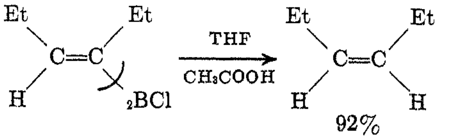
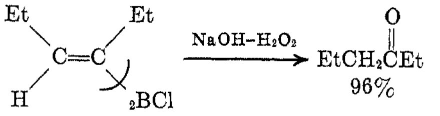
hydrofuran to give stereochemically pure olefins (eq 5 and 6). Oxidation of dialkenylchloroboranes with alkaline hydrogen peroxide gives the corresponding carbonyl compounds (eq 7 and 8).

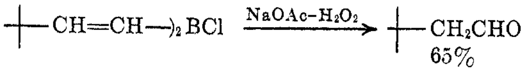


(5)

$$n\text{-}C_4H_9CH{=}CH{-})_2BCl \xrightarrow[CH_3COOH]{THF} n\text{-}C_4H_9CH{=}CH_2 \quad 90\% \tag{6}$$



(7)

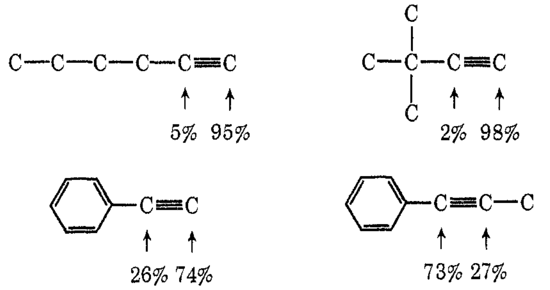


(8)

The directive effect in the monohydroboration of representative alkynes with $BH_2Cl \cdot OEt_2$ was examined. Analysis of the hydroboration mixture for residual alkyne and hydride established that quantitative conversion to the dialkenylchloroborane was achieved. The reaction mixture was then oxidized and the resulting carbonyl products were reduced to the alcohols with alkaline sodium borohydride. The alcohols were analyzed by gc. In the case of terminal alkynes, the amount of the internal alcohols found corresponds to the fraction of boron in the internal position. Since the formation of dialkenylchloroborane was quantitative, the remainder of the boron must have gone to the terminal position. (Oxidation of terminal vinylboranes to aldehydes in quantitative yield is more difficult.) The results are presented in Chart I. The results reveal that the directive effect in the hydroboration of terminal acetylenes with $BH_2Cl \cdot OEt_2$ is less than that observed in the hydroboration of olefins with this reagent.[5] However, it is not possible to compare the directive effects achieved with $BH_2Cl \cdot OEt_2$ with those of borane itself, because the latter reagent converts terminal acetylene predominantly to the dihydroboration product.[4,6] The greater control of monohydroboration of acetylenes provided by chloroborane represents a major advantage of this reagent.

CHART I

DISTRIBUTION OF BORON IN THE MONOHYDROBORATION OF ALKYNES WITH $BH_2Cl \cdot OEt_2$



The following experimental procedures for the synthesis and reactions of bis(*cis*-3-hexenyl)chloroborane are representative. To a solution of 100 mmol of 3-hexyne in 15 ml of ethyl ether was added dropwise 50 mmol of BH_2Cl in ethyl ether[1] (37 ml) at 0° and this mixture was stirred under nitrogen for 2 hr. The ether was removed using a water aspirator and the bis(*cis*-3-hexenyl)chloroborane was distilled at 66–68° (0.1 mm). The product, obtained in 88% yield, was characterized by pmr and elemental analysis. In the experiment involving terminal alkynes, the procedure was identical except that 140 mmol of alkyne (40% excess) was used instead of the stoichiometric amount.

