pound assigned the *trans*-4-*t*-butyl-1-methylcyclohexyl chloride structure by Greene.[23]

Anal. Calcd for $C_{11}H_{21}Cl$: C, 70.02; H, 11.14. Found: C, 70.29; H, 11.21.

A solution was prepared from 1 g of 4-*t*-butyl-1-methylcyclohexyl chloride (*cis–trans* mixture) in 5 ml of ethyl alcohol and was added to 650 mg of freshly prepared sodium methoxide. The mixture was refluxed overnight, and was poured into ice water and extracted with ether. The ether layer was separated and washed with water. After drying of the solution and removal of the solvent, vpc analysis of the residue showed a peak at 4 min (4-*t*-butyl-1-methylcyclohexene) followed by peaks at 17 and 21 min in the ratio 1:1. The latter was collected and the infrared spectrum was identical with that of the compound assigned the *cis* structure by Greene.[23]

1-Methylcyclohexyl Chloride.—1-Methylcyclohexyl chloride was prepared from 1-methylcyclohexanol [bp 49–50° (8 mm)] and concentrated hydrochloric acid according to Brown,[24] bp 30–31° (6 mm) [lit[24]. bp 65.2–65.5° (44 mm)].

1,4,4-Trimethylcyclohexyl Chloride.—4,4-Dimethylcyclohexanone (240 mg) underwent the Grignard reaction as described for 4-*t*-butylcyclohexanone. The formation of 1,4,4-trimethylcyclohexanol was verified by the disappearance of 1680-cm^{-1} band. The alcohol (200 mg) was dissolved in 5 ml of dry ether and treated with 70 mg of anhydrous hydrogen chloride at 0°. The reaction mixture was allowed to stand overnight and was diluted with ether, washed with water, and dried over magnesium sulfate. The solvent was removed *in vacuo*, and vpc analysis using column B at 120° and 9 psi gave a peak with a retention time of 5 min. This fraction was collected.

Anal. Calcd for $C_9H_{17}Cl$: C, 67.29; H, 10.59. Found: C, 68.08; H, 10.39.

(23) Professor F. D. Greene, private communication.

(24) H. C. Brown, R. S. Fletcher, and R. B. Johannesen, *J. Am. Chem. Soc.*, **73**, 212 (1951).

Registry No.—Chlorocyclohexane, 542-18-7; 1-chloro-1-methylcyclohexane, 931-78-2; *cis*-4-*t*-butyl-1-chlorocyclohexane, 13131-74-3; *trans*-4-*t*-butyl-1-chlorocyclohexane, 13145-48-7; *cis*-4-*t*-butyl-1-chloro-1-methylcyclohexane, 13145-49-8; *trans*-4-*t*-butyl-1-chloro-1-methylcyclohexane, 13131-75-4; 1-chloro-1,4,4-trimethylcyclohexane, 13145-50-1.

Acknowledgment.—The authors are indebted to Professor Robert Taylor, University of Michigan, Dr. Margaret Griffing, Ethyl Corp., and Dr. J. A. Hirsch, of this department, for the infrared spectra. We also would like to thank Professor F. D. Greene, Massachusetts Institute of Technology, for making available to us his unpublished data on the compounds as discussed in the text. Finally, we would like to thank Mrs. G. L. Wang for furnishing the sample of 4,4-dimethylcyclohexanone used in this work.

Conformational Analysis. X.[1] Determination of Intramolecular Hydrogen Bonding by Hydroxyl Proton Magnetic Resonance[2]

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Dilution studies of the hydroxyl proton magnetic resonance of a number of isomeric alcohols containing the bicyclo[2.2.1]heptane skeleton have been made, and the limiting chemical shift–concentration dependence relationships have been determined. In the compounds investigated, a distinction has been made between pairs of isomers in which one compound can intermolecularly hydrogen bond to an acceptor site and the second compound cannot. Compounds which are intramolecularly hydrogen bonded exhibit small limiting slopes compared with isomeric compounds which cannot intramolecularly hydrogen bond. The compounds which cannot intramolecularly hydrogen bond to an acceptor site may intermolecularly hydrogen bond to it. The degree of intermolecular hydrogen bonding is indicated by the difference in the observed chemical shift concentration curve from that predicted from model compounds lacking the acceptor site.

