

¹H Nuclear Magnetic Resonance Spectra of Cyclic Monoenes: Hydrocarbons, Ketones, Heterocycles, and Benzo Derivatives

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I. Scope

Interest in the high-resolution ¹H NMR spectra of cyclic olefins originates from various sources. Besides the aspect of basic structure determination that certainly ranges among the most important applications, the conformational analysis of cyclic olefins has been tremendously advanced through the information obtained from chemical shifts and spin-spin coupling constants. In addition, these parameters are dependent on the electronic structure of the individual systems and valuable details about chemical bonding became available.

On the other hand, the NMR spectra of cyclic olefins with known stereochemistry have served as an important source of experimental data that paved the way for a better understanding of the mechanisms which determine chemical shifts and coupling constants of protons in organic molecules. Empirical

NMR/chemical structure correlations could thus be established and theoretical investigations were stimulated.

Besides these static parameters related to molecular geometry and bonding, the sensitivity of the NMR method to intramolecular rate processes has led to a wealth of information related to the dynamic properties of molecules, including conformational equilibria as well as valence isomerizations. The temperature dependence of the spectrum has thus been studied for many systems.

It is therefore not surprising that a large number of NMR investigations dealing with cyclic olefins has appeared in recent years, and as a first step in an attempt to summarize the results obtained this review covers work concerned with cyclic monoenes. The emphasis lies on simple cycloalkenes and their benzo derivatives, but unsaturated ketones, heterocycles, bicyclic compounds, and cycloalkynes are treated as well though less exhaustively. The main interest is focussed on high-resolution NMR work in isotropic solvents; however, investigations on systems partially oriented in the nematic phase are also included. Structural and theoretical work dealing with the specific systems is cited. In cases where ¹⁹F NMR work contributed significantly to our knowledge of structure and conformation, these investigations have also been included, whereas ¹³C NMR work is generally not considered.

The material is arranged in main divisions following ring size. Since there are practically no investigations that treat rings larger than cyclodecene, this compound quite naturally sets the limit for our survey. The main accent was put on those papers that are primarily concerned with the NMR spectrum of the individual compounds and where efforts have been made to measure the NMR parameters of the system as accurately and as completely as possible. On the other hand, many data of general interest are contained in references dealing with aspects of synthesis or reaction mechanism, and these sources have been cited frequently, but no attempt was made to cover them completely. Also, for data of trivial nature, the reader is referred to compilations of NMR parameters.¹⁻³ Efforts have been made to screen the literature as thoroughly as possible, including journals received up to the middle of 1976. Work that appeared or came to our attention past this date is collected in the Addendum that should be consulted by the reader parallel to the main text. Even so we are aware of the possibility that we may have missed some important articles, and apologies are made for these shortcomings in advance.

Structural formulas are given for all compounds whose NMR spectra are discussed in some detail. Particular protons are indexed by numbers or letters that are used in turn to identify the NMR parameters. The numbers generally do not conform with the labeling of the carbon skeleton laid down by chemical nomenclature. If for a particular compound two or more parameters are identical for reasons of molecular symmetry, only one of

them is listed in the table. Chemical shifts are given in ppm on the δ scale with positive values downfield from the reference signal, if not stated otherwise that of tetramethylsilane (TMS). Coupling constants are in Hz. Those cited to two decimal places are believed to be reliable within 0.1 Hz or less; other data may be in error by 0.2 Hz or more.

Quite naturally, the quality of the various contributions to the field differs widely, and the amount of material presented could have been easily reduced by a factor of 0.5 or so if a strict standard as to the accuracy of the experimental and theoretical work would have been followed. Most authors do not give experimental errors for frequency measurements and in many cases poor spectra are reported. In addition, first-order treatments are still popular in cases where with some extra effort more reliable data could have been obtained. On the other side, one must admit that in a number of cases even the most qualitative information from a poorly resolved spectrum may be of chemical interest and of importance for a specific problem. We therefore refrained from ignoring such sources completely. We would, however, like to stress the need for accurate work and refer to the discussion of details connected to experiment and to the theory of spectral analysis given by Abraham.⁴ Also, an astonishingly large number of papers does not quote experimental details like the concentration of the solution used for the measurement.

II. Related Reviews

Several reviews treating material closely related to the present subject have appeared. Of special interest are Sternhell's discussions of H,H coupling constants in general^{5,6} and the survey of H,H long-range coupling constants given by Barfield and Chakrabarti.⁷

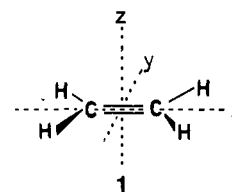
The results of conformational analysis of seven-membered rings have been treated by Tochtermann,⁸ and an extensive account of the NMR work on cyclopentadienyl compounds has been presented by Sergejev.⁹ The NMR investigations of conformational changes in general have been surveyed by Thomas¹⁰ and Sutherland,¹¹ and a recent monograph on "Dynamic NMR Spectroscopy"¹² contains reviews by Binsch on NMR bandshape analysis and by Anet on the conformation of ring compounds. The *R*-value method, developed to derive information about the geometry of cyclic compounds from H,H coupling constants, was discussed by Lambert,¹³ and the numerous data obtained for annulenes (only of peripheral interest in the present context) have been collected by Haddon, Haddon, and Jackman.¹⁴ The NMR spectra of simple heterocycles are the topic of a thorough treatment by Batterham,¹⁵ and most of the material discussed there is not included in the present survey. Finally, the theoretical methods used to calculate spin-spin interactions that are relevant to our discussion have been reviewed by Barfield and Grant¹⁶ and by Murrell.¹⁷

III. Introduction

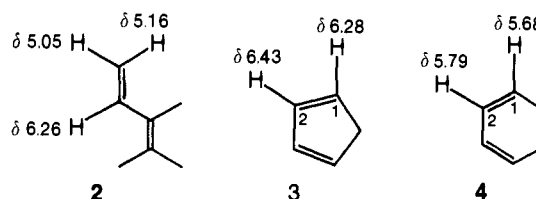
Before starting to present the results obtained for individual systems in detail, it seems practical to discuss some general aspects of chemical shifts and spin-spin coupling constants for protons in cyclic olefins.

A. Chemical Shifts

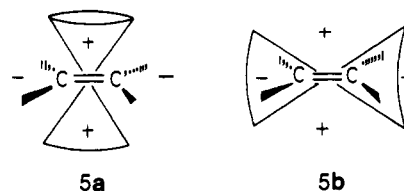
In the absence of special substituent effects the diamagnetic anisotropy of the double bond will be the dominating factor that influences the resonance frequencies. It is generally agreed today that protons above or below the plane of the double bond and near the *z* axis (1) are shielded, whereas deshielding exists in the *x,y* plane. The calculations,^{18,19} the results of which have been presented in graphical form,³ disagree with respect to the sign of the effect near the *x* axis, where shielding¹⁹ as well as



deshielding¹⁸ has been predicted. Only the second alternative, however, seems supported by the majority of the experimental findings. In buta-1,3-diene (2), existing predominantly in the *s*-trans conformation,^{20,21} the protons near the *x* axis of the second double bond are deshielded.²² Similar results are found for the inner protons of the diene systems of cyclopenta-1,3-diene (3) and cyclohexa-1,3-diene (4).²³

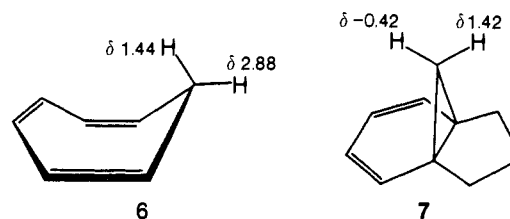


In still another calculation^{24,25} it was found that shielding instead of deshielding might also occur in the *x-y* plane of the double bond. To substitute the older picture for the shielding cone of the C=C bond (5a),²⁶ model 5b was proposed. [It should be



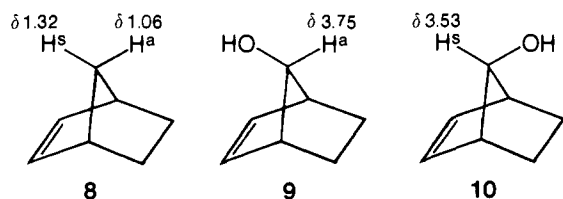
remembered that shielding cones of type 5a or 5b with an opening angle of 109.4° apply only for groups with axial symmetry. In the present context they are simplified representations of the true anisotropy effect of the CC double bond.] However, since in only 6 out of 21 experimental data used for the evaluation of the diamagnetic anisotropies of the double bond the contribution of the double bond to the shielding was predominant and since none of these came from protons near the *y* axis, it seems premature to discard 5a in favor of 5b. On the contrary, the chemical shifts for 2, 3, and 4 strongly support model 5a. In 2 the central protons that come close to the *y* axis of the second double bond are the most strongly deshielded. In going from 4 to 3 H(1) moves to the *y* axis of the opposite C=C bond, and again deshielding is observed. Other examples will be cited in section IV.A.

From the numerous cases of protons situated in the shielding region near the *z* axis of the double bond, a few examples from the class of cyclic olefins are cited to demonstrate the effect. In cyclohepta-1,3,5-triene (6) the 3,4 double bond is responsible

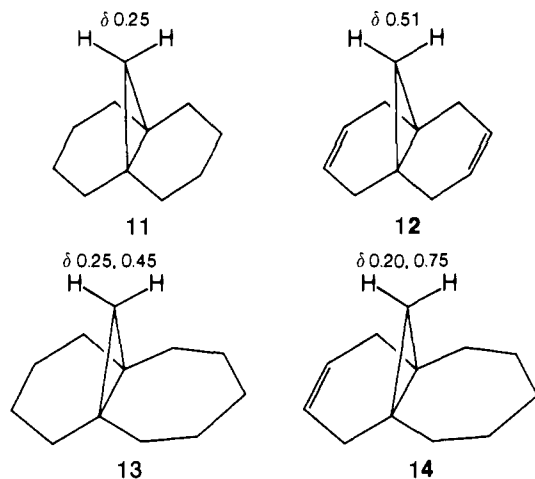


for the shielding of the quasi-axial methylene proton,²⁷ and in the norcaradiene system^{28,29} (7) a large shift difference for the cyclopropane protons results from the combined effect of the two double bonds. Of special interest are the observations made for the norbornenes.^{30,31} In *syn*-7-methylnorbornene the CH₃ resonance is shifted to higher field by 0.09 ppm as compared with the same resonance in the *anti* isomer.³ In hydrocarbon 8

the syn proton at C(7), however, is deshielded with respect to the anti proton, whereas the same proton is shielded in a pair of syn- and anti-substituted norbornenes³⁰ (9, 10). Predictions

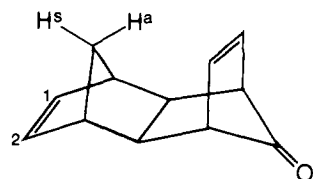


as to the sign of the anisotropy effect are, therefore, difficult to make, if the proton considered is located near the borderline between the shielding and the deshielding region of the double bond. This uncertainty is due in most cases to an insufficient knowledge of the molecular geometry, and occasionally to the small magnitude of the effect in this region and to the approximate nature of the calculations.



Other examples of similar unexpected deshielding effects of the double bond are provided by compounds 11 to 14.³² An explanation for the surprising downfield shift of the bridge methylene resonance in 12 as compared to 11 is offered by the assumption that the anti proton is deshielded by the double bond more strongly than the syn proton is shielded. If this is true, the assignment $\delta(H_{syn}) = 0.25$ and 0.20 , $\delta(H_{anti}) = 0.45$ and 0.75 ppm for the bridge protons in 13 and 14, respectively, results. Consequently, for these protons in 12 an overall effect of $\Delta\delta = +0.25$ ppm is predicted if similar geometry is assumed, in perfect agreement with the experimental observation.

Special situations arise in cases where steric compression leads to large deshielding effects. An example was found with compound 15 and the corresponding ketal, where H^a resonates



15

at δ 2.44 and 2.55, that is, 1.38 and 1.49 ppm at lower field than the anti-methylene proton in norbornene, despite its location near the z axis of the second double bond.³³ A strong van der Waals interaction³⁴ between the hydrogen 1s orbital and the π cloud of the double bond was invoked to explain this observation. H^s, on the other hand, is shielded by 0.38 and 0.43 ppm, respectively, and it seems reasonable to assume that the electron density is raised at this position as a consequence of the van der Waals effect. Also, the steric interaction may force H^s closer to the z axis of the C(1)=C(2) bond.

For substituted derivatives, additional shielding effects of the

various groups present (anisotropy, ring current, electric field, and van der Waals effects³) have to be considered to account for the observed chemical shifts. Substitution at the π system will furthermore influence the π -charge density at the carbon atoms, and this effect may be evaluated using the empirical relation

$$\Delta\sigma = K\Delta Q_\pi$$

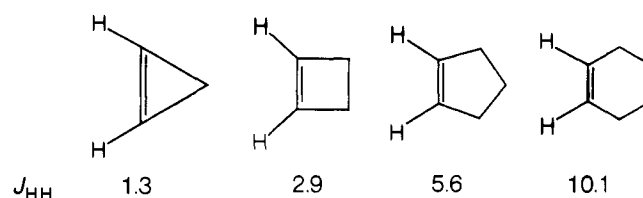
where $\Delta\sigma$ is the change in the proton shielding constant. ΔQ_π is the excess charge density, and K is a proportionality constant with a magnitude in the order of 8–12 ppm/electron.^{35–40}

In the case of fully conjugated cyclic π systems, the "ring current effect" has a major influence on the proton resonance frequencies, and this aspect has been discussed in detail.¹⁴ Both diamagnetic⁴¹ and paramagnetic⁴² "ring current effects" have been theoretically predicted and experimentally verified in cases of delocalized $(4n + 2)$ and $(4n)$ π systems, respectively, thus making proton NMR one of the most powerful methods for the elucidation of the electronic structure of cyclic unsaturated compounds. The magnetic behavior of annulenes as well as cyclic olefins was also the object of susceptibility measurements by the NMR method⁴³ and of studies concerned with specific solvent-solute interactions, where solvent shifts of the proton resonance frequency in chloroform⁴⁴ or acetonitrile⁴⁵ have been employed to detect magnetic anisotropies.

B. H,H Coupling Constants

Spin-spin coupling constants between protons in cyclic olefins are expected to yield a great deal of information concerning structure and conformation. Indeed, cyclic olefins have been used frequently to demonstrate certain relations that exist between the magnitude and sign of the coupling constants and the molecular geometry.⁴⁶

In the case of vicinal coupling, the dependence of 3J on the magnitude of the HCC valence angles⁴⁷ became clear from the observation made for cyclic monoenes, where increasing values for 3J across the double bond have been found with increasing ring size:^{48–51}



In addition, cyclic olefins were used to derive the equation^{52,53}

$$^3J = -35.10R_{\mu\nu} + 56.65$$

that correlates vicinal coupling constants across the double bond in six-membered rings with the CC bond length $R_{\mu\nu}$. Using HMO bond orders $P_{\mu\nu}$, the relation

$$^3J = 7.42P_{\mu\nu} + 2.69$$

was found⁵² to hold for olefinic systems of this particular ring size. Data for fulvenes, on the other hand, led to

$$^3J = -32.26R_{\mu\nu} + 48.45$$

suitable both for isolated and for conjugated double bonds.⁵⁴

On the basis of these correlations between 3J and CC bond length or π bond order (also proposed theoretically^{47,55} and first established experimentally for benzenoid aromatics⁵⁶), many important informations about the ground-state properties of cyclic π systems have been obtained. In particular, the alternation or nonalternation of vicinal coupling constants on neighboring HC=CH fragments may be used in suitable cases

TABLE I. Survey of ^1H and ^{13}C NMR Parameters of Cycloalkenes^a

Ring size ^k	$\delta(\text{=CH})$	$\delta(\text{=CCH}_2\text{-})$	$\delta(\text{=CCCH}_2)$	$^3J(\text{HC=CH})$	$^1J(\text{=}^{13}\text{C-H})$	$\delta(\text{=}^{13}\text{C-})$	$\delta(\text{=C-}^{13}\text{CH}_2)$	Lit.
3	7.01	0.92		1.3	228.2	108.7	2.3	b-d
4	6.03	2.57		2.85	170	137.2	31.4	d-f
5	5.60	2.28	1.90	5.57	161.6	130.8	32.8	d,g,f
6	5.59	1.96	1.65	10.11	158.4	127.4	25.4	d,g,f
7	5.71	2.11	1.62, 1.49	11.02	156.2	132.7	29.6	d,g,f
c-8	5.56	2.11	1.50	10.41	156.0	130.4	26.0	d,g,f
t-8	5.40			16.0	151			h,i
c-9				10.7				j
t-9	5.2							h
c-10	5.36			10.8				j
t-10	5.43			15.1				j

^a Chemical shifts refer to tetramethylsilane as standard. ^b Reference 90. ^c Reference 83. ^d Reference 102. ^e Reference 110. ^f Reference 84. ^g Reference 51. ^h Reference 85. ⁱ Reference 479. ^j Reference 49. ^k c = cis; t = trans.

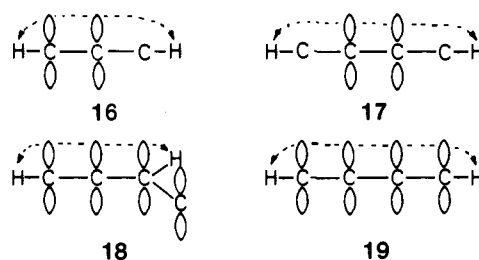
to distinguish localized (olefinic) from delocalized (aromatic or anti-aromatic) cyclic π systems.⁵⁷⁻⁵⁹ In an extension of the earlier approach,⁵⁸ the vicinal H,H coupling constants in the benzene ring of benzo[*n*]annulenes are now used to determine the electronic ground-state properties of the respective [*n*]annulenes.^{60,61}

Turning to long-range coupling constants, we find that, in particular, the magnitude and sign of the allylic coupling $^4J_{\text{trans}}$ and its dependence on conformation have been evaluated using experimental data derived from the NMR spectra of cyclic olefins.^{62,63} Recent MO calculations⁶⁴ using the INDO method⁶⁵ are in good agreement with the experimental results. The same is true for the homoallylic coupling constant 5J , whose dependence on geometry has been investigated in detail.⁶⁶ Calculations⁶⁷ for H,H coupling constants in several cycloalkenes performed with the finite perturbation method⁶⁸ within the INDO approximation⁶⁵ substantiate all these findings and demonstrate that this approach is a reliable tool for the interpretation of experimental results.

In this review, vicinal coupling constants will be discussed on the basis of the Karplus theory.^{47,69} For long-range couplings, the σ - π separation model⁷⁰⁻⁷² will be adopted since the interpretation of experimental data from unsaturated compounds in terms of separate contributions by the σ and π framework, $J(\sigma)$ and $J(\pi)$, respectively, has proved successful. The usefulness of this concept has been convincingly demonstrated by investigations dealing with acyclic polyenes.⁷³ A correction of the older theory,⁷² however, was found necessary.⁷⁴⁻⁷⁷ The π contributions to H,H coupling constants are characterized by⁷³ (1) independency of configuration, i.e., for $2^4J_{\text{cis}}(\pi) = ^4J_{\text{trans}}(\pi)$; and (2) by the observation that the replacement of a hydrogen atom in a C(sp²)-H bond by a methyl group changes the sign of $J(\pi)$ but only slightly the magnitude.⁷⁸ More recently, $J(\pi)$ is evaluated using MO theory and comparing results of calculations performed with INDO and CNDO/2 wave functions or INDO wave functions obtained with partial neglect of one-center exchange integrals.^{79,80} In the CNDO/2 method⁶⁵ one-center σ - π exchange integrals that transmit electron spin information from the σ to the π system are completely neglected. Thus, the difference $J_{\text{calcd}}(\text{INDO}) - J_{\text{calcd}}(\text{CNDO}/2)$ allows an estimate of the π -electron contribution to the particular coupling constant.^{65,79}

In addition to the conventional allylic and homoallylic π -coupling path, characterized by spin correlations of types **16** and **17**, respectively, spin correlations of type **18** and **19** will contribute to the coupling in conjugated systems. These mechanisms have been termed "vinylic"⁸¹ or $J(\pi)_{\text{conj}}$ ⁸² and were first considered in aromatic compounds by McConnell.^{70,71}

In the following text the notation used for H,H coupling constants complies to the present usage. nJ stands for coupling over *n* bonds and $^nJ_{\text{cis}}$ and $^nJ_{\text{trans}}$ designate coupling between protons in a cis or trans arrangement at a double bond or a single bond



in a conformationally rigid compound with dihedral angles near 0 or 180°, respectively; J_{aa} , J_{ae} , J_{ee} describe couplings of protons in axial and equatorial positions.

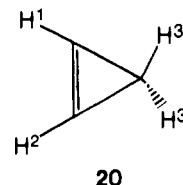
The terms "axial" and "equatorial", while strictly applicable only in the cyclohexane system, are used to describe stereochemically similar situations in other ring systems, usually with the prefixes "quasi" or "pseudo".

Finally, as an introductory survey, the NMR data of cycloalkenes, including ^{13}C chemical shifts, are presented in Table I. In addition, reference is made to a ^{19}F NMR investigation of various fluorinated cycloalkenes.⁸⁶

IV. Individual Compounds

A. Cyclopropene

Because of molecular C_{2v} symmetry, the protons of cyclopropene (**20**), whose structure has been determined by electron diffraction⁸⁷ and by microwave spectroscopy,^{88,89} give rise to a classic A_2X_2 system with $\delta(1,2)$ 7.01, $\delta(3,3')$ 0.92, and $J(1,3) = 1.75$ Hz.⁹⁰ The magnitude of $J(1,2)$ was obtained from the ^{13}C satellites of the olefinic protons, which yielded 1.3 Hz for this interaction and in addition $^1J(^{13}\text{C}, ^1\text{H}) = 226$ Hz; 228.2 Hz was measured for the same constant in the ^{13}C NMR spectrum of **20**.⁸³ From these experiments it was not possible to deduce the



magnitude of the geminal H,H coupling constant as well as the sign of this and the other spin-spin interactions, and these parameters remain unknown. For 1-methylcyclopropane $^1J(^{13}\text{C}, ^1\text{H}) = 172$ Hz was found at the CH_2 group,⁹¹ whereas ^{13}C NMR again yielded a slightly different value (169.0 Hz).⁸³ The other one-bond $^{13}\text{C}, ^1\text{H}$ coupling constants for **20** and its 1- and 3-methyl derivative are as follows:⁸³ **20** C-3 167.0 Hz; 1-Me-**20** C-2 224.7 Hz, CH_3 129.0 Hz; 3-Me-**20** C-1 224.0 Hz, C-3 162.4 Hz, and CH_3 124.5 Hz.

NMR data for a number of methyl- and chloro-substituted

TABLE II. NMR Data of Cyclopropenes and Cyclopropenones

Compound	Solvent	$\delta(1,2)$	$\delta(3,3')$	$\delta(\text{CH}_3)$	$J(1,2)$	$J(1,3)$	$^1J(^{13}\text{C}, ^1\text{H})^a$	Ref
Cyclopropene	Neat	7.06	0.93		1.3	1.75	226, 228.2	83, 90, 102
	CCl_4^f	7.01	0.92					
1-Methyl-		6.40	0.83	2.13			224.7	83, 92
3,3-Dimethyl- ^b		7.32		1.15			221	91, 93
1,3,3-Trimethyl- ^c		6.65		1.06 (6 H): 2.00 (3 H) 0.99: 1.90			218	91, 94
1,2,3,3-Tetramethyl-								94
1-Chloro-	CCl_4	6.65	1.61			1.5		95
3-Chloro-	CCl_4	7.57	4.23			1.5		95
1,2-Dichloro-	CCl_4		2.07					95
1,3-Dichloro-	CCl_4	7.20	4.48					95
3,3-Dichloro-	CCl_4	8.00					239 \pm 2	95
1,3,3-Trichloro-	CCl_4	7.67					240 \pm 2	95
1,2,3-Trichloro-	CCl_4		4.72					95
1,2-Diphenyl-	CDCl_3		1.52					96
Cyclopropenone	CDCl_3	9.08			3.9 \pm 0.1		217 \pm 1	97
	H_2SO_4^g				1.3 \pm 0.1		250	97
1-Methyl-	CCl_4	8.66		2.40			213 \pm 4	<i>d</i>
1,2-Dimethyl-	CCl_4			2.25				<i>d</i>
1- <i>n</i> -Propyl-		8.68						<i>e</i>

^a Olefinic position. ^b $J(\text{CH}_3, \text{H}) = 0.7$ Hz. ^c Allylic $J(\text{CH}_3, \text{H}) = 1.1$ Hz. ^d Reference 99. ^e Reference 100. ^f 15% v/v. ^g Concentrated.

cyclopropenes have been reported,⁹²⁻⁹⁶ as well as those for cyclopropenone,⁹⁷ where earlier data^{95,98} were in error (Table II).

The unique position of **20** among the cycloalkenes is apparent from its chemical shifts, where additional factors cause an up-field shift for the CH_2 resonance of 1.65 ppm and a downfield shift for the $=\text{CH}$ -resonance of 0.98 ppm if cyclobutene is taken as reference. A ring current effect within the σ skeleton, which received new experimental support in the case of cyclopropene,¹⁰¹ was proposed as the origin of these shifts.¹⁰² It was also suggested⁹¹ that at least part of the deshielding of the olefinic protons is due to the higher *s* character in the CH bonds. From $^1J(^{13}\text{C}, ^1\text{H})$ one calculates approximately 44% on the basis of the empirical Muller-Pritchard relation.¹⁰³

Compared to cyclopropane, the CH_2 protons of **20** are deshielded by 0.7 ppm. Assuming similar shielding contributions from the σ bonds in both three-membered rings, this additional effect can be ascribed to the diamagnetic anisotropy of the double bond in **20**. An angle of 64° between the *z* axis and the vector leading from the midpoint of the $\text{C}=\text{C}$ bond to one of the methylene protons is calculated from the structural data.⁸⁸ Deshielding is thus expected according to model **5a**, in agreement with the experimental findings.

The existence of a diamagnetic ring current in **20** has also been postulated on the basis of microwave studies¹⁰⁴ that led to the determination of magnetic anisotropies $\Delta\chi$ (out-of-plane minus average in-plane magnetic susceptibility) of several three-membered ring compounds from the measurement of their molecular Zeeman effect (Table III). These data suggest additivity for $\Delta\chi$ contributions originating from the cyclopropane σ skeleton and the double bond. They support, therefore, the analysis of the proton chemical shifts in **20** given above.

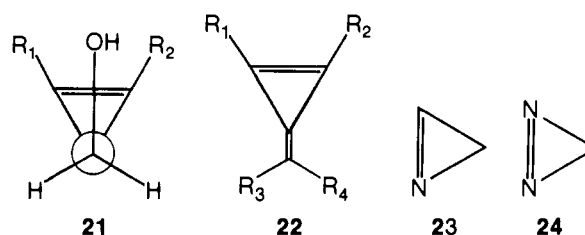
Compared to **20**, the olefinic protons in cyclopropenone are less shielded by 2 ppm, a result that is most likely due to the combined effect of: (a) the diamagnetic anisotropy of the carbonyl group, (b) the partial positive charge induced in the 2,3 positions, and (c) the electric field effect caused by the dipole moment of 4.39 D. Finally, the high-field shift found for the olefinic resonance in 1-chlorocyclopropene was attributed to the large CCCl angle that exists in the three-membered ring (150°), since the proton is now in the diamagnetic shielding region of the $\text{C}-\text{Cl}$ bond.⁹⁵

In an investigation of the conformational behavior of primary and tertiary cyclopropenylcarbinols using vicinal coupling and pyridine-induced solvent shifts, it was found that conformation

TABLE III. Magnetic Susceptibility Anisotropies $\Delta\chi$ of Three-Membered Rings¹⁰⁴

Compound	$\Delta\chi, 10^{-6}$ erg/(G ² mol)	Ref
Cyclopropane	-10.0	<i>a</i>
Methylenecyclopropane	-16.6 \pm 0.6	<i>b</i>
Cyclopropene	-17.0 \pm 0.5	<i>a</i>
Cyclopropenone	-17.8 \pm 1.0	104
Propene	-6.4 \pm 0.8	<i>c</i>

^a Reference 105. ^b Reference 106. ^c Reference 107.



21 is the least favored.¹⁰⁸ No definite results with respect to the rotation around the $\text{C}-\text{O}$ bond could be obtained from $^3J(\text{HCOH})$. Substituted methylenecyclopropenes of type **22** were synthesized¹⁰⁹ in order to study rotational isomerism about the exocyclic double bond. From the temperature-dependent NMR spectra activation barriers ΔG^\ddagger of 14.0 to 21.0 kcal/mol were determined at the coalescence temperatures. Steric and electronic factors determining the barriers were discussed. Finally, the scattered NMR data for azirine (**23**) and diazirine (**24**) have been summarized, and evidence for the shielding properties of the diazirine ring is available.¹⁵

B. Cyclobutene

The spectrum of cyclobutene (**25**) shows two sharp lines at δ 2.57 and 6.03, indicating deceptive simplicity. Analysis¹¹⁰ was

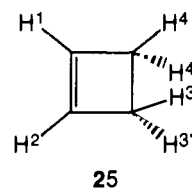


TABLE IV. NMR Parameters of Cyclobutene¹¹⁰

$\delta(1,2)$	(a) Chemical Shifts (CCl ₄)		2.57
	6.03	$\delta(3,4)$	
	(b) Coupling Constants		
$J(1,2)$	+2.85	$J(^{13}\text{C},\text{H}^1)$	170
$J(1,3)$	-0.35 (-1.00) ^a	$J(^{13}\text{C},\text{H}^3)$	140
$J(1,4)$	+1.00 (0.35) ^a	$J(^{13}\text{CCH}^1) - J(^{13}\text{CCH}^2)$	+4.0
$J(3,3')$	-12.00	$J(^{13}\text{CCH}^4) - J(^{13}\text{CCH}^3)$	+7.0
$J(3,4)$	+4.65		
$J(3,4')$	+1.75		

^a Alternative assignment.

