^{13}C Nuclear Magnetic Resonance Studies. Part 48. ^{13}C Spectra of a Variety of Bicyclic Ketones[1]

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The ^{13}C n.m.r. spectra of a series of 37 bicyclic ketones have been recorded to examine the variations in ^{13}C shieldings with structure and with methyl substitution. Several examples of six skeletal types were included: bicyclo[4.4.0]decanones, bicyclo[4.1.0]heptanones, bicyclo-[3.1.0]hexanones, bicyclo[3.2.2]nonanones, bicyclo[3.2.1]- and -[3.3.0]octanones as well as bicyclo[2.1.1]hexan-2-one, nopinone (6,6-dimethylbicyclo[3.1.1]heptan-2-one), and two methyl derivatives of the latter. The observed trends associated with methyl substitution follow well-defined patterns and offer further support for the application of ^{13}C shieldings as aids for stereochemical assignments especially through the well known γ effects. The variation in the shieldings of the carbonyl carbons in these systems suggested that bond eclipsing interactions have an important influence on this parameter. With this notion, the heretofore puzzling variations observed for the cycloalkanones are readily interpretable in terms of their favored conformations.

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On a déterminé les spectres r.m.n. du ^{13}C d'une série de 37 cétones bicycliques pour examiner les variations du blindage du ^{13}C en fonction de la structure et de la substitution par des groupements méthyles. Plusieurs exemples de six types de squelettes sont inclus: bicyclo-[4.4.0]déconones, bicyclo[4.1.0]heptanones, bicyclo[3.1.0]hexanones, bicyclo[3.2.2]nonanones, bicyclo[3.2.1] et [3.3.0]octanones de même que bicyclo[2.1.1]hexanone-2, nopinone (diméthyl-6,6 bicyclo[3.1.1]heptanone-2) de même que deux dérivés méthylés de cette dernière. Les tendances observées, associées avec la substitution du méthyle, suivent des patrons bien définis et offrent un support supplémentaire pour l'application des blindages du ^{13}C comme aide pour l'attribution stéréochimique spécialement grâce aux effets γ bien connus. La variation dans les blindages du groupe carbonyle dans ces systèmes suggère que des interactions provenant des éclipsages des liens ont une influence importante sur ce paramètre. Avec cette notion, les variations un peu surprenante observées jusqu'à maintenant dans les cycloalcanones sont facilement interprétables en termes des conformations les plus favorisées.

[Traduit par le journal]

Introduction

One of the most important and interesting features of ^{13}C nuclear shieldings is their remarkable sensitivity to stereochemical environment. Although this has been recognized for several years (1), a satisfactory theoretical interpretation has yet to be presented. Nevertheless, stereochemical assignments for a wide variety of systems have been obtained empirically (2) through the knowledge that the relative orientation of vicinal carbons, or of a carbon vicinal to a heteroatom, has a pronounced effect on the observed shieldings, attributed to 1,4-nonbonded interactions. The general trends and relative magnitudes of these shifts, termed γ effects, have been determined through systematic studies of series of model compounds, primarily, in cyclic systems. Much of the attention has been focussed on mono- and polycyclic six-membered ring systems because of their well-defined geometries although several bicyclic systems with other ring sizes are also attractive models. Of the latter, however, only the bicyclo[2.2.1]heptanes (ref. 3 and references therein) and bicyclo[2.2.2]octanes (4) have been examined in some detail. In these studies, a common approach has been to examine the effects of methyl substitution on the shieldings of the skeletal carbons as a function of methyl orientation since the latter is well defined. In this way, the influence of molecular geometry on the ^{13}C shieldings can be determined with minimum alteration of the bonding contributions.

Another aspect of stereochemical effects in ^{13}C spectra concerns the variation of carbonyl carbon shieldings with ring size. While the trend was

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illustrated several years ago (5), no satisfactory explanation has been put forward although a conformational origin may be suspected. The relative rigidity of bicyclic skeletons, however, provides a means whereby potential conformational contributions can be controlled and tested.

For these reasons, a series of 37 bicyclic ketones, embracing 8 skeletal types, **1–8**, was selected for ^{13}C n.m.r. examination. We wish to report the ^{13}C shieldings for this series for comparison of the methyl substituent effects with other well-defined systems. The carbonyl shieldings for this series have led to an interpretation of the variation of carbonyl shieldings in the cycloalkanones (C_4–C_{17}) in terms of their preferred conformations. Both features have potential application for stereochemical elucidations.

