$$\left(\frac{\Delta H}{H}\right)_i = -a_i \frac{\gamma_e}{\gamma_H} \frac{g\beta S(S+1)}{6kT} \tag{1}$$

on the aromatic carbon atoms by eq. 2[6] we obtained the

$$a_i = Q\rho_i \tag{2}$$

results shown in Table I. Also given are the observed room temperature shifts.

TABLE I

RESULTS FROM EQUATIONS 1 AND 2

	$\Delta H_i{}^a$	$a_i{}^b$	$\rho_i{}^c$
$Co[P(C_6H_5)_3]_2Br_2$			
meta-H	−486.2	+0.0403	−0.00179
para-H	+720.2	−.0521	+.00231
$Co[P(C_7H_7)_3]_2Br_2$			
meta-H	−486.9	+.0407	−.00181
−CH₃	−721.4	+.0559	

^{a} Shifts in c.p.s. at 25°.　^{b} Gauss.　^{c} $Q_{CH} = -22.5$ gauss.

The triphenylphosphine complex, described by Cotton and co-workers[7] contains tetrahedrally coordinated cobalt(II). Magnetic measurements[7] indicate that the cobalt is in an $S = {}^3/_2$ state and from $\mu_{eff} = 4.52$ Bohr magnetons we estimate a g-factor of 2.33. The temperature dependences of the meta- and para-hydrogen resonance shifts in $Co[P(C_6H_5)_3]_2Br_2$ are shown in Fig. 1. The linearity of these plots indicates that no free energy term such as used by Eaton, et al.,[1–4] in the analysis of the spectra of Ni(II) aminotroponeimineates is necessary. These cobalt phospine complexes have a spin free d⁷ configuration and no diamagnetic–paramagnetic equilibrium is possible.

Previous work[3,8] has indicated that substitution of a methyl group for a hydrogen at various positions on a phenyl ring does not appreciably alter the spin densities at the aromatic carbon atoms. In our case, if we assume no change in the ratio of spin densities between the meta and para positions in the phenyl and p-tolyl derivatives, we obtain a value of Q_{CH_3} of 23.9 gauss from the observed shift of the methyl resonance. This value is lower than that found from e.s.r.[9] measurements and in the N-substituted p-tolyl derivative of Ni(II) aminotroponeimineate.[3] The work of Eaton, et al.,[3] indicates that in paramagnetic conjugated systems containing methyl groups, Q_{CH_3} varies considerably, and this variation is attributed to differences in the size of the conjugated system to which the methyl group finds itself attached. Spectroscopic evidence[10] indicates that in coordinated triphenylphosphine the phenyl groups are not conjugated with one another.

We were, however, able to obtain identical spin densities at the para-carbon atom in both the phenyl- and p-tolylphosphine complexes with larger values of Q_{CH_3} by considering a pseudo contact interaction.[3,11,12] This interaction causes a shift of all resonances in proportion to the reciprocals of the cubes of the distance of the resonating nuclei from the paramagnetic ion. For example, a pseudo contact interaction which at 25° produces an upfield shift of the meta-hydrogen resonance 60 c.p.s., the para-hydrogen 40 c.p.s., and the methyl-hydrogens 27 c.p.s., yields a Q_{CH_3} of +27.0 gauss. The actual value of Q_{CH_3} in our system is, of

(6) H. M. McConnell, J. Chem. Phys., 24, 632 (1956).

(7) F. A. Cotton, O. D. Faut, D. M. L. Goodgame, and R. H. Holm, J. Am. Chem. Soc., 83, 1780 (1961).

(8) J. R. Boulton, A. Carrington, and A. D. McLachlan, Mol. Phys., 5, 31 (1962).

(9) R. W. Fessenden and R. H. Schuler, J. Chem. Phys., 33, 935 (1960).

(10) H. H. Jaffé, ibid., 22, 1430 (1954).

(11) H. M. McConnell and R. E. Robertson, ibid., 29, 1361 (1958).

