Nuclear Magnetic Resonance Spectroscopy. Conformational Equilibria and Equilibration of 5,5-Difluoro-*cis*-hydrindan and 9-Methyl-5,5-difluoro-*cis*-hydrindan[1]

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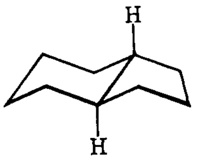
Received April 24, 1968

Abstract: The rate of ring inversion and conformational equilibration of 5,5-difluoro-*cis*-hydrindan has been determined from the temperature dependence of its fluorine magnetic resonance spectrum. The activation energy for ring inversion was found to be 6.9 ± 0.2 kcal/mol. Introduction of an angular methyl group at the 9 position resulted in an increase in the activation energy to 8.1 ± 0.3 kcal/mol.

Fluorine magnetic resonance (fmr) spectroscopy of *gem*-fluoro groups has been used in studies[3] of conformational equilibria and equilibration of cyclobutanes,[4] cyclohexane,[5] cycloheptanes,[6a,b] cyclooctanes,[6c] *cis*-decalins,[7] and *cis*-decalones.[8] The technique is here extended to 5,5-difluoro-*cis*-hydrindan and the corresponding 9-methyl derivative, substances which provide models for the C, D part of the steroid ring system. Although *trans*-hydrindan (**1**) has only one favorable conformation with a chairlike six-membered ring, *cis*-hydrindan, like *cis*-decalin,[7] is expected to have two reasonably favorable nonequivalent conformations (**2** and **3**) which are anticipated to be rapidly interconverted at normal temperatures, thus leading to averaging of the resonances of the axial and equatorial hydrogens in the proton resonance spectrum. The energy barrier of this interconversion has been studied[9] with the aid of the temperature dependence of the proton spectra. The signals due to the protons in the five- and six-membered rings appeared as two reasonably sharp singlets at 25° but gave only one broad resonance at −127°, which was unchanged on further cooling to −140°. The enthalpy of activation ($\Delta H^{\ddagger}$) was estimated to be 6.4 kcal/mol assuming a negligibly small entropy of activation.



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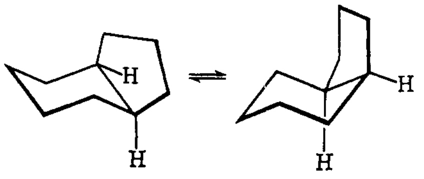
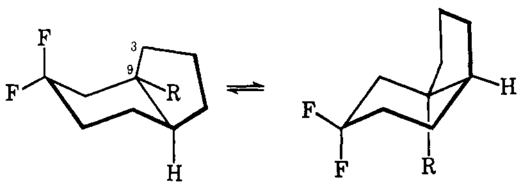


2 **3**

Introduction of a *gem*-fluoro group in position 5 of *cis*-hydrindan is expected to permit direct observation of the resonances of conformations **4** and **5** if the rate of interconversion can be sufficiently slowed at low temperature. Conformers **4** and **5** are not anticipated to be energetically equivalent and **5**, in which the axial fluorine atom suffers only 1,3-diaxial interaction with hydrogen atoms, should be favored over **4** where there should be at least some hindrance between the axial fluorine and the ring methylene at position 3. Introduction of a 9-methyl group gives the conformers **6** and **7**, and in **7** there is an additional 1,3-diaxial methyl–fluorine interaction which is not present in **6**.

