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Application of the model-free approach to low molecular weight systems with hindered internal rotation: cinnamoylmesitylene

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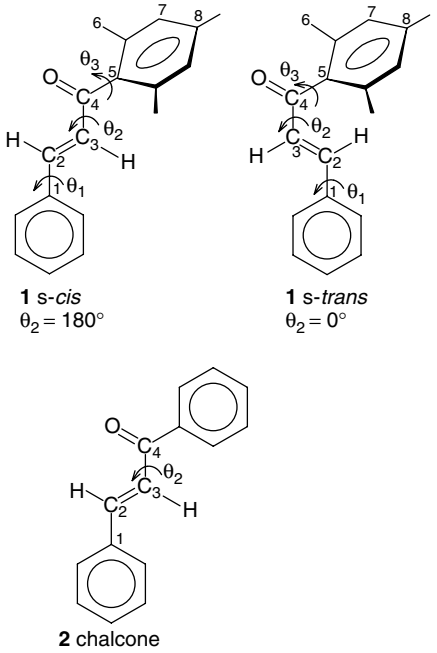
We investigated the molecular dynamics of the molecule of cinnamoylmesitylene, a substituted chalcone. Known rotation barriers for the O═C-4—C-3═C-2 bond of substituted chalcones are in the range of values accessible to modern NMR techniques. The internal rotation about the C-3—C-4 bond is found to be fast relative to the complete lineshape analysis (CLSA) time-scale. To determine the activation parameters of overall and internal motions of the molecule, the Lipari–Szabo model-free analysis of the relaxation times and heteronuclear NOE data was used instead. Simultaneous analysis of both heteronuclear spin–lattice relaxation times and NOE data for the two carbon atoms C-2 and C-7 in the O═C-4—C-3═C-2 and mesitylene fragments at different temperatures was performed. The correlation times and activation energies of overall and internal motions and the generalized order parameter, which are measures of the molecular mobility, were thus determined. The standard enthalpies of activation, $\Delta H^{\neq}$, calculated from the experimental data for C-2 and C-7, are 5.6 and 6.6 kcal mol^{-1}, respectively. Theoretical estimates of the barriers to internal rotations by *ab initio* MO calculations were made to verify the experimental results. The agreement between the NMR and theoretical results was good. Copyright © 2003 John Wiley & Sons, Ltd.

KEYWORDS: NMR; ^{13}C NMR; NOE; hindered internal rotation; model-free approach; cinnamoylmesitylene

INTRODUCTION

Nucleophilic addition of bulky organometallic reagents to cinnamoylmesitylene (**1**) is highly regio- and stereoselective,[1] which has been attributed to the sterically blocked carbonyl group and also to hindered rotation within the conjugated system.[2–5] The observed regio- and stereoselectivity effects also show significant temperature dependences, leading to the problem of determining the barriers to internal rotation in this compound (Scheme 1). Compound **1** is a substituted chalcone (**2**). Known rotation barriers for the O═C-4—C-3═C-2 bond of this class of compounds[2–5] are in the range of values accessible to modern NMR techniques.

The most widely used NMR method for investigating internal rotation is complete lineshape analysis (CLSA) of NMR spectra measured at variable temperature.[6] The lineshape analysis is restricted to lifetimes between 1 and 10^{-4}–10^{-5} s, i.e. the range of reliably measurable rate constants is between ca 1 and 10^4–10^5 s^{-1}. This method is not applicable when the exchange process is fast relative to the so-called 'chemical shift time-scale.' If NMR lifetimes are so short as to play the role of correlation times in nuclear relaxation, the spin–lattice relaxation time T_1 and the



Scheme 1

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nuclear Overhauser effect (NOE) can be used to determine the exchange rates. Interpretation of the experimental data within the framework of the model-free approach[7,8] allows one to determine the correlation times of overall and internal motions and the generalized order parameter, which are measures of molecular mobility. Clore and co-workers[9,10] further extended the method to account for the presence of both slow and very fast internal motions. Analysis of the temperature dependence of the spin–lattice NMR relaxation times and NOE can be used to extract the activation parameters of the motions responsible for nuclear relaxation.