(12) Subsequent to submitting this communication an article appeared [J. A. Happe and R. L. Ward, ibid., 39, 1211 (1963)] wherein pseudo contact shifts in octahedrally coordinated Co(II) complexes were reported.
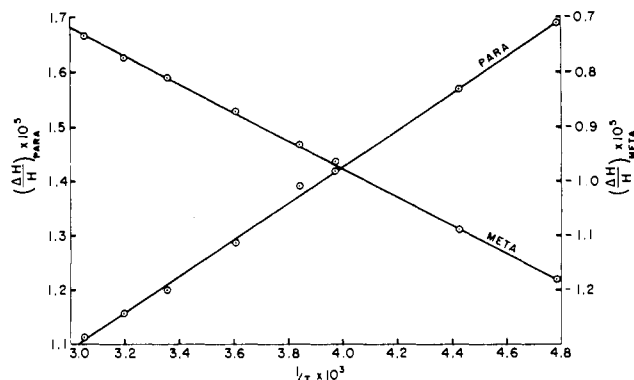
Fig. 1.—Fractional observed shifts for meta- and para-hydrogens in $Co[P(C_6H_5)_3]_2Br_2$ vs. $1/T$.

course, unknown and further work is indicated, but it is not unlikely that there is some pseudo contact contribution to the observed resonance shifts. We expect the pseudo contact interaction to be large when there is a large anisotropy in the g-value. Due to the dissimilarity in ligands and their positions in the spectrochemical series[7] a fairly large C_{2v} component in the ligand field is not unlikely; this is consistent with a moderately anisotropic g-value. The ratio of the absolute values of the para spin density to the meta spin density is lower than found for most of the compounds measured by Eaton, et al.,[1–4] but it may be significant that the ratio is fairly close to that found in a chelate containing a phenyl group bonded to a sulfur atom.[1]

We have observed resonances in other tetrahedral cobalt complexes and in the analogous nickel compounds. Arsine and phosphine oxide complexes are being investigated and the results will be reported in a subsequent publication.

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The Esterolytic Catalysis of Poly-4(5)-vinylimidazole and Poly-5(6)-vinylbenzimidazole

Sir:

We wish to report an unusual catalytic effect of poly-4(5)-vinylimidazole and poly-5(6)-vinylbenzimidazole.

The role of imidazole in the multifunctional catalysis of chymotrypsin has been recognized.[1] pH–rate profiles of chymotrypsin have sigmoid or bell-shaped curves. Recently a sigmoid profile has been identified with a rate-determining deacylation step, involving one functional group (probably imidazole).[2] A bell-shaped curve has been identified with a rate-determining acylation step in which a second group besides imidazole is involved.[2] This group may be the hydroxyl group

(1) H. Gutfreund and J. M. Sturtevant, Biochem. J., 63, 656 (1956); L. Weil, S. James, and A. R. Buchert, Arch. Biochem. Biophys., 46, 266 (1953); J. R. Whitaker and B. J. Jandorf, J. Biol. Chem., 223, 751 (1956); V. Massey and B. S. Hartley, Biochim. Biophys. Acta, 21, 361 (1956); G. Schoellmann and E. N. Shaw, Biochemistry, 2, 252 (1962). For a review see J. A. Cohen, R. A. Oosterbaan, H. S. Jansz, and F. Berends, J. Cellular Comp. Physiol., 54, 231 (1959); E. A. Barnard and W. D. Stein, "Advances in Enzymology," Vol. 20, F. F. Nord, Ed., Interscience Publishers, Inc., New York, N. Y., 1958, p. 51.