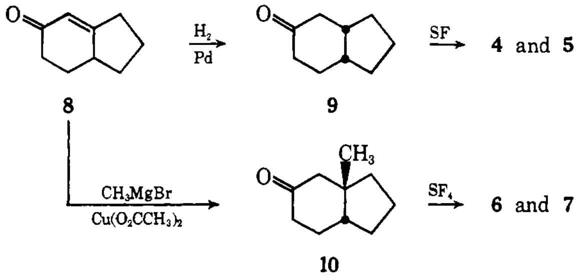


4, R = H
6, R = CH_3

5, R = H
7, R = CH_3

Syntheses and Results

Cyclopentanone was converted to the pyrrolidine enamine which, with methyl vinyl ketone,[10] followed by hydrolysis, gave the α,β-unsaturated ketone **8**. Hydrogenation of **8** over palladium on charcoal in neutral or acid conditions gave *cis*-hydrindan-7-one (**9**),[11] which, with sulfur tetrafluoride[12] at room temperature for 17 hr, yielded the *cis*-5,5-difluorohydrindan **4** and



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(1) Supported in part by the National Science Foundation.

(2) On leave of absence from the Department of Organic Chemistry, The University of Sydney, Sydney, Australia.

(3) J. D. Roberts, *Chem. Brit.*, **2**, 529 (1966).

(4) J. B. Lambert and J. D. Roberts, *J. Amer. Chem. Soc.*, **87**, 3884 (1965).

(5) (a) J. D. Roberts, *Angew. Chem.*, **75**, 20 (1963); *Angew. Chem. Intern. Ed. Engl.*, **2**, 53 (1963); (b) F. A. Bovey, E. W. Anderson, F. P. Hood, and R. L. Kornegay, *J. Chem. Phys.*, **40**, 3099 (1964); (c) S. Spassov, E. S. Glazer, D. L. Griffith, K. Nagarajan, and J. D. Roberts, *J. Amer. Chem. Soc.*, **89**, 88 (1967).

(6) (a) J. D. Roberts, Abstracts of 19th National Organic Chemistry Symposium of the American Chemical Society, Tempe, Ariz., June 1965, pp 77–85; (b) R. Knorr, E. S. Ganter, and J. D. Roberts, *Angew. Chem.*, **79**, 577 (1967); (c) J. E. Anderson, E. S. Glazer, D. L. Griffith, R. Knorr, and J. D. Roberts, *J. Amer. Chem. Soc.*, in press.

(7) J. T. C. Gerig and J. D. Roberts, *ibid.*, **88**, 279 (1966).

(8) R. E. Lack, C. Ganter, and J. D. Roberts, *ibid.*, **90**, 7001 (1968).

(9) W. B. Moniz and J. A. Dixon, *ibid.*, **83**, 1671 (1961).

(10) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkoviez, and R. Terrell, *ibid.*, **85**, 207 (1963).

(11) R. L. Augustine, *J. Org. Chem.*, **28**, 152 (1963).

(12) W. R. Hasek, W. C. Smith, and V. A. Engelhardt, *J. Amer. Chem. Soc.*, **82**, 543 (1960).

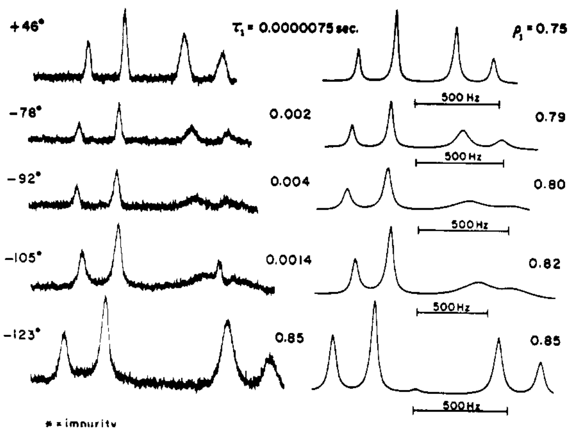

Figure 1. Fluorine magnetic resonance spectra at 56.4 MHz of 5,5-difluoro-*cis*-hydrindan as a function of temperature in acetone. The curves on the right side are theoretical spectra calculated as a function of τ_1 and p_1 (the subscripts referring to the dominant conformation **5**).

