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Carbon-13 Shifts in 1-Hetera-2,6-diaryl-4-cyclohexanones and a Few Corresponding 1-Hetera-4-cyclohexanols

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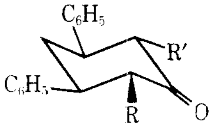
The ^{13}C NMR spectra of variously substituted 1-hetera-4-cyclohexanones and some of the corresponding heteracyclohexanols have been measured and utilized in conformational analysis. The results have been interpreted in terms of deshielding effects for α and β carbons as exerted by the heteroatom. The data indicate an α-substituent effect in the order O > NCH_3 > NH > S. A γ effect was observed for C(4) (C═O) which parallels that found for simple 1-hetera-4-cyclohexanones: S < NH < O. Reductions of the ketones gave the corresponding alcohols, and conformations are assigned to a few 1-heteracyclohexanols on the basis of ^{13}C chemical shifts also. Significantly greater $^1J_{^{13}CH}$ coupling values were observed for carbon atoms attached directly to sulfur compared to $^1J_{^{13}CH}$ values for the C(3),C(5) carbons. Heteroatoms N and O cause greater chemical shifts in the resonances of antiperiplanar carbons than the sulfur counterpart as compared with model systems. Interestingly, $^1J_{C-D}$ values for the carbon α to the C═O group or α to the hydroxyl-bearing carbon in the corresponding alcohols did not vary significantly (~20 Hz) in several cases.

Although the ^{13}C NMR spectra of a number of substituted cyclohexanones[1] and cyclohexanols[2,3] have been recorded, there has been little work published on *substituted* 1-hetera-4-cyclohexanones,[4] and we could not find a report on substituted 1-hetera-4-cyclohexanols. The purpose of the present study was to measure the ^{13}C chemical shifts and the $^1J_{^{13}C-H}$ and $^1J_{^{13}C-D}$ values in order to perform a conformational analysis on some substituted heterocyclic systems in the families cited. Assignments have been made on the basis of signal multiplicity found in the off-resonance decoupled spectra, the magnitude of the $^1J_{^{13}C-H}$ coupling (which was largest for carbon attached directly to sulfur),[5] and the known effects of deuterium substitution on ^{13}C chemical shifts.[6]



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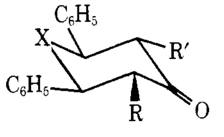
b, R = CH_3; R′ = H



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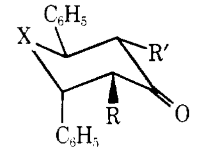
c, X = S; R = C_2H_5; R′ = H
d, X = NH; R = R′ = H
e, X = NH; R = CH_3; R′ = H
f, X = NH; R = R′ = CH_3
g, X = NH; R = C_2H_5; R′ = H
h, X = NCH_3; R = R′ = H
i, X = NCH_3; R = CH_3; R′ = H
j, X = NCH_3; R = R′ = CH_3
k, X = NCH_3; R = C_2H_5; R′ = H
l, X = O; R = R′ = H
m, X = O; R = CH_3; R′ = H
n, X = O; R = R′ = CH_3
o, X = O; R = C_2H_5; R′ = H



3a, X = S; R = R′ = H
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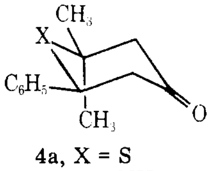
c, X = S; R = C_2H_5; R′ = H
d, X = O; R = R′ = H



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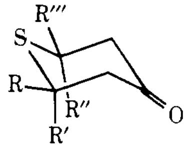

5a, R = R′ = R″ = R‴ = H
b, R = R‴ = CH_3; R′ = R″ = H
c, R′ = R‴ = CH_3; R = R″ = H
d, R = R′ = H; R″ = R‴ = CH_3
e, R = R′ = R″ = R‴ = CH_3

Results

All ^{13}C chemical shifts, shift differences, and J_{CH} values are recorded in Tables I–VI. Table I lists ^{13}C shift data for the standards 1 and 1-hetera-2,6-diaryl-4-cyclohexanones 2 as well as related systems 3–5. The chemical shifts of carbon nuclei oriented anti to a γ heteroatom have been included in Table

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Table I. ^{13}C Chemical Shifts for 1-Hetera-2,6-diaryl-4-cyclohexanones and Other Related Systems