The hydroxyl proton magnetic resonance has been examined quantitatively for only a few simple compounds. This widely occurring resonance has been ignored as a result of its concentration dependence. At concentrations normally employed in nmr, the hydroxyl signal is a time average of a weighted average of the various hydrogen-bonded species present in solution. We have shown in several reports that the chemical shift of the hydroxyl proton is linearly related to concentration in carbon tetrachloride in the 0.015–0.002 mole fraction range.[4] By extrapolation to infinite dilution, the chemical shift of the monomeric hydroxyl proton can be determined. At infinite dilution the chemical shift is solely a function of magnetic environment, and this resonance signal has been used as a conformational probe in the cyclohexane series.[4] However, the limiting resonances for a large number of simple alcohols investigated in this laboratory have been shown to be located in a relatively narrow high-field region. Therefore, another method was sought in order to provide additional structural information from the nmr of alcohols. An alternate approach, which offers a quantitative method of evaluating the steric environment of the hydroxyl proton, involves the use of the limiting slope of the chemical shift–concentration curve. This technique has been shown to be useful in determining the steric environment of the hydroxyl group in some rigid bicyclic compounds.[5]

The limiting-slope method is derived from the early work of Becker, Liddel, and Shoolery,[6] who carried out a detailed study of the dilution shift of the hydroxyl proton of ethanol in carbon tetrachloride. With decreasing concentration the hydroxyl resonance shifts to a higher field and the dilution curve linearly approaches a limiting value at infinite dilution. The linear relationship has been interpreted in terms of a

(1) Conformational Analysis. IX: R. J. Ouellette, D. L. Marks, and D. Miller, *J. Am. Chem. Soc.*, **89**, 913 (1967).

(2) The authors acknowledge a grant from the Petroleum Research Fund of the American Chemical Society in support of this research.

(3) National Science Foundation Undergraduate Research Participant.

(4) R. J. Ouellette, *J. Am. Chem. Soc.*, **86**, 3089, 4378 (1964); R. J. Ouellette, K. Liptak, and G. E. Booth, *J. Org. Chem.*, **31**, 546 (1966).

(5) R. J. Ouellette, G. E. Booth, and K. Liptak, *J. Am. Chem. Soc.*, **87**, 3436 (1965).

(6) E. D. Becker, V. Liddel, and J. N. Schoolery, *J. Mol. Spectry.*, **2**, 1 (1958).

monomer–dimer equilibrium. Huggins, Pimentel, and Shoolery[7] have shown that, if a system is governed by monomer–dimer equilibrium, the limiting slope of the dilution curve is related to the equilibrium constant for dimer formation by

$$\left(\frac{\partial\delta}{\partial\chi}\right)_{\chi=0} = 2K\Delta_D$$

In the above expression, $K = \chi_D/\chi_M^2$ where χ_D and χ_M are the mole fraction of dimer and monomer, respectively. The symbol Δ_D is equal to the difference between the chemical shifts of the dimer and the monomer, $\delta_D - \delta_M$. The equilibrium constant for the monomer–dimer equilibrium could be evaluated if the limiting slope and the chemical shifts of the dimer and monomer were available. The limiting slope and the chemical shift of the monomer are directly available from dilution studies. However, the chemical shift of the dimer is not directly observable.