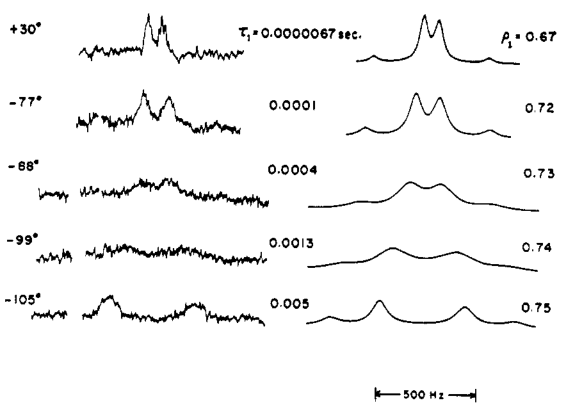

Figure 2. Fluorine magnetic resonance spectra at 56.4 MHz of 9-methyl-5,5-difluoro-*cis*-hydrindan as a function of temperature in acetone. The curves on the right side are theoretical spectra calculated as a function of τ_1 and p_1 (the subscripts referring to the dominant conformation, it not being known whether this is **6** or **7**).

5. The fluorine spectrum showed no evidence of the temperature-independent resonances expected for the *trans* isomer which is in agreement with the results reported by Augustine,[11] namely, that hydrogenation of the α,β-unsaturated ketone **8** under a variety of conditions gives only the *cis* product. Clearly, also, no change in configuration of the ring junction took place during the sulfur tetrafluoride reaction.[7,8]

9-Methyl-*cis*-hydrindan-5-one (**10**) was prepared by 1,4 addition of methylmagnesium bromide to the α,β-unsaturated ketone **8** in the presence of cupric acetate[13] and this was converted with sulfur tetrafluoride[12] to 9-methyl-5,5-difluoro-*cis*-hydrindan, **6** and **7**. The fluorine spectrum again showed no sign of the temperature-independent resonances expected for the *trans* isomer.

The fluorine spectrum of 5,5-difluoro-*cis*-hydrindan at room temperature and at −70° appeared as a single averaged AB quartet (Figure 1) because of rapid interconversion of conformers **4** and **5**. At about −105°, the low-field pair of signals were still reasonably sharp but the broader high-field pair had become grossly flattened. At −130°, two overlapping AB quartets were observed. The rather different appearance of the temperature dependence of the spectra of 5,5-difluoro-*cis*-hydrindan compared to those of the *gem*-fluoro-*cis*-decalins[7] and -*cis*-decalones[8] can be understood if it is assumed that the equatorial fluorine atom of **5** appears at δ 640 Hz and is averaged at high temperatures with the axial fluorine of **4** at δ 804 Hz. At the same time, we take the resonance of the axial fluorine of **5** to come at δ 1466 Hz and consider this to be averaged with the resonance of the equatorial fluorine of **4** at δ 452 Hz. The logic of these assignments will be considered in more detail later.

The room-temperature fluorine spectrum of 9-methyl-5,5-difluoro-*cis*-hydrindan also appears as an averaged AB spectrum (Figure 2), each peak being split by proton coupling into a quintet as in various 1,1-difluorocyclohexanes[5b] and 6,6-difluoro-*cis*-decal-2-one.[8] The splitting in the downfield quintets is about 13 Hz and in the upfield quintets about 16 Hz. This is expected on the basis that the observed H–F couplings are average values and will be smaller the more nearly equatorial the fluorines are on the average. At −88°, the spectrum still shows an averaged AB pattern but, on decreasing the temperature to −99°, the signals broaden and, at −105°, what appears to be a single AB quartet emerges with a much larger chemical shift than the averaged room-temperature spectrum.