compd[a]	X	C(2)	C(3)	C(4)	C(5)	C(6)	other
1a[b]	S	43.63	48.23	208.82	48.23	43.62	
2a	S	48.15	50.24	206.78			Ar, 139.06, 128.43, 127.61, 126.78
2b	S	55.14	51.37	208.59	52.46	48.68	CH_3, 12.04; Ar, 139.18, 138.40, 128.51, 127.69, 126.88
2c	S	53.96	59.25	208.73	52.14	49.21	$\mathbf{CH_2}CH_3$, 18.96; $CH_2\mathbf{CH_3}$, 11.96; Ar, 139.19, 138.38, 128.58, 127.78, 126.94
2d	NH	60.89	50.10	206.68			Ar, 142.60, 128.36, 127.48, 126.31
2e	NH	68.20	51.38	208.32	50.63	61.31	CH_3, 10.09; Ar, 142.55, 141.69, 128.24, 127.57, 127.04
2f	NH	68.64	51.37	210.13			CH_3, 10.39; Ar, 141.96, 128.12, 127.41
2g	NH	66.61	58.29	208.14	51.35	61.62	$\mathbf{CH_2}CH_3$, 17.84; $CH_2\mathbf{CH_3}$, 12.19; Ar, 142.57, 141.69, 128.27, 127.60, 127.46
2h	NCH_3	69.89	50.48	205.81			NCH_3, 40.53; Ar, 142.84, 128.45, 127.23, 127.03
2i	NCH_3	77.18	50.88	207.48	50.63	70.41	NCH_3, 41.05; CH_3, 11.00; Ar, 143.10, 142.05, 128.48, 128.30, 127.67, 127.34, 127.28, 126.70
2j	NCH_3	77.56	50.62	209.16			NCH_3, 41.29; CH_3, 11.12; Ar, 142.23, 128.22, 127.55, 127.25
2k	NCH_3	75.48	57.69	207.23	51.24	70.65	NCH_3, 41.03; $\mathbf{CH_2}CH_3$, 18.55; $CH_2\mathbf{CH_3}$, 12.05; Ar, 143.21, 142.05, 128.50, 128.30, 127.83, 126.70
2l[c]	O	78.64	49.46	205.20			A 140.59, 128.08, 128.01, 125.37
2m	O	85.97	51.65	207.09	50.16	79.39	CH_3, 9.48; Ar, 140.62, 139.55, 128.34, 127.78, 126.99, 125.44
2n	O	86.35	51.77	208.25 201.22			CH_3, 14.84, 9.80; Ar, 139.59, 138.51, 136.59, 135.68, 129.29, 128.91, 128.1, 126.87
2o	O	84.62	58.33	206.80	50.86	79.57	$\mathbf{CH_2}CH_3$, 17.36; $CH_2\mathbf{CH_3}$, 11.96; Ar, 140.64, 139.54, 128.72, 128.36, 127.78, 127.19, 125.45
3a	S	43.78	48.41	207.75			Ar, 140.11, 128.39, 127.31, 127.19
3b	S	51.04	49.81	209.87	49.81	43.77	CH_3, 13.55; Ar, 139.50, 139.36, 128.39, 128.33, 127.87, 127.52, 127.17
3c	S	53.96	59.25	209.55	52.14	49.21	$\mathbf{CH_2}CH_3$, 19.67; $CH_2\mathbf{CH_3}$, 11.80; Ar, 139.69, 139.25, 128.37, 128.28, 127.47, 127.15, 126.94
3d	O	73.27	46.19	205.87			Ar, 139.66, 128.37, 127.79, 126.45
4a	S	45.52	56.70	207.67	49.78	44.68	CH_{3e}, 30.51; CH_{3a}, 28.41; Ar, 139.01, 128.33, 127.46, 126.93
4b	NH	53.58	53.92	208.32	49.55	55.76	CH_{3e}, 31.95; CH_{3a}, 28.10; Ar, 142.82, 128.25, 127.31, 126.31
4c	NCH_3	57.77	55.35	207.06	50.47	64.56	NCH_3, 33.90; CH_{3e}, 30.81; CH_{3a}, 15.60; Ar, 143.56, 128.45, 127.42, 126.96
5a[d]	S	29.83	43.83	207.07			
5b[e]	S	38.44	51.27	207.67			CH_3, 21.43
5c[e]	S	35.58	50.63	207.90			CH_3, 21.08
5d	S	45.67	57.86	208.25	42.37	29.28	CH_{3e}, 29.28; CH_{3a}, 26.34
5e	S	46.40	55.80	208.86			CH_3, 32.29

[a] All data are given in ppm downfield from Me_4Si; solutions used were 1.5 M in $DCCl_3$. Standards for comparison were the following: cyclohexanone,[4] 41.90 [C(2)], 27.1 [C(3)], 25.0 [C(4)], 211.5 [C(1)] ppm; 1-methyl-4-piperidone,[4] 55.3 [C(2)], 41.0 [C(3)], 207.1 [C(4)] ppm; tetrahydropyran-4-one,[4] 67.7 [C(2)], 42.8 [C(3)], 206.2 [C(4)] ppm. [b] C(4), 40.68 ppm. [c] Examined as a cis,trans mixture. [d] Reference 4: 30.00 [C(2)], 208.00 [C(4)] ppm. [e] Examined as a cis,trans mixture.

II. Chemical shift differences and J_{CH} values for ring carbons in the heteracyclohexanones and heteracyclohexanols have been tabulated, using the nonsubstituted parent compounds as standards (Tables III and IV). Recorded in Table V are the ^{13}C chemical shifts for many of the corresponding alcohols. Coupling constants $^1J_{^{13}C-H}$ and $^1J_{^{13}C-D}$ of selected heterocyclic compounds are found in Table VI.

Discussion

1-Hetera-4-cyclohexanones. In analyzing the results, it is useful to compare chemical shifts of carbons in certain heterocycles with a standard, which we selected to be *cis*-3,5-diphenylcyclohexanone (**1a**). The chemical shift in the 1-hetera-2,6-diaryl-4-cyclohexanones should give information about the electrostatic effect in the system due to the heteroatom. Moreover, introduction of the heteroatom in either

Table II. Shielding Effects of Heteroatoms Anti to Carbon

heteroatom	compd	$\delta(^{13}C)$ for C(2) methyl[b]	γ effect (shift difference)[a]
	1a	13.94	0.00
S	**2b**	12.04	−1.90
NH	**2e**	10.09	−3.85
NH	**2f**	10.39	−3.55
NCH_3	**2i**	11.00	−2.94
NCH_3	**2j**	11.12	−2.82
O	**2m**	9.48	−4.48
O	**2n**	9.80	−4.14

[a] *r*-2-Methyl-*trans*-3,*trans*-5-diphenylcyclohexanone[10] (**1b**) is the reference system [$\delta(^{13}C$ ref)] in the present investigation. ^{13}C shifts for **1b:** 13.94 (CH_3), 50.27 [C(2)], 56.84 [C(3)], 43.50 [C(4)], 46.72 [C(5)], 50.27 [C(6)], 209.15 [C(1)] ppm. [b] In ppm from Me_4Si.

