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^{1}H and ^{13}C NMR Studies of Conformational Substituent Effect in 4- and 5-Monosubstituted Derivatives of Benzocycloheptene

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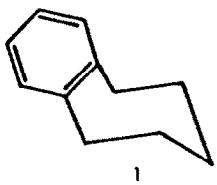
Abstract -Values of $-\Delta G^{\circ}$ for the axial⇌equatorial conformational equilibrium of the chair form of 5-substituted (2-8) and 4-substituted (9-14) derivatives of benzocycloheptene were measured from their ^{1}H and/or ^{13}C NMR spectra recorded under conditions of slow exchange ($T < 80^{\circ}C$). Strikingly different conformational substituent effects are noted in each series of compounds. The results are compared with equivalent energy parameters published for analogous six-membered cyclic derivatives and interpreted in terms of steric and electrostatic interactions. Substituent effects on ^{13}C NMR chemical shifts were measured and are compared to those reported for the cyclohexane ring.

As part of our continuing effort to thoroughly define the conformational properties of seven membered ring systems and as a sequel to a detailed study [1] reported some time ago on the conformation of benzocycloheptene (1), we have prepared several 4- and 5-monosubstituted derivatives(2-14) and studied their conformational features by ^{1}H and ^{13}C dynamic NMR methods. [2]



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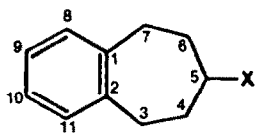
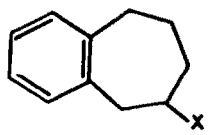
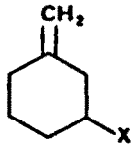




2 ; X = OCH_3
3 ; X = $OCOCH_3$
4 ; X = $OCOCF_3$
5 ; X = OTMS
6 ; X = Cl
7 ; X = OH
8 ; X = CH_3

9 ; X = OCH_3
10 ; X = $OCOCH_3$
11 ; X = OTMS
12 ; X = Cl
13 ; X = OH
14 ; X = CH_3

Our interest in these compounds derived in part from the fact that, contrary to the vast amount of information available in the literature on the conformational energy of substituents on six-membered ring systems,[3] very little attention had so far been given to the determination of substituent energy for seven-membered cyclic compounds. Our objective was therefore to measure the relative populations of equatorial and axial chair conformers present at equilibrium for these compounds and to compare them with corresponding values already known for analogous six-membered cyclic molecules. Compounds 2-8 are considered analogs of cyclohexane derivatives while compounds 9-14 have features in common with 3-substituted methylenecyclohexane derivatives (15) studied by Lambert and coworkers [4].



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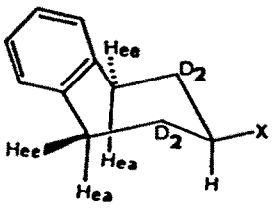
A second aspect of our work was concerned with the determination of α, β, γ and δ substituent effects on ^{13}C NMR chemical shifts. Again, whereas such effects have been extensively studied in the cyclohexane system,[5] relatively little is known for the seven-membered ring. We wanted to determine whether the significantly greater puckering of the seven-membered chair would lead to appreciable differences.

It is pertinent to recall that earlier studies[1] have shown that benzocycloheptene exists exclusively in the chair conformation and that its relatively high activation energy for chair inversion (10.9 kcal/mol) makes its conformational features amenable to studies by dynamic NMR methods. Furthermore, it is well known that of the various methods available to determine $-\Delta G^{\circ}$ values for substituents on cyclic systems, NMR peak integration under conditions of slow exchange is the most reliable.[3] Therefore signal integrations from both ^1H and ^{13}C low temperature spectra of compounds 2 to 14 were used to measure the relative amounts of axial and equatorial conformers.

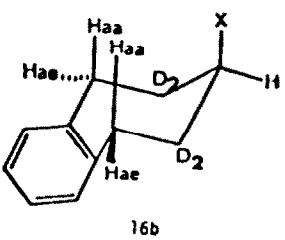
RESULTS

^1H NMR spectra. With the exception of the two methyl derivatives (8 and 14), all ^1H NMR analyses were performed on β, β'-tetradeuterio derivatives of each compound; compounds 2-7 were deuterated at the 4 and 6 positions while compounds 9-13 were deuterated at the 3 and 5 positions. In all cases, the methine proton gives a singlet at room temperature for spectra recorded under deuterium decoupling conditions. All tetradeuterio derivatives are identified by adding the suffix $-d_4$ to the number of each compound (e.g. 2-d_4). All ^1H NMR analyses were performed at 100 MHz in the CW mode.

Room temperature ^1H spectra of compounds 2-d_4 to 7-d_4 present the same overall characteristics (Figure 1). The aromatic protons appear as singlets at ~ 7 ppm; the H-5 protons also appear as singlets in the deuterium decoupled spectra, while the methylene protons on carbons 3 and 7 constitute an AA'BB' multiplet which appears as a simple AB since ^5J coupling constants are small and make each side of the molecule essentially independant from the other. On lowering the temperature a spectral change is observed, and below -80°C the slow exchange spectrum recorded consists of the superimposition of characteristic features for the axial and the equatorial conformers. The signal of the H-5 proton has split into two singlets of unequal intensity: the high field singlet being due to the axial proton of the equatorial conformer while the low field less intense singlet is due to the equatorial proton of the axial conformer. This assignment is deduced from line-widths of the methine protons in the absence of deuterium decoupling whereby the axial protons are broader than the equatorial ones. The benzylic protons give rise to two AB patterns; the more intense one is assigned to the H-3,7 protons of the equatorial conformer (16a) and Figure 1 shows that it is effectively an A_2 singlet because of the small chemical shift difference between the axial and equatorial benzylic protons while the less intense AB quartet belongs to the axial conformer 16b for which the chemical shift difference between the benzylic protons ranges from 78 to 105 Hz and J_{AB} ranges from -13.9 to -15.0 Hz depending on the substituent. No ^1H spectral change was observed for compound 8. The ^1H parameters for compounds 2-d_4 to 7-d_4 are summarized in Table I.



