*	—	6·89[7]	−3·46	—	−3·55
CCl_3COOH	—	4·92[8]	—	—	−4·84	—

* Ostwald's value.

The alcohol values must be considered since no accurate value for trichloracetic acid in water is available. As mean values for pK_r, therefore, we have −1·92, −3·50, −4·84. The equation (2) given, with $s = -1{\cdot}92$, $t = 0{\cdot}30$ predicts (−1·92) −3·52, −4·82 within the experimental error.

Further, since t is related to the bond-polarizability, for the fluor-acids it should be smaller, for the bromo- and iodo-acids larger, than for the chloracids. The only extant data are for propionic, α-brompropionic, and αα-dibrompropionic acids[9]: pK 4·87, 2·97, 1·48[9]. If equation (2) is valid, $s = -1{\cdot}90$, $t = 0{\cdot}41$ as compared with 0·30—in the right direction. It is suggestive that Wegscheider[10] found the largest deviation from equation (1) for substituted benzoic acids if the groups were 1 : 2 : 3, or 1 : 2 : 6 (carboxyl at 1), when the mutual interference must be a maximum. Exact calculation of the t term is not at present possible, but the order is reasonable[3,4].

Although explanations in terms of resonance and polarizability are not fundamentally opposed, Jenkins' relations between pK and n are of doubtful significance; resonance energy is not, in general, linear in the number of canonical forms. Finally, the resonance possibilities of the undissociated acids are very similar to those of their anions.

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[3] Smyth, C. P., and McAlpine, *J. Chem. Phys.*, **1**, 190 (1933).
[4] Compare also Sutton and Brockway, *J. Amer. Chem. Soc.*, **57**, 473 (1935).
[5] Harned and Ehlers, *J. Amer. Chem. Soc.*, **55**, 652 (1933).
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Nature of the Cyanide-stable Portion of Cellular Respiration

IN a recent and interesting review by Commoner[1], on the cyanide inhibition of cellular respiration, it is suggested that the cyanide-stable respiration is mediated through the yellow-enzyme system and is concerned with the oxidation of fatty substances, that is, compounds with a low O/C ratio. As tentative support for this hypothesis Commoner instances the relatively high Q_O^{CN} of liver, kidney and heart, the high flavin content of these tissues, and their low respiratory quotient ($R.Q.$) values.

Unfortunately, in advancing these ideas, no account has been taken of the possible contribution of purine oxidation to the cyanide-stable respiration. In the case of ox-liver it may be shown that such oxidation possibly accounts for the whole of this cyanide-stable respiration. From previous data of mine[2] the Q_{O_2} of 'minced' ox-liver may be calculated to be 1·8, of which the greater part was shown to be due to purine-base oxidation, and which is only slightly inhibited by cyanide. This value for Q_O^{CN} agrees quite well with that of 1·5–2·4 deduced by Commoner. For ox-liver, where uricase activity is absent, the $R.Q.$ for purine-base oxidation is nil, so that if such oxidations account for any great part of the total respiration, the $R.Q.$ value for the whole tissue will be much lower than unity. The low $R.Q.$ values for liver do not therefore necessarily prove that fat oxidation is predominant. The high flavin-content of these tissues may also be accounted for by its xanthine oxidase activity in view of the identification of this enzyme as a flavin.

The evidence quoted in favour of Commoner's hypothesis is thus equally in favour of the view that the cyanide-stable respiration in mammalian tissues is to be identified with purine-base oxidation.

It is worth while pointing out that, with some plant tissues, notably those of carrot leaf and tea leaf, considerably higher concentrations of cyanide ($m./100$) are required to bring about maximum inhibition of respiration. I have also recently shown that $m./100$ cyanide is necessary for full inhibition of oxidation of catechols and p-phenylenediamine by a preparation of tea oxidase believed to be a cytochrome oxidase.

If, as seems likely, a cytochrome system is operating in these tissues the cyanide sensitivity of cytochrome must vary considerably according to the nature of the tissue. Until this variation has been properly