This behavior is rather similar to that observed for 4-ethyl-4-methyl-1,1-difluorocyclohexane[5b] and is the result of having near coincidence of the chemical shifts of the axial fluorines and also of the equatorial fluorines of **6** and **7**. Apparently there is a balancing of the effects of the 9-methyl *vs.* 5-fluorine interaction on one side of the ring and the 3-methylene *vs.* the other 5-fluorine interaction on the opposite side of the ring. Somewhat similar (but smaller) balancing trends can be seen with 9-methyl-2,2-difluoro-*cis*-decalin[7] and the corresponding *cis*-decalone[8] (Table I). The relative proportions of **6** and **7** are clearly not equal at room temperature because with equal proportions and equal chemical shifts a single A_2 resonance would be observed at room temperature. The center of the AB pattern at room temperature was found to be shifted upfield by 35 Hz from the center of the AB pattern at −100° and the intermediate spectra could only be matched satisfactorily by assuming a 30-Hz downfield shift of the resonances of the equatorial fluorines, relative to trifluoroacetic acid as internal standard with a 100° decrease in temperature. The same sort of increase of about 30 Hz in the chemical-shift difference between axial and equatorial fluorine atoms for a 100° decrease in temperature has been noted before.[5b,8,14] However, it is a small effect as far as measurements of τ go, and, if ignored, introduces negligible error, provided that the line shapes rather than line positions are used to determine τ.[3]

Theoretical spectra were generated by an IBM 7094 computer using the Gerig[7] modification of Alexander's[15] equations as a function of τ and the other spectral parameters for the conformational equilibration.

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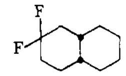
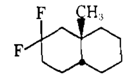
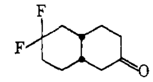
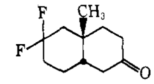
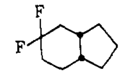
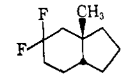
[13] A. J. Birch and M. Smith, *Proc. Chem. Soc.*, 356 1962); S. Boatman, T. M. Harris, and C. R. Hauser, *J. Amer. Chem. Soc.*, **87**, 82 (1965); R. F. Church, R. E. Ireland, and D. R. Shridhar, *J. Org. Chem.*, **27**, 707 (1962).

[14] R. A. Newmark and C. H. Sederholm, *J. Chem. Phys.*, **43**, 602 (1965).

[15] S. Alexander, *ibid.*, **37**, 967 (1963).

Table I. Nmr and Kinetic Parameters for 5,5-Difluoro-*cis*-hydrindan and 2,2-Difluoro-*cis*-decalin Derivatives

		δ upfield from CF_3COOH, Hz								
Compound	Solvent	Equatorial	Axial	δ_{F-F}	J_{F-F}, Hz	% of conformation	E_a, kcal/mol	ΔG^*, kcal/mol	ΔH^*, kcal/mol	ΔS^*, eu
	Acetone	593	1354	761	234	74^a	15.0 ± 0.9	12.3		8
		528	875	347	236	26^b	14.5 ± 0.9	11.7		
	Propene	451	995	544	239	52^a	9.1 ± 0.6	12.1		−13
		302	699	397	242	48^b	9.2 ± 0.6	12.0		
	Ether	637	1326	688	241	65^a	11.3 ± 0.3	9.5	10.8	6
		570	890	320	241	35^b	10.5 ± 0.3	9.1	10.1	4
	Acetone	524	912	288	237	$75^{a,c}$	9.5 ± 0.1	10.4	9.1	−5
		371	704	333	237	$25^{b,c}$	9.2 ± 0.1	9.8	8.4	−5
	Acetone	655	1465	810	223	$70^{a,d}$	6.9 ± 0.2	7.6	6.5	−6
		457	804	347	223	$30^{b,e}$	6.2 ± 0.25	7.0	5.8	−7
	Acetone	428	1010	572	237	67	8.1 ± 0.36	7.8	7.8	0
		428	1010	572	237	33	7.7 ± 0.4	7.4	7.3	0.5

[a] Conformation with the fluorine *cis* to the bridgehead hydrogens in the axial position. [b] Conformation with the fluorine *cis* to the bridgehead hydrogens in the equatorial position. [c] The assignment of configuration here is arbitrary. [d] **5**. [e] **4**.