16a



16b

Table I: ^{1}H Parameters for compounds 2-d_4 - 7-d_4 and 9-d_4 - 14. *

X	Solvent	Room temperature (~ 25°C)				Low temperature (-85°C)						X	Solvent	+25°	-85°	
		H-5	H-3,7			H-5a	H-5e	H-3,7						H-4	H-4a	H-4e
			δ_A	δ_B	J_{AB}			A_{2e} [1]	δ_A [2]	δ_B [2]	J_{AB}					
OCD_3	CS_2	3.29	2.92	2.40	14.1	3.12	3.51	2.58	3.08	2.22	13.9	OCD_3	CS_2	3.02	2.81	3.51
2	$CHFCl_2$	3.41	2.94	2.56	14.6	3.32	3.67	2.71	3.05	2.27	14.9	9	$CHFCl_2$	3.16	3.01	3.73
$OCOCH_3$	$CHFCl_2$	5.03	2.91	2.66	14.5	4.94	5.23	2.76	3.28	2.48	14.0	$OCOCH_3$	CS_2	4.58	4.32	4.86
3	THF-d_8	5.22	2.92	2.70	14.4	5.16	5.39	2.89	3.19	2.51	15.0	10	$CHFCl_2$	4.76	4.59	5.12
$OCOCF_3$	CD_3OD	5.21	2.84	2.64	14.7	5.16	5.41	2.78	--[3]	-- [3]	-- [3]	OTMS	CS_2	3.49	3.35	4.11
4	$CHFCl_2$	5.29	3.53	3.25	14.5	5.09	5.42	3.33	3.79	3.10	14.9	11	$CHFCl_2$	3.58	3.51	--
	CD_3COCD_3	5.33	3.15	2.73	14.6	5.26	5.52	2.82	3.18	2.55	14.1	Cl	CS_2	3.87	3.66	4.43
OTMS	CS_2	3.89	2.91	2.41	14.8	3.62	4.11	2.57	3.24	2.18	14.2	12	$CHFCl_2$	4.07	3.93	4.71
5	$CHFCl_2$	3.93	2.93	2.55	14.7	3.79	4.22	2.71	3.35	2.36	14.3	OH	CS_2	3.54	3.47	4.17
Cl	CS_2	4.22	2.97	2.56	14.6	3.94	4.55	2.65	3.27	2.39	14.8	13	CD_3COCD_3	3.51	3.45	4.23
6	$CHFCl_2$	4.30	3.02	2.62	14.3	4.19	4.73	2.76	3.39	2.55	15.0	CH_3	CS_2	.93 (6.3)	.61 (7.2)	1.03 (5.4)
OH	CD_3COCD_3	3.36	2.90	2.61	14.6	3.77	4.17	2.69	3.36	2.36	14.0	14	$CHFCl_2$	.97 (6.3)	.64 (7.2)	1.03 (5.4)
7																

* Chemical shifts are in ppm from TMS; coupling constants are in Hz.

1 Chemical shift of H-3,7 protons of the equatorial conformer (A_2, see text).

2 Chemical shift of H-3,7 protons of the axial conformer (AB quarter, see text).

3 Partial overlapping with solvent signals.

4 Chemical shift of methyl signal; coupling constants are in brackets.

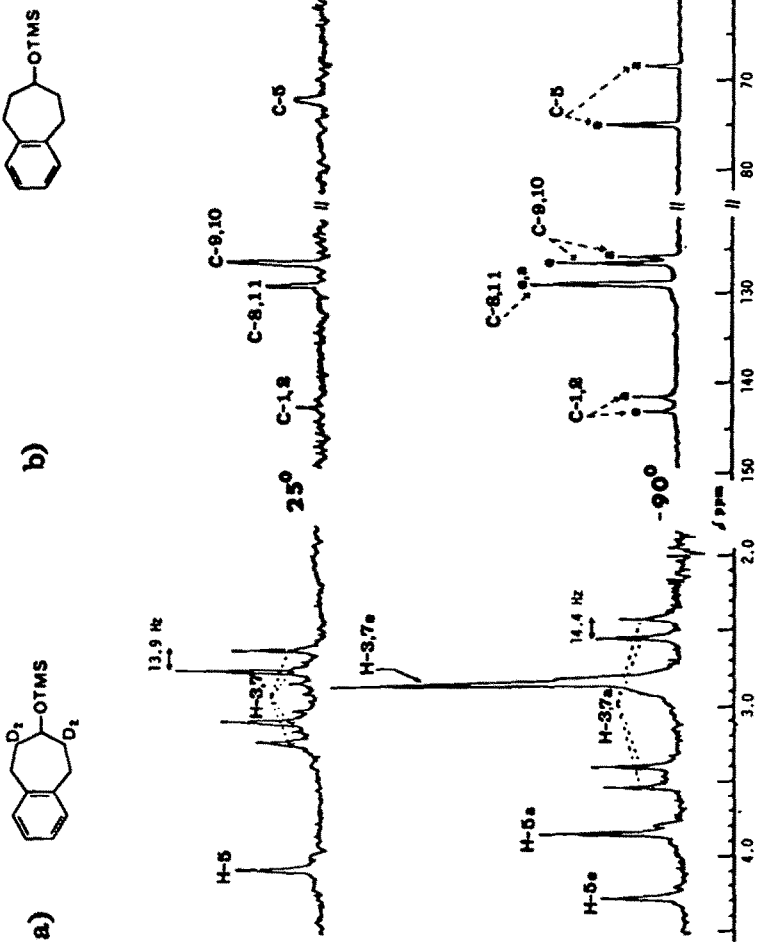


Figure 1. a) Partial 100 MHz ^{1}H NMR spectra of compound 2-d_4 in CS_2 at 25°C and -90°C;
b) Partial 22.63 MHz ^{13}C NMR spectra of compound 2 in CS_2 at 25°C and -90°C
(e = signal of the equatorial conformer, a = signal of the axial conformer).

The room temperature ^{1}H NMR spectra of compounds 9-d_4 to 13-d_4 also present the same overall characteristics. The aromatic protons again appear as a singlet at ~7 ppm, the H-4 proton appears as a singlet in the deuterium decoupled spectra with its position ranging from 3.02 to 4.75 ppm depending on the substituent and the methylene protons on carbon 7 appear as a more or less resolved multiplet between 2.63 and 2.77 ppm while the methylene protons on carbon 6 appear as a non symmetrical pair of multiplets between 1.0 and 2.2 ppm.

On lowering the temperature a spectral change occurs and below -80°C the H-4 singlet has split into two components of unequal intensity; line width arguments show that the high field singlet belongs to the axial proton of the equatorial conformer while the low field singlet arises from the equatorial proton of the axial conformer.

The room temperature ^{1}H NMR spectrum of 14 shown partly in Figure 2 presents the following features: the aromatic protons appear as a singlet at 6.91 ppm while the H-3 and H-7 protons appear as a multiplet betwen 2.9 and 2.5 ppm. Protons on carbons 4, 5 and 6 give rise to a non-resolved multiplet between 2.2 and 1.2 ppm. Finally, the methyl group appears as a doublet at 0.93 ppm with a coupling constant to the methine proton of 6.3 Hz. On lowering the temperature below -85°C, the methyl signal splits into two doublets; the less intense one observed at 0.61 ppm is assigned to the axial conformer. Its coupling constant is 7.2 Hz while the more intense doublet for the equatorial methyl group observed at 1.03 ppm shows a coupling constant of 5.4 Hz.

The pertinent ^{1}H NMR parameters for compounds 9-d_4 to 13-d_4 and 14 are summarized in Table I.

^{13}C NMR Spectra. All ^{13}C NMR spectra were recorded at 22.63 MHz with broad band proton decoupling. The room temperature ^{13}C NMR spectrum of benzocycloheptene (1) has already been assigned in the literature[6]. On lowering the temperature, no spectral change is observed in agreement with earlier findings [1] that benzocycloheptene exists exclusively in the chair conformation.

The room temperature ^{13}C NMR spectra of compounds 2-8 share similar characteristic features. Symmetry considerations allow for only 6 signals to be observed for the 11 carbons of the benzocycloheptene system. The assignments given in Table II were made from chemical shift considerations and by comparaison with the spectra of the tetradeutero derivatives.