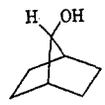
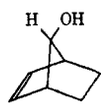
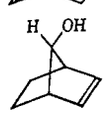
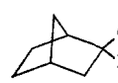
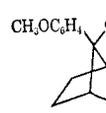
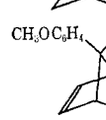
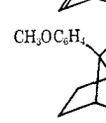
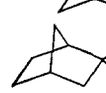
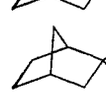
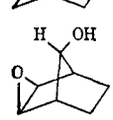
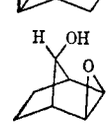
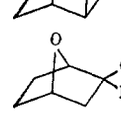
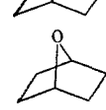
As a first approximation, the quantity $\delta_D - \delta_M$ can be assumed to be constant for a series of closely related alcohols. The assumed near constancy of the quantity $\delta_D - \delta_M$ is reasonable, as all individual contributions to the shielding of the proton save the difference that results from the formation of a hydrogen bond should cancel. The effect of structural features on the chemical shift of the monomeric hydroxyl proton is of a lower order of magnitude than the shift caused by hydrogen bonding. Our observations on the limiting slopes of the chemical shift–concentration dependence provide some support for the assumption of a constant value for $\delta_D - \delta_M$. If the alcohols are not structurally similar, the assumption may not be correct. However, providing that the differences in $\delta_D - \delta_M$ are smaller than the differences in K, the method may still be qualitatively useful.

In order to further expand the method of using the chemical shift–concentration dependence of the hydroxyl proton in organic chemistry, we have examined compounds in which intramolecular hydrogen bonding can occur in one member of a pair of isomeric alcohols. If intramolecular hydrogen bonding can occur, then the mole fraction of dimeric alcohol which results from intermolecular hydrogen bonding should be smaller at a given concentration than the mole fraction of dimer of an alcohol which cannot intramolecularly hydrogen bond. The limiting slope of the dilution curve for an alcohol which can intramolecularly hydrogen bond should be smaller than for the alcohol which cannot intramolecularly hydrogen bond. Therefore, it was anticipated that nmr dilution studies of alcohols that can intramolecularly hydrogen bond would provide a complimentary analytical tool to the more commonly used infrared techniques for detecting the presence of intramolecular hydrogen bonds.

Results and Discussion

The chemical shift–concentration dependence of the hydroxyl proton for 15 alcohols has been determined in the 0.002–0.01 mole fraction range. For each compound the limiting slope and extrapolated chemical shift at infinite dilution were evaluated and are listed in Table I. All chemical shifts were determined in carbon tetrachloride relative to tetramethylsilane which was approximately 0.003 mole fraction. The experimental procedure has been described previously.[4] All spectra were determined at 40°, and the assigned hydroxyl resonance was confirmed by exchange with deuterium oxide.

TABLE I

No.	Compound	Limiting slope, cps/N	Limiting chemical shift
1		2650	40.0
2		2380	60.5
3		320	121.0
4		2320	45.5
5		660	56.2
6		590	71
7		55	138.2
8		1170	46.0
9		1860	52.5
10		3580	44.0
11		85	192.0
12		4800	66.7
13		4860	46.2
14		3500	44.0
15		3450	44.0

Both the limiting slopes and limiting chemical shifts of 7-bicyclo[2.2.1]heptanol (**1**) and *exo*-2-bicyclo[2.2.1]-heptanol (**4**) are very similar. If the terms $\delta_D - \delta_M$ are equal for these two compounds, then it could be concluded that the 7 position is sterically less hindered than the 2 position. Introduction of a double bond into the ring system affects both the limiting slope and

(7) C. M. Huggins, G. C. Pimentel, and J. N. Shoolery, *J. Phys. Chem.*, **60**, 1311 (1956).

limiting chemical shift of the hydroxyl group at the 7 position. The slightly smaller slope for *anti*-7-bicyclo-[2.2.1]heptenol (**2**) as compared to 7-bicyclo[2.2.1]-heptanol (**1**) suggests that the double bond alters the geometry of the ring system so as to decrease the local steric environment at the hydroxyl group. While there is also a change in limiting chemical shift, as might be expected from the introduction of the anisotropic double bond, this difference is not very significant.