Experimental

Materials

Apart from bicyclo[3.2.1]octan-2-one, *trans*-decal-1- and -2-one which were commercially available, the ketones were prepared by published procedures. These include bicyclo[3.1.0]hexan-3-one by CrO_3 oxidation of bicyclo[3.1.0]hexan-3-ol (6), 6,6-dimethylbicyclo[3.1.1]-heptan-2-one (nopinone) by ozonolysis of β-pinene (7), *cis*-bicyclo[3.3.0]octan-2-one (8), bicyclo[3.2.1]octan-3-one (9) and -6-one (10). Several samples were available from earlier work in this laboratory: the bicyclo[3.1.0]hexan-2-ones (11), the bicyclo[4.1.0]heptan-2-ones (11), and the 10-methyldecalones (12). Professors R. R. Fraser and J. L. Charlton kindly provided samples of bicyclo[3.2.2]nonan-6-one and bicyclo[2.1.1]hexan-2-one, respectively. 3,3-Dimethylbicyclo[3.3.0]octan-2-one was isolated as the rearrangement product obtained by homoenolization of 3,3-dimethylbicyclo[3.2.1]octan-2-one (13). Ring expansion of norcamphor with diazoethane furnished *endo*-2-methylbicyclo[3.2.1]octan-3-one (14) which upon equilibration with trifluoroacetic acid gave a mixture of the *exo* and *endo* isomers (37:63). This ring expansion reaction also gave *exo*-3-methylbicyclo[3.2.1]octan-2-one but, contrary to the original report, attempted epimerization with sodium methoxide failed to produce detectable amounts of the *endo*-3-methyl isomer. To confirm enolate formation under these conditions, an experiment with MeO^-/MeOD was carried out giving only the *endo*-3-deuterio-*exo*-3-methyl isomer in high yield. Norcamphor also served as the starting material for 2,2-dimethylbicyclo[3.2.1]octan-3-one which was generated from the 2-methyl-2-chloromethyl derivatives (15) by reduction with *t*-BuO^-/*t*-BuOH followed by CrO_3 oxidation to furnish the desired ketone identical to that reported by another route (16). The remaining examples were obtained by methylation using the sodamide – methyl iodide procedure (17). The mono- and dimethyl derivatives were, in most cases, readily separated by g.c. on SE-30 columns. The preparations and physical constants of the new compounds obtained in this work are described below.

3,3,6,6-Tetramethylbicyclo[3.1.1]heptan-2-one

Methylation of nopinone using sodamide and methyl iodide (17) afforded a mixture (550 mg) of three ketones. Gas chromatographic analysis and separation on SE-30 columns showed the mixture to contain nopinone (52%), *cis*-nopinone, the *exo*-3-methyl derivative (34%), and the desired 3,3-dimethylnopinone (14%). A sample of *cis*-nopinone, *exo*-3,6,6-trimethylbicyclo[3.1.1]heptan-2-one, exhibited the same i.r. and n.m.r. spectra as those reported (18).

Mol. wt. Calcd. for $C_{10}H_{16}O$: 152.1200. Found (*m/e*): 152.1199.

A sample of 3,3,6,6-tetramethylbicyclo[3.1.1]heptan-2-one had the following properties: $\nu_{max}(CCl_4)$ 1700 cm^{-1}; ^1H n.m.r. 0.84 (s, 3H), 1.24 (s, 3H), 1.31 (s, 3H), 1.33 p.p.m. (s, 3H).

Mol. wt. Calcd. for $C_{11}H_{18}O$: 166.1357. Found (*m/e*): 166.1359.

2,4-Dinitrophenylhydrazone, m.p. 117.5–118.5°.

7,7-Dimethylbicyclo[3.2.2]nonan-6-one

Methylation of bicyclo[3.2.2]nonan-6-one using $NaNH_2$–CH_3I (17) gave a mixture containing unreacted starting material (20%), the monomethyl ketones (43%), and 7,7-dimethylbicyclo[3.2.2]nonan-6-one (37%). The latter was isolated by preparative g.c. on a SE-30 column and found to have the following properties: $\nu_{max}(CCl_4)$ 1711 cm^{-1}; ^1H n.m.r. 1.14 p.p.m. (s, 6H); m.p. 89–90°.

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.56; H, 10.78.

The 7-methylbicyclo[3.2.2]nonan-6-ones, however, could not be separated but the mixture gave methyl signals in its ^1H spectrum at 1.16 (d, $J \sim 7.5$ Hz) and 1.13 p.p.m. (d, $J \sim 6.5$ Hz) assigned to the *exo* and *endo* isomers on the basis of the ^{13}C spectrum (see Discussion) which indicated that the two ketones were present in a 2:3 (*exo/endo*) ratio.

Anal. Calcd. for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.85; H, 10.64.

endo-7-Methylbicyclo[3.2.1]octan-6-one

The usual methylation procedure employed for this series gave only 4% of the *endo*-7-methyl derivative of bicyclo[3.2.1]octan-6-one. The major monomethyl derivative was found to be identical to that described by Kubota *et al.* (19) and subsequently shown to be the 7-*exo*-methyl isomer. A sample of the latter (400 mg) was dissolved in 10 ml of 3% sodium methoxide in methanol and the solution refluxed for 7 h in a nitrogen atmosphere. After dilution with 15 ml of ice water, the ketone product was isolated by pentane extraction. Gas chromatographic analysis on 20% Carbowax 4000 showed that the mixture (400 mg) contained 45% of the *exo*-7-methyl isomer and 55% of the desired *endo*-7-methylbicyclo[3.2.1]octan-6-one. Separation by preparative g.c. gave a sample of the latter having the following properties: $\nu_{max}(CCl_4)$ 1710 cm^{-1}; ^1H n.m.r., 1.10 p.p.m. (d, 3H, $J \sim 7$ Hz); 2,4-dinitrophenylhydrazone, m.p. 203.5–204.5°.

Anal. Calcd. for $C_{15}H_{18}N_4O_4$: C, 56.59; H, 5.70; N, 17.60. Found: C, 56.63; H, 5.88; N, 17.42.

As an aid for some of the assignments, several of the ketones were refluxed with 5% MeO^-/MeOD to exchange the α-protons. Specific examples are noted in the Results section. In each case, the ketone was recovered in high yield.

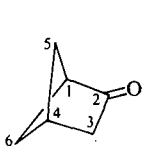
Spectra

Proton spectra were recorded with either Varian T-60 or HA-100 spectrometers while ^{13}C spectra were ob-

tained using a Varian XL-100-15 system operating in the Fourier transform mode, as described previously (3). The data were determined for $CDCl_3$ solutions (5–15% w/v) containing a few drops of TMS as an internal standard in 5 mm sample tubes. Peak positions were measured relative to TMS to within ±1 Hz; thus the shieldings have precisions greater than 0.1 p.p.m.

