(18) L. F. Johnson and W. C. Jankowski, "Carbon-13 NMR Spectra", Wiley-Interscience, New York, N.Y., 1972, cf. spectrum no. 479.
(19) Since the chemical shift differences ($\delta\Delta$) between C-(1) and C-(2) in **10** and **11** is $\simeq$ 4–5 ppm and the $\delta\Delta$ between C-1(A) and C-2(A) in **1** is 5.1 ppm, a reversal of the relative chemical shifts between the morphinanes and lithospermic acid would involve a shielding of C-2 by $\simeq$ 5 ppm and a simultaneous deshielding of C-1 by the same amount. The principal structural differences between **1** and **10/11**, i.e., the tertiary vs. quaternary center α to C-2 and the unsaturated side chain vs. the β-ammonium-substituted fused [C-(1) to C-(2)] cyclohexane ring, are in all probability insufficient to cause so large a chemical shift change.[20]
(20) In simple models, e.g., isopropylbenzene vs. *tert*-butylbenzene, the additional β effect of the third methyl group is <1 ppm, and similarly, the $\delta\Delta$ of C-1 between *o*-xylene and tetralin is also <1 ppm.[2a] Interestingly, in models lacking all substitution at C-2, i.e., Dopa (**8**), with a saturated side chain bearing a β-ammonium ion, vs. caffeate esters **2** and **5**, the resonances of C-1 and C-1(A) are virtually identical (see Table I). This observation further supports our use of morphinanes as models for ring A of **1**.
(21) Cf. ref 18, spectrum no. 356.

The 1-Hetera-4-cyclohexanone System. Proton and Carbon-13 Magnetic Resonance, Transannular Effects, and Conformational Analysis

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Proton (^{1}H NMR) and carbon-13 (^{13}C NMR) magnetic resonance have been applied to a series of 1-hetera-4-cyclohexanones in order to acquire information about ring conformations. The ^{1}H NMR results require evaluation of long-range couplings through the carbonyl groups prior to R-value analysis. Comparison of the ^{13}C NMR data with that from a series of 1-heteracyclohexanes and from acyclic analogues indicates (a) that the effects α and β to the heteroatom groups in the 1-hetera-4-cyclohexanones are proportional to the effects in the same positions in the 1-heteracyclohexanes except for cyclohexane-1,4-dione, and, therefore, indicate chair conformations; (b) that additivity relationships from the 1-heteracyclohexanes may be used as indications of chair or twist conformations in 1,4-diheteracyclohexanes and 1-hetera-4-cyclohexanones; and (c) that upfield carbonyl shifts in 1-hetera-4-cyclohexanones and related systems do not contain transannular electron-transfer components. Previous suggestions that upfield carbonyl shifts of approximately 10 ppm or less may be used to indicate transannular electron donation are refuted. An ordering of heteroatom group effects is presented based on ^{13}C NMR α shifts in these cyclic systems.

Cyclohexane and its derivatives have been subjected to extensive conformational analyses.[2] Numerous examples have been reported of both chair[2] and nonchair[2,3] preferences. In view of the predominantly twist nature of cyclohexane-1,4-dione[4,5] (**1a**) and its derivatives[4,6] and the predominantly chair nature of 1,4-dimethylenecyclohexane[4,7] and its analogues,[7,8] the question may be raised as to the extent to which sp^2-like hybridizations and electronic interactions cause this conformational dichotomy. A useful type of compound to help answer this question is the 1-hetera-4-cyclohexanone system (**1b–n**).

Various representative 1-hetera-4-cyclohexanones have been readily available for some time. Allinger and Jindal[9] investigated 1-acetyl-4-piperidone (**1b**) and 1-methyl-4-piperidone (**1c**) using Z values with n $\rightarrow \pi^*$ transitions, dipole moments, and infrared spectroscopy, and concluded that both compounds were predominantly in chair conformations. In particular, the N-acetyl system **1b** was not believed[9] to exhibit a transannular charge-transfer electrostatic interaction between the carbonyl groups in a boat conformation. However, no Z-value correlation was observed for this compound.

A series of papers by Katritzky and co-workers[10] has reported the cis–trans equilibrations of 3,5-dimethyl-1-hetera-4-cyclohexanones. These workers assumed that only chair conformations were significant; e.g., ". . . it is generally accepted that these compounds exist in a chair form".[10] Their base-catalyzed equilibrations were accomplished simultaneously with deuteration at the position α to the carbonyl group to simplify the proton magnetic resonance (^{1}H NMR) spectra, thereby eliminating the possibility of a concurrent R-value[4] type of conformational analysis.

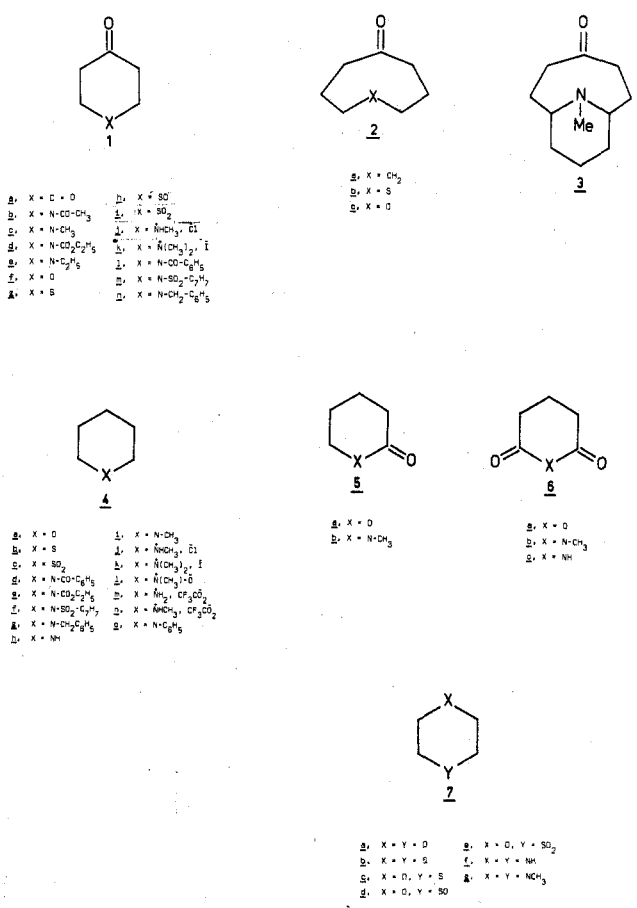

Table I
Results of Dahn, Schlunke, and Temler[13]

Compd	^{17}O NMR signal[a]	Rate of hydration[b]
Cyclohexanone	−564, −561	6
1e (X = NC_2H_5)	−561	19
1f (X = O)	−568	14
1g (X = S)	−569	20

[a] In parts per million relative to water. Measured on dioxane solutions at 28 ± 2°. [b] Determined by ^{17}O NMR on 8:1 dioxane–water solutions at 28 ± 2° in pH 5 acetate buffer.