For the synthesis of diene, 50 mmol of bis(*cis*-3-hexenyl)chloroborane (ether removed, but not distilled) was dissolved in 40 ml of tetrahydrofuran. Aqueous sodium hydroxide (3 *M*, 200 mmol) was then added at 0°, followed by dropwise addition of tetrahydrofuran solution of iodine until a slight color of iodine persisted. The excess iodine was destroyed by stirring with excess sodium thiosulfate solution at 25°. The diene was extracted into pentane, washed with dilute thiosulfate solution, dried, and distilled at 62–64° (8 mm). The *cis,trans*-4,5-diethyl-3,5-octadiene, obtained in 83% yield, was characterized by pmr.[3]

To achieve the protonolysis, 4 mmol of bis(*cis*-3-hexenyl)chloroborane was dissolved in 2 ml of tetrahydrofuran and stirred with 2 ml of glacial acetic acid at 25° for 3 hr. The yield of *cis*-3-hexene formed was 92% (gc analysis).

Oxidation of 10 mmol of bis(*cis*-3-hexenyl)chloroborane in 10 ml of ether was carried out by adding, at 0°, 20 mmol of aqueous sodium hydroxide (3 *M*), followed by 2 ml of 30% hydrogen peroxide (dropwise) and 10 ml of ethanol, and stirring at 25° for 30 min. The yield of 3-hexanone was 96% (gc analysis).

The present development provides, for the first time, a general convenient procedure for the synthesis of dialkenylchloroboranes.[7] The ready availability of these compounds by the present simple procedure should facilitate the exploration of the chemistry of this interesting class of compounds. Diene formation, protonolysis, and oxidation are synthetically useful reactions of these compounds, and other interesting applications may be anticipated.

---

(5) H. C. Brown and N. Ravindran, *J. Org. Chem.*, **38**, 182 (1973).

(6) G. Zweifel and H. Arzoumanian, *J. Amer. Chem. Soc.*, **89**, 291 (1967).

(7) The only compound of this class reported to date is the diethenylchloroborane obtained in 35% yield by the fractionation of a mixture of products from the reaction of tetraethenyltin with boron trichloride at 60°: F. E. Brinckman and F. G. A. Stone, *J. Amer. Chem. Soc.*, **82**, 6218 (1960).

(8) Postdoctoral research associate on National Science Foundation Grant No. 27742X.

RICHARD B. WETHERILL LABORATORY
PURDUE UNIVERSITY
LAFAYETTE, INDIANA 47907

HERBERT C. BROWN*
N. RAVINDRAN[8]

RECEIVED JANUARY 12, 1973

Conformational Effect on Observable Magnetic Nonequivalence of Diastereotopic Protons.

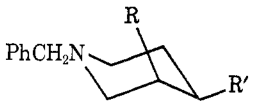
III. 3-Axial Alkyl Effect[1]

Summary: The diastereotopic, benzylic protons of a substituted 1-benzylpiperidine appear as an AB quartet in the nmr spectrum if a 3-alkyl substituent is either axially oriented or is a branched chain and equatorial.

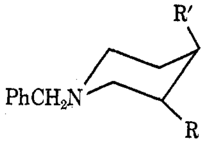
Sir: The diastereotopic relationship of two hydrogens is a necessary but not a sufficient requirement for them to have pmr signals showing different chemical shifts. It has been shown that the diastereotopic protons of the methylene group of an *N*-benzylpiperazine or -piperidine appear to have identical chemical shifts if the lack of symmetry results from a 2-axial group or from a 3 substituent.[1,2] These relationships have permitted a qualitative conformational analysis of substituted *N*-benzyl six-membered heterocycles.[3]

An extension of this investigation has provided another generalization which will be of value in the stereochemical studies of nitrogen heterocycles. A 3-axial but not a 3-equatorial alkyl substituent on a 1-benzylpiperidine causes observable nonequivalence of the benzylic, methylene protons.

A series of 1-benzyl 3,4-disubstituted piperidines (**1**) were prepared by hydrogenation of the corresponding pyridines. The reactions gave primarily one isomeric form of the product shown to be the cis isomer **1**. On the basis of the previous results[2,3] it was anticipated that the products **1** and **2** would show singlets for the methylene protons of the *N*-benzyl group due to undetectable chemical shift differences, and indeed this was the nmr observation made with **2**. The signals for these protons in the cis isomers **1a–c**, however, all appeared as AB quartets of ~10–12-Hz difference in chemical shifts of the diastereotopic hydrogens when measured with a 100-MHz spectrometer.