Results

The shielding data for this series of ketones are collected in Table 1. In each case, both noise and off-resonance decoupled spectra were obtained to distinguish between carbon types, the first step for the assignments. The carbonyl carbons were readily assigned from their characteristic low-field positions (1) and in the parent systems, the



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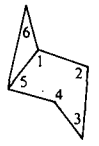

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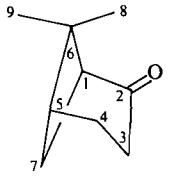

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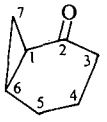

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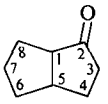

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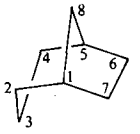

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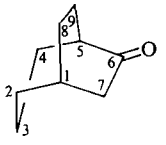

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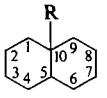

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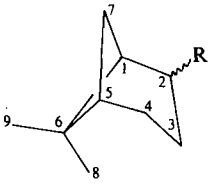
nonequivalent bridgehead carbons could be distinguished readily since that closer to the carbonyl is consistently less shielded. For the symmetrical compounds, the relative intensities led to straightforward assignments. From these features, the assignments for 2-oxo-**1**, 3-oxo-**2** and -**6** were completed.

The 2-oxo-**2** derivatives each have three methylene carbons which were distinguished in the monomethyl derivatives by deuterium exchange of the α-methylene protons. In the spectra of the dideuterated derivatives, one methylene signal essentially disappeared, one was shifted to higher field by ~0.2 p.p.m., by the geminal isotope effect, while the third was unaffected, establishing these as the C-3, C-4, and C-6 signals, respectively (3). From the methyl shieldings for the monomethyl derivatives, it followed that the more shielded methyl signal for the 1,5-dimethyl derivative was due to the 1-methyl carbon. In a similar manner, the assignments for the **4** derivatives were completed, again, utilizing the results for the 3,3-dideuteriomonomethyl isomers to identify the different methylene signals.

To aid the assignment for nopinone (**3**) and its derivatives, the ^{13}C spectra of apopinane (**9***a*), *cis*-pinane (**9***b*), and the nopinols (**9***c* and *d*) were also recorded; these data appear in Table 2. For **9***a*, the C-1, -2, -4, -5, and -6 assignments were straightforward and it remained to distinguish the C-3 from the C-7 signal and the *gem*-dimethyl resonances. The consistent appearance of a methylene signal near 26 p.p.m. in all spectra of the [3.1.1] series led to its assignment as C-7 since C-2 substitution could be expected to have little effect at this position. Since C-8 is essentially axial with respect to the six-membered ring and C-9 is equatorial, it was expected that C-8 would be the more shielded of the *gem*-dimethyl carbons. This was supported by an examination of the relative shifts in **3** upon addition of $Eu(fod)_3$, since the higher field methyl signal exhibited a greater downfield shift. With two methyl signals near 23 p.p.m. for **9***b* the assignments of C-8 and



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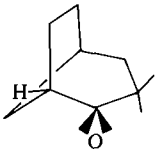
a R = H
b R = α-Me
c R = α-OH
d R = β-OH



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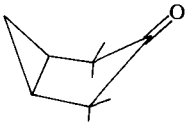

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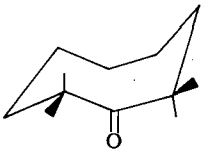

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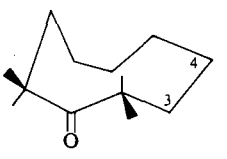

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TABLE 1. ^{13}C shieldings of several bicyclic ketones[a]

Skeleton	Substituent	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	Me[b]
[2.1.1] (1)	2-Oxo	56.0	214.0	40.8	35.8	40.9	40.9					
[3.1.0] (2)	3-Oxo	12.2	40.9	217.9	40.9	12.2	13.3					
	2-Oxo	27.4	215.1	31.4	22.6	21.6	13.5					
	2-Oxo-1-Me	32.6	215.8	32.0	21.7	28.7	20.5					13.9
	2-Oxo-5-Me	35.0	214.5	33.6	29.1	30.0	20.9					21.2
	2-Oxo-1,5-Me_2	37.2	215.9	32.5	28.8	33.4	26.8					10.5 (C-1) 18.5 (C-5)
[3.1.1] (3)	2-Oxo-6,6-Me_2	57.9	214.3	32.7	21.4	40.4	41.0	25.2				22.1 (*syn*) 25.8 (*anti*)
	2-Oxo-3,6,6-Me_3	57.1	216.1	37.1	30.9	41.1	41.2	25.4				14.1; 21.9; 26.3
	2-Oxo-3,3,6,6-Me_4	58.5	219.9	43.0	37.6	42.1	40.9	25.9				22.7; 26.4; 27.6; 33.8
[4.1.0] (4)	2-Oxo	25.7	208.7	36.6	17.9	21.3	17.4	10.2				
	2-Oxo-1-Me	29.8	210.2	36.4	19.3	21.8	26.3	18.1				19.8
	2-Oxo-6-Me	34.3	208.7	35.8	18.1	28.1	23.9	17.5				24.8
	2-Oxo-1,6-Me_2	35.4	209.9	36.0	18.3	29.4	28.5	24.1				14.3 (C-1) 21.2 (C-6)
[3.3.0] (5)	2-Oxo	52.0	223.0	37.9	(26.4)	41.0	33.5	(26.2)	29.8			
	2-Oxo-3,3-Me_2	50.3	224.6	47.6	43.5	36.3	33.6	25.0	29.4			23.1 (*endo*) 25.3 (*exo*)
	2-Oxo-1,3,3-Me_3	56.4	225.1	46.9	42.4	45.5	31.8	24.4	37.4			24.9 (1-Me) 24.4 (*endo*) 25.8 (*exo*)

