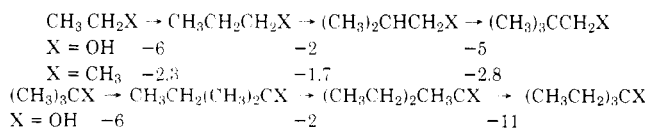


Scheme II. SCS Values for γ -Methyl Substitution

roduction at C₂ of ethanol causes shielding, with the first and third methyl prompting larger changes than the second methyl. This same sort of behavior is observed for the ¹³C shifts of the terminal CH₃ in the X = CH₃ series. This is, of course, the well-known γ effect⁹ in ¹³C NMR which is traditionally rationalized in terms of 1,4-gauche interactions. The relative magnitudes of the γ steric shifts in the two series correlate qualitatively with the increase in gauche relationships of the nucleus under observation.

A second series illustrating the effect of an increasing number of γ -methyls consists of the tertiary alcohols also shown in Scheme II. The γ shifts are similar to those of the first series with the exception of an especially large SCS for the third substitution. Models suggest that interactions among the ethyl groups of triethylcarbinol should promote the population of conformers in which the OH group is subjected to gauche interactions.

An argument based on γ interactions also rationalizes the chemical shifts of cyclopentanol and cyclohexanol, which are significantly deshielded relative to an acyclic analogue such as 3-pentanol. Incorporation of the γ carbons into a five- or six-membered ring reduces gauche interactions with the OH group. Thus, cyclohexanol, which in its equatorial form is devoid of such interactions, has a similar chemical shift to isopropyl alcohol, a model without γ substituents. Some gauche interaction is present for the conformationally more flexible cyclopentanol and its chemical shift is intermediate to those of cyclohexanol and 3-pentanol.

The introduction of δ -alkyl groups does not generally appear to cause important changes in the ¹⁷O chemical shifts of alcohols, although a slight deshielding trend can be deduced from the data (i.e., 5 \rightarrow 8 \rightarrow 9 \rightarrow 10; 12 \rightarrow 13; 5 \rightarrow 11; but see 6 \rightarrow 14).

The presence of heteroatomic substituents γ to the OH group also provokes shielding, which is usually larger than that of CH₃: CH₃, -6; OH, -11; N(CH₃)₂, -12; Cl, -8; and SCH₃, -2 ppm. Finally, trifluoroethanol is about 30 ppm more shielded than ethanol.

In summary, ¹⁷O chemical shifts of simple alcohols show a strong resemblance to the ¹³C behavior of a CH₃ group analogously situated, although the magnitudes of the substituent effects are generally much larger at the oxygen center. We are currently expanding our study to other functional groups.¹⁰

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- Spectra were obtained using a Varian XL-100-15 spectrometer equipped for Fourier transform operation. A pulse width of 22 μ s with an interval of 0.11 s was employed with a spectral window of 10 000 Hz. Proton decoupling was performed concurrently. Anywhere from 10 000 to 200 000 scans were accumulated depending on the sample. An ¹⁷O-enriched H₂O sample (otherwise isotopically normal) at 28 °C was used as an external reference. The spectra were generally run at 65 °C on pure, natural abundance samples from commercial sources.
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- Support of this work by a research grant from the National Science Foundation is gratefully acknowledged. Fellowship support to Manuel A. Centeno was provided by the Universidad de Oriente, Venezuela.

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Received September 12, 1978

Oxygen-17 Nuclear Magnetic Resonance. 2.
Cyclohexanones

Summary: The ¹⁷O chemical shifts of several substituted cyclohexanones have been measured. Substituent shifts have been derived for methyl substitution at various sites and it appears that the substituent shift for methyl substitution at the carbon adjacent to a carbonyl depends on the dihedral angle between these two groups.

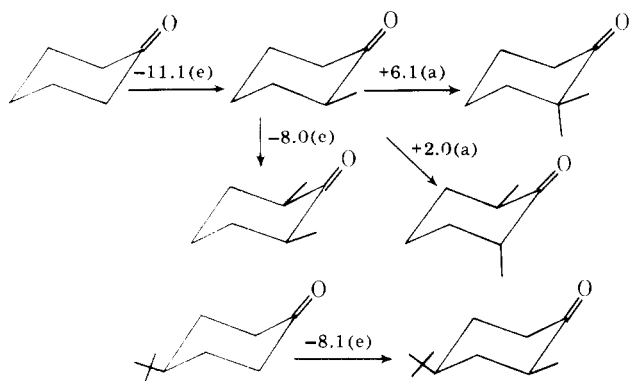
Sir: In connection with a study of the ¹⁷O NMR characteristics¹ of the carbonyl oxygen of aldehydes,^{2,3} ketones,^{2,3} esters,⁴ etc., we have measured the ¹⁷O chemical shifts for a number of cyclohexanones. The well-defined conformational situation for cyclohexane derivatives allows for the empirical definition of substituent effects as a function of molecular geometry. Such information should prove invaluable in the application of conformational analysis to the interpretation of ¹⁷O data for acyclic carbonyl compounds.

