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Conformationally Favored CH---O Intramolecular Interaction and Restricted Rotation in Sterically Crowded Ester

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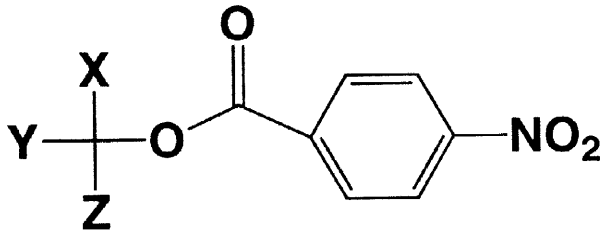
Abstract : Restricted rotation of a sterically crowded ester, which has two *tert*-butyl groups and one isopropyl group, was studied by dynamic NMR spectroscopy. The intramolecular through-space interaction between the methine hydrogen of the isopropyl group and the carbonyl oxygen exists in the ester. Bulky alkyl substituents in close proximity cause both restricted rotation of the $C(sp^3)$-$C(sp^3)$ single bond and CH---O intramolecular interaction. © 1998 Elsevier Science Ltd. All rights reserved.

Weak molecular interactions such as CH---π [1], CH---N[2], and CH---O[2] play important roles in both biological and material sciences. Recently we reported intramolecular through-space interaction between the γ-methyl hydrogen and the oxygen lone pair (CH_3---O) in sterically crowded alcohols identified by ^{17}O NMR spectroscopy.[3]

In this paper, we describe very interesting findings about restricted rotation and an intramolecular CH---O interaction in the sterically crowded ester (**1a**) studied by NMR spectroscopy.

2-Methyl-1,1-di-*tert*-butylpropyl *p*-nitrobenzoate (**1a**) was prepared from *tert*-butyllithium, *iso*-butyryl chloride, and *p*-nitrobenzoyl chloride as previously reported.[4] For 1,1-diethyl-2-methylpropyl *p*-nitrobenzoate (**1b**), the corresponding alcohol and *p*-nitrobenzoyl chloride were used for the synthesis.



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1a : X=Y=^{t}Bu, Z=^{i}Pr

1b : X=Y=Et, Z=^{i}Pr

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For NMR spectroscopy, samples were prepared by dissolving ca. 50 mg ml^{-1} of material in a mixture of 90% CD_2Cl_2 and 10% $CDCl_3$. The ^1H and ^{13}C NMR spectra were recorded on a JEOL α-500 spectrometer operating at 499.65 MHz for ^1H nuclei and at 125.77 MHz for ^{13}C nuclei, respectively. A Bruker DMX-750 spectrometer was also used for ^{13}C NMR spectra (operating at 188.64 MHz). Tetramethylsilane was used as an internal standard.

At room temperature, the ^{13}C NMR signal (22.6 ppm at 297.0 K) of a methyl carbon in the isopropyl group of **1a** was slightly broader than other signals (Fig. 1-a). As the temperature decreased, the signal broadened significantly as shown in Fig. 1-b and finally split into two signals with equal intensity (Fig. 1-c). A similar line-shape change was observed about the quaternary carbon signal (45.1 ppm at 297.0 K) of the *tert*-butyl group of **1a**. There were no line-broadening nor splitting in the signals of the methine carbon (32.8 ppm at 297.0 K) in the isopropyl group and the quaternary carbon (103.3 ppm at 297.0 K) connected with the ester group. These phenomena can be explained by the restricted rotation around the $C(sp^3)$-$C(sp^3)$ single bond between the methine carbon of the isopropyl group and the quaternary carbon connected with the ester group.