TABLE 1—*Continued*

Skeleton	Substituent	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	Me[b]
[3.2.1]	2-Oxo	51.2	214.0	34.7	32.1	34.1	(28.1)	(28.0)	38.3			
(**6**)	2-Oxo-3-Me	51.1	214.7	38.3	42.5	34.8	28.4	27.9	39.4			14.5
	2-Oxo-3,3-Me_2	50.9	218.2	42.1	46.0	35.1	28.7	28.1	35.7			30.6 31.2
	3-Oxo	35.3	50.3	211.9	50.3	35.3	29.3	29.3	37.8			
	3-Oxo-2-*exo*-Me	41.6	53.1	218.1	47.7	35.3	28.5	30.1	32.1			17.6
	3-Oxo-2-*endo*-Me	42.7	51.4	213.0	49.8	36.6	29.2	24.3	39.8			12.8
	3-Oxo-2,2-Me_2	47.7	49.7	216.3	47.1	35.9	28.4	25.4	34.1			22.9 (*endo*) 26.4 (*exo*)
	6-Oxo	32.2	(30.5)	18.9	(30.7)	46.2	221.4	43.5	37.2			
	6-Oxo-7-*exo*-Me	39.4	31.4	19.3	30.5	(46.7)	224.2	(46.9)	34.4			15.6
	6-Oxo-7-*endo*-Me	36.8	26.1	19.1	30.8	45.7	223.4	48.4	36.4			8.5
	6-Oxo-7,7-Me_2	43.1	28.1	19.2	31.2	45.8	225.4	48.1	34.4			25.2 (*exo*) 17.9 (*endo*)
[3.2.2]	6-Oxo	28.5	34.1	21.6	31.9	46.9	216.2	44.3	24.4	23.2		
(**7**)	6-Oxo-7-*exo*-Me	35.2	35.4	21.4	30.9	46.9	218.9	47.5	20.1	22.9		17.4
	6-Oxo-7-*endo*-Me	34.1	29.1	21.1	31.1	46.5	218.0	46.5	25.9	22.9		12.7
	6-Oxo-7,7-Me_2	39.6	31.4	21.0	31.4	47.0	220.1	46.4	23.3	22.7		23.2 (*endo*) 26.9 (*exo*)
[4.4.0]	1-Oxo	211.9	41.6	(25.4)	33.0	44.9	34.3	(25.1)	(25.8)	26.5	54.9	
(**8**)	1-Oxo-10-Me	215.6	37.4	26.2	(27.7)	46.1	(28.0)	26.2	21.4	32.5	48.3	15.7
	2-Oxo	48.5	210.5	41.4	(32.7)	41.6	34.2	26.1	25.6	(33.6)	43.3	
	2-Oxo-10-Me	56.8	211.2	41.3	28.0	43.7	29.4	26.6	21.1	41.6	37.6	16.5
	3-Oxo-10-Me	40.3	38.1	210.6	44.8	44.6	29.0	26.0	21.6	41.0	33.1	14.9
	4-Oxo-10-Me	40.8	20.5	40.8	210.9	57.6	22.6	25.6	21.2	41.3	39.6	16.9

[a]In p.p.m. from internal TMS in $CDCl_3$ solutions. Assignments for similar values in parentheses may be reversed.
[b]*Syn* with respect to the carbonyl group; *endo* with respect to the larger ring.

TABLE 2. ^{13}C shieldings[a] of some bicyclic nydrocarbons and alcohols

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
9*a*	41.1	25.4	22.4	25.4	41.1	39.1	26.7	20.5	26.8	
9*b*	48.1	36.0	33.9	23.9	41.4	38.7	26.6	(22.9)	28.3	(23.2)
α-Nopinol (**9***c*)	47.9	73.1	28.3	24.8	41.0	37.4	25.5	22.4	27.3	
β-Nopinol (**9***d*)	48.0	69.4	23.3	22.7	40.5	39.4	25.7	20.0	26.7	
6	35.2	32.8	19.1	32.8	35.2	28.9	28.9	39.7		
7	29.0	35.7	22.2	35.7	29.0	25.9	25.9	25.9	25.9	
trans-Decalin[b]	34.3	26.9	26.9	34.3	43.7	34.3	26.9	26.9	34.3	43.7
10-Methyl-*trans*-decalin[c]	42.1	22.1	27.2	29.3	45.8	29.3	27.2	22.1	42.1	33.9

[a]In p.p.m. from internal TMS. Measured for 5–15% (w/v) solutions in $CDCl_3$.
[b]From ref. 12.
[c]From ref. 20; the methyl shielding is 15.7 p.p.m.

C-10 are uncertain and for 3,3,6,6-tetramethyl-**3** the methyl assignments may not be correct; the present assignments are discussed more fully later.

As noted earlier, 3,3-dimethyl-*cis*-bicyclo-[3.3.0]octan-2-one was obtained by homoenolization of 3,3-dimethylbicyclo[3.2.1]octan-2-one. Deuterium exchange under homoenolization conditions, coupled with ^2H n.m.r. examination, permitted unequivocal identification of C-6, -7, and -8 (13) in the ^{13}C spectrum and completed the assignments, from which those for **5** and its trimethyl derivative followed readily.