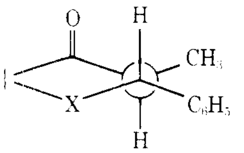
Table III. Methyl ^{13}C Chemical Shift Parameters[a] (ppm) for 1-Hetera-2,6-diarylcyclohexanones and Selected Heterocyclohexanols

compd	C(2)	C(3)	C(4)	C(5)	C(6)
2b	+6.99	+1.13	+1.81	+2.22	+0.53
2e	+7.31	+1.28	+1.64	+0.53	+0.42
2f	+7.75	+1.27	+3.45		
2i	+7.29	+0.40	+1.67	+0.15	+0.52
2j	+7.67	+0.14	+3.35		
2m	+7.33	+2.19	+1.89	+0.70	+0.75
2n	+7.71	+2.31	+3.05		
8b	+6.13	+2.15	+4.96	+0.69	−0.62
8e	+7.08	+0.54	+5.33	−0.46	+0.05
8f	+6.93	−0.32	+10.60		
10b	+5.67	+1.45	+5.01	+1.45	−0.52
10e	+6.28	+0.36	+4.56	−0.94	−0.35
10f	+5.95	−0.33	+9.51		

[a] Shift differences between methyl-substituted heterocycles and model compounds from which the above shifts were calculated. The systems (model compounds) are **2b (2a), 2e (2d), 2f (2e), 2i (2h), 2j (2h), 2m (2l), 2n (2l), 8b (8a), 8e (8d), 8f (8d), 10b (10a), 10e (10d),** and **10f (10d).** A + sign indicates a downfield shift, and a − sign indicates an upfield shift.

ketone **2** or **3** changes the electron density at C(2),C(6), and this is reflected in the downfield shift of these α carbons compared with the shift for C(3),C(5) in **1a** as shown in Table I. Examination of the data reveals an α-substituent effect in the order O > NCH$_3$ > NH > S as was noted very recently by Hirsch and Havinga[4] in a few simple cases. The heteroatom also causes an upfield shift in the carbonyl resonance (relative to the comparable signal in **1a**). As suggested by Jones and Hassan[7] and Dutch[8] for simple systems, the upfield γ shift in our 1-hetera-2,6-diaryl-4-cyclohexanones probably arises from a field effect. Eliel and co-workers have proposed a hyperconjugative-type interaction of an electron pair on a heteroatom through the C_α–C_β bond (in certain heteracyclohexanes), consequently affecting the shift of the γ-antiperiplanar carbon atom.[9]

Inspection of the data in Table II reveals that heteroatoms N and O cause significant upfield shifts of methyl carbons in 1-hetera-2,6-diaryl-3-methyl-4-cyclohexanones [compared to the signals for the methyl carbon in *r*-2-methyl-*trans*-3,5-diphenylcyclohexanone (**1b**)], which substantiates the observation here (as found in other heterocyclic and cyclohexyl systems)[9] that heteroatoms significantly alter the chemical shift of anti carbon nuclei. The carbonyl carbon atoms in ketones **3a–c** and **3d** experience a downfield shift of ~1 ppm relative to carbonyl carbon shift in the all-equatorial isomers **2a–c** and **2l**, respectively. Recent X-ray data[10] have indicated that one ortho hydrogen atom in the axial phenyl group was in close proximity to the carbonyl carbon in crystalline **3b** and **3c**. Thus, the downfield shift presumably is due to the deshielding effect of the aromatic ring.



The effect of methyl substitution on the methyl-bearing carbon resonance has been recognized in methylcyclohexanes[11] and certain piperidine derivatives.[7] A downfield shift of 1.13 ppm (Table III) is observed in **2b** for C(3) on which an equatorial methyl group resides. No significant downfield ^{13}C shift is found for **2i** or **2j** for the methylated carbons C(3) or C(5). A downfield shift of 2.31 ppm (due to methyl substitution) is observed for C(3) and C(5) in **2n** compared to the corresponding signals found for C(3),C(5) in **2l.** However, a downfield shift of 3–4 ppm has been detected for the methyl-substituted carbon in some cyclohexanones[11] and piperidones.[7] An appreciable deshielding effect (7–9 ppm) is noted for C(3) in **2c, 2g,** and **2k,** apparently due to the ethyl group (as compared to the same resonances in **2a, 2d,** and **2h,** respectively).

Table IV. Phenyl ^{13}C Chemical Shift Parameters[a] (ppm) for 1-Hetera-2,6-diaryl-4-cyclohexanones and Related Systems

compd	C(2)	C(3)	C(4)
1a	+16.53	+6.33	−2.68
2a	+18.32	+6.41	−0.69
2h	+14.59	+9.48	−1.29
2l	+10.94	+6.66	−1.00

[a] Shift differences between phenyl-substituted compounds and standard compounds from which the above shifts were calculated. The standards selected are given in parentheses following the compound: **1a** (cyclohexanone);[4] **2a (5a); 2h** (1-methyl-4-piperidone);[4] **2l** (4-thianone).[4] A + sign indicates a downfield shift, and a − sign indicates an upfield shift from the standard.

The carbonyl carbon [C(4)] resonances in **2b, 2e, 2i,** and **2m** are shifted downfield by ~1.5 ppm compared to the C(4) signals in **2a, 2d, 2h,** and **2l.** Interestingly, this deshielding effect for C(4) in **2b, 2e, 2i,** and **2m** is close in value to that found for C(1) in 2-methylcyclohexanone, which was deshielded 1.5 ppm compared to the C(1) signal in cyclohexanone.[1] The effect of alkyl substituents on the C(4) resonance appears to be roughly additive. For example, in comparing **2d** with **2e** and **2f,** a difference is noted for the C(4) resonances that amounts to 1.64 and 3.45 ppm, respectively. With the NCH$_3$ analogues, comparing **2h** with **2i** and **2j** gives shift differences of 1.67 and 3.55 ppm, respectively, for C(4) (Table III). An interesting situation is found in comparing **5a** with **5b** and **5d,** which shows shift differences of 8.61 and 15.84 ppm, respectively, *for C(2).*