Reported ^1H NMR analyses of 4-piperidones[11] indicate "the near-symmetrical pattern of an AA'BB' system" for the ring protons in 1-methyl-4-piperidone (**1c**). This suggests that an *R*-value approach[4] might be useful in a related heterocyclic system, but raises the question of the cause of the lack of symmetry in the spectrum. A conclusion drawn[11] on the basis of first-order coupling constants that 1-*tert*-butyl-*trans*-3,5-dimethyl-4-piperidone is nonchair must be viewed with some skepticism.[3] A subsequent report[12] of the ^1H NMR spectrum of 1-carboethoxy-4-piperidone (**1d**) provided little useful conformational information.

Other spectrometric and kinetic techniques have been applied to members of this series to probe interactions between the heteroatom and the carbonyl group. Dahn and co-workers[13] have examined the *N*-ethyl (**1e**), O (**1f**), and S (**1g**) systems using ^{17}O-labeled ketones, and report that neither ^{17}O NMR spectra nor rates of hydration of the carbonyl groups provide any evidence for transannular interactions (Table I). Nevertheless, their results do indicate the presence of some type of heteroatom effect whose nature is not discussed. Changing the heteroatom must introduce some effect[14] related to the electronegativity of the heteroatom (and its substituents), and this electronegativity effect, whether through bonds or through space,[14] must be evaluated before any additional transannular interaction can be postulated or dismissed.

Some sulfur-containing members of this series (**1g–i**) have been subjected to mass spectrometric investigation.[15,16] Changing the nature of the heteroatom or its substituents influences the fragmentation pattern primarily by affecting the relative amounts of charge localization at the various possible sites on ionization. No definitive functional group interactions as such[17] were encountered. However, in a more extensive study[18] of the analogous 1-hetera-3-cyclohexanones, Djerassi and co-workers concluded that few fragmentations occur in such difunctional compounds which directly reflect the fragmentation patterns of the individual monofunctional systems (the heterocycle and the cyclohexanone).

Another technique which might be a useful probe for conformational analysis and/or transannular interactions is carbon-13 nuclear magnetic resonance spectroscopy[19,20] (^{13}C NMR). Jones and Hassan[21] have reported ^{13}C NMR data for 1-methyl-4-piperidone (**1c**), a series of ring-methylated analogues, and their hydrochloride and methiodide salts (including hydrochloride **1j** and methiodide **1k**). The observed ^{13}C NMR chemical shifts were analyzed in terms of the equatorial and axial positions of the methyl groups and of the nitrogen substituents in chair conformations (based on previous[11] ^1H NMR studies). Additivity substituent parameters were derived and compared to the corresponding cyclohexane, cyclohexanone, and piperidine substituent parameters. The *N*-methyl, N^+, and C=O centers were considered as electronegative substituents in the cyclohexane system in order to rationalize smaller substituent parameters in the piperidone series. Since the observed effects of protonation and methiodation were small, Jones and Hassan[21] concluded that, by analogy with the piperidines[22] and the cyclohexanones, the major effect of the nitrogen and carbonyl groups on the carbons to which they are bonded is an inductive[19] (through-bond[14]) one, but that the effects of the tertiary and quaternary nitrogens on C-4, the carbonyl carbon in the piperidones, require postulation of an electric field effect.[19,22]

Table II
^{13}C NMR of Carbonyl Carbons in 5-Heteracyclooctanones[23]

Compd	δ^a (C_6H_{12})	$\Delta\delta^b$	δ^a (1:9 C_6H_{12}–$CHCl_3$)	$\Delta\delta^b$
2a	212.4		218.2	
2b	210.9	−1.5	215.8	−2.4
2c	208.7	−3.7	214.3	−3.9
3	199.6	−12.8	129.7	−88.5

[a] In parts per million relative to Me_4Si as reported by ref 24. [b] In parts per million relative to **2a**.

The sensitivity of ^{13}C NMR to transannular electron donation to carbonyl groups has been suggested by Nakashima and Maciel[23] using 5-heteracyclooctanones (**2a–c, 3**). Results in cyclohexane and 1:9 cyclohexane–chloroform (Table II[24]) are reported to provide evidence for transannular electron donation from the heteroatom to the carbonyl group in the upfield shifts of the ^{13}C NMR signals of the carbonyl carbons, thereby extending conclusions based primarily on the behavior of **3** in other investigations.[13,23] Nevertheless, Nakashima and Maciel[23] point out that it is possible that the observed effects for **2b** and **2c** may be partly inductive, but suggest that such an inductive effect through four σ bonds would probably not have such a magnitude. Only two possible interactions are considered—a through-bond effect and an electron-transfer bonding transannular effect. The possibility of a dipolar through-space ("field") effect[14] is not differentiated from the bonding type of transannular effect, as it must be. It would be useful to be able to compare the cyclooctanone series with the corresponding heteracyclooctane compounds so as to treat the data[19,20] as ($\delta_{ketone} - \delta_{hydrocarbon}$) and better evaluate the inductive and field effects.

It is the intent of this work to investigate the ^1H NMR and ^{13}C NMR characteristics of representative 1-hetera-4-cyclohexanones (**1**) in the hope of being able to draw definite conclusions with respect to ring conformation[68] and with respect to the types of interactions existing between the heteroatom and the carbonyl group. The ^{13}C NMR of related 1-heteracyclohexanes (**4**), 1-hetera-2-cyclohexanones (**5**), and 1-hetera-2,6-cyclohexanediones (**6**) were determined for comparison purposes.

Experimental Section

All ^{13}C NMR spectra were recorded on a JEOL PS-100 NMR spectrometer equipped with a JEOL-JNM-PFT-100 pulse unit and a JEOL-JEC-6 computer. Field–frequency stabilization was established by the deuterium signal of the solvent utilized [$CDCl_3$ or $(CD_3)_2SO$]. The chemical shifts are expressed in parts per million relative to internal Me_4Si at 26 ± 2°C (unless otherwise indicated) and are believed to be accurate to 0.2 ppm.[25] The spectra were obtained under conditions of proton-noise decoupling, with off-resonance decoupling used to verify peak assignments where needed. All ^1H NMR spectra were recorded on the above JEOL spectrometer or on a Varian A-60A spectrometer, and are expressed in parts per million relative to internal Me_4Si.