In the [3.2.1] series, the parent hydrocarbon was also examined (Table 2). For the 2-oxo compounds, the spectra of the 3,3-dideuterio, 3-deuterio-3-methyl, and 1,7,7,9,10-pentadeuterio-3,3-dimethyl derivatives were also determined; the latter isomer was obtained from homoenolization experiments (13). With these data the assignments for the 2-oxo derivatives were readily completed. For the 3-oxo derivatives, the well-separated methine signals permitted straightforward assignments while the C-6 and C-7 methylene resonances were identified on the basis of an expected shielding influence of an *endo*-2-methyl at C-7 but for the *exo*-2-methyl isomer these methylene signals were not so readily assigned. By analogy with *exo*-3-methylnorcamphor (3), however, one may predict that the *exo*-2-methyl group would tend to deshield C-7 slightly and, on this basis, the C-6 and C-7 signals were taken to be those at 28.5 and 30.1 p.p.m., respectively. A comparison of the data for the 6-oxo series with that for the parent hydrocarbon led to the assignments given in Table 1 for these four derivatives. A sample of 7,7-dimethylbicyclo[3.2.1]octan-6-one containing deuterium at C-3, -4, -5, and -9 was available from homoenolization studies (20) to confirm its assignments and provide supporting evidence for those for the other 6-oxo derivatives.

For the bicyclo[3.2.2]nonan-6-ones, the spectra of the 7,7-dideuterio, 7-deuterio-7-*exo*-methyl, and 7-deuterio-7-*endo*-methyl derivatives as well as the parent hydrocarbon (Table 2) were also recorded. This permitted a ready distinction between the methine signals for the monomethyl cases. Since one signal was essentially eliminated, one was shifted upfield by 0.1 p.p.m. while the third methine signal was unaffected in the spectra of the deuterated compounds, these arose from C-7, C-1, and C-5, respectively. In addition, one of the methylene signals in each was significantly broadened, identifying the vicinal methylene carbon *anti* to the deuterium (21). Of the remaining methylene peaks, the highest field signal, ~21 p.p.m., was assigned to C-3 in the four ketones because of its similarity with C-3 in the hydrocarbon and the fact that it should be little affected by 7-substitution. All four ketones exhibited methylene absorption near 31 p.p.m. which was assigned to C-4 since this carbon should be little affected by 7-substitution. Supporting this assignment, the spectrum for 7,7-dideuteriobicyclo-[3.3.2]octan-6-one showed broadening due to vicinal C–D coupling for the 24.4 and 34.1 p.p.m. resonances. Thus it also followed that C-9 gave rise to the signal near 23 p.p.m. in the four ketones.

For the *trans*-decalones, the methylene assignments were made by comparison with the results for *trans*-decalin and 10-methyl-*trans*-decalin (Table 2) in a manner analogous to that described for the decalols (12) and some more highly substituted decalones (22). In the 2- and 3-oxo derivatives, the carbonyl group has little effect on the C-6, -7, -8, and -9 shieldings while the α-meth-

TABLE 3. Methyl substituent effects[a] in some bicyclic ketones and cyclohexanone

Skeleton	Substitution	Substituent effects					
			β		γ		
		α	C=O	$CH(CH_2)$	*gauche*	*anti*	CH[b]
[2.2.1][c]	2-Oxo-3-*exo*-Me	3.1	2.6	6.2	−3.2	0.9	−0.3
[3.2.1]	6-Oxo-7-*exo*-Me	3.4	2.8	7.2	−2.8	0.9	+0.5
[3.2.2]	6-Oxo-7-*exo*-Me	3.2	2.7	6.7	−4.3	1.3	0.0
[2.2.2][d]	2-Oxo-3-Me	2.6	3.4	6.0	−4.6	1.3	0.0
[2.2.1][c]	2-Oxo-3-*endo*-Me	3.1	2.4	5.1	−6.2	−0.4	0.5
[3.2.1]	6-Oxo-7-*endo*-Me	4.9	2.0	4.6	−4.4	−0.8	−0.5
[3.2.2]	6-Oxo-7-*endo*-Me	2.2	1.8	5.6	−5.0	1.5	−0.4
[3.2.1]	2-Oxo-3-*exo*-Me	3.6	0.7	10.4		−0.1(C-1)	
						0.7(C-5)	
	3-Oxo-2-*endo*-Me	1.1	1.1	7.4	−5.0(C-7)	−0.5(C-4)	
						2.0(C-8)	
$C_6H_{10}O$[e]	2-Me(equatorial)	3.4	1.0	9.1		0.2(C-4)	
						−0.1(C-6)	
$C_6H_{10}O$[e]	2-Me(axial)	3.6	3.6	6.0	−5.9(C-4)		
					−6.2(C-6)		
[3.2.1]	3-Oxo-2-*exo*-Me	2.8	6.2	6.3	−2.6(C-4)	0.8(C-7)	
					−5.7(C-8)		
[4.4.0]	1-Oxo-10-Me	−6.6	3.7	1.2(C-5)	−4.2(C-2)		
				6.0(C-9)	−5.3(C-4)		
					−6.3(C-6)		
					−4.4(C-8)		
	2-Oxo-10-Me	−5.7		8.3(C-1)	0.7(C=O)		
				2.1(C-5)	−4.7(C-4)		
				8.0(C-9)	−4.8(C-6)		
					−4.5(C-8)		
	3-Oxo-10-Me	−8.5		7.6(C-1)	−3.3(C-2)		
				1.3(C-5)	−3.7(C-4)		
				6.8(C-9)	−4.6(C-6)		
					−4.5(C-8)		
	4-Oxo-10-Me	−5.3		7.8(C-1)	−4.9(C-2)		
				2.7(C-5)	−1.0(C=O)		
				7.0(C-9)	−3.9(C-6)		
					−3.9(C-8)		

