

effects from two *m*-methyl groups, at least insofar as its effect on adsorption affinity of phenols is concerned.

The 2,6-disubstituted phenols show a very marked decrease in adsorption affinity over their monosubstituted analogs. This is clearly evident even with the relatively small methyl group.

The data obtained in this study substantiate the hypothesis that the steric hindrance of the alkyl substituent is the most important influence of that group on the chromatographic adsorption of *ortho*-alkyl substituted phenols. Equally important from

the point of view of a practical application, this information affords the chromatographer a simple method for the separation of *ortho* and *para* isomers of these alkyl phenols. It can also serve as a simple purification procedure for small quantities of the *ortho*-substituent.

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COMMUNICATIONS TO THE EDITOR

SPECIFIC MEDIUM EFFECTS IN NUCLEAR MAGNETIC RESONANCE SPECTRA OF LIQUIDS

Sir:

It has been accepted generally that two molecular properties affect \mathcal{H} (the strength of the applied field necessary to induce resonance) in the high-resolution nuclear magnetic resonance spectra of liquids: (1) intramolecular diamagnetic shielding by the valence electrons, and (2) alteration of the effective field at the molecule by the bulk of the liquid. The latter effect is usually assumed to be strictly derivable from the shape of the sample and the volume susceptibility (κ) of the liquid.¹ For a molecule residing in a spherical cavity in a cylindrical liquid sample oriented transversely to the magnetic field, the prediction of classical magnetostatics is a decreasing \mathcal{H} with decreasing volume susceptibility of the liquid. In agreement with this model, methylene chloride ($\kappa = -0.73 \times 10^{-6}$)² shows³ a lower \mathcal{H} by 6.1 ± 0.2 milligauss when diluted with nine volumes of methylene bromide ($\kappa = -0.95 \times 10^{-6}$).² However, when methylene chloride is dissolved in tetrachloroethylene ($\kappa = -0.83 \times 10^{-6}$)² no change in \mathcal{H} is observed.

In our experience *such anomalies may arise whenever there is a possibility of a preferred orientation of magnetically anisotropic molecules adjacent to the molecule under study.* This orientational interaction will be a highly specific one. Therefore, the addition to several liquids of a single substance intended to serve as a reference may result in unpredictable shifts in the \mathcal{H} for the added substance, which thereby loses its value as a standard. Moreover, \mathcal{H} for the aromatic hydrogens of *t*-butylbenzene is unaltered on dilution with nine volumes of carbon tetrachloride while \mathcal{H} for the methyl hydrogens is lowered by 5.1 ± 0.5 milligauss.

(1) B. P. Dailey and J. N. Shoolery, *THIS JOURNAL*, **77**, 3977 (1955), who point out, however, that non-ideal behavior is observed in the case of mixtures of methyl iodide and benzene.

(2) P. Pascal, *Ann. Chim.*, (8) **19**, 5 (1910).

(3) Measurements were made on a Varian NMR Spectrometer at 40 megacycles using a 5-mm. spinning sample tube containing a 1-mm. sealed capillary of reference substance. Separate experiments have shown that \mathcal{H} for the reference is independent of sample susceptibility in this geometry.

Thus, extreme care must be exercised in the use of so-called internal standards.

This orientational effect may be largely eliminated by surrounding the molecule with solvent molecules which are more nearly magnetically isotropic. For example, Table I displays \mathcal{H} for the *para*-hydrogen⁴ in several mono-substituted benzenes as found by measurement on the pure liquid, and as extrapolated for the infinitely dilute solution in carbon tetrachloride from data obtained on five and ten volume-per cent. concentrations.

TABLE I
para-HYDROGEN RESONANCES IN MONOSUBSTITUTED
BENZENES

Substituent	\mathcal{H} (milligauss) ^a		σ_p ^c
	Pure liquid	Extrapolated ^b	
—NH ₂	+10.2	+3.8	−0.66
—OCH ₃	+ 2.6	+0.8	−0.27
—CH ₃	+ 4.5	+0.5	−0.17
—H	+ 5.7	0.0	0.0
—C(CH ₃) ₃	+ 0.2	−0.2	−0.20
—Cl	+ 3.1	−1.5	+0.23
—Br	+ 4.5	−1.3	+0.23
—I	+ 0.5	−1.5	+0.28
—CN	+ 0.9	−4.5	+1.00
—CHO	− 0.2	−5.8	+1.13
—NO ₂	+ 1.9	−6.3	+1.27

^a Relative to the extrapolated \mathcal{H} for benzene in carbon tetrachloride. All measurements with a probable error of ± 0.5 milligauss. ^b See text. ^c Reference 5.