The limiting slope of *syn*-7-bicyclo[2.2.1]heptanol (**3**) is an order of magnitude smaller than the *anti* isomer. In addition a downfield shift of 60 cps is observed. An increase in the limiting slope would be expected since the hydroxyl group is sterically more accessible in the *syn* compound as compared to the *anti* compound. Therefore, the decrease in the limiting slope must be due to an intramolecular hydrogen bond which is geometrically favorable in the *syn* compound. That the limiting chemical shift appears at lower field in the *syn* compound also supports the hypothesis of intramolecular hydrogen bonding. Owing to the anisotropic effect of the double bond, a proton located above the plane of the double bond would be expected to experience an upfield shift. The fact that a downfield shift is observed can be explained by the formation of a hydrogen bond to the π system.

The limiting slopes of 7-(*p*-anisyl)-7-bicyclo[2.2.1]-heptanol (**5**) and *anti*-7-(*p*-anisyl)-7-bicyclo[2.2.1]-heptenol (**6**) are similar. As previously noted with compounds **1** and **2**, the *anti* double bond causes a downfield shift and a slight decrease in the limiting slope. That the slopes are less than for the compounds without the anisyl groups is probably the result of altering the steric environment by the introduction of an anisyl group. This hypothesis is supported by the slope of 2-methyl-2-*endo*-bicyclo[2.2.1]heptanol (**8**) as compared with 2-*endo*-bicyclo[2.2.1]heptanol (**9**). If a methyl group decreases the slope of the concentration–chemical shift plot by a factor of 0.6, then it is not unreasonable for the sterically larger anisyl group to decrease the slope by a factor of 0.25. The limiting slope of 7-(*p*-anisyl)-*syn*-7-bicyclo[2.2.1]heptenol (**7**) is an order of magnitude smaller than the isomeric *anti* compound. In addition the chemical shift at infinite dilution of the *syn* compound appears at lower field than the *anti* compound by 67 cps. Both the limiting slope and the limiting chemical shift indicate that a π hydrogen bond is present in the *syn* compound.

The placement of a 2,3-epoxy bridge in the bicyclo-[2.2.1]heptane ring system provides further evidence for the utility of chemical shift–concentration slopes in distinguishing compounds where intramolecular hydrogen bonding may or may not be possible. The limiting slope of *anti*-2,3-epoxy-7-bicyclo[2.2.1]heptanol (**10**) is 400 times larger than the *syn* isomer (**11**). In the *syn* isomer intramolecular hydrogen bonding is favorable, as the epoxide ring is geometrically close to the hydroxyl group. The limiting chemical shift of the *syn* compound is displaced strongly downfield by the formation of the hydrogen bond. While the limiting slope of the *syn*-epoxy compound is predictably small, the limiting slope of the *anti* compound is larger than would be expected on the basis of the similar steric environment of the hydroxyl group in 7-bicyclo[2.2.1]heptanol (**1**). The large slope for the *anti*-epoxy compound can be attributed to the presence of two acceptor sites per molecule, since it is more probable that intermolecular hydrogen bonding will occur in this compound as compared to 7-bicyclo[2.2.1]-heptanol (**1**).

In compounds containing π electron or oxygen acceptor sites in rigid ring systems of proper geometry, assignment of stereochemistry is possible if each member of an isomeric pair of compounds is available. In addition, since intramolecular hydrogen bonding decreases the slope of the chemical shift–concentration line relative to model compounds, a tentative assignment of stereochemistry might be made for the hydrogen-bonded compound if the decrease in slope is substantial. Intermolecular hydrogen bonding with an oxygen acceptor site increases the slope of the chemical shift–concentration line over that of model compounds. In the case of weak acceptor sites, such as π bonds, the degree of intermolecular hydrogen bonding may be very small. In the case of *anti*-7-bicyclo-[2.2.1]heptenol the slope is actually smaller than that of saturated model compound 7-bicyclo[2.2.1]heptanol. There must be differences in the steric environments of the hydroxyl group of the two compounds which cause a decrease in the slope of the unsaturated compound. Therefore, an intermolecular hydrogen bond with a π acceptor site is probably either masked or absent.