[a]In p.p.m. Positive values denote deshielding effects.
[b]Bridgehead carbon: C-1 in [2.2.1] and [2.2.2] ketones; C-5 in [3.2.1] and [3.2.2] series.
[c]Reference 3.
[d]Reference 4*b*.
[e]Cyclohexanone, data from ref. 23.

ylene carbons were readily identified by their characteristic shifts to lower field. In the 1- and 4-oxo derivatives, the *gauche* vicinal methylene carbon (C-9 and C-6, respectively) was characterized by its upfield shift caused by the γ effect of the carbonyl oxygen while the remaining methylene carbons in the unsubstituted ring are essentially unaffected (22), as are the β- and γ-methylene carbons in the substituted ring. Thus, the assignments for these decalones were readily completed.

Discussion

In one of the first systematic studies of substituent effects in alicyclic systems, Dalling and Grant (23) showed the remarkable reproducibility and stereochemical dependence of the effects of methyl groups on the shieldings of cyclohexane ring carbons. Similar results were subsequently obtained for the norbornane system by Roberts and co-workers (24) and in this laboratory (3) for the bicyclo[2.2.2]octanones (4*b*) and for several cyclohexanones and cyclopentanones (25). In each case, the carbons γ to the site of substitution are significantly shielded if *gauche* to the methyl group and tend to be deshielded slightly, if *anti*. To examine the trends for α-methyl substitution in the present ring systems, some pertinent data are given in Table 3, which contains the shifts observed for the skeletal

carbons in the monomethyl derivatives from their positions for the parent ketones. The first seven entries have the carbonyl in a two-carbon bridge with the α-methyl *gauche*, or approximately so, to either a one- or two-carbon bridge. It is apparent that the latter arrangement produces the larger upfield shift, as might be expected because of the smaller dihedral angle between the two γ centers; the relative shieldings of the methyl carbons exhibit the same trend. For each *exo*/*endo* pair, the β effects are somewhat diminished in the isomer having the greater negative γ shift. The last three entries in the first column of Table 3 have an equatorial α-methyl nearly eclipsed with the carbonyl group, with only one having a *gauche* γ interaction, which presumably accounts for the attenuated β effect at the adjacent bridgehead carbon. It has been generally found that the shielding of all carbons in the γ *gauche* fragment are upfield from those in the corresponding arrangement lacking the *gauche* interaction (1, 2). The remaining six entries in Table 3 are closely related, each having the methyl group in an axial orientation on a six-membered ring. The variety of γ *gauche* effects are consistently upfield for sp^3 carbons while the carbonyl carbon is much less affected. It is interesting that with three or four γ *gauche* interactions the methyl group no longer deshields the carbon to which it is bonded; also the β effects at the methine carbons are very much less than those at the methylenes. From Table 1, it is apparent that methyl substitution at the ring junctions in the [3.1.0] and [4.1.0] systems does not produce distinctive upfield shifts for the γ-carbons. This is consistent with the relatively large dihedral angles, ~120°, relating these centers. The γ shielding interactions between the nearly eclipsed vicinal methyls in the dimethyl derivatives, however, are clearly evident from the methyl carbon shieldings.

To examine the effect of the carbonyl group on the shieldings of the neighboring carbons, the relevant data are listed in Table 4, obtained by comparison of the results for the unsubstituted ketones with those for the parent hydrocarbons. The earlier data for norcamphor (3) and bicyclo[2.2.2]octanone (*4b*)[3] are included. In general, the α-methylene carbons are more strongly deshielded in the bicyclic systems than in cyclopentanone or cyclohexanone. It is also interesting that the carbonyl group tends to shield the γ-carbons in all cases. There seems to be no ready explanation for either of these trends. The upfield shifts exhibited by the β-methylene carbons, however, are consistent with γ interactions involving the carbonyl oxygen and, as expected, the effects are larger with smaller dihedral angles such that a trend is discernible. The maximum upfield shifts are found for the three decalones having the carbonyl group at either C-1 or C-4, in which cases the carbonyl oxygen must be nearly eclipsed with C-9 or C-6, respectively. The smallest shifts occur in the systems for which the carbonyl oxygen and β-methylene carbon are separated by relatively large dihedral angles, ~120°. Presumably the interaction producing these upfield shifts involves the hydrogen bonded to the affected carbon. For the β-bridgehead carbons, the bridgehead hydrogen and carbonyl oxygen are much too far apart to interact and there is no apparent trend in these data. It may be noted that in two cases the quaternary β-carbons are markedly deshielded by the carbonyl groups but this is probably a result of the elimination of a *gauche* γ interaction of the angular methyl bonded to the quaternary carbon by placement of the carbonyl at C-2 or C-4 in the decalone skeleton.