Analysis of heteronuclear relaxation data (^{13}C and/or ^{15}N) and NOE by means of the model-free approach has been widely used to investigate molecular dynamics of large molecules (e.g. proteins), where the overall slow motion and the fast internal motions occur on two different time-scales.[11–14] Measurements of ^{13}C spin–lattice relaxation times and NOE have also been used to investigate the molecular dynamics of medium-sized molecules with fast internal motions. Gillies and co-workers[15–20] studied the molecular motion and the rotational barriers in a series of dicyclohexyl compounds with two or three carbon atoms between the cyclohexyl rings. The experimental data were successfully analyzed by a two-correlation times approach. Wang *et al*.[21] studied the restricted group internal rotation and anisotropic overall molecular tumbling in some steroid natural products by using a similar approach. The method has also been applied to di- and tetrasaccharides.[22]

The aim of this study was to investigate the molecular dynamics of cinnamoylmesitylene. The internal rotation about the C-3—C-4 bond was found to be fast relative to the CLSA time-scale: we failed to observe either intermediate or slow exchange spectra even at the lowest temperatures used. The Lipari–Szabo model-free approach was used instead to determine the activation parameters of overall and internal motions of the molecule. Theoretical estimates of the barriers to internal rotations by *ab initio* MO calculations were made to verify the experimental results.

EXPERIMENTAL

The synthesis of **1** is described in Ref. 1.

A sample for NMR measurements was prepared by dissolving 40 mg of **1** in 0.6 ml of methylene-d_2 chloride (CD_2Cl_2). The solution was degassed by several freeze–pump–thaw cycles on a vacuum line to remove the dissolved oxygen and the NMR tube was then sealed.

NMR spectra

NMR spectra were recorded on a Bruker DRX-250 spectrometer, operating at 250.13 MHz for ^{1}H and 62.9 MHz for ^{13}C, using a 5 mm dual ^{1}H–^{13}C probehead.

^{13}C spin–lattice relaxation times, T_1, were measured at nine temperatures in the range 171.6–297.0 K. All measurements were performed using the inversion–recovery pulse sequence with power gated decoupling to obtain decoupled ^{13}C signals. The spectral width was 200 ppm and the number of data points was 16K. At least 10 τ values were used to obtain the experimental data points for the T_1 relaxation curve. The number of transients for each delay was 128 and a relaxation period of 30 s (at least five times the longest T_1) was used. The T_1 values were derived from a three-parameter exponential fit, integrated in the Bruker software. All values are average of at least two measurements.

The NOEs were calculated as the ratio of signal amplitudes measured from two ^{13}C spectral data sets. The first data set was collected with power gated decoupling, that is, the decoupler was gated on before and during the acquisition period, thus producing decoupled ^{13}C spectra with signals enhanced by NOE. The spectra in the second data set were acquired by irradiating the protons only during the acquisition period and the decoupler was off during the recovery delay. In this case, the signals in the ^{13}C spectra are without NOE but decoupled from protons. To avoid heating effects, thus disturbing the temperature stability, a composite pulse decoupling with the WALTZ16 pulse sequence was applied. A relaxation delay >10 times the longest proton T_1 at the temperature of measurement was used in each experiment. An exponential multiplication of 1 Hz line broadening was applied before Fourier transformation of the spectra. The NOE values were calculated as the average of two measurements. The spectra were recorded at the same temperatures as for the T_1 measurements.

Variable-temperature measurements

Variable-temperature measurements were carried out with a standard Bruker variable-temperature VT-1000 unit. The sample temperature was independently measured with a capillary in the sample tube containing a mixture of CCl_3F, CD_3OD, CF_3COOH and CH_2Cl_2 in volume ratio of 8 : 6 : 1 : 1.[23] The internal temperature of the sample was calculated by using the following equation:

$$T(\mathrm{K}) = 256.9 + 0.401\Delta\nu - 6.9696 \times 10^{-4}\Delta\nu^2 + 1.728 \times 10^{-6}\Delta\nu^3 \quad (1)$$

where $\Delta\nu = \nu_{CH_2Cl_2} - \nu_{OH}$ Hz at a 250.13 MHz spectrometer proton frequency. The temperature was measured before and after each experiment and the temperature stability was found to be ±0.1–0.5 K.

