An Analysis of Diastereotopic Protons[1] in the 2-Halodimethylaminomethylferrocenes[2]

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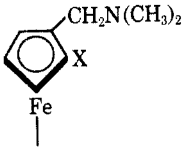
The two factors, conformational preference and intrinsic asymmetry, that contribute to geminal group magnetic nonequivalence in asymmetric compounds have been the topic of much conjecture. Synthesis of the 2-halodimethylaminomethylferrocenes gave us a series of compounds that should in fact minimize the alteration of electronic factors and maximize the relative importance of conformational preferences brought about by steric interactions. The results suggest that there is a steric interaction, but not in the "hard-core" sense of the word. The data do, however, suggest that there is a significant contact effect and a negligible anisotropic effect due to the halogen.

Magnetic nonequivalence has been observed when methylene or geminal dimethyl protons are proximate to a center of asymmetry or to some element of dissymmetry;[4] these elements can be as much as seven bonds removed from the perturbing groups.[5] The two factors presumably responsible for the diastereotopic[1] relationships of geminal groups are conformational (steric) effects[6] and electronic perturbations arising from an "intrinsic" asymmetry of the molecule.[7] Although the data recorded in this paper cannot be rationalized on the basis of either an asymmetry or a steric effect, certain trends in the data suggest that other effects may be operating. New approaches to the interpretation of the magnetic nonequivalence of diastereotopic protons are certainly desirable. Recently intramolecular coordination was proposed as one means of promoting strong magnetic nonequivalence in diastereotopic groups.[8] We propose in the present paper that in suitable systems a contact interaction may also be of significant importance in the analysis of magnetic nonequivalence.

Since the difference in the chemical shift of the two methylene protons in certain 1,2-disubstituted ferrocenes previously reported[9] were all about an order of magnitude greater than in most other systems exhibiting this behavior,[10] it was anticipated that the chemical shift of the protons of the 2-substituted dimethylaminomethylferrocene system would be most sensitive to changes in the substituent X. The model compounds selected for this study were the 2-halodimethylaminomethylferrocenes. This series should in fact decrease the importance of electronic factors while making conformation factors much easier to analyze than those of our earlier systems.[9]



Ia, X = Cl
b, X = Br
c, X = I

The results of this study indicate that a contact interaction between a methylene proton and the respective halogen may be operating in these systems. Furthermore, some of our observations have led us to suggest a revision of an nmr method of distinguishing certain 1,2- from 1,3-disubstituted ferrocenes.[11]

Experimental Section

All spectra were recorded on a Varian A 56-60 spectrometer at 44° with internal TMS standard. Each solution was approximately 10% 2-halodimethylaminomethylferrocene by volume.

The 2-halodimethylaminomethylferrocenes were prepared by the methods of Rockett, *et al.*[12] and Hauser, *et al.*[13] All physical properties noted were in accord with their reported values.

In addition we would like to report the following preparation of 2-iododimethylaminomethylferrocene.

Preparation of 2-Iododimethylaminomethylferrocene (Ic).—Dimethylaminomethylferrocene (2.43 g, 10 mmol) in 20 ml dry ether was treated with *n*-butyllithium in hexane (25 mmol).[14] After stirring for 1 hr., the reaction mixture was cooled to Dry Ice–acetone temperature and treated with methylene iodide. The resulting solution was stirred for 0.25 hr and then hydrolyzed with water. The ethereal layer was separated immediately and placed without concentrating on an alumina chromatography column. Rapid elution with petroleum ether–benzene mixture (50:50) produced a solid band which was cut into 250-ml fractions. Ir and nmr spectra of the first two fractions (0.125 g, 3.3%) proved to be identical with those of an authentic sample of iodamine, Ic. The low crude yield and extreme difficulty of purification of the product from this procedure prompts us to recommend use of the boronic acid route.[12]

Results

Appropriate nmr data of the 2-halodimethylaminomethylferrocenes are summarized in Tables I and II, chemical shifts being reported in cycles per second downfield from an internal tetramethylsilane standard.

