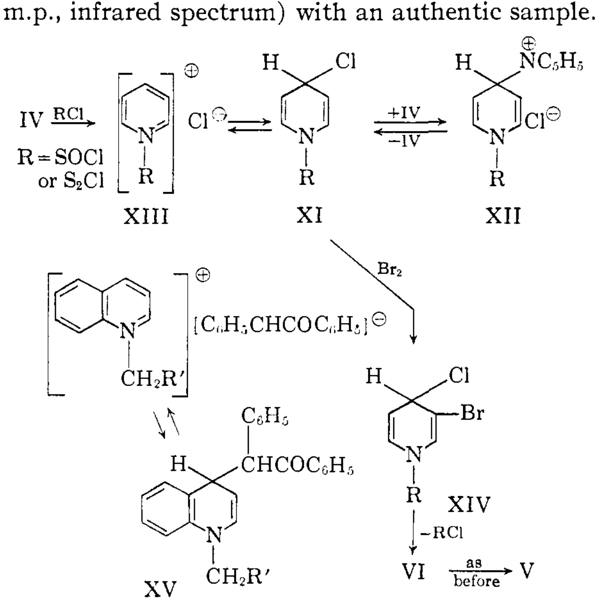
an authentic sample. From the steam distillate a small amount of 3-bromopyridine (VI) and about 25% of unchanged IV were isolated. Replacement of II by sulfur monochloride (VII) permitted a higher reaction temperature (125–130°), an easier work-up, and increased the yield of V to 33–40%, VI in II and in VII afforded V in 15[13] and 50% yields, respectively.

Quinoline (VIII) is much more reactive than IV toward bromination in a solution of VII. Best results were obtained by use of equimolar amounts VIII, VII and IV with a slight excess of bromine, the reagents being added (cooling) to VIII in the order named. On heating the solution in a bath at about 95° for about 1 hr. a solid formed. The filtered solid was treated with aqueous alkali, sulfur removed by filtration, the filtrate extracted with ether, and the extract distilled to yield 65% of almost analytically pure 3-bromoquinoline (IX),[14] b.p. 115–120° at 1 mm., $n^{25}$D 1.6613, whose infrared spectrum was identical with that of an authentic sample[15] kindly supplied by Dr. J. Eisch.

Bromination of isoquinoline in VII has not yet been studied thoroughly, but we have obtained 4-bromoisoquinoline, m.p. 34–37°, identical (mixed m.p., infrared spectrum) with an authentic sample.



R' = 2,6-dichlorophenyl

Characteristic of these reactions is the entry of the bromine at the beta-position to the ring nitrogen, regardless of the nature of the substituent (—H, —Br, or —COCl) already present. The mild conditions used, even with I, militate against a straightforward electrophilic substitution. Much more likely is the view that the species being brominated is a 1,2- or 1,4-dihydropyridine derivative (XI) or its reaction product (XII) with IV, all of which probably exist in equilibrium with the pyridinium salt formed by addition of either VII or II to IV. Electrophilic bromination of XI or XII (each has a vinylamine structure) would certainly proceed readily to yield (from XI) XIV, which could lose RCl to form the observed products. It is noteworthy that XII has been suggested as an intermediate in the reaction of IV with either II or VII to form the 4-pyridyl-pyridinium chloride hydrochloride.[16,17] The mechanism is strikingly similar to those independently suggested to explain the bromination of compounds like XV[18] and the nitration (with benzoyl or acetyl nitrate) of quinoline 1-oxide,[19] both of which occur at the 3-position under very mild conditions.

It seems likely that the above ideas can be extended to other pyridine-type heterocycles and to other substitution reactions. Furthermore, II and VII probably can be replaced by a variety of similar reagents. Work along some of these lines is in process in this Laboratory. We believe that reactions like those described open important new perspectives in the chemistry of pyridine-type heterocycles.

DEPARTMENT OF CHEMISTRY
FORDHAM UNIVERSITY
NEW YORK 58, NEW YORK

EDWARD E. GARCIA
CLAUDE V. GRECO
I. MOYER HUNSBERGER[20]

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[13] No attempt was made to achieve maximum yield.

[14] A. Edinger [*Ber.*, **29**, 2456 (1896)] reported a low yield of IX from the exothermic reaction of VIII with sulfur monobromide (X), free bromine being produced by decomposition of X.

[15] J. Eisch, *Chemistry and Industry*, 1449 (1959).

[16] E. Koenigs and H. Greiner, *Ber.*, **64**, 1049 (1931).

[17] E. Koenigs and H. Greiner, German Patents 536, 891 (1931), and 566,693 (1932), as cited by H. Maier-Bode and J. Altpeter in "Das Pyridin und seine Derivate," Verlag von Wilhelm Knapp, Halle (Saale), 1934, Photo-Lithoprint Reproduction by Edwards Brothers, Inc., Ann Arbor, Mich., 1943, pp. 99, 289, and 292.

