them as deoxy-CDP-X and CDP-X, but the nature of X remained uncertain although it was noted that it was basic.

I am indebted to Dr. Reiji Okazaki of Nagoya University for preparing lyophilized samples of unfertilized sea urchin eggs.

RESEARCH LABORATORIES OF
TAKEDA PHARMACEUTICAL INDUSTRIES, LTD.
OSAKA, JAPAN YUKIO SUGINO

RECEIVED JULY 17, 1957

CORRELATION OF CARBANION REACTIVITIES BY σ_R^- PARAMETERS[1]

Sir:

The definition of nucleophilic resonance parameters, σ_R^-, has been made recently according to the equation[2]

$$\sigma_R^- = \sigma^- - \sigma_I \quad (1)$$

where σ^- is the dual Hammett sigma value which pertains to the reactions of *p*-substituted derivatives of aniline and phenol,[3] and σ_I is the inductive substituent constant.[2] The σ_R^- values provide a scale of the powers of substituent groups to delocalize negative charge by conjugation.

Useful applicability of the σ_R^- scale to certain nucleophilic reactivities is suggested by the correlation of the rates of carbanion formation of substituted methanes in water at 25° by the equation

$$\log k_1 = (26.0)\sigma_R^- + (4.0)(\Sigma\sigma_I) - 24.8 + \log n_H \quad (2)$$

The term $\log n_H$ is a statistical correction term, n_H being the number of ionizable H atoms. The rate constants, k_1, are those tabulated by Pearson and Dillon.[4] The correlation, shown in Fig. 1, holds over a spread of rates of eight powers of ten with an average deviation of 0.25 log unit. This is quite satisfactory since the precision of σ_R^- values is no better than ± 0.03. Figure 1 shows a plot of log (k_1/n_H) *vs.* the quantity $(26.0)\sigma_R^- + (4.0)\Sigma\sigma_I$. The full line is one of unit slope.

The term $(4.0)\Sigma\sigma_I$ presumes to measure the inductive contribution, and the term $(26.0)\sigma_R^-$, the resonance contribution to the logarithm of the ionization rate. The enormous (and therefore rather crude) constant for susceptibility to resonance interaction, 26.0 (compared to 4.0 for susceptibility to inductive interaction), indicates that a much greater stabilization by resonance than inductive interaction results from the substitution of conjugated groups directly at the carbanion carbon compared to the corresponding interactions of these groups acting through the ring system of *p*-substituted benzene derivatives.

Equation (2) is unique in that resonance parameters determined from reactivities in the aromatic series are used to correlate the effects of corresponding substituents in the aliphatic series. This usage completes a cycle wherein inductive effects from the aliphatic series (σ_I parameters) have been used to evaluate from aromatic series reactivities (equation (1)), the resonance parameter, σ_R^-. This parameter is now applied to the correlation of resonance effects in the aliphatic series.

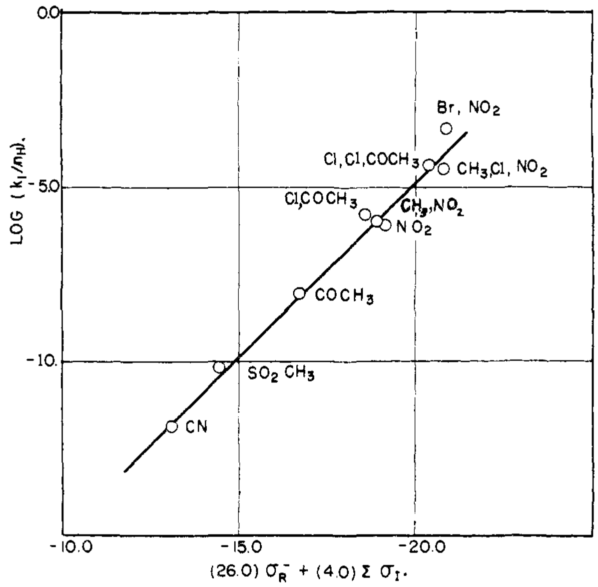


Fig. 1.—Correlation by equation (2) of rates of carbanion formation: $X_1X_2X_3CH + H_2O \longrightarrow [X_1X_2X_3C]^- + H_3O^+$, where X_1 is as indicated and $X_2 = X_3 = H$ unless otherwise indicated. A line of unit slope is shown.

It has been assumed in using equation (2) that σ_R^- values for the substituents Br, Cl, and CH_3 (in the presence of a single conjugating group such as NO_2, CH_3CO, CH_3SO_2, or CN) are zero, and that the former substituents contribute only to the $\Sigma\sigma_I$ term. If equation (2) is applied to polysubstitution of conjugating substituents (using $\Sigma\sigma_R^-$) substantial deviations are obtained (Table I lists some typical deviations).