All samples exhibited properties corresponding to literature data and were donated, purchased, or prepared as indicated: cyclohexane-1,4-dione[26] (**1a**), tetrahydropyran[27] (**4a**), tetrahydropyran-4-one[28] (**1f**), δ-valerolactone[26] (**5a**), pentamethylene sulfide[27] (**4b**), tetrahydrothiopyran-4-one[29] (**1g**), pentamethylene sulfone[30] (**4c**), tetrahydrothiopyran-4-one 1,1-dioxide[31] (**1i**), 1-methyl-2-piperi-

Table III
^{13}C NMR Data[a] for 1-Hetera-4-Cyclohexanones (1)

Compd	X	Solvent	α to X	α to C=O	C=O	Other
1a	C=O	$CDCl_3$	36.5	36.5	208.8	
1c	NCH_3	Neat[b]	55.4	40.9	206.2	NCH_3, 45.1
		$CDCl_3$[c]	54.7	40.9		NCH_3, 44.6
		$CDCl_3$	55.3	41.0	207.1	NCH_3, 45.4
		$(CD_3)_2SO$	55.1	40.8	207.4	NCH_3, 45.1
1d	$NCO_2C_2H_5$	$CDCl_3$	43.0	40.9	207.2	NCO, 155.3; OCH_2, 61.6; CH_3, 14.7
		$(CD_3)_2SO$	42.5	40.6	207.1	NCO, 155.0; OCH_2, 61.3; CH_3, 14.7
1f	O	$CDCl_3$	67.7	42.8	206.2	
1g	S	$CDCl_3$	30.0	44.0	208.0	
		$(CD_3)_2SO$	28.8	43.4	207.7	
1i	SO_2	$(CD_3)_2SO$	48.2	37.7	203.1	
1j	$^+NHCH_3,Cl^-$	$CDCl_3$[b]	52.0	38.4	203.1	NCH_3, 42.2
1k	$^+N(CH_3)_2,I^-$	$(CD_3)_2SO$[b]	60.6	35.9	201.7	NCH_3, 51.8
1l	$NCOC_6H_5$	$CDCl_3$[d]	43.9	41.0	206.0	NCO, 170.6; Ar, 135.5, 130.0, 128.5, 126.9
1m	$NSO_2C_7H_7$	$CDCl_3$	45.7	40.4	205.6	CH_3, 21.4; Ar, 144.0, 133.2, 129.8, 127.5
		$(CD_3)_2SO$	45.1	39.8	205.3	CH_3, 21.0; Ar, 144.7, 133.1, 130.0, 127.4
1n	$NCH_2C_6H_5$	$CDCl_3$	52.8	41.0	207.7	$ArCH_2$, 61.8; Ar, 138.1, 128.6, 128.3, 127.2

[a] Chemical shifts in parts per million relative to internal Me_4Si. [b] Reference 21. [c] Reference 45b. [d] At 60°C, ref 38.

done[26] (**5b**), 1-methyl-4-piperidone[26] (**1c**), *N*-methylglutarimide[27] (**6b**), 1-benzoylpiperidine[32] (**4d**), 1-benzoyl-4-piperidone[32] (**11**), 1-carboethoxypiperidine[33] (**4e**), 1-carboethoxy-4-piperidone[26] (**1d**), 1-tosylpiperidine[34] (**4f**), 1-tosyl-4-piperidone[35] (**1m**), 1-benzylpiperidine[36] (**4g**), and 1-benzyl-4-piperidone[32] (**1n**). A sample of tetrahydrothiopyran-4-one 1-oxide (**1h**) was prepared,[37] but is not included because of solubility difficulties and facile hydration and decomposition reactions.

Results and Discussion

^1H NMR Results. Spectra were obtained for compounds **1c, 1d, 1g, 1i,** and **1m,** and were compared with available spectra for **1c**,[11] **1d**,[12] and **11**.[32] Only spectra exhibiting a first-order appearance were obtained at 60 and 100 MHz over a range of temperatures (−50 to 70°C) except for compounds **1g** and **11**.[38] The spectrum of tetrahydrothiopyran-4-one (**1g**) appeared as an unsymmetrical AA′BB′ system. Analysis with the aid of the iterative computer program LAME[27] (LAOCOON with magnetic equivalence) using estimated J_{gem} values[4,39] suggested that the lack of symmetry resulted from long-range couplings[40] through the carbonyl group and that a complete analysis[4] was not reasonable because of insufficient spectral resolution. After completion of these experiments, ^1H NMR data for *N*-alkyl-3,5-diphenyl-4-piperidones were reported[41] and analyzed in detail. The results[41] indicate chair conformations and both equatorial–equatorial and equatorial–axial long-range couplings through the carbonyl group.

^{13}C NMR Results. Spectra were obtained for cyclohexane-1,4-dione (**1a**) and 1-hetera-4-cyclohexanones **1c,d,f,g,i,l,m,n** (Table III), 1-heteracyclohexanes **4a–g** (Table IV), 1-hetera-2-cyclohexanones **5a** and **5b** (Table V), and 1-hetera-2,6-cyclohexandiones **6a–c** (Table V) and were compared with literature values for these[19–22,42–51] and analogous[47,49,52] systems. Spectra were obtained in $CDCl_3$ as a primary solvent. Since some compounds were not sufficiently soluble in this solvent, $(CD_3)_2SO$ was also used. Sufficient compounds were determined in both solvents to indicate the presence of small but reasonable consistent solvent effects.[19,20,23,53] In order to minimize such solvent effects, a given signal in a 1-hetera-4-cyclohexanone (**1**) is considered only relative to the analogous signal in the corresponding 1-heteracyclohexane (**4**) in the same solvent (except where literature values are used and not redetermined). Data for the *N*-benzoyl compounds **11** and **4d** are reported at temperatures sufficiently high[38] to ensure conditions of rapid exchange. An attempt to consider the 1-hetera-4-cyclohexanones (**1**) as analogues of 1,2-disubstituted ethanes[54] and to thereby compare the cyclic and acyclic cases[55] was prevented by lack of data on common substituents in the two systems.

Before attempting to evaluate the ^{13}C NMR resonances in the 1-hetera-4-cyclohexanones (**1**), some reference point must be established for the electrostatic effects of the heteroatoms (and their substituents) in the absence of transannular interactions and/or conformational distortions. Since all of the carbon-unsubstituted 1-heteracyclohexanes (**4**) analyzed to date are believed to prefer chair conformations, chemical shifts in the 1-heteracyclohexanes (relative to cyclohexane as a standard[56]) should reflect primarily the heteroatom group electrostatic effects. Plots (Figure 1) of the chemical shifts (Table IV) of the carbon resonances α to X ($\delta^{\alpha}_{C_5H_{10}X} - \delta_{C_6H_{12}}$) against the methyl chemical shifts[57] of the corresponding acyclic CH_3XCH_3 and against the methylene chemical shifts[58] of the corresponding acyclic $CH_3CH_2XCH_2CH_3$ appear to be linear[60] within the limitation of the available data. The results in Figure 1, therefore, support the assumption of consistent (chair) conformations in these heterocyclic systems.