[18] F. Kröhnke and I. Vogt, *Chem. Ber.*, **90**, 2227 (1957).

[19] E. Ochiai and C. Kaneko, *Pharm. Bull.* (*Tokyo*), **5**, 56 (1957); *Chem. Pharm. Bull.* (*Tokyo*), **7**, 267 (1959).

[20] To whom all inquiries should be sent at Department of Chemistry, University of Massachusetts, Amherst, Massachusetts.

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### THEORY OF PROTON COUPLING CONSTANTS IN UNSATURATED MOLECULES

*Sir:*

A number of recent papers[1–5] concerned with the n.m.r. spectra of unsaturated molecules have reported the magnitudes of 1.5 to 7 c.p.s. for the coupling constants between protons separated by three or four carbon atoms. Since theoretical calculations[6] and experimental measurements[7] have shown that the sigma-electron contribution to such coupling constants is less than 0.5 c.p.s., the large size of the observed values has aroused some interest. We wish to point out in this communication that the inclusion of pi-electron terms in the coupling interaction provides a quantitative explanation of the experimental results.

A second-order perturbation formalism has been developed for the calculation of the pi-electron contribution to the proton coupling constants for unsaturated systems in which the formal separation into sigma and pi electrons is possible. The

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[1] S. Alexander, *J. Chem. Phys.*, **28**, 355 (1958); J. Waugh, *ibid.*, **30**, 944 (1956); C. N. Banwell, A. D. Cohen, N. Sheppard and J. J. Turner, *Proc. Chem. Soc.*, 266 (1955).

[2] E. B. Whipple, J. H. Goldstein, L. Mandell, G. S. Reddy and G. R. McClure, THIS JOURNAL, **81**, 1321 (1959); P. T. Narasimhan and M. T. Rogers, *J. Chem. Phys.*, to be published.

[3] E. B. Whipple, J. H. Goldstein and L. Mandell, *ibid.*, **30**, 1109 (1959); E. B. Whipple, J. H. Goldstein and W. E. Stewart, THIS JOURNAL, **81**, 4761 (1959).

[4] R. R. Fraser, *Can. J. Chem.*, **38**, 549 (1960).

[5] N. Muller and D. E. Pritchard, *J. Chem. Phys.*, **31**, 768 (1959).

[6] M. Karplus, unpublished calculations.

[7] P. T. Narasimhan, private communication; Shimizu, Matsuoka, Hafferi and Seudo, *J. Phys. Soc.* (*Japan*), **14**, 683 (1959).

coupling interaction arises from sigma–pi exchange terms in the Hamiltonian operator. Recognition of the correspondence between these exchange terms and those occurring in related pi-electron radicals[8] makes possible a considerable simplification of the theory. Although the general result obtained by this procedure is still rather complicated, a number of approximations permit the pi-electron contribution $A_{\mathrm{HH}'}(\pi)$ to be written in the very simple form

$$A_{\mathrm{HH}'}(\pi) = K \sum_{T} \frac{a_{\mathrm{H}}(T)a_{\mathrm{H}'}(T)}{\Delta\pi(T)} \qquad (1)$$

Here $a_{\mathrm{H}}(T)$ and $a_{\mathrm{H}'}(T)$ are the hyperfine splitting constants for the pair of pi-electron radical fragments that correspond to the triplet state $T$ and $\Delta\pi(T)$ is the singlet–triplet transition energy. The sum in Eq. (1) is over all the pi-electron triplets $T$ that make a significant contribution. If $A_{\mathrm{HH}'}(\pi)$, $a_{\mathrm{H}}(T)$, and $a_{\mathrm{H}'}(T)$ are expressed in c.p.s. and $\Delta\pi(T)$ in eV., the constant $K$ is equal to $2.1 \times 10^{-15}$.

To clarify Eq. (1), we consider a simple application. The 1,3-proton coupling in propylene can be estimated by including only the lowest pi-electron triplet state. This state corresponds to the two radical fragments H–$\dot{\mathrm{C}}$ and H–C–$\dot{\mathrm{C}}$ for which hyperfine splitting constants $a_{\mathrm{H}}$ of $-65 \times 10^6$ c.p.s.[9] and $+75 \times 10^6$ c.p.s.,[10] respectively, are appropriate. With the transition energy $\Delta\pi(T)$ set equal to 6 e.V., the most likely value for ethylene,[11] a value of $-1.7$ c.p.s., is obtained for $A_{\mathrm{HH}'}(\pi)$.

