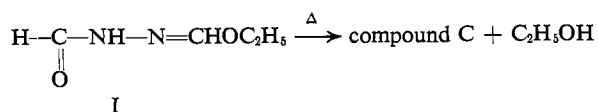


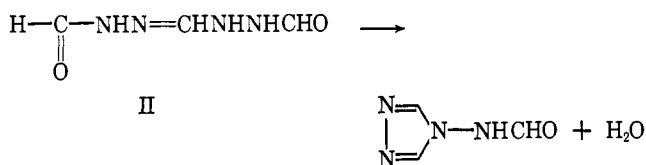
The thermolysis of ethyl formate formylhydrazone (I)



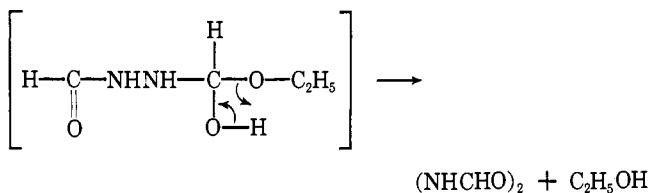
at atmospheric pressure gave 1,3,4-oxadiazole, a liquid at room temperature, b.p. 150°. *Anal.* Calcd.: C, 34.29; H, 2.88; N, 40.00. Found: C, 34.56; H, 3.19; N, 39.71; mol. wt., 70 (mass spectrometry); *m/e* (relative intensity, %) 13 (3.0), 14 (3.7), 18 (2.3), 27 (5.0), 28 (2.5), 29 (23.0), 31 (1.4), 41 (14.0), 42 (69.0), 43 (3.4), 55 (1.6), 70 (100.0), and 71 (3.2);  $n_{\text{D}}^{25}$  1.4300; n.m.r.  $\tau$  0.60 (neat), 1.27 (CDCl<sub>3</sub>); no ultraviolet maximum above 200 m $\mu$ ; infrared  $\lambda_{\text{max}}$  3.17, 6.50, 6.67, 7.83, 9.17, 10.46, 10.82, and 11.57  $\mu$  (CHCl<sub>3</sub>).

Ethyl formate formylhydrazone (I) was formed by heating an ethanol solution of formic acid hydrazide and excess triethyl orthoformate. Compound I showed unusual n.m.r. spectral data, which will be the subject of a separate communication.

Reaction, under anhydrous conditions, of very pure formic acid hydrazide and (a) excess triethyl orthoformate heated under reflux, or (b) an equimolar quantity of compound I heated at 100°, or in ethanol at reflux, gave the same two products. These products are N,N'-diformylhydrazine and 4-formylamino-1,2,4-triazole. Seemingly, N,N'-di(formamido)formimidine (II), formed from the reaction of compound I and formic



acid hydrazide by the elimination of 1 mole of ethanol, readily lost a molecule of water to give the triazole. The water so formed reacted with compound I to give



N,N'-diformylhydrazine and ethanol.

The reaction has been extended by the use of appropriate starting materials to include the preparation of the unreported monoalkyl and unsymmetrical 2,5-dialkyl-1,3,4-oxadiazoles. A detailed report of the study is in preparation.

**Acknowledgment.** The microanalyses were performed by W. L. Brown and associates. The physical measurements were made by L. G. Tensmeyer, W. Hargrove, and associates.

(3) The CEC 21-110 mass spectrometer was used: reservoir temperature 250°, ionization voltage 70 v., acceleration voltage 8 kv., and block temperature 200°.

(4) Determined with a Varian HA-60 spectrometer.