The spectral assignment of compound 5 is used for illustrative purposes. The aliphatic region, shown partially in Figure 1b, contains 4 signals. The lower field signal (72.59 ppm) is assigned to the substituent bearing carbon since substitution with an oxygen group is expected to deshield the α carbon by ~50 ppm. [5] Substituent signals are easily assigned from predictable chemical shift and intensity arguments and, for 5, the trimethylsilyl carbons appear at 0.26 ppm. Comparaison of the spectra with those of the deuterated derivatives allows the assignment of the highest field signal (30.09 ppm for 5) to the benzylic carbons C-3,7 since its intensity remains unchanged in the $-d_4$ derivative spectrum while the lower field signal (36.85 ppm for 5) has disappeared owing to the fact that the CD_2-4,6 quintuplet is not observed under the recording conditions used because of a long T_1 and the absence of NOE for these non protonated carbons. [7]

The aromatic region of 5 contains 3 signals. The low intensity of the signal at 142.26 ppm indicates that it arises from the C-1,2 quaternary carbons. By analogy with benzocycloheptene, the signals at 128.81 and 126.08 ppm are assigned to the C-8,11 and C-9,10 carbons respectively.

Table II: ^{13}C NMR chemical shits * and substituent effects of compounds 2, 3, 5, 7, 8.

X	Solvent	T°C		C-1,2	C-3,7	C-4,6	C-5	C-8,11	C-9,10	Cx	α	β	γ	δ	$C_6H_{11}X$ [4] α	β	γ	δ
H	CS_2	25		142.85	36.91	28.66	33.14	128.94	125.95									
1		-80		142.78	36.59	28.27	33.02	128.81	125.76									
OCH$_3$	CS_2	25		142.26	30.16	32.69	80.85	128.81	126.15	55.37								
2		-80	[1] a	152.65	28.47	31.00	76.95	128.62	125.82	[2]	43.93	2.73	-8.12	-0.13	47	2	-7	-1
			e	141.35	31.00	32.95	83.84	128.62	126.21		50.82	4.68	-5.59	-1.43	52	4	-3	-2
OCOCH$_3$	CS_2	25		141.48	30.54	33.01	74.60	128.87	126.40	20.80								
3		-83	a	141.97	29.07	31.56	71.37	128.65	126.06	21.04	38.35	3.29	-7.52	-0.81	42	3	-6	--
			e	140.90	30.75	32.85	76.11	128.87	126.39	21.04	43.09	4.58	-5.84	-1.88	46	5	-2	-2
OTMS	CS_2	25		142.26	30.09	36.85	72.59	128.81	126.08	0.26								
5		-90	a	142.91	28.27	35.09	68.43	128.75	125.69	0.00	35.41	6.82	-8.32	0.13				
			e	141.29	31.07	37.04	75.13	128.75	126.21	0.00	42.11	8.77	-5.52	-1.49				
OH	THF-d_8			143.00	30.93	37.30	68.04	129.26	126.60									
7		-100	a	144.02	[3]	35.30	[3]	129.33	126.73	--		6.83		-0.32				
			e	142.65	31.52	37.56	74.87	129.33	126.73	--	41.85	9.09	-5.27	-1.69				
CH$_3$	CS_2	25		142.52	35.29	36.46	38.60	128.75	125.95	23.98								
8		-85	a	--	--	--	--	--	--	--					1.4	5.4	-6.4	0
			e	142.39	35.35	36.07	38.93	128.62	125.82	24.50	5.91	7.80	-1.24	-0.39	6.0	9.0	0	-0.2

* in ppm from TMS.

1 a = signals of axial conformer, e = signals of equatorial conformer.

2 under CD_2Cl_2 signals.

3 under THF-d_8 signals.

4 values taken from reference 7.

Table III: ^{13}C NMR chemical shifts* and substituent effects for compounds 9 - 11, 13 and 14

X	Solvent		T °C	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9,10	C-11	subst	α	β C-3	β C-5	γ	δ
OCH_3	CS_2		25	143.18	137.42	41.53	78.51	37.56	25.09	36.04	128.81	126.21,126.41	130.11	55.37					
9		e [1]	-100	143.11	136.87	41.53	79.16	38.08	25.87	35.34	128.75	126.21,125.76	129.79	55.63	50.89	4.94	5.06	-2.40	-1.25
		a		142.52	137.19	39.06	74.93	36.52	21.77	--	--	--	130.57	-- [2]	46.66	2.47	3.50	-6.50	--
$OCOCH_3$	$CHFCl_2$		25	144.00	137.10	41.95	72.80	37.72	25.24	36.03	129.50	126.96,127.43	130.97	21.36					
10		e	-100	144.26	136.75	42.51	73.36	37.85	25.63	35.34	129.63	127.00,127.43	130.79	21.97	44.89	5.72	4.83	-2.84	-1.45
		a		143.74	137.27	38.61	69.85	36.10	22.51	--	129.18	126.67, --	131.31	21.62	41.38	1.82	3.08	-5.96	--
OTMS	CS_2		25	143.04	137.39	46.34	70.58	41.98	25.80	35.81	128.81	126.28,126.47	130.11	0.00					
11		e	-100	143.43	137.52	46.73	70.77	42.31	26.58	35.55	129.20	126.66,126.86	130.24	0.454	42.50	10.14	9.29	-1.69	-1.04
		a		--	--	--	67.21	--	22.13	--	--	-- --	--	--	38.94	--	--	-6.14	--
OH	$THF-d_8$		25	144.02	138.43	46.40	68.04	41.98	26.13	36.26	129.20	126.67	130.63	--					
13		e	-100	143.95	138.23	46.66	-- [3]	42.18	-- [3]	35.81	129.27	126.80	130.37	--	--	9.87	9.16	--	-1.58
		a		--	--	--	--	39.74	--	32.96	--	--	--	--	--	--	--	--	--
CH_3	CS_2		25	142.72	140.92	44.19	33.21	40.80	27.17	36.26	128.55	125.76	129.20	23.40					
14		e	-100	142.78	141.29	44.39	33.79	41.33	28.01	36.07	128.62	125.82	129.01	25.35	5.52	7.80	8.31	-0.26	-0.52
		a		--	--	--	29.04	38.29	22.49	--	--	--	--	25.97	0.77	--	5.27	-5.72	--

* in ppm from TMS.

1 e = signals of equatorial conformer, a = signals of axial conformer

2 under CD_2Cl_2 signals.

3 under $THF-d_8$ signals.

