

reported compounds. No evidence of sodium retention was obtained for this series of compounds.

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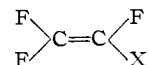
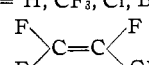
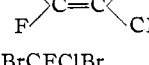
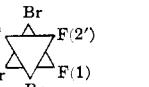
RELATIVE SIGNS OF FLUORINE-19-FLUORINE-19 AND HYDROGEN-1-FLUORINE-19 N.M.R. COUPLING CONSTANTS¹

Sir:

The importance of the relative signs of n.m.r. coupling constants has only recently been realized in the analyses of high resolution n.m.r. spectra. The use of double resonance techniques for the determination of the relative signs of coupling constants is rather more attractive than the previously exploited long and tedious iterative high-resolution approach. In this communication we wish to give the results of some double resonance studies which have given the relative signs of several important types of F^{19} - F^{19} and H^1 - F^{19} coupling constants.

In Table I are summarized results from F^{19} - F^{19} double resonance studies on a number of fluorocarbon

TABLE I
RELATIVE SIGNS OF F^{19} - F^{19} COUPLING CONSTANTS

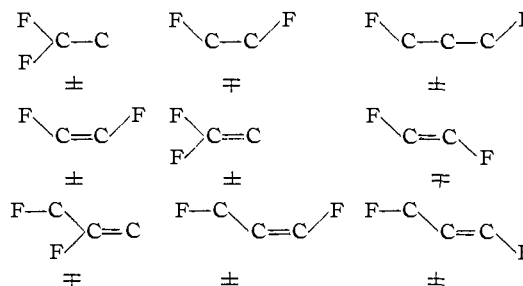
	k_2	Ref.
(1) 	(3) $J_{12} \pm, J_{13} \pm, J_{23} \mp$	^{a, b, c}
(X = H, CF ₃ , Cl, Br, I)		
(1) 	(3) $J_{12} \pm, J_{13} \pm, J_{23} \mp$	^{a, c}
(2) 	(4) $J_{14} \pm, J_{24} \pm, J_{34} \mp$	
CF ₂ BrCFClBr	$J_{12} \mp, J_{12'} \mp, J_{22'} \pm$	
(2, 2') (1)		
CF ₂ ClCFClH	$J_{12} \mp, J_{12'} \mp, J_{22'} \pm$	
(2, 2') (1)		
CF ₂ BrCFBrH	$J_{12} \mp, J_{12'} \mp, J_{22'} \pm$	
(2, 2') (1)		
(2) 	$J_{12} \mp, J_{12'} \mp, J_{22'} \pm$	^{c, d}
CF ₃ CF ₂ CF ₂ Br	$J_{12} \mp, J_{23} \mp, J_{13} \pm$	
(3) (2) (1)		
CF ₃ CF ₂ CF ₂ I	$J_{12} \mp, J_{23} \mp, J_{13} \pm$	
(3) (2) (1)		
CF ₃ CFClCFCl ₂	$J_{12} \mp, J_{23} \mp, J_{13} \pm$	
(3) (2) (1)		
CF ₃ CClCF ₂ Cl	$J_{13} \pm, J_{1'3} \pm, J_{11'} \pm$	
(3) (1, 1')		

^a D. F. Evans, *Mol. Phys.*, **5**, 183 (1962). ^b D. D. Elleman and S. L. Manatt, *J. Chem. Phys.*, **36**, 1945 (1962). ^c D. D. Elleman and S. L. Manatt, presented at Third Conference on Experimental Aspects of N.M.R. Spectroscopy, Mellon Institute, Pittsburgh, Penna., March 2, 1962. ^d S. L. Manatt and D. D. Elleman, *J. Am. Chem. Soc.*, **84**, 1305 (1962).

compounds. Some of these results have been previously reported by us.^{2,3,4} Four different halogen

- (1) Presented in part at the Symposium on High-Resolution N.M.R. Spectroscopy, University of Colorado, Boulder, Colorado, July 3, 1962.
- (2) D. F. Evans, *Mol. Phys.*, **5**, 183 (1962).
- (3) D. D. Elleman and S. L. Manatt, *J. Chem. Phys.*, **36**, 1945 (1962).
- (4) S. L. Manatt and D. D. Elleman, *J. Am. Chem. Soc.*, **84**, 1305 (1962).