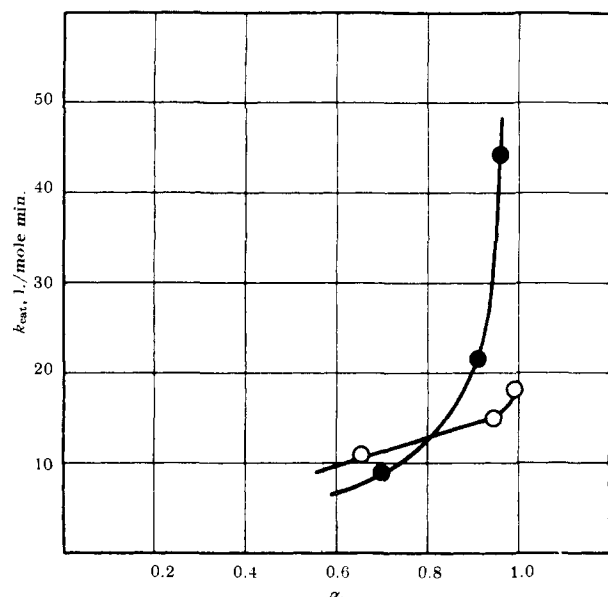(2) M. L. Bender, G. E. Clement, F. J. Kézdy, and B. Zerner, J. Am. Chem. Soc., 85, 358 (1963).

Fig. 1.—Solvolysis of p-nitrophenyl acetate catalyzed by imidazole, O, and by poly-4(5)-vinylimidazole, ●.

of serine with a strongly modified nucleophilicity toward the substrate.[2-4]

As simple models for chymotrypsin we have synthesized the homopolymers and appropriate copolymers of 4(5)-vinylimidazole[5] and 5(6)-vinylbenzimidazole.[6] We now wish to report the kinetic data for the esterolytic activity of the homopolymers.[7] As substrates p-nitrophenyl acetate (PNPA) and 3-nitro-4-acetoxybenzoic acid (NABA) have been employed. Rates were determined in alcohol–water mixtures containing TRIS buffers at constant ionic strength at $26.0°$.[8] The rates were followed by the measurement of the ultraviolet absorption of the phenols evolved.[9] In every case rates were first order both in catalyst and substrate up to 70% conversion or more. The catalysis of the polymers was compared to that of imidazole and benzimidazole. In Table I the catalytic rates of hydrolysis of PNPA by poly-4(5)-vinylimidazole and imidazole are presented.

With the neutral substrate PNPA we have discovered an unusual polymeric effect. At high pH values the catalytic rate of the polymers was higher than that of the monomers, and the enhanced rate was pH dependent.

It appears that above pH 8.0 the polymer is a better catalyst than the monomer. Ultraviolet titration af-

(3) A. K. Balls and E. F. Jansen, "Advances in Enzymology," Vol. 13, F. F. Nord, Ed., Interscience Publishers, Inc., New York, N. Y., 1952, p. 321; N. K. Schaffer, S. C. May, Jr., and W. H. Summerson, *J. Biol. Chem.*, **202**, 67 (1953); N. K. Schaffer, L. Simet, S. Harshman, R. R. Engle, and R. W. Drisko, *ibid.*, **225**, 197 (1957); B. F. Erlanger and W. Cohen, *J. Am. Chem. Soc.*, **85**, 348 (1963).

(4) The change in nucleophilic capacity may be tied up with a considerable change of pK_a of the hydroxyl group; see ref. 2, and *cf.* T. C. Bruice, T. H. Fife, J. J. Bruno, and N. E. Brandon, *Biochemistry*, **1**, 7 (1962).

(5) C. G. Overberger and N. Vorchheimer, *J. Am. Chem. Soc.*, **85**, 95 (1963).

(6) In preparation.

(7) A detailed study of the esterolytic activity of monomeric imidazoles has been carried out by M. L. Bender and B. W. Turnquest, *J. Am. Chem. Soc.*, **79**, 1652, 1656 (1957); T. C. Bruice and G. L. Schmir, *ibid.*, **79**, 1663 (1957); T. C. Bruice and J. M. Sturtevant, *ibid.*, **81**, 2860 (1959); B. M. Anderson, E. H. Cordes, and W. P. Jencks, *J. Biol. Chem.*, **236**, 455 (1961). For a general review see M. L. Bender, *Chem. Rev.*, **60**, 53 (1960).