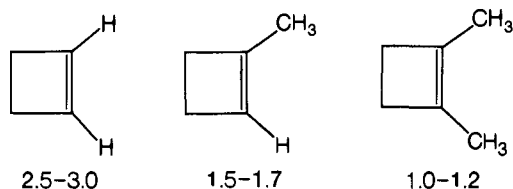
performed using the ¹³C satellites of olefinic and methylene protons as well as information obtained from di- and trideuterated species. The results are given in Table IV.

The calculated spectrum was sensitive to the difference of the long-range ¹³C,H coupling constants but was not affected by an interchange of $J(1,3)$ and $J(1,4)$ in combination with a sign reversal. The assignment given for these parameters is based on the observation that in the spectrum of the mixture of 1,3,3-trideuterio- and 2,3,3-trideuteriocyclobutene the CH₂ absorption at higher field shows a smaller splitting than that at lower field. Because it is known that deuterons exert generally a shielding effect on neighboring protons,¹¹¹ the high-field absorption was assigned to the 1,3,3 isomer.

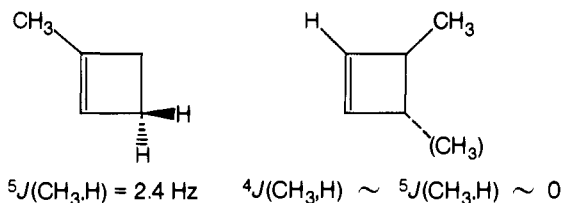
A reasonably good fit between calculated and observed spectra was also obtained using the combination $J(1,3) = +0.3$ and $J(1,4) = -0.9$ Hz. This solution can, however, be discarded since the positive sign of vicinal coupling H,H constants is well established.³

The proton spectrum of **25** oriented in a nematic liquid crystal solvent has also been analyzed,¹¹² and the geometry obtained was found in excellent agreement with that derived from microwave spectroscopy.¹¹³

In a careful study¹¹⁴ the ¹H NMR data for 19 differently substituted cyclobutenes, methylenecyclobutenes, and 1,2-bis-(methylene)cyclobutenes were determined, together with the one-bond ¹³C,¹H coupling constants. Data were derived directly from the mostly complicated spectra through the extensive use of double and triple resonance experiments and the inspection of the ¹³C satellite spectra. Computer simulation was employed to confirm the results by comparison between theory and experiment, but no iterative analyses were performed. The discussion is focussed on the influence that structural changes, which are introduced by the increasing number of sp² carbons within the four-membered ring, have on ¹J(¹³C,¹H). For ³J_{cis} and the allylic and homoallylic H,H coupling constants, the following ranges were found typical:



In another investigation,¹¹⁵ long-range coupling constants of similar magnitude were observed for methyl groups that occupy an olefinic position due to the favorable geometry of σ and π bonds. On the other hand, a methyl group in 3 or 4 position shows no coupling to the olefinic protons:^{114,115}

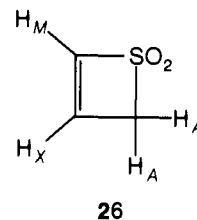


A number of fluoro-substituted cyclobutenes have been studied¹¹⁶ with the following results for the various $J(\text{H},\text{H})$ values:

$J(1,2)$	+3	$J(3,3')$	-12 to -15
$J(1,3)$	-0.5	$J(3,4)$	+4 to +6
$J(1,4)$	+1 to +2	$J(3,4')$	+1 to +4

For 3,3,4,4-tetrafluorocyclobutene $J(1,2) = 3.48$ Hz was found.¹¹⁷ The increase of this coupling as compared with the analogous interaction in the hydrocarbon is expected on the basis of the known alternation of substituent effects on vicinal coupling constants.^{118,119} The absolute magnitude of the change (0.63 Hz) is, however, much smaller than that found, for example, in fluorobenzene, where one substituent is sufficient to raise ³J by 0.81 Hz over the benzene value.¹²⁰ A possible explanation seems to be that in the present case the effect of one CF₂ group is partly cancelled by the second CF₂ group, since the number of intervening bonds is either (1) leading to an increase of $J(1,2)$ or (2) leading to a decrease of $J(1,2)$.

For several other systems that contain a partial cyclobutene, structure NMR data have been reported¹²¹⁻¹²⁴ (Table V). In a careful study of thiete 1,1-dioxide (**26**) all H,H and ¹³C,¹H coupling



constants were determined from ¹H and ¹³C NMR spectra.¹²⁵ Sign determinations were performed by tickling and triple resonance experiments. The spectrum is of the A₂MX type and yielded $\delta(\text{A}) = 4.580$, $\delta(\text{M}) = 6.785$, $\delta(\text{X}) = 7.178$ ppm; $J(\text{A},\text{X}) = +1.60$, $J(\text{A},\text{M}) = -0.52$, and $J(\text{M},\text{X}) = +4.10$ Hz. Earlier chemical shift assignments were confirmed by deuteration. Noteworthy is the increase found for ³J_{cis} as a result of the introduction of the bulky sulfur atom into the cyclobutene ring that apparently leads to severe changes for the CCC and HCC valence angles. Sign and magnitude of $J(\text{A},\text{X})$ and $J(\text{A},\text{M})$ support the first assignment given for $J(1,3)$ and $J(1,4)$ in **25** (see Table IV). The consequences of the different geometry on these parameters are, however, not known. In general it appears that the relation $|J(1,3)| < |J(1,4)|$ seems sensitive to geometry and substituent effects since frequently the opposite ratio has been given^{114,121} (cf. Table V).

For cyclobutenone (**27**),¹²⁷ isopropylidenecyclobutenone (**28**),¹²⁸ and phenylcyclobutenedione (**29**),¹²⁸ the particular

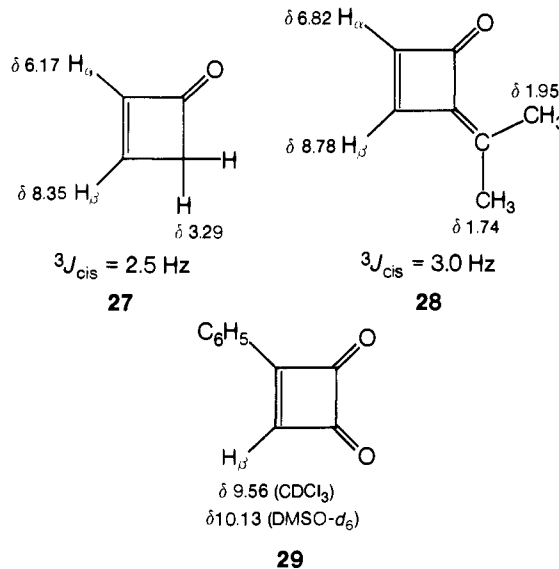


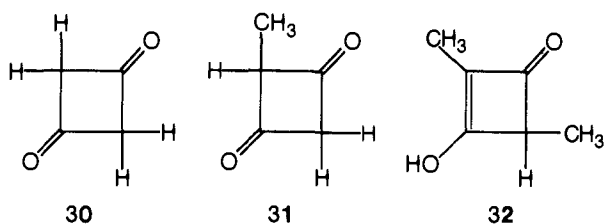
TABLE V. NMR Data of Miscellaneous Cyclobutenes

	$\delta(1)$	$\delta(2)$	$\delta(3)$	$\delta(4)$	$J(1,2)$	$J(1,3)^a$	$J(1,4)$	$J(2,3)$	$J(2,4)^a$	$J(3,4)$	Solvent	Ref
	6.23	6.23	5.06	5.06	2.5	1.6	0.9	0.9	1.6	3.2	CCl ₄	114
	¹ J(¹³ C, ¹ H): C(1) 181.0, C(3) 166.7											
	6.40	6.40	4.14	4.14		0.7	1.8	1.8	0.7	3.9	CDCl ₃	115
	5.84	6.12	3.3	4.8	2.8	1.5	0	0	2.8		CCl ₄	121
	5.88	6.38	3.19		2.8	1.5	0				CDCl ₃	122
	6.04	6.42			2.6						CDCl ₃	122

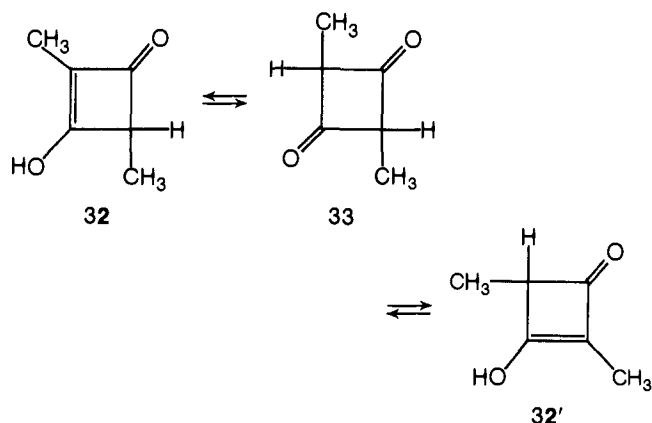
^a Sign not determined.

low-field absorption of the olefinic β proton is most probably a consequence of two factors: charge density effects and deshielding by the diamagnetic anisotropy of the carbonyl group.³ For H _{β} ¹J(¹³C, ¹H) values of 177.0 Hz (CCl₄) for **28** and 181.7 (CDCl₃) and 185.4 (DMSO-d₆) Hz for **29**, respectively, were found.¹²⁸

Interesting tautomeric phenomena have been detected for cyclobutane-1,3-diones. Whereas the parent compound (**30**)



seems to exist in equilibrium with the enol,^{129,130} the enol is heavily favored in the case of 2-methyl-1,3-cyclobutanedione (**31**).¹³¹ A detailed NMR study of 3-hydroxy-2,4-dimethylcyclobutanone (**32**) revealed the temperature dependence of the spectrum that consists of two CH₃ doublets centered at 1.1 and 1.42 ppm ($J = 7.0$ and 2.5 Hz, respectively) and a methine proton multiplet (13 resolved lines out of 16 theoretical ones) in DMSO at room temperature. In H₂O the methyl resonances broaden and

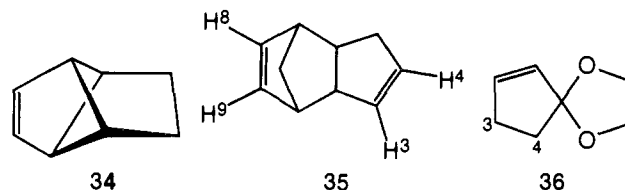


finally collapse to a singlet at elevated temperatures.¹³² The various proton exchange mechanisms explaining this behavior have been tested using line-shape calculations based on the Anderson-Kubo-Sack theory.¹³³⁻¹³⁵ Activation parameters for the keto-enol tautomerism **32** \rightleftharpoons **33** \rightleftharpoons **32'**, the most likely of two remaining possibilities, were obtained. Later,¹³⁶ the effect of pH on the spectrum of **32** was studied, and the results again demonstrate the existence of **33** as an intermediate which is approached through the enolate anion of **32**.

C. Cyclopentene

1. The Hydrocarbon and Its Derivatives

No complete analysis of the cyclopentene spectrum has so far been achieved. ³J_{cis} = 5.57 Hz was determined for the olefinic protons from the ¹³C satellites under simultaneous decoupling of the allylic CH₂ protons.⁵¹ In the same experiment ¹J(¹³C, ¹H) = 161.6 Hz was found in the olefinic position. The value of ³J_{cis} drops to 5.1 Hz and ¹J(¹³C, ¹H) increases to 167 \pm 1 Hz in the strained system **34**.¹³⁷



For *exo*- and *endo*-tricyclo[5.2.1.0^{2,6}]deca-3,8-diene (**35**), values of 5.6 and 5.8 Hz have been reported for $J(3,4)$ and $J(8,9)$, respectively,¹³⁸ and a number of cyclopentadiene dimers substituted in various positions have been treated in detail.¹³⁹

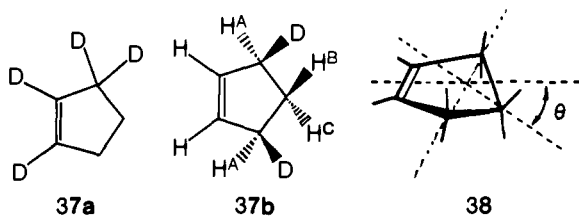
The CH₂-CH₂ segment of cyclopentene was studied in the diketal **36**, and values of 8.6 and 4.2 Hz were found for $J(3,4) = ^3J_{cis}$ and $J(3,4') = ^3J_{trans}$.¹⁴⁰ In two other investigations the partially deuterated compounds **37a**¹⁴¹ and **37b**¹⁴² were studied. For the former, the AA'BB' system of the dimethylene fragment was analyzed with simultaneous ²H decoupling.¹⁴¹ ³J_{cis} = 9.36 and ³J_{trans} = 5.72 (± 0.04) Hz were found. These values showed no temperature dependence between 220 and 360 K, indicating the presence of a single conformation or a group of equal energy

TABLE VI. NMR Data of Substituted Cyclopentenes

Substitution	$\delta(1,2)$	(a) Chemical Shifts			Solvent ^a	Ref
		$\delta(3,5)$	$\delta(4\alpha)$	$\delta(4\beta)$		
<i>cis</i> -3,5-Dibromo-	6.13	5.06	2.72	3.08	CCl ₄	153
		5.0	2.68	3.03	CS ₂	152
<i>cis</i> -3,5-Dihydroxy-	5.77	4.44	1.29	2.56	DMSO- <i>d</i> ₆	153
	5.88	4.66	1.51	2.66	CDCl ₃	153
	5.87	4.59	1.41	2.73	CD ₃ OD	<i>b</i>
<i>cis</i> -3,5-Dibenzhydryl-	6.23	5.72	2.03	3.11	DMSO- <i>d</i> ₆	153
	6.28	5.88	2.07	3.10	CDCl ₃	153

Substitution	² <i>J</i> (4 α ,4 β)	(b) Coupling Constants		³ <i>J</i> (1,5)	⁴ <i>J</i> (1,4 α)	⁴ <i>J</i> (1,4 β)	Solvent ^a	Ref
		³ <i>J</i> (4 β ,5 β) (³ <i>J</i> _{cis})	³ <i>J</i> (4 α ,5 β) (³ <i>J</i> _{trans})					
<i>cis</i> -3,5-Dibromo-	-16.5	6.5	1.8	1.0			CCl ₄	153
	-16.4	6.9	1.5		0.4	0.2	CS ₂	152
<i>cis</i> -3,5-Dihydroxy-	-13.0	7.3	5.8	1.0		0.6	DMSO- <i>d</i> ₆	153
	-14.7	7.3	3.6	1.0	0.5		CDCl ₃	153
	-13.7	6.9	5.3			0.5	CD ₃ OD	<i>b</i>
<i>cis</i> -3,5-Dibenzhydryl-	-14.7	7.3	3.8	0.8			DMSO- <i>d</i> ₆	153
	-15.0	7.5	4.0	0.8			CDCl ₃	153

^a Concentration max. 10%. ^b Reference 157.

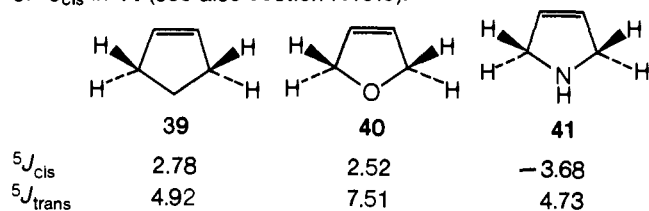


conformers. The *R* value method¹³ was not applicable to derive quantitative information about the puckering angle but indicated that **37a** is more flat than other five-membered rings not containing two sp² carbons. On the basis of the Karplus theory, the magnitudes of the vicinal coupling constants are in accord with the expectations for the envelope conformation **38** that has been established by various structural methods.¹⁴³⁻¹⁴⁸ A puckering angle θ of 22-23° has been found by microwave^{143,144} and IR spectroscopy,¹⁴⁵ whereas electron diffraction¹⁴⁷ yielded 29°. For the ring-puckering barriers 660 and 700 cal/mol were determined.^{145,146} Calculations^{149,150} reproduce the essential features of these results quite well. The spectrum of **37b** was analyzed under the condition of both the deuterons and the olefinic protons decoupled.¹⁴² The observed A₂BC-type spectrum yielded the following data:

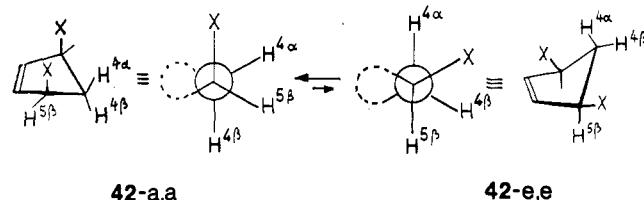
$$\begin{aligned} \delta_A &= 2.282 \text{ ppm} & J(A,B) (J_{trans}) &= 5.63 \pm 0.04 \text{ Hz} \\ \delta_B &= 1.797 \text{ ppm} & J(A,C) (J_{cis}) &= 9.46 \pm 0.04 \text{ Hz} \\ \delta_C &= 1.808 \text{ ppm} & J(B,C) (J_{gem}) &= -12.74 \pm 0.02 \text{ Hz} \end{aligned}$$

Noteworthy is the stereochemical isotope effect of 0.011 ppm on the chemical shift of H^B, in *cis* position to the deuterons. The coupling constants agree well with those obtained for **37a**.¹⁴¹

An ample study of homoallylic coupling has been performed for cyclopentene and its 4-hetero derivatives using the finite perturbation method and INDO wave functions.¹⁵¹ The most important result is the finding ⁵*J*_{trans} > ⁵*J*_{cis}, not apparent if only π -electron contribution are considered. The values for the planar structures **39**, **40**, and **41** have been calculated as shown. Agreement with experiment is good, except for the negative sign of ⁵*J*_{cis} in **41** (see also section IV.C.3).



Conformational analysis of cyclopentenes has so far been attempted in relatively few cases. Computer simulation was used to analyze the ABMM'XX' system of *cis*-3,5-dibromocyclopentene.¹⁵² Other studies^{153,154} on *cis*-3,5-dihydroxy- and *cis*-3,5-dibenzhydroxycyclopentene are based on first-order treatments and double resonance. From the results (Table VI) the following conclusion can be drawn. From the vicinal coupling constants only ³*J*_{trans} = *J*(4 α ,5 β) is significantly influenced by the conformation. This finding points to an equilibrium between two envelope conformations with either diaxial or diequatorial substituents (**42-a,a**, **42-e,e**), as the relevant Newman projections



indicate. For the dibromide and the diol (in CDCl₃) the small magnitude of ³*J*_{trans} suggests a trans-coplanar arrangement of the C(5)-X and the C(4)-H^{4 β} bond, where a maximum effect of the electronegative substituent is expected.^{155,156} The conformation **42-a,a**, therefore, is favored, and its concentration was estimated to 80%.¹⁵⁴ In polar solvents, on the other hand, solvation shifts the equilibrium toward the e,e conformation (64%¹⁵⁴). For the diol, IR measurements support these interpretations.¹⁵³

Of further significance are the long-range coupling constants between the olefinic and the methylene protons at C(4) that profit from the M-mechanism. For **42-a,a** ⁴*J*(1,4 α) ~ 0.5 and ⁴*J*(1,4 β) ~ 0, whereas for **42-e,e** the opposite ratio is found.

For trans-3,5-disubstituted compounds the methylene protons are equivalent, indicating a planar conformation or a fast equilibrium **42-a,e** \rightleftharpoons **42-e,a**. The latter is supported by IR results that established two nonequivalent OH groups for the diol;¹⁵³ 4-substituted systems slightly prefer the axial conformation (~65%), the concentration of which is raised in polar solvents.¹⁵⁴

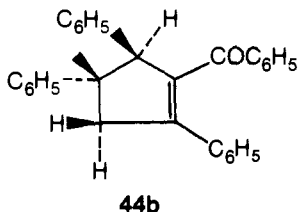
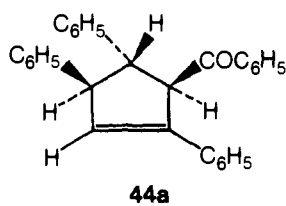
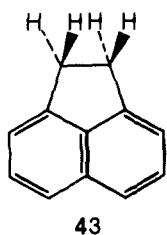
As a general result the fact emerges that substituents strongly influence the geometry of cyclopentene. The conformation of this ring system is therefore less predictable than that of other ring compounds, for instance, cyclohexene.

In this context, investigations dealing with acenaphthene (**43**) are of interest, since the CH₂CH₂ fragment of this compound may

TABLE VII. NMR Data of Cyclopent-2-enones

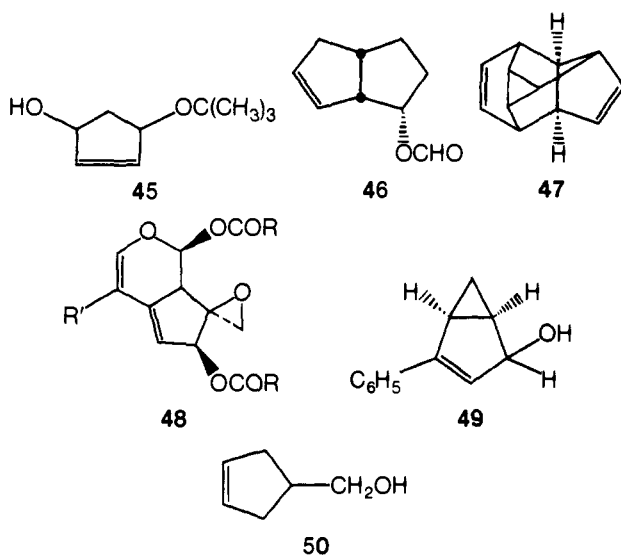
	$\delta(2)$	$\delta(3)$	$\delta(4)$	$\delta(4')$	$\delta(5)$	$\delta(5')$	Solv ^a	Ref
51	6.10	7.71		2.2		2.66	CCl ₄	c
4-Benzoyl-51	6.28	7.58	5.98		2.38	2.38	CCl ₄	153
4-Benzoyl-51	5.82	6.90	5.53		2.07	2.83	C ₆ D ₆	153
4-Bromo-51	6.17	7.62	5.15		2.56	2.92	CS ₂	153
	$J(2,3)$	$J(2,4)$	$J(3,4)$	$J(4,5)$	$J(4',5)$	M^b	Solv	Ref
51	5.70	-2.14	2.60	7.20	2.24	0.36	Neat	170
4-Benzoyl-51	5.7	-1.3	2.7	6.6	2.3		CCl ₄	153
4-Benzoyl-51	5.9	-1.2	2.5	6.6	2.3		C ₆ D ₆	153
4-Bromo-51		-1.2	2.6	6.4	1.8		CS ₂	153

^a Concentration max. 10%. ^b $M = J(4,4') - J(5,5')$. ^c Reference 173.



serve (with some reservations as to the similarity of bond lengths and bond angles) as a model for a planar structure. ³J_{C1s} = 9.2 and ³J_{trans} = 3.8 Hz were found from the analysis of the ¹³C satellites.¹⁵⁸ The α -bromo derivative yielded values of 6.8 and 2.7 Hz for the same constants.¹⁵⁹ Other mono- and disubstituted systems have been studied.^{158,160}

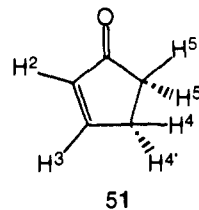
Additional NMR data have been reported for the highly substituted isomers **44a** and **44b**,¹⁶¹ for *cis*- and *trans*-**45**,¹⁶² as well



as for systems containing a partial cyclopentene structure (**46**,¹⁶³ **47**,¹⁶⁴ **48**,¹⁶⁵ **49**¹⁶⁶), and the influence of tris(dipivaloylmethanato)europium(III) [Eu(dpm)₃] on the spectrum of 3-cyclopentenyl-1-methanol (**50**) was recorded and the average structure of the 1:1 complex computed from the pseudocontact shifts by an iterative procedure.¹⁶⁷

2. Cyclopentenones

The introduction of a third sp²-hybridized carbon atom into the five-membered ring renders cyclopent-2-enone (**51**) practically planar. It has been estimated¹⁶⁸ that the dihedral angle between the planes determined by the carbon segments C(1) to C(4) and C(4)-C(5)-C(1), respectively, has a maximum value of 10°. The microwave spectrum of **51** was later found consistent with a planar structure.¹⁶⁹



The ¹H NMR spectrum of **51** has been examined by several authors,^{46,170} and the data given in Table VII were obtained. In addition, the spectra of cyclopent-2-enones substituted in the 4 position have been described,¹⁵³ and these results are also included in the table. The spectrum of 3-*tert*-butyl-4-bromocyclopent-2-enone was discussed particularly as an example of an ABX system.¹⁷¹

In an extensive investigation of 26 cyclopent-2-enones mono-, di-, and trisubstituted (R = CH₃, Cl, Br) in position 4 and 5, evidence for nonplanar conformations that result from eclipsed interactions of the substituents was obtained from chemical shifts and coupling constants and supported by IR measurements.¹⁷² From an analysis mainly of the vicinal coupling constants it was concluded that (1) in *trans*-4,5-dihalo-**51** from the conformation with diequatorial or dlaxial substituents the latter is preferred, (2) in *trans*-5-chloro-4-alkyl-**51** the substituents occupy the axial positions with increasing size of the alkyl group, and (3) in *cis*-4-chloro-5-alkyl-**51** none of the two conformations dominates, the ring deformation being the same for alkyl groups of different size.

A twist of ~20° around the C(4)-C(5) bond was estimated for the nonplanar conformations. For case 3 the NMR findings do not rule out a planar structure.

NMR data for various other substituted cyclopent-2-enones have been reported in a number of studies that used first-order treatments only and were aimed primarily on structural assignments.¹⁷⁴⁻¹⁸¹ No NMR investigation of cyclopent-3-enone, which like its isomer **51** is planar,^{182,183} has, to our knowledge, been published.

3. Heterocyclic Systems

A great deal of NMR work has been performed in order to establish the structure and conformation of five-membered heterocycles containing one double bond, especially since these compounds are widely occurring as partial structures in many

TABLE VIII. NMR Data of Compounds of Types 52 and 53

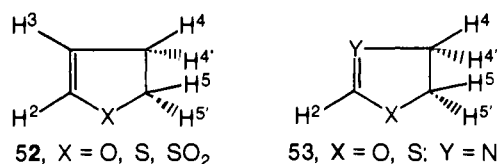
	$\delta(2)$	$\delta(3)$	$\delta(4)$	$\delta(5)$	Solv	Ref
52, X = O	6.31	4.95	2.60	4.38	CDCl ₃	a
52, X = S	6.17	5.63	2.74	3.22	CDCl ₃	a
52, X = SO ₂	6.66	6.81	2.92	3.19	CDCl ₃	a
53, Y = N; X = O	6.92		3.73	4.15	CDCl ₃	a
53, Y = N; X = S	7.96		4.27	3.23	CDCl ₃	a

	$J(2,3)$	$J(2,4)$	$J(3,4)$	$J(4,5)$	$J(4,5')$	M^b	Ref
52, X = O ^c	2.43	-2.36	2.46	10.76	8.13	6.09	170
52, X = S ^c	5.98	-2.23	2.78	9.99	7.53	5.09	170
52, X = SO ₂ ^d	6.62	-2.29	3.12	9.00	4.20	4.74	170
53, Y = N; X = O ^c		-2.20			19.44		170
53, Y = N; X = S ^d		-2.24		9.76	7.95	4.53	170

^a Reference 187. ^b $M = J(4,4') - J(5,5')$. ^c Neat. ^d 1:1 in CDCl₃.

natural products. The earlier efforts in this field have been extensively reviewed,¹⁵ and what follows concentrates on the more recent findings.

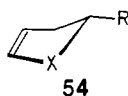
Interesting data concerning the mechanism of vicinal H,H coupling constants were obtained from a study of compounds of type 52 and 53.^{170,184} The protons of the CH₂CH₂ fragments



of these molecules yield spectra of the AA'BB' type,¹⁸⁵ most of them formerly misinterpreted as A₂B₂ systems with the incorrect assumption $^3J_{\text{cis}} = ^3J_{\text{trans}}$. The authors¹⁷⁰ determined all vicinal coupling constants, whereas the geminal constants could not be secured since it proved impossible to measure the parameter *K*. Selected results are collected in Table VIII.

Compared to 36 a strong increase for the magnitude of the vicinal coupling constants over the single bond was found for 52 and 53. This is still true in the light of the new data now available for 37,^{141,142} in particular, in the case of 2,3-dihydrofuran (52, X = O). This finding could not be explained with changes in bond length, bond angles, and/or the electronegativity of the heteroatom, even if the dependence of the latter factor on the relative orientation of the electronegative X group and the CH bonds of the dimethylene fragment^{155,156,186} was considered. It was assumed that a further mechanism influencing the 3J values in these systems must operate and that presumably the free electron pairs of the heteroatoms are responsible for the observed effect.