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Received October 15, 1965

## Deuteron Magnetic Resonance Spectroscopy of Large Molecules. Spectrum of Chlorophyll a-d<sub>72</sub><sup>1</sup>

Sir:

By comparison to proton magnetic resonance spectroscopy, deuteron magnetic resonance (d.m.r.) is as yet little explored, and its scope remains to be defined. Diehl and Liepert<sup>2</sup> have made the most extensive investigation of d.m.r. so far reported and have shown its applicability to compounds of low molecular weight. For large, unsymmetrical molecules, the increase in correlation time combined with the deuterium electric quadrupole relaxation<sup>3</sup> could conceivably broaden the resonance lines sufficiently to obliterate the d.m.r. spectrum. The successful culture of fully deuterated microorganisms makes available a great variety of fully deuterated compounds,<sup>4</sup> many of the more interesting of which have molecular weights in the range 300 to 1000. We can now report the first d.m.r. data that have been obtained for a large and complex natural product and are able to show that useful d.m.r. spectra can be obtained with highly anisotropic large molecules.

Table I lists the principal lines in a 15.4-Mc. spectrum<sup>5</sup> of methyl (CH<sub>3</sub>) deutero pheophorbide a. The observed line widths of 2 to 7 c.p.s. are considerably

Table I. Chemical Shifts ( $\delta$ , p.p.m.) in Methyl Pheophorbide<sup>a</sup>

Position <sup>b</sup>	D.m.r. Methyl deutero-pheophorbide a (0.12 M)	P.m.r. <sup>c</sup> Methyl pheophorbide a (0.12 M)	$\Delta$ , (d.m.r.) - (p.m.r.)
11	3.33	3.38	-0.05
5	3.64	3.65	-0.01
1	3.96	4.00	-0.04
3	4.31	4.35	-0.04
4	5.71	5.67	+0.04

<sup>a</sup> Chemical shifts are given in p.p.m. from internal CDCl<sub>3</sub> and CHCl<sub>3</sub>; high-field values are positive. The d.m.r. chemical shifts represent the average of ten measurements with standard deviations not greater than  $\pm 0.03$  p.p.m. <sup>b</sup> See ref. 6 for chlorophyll position numbering. Protons no. 1, 3, and 5 are methyl groups attached directly to the macrocycle; no. 4 is the CH<sub>3</sub> of the ethyl group at position 4; and no. 11 is the methyl group of the carbomethoxy group at carbon 10 in the isocyclic ring V of chlorin. <sup>c</sup> Reference 6.

larger than those commonly observed in p.m.r., but they are quite comparable to the d.m.r. line widths for low molecular weight alcohols observed by Diehl and Liepert.<sup>2</sup> The deuteron chemical shifts (p.p.m. from CDCl<sub>3</sub> as solvent and internal standard) for deutero pheophorbide a are directly comparable to the proton chemical shifts for the same groups in ordinary methyl pheophorbide a<sup>6</sup> at the same concentration. The

(1) Based on work performed under the auspices of the U. S. Atomic Energy Commission.

(2) P. Diehl and Th. Liepert, *Helv. Chim. Acta*, **47**, 545 (1964).

(3) A. Abragam, "The Principles of Nuclear Magnetism," The Clarendon Press, Oxford, 1961, p. 313 ff.

(4) J. J. Katz, 39th Annual Priestley Lectures, The Pennsylvania State University, University Park, Pa., 1965.

(5) The d.m.r. spectra reported here were recorded at a magnetic field of about 23.4 kgauss by the use of a slow sweep unit with a Varian V-4311 n.m.r. spectrometer, operated in the high-resolution mode. A conventional side-band technique (with high modulation indexes) was used for the calibrations. The samples were contained in standard 5-mm. tubes.

(6) G. L. Closs, J. J. Katz, F. C. Pennington, M. R. Thomas, and H. H. Strain, *J. Am. Chem. Soc.*, **85**, 3809 (1963).

largest difference between the two sets of chemical shift data is 0.05 p.p.m., in agreement with Diehl and Liepert's observations on small molecules.