The limiting slopes for *exo*-2-hydroxymethyl-7-oxabicyclo[2.2.1]heptane (**12**) and *endo*-2-hydroxy-methyl-7-oxabicyclo[2.2.1]heptane (**13**) are identical. Therefore, it appears that intramolecular hydrogen bonding does not occur to any significant extent in the *exo* compound. There is a small downfield shift in the *exo* compound as compared to the *endo* compound, which could be due to an anisotropic contribution of the heteroatom. Examination of models indicates that the geometry of the *exo* might allow the formation of an intramolecular hydrogen bond *via* a six-membered ring. The minimum oxygen–oxygen distance is 2.6 A which is within the proper range for a hydrogen bond between two oxygen atoms. However, the orbital geometries at the two oxygen atoms are not ideally situated with respect to the bridging hydrogen atom. Finally, the rotamer about the carbinol carbon and ring carbon bond that allows hydrogen bonding is energetically less favorable with respect to nonbonded interactions as compared to the other two rotamers. Therefore, both entropy and enthalpy terms should tend to decrease the mole fraction of the rotamer which is suitable for hydrogen bonding. Since this nmr method involves interpretation of an experimental term which is a time average of a weighted average of the species in solution, there are distinct limitations on the detection of weak hydrogen bonding or limited hydrogen bonding in flexible molecules.

The limiting slopes of *exo*-2-hydroxymethylbicyclo-[2.2.1]heptane (**14**) and *endo*-2-hydroxymethylbicyclo-[2.2.1]heptane are identical (**15**). The large slopes are as expected for primary alcohols. Although we have shown that the degree of substitution at the β carbon of an alcohol affects the limiting slope, it appears that there is little noticeable effect owing to differences in geometry of the γ-carbon branches. While the limiting chemical shifts of *endo*-2-hydroxymethyl-7-oxabicyclo-

[2.2.1]heptane (**13**) and *endo*-2-hydroxymethylbicyclo-[2.2.1]heptane (**15**) are very close, there is a considerable difference in their limiting slopes. The steric environments of the hydroxyl groups are similar and, therefore, the larger slope for the oxa compound must be the result of two acceptor sites within the same molecule.

Registry No.—**1**, 2566-48-5; **2**, 694-70-2; **3**, 13118-70-2; **4**, 497-37-0; **5**, 13118-71-3; **6**, 13118-72-4; **7**, 13143-81-2; **8**, 6196-84-5; **9**, 497-36-9; **10**, 13118-75-7; **11**, 13118-76-8; **12**, 13118-77-9; **13**, 13118-78-0; **14**, 13118-79-1; **15**, 13137-31-0.

Acknowledgment.—The authors wish to thank Dr. Paul G. Gassman, The Ohio State University, for samples of compounds **5**, **6**, **7**, **10**, and **11** used in this study.

A Novel 1,4-Elimination Reaction of 1-Chloro-2-alkylperfluorocycloalkenes with Alkoxide Ion

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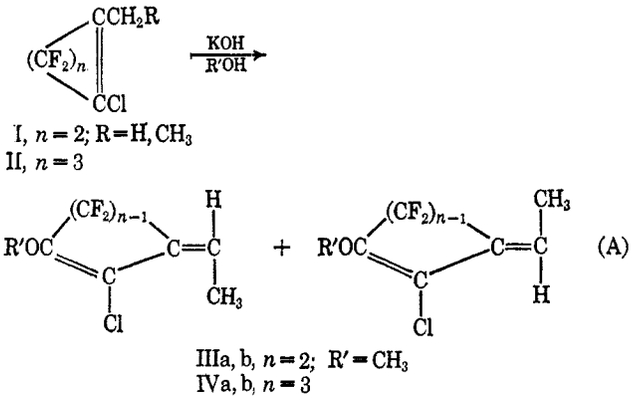
The nucleophilic attack by alkoxide ion on 1-chloro-2-alkylperfluorocyclobutene and -pentene brought about a novel 1,4-elimination reaction which yielded the corresponding 1-alkoxy-2-chloro-3-methyleneperfluorocyclobutene and 1-alkoxy-2-chloro-3-ethylideneperfluorocyclopentene. The physical properties of these compounds along with their nmr data are also presented.