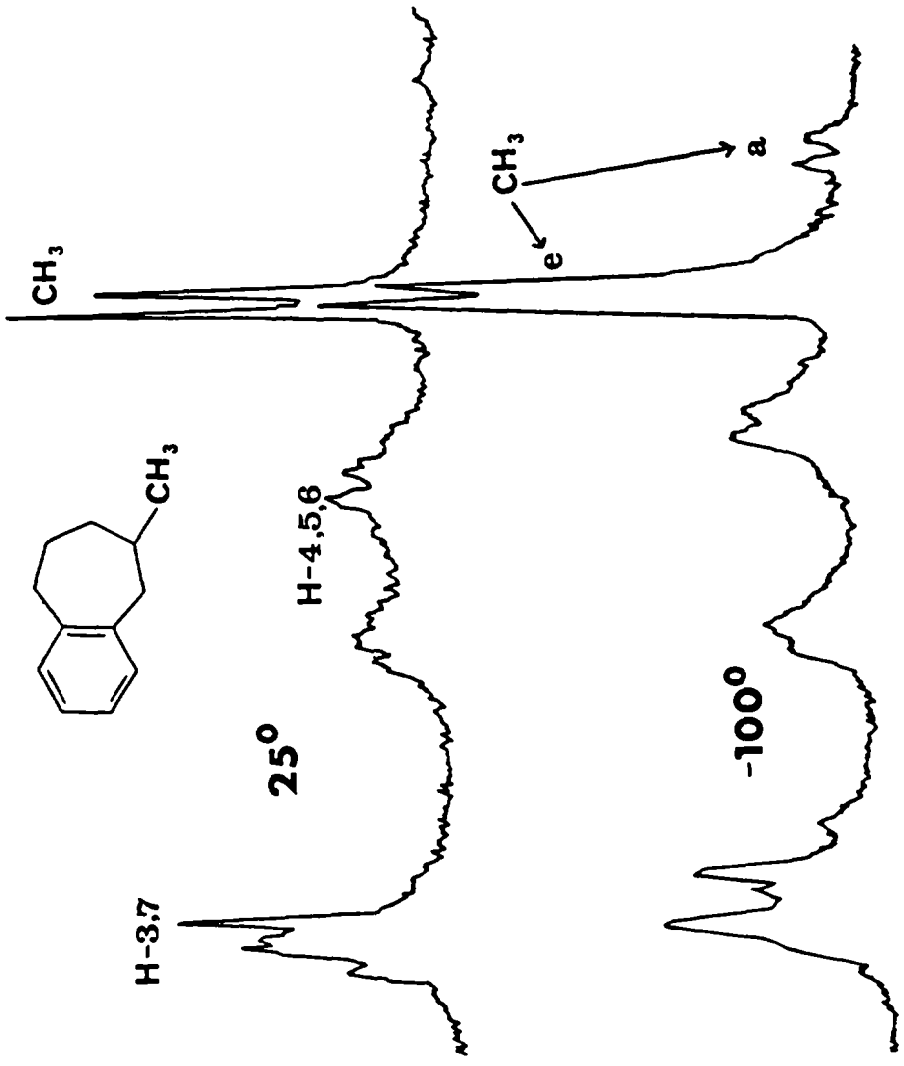


Figure 2. Partial 100 MHz ^1H NMR spectra of compound 14 in CS_2 at 25°C and -100°C (e = signal for the equatorial conformer, a = signal of the axial conformer).

On lowering the temperature a spectral change is observed and below -90°C the ring carbon signals of most compounds have split into two components. In the aliphatic region signals of the less intense axial conformer appear at higher field than the signals of the equatorial conformer. This is consistent with the known α_e, β_e, γ_e, and α_a, β_a, γ_a effects of oxygen derivatives of cyclohexane.

In the aromatic region, however, the less intense C-1,2 signal of the axial conformer appears at lower field than that of the corresponding signal of the equatorial conformer. The C-9,10 line has also split into two unequal components with the less intense signal of the axial conformer appearing at higher field that the more intense signal of the equatorial conformer. The C-8,11 line has not split as seen in Figure 1b.

The absence of symmetry in compounds 9-14 accounts for the observation of a ^{13}C NMR signal for each of the 11 carbons on the benzocycloheptene ring. The assignments reported in Table III are based on calculations of chemical shifts using benzocycloheptene as the reference molecule together with substituent effects determined for compounds 2-8, and comparison with the spectra of the tetradeuterated derivatives. On lowering the temperature, splitting of various signal occurs and the chemical shift data are also reported in Table III. The spectrum of the methoxy derivative 9 in CS_2 will serve as an illustration.

At low temperature, most of the ring carbon signals of 9 split into two components. In the aliphatic region, the C-4 doublet has a low field intense component at 79.16 ppm which is assigned to the equatorial conformer and a less intense higher field component at 74.93 ppm which is assigned to the axial conformer. As was the case for the 5-substituted derivatives, this assignment is made from the α_e and α_a effects determined for the OCH_3 group in 2 and from the positive value of $-\Delta G^{\circ}$ derived from the ^{1}H spectra which indicates a predominance of the equatorial conformer. Carbons 3, 5 and 6 all show an axial component at higher field than the equatorial component while C-7 shows only one signal. This is easily explained by the fact that this carbon is only slightly influenced by the presence of a δ substituent.

In the aromatic region, only the signals of C-1 and C-2 have split into two components. The more intense, lower field line of the equatorial conformer appears at 143.11 ppm while its axial counterpart appears at 142.52 ppm. Carbon-2 which is influenced by a γ-effect from the substituent has its equatorial component at 136.87 ppm and its axial component partially superimposed at 137.19 ppm.

DISCUSSION

Values of $-\Delta G^{\circ}$ were obtained from the equation $-\Delta G^{\circ} = RT \ln K$ where $K = [E]/[A]$; [E] is the relative population of the equatorial conformer and [A] is the relative population of the axial conformer. These populations were determined by integration of ^{1}H and/or ^{13}C signals.

It is well known that FT ^{13}C NMR signal integrations should not be used to evaluate molecular proportions unless certain conditions are met. Having found that the T_1 relaxation times of the carbons of 2,4-dimethyl piperidine were in a 0.26 - 0.43 seconds range at -67°C, Booth and Jozefowicz [8] concluded that integrations from ^{13}C Fourier transform spectra can be used to measure molecular proportions provided that the temperature is lower than -53°C, that comparisons are made between carbons bearing the same number of protons and that the repetition rate is longer than 2 seconds.

Values of $-\Delta G^{\circ}$ reported in Table IV were determined using either or both ^{1}H and ^{13}C NMR spectra recorded below -80°C, the latter using a pulse repetition

Table IV. Values of $-\Delta G^{\circ}$ determined for 5-substituted

X	Solvent	T (°C)	%eq	%ax	K	$-\Delta G^{\circ}$ (kcal/mol)	Method	A [1] (kcal/mol)
OCH_3 **2**	$CHFCl_2$	-80	70	30	2.3	.32	^{13}C*	.55
	$CHFCl_2$	-80	71	29	2.5	.35	^{1}H	
	CS_2	-80	41	59	0.7	-.13	^{13}C	
	CS_2	-80	34	66	0.5	-.26	^{1}H	
$OCOCH_3$ **3**	$CHFCl_2$	-80	72	28	2.6	.37	^{1}H	.71
	CS_2	-83	73	27	2.7	.38	^{13}C	
$OCOCF_3$ **4**	THF-d_8	-90	74	26	2.8	.37	^{1}H	.54
	CD_3OD	-90	73	23	3.3	.43	^{1}H	
OTMS **5**	$CHFCl_2$	-80	88	12	7.7	.78	^{1}H	.74 [2]
	CS_2	-80	66	34	1.9	.25	$^{13}C(^{1}H)$	
	CS_2	-80	54	46	1.2	.06	^{1}H	
Cl **6**	$CHFCl_2$	-80	68	32	2.1	.28	^{1}H	.51
	CS_2	-95	52	48	1.1	.03 [5]	^{1}H	
OH [6] **7**	THF-d_8	-100	73	27	2.7	.34	^{13}C	.97
CH_3 **8**	CS_2	-85	~100	~0	> 50	> 1.5 [5]	^{13}C	1.7 [3]

*All ^{13}C NMR solutions contain 13% of CD_2Cl_2 for field locking purposes. Consequently the $-\Delta G^{\circ}$ values in CS_2 determined by ^{13}C NMR are less accurate because the CD_2Cl_2 changes the polarity of the medium. This is particularly important for **2**, **3**, **5**, and **11** (vide infra).

1. The A values are taken from reference 3.
2. The A value for OTMS is taken from reference 11.
3. The A value for CH_3 is taken from reference 9.
4. The A_w values are taken from reference 4. Instead of CS_2 the nonpolar solvent used was CF_2Cl_2.
5. These values are taken from reference 12.
6. Derivatives **7** and **13** are not soluble in common nonpolar solvents suitable for low temperature studies such as CS_2 or CF_2Cl_2.

and 4-substituted derivatives of benzocycloheptene.