The situation is more complicated in the case of deuteriochlorophyll, for the presence of magnesium and the phytol chain affects the correlation time, and this should make a substantial difference in the d.m.r. spectrum. We have therefore measured the d.m.r. spectrum of chlorophyll *a*-*d*<sub>72</sub> in 50% tetrahydrofuran-chloroform-*d*<sub>1</sub> (v./v.). The natural line width is increased by the phytol chain and the magnesium to the extent that the methyl resonances are no longer fully resolved, but the chemical shift values for the envelope of resonances are directly comparable with the chemical shifts of the ring methyl groups in solutions of monomeric chlorophyll *a*. The phytol deuterium resonances, however, surprisingly exhibit a very considerable upfield shift. The strongest peak in the deuterium phytol resonance (6.95 p.p.m. upfield from CDCl<sub>3</sub>) corresponds to a chemical shift of 0.83 p.p.m. in hydrogen phytol, and is fully 0.63 p.p.m. higher in field than the terminal methyl groups in either ordinary phytol or the phytol of chlorophyll.<sup>7</sup> The minor changes in the chemical shift of the low-field methyl groups rule out the possibility that the change in the deuterium phytol shift is caused by changes in the bulk properties of the solution. Although the d.m.r. shift may arise from differences in the association of the phytol chain in deuteriochlorophyll with the porphyrin ring as compared to the situation in ordinary chlorophyll, and large shifts in proton resonances occur in chlorophyll as a function of aggregation,<sup>6</sup> we prefer at this time to attribute the difference in chemical shift to deuterium isotope effects.

Nucleus-electron interactions and primary isotope effects on local electron density may be important factors in the d.m.r. shifts as in other isotope effects. We believe that differences in electronic properties between bonds to hydrogen and bonds to deuterium may be correlated, not with differences in infrared vibrational frequencies, but with differences in infrared absorption peak intensities.<sup>8</sup> Bonds to hydrogen and corresponding bonds to deuterium may have very different intensities in the infrared.<sup>11</sup> Since the absolute intensity is related to variations of the dipolar moment of a C-H bond by  $|A| = N\pi/3c(\partial\mu/\partial Q)^2$ , the generally smaller values of  $|A|$  for C-D bonds suggest a smaller value of  $(\partial\mu/\partial Q)$ , and a higher value for the electron density near a deuterium atom. Deuterium should thus experience an upfield shift relative to protium, and an adjacent proton should experience an upfield shift also. Since n.m.r. shifts measure only the differences in shielding for different chemical species, the close agreement of the <sup>1</sup>H and <sup>2</sup>H chemical shifts in Table I

(7) The chemical identity of ordinary and deuteriochlorophylls is established by their chromatographic behavior.

(8) Jouve, *et al.*,<sup>9</sup> have shown a good correlation between the absolute intensity of an infrared absorption peak and chemical shifts in proton magnetic resonance. Such a correlation is not surprising in the light of well-recognized relations between infrared band intensities and substituent effects.<sup>10</sup>

(9) P. Jouve, M. Teulier, and G. Levi, *Compt. rend.*, [9] **258**, 2545 (1964).

(10) Cf. T. L. Brown, *J. Phys. Chem.*, **64**, 1798 (1960); D. Hadži in "Infrared Spectroscopy and Molecular Structure," M. Davies, Ed., Elsevier Publishing Co., Amsterdam, 1963, Chapter VII, pp. 249-257.

(11) See, for example, R. M. Adams and J. J. Katz, *J. Opt. Soc. Am.*, **46**, 895 (1956); H. H. Strain, M. R. Thomas, H. L. Crespi, and J. J. Katz, *Biochem. Biophys. Acta*, **52**, 517 (1961).

is not surprising. Although the mechanism is not entirely clear, it appears qualitatively that an integrated isotope effect may suffice to account for the observed differences in the chemical shift of hydrogen and deuterium in the phytol residue.

The solvent dependence of the chlorophyll *a*-*d*<sub>72</sub> d.m.r. spectrum has also been examined, and the line width is found to be highly dependent on the aggregation state of the chlorophyll.<sup>6</sup>

(12) Resident Research Associate, 1963-1965.

