

CCCIV.—*The Effects of the Spatial Position of Substituent Groups on Acidic Strength.*

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IN an investigation on the rotatory powers of a number of the homologous menthyl alkyloxyacetic and hydrogen dicarboxylic esters (Rule, Hay, and Paul, this vol., p. 1347), it was observed that the maxima in the rotation curves of the one series corresponded to the minima in the other. From these results it was concluded that the terminal alkyloxy- and carboxy-groups of the growing chains give rise to opposite changes in rotatory power when they return to the neighbourhood of the asymmetric atom, and, further, that the characteristic influence of *o*-substituents in the optically active benzoic esters is propagated through space rather than through the chain of intervening atoms. In support of these conclusions the authors observed that parallel phenomena may be found in the influence of substituents on the acidity of geometrically isomeric acids.

There appears, however, to be little justification for this generalisation, and available data on the dissociation constants of acids of the type of crotonic acid (as well as of other acids) show that it is not possible to correlate the two phenomena. Recent work on the configuration of the crotonic acids, both from the chemical and physical standpoint, shows that crotonic acid (m. p. 72°) has the *trans*-configuration (Errera and Henri, *Compt. rend.*, 1925, **181**, 548; Langseth, *Z. physikal. Chem.*, 1925, **118**, 49; Auwers and Wissebach, *Ber.*, 1923, **56**, 715). The dissociation constants of the two crotonic acids, and of other acids of the same type on which there is now little doubt with regard to their configuration, are given below :

$\begin{array}{c} \text{CH}_3 \cdot \underset{\text{H}}{\underset{ }{\text{C}}} \cdot \text{H} \\ \text{H} \cdot \underset{\text{H}}{\underset{ }{\text{C}}} \cdot \text{CO}_2\text{H} \end{array}$ Crotonic acid, 0.22×10^{-4} .	$\begin{array}{c} \text{H} \cdot \underset{\text{H}}{\underset{ }{\text{C}}} \cdot \text{CH}_3 \\ \text{H} \cdot \underset{\text{H}}{\underset{ }{\text{C}}} \cdot \text{CO}_2\text{H} \end{array}$ <i>iso</i> Crotonic acid, 0.36×10^{-4} .	$\begin{array}{c} \text{Cl} \cdot \underset{\text{H}}{\underset{ }{\text{C}}} \cdot \text{CH}_3 \\ \text{H} \cdot \underset{\text{H}}{\underset{ }{\text{C}}} \cdot \text{CO}_2\text{H} \end{array}$ β -Chloro <i>isocrotonic</i> acid, 0.95×10^{-4} .	$\begin{array}{c} \text{CH}_3 \cdot \underset{\text{H}}{\underset{ }{\text{C}}} \cdot \text{Cl} \\ \text{H} \cdot \underset{\text{H}}{\underset{ }{\text{C}}} \cdot \text{CO}_2\text{H} \end{array}$ β -Chlorocrotonic acid, 1.44×10^{-4} .
$\begin{array}{c} \text{CH}_3 \cdot \underset{\text{H}}{\underset{ }{\text{C}}} \cdot \text{H} \\ \text{CH}_3 \cdot \underset{\text{H}}{\underset{ }{\text{C}}} \cdot \text{CO}_2\text{H} \end{array}$ Tiglic acid, 0.09×10^{-4} .	$\begin{array}{c} \text{H} \cdot \underset{\text{H}}{\underset{ }{\text{C}}} \cdot \text{CH}_3 \\ \text{CH}_3 \cdot \underset{\text{H}}{\underset{ }{\text{C}}} \cdot \text{CO}_2\text{H} \end{array}$ Angelic acid, 0.50×10^{-4} .	$\begin{array}{c} \text{CH}_3 \cdot \underset{\text{H}}{\underset{ }{\text{C}}} \cdot \text{H} \\ \text{Cl} \cdot \underset{\text{H}}{\underset{ }{\text{C}}} \cdot \text{CO}_2\text{H} \end{array}$ α -Chlorocrotonic acid, 7.2×10^{-4} .	$\begin{array}{c} \text{H} \cdot \underset{\text{H}}{\underset{ }{\text{C}}} \cdot \text{CH}_3 \\ \text{Cl} \cdot \underset{\text{H}}{\underset{ }{\text{C}}} \cdot \text{CO}_2\text{H} \end{array}$ α -Chloro <i>isocrotonic</i> acid, 15.8×10^{-4} .