These spectra reproduce the line positions, shapes, and relative intensities of the experimental spectra for **4** ⇌ **5** and **6** ⇌ **7** as can be seen from Figures 1 and 2.

The resonance peaks of the fluorines in the minor conformer of 5,5-difluoro-*cis*-hydrindan at −130° were overlapped by the resonances of the equatorial fluorines of the major conformer and the chemical shifts were estimated by requiring that the low-temperature chemical shifts (corrected for the usual change with temperature) reproduce the averaged room-temperature spectrum.

The Arrhenius parameters for ring inversion were obtained from least-squares fits of plots of log $(1/\tau)$ against $1/T$. The free energies, enthalpies, and entropies of activation calculated in the usual way are presented along with nmr parameters for the separate conformations and some comparison substances in Table I.

Discussion

The conformers responsible for the various fmr resonances of 5,5-difluoro-*cis*-hydrindan (**4** and **5**) can be identified with reasonable certainty by the chemical shifts. The major conformer appears to be **5** with its axial fluorine assigned to the resonance at δ 1465 by analogy with the 1354-Hz resonance of the corresponding *cis*-decalin.[7] For the minor conformer, the axial fluorine atom is found at δ 804 because of a steric interaction with the 3-methylene group. This compares well with the 875-Hz resonance of the corresponding *cis*-decalin. The respective chemical shifts of the equatorial fluorines follow the same pattern, being 452 (528) Hz for **4** and 640 (593) Hz for **5** (the parenthetical numbers referring to the corresponding *cis*-decalin conformations). The general agreement is probably better than should be expected because of the substantial distortion of the six-membered ring by *cis* fusion with the five-membered ring.[16]

Identification of the major conformer of the 9-methyl derivative (**6** ⇌ **7**) is uncertain because the conformers have identical, or closely similar, chemical shifts for their axial and equatorial fluorines. The axial fluorine resonances appear at 1010 Hz downfield from trifluoroacetic acid which seems to indicate less steric interaction from the methyl group in **7** than appears to be the case for the corresponding methyl-*cis*-decalin[7] or methyl-*cis*-decalones.[8] The expected distortion of the chair structure of the six-membered ring by the five-membered ring involves pulling the methyl group away from a true axial-type position and thus should reduce the interaction of the methyl with the axial fluorine atom in conformation **7**. An expected[8] (and observed) result of this smaller than usual methyl–fluorine interaction is the smaller downfield shifts of the axial and equatorial fluorines of **7** as compared to the corresponding conformation of 2,2-difluoro-9-methyl-*cis*-decalin (see Table I). No solid basis exists for deciding whether **6** or **7** is the major conformation. The chemical shifts of course provide no help.

The angular methyl group in the *cis*-decalins[7] and *cis*-decalones[8] causes a *decrease* in the activation energy of inversion compared to the substances without the angular methyl group. The opposite is observed for the *cis*-hydrindans. The activation energy for inversion of the major conformer of 5,5-difluoro-*cis*-hydrindan was found to be 6.9 ± 0.2 kcal/mol while that for the major conformer of 9-methyl-5,5-difluoro-*cis*-hydrindan is 8.1 ± 0.35 kcal/mol. Possible reasons for this become clear on examination of molecular models. First, the chair–chair conformations of 2,2-difluoro-*cis*-decalin are expected to be less strained than the corresponding conformations of 5,5-difluoro-*cis*-hydrindan because of the fusion of the five-membered ring onto the six-membered ring. However, in the transition states for inversion, which involve essentially

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(16) E. L. Eliel and C. Pillar, *J. Amer. Chem. Soc.*, 77, 3600 (1955).