(8) For poly-4(5)-vinylimidazole and imidazole 28.5% ethanolic solutions were employed, with 0.02 *M* TRIS as buffer and the ionic strength 0.02. For poly-5(6)-vinylbenzimidazole 30% propanol–water solutions were employed, with 0.01 *M* TRIS and ionic strength 0.01. Catalyst concentrations were 5×10^{-4} *M* and substrate concentrations 5×10^{-5} *M*. No change in catalytic rate was observed when catalyst concentration was dropped to 5×10^{-5} *M*.

(9) For p-nitrophenol the wave length selected was 400 and for 3-nitro-4-hydroxybenzoic acid it was 416 mμ.

	k_{cat}, l./mole min.	
pH	Poly-4(5)-vinylimidazole	Imidazole
7.2	9.1	11.4
8.2	21.4	15.0
9.0	44.2	17.8

forded the first pK of poly-4(5)-vinylimidazole and the empirical relationship between α_1[10] and pH in the following expression[11]

$$pK = 6.6 = pH + 1.6 \log \frac{1 - \alpha_1}{\alpha_1}$$

Plots of rates vs. α_1 appear in Fig. 1. It shows that at $\alpha_1 = 0.8$ the catalytic rates of polymer and monomer are the same. Evidently the relatively strong enhancement of the catalytic rate of the polymer at higher pH values cannot be rationalized on the basis of α_1.
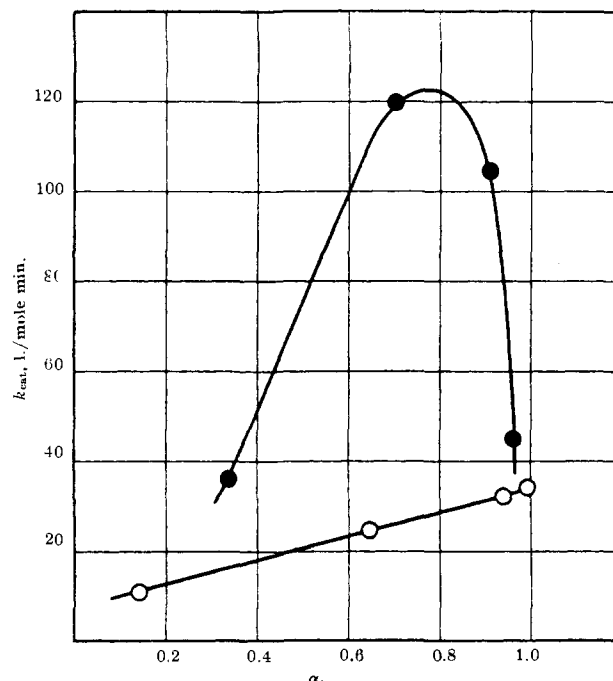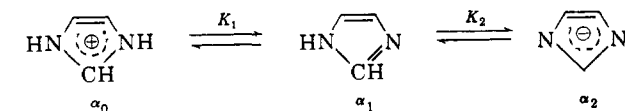

Fig. 2.—Solvolysis of 3-nitro-4-acetoxy benzoic acid catalyzed by imidazole, O, and by poly-4(5)-vinylimidazole, ●.

At these pH values the polymer of 5(6)-vinylbenzimidazole is a better catalyst than benzimidazole (Table II). By ultraviolet titration its first pK was

	k_{cat}, l./mole min.	
pH	Poly-5(6)-vinylbenzimidazole	Benzimidazole
7.8	1.2	0.4
8.6	3.2	0.7
9.7	17.0	2.7

(10) Imidazole is an ampholyte having two pK units. The total catalytic rate is composed of the contributions of the neutral (α_1) and anionic (α_2)

$$HN\overset{\oplus}{\underset{CH}{\diamond}}NH \underset{}{\overset{K_1}{\rightleftharpoons}} HN\underset{CH}{\diamond}N \underset{}{\overset{K_2}{\rightleftharpoons}} N\overset{\ominus}{\diamond}N$$

$$\alpha_0 \qquad\qquad \alpha_1 \qquad\qquad \alpha_2$$

fractions

$$k_{cat} = f_{neutral} \, \alpha_1 + f_{anionic} \, \alpha_2$$

(11) A. Katchalsky and P. Spitnik, *J. Polymer Sci.*, **2**, 432 (1957); A. Katchalsky, N. Shavit, and H. Eisenberg, *ibid.*, **13**, 69 (1954); I. Kagawa and H. P. Gregor, *ibid.*, **23**, 477 (1957).