The dissociation constants of the above acids indicate that the spatial proximity of a CH₃ or Cl group to the carboxyl group in every case increases the acidic strength, and that the change thus pro-

duced is in the same direction as (though smaller in magnitude than) that produced by the carboxyl group in fumaric and maleic acids ($K = 10 \times 10^{-4}$ and 150×10^{-4} respectively). From these observations it will be seen that it is not possible to adduce corroborative evidence from this source as claimed by Rule, Hay, and Paul, who infer that the spatial proximity of a CH_3 or Cl group to the carboxyl group produces a lowering of the dissociation constant, *i.e.*, an effect in the opposite direction to that produced by the carboxyl group. The analogy between the two phenomena cited by them is therefore invalid.

The increase in the acidic strength of these acids by the spatial proximity of substituents is in close conformity with the behaviour of substituted benzoic acids, and it is possible to observe a close analogy between the effect of *o*-substitution, which is known always to increase the strength of a benzoic acid independently of the polar character of the substituent, and *cis*-substitution, which is seen to have an effect of the same type on acids of the acrylic acid series. In both cases the increase may be attributed to steric inhibition to the return of the hydrogen ion.

In the case of ortho-substituted benzoic acids (*i.e.*, β -substitution), the increase in the dissociation constant is considerably greater than the increase in the corresponding β -substituted aliphatic acids, due to the superimposed secondary effect of the spatial proximity of the groups. On the other hand, with the meta- and para-acids, the increase is in nearly every case of the same order of magnitude as is met with in corresponding γ - and δ -substituted acids of the aliphatic series. This is clearly illustrated in the following table of dissociation constants (taken from Landolt-Börnstein, "Tabellen").

Benzoic acid, $K \times 10^4 = 0.66$.

Acid.	$K \times 10^4$.	Acid.	$K \times 10^4$.	Acid.	$K \times 10^4$.
<i>o</i> -Chlorobenzoic	13.0	<i>m</i> -Chlorobenzoic ...	1.5	<i>p</i> -Chlorobenzoic	0.93
<i>o</i> -Bromobenzoic	14.5	<i>m</i> -Bromobenzoic ...	1.37	<i>p</i> -Bromobenzoic	0.59
<i>o</i> -Hydroxybenzoic ...	10.0	<i>m</i> -Hydroxybenzoic ...	0.83	<i>p</i> -Hydroxybenzoic ...	0.29
Phthalic	12.0	Homophthalic	2.9	Terephthalic	—
<i>o</i> -Toluic	1.2	<i>m</i> -Toluic	0.56	<i>p</i> -Toluic	0.43

Propionic acid, $K \times 10^4 = 0.14$.

β -Chloropropionic ...	0.85	γ -Chlorobutyric ...	0.3	δ -Chlorovaleric	0.204
β -Bromopropionic ...	0.98	γ -Bromobutyric ...	0.26	δ -Bromovaleric	0.191
β -Hydroxypropionic...	0.31	γ -Hydroxybutyric ...	0.19	δ -Hydroxyvaleric ...	0.2
Succinic	0.66	Glutaric	0.47	Adipic	0.37
Butyric	0.148	Valeric	0.16	Caproic	0.145

With the ortho-substituted acids, the configuration of the molecule is such that the substituent group is permanently maintained at an effective distance from the carboxyl group, and the resulting spatial proximity of the groups is shown in the abnormal increase in the dissociation constant. From these considerations, it would be

expected that *cis*-substitution in like manner would result in an increase in dissociation constant (when compared with *trans*-substitution), and if the new configurations for the crotonic acids are accepted, this analogy is borne out in fact.

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