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[1] K. Mislow and M. Raban in "Topics in Stereochemistry," Vol. I, N. L. Allinger and E. L. Eliel, Ed., John Wiley & Sons, Inc., New York, N. Y., 1967, pp 7, 8.

[2] Presented in part at the 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 1968, Abstracts M, paper 106.

[3] NASA fellow, Southern Illinois University.

[4] For a recent review, *cf.* M. Martin and G. J. Martin, *Bull. Soc. Chim. Fr.*, 2117 (1966).

[5] G. M. Whitesides, D. Holtz, and J. D. Roberts, *J. Amer. Chem. Soc.*, **86**, 2628 (1964).

[6] G. M. Whitesides, F. Kaplan, K. Nagarajan, and J. D. Roberts, *Proc. Natl. Acad. Sci. U. S.*, **48**, 1113 (1962).

[7] H. S. Gutowsky, G. G. Belford, and P. E. McMahon, *J. Chem. Phys.*, **36**, 3353 (1962); H. S. Gutowsky, *ibid.*, **37**, 2196 (1962).

[8] E. F. Kiefer, W. L. Waters and D. A. Carlson, *J. Amer. Chem. Soc.*, **90**, 5127 (1968); E. F. Kiefer and W. Gericke, *ibid.*, **90**, 5131 (1968).

[9] P. Smith, J. J. McLeskey, III, and D. W. Slocum, *J. Org. Chem.*, **30**, 4356 (1965).

[10] Two examples of systems involving a methylene AB quartet having extremely large differences in chemical shift have been published; *cf.* A. H. Lewin, J. Kipowitz, and T. Cohen, *Tetrahedron Lett.*, 1241 (1965), and P. L. Southwick, J. A. Fitzgerald, and G. E. Milliman, *ibid.*, 1247 (1965).

[11] G. R. Knox, P. L. Pauson, and G. V. D. Tiers, *Chem. Ind.* (London) 1046 (1959).

[12] G. Marr, R. E. Moore, and B. W. Rockett, *J. Organomet. Chem.*, **7**, P11 (1967); G. Marr, R. E. Moore and B. W. Rockett, *J. Chem. Soc.* (C), 24 (1968).

[13] R. L. Gay, T. F. Crimmins, and C. R. Hauser, *Chem. Ind.* (London), 1635 (1966).

[14] D. W. Slocum, B. W. Rockett, and C. R. Hauser, *ibid.*, 1831 (1964); D. W. Slocum, B. W. Rockett, and C. R. Hauser, *J. Amer. Chem. Soc.*, **87**, 1241 (1965).

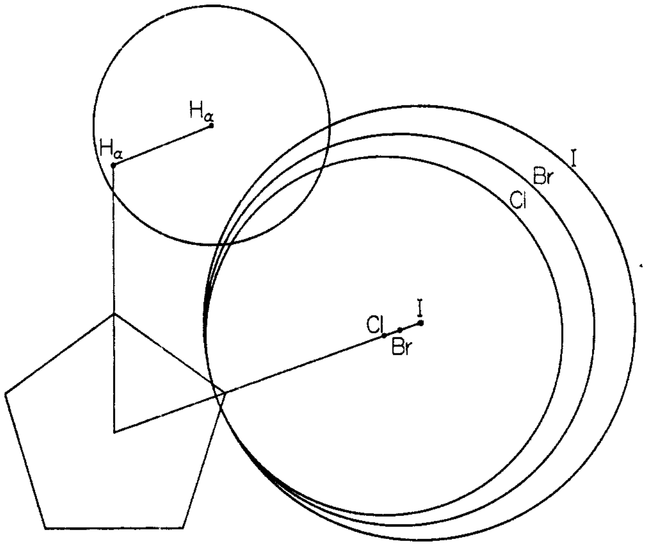

Figure 1 was constructed by superimposing the van der Waals radii of the halogen atoms (E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart, and Winston, New York, N. Y., 1959, p 51) on the respective carbon–halogen bond distances. The projection involves placing all bonds in the same plane as that of the cyclopentadienyl ring. This should not be the most stable conformation (*cf.* Discussion) but does demonstrate clearly the increasing "hard core" steric interaction through the series.