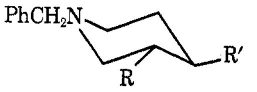


axial (ax)



equatorial (eq)

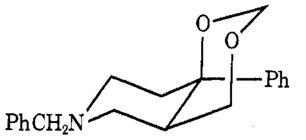
	Δδ
1a, R = CH_3; R′ = CH_2CH_3	12.2
b, R = CH_2CH_3; R′ = CH_3	10.4
c, R = CH_3; R′ = CH_3	10.0



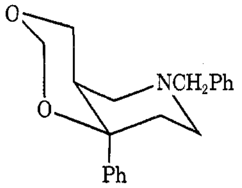
2, R = CH_3; R′ = CH_2CH_3 (s)

A consideration of the relative stability of the two chair conformers of **1** (ax-**1** and eq-**1**) leads to the prediction that the 4-axial substituent of eq-**1** should introduce an unfavorable steric strain, described in terms of $-\Delta G_{\mathrm{CH_3}}°$, of ~1.8 kcal/mol. The 3-axial substituent of ax-**1** should cause a smaller unfavorable steric interaction by ~0.6–0.8 kcal/mol, since one syn axial hydrogen has been replaced by the nitrogen free pair.[4] Thus ax-**1** should be present in excess to the extent of ~70% in the conformational equilibrium of **1**. Since the 4 substituent in any conformation is symmetrically disposed toward the N substituent, it is apparent that it is the 3-axial substituent that is causing the observed nonequivalence of the diastereotopic protons of the methylene of the *N*-benzyl group. The 3-equatorial alkyl groups of 3-methyl- (**7a**),[5] 3-ethyl- (**7b**), and *trans*-3-methyl-4-ethyl-1-benzylpiperidine (**2a**) led to singlets for the benzylic methylene protons. That the 3-axial alkyl group produces a *detectable* magnetic anisotropic effect on the diastereotropic protons of the N substituent should have been expected in view of the recent observations of the anomalous 3-axial substituent effect on the optical rotatory dispersion of cyclic six-membered-ring ketone.[6] Both of these experimental observations result from the close steric proximity of a 3-axial substituent to the tercovalent ring atom at position 1.

The application of this observation can be illustrated by providing confirmation for the assignment based on long range coupling made by Casy and coworkers[7] of the "O inside" conformation (**4**) rather than the "O outside" form (**5**) for the product of the Prins reaction with 1-benzyl-4-phenyl-1,2,3,6-tetrahydropyridine. The product gave a singlet for the methylene protons of the 1-benzyl group requiring that there be no axial 3 substituent such as that present in **5**.

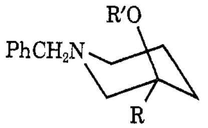


4



5

A 3-axial hydroxyl or acetoxyl group did not lead to an observable AB quartet for the diastereotopic benzylmethylene in three 1-benzyl 3,3-disubstituted piperidines (**6a–c**). The AB quartet observed for 1-benzyl-3-acetoxy-3-ethylpiperidine (**6d**) may result from an



	Δδ
6a, R = C_2H_5; R′ = H	s
b, R = Ph; R′ = H	s
c, R = Ph; R′ = Ac	s
d, R = C_2H_5; R′ = H	7.2

effect of the ethyl group, for it was found that, unlike an equatorial 3-methyl group (**7a**), a larger substituent such as a 3-benzyl (**7c**), isopropyl (**7d**), or *tert*-butyl (**7e**) group in the equatorial conformation of 1-benzylpiperidine gave AB quartets for the benzylic methylene protons in the pmr spectra. A consideration of the relative stabilities of the rotomers about the bond attaching these groups to the 3 position shows that the

---

[1] For previous papers in this series, see (a) R. E. Lyle and J. J. Thomas, *Tetrahedron Lett.*, 897 (1969); (b) R. E. Lyle, J. J. Thomas, and D. A. Walsh, in "Conformational Analysis," G. Chiurdoglu, Ed., Academic Press, New York, N.Y., 1971, pp 157–164.

[2] (a) R. K. Hill and T. H. Chan, *Tetrahedron*, **21**, 2013 (1965); (b) Y. L. Chow and C. J. Colon, *Can. J. Chem.*, **5**, 2559 (1967).