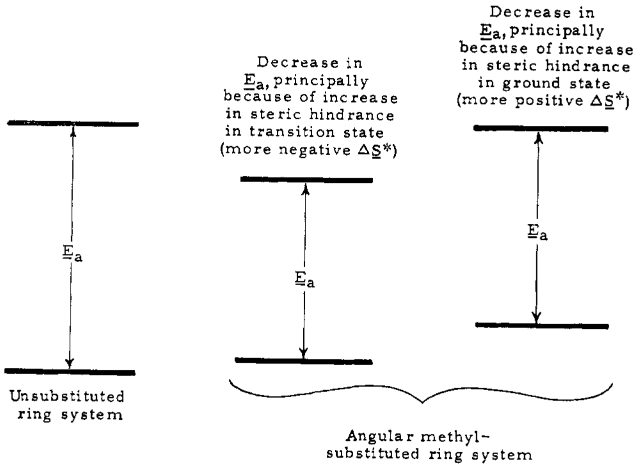

Figure 3. Schematic energy diagram showing possible effects of angular methyl substitution on energies of ground and transition states for *cis*-decalin derivatives.

boat-shaped six-membered rings in either case, the degree of strain should be more nearly comparable and for this reason we expect the hydrindan compounds to invert more rapidly, as they do. The steric effect of the angular methyl group in the ground-state conformations of 9-methyl-2,2-difluoro-*cis*-decalin[7] is expected to be larger than for 10-methyl-6,6-difluoro-*cis*-decal-2-one,[8] because, in the ketone, the methyl group is substantially pulled away from perfect axial positioning.[16] Similar effects of the methyl in **6** and **7** seem apparent in the fmr chemical shifts of these substances as mentioned above. On top of this, the reasonable-looking inversion transition state for 9-methyl-5,5-difluoro-*cis*-hydrindan appears to be somewhat more congested than that for 9-methyl-2,2-difluoro-*cis*-decalin and if so, this would also tend to lead to a relatively larger E_a for substitution of an angular methyl group in the hydrindan series than in the decalin series.

Although there is considerable uncertainty to the accuracy of the figures for the entropies of activation given in Table I, it is clear that there are substantial differences in ΔS^* associated with angular-methyl substitution in the *cis*-decalin[7,16] and *cis*-hydrindan series (Table I). Thus ΔS^* goes from $+8$ eu for 2,2-difluoro-*cis*-decalin[7] to -13 eu for the 10-methyl derivatives.[7] An opposite (and smaller) effect appears to be operative in the *cis*-hydrindan series.

A number of symmetrically 9,10-disubstituted *cis*-decalins have recently been reported[17] to have ΔS^* values for inversion around $+13$ eu similar to those found for unsubstituted *cis*-decalins.[7] It was suggested[17] that large positive entropies of activation for these compounds could be ascribed to a difference in symmetry between the ground and transition states which is not possible for the monosubstituted *cis*-decalins. However, the total variation in ΔS^* from $+13$ eu for disubstituted and -13 eu for the monosubstituted *cis*-decalins seems rather too large for differences in symmetry between the ground and transition states. It seems more reasonable that there are substantial contributions to the entropies of activation through changes in the degree of ordering of the parts of the molecule with respect to one another. The greater freedom in the transition state relative to the ground state, the greater will be the activation entropy.

The data of Table I seem to indicate a qualitative relationship between E_a and ΔS^* as the result of substitution of an angular methyl group. For the three available examples, ΔS^* is seen to become more negative when E_a decreases and more positive when E_a increases. Rather similar behavior is observed with some of the 4-substituted 1,1-difluorocyclohexanes studied earlier.[5c] If this parallelism is real, it may well indicate that our earlier[5c,7,8] interpretations of the effect of angular methyl substitution on the E_a values are incorrect. The argument follows (see also Figure 3).