COMPUTATIONAL PROCEDURES

Analysis of ^{13}C spin–lattice relaxation times (T_1) and heteronuclear NOE data (η) by the model-free approach

Relaxation of ^{13}C nuclei that have one or more directly attached protons is dominated by dipole–dipole interactions with protons. In such cases, longitudinal relaxation rate, $R_1 = 1/T_1$, and the NOE factor, η, are given by the following equations:

$$R_1 = \frac{1}{T_1} = \frac{\hbar^2\gamma_C^2\gamma_H^2}{4r_{CH}^6}\left(\frac{\mu_0}{4\pi}\right)^2 [J(\omega_H - \omega_C) + 3J(\omega_C) + 6J(\omega_H + \omega_C)] \quad (2)$$

$$\eta = \frac{\gamma_H[6J(\omega_H + \omega_C) - J(\omega_H - \omega_C)]}{\gamma_C[J(\omega_H - \omega_C) + 3J(\omega_C) + 6J(\omega_H + \omega_C)]} \quad (3)$$

where $\hbar = \frac{h}{2\pi}$ is the modified form of Planck's constant, γ_H and γ_C are gyromagnetic ratios of ^1H and ^{13}C, respectively, ω_H and ω_C are ^1H and ^{13}C Larmor frequencies, r_{CH} is the C—H bond length and $J(\omega)$ is the spectral density function for the motion of the CH vector.

In the case of isotropic rotation of a rigid molecule, $J(\omega)$ is a simple Lorentzian:

$$J(\omega) = \frac{2\tau_M}{1 + \omega^2\tau_M^2} \tag{4}$$

where τ_M is the molecular rotational correlation time.

In the presence of anisotropic rotation or internal motions, they additionally modulate the nuclear relaxation and the Lorentzian model with one correlation time is no longer valid. For such systems, the relaxation data can be analyzed within the framework of the so-called model-free approach, developed by Lipari and Szabo.[7,8] The advantage of this method in comparison with other methods for the analysis of relaxation data[24–26] is that it does not require any specific model for molecular motion to be invoked. In the model-free analysis, the motion of a flexible molecule is described by three parameters: (1) a generalized order parameter, S^2, (2) an effective correlation time, τ_e, and (3) another correlation time, τ_M. The model-free approach is based on the assumption for two statistically independent types of motions, a rapid, local (internal) reorientation, depicted by the correlation time τ_e, and a slower, global molecular tumbling, described by τ_M. The generalized order parameter S^2 is a measure of the degree of spatial restriction of the local motion. In the model-free approach, the spectral density function is given by the following equation:

$$J(\omega) = \frac{2}{5}\left[\frac{S^2\tau_M}{1 + (\omega\tau_M)^2} + \frac{(1 - S^2)\tau}{1 + (\omega\tau)^2}\right] \tag{5}$$

with $\tau^{-1} = \tau_M^{-1} + \tau_e^{-1}$.

The limiting values of the generalized order parameter S^2 ($0 \le S^2 \le 1$) have the following meaning: when $S^2 = 0$ all conformations occur with equal probability, whereas when $S^2 = 1$ the molecule is restricted to a single conformation.

When the internal motion is extremely fast ($\omega\tau \ll 1$) and the order parameter is not too small, $S^2\tau_M \gg (1 - S^2)\tau$, the spectral density function can be reduced to depend on the overall correlation time, τ_M, only:

$$J(\omega) = \frac{2}{5}\frac{S^2\tau_M}{1 + \omega^2\tau_M^2} \tag{6}$$

The correlation times can be considered as rate parameters and their temperature dependence can be treated by the Arrhenius equation to derive the activation energy of the respective molecular motion:

$$\tau_c = \tau_{c0}\exp\left(\frac{E_{ca}}{RT}\right) \tag{7}$$

where subscripts c ≡ M or e apply for overall (molecular) or internal motions, respectively, and E_a is the Arrhenius activation energy. The generalized order parameter S^2 is considered to be independent of temperature.