X	Solvent	T (°C)	%eq	%ax	K	$-\Delta G^{\circ}$ (kcal/mol)	Method	A_{π}[4] (kcal/mol)
OCH_3 **9**	$CHFCl_2$	-100	63	37	1.8	.18	^{13}C	.11
	$CHFCl_2$	-100	68	32	2.1	.26	^{1}H	
	CS_2	-100	78	22	3.5	.43	^{1}H	.80
$OCOCH_3$ **10**	$CHFCl_2$	-100	81	19	4.2	.49	^{13}C	.38
	$CHFCl_2$	-100	81	19	4.2	.49	^{1}H	
	CS_2	- 90	80	20	4.0	.50	^{1}H	.61
OTMS **11**	$CHFCl_2$	- 90	~100	~0	>50	>1.5	^{13}C	
	$CHFCl_2$	- 90	~100	~0	>50	>1.5	^{1}H	
	CD_2Cl_2	- 90	96	4	25	1.2	^{1}H	
	CS_2	-100	89	11	8	.72	^{13}C	
	CS_2	- 90	80	20	4.0	.50	^{1}H	
Cl **12**	$CHFCl_2$	- 95	66	34	1.9	.24[5]	^{1}H	
	CS_2	- 95	88	12	7.3	.70[5]	^{1}H	
OH[6] **13**	THF-d_8	-100	96	4	25	1.2	^{1}H	1.12
CH_3 **14**	$CHFCl_2$	-100	93	7	13	.88	^{13}C	.70
	$CHFCl_2$	-100	93	7	13	.88	^{1}H	
	CS_2	-100	92	8	12	.85	^{13}C	.80
	CS_2	-100	93	7	13	.91	^{1}H	

rate of 4 seconds. The results derived from ^{13}C measurements involved various signals. For compounds 2-7, the only signals with a chemical shift difference large enough for accurate integration were those of C-5 while for compounds 9-13 calculations were carried out for the C-4 and C-6 signals. Finally, the C-5 and C-7 signals were used for 13 and C-6 was used for 14. Determinations of $-\Delta G^{\circ}$ from ^{1}H NMR measurements also involved several signals. For compounds 2-d_4, 7-d_4 and 9-d_4 to 13-d_4, the methine proton signal on the substituent bearing carbon was used to determine K while for 14, the methyl signal was used.

For compounds 2, 3, 5, 9, 10, 11 and 14, $-\Delta G^{\circ}$ values were determined from both ^{1}H and ^{13}C NMR spectra. For $CHFCl_2$ solutions, the two values obtained were within experimental error of each other while for CS_2 samples, important differences were noted. These differences however, were thought to arise from the difference in polarity between the ^{1}H and ^{13}C NMR CS_2 solutions because the ^{13}C samples also contained 13% of CD_2Cl_2 for locking purpose. This was confirmed by determining $-\Delta G^{\circ}$ values from ^{1}H spectra of samples prepared using CS_2 containing 13% CD_2Cl_2; excellent agreement with the ^{13}C NMR values was then observed.

Values of $-\Delta G^{\circ}$ are reported in Table IV together with the corresponding values of the cyclohexane (A values) and 3-substituted exo-methylenecyclohexane (A_{π}) systems. It was believed that the greater puckering of the chair form of benzocycloheptene [1] relative to that of cyclohexane would modify 1,3-syn axial interactions and be reflected on the conformational free energy of substituents on the seven-membered ring. A comparaison of the $-\Delta G^{\circ}$ values determined for the polar 5-substituted derivatives of benzocycloheptene with the corresponding A values shows that the former parameters are almost always smaller than the latter. This suggests that the interactions responsible for the equatorial preference in cyclohexane are less important or that other factors exert a strong conformational effect in the seven-membered ring. It can also be noted that the trends for $-\Delta G^{\circ}$ and A values are not the same. The most important differences are noted for the OCH_3 and OTMS substituents.

The behavior of the $-\Delta G^{\circ}$ values for the 4-substituted derivatives is significantly different. In this series, structural characteristics suggest that the $-\Delta G^{\circ}$ values should not be compared with A values, but rather with A_{π} values [4] as will be discussed later.

Jensen and Bushweller [3] have suggested that A values can be rationalized in terms of steric interactions between axial substituents and syn-axial protons and are therefore influenced by parameters such as the van der Waals radius, the polarisability and electronic density of each substituent. The following considerations constitute an attempt to demonstrate that, in the benzocycloheptene system, steric interactions alone cannot account for the results observed and that $-\Delta G^{\circ}$ is most strongly dependent on electrostatic effects.

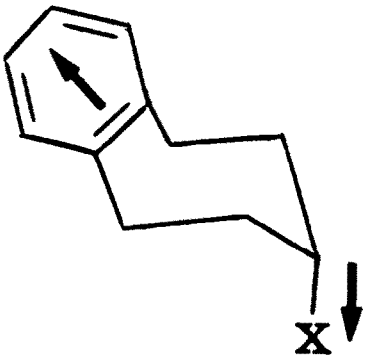
The values observed for the methyl derivatives 8 and 14 are of special importance because the non-polar methyl substituent ought not to involve significant electrostatic or dipolar effects; these compounds should therefore provide useful reference point. The absence of a spectral change at low temperature for compound 8 means that the population of the axial conformer is less than 2%; consequently $-\Delta G^{\circ}$ for this compound is greater than 1.5 Kcal/mole and is most probably not smaller than the 1.7 Kcal/mole observed for methylcyclohexane. [9] Thus, 1,3-syn-axial interactions are at least as strong in the seven-membered ring of 8. The $-\Delta G^{\circ}$ value of 0.88 Kcal/mole determined for 14 (8% of axial conformer present at equilibrium at -100°C) indicates that

steric interaction are less important when the substituent location is changed from the 5 to the 4-position. Structural changes whereby one of the 1,3-syn-axial proton has been replaced by the benzo group can account for the reduction. The π electrons therefore have less repulsive steric character than a saturated CH_2 group as Lambert and coworkers [4] noted for 3-methyl-exo-methylenecyclohexane. Consequently, the axial methyl group is less destabilized for both compounds.

Finally, the observation that the $-\Delta G^{o}$ values obtained for compound 14 are independent of the nature of the solvent confirms the hypothesis that the methyl group does not give rise to a significant electrostatic conformational effect [10] as in the case for most polar substituents in both seven-membered series where solvent changes are useful to identify the origin of the conformational effects observed. The underlying concepts suggest that in a relatively nonpolar solvent such as CS_2, the intramolecular electrostatic interactions should achieve greatest importance while in the more polar $CHFCl_2$ solvent, the electrostatic interactions should be significantly reduced. The observation [13] that solvent effects are small for certain monosubstituted cyclohexanes suggests that electrostatic forces are significant in the seven-membered ring compounds.

The results for compounds 2 to 7 given in Table IV do show large conformational perturbations on solvent change. For example, the $-\Delta G^{o}$ values are reduced significanlty for derivatives 2 (OCH_3), 5 (OTMS) and 6 (Cl) by decreasing the polarity of the solvent from $CHFCl_2$ to CS_2. For reasons given earlier, the appropriate $-\Delta G^{o}$ value for 5 in CS_2 is 0.06 and not 0.25 which represents a value obtained by ^{13}C NMR in CS_2 containing CD_2Cl_2.