The variation of the carbonyl carbon shieldings in this series of bicyclic ketones seems particularly interesting. The values span a range of 14 p.p.m., δ_C 208.7–223.0 for the parent ketones, and there appears to be a trend which may account for the well-known but unexplained, variation of carbonyl shieldings in the monocyclic series (5). The remarkable sensitivity of this shielding to ring size has only been attributed to conformational factors in the most general terms. Although most of these bicyclic ketones can be regarded as either substituted cyclohexanones or cyclopentanones, the observed carbonyl shieldings seem to depend primarily on features other than ring size. For the simple five- and six-membered rings the carbonyl shieldings differ by 8 p.p.m. (5, 25), 220.5 and 212.0 p.p.m., respectively, in $CDCl_3$ but in **1** and **3** this absorption is near 214 p.p.m., even though their carbonyl groups are in different sized rings. As a possible explanation, it can be suggested that the number of α-bond eclipsing interactions present in each case is the more important feature. Cyclohexanone has two bond eclipsing interactions, whereas **1** and **3** have one, and cyclopentanone can be viewed as lacking such inter-

[3]The methylene shielding for bicyclo[2.2.2]octane is incorrect in the earlier paper and should read 26.1 p.p.m.

TABLE 4. Carbonyl substituent effects[a]

Skeleton	Substituent	α-C		β-C		γ-C
		CH	CH_2	CH	CH_2	
[2.2.2][b]	2-Oxo	18.3	18.5	3.9	−2.7(C-6, 7)	−1.3(C-5, 8)
[3.2.2]	6-Oxo	17.9	18.4	−0.5	−3.8(C-4)	−1.6(C-2)
					−2.7(C-9)	−0.6(C-3)
						−1.5(C-8)
[2.2.1][c]	2-Oxo	13.4	15.5	−1.0	−5.4(C-6)	−2.5(C-5)
					−0.7(C-7)	
[3.2.1]	6-Oxo	11.0	14.6	−3.0	−2.1(C-4)	−2.3(C-2)
					−2.5(C-8)	−0.2(C-3)
	2-Oxo	16.0	15.6		−0.7(C-4)	−1.1(C-5)
					−0.9(C-7)	−0.8(C-6)
					−1.4(C-8)	
	3-Oxo		17.5	0.1		0.4(C-6, 7)
						−1.9(C-8)
[4.4.0]	1-Oxo	11.2	14.7	1.2	−1.5(C-3)	−1.3(C-4)
					−7.8(C-9)	0.0(C-6)
						−1.1(C-8)
	1-Oxo-10-Me	14.4	15.3	+0.3	−1.0(C-3)	−1.6(C-4)
					−9.6(C-9)	−1.3(C-6)
						−0.7(C-8)
	2-Oxo		14.2(C-1)	−0.4	−1.6	−2.1(C-5)
			14.5(C-3)			−0.7(C-9)
	2-Oxo-10-Me		14.7(C-1)	3.7[d]	−1.3	−2.1(C-5)
			14.1(C-3)			−0.5(C-9)
	3-Oxo-10-Me		16.0(C-2)	−1.2	−1.8	−0.3(C-6)
			15.5(C-4)			−0.8(C-10)
	4-Oxo-10-Me	11.8	13.6	5.7[d]	−1.6(C-2)	−1.3(C-1)
					−6.7(C-6)	−1.6(C-7)
						−0.8(C-9)
Cyclopentanone[e]			11.6		−3.3	
Cyclohexanone[e]			14.2		−0.6	−2.7

[a]In p.p.m. Positive values denote deshielding effects.
[b]Reference 4*b*.
[c]Reference 3.
[d]Quaternary carbons.
[e]Reference 23.

actions, since its favored conformation is the half-chair (26). Inspection of molecular models indicates that α-bond eclipsing interactions should be minimal in **5** and 6-oxo-**6** and their carbonyl shieldings of 223.0 and 221.4 p.p.m., respectively, are comparable to the cyclopentanone value. The carbonyl shieldings for 3-oxo-**6** and five of the six decalones (210.5–211.9 p.p.m.) are essentially the same as that of cyclohexanone and each of these has comparable bond eclipsing. In *trans*-10-methyl-1-decalone, the somewhat lower carbonyl shielding of 215.6 p.p.m. may result from a greater degree of flattening in the ring containing the carbonyl group which would tend to reduce the *syn* axial interaction of the angular methyl at C-2. Ring flattening increases the dihedral angle between the α C—H bond and the carbonyl π-bond, thereby reducing the eclipsing interaction. The fact that the γ effect of the angular methyl group at C-2 (Table 3) is significantly less than that at C-4 and C-6 is consistent with this interpretation. The carbonyl shieldings of **7**, bicyclo[2.2.2]octanone (4*b*), and norcamphor (3) are 216.2, 216.7, and 217.4 p.p.m., respectively, which on the basis of the present proposal suggest that the carbonyl group has a single bond eclipsing interaction somewhat smaller than that in the more rigid **1** skeleton. Again, molecular models indicate that this is a reasonable interpretation. On similar grounds, the carbonyl absorption of 214.0 p.p.m. for 2-oxo-**6** can be interpreted in terms of **10** as the favored conformation having the 3-carbon bridge nearly planar.