These data indicate an α substituent effect in the order $O > {}^+N(CH_3)_2 \gg NCH_3 > {}^+NHCH_3 > NCH_2C_6H_5 > NC_6H_5 > SO_2 > NH > NSO_2C_7H_7 > NCOC_6H_5 > C{=}O \gg S$. It is not resonable to consider the effects of the charged species on the same basis as the uncharged species because of monopole-induced effects. In addition, the charged species and the sulfone group contain both equatorial and axial substituents on the heteroatom, requiring consideration of conformationally dependent substituent effects,[19,20] while the nitrogen species will also have different steric components. Because of the observed correlation with acyclic ^{13}C NMR chemical shifts, it seems consistent with current terminology[19] to describe the order of the observed substituent effects of the uncharged species as indicating relative electron-withdrawing abilities.[70] However, the order within the uncharged nitrogen species is itself, at first glance, somewhat surprising. The usual approach[14,61] is to consider an alkyl group on nitrogen as electron donating and an amide or sulfonamide group as electron withdrawing, suggesting a relative electron-withdrawing order of NCO, $NSO_2 > N$-alkyl. The opposite order observed here may be discussed in several ways. The benzoyl, sulfonyl, and ethoxycarbonyl groups delocalize the lone pair on nitrogen, effecting a rehybridization with diminished electron density at the nitrogen. The nitrogen has less tendency to withdraw electrons from the adjacent carbon (and hy-

Table IV
^{13}C NMR Data[a] for 1-Heteracyclohexanes (4)

Compd	X	Solvent	α to X	β to X	γ to X	Other	Ref
4a	O	Neat	69.5	27.7	24.9		20, 42
		Neat	69.7	27.9	25.1		19, 42
		$(CD_3)_2CO$	69.8	27.4	24.3		43
		$CDCl_3$	68.7	26.9	23.8		Here
4b	S	Neat	all 30 ± 2.5				19, 20, 42
		$CDCl_3$	29.1	27.9	26.6		Here
4c	SO_2	$(CD_3)_2SO$	51.2	24.1	22.8		Here
4d	$NCOC_6H_5$	$CDCl_3$[b]	45.8	26.1	24.5	NCO, 170.0; Ar, 136.8, 129.2, 128.2, 126.8	Here
		$(CD_3)_2SO$[b]	45.2	25.7	24.3	NCO, 168.9; Ar, 136.8, 129.2, 128.4, 126.7	Here
4e	$NCO_2C_2H_5$	$CDCl_3$	44.8	25.8	24.6	NCO, 155.4; OCH_2, 60.9; CH_3, 14.8	Here
		$(CD_3)_2SO$	44.5	25.7	24.4	NCO, 154.8; OCH_2, 60.7; CH_3, 14.8	Here
4f	$NSO_2C_7H_7$	$CDCl_3$	47.0	25.1	23.4	CH_3, 21.5; Ar, 143.3, 133.1, 129.6, 127.7	Here
		$(CD_3)_2SO$	46.6	24.8	22.9	CH_3, 21.0; Ar, 143.3, 133.2, 129.7, 127.4	Here
4g	$NCH_2C_6H_5$	$CDCl_3$	54.6	26.0	24.5	$ArCH_2$, 64.0; Ar, 138.6, 129.1, 128.0, 126.8	Here
4h	NH	Dioxane	47.9	27.8	25.9		44
		Neat	47.7	27.5	26.1		19, 22
		Neat (?)	48.2	28.0	26.0		19, 45a
		c	47.1	27.0	24.5		46
		Neat[d]	47.9	27.9	25.9		47a
		Neat	50.2	28.6	26.8		48a
		$CDCl_3$	47.9	27.9	26.2		48b
		C_6D_6	47.9	27.7	25.9		47b
4i	NCH_3	Neat	57.4	26.6	26.6	NCH_3, 47.9	19, 20, 42
		Neat	56.7	26.2	24.3	NCH_3, 46.9	19, 22
		Neat	57.9	27.3	25.3	NCH_3, 48.0	48a
		Neat[d]	57.0	26.6	24.6	NCH_3, 47.1	47a
		c	56.7	26.0	24.1	NCH_3, 46.6	46
		$CDCl_3$	57.4	26.7	22.7	NCH_3, 47.7	48b
4j	$^+NHCH_3$, Cl^-	e	55.2	23.7	21.8	NCH_3, 44.3	19, 22
		c	55.7	23.9	21.7	NCH_3, 44.3	46
4k	$^+N(CH_3)_2$, I^-	e	63.3	20.6	21.0	NCH_3, 52.7	19, 22
		c	63.8	20.8	21.3	NCH_3, 52.8	46
4l	$^+N(CH_3)O^-$	C_6H_6	66.1	21.1	21.7	NCH_3, 59.6	19, 22
4m	$^+NH_2$, $CF_3CO_2^-$	CF_3CO_2H[f]	47.4	23.8	22.9		48a
4n	$^+NHCH_3$, $CF_3CO_2^-$	CF_3CO_2H[f]	57.8	24.5	22.0	NCH_3, 45.3	48a
4o	NC_6H_5	Neat	52.4				19, 45a

[a] Chemical shifts in parts per million relative to internal Me_4Si or converted to this basis. [b] At 56°C.[38] [c] 50% aqueous dioxane. [d] With 10% cyclohexane. [e] Water or dioxane; not clearly specified. [f] Results vary with mole fraction CF_3CO_2H; see ref 48a.