In Table II protons 1 and 2 refer to the methylene protons and ν_1 and ν_2, respectively, are their calculated chemical shifts,[15] $\delta_{1,2}$ the difference in the 1,2 proton chemical shifts, and $\bar{\nu}_{1,2}$ the chemical shift of the central position in the AB pattern. For reasons outlined in the discussion section, the H_1 signal was assigned to the downfield single-proton absorption and the H_2 signal to that upfield.

TABLE I

DIFFERENCES IN CHEMICAL SHIFT[a] OF THE METHYLENE PROTONS OF THE 2-HALODIMETHYLAMINOMETHYLFERROCENES (I′ a–c) AS A FUNCTION OF SOLVENT AND SUBSTITUENT

	Substituent		
Solvent	Cl	Br	I
CCl_4	s[b]	s[b]	s[b]
$CDCl_3$	9.6	3.9	s[b]
C_6H_6	14.2	12.3	8.9
$C_6H_5CH_3$	12.9	10.8	7.2
CH_3CN	11.5	8.9	s[b]
DMSO-d_6	s[b]	s[b]	s[b]

[a] In cycles per second. [b] s refers to singlet.

When a measurable value for the difference in the chemical shift could be observed, the difference was found to decrease without regard to solvent as the van der Waals radius of the 2 substituent increased (Table I). The chemical shift values of the H_1 (*exo*) proton moved to higher field strengths as the van der Waals radius of the 2 substituent increased (Table II). The chemical shift values of the H_2 (*endo*) proton likewise moved to higher field strengths as the van der Waals radius of the 2 substituent increased (Table II), but to a much less pronounced extent. Likewise, it was found that the C_5H_5 signal shifted progressively upfield in the 2-halo series.

Attempts to study the spectra of these compounds at higher temperatures led to apparent decomposition.

Discussion

The simplest treatment of the 2-halodimethylaminomethylferrocene system suggested that an increase in the size of the halogen in the 2 position would cause the methylene protons to experience a progressively higher conformational energy barrier to passage by the respective halogen. This might well be reflected in a slowing of conformational interconversion such that on an nmr time scale the difference in magnetic environment of H_1 and H_2 would become progressively greater, this being reflected in a greater δ_{AB}. Figure 1 illustrates an idealization of the increasing steric interaction through the halogen series (Cl, Br, I) of a methylene proton and halogen. Such a model may be unreliable since it is thought that iodine is much "softer" than the other halogens so that it is difficult to assign to it a suitable van der Waals radius. Likewise the bending force constants of the carbon–halogen bond decrease through the series, Cl, Br, I,[16] indicating that the bulkier halogen should be the easier to bend out of the path of the interconverting methylene protons. Since the difference in chemical shift observed for these systems in all solvents where AB patterns were observed progressively decreased as the halogen became larger, the interference model cannot be invoked unless it is assumed that the "softness" or bending factors actually reverse the order of size in these systems. As a matter of fact, a recent related nmr publication[17] suggests that size decreases Br > Cl ∼ I, at least in the instance of the molecules studies. Bending force constants are much smaller in magnitude than stretching force constants and are of the order of conformational change; hence the effective van der Waals radii in our system, from the point of view of the conformational change of the methylene group, may be quite different from that illustrated in Figure 1.[18]

The chemical shift data are contrary to those expected if the methylene protons are experiencing an anisotropic influence of the halogen. If the anisotropic affect were the dominating factor, the chemical shift values of the methylene protons would be expected to progress to lower fields as the halogen was varied from Cl to Br to I. That the opposite order is observed is strongly indicative that some entirely different effect is operating.

A downfield shift occurring in the order Cl > Br > I parallels that predicted on the basis of electronegativity concepts. The use of such an argument is, however, diminished by the number of bonds through which this effect must be transmitted. For instance, in the σ framework systems illustrated by the ethylhalogermanes $[Et_{4-n}GeX_n]$ inductive effects accounted for 3–10% of the methylene shifts and were only marginal for the methyl shifts; these interpretations were corrob-

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(15) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance", McGraw-Hill Book Co., Inc., New York, N. Y., 1959, Chapter 6.