A decrease in E_a on substitution of an angular methyl which arises from steric interactions could result primarily either from an *increase* in steric interactions in the *ground* state relative to the transition state or from a *decrease* in the steric interactions in the *transition* state relative to the ground state. A net increase in steric interaction in the ground state with respect to the transition state would be expected to increase the relative degree of molecular ordering in the ground state and lead to a more positive ΔS^*. The opposite trend in ΔS^* should be associated with increases of steric interactions in the transition state relative to the ground state and this, of course, is what is observed. However, it is our view that this interpretation should not be accepted as final until data on more systems are available, particularly because of the known uncertainties in determination of ΔS^* values by the nmr method.

The activation energy can become larger with substitution of the angular methyl in *cis*-hydrindan (whereas it becomes smaller with *cis*-decalin) because of (a) smaller steric interactions in the ground state along with (b) somewhat greater steric congestion in the transition state, and at the same time results in a more positive ΔS^* with the angular methyl group present.

Experimental Section

Melting and boiling points are uncorrected. Vapor phase chromatographic separations were performed with an Aerograph Model 760 "Autoprep" gas chromatograph, using an SE 30 column. Elemental analyses were carried out by Elek Microanalytical Laboratories, Torrance, Calif. Proton magnetic resonance spectra were taken at room temperature with the Varian Model A-60A spectrometer with tetramethylsilane as internal standard. Fluorine magnetic resonance spectra were recorded at 56.4 MHz with the Varian Model A-56/60A spectrometer (9-methyl-5,5-difluoro-*cis*-hydrindan) or with the Varian Model V4300D spectrometer (5,5-difluoro-*cis*-hydrindan). The reported fluorine chemical shifts are in hertz upfield from trifluoroacetic acid as internal standard. The spectra were calibrated with audio side bands of the reference signal using a Hewlett-Packard Model 200AB audio oscillator and Model 521-C frequency counter.

For 9-methyl-5,5-difluoro-*cis*-hydrindan, a sweep width of 1500 Hz was required and the spectrum was intensified using several scans with a Varian C-1024 computer.

5,5-Difluoro-*cis*-hydrindan. Cyclopentanone (42 g, 0.5 mol) and pyrrolidine (71 g, 1 mol) were heated under reflux in 150 ml of benzene for 4 hr with the water formed being separated by azeotropic distillation. The product was hydrolyzed with a mixture of 25 ml of acetic acid, 25 ml of water, and 12.5 g of sodium acetate. The resulting α,β-unsaturated ketone **8**, bp 70–72° (1 mm) (lit.[10] bp 80–81° (4 mm)), gave an nmr spectrum showing one vinyl proton at δ 5.72. The ketone **8** (1 g) in 150 ml of ethanol containing 5 ml of 3 *N* hydrochloric acid was shaken with hydrogen over 500 mg of palladium on charcoal until hydrogen absorption ceased. A 2-g sample of crude *cis*-hydrindan-5-one (**9**) prepared in this way was mixed with 0.26 ml of water and 20 ml of methylene chloride and treated with 15.8 g of sulfur tetrafluoride in a steel reaction vessel for 17 hr at 20°. The dark-brown solution was washed with sodium bicarbonate solution, dried over sodium sulfate, purified by chro-

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(17) J. Altman, H. Gilboa, D. Ginsburg, and A. Loewenstein, *Tetrahedron Lett.*, 1329 (1967).

matography on neutral alumina (Woelm), distilled, and finally separated from traces of impurities by preparative vpc to give 5,5-difluoro-*cis*-hydrindan (**4** and **5**), bp 170–171°. The proton nmr spectrum of the products showed no low-field absorptions and the ^{19}F spectrum showed an AB quartet at 20° which was temperature dependent, appearing as two overlapping AB quartets at −130°.

Anal. Calcd for $C_9H_{14}F_2$: C, 67.5; H, 8.8. Found: C, 68.1; H, 8.8.