Table V
^{13}C NMR Data[a] for Other Relevant Systems

Compd	X (Y)	Solvent	C-2	C-3	C-4	C-5	C-6	Other	Ref
Cyclohexanone		Neat	40.7	26.8	24.1	26.8	40.7	CO, 208.8	19, 20, 49
		$CDCl_3$	41.9	27.1	25.1	27.1	41.9	CO, 211.3	44
		$CDCl_3$	41.9	27.1	25.0	27.1	41.9	CO, 211.5	50
5a	O		167.5						19
			175.2						20
		$CDCl_3$	171.2	29.9	19.1	22.3	69.3		Here
5b	NCH_3		170 ± 3						21
		$CDCl_3$	169.2	32.4	21.8	23.3	49.9	NCH_3, 34.3	Here
6a	O		168.2						20
		$CDCl_3$	167.8	29.6	16.1	29.6	167.8		51
		$(CD_3)_2CO$	168.5	30.1	16.7	30.1	168.5		51
6b	NCH_3	$CDCl_3$	172.8	32.6	17.2	32.6	172.8	NCH_3, 26.0	Here
6c	NH	$(CD_3)_2CO$	173.8	32.2	18.7	32.2	173.8		51
7a	O, O	$CDCl_3$	67.8	67.8		67.8	67.8		52
7b	S, S	$CDCl_3$	29.1	29.1		29.1	29.1		52
7c	O, S[c]	$CDCl_3$	68.5	27.0		27.0	68.5		52
7d	O, SO[c]	$CDCl_3$	59.0	46.2		46.2	59.0		52
7e	O, SO_2[c]	$CDCl_3$	66.0	52.8		52.8	66.0		52
7f	NH, NH	Neat[b]	47.9	47.9		47.9	47.9		47a
7g	NCH_3, NCH_3	Neat[b]	55.7	55.7		55.7	55.7		47a

[a] Chemical shifts in parts per million relative to internal Me_4Si. [b] With 10% cyclohexane. [c] Oxygen at position 1.

drogen) atoms than the NH or *N*-alkyl groups. The validity of this type of reasoning is supported by the position of NC_6H_5 relative to *N*-alkyl in the sequence. In a sense, this behavior of the various nitrogen groups[48a] is another manifestation of the Pople–Gordon suggestion[14,62] that through-bond inductive effects exhibit an alternation in magnitude of polarity in saturated systems.

An additional (or alternative) qualitative electron-density argument may be developed from considerations of dipole-induced σ polarizations. The different orientations

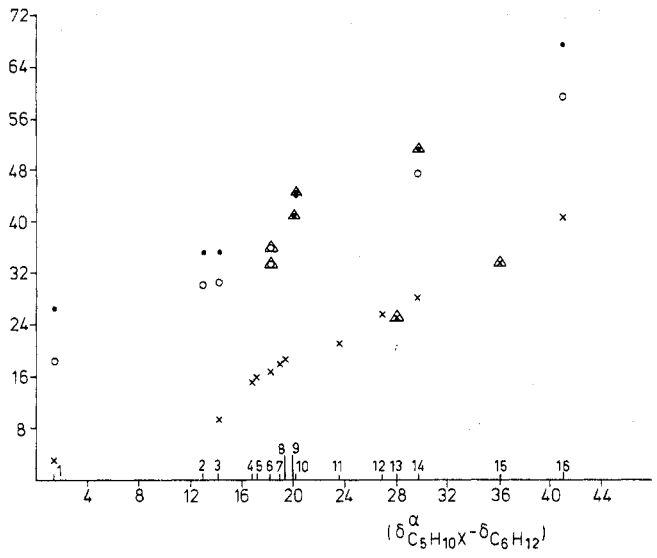

Figure 1. Comparison of the chemical shifts of the carbons α to the heteroatom in **4** (relative to cyclohexane) with (a) the chemical shifts α to the heteroatom in $(CH_3CH_2)_2X$ (●), (b) in $(CH_3)_2X$ (○), and (c) in **1** (relative to the position β to the carbonyl in cyclohexanone) (x). Points involving comparisons in different solvents are indicated by Δ. Heteroatomic group and number assigned: S, 1; C=O (neat), 2; C=O, 3; $NCO_2C_2H_5(Me_2SO)$, 4; $NCO_2C_2H_5$, 5; $NCOC_6H_5$, 6; $NSO_2C_7H_7(Me_2SO)$, 7; $NSO_2C_7H_7$, 8; NCH_3, 9; NH, 10; SO_2, 11; $NCH_2C_6H_5$, 12; $NHCH_3$, 13; NCH_3, 14; $^+N(CH_3)_2$, 15; O, 16.

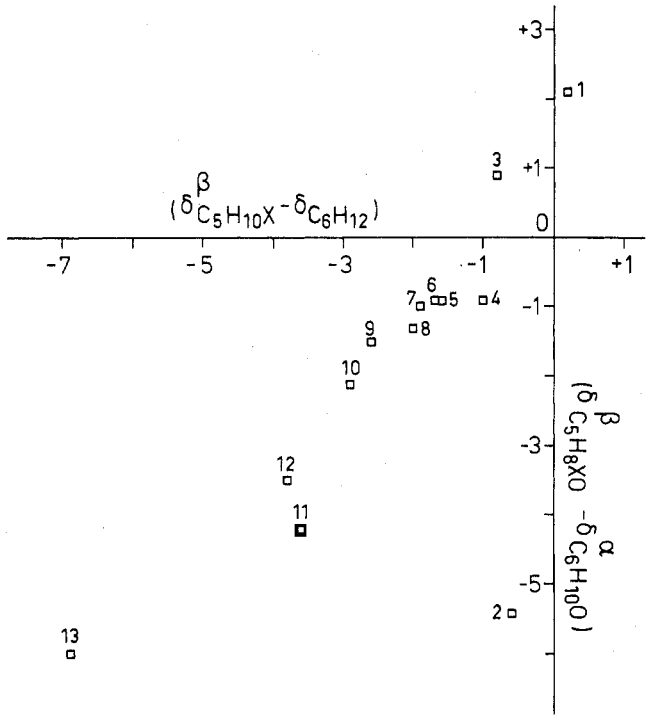

Figure 2. Comparison of the chemical shifts of the carbons β to the heteroatom in **4** (relative to cyclohexane) with the chemical shifts of the carbons β to the heteroatom in **1** (relative to the position α to the carbonyl in cyclohexanone): X = S, 1; C=O, 2; O, 3; NCH_3, 4; $NCOC_6H_5$, 5; $NCH_2C_6H_5$, 6; $NCO_2C_2H_5$, 7; $NCO_2C_2H_2(Me_2SO)$, 8; $NSO_2C_7H_7$, 9; $NSO_2C_7H_7(Me_2SO)$, 10; SO_2, 11; $^+NHCH_3$, 12; $^+N(CH_3)_2$, 13.

and magnitudes of the group dipole moments in the *N*-alkyl and benzamide–urethane–sulfonamide systems would induce different charge densities at the α and β carbons in these two types of structures. Combination of such a dipole-induced dipole interpretation with nitrogen hybridization effects may best explain the order of both the α and β chemical shifts. The fact that the α shifts are downfield and the β shifts are upfield illustrates the complexity of these phenomena.