In a study of 5-substituted 2,3-ring-fused heterocycles of type 52 (X = O, S) the spectrum of the CHCH₂ fragment was carefully analyzed.¹⁸⁸ Again large values for $^3J_{\text{trans}} = J(4,5')$ were found (6.6–7.2 Hz), leading to a $^3J_{\text{cis}}/^3J_{\text{trans}}$ ratio of 1.2–1.4, considerably smaller than that expected on the basis of the Karplus theory⁴⁷ for an eclipsed CH₂CH₂ fragment (~2.5; see, for instance, 43, section IV.C.2). Similar findings were earlier reported for 2- and 3-methyl-5-phenyl-4,5-dihydrofuran ($^3J_{\text{cis}} = 10.2$, $^3J_{\text{trans}} = 8.4$, 8.6 Hz).¹⁸⁹ This observation was explained¹⁸⁸ with the nonplanarity of the compounds, and the predominance (>90%) of an envelope conformation 54 with pseudo-equatorial



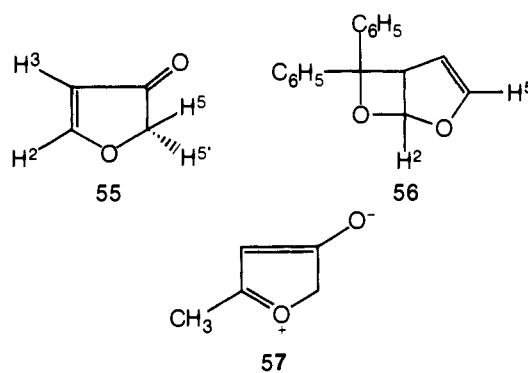
substituents in the 5 position was proposed. This view is supported by earlier IR results for 2,3-dihydrofuran (52, X = O) which established an envelope or C_s conformation in solution with an angle of buckle of 19° and a barrier to planarity of only 0.24

TABLE IX. NMR Data of Compounds 58–60

	58	59	60
$^3J(\text{H,H})$	1.5	7.12	8.33
$^1J(^{13}\text{C}, ^1\text{H})$	220.1	189.50	190.73
$^2J(^{13}\text{C}-\text{C}-\text{H})$	17.5	4.66	3.97
$^3J(^{13}\text{C}-\text{C}-\text{C}-\text{H})$	9.3	8.70	10.42
$\delta(\text{H})$	7.025	7.211	6.833
Solvent/concn	CS ₂ /sat. soln	CS ₂ /sat. soln	CS ₂ /sat. soln
Ref	194, 195	195	195

kcal/mol.^{190,146} Nonplanarity was also found for 2,3-dihydrothiophene (52, X = S).¹⁴⁶ The authors¹⁸⁸ did not comment on a possible lone-pair effect for 3J .

Several furenidone systems of type 55 (3-oxo-2,3-dihydrofuran) have been investigated in detail.¹⁹¹ Large deshielding exists here for H² (δ 8.23 ppm) owing to the presence of the carbonyl function and the ether oxygen. Allylic coupling (0.8 Hz) was established between H² and the CH₂ group, presumably transmitted through the heteroatom. $J(2,5) = 0.8$ Hz was also observed in 56.¹⁹² The 5-methyl derivative of 55 shows a



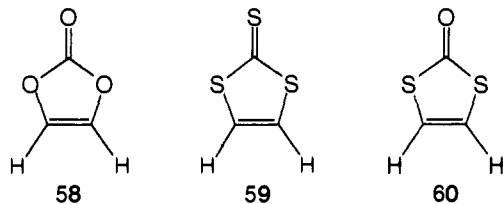
homoallylic coupling between CH₃ and CH₂ protons of the same magnitude (0.9 Hz).¹⁹¹ This was attributed to a partial double-bond character for the C(5)–O bond, represented by the resonance structure 57.

$^3J_{\text{cis}}$ and several $^{13}\text{C}, ^1\text{H}$ coupling constants have been measured for the planar molecule vinylene carbonate (58), which is close to being a perfect pentagon with internal CCC angles near 108°,¹⁹³ and its sulfur analogues 59 and 60^{194,195} (Table IX). Data for the structurally similar maleic anhydride are $J(\text{H,H}) = 5.72 \pm 0.18$ and $^1J(^{13}\text{C}, ^1\text{H}) = 189.5 \pm 0.7$ Hz.¹⁹⁶ Both values are considerably different from those in the open-chain analogue maleic acid, being 12.2 ± 0.1 and 169.3 ± 0.3 Hz, respectively. In a number of studies solvent, concentration, and temperature effects for the NMR parameters of maleic anhydride, mainly the proton chemical shift, were traced to study donor–acceptor interactions notably with aromatic compounds.¹⁵

TABLE X. NMR Data of Compounds 61–63^a

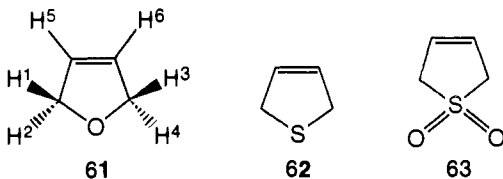
	$\delta(1)$	$\delta(5)$	$J(1,3)^b$	$J(1,4)^c$	$J(1,5)$	$J(1,6)$	$J(5,6)$	Solv	Ref			
61	4.514	5.851	7.07 (4.59) ^d 4.19 ± 0.10 2.5 ± 0.7	4.59 (7.07) ^d 6.66 ± 0.09 4.4 ± 0.8	1.63 0.66 ± 2.49	-2.51 -2.68 ± 0.93	6.33 5.95 ± 0.12 5.6 ± 1.1	Neat EBBA ^{e,f} EBBA ^{e,g} Neat	197 198 217 197			
62	3.664	5.794	6.60 (3.24) ^d	3.24 (6.60) ^d	2.52	-2.36	6.31	Neat	197			
63	3.716	6.109	1.94 (1.27) ^d 0.7 ± 0.4	1.27 (1.94) ^d 1.2 ± 0.4	2.89 -0.8 ± 0.5	-2.34 0 ⁱ	8.57 8.6 ± 0.5	Acetone ^h	197 199			
	$\delta(2)$	$\delta(3)$	$\delta(4)$	$\delta(5)$	$\delta(6)$	Solv	Ref					
R-61^j	5.116	4.767	4.649	5.808	6.024	CCl ₄ ^k	207					
R-61^l	5.956	4.814	4.731		6.298	CCl ₄ ^m	207					
	$J(2,5)$	$J(2,6)$	$J(2,3)^c$	$J(2,4)^b$	$J(3,4)$	$J(3,5)$	$J(3,6)$	$J(4,5)$	$J(4,6)$	$J(5,6)$	Solv	Ref
R-61^j	+1.87	-2.46	+6.40	+3.22	-13.00	-2.61	+1.58	-2.45	+1.69	+6.19	CCl ₄ ^k	207
R-61^l		-1.85	+5.87	+3.21	-13.81		+1.78		+2.04		CCl ₄ ^m	207
	$^1J(^{13}C_{\alpha},H^1)$	$^1J(^{13}C_{\beta},H^5)$	$^2J(^{13}C_{\alpha},H^5)$	$^3J(^{13}C_{\alpha},H^6)$	$^2J(C_{\beta},H^1) - ^4J(C_{\beta},H^3)$	Ref						
61	146.7 ± 0.1	168.04 ± 0.03	7.5 ± 1.2	5 ± 1	-9.5 ± 0.2	197						

^a If not stated otherwise, the error in the coupling constants is ±0.02 Hz. ^b ⁵J_{cis}. ^c ⁵J_{trans}. ^d Most likely assignment (see text). ^e EBBA = *N*-(*p*-ethoxybenzylidene)-*p*-*n*-butylaniline. ^f Concentration 19.5 mol %, temp 18 °C. ^g Concentration 10 mol %, temp 30 °C. ^h Saturated solution. ⁱ Assumed. ^j R = 2-methoxycarbonyl (H¹ = COOCH₃). ^k Concentration 9.2%. ^l R = 2,3-diphenyl (H¹ = H⁵ = C₆H₅). ^m Concentration 13.5%.



An inverse linear relation between ³J(*H*-C-C-*H*) and ²J(¹³C-C-*H*) at the double bond was noted for **58–60** as well for the other unsaturated systems.¹⁹⁵ Points for olefinic and aromatic compounds define different lines, and this observation indicates a possible correlation between the ratio of these two coupling constants and the electronic structure of cyclic π systems. Carbon-13 isotope shifts on $\delta(H)$ of 0.0035 ppm for directly bonded protons and 0.0013 ppm for a proton separated by three bonds from ¹³C were found.

Turning now to 2,5-dihydro heteroaromatics, one finds a minute treatment of the spectra of 2,5-dihydrofuran (**61**), 2,5-dihydrothiophene (**62**), and 2,5-dihydrothiophene 1,1-dioxide (butadiene sulfone, **63**),¹⁹⁷ as well as studies of **61** and **63** partially oriented in a nematic solvent.^{198,199}



The spectra of **61–63** are deceptively simple under conditions of low resolution owing to the small value of the sum $J(1,5) + J(1,6)$, showing only two lines.²⁰⁰ High resolution and high gain now¹⁹⁷ enabled the observation of weak transitions symmetrically flanking the main peaks, and an iterative analysis of the AA'XX'X''X''' systems was carried out using the method of Brailion and Barbet.²⁰¹ Only the geminal coupling constants could not be obtained because the small difference of $J(1,3)$ and $J(1,4)$ that makes the methylene protons nearly magnetically equivalent. The symmetry of the spin system did not allow the

distinction of $J(1,5)$ from $J(1,6)$ nor ⁵J_{cis} from ⁵J_{trans}. The former were assigned on the basis of their signs and the latter on the basis of the homoallylic coupling constants in cyclohexa-1,4-diene.²⁰² As we shall discuss below, the second assignment most probably is incorrect. In the case of **61** an analysis of ¹³C side bands was also achieved. The results are collected in Table X.

The main interest of the authors was directed at the cross-ring coupling constants of the homoallyl type [$J(1,3) = ^5J_{cis}$, $J(1,4) = ^5J_{trans}$]. They developed a semiempirical theory in terms of "orbital coupling factors", based on earlier work,^{203,204} and analyzed possible σ and π contributions to these interactions. They found hyperconjugation of the methylene groups with the π bond and the lone pairs as the most efficient coupling mechanisms. Thus, these couplings may also be regarded as ⁴J values. Contrary to the INDO results¹⁵¹ discussed above and to the results suggested by the liquid crystal studies,^{198,199} ⁵J_{cis} > ⁵J_{trans} was obtained. Because of the numerous and drastic approximations, the theory will most probably be of limited value for the actual calculation of *J* values, but might be helpful for an analysis of spin-spin coupling in terms of "chemical significance", i.e., MO models.

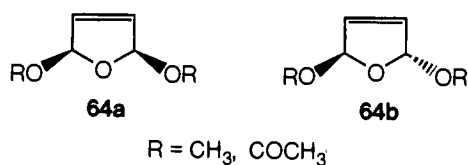
The NMR work on partially oriented **61**¹⁹⁸ and **63**¹⁹⁹ is of interest here with respect to the assignment of ⁵J_{cis} and ⁵J_{trans}, since in both studies the dipolar as well as the scalar coupling constants were determined independently. For both systems ⁵J_{cis} < ⁵J_{trans} was found (Table X). Whereas for **63** several assumptions and the large experimental error render the results somewhat uncertain, the data for **61** are more reliable. They agree reasonably well with those calculated by the finite perturbation method¹⁵¹ (see section IV.C.1) and reinforce the conclusions that the first assignment for the ⁵J values given in Table X must be reversed.

Further support for this comes from an investigation of *cis*- and *trans*-2,5-disubstituted-2,5-dihydrofurans **64a** and **64b**.²⁰⁵ The stereochemistry of both systems was elegantly established from the NMR spectra of their 3,4-addition products: *trans*-bromination leads to an AA'XX' system for the dibromide of **64b**, whereas the adduct of **64a** has no symmetry. The reverse is true for the formation of the *cis* diols. Since the AA'BB' systems of

TABLE XI. Comparison of Liquid Crystal NMR Studies of 2,5-Dihydrofuran (61)

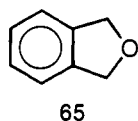
Reference	198	216	217	218			
Paper received	Aug 7 1973	Oct 10 1973	Nov 26 1973	Jan 14 1974			
Field strength, MHz (mode)	220 (CW)	100 (CW)	240 (FT)	100 (CW)			
Solvent	EBBA	EBBA	<i>a</i>	EBBA			
Concn	19.5 mol %	5% w/w	10 mol %	18.4 mol %			
Temp, °C	18		30	25			
Exptl error in line position		±2.0		±1.5			
Scalar couplings included in iterative analysis	Yes	No	Yes	No			
RMS error of fit (number of lines used)	0.44 (77)	0.113		1.65 (70)			
Vibr correct	No	Yes	No	No			
r_{13}/r_{12}	1.936	1.964	1.945	1.953	1.934	1.942 ^b	0.017 ^c
r_{14}/r_{12}	2.179	2.204	2.187	2.194	2.176012.184	0.015	
r_{15}/r_{12}	1.449	1.472	1.462	1.430	1.445	1.446	0.019
r_{16}/r_{12}	2.218	2.244	2.228	2.215	2.210	2.217	0.010
r_{56}/r_{12}	1.455	1.461	1.454	1.466	1.445	1.455	0.011
Tested structure	Rigid planar	Puckered	Rigid planar	Rigid planar	Rigid planar, puckered		
Proposed structure		Puckered		Rigid planar	Rigid planar		

^a *p,p'*-Ethoxybenzoxymethylphenyl carbonate. ^b Average value for data of rigid planar structures. ^c Largest difference between two values for rigid planar structures.



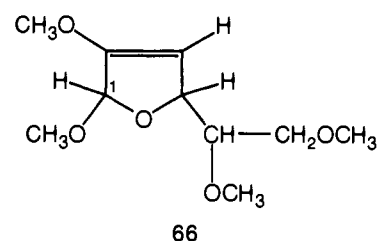
64a,b proved difficult to analyze because of $N \sim 0$ as a consequence of the opposite sign of J and J' , the vicinal and allylic coupling constants, the parameters were partly extracted from the ¹³C satellites. $^5J_{\text{cis}} = 0.4$ Hz and $^5J_{\text{trans}} = 4.0$ and 3.5 Hz was obtained, a result which is qualitatively also apparent from the experimental spectra: For **64a** one estimates $K \approx M$,¹⁸⁵ whereas for **64b** $K \neq M$ is indicated. A later, more accurate analysis of **64a,b** (R = COCH₃) confirmed the earlier results with slightly different numerical values.²⁰⁶

In what appears to be the latest study of the 2,5-dihydrofuran system (**61**) complete iterative analyses—including sign determination—for 2-methoxycarbonyl-**61**, 2,3-diphenyl-**61**, and for five derivatives of phthalan (**65**) were reported.²⁰⁷ The data



for the first two compounds are included in Table X. The discussion was focussed again at the relative magnitude of $^5J_{\text{cis}}$ and $^5J_{\text{trans}}$ (both of positive sign), and the relation $^5J_{\text{cis}} < ^5J_{\text{trans}}$ suggested by the results described above was confirmed. With the necessary care it can be used to assign stereoisomeric molecules. The finite perturbation theory⁶⁸ in the INDO approximation⁶⁵ was used to trace the experimental findings by calculations with special emphasis on conformational effects important for the above-mentioned long-range interactions via the dual path as 5J through the CC double bond and as 4J through the heteroatom. The results, given also in graphical form, showed these parameters to be very sensitive to the puckering angle θ between the planes formed by C(2)—O—C(5), and C(2)—C(3)—C(4)—C(5). It seems important to note the predictions for strongly folded conformations ($\theta \sim 25^\circ$), where $^5J_{\text{trans}}$ and $^4J_{\text{cis}}$ between the pseudoaxial hydrogens become equal and $^5J_{\text{cis}}$ between the pseudoequatorial hydrogens vanishes. The authors discussed literature relevant to their observations, notably studies dealing with oxazolines. They felt that the possibility of a simple extension of their results to other 2,5-dihydro heteroaromatics does not exist (see, however, discussion for **67** and **68**).

$^5J_{\text{cis}}$ and $^5J_{\text{trans}}$ values in line with the above findings are reported in an investigation of 17 3-oxazolines where five cis/trans pairs were assigned.²⁰⁸ In another study, an earlier assignment of the stereochemistry of two C-1 epimers of dehydrofuranose (**66**) was reversed on the basis of the two observed homoallylic interactions of 0.9 and 4.0 Hz.²⁰⁹



The NMR study of partially oriented **61**¹⁹⁸ also yielded detailed structural data for this compound, where only an early electron diffraction study was available.²¹⁰ Compared to calculations that were based on a rigid planar structure, improved agreement between experimental and calculated dipolar coupling constants was achieved with corrections to the structure for ring puckering and methylene rocking motions. A puckering angle of 16° resulted between the planes determined by C(2) to C(5) and C(5)—O—C(2), respectively. Thus as suggested by far-IR work,²¹¹ and contrary to earlier results,^{146,212-214} **61** has a structure similar to cyclopentene (cf. section IV.C.1). As to the absolute values for the bond lengths and angles some uncertainty remains, since the NMR method ultimately relies on the assumption of one structural parameter to scale the results. This undoubtedly must be regarded as the largest drawback, despite all sophistication and accuracy achieved in today's liquid crystal NMR work.²¹⁵

This latter aspect is especially illuminated by the fact that in addition to ref 198 three other independent groups investigated compound **61** simultaneously.²¹⁶⁻²¹⁸ As a consequence of this coincidence **61** now turns out to be a test case for the reliability of results obtained from liquid-crystal NMR studies. In Table XI we summarize experimental data and as structural information the calculated ratios of interproton distances. Since these are based on an assumed structure, the data for the rigid planar structure must be compared. They agree fairly well, the largest deviations between two values of the series ranging from 1 to 2%. Larger discrepancies, however, are found for the final structural parameters given in three of these studies^{198,217,218} because of the various assumptions introduced. The largest disadvantage seems the lack of unequivocal criteria that could

TABLE XII. NMR Data of 3,4-Dehydroprolinamide (67)²⁰⁹

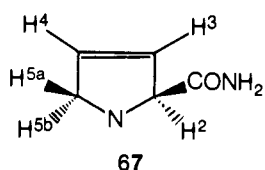
$\delta(2)$	$\delta(3)$	$\delta(4)$	$\delta(5a)$	$\delta(5b)$	Solvent	
4.549	5.896	5.864	3.785	3.911	CDCl ₃ ^a	
4.551	5.853	6.074	3.792	3.792	D ₂ O ^{a,b}	
$J(2,3)$	$J(2,4)$	$J(2,5a)$	$J(2,5b)$	$J(3,4)$	$J(3,5a)$	$J(3,5b)$
2.10	-2.54	5.81	3.76	5.86	-2.47	-2.21
2.13	-2.40		4.18 ^c	5.92		-2.40 ^c
$J(4,5a)$	$J(4,5b)$	$J(5a,5b)$	Solvent			
1.99	1.97 ^c	1.86	-14.73			
					CDCl ₃ ^a	D ₂ O ^{a,b}

^a Saturated solution. ^b Reference compound sodium salt of 3-trimethylsilylpropane-1-sulfonic acid or sodium terephthalate. ^c Average value.

aid the search for the best solution. Consequently, in two of the treatments,^{216,217} the possibility of a puckered structure was not considered.

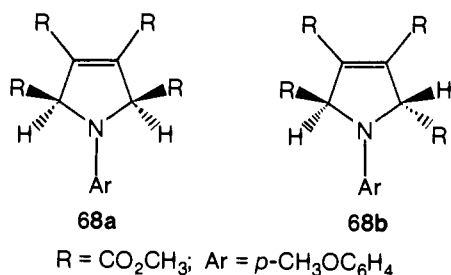
For **63** planarity was found,¹⁹⁹ in agreement with x-ray results,²¹⁹ but the possibility of ring puckering was not rigorously tested.

The abundance of nitrogen heterocycles has led to a considerable number of NMR investigations in this field. For 2,5-dihydropyrrole systems again the determination of the homoallylic coupling constants was of interest and the spectrum of 3,4-dehydroprolinamide (**67**) was analyzed^{220,209} using an



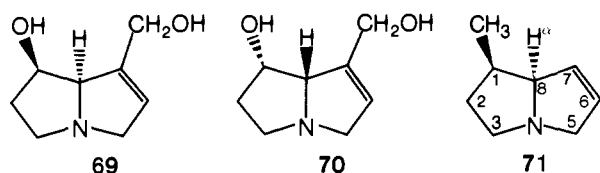
ABXYM and ABCDE approach. The latter gave after iterative refinement the data collected in Table XII.

From the ¹³C satellites of the *cis*- and *trans*- Δ^3 -pyrrolines **68a** and **68b** coupling constants of 3.0 and 7.2 Hz, respectively, were



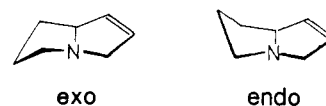
obtained.²⁰⁹ The finding ⁵J_{cis} < ⁵J_{trans} established by these results has later been used to clarify the stereochemistry in related compounds.^{221,222}

A study of 40 pyrrolizidine alkaloids yielded general information about chemical shifts and the magnitude of coupling constants.²²³ The three systems retronecine (**69**), heliotridine (**70**)—two diastereoisomers—and heliotridene (**71**) were later



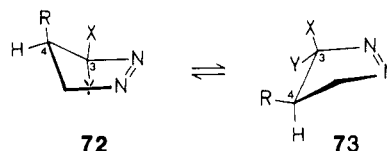
selected for detailed investigations.^{224,225} Conformational analysis was achieved with the help of the observed coupling constants. For all three systems a planar unsaturated ring seems well established. The pyrrolidine ring, on the other side, is exo-buckled in **69**, whereas rapidly interconverting *exo*- and *endo*-

buckled envelope conformers exist in the case of **70** and **71** with an estimated angle of buckle of ca. 45° for the latter:



The **71** *exo/endo* ratio is changed from 1:1 to 1:3 upon protonation of the nitrogen atom effected by adding concentrated HCl to the CDCl₃ solution of **71**. The concentration of *endo*-**71** also increased at low temperature showing this conformer to be energetically favored. Considerable changes of chemical shifts and coupling constants were observed on protonation, and the former allowed an identification of the individual proton resonances at the C(3) and C(5) methylene groups through the registration of protonation shifts of similar magnitude for H(3 α), H(5 α), and H(8 α). Following these findings²²⁵ the assignment for $\delta(5\alpha)$, $\delta(5\beta)$, $J(5\alpha,8\alpha)$ (⁵J_{cis}), and $J(5\beta,8\alpha)$ (⁵J_{trans}) given in the earlier work on **69** and **70**²²⁴ has to be reversed. An interesting observation is the absence of homoallyl coupling in the pyrrolidine ring of **71** [$J(3,8\alpha) = 0$], since it suggests that the lone pair of the heteroatom does enhance these interactions only in the presence of the double bond (cf. discussion for **61** and **62**).¹⁹⁹

Of systems with more than one heteroatom in the ring we note studies dealing with the conformation of *cis*- and *trans*-3,5-dimethyl-3-methoxycarbonyl- Δ^1 -pyrazolines²²⁶ as well as that of 3,3,4-trisubstituted- Δ^1 -pyrazolines.²²⁷ Like cyclopentene (**38**) these systems possess an envelope conformation with a folding angle of ~25 to ~36°. In the first study²²⁶ the existence of only one conformation was assumed, whereas in the second study²²⁷ both forms with axial and equatorial substituent at C(4) (**72** and **73**, respectively) were found, their relative energy being dependent on the nature of the substituents at C(3): for diesters (X

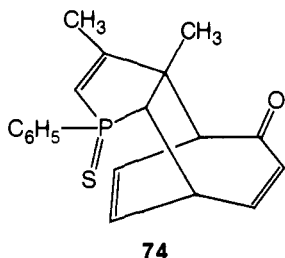


= Y = COOCH₃) increasing size of an alkyl group at C(4) favors **72**, while for diketones (X = Y = COR; R = CH₃, C₆H₅) with methyl and phenyl substitution at C(4) **73** dominates.

For Δ^2 -pyrazolines, the influence of substitution on NMR parameters and conformation has been investigated.^{228,229} The AA'BB' systems of the CH₂CH₂ fragments in 1,3-diphenyl- Δ^2 -pyrazoline and 3-phenylisoxazoline were analyzed, and substituent effects for proton resonance frequencies were obtained for 36 and 23 derivatives of these two systems, respectively.²³⁰ For the vicinal coupling constants ³J_{cis} > ³J_{trans} was observed in all cases. Further work on pyrazolines and pyrazolones as well as on reduced pyrroles and pyrrolidones has been summarized,¹⁵

and as a guide to the more recent literature in this field we only mention three studies dealing with rotational isomerism in acyl- Δ^2 -pyrazolines,²³¹ and first-order spectra of Δ^3 -pyrazolines²³² and 3-aminoisoxazolines.²³³

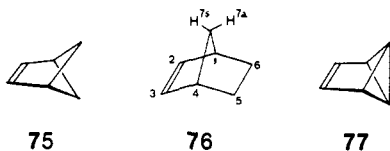
Finally, stereochemical information has been obtained by NMR using shifts reagents and $^2J(^{31}\text{P}, ^1\text{H})$ data for the cycloaddition products of 3,4-dimethyl-1-thio-1-phenylphosphole with tropone that contain a phosphorus heterocycle (**74**),²³⁴ and earlier sources of NMR information for various dihydrophospholes and their salts have been cited.¹⁵



4. Bicyclic Systems

Several bicyclic systems contain a cyclopentene ring as partial structure, and from this class of compounds papers dealing with bicyclo[2.1.1]hex-2-ene (**75**) and norbornene (bicyclo[2.2.1]hept-2-ene, **76**) and their derivatives will be reviewed in this section.

Only limited NMR information is available for **75**²³⁵ and the related benzvalene (**77**).²³⁶ Since first-order treatments have

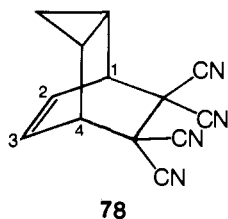


been used and deceptive simplicity present in many of these spectra was not considered, reliability is confined to the chemical shift information. Some coupling constants were determined for benzo-**75**,²³⁷ and its 4-methyl carboxylate,²³⁸ but since no iterative analysis was employed, the precision of the reported values is probably low.

The spectrum of norbornene (**76**) and those of many of its derivatives are also deceptively simple, and the parameters were obtained from an investigation of the ^{13}C satellites^{239,240} and with the help of solvent shifts.²⁴⁰ The following ranges for the coupling constants were given (in Hz):²⁴⁰

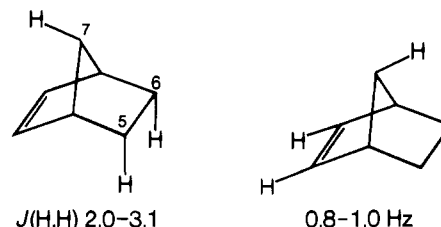
$J(1,2)$	2.8–3.0	$J(1,7^s)$	1.8–2.0	$J(^{13}\text{C}, \text{H}^2)$	164–166
$J(1,3)$	0.5–0.7	$J(1,7^a)$	<1.3–1.5		
$J(2,3)$	5.5–5.8	$J(7^s, 7^a)$	8.5–9.5		

For the parent system the treatment was later refined using double resonance experiments to decouple all methylene protons from H^1 to H^4 . The resonance of the olefinic protons could thus be observed and analyzed as the AA' part of an $\text{AA}'\text{XX}'$ system, including ^{13}C -satellite lines.²⁴¹ From this work $J(1,2) = 2.89$, $J(1,3) = 0.77$, $J(1,4) = 1.12$, and $J(2,3) = 5.77$ Hz resulted. $J(2,3) = 5.68$ and $J(^{13}\text{C}, \text{H}^2) = 166.8$ Hz were reported by another group.⁵¹ The CH_2CH_2 fragment of **76** has not yet been analyzed with the necessary accuracy. The strain effect present in **76** for the vicinal coupling constants becomes clear from a



comparison with the data of the closely related bicyclo[2.2.2]oct-2-ene (**78**), where the following values were found:²⁴² $J(1,2) = 6.91$, $J(1,3) = 1.31$, $J(2,3) = 8.12$, and $J(1,4) \sim 0$ Hz. For $J(1,2)$ the large difference (4.02 Hz) indicates that changes in CCH bond angles are accompanied by a reduction of the dihedral angle.

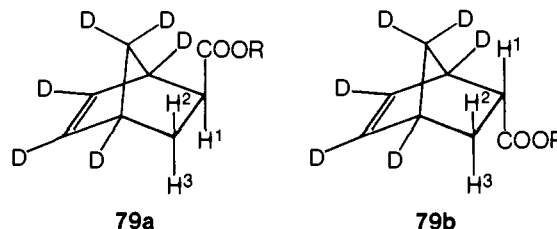
Because of its rigidity the norbornene system served as a popular model to establish stereospecificity of coupling pathways and substituent induced chemical shifts. One of the early examples was the demonstration of the M or W mechanism favoring large couplings over four σ bonds.^{64,243–245} Two types of interactions have been observed:²⁴⁶



The fact that only the endo protons at C(5) and C(6) are appreciably coupled to H^{7s} emerged as an important criterion for the evaluation of the configuration of 5-, 6-, and 7-substituted norbornenes. It allowed on the other side an unequivocal assignment of $\delta(\text{H}^{7s})$ and $\delta(\text{H}^{7a})$.²⁴⁷ Using *anti*-7-deuterio-**76**³¹ and *exo*-, *exo*-5,6-dideuterio-**76**,³⁰ it was shown independently by two other groups that in **76** H^{7s} resonates at lower field than H^{7a} . The assignment was later confirmed through the synthesis and NMR spectrum of *endo*, *endo*-5,6-dideuterio-**76**.²⁴⁸ The proton resonance frequencies of **76** are therefore as given in Table XIII.