While the \mathcal{H} 's for the pure liquids do not seem to fall in any recognizable order, those found by extrapolation follow the order expected from the electrical effects of the substituents, and, within experimental error, fit the equation

$$\mathcal{H} - \mathcal{H}_0 = -5.0\sigma_p$$

where \mathcal{H}_0 is the extrapolated \mathcal{H} for benzene, and σ_p is Hammett's *para* substituent constant.⁵ Other classes of substances show similar trends toward order consistent with known molecular properties when treated in a corresponding manner.

(4) E. B. Baker, *J. Chem. Phys.*, **23**, 984 (1955).

(5) L. P. Hammett, "Physical-Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 188.

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PARAMAGNETIC RESONANCE OF
OCTACYANOTUNGSTATE(V)¹

Sir:

The paramagnetic resonance of crystalline potassium octacyanotungstate and its aqueous solutions has been observed. A polycrystalline sample of composition $K_3W(CN)_8 \cdot 0.55H_2O$ yields a single almost symmetrical resonance at room temperature. The g value at the center of the peak is 1.98. The breadth of the peak between points of extreme slope is 30 oersteds.

An aqueous solution, approximately 0.01 M in $W(CN)_8^{4-}$, yields a symmetrical resonance of three lines. The central intense line occurs at $g = 1.972$ with breadth between points of extreme slope of 9.3 oersteds. The two satellites, each of intensity $7 \pm 3\%$ of that of the central peak are separated by 52 oersteds. The central peak in all probability arises from ions containing W^{184} which has zero nuclear spin and is 86% abundant; the satellites are the hyperfine components associated with W^{183} which has spin $1/2$ and is 14% abundant.

The spectrum of the aqueous solution is unusual in its sharpness. Owing to rapid relaxation processes, most paramagnetic compounds of heavy elements have lines so broad at room temperature, that the resonances are not easily observed. The hyperfine coupling constant is unusually large, corresponding to a magnetic field of 6×10^5 oersteds at the tungsten nucleus. The results suggest the possible usefulness of $W(CN)_8^{4-}$ in experiments involving alignment of the nuclei of some of the radioactive isotopes of tungsten.

The conventional description of $W(CN)_8^{4-}$ ascribes the paramagnetism to an unpaired electron occupying a d orbital. The isotropic hyperfine interaction here described requires admixture of a configuration containing unpaired electrons in s orbitals.² Further experiments with dilute solid solutions of $W(CN)_8^{4-}$ in single crystals of a diamagnetic substance are required for more complete determination of the nature of the electronic wave function.

An attempt was made to measure the rate of electron exchange between $W(CN)_8^{4-}$ and $W(CN)_8^{3-}$ by the observation of the spectrum of the former in the presence of the latter. At concentrations of $W(CN)_8^{3-}$ lower than 0.02 M no broadening of the hyperfine components of $W^{183}(CN)_8^{3-}$ was observed. With $W(CN)_8^{3-}$ at

(1) This work has been supported in part by the United States Air Force through the Office of Scientific Research of the Air Research and Development Command and by the United States Atomic Energy Commission under Contract AT(11-1)-34 with the University of California.

(2) A. Abragam, J. Horowitz and M. H. L. Pryce, *Proc. Roy. Soc. (London)*, **A230**, 169 (1955).

0.04 M a slight broadening, of the order of one oersted, was observed. If the broadening arises from the electron exchange reaction, the rate constant for the bimolecular exchange is 4×10^8 liter mole⁻¹sec.⁻¹. The absence of broadening at lower concentrations establishes this value as an upper limit, *i.e.*, $k \leq 4 \times 10^8$ liter mole⁻¹sec.⁻¹. Previous work with radioactive tracers^{3,4} has indicated that $k > 4 \times 10^4$ liter mole⁻¹sec.⁻¹.

(3) E. L. Goodenow and C. S. Garner, *THIS JOURNAL*, **77**, 5272 (1955).