Table I. ¹⁷O and ¹³C Carbonyl Chemical Shifts of Substituted Cyclohexanones

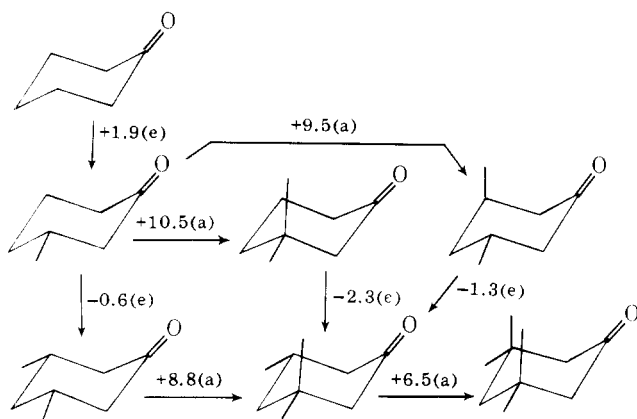
cyclohexanone	$\delta^{17}\text{O}^a$	$\delta^{13}\text{C}^b$
parent	559.9	207.4
2-methyl	548.8	209.9
3-methyl	561.8	207.0
4-methyl	560.1	207.9
2-ethyl	553.3	208.6
2-isopropyl	558.7	208.6
2- <i>tert</i> -butyl	561.9	208.5
2- <i>n</i> -propyl	552.2	209.1
3- <i>tert</i> -butyl	561.4	207.6
4- <i>tert</i> -butyl	557.4	207.2
2,2-dimethyl	554.9	211.2
3,3-dimethyl	572.3	207.1
4,4-dimethyl	561.4	207.4
<i>cis</i> -2,6-dimethyl	540.8	210.1
<i>trans</i> -2,6-dimethyl	550.8	212.4
<i>cis</i> -3,5-dimethyl	561.2	206.5
<i>trans</i> -3,5-dimethyl	571.3	207.0
<i>cis</i> -2-methyl-4- <i>tert</i> -butyl	549.3	208.9
3,3,5-trimethylcyclohexanone	570.0 ^c	207.2
3,3,5,5-tetramethylcyclohexanone	576.5	207.2

^a In ppm relative to external H₂O; 30% by weight in dioxane with a drop of H₂¹⁷O. ^b In ppm relative to internal Me₄Si; 10% by weight in CCl₄. ^c Neat.

Scheme I



Scheme II



The ^{17}O chemical shifts at 13.56 MHz for several substituted cyclohexanones relative to external H_2O are given in Table I.⁵ Also listed in Table I are the carbonyl ^{13}C chemical shifts for 10% solutions in CCl_4 .⁶ In Scheme I are shown several pairs of compounds differing only in the presence of a methyl substituent at a carbon adjacent to the carbonyl unit. When the added methyl substituent is oriented equatorially, there is a large shielding (i.e. negative) substituent shift (-8 to -12 ppm) as indicated by the SCS⁷ values given over the arrows. On the other hand, an axial methyl causes a smaller deshielding effect. There appears to be some variation in the SCS value (2–6 ppm) depending upon the other substituents present, but the general trends are clear. Appreciable changes in the carbonyl ^{13}C shifts accompany substitution adjacent to the carbon and are deshielding in all cases. A more extensive ^{13}C study confirms this observation and indicates that an axial methyl has a larger effect.⁶

There is also an important geometrical dependence of the ^{17}O shifts attending substitution at a carbon center one-removed from the carbonyl group as illustrated in Scheme II. An axial methyl at this site induces marked deshielding (7–10 ppm) of the ^{17}O signal, whereas equatorial substitution results in only small shifts, generally deshielding. Interestingly, only small changes are observed in the ^{13}C chemical shifts of the carbonyl carbons.⁶

Increasing the size of a C_2 alkyl group as depicted in Scheme III also adds methyls three bonds removed from the carbonyl, albeit with more conformational ambiguity.⁸ The indicated deshielding effects (3–5 ppm) are similar to those for axial C_3 substitution, although somewhat smaller in magnitude. Only the first pair of compounds differs significantly in their carbonyl ^{13}C shifts.