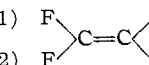
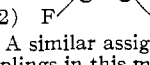
substituted 1,1,2-trifluoroethanes, which due to asymmetry show ABX n.m.r. spin systems,⁵ were studied. It was determined that the vicinal and geminal coupling constants have different signs in the three ethane derivatives studied at room temperature and the one which was frozen into its separate conformers.⁴ From the four halogen substituted fluoropropanes studied it was found that the vicinal coupling has a sign different from the geminal and 1,3-couplings. From the data presented above the relative sign relationships between the most commonly encountered F^{19} - F^{19} n.m.r. coupling constants can be tabulated



The one assumption involved in this correlation is that the $\begin{matrix} F \\ | \\ C-C \end{matrix}$ coupling constant has the same sign as that of the $\begin{matrix} F \\ | \\ C=C \end{matrix}$ coupling. This may be a reasonable assumption on grounds that these coupling constants are all fairly large in magnitude (ranging from about 28-224 c.p.s.) and that the contributions to these two types of geminal couplings may be similar. The fact that the $F-C-C-F$ coupling has the same sign as that of the $F-C-CF=C$ coupling with this assumption is interesting and suggests that the contributions to these two types of vicinal coupling may also be similar. Appropriate compounds to test this assumption are in preparation.

Table II summarizes some results for H^1 - F^{19} couplings obtained either by H^1 - H^1 or F^{19} - F^{19} decoupling.

TABLE II
RELATIVE SIGNS OF H^1 - F^{19} COUPLING CONSTANTS

CH ₃ CH ₂ F ^a	} $J \begin{matrix} F \\ \\ C \\ \\ H \end{matrix} \pm, J \begin{matrix} F & & H \\ & \diagdown & / \\ & C-C & \end{matrix} \pm$
CH ₃ CHF ₂	
CF ₃ CFH ₂	
CF ₃ CF ₂ H	
CF ₂ BrCFBrH	
CF ₃ CF ₂ CF ₂ H	
CF ₂ HCF ₂ CFH ₂	
(1) 	(3) ^{b, c} $J_{14} \pm, J_{24} \mp, J_{34} \pm$
(2) 	(4)

^a A similar assignment of the relative signs of the H^1 - F^{19} couplings in this molecule also has been obtained from high-resolution analyses at two frequencies by S. L. Stafford and J. D. Baldeschwieler, *J. Am. Chem. Soc.*, **83**, 4473 (1961). ^b D. F. Evans, *Mol. Phys.*, **5**, 183 (1962). ^c D. D. Elleman and S. L. Manatt, presented at Third Conference on Experimental Aspects of N.M.R. Spectroscopy, Mellon Institute, Pittsburgh, Penn., March 2, 1962.

It was found that the $\begin{matrix} F \\ | \\ C \\ | \\ H \end{matrix}$ and $\begin{matrix} F & & H \\ & \diagdown & / \\ & C-C & \end{matrix}$ couplings are of the same sign in every case regardless of the substituents present.