$\delta(7s) > \delta(7a)$ is also true for benzo-**76**, where 1.77 and 1.48 ppm were found²⁴⁷ contrary to earlier assignments.²⁴⁹ For 7-substituted norbornenes, however, the situation is reversed,²⁴⁶ since for a pair of isomers H^{7s} now resonates at higher field than H^{7a} . Small changes of the molecular geometry apparently induced by substitution at C(7) seem to shift H^{7s} from the paramagnetic to the diamagnetic shielding region of the C(2)–C(3) double bond. The values for the carbinol have been given above (cf. section III.A). In the case of 7-*syn*- and 7-*anti*-carboethoxy-**76** δ values of 4.50 and 4.23 ppm were found for H^{7a} and H^{7s} , respectively.²⁴⁶

In order to settle the question of the relative magnitude of $^3J_{\text{cis}}$ values in the CH_2CH_2 fragment of **76** raised by results of earlier investigations,^{250,251} a detailed NMR analysis of the ABX systems in the CH_2CHR part of 5-*exo*- and 5-*endo*-norbornylcarboxylate (**79a**, **79b**) fully deuterated in all other positions was performed.²⁵² The spectra of both compounds were observed with ^1H $\{^2\text{H}\}$ decoupling and the results of the analysis (Table XIII) were confirmed by INDOR experiments. $^3J(\text{H}, \text{H})_{\text{endo}} \approx ^3J(\text{H}, \text{H})_{\text{exo}}$, i.e., $J(1,3)$ in **79a** $\approx J(1,2)$ in **79b**, was firmly established, showing that the earlier results were in error.



For halogenated norbornenes the magnetic anisotropy effect of the halogen substituents at C(5) and C(6) on the resonance frequencies of H^{7s} and H^{7a} have been discussed.²⁵³ A comprehensive analysis of the spectrum of *endo*-*cis*-5,6-dibromo-**76** was presented later²⁵⁴ with the results given in Table XIII. For a series of chlorinated norbornenes of type **80** the influence of various substituents ($\text{X} = \text{OH}, \text{OAc}, \text{Cl}, \text{C}_6\text{H}_5, \text{COOH}, \text{CN}$) on the

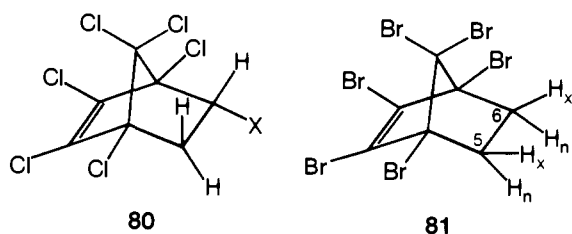
TABLE XIII. NMR Data of Norbornene (76) and Several Substituted Norbornenes^a

	$\delta(1,4)$	$\delta(2,3)$	$\delta(5x,6x)$	$\delta(5n,6n)$	$\delta(7s)$	$\delta(7a)$	$J(1,2)$	$J(1,3)$	$J(1,4)$	$J(2,3)$	Solvent (concn)	Ref
76	2.85	5.91	1.59	0.96	1.32	1.06	2.89	0.77	1.12	5.77 5.68		30, 31, 51, 240, 247
	$\delta(1)$	$\delta(2)$	$\delta(3)$	$J(1,2)$	$J(1,3)$	$J(2,3)$						
79a	2.143	1.898	1.300	4.4	9.0	-11.8						252
79b	2.863	1.848	1.380	9.4	4.2	-11.8						252
b	$\delta(1,4)$	$\delta(2,3)$	$\delta(5,6)$	$\delta(7s)$	$\delta(7a)$						CCl ₄ (20% w/v)	253
	3.25	6.23	4.45	1.80	1.47							
	$J(1,2)$	$J(1,3)$	$J(1,4)$	$J(1,6)$	$J(1,7s)$	$J(1,7a)$	$J(2,3)$	$J(2,7a)$	$J(5,6)$	$J(7a,7s)$	CCl ₄ (1 M)	254
	3.0	0.6	1.35	3.3	2.05	1.5	5.7	0.6	7.65	(-)9.7		
81	$\delta(5x)$	$\delta(5n)$	$J(5x,5n)$	$J(5x,6n)$	$J(5x,6x)$	$J(5n,6n)$						258
	2.61	2.01	-12.3	3.7	9.6	8.9						
c	$\delta(1)$	$\delta(2)$	$\delta(3)$	$\delta(4)$	$\delta(5x)$	$\delta(6x)$	$\delta(6n)$	$\delta(7s)$	$\delta(7a)$	$J(1,2)=J(3,4)$	$J(1,3)$	260
	2.95	6.01	5.97	3.02	1.130	1.945	1.03	1.497	1.217	2.85	1.2	
	$J(1,4)$	$J(1,6x)$	$J(1,6n)$	$J(1,7s)=J(4,7s)$	$J(1,7a)=J(4,7a)$	$J(2,3)$	$J(2,4)$	$J(2,7s)=J(3,7s)$				
	0.9	3.80	0.5	1.8	1.55	5.7	1.2	~0.3				
	$J(2,7a)=J(3,7a)$	$J(4,5x)$	$J(5x,6x)$	$J(5x,6n)$	$J(6x,6n)$	$J(6n,7s)$	$J(7s,7a)$	$J(2,5x), J(3,5x)$				
	0.65	2.85	9.30	5.55	(-)10.8	1.8	(-)7.70	~0.4				

^a For proton numbering see appropriate formula. ^b *endo-cis*-5,6-Dibromo-76. ^c *endo*-5-Trimethylsilyl-76.

NMR parameters of the remaining protons was studied.²⁵⁵ This work allowed an isolation of the electronegativity effect exerted by the X groups on H,H coupling constants and internal chemical shifts, since because of the rigid geometry of **80** the other factors influencing these parameters can be regarded to a good approximation as constant. In the electronegativity range of 3.80–2.49 determined for the series of X groups given above by the NMR method,²⁵⁶ linear variations of ³J_{trans} (2.5–4.6 Hz), ³J_{cis} (7.6–9.3 Hz), and ²J (–13.3 to –12.6 Hz) were found. The internal chemical shifts also showed a linear dependence on the substituent electronegativity.

In another investigation,²⁵⁷ **80** (X = PO(OCH₃)₂) was used, together with other systems, to establish the angular dependence of ³¹P–C–C¹H coupling constant. A general Karplus-type behavior was found. Data similar to those reported for **80** have been



obtained from the analogous bromo compounds.²⁵⁸ The parent system **81** yielded results (Table XIII) that support the findings for the two ³J_{cis} values cited above.²⁵² In context with a new theoretical study using both MO and VB formalism in their recent versions adequate for treating nuclear spin–spin coupling to elucidate the conformational dependence of ⁴J values, the spectra of *endo,endo*- and *endo,exo*-5,6-dimethyl-**80** as well as that of *endo*-5-methyl-**80** were analyzed.²⁵⁹ Small negative ⁴J(CH₃–C–C–H) data were found, in agreement with the calculations that predict negative interactions of this type for dihedral angles of between 30 and 120°. The stereochemistry of *endo*-5-trimethylsilyl-**76** was established in an ample study²⁶⁰ that used high-field NMR (250 and 300 MHz), double resonance, and INDOR experiments. Computer simulation was employed to test the data (Table XIII) that include several hitherto unobserved long-range coupling constants.

Several authors investigated the effect of shift reagents on the ¹H NMR spectra of norbornenes. 5-*endo*-Hydroxymethyl-**76**

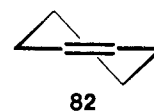
was used to study a possible influence of the shift reagent Eu(dpm)₃ on H,H coupling constants.²⁶¹ Within the limits of the experimental error, given as 0.1 Hz, no such changes were observed, with the exception of couplings involving protons at C(8), the carbon in α position to the coordination site. This agrees with results of another group¹⁶⁷ who studied the same compound under similar conditions and observed contact shifts only for the CH₂–O resonance. The average structure of the alcohol-Eu(dpm)₃ complex was derived by a least-squares fit of calculated on observed proton shifts. The power of the lanthanide shift reagents for the simplification of spectra and for structure elucidation was nicely demonstrated in the case of 5-*exo*-methyl-6-*endo*-hydroxymethyl-**76** and its 5-*endo*-6-*exo*- isomer.²⁶² Of importance is the finding that only a dynamic model for the complex which considered rotamers about the C–O as well as the C–CH₂ O bond could adequately explain the experimental results.

Finally, we mention an investigation dealing with 5,6-dicarboxymethoxynorbornenes,²⁶³ the observation of deshielding for the ¹H resonance caused by steric compression in the system **15** cited in section III.A,³³ and the use of the NMR parameters of **76** to establish the structure of norbornadiene–cyclopentadiene addition products,²⁶⁴ as well as that of benzo[3,4]bicyclo[3.2.1]octa-3,6-dienes.²⁶⁵ Long-range shielding effects of the three-membered ring in tricyclo[3.2.1.0^{2,4}]octenes and their benzo derivatives with *exo*- and *endo*-cyclopropane ring have been given.²⁶⁶

D. Cyclohexene

1. The Hydrocarbon and Its Derivatives

The structure of cyclohexene has been determined by electron diffraction,^{267–270} and the half-chair **82**, already proposed in



1937,²⁷¹ was found to be the stable conformation. Similar conclusions were drawn from IR and Raman measurements²⁷² and from x-ray investigations of substituted cyclohexenes.^{273,274} The half-chair was also predicted by calculations^{275,276} that

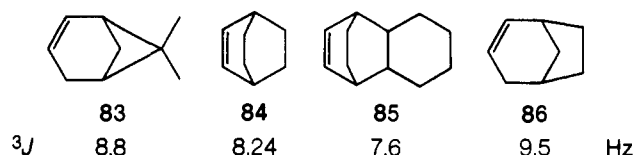
TABLE XIV. Data for the Conformational Interconversion of Cyclohexenes

Cyclohexene	T_c , °C ^a	$\nu_e - \nu_a$ ^b	ΔG^\ddagger ^c	E_4 ^d	Solvent	Ref
1,4-Dihydroperdeuterio-	-166.7	19	5.37		<i>f</i>	283
4-Fluoro-	-151.8	728 ^g	5.3	0.014	CD ₂ CDCI	283
4-Chloro-	-151.8	27	6.3	0.200	CD ₂ CDCI	283
4-Bromo-	-149.3	27	6.3	0.077	CD ₂ CDCI	283
1,4-Dihydro-4-bromoperdeuterio-	-148.0		6.3		CD ₂ CDCI	283
4-Iodo-	-146.3	27	6.5	-0.016	CD ₂ CDCI	283
<i>cis</i> -4,5-Dicarbomethoxy-	-135.5		7.4		CD ₂ CDCI	283
Perfluoro-	-111.5	19.4 ^{e,g}	6.83 ^h		CF ₂ Cl ₂	286
1,2-Dichloroperfluoro-	-111.5	12.7 ^{e,i}	6.28 ^j		CF ₂ Cl ₂	286
3,3,6,6-Tetramethyl-	-117.5		8.4		<i>k</i>	290
3,3-Dimethyl-1,2,5,5-tetra-deuterio-	-146.8		6.3		CF ₂ Cl ₂	290
4,4-Dimethyl-	-155.8		6.1		CF ₂ Cl ₂	290

^a Coalescence temperature ($\pm 0.5^\circ$). ^b Chemical shift difference between equatorial and axial H at C(4) (Hz at 60 MHz). ^c In kcal/mol (± 0.1). ^d In kcal/mol. ^e Chemical shift difference between equatorial and axial fluorine (in Hz at 56.4 MHz). ^f 40% (v/v) in deuteriovinyl chloride/chlorotrifluoroethylene (1:2). ^g $J(F,F) = 287$ Hz. ^h $\Delta H^\ddagger = 7.2 \pm 0.2$ kcal/mol; $\Delta S^\ddagger = 2.6 \pm 1.6$ eu. ⁱ ${}^2J(F,F) = 280$ Hz. ^j $\Delta H^\ddagger = 6.3 \pm 0.2$ kcal/mol; $\Delta S^\ddagger = 0.2 \pm 1.5$ eu. ^k Vinyl chloride/CF₂Cl₂ (85:15).

showed **82** to be essentially strainfree.²⁷⁷

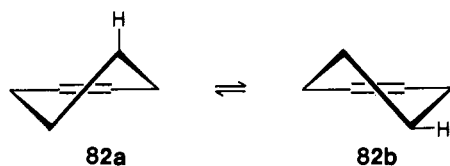
For 1,2,3,3,6,6-hexadeuteriocyclohexene values of 8.94 and 2.95 Hz were determined²⁷⁸ for ${}^3J_{\text{trans}} [(J_{\text{aa}} + J_{\text{ee}})/2]$ and ${}^3J_{\text{cis}} (= {}^3J_{\text{ae}})$, respectively, and from the ratio, the *R* value¹³ of 3.03 and a torsional angle of 63° were calculated²⁷⁹ for the twist around the C(4)-C(5) bond, in good agreement with the structural data. From the ¹³C satellites of the olefinic protons, ${}^3J(1,2) = 10.11$ Hz and ${}^1J({}^{13}\text{C}, {}^1\text{H}) = 158.4$ Hz were determined under simultaneous decoupling of the allylic protons,⁵¹ the complete analysis being prevented by the complexity of the spin system, a fact equally true for all the higher cycloalkenes. Considerable reduced 3J values across the double bond were found by the same technique in compounds **83** to **86**.⁵¹ Geminal coupling



constants for the allylic CH₂ group in 18 cyclohexenes and compounds of related structure were collected.²⁸⁰ The data are in the range from (-)15 to (-)19 Hz, and their dependence on conformation of the systems was discussed.

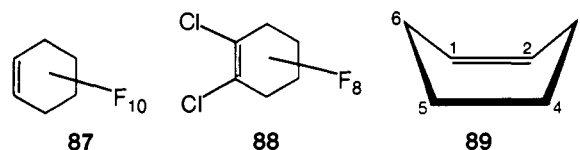
Starting with **82**, the conformational equilibria of the larger rings are characterized by energy barriers that are in many cases high enough to allow the detection of individual conformers using low-temperature NMR. Therefore, the interest of the application of NMR to these systems originates not only from the usefulness of their NMR parameters for structural investigations, but also from the possibility to measure conformational free energies and activation parameters in order to gain knowledge about the dynamic behavior of such molecules.

In the present case, a ring inversion process between two equivalent half-chair conformations **82a** and **82b** was de-



tected.²⁸¹⁻²⁸³ A free enthalpy of activation ΔG^\ddagger of 5.4 kcal/mol resulted at -167°C from measurements on 1,4-dihydroperdeuterio-**82**,^{282,283} that was chosen for the purpose of spectra simplification through ${}^1\text{H}\{^2\text{H}\}$ double resonance. At this temperature the chemical shift difference between axial and equatorial methylene protons at C(4) amounts to 0.3 ppm, 0.2 ppm less than in cyclohexane.

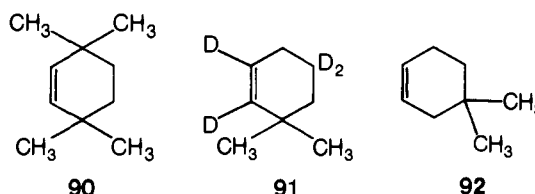
For 3- and 4-substituted cyclohexenes equilibria between conformers with axial and with equatorial substituents are possible, and E_3 and E_4 values similar to the *A* values for substituted cyclohexanes²⁸⁴ were introduced for these systems in order to characterize the ΔG° data.²⁸³ The general features of cyclohexene conformational analysis as well as some earlier experimental results have been reviewed.²⁸⁵ In Table XIV we present the results of measurements made for 4-substituted systems and for the fluoro-substituted compounds **87** and **88**. For the latter a complete line-shape analysis was employed²⁸⁶ to extract the rate constants from the ¹⁹F NMR spectra.



A major point of interest and the subject of a number of theoretical studies was the mechanism of cyclohexene ring inversion. Reviews of the earlier results worth reading are given in ref 286 and 289. The boat form **89** was regarded by some



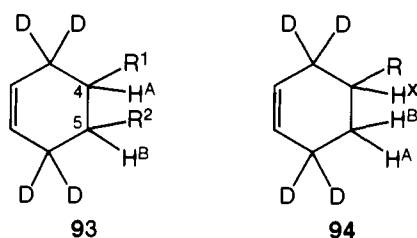
authors as intermediate (energy profile a),^{281,287} and by others as the transition state of the inversion (energy profile b).^{283,288,289} It is now accepted that the latter interpretation is correct, especially since recent improved calculations¹⁵⁰ agree with the earlier data.²⁸⁸ The results for the 4-substituted cyclohexenes²⁸³ (Table XIV) suggested energy profile b, since an increase of the barrier was found with increasing size of the substituent at C(4). The origin of this effect was seen in the eclipsing of the C(4)-X and C(5)-H bonds possible in **89**. More recently, the *gem*-dimethyl-substituted systems **90**, **91**, and **92** were studied to find



further support for this interpretation.²⁹⁰ The ΔG^\ddagger values given in Table XIV were found at the coalescence temperature, that

for **90** being the highest so far measured for a substituted cyclohexene. This finding clearly supports the boat form as the transition state, since a large steric interaction is expected for the methyl groups at the "prow" of **89**. A similar effect is still present in **91**, and a comparison with the energy of CH₃CH₃ and CH₃H 1,3-diaxial interactions in cyclohexane suggests that indeed the barrier increase found for **90** and **91** with respect to the parent compound originates from van der Waals repulsion. The data for **92** support the conclusions reached earlier for the 4-substituted systems, where the barrier rise was attributed to torsional energy in the transition state (see above).

Information about the geometry and conformation for a considerable number of substituted cyclohexenes has been derived from their NMR spectra, even if the majority of these measurements were performed in the region of fast exchange. A number of 4,5-disubstituted systems was studied,²⁹¹ and from these *cis*- and *trans*-4,5-dimethylcyclohexene retained their conformational mobility even at -161 and -153°, respectively, as was concluded from the absence of line broadening in their spectra. For the *trans* compound H⁴ and H⁵ resonate at higher field than in the *cis* isomer (δ 1.45 vs. 1.95), and this observation was attributed to their predominate axial orientation, in contrast to the average axial-equatorial orientation in the *cis* compound. Complete deuteration at C(3) and C(6) was employed in other studies^{292,293} in order to simplify the spectra of 4,5-disubstituted as well as 4-substituted cyclohexenes (**93**, **94**). The AB spectra

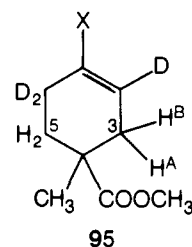


of the methine protons yielded average ³J values of 10–11 Hz and for the ABX systems of **94** the sum J_{AX} + J_{BX} ranging from 11.3 to 14.1 Hz was extracted directly from the spectra. Assuming limiting values for J_{aa}, J_{ae}, and J_{ee}, the spin-spin interaction between axial and equatorial protons, the conformational preferences in **93** and **94** were estimated. In all cases the more stable conformer was that with equatorial substituents, in agreement with other findings, however, the contribution of the axial conformer was found larger than in the corresponding cyclohexanes. This fact was attributed to the reduction of 1,3-diaxial interactions from two in cyclohexane to only one in cyclohexene. For polar substituents, a destabilization of the diequatorial form of **93** was noted. Later, more accurate data for *trans*-4,5-disubstituted systems of type **93** were obtained through ¹H{²H}-decoupling experiments.²⁹⁴ The temperature dependence of ³J(4,5) was observed, and an iterative procedure²⁹⁵ was employed to extract the individual NMR parameters J_{ae} and J_{aa} (J_{gauche} and J_{trans}, respectively) as well as the ΔH° and ΔS° data. The diequatorial conformer was present to 70–80%, with the exception of CCl₃-substituted systems, where this percentage dropped to 60%. Considerable variations for the calculated values of the coupling constants were found over the whole series of compounds. In the light of the uncertainties inherent in the iterative method,²⁹⁶ the reliability of the quantitative results seems, however, doubtful.

Analysis of the deuterium decoupled ABX spectra of 4-cyano-, 4-chloro-, and 4-ethoxycarbonyl- **94** was also performed in a variety of different solvents.²⁹⁷ Using dihedral angles of φ_{ae} = 58° and φ_{ee} = 62° and a simple cos² dependence for ³J, the mole fraction of the equatorial conformer was estimated from the ratio R = J_{AX}/J_{BX} of the two vicinal interactions. Values of ~50, ~60, and ~100% resulted for the three systems. Later the stereoisomeric *cis*- and *trans*-3-methyl-4-R-3,6,6-trideuteriocyclohexenes with R = COOCH₃, CH₂OH, CH₂Cl were

studied.²⁹⁸ The conformational behavior of these systems is complicated by the nonequivalence of the axial and equatorial position at C(3) and C(4). The large value found for one vicinal coupling constant of the ABX system formed by the methine proton at C(3) and the methylene protons at C(4) (10.4–12.9 Hz) indicates the equatorial preference of the R group in all cases. The magnitude of the other vicinal coupling constant was only 3.7–2.1 Hz. ΔG° values of 1–2 kcal/mol were estimated with the help of several assumptions concerning dihedral angles and limiting values for the coupling constants.

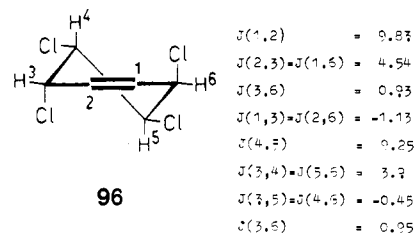
Studies of a series of compounds of type **95** (X = OCH₃, Cl,



H, C₆H₅, COOCH₃, CN, CONH₂, OCOCH₃, N(CH₂CH₂)₂O) were performed to investigate the effect of β-substitution on ²J values.²⁹⁹ Agreement with theory³⁰⁰ was found as electron-withdrawing substituents caused a negative shift, and electron-donating substituents caused a positive shift for ²J, the total range being 2.9 Hz. A correlation of Δ²J with the shielding of the olefinic proton adjacent to the CH₂ group suggested that resonance interactions between X and the π-bond affected the hyperconjugative electron transfer to and from the CH₂ bond orbitals. ⁴J values between the methylene protons at C(3) and C(5) were also determined.

The spectra of several stereoisomeric 3,4,5,6-tetrahydrocyclohexenes, the so-called conduritols, have been analyzed in detail, and their conformations were deduced from the observed H,H coupling constants.³⁰¹ In all cases the half-chair was found to be the most stable conformer. Small negative ⁴J values were observed between protons in axial and equatorial positions (⁴J_{aa}, ⁴J_{ae}) in support of the earlier theory of ⁴J coupling.²⁴⁵ Recent theoretical work substantiates these findings.²⁵⁹

Conformational studies have also been performed for 3,4,5-trichloro-6-bromo- and 3,4,5,6-tetrachlorocyclohexenes using 300-MHz spectra that facilitated the determination of coupling constants and readily allowed an assignment of the configuration.³⁰² The spectrum of the tetrachloro compound **96**



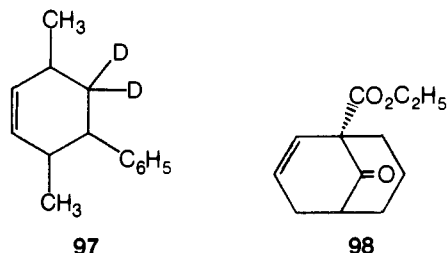
showed AA'XX' half-spectra for the olefinic as well as for the methine protons at C(4) and C(5) that upon analysis gave the coupling constants as shown.

In another study of 3-aryl-1,3,5,5-tetramethyl-Δ¹- and Δ⁶-cyclohexenes,³⁰³ it was found that an aryl- and an α-naphthyl group remained strictly in an axial position, thus allowing the majority of the methyl groups to occupy the equatorial positions. The arguments in favor of these conformations were derived mainly from chemical shifts that are given also for the model systems 1-methyl- and 1,3,3,5,5-pentamethylcyclohexene. Evidence for the preferred rotamer with respect to α-naphthyl rotation was also deduced from the ring current effect of the naphthyl ring.

Based on findings for several 3,4-disubstituted cyclohexenes, the conformational free energy of an allylic *tert*-butyl group was

estimated to be much less (ca. 50%) than the corresponding value for this substituent in cyclohexane.³⁰⁴ Partial deuteration with $^1\text{H}\{^2\text{H}\}$ spin decoupling was used to determine chemical shifts and coupling constants. For *trans*- and *cis*-3,4-disubstituted systems several cases of conformational heterogeneity were observed, indicating that a gauche interaction between a neighboring substituent and the *tert*-butyl group is of similar magnitude or even larger than the conformational free energy of the latter group. On the other hand, for 3,6-disubstituted systems the *e,e* conformation dominates. In addition, data for 1- and 2-*tert*-butyl-4-methoxycarbonyl-**82** are reported and compared with results found earlier for 4-methoxycarbonyl-**82**²⁹² and its 1,2-dimethyl derivative.³⁰⁵ Only minor changes of conformation following the introduction of a *tert*-butyl group in 1 or 2 position are indicated, the ester group always occupying dominantly (ca. 80%) the equatorial position.

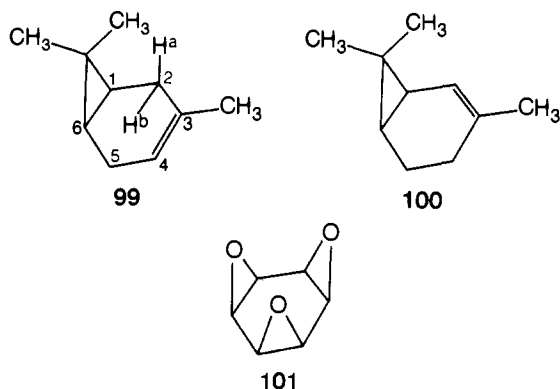
Finally, we mention work on cyclohexene partial structures in the natural products codeine and isocodeine,³⁰⁶ in Diels–Alder adducts (**97**),³⁰⁷ and in bicyclic ketones (**98**).³⁰⁸ Relevant to the



material presented here are also a recent review on chair–chair interconversion of six-membered rings³⁰⁹ and the complete analysis of the spectrum of the CH_2CH_2 fragment of the chair form of cyclohexane.³¹⁰

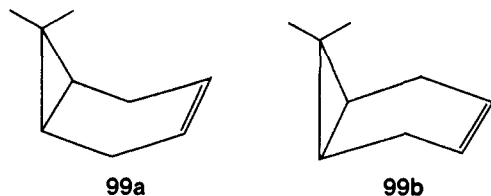
2. Bicyclic and Tricyclic Systems

The conformation of cyclohexene is drastically altered if one of the CC single bonds is replaced by a three-membered ring, which imposes similar constraints on bond and torsional angles like an additional CC double bond. It is therefore to be expected that the conformation of 3-carene (**99**) resembles that of cyclohexa-1,4-diene, whereas that of 2-carene (**100**) should show



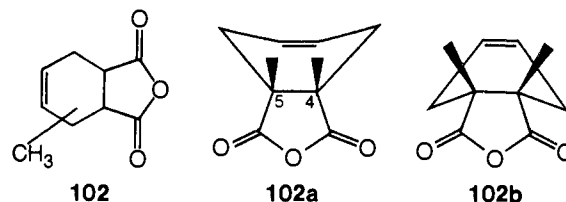
a relationship to the shape of cyclohexa-1,3-diene. As an interesting observation that illuminates this point, we mention the structure of benzene trioxide (**101**)³¹¹ that can formally be regarded as the first planar cyclohexane derivative.

Conflicting interpretations of the NMR data of **99** are available. Two boat forms, **99a** and **99b**, were discussed,³¹² and from the



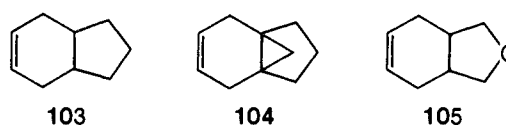
chemical shifts it was deduced that **99a** is favored. Examination of the 220-MHz spectrum,³¹³ on the other hand, led to the conclusion that the six-membered ring of **99** is essentially flat, since the coupling constants $J(1,2a) = 7.5$ and $J(1,2b) = 0$ Hz were in good agreement with calculated values based on a Karplus-type relation $J = 10 \cos^2 \phi$ derived for 3J values in substituted cyclopropanes. Since in addition the electron diffraction pattern of **99** was interpreted solely in terms of conformation **99a**,³¹⁴ further work is clearly needed to derive a more satisfactory answer about the conformation of this compound and that of its isomer **100**. For some substituted 3-carenes first-order NMR data are available,³¹⁵ as well as for 2-norcarenones.³¹⁶

A detailed discussion of the conformations of 21 methyl-substituted cyclohexene-4,5-dicarboxylic acid anhydrides of type **102** was given.³¹⁷ For the *trans* compounds, only the rigid half-chair with diequatorial CO groups is possible. For the *cis* compounds, however, the large values found for $^3J(\text{H}^4, \text{H}^5)$ of 9.4 to 10 Hz indicated that the respective CH bonds are eclipsed, and a boat geometry (**102a**) was proposed for the six-membered ring.