(16) J. W. Russell, C. D. Needham, and J. Overend, *J. Chem. Phys.*, **45**, 3383 (1966).

(17) G. M. Whitesides, J. P. Sevenair, and R. W. Goetz, *J. Amer. Chem. Soc.*, **89**, 1135 (1967).

(18) Rigorous analysis of this system would involve estimations from the contributions of the dihedral angles formed by each C–H bond, and the ring plane, and each N–C bond. Inversion at nitrogen must also be considered. Such analysis would be exceedingly difficult. The following arguments are therefore only qualitative at best. Recent theoretical treatments of the "ortho effect" have determined that it is primarily electrical in nature. *Cf.* M. Charton, *ibid.*, **91**, 615 (1969).

TABLE II

CHEMICAL SHIFT VALUES FOR METHYLENE PROTONS H_1 AND H_2[a] AS A FUNCTION OF SOLVENT AND SUBSTITUENT

	Solvent					
Substituent (X)	CCl_4	$CDCl_3$	C_6H_6	$C_6H_5CH_3$	CH_3CN	DMSO-d_6
		endo proton values, ν_2				
Cl		204.2	198.0	197.8	201.7	
Br		203.6	195.9	197.7	201.8	
I		200.8	193.7	193.4	197.3	
		exo proton values, ν_1				
Cl		213.8	212.2	210.6	213.2	
Br		207.4	208.2	208.5	210.6	
I		200.8	202.7	200.6	197.3	
	Central position of $\bar{\nu}_{1,2}$					
Cl	206.8	209.0	205.1	204.2	207.5	203.5
Br	204.5	205.5	202.0	203.1	206.2	202.0
I	195.4	200.8	198.2	197.0	197.3	197.5

[a] Cycles per second downfield from TMS.

orated by ^{13}C coupling measurements.[19] As such the electronegativity effect in the proton spectrum probably accounts for only a very slight shift. Hence it follows that electronegativity plays only a minor role in this system. It should also be pointed out that each methylene proton should experience to a first approximation an equal shift due to electronegativity. An effect that differentiates the two protons must actually be operating, however.

Since each proton appears to behave somewhat independently of the other, it seemed logical to explore some other type of interaction. Included in the study of the halogen-substituted ethylgermanes[19] was an anomalous upfield shift which was attributed to a contact of the methyl group protons with the induced electronic circulation of the halogen atom. This type of effect could also operate in the 2-halo dimethylaminomethylferrocene system since only rotation about the C–C bond containing the methylene hydrogens is of major importance in an argument of this nature.

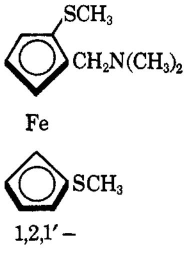
Analysis of each methylene proton separately should serve to illustrate the relative importance of a contact effect on the individual proton. Seemingly, the most stable conformation in this system would place the dimethylaminomethyl group away from the halogen atom which would allow the two methylene protons to flank the halogen atom above and below.[20] That proton which flanks the halogen above the ferrocene system is termed *exo* while that extending down towards the iron atom is termed *endo*. There may be slight conformational variation within the series to bring about the actual "most stable contact" conformation. Since it is thought that a proton in the vicinity of a metal atom experiences an upfield shift,[21] the upfield portion of the AB pattern may be assigned to that methylene proton which is time averaged in the *endo* position. The relatively small but regular variations through the series in the chemical shift data of the H_2 proton in any one solvent indicate that there is minor contact between the halogen substituent and the *endo* proton.

