A comparison of the DNMR behaviour of methyl 5,6-bis(2-methoxyphenyl)-1,4-dimethyl-7-oxobicyclo[2.2.1]hept-5-en-2-endo-carboxylate and its 7-oxa analogue

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Methyl 5,6-bis(2-methoxyphenyl)-1,4-dimethyl-7-oxobicyclo[2.2.1]hept-5-en-2-endo-carboxylate, a moderately crowded norbornene ester, exhibits complex VT-DNMR behaviour. A similar behaviour is not seen in its 7-oxa analogue, showing that conformational transmission from position 7 has a crucial influence on the distance parameters that govern the dynamic processes involving the substituents on the bicycloheptene framework.

The norbornene endo ester 1a exhibits \( ^1 \)H NMR detectable, temperature-variable dynamic behaviour\(^1 \) [compare sample spectra reproduced in Figures 1a and 1b illustrating the changes observed on lowering the temperature from 293 to 223 K; the population ratio of the two forms stabilized at low temperature was estimated at \( \sim 10:1 \) from the relative intensities of the salient –OMe lines in the original 223 K spectra]. Hindrance offered by the C(2) endo-ester function to the rotation of the magnetically highly anisotropic \( o \)-methoxyphenyl groups about the bonds of their attachment to the bicycloheptene framework was suspected as the factor underlying the dynamic processes. However, partial overlap and complexity of changes observed during high-to-low and low-to-high VT-NMR experiments, possibly arising from differences in the rates of change of line-widths of the different signals, effectively prevented keeping track of the line associations and, since coalescence temperatures could not be determined with any precision, no thermodynamic parameters could be extracted.

The preferred rotational orientations of the aryl rings of the cis-stilbene part of a 1,2-cyclopentene, restricted to an envelope conformation in the bridged bicyclic system 1a, could well be the resultants of additional intramolecular steric forces from the bridgehead methyls, and electrostatic influences as well, from the C(2) endo ester function. The \( o \)-methoxyphenyl groups were, therefore, taken as attaining conformational stabilization at high rotational angles in relation to the C(5)-C(6) bond as the temperature was lowered in order that mutual interactions be brought to a minimum. A recent X-ray crystallographic\(^2 \) determination has confirmed not only that this is the case (for the crystalline phase of 1a) but also that the C(2) ester function has the endo configuration.

A mechanical analogy, based on an assumption that bonds tend to maintain optimal overlap, hinted at a possibility that replacement of the carbonyl at position 7 in 1a by an ether linkage may alter the distance parameters among the substituents of the bicycloheptenone (by some form of conformational transmission) that VT-DNMR behaviour would not be observable any longer. In the schematic above, A could represent an initial situation where X happens to be \( sp^2 \) hybridized (\( >C=O, >C=NR \)). Angle C(1)-X(7)-C(4) tends to attain the "trigonal value" of \( \sim 120^\circ \), moving C(1) and C(4) apart and bringing the R’s closer. A reduction in the magnitude of angle C(1)-X(7)-C(4) to a "tetrahedral value" (\( \sim 109^\circ \)) on replacement of \( sp^2 \) X with an \( sp^3 \) X (\( >CHOH, heteroatom \)) could allow the R’s to move apart and, as shown in B, hindrance to their rotation could be
Figure 1a—$^1$H NMR spectrum of 1a. Temperature 293 K; Solvent CDCl$_3$.

Figure 1b—$^1$H NMR spectrum of 1a. Temperature 223 K; Solvent CDCl$_3$. 
lessened even though that could be at the cost of some increase in R–Me nonbonded interaction.

X-ray crystallographic studies disclosed, however, that the existing situation in 1a (and in similarly substituted C(7) sp² bicycloheptenones) is better described by B than A: angle C(1)-C(7)=O-C(4), at a value close to 99°, is considerably strained and the external angles C(6)-C(5)-R and C(5)-C(6)-R opened out somewhat (~127°), showing that R–R interaction may have already been attenuated. The closing-in of angle C(1)-X(7)-C(4) was, presumably, a constraint imposed by a need to maintain a certain nonbonded C(1)-C(4) distance in the boat form of a cyclohexene and, since it was nearer in magnitude to a C(1)-sp³ X(7)-C(4) angle, replacement of sp² X by an sp³ X at position 7 could only be expected to lead to some relief of local angle strain and not to any greater optimization of internal strain by conformational transmission of the type suggested by the mechanical analogy. The VT-DNMR behaviour of the 7-oxa analogue 1a, for example, could not be expected to be very different from that of 1a itself.

Compound 1a was the major component in a mixture of products obtained from the [4π + 2π] cycloaddition of methyl methacrylate (Mma) to cyclopenta-
dienone Cp (Scheme I). Efforts to obtain its 7-oxa analogue via a parallel procedure, employing furan Fu as the diene, were not successful, there being no reaction. In some trials, under the so-called “catalyzed” condition of adding BF₃-Et₂O to the reaction mixture, the cycloaddition of methyl acrylate (Ma) to Fu did not stop at the desired stage of the formation of the bridged bicyclic 7-oxa adduct, but proceeded to give, by oxygen extrusion followed by aromatization, methyl 2,5-dimethyl-3,4-bis(2-methoxyphenyl)benzoate, an o-terphenyl, as the sole product. In further attempts, a mixture of Ma and Fu was let stand over a period of several days in the absence of any added “catalyst” and the reaction was monitored by TLC. Slow formation of two major, apparently closely related products in an approximate ratio of 3:7 was noticed. Isolated as semi-crystalline, waxy solids, they could not be wholly freed from cross-contamination (attempted purification by chromatographic means led to severe loss of material). While IR spectra disclosed the presence of an ester carbonyl, a double bond and aromatic rings in each component, HRMS data gave definite indication that they were indeed isomeric: the less abundant component - Mass Found 394.1789; the more abundant component - Mass Found 394.1790.
Figure 2a—$^1$H NMR spectrum of 2a. Temperature 303 K; Solvent CDCl$_3$.