Introduction of a methyl group at C(3) causes a large β effect (~6–7 ppm compared to the nonmethylated compounds) at C(2) in all methyl-substituted heterocycles reported in the particular heterocyclics studied. For example, a downfield shift of 7.29 ppm is detected for C(2) in **2i** compared to the corresponding resonance for C(2) in **2h.** In comparison, methyl groups added at the 2,6 positions in **5b** also result in a downfield shift at C(2) and C(6) of approximately 8 ppm relative to that found in **5a.** However, the C(2) and C(6) signals are deshielded in trans isomer **5c** only by 5.75 ppm compared to that in **5a.** Carbon-2 in *trans*-**5c** is *shielded* by −2.86 ppm compared to C(2) in *cis*-**5b.** This is ascribed to a 1,3-type interaction or steric effect of the axial methyl in **5c.**

The same trend is found in *trans*-2,6-diphenyl-4-thianone (**3a**). A large downfield shift of 13.95 ppm is found for C(2) in **3a** (due to the phenyl groups) compared to C(2) in **5a.** The presence of the axial phenyl in **3a** causes an *upfield* shift (Table IV) of 4.37 ppm at C(2),C(6) relative to C(2),C(6) in **2a.** In general, cis phenyl groups at C(2),C(6) in the heteracyclohexanones cause a *deshielding effect* of the C(2) compared to the C(2) of the unsubstituted standard 1-hetera-4-cyclohexanones (see Table IV). To illustrate, a downfield shift of 18.32 ppm is observed for C(2),C(6) in **2a** compared to the corresponding resonances for C(2),C(6) in **5a.** This effect of phenyl substitution at C(2),C(6) appears to decrease as the *electronegativity of the heteroatom increases.* Phenyl groups at the 2,6 positions in **2a** also result in a downfield shift at C(3) and C(5) of approximately 6 ppm relative to that found in **5a.** Note the similarity in shift for C(2) in **3a** (43.78 ppm) to that for C(3),C(5) in **2a** (43.63 ppm). Obviously, the deshielding effect of the heteroatom in **3a** is offset by the shielding effect

Table V. One-Bond Coupling Constants $^1J_{^{13}C-H}$ and One-Bond Carbon-Deuterium Coupling Constants $^1J_{^{13}C-D}$ of Selected Compounds[a]

compd	$^1J_{^{13}C-H}$ (carbon), Hz	$^1J_{^{13}C-D}$ (carbon), Hz
14a	141.00 (2,6)	20.00 (3,5)
14b	141.90 (2,6)	19.60 (3,5)
14c	142.70 (2) 142.66 (6)	
14d	142.50 (6)	19.95 (5)
15a	139.00 (2,6)	18.00 (3,5)
15b	139.70 (2,6)	19.50 (3,5)
15c	139.77 (2) 139.03 (6)	20.00
15d	139.55 (6)	20.00 (3,5)
16b	142.83 (2,6)	20.00 (3,5)
16c	142.42 (2) 142.51 (6)	
16d	139.63 (6)	20.00 (3,5)

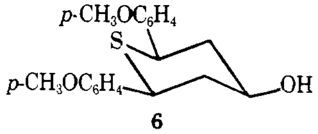
[a] $^1J_{^{13}C-H}$ for 3,5 carbons in the corresponding nondeuteriated compounds are (in Hz) the following: **5a** (126.20), **2a** (125.80), **2b** (127.10), **4a** (126.40), **13a** (126.30), **8a** (128.00), **8b** (127.00), **9a** (125.50), **10a** (126.4), **10b** (126.10), and **11a** (125.20).

of the axial phenyl group at C(2). From examination of the spectra of 2,2-dimethyl- (**5d**) and 2,2,6,6-tetramethyl-4-thianone (**5e**), it is clear that the gem dimethyl group causes a downfield shift (average 16 ppm) at C(2) and C(6) carbons relative to C(2),C(6) in **5a**.

The shielding effects of methyl groups are also reflected in the nitrogen family. This is seen, for example, in the *N*-methyl group, which normally appeared at 41 ppm in all of the 1-aza-2,6-diaryl-4-cyclohexanones. However, the ^{1}H signal for the *N*-methyl group in **4c** is shifted upfield by 7 ppm. Such steric effects on ^{13}C shifts have been reported for 1,2-dimethyl- and 1,2,5-trimethyl-4-piperidone[7] and in methylcyclohexanes.[11]

To simplify the assignment of the carbon signals in the present investigation, we examined the ^{13}C NMR spectra of some deuterioheterocyclohexanones and derivatives thereof and observed upfield isotope-induced shifts (~0.5 ppm) of the ^{13}C signals for the α carbons as well as the long range ^{13}C–D coupling (Table V). Similar isotope-induced upfield shifts for the α carbons and the long range ^{13}C–D coupling have been reported[6] for long chain aliphatic compounds. In our systems, the signals for the α positions were a triplet and quintet for the tertiary and secondary deuteriated carbons, respectively, with $J_{^{13}C-D}$ of about 20 Hz. In most cases the carbon–deuterium multiplets were very weak, and in some instances no signals were observed for secondary deuterio carbons, presumably due to increased T_1[12,13] values and decreased Overhauser effects.