On substituting the full or reduced density functions [Eqn (5) or (6)] into Eqns (2) and (3), one obtains the interdependences of the measured data, R_1, η, the correlation times, τ_M, τ_e, and the generalized order parameter, S^2. Equation (7) is also incorporated in the set of Eqns (2) and (3), thus introducing the activation energies E_{aM} and E_{ae}, which are in fact the parameters we are seeking. As a result, we obtain the five parameters that characterize the molecular dynamics: S^2, τ_M, τ_e, E_{aM} and E_{ae}. These are evaluated by simultaneously solving Eqns (2) and (3). The total number of the available experimental data is $N_{total} = N_{R_1} + N_\eta$.

Programs used for the evaluation of these motional parameters from the NMR data and the respective error analysis were written in FORTRAN. The minimization procedure and the definition of the target function can be obtained from the authors on request.

As an alternative, it is also possible to combine Eqns (2) and (3) by multiplying them:

$$R_1 \times \eta = \frac{\hbar^2\gamma_C^2\gamma_H^2}{4r_{CH}^6}\left(\frac{\mu_0}{4\pi}\right)^2\frac{\gamma_H}{\gamma_C}[6J(\omega_H + \omega_C) - J(\omega_H - \omega_C)] \tag{8}$$

This equation could be used to find the five parameters of interest. However, in this case the number of the data set is reduced to half of the total number of all data: $N_{total} = N_{R_1} = N_\eta$. This means that the accuracy of the calculation is greatly reduced. That is why we used the former approach.

Ab initio calculations

To obtain theoretical estimates of the rotational barriers in the molecule of **1** with respect to the two single bonds with potentially hindered rotation, we use *ab initio* MO calculations with complete optimization of the molecular geometry at fixed values of angles θ_1 (phenyl rotation) and θ_2 (mesitoyl rotation) (see Scheme 1). We assume that the rotation defined by θ_3 is too strongly hindered,[27] and optimize the geometry with no constraints on this dihedral angle.

The calculations are carried out with the GAMESS-US program.[28] The geometries of conformers between 0° (s-*cis*) and 180° (s-*trans*) for θ_1 and θ_2 were completely optimized at the RHF/3–21G and 6–31G* basis set levels.[29] To obtain more reliable rotational barriers we carried out single-point energy calculations for conformations at values of $\theta_2 = 0°$ and 180° (equilibrium) and 90° (maximum) at the MP2/6–31G*//RHF//6–31G* level of theory.

RESULTS AND DISCUSSION

The assignment of the signals in the ^1H and ^{13}C NMR spectra of **1** was done by taking into consideration the magnetic anisotropy effect of the neighboring groups and was confirmed by two-dimensional inverse detected heteronuclear (C–H) correlation through one bond (HMQC experiment). The non-protonated carbons have long T_1 relaxation times and small NOE factors. In this respect they are prone to larger experimental errors and were not used in the calculations.

It is expected that the reorientation around the C-3—C-4 bond (see Scheme 1) is restricted owing to steric hindrance. The ^{13}C and ^{1}H NMR spectra recorded at different temperatures show that even at the lowest temperature (162.1 K) the barrier to internal rotation is still very low to be investigated by CLSA. The width and the shape of the spectral lines do not show significant temperature changes, so the application of CLSA to investigate the interconversion of the rotamers is not possible.