Having established the electrostatic nature of the heteroatom group effects on the α carbons in the 1-heteracyclohexanes (**4**), comparison of the heteroatom effects in the 1-hetera-4-cyclohexanones (**1**) to those in **4** is required. A plot (Figure 1) of the chemical shifts (Table III) of the carbons α to the heteroatom in **1** relative to the chemical shift of the corresponding position (β to the carbonyl) in cyclohexanone (Table V, from ref 44) ($\delta^{\alpha}_{C_5H_8XO} - \delta^{\beta}_{C_6H_{10}O}$) against the chemical shifts of the α carbons in **4** relative to cyclohexane ($\delta^{\alpha}_{C_5H_{10}X} - \delta_{C_6H_{12}}$) gives a good linear relationship except for cyclohexane-1,4-dione (**1a**). Since the latter compound is believed[4,5] to exist predominantly in a twist conformation in solution, the linear relationship observed in Figure 1 for all of the other 1-hetera-4-cyclohexanones suggests that they all possess similar chairlike conformations.[68]

A similar plot of ($\delta^{\beta}_{C_5H_{10}X} - \delta_{C_6H_{12}}$) against the methyl chemical shifts[58] of the $CH_3CH_2XCH_2CH_3$ series indicates no obvious relationship. The order of these β shifts in the 1-heteracyclohexanes (**4**) is different from that of the α shifts. Explanations based on conformational influences in the acyclic compounds[55] and conformational effects[48a] in the heterocyclic compounds related to positions of monopoles, lone pairs, and dipoles on the heteroatomic groups are reasonable.

Reasonably strong evidence for chair conformations of **1** is provided in Figure 2, where ($\delta^{\beta}_{C_5H_8XO} - \delta^{\alpha}_{C_6H_{10}O}$) is found to be proportional to ($\delta^{\beta}_{C_5H_{10}X} - \delta_{C_6H_{12}}$) except for cyclohexane-1,4-dione. Any conformational dependence of the σ inductive effect[48a] in **1** is cancelled by the analogous conformational effect in **4** if each series of compounds exists in similar (chair) conformations. The dramatically divergent behavior of **1a** suggests that such β shifts may be the most useful ^{13}C NMR probe of ring conformational preference.[70]

It may be argued that the "abnormal" behavior of cyclohexane-1,4-dione (**1a**) in both Figure 1 and Figure 2 is not the result of a conformational difference, but arises from the symmetry of this compound, where all of the methylene carbons are equivalent. If this were true, discrepancies would be observed whenever symmetrical structures (e.g., **7**) were compared with similar unsymmetrical ones. As shown in Figure 3, comparison of observed ^{13}C NMR chemical shifts (Tables III and V) and chemical shifts calculated from monosubstituted systems (Table IV) by assuming additivity relationships illustrates the validity of the additivity relationships (within ±2.5 ppm) for all of the compounds listed other than cyclohexane-1,4-dione. An explanation of these results on other than conformational grounds does not seem reasonable.

Further support for the validity of the conclusion that the ^{13}C NMR results of Figures 1 and 2 require chair conformations for the 1-hetera-4-cyclohexanones (**1**) (other than **1a**) may be found in a comparison (Figure 4) of the 1-hetera-4-cyclohexanones with the 1-hetera-2-cyclohexanones (**5**) and the 1-hetera-2,6-cyclohexanediones (**6**) (Table V[63]), neither of which exists in a normal chair conformation.[39,51] Additivity relationships do not hold, which should be expected since **5** and **6** might better be considered as containing single new functional groups. Any possible correlation similar to Figures 1 and 2 would have significantly different slopes. Treatment of **5** and **6** as containing a new functional group set and comparison with the corresponding acyclic esters, amides, anhydrides, and imides

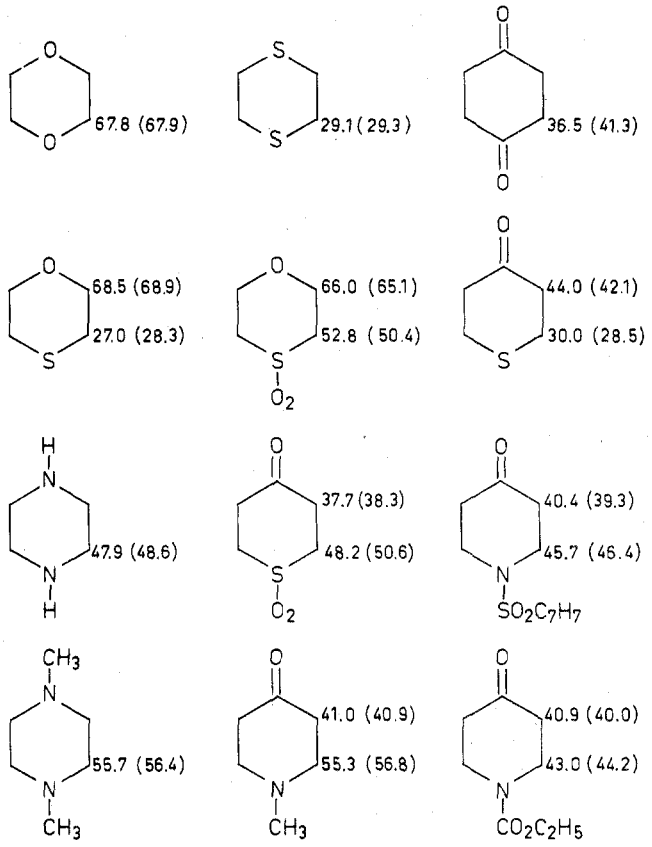

Figure 3. Comparison of observed ^{13}C NMR chemical shifts with those calculated (in parentheses) assuming additivity of effects from monosubstituted compounds.

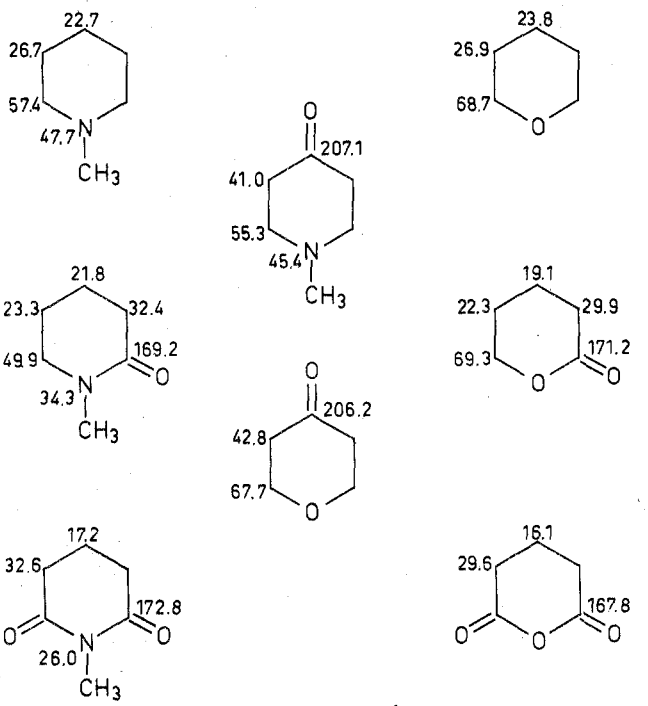

Figure 4. ^{13}C NMR comparison of 1-oxa- and 1-azamethylcyclohexanes, -2-cyclohexanones, -4-cyclohexanones, and -2,6-cyclohexanediones.