1-Hetera-4-cyclohexanols. A few 1-hetera-2,6-diaryl-4-cyclohexanols, 6–13 (and certain related deuterated systems, 14–16), were prepared and may be biased at least to some degree (Table VI). The carbinyl carbon shielding depended largely upon the conformation of the hydroxyl group; an axial hydroxyl group shielded the hydroxyl-bearing carbon by about 5 ppm. The C(2),C(6) and C(3),C(5) carbons were also shielded by ~5 and 3 ppm, respectively, in the axial isomer. Such chemical shift differences for epimeric alicyclic alcohols have been clearly established.[3a] Proton NMR studies on related piperidinols showed the phenyl groups to be equatorial at C(2),C(6) in this nitrogen system.[3b]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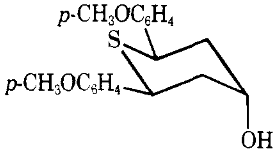
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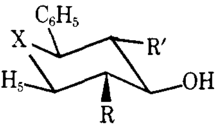
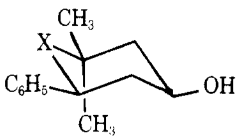
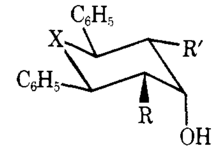


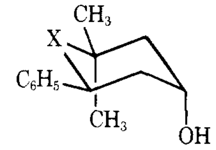
8a, X = S; R = R′ = H
b, X = S; R = CH_3; R′ = H
c, X = S; R = C_2H_5; R′ = H
d, X = NCH_3; R = R′ = H
e, X = NCH_3; R′ = H; R = CH_3
f, X = NCH_3; R = R′ = CH_3
g, X = NCH_3; R = C_2H_5; R′ = H



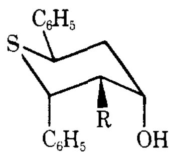
9a, X = S
b, X = NCH_3



10a, X = S; R = R′ = H
b, X = S; R = CH_3; R′ = H
c, X = S; R = C_2H_5; R′ = H
d, X = NCH_3; R = R′ = H
e, X = NCH_3; R = CH_3; R′ = H
f, X = NCH_3; R = R′ = CH_3
g, X = NCH_3; R = C_2H_5; R′ = H



11a, X = S
b, X = NCH_3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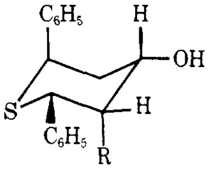
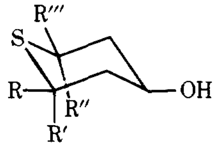
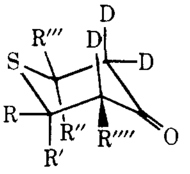

12′

a, R = H
b, R = CH_3
c, R = C_2H_5



13a, R = R′ = R″ = R‴ = H
b, R = R′ = R″ = R‴ = CH_3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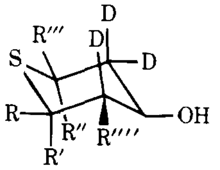
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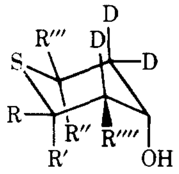

16

a, R = R′ = R″ = R‴ = H; R⁗ = D
b, R = R‴ = C_6H_5; R′ = R″ = H; R⁗ = D
c, R = R‴ = C_6H_5; R′ = R″ = H; R⁗ = CH_3
d, R = C_6H_5; R′ = H; R″ = R‴ = CH_3; R⁗ = D

The ^{13}C chemical shifts of the carbinyl carbons in **9a**, **11a**, **9b**, and **11b** are similar. The upfield shift of the carbon bearing the equatorial hydroxyl group in **9a** and **9b** relative to that shift in **8a** and **8d** is probably a consequence of the steric interaction of the axial methyl group (see Table II). On this basis,[3] one would expect a greater upfield shift of the carbinyl carbon for **11a** and **11b** relative to that found in **10a** and **10d.** However, the ^{13}C chemical shift (67.78 ppm) of C(4) in the equatorial isomer **9a** is not much lower than the chemical shift (67.58 ppm) for C(4) in the axial isomer **11a**. It is suprising to note that the ^{13}C chemical shift (65.98 ppm) for C(4) in the axial isomer **11b** was slightly greater than the chemical shift (65.48 ppm) for C(4) in the equatorial isomer **9b.** This would

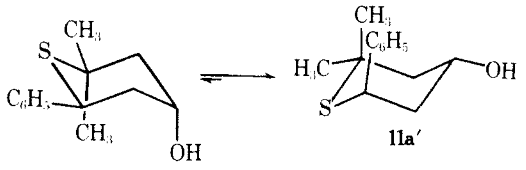
Table VI. Chemical Shifts of Carbons of Some 1-Hetera-2,6-diarylcyclohexanols and Related Systems[a,b]