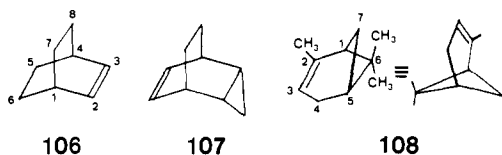
Ring inversion must then lead to a second boat conformer (**102b**), and from the coupling constants it was concluded that either one can be favored depending on a *cis* or *trans* substitution at C-3 and/or C-6. Since the accuracy of the measured J values is low and only 3J data were considered, the results are only indicative for the general picture. In particular, the authors did not comment on the possibility of a planar six-membered ring and the fact that substitution inevitably will lead to deformations of the geometry, and as a consequence one is dealing with a whole family of conformations in this series of compounds. This limitation, however, applies to a large number of other studies as well, as discussed above. In another paper the configuration of various Diels–Alder adducts of alkylbutadienes and maleic anhydride was established from chemical shift measurements.³¹⁸

The model pair **103** and **104** was used to estimate the influ-



ence of the diamagnetic anisotropy of the three-membered ring on the chemical shifts of the vinyl protons;⁸² δ values of 5.58 and 5.43 ppm, respectively, were found. Using the point dipole approximation³¹⁹ with $\Delta\chi = -20 \times 10^{-6} \text{ cm}^3/\text{mol}$ for the cyclopropane ring³²⁰ and the bond anisotropy model,³²¹ the experimentally observed shielding of +0.15 ppm was excellently reproduced, regardless whether a conformational equilibrium between two boat conformations analogous to **102a** and **102b**, respectively, or a planar six-membered ring was assumed. An attempted conformational analysis for *cis*-8-oxabicyclo[4.3.0]non-3-ene (**105**) failed because an incorrect treatment was used for the interpretation of a poorly resolved spectrum.³²²

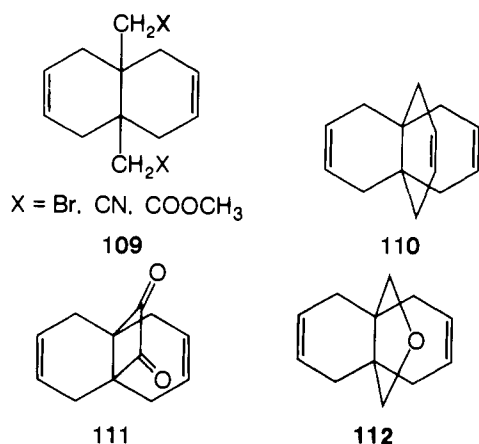
For the bicyclo[2.2.2]oct-2-ene system (**106**) first-order treatments are available^{323–325} that discuss anisotropy effects of the double bond as well as that of the benzene ring in the corresponding benzoderivatives and that of the three-membered ring in the structurally related tricyclo[3.2.2.0]nonenes (**107**).³²¹ In 3-substituted derivatives of **106** the magnitude of $^4J(\pi)$ apparently is proportional to the electron density at the double bond which in turn is a function of the substituents.³²⁵ Data for the structurally related system **78**²⁴² have already been given in section IV.C.4.



The stereochemistry of the four isomeric 5-hydroxy-6-methylbicyclo[2.2.2]oct-2-enes was assigned with the help of lanthanide-induced shifts (LIS) using Eu(fod)₃ as the shift reagent.³²⁶ The qualitative assignment based on the concentration dependence of the LIS data and reasonable assumptions concerning the structure of the complex was confirmed on a quantitative basis using a computer program to assign less well determined resonances. The agreement factor *R*³²⁷ served as criterion for the correct solution.

Bicyclo[3.1.1]hepta-2-enes have been treated in more detail with the spectral analysis of the natural occurring terpenoids verbenone, myrtenal, α -pinene, and 11 α -pinene derivatives.³²⁸⁻³³⁰ These systems can be regarded as bridged cyclobutanes (**108**), and the findings were related to the data of other strained four-membered rings in a number of bicyclic compounds.³³⁰ It was found that the correlation of ²*J* values with the CCC bond angle differs markedly for these systems from that found for other hydrocarbons of different ring size, a fact already noted earlier.²⁸⁰ Large ⁴*J* couplings of positive sign (5.9 to 6.4 Hz) were found between the quasi-equatorial bridgehead protons H¹ and H⁵, and the influence of the cyclobutane folding angle on the magnitude of these couplings was traced with INDO calculations and by geometric considerations concerned with the possibility of a direct coupling mechanism. The results of both approaches compared well with the experimental findings. From the presumably negative geminal coupling constant of 18 Hz at the C(4) methylene group it was concluded that the C(1)-C(5) fragment of **108** is essentially planar. ³*J*_{cis} across the double bond was found to agree with data of other bridged cyclohexenes. Induced chemical shifts for CH₃ and OH substituents were reported. However, attempts to reproduce these data with the help of various model calculations^{331,332} were unsuccessful. In addition we mention results for benzo[6,7]bicyclo[3.2.1]octa-3,6-dienes²⁶⁵ that are of related interest here.

The conformational behavior of 9,10-disubstituted cis- $\Delta^{2,6}$ -hexalins (**109**) and of [4.4.4]propella-3,8,12-triene (**110**),



both containing cyclohexene substructures, was the goal of a dynamic NMR study.³³³ In the hexalins the AB system of the angular CH₂ protons was used to monitor the ring inversion process by line-shape calculations over a temperature range of ca. 70°. The relatively high barrier found [ΔG^\ddagger (300 K) 12.2, 13.4, and 14.2 kcal/mol for X = Br, CN, COOCH₃, respectively] was taken as evidence for a mechanism that assumes the boat form as transition state and requires simultaneous inversion of both rings, thus making the barrier much higher than in cyclohexene. In contrast, ring inversion in cis-decalin proceeds ap-

parently independently for both rings, and the barrier is only slightly larger than in cyclohexane.^{309,334}

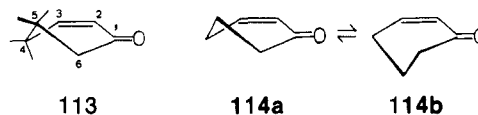
In the case of **110** an AA'BB'-type spectrum was observed for the allylic protons when the vinylic protons were decoupled. Because of the degeneracy of many transitions, an approximate line-shape analysis assuming an AB system was possible. A further increase in barrier was found (ΔG^\ddagger (300 K) 16.7 kcal/mol), indicating that most probably the inversion is concerted for all three rings. The ground-state conformation of **110** was later found to be of *D*₃ symmetry with all three rings adopting a cyclohexene-like half chair conformation.³³⁵ In contrast, a boat conformation is adopted by the six-membered rings of the dione **111**,³³⁶ possibly as a consequence of the bond angle changes associated with the introduction of a four-membered ring. This leads to a situation that is close to that in cyclohexa-1,4-diene where a flat boat conformation was established.³³⁷ Lanthanide shift reagents were used to distinguish the allylic proton resonances cis and trans to the ether bridge in the propellane **112** in order to investigate the steric course of the homogenous 1,4-hydrogenation of the tetraene precursor.³³⁸

3. Cyclohexenones

There is a paucity of precise NMR data for cyclohexenones since the spectra of the parent compounds have so far not been analyzed and only first-order treatments have been used to collect data for a number of derivatives.

It is generally assumed³³⁹ that cyclohex-2-enone possesses an envelope conformation **113** in which the oxygen and five carbons are coplanar and only C(5) deviates from this plane (sofa or envelope form). This view is supported by a recent microwave study³⁴⁰ and was adopted in two NMR investigations^{341,342} where the authors, however, used the misleading term half-chair.

Whereas for the parent compound a fast equilibrium between the two enantiomers **114a** and **114b** exists,³⁴⁰ most substituted



systems investigated so far adopt predominantly a single conformation. For several 3-methylcyclohex-2-enones phenyl substituted in positions 5 and 6, evidence for the preferred equatorial orientation of the C(5) substituent was derived.³⁴¹ Similar studies for methyl- and *tert*-butyl-substituted systems³⁴² used 220-MHz spectra and shift reagents to achieve first-order analysis. Again it was concluded that the 5-substituent occupies the equatorial position. The conformational analysis was based primarily on the coupling constants, notably ³*J*(3,4e), ³*J*(3,4a) and ⁴*J*(3,5e), ⁴*J*(3,5a) (cf. **113**). For the latter, a rigid conformation is supposed to yield values of 1.7 Hz for ⁴*J*(3,5e) because of a typical W arrangement of the σ bonds, and ~ 0 for ⁴*J*(3,5a), whereas ~ 0.8 Hz is observed for the average coupling ⁴*J*(3,5) = [⁴*J*(3,5e) + ⁴*J*(3,5a)]/2 in flexible forms. Using the same approach, mono-, di-, tri-, and tetramethyl-substituted systems and their BF₃ complexes were studied by others.³⁴³ From the findings it was concluded that complexation does not change the conformational equilibrium but leads to drastic charge transfer from the double bond to the carbonyl group as indicated by considerable downfield shifts observed for H(2) (0.84-1.04 ppm) and H(3) (0.87-0.94 ppm). This again supports a planar arrangement of C(1) to C(3).

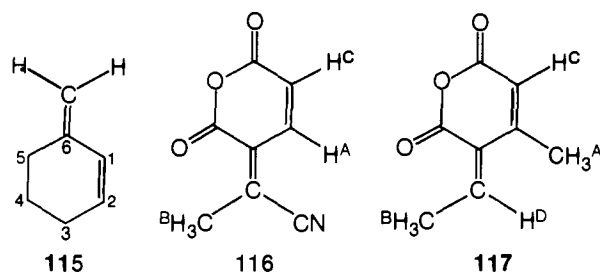
Vicinal and allylic coupling constants were employed to gain information about the geometry of the partial cyclohex-2-enone structure in various natural products^{344,345} after NMR/structure correlations had been uncovered by earlier investigations dealing with Δ^4 -3-ketosteroids.³⁴⁶ In addition, shift reagents were used for general structure determinations of systems with cyclohex-2-enone subunits.³⁴⁷ Bridged cyclohex-2-enones were

TABLE XV. Coupling Constants for Compounds 116 and 117³⁵¹

	$J(A,B)$	$J(A,C)$	$J(A,D)$	$J(B,C)$	$J(B,D)$	$J(C,D)$	Solvent
116	-1.30	+0.92	-0.66	0.1	-0.20	+7.60	CDCl ₃
117	-1.39		-0.77		-0.32		CDCl ₃

treated in the studies mentioned above^{328,330} and in an investigation where the chemical shift of the olefinic β -proton was utilized to estimate the twist angle of the conjugated system in compounds possessing a methylene bridge between positions 2 and 6 or 2 and 4.³⁴⁸ Miscellaneous 2J data in cyclohexenones and related molecules have been reviewed.³⁴⁹

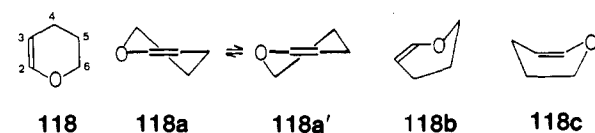
Structurally related to 113 are *exo*-methylene cyclohexene (115) and the two anhydrides 116 and 117. Several derivatives



of 115 substituted at carbons 3 and/or 4 were investigated qualitatively by first-order analysis and double resonance experiments.³⁵⁰ For 116 and 117, an ample study established the magnitude and the absolute signs of long-range H,H coupling constants over four, five, and six bonds³⁵¹ with the help of spin-decoupling and spin-tickling experiments. The results (Table XV) were found in excellent agreement with theoretical predictions and experimental data from acyclic dienes.

4. Heterocyclic Systems

A good deal of work exists again for heterocyclic systems derived from cyclohexene by replacement of one or more methylene groups by oxygen, nitrogen, or sulfur. In the oxygen series several studies concerned with the conformation of 5,6-dihydro-4*H*-pyran (118) are available and, using the calculations for cyclohexene^{275,288} as a guideline, three conformations for 118 have been considered in the discussions of the NMR results:³⁵² the half-chair 118a, calculated to be of lowest en-



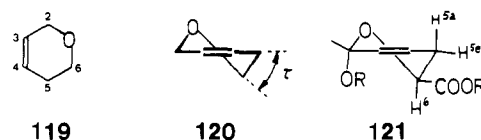
ergy,^{275,288} the envelope or "sofa" conformation 118b,³⁵³ destabilized by 1.2 kcal/mol, and the boat form 118c. Line-shape changes in the low-temperature spectrum of 118 were attributed to a conformational equilibrium of the two half-chairs 118a and 118a'.³⁵⁴ At -156 °C the methylene protons in the α position to the oxygen appear as the AB part of an ABXY system with the axial proton at higher field. A ΔG^\ddagger of 6.6 ± 0.3 kcal/mol was derived at the coalescence temperature (-140 °C), a surprisingly high value in the light of results that indicate a barrier decrease in cases where a CH₂ group is replaced by an oxygen.³⁵⁵⁻³⁵⁹ However, this applies to situations where only torsional energy (eclipsing of CH bonds) is important. In the present case, the origin of the barrier increase compared to the hydrocarbon ($\Delta\Delta G^\ddagger = 1.2$ kcal/mol; cf. section IV.D.1) was attributed to ground-state stabilization by conjugation between the π bond and the heteroatom.

Evidence for the half-chair conformation was also derived from the spectrum of D-glucal triacetates³⁶⁰ and more recently from that of 4-*tert*-butyl-118.³⁶¹ Shift reagents were used in this case successfully to simplify the spectrum for first-order analysis

that allowed the determination of 3J and 4J value. The similarity of the vicinal coupling constants in the C(5)-C(6) fragment with those of cyclohexane strongly supports 118a as the ground-state conformation of 118. On the other hand, 118b was favored in a discussion of results obtained for several substituted compounds, but the arguments presented are not fully convincing.³⁵² An interesting graphical method was developed to analyze the observations made for annelated and substituted dihydropyrans on the basis of an equilibrium $118a \rightleftharpoons 118a'$.³⁶² The authors correctly emphasized the limited nature of the NMR method that uses the Karplus equation to derive quantitative data for a series of differently substituted systems. Nevertheless, a general insight into the conformation and geometry of the compounds studied was possible, indicating that in the *trans* compounds the 4-phenyl group prefers the pseudo-equatorial position, whereas a 2-alkoxy group prefers the pseudo-axial position. In the *cis* compounds a slight dominance of the conformer with both groups in pseudo-axial positions was indicated; 2,3-annulation alters these preferences due to peri interactions with the 4-substituent. Strong changes are also caused by substituents in the phenyl group. Further evidence for general substituent effects on the conformation of 118 comes from investigations dealing with unsaturated carbohydrates, where α and β isomers exist in different half-chairs.³⁶³

Results bearing on the conformation of 118 have also been obtained from flavans (2,3-benzo-118).³⁶⁴⁻³⁶⁸ It was pointed out³⁶⁵ that the accuracy of the Karplus equation is insufficient to allow a decision in favor of either the half-chair or the envelope conformation. The cyclohexane-like effect of electronegative substituents on 3J values found for the flavans, however, again supports the half-chair. This and the other observations in favor of 118a as the stable conformation of 118 in the liquid state are strongly supported by the results of far-IR work that established 118a in the gas phase and in addition yielded a ring inversion barrier of 8.4 kcal/mol.³⁷⁵

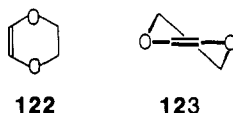
Conclusions based on the Karplus equation are also available for derivatives of 3,6-dihydro-2*H*-pyran (119), where the microwave spectrum of the parent compound was studied.³⁶⁹ A twisted or half-chair conformation 120 similar to that of cyclohexene (see section IV.D.1) was found with a twist angle τ of $31.5 \pm 3^\circ$.



In the NMR studies of 2,6-disubstituted derivatives of 119 a half-chair (121) was assumed.³⁷⁰ From the large value obtained for the sum of $J(6,5a) + J(6,5e)$ and the dihedral angles estimated from Dreiding models, it was concluded that the "trans" compounds exist predominantly in the conformation 121. For the "cis" compounds a ca. 1:1 mixture of the a,a and e,e conformer was considered. Later, ΔG° values were derived from temperature variations in the coupling constants.³⁷¹ As in other cases, the numerous assumptions necessary to obtain this information leaves the reader with mixed feelings about the significance of quantitative results.

From those compounds containing two oxygen atoms 1,4-dioxene (122) was studied most extensively.^{372,373} The NMR spectrum of 122 consists at room temperature of two singlets at δ 3.96 and 5.86 ppm and shows at -144.5 °C an AA'BB' system for the CH₂CH₂ fragment which gave after iterative

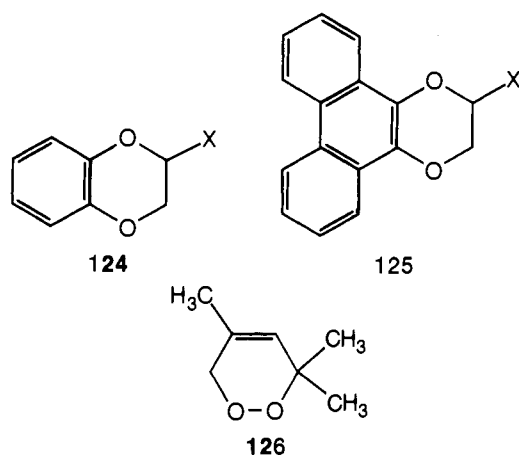
analysis the following data: δ_a 3.886, δ_e 4.044 ppm; ${}^2J = -11.88$, ${}^3J_{aa} = 9.98$, ${}^3J_{ee} = 1.08$, and ${}^3J_{ea} = 2.02$ Hz. Considering the effect of oxygen on the 3J values the coupling constants compare favorably with those of cyclohexane.³¹⁰ Thus the half-chair **123** must be the ground-state conformation of **122**.



The twist angle was calculated from the vicinal coupling constants as 26.8° .³⁷³ This result is in good agreement with the conclusions drawn from dipole moment measurements,³⁷⁴ far-infrared work,³⁷⁵ and the microwave spectrum.³⁷⁶ From the latter a twist angle of 29.9° was deduced and the molecule is believed to possess little, if any, strain.

From the temperature dependence of the NMR spectrum it was also possible to extract the activation parameters for the ring inversion of **122** using complete line-shape calculations.³⁷² Again, as in the case of **118**, the barrier is rather high ($\Delta G^\ddagger = 7.32 \pm 0.21$, $\Delta H^\ddagger = 7.32 \pm 0.15$ kcal/mol). A similar result was presented in the IR work³⁷⁵ that in addition gave evidence for the presence of ca. 7% of a bent conformer, destabilized by 561 cm^{-1} with respect to **123**.

Compound **122** was also studied in partially oriented form using a liquid crystal matrix.³⁷⁷ For the analysis of the spectrum the indirect coupling constants were largely neglected. Test calculations showed them to be of minor importance for the correct reproduction of the spectrum. Only a twisted geometry could explain the results, the twist angle being 29.1° , in excellent agreement with the above-mentioned findings. This observation shows that the reorientation of **122** in the liquid crystal is fast compared to the ring inversion process.



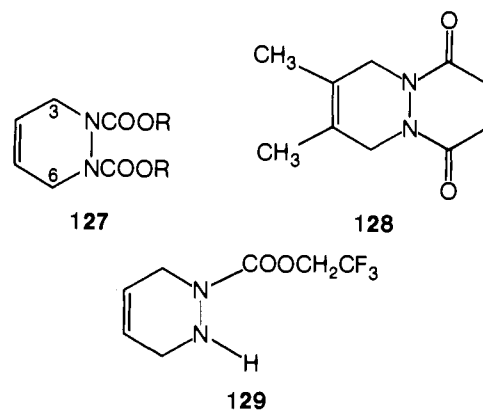
Conformational analysis has been performed for 2-substituted 5,6-benzodioxenes (**124**),^{378,379} The coupling constants for the parent compound were determined from an analysis of the ${}^{13}\text{C}$ satellite spectrum as $J = 5.92$ and $J' = 2.28$ Hz, indicating a fast equilibrium between two half-chairs. For derivatives with $X = \text{CN}$, $\text{CO}_2\text{C}_2\text{H}_5$, CO_2CH_3 , and COCl , a pseudo-axial preference was found for the substituent, whereas for system with $X = \text{COCH}_3$, $\text{CONCH}_3\text{C}_6\text{H}_5$, and $\text{C}(\text{OH})(\text{CH}_3)_2$, the substituent occupies the pseudo-equatorial position.

Similar results were obtained from the analysis of the ABX spectra of 2-substituted phenanthrodioxenes (**125**).³⁸⁰ Bulky groups like phenyl and naphthyl are exclusively pseudo-equatorial oriented, whereas for $X = \text{SC}_2\text{H}_5$, OC_2H_5 , OC_6H_5 , and Cl , increasing concentrations of the pseudo-axial conformer are found. The configuration of 2,3-disubstituted systems (cis or trans) was established from the coupling constants since for the average value ${}^3J(\text{cis}) > {}^3J(\text{trans})$ is valid.

A significant increase for the barrier of ring inversion was

reported in a preliminary dynamic NMR study of 1,3,3-trimethyl-4,5-dioxacyclohexene (**126**, 4,5,6-trimethyl-1,2-diox-4-ene), a cyclic peroxide.³⁸¹ From the temperature dependence of the *gem*-dimethyl signals, a ΔG^\ddagger of 11 kcal/mol was obtained, determinations of the Arrhenius parameters being less accurate owing to the use of approximate methods for the extraction of the rate constants. Since the half-chair is the most likely ground-state conformation of **126**, the reason for the barrier increase as compared to the ring inversion of cyclohexene ($\Delta\Delta G^\ddagger = \text{ca. } 6$ kcal/mol) might be seen in additional lone-pair interactions and bond angle strain present in the transition state. Similar barrier raises due to the O-O grouping are known for saturated systems.^{382,383}

In the field of nitrogen-containing compounds a considerable amount of work has been invested to uncover the conformational behavior of the tetrahydropyridazine system **127**. The first report³⁸⁴ dealt with 3,6-diphenyl-**127**, $R = \text{CH}_3$, C_2H_5 , and showed



the presence of two rate processes associated with energy barriers ΔG^\ddagger of 18.9 kcal/mol (at 97°C) and 14.8 kcal/mol (at -3°C). These were attributed to cyclohexene-like ring inversion and hindered rotation about the N-COOR bonds. For the former process a line-shape analysis yielded $\Delta H^\ddagger = 16.4 \pm 1$ kcal/mol and $\Delta S^\ddagger = -7 \pm 3$ eu.³⁸⁵ At 30°C the coupling constants of the compound are in accord with the half-chair conformation found for cyclohexene (cf. section IV.D.1). Compared to the hydrocarbon, however, and analogous to the situation discussed for **126**, the introduction of the N(COOR)-N(COOR) fragment into the six-membered ring greatly increases the barrier for ring inversion ($\Delta\Delta H^\ddagger \sim 10$ kcal/mol). That has been attributed to steric hindrance between the COOR groups in the transition state leading to a high rotational barrier around the N-N bond,³⁸⁵ an interpretation supported by experimental findings for compound **128**,³⁸⁶ where the possibility of rotation around the N-COOR bonds and nonbonded interactions between the ester groups have been eliminated. An upper limit of ΔG^\ddagger (-60°C) = 10.4 kcal/mol was found in this case for the ring inversion barrier. Additional evidence that the barrier height depends on the resistance to rotation around the N-COR bond was presented.³⁸⁶

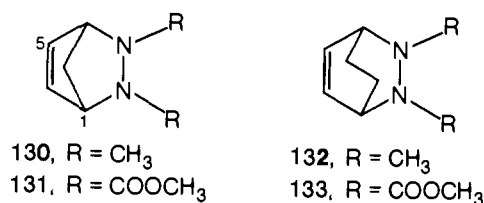
The above assignment of the two barriers was criticized³⁸⁷ and restricted rotation instead proposed as the origin of the high-energy process, but the original arguments³⁸⁴ found support by others³⁸⁸⁻³⁹⁰ and are now accepted insofar as recent work³⁹¹ at 100 MHz established a similar activation barrier for **127**, $R = \text{C}_2\text{H}_5$ (Table XVI), and revealed a much lower value ($\Delta G^\ddagger < 10$ kcal/mol) for the model compound **129**, thus again indicating that a removal of the above-mentioned steric crowding in the transition state considerably lowers the ring inversion energy.

Whereas agreement about the origin of the high-energy process has thus been reached, arguments in favor of restricted rotation,^{384,385} nitrogen inversion,³⁹² and a combination of both³⁹¹ have been advanced to explain the low-temperature rate process. In order to shed more light on this problem, the bicyclic compounds **130-133** were studied.^{386,393-395} Since these are

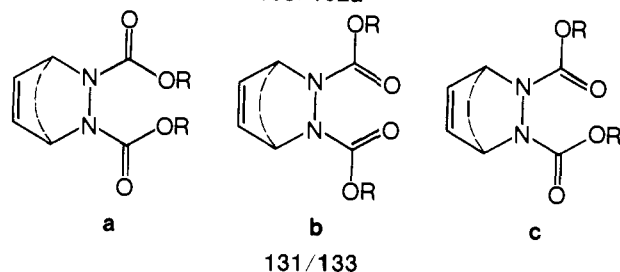
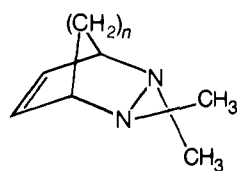
TABLE XVI. Energy Barriers for Dynamic Processes in Tetrahydropyridazines and Related Compounds

Compound	Solvent	ΔG^\ddagger (°C) ^a	ΔH^\ddagger ^a	ΔS^\ddagger ^b	Barrier origin	Ref
127, R = C ₂ H ₅	Cyclohexane	20.5 (25)	20.7 ± 1.4	0.6	Ring inversion	391
	CH ₃ COOH	21.1 (25)	22.9 ± 1.2	6.0	Ring inversion	391
128	CHCl ₃	<10.4 (-60)			Ring inversion	386
129	CHCl ₃ ^c	14.2	11.2	-11.0	Restricted rotation	391
	CHCl ₃	<10(-60)			Ring inversion	391
3,6-Ph ₂ -127, R = CH ₃	C ₂ Cl ₄	18.9 (97)	16.4 ± 1.0	-7 ± 3	Ring inversion	384, 385
	CDCl ₃	14.8 (-3)			Restricted rotation	384, 385
130	CDCl ₃ ^d	14.5 ± 0.2 (-9)	16.9 ± 0.6	8.3 ± 2.1	Nitrogen inversion	394
	Pentane ^d	13.9 ± 0.2 (-5)	16.2 ± 0.8	7.6 ± 2.6	Nitrogen inversion	394
131	CDCl ₃ ^d	13.7 (-5)			Restricted rotation	395
132	CDCl ₃ ^d	12.2 ± 0.2(-9)	14.9 ± 0.8	10 ± 3	Nitrogen inversion	394
	Pentane ^d	11.8 ± 0.3(-5)	12.4 ± 0.6	2.8 ± 2.5	Nitrogen inversion	394
133	CDCl ₃ ^d	16.4 (27.5)			Bridge flipping	395
	D ₂ O	16.6 (32)			Bridge flipping	395
135	CF ₂ Cl ₂	12.0 (-20)			Nitrogen inversion ^e	399
	CF ₂ Cl ₂	8.5 (-109)			Ring inversion ^e	399

^a In kcal/mol. ^b In eu. ^c 10% (v/v). ^d Ca. 0.5 M. ^e For alternative assignment see ref 400 and section V.



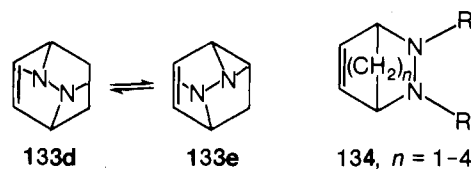
rigid systems, it was hoped to analyze nitrogen inversion and restricted rotation without the interference of the ring inversion process. The low-temperature spectra of **130–133**, obtained in the slow exchange region revealed two distinct CH₃ signals for the methyl compounds and three to four different CH₃ signals for the esters, thus indicating the presence of conformers **130/132a** and their mirror images, and **131/133a–c**, respectively. For **130** and **132** consecutive inversion of both nitrogens was found^{393,394} (Table XVI), and for **131** and **133** restricted rotation was favored^{394,395} over nitrogen inversion.³⁹³ For **133**, coalescence of the individual COOR signals was obtained



practically in the same temperature range as for **131** (-10 to -50 °C). In the case of a nitrogen inversion process, on the other side, a barrier decrease should be observed for the less strained system **133**, as was indeed found for the pair **130/132** (Table XVI), where only inversion can be responsible for the spectral changes.

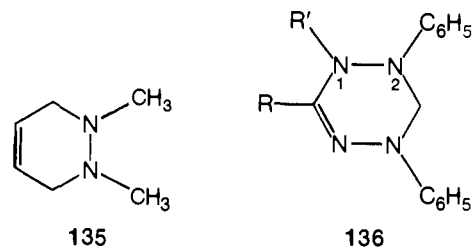
In addition, a bridge flipping process of the twisted NCOOR–NCOOR bridge containing the two nitrogens in the nearly planar state was discovered in the [2.2.2] system (**133d** ⇌ **133e**, Table XVI). No solvent effect on the barrier height was observed. In contrast, the activation energy for the pyramidal nitrogen in-

version in **130** was found to increase by 2.3 kcal/mol when pentane was replaced by D₂O as solvent.³⁹⁴ This work was later extended to 1- and 5-monosubstituted systems of type **130** and **131**³⁹⁶ and the conformational flexibility of systems of type **134**



was investigated.³⁹⁷ It is interesting to note that in the case of the ethyl ester the chirality of **133** is documented not only by the presence of two distinct ethyl absorptions but also by the diastereotopic nature of the methylene protons, thus giving rise to two ABC₃ type spectra in the slow-exchange region.