A detailed discussion of the behavior observed is difficult to formulate quantitatively because electrostatic calculations are frought with uncertainties[4c] owing to serious limitations arising from the absence of precise geometrical information for the various conformers. Consequently, only a qualitative rationalization of the results is attempted here in terms of the simple formalism proposed by Kaloustian [10a] to describe the conformational consequence of dipolar interactions and solvation. Two terms describe the electrostatic contribution, the first, E_D, is the dipole-dipole interaction (maximum in the vapor phase, it tends towards zero in polar solvents) while the second E_s, is the solvation stabilization energy (zero in the vapor phase, it becomes important in polar solvents favoring that conformation with the larger dipole moment). Because E_D and E_S can have opposite signs, their sum may reinforce or offset steric effects depending on the relative orientation of the individual dipoles.



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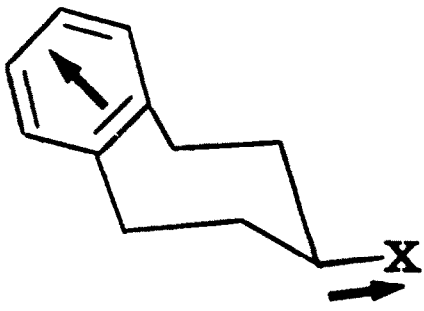

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The greater amount of axial form observed for 6 in CS_2 relative to chlorocyclohexane could result from a stabilizing electrostatic term favoring the axial form since steric repulsion of an axial substituent should be larger in the seven-membered ring, owing to greater puckering of the chair conformation or alternatively, it could be due to a stronger destabilizing interaction in the equatorial form. An increase in solvent polarity, such as for $CHFCl_2$, displaces the equilibrium towards the equatorial form (i.e. $-\Delta G^o$ changes from 0.03 to 0.28) because, as is shown below, the importance of the electrostatic E_D term is reduced as a result of the insulation of one polar moiety from the other by the surrounding solvent molecules.

In order to assess the relative importance of the dipolar contribution to electrostatic interactions, it is necessary to assign the direction of the dipoles for the relevant fragments within the 5-substituted-benzocycloheptene derivatives. For the benzo group, the negative end of the dipole should point away from the alkyl portion of benzocycloheptene as alkyl groups are electron donating (i.e. o-dimethylbenzene [14a], μ = 0.64 D; benzocycloheptene [14b], μ = 0.63 D). The dipole orientation for the various substituents is more difficult to describe as it will be different for X = Cl or OCH_3. For the halogen its direction ought to be along the C-X bond so that 17 and 18 provide useful illustrations while for X = OCH_3, the dipole should approximately bisect the CH-O-CH_3 angle and various substituent rotamers must be taken into account. [4c,10b]

Although calculations of dipole-dipole interactions are not expected to be very accurate owing to the absence of adequate geometrical information [4,10b], simple calculations [15] suggest that 18 is more destabilized than 17 for X = Cl because although both conformers are found to have a positive E_D term, 18 has the larger one.

Table IV reveals that compound 2 (OCH_3) exhibits the most striking conformational behavior. Indeed in CS_2 the axial form predominates whereas in the more polar $CHFCl_2$ the equatorial form is more abundant. Here also the data is compatible with a greater dipole-dipole destabilization of the equatorial form. The fact that the methoxy group dipole should bisect the CH-O-CH_3 angle and be affected by rotamer populations [4c] could account for some of the difference between 2 and 6. It is interesting to point out that a similar solvent effect was observed for 4-methoxy-exo-methylene cyclohexane [16] for which $-\Delta G^o$ values are 0.31 in CF_2Cl_2 and 0.50 in $CHFCl_2$. In addition, work by Stolow and coworkers [17] on 4-substituted cyclohexanones has pointed to similar polar effects involving a significant destabilization of the equatorial form. On the other hand, the study of the conformational preference of the methoxy group in 5-substituted 1,3-dioxanes [10b,18] for which a stronger repulsive dipolar interaction exists in the axial form (instead of the equatorial one) has shown a solvent effect which is opposite to the above.

Thus it appears that the solvent induced conformational effect favoring 17 relative to 18 in CS_2 arises mainly through differences in the E_D term. The solvent change to the more polar $CHFCl_2$ therefore attenuates the destabilizing electrostatic forces present and effectively shift the equilibrium in favor of the equatorial conformation. But because the axial conformer (17) for X = Cl is expected to have a larger dipole moment [19] than 18, it should be better solvated in $CHFCl_2$, that is 17 should be stabilized by the E_s term. The observation that the $-\Delta G^o$ values for 2 and 6 are smaller than the corresponding A values is compatible with these two contributions having opposite effects on solvent change from CS_2 to $CHFCl_2$. Thus, as E_D becomes smaller in $CHFCl_2$, the expected increase in the equatorial form does not take place because the E_s term favors the more polar axial conformer. Unfortunately

it not possible to assess quantitatively the importance of each factor in $CHFCl_2$ with respect to the increased steric interation expected in the axial form as a result of the larger puckering of the seven-membered ring.

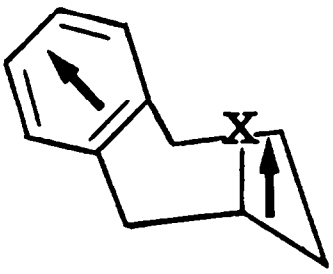
Compound 5 (OTM) also exhibits the same trend although the $-\Delta G^{o}$ values in the two solvents reveal conformer populations different from Cl and OCH_3. Back bonding to d orbitals of the Si atom ought to change the electronic density on the oxygen atom and thereby modify the magnitude of the dipole-dipole interactions.

Contrastingly compound 3 ($OCOCH_3$) and 4 ($OCOCF_3$) show very little conformational change on changing the solvent from CS_2 to $CHFCl_2$. Such a levelling off effect has also been observed previously [4b] and is thought to be related to changes in electronic density of the oxygen atom as a result of delocalization of the oxygen lone pairs with the carbonyl group. Marked differences between $OCOCH_3$ and OCH_3 groups have also been noted for 5-substituted 1,3-dioxanes [10b] and rationalized in terms of a so-called charge attraction mechanism favoring the axial conformer. If such an attraction existed in 3, it would most probably be accompanied by modifications in the dipolar interaction which could become less important. Hence, the relative insensitivity to solvent changes.