compd	X	C(2)	C(3)	C(4)	C(5)	C(6)	other
6	S	46.51	55.15	71.37			O–CH_3, 43.65; Ar, 158.77, 132.68, 128.43, 113.89
7	S	41.17	55.11	66.75			O–CH_3, 40.47; Ar, 158.56, 133.55, 128.43, 113.80
8a	S	47.22	43.43	71.19			Ar, 140.40, 128.42, 127.36, 127.23
8b	S	53.35	45.58	76.15	44.12	46.60	CH_3, 15.13; Ar, 140.35, 139.24, 128.36, 127.93, 127.11
8c	S	50.01	50.33	72.17	46.57	44.52	$\mathbf{C}H_2CH_3$, 20.03; $CH_2\mathbf{C}H_3$, 9.01; Ar, 140.32, 139.01, 128.34, 127.98, 127.11
8d	NCH_3	68.61	45.28	68.41			NCH_3, 41.15; Ar, 144.49, 128.25, 127.03, 126.79
8e	NCH_3	75.69	45.82	73.74	44.82	68.66	NCH_3, 41.75; CH_3, 14.89; Ar, 144.62, 142.94, 128.61, 127.06, 126.88
8f	NCH_3	75.54	44.96	79.01			NCH_3, 42.14; CH_3, 15.11; Ar, 143.88, 127.94, 127.45, 126.63
8g	NCH_3	72.13	50.54	70.12	44.96	68.50	NCH_3, 41.66; $\mathbf{C}H_2CH_3$, 19.98; $CH_2\mathbf{C}H_3$, 9.42; Ar, 144.58, 142.78, 128.21, 128.04, 126.99
9a	S	43.66	49.76	67.78	43.92	43.54	CH_{3e}, 31.41; CH_{3a}, 28.38; Ar, 140.49, 128.28, 127.26, 127.17
9b	NCH_3	55.20	49.17	65.48	45.67	63.49	NCH_3, 34.28; CH_{3e}, 31.16; CH_{3a}, 15.86; Ar, 144.64, 128.18, 127.31, 126.73
10a	S	41.85	40.30	66.58			Ar, 141.25, 128.31, 127.34, 127.14
10b	S	47.52	41.75	71.59	41.75	42.37	CH_3, 15.13; Ar, 140.93, 140.00, 128.25, 127.93, 127.37, 127.08
10c	S	47.12	47.90	66.59	42.25	41.53	$\mathbf{C}H_2CH_3$, 21.84; $CH_2\mathbf{C}H_3$, 11.33; Ar, 140.96, 140.06, 128.25, 128.02, 127.37, 127.05
10d	NCH_3	63.76	42.92	64.89			NCH_3, 41.73; Ar, 145.15, 128.22, 127.20, 126.62
10e	NCH_3	70.04	43.28	69.45	41.98	63.41	NCH_3, 41.82; CH_3, 15.79; Ar, 145.35, 143.57, 128.19, 127.96, 127.14, 126.58
10f	NCH_3	69.68	42.59	74.40			NCH_3, 41.92; CH_3, 15.86; Ar, 143.88, 127.94, 127.66, 126.63
10g	NCH_3	69.54	48.15	64.77	43.26	63.32	NCH_3, 41.90; $\mathbf{C}H_2CH_3$, 21.18; $CH_2\mathbf{C}H_3$, 11.20; Ar, 145.49, 143.68, 128.18, 127.95, 127.11
11a	S	41.79	45.90	67.58	40.68	38.38	CH_{3e}, 32.58; CH_{3a}, 30.85; Ar, 141.55, 128.24, 127.43, 126.93
11b	NCH_3	53.65	45.87	65.98	43.27	58.93	NCH_3, 34.80; CH_{3e}, 31.97; CH_{3a}, 18.23; Ar, 145.22, 128.15, 127.89, 126.58
12a	S	43.83	40.28	66.32	43.67	43.22	Ar, 140.93, 140.76, 128.39, 128.13, 127.31, 126.40
12b	S	42.22	48.32	69.17	33.77	41.84	CH_3, 6.70; Ar, 140.58, 140.18, 128.21, 127.96, 127.60, 127.35, 127.03, 126.79, 126.36
12c	S	39.80	47.79	69.17	38.37	39.80	$\mathbf{C}H_2CH_3$, 20.50; $CH_2\mathbf{C}H_3$, 13.42; Ar, 141.55, 140.87, 128.54, 128.18, 127.90, 127.48, 127.08, 126.97, 126.74, 126.56
13a	S	26.48	36.07	68.49			
13b	S	43.72	50.37	65.48			CH_{3e}, 33.30; CH_{3a}, 31.35

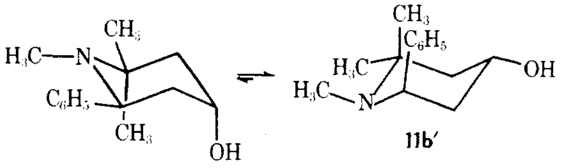
[a] Given in parts per million downfield from Me_4Si; data were obtained using 0.3 M solutions in $DCCl_3$. [b] Cyclohexanol (present study): 35.53 [C(2)], 24.39 [C(3)], 25.67 [C(4)], 69.97 [C(1)] ppm; these values were obtained on a solution in $DCCl_3$.

lead to the conclusion that the contribution to the equilibrium by conformations **11a** and **11b** with an axial hydroxyl group is small and that the compounds largely exist in the alternate chair conformations **11a′** and **11b′**. However, this does not seem entirely resonable. The syn diaxial CH_3–C_6H_5 interaction in **11a′** and **11b′** should be severe enough to make the chair conformation highly strained. Consequently, it is not unreasonable to suppose that **11a** and **11b** may favor a nonchair conformation. Conceivably, the system may exist in twist conformations or as deformed chairs in which the nonbonded steric interactions have been relieved to a large extent.

It is noteworthy that the additivity of the alkyl group (as observed with the ketones) is detected in the alcohols. Comparing **8d** with **8e** and **8f**, shift differences of 5.33 and 10.60 ppm for C(4) are found in Table III. Similarly, differences of



11a **11a′**



11b **11b′**

4.56 and 9.51 ppm are noted when **10d** is compared with **10e** and **10f**.

Preliminary evidence[14] indicates that in the reduction of **3b** with $LiAlH_4$ an equatorial alcohol was formed, but of structure **12′** rather than **12**. Hence, it appears that hydride transfer from lithium aluminum hydride[10] probably occurs from the least hindered equatorial side to give an *axial alcohol* which undergoes ring reversal to give **12′**. Further extrapolation to the other alcohols in this family does not seem warranted at this time, but work is continuing in this complex area.