For the ketones containing a three-membered ring, an earlier study (11) of the carbonyl shieldings led to the conclusion that cyclopropylcarbonyl conjugation could be a contributing

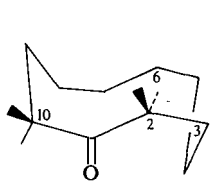
TABLE 5. ^{13}C shieldings of some cycloalkanones[a]

Ring	C=O	α-CH_2								ω-CH_2
4	209.1	47.7								9.7
5	220.5	38.3	23.3							
6	212.0	42.0	27.1							25.1
7	215.2	43.9	30.5	24.4						
8	218.1	42.0	27.3	25.7						24.8
9	218.1	43.6	27.0	25.1	24.4					
10	214.7	42.1	25.0	24.9	23.5					25.2
11	214.3	42.0	26.1	25.0	24.5	22.6				
12	212.7	40.4	24.8	24.7	24.3	22.6				22.5
13	212.7	42.0	26.6	25.9	25.8	24.6	23.3			
14	211.9	40.9	26.1	25.9	25.4	25.3	23.0			24.5
15	212.6	42.2	27.7	26.8_8	26.8_5	26.6	26.4	23.5		
16	212.2	42.1	27.7	27.3	27.1	26.6_2	26.5_7	23.5		26.6
17	212.1	42.4	28.3	27.9	27.7	27.3_4	27.2_6	27.0	23.8	

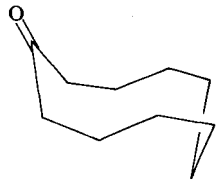
[a]1 *M* solutions in $CDCl_3$.

factor. This still seems reasonable for bicyclo-[4.1.0]heptan-2-one since its carbonyl signal at 208.7 p.p.m. is at appreciably higher field than that for cyclohexanone. For bicyclo[3.1.0]hexan-2-one, however, the observed shielding of 215.1 p.p.m. is also consistent with the presence of one bond eclipsing interaction, which on the basis of the foregoing, would tend to increase the carbonyl shielding from that found for cyclopentanone, as is observed. In bicyclo[3.1.0]hexan-3-one, the absorption at 217.9 p.p.m. is not so greatly different from cyclopentanone but could conceivably represent the shielding for the envelope conformation **11** since the three-membered ring probably precludes the half-chair conformer and in **11** bond opposition strain between the C-3 (C-4) and C-2 (C-5) hydrogens is minimized. The alternative envelope conformer maximizes this contribution.

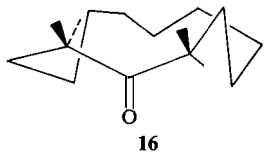
Since the variations in the carbonyl shieldings in these bicyclic systems are explicable in terms of the number of bond eclipsing interactions it seems reasonable to reexamine the trends found several years ago for the monocyclic ketones (5). The data for 1 *M* solutions in $CDCl_3$ are listed in Table 5 from which it is apparent that the carbonyl carbons in 8- and 9-membered rings are appreciably deshielded relative to cyclohexanone, whereas the 7-, 10-, and 11-membered ring examples are somewhat less shielded than cyclohexanone. For the larger rings the carbonyl shieldings are essentially the same as cyclohexanone. These trends are identical to those originally reported (5) but in $CDCl_3$ the carbonyl carbons are deshielded by *ca.* 3 p.p.m., relative to the values for CS_2 solutions, presumably because of hydrogen bonding in $CDCl_3$. On the basis of bond eclipsing contributions to the carbonyl shieldings, the observed values for cyclooctanone and cyclononanone indicate that these favor conformations with one eclipsing interaction such as **12** and **13**, respectively. These are boat-chair (BC) conformations with **13** somewhat distorted to relieve bond opposition strain at C-3 and C-4. Anet and his co-workers have established that **12** is the favored conformation for cyclooctanone (27) and have shown that cyclononanone very likely exists in a single conformation of the same symmetry (28). For cyclodecanone, two of the possible boat-chair-boat (BCB) conformations are **14** and **15**. If **15** were



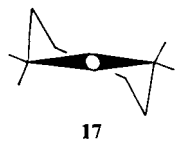
14 (BCB-3)



15 (BCB-1)



16



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favored, one could anticipate a carbonyl shielding essentially the same as that for cyclohexanone whereas in **14** transannular interactions tend to maximize the separation between closely approaching hydrogens (*e.g.* on C-2 and C-6 in **14**) thereby reducing the bond eclipsing interactions of the carbonyl group (*i.e.* with the C_2—C_3 bond

and one of the α-hydrogens at C-10) and decreasing the carbonyl shielding. The observed shielding of 214.7 p.p.m. is significantly less than the cyclohexanone value of 212.0 p.p.m. The remaining BCB-2 conformation for cyclodecanone has the carbonyl group in an environment very similar to that for cyclohexanone, always eclipsed with two hydrogens on the α- and α′-carbons. Thus the carbonyl shielding results favor **14** as the preferred conformation. Anet *et al.* (28) have recently presented evidence that cyclodecanone strongly favors **14** (BCB-3) over the BCB-2 conformer and their results clearly eliminate **15** as a major contributor. Since the carbonyl shielding of cycloundecanone (214.3 p.p.m.) is very close to that for cyclodecanone, a similar preferred conformation is indicated and it has been shown that the 11-membered ring ketone probably exists as a single conformer in solution (28). The conformation of the crystalline state has recently been established (29). Anet *et al.* have also shown that cyclododecanone very probably has the same ring skeleton as cyclododecane, a "square" D_4 form, as represented by **16** with the carbonyl group at a noncorner position (28). This conformation has two bond eclipsing interactions for the carbonyl group and the observed shielding of 212.7 p.p.m. fits very well with the present interpretation. Finally it may be noted that the bond eclipsing for the carbonyl group in a twist-chair seven-membered ring (**17**) would appear to be less than that for cyclohexanone, as judged by inspection of molecular models, and the observed shielding of 215.2 p.p.m. seems very reasonable.

Although the notion that bond eclipsing interactions are important factors governing carbonyl carbon shieldings is speculative, the favored conformations indicated by the observed shieldings for the cycloalkanones are in excellent agreement with those deduced on the basis of much more rigorous information. This suggests that carbonyl shielding data may be helpful for conformation assignments in a variety of systems.

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