Figure 2b—$^1$H NMR spectrum of 2b. Temperature 303 K; Solvent CDCl$_3$. 
Figure 3a—$^1$H NMR spectrum of 1b. Temperature 303 K; Solvent CDCl$_3$.

Figure 3b—$^1$H NMR spectrum of 1b. Temperature 223 K; Solvent CDCl$_3$. 
[C\textsubscript{2}H\textsubscript{5}O\textsubscript{3}] (on the basis of structures 2) requires 394.1780\superscript{2}.

With the exception of the extra presence of two deshielded 3H singlets, clearly ascribable to the ary1-\textit{OMe} groups, the \textsuperscript{1}H NMR spectra of the less and more abundant components (Figures 2a and 2b) closely resembled, respectively, those of the earlier synthesized methyl 5,6-diphenyl-1,2,4-trimethyl-7-oxabicyclo[2.2.1]hept-5-ene-2-exo- and -2-endo-carboxylates\superscript{3,6}, analogues of 2a and 2b which, without o-methoxy substitution on the aryl rings, could not be expected to exhibit NMR-detectable dynamic phenomena. Formed in the approximate ratio of 3:7, the -\textit{OMe} chemical shifts in these two esters were \(\delta \text{ 3.80 and 3.40, configurational assignments were based on the criteria that exo isomers are not dominant in the formation of bicyclo[2.2.1]hept-5-ene-2-carboxylic esters by }[4\pi + 2\pi]\text{ cycloadditions and that the -\textit{OMe} singlets in the exo methyl esters occur at lower fields than in their endo analogues. For example, the endo-ester dominates in the formation of methyl 5,6-diphenyl-1,2,4-trimethyl-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxylate and the chemical shift of the -\textit{OMe} singlet is, in its case, \(\delta \text{ 3.46, while that in the less abundant exo ester it is } \delta \text{ 3.72.}\)

Since the ester -\textit{OMe} chemical shifts in the minor and major products of cycloaddition of Ma to Fu were, respectively, \(\delta \text{ 3.62 and 3.4, structures 2a and 2b could be clearly assigned to them on the same bases. The similarity of the } \text{\textsuperscript{1}H NMR spectra of these products with those of their unmethoxylated analogues included analogous differences in chemical shifts of the pairs of -\textit{CMe} lines in the exo and endo isomers. The component assigned the exo configuration 2a had -\textit{CMe} lines, at \(\delta \text{ 1.41 and 1.56 (}\Delta\delta\text{ 0.15 ppm), less separated than in that assigned the endo configuration 2b where the -\textit{CMe} lines, at } \delta \text{ 1.53 and 1.82 (}\Delta\delta\text{ 0.29 ppm), were separated to a greater extent. The corresponding shifts in the unmethoxylated analogues were, respectively, } \delta \text{ 1.64 and 1.76 (}\Delta\delta\text{ 0.12 ppm) and } \delta \text{ 1.64 and 1.96 (}\Delta\delta\text{ 0.32 ppm). Additionally, the components of the 3-spin patterns seen in the } \delta \text{ 2-3.5 regions (not yet individually assigned to the C(2) and C(3) exo and endo protons), clearly different from each other, resembled closely the patterns seen in the respective unmethoxylated analogues.}

A direct comparison of the two 7-oxa-ester components with the 7-oxo ester 1b, the C(2) desmethylylated analogue of 1a, was immediately possible because 1b had been shown earlier\superscript{1} to resemble 1a closely in its VT-DNMR behaviour (compare Figures 3a and 3b with Figures 1a and 1b). The room temperature \textsuperscript{1}H NMR spectrum of 2b (Figure 2b) showed no evidence of broadening of any of the salient lines (-\textit{CMe}, -\textit{OMe}) even remotely resembling the features seen in the room temperature spectrum of 1b (Figure 3a). The line-widths at 30\textsuperscript{2} K of salient lines remained as narrow as those in the 303 K \textsuperscript{1}H NMR spectrum (Figure 2a) of its exo ester analogue 2a which cannot be expected to show VT-DNMR behaviour. On the other hand, it bore essential resemblance to the low temperature spectrum of 1b (Figure 3b). Even though it was unlikely that one was operating in a post-coalescence regime at room temperature in the case of 2b, the sample was cooled to 223 K and its \textsuperscript{1}H NMR spectrum recorded. Barring some slight broadening, no bifurcation of any of the lines was observed. The conclusion that activation energies associated with interconversions between the stabilized forms of 1a have been lowered enough on replacement of the carbonyl at position 7 by an ether linkage to render VT-DNMR behaviour unobservable in 2b seems inescapable.

X-ray crystallographic analysis, which may provide answers to the precise manner in which hindrance to the rotation of the o-methoxyphenyl groups is attenuated in 2b compared with 1b, must await success of our current efforts to obtain a suitable crystal of the pure material.

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Reference
NOTES


2 Houk K N & Luskus L J, J Am Chem Soc, 93, 1971, 4606; the endo-methyl, exo-ester analogue of 1a has been isolated from the product mixture by Dr I N N Namboothiri in more recent work.