TABLE I

DEVIATIONS FROM EQUATION (2) OF RATES OF IONIZATION OF POLYSUBSTITUTED METHANES WITH MORE THAN ONE CONJUGATING GROUP

Substituted methane	$\log(k/n_H)$ exptl.	$\log(k/n_H)$ calcd. eqn. (2)	Deviation log units
$CNCH_2CN$	−0.3	+ 1.2	+ 1.5
$CH_3COCH_2COCH_3$	−0.3	+ 8.6	+ 8.9
$CH_3COCH(Br)COCH_3$	−0.3	+10.4	+10.7
$CH_3COCH(CH_3)COCH_3$	−2.8	+ 8.4	+11.2
$CH_3COCH_2NO_2$	0.0	+11.0	+11.0
$NO_2CH_2NO_2$	+1.4	+13.5	+12.1

It is apparent from Table I that steric inhibition of resonance (and possibly other steric effects) of the second by the first conjugated substituent (and by bulky substituents, *e.g.*, Br, CH_3) contributes appreciably to the failure of equation (2). For example, the rate of ionization of dinitromethane is twelve powers of ten slower than predicted by equation (2). On the other hand, the

(1) This work was supported in part by the Office of Naval Research Project NR055-328. Reproduction in whole or in part is permitted for any purpose of the United States Government.

(2) R. W. Taft, Jr., THIS JOURNAL, **79**, 1045 (1957); *cf.* also M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., N. Y., 1956, p. 578, 594, and J. D. Roberts and W. T. Moreland, Jr., THIS JOURNAL, **75**, 216 (1953).

(3) *Cf.* (a) reference (2); (b) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 184; (c) H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953).

(4) R. G. Pearson and R. L. Dillon, THIS JOURNAL, **75**, 2439 (1953). These authors have noted qualitatively the correlation given by equation (2) *cf.* footnote (35).

sterically more compact CN groups of $CH_2(CN)_2$ lead to a deviation of only 1.5 powers of ten greater rate, according to equation (2), than that observed. The results listed in Table I also suggest that saturation of resonance stabilization in the ionization state contributes to the failure of equation (2) since the deviations increase with increasing values of $\Sigma\sigma_R^-$.[5]

(5) The logarithms of the ionization constants of substituted methanes (reference 4) also appear to follow equation (2) with $\rho_R \cong 30$, $\rho_I \cong 7$, and log K_a of methane $\cong -40$. However, the ionization constants for $CH_3SO_2CH_3$ and CH_3CN are so crude that the quantitative significance of the relationship is uncertain. Two points are worthy of comment. Nitromethane deviates (greater acidity) by about six log units, which is the same magnitude as the deviation of this compound from the norm in a plot of log k_1 *vs.* log K_a (*cf.* Fig. 1, reference 4). Thus the deviation apparently can be attributed to the abnormally slow recombination rate of "nitrocarbanion" with hydrogen ion. On the other hand, the relationship is followed reasonably well by both $CH_2(CN)_2$ and $CH(CN)_3$. $(CH_3CO)_2CH_2$ and $(CH_3CO)_3CH$ deviate substantially (weaker acids) in the direction expected for steric inhibition of resonance in the carbanion ion.

COLLEGE OF CHEMISTRY AND PHYSICS
THE PENNSYLVANIA STATE UNIVERSITY
UNIVERSITY PARK, PENNSYLVANIA ROBERT W. TAFT, JR.

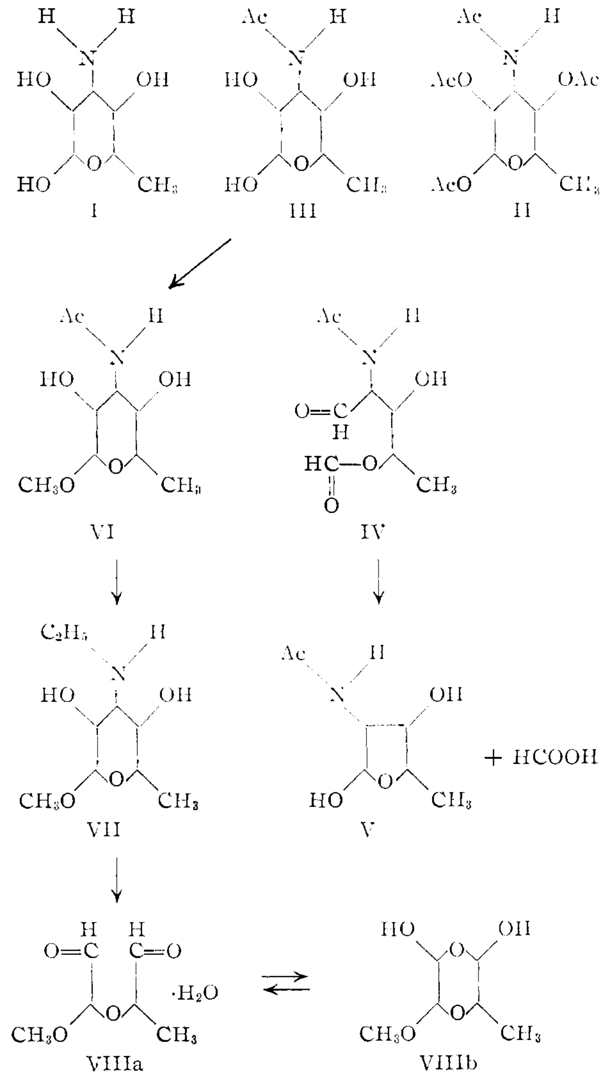
RECEIVED AUGUST 7, 1957

THE STRUCTURE OF MYCOSAMINE

Sir:

We wish to report in this communication on the structure of an amino-sugar mycosamine,[1] which represents the nitrogen-containing moiety of the antifungal antibiotics, nystatin,[2] $C_{46}H_{77}NO_{19}$,[3,4] and amphotericin B, $C_{46}H_{73}NO_{20}$.[1,5] This amino sugar was isolated in the form of its tetraacetate[1] from the mixture of products resulting from the sulfuric acid catalyzed acetolysis of either the antibiotics or their hydrogenated derivatives. Structure I is assigned to the parent amino sugar on the basis of the following evidence:

Chromatographic fractionation on alumina of the chloroform soluble portion of the acetolysis products yielded tetraacetylmycosamine (II, m.p. 159–161°, $[\alpha]^{23}D$ +39° (*c*, 1.0 in ethanol); calcd. for $C_6H_9NO_4.4CH_3CO$: C, 50.75; H, 6.39; N, 4.23; acetyl (total), 52.0. Found: C, 50.40; H, 6.44; N, 4.26; acetyl, 50.9), hydrolyzable by barium methoxide in methanol to N-acetylmycosamine[1] (III, m.p. 191–192°, $[\alpha]^{23}D$ −46° (*c*, 1.0 in ethanol); calcd. for $C_6H_{12}NO_4 \cdot CH_3CO$: C, 46.82; H, 7.37; N, 6.83; N-acetyl, 21.0. Found: C, 46.58; H, 7.22; N, 7.07; N-acetyl, 21.2), which reduces hot Fehling solution only slowly and gives a positive iodoform test. Treatment of III with periodic acid (consumption 1 mole) yielded 2-acetamido-3-hydroxy-4-formoxypentanal IV (amorphous, calcd. for $C_8H_{13}NO_5$: C, 47.29; H, 6.45; N, 6.85. Found: C, 47.22; H, 6.84; N, 6.93) which gives a positive Morgan–Elson test for 2-acetamido aldoses, reduces Fehling solution more readily than III, and consumes one mole of base to yield formic acid and the 2-acetamido-2,5-dideoxypentose, V (m.p. 128–130°, $[\alpha]^{23}D$ −81° (*c*, 1.0 in ethanol); calcd. for $C_7H_{13}NO_4$: C, 47.99; H, 7.48; N, 8.00. Found: C, 47.86; H, 7.41; N, 8.09).



Furthermore, methyl N-acetylmycosaminide VI (m.p. 168–170°, $[\alpha]^{23}D$ +47° (*c*, 0.9 in ethanol); calcd. for $C_9H_{17}NO_5$: C, 49.30; H, 7.82; N, 6.39; OCH_3, 14.1. Found: C, 49.00; H, 7.56; N, 6.13; OCH_3, 13.5), obtained from III with methanolic hydrogen chloride, was reduced with lithium aluminum hydride to methyl N-ethylmycosaminide, VII, (m.p. 90.5–92.5°, $[\alpha]^{23}D$ +25° (*c*, 1.0 in water); calcd. for $C_9H_{19}NO_4$: C, 52.66; H, 9.33; N, 6.83; mol. weight, 205. Found: C, 52.51; H, 9.19; N, 6.84; neut. eq. (perchloric acid titration), 211), and this base was degraded with sodium periodate (2 moles) to the known[6] D′-methoxy-D-methyldiglycolic aldehyde VIII (m.p. 99–102°, $[\alpha]^{23}D$ +131 (*c*, 0.5 in water); calcd. for

(1) J. D. Dutcher, M. B. Young, J. H. Sherman, W. E. Hibbits and D. R. Walters, "Antibiotics Annual," 1956–1957, Medical Encyclopedia, Inc., New York, N. Y., 1956, p. 866.

(2) The E. R. Squibb and Sons trademark for nystatin is "Mycostatin."

(3) J. D. Dutcher, G. Boyack and S. Fox, "Antibiotics Annual," 1953–1956, Medical Encyclopedia, Inc., New York, 1953, p. 191.

(4) J. D. Dutcher, D. R. Walters and O. P. Wintersteiner, "Therapy of Fungus Diseases," Little, Brown and Company, Boston, Mass., 1955, p. 168.

(5) J. Vandeputte, J. L. Wachtel and E. T. Stiller, "Antibiotics Annual," 1955–1956, Medical Encyclopedia, Inc., 1955, p. 587.

(6) W. D. Maclay, R. M. Hann and C. S. Hudson, THIS JOURNAL, **61**, 1660 (1939).