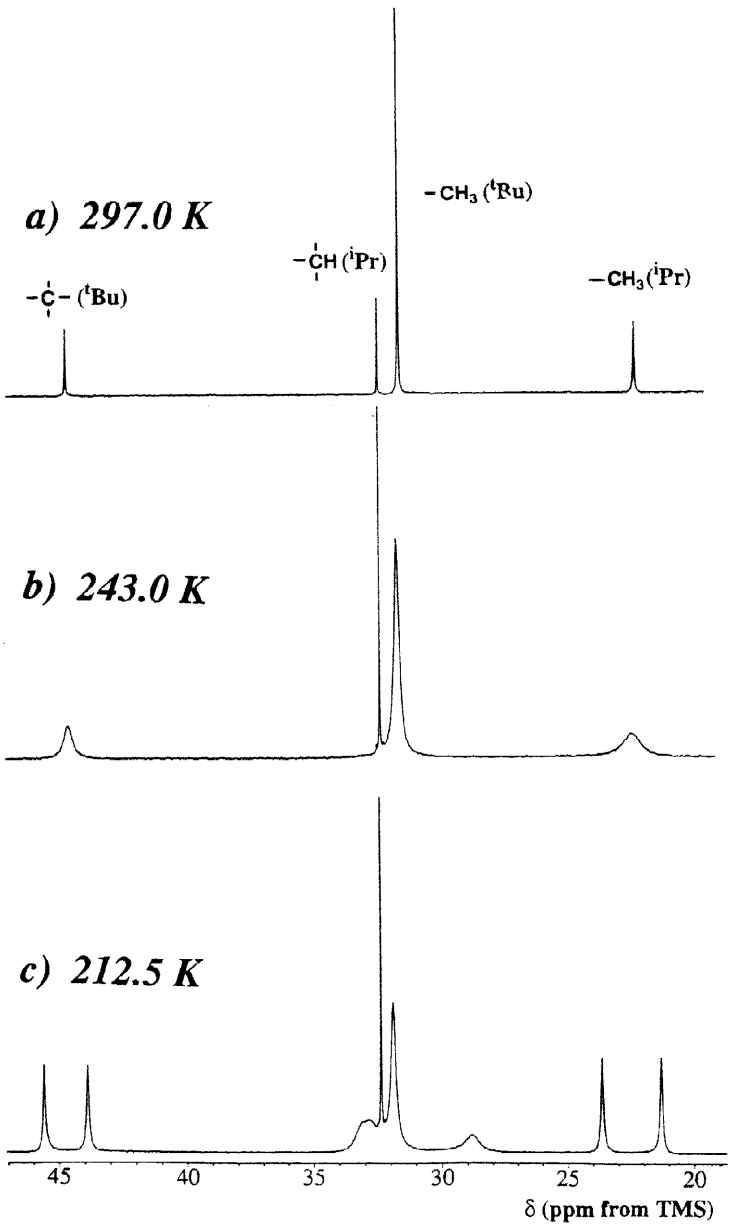
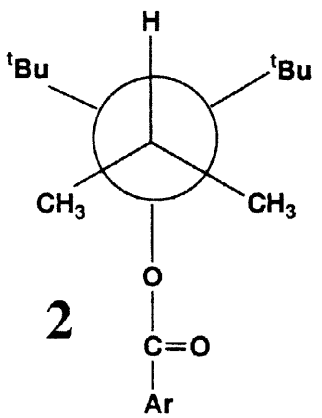
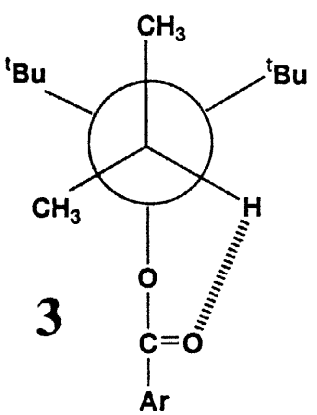
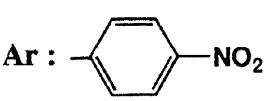


Fig. 1. Temperature-dependent ^{13}C NMR spectra of the alkyl region in **1a** at 125.77 MHz.







Two methyl carbons of the isopropyl group are magnetically equivalent in the anti conformer, **2**. In the gauche conformer, **3**, however, these two carbons exist in the magnetically nonequivalent conformation during the freezing of the internal rotation around the bond. As the two equal intensity signals were observed for the methyl carbons, conformer **2** does not exist at the low temperature as 212.5 K. The conformer **3** and its enanthiomer **3'**, both of which are magnetically equivalent, exist at low temperature. So the temperature dependent spectra as shown in Fig. 1 reflect the exchange between conformers **3** and **3'**. In the case of **1b**, no line-broadening nor splitting in the signals were observed at the temperatures between 298 K and 178 K. This suggests that the steric hindrance among the two *tert*-butyl groups and the isopropyl group in **1a**, which exist in close proximity, produces the higher rotational barrier.

The exchanging rates for the rotation of the $C(sp^3)$-$C(sp^3)$ single bond of **1a** described above were determined by the complete line-shape analyses. Calculations for complete line-shape analyses were performed with a FACOM M-1800/30 computer using the computer program EXNMR0[5] which is based on the modified Bloch equation method.[6] The activation parameters for the rotation were obtained by using the Eyring equation[7] as follows;

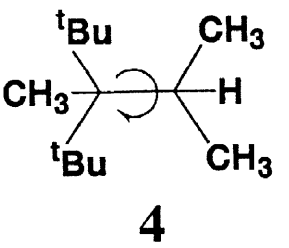
Rotational barrier obtained from the analysis of the methyl carbons of the isopropyl group:

$\Delta G^{\ddagger}$=11.3±0.5 kcal/mol, $\Delta H^{\ddagger}$=9.1±0.3 kcal/mol, $\Delta S^{\ddagger}$=-7.7±0.7 e.u. at 298.0 K

Rotational barrier obtained from the analysis of the quaternary carbons of *tert*-butyl groups:

$\Delta G^{\ddagger}$=11.3±0.5 kcal/mol, $\Delta H^{\ddagger}$=9.3±0.3 kcal/mol, $\Delta S^{\ddagger}$=-6.7±0.7 e.u. at 298.0 K

These experimentally obtained values are equivalent within the experimental error and reveal the rotational barrier around the bond between the methine carbon of the isopropyl group and the quaternary one connected with the ester group. This rotational barrier in **1a** is similar as that in highly-branched hydrocarbon (**4**, $\Delta G^{\ddagger}$=11.0 kcal/mol).[8] This suggests that the transition state for the rotation in **1a** exists in very overcrowded environment.