(4) H. Baadsgaard and W. D. Treadwell, *Helv. Chim. Acta*, **38**, 1669 (1955).

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THE PARTIAL STRUCTURE OF NOVOBIOCIN
(STREPTONIVICIN),¹ II.

Sir:

The isolation and properties of novobiocin have been described.²⁻⁴ The present studies, added to those previously reported,⁵ indicate that it is a C_9 sugar attached glycosidically to the 7-position of 3-[4-hydroxy-3-(3-methyl-2-butenyl)-benzamido]-4,7-dihydroxy-8-methylcoumarin.

Novobiocin (I) ($C_{31}H_{36}N_2O_{11}$), is cleaved by the action of hot acetic anhydride to yield 4-acetoxy-3-(3-methyl-2-butenyl)-benzoic acid (II) and a neutral compound, $C_{23}H_{26}N_2O_{10}$ (III).⁵ Hydrolysis of I by 4 N hydrochloric acid in 60% ethanol gave an optically inactive acid, $C_{22}H_{21}NO_6$ (IV), which upon cleavage with hot acetic anhydride yielded 2,2-dimethyl-6-chromancarboxylic acid (VI) and an optically inactive neutral compound, $C_{14}H_{11}NO_5$ (VII).⁵

In addition to IV, the acid hydrolysis affords an

(1) The Upjohn Company Registered Trade Mark for novobiocin is Albamycin. Our previous Communication⁵ on the structure of this antibiotic is listed under our former generic name, streptonivicin, now abandoned. The isolation of the same material by the Merck group has been described in *THIS JOURNAL*, **77**, 6404 (1955). The comparisons establishing identity are described by Henry Welch and W. W. Wright in *Antibiotics and Chemotherapy*, **5**, 670 (1955).

(2) (a) Streptonivicin, A New Antibiotic. I. Discovery and Biologic Studies, C. G. Smith, A. Dietz, W. T. Sokolski and G. M. Savage, *Antibiotics and Chemotherapy*, in press, February, 1956. (b) II. Isolation and Characterization, H. Hoeksema, M. E. Bergy, W. G. Jackson, J. W. Shell, J. W. Hinman, A. E. Fonken, G. A. Boyack, E. L. Caron, J. H. Ford, W. H. DeVries, and G. Crum, *ibid.* (c) III. *In Vitro* and *In Vivo* Evaluation, J. R. Wilkins, C. Lewis and A. R. Barbiers, *ibid.* (d) IV. A Biological Assay for Body Tissues and Fluids, R. M. Taylor, W. T. Sokolski, G. M. Savage and M. J. Vander Brook, *ibid.* (e) V. Absorption, Distribution and Excretion, R. M. Taylor, W. L. Miller and M. J. Vander Brook, *ibid.* (f) VI. Toxicology, E. John Larson, N. E. Connor, O. F. Swoap, R. A. Runnells, M. C. Prestrud, T. E. Eble, W. A. Freyburger, W. Veldkamp and R. M. Taylor, *ibid.*, March, 1956.

(3) Streptonivicin (Albamycin) A New Antibiotic; Preliminary Report, F. R. Heilman, D. R. Nichols, W. E. Wellman, and J. E. Geraci, *Proc. Staff Meetings Mayo Clinic*, **30**, 540 (1955).

(4) Streptonivicin, Laboratory and Clinical Studies in the Pediatric Age Group, Feng-Kai Lin and L. L. Coriell, Third Annual Symposium on Antibiotics, November 2-4, 1955; "Antibiotics Annual, 1955-1956," Welch and Marti-Ibanez, Medical Encyclopedia, Inc., New York, N. Y., in press.

(5) Herman Hoeksema, James L. Johnson, and Jack W. Hinman, *THIS JOURNAL*, **77**, 6710 (1955). New analytical data for I and III have been obtained as follows: Calcd. for $C_{31}H_{36}N_2O_{11}$ (I): C, 60.77; H, 5.92; N, 4.58. Found: C, 60.62; H, 5.91; N, 4.54. Calcd. for $C_{23}H_{26}N_2O_{10}$ (III): C, 56.33; H, 5.35; N, 5.71. Found: C, 56.53; H, 5.33; N, 5.68.