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## Reactions of the 2-Halo-3-(2-hydroxyethoxy)cyclohexenes with Potassium *t*-Butoxide in Dimethyl Sulfoxide<sup>1</sup>

Sir:

As part of a program directed toward determining the scope and limitations of reactions of 2-haloallyl compounds with base,<sup>2</sup> we prepared the 2-halo-3-(2-hydroxyethoxy)cyclohexenes **1** and **2** and studied their reactions with potassium *t*-butoxide in dimethyl sulfoxide (DMSO). Our results show that cyclohexenyl halides can undergo reactions with strong base by mechanisms other than those involving cyclohexenes.<sup>3</sup>

Using procedures similar to that described for the preparation of 2-bromoallyloxyethanol,<sup>2a</sup> 2-bromo-3-(2-hydroxyethoxy)cyclohexene (**1**),<sup>4</sup> b.p. 96° (1 mm.), *n*<sup>20</sup><sub>D</sub> 1.5222, and its chloro analog **2**,<sup>4</sup> b.p. 108° (5 mm.), *n*<sup>24</sup><sub>D</sub> 1.4962, were prepared in >50% yield from the corresponding 2,3-dihalocyclohexene<sup>5,6</sup> and sodium ethylene glycolate in ethylene glycol. Treatment of **1** with 2.2 equiv. of 1.23 *M* potassium *t*-butoxide in DMSO at 60° for 6 hr. gave a 71% yield of a mixture of two compounds, **3** and **4**, b.p. 51° (2 mm.), in nearly equal amounts. Similar treatment of **2** gave a 42% yield of a mixture that was 8% **3** and 92% **4**. The components were separated by gas chromatography (20% Carbowax 20M on alkaline firebrick at 162°), and **3**,<sup>4</sup> *n*<sup>24</sup><sub>D</sub> 1.4764, was found to have infrared and n.m.r. spectra that were indistinguishable from those of cyclohex-2-enone ethylene ketal<sup>4</sup> prepared from cyclohex-2-enone<sup>7</sup> and ethylene glycol.<sup>8</sup> Spectral and

(1) (a) Supported by Grant No. GM-10606 from the National Institute of General Medical Sciences, U. S. Public Health Service; (b) abstracted from the Ph.D. Thesis of W. Schear, University of California, Davis, 1965.

(2) (a) A. T. Bottini, F. P. Corson, and E. F. Böttner, *J. Org. Chem.*, **30**, 2988 (1965); (b) A. T. Bottini, J. A. Mullikin, and C. J. Morris, *ibid.*, **29**, 373 (1964); (c) A. T. Bottini and E. F. Böttner, *ibid.*, in press.

(3) See L. K. Montgomery, F. Scardiglia, and J. D. Roberts, *J. Am. Chem. Soc.*, **87**, 1917 (1965).

(4) The experimental and theoretical carbon and hydrogen analyses agreed to within 0.3%, and the infrared and 60-Mc. n.m.r. spectra were compatible with the assigned structure.

(5) J. Sonnenberg and S. Winstein, *J. Org. Chem.*, **27**, 748 (1962).

(6) E. Bergman, *ibid.*, **28**, 2210 (1963).

(7) F. C. Whitmore and G. W. Pedlow, Jr., *J. Am. Chem. Soc.*, **63**, 758 (1941).

(8) For the method used, see R. F. Fischer and C. W. Smith, *J. Org. Chem.*, **25**, 319 (1960). Acid hydrolysis of **3** gave cyclohex-2-enone (2,4-dinitrophenylhydrazone, m.p. 163.5-165.5°) and ethylene glycol (*p*-nitrophenylurethan, m.p. 128-132°). **3** has also been prepared by dehydrohalogenation of the 2-halocyclohexanone ethylene ketals.<sup>9</sup>

(9) H. W. Wanzlich, G. Gollman, and H. Milz, *Chem. Ber.*, **88**, 69 (1955).