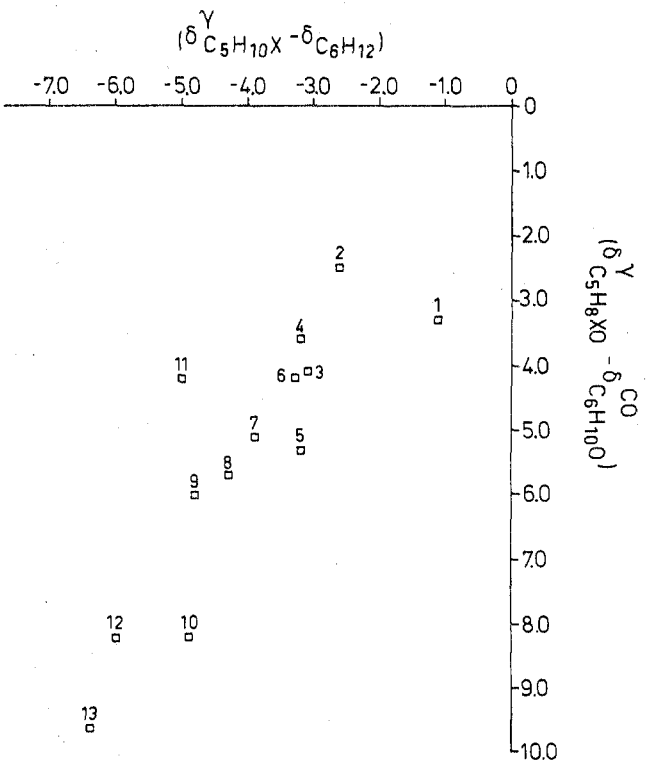

Figure 5. Comparison of the chemical shifts of the carbons γ to the heteroatom in **4** (relative to cyclohexane) with the chemical shifts of the carbonyl carbons in **1** (relative to the carbonyl carbon in cyclohexanone): X = S, 1; C=O, 2; $NCO_2C_2H_5$, 3; $NCH_2C_6H_5$, 4; $NCOC_6H_5$, 5; $NCO_2C_2H_5(Me_2SO)$, 6; O, 7; $NSO_2C_7H_7$, 8; $NSO_2C_7H_7(Me_2SO)$, 9; SO_2, 10; NCH_3, 11; $NHCH_3$, 12; $^+N(CH_3)_2$, 13.

(where available[64]) gives a more or less parallel correlation to those in Figure 1 (although solvent corrections must be introduced for meaningful correlation). Conformational changes in going from **4** to **5** and to **6** are consistent in the two heteroatom series, but correlation with **1** does not occur.

The final question is the extent to which a field effect or an electron transfer occurs in the 1-hetera-4-cyclohexanones. As suggested by the calculations of Jones and Hassan[21] and Duch,[19,22] an electric field effect is probably the major interaction between the heteroatom group and the γ position in these systems. In all members of compound sets **1** and **4**, the γ carbon is shifted upfield (relative to cyclohexane in **4** and relative to the cyclohexanone carbonyl in **1**) (Tables III and IV). As shown in Figure 5, a plot of the γ chemical shifts in **1** against those in **4** appears as clustering about a possible linear relationship. The γ upfield shifts in **1** are larger than in **4** [except for cyclohexane-1,4-dione (**1a**)], an effect ascribable to the greater sensitivity of the carbonyl group to electrostatic effects through polarization of the π electrons. Since the largest shifts are for quaternary nitrogen heterocycles, which cannot donate electrons to carbonyl groups, any transannular electron donation must be minimal in the 1-hetera-4-cyclohexanones (**1**).[65]

A recent publication by Eliel et al.[66] provides greater insight into heteroatom effects on both gauche and anti γ carbons. Incremental γ upfield shifts on anti positions are greater than on gauche positions and are most pronounced for second-row heteroatoms. These authors propose a hyperconjugative-type interaction of free-electron pairs centered on second-row heteroatoms with the C_α–C_β bond accompanied by a subsequent alternation of the electron density at the γ anti-periplanar carbon. Electrostatic through-space field effects are discounted because of observed dependence on heteroatom row and not on heteroatom electronegativity. Enhanced γ anti effects in positively charged systems require an additional monopole-induced σ-inductive effect or electrostatic field effect. Simple steric arguments[19,20] may still be important in γ gauche relationships

and may not be discarded. While these new data[66] are extremely significant, they do not appear to materially affect the conclusions reached herein.

According to Nakashima and Maciel,[23] an upfield shift in the carbonyl carbon resonance provides evidence for transannular electron donation. While the heteroatom is fewer σ bonds distant from the carbonyl group in **1** than in **2** and **3**, the upfield shifts of the carbonyl carbons in **1** and the γ carbons in **4** are larger than the upfield shifts reported for **2b** and **2c**, requiring the conclusion that Nakashima and Maciel only observed transannular electron donation in **3**. The observed upfield shifts in **2b** and **2c** relative to **2a** must be ascribed to the normal effects of the heteroatoms in these molecules.

The ^{13}C NMR results reported herein indicate unambiguously that the hybridization at nitrogen does affect the electron density at each ring carbon in a six-membered nitrogen heterocycle. Assumptions[67] that hybridization at nitrogen is of little significance and that rotational barriers in *N*-acetylpiperidines and *N*-nitrosopiperidines provide an indirect method to evaluate conformational equilibria (such as ΔG° for 2-methyl substituents) in the corresponding piperidines must be accepted with caution.

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Registry No.—**1a,** 637-88-7; **1c,** 1445-73-4; **1d,** 29976-53-2; **1f,** 29943-42-8; **1g,** 1072-72-6; **1i,** 17396-35-9; **1j,** 34737-83-2; **1k,** 26822-37-7; **1l,** 24686-78-0; **1m,** 33439-27-9; **1n,** 3612-20-2; **4b,** 1613-51-0; **4c,** 4988-33-4; **4d,** 776-75-0; **4e,** 5325-94-0; **4f,** 4703-22-4; **4g,** 2905-56-8; **5a,** 542-28-9; **5b,** 931-20-4; **6b,** 25077-25-2.