More remote substitution in the ring or on the side chains does not result in ^{17}O chemical shift changes much larger than experimental uncertainty; the ^{13}C variations are also small.

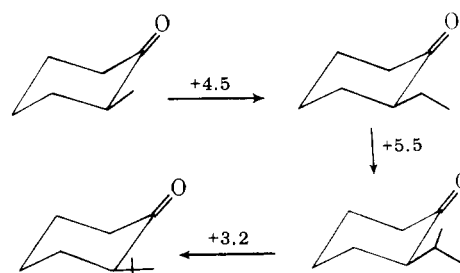
Other geometrical relationships for substitution adjacent

Table II. ^{17}O and ^{13}C Carbonyl Chemical Shifts of Some Bicyclic Ketones

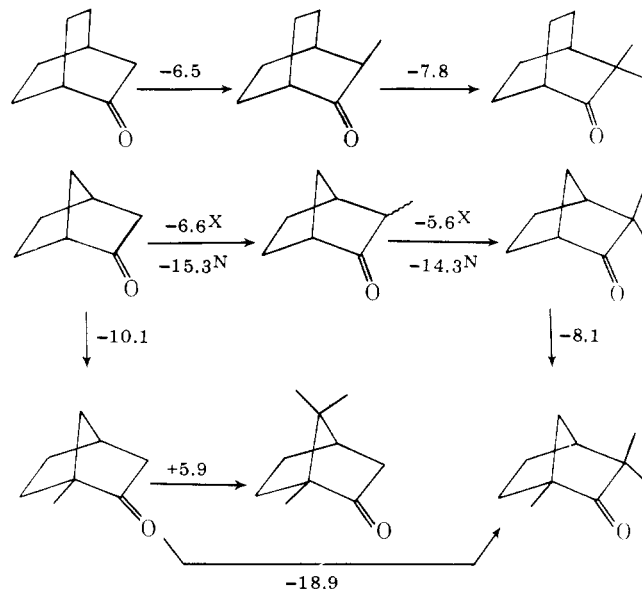
compounds	$\delta^{17}\text{O}^a$	$\delta^{13}\text{C}^b$
bicyclo[2.2.1]heptan-2-one	524.3	213.1
1-methylbicyclo[2.2.1]heptan-2-one	514.2 ^c	213.8
exo-3-methylbicyclo[2.2.1]heptan-2-one	517.7 ^c	215.7
endo-3-methylbicyclo[2.2.1]heptan-2-one	509.0 ^c	215.4
3,3-dimethylbicyclo[2.2.1]heptan-2-one	503.4	217.6
1,3,3-trimethylbicyclo[2.2.1]heptan-2-one	495.3	218.6
1,7,7-trimethylbicyclo[2.2.1]heptan-2-one	520.1	214.3
bicyclo[2.2.2]octan-2-one	545.9	212.1
3-methylbicyclo[2.2.2]octan-2-one	539.4	215.4
3,3-Dimethylbicyclo[2.2.2]octan-2-one	531.6 ^c	217.4

^a In ppm relative to external H_2O ; 30% by weight in dioxane with a drop of H_2^{17}O . ^b In ppm relative to internal Me_4Si ; 10% by weight in CCl_4 . ^c 10% by weight in dioxane.

Scheme III



Scheme IV



to the carbonyl group have been explored for the nonchair cyclohexanones incorporated in the bridged bicyclic ketones of Table II. Thus, the carbonyl group of bicyclo[2.2.2]octanones bisects the dihedral angle of the C_3 substituents. Methyls at C_3 give SCS values of -6 to -8 ppm, i.e., *shielding* as for equatorial substitution in a chair cyclohexanone, but slightly smaller in magnitude. A qualitatively similar situation obtains in the bicyclo[2.2.1]heptanone series as shown in Scheme IV, although the SCS values for the more sterically hindered *endo*-methyls are strikingly larger (ca. -15 ppm). The substituent shifts for methyl introduction at C_1 are also large and shielding (-8 to -10 ppm). Important deshielding effects of the carbonyl ^{13}C signals accompany these substitutions adjacent to the carbonyl.⁹ Finally, a 6-ppm deshielding effect on the ^{17}O resonance is promoted by the introduction

of two methyls at C₇. The *syn*-methyl, which has a geometrical relationship to the carbonyl group not unlike that of an axial C₃ methyl in a chair cyclohexanone, is probably the critical influence here, although this point needs to be checked.