determined as 3.5; pK_1 of benzimidazole was found as 5.4. Since at these pH values α_1 for both is equal to 1.0, the increase of rate with pH results from α_2 mainly.

The enhanced rates of the polymers *vs.* the monomers in these particular cases is therefore mainly due to a modified contribution of the *anionic* fractions of the polymers.

With poly-4(5)-vinylimidazole and the negatively charged substrate NABA the results were similar to those previously observed by Letsinger and Savereide[12] for analogous systems. The protonated sites (α_0), which do not catalyze the hydrolysis of PNPA, serve as binding sites for NABA. As a result a bell-shaped pH–rate profile was observed (Fig. 2) with a strong maximum near pH 7.5. At this point the catalytic rate of poly-4(5)-vinylimidazole is five times faster than that of imidazole with NABA, and *ca.* 12 times the latter's rate with PNPA. On the other hand, while at pH 8.0 the catalytic activity of poly-5(6)-vinylbenzimidazole with NABA was found comparable to that of benzimidazole, at pH 10.0 the polymer was found to be 50-fold faster than the monomer. Since at these pH values α_0 for this polymer is zero, the enhancement in this case can be only explained as for the neutral substrate.

Acknowledgment.—The authors are indebted to Professor Herbert Morawetz for his stimulating and helpful advice. Financial support by the United States Chemical Corps is gratefully acknowledged.

(12) R. L. Letsinger and T. J. Savereide, *J. Am. Chem. Soc.*, **84**, 114, 3122 (1962); and also *cf.* H. Ladenheim, E. M. Loebl, and H. Morawetz, *ibid.*, **81**, 20 (1959).

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Conformer Populations and Thermodynamic Data from Temperature Dependent Circular Dichroism Measurements[1,2]

Sir:

Recent measurements[3] of circular dichroism (C.D.) curves over relatively large ranges of temperature open a new door to comparatively accurate information on the population of conformers in flexible, optically active molecules. Under favorable circumstances, ΔG°, ΔH°, and ΔS° pertinent to the distribution of conformers may be derived from the C.D. data. In addition, similar information relating to solvation of an optically active species can sometimes be obtained. We confine ourselves in the present note to a quantitative treatment of a two-conformer equilibrium, and adapt to our purposes a type of analysis used previously in connection with monochromatic rotations.[4]

For a particular absorption band, the *observed* total rotational strength R_0^T at temperature T can be derived[5] from the relevant C.D. curve. If R_a and R_b denote the rotational strengths associated with the lower energy conformer a and the higher energy conformer b, respectively, then assumption of a Boltz-

(1) Paper XCIII in the Stanford series "Optical Rotatory Dispersion Studies." For preceding article see C. Djerassi, J. Burakevich, J. W. Chamberlin, D. Elad, T. Toda, and G. Stork, *J. Am. Chem. Soc.*, in press.

(2) Financial support from the Alfred P. Sloan Foundation (A.M.) and the National Science Foundation (Grant G-19905 to Stanford University) is gratefully acknowledged.

(3) K. M. Wellman, E. Bunnenberg, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 1870 (1963). Some of the data and representative C.D. curves used in the present analysis may be found here.

(4) W. W. Wood, W. Fickett, and J. G. Kirkwood, *J. Chem. Phys.*, **20**, 561 (1952).