In summary, ^{13}C NMR analysis of several substituted 1-hetera-4-cyclohexanones indicates that the order of deshielding for the α carbon decreases but parallels the order of decreasing electronegativity of the heteroatom. That is, the order is O > N > S. In 1-hetera-*cis*-2,6-diphenyl-4-cyclohexanones, the ^{13}C NMR resonance for C(2) is more deshielded than in the trans isomer, which presumably is a rapidly inverting ring system so that the C(2) signal is an average of signals for C(2) and C(6) in the sulfur (**2a** and **3a**) and oxygen (**2l** and **3d**) analogues. In the cis isomers **2a** (S), **2d** (NH), and **2l** (O), the C(4) resonances *increase* in shielding in the order S (206.78 ppm) < NH (206.68 ppm) < O (205.20 ppm). A similar trend is observed in the methyl-substituted [methyl at C(3)] compounds **2b** (S), **2e** (NH), and **2m** (O) (208.59 vs. 208.32 vs. 207.09 ppm). Likewise, the situation is similar in the ethyl-substituted compounds **2c** (S, 208.73 ppm), **2g** (NH, 208.14 ppm), and **2o** (O, 206.80 ppm). Thus, although steric interactions may increase slightly between C=O and equatorial R [at C(3)] as R changes from H to CH_3 to C_2H_5 with resulting changes in the ^{13}C signals for C(4), the order for $\delta_{^{13}C}$ remains S > N > O in the systems studied. This seems to argue for comparable geometry in all three systems.

A "γ effect" for C(4) [C=O] resonances parallels that found for simple 1-hetera-4-cyclohexanones.[4] Namely, C(4) in an antiperiplanar arrangement with respect to the heteroatom is shifted upfield the largest extent in the oxygen systems. For example, the order of *increasing* upfield shift for C(4) in the two series studies is **2a** (S, 206.78 ppm) < **2d** (NH, 206.28 ppm) < **2l** (O, 205.20 ppm) and **2b** (S, 208.59 ppm) < **2e** (NH, 208.32 ppm) < **2m** (O, 207.09 ppm). All of these shifts are comparable to the model systems **1a** (X = CH_2; R = R′ = H) and **1b′** (X = CH_2; R = CH_3; R′ = H). This order of shielding has recently been observed also in heteracyclohexanes and related molecules.[9]

In the few 4-thianols obtained, the ^{13}C NMR resonance found for C(4) (C-OH) was dehielded the largest extent (71.19 ppm) in the all-equatorial isomer *cis*-2,6-diphenylthian-*r*-4-ol (**8a**). This shielding, compared to the value of 66.58 ppm found for the isomer **10a** with an axial hydroxyl group, is certainly of diagnostic importance for stereochemical assignment. Interestingly, the ^{13}C resonance for C(4) in *cis*-2,*trans*-6-diphenylthian-*r*-4-ol (**12a**) was detected at 66.32 ppm. Such increased shielding may result from an anisotropic effect on C(4) by the phenyl group (axial) at C(2). However, the alcohols of this family will require further examination with many other members before any definitive assignments can be made.

Experimental Section

Proton noise-decoupled ^{13}C NMR spectra were recorded at 25.2 MHz on a Varian XL-100(15) NMR spectrometer equipped with a Nicolet TT-100 Fourier transform accessory. Chemical shift data encompassing a 6000-Hz spectral region were collected into 8K data points. Single-frequency, off-resonance spectra were obtained by irradiating with a continuous wave frequency at about δ −5 compared to Me_4Si in the proton spectrum. The samples were run as 0.3 and 1.5 M solutions in $DCCl_3$ containing tetramethylsilane as an internal reference. The spectra of all samples were recorded at 37 °C.

The preparation of the compounds **2b, 2c, 3b, 3c, 6, 7, 8b, 8c, 9a, 10b, 10c, 11a, 12b, 12c, 14a–d, 15a–d,** and **16b–d** will be reported elsewhere.[10] Nitrogen heterocycles **2d–k, 4b, 4c, 8d–g, 9b, 10d–g,** and **11b** were synthesized by previously described methods.[15] All other samples were prepared as indicated: 4-thianone[16] (**5a**); 4-thianol[17] (**13a**); *cis*-2,6-di-*p*-anisyl-4-thianone[19] (precursor of **6** and **7**); *cis*-2,6-diphenylthian-*r*-4-ol[18] (**8a**); *trans*-2,6-diphenylthian-*r*-4-ol[18] (**10a**); *cis*-2,*trans*-6-diphenylthian-*r*-4-ol[18] (**12a**); 2,2-dimethyl-4-thianone[20] (**5d**); 2,2,6,6-tetramethyl-4-thianone[17] (**5e**); *cis*-2,6,-*trans*-2,6-tetramethylthian-*r*-4-ol[17] (**13b**); 2,2-dimethyl-6-phenyl-4-thianone[21] (**4a**); *cis*-2,6-diphenyltetrahydropyran-4-one (**2l**);[22] *trans*-2,6-diphenyltetrahydropyran-4-one[22] (**3d**); *r*-2,*cis*-6-diphenyl-*trans*-3-methyltetrahydropyran-4-one (**2m**);[22] *r*-2,*cis*-6-diphenyl-3,5-dimethyltetrahydropyran-4-one (**2n**);[23] *r*-2,*cis*-6-diphenyl-*trans*-3-ethyltetrahydropyran-4-one[14] (**2o**); *cis*- (**5b**) and *trans*-2,6-dimethyl-4-thianone (**5c**);[24] and *cis*-3,5-diphenylcyclohexanone (**1a**).[25]