Thus, it appears that methyl substitution at a carbon adjacent to the carbonyl results in variable substituent shifts depending on the dihedral angle such that the shift is largest when the methyl group is eclipsed with the carbonyl and decreases with increasing dihedral angle, ultimately changing sign somewhere between 60 and 120°. The opposite trends observed for the ¹⁷O and ¹³C chemical shifts of most of these carbonyl compounds may be a result of an important contribution from carbonyl group polarization by the substituents.

The large deshielding ¹⁷O shift induced by an axial C₃ methyl is more difficult to understand. A through-space interaction seems most reasonable, but this must surely take place through the intermediacy of the intervening carbonyl carbon, a center which is itself not affected very much by the substituent. Nonetheless, it should be noted that the substituent carbon-carbon bond in such compounds is reasonably proximate and roughly parallel to the axis of the carbon orbital involved in the π system of the carbonyl group, a situation which also obtains for an axial C₂ methyl and for the C₂-substituted series of Scheme III. Whether such interactions are a common source of the deshielding substituent effects in these diverse situations, however, remains to be established.

We are currently applying the information obtained in this study to the utilization of ¹⁷O data in the conformational analysis of acyclic systems.¹⁰

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- Spectra were obtained using a Varian XL-100-15 spectrometer equipped for Fourier transform operation at 13.56 MHz. A pulse width of 22 μs with a pulse interval of 0.11 s and a spectral width of 10 000 Hz was generally employed with 5000–20 000 scans. The reproducibility of chemical-shift measurements is estimated to be ±1 ppm. An ¹⁷O-enriched H₂O sample (otherwise isotopically normal) at 28 °C was used as an external reference. The spectra were generally obtained on dioxane solutions to which a drop of H₂¹⁷O was added a few minutes prior to measurement in order to isotopically enrich the carbonyl oxygen.
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- Support of this work by a research grant from the National Science Foundation is gratefully acknowledged. Manual A. Centeno was the recipient of a fellowship from Universidad de Oriente, Venezuela. We thank Norsk Hydro for a generous gift of ¹⁷O-labeled H₂O.

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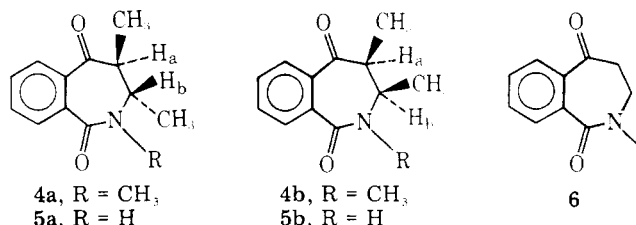
Received September 12, 1978

Photochemical Addition of Alkenes to *N*-Methylphthalimide. Stereochemistry of the Addition

Summary: Irradiation of *N*-methylphthalimide in the presence of *cis*- and *trans*-2-butene gave *cis*-1,6,7-trimethyl- and *trans*-1,6,7-trimethyl-3,4-benzo-6,7-dihydroazepine-2,5-dione, respectively, with greater than 95% stereospecificity, suggesting that the addition proceeds via a concerted π₂ + σ₂ addition.

Sir: We recently reported the photochemical addition of dienes,¹ alkenes,² and vinyl ethers³ to *N*-methylphthalimide to give 3,4-benzo-6,7-dihydroazepine-2,5-diones and have shown that the remarkable sensitivity of the addition process to alkene ionization potential² is due to competitive electron transfer quenching of the phthalimide excited state by the alkene.⁴ Similar results have been found by Maruyama's group,⁵ but the mechanism of the photochemical addition reaction is still open to question. Our initial suggestion on the gross mechanistic features of the reaction included either a two-step process involving a biradical intermediate (2) which could close to 3⁷ and subsequently open to the observed product, or a π₂ + σ₂ addition of the alkene to the C(=O)N bond of the imide to give 3 directly as outlined in Scheme I.

These mechanistic alternatives are amenable to a simple test; the direct π₂ + σ₂ process must be stereospecific, whereas the biradical intermediate 2 could result in loss of stereochemistry on the alkene moiety. Our substrate of choice for this investigation was 2-butene and irradiation of a mixture of *cis*- and *trans*-2-butene provided a mixture of 4a and 4b.



The determination of the stereochemistry of 4a and 4b is crucial to the study and should follow from analysis of the couplings observed for H_b in the two isomers. The spectrum of the mixture shows two doublets of quartets at δ 4.46 (*J* = 2.3, 7 Hz) and 3.96 (*J* = 9.9, 7 Hz). Stereochemical assignments for 5a and 5b have been made on the basis of equilibration results⁸ in which the most stable isomer, with *J*_{H_aH_b} = 2.3 Hz, was assigned the *trans* geometry (5a) and the isomer with