The *exo* proton (that ascribed to the ν_1 data, Table II) is found to shift appreciably with a change in halogen. The shifts to higher field follow the change in the halogen from Cl to Br to I. Figure 1 can be taken to illustrate the approximate position of closest approach for the *exo*- methylene hydrogen and the various halogens. The direction and magnitude of the chemical shift changes indicate that the major effect imposed on the *exo* proton is due to a contact interaction of the groups.[19]

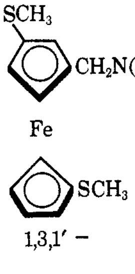
The above discussion has served to illustrate the relative importance of the contact interaction with respect to the diamagnetic anisotropic shift on the individual methylene protons. The principal effect imposed on the H_1 proton is a shift to higher field with negligible contribution from anisotropy. On the other hand the H_2 proton experiences smaller effects from either a contact or a magnetic anisotropic contribution from the halogen atom. These results indicate that an electronic influence on nonequivalent methylene protons can be imposed if the electronic nature of the substituent is understood.[18]

The hypothesis that a contact interaction was operating between the methylene protons and halogen suggested that a similar effect might be operating between the C_5H_5 ring protons and halogen. It is notable that an upfield shift of the C_5H_5 protons occurs through the same series. Compounds are in preparation which will test this idea in detail.

One interesting side light emerged from our studies. It has previously been proposed[11] for the particular case of the 1,2,1′- and 1,3,1′-dithiomethyldimethyl-



1,2,1′-



1,3,1′-

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[19] K. M. Mackay and R. Watt, *J. Organometa. Chem.*, **6**, 336 (1966).

[20] A similar analysis of a related system has recently been published: R. E. Lyle and J. J. Thomas, *Tetrahedron Lett.*, 897 (1969). However, see our discussion in ref 18.

[21] Apparently, the assignment of the *endo* proton to the high field signal is controversial. Support for the assignment used in this paper can be found in the chapter by M. L. Maddox, S L. Stafford, and H. D. Kaesz in *Advan. Organometal. Chem.*, **3** (1965), and in the upfield shift of the methyl protons of (*endo*-methylcyclopentadiene)cyclopentadienylcobalt [M. L. H. Green, L. Pratt, and G. Wilkinson, *J. Chem. Soc.*, 3753 (1959)]. However, as a referee has pointed out, the molecular anisotropy studies of L. N. Mulay and M. E. Fox [*J. Chem. Phys.*, **38**, 760 (1963)] suggest that such *endo* protons in ferrocenes should be deshielded. Other authors have made assignments based on the observations of Mulay and Fox [*cf.* M. Rosenblum and F. W. Abbate, *J. Amer. Chem. Soc.*, **88**, 4178 (1966)]. There seems reason to believe that the statement, protons in the vicinity of a metal atom experience an upfield shift, requires serious examination and may be system dependent. Compounds are in preparation to test certain aspects of this hypothesis.

aminomethylferrocenes that the 1,2 isomer could be distinguished from the 1,3 isomer by the presence of a methylene AB quartet in the nmr spectrum of the 1,2 isomer. This method appears to be solvent dependent, since in the present study the 2-iodo compound gave singlets in both DMSO-d_6 and acetonitrile. More importantly each of those 2-haloferrocene derivatives exhibited methylene singlets in CCl_4, the solvent utilized in the original study.

Registry No.—Ia, 12085-94-8; Ib, 12110-60-0; Ic, 12302-05-5.

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Oxidation of Substituted Styrenes by Thallium Triacetate[1]

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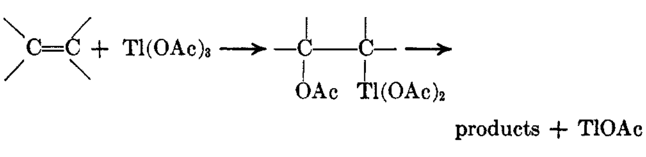
The products and kinetics of the oxidation of six ring-substituted styrenes by thallium triacetate in acetic acid have been determined. Two products, 1-aryl-1,2-ethanediol diacetate and 2-aryl-1,1-ethanediol diacetate, are obtained, with the latter predominating as the electron-donating ability of the ring substituent increases. A correlation of the logarithm of the product ratio with Brown σ^+ values has been found with $\rho^+ = -1.7$. 1-Deuteriostyrene yields 1-deuterio-1-phenyl-1,2-ethanediol diacetate and 1-deuterio-2-phenyl-1,1-ethanediol diacetate. The rate of oxythallation of styrenes is second order, first order in each reactant. A Hammett-type correlation with Brown σ^+ values has been established with $\rho^+ = -2.2$. The activation parameters $\Delta H^{\ddagger} =$ 7.9 kcal/mol and $\Delta S^{\ddagger} = -41$ cal/deg for the reaction of *p*-methylstyrene have been evaluated from rate data at 19.7, 50.1, and 75.0°. The activated complex for oxythallation has approximately the same carbonium ion character as for oxymercuration. The effect of styrene structure on product distribution suggests that the decomposition of an oxythallated adduct proceeds *via* a carbonium ion intermediate resulting from loss of thallium(I).