[3] L. N. Pridgen, Ph.D. Thesis, University of New Hampshire, 1972.

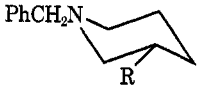
[4] P. J. Brignell, K. Brown, and A. R. Katritzky, *J. Chem. Soc. B*, 1462 (1968); F. G. Ridell, *Quart. Rev.*, **21**, 364 (1967).

[5] Y. L. Chow, S. Black, J. E. Blier, and M. M. Tracy, *Can. J. Chem.*, **48**, 2134 (1970).

[6] (a) Y. H. Pao and D. P. Santry, *J. Amer. Chem. Soc.*, **88**, 4157 (1966); (b) G. Snatzke, B. Ehrig, and H. Klein, *Tetrahedron*, **25**, 5601 (1969); (c) M. E. Herr, *et al.*, *J. Org. Chem.*, **35**, 3607 (1970); (d) C. Coulombeau and A. Rassat, *Bull. Soc. Chim. Fr.*, 516 (1971); (3) G. Snatzke and H. Klein, *Chem. Ber.*, **105**, 244 (1972); (f) D. N. Kirk, W. Klyne, and W. P. Mose, *Tetrahedron Lett.*, 1315 (1972); (g) H. J. C. Jacobs and E. Havinga, *Tetrahedron* **28**, 135 (1972); (h) G. Snatzke and K. Kinsky, *Tetrahedron*, **28**, 295 295 (1972); (i) J. F. Tocanne, *Tetrahedron*, **28**, 389 (1972), and references therein.

[7] A. F. Casy, A. B. Simmonds, and D. Staniforth, *J. Org. Chem.*, **37**, 3189 (1972).

more stable rotomer or rotomers have a methyl or phenyl group in a pseudoaxial arrangement for **7c**, **7d**, and **7e**.



	Δδ
7a, R = CH$_3$	s
b, R = CH$_3$CH$_2$	s
c, R = PhCH$_2$	12.9
d, R = (CH$_3$)$_2$CH	6.7
e, R = (CH$_3$)$_3$C	13.0

The appearance of the diastereotopic protons of the methylene group of an *N*-benzyl substituent as an AB quartet in the nmr spectrum of an alkylated piperidine or piperazine has been shown to be positive evidence for a 2-equatorial alkyl, a 3-axial alkyl or a large 3-equatorial alkyl substituent. The appearance of the methylene signal as a singlet is evidence for the absence of these conformational features.

Acknowledgment.—The nmr spectra were determined with a Joel MH-100 obtained from Grants NSF GP 29176 and NIH 5S05-FR-07108. The authors also wish to express appreciation to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of the research. Appreciation is also expressed to Dr. H. C. Brown for a generous sample of 3-*tert*-butylpyridine and to Dr. O. Frank Beumel and Foote Mineral for *n*-butyllithium used in this research.

---

(8) This research was abstracted from the thesis of L. N. P submitted to the Graduate School of the University of New Hampshire in partial fulfillment of the Ph.D. degree. Martin Luther King and Petroleum Research Fund Fellow, 1969–1972.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF NEW HAMPSHIRE
DURHAM, NEW HAMPSHIRE 03824

ROBERT E. LYLE*
LENDON N. PRIDGEN[8]

RECEIVED FEBRUARY 5, 1973

Fundamental Studies of Substituted Ferrocenes. VII.[1] Proton Magnetic Effects in Trimethylsilylferrocene

Summary: Specific deuterium labeling of trimethylsilylferrocene shows that the upfield two-proton apparent triplet at δ 4.07 ppm can be assigned to the 2,5-position protons and thus the downfield two-proton apparent triplets at δ 4.30 ppm can be assigned to the 3,4-position protons.

Sir: In a previous publication[2] we had advanced the hypothesis based on chemical shift data that the response of a ferrocene ring to an electron-donating substituent (typified by an amino group) was "principally manifested at the 3,4 positions," care being taken at that time to avoid use of the term resonance. Since then other monosubstituted ferrocenes containing electron-donating substituents have been shown to exhibit similar pmr behavior.[1,3] We now propose that this phenomenon be interpreted as a resonance effect[4] and offer as proof the herein documented observation of electron withdrawal from the 3,4 positions of trimethylsilylferrocene as determined by pmr. Since the trimethylsilyl group in several instances has been found to participate in (p–d) π-electron withdrawal[5] (although in most instances the result is not marked), our proposal amounts to suggesting that correct assignment of chemical shifts according to two distinct π-resonance effects in an unknown system constitutes satisfactory identification of such effects in said system.