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Registry No.—**1a,** 21152-23-8; **1b,** 68226-26-6; **2a,** 18456-44-5; **2b,** 68226-04-0; **2c,** 68226-05-1; **2d,** 54750-61-7; **2e,** 54716-97-1; **2f,** 18699-96-2; **2g,** 68226-06-2; **2h,** 39653-65-1; **2i,** 60598-63-2; **2j,** 18700-01-1; **2k,** 68226-07-3; **2l,** 18458-71-4; **2m,** 68226-08-4; **2n,** 68226-09-5; **2o,** 68226-10-8; **3a,** 18456-45-6; **3b,** 68296-29-7; **3c,** 68296-30-0; **3d,** 18458-72-5; **4a,** 68226-11-9; **4b,** 24522-15-4; **4c,** 19340-13-7; **5a,** 1072-72-6; **5b,** 68226-12-0; **5c,** 68226-13-1; **5d,** 2323-13-9; **5e,** 22842-41-7; **6,** 68296-34-4; **7,** 68296-35-5; **8a,** 18456-47-8; **8b,** 68226-14-2; **8c,** 68226-23-3; **8d,** 68296-36-6; **8e,** 43051-67-8; **8f,** 43051-69-0; **8g,** 42180-04-1; **9a,** 68226-24-4; **9b,** 24557-56-0; **10a,** 18456-46-7; **10b,** 68296-31-1; **10c,** 68296-37-7; **10d,** 68296-38-8; **10e,** 43051-66-7; **10f,** 43051-68-9; **10g,** 43051-56-5; **11a,** 68226-25-5; **11b,** 24578-00-5; **12a,** 18456-50-3; **12b,** 68296-39-9; **12c,** 68296-40-2; **13a,** 29683-23-6; **13b,** 20931-54-8; **14a,** 22842-37-1; **14b,** 68226-15-3; **14c,** 68226-16-4; **14d,** 68226-17-5; **15a,** 68226-18-6; **15b,** 68226-19-7; **15c,** 68226-20-0; **15d,** 68226-21-1; **16b,** 68296-32-2; **16c,** 68296-33-3; **16d,** 68226-22-2.

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Preparation and Stereochemistry of Some Substituted 4-Thianones and 4-Thianols. Single-Crystal Analysis of *r*-2,*trans*-6-Diphenyl-*cis*-3-methyl-4-thianone and *r*-2,*trans*-6-Diphenyl-*cis*-3-ethyl-4-thianone

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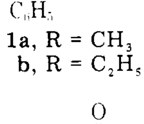
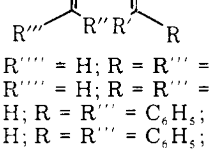
A number of substituted 4-thianones and 4-thianols have been prepared. Methods of formation, IR, ^{1}H NMR, and ^{13}C NMR analysis indicated the conformation of the heterocyclic ring in the cases studied to be predominantly of the chair form. The structures of *r*-2,*trans*-6-diphenyl-*cis*-3-methyl- and *r*-2,*trans*-6-diphenyl-*cis*-3-ethyl-4-thianone were determined by single-crystal X-ray diffraction studies. The space group for the two compounds is *Iba*2, with unit cell dimensions of a = 39.389, b = 10.5224, and c = 7.1062 Å for the methyl derivative and a = 39.414, b = 10.8315, and c = 7.3941 Å for the ethyl derivative. The structures were solved from diffractometer data and refined to $R-$ values of 0.060 and 0.058, respectively.

Simple six-membered sulfur heterocyclics are known to exist mostly in the chair conformation.[1-8] In contrast, a few six-membered nitrogen heterocyclics with a preferred boat conformation are recorded. For example, pseudotropine,[9] phenyl 3α-phenyl-3β-tropanyl ketone,[10] and 1,2,2,6,6-pentamethyl-4-phenyl-4-piperidinol[11] have been reported to exist in the boat form. In connection with a study on ^{13}C NMR spectra of some substituted thiane derivatives, we had an occasion to prepare a number of substituted 4-thianones and 4-thianols and certain derivatives thereof. We now report the methods of preparation and present evidence for the configuration and conformation of the saturated sulfur heterocycles. The first single-crystal analysis of a substituted 4-thianone is also recorded.



1a, R = CH_3
b, R = C_2H_5



2a, R′ = R″ = R'''' = H; R = R''' = C_6H_5
b, R′ = R″ = R'''' = H; R = R''' = $C_6H_4OCH_3$-*p*
c, R′ = R″ = H; R = R''' = C_6H_5; R'''' = CH_3
d, R′ = R″ = H; R = R''' = C_6H_5; R'''' = C_2H_5
e, R = C_6H_5; R′ = H; R″ = R''' = CH_3; R'''' = H

Results and Discussion

The preparation of 2,6-diphenyl-4-thianone was first reported by Arndt and co-workers.[12] The reaction of dibenzalacetone with H_2S in the presence of sodium acetate leads to the formation of both *cis*- and *trans*-2,6-diphenyl-4-thianone. Although this method gives good yields, it is limited by the number of appropriate precursors available, such as **1** and **2**. In the present investigation, the unsymmetrical distyryl ketones **2c** and **2d** were prepared by the condensation of monobenzilidine derivatives **1a** and **1b** with benzaldehyde in the presence of aqueous sodium hydroxide under controlled conditions. Incidentally, the reaction of benzaldehyde and methyl ethyl ketone with concentrated hydrochloric acid has been reported by Metayer[13] to furnish **2d** as a side product.

$$\mathbf{1a}\ (\text{or } \mathbf{1b}) \xrightarrow[2.\ C_6H_5CHO]{1.\ NaOH/H_2O} \mathbf{2c}\ (\text{or } \mathbf{2d})$$

In our hands, reaction of unsymmetrical 1,4-pentadien-3-one (**2c**) with H_2S in the presence of sodium acetate or Triton B led to the formation of both *r*-2,*cis*-6-diphenyl-*trans*-3-methyl-4-thianone (**3c**) and *r*-2,*trans*-6-diphenyl-*cis*-3-methyl-4-thianone (**4b**), but under different *conditions*. Higher ratio of base/dienone concentration, lower temperature, and shorter reaction time favored the formation of thermodynamically less stable **4b.** If the concentration of the sodium acetate was *decreased* and the temperature of the reaction and the heating time were both increased, the **3c** predominated. The syntheses for **3a–e** and **4a–c** were similar, and details are in the Experimental Section.

Stereochemistry of the 4-Thianones. If the chair conformation is assumed for the heterocyclic ring, the two aryl groups and the methyl group in **3c** or the ethyl group in **3d**

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