The temperature-dependent NMR spectra of tetrahydropyridazines **135** were also investigated by several groups.^{398–400}



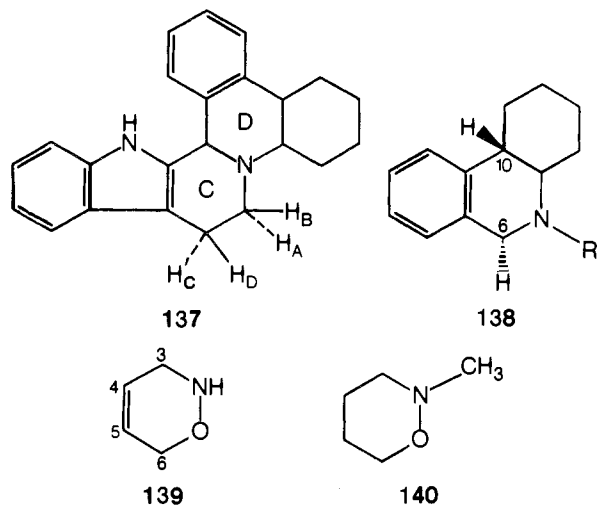
The most stable conformation of these systems has one axial and one equatorial N–CH₃ group, a fact also supported by dipole moment measurements.⁴⁰⁰ Two dynamic processes with energy barriers as shown in Table XVI were detected and attributed to nitrogen inversion and ring inversion, respectively.³⁹⁹ In an earlier study on related systems⁴⁰¹ only the high-energy process ($\Delta G^\ddagger \sim 12$ kcal/mol) was described.

Notwithstanding the correctness of the above-mentioned assignment, the ring inversion barrier in these systems is much lower than that for **127**. The possibility of a ring inversion process which does not involve a passing of the two N–CH₃ groups and therefore requires less energy was suggested for **135** and the above assignment for the nitrogen inversion barrier was criticized.⁴⁰⁰ These authors instead connected the high barrier to inversion processes (nitrogen or ring) with passing of the N substituents and the low barrier to inversion processes (nitrogen or ring) without passing of the N substituents. It seems that more work is needed to understand the conformational dynamics of these molecules (see section V).

Finally, evidence for a slow nitrogen inversion process at N-2 with barriers between 12.4 and 20.4 kcal/mol was found for

substituted tetrahydro-*s*-tetrazines (136).⁴⁰²

In a 270-MHz study the problem of the stereochemistry of three isomeric indoloquinolizines (137), containing the 3,6-dihydropyran partial structure, was attacked by an iterative spectral analysis of the ABCD system, supported by INDOR experiments.⁴⁰³ The stereochemistry at rings C and D was discussed on the basis of ²J(A,B) and the chemical shift difference $\nu_A - \nu_B$, both parameters that are sensitive to the orientation of the nitrogen lone pair relative to the C-H_A and C-H_B bonds. In the related octahydrophenanthridine 138 a formerly assumed

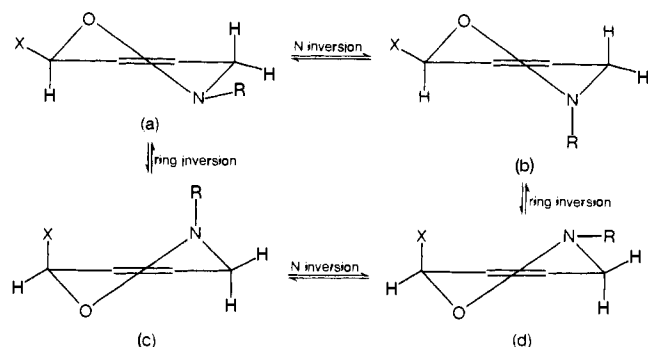


non-*W* ⁴J coupling was recognized as the homobenzylic coupling of 1.88 Hz between the pseudo-axial protons at C(6) and C(10) by a double resonance study.⁴⁰⁴

In the field of compounds containing two different heteroatoms we note a study of H,H coupling constants in 1,2-oxazines (139).⁴⁰⁵ For 13 differently substituted systems first-order analysis aided by spin decoupling was applicable. Homoallylic, allylic, and vicinal coupling constants were observed. It was concluded that the ⁵J coupling (2.0–2.5 Hz) is transmitted to an appreciable amount across the N–O bond. Because of the electronegativity effect of the two heteroatoms, the magnitude of the ³J values is rather small (*J*(3,4) 3.4–3.7, *J*(5,6) 2.9 Hz).

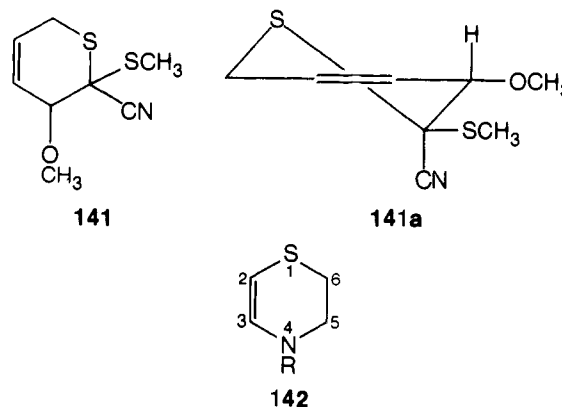
The dynamic behavior of N-substituted (CH₃, *t*-C₄H₉) 4,5-benzo-139 and 6-phenyl-139 was the main interest of a related investigation that used low-temperature NMR studies at 60, 100, and 220 MHz.⁴⁰⁶ Ring and nitrogen inversion can be assumed for these systems according to Scheme I. Only one of these processes, however, could be slowed down sufficiently to effect the NMR line shape that changed from an A₂ to an AB system for the N-CH₂ and O-CH₂ protons but remained a singlet for the N-CH₃ and N-*t*-C₄H₉ resonance. This information was not enough to decide which of the two inversions shown in Scheme I is slow on the NMR time scale. In view of the barrier height determined at coalescence temperature (ΔG^\ddagger (3 °C) 11.0 kcal/mol) the authors voted in favor of slow nitrogen inversion.

SCHEME I

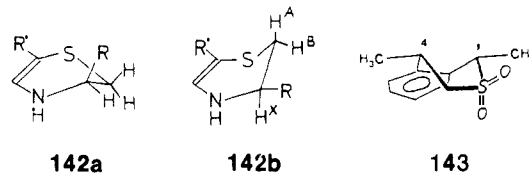


Support for this interpretation was seen in the 13.7-kcal/mol barrier found for nitrogen inversion in the saturated system tetrahydro-2-methyl-1,2-oxazine (140)⁴⁰⁷ on one side and the low barrier for ring inversion in cyclohexene on the other side. However, since ring inversion in the 1,2-dioxin 126 requires much higher energy (see above), the possibility that the same process is responsible for the spectral changes observed for 139 seems not yet ruled out, especially since solvent effects, known to influence strongly the barrier for nitrogen inversion,^{407,408} have not been investigated. In a preliminary note,⁴⁰⁹ barriers [$\Delta G^\ddagger(T_c)$] of 13.0 to 13.8 kcal/mol are given for a series of alkyl-substituted derivatives of 139. Again nitrogen inversion was invoked; the solvent effects observed in some cases are, however, rather small and probably within experimental error. In summary, it appears that the difficulties associated with a correct assignment of the various dynamic processes present in nitrogen heterocycles are still persistent, a statement underlined by a recent controversy on this matter.^{409,410}

From sulfur-containing systems the 3,6-dihydrothiopyran 141 was investigated at 220 MHz and the half-chair conformation 141a was found compatible with the H,H coupling constants.⁴¹¹ Another conformational analysis deals with the dihydro-1,4-thiazine system 142.⁴¹² The ABX systems of the aliphatic pro-



tons of derivatives substituted at C(2) and C(5) were analyzed and the results discussed in terms of the two "sofa", or "envelope", conformations 142a and 142b where electronic conjugation was seen as the driving force for the assumed coplanarity of atoms 1 to 5. With the help of the NMR parameters from a conformationally rigid model compound it was shown that for 142, R = R' = CO₂CH₃, in pyridine and acetone-*d*₆, 142a with R in a quasi-axial environment dominates, leading to *J*(A,X) ≈ *J*(B,X), whereas in CDCl₃ *J*(A,X) > *J*(B,X), indicating an appreciable population also of conformation 142b. The importance of intramolecular hydrogen bonding between R and the NH proton for the stabilization of 142b was demonstrated and confirmed by IR studies. Conformational equilibria for different solvents



were later determined from the magnitudes of *J*(A,X) and *J*(B,X).⁴¹³ The work was extended to the corresponding sulfoxides,⁴¹⁴ and evidence for an overwhelming preference of the conformation with the oxide function in the axial position—also found in saturated systems⁴¹⁵—was presented. However, the claim to have evaluated the NMR parameters from the AB region of the ABX systems by first-order analysis renders the accuracy of the quantitative aspect of this work somewhat doubtful. Finally, we mention an x-ray study of *cis*-1,4-dimethylisothiochroman dioxide which showed this system to adopt a boat form 143 in the solid state instead of the half-chair.⁴¹⁶ The same confor-

mation presumably is present in solution since the NMR spectrum yielded for H(4) a 3J coupling of 12 Hz showing this proton to be in an axial position. Similar findings were reported for the *trans*-1,3-dimethyl sulfone, whereas the *cis*-1,3-dimethyl compound presumably adopts a half-chair conformation.

A number of earlier studies, notably on dimeric pyridones, 2,3-dihydro 4-pyrones, and tetrahydropyridines, are cited in ref 15.

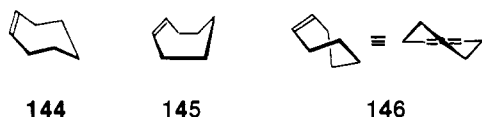
E. Cycloheptene

1. The Hydrocarbon and Its Benzo Derivatives

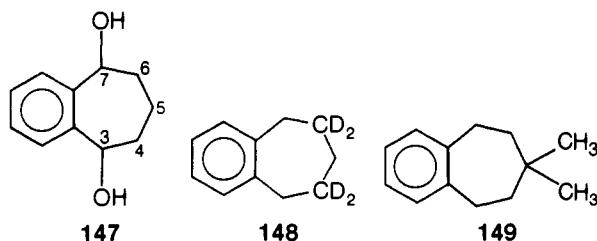
Compared to the six-membered ring, the investigation of the conformational processes present in the larger rings is more complicated because the barriers to pseudorotation and ring inversion are of comparable magnitude. The assignment of the activation parameters determined from the NMR line-shape changes to specific conformational transformations are, therefore, not always possible. Furthermore, the increased flexibility of the larger ring systems as well as their more complex spectra—a simple consequence of the increased number of protons present—strongly reduces the possibility to obtain exact chemical shifts and coupling constants unless partial deuteration and $^1H\{^2H\}$ double resonance experiments are employed.

Experimental results for the conformational behavior of cycloheptene that were obtained prior to 1970 have been reviewed in detail.⁸ We mention these investigations only briefly and concentrate on the more recent findings.

Three conformations, the chair **144**, the boat **145**, and the twist boat **146** are considered for cycloheptene.^{417,418} First information that indicated the chair to be the most stable one came from investigations of benzocycloheptenes **147–149**.^{419–422} For



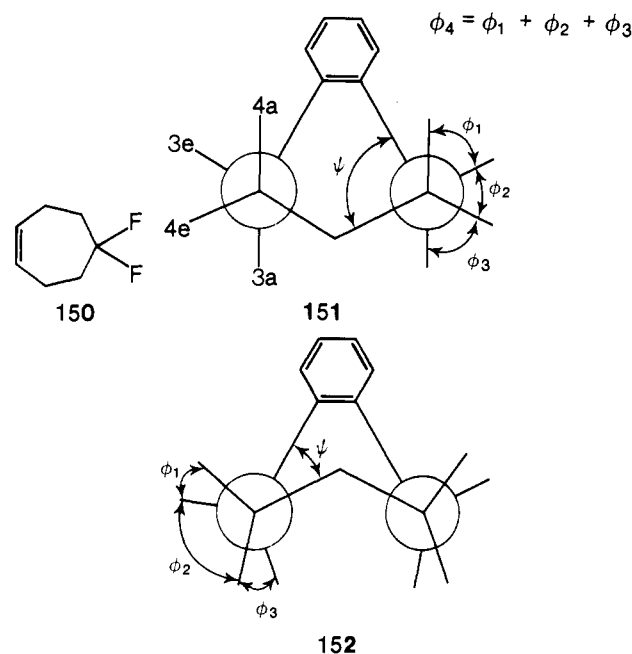
148 and **149** the nonequivalence of the CH and C-CH₃ bonds at C(5), respectively, was demonstrated by the observation of an AB system and nonequivalent methyl groups in the low-temperature NMR spectra (< -60 °C).^{420–422} This allowed the exclusion of **146** as the ground-state conformation. A decision



between **144** and **145** was then possible on the basis of H,H coupling constants and chemical shifts. The diol **147** and its acetate were examined,⁴¹⁹ and the single vicinal coupling of 9 Hz observed between the pseudo-axial benzylic hydrogen at C(3,7) and its neighboring CH₂ protons was found compatible only with the chair conformation, where—following models—dihedral angles between the C(3)-H and C(4)-H bonds of 90 and 115° are expected, while for **145** these angles are probably 15 and 150°, respectively. Extended investigations of a large number of substituted benzocycloheptenes confirmed this interpretation.^{420–422} Considering the ring current effect on the chemical shift of the CH₂ protons and the methyl groups at C(5) in both conformations **144** and **145**, the observed shift differences between pseudo-axial and pseudo-equatorial positions were found to agree only with that expected for the chair **144**.

Further evidence against the twist-boat ground state came from a study of 5,5-difluorocycloheptene (**150**)^{423,424} that showed dynamic behavior in the ¹⁹F NMR spectrum with coalescence at -92 °C and an AB system ($\Delta\nu = 1602$ Hz, $J(A,B) = 248$ Hz) in the slow exchange limit. Line-shape analysis between -44 and -147 °C yielded $\Delta H^\ddagger = 7.4 \pm 0.1$ kcal/mol and $\Delta S^\ddagger = 0.2 \pm 0.1$ eu. From their data alone the authors could not exclude the boat, but they favored the chair conformation, and their choice is supported by the findings discussed above. In addition, all investigations cited so far agree in that no second conformation was detected in the low-temperature spectra, thus showing the chair to be by far the most stable one. This is in accord with Raman and IR data⁴²⁵ that proved **144** to be the conformation of crystalline cycloheptene. In the liquid phase, however, additional bands were attributed to the boat conformation.

In order to further characterize the chair conformation **144**, spectral analysis of several partially deuterated benzocycloheptenes was carried out at -120 °C, where—on the NMR time scale—"frozen" conformations exist for these system.⁴²⁶ As in the earlier studies,^{419–422} from the now more accurately determined vicinal H,H coupling constants $J(3a,4a) = 12.6$, $J(3a,4e) = 1.1$, $J(3e,4a) = 1.1$, and $J(3e,4e) = 6.6$ Hz (errors ± 0.1 – 0.2 Hz), dihedral angles of $\phi_1 = \phi_3 = 73^\circ$, $\phi_2 = 44^\circ$, and $\phi_4 = 189^\circ$ (see **151**) were derived using a Karplus-type relation of $^3J = 12.95 \cos^2 \phi$ adjusted empirically for cyclohexane.³¹⁰ As indi-



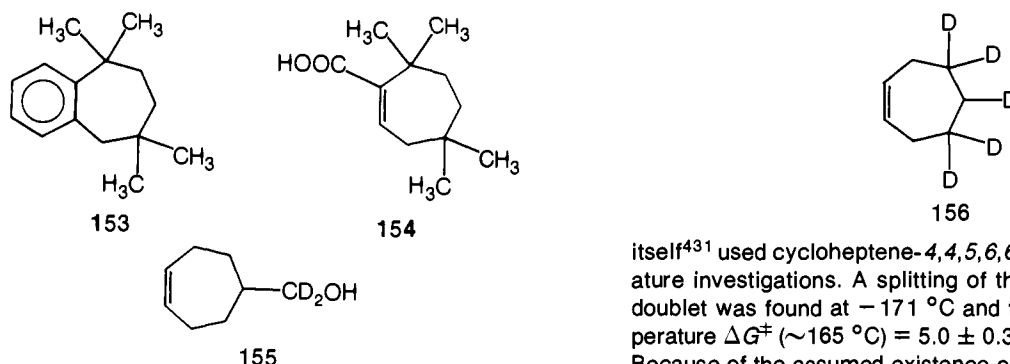
cated by **152**, the boat is not compatible with these results. Compared to cyclohexane, the seven-membered ring in **151** was found more puckered, showing a smaller ϕ_2 and a larger puckering angle ψ (cf. **151**) than the six-membered ring. For the chemical shifts, the axial proton at C(3) was found less shielded than the pseudo-equatorial one, most probably as a consequence of the ring current effect of the annelated benzene ring. At C(4) $\delta_a < \delta_e$ was observed, as in cyclohexane. In this context we also mention the results of a different study that determined $^3J_{cis}$ across the double bond as well as $^1J(^{13}C, ^1H)$ in the olefinic position of cycloheptene itself with values of 11.02 and 156.2 Hz, respectively.⁵¹

A compound diverging from the line developed so far apparently is 3,3,6,6-tetramethylbenzocycloheptene (**153**)⁴²⁷ where four C(4)-methyl signals (two 1:1 pairs of different intensity) are observed in the slow exchange limit (-81 °C).⁴²⁸ Accordingly two conformations, presumably boat and chair, are present, a result that agrees well with the predictions of model calculations⁴²¹ that showed both conformers to be of equal energy.

TABLE XVII. Activation Parameters for Dynamic Processes in Cycloheptenes, Benzocycloheptenes, and Tetramethylthiacycloheptyne (171)

Compound	ΔG^\ddagger , °C ^a	ΔH^\ddagger ^a	ΔS^\ddagger ^b	Solvent (concn)	Ref
148	10.7 (-57)	13.0 ± 1.5 (<i>E_a</i>)	15.0 ± 1.6 (log <i>A</i>)	CS ₂ (5-10%)	422
150	7.45 (-92)	7.7 ± 0.4 (<i>E_a</i>)	0.2 ± 2	CF ₃ Br/propene (10%)	424
153		12.6	-1	CS ₂ (5-10 wt%)	428
		9.3	-10		428
154	12.2 (-40)			CDCl ₃	429
156	5.0 ± 0.3 (-165)			H ₂ C=CHCl/CHF ₂ Cl 85:15 v/v (5%)	431
160	<5			CHF ₂ Cl (5%)	437
Benzo-160	10.3 (-73)			CS ₂ (5-10%)	422
161	6.0 (-153)			CHF ₂ Cl (5%)	437
Benzo-161	11.3 (-45)			CS ₂ (5-10%)	422
162	6.2 (-140)			CHF ₂ Cl (5%)	437
Benzo-162	11.8 (-45)			CS ₂ (5-10%)	422
163	7.7 (-117)			CHF ₂ Cl (5%)	437
Benzo-163	10.4 (-63)			CS ₂ (5-10%)	422
168	9.5 ± 0.2 (-57)	9.9 ± 0.2	1.5 ± 1.2	CHF ₂ Cl	443
171	9.2 (-100)	9.4 ± 0.3	1.3 ± 1.5	CD ₂ Cl ₂	455

^aIn kcal/mol. ^bIn eu.



From the experimental intensity ratios below coalescence and the line positions in the averaged spectra, $\Delta H^\ddagger = 0.3$ kcal/mol was extracted and from an approximate treatment of the line-shape changes activation parameters of $\Delta H^\ddagger = 9.3$ kcal/mol, $\Delta S^\ddagger = -10$ eu., and $\Delta H^\ddagger = 12.6$ kcal/mol, $\Delta S^\ddagger = -1$ eu., were derived for the dynamic processes attributed to chair \rightleftharpoons boat and chair \rightleftharpoons chair interconversions, respectively. It was suggested by others that one of these processes is associated with pseudorotation.⁴²²

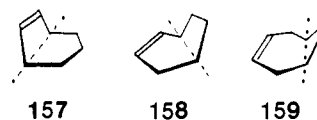
In a later study dealing with the structurally related system **154**, however, a different interpretation of the experimental observations was proposed.⁴²⁹ Spectral changes similar to those found for **153** were observed for the C(3) methyl groups of **154** that resulted in the appearance of two 1:1 doublets having different intensity. Since the IR spectra of **154** in the solid and in CS₂ solution were found identical, the author attributed the second doublet in the low-temperature NMR spectrum to lines of the C(4) and C(5) methylene protons and assumed that only one conformer, either chair or boat, is present.

Paramagnetic shift reagents and first-order analysis were employed to establish the most stable conformation of cycloheptene-5-carbinol- α, α -d₂ (**155**).⁴²⁰ Evidence of a chair form with pseudo-equatorial substituent was found. The spectra are, however, poorly resolved, and a more accurate investigation still seems desirable.

Besides the attempts to determine the ground-state conformation of cycloheptene and its derivatives, efforts have been made to uncover the details of its dynamic behavior. In addition to the dynamic NMR study of the 5,5-difluoro compound already mentioned, the activation parameters of the dynamic process responsible for the line-shape changes in the spectrum of the benzo compound **148** were determined.⁴²² ΔG^\ddagger (-57 °C) = 10.7 kcal/mol was found. A study dealing with the parent system

itself⁴³¹ used cycloheptene-4,4,5,6,6-d₅ (**156**) for low-temperature investigations. A splitting of the C(5)-H resonance in a doublet was found at -171 °C and for the coalescence temperature ΔG^\ddagger (~165 °C) = 5.0 ± 0.3 kcal/mol was calculated. Because of the assumed existence of intermediates (**145**, **146**) in the inversion process, a transmission coefficient of 1/2 was used for the ring inversion.

The detailed discussion of these experimentally determined activation parameters that are summarized in Table XVII is only possible by recourse to theoretical results as a guideline since no direct information about the geometry of transition states are available from the NMR method, and in a series of transformations only that with the highest barrier is measured. It is therefore gratifying that a considerable number of theoretical investigations of the cycloheptene conformations and their interconversion pathways are available.^{150,276,421,432-434} Except for the two earliest treatments^{287,417} all calculations agree in that the chair **144** is the most stable conformation for the hydrocarbon as well as its benzo derivative and that the twist boat is a true intermediate for the chair \rightleftharpoons chair interconversion. Furthermore, the rate-determining step is that of the chair-boat or chair-twist boat transition and not one of a pseudorotation within the boat family. The experimentally determined barriers are then connected to these local ring inversions (for a definition see F. A. L. Anet in ref 12). For the overall energetics of cycloheptene ring inversion, however, different results have been obtained, and these are summarized in Figure 1. Besides the true conformations **144-146** characterized by energy minima, transition-state geometries **157** to **159** have been calculated. Whereas for



treatments a-d molecular mechanics or force-field calculations⁴³⁵ were used, treatments e and f are based on the MINDO/II method.⁴³⁶ Here a different inversion path was found for cycloheptene and benzocycloheptene,^{433,434} the latter being in

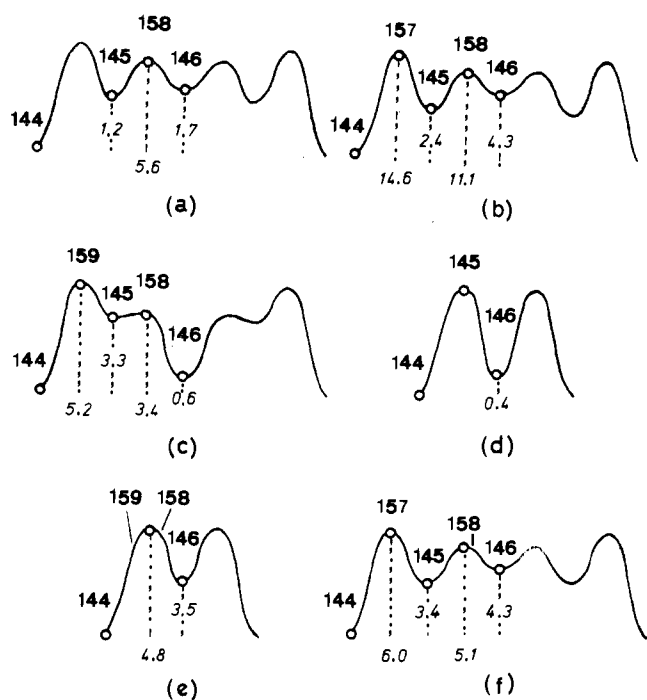
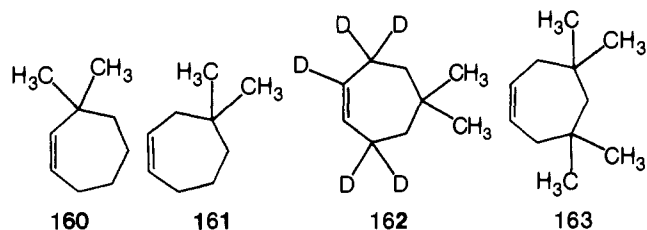


Figure 1. Schematic representation of calculated conformational interconversion mechanisms for cycloheptene (a, c, d, e) and benzocycloheptene (b, f): (a) ref 276; (b) ref 421, 422; (c) ref 150; (d) ref 432; (e) ref 433; (f) ref 434. Energies are in kcal/mol relative to the energy of the chair conformation 144.

qualitative agreement with study b. On the other hand, treatments d and e for cycloheptene agree in that both show the boat to be no intermediate at all and thus predict the disappearance of a separate pseudorotation barrier. Furthermore, it seems that the twist boat is preferred over the boat in the more recent results for the parent system.

An intriguing feature certainly is the difference in barrier height found for cycloheptene and benzocycloheptene ($\Delta\Delta G^\ddagger = 5.7$ kcal/mol). Various explanations have been offered. An increase in bending energy for the internal angles C(1)–C(2)–C(3) and C(2)–C(7) in the transition state 157⁴³¹ and nonbonding H,H repulsion were discussed,¹⁵⁰ while others preferred to interpret the change in ΔG^\ddagger as a documentation of the existence of different inversion mechanisms.^{433,434}

An attempt to decide this alternative experimentally was made with the investigation of compounds 160 to 163,⁴³⁷ whose benzo analogues had been studied earlier.⁴²² The spectrum of 160 did

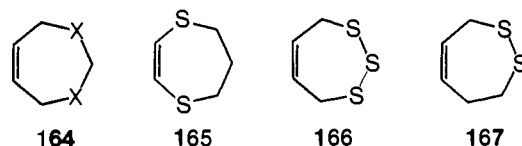


not show changes attributable to a dynamic process even at -170°C ; that of 161 gave a doublet for the methyl groups below -153°C . In the case of 162 deuterium decoupling was employed and the CH_2 resonances were found to change from an A_2 to an AB system ($T_c = 140^\circ\text{C}$). Finally, for 163 an unsymmetrical AB-type absorption and a doublet were observed in the slow exchange region for the methylene protons at C(3) and C(7) and the CH_3 resonances, respectively, while the C(5) methylene proton absorption remained a singlet even at -170°C . The barriers calculated at the various coalescence temperatures are compared in Table XVII with those of the corresponding benzo systems. In all cases, with the exception of the pair 163/

benzo-163, one finds within experimental error the same barrier increase in going from the parent compound to the benzo derivative ($\Delta\Delta G^\ddagger = 5.4$ kcal/mol). This was taken as a strong evidence for a common inversion path in both series of compounds, and this finding thus diverges from the results of the theoretical studies e and f discussed above. For the last pair of compounds $\Delta\Delta G^\ddagger$ only amounts to 2.7 kcal/mol and two possibilities to explain this result, which mainly originates from the barrier increase in the parent system 163, were suggested. Both imply an energy increase for the supposed transition state of pseudorotation (structure 158), which can be reached from the chair or from the twist boat as possible stable conformations of 163. The latter possibility is supported by the fact that the methylene resonance at C(5) remained a singlet even at the lowest temperature reached (-170°C).

2. Heterocyclic Systems

The earlier work on heterocycloheptenes of types 164 to 167 (X = S, O) and/or their *gem*-dimethyl derivatives as well as the



corresponding benzo systems^{417,438–442} has again been reviewed in detail.^{8,11} For the sulfur heterocycles several interesting features were discovered.

(1) In many cases two conformations of comparable energy exist. One of these is the chair and the other one may be either twist boat or boat.

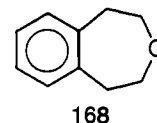
(2) Barriers for local ring inversion of the chair to the boat family and for pseudorotation within the boat family could be measured separately, energy differences between the two processes being in the order of 3–8 kcal/mol.

(3) The replacement of a methylene group by sulfur leads to an increase in the activation barriers which become >15 kcal/mol in the case of benzo-166.

(4) Several α,α' -disubstituted benzo trisulfides crystallize within the limits of detection in a single conformation (twist boat or chair), and the appearance of the conformational equilibrium could be followed by NMR at -40°C , thus allowing an independent determination of ΔG^\ddagger values.

For the oxygen-containing systems 164, and 5,5'-dimethyl-164 (X = O), and their corresponding benzo derivatives, the slow exchange limit was reached only for 5,5'-dimethylbenzo-164, yielding $\Delta G^\ddagger (-76^\circ\text{C}) = 9.7$ kcal/mol at coalescence, again lower by 2.1 kcal/mol than in the hydrocarbon (149).