In a limited comparative product study, Kabbe[2] found that the oxidative properties of thallium triacetate toward some styrenes are between those of mercuric acetate and lead tetraacetate. The products of the reaction of styrene with thallium triacetate in acetic acid are 2-phenyl-1,1-ethanediol diacetate (8.5% yield) and 1-phenyl-1,2-ethanediol diacetate (71% yield). Only 2-(*p*-methoxyphenyl)-1,1-ethanediol diacetate was reported for the reaction with *p*-methoxystyrene. The products obtained have been rationalized as being derived from an olefin–metal salt adduct which may then decompose under reaction conditions *via* carbonium ion intermediates. The metal has gained two electrons in the process and is therefore reduced.



The first step has analogy in the well-known oxymercuration reaction. While the mercuric acetate–olefin adducts can be obtained easily,[3] only two thallium triacetate–olefin adducts have been isolated and characterized.[2,4]

No quantitative information exists on the rates of oxythallation of olefins by $Tl(OAc)_3$ in acetic acid. Therefore, the exact nature of this process and its possible similarity to oxymercuration of olefin by $HgOAc_2$ has yet to be determined. However, the kinetics of oxymercuration[5] by Hg^{2+} and oxythallation[6] by Tl^{3+} have been determined in aqueous perchloric acid.

There are no systematic studies of a series of related olefins which would provide quantitative information about the postulated solvolytic decomposition of oxythallated adducts compared with oxymercurated adducts. The solvolytic stability of carbon–metal bonds decreases in the order Hg > Tl > Pb. The likelihood of isolating oxythallated adducts and being able to determine their reactivity makes these compounds invaluable models for elucidating the parameters controlling lead tetraacetate oxidations.[7,8]

Results

Product Studies.—A series of substituted styrenes was treated with thallium triacetate in anhydrous acetic acid at 75°. Thallium triacetate was prepared and used *in situ* by the addition of thallic oxide to anhydrous acetic acid containing about twice the amount of acetic anhydride needed to remove the water produced in the formation of the thallium triacetate.[9,10] To this solution the styrene was added

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[1] The authors gratefully acknowledge Grant GP 3873 from the National Science Foundation in support of this work.

[2] H. J. Kabbe, *Ann.*, **656**, 204 (1962).

[3] J. Chatt, *Chem. Rev.*, **48**, 7 (1951).

[4] K. C. Pande and S. Winstein, *Tetrahedron Lett.*, 3393 (1964).

[5] J. Halpern and H. B. Tinker, *J. Amer. Chem. Soc.*, **89**, 6427 (1967).

[6] P. M. Henry, *ibid.*, **87**, 4423 (1965).

[7] A. South, Jr., and R. J. Ouellette, *ibid.*, **90**, 7064 (1968).

[8] R. J. Ouellette, D. Miller, A. South, Jr., and R. D. Robins, *ibid.*, **91**, 971 (1968).

[9] A. South, Jr., Ph.D. Thesis, The Ohio State University, 1966.

[10] South[9] has shown that the reaction of phenylcyclopropane with thallium triacetate prepared *in situ* proceeds to give the same product ratio as the reaction with pure thallium triacetate. Therefore, it was assumed that the reaction of styrene with thallium triacetate prepared *in situ* proceeds in a manner identical with the reaction of styrene with pure thallium triacetate which was employed in the kinetic studies.