Banwell and Sheppard recently have reported the relative signs between all the coupling constants in vinyl fluoride⁶ and Beaudet and Baldeschwieler⁷ have

- (5) See for example P. M. Nair and J. D. Roberts, *ibid.*, **79**, 4565 (1957).
- (6) C. N. Banwell and N. Sheppard, *Proc. Roy. Soc. (London)*, **A263**, 136 (1961).
- (7) R. A. Beaudet and J. D. Baldeschwieler, *J. Mol. Spectroscopy*, **9**, 30 (1962); private communication from R. A. Beaudet.

tentatively assigned the relative signs of coupling constants in *cis* and *trans* 1-fluoropropene. These studies^{6,7} based on high-resolution analyses at several frequencies then establish the relation between the various types of H^1-F^{19} and H^1-H^1 couplings. In both these studies^{6,7} it was noted that the *cis* $F-C=C-H$ coupling, which is a rather small coupling, has the same relative sign as the $F-C=C$ coupling and thus a sign reversal takes place for the *cis* coupling on going from trifluoroethylene to derivatives with one fluorine on the double bond.

Subsequent publications from our laboratories will contain the details and discussion of the results of the double resonance studies reported here.

NOTE ADDED IN PROOF.—The assumption made above that the relative signs of the $C-C\langle\begin{smallmatrix} F \\ F \end{smallmatrix}\rangle$ and $C=C\langle\begin{smallmatrix} F \\ F \end{smallmatrix}\rangle$ couplings are the same has now been verified. From double resonance studies the relative signs of the

coupling constants in $\begin{matrix} Cl & & F(2) \\ & \diagdown & / \\ & C=C & \\ & / & \diagdown \\ (1)F & & CFCICFCl_2 \\ & & (3) \quad (4) \end{matrix}$ have been

found to be J_{12}^\mp , J_{34}^\mp , J_{23}^\mp , J_{13}^\mp , J_{14}^\pm and J_{24}^\pm .

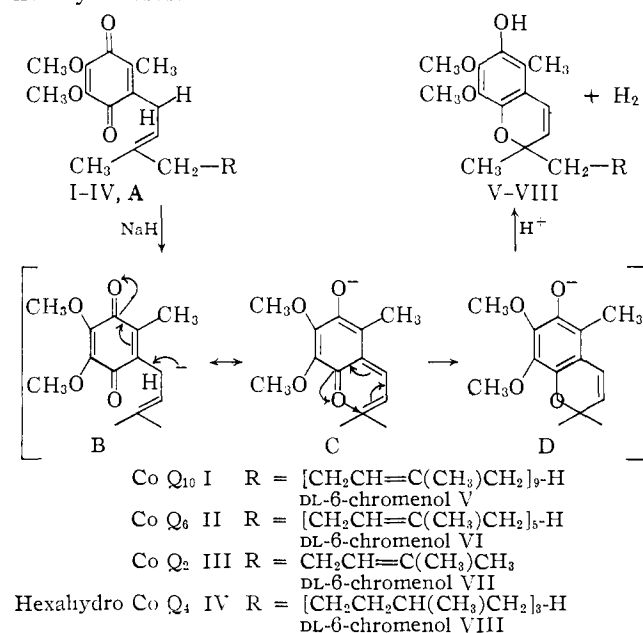
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COENZYME Q. XXXVIII. CYCLIZATION OF COENZYME Q TO THE CORRESPONDING CHROMENOLS WITH SODIUM HYDRIDE

Sir:

Quinones of the coenzyme Q group (I–IV) have been converted to the corresponding DL-chromenols (V–VIII) in good yield by a novel procedure, cyclization with sodium hydride. This reaction is of general applicability for preparing DL-chromenols from the coenzyme Q group and for the first time makes these compounds readily available for biological research. Chromenol VII is new, and this reaction will facilitate new syntheses.



The isolation of the 6-chromenol of coenzyme Q₁₀ (ubichromenol-50) (V) from human kidney has been reported.¹ Artfactual conversion of coenzyme Q₁₀ (ubiquinone-50) (I) during actual and simulated isolation procedures, by saponification of animal tissues^{2,3} and upon column chromatography over alumina,⁴⁻⁷ has been disclosed. Study³ of the isolation procedure indicated that part of ubichromenol-50 is artifactual, but part may be of natural origin. Although there are other reports of analytical data on ubichromenol in tissues or natural materials, unambiguous proof for the natural occurrence of ubichromenol-50 is not yet available.