From a low-temperature NMR study of 5-oxabenzocycloheptene⁴⁴³ (168) and the analysis of the ABCD spin system of the CH_2CH_2 fragment at -105°C —aided by the use of partially

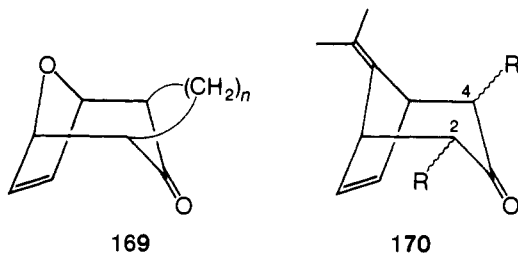


deuterated compounds and $^1\text{H}\{^2\text{H}\}$ decoupling—it was possible to show that this system exists also predominantly in a chair conformation. The NMR parameters are compared with that of 151 in Table XVIII. The differences between both sets of coupling constants could be attributed partly to the electronegativity effect of the oxygen and to a slightly more flattened seven-membered ring in 168. The line-shape changes from the AA'XX' system obtained in the fast exchange limit to the ABCD system measured at -105°C were calculated using the DNMR-2 program⁴⁴⁴ and from the rate constants obtained between -41.6 and -91.4°C the activation parameters given in Table XVII were calculated. The ring inversion process is thus again lowered by the

introduction of an oxygen ($\Delta\Delta G^\ddagger = 1.2$ kcal/mol in comparison to **148**). A new type of long-distance isotope effect on the chemical shifts in the deuterated compounds was noted.

The spectra of a number of methyl-substituted 1,5-benzodiazepines and 1,5-benzothiazepines have been analyzed by the iterative procedure in the fast exchange limit, and chemical shifts and coupling constants are reported.⁴⁴⁵ The conformations of the compounds were qualitatively discussed on the basis of a modified Karplus relation using the ³J values obtained. The conclusions drawn are necessarily based on many assumptions since no information from "frozen" conformers could be gained in the temperature range used.

Finally we mention two investigations that deal with bridged systems **169** and **170** that contain a cycloheptenone partial structure.^{446,447} In the case of **169** the bridges prevent the

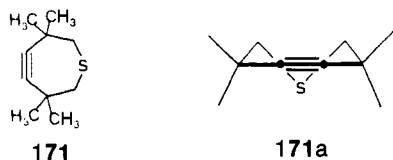


molecule from adopting a twist conformation and a true chair \rightleftharpoons boat equilibrium, favoring the boat conformation, is obtained. A line-shape analysis carried out in CCl₄ and acetone-*d*₆ yielded $\Delta G^\ddagger = 16.0$ and 16.4 kcal/mol, respectively, for **169**, *n* = 9; $\Delta H^\ddagger = 16.7$ kcal/mol and $\Delta S^\ddagger = 1.5$ eu were obtained. These activation parameters are very sensitive to the size of the methylene bridge; for **169**, *n* = 10, the slow exchange limit could not be reached at -80 °C ($\Delta G^\ddagger < 8$ kcal/mol), and for **169**, *n* = 8, no dynamic behavior was detected even at 140 °C, which means that the barrier for ring inversion exceeds ca. 22 kcal/mol. For **170** that was substituted in positions 2 and 4, *cis* and *trans* isomers were investigated. In the former the cycloheptenone ring adopts a chair conformation in case of 2 β ,4 β substitution. This conformation was also predicted earlier for the parent ketone.⁴⁴⁸ In addition, as a reference to related material, we refer to two recent studies dealing with cycloheptane⁴⁴⁹ and cycloheptene oxide.⁴⁵⁰

3. Cycloheptyne

The seven-membered ring is the first cycle where stable derivatives containing a CC triple bond were isolated, thus allowing structural and conformational studies. We therefore include here and in the following sections investigations dealing with cyclic acetylenes.

Cycloheptyne itself, while detected as a short-lived intermediate,⁴⁵¹ is still too reactive to allow its isolation. Even the 3,3,7,7-tetramethyl derivative, while more stable than the parent hydrocarbon, has a half-life of only 1 day in solution.⁴⁵² The sulfur derivative **171**, however, was prepared⁴⁵³ and investigated.



Electron diffraction studies showed that **171** possesses conformation **171a** and with 145.8° the smallest CCC angle at the triple bond known so far.⁴⁵⁴ At room temperature the NMR spectrum of **171** consists of two singlets at 2.784 and 1.186 ppm for the CH₂ and CH₃ protons, respectively.^{453,455} At lower temperature line-shape changes are observed and at -108 °C a CH₂-AB system [$\delta(A)$ 2.970, $\delta(B)$ 2.725 ppm, $J(A,B) = (-) 13.7$ Hz] and two methyl singlets (δ 1.283, 1.132 ppm) are found, in

TABLE XVIII. NMR Parameters of Benzocycloheptene (**151**)⁴²⁶ and 5-Oxabenzocycloheptene (**168**)⁴⁴³

	151 ^a	168 ^b
$\delta(3a)$	2.83	3.230
$\delta(3e)$	2.72	2.726
$\delta(4a)$	1.23	3.359
$\delta(4e)$	1.97	4.122
² J(3a,3e)	-14.1 \pm 0.1 ^c	-15.3 \pm 0.2 ^c
² J(4a,4e)	-13.8 \pm 0.2	-11.8 \pm 0.2
³ J(3a,4a)	12.6 \pm 0.2	11.2 \pm 0.2
³ J(3a,4e)	1.1 \pm 0.1	2.0 \pm 0.2
³ J(3e,4a)	1.1 \pm 0.1	0.6 \pm 0.2
³ J(3e,4e)	6.6 \pm 0.2	5.0 \pm 0.2

^a Values obtained from various partially deuterated systems at -120 °C in CHClF₂. ^b At -105 °C in CHClF₂. ^c Estimated errors.

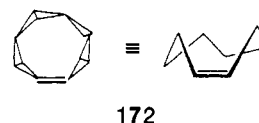
accord with the expectation based on **171a**.⁴⁵⁵ From the line-shape analysis of the AB \rightleftharpoons BA exchange between -30.0 and -95.5 °C activation parameters given in Table XVII were derived for the dynamic process that is best ascribed to ring inversion. The rather low barrier found for this strained system most probably is a consequence of the flexibility of the C \equiv C-C valence angles. Following the observations made for other sulfur heterocycles as cited above (section IV.E.2), the ring inversion barrier for the parent hydrocarbon is expected to lie below 9 kcal/mol.

F. Cyclooctene

Whereas the seven-membered ring was the first to accommodate a triple bond, cyclooctene is the first cycloalkene where both the *cis* and *trans* isomers have been isolated. The spectra of both isomers show considerable differences in the methylene region as well as in the olefinic region, the latter with absorptions centered at δ 5.40 and 5.51 ppm for the *cis* and *trans* compounds, respectively.⁸⁵ These variances are a consequence of the differences in geometry and conformational behavior that will be discussed in the following sections.

1. cis-Cyclooctene

The detailed structure of *cis*-cyclooctene has not yet been determined, but conformation **172** was predicted for this compound⁴⁵⁶ on the basis of x-ray evidence for cyclooctenimine.⁴⁵⁷



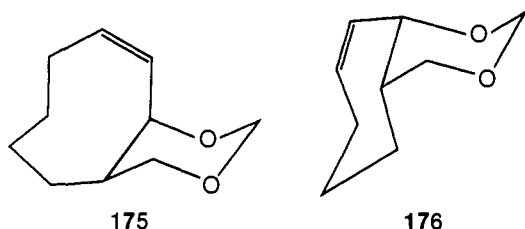
Calculations^{150,276,432} yielded similar geometries as energy minima. Other forms have been discussed^{458,459} and could be eliminated because of the small (1 Hz) coupling constant found for *cis*-5,6-dihydrocyclooctene-*d*₁₂, indicating a dihedral angle of ca. 90° between the C(5)-H and C(6)-H bonds.

Two dynamic processes were found for *cis*-cyclooctene by NMR^{458,459} and attributed to pseudorotation ($\Delta G^\ddagger = 5.8$ kcal/mol) and ring inversion ($\Delta G^\ddagger = 8.2$ kcal/mol), but no detailed account on this investigation has so far appeared. In a study that used variable-temperature ¹⁹F NMR, two structureless signals separated by 6.4 ppm were observed at -156 °C for 1-fluoro-*cis*-cyclooctene, indicating the presence of two conformations, presumably **173** and **174**.⁴⁶⁰ From the peak area ratio of 3:2, an



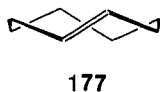
energy difference of 95 kcal/mol was calculated. Coalescence was observed at -129°C and an energy barrier of 6.1 kcal/mol estimated for the dynamic process responsible for the line-shape changes. Either pseudorotation or ring inversion could explain equally well this finding, but in a recent review on multistep conformational interconversion mechanisms⁴⁶¹ two pathways for the dynamic behavior of *cis*-cyclooctene were proposed that allow a unique interpretation of the NMR data. One is a pseudorotation that introduces a C_2 axis on the NMR time scale. It must be assigned to the low-energy process in view of the NMR evidence.⁴⁶² It also interchanges the two fluorine sites. The barrier for the high-energy process that is necessary for complete geminal exchange to occur and that conforms to ring inversion is characterized by a plane of symmetry.

A 300-MHz spectrum of *cis*-bicyclo[6.4.0]-10,12-dioxa-2- and 3-dodecene showed the former to exist predominantly in conformation **175** with axial alkene group despite an expected strain effect of ca. 2.25 kcal/mol for this orientation of the double bond.⁴⁶³ The reason for this observation was seen in nonbonding interactions between internal hydrogens and oxygen expected for the alternative conformation **176**.



2. *trans*-Cyclooctene

trans-Cyclooctene, first isolated in 1910,⁴⁶⁵ recognized as the *trans* isomer in 1950,⁴⁶⁵ and resolved into optical isomers in 1963,⁴⁶⁶ has a twist or distorted crown conformation **177**.⁴⁶⁷ It is rigid on the NMR time scale, the barrier to ring inversion accompanied by racemization for the pure isomers being 35.6 kcal/mol.⁴⁶⁸ **177** was determined by recent electron diffraction



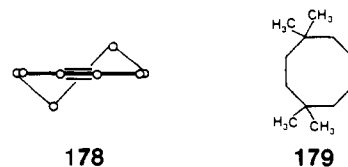
measurements⁴⁶⁷ and agrees with the result of various x-ray investigations of *trans*-cyclooctene metal complexes,⁴⁶⁹⁻⁴⁷¹ iodo-*trans*-cyclooctene,⁴⁷² and *trans*-2-cyclooctenyl dinitrobenzoate.⁴⁷³ In an earlier electron diffraction analysis a chair conformation was proposed,⁴⁷⁴ but it seems that this result is in error. The twist conformations is also supported by the outcome of recent theoretical calculations.^{150,432} One group⁴⁷⁵ found a distorted chair as the most stable form, but this result was not confirmed.⁴³² An interesting feature of **177** is the twisted double bond that shows a dihedral angle of 136° . This possibility had been suggested already in connection with the interpretation of dipole moment⁴⁷⁶ and optical activity data.^{477,478}

A first-order interpretation of the ^{13}C satellites of the olefinic protons of **177** yielded $^1J(^{13}\text{C}, ^1\text{H}) = 151$, $^3J(1,2) = ^3J_{\text{trans}} = 16.0$, $^3J(2,3) = 10.0$, and $^3J(2,3') = 4.5$ Hz.⁴⁷⁹ The one-bond $^{13}\text{C}, ^1\text{H}$ coupling constant is thus considerable smaller than in the *cis* isomer (see Table I), and this agrees with the rehybridization of the olefinic carbons discussed earlier¹⁵⁰ in connection with the twisted double bond, where some s-character was introduced into the π -bond thereby lowering the s-character in the C-H bonds. Vicinal coupling constants in the same order as for **177** were found also for *trans*-cyclooctenyl derivatives.^{480,481} A consideration of the effect of the double bond anisotropy on the chemical shift of the methylene protons yielded support for the twist conformation,⁴⁷⁹ and the thermal transformation of configurationally pure 2-bromo-3-methoxy-*trans*-cyclooctene into

its diastereoisomer (20%) and the *cis* compound (30%) was detected by NMR.⁴⁸²

3. Cyclooctyne

The structure of cyclooctyne has been determined by electron diffraction as the "half-chair" **178** that has the unique feature

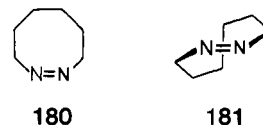


of six coplanar carbon atoms.⁴⁸³ The $\text{C}\equiv\text{C}-\text{C}$ angle (158.5°) is larger than in the seven-membered cyclic acetylene **171**, and an increased flexibility of the compound is expected.

In order to simplify the spectrum of **178**, 4,4,7,7-tetramethylcyclooctyne (**179**) was synthesized and investigated.⁴⁸⁴ At 35°C three signals at 0.99, 1.44, and 1.82 ppm were observed and assigned to the CH_3 , $\gamma\text{-CH}_2$, and $\alpha\text{-CH}_2$ protons, respectively. At low temperature the methyl signal splits into a doublet and partially overlapping AA'BB' systems are observed for the methylene protons. From coalescence measurements at 60 and 220 MHz for both absorptions a ΔG^{\ddagger} value in the order of 12.5 kcal/mol could be extracted and was assigned to ring inversion. The barrier is surprisingly high if one considers the results for **171** (cf. section IV.E.3) and the assumed barrier-raising effect of the sulfur. This finding shows that the effect of dimethyl substitution on barrier height apparently has a strong positional dependence. Models suggest that ring inversion in **179** involves CH_3, CH_3 repulsion, whereas in **171** only CH_3, H repulsion is present.

4. Heterocyclic Systems

Recently, NMR data for *cis*- and *trans*-1,2-diaza-1-cyclooctene (**180** and **181**, respectively) and their *cis*- and *trans*-3,8-diphenyl



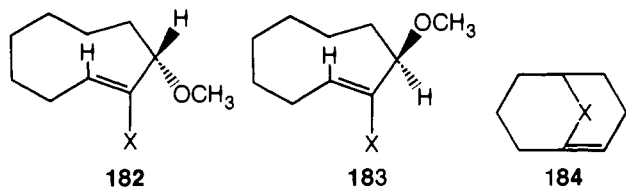
derivatives was reported.⁴⁸⁵ As expected, both isomers show different NMR spectra, but both are temperature dependent. In the 3,8-diphenyl series the fact that *cis*-3,8-diphenyl-**181** is the only isomer that possesses diastereotopic methine protons was used for structural assignment. For *cis*-3,8-diphenyl-**180** a dynamic process characterized by a barrier ΔG^{\ddagger} of 18.1 ± 0.3 kcal/mol as determined from the ^{13}C NMR spectrum was reported.

G. Cyclononene

There is a paucity of NMR as well as structural data for cyclononenes. An early analysis of the olefinic splitting pattern in *cis*-cyclononene yielded $^3J(1,2) = ^3J_{\text{cis}} = 10.7$, $^3J(2,3) = 8.2$, and $^4J(1,3) = -0.7$ Hz,⁴⁸⁶ and dihedral angles were estimated from these data,⁴⁹ but the results are probably not accurate enough to allow conclusions about the conformation. The spectrum of the *trans* compound was compared qualitatively with that of *cis*- and *trans*-cyclooctene.⁸⁵

Force field calculations have been performed for *cis*- and *trans*-cyclononene,^{276,432,475} however, the results can only be compared⁴³² with structural data obtained for caprylolactam and its hydrochloride.⁴⁸⁷ The resolution of enantiomeric *trans*-cyclononenes was attempted, but only partially successful even at low temperatures.⁴⁸⁸ A racemization barrier of 20 ± 2 kcal/mol was found, much lower than that for *trans*-cyclooctene.

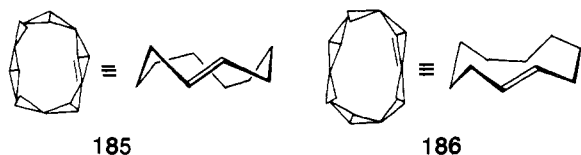
Diastereomeric 2-halo-3-methoxy-*trans*-cyclononenes (**182** and **183**) were detected by NMR at 35 °C, while at higher temperatures their increased interconversion rate led to coalescence of the methoxy signals (92 °C).⁴⁸²



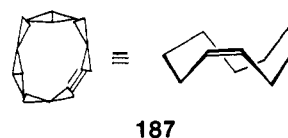
First-order NMR data are available for *cis*- and *trans*-1,3-dibromocyclononene⁴⁸⁹ and for bicyclic systems of type **184** (X = CH₂^{490,491}, O,⁴⁹² S⁴⁹³) that contain a cyclononene ring. In the former case the stereochemical assignment of the double bond in both isomers was based on a deshielding effect exerted by bromine on the vinylic proton in a *cis* arrangement that was indicated by results from various model compounds; $\delta = 6.11$ and 5.89 ppm was found for the *cis* and *trans* isomers, respectively. In the bicyclic series the vinylic proton ($\delta = 5.57$ for X = O, $\delta = 6.25$ for X = S, $\delta = 5.68$ for X = CH₂) in the ether and the sulfide is deshielded by 1.4 and 0.9 ppm, respectively, in comparison to the resonance of the β proton in untwisted vinyl ethers and sulfides. This was taken to indicate the absence of dative interactions between the heteroatom and the double bond in **184** due to unfavorable geometry.⁴⁹³

H. Cyclodecene

The possible conformations of *cis*- and *trans*-cyclodecene have been discussed in more detail,^{461,494,495} and experimental as well as theoretical treatments are available. X-ray investigations of the silver nitrate complexes of both olefins^{496,497} and of a cyclodeceny-*p*-nitrobenzoate of the *trans* compound⁴⁹⁵ have been performed, and the problem of conformation and conformational interconversion has been attacked by calculations.^{150,432,475} The latter disagree in their predictions for the most stable geometries of the two olefins, and according to the x-ray results, the *trans* compound adopts different conformations in the AgNO₃ complex and in the *p*-nitrobenzoate crystals, where only the major component present to 70–80% could be characterized. The observed forms are **185** for the complex⁴⁹⁶ and **186** for the *p*-nitrobenzoate.⁴⁹⁵

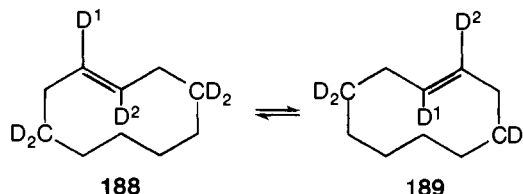


An interesting feature of **185** is the twisted *trans* double bond that has a torsional angle of 138°, practically the same value as found for *trans*-cyclooctene.⁴⁶⁷ A further point of interest is the increased flexibility of the ten-membered ring even in the *trans* compound that prevents the isolation of optical isomers.⁴⁸⁸ Half-lives of 10⁵ years, 10 s, and 10⁻⁴ s at room temperature have been calculated⁴⁹⁸ for the enantiomers of the eight-, nine-, and ten-membered cyclic *trans* olefins, respectively. However, at -60 °C diastereoisomers were also observed for 2-bromo-3-methoxy-*trans*-cyclodecene,⁴⁸² coalescence of the methoxy signal occurring now at 5 °C. Calculations⁴³² indicate that the free *trans* olefin might adopt a conformation that differs appreciably from that of the AgNO₃ complex (**185**), whereas for the *cis* isomer, both the complex and the free olefin, closely follow conformation **187** found experimentally for the complex.⁴⁹⁷ [We would like to point out that the stereoforulas given for **185**–**187** were based on the experimental results and chosen to illustrate the main features of the conformations. They contain some "artistic intuition" and must by no means be mistaken as exact



representations of structural parameters as bond lengths and bond angles.] Thus, the situation met with the two isomers of cyclodecene can be summarized as follows:⁴⁹⁵ "*cis*-cyclodecene has a well-defined conformation, related to the stable cyclodecane conformation, with a planar double bond system." For *trans*-cyclodecene the available evidence "points to a number of rather ill-defined conformations of roughly equal energy, all destabilized by the presence of twisted double bond systems."

Except for an earlier report on H,H coupling constants of the olefinic protons in *cis*- and *trans*-cyclodecene⁴⁹ (cf. Table I), NMR investigations deal exclusively with *trans*-cyclodecene. A detailed study was performed on 1,2,4,9,9-hexadeuterio-*trans*-cyclodecene, where the allylic protons were used as a probe to uncover the dynamic behavior of this olefin.⁴⁹⁸ At room temperature these protons give rise to a single resonance at $\delta = 2.05$ ppm, whereas at -74 °C an AB system with $\Delta\delta(A,B) = 0.19$ ppm and $J(A,B) = 12.8$ Hz is observed. A complete line-shape analysis in the temperature range from -7 to -74 °C yielded $E_a = 10.7 \pm 0.3$ kcal/mol, $\log A = 11.7 \pm 0.3$, $\Delta S^\ddagger = -6.8$ eu, and $\Delta G^\ddagger(2.8 \text{ }^\circ\text{C}) = 12.0$ kcal/mol for the rate process responsible for these spectral changes. Models and their interconversions as well as the experimentally measured exchange mode indicated that the observations originate from a rotation of the *trans* double bond through the loop of the methylene groups (**188** \rightleftharpoons **189**). Another dynamic process with an appar-



ently slightly higher barrier documents itself in a broadening of the other CH₂ resonances at $\delta = 1.37$ and was attributed to restricted rotation around the C(6)–C(7) bond. At lower temperatures (-143 to -164 °C) further motions are apparently slowed down sufficiently to affect the spectrum; however, their identification was not possible. In particular, a third dynamic process, the flipping of the C(4) and C(9) methylene groups, was expected to be too fast for NMR detection.

The choice of the relative population of the six conformations chosen above for *trans*-cyclodecene⁴⁹⁸ was later criticized on the basis of the x-ray results for the AgNO₃ complex that showed **185** to be the most stable form.⁴⁹⁶ In a subsequent ¹⁹F NMR investigation of 3,3-difluoro-*trans*-cyclodecene, no experimental evidence was found against this prediction.⁴⁹⁹ This study confirmed the presence of three dynamic processes, "frozen out" at temperature ranges of +17 to -11, -11 to -30, and -30 to -150 °C, and documented by the following spectral changes: (a) transformation of the ¹⁹F singlet to an AB system, (b) changes of the separation of the two inner lines of this AB system, and (c) the appearance of at least four different AB systems at -152 °C with the relative population of 0.78, 0.14, 0.05, and 0.03, as well as additional minor absorptions. The authors concluded that at least five different conformations are present at -152 °C, an interpretation that is supported by the results of calculations which yield six conformations within an energy range of 2.5 kcal/mol.⁴³² The activation parameters derived from the A₂ \rightleftharpoons AB exchange are $E_a = 14.9 \pm 0.4$ kcal/mol, $\log A = 14.68 \pm 0.28$, $\Delta G^\ddagger(2.8 \text{ }^\circ\text{C}) = 12.4$ kcal/mol, and $\Delta S^\ddagger = +6.9$ eu. Whereas the ΔG^\ddagger value agrees with that obtained from the

TABLE XIX. NMR Parameters of Benzocycloalkenes (191, 198) and Benzocycloalkanediones (194–196)

Compound	$\delta(1,4)$	$\delta(2,3)$	$\delta(\alpha\text{-CH}_2)$	$J(1,2)$	$J(2,3)$	$J(1,3)$	$J(1,4)$	Rms	Solv	Ref
191, $n = 1$	7.149 ^a	7.189	3.11	6.04	7.63	0.33	1.85	0.04	CDCl ₃ ^e	503, 504
191, $n = 2$	6.907 ^a	6.764	3.11	7.36	7.79	1.00	1.03	0.03	CDCl ₃ ^e	503, 504
					7.36	7.78	0.92	0.04	CCl ₄ ^f	/
	6.76 ^b	6.90								506
191, $n = 3$	7.073 ^a	6.990	2.80	7.59	7.20	1.17	0.48	0.04	CDCl ₃ ^e	502, 504
191, $n = 4$			2.65						CCl ₄ ^g	502
191, $n = 5$			2.74						CCl ₄ ^g	502
191, $n = 6$			2.78						CCl ₄ ^g	502
194	8.080 ^c	7.856		7.71	7.15	0.77	1.24	0.03	CDCl ₃ ^e	504
195	7.963 ^c	7.845		7.73	7.34	1.05	0.83	0.02	CDCl ₃ ^e	504
196	8.045 ^c	7.733		7.81	7.34	1.30	0.58	0.01	CDCl ₃ ^e	504
198	7.483 ^d	7.606		6.86	7.45	0.34	1.89	0.03	CCl ₄ ^h	513

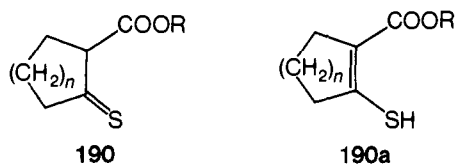
^a Assignment based on H,H long-range coupling. ^b Assignment based on width of ¹³C satellites. ^c Assignment based on benzene solvent shifts. ^d Assignment based on H,F coupling constants: $J(1,F) = 3.64$, $J(2,F) = -0.33$ Hz. ^e Concentration 10–20% w/v or v/v. ^f 0.6 M. ^g At infinite dilution. ^h 25% v/v. ⁱ Reference 507.

earlier proton NMR work, the other parameters differ considerably, a fact that was attributed to systematic errors of unknown origin.

An interconversion scheme, where eight possible conformational classes of *trans*-cyclodecene were connected by the types of motions mentioned above (rotation of the C=C and C(6)—C(7) bonds and flipping of the methylene groups) was given.⁴⁹⁹ Clearly, at room temperature all three of these processes are rapid on the NMR time scale. For the line-shape changes, however, only a tentative assignment was possible, the proposed order being now bond rotation (C=C or C—C), CH₂ flipping, and bond rotation (C—C or C=C).

More recently, an interconversion path for *trans*-cyclodecene was proposed⁴⁶¹ that renounced high-energy C(6)—C(7) bond rotation. A family of four conformations, among them that found for the AgNO₃ complex (185) and for the *p*-nitrobenzoate (186), is interchanging with each other via corner-moving steps of low energy, and connected by C=C bond rotation as the high-energy process followed by successive passage through four unpopulated forms to the inverted crystal conformation 186', thereby achieving geminal exchange. This scheme explains the NMR findings except for the postulated second high-energy process. Clearly, this problem requires further studies, especially since the experimental evidence for this second high-energy process seems less clearcut than for the other intramolecular motions.

Finally, we mention a study that deals with tautomerism in ethyl 2-thioxocycloalkanecarboxylates of ring sizes 5 to 12 (190, $n = 1-8$).⁵⁰⁰ For the smaller rings up to 190, $n = 5$, the *cis* enethiols 190a dominate, most probably as equilibrium mixtures

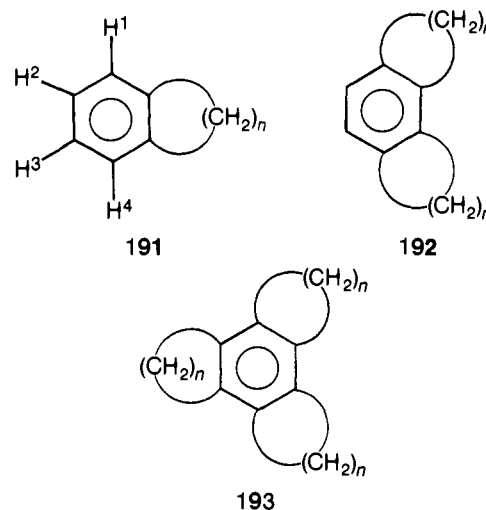


of COOR rotamers. The spectra of the larger ring compounds (ring size 10–12, 190, $n = 6-8$) show additional signals attributable to *trans* enethiols and thione forms, and the concentration of the former increases with increasing ring size. Equilibrium concentrations as calculated from the NMR intensities are given.

I. Benzocycloalkenes

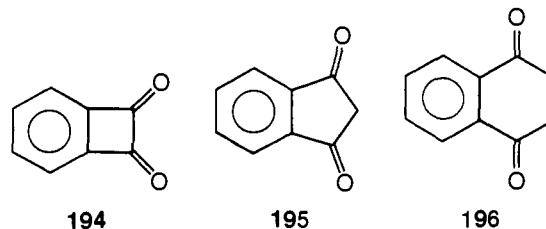
Results for benzocycloalkenes have already been treated in the appropriate former sections if the findings were of relevance to the properties of the parent cycloalkene. We now discuss work especially concerned with the benzo systems themselves irrespective of a particular ring size.

The NMR parameters of simple benzocycloalkenes (191) are summarized in Table XIX. They have been discussed under the aspect of a possible perturbation of the π -electron sextet by strain effects, a phenomenon known as the Mills–Nixon effect.⁵⁰¹ From the chemical shifts measured for the benzylic protons in mono-, di-, and tricycloalkenobenzenes of type 191–193 ($n = 3-6$), it



was concluded that the "ring current effect" of the aromatic ring in these systems is diminished by strain since in comparison to model compounds (cycloalkenes, *exo*-methylene cycloalkenes) a less pronounced downfield shift was found with decreasing ring size.⁵⁰² The measured chemical shift data for benzocyclobutene and benzocyclopropene,⁵⁰³ however, cast doubt on this argument. In these compounds ring strain is expected to be large, and a distinct upfield shift for the resonance frequencies of all protons should result if cyclic delocalization is appreciably quenched. This is not the case (Table XIX), and the observed effects are most probably of different origin.