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For methyl carbon of the *tert*-butyl group, the signal became significantly broader as the temperature decreased (Fig. 1-b and 1-c). At very high magnetic field (188.64 MHz for ^{13}C nuclei, which corresponds to 750.13 MHz for ^{1}H nuclei) and low temperatures, the six signals with almost equal intensities could be observed as shown in Fig. 2. These line-shape changes are explained by the restricted rotation around the $C(sp^3)$-$C(sp^3)$ bond between the quaternary carbon of the *tert*-butyl group and the quaternary carbon connected with the ester group. Unfortunately, the line-shape changes were so complicated that the activation parameters for the rotation could not be obtained. The existence of the six signals for the two *tert*-butyl groups of **1a** means that the six carbons are in magnetically non-equivalent environments. These signals spread over about 5 ppm in width, so the environments of

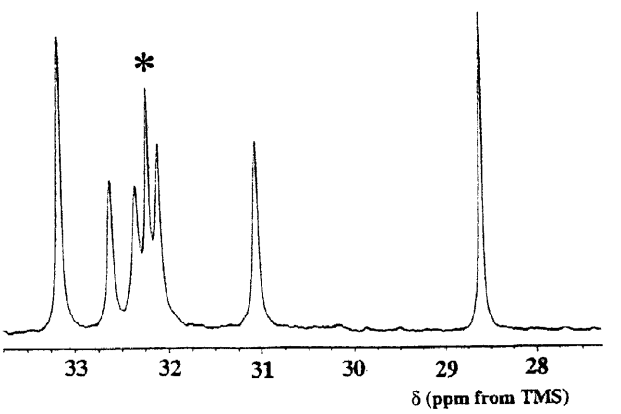

Fig. 2. The ^{13}C NMR spectrum of the alkyl region in **1a** at 188.64 MHz and at 187.7K.
* The methine signal of the isopropyl group.

the six methyl groups are very different from each other. It is necessary to consider some kinds of interaction, as the six methyl signals become non-equivalent. Both repulsion of the bulky substituents and the CH---O interaction as discussed below are possible reasons for the non-equivalency.

In the ^{1}H NMR spectra of **1a**, as is similar in the ^{13}C NMR spectra, line-shape changes of methyl protons in both isopropyl and *tert*-butyl groups occurred as the temperature decreased. Besides these phenomena, one more characteristic thing is that a chemical shift of the isopropyl methine proton of **1a** is observed in such remarkably low field of 3.961 ppm in $CDCl_3$ at 295.2 K. The ^{1}H NMR chemical shift of the corresponding proton in **1b** is 2.568 ppm under the same conditions. Because the extent of the chemical shift difference is too large, as large as 1.4 ppm between **1a** and **1b**, CH---O interaction such as a weak hydrogen bonding is the reason for this extremely low field shift in **1a**. Chemical shift anisotropy of the aromatic ring and/or the carbonyl group should be considered. However, the large chemical shift difference indicates that the CH---O interaction is the dominant reason for the low field shift. The non-bonding length between the methine hydrogen of the isopropyl group and the oxygen of the carbonyl group is approximately 2.2 Å, calculated by the structural optimization of MM2 program using Molskop system (JEOL). It suggests that this molecule can take the conformation which has the CH---O interaction between the methine hydrogen of the isopropyl group and the oxygen of the carbonyl group. Many intramolecular interactions of CH---O with short distance have so far been found, and most of these CHs belong to acidic type of the CH group activated by the neighboring functional group.[2] However, the presence of CH---O interaction in non-activated aliphatic hydrogen is rare example to our knowledge.[9,10] Thus, the CH---O interaction in **1a** is an important case.

In conclusion, the strongly restricted rotation of the isopropyl group and the *tert*-butyl group in **1a** due to the steric hindrance of these substituents is clearly observed by the temperature dependent ^{13}C NMR spectroscopy. It is also observed that the CH---O interaction between the methine proton of the isopropyl group and the carbonyl oxygen occurred in the ester. These findings are explained by the severely overcrowded substituents, which exist in close proximity, in **1a**.

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