In the course of our studies of nucleophilic attack by alkoxide ion on alicyclic polyfluoro olefins, a novel 1,4-elimination reaction was encountered when 1-chloro-2-alkyltetrafluorocyclobutene-1 (I) and 1-chloro-2-alkylhexafluorocyclopentene-1 (II), respectively, were treated with alcoholic potassium hydroxide (reaction A). A mixture of geometrical isomers of the corresponding 1-alkoxy-2-chloro-3-alkylideneperfluorocycloalkene-1 and 1-alkoxy-2-chloro-3-methyleneperfluorocycloalkene-1 was obtained in high yield. Thus, ab-

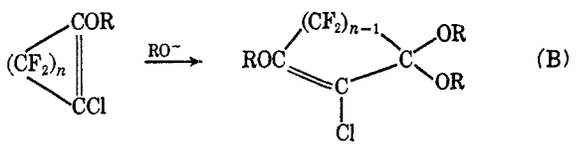


I, $n = 2$; R = H, CH_3
II, $n = 3$

(A)

IIIa, b, $n = 2$; R' = CH_3
IVa, b, $n = 3$

straction of an α hydrogen from the alkyl group by alkoxide ion is apparently preferred to the "normal" nucleophilic displacement of vinylic allylic halogen (reaction B). The acidity of these protons (reaction



(B)

A) can be attributed both to the allylic nature of the protons on the α carbon and their proximity to a highly fluorinated ring structure.[2]

(1) This paper represents part of a Ph.D. thesis submitted to the Graduate School, University of Colorado, 1967.

Although no other example of an analogous 1,4-elimination of hydrogen fluoride involving proton abstraction from a carbon atom has been reported to the best of our knowledge, a similar mechanism may be involved in the reaction of alicyclic polyfluoro olefins with an excess of amines,[3] hydroxylamine,[4] or potassium hydroxide in polar aprotic solvents.[5]

McBee[4] reported that both 1,2-dichlorohexafluorocyclopentene-1 (V) and octafluorocyclopentene-1 (VI) gave 1,3-iminoamines upon treatment with hydroxylamine. Two competitive reaction paths are available to initially formed 1-halo-2-hydroxylaminohexafluorocyclopentene-1 in this reaction: elimination of hydrogen fluoride or additional attack by hydroxylamine (Scheme I). The isolation of the 1,3-iminoamine from VI was cited as evidence against the latter possibility since all previous studies in these systems indicated that the remaining vinylic fluorine would be displaced preferentially.[6]

A similar conclusion has recently been suggested by Stockel and co-workers[5] concerning the hydrolysis of polyhalo olefins with potassium hydroxide in polar aprotic solvents. Two plausible reaction paths were advanced and are illustrated in Scheme II. Path B is capable of explaining why the reaction of VI with hydroxide ion differs from that with alkoxide ion[6] since the formation of enolate ion is not possible in the latter case. The over-all similarity of these reactions is apparent if the heteroatom in the previously mentioned examples is equated with the α carbon of the ethyl group in I and II.

Failure of recovered I to exhibit deuterium incorporation in the allylic position when methanol-OD was

(2) The inductive effect of the γ-carbon fluorines in this example may be relatively unimportant. However, the acidity of a proton with adjacent β-difluoro groups is well documented: A. Streitwieser, Jr., and D. Holtz, Abstracts, 152nd National Meeting of the American Chemical Society, Sept 1966, New York, N. Y., p K-30.

(3) R. L. Pruett, J. T. Barr, *et al.*, *J. Am. Chem. Soc.*, **72**, 3646 (1950).

(4) E. T. McBee, J. J. Turner, C. J. Morton, and A. P. Stefani, *J. Org. Chem.*, **30**, 3698 (1965).

(5) R. F. Stockel, M. T. Beachem, and F. H. Megson, *ibid.*, **30**, 1629 (1965).

(6) R. D. Chambers and R. H. Mobbs, *Advan. Fluorine Chem.*, **4**, 50 (1965).