The detailed analysis of the AA'BB' spin systems of 191, $n = 1-3$, and several benzoalkanediones (194–196) yielded pre-



cise data for the coupling constants, and a strong variation of the long-range coupling constants ⁴ J (J_{meta}) and ⁵ J (J_{para}) with ring size was noted⁵⁰⁴ (Table XIX). Considering also the values

TABLE XX. NMR Parameters ^a of α -Tetralone (199)⁵²³

A. Aliphatic Protons					
	I ^b	II ^c		I	II
$\delta(2)$		2.4609	$J(4,4')$	-16.21	
$\delta(3)$	1.9887	1.9839	$J(2,3)$		8.76
$\delta(4)$	2.8252		$J(2,3')$		4.26
			$J(3,4)$	7.98	
$J(2,2')$		-16.67	$J(3',4)$	4.29	
$J(3,3')$	-13.00	-13.20			

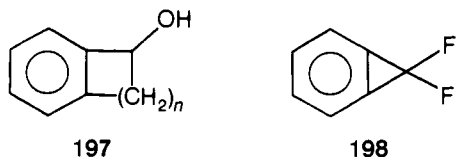
B. Aromatic Protons					
	I	II		I	II
$\delta(5)$	7.0983	7.0997	$J(5,8)$	0.54	0.60
$\delta(6)$	7.2973	7.3000	$J(4,6)$	0.33	
$\delta(7)$	7.1476	7.1500	$J(6,7)$	7.24	7.24
$\delta(8)$	7.8764	7.8695	$J(6,8)$	1.46	1.60
			$J(4,7)$	-0.61	
$J(4,5)$	-0.91		$J(7,8)$	7.67	7.87
$J(5,6)$	7.67	7.88	$J(4,8)$	0.43	
$J(5,7)$	1.26	1.30			

^a Errors in chemical shifts 0.001–0.002 ppm, in coupling constants 0.03–0.11 Hz for aliphatic protons, those for aromatic protons being smaller. Solvent/concn: CCl₄/15 wt %. ^b 2,2'-Dideuterio-199. ^c 4,4'-Dideuterio-199.

of these parameters in α -di-*tert*-butylbenzene,⁵⁰⁵ it appears that the long-range coupling constants are indicative of the strain effects operating in the various systems: ⁴*J* increases with decreasing ring size, i.e., increasing strain, whereas ⁵*J* shows the opposite trend. The changes observed for the vicinal coupling constants were found less systematic. This paper also reports correct values for H,H coupling constants in *cis*- and *trans*- α,α' -dibromo-191, *n* = 2, and the corresponding tetrabromide.

The spectrum of 191, *n* = 1, is complicated by the small chemical shift difference between the aromatic α and β protons, and for 191, *n* = 4, $\Delta\delta$ is too small to allow an analysis, even at high field strength (220 MHz). Assignments of proton resonance frequencies were based on the assumption that the benzylic protons couple more strongly with the aromatic α protons than with the β protons. Recently, the assignment given for indan (191, *n* = 3) was confirmed, but for 191, *n* = 2, the reverse assignment was proposed.⁵⁰⁶ For completeness, we also mention here investigations dealing with the ¹³C NMR chemical shifts^{508,506} and the ¹³C,¹³C coupling constants⁵⁰⁹ of these systems.

An interesting study of the spectra of benzocycloalkenols (197, *n* = 1–3), measured at high field strength (220, 300 MHz) and in the presence of Eu(dpm)₃ in order to overcome the dif-



iculties that result from the small chemical shift differences between the aromatic protons in the hydrocarbons, has appeared.⁵¹⁰ It bears on the problem of lanthanide shift reagent induced changes of H,H coupling constants that has also been discussed in a recent review⁵¹² and in ref 361. The determined values—especially the para-coupling constant $J(1,4)$ —differ considerably from the exact parameters found for the parent systems. Using statistical methods for an error analysis the authors concluded that the observed deviations are real and indicative for a coupling constant change caused by Eu(dpm)₃. No conclusions as to the origin of this effect were, however, possible. In view of the severe line broadening brought about by the shift reagent, the difficulties of obtaining correct errors for NMR parameters that also include the experimental error in the measured line positions, and the unfavorable ratio of experimental information (number of lines) to unknown spectral parameters (coupling constants, chemical shifts) met especially for the AA'BB' system because of its symmetry, the possibility that the observed differences originate from random errors seems not fully excluded.

The spectrum of 1,1-difluorobenzocyclopropene (198) has also been analyzed completely.⁵¹³ Here the relative chemical shift $\Delta\delta(A,B)$ is much larger than in the hydrocarbon, and the analysis of the spectrum, performed for the proton AA'BB' spin system with ¹⁹F decoupling as well as for the full six-spin system, presented no problem. Relative signs of H,F coupling constants were determined by spin-tickling experiments. The vicinal H,H coupling constants found (Table XIX) differ from the values in the hydrocarbon 191, *n* = 1, but no satisfactory explanation for this finding could be presented.

First structural information on benzocyclopropenes came from a study of 191, *n* = 1, and 198 partially oriented in a nematic phase.⁵¹⁴ It was found that within experimental error both compounds possess the same proton geometry in the six-membered ring. The benzene ring is distorted in the sense that CCC bond angles at C(α) and C(α') are smaller and those at C(β) and C(β') are larger than 120°. This conclusion found support by the results of an x-ray analysis of 1,1-dicarbomethoxy-2,5-diphenyl-191, *n* = 1,⁵¹⁵ and a recent microwave investigation of 198.⁵¹⁶ Similar distortions of the benzene ring have been reported for 194.⁵¹⁷

CNDO/2 calculations for benzocycloalkenes have been performed in order to detect structural peculiarities and to explain the experimental findings for the H,H coupling constants.^{518,519} Geometries were derived using an energy minimization procedure, and the spin-spin interactions were calculated on the basis of the Pople-Santry theory.⁵²⁰ The observed trends for the $J(H,H)$ values were reproduced quite well; the bond lengths found for 191, *n* = 1, are on the other side in disagreement with the results of the x-ray work cited above. In this connection we mention a recent review on the chemistry and properties of benzocyclopropenes.⁵²¹

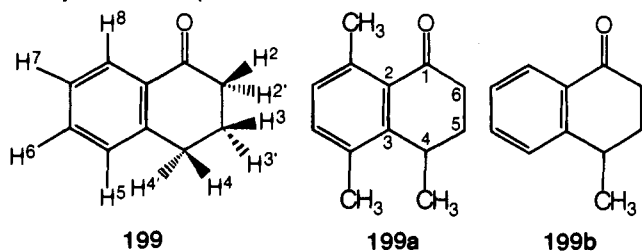
Conformational aspects for a substituted indan²⁵⁷ and 4,5-disubstituted tetralins^{291,522} have been followed with the help of H,H coupling constants. For *trans*-4,5-dimethyltetralins²⁹¹ a preferred diequatorial orientation of the methyl groups was de-

TABLE XXI. NMR Parameters of Methylene Protons in Five- and Six-Membered Rings of Compounds 200–204⁵³⁶

Compd	$\Delta\nu^a$	³ <i>J</i> _{cis}	³ <i>J</i> _{trans}	² <i>J</i> _{gem}	² <i>J</i> ' _{gem}	<i>R</i>	ψ	Solvent
200	33.04	8.61	3.49	-17.67	-19.46	0.41	23	CS ₂
201 ^b	16.0	7.0	6.2	(-15.0)	(-15.0)	0.89	42	CS ₂
201 ^c						(1.13)	(47)	
202	15.54	8.63	5.51	-15.23	-18.53	0.64	36	CHCl ₃
203	18.88	3.45	9.44	-13.73	-17.23	2.73	61	CS ₂
204	19.42	4.14	8.92	-17.38	-21.51	2.16	58	CHCl ₃

^a Chemical shift difference between A and B protons in Hz at 60 MHz. ^b Noniterative solution. ²*J*_{gem} not determined. ^c Alternative assignment for vicinal coupling constants.

rived, whereas for dihalo-substituted systems⁵²² a strong predominance of the diaxial conformer seems to exist, a conclusion mainly based on dipole moment measurements.

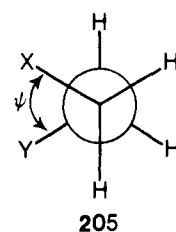


A detailed investigation was performed on α -tetralone (**199**), where the complete computer analysis was aided by the use of deuterated species and $^1\text{H}\{^2\text{H}\}$ decoupling.⁵²³ The results, given in Table XX, show the stable conformation with the C=O group essentially coplanar with the aromatic ring and the three CH_2 groups in a perfectly staggered relationship to one another. This corresponds to the sofa or envelope conformation discussed for **113** in section IV.D.3. Long-range coupling constants over four, five, and six bonds were obtained, and their magnitude and sign agreed well with the results of previous calculations⁵²⁴ if rapid ring inversion, leading to average values, was assumed. A subsequent 220-MHz investigation⁵²⁵ deals with the methyl-substituted tetralone **199a** and **199b**. From the coupling constants of **199a** extracted by first-order analysis, support for a probably distorted sofa conformation with an axial 4-methyl group was obtained by the *R*-value method. The latter yielded $\psi = 51^\circ$ for the internal dihedral angle between the C(4)–C(5) and C(6)–C(1) bonds. For **199** 57° was found for this parameter.⁵²³ In contrast, for **199b** a 1:1 mixture of two half-chairs was assumed since equal cis and trans 3J values across the C(5)–C(6) bond were found.

Benzo derivatives of norbornene (**76**) and bicyclo[2.2.2]-octene (**106**) have been studied extensively. Several investigations have already been cited^{248,265,266} in the appropriate sections (IV.C.4, IV.D.2). Others deal with systems derived from the parent compound by the introduction of a cyclopropane,⁵²⁶ oxirane, and aziridine ring,⁵²⁷ and discuss the shielding properties of these three-membered rings. The nonequivalence of the two one-bond $^{13}\text{C}, ^1\text{H}$ coupling constants at C(7) of **76** and benzo-**76** was established with values of 136.0 and 130.0, and 136.0 and 132.0 Hz, for $^1J(^{13}\text{C}, \text{H}^{7\text{s}})$ and $^1J(^{13}\text{C}, \text{H}^{7\text{a}})$, respectively, in the two compounds.⁵²⁸ In addition, paramagnetic contact shifts^{529,530} have been observed in 6-aminobenzo-**76**⁵³¹ using bis(acetylacetonato)nickel(II) in order to obtain long-range ESR hyperfine splittings across σ bonds and their signs. Similar studies for 6-aminobenzo-**106**⁵³² were undertaken in order to gain quantitative information about the dihedral angle dependence of β -proton ESR hyperfine coupling constants in radicals. First-order NMR data for dihalo- and other disubstituted benzo-norbornenes have been reported⁵³³ and were found generally in line with observations made for **76** itself.^{251,253} Finally, we mention a study⁵³⁴ that contains data on benzobicyclo[3.2.1]-octene and an investigation⁵³⁵ that deals with several polycyclic systems where information about the relative strength of the shielding cones of ketonic and olefinic linkages became available.

As for benzoheterocycles, numerous investigations exist, but within the limits of the present review we refrain from covering this field. Some examples have been included in the former sections in connection with work on the parent systems, and earlier studies (up to 1969) have been treated in ref 15. Unfortunately, many of them suffer from low-sensitivity spectra and the use of first-order treatments. An example what can be done is given in a paper dealing with the geometry of the five- and six-membered rings in 1-indanone (**200**), 1-indanone ethylenedithiol ketal (**201**), benzothiophene dioxide (**202**), 4-thiochroman (**203**), and 4-thiochroman 1,1-dioxide (**204**).⁵³⁶ Iterative

analysis of well-resolved AA'BB'-type spectra yielded reliable coupling constants that were in turn used to determine the internal dihedral angles ψ (cf. **205**) by the *R*-value method^{13,279}



(Table XXI). As can be seen, the alicyclic ring in **203** is slightly puckered (for cyclohexane, $\psi = 56^\circ$), and that of the dioxide **204** is virtually without distortion. In the five-membered rings care must be exercised in the assignment of the two vicinal coupling constants $^3J_{\text{cis}}$ and $^3J_{\text{trans}}$. *R* values and torsional angles were calculated for the two possible choices, and except for **201** a unique decision as to the correct solution was possible. It was concluded that the flattening of the five-membered rings becomes less pronounced on passing from **200** as the most flattened compound to **202** and **201**.

V. Addendum

Section IV.A and B. Interest in the structure of small ring compounds continues, and as a supplementation we mention microwave investigations for 3,3-difluorocyclopropene⁵³⁷ and *exo*-methylenecyclobutenone,⁵³⁸ a study of the vibrational spectra of cyclopropenone,⁵³⁹ as well as x-ray work on *cis*-cyclobutene-3,4-dicarboxylic acid.⁵⁴⁰ There are also several attempts to calculate the geometries of cyclopropene and cyclopropenone by improved ab initio methods.^{541–543} For cyclobutenedione $\delta(\text{H}) = 9.73$ ppm was reported,⁵⁴⁴ and recent reviews on the chemistry of cyclopropenone and related compounds^{100,545} also discuss the physical properties of these systems.

Section IV.C. An x-ray investigation of 1,2-diphenylcyclopentene⁵⁴⁶ has established the C_s envelope conformation **38** for the cyclopentene ring with a puckering angle of 17.2° , somewhat less than that found for cyclopentene itself (see above). Ring puckering potential functions and the conformations were also the aim of a CNDO/2 study of several unsaturated five membered rings, including **38**, cyclopent-3-enone, and the dihydrofurans.⁵⁴⁷ Further insight into the geometry of the cyclopentene ring comes now from a detailed study of the ^1H NMR spectra of the four symmetrical dichlorocyclopentenenes (1,2-, 4,4-, *cis*-3,5-, and *trans*-3,5-dichloro-**38**).⁵⁴⁸ Iterative analysis was used to determine the NMR parameters, including the signs of the majority of the coupling constants. Envelope conformations were found for the 1,2, *trans*-3,5, and *cis*-3,5 isomer with an equilibrium displaced by approximately 70% to the side of the diaxial form **42-a,a** in the case of the latter compound, in accord with earlier findings. Precise values for the interactions $^4J(1,4\alpha)$ and $^4J(1,4\beta)$ (+0.47 and -0.24 Hz, respectively) were measured. For the homoallylic interactions again $^5J_{\text{trans}} > ^5J_{\text{cis}}$ was observed in all cases with the exception of the 4,4 isomer, where 1.34 Hz was found for both couplings. On the basis of the large allylic interaction $^4J(1,3)$ (-2.14 Hz) and the increase observed for $^3J(1,2)$ ($\Delta J = 0.89$ Hz compared with that for **38**), a planar structure was proposed for this compound. The finding $^5J_{\text{trans}} = ^5J_{\text{cis}}$ is then at variance with the theoretical predictions (cf. **39**).^{151,207} With this additional information at hand more precise measurements for natural products containing cyclopentene moieties^{549,550} should yield more satisfactory results.

The planarity of cyclopent-2-enone has been further established by IR and Raman measurements,⁵⁵¹ and a slow interconversion between "free" and hydrogen-bonded forms of

substituted 4-hydroxycyclopent-2-enones in acetone solution has been established by double resonance.⁵⁵² The work dealing with compounds **58–60**^{194,195} has now been extended to 1,3-dioxole (**58**, CO=CH₂) and bis-1,3-dioxolyl.⁵⁵³ Chemical shifts and H,H as well as ¹³C, ¹H coupling constants are given, including sign determinations by iterative analysis and double resonance experiments. A particular large geminal ¹³C, ¹H coupling constant of 20.04 Hz and a remarkable small ³J(H,H) value of 1.21 Hz (the smallest measured so far for this type of interaction) were found in the olefinic fragment of 1,3-dioxole. For the bicyclic compound the temperature variation for ³J(H,H) across the single bond indicated that in polar solvents such as acetone the gauche conformer is that of higher energy, in contrast to the behavior of other tetrasubstituted ethanes. In a subsequent paper⁵⁵⁴ the spectrum of 1,3-dioxole served to demonstrate line broadening effects caused by the phenomenon known as "radiation damping".⁵⁵⁵ It was shown that for relatively strong resonance lines nonnegligible intensity changes and peak distortions result and may in turn cause erroneous line assignments and loss of information.

From the field of nitrogen heterocycles we cite two additional investigations that deal with the conformation of 5-substituted Δ²-1,2,3-triazolines⁵⁵⁶ and Δ²-pyrazolines.⁵⁵⁷ Evidence for an envelope conformation with pseudo-axial substituent was found for the triazolines.

Further investigations of bicyclic compounds deal with the stereochemistry of norbornene derivatives disubstituted at position 2 (cf. **76**)^{558,559} and the influence of exo-cis and endo-cis 5,6-substituents on the chemical shifts in **76**.⁵⁶⁰ An interesting linear correlation between δ(H) of the C(7) methylene protons and Taft's σ₁ values was found. For derivatives with endo-hydroxymethyl groups in positions 5 and 6, evidence for the preferred conformation of the substituents was derived from the measured ³J(H,H) data.⁵⁶¹ Rotational isomerism was also investigated for the two diastereomers of 5-endo-(2-hydroxyethyl)-**76** using first-order analysis of the 220-MHz spectrum and LIS studies.⁵⁶² It turned out that the information derived from the LIS data was insufficient to support the conclusions drawn from chemical shift data alone. Independent evidence was thus derived from the ¹H NMR spectra of the cyclization products of both alcohols. A comprehensive NMR study of a large number of substituted endo-tricyclo[3.2.1.0^{2,4}]oct-6-enes has appeared.⁵⁶³ ⁴J interactions involving a non-W path were reported,⁵⁶⁴ but for **76** again ⁴J(H^{7s},H⁵ⁿ) > ⁴J(H^{7s},H^{5x}) was confirmed with values of 2.1 and 0.4 Hz, respectively. Two other investigations deal with the spectra of 5- and 6-chloro-substituted **76**⁵⁶⁵ and with the solvent effects for 7-hydroxy-**76**.⁵⁶⁶ Characteristic differences in the splitting pattern observed for the phenyl resonances in exo and endo adducts of tetracyclone (tetraphenylcyclopentadienone) with cyclohexene were found and ascribed to rotational isomerism of the phenyl groups in the 1,4 position.⁵⁶⁷ It appears from other data that these "fingerprints" may serve as an empirical method to establish the stereochemistry of such adducts. LIS studies on endo and exo 5,6-dicarboxylic acid anhydrides of **76** and derivatives with the spiro substituents at C-7 were performed in order to investigate complex formation with bifunctional systems containing donors of different basicity.⁵⁶⁸ It was found that, in the absence of steric effects, carbonyl oxygen is favored over ether oxygen attachment. Finally, we only mention a few leading references that deal with the nitrogen inversion⁵⁶⁹ and n,π* interactions^{570–572} in 7-azanorbornene and related compounds.

Section IV.D. Theoretical calculations of the H,H coupling constants for the cyclohexene half-chair **82** have been performed⁵⁷³ using the Pople-Santry theory⁵²⁰ and the finite perturbation method.⁶⁸ Qualitative agreement with experimental data was found for most values, somewhat better for the second approach. The calculated allylic coupling constants are different in magnitude and sign from those derived in ref 67. The ³J values

agree well with those cited above for the parent compound if the conformational equilibrium **82a** ⇌ **82b** is taken into account. Still, the uncertainties of such calculations are too large to allow such data to be used as a sound basis for conformational analysis, a possibility that would be of particular interest in the case of systems like **82** where, because of the complex NMR spectrum, experimental values are difficult to obtain.

Conformational analysis of substituted cyclohexenes has continued,⁵⁷⁴ including polyalcohols and their acetates derived from aromatic hydrocarbons.⁵⁷⁵ In the latter study the results obtained for conduritols³⁰¹ were used as a guideline. For some of the systems a boat or flattened chair conformation was indicated, and hydrogen bonding in NHR-substituted systems even leads to conformations with all substituents in axial positions. ¹H NMR was also used to investigate the stereochemistry of cyclohexene alcohols formed by reduction of cyclohex-2-enones,⁵⁷⁶ and a recent review on conformational processes in cyclic compounds also summarizes the results obtained for cyclohexene ring inversion.⁵⁷⁷

The formerly unresolved question of the geometry of **105** has again been investigated and evidence for the "open" conformation corresponding to **102b** was derived from LIS measurements.⁵⁷⁸ Additional data on the bicyclo[2.2.2]octene system (**106**) are available^{579,580} with an especially detailed discussion of the NMR parameters in ref 579.

The earlier NMR results on the conformation of substituted cyclohex-2-enones³⁴² were confirmed by a CD study,⁵⁸¹ and hindered rotation about the aryl-C(3)-cyclohex-2-enone bond in naphthalenes substituted by a cyclohex-2-enone ring was observed.⁵⁸² A preliminary account on the stereochemistry of spiro[5.5]undeca-1,8-dien-3-ones, containing a cyclohex-2-enone and a cyclohexene partial structure, has appeared.⁵⁸³

As for heterocyclic systems, a major step forward was made in the conformational analysis of the 5,6-dihydropyran system (**118**) by a rigorous analysis of the spectra of acetylated glycols⁵⁸⁴ that were already the subject of earlier studies by this group and by others.⁵⁸⁵ Iterative computer analysis was supplemented by double resonance experiments to assure sign determinations for the coupling constants. Thus a reliable set of experimental J(H,H) values was at hand for a least-squares analysis based on the assumption that the observed data are weighted averages of the constants corresponding to the two half-chair conformations. Neglecting β-configurational and minor substituent effects, the set of 46 observed coupling constants yielded optimized values characteristic of the individual half-chairs, as well as the mole fractions. ΔG° values ranging from 0.2 to 1.8 kcal/mol for seven different conformational equilibria were thus obtained. The observed temperature dependence of the J values further supports the dynamic nature of the systems. Rotational isomerism for the CH₂OAc side chain was also investigated. Some of the earlier treatments of unsaturated carbohydrates are cited in a review on NMR applications in this field.⁵⁸⁶

The half-chair conformation for 3,6-dihydropyran (**118**) as well as for 1,4-dioxene (**122**) received further support from a Raman study⁵⁸⁷ that yielded barriers for ring inversion in the gas phase of 7.6 ± 0.6 kcal/mol for **118** and **122** as well as for cyclohexene.

1,4-Dioxene was again subject of a detailed NMR analysis including this time the ¹³C satellites in the ¹H spectrum, the ¹³C spectrum, and the ¹H spectrum of **122** oriented in two different lyotropic mesophases.⁵⁸⁸ Nearly all spin-spin interactions of this molecule have now been determined and from the liquid crystal work twist angles close to 28° were derived, in good agreement with the results of other studies.^{373,376,377} Extended Hückel calculations nicely reproduced the twist angle as well as the inversion barrier.³⁷² The AA'BB' system of the CH₂-CH₂ fragment of 2-chloro-**122** was analyzed⁵⁸⁹ with results practically identical with those of the parent compound. To extract chemical

shifts and coupling constants for 1,3-dioxene and three methyl-substituted derivatives 300-MHz spectra were used.⁵⁹⁰ It was concluded that the envelope conformation corresponding to **118b** (C(5) = O) is the most stable form. ΔG^\ddagger (-123°C) ~ 7.2 kcal/mol was estimated for the dynamic process detected for the parent compound and ascribed to ring inversion. Since, according to these results, 1,3-dioxene has a unique position among simple cyclohexene analogues, further studies to substantiate the above conclusions seem desirable.

Evidence for the preferred orientation of the substituents in several 5,6-dihydro-4H-1,3-oxazines was also derived from H,H coupling constants determined by first-order analysis.⁵⁹¹ The discussion was based on an envelope conformation of the oxazine ring found in an x-ray study of a highly substituted derivative.⁵⁹²

Considerable progress in understanding the dynamic behavior of the tetrahydropyridazines **130**, **132**, and **135** was possible through the application of ^{13}C NMR^{593,594} and photoelectron (PE) spectroscopy⁵⁹⁵ as well as the low-temperature cyclic voltametry,⁵⁹⁶ and we describe these results in order to report on the present state of the development in this field. The discrimination between inversion processes that involve the nitrogens or the ring and that are characterized either by passing (high-energy process) or by nonpassing (low-energy process) of the methyl groups⁴⁰⁰ has proven a fruitful concept. It is now accepted that **135** has an a,e conformation³⁹⁹ (half-chair with axial and equatorial methyl group), and the low-energy process (cf. Table XVI) is attributed to an a,e \rightleftharpoons e,a equilibrium via nitrogen inversion without passing of the methyl groups and involving the a,a conformation as intermediate:⁵⁹⁴ ΔG^\ddagger (298 K) = 7.68 ± 0.21 , ΔH^\ddagger = 8.8 ± 0.35 , ΔS^\ddagger = 3.9 ± 1.9 eu (solvent acetone- d_6). Ring inversion of the nonpassing type connects the a,a to an e,e form. Both are present in only minor concentrations and have so far escaped direct detection. Estimates for the amount of e,e conformation present yield approximately 0.2%.⁵⁹⁶ An interconversion scheme between the eight possible conformations has been given.⁵⁹⁶ Of importance in this context are also the results for the saturated analogues of **135**, where new data for the high energy processes could be obtained.⁵⁹⁷

For the bicyclic compounds, PES results⁵⁹⁵ confirm the trans arrangement of the CH_3 groups, and an improved line-shape analysis of the ^{13}C spectrum yielded more precise activation parameters for the nitrogen inversion in **132** still believed to be consecutive:⁵⁹³ ΔH^\ddagger = 11.70 ± 0.24 kcal/mol, ΔS^\ddagger = -2.11 ± 0.96 eu, ΔG^\ddagger (298 K) = 12.33 ± 0.05 kcal/mol (in acetone- d_6). Notably different from the earlier results³⁹⁴ is the negative activation entropy.

Section IV.E-H. In a preliminary report⁵⁹⁸ a chair conformation with axial phenoxy group has been proposed for the cyclic phosphite **164**, $\text{X-CH}_2\text{-X} = \text{O}(\text{POC}_6\text{H}_5)_2$, on the basis of the $^3\text{J}(\text{P,H})$ coupling constants of 13.0 and 7.0 Hz observed between ^{31}P and the allylic methylene protons, and the assumption that the phenoxy group strongly prefers the axial orientation. The coupling constants did not change over a temperature range from -60 to 80°C . In contrast, the corresponding benzo compound showed nearly equal couplings (9.5, 10.5 Hz) and moreover a strong temperature dependence of these parameters. An equilibrium between a chair and a twist boat conformation was proposed in this case. For the analogous sulfites (**164**, $\text{X-CH}_2\text{-X} = \text{O}(\text{SO})_2$), and the corresponding benzo derivative) preliminary data point to a twist boat conformation and a chair/twist boat equilibrium, respectively.⁵⁹⁹ Evidence for a twist boat conformation was also gathered from the ^{13}C NMR results in the case of alkyl-substituted 1,3-dioxocyclohept-5-enes (**164**, $\text{X} = \text{O}$).⁶⁰⁰

The conformation of a trans cyclodecenone ring (present as a partial structure in a 5,10-secosteroid) was investigated by x-ray and NMR analysis.⁶⁰¹ In the solid an extended crown conformation of approximate C_{2h} symmetry was found. In

contrast to other trans cyclodecene structures (see above), the double bond deviates only slightly from planarity (torsional angle 175°). Transannular attraction between the $\text{C}=\text{C}$ and $\text{C}=\text{O}$ double bonds was invoked to explain this finding. In solution, the NMR results (^1H and ^{13}C) supported the presence of the crown conformation, but at the same time indicated the existence of the second form resembling conformation **185**.⁴⁹⁶

Section IV.I. Benzene derivatives of type **192** with $n = 2$ or $n = 2$ and 1 (the latter linear annelated) have recently been synthesized,^{602,603} and the question of strain effects on chemical shifts or ring current intensity is again of interest. In line with our discussion above, the data for these systems do not indicate the presence of any unusual mechanism for proton shielding, the $\delta(\text{H})$ values of the aromatic protons (6.74 and 6.85 ppm, respectively) being close to the resonance of these protons in durene (6.74 ppm⁶⁰⁴). Since systematic investigations, especially those including dilution measurements, of these and other strained systems are missing, chemical shift arguments in the discussion of the bonding situation in the benzene ring of these molecules⁶⁰⁵ should be used with caution. The peculiar equivalence of the methylene resonances in the compounds cited above (δ 3.08 ppm) seems worth mentioning.

Iterative computer analysis of the methyl tetralone spectra⁵²⁵ was now presented.⁶⁰⁶ The authors voted in favor of a half-chair instead of an envelope or sofa conformation⁵²³ in the case of the monomethyl compounds. Non-half-chair forms were proposed for the trimethyl compounds. Finally, for recent studies on benzo heterocycles, we mention work on chromans⁶⁰⁷ and flavans⁶⁰⁸ as well as on tetrahydroisoquinoline⁶⁰⁹ and 3,4-dihydro-1,6-benzodiazocine-2,5-diones.⁶¹⁰

VI. Conclusion

As the material discussed in this review demonstrates, ^1H NMR has enormously extended and deepened our knowledge about structure and dynamic behavior of cyclic monoenes. Naturally, the picture is fairly complete for the smaller rings, but there is definitely less information on medium and large rings. Already the difficulties in understanding the dynamic behavior in the cycloheptene series are far from being completely removed. Furthermore, it is now increasingly realized that for substituted systems important parameters of the conformation established for the parent compound may have changed, and the detection of such differences will be the goal of further work. Also, as in other fields of dynamic NMR studies, the correct determination of activation entropies that could yield important informations about transition states and the pathways of conformational equilibria is only in its beginnings. Certainly, the high sensitivity and precision attainable through ^1H Fourier transform techniques, the use of high-field spectrometry, allowing also increased spectra simplification by double resonance methods, and the new information derived from ^{13}C NMR will lead to future progress, especially if the potential available through these experimental techniques in combination with rigorous spectral analyses and the application of advanced theories is fully exploited.

VII. References

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