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(26) Aldrich Chemical Co.
(27) Kindly provided by Dr. F. J. Koer and Dr. C. Altona.
(28) Kindly provided by Professors L. A. Paquette and H. Dahn.[13]
(29) Prepared by R. W. Kosley, Jr., by method of P. Johnson and G. A. Berchtold, *J. Org. Chem.*, **35**, 584 (1970), or by sublimation of material purchased from Aldrich Chemical Co.
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(56) A value of δ 27.7 was used for neat cyclohexane.[19,20]
(57) Reference 19: $(CH_3)_2O$ δ 59.4 (neat); $(CH_3)_3N$ δ 47.5 (neat); $(CH_3)_2S$ δ 19.5 (neat); $(CH_3)_2CO$ δ 30.2 (neat). Reference 44: $(CH_3)_2CO$ δ 30.6 ($CDCl_3$); $(CH_3)_2NCHO$ δ 31.1 and δ 36.2 ($CDCl_3$) for average of δ 33.6; $(CH_3)_2NCOCH_3$ δ 34.5 and δ 37.5 (dioxane) for average of δ 36.0.
(58) Reference 19: $(CH_3CH_2)_2O$ α δ 67.4, β δ 17.1 (neat); $(CH_3CH_2)_2S$ α δ 26.5, β δ 15.8 (neat); $(CH_3CH_2)_2NH$ α δ 44.1, β δ 15.4 (neat); $(CH_3CH_2)_2CO$ α δ 35.3, β δ 7.3 (neat). Reference 44: $(CH_3CH_2)_2CO$ α δ 35.4, β δ 7.9 ($CDCl_3$). Reference 59: $(CH_3CH_2)_2NH$ α δ 44.4, β δ 15.7 (C_6D_6); $(CH_3CH_2)_2NCH_3$ α δ 51.4, β δ 12.8, NCH_3 δ 41.0 (C_6D_6).
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Carbon-13 Nuclear Magnetic Resonance Spectra of Chlorinated Pentacyclo[5.3.0.0^{2,6}.0^{3,9}.0^{4,8}]decanes

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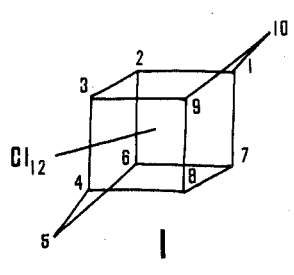
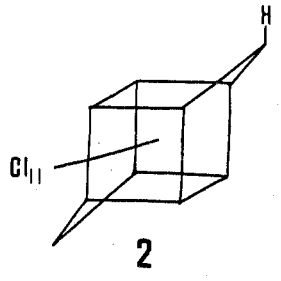
The ^{13}C NMR spectra of dodecachloropentacyclo[5.3.0.0^{2,6}.0^{3,9}.0^{4,8}]decane and four of its hydrogen-substituted derivatives have been obtained. The assignment of the ^{13}C resonances was based on chemical shifts, coupling constants, and Overhauser enhancements of the signals. Good correlation was found between the observed chemical shifts and those predicted from substituent parameters and between ^{1}H chemical shifts and ^{13}C chemical shifts. Some unusual variations in the two- and three-bond coupling constants were observed.

Proton-coupled ^{13}C NMR studies have generally been limited to simple molecules because of the complexity of the spectra and the low sensitivity associated with this technique. The availability of dodecachloropentacyclo[5.3.0.0^{2,6}.0^{3,9}.0^{4,8}]decane (compound 1) and some of its hydrogen derivatives provided an excellent opportunity to investigate the ^{1}H–^{13}C coupling and the inductive effects in a set of closely related and relatively large molecules. These compounds have a rigid carbon skeleton, and on account of its symmetry, 1 contains only three sets of magnetically different carbons. Four hydrogen derivatives of 1 were available from photochemical reactions[2-4] and other synthetic routes.[5]

Compound 1 was first synthesized in 1945 by Prins.[6] Its structure was deduced from infrared,[7] x-ray,[8] and mass spectral[9] data. This compound has been used commercially as a pesticide (Mirex)® and a fire retardant (Dechlorane)® and has been the subject of pyrolysis,[10] chemical,[5,8] and photochemical[2-4] investigations. The structures of compounds **2, 3,** and **5** were assigned from NMR, infrared, and mass spectral data.[2-4] The geometry of compound **4** was deduced in this study.



1



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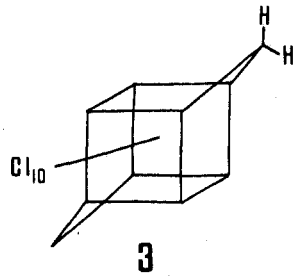

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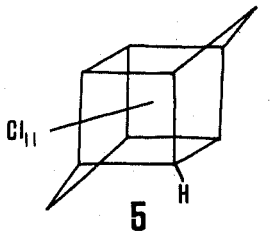

5

Experimental Section

The ^{13}C NMR spectra were obtained at 22.6 MHz with a Bruker HX-90 spectrometer, operated in the single coil configuration with a heteronuclear ^{19}F lock and equipped for fast Fourier transformation with a Nicolet 1083 data system. ^{1}H NMR spectra were obtained at 90 MHz in the continuous wave mode with a homonuclear lock.

Chemical shifts were measured while employing noise-modulated ^{1}H decoupling[11] at ambient probe temperature (approximately 25°C). Saturated solutions in carbon disulfide containing 5% (v/v) hexafluorobenzene and 10% (v/v) tetramethylsilane were used for the lock and chemical shift reference, respectively. Approximately 1.3 ml of sample solution was contained in 10-mm o.d. sample tubes fitted with vortex plugs. Chemical shift data encompassing a 5000-Hz spectral region were collected into 8K data points, yielding a computer resolution of 1.2 Hz (0.04 ppm). Typically, 20 000 scans with a delay time of 2 sec between scans were necessary to obtain a good spectrum.

Gated, noise-modulated ^{1}H decoupling was applied in order to observe long-range ^{13}C–^{1}H coupling.[12,13] The BSV-2 decoupler was on for 1.8 sec and off 0.2 sec prior to the data acquisition, using circuitry similar to that of Dorn et al.[14]

Compound 1 (98%), obtained from Allied Chemical Corp., was recrystallized from benzene. Two hydrogen-substituted derivatives of compound 1 were prepared by the methods of Dilling.[5] Two other derivatives were prepared by the photolysis of compound 1 as described elsewhere.[2,3]

Discussion

The ^{13}C spectrum for compound 1 (Table I) consisted of three singlets at 91.6, 82.4, and 76.5 ppm downfield from Me_4Si with relative areas of 1:3:2. The peak at the lowest field and with the smallest intensity was assigned to the di-