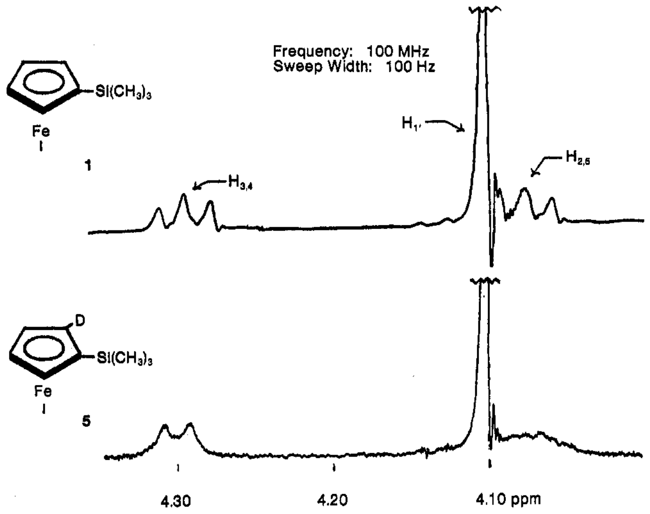


Figure 1.

Trimethylsilylferrocene (**1**) possesses chemical shift shielding values for the H$_{2,5}$ and H$_{3,4}$ proton resonances in accordance with resonant electron withdrawal by the trimethylsilyl group from the 3,4 positions. The pmr spectrum of **1** exhibits two unsymmetrical triplets[6,7] for the homoannular proton resonances. Assignments for these resonances have been made on the basis of comparative spectra of trimethylsilylferrocene and 2-deuteriotrimethylsilylferrocene (CDCl$_3$) as shown in Figure 1. Attenuation of the resonance at δ 4.07 ppm and the change in splitting of the resonance of δ 4.30 ppm from a triplet to a doublet with introduction of a deuterium at the 2 position permits equivocal assignment of the resonance at high field to the H$_{2,5}$ protons and that at low field to the H$_{3,4}$ protons.

The deuterated trimethylsilylferrocene was prepared by the series of reactions shown in Scheme I. Treatment of chloroferrocene (**2**) with *n*-butyllithium under conditions reported[8,9] to give metalation of chloroferrocene and now documented to provide 2 metalation,[1] followed by addition of trimethylchlorosilane, afforded 2-chlorotrimethylsilylferrocene (**3**) as an oil. Sodiation of **3** with dispersed sodium and deuterolysis of the sodiated intermediate (**4**) with excess deuterium oxide produced trimethylsilylferro-

---

[1] Part VI: D. W. Slocum, W. E. Jones, and C. R. Ernst, *J. Org. Chem.*, **37**, 4278 (1972).

[2] D. W. Slocum, P. S. Shenkin, T. R. Engelmann, and C. R. Ernst, *Tetrahedron Lett.*, 4429 (1971).

[3] D. W. Slocum, B. P. Koonsvitsky, and C. R. Ernst, *J. Organomet. Chem.*, **38**, 125 (1972).

[4] Other effects such as field, inductive, and (for pmr) anisotropy would be expected to be strongest at the 2,5 positions.

[5] M. E. Freeburger and L. Spialter, *J. Amer. Chem. Soc.*, **93**, 1894 (1971).

[6] M. D. Rausch and M. Mark, *J. Org. Chem.*, **28**, 3225 (1963).

[7] M. I. Levenberg and J. H. Richards, *J. Amer. Chem. Soc.*, **86**, 2634 (1964).

[8] J. Huffman, L. Keith, and R. Ausbury, *J. Org. Chem.*, **30**, 1600 (1958).

[9] A. N. Nesmeyanov, *Dokl. Akad. Nauk SSSR*, **176**, 598 (1968).