(5) C. Djerassi, "Optical Rotatory Dispersion," McGraw–Hill Book Co., New York, N. Y., 1960, p. 164.

mann distribution for the conformers leads to the following expression relating R_0^T to R_a and R_b

$$R_0^T = (R_a - R_b)[1 + \exp(-\Delta G^\circ/NkT)]^{-1} + R_b \quad (1)$$

Here N is Avogadro's number, k is Boltzmann's constant, and ΔG° is the standard Gibbs free energy change for the reaction a $\rightleftharpoons$ b. The equilibrium constant K can be written as

$$K = (R_a - R_0^T)/(R_0^T - R_b) \quad (2)$$

According to eq. 1, a plot of R_0^T *vs.* $1/[1 + \exp(-\Delta G^\circ/NkT)]$ should yield a straight line for the proper temperature-dependent values of ΔG°. If ΔG° is in fact a constant over the temperature range studied, then substitution of various trial values for ΔG° into eq. 1 yields a family of curves, only one of which (that for the proper ΔG°) is a straight line.[6,7] From the slope and intercept of this line one can obtain the correct values for R_a and R_b, which, when substituted into eq. 2, provide an explicit temperature-dependent expression for K in terms of the experimental R_0^T.

It is noteworthy that one obtains specific values for the rotational strengths (R_a and R_b) of the nonisolatable forms a and b. Without solvent corrections, these values refer to the apparent rotational strengths in solution, rather than their values *in vacuo*. However, because K appears as a ratio of R-values, the equilibrium constant can be shown to be largely independent of these solvent corrections if the solvation effects themselves are not markedly temperature dependent, as often seems to be the case.[8] Hence the K-value obtained is a reasonable reflection of the population of conformers present. Moreover, it follows as a corollary that once one obtains R_a and R_b values in one solvent, K can be found in any other solvent at any temperature T simply by measuring R_0^T for that solvent. *A facile means for obtaining K in a variety of solvents is therefore available.*

By way of specific example, we consider the equilibrium $I_e \rightleftharpoons I_a$ in (+)-*trans*-2-chloro-5-methylcyclohexanone in EPA.[3] Some of the curves corresponding to the plot of eq. 1 are indicated in Fig. 1. An optimized[6] straight line is obtained for $\Delta G^\circ = 1.72$ kcal./mole, with $R_a = +2.34 \times 10^{-40}$ c.g.s. and $R_b = -34.7 \times 10^{-40}$ c.g.s. This value for ΔG° is good to ± 0.09 kcal./mole. Since ΔG° is assumed to be temperature-independent, $\Delta H^\circ = \Delta G^\circ$, and $\Delta S^\circ = 0$ for the equilibrium $I_e \rightleftharpoons I_a$.

Conformer populations in various solvents at 25°, calculated from the preceding values of R_a and R_b in conjunction with measured[3] values of R_0^{298}, are given in Table I along with estimates obtained previously from ultraviolet and optical rotatory dispersion data. The three sets of percentages agree within the stated error limits.

(6) A minimal least-squares fit to a straight line can be used to obtain a better value for ΔG° than can be achieved visually from the plot. In the example of *trans*-2-chloro-5-methylcyclohexanone (1) discussed later, we used such a least-squares procedure. In this case, the eye could distinguish easily to better than 0.05 kcal./mole.

(7) Equations of the mathematical forms 1 and 2 appear in connection with a variety of kinetic and spectroscopic measurements [see E. L. Eliel, *J. Chem. Educ.*, **37**, 126 (1960)]. Data from such measurements are amenable to the present method of analysis so long as the quantities analogous to R_a and R_b (*e.g.*, n.m.r. chemical shifts for pure conformers) are temperature independent, and the other stated assumptions are met.

(8) Calculation of R_0^T from the raw experimental data must take account of the concentration changes accompanying the volume variation with temperature, which also produce changes in the index of refraction of the medium. According to the simple $(n^2 + 2)/3$ Lorentz-type correction factor, this implies a further correction for R_0^T. However, in those steroids studied so far which one may expect to be rigid, the differences between R_0^T at 25° and $-192°$ generally represent changes of less than 4%, and these differences have been both positive and negative. Hence, in the absence of further information, we have ignored any corrections due to changes in the index of refraction with temperature.