The results obtained for the series of 4-substituted derivatives reported in Table IV show striking differences compared to observations made for analogous 5-substituted derivatives. It is seen that in CS_2 all $-\Delta G^{o}$ values are larger and that the solvent change to the more polar $CHFCl_2$ reduces $-\Delta G^{o}$ (i.e. accrued axial preference instead of equatorial preference noted for the 5-substituted family of compounds) for 9 (OCH_3) and 12 (Cl) while for 11 (OTMS) the trend is opposite. These effects no doubt arise from the proximity of the π-electron centre which can influence conformational preference through mechanisms identified recently for 3-substituted exo-methylene cyclohexanes. [4c]

For the 4-methyl derivative 14, the equatorial conformer is preferred by only 0.88 kcal/mole and this $-\Delta G^{o}$ value is virtually independent of solvent. The difference between this value and the 1.7 kcal/mole preference for the equatorial conformation in cyclohexane [9] (the A value) is due to a reduction of the steric interaction arising from the replacement of a syn-axial proton by π-electrons of the aromatic ring. It is therefore clear that for the polar substituents steric repulsion also ought to be less in this family of compounds. Furthermore, it is pertinent to point out that the $-\Delta G^{o}$ value of the methyl group in 14 is similar to that of 3-methyl-exo-methylenecyclohexane [4b] (15, X = CH_3; $-\Delta G^{o}$ = 0.80 $\equiv A_{\pi}$ in the Table IV). It is therefore reasonable to assume at the outset that forces at work in the six-membered ring should be relevant for the seven-membered ring. Thus dipole-dipole interations ought to be considered first to explain the observations for 12 (Cl) and 9 (OCH_3) in a qualitative manner. Dipole orientations shown in structures 19 and 20 indicate that when X = Cl repulsive dipole-dipole interactions (larger E_D term) exist in the axial form 19 whereas for the equatorial form 20 the interaction is either less repulsive or weakly attractive [4c]. Therefore, in a non-polar solvent such as CS_2, the axial form will be destabilized whereas in a more polar solvent such as $CHFCl_2$, dipolar repulsion will become smaller so that the amount of the axial form should increase. Furthermore, solvation in $CHFCl_2$ should also stabilize the more polar axial form so that both E_D and E_S terms favor the axial form in the more polar solvent.

The case of 9 is slightly more complex owing to the possibility of substituent rotation and a different substituent dipole orientation which should bisect the $CH-O-CH_3$ angle. Recently published results [4b,c] for 3-methoxy-exo-methylenecyclohexane (15, X = OCH_3) are pertinent because they



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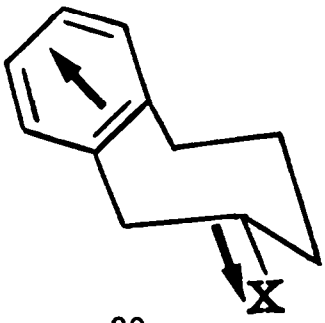

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indicate that a repulsive dipole-dipole interaction in the axial form is responsible for a $-\Delta G^0$ value of 0.80 in CF_2Cl_2 which becomes 0.11 in $CHFCl_2$ as a consequence of the attenuation of the dipolar interaction. In the case of 9, the average $-\Delta G^0$ value of 0.22 in $CHFCl_2$ is quite close to 0.11 as expected whereas the value of 0.43 in CS_2 is smaller than the value of 0.80 for the six-membered analog in CF_2Cl_2. Different dipole orientation caused by differences in ring geometry could account in large part for the different values. Furthermore, a quadrupolar contribution could be more significant for 9. Nevertheless, the trend is the same for both ring sizes.

The acetate derivative 10 is rather insensitive to solvent change as is the case for the analogous six-membered compound. A change in the nature of dominant mechanism to charge attraction could account for this feature.

Surprisingly, 11 (OTMS) shows an unexpected conformational change whereby an increase in solvent polarity favor the equatorial form relative to the axial form. The reason why 11 would show an apparently abnormal behavior, while 5 dit not in the 5-substituted series, is not obvious. Why does the increase in solvent polarity favor the equatorial form for 11 alone? One possibility is that solvation overrides the accrued axial stabilization when the dipolar repulsion is removed.

Preferential solvation of the equatorial form could exist although it is not clear why. Possibly hydrogen bonding of the $CHFCl_2$ molecules could be stronger because of a specific interaction with the OTMS substituent and for steric reasons would be stronger in the equatorial than in the axial form. The very strong equatorial preference for 5 in $CHFCl_2$ may also be a consequence of such a specific interaction of the $CHFCl_2$ molecules with the equatorial OTMS substituent. Back-bonding (p→d) in the O-Si bond might be responsible for this specificity.

It is interesting to point out other cases where the $O-Si(CH_3)_3$ substituent shows accrued equatorial preference. Trans-2,3-di(trimethylsiloxy)-1,4-dioxane 20 is such a case even though the cause may be different from that of 11 although fundamentally related.

^{13}C NMR parameters. Substituent effects determined from room temperature spectra are not significant because they represent a population dependent average of the effect of the substituent in an axial and equatorial position.

Observed α effects in both series of seven-membered compounds are very similar to those observed in the cyclohexane system.[5] The α effect being mostly dependent on the electronegativity of the substituent, the order of increasing α effects is the same in both series as in cyclohexane, i.e. $OCH_3 > OCOCH_3 > OH > CH_3$.

Furthermore, β effects are also very similar to those observed for monosubstituted cyclohexane derivatives. However, differences exist between the β effects determined for carbon 3 and carbon 5 in the 4-substituted series and most probably reflect geometrical differences due to the absence of symmetry with respect to the C-X bond.

Important differences are noted for γ effects between the two series and between values reported for the cyclohexane system. It is noteworthy to point out that for the 4-series only C-6 is actually considered because the other γ-carbon (C-1) is an sp^2 carbon.

The γ_e values for the 5-series reported in Table II are appreciably more negative than those of corresponding cyclohexane derivatives. In addition to the upfield shift, throught the so-called γ_{anti} effect, exerted by polar substituents, there appears to be another contribution due to differences in ring geometries [21] for the two ring size as is most clearly seen for the γ_e of the CH_3 group. γ_a values are also more negative for the seven-membered compounds. Constrastingly, the data for the 4-substituted series are closer to that for cyclohexanes. Differences in dihedral angles are most probably the cause. [21]

Finally, observed δ effects are small (-1 to -2 ppm) and similar to those observed for monosubstituted cyclohexane derivatives.

EXPERIMENTAL

Melting points are uncorrected and were determined using a Buchi melting point apparatus. The vpc analyses and separations were carried out on a Varian Aerograph model 920 instrument using helium as carrier gas.

The variable temperature ^{1}H spectra were recorded with a JEOL model JNM-4-H-100 instrument operating in the CW mode at 100 MHz. Deuterium decoupling was performed with a heteronuclear decoupling unit JEOL model JNM-SC-HC. The ^{13}C spectra were recorded with broad band ^{1}H decoupling on a Bruker WH-90 instrument operating at 22.63 MHz with a pulse angle between 30° and 65°, SW= 6000 Hz, data size = 8K, AQ = 0.679s. For most spectra, the pulse repetition time was approximately equal to the acquisition time except for the spectra used for integrations, for which it was 4 sec.

All ^{1}H analyses were performed on samples of 20-30 mg of the compound in 0.5 ml of solvent in standard 5 mm tubes. All ^{13}C analyses were performed on samples of 100-300 mg of the compound in 2.5 ml of solvent containing 13% (v/v) of CD_2Cl_2 (for locking purposes) in standard 10 mm tubes. All samples were degassed and sealed.

The values of K reported from ^{1}H measurements are a mean of 5 integrations using the electronic integrator on the instrument. The precision is estimated from the standard deviation. When measurements of K are made from ^{13}C spectra, most authors use a mean of the results obtained for several pairs of carbons in the molecule.

When only one pair of signals could be used to determine K, the value reported is a mean of 5 to 10 integrations using the electronic integrator and the precision is estimated from the standard deviation. If more than one pair of signals was used the value reported is a mean of the values determined for each pair. Typically the precision on $-\Delta G^{\circ}$ values ranges from .01 to .06 Kcal/mole while the uncertainty on relative conformer populations does not exceed 4%.