9-Methyl-5,5-difluoro-*cis*-hydrindan. Cupric acetate (500 mg) was added to a solution of methylmagnesium bromide prepared from 2 g of magnesium and 7 g of methyl bromide in tetrahydrofuran. The α,β-unsaturated ketone **8** (5 g) in tetrahydrofuran was added over 30 min and the mixture heated under reflux for a further 5 hr. The resulting crude 9-methyl-*cis*-hydrindan-5-one (**10**) had a proton spectrum showing the 9-methyl group at δ 1.04 and no low-field protons. A 2-g sample of the crude ketone in 20 ml of methylene chloride and 0.24 ml of water was treated in a steel reaction vessel with 14.2 g of sulfur tetrafluoride for 16 hr at 20°. The usual isolation procedure gave a crude dark-brown product which was purified by chromatography on alumina prepared in pentane. Elution with pentane gave 0.9 g of 9-methyl-5,5-difluoro-*cis*-hydrindan whose ^{19}F spectrum showed a single AB quartet at 20°. Attempts to purify further the compound by preparative vpc were unsuccessful.

Nuclear Magnetic Resonance Spectroscopy. Conformational Equilibria and Equilibration of 4,4-Difluorocyclohexanone and 6,6-Difluoro-*cis*-decal-2-ones[1]

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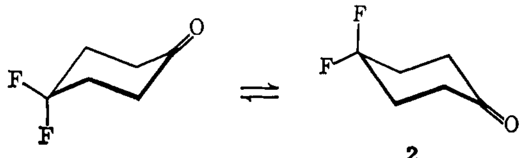
Received April 24, 1968

Abstract: The rates of ring inversion and conformational equilibration of 6,6-difluoro-*cis*-decal-2-one and 10-methyl-6,6-difluoro-*cis*-decal-2-one have been determined using fluorine magnetic resonance spectroscopy. The activation energies were found to be 11.3 ± 0.3 and 9.5 ± 0.1 kcal/mol, respectively. 4,4-Difluorocyclohexanone, however, appears to exchange its fluorines between conformationally nonequivalent sites rapidly on the nmr time scale even at −180°.

Nuclear magnetic resonance spectroscopy has been employed very extensively for conformational analysis and determination of rates of conformational equilibration.[3] Recently, emphasis has been placed on the use of fluorine magnetic resonance spectroscopy as an aid to conformational analysis, because fluorine chemical shifts are much more sensitive to chemical environment[4] than those of protons. The advantages of fluorine magnetic resonance spectroscopy for studies of conformational equilibration have recently been reviewed.[5] Among the successful applications are those to cyclobutane,[6] cyclohexane,[7] cycloheptane,[5,8] cyclooctane,[8] and *cis*-decalin[9] derivatives.

The "fluorine-labeling" technique was used in the present study of cyclohexanone and of some *cis*-decal-2-ones which have special interest as models of the A, B rings of the 3-keto steroids.

So far, no reports are available of the successful use of proton magnetic resonance to detect "freezing out" of the chair–chair interconversion of cyclohexanone at low temperatures.[10] Here, "fluorine labeling" might be expected to be helpful in studies of the interconversion of the cyclohexanone forms **1** and **2** because of the generally much larger chemical-shift differences between axial and equatorial fluorines than between axial and equatorial hydrogens.[7]



1 **2**

The inversion of cyclohexanone rings in other systems has not been studied. Molecular models show that *cis*-decal-2-one (**3**) like *cis*-decalin would be expected to interconvert between the two diasteromeric conformations **4** and **5**.[11] Introduction of *gem*-fluorines at the 6 position of **3** provides two conformations, **6** and **7**.

The equilibrium constant connecting **6** and **7** is not expected to be unity because the axial fluorine atom in

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[1] Supported in part by the National Science Foundation.

[2] On leave of absence from the Department of Organic Chemistry, The University of Sydney, Sydney, Australia.

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[11] The existence of the enantiomeric forms of **4** and **5** and related substances to be discussed later is taken to be understood.