TABLE I

PROTON SPIN COUPLING CONSTANTS

| Proton linkage | $A_{\mathrm{HH}'}(\pi)$ (c.p.s.) (theor.) | $A_{\mathrm{HH}'}$ (c.p.s.) (exp.) |
|---|---|---|
| H—C=C—C—H | $-1.7$ | $-1.4$ to $-1.8$[1] |
| H—C=C=C—H | $-6.7$ | 6.1 to 7.0 (unknown sign)[2] |
| H—C—C=C—C—H | $+2.0$ | 1.2 to 1.5 (unknown sign)[3] |
| H—C=C=C=C—H | $+7.8$ | Not measured |

Substitution of available values for the hyperfine constants and triplet state energies into Eq. (1) yields the results given in Table I. Only systems containing a double bond with the protons separated by three or four carbon atoms have been included. Where possible the absolute signs of the theoretical results are compared with the relative signs obtained by the analysis of n.m.r. spectra.[12] It is seen that the calculated values for the coupling constants are in agreement with the available experimental measurements. The large value predicted for butatriene has yet to be verified, as do the signs in several of the systems for which only the magnitudes are available.

From the theory presented in this paper it is evident that the pi electrons provide the dominant contribution to the coupling constant in certain unsaturated molecules. Corresponding results are found for similar couplings in systems that contain a triple bond (*e.g.*, methylacetylene). A more detailed discussion of the theoretical development leading to Eq. (1) and other applications are to be published in the *Journal of Chemical Physics.*

NOYES CHEMICAL LABORATORY
UNIVERSITY OF ILLINOIS
URBANA, ILLINOIS
MARTIN KARPLUS

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(8) See H. M. McConnell, *J. Mol. Spect.*, **1**, 11 (1957); *J. Chem. Phys.*, **30**, 126 (1959), for a corresponding device applied to aromatic molecules.

(9) H. M. McConnell, *J. Chem. Phys.*, **24**, 764 (1956); H. S. Jarret, *ibid.*, **25**, 1289 (1956); M. Karplus, *ibid.*, **30**, 15 (1959).

(10) R. Bersohn, *J. Chem. Phys.*, **24**, 1066 (1956); A. D. McLachlan, *Mol. Phys.*, **1**, 233 (1958).

(11) W. J. Potts, Jr., *J. Chem. Phys.*, **23**, 65 (1955).

(12) The theoretical sign of $A_{\mathrm{HH}}$ is defined as positive if the nuclear spin state with the proton spins paired is of lower energy. The experimental sign is relative to the HCCH coupling, which is taken to be positive.

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## UNSPECIFIC TRITIUM LABELLING ACCELERATED BY MICROWAVE, ALTERNATING CURRENT AND DIRECT CURRENT ELECTRICAL DISCHARGES AND BY ULTRAVIOLET RADIATION

*Sir:*

In a recent publication Westermark, *et al.*,[1] presented electrical discharges for accelerating unspecific labelling. Systematic studies based on high frequency (2425 mc./sec.) microwave discharge, low frequency glow discharges and ultraviolet radiation have now been performed on a variety of organic substances ranging from high polymeric substances of known characteristics to liquids of low boiling points.

A short record of some findings will be given. Detailed experimental techniques and discussions will be published elsewhere.[2]

Most of the radioactivity measurements were made in an Ekco liquid scintillation counter. Polystyrene and polymethyl methacrylate were purified by precipitating in excess of ice-cooled methanol, and then filtering and drying at 80° for 24 hr. Tritium was supplied in small ampoules with fragile hook seals from the Radiochemical Centre, Amersham.

With polystyrene (200 mg.) and 50–100 mC. of tritium in evacuated Pyrex tubes under microwave discharge in a silver plated brass cavity, specific activities of about 100 mC./g. in the purified product were reached for an energy input of about 5000 watt sec. The percentage of tritium fixed was about 10–20% and the yield of fixation 0.002 mC./watt sec. This activity tended to decrease at higher energy inputs. The pressure of tritium was found to decrease with energy unless too much energy was put in. There was no difference between the labelled material and the original polystyrene in the ultraviolet absorption spectra taken over a wide range of wave lengths. In an experiment with 20 mg. placed 2.5 cm. away from the plasma region in a bent section of the tube, the tritium pressure decreased more slowly but the activity finally obtained was 426 mC./g.; typical treatment time was 1660 sec. This result suggests that tritiation occurs via T atoms as it is not probable that significant amounts of gaseous ions would reach the material under the above conditions. Further evidence in favor of this hypothesis is given below. Except for the effect of reflected photons the bent-tube method eliminates the destruction of organic material from short wave length ultraviolet light from the plasma zone.

(1) T. Westermark, H. Lindroth and B. Enander, *J. Appl. Radiation and Isotopes*, **7**: **4**, 331 (1960).

(2) N. A. Ghanem and T. Westermark, paper to be presented before the I.A.E.A. isotope conference in Copenhagen, Sept., 1960.