SYNTHESIS OF COMPOUNDS

4,5-Benzocycloheptenone(21)

A solution of 4.6 g (0.029 mol) of 4,5-benzocycloheptatrienone [22] in ethyl acetate was hydrogenated using 800 mg of palladium-on-charcoal (5%) at room temperature and a pressure of 1.7 atm during 18 hours. An oily substance (4.6 g; 98%) was obtained after evaporation of the

solvent at reduced pressure. The known compound [14b] 21 was identified by its ^1H NMR spectrum in CCl_4: δ 7.1 (4H, s), δ 2.68 (8H, AA'BB', H-2,3,6,7).

4,5-Benzocycloheptenone-2,2,7,7-d_4 (21-d_4).
A mixture of 1.6 g (0.10 mol) of 21, 4.6 g of anydrous K_2CO_3 and 47 ml of D_2O was stirred under reflux for 24 hours. After cooling, the mixture was extracted with ether and the organic fraction dried over $MgSO_4$. Evaporation of the solvent under reduced pressure yielded 1.65 g of 21-d_4 as an oil which was characterized by its ^1H NMR spectrum in $CDCl_3$; 7.2 ppm (4H, s, Ar), 2.8 ppm (4H, s, H-3,6).
Compounds 2-8 were prepared either from 21 or 21-d_4 by published methods. We report below the procedures used to prepare the deuterated derivatives of 2-7 and 8. Analytical ^1H NMR spectral data is given for each compound while the ^{13}C NMR data is summarized in Table II.

5-Hydroxy-benzocycloheptene-4,4,6,6-d_4 (7-d_4)
A solution of 0.47 g (.003 mol) of 21-d_4 in 5 ml of anhydrous diethyl ether was slowly added to a slurry of 0.3 g (.008 mol) of $LiAlH_4$ in 12 ml of anhydrous ether. The mixture was stirred at room temperature overnight. The flask was cooled in an ice-bath and 10 ml of 10% H_2SO_4 were cautiously added. The aquous layer was extracted with ether (2 x 40 ml) and the combined organic fractions were dried over $MgSO_4$. Evaporation of the solvent under reduced pressure yielded 0.48 g (100%) of a white solid. M.P.= 90°C. ^1H NMR, δ ($CDCl_3$): 7.1 ppm (4H, s, Ar), 4.0 ppm (1H, broad singlet, H-5), 2.8 ppm (4H, AB quartet, H-3,7) 1.5 ppm (1H, broad singlet, hydroxyl proton).

5-Methoxy-d_3 benzocycloheptene-4,4,6,6-d_4 (2-d_4)
A suspension of 0.5 g of NaH in 5ml of diglyme was slowly added to an ice-cooled solution of 300 mg (.002 mol) of 7-d_4 and 2 g (.014 mol) of Cd_3I in 5 ml of diglyme. The mixture was stirred at room temperature for 4 hours. The flask was again cooled in an ice bath an 10 ml of methanol were cautiously added. Water and ether were separated. The organic layer was washed with water to eliminate diglyme and dried over $MgSO_4$. The solvent was evaporated to a total volume of about 2 ml and 50 µl fractions of this solution were purified by gas chromatography on a SE-30 column (30%, 6m X 1 cm). A colorless liquid (100 mg; 30%) was obtained. ^1H NMR, δ ($CDCl_3$): 7.1 ppm (4H, s, Ar), 3.4 ppm (1H, s, H-5), 2.7 ppm (4H, AB quartet, H-3,7).

5-O-Acetyl – benzocycloheptene-4,4,6,6-d_4 (3-d_4)
A solution of 100 mg (.0006 mol) of 7-d_4, 2.4 ml of distilled pyridine and 1.2 ml of acetic anhydride was stirred at room temperature for 20 hours. HCl 3% (20 ml) was added and the mixture was extracted with ether (3 X 25 ml). The combined organic fractions were washed with a saturated solution of $NaHCO_3$ and dried over $MgSO_4$. The solvent was evaporated to a total volume of about 2 ml and 50 µl fractions of this solution were purified by gas chromatography on a SE-30 column (30%, 6 m X 1 cm) to yield 55 mg (44%) of a white solid. M.P. = 86 °C. ^1H NMR, δ ($CDCl_3$): 7.1 ppm (4H, s, Ar), 5.1 ppm (1H, s, H-5), 2.8 ppm (4H, AB quarter, H-3,7), 2.0 ppm (3H, s, $OCOCH_3$).

5-O-Trifluoroacetyl-benzocycloheptene-4,4,6,6-d_4 (4-d_4)
A solution of 300 mg (.002 mol) of 7-d_4 and 0.6 ml of trifluoro acetic anhydride was stirred at 35°C for 20 minutes and at room temperature overnight. The excess anhydride was distilled and the ester was dissolved in 1 ml of CCl_4. Fractions of 50 µl of this solution were purified by gas chromatography on a SE-30, 30% column (6 m X 1 cm) to yield 120 mg (28%) of a white solid. M.P. = 67-68° C. ^1H NMR, δ($CDCl_3$); 7.2 ppm (4H, s, Ar), 5.3 ppm (1H, s, H-5), 2.8 ppm (4H, AB quartet, H-3,7).

5-Chloro – benzocycloheptene-4,4,6,6-d_4 (6-d_4)
A solution of 1.0 g (.006 mol) of 7-d_4 in 10 ml of CCl_4 was stirred for 10 minutes and 2.0 g of dry triphenyl phosphine were added. The solution was stirred under reflux for 1 hour then cooled to room temperature and left to stand overnight. A

precipitate formed which became more abundant when 10 ml of n-pentane were added. After filtration, the solvent was evaporated and the remaining yellow oil was purified by gas chromatography. There was ample formation of an aerosol and only a small quantity of pure 6-d_4 was obtained. The melting point is close to room temperature and the product exists in both liquid and solid state, ^{1}H NMR, $\delta(CDCl_3)$: 7.0 ppm (4H, s, Ar), 4.2 ppm (1H, s, H-5), 2.6 ppm (4H, AB quartet, H-3,7).

5-Methyl-Benzocycloheptene (8)

A solution of 0.61 g (.0039 mol) of 5-exo-methylene benzocycloheptene (prepared on adaptation of the method of Bertini and coworkers [23,24]) in 25 ml of methanol was hydrogenated in 2 atms of H_2 at room temperature for 19 hours using 0.18 g of palladium (5%) over charcoal as catalyst. Evaporation of the solvent under reduced pressure yielded 0.58 g (94%) of 8 which was purified by gas chromatography on a SE-30, 30% colum (6 m X 1.0 cm). The ample formation of an aerosol accounts for the low yield (0.12 g, 20%) of the purification. The product was obtained as a colorless liquid. ^{1}H NMR, $\delta(CS_2)$: 7.1 ppm (4H, s, Ar), 2.9 ppm (4H, multiplet, H-3,7), 2.0 ppm (4H, multiplet, H-4,6), 1.1 ppm (4H, doublet + multiplet, CH_3 + H-5).

3,4-benzocycloheptenone (22). This compound was prepared from benzosuberone by a procedure already published [25]. It was identified by its ^{1}H NMR spectrum which was identical to that reported [24].

Derivatives of 3,4-benzocycloheptenone

Compound 9-13, their tetradeutero analogs, and 14 were prepared from 22 according to the same procedure as that described for the corresponding 5-substituted derivatives. Their ^{1}H and ^{13}C NMR spectra were consistent with their structure (Tables I and III).

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