Reports on the prevention⁸ of the resorption-gestation syndrome in rats by the DL-6-chromenol from coenzyme Q₁₀ (V), and the maintenance of motility⁹ of chicken sperm by the DL-6-chromenol from hexahydrocoenzyme Q₄ (VIII), gives additional importance to the study of the chromenols.

We^{6,8} reported preparation of the chromenols V and VIII from coenzyme Q₁₀ and hexahydrocoenzyme Q₄ by conversion on columns of basic alumina; the products were eluted with methanol-ether and purified by chromatography on Florisil or silica gel. The yields were low, 13–38%, and the starting material was hardly recoverable. A new method for the conversion of coenzyme Q to the chromenols has been sought. McHale and Green¹⁰ have just reported that ubiquinone-30 is converted into the corresponding ubichromenol in refluxing pyridine solution.

We have found that coenzyme Q may be converted to chromenols in good yields, 45–90%,¹¹ by reaction of the quinones with sodium hydride. The quinone was stirred with excess sodium hydride (5.0 molecular equivalents of a 50% sodium hydride dispersion in mineral oil obtained from Metal Hydrides, Incorporated) in refluxing, dry benzene for two hours. Following acidification of the cooled reaction mixture with dilute acetic acid, the benzene layer yielded a residue which was composed primarily of the DL-chromenol, unreacted quinone and mineral oil. Column chromatography on silica gel or Florisil using ether-iso-octane eluents provided purification of the chromenol and recovery of the quinone. Coenzymes Q₁₀ (I), Q₆ (II), Q₂ (III) and hexahydrocoenzyme Q₄ (IV) gave the corresponding DL-chromenols: V (*Anal. Found*: C, 81.82; H, 10.80.), VI (*Anal. Found*: C, 78.87; H, 9.64), VII (*Anal. Found*: C, 71.51; H, 8.21) and VIII (*Anal. Found*: C, 75.64; H, 10.63), respectively. Ultraviolet absorption data are given in Table I. N.m.r. data⁶ were consistent with the chromenol structures, V–VIII.

The mechanism of this reaction appears to be a base catalyzed cyclization, presumably similar to that⁴ for the cyclization of coenzyme Q₁₀ over basic alumina.

(1) D. L. Laidman, R. A. Morton, J. Y. F. Paterson and J. F. Pennock, *Biochem. J.*, **74**, 541 (1960).

(2) H. H. Draper and A. S. Scallany, *Biochem. Biophys. Res. Comm.*, **2**, 307 (1960).

(3) F. W. Hemming, D. L. Laidman, R. A. Morton, and J. F. Pennock, *ibid.*, **4**, 393 (1961).

(4) J. Links, *Biochim. Biophys. Acta*, **38**, 193 (1960).

(5) J. Green, E. E. Edwin, A. T. Diplock and D. McHale, *Biochem. Biophys. Res. Comm.*, **2**, 269 (1960).

(6) C. H. Shunk, F. R. Koniuszy, E. L. Wong, N. R. Trenner, B. H. Arison and K. Folkers, *ibid.*, **3**, 228 (1960).

(7) F. W. Hemming, R. A. Morton and J. F. Pennock, *Biochem. J.*, **80**, 445 (1961).

(8) B. C. Johnson, Q. Crider, C. H. Shunk, B. O. Linn, E. L. Wong, and K. Folkers, *Biochem. Biophys. Res. Comm.*, **5**, 309 (1961).

(9) A. C. Page, Jr., M. C. Smith, P. H. Gale, D. Polin and K. Folkers, *ibid.*, **6**, 141 (1961).

(10) D. McHale and J. Green, *Chemistry and Industry*, 1867 (October 27, 1962).

(11) Yields based upon amount of coenzyme Q consumed. Amount of chromenol obtained was 45–60%. Quinone is recovered.