The Lipari–Szabo model-free analysis of the relaxation times and heteronuclear NOE data can be used instead to calculate the activation parameters of the process. In the presence of restricted internal motion, the averaging of angular fluctuations of the C—H vectors is no longer possible and the nuclear relaxation is influenced in a characteristic way by the rate of these fluctuations. This means that the relaxation of C-2 and C-3, which is governed mainly by the dipole–dipole interactions with the attached protons, is modulated not only by the overall molecular tumbling but also by the contribution of hindered internal rotation. At most temperatures, the C-3 signal is overlapped by the signals of the benzene ring and, consequently, cannot be used in the calculations.

The *ab initio* calculations show that the rotation of the mesityl fragment is strongly hindered and the fragment assumes a dihedral angle of 90° relative to the plane formed by the two double bonds, O═C-4—C-3═C-2 (see Scheme 1). This means that the contribution of the mesityl rotation to the relaxation behavior of C-7 can be neglected. That is why we suppose that the relaxation of C-7 from the mesityl fragment is modulated by the same processes as that of C-2 and C-3, i.e. by the overall molecular motion and the restricted internal rotation about the C-3—C-4 bond.

The relaxation of the protonated carbon atoms from the benzene ring is mainly affected by the fast internal rotation of the benzene ring itself and cannot be used for evaluation of the correlation times of overall and internal rotation around the C-3—C-4 bond.

The experimental data (relaxation rates and NOE values) for C-2 and C-7 taken at different temperatures were simultaneously fitted to Eqns (2) and (3) to optimize the five parameters, S^2, τ_M, E_{aM}, τ_e and E_{ae}, using Eqns (7) and (5). For comparison, calculations with the reduced spectral density function, Eqn (6), were also carried out. This model is applicable in case of very fast internal motions when $\tau_e \ll \tau_M$.[7,8] We assume that the global molecular motion is isotropic, which is a widely used approximation.[30–32] The generalized order parameter S^2 is considered to be independent of temperature, as it is not a rate parameter. The results for carbon atoms C-2 and C-7 are given in Table 1. The last column in Table 1 shows the values of χ^2, which can be interpreted as a criterion for goodness of fit. The values of the activation energy for the global motion, E_{aM}, calculated by the full and the reduced spectral density function are very close. Fitting of the experimental data with a two-correlation times function, however, gives a smaller χ^2 value than fitting with a one-correlation time function. This result means that the relatively restricted internal rotation around the C-3—C-4 bond indeed makes a definite contribution to the relaxation parameters of the carbon atoms C-2 and C-7. The results obtained from C-2 and C-7 are in good agreement, which supports the adequacy of the two-correlation times model. The average value of $S^2 \approx 0.5$, which is a measure of the spatial restriction of the internal motions, indicates that the rotation around the C-3—C-4 bond is neither completely free nor entirely restricted.

Figure 1(a) and (b) present the temperature dependence of the relaxation rates, R_1 (circles) and the best fit (solid curves) obtained by simultaneously fitting the experimental relaxation and NOE data to a two-correlation times function (five-parameter fit) for C-2 and C-7, respectively. The dashed line represents the best simultaneous fit of the experimental R_1 and NOE data with the reduced Lorentzian spectral density, assuming one correlation time (three-parameter fit). Figure 2(a) and (b) present the temperature dependence of the experimental NOE data and the best fit to the full (solid line) and the reduced (dashed line) spectral density function. It is evident that the two-correlation times spectral function (five-parameter fit) gives better results.

The activation energy, E_{ae} of the intramolecular rotation around the C-3—C-4 bond can be interpreted as an energy barrier to interconversion of the two rotamers presented in Scheme 1, characterized by the standard enthalpy of activation, $\Delta H^{\neq}$. The relation between the two quantities is defined as

$$E_a = \Delta H^{\neq} + RT \tag{9}$$

The $\Delta H^{\neq}$ value for rotation around the C-3—C-4 bond calculated from the NMR data (Table 1) was compared with the results from the *ab initio* calculations. The results of the MO calculations for the internal rotation around the C-3—C-4 bond (θ_2) at three different theoretical levels are given in Table 2. The barriers to internal rotation, given by $\Delta H^{\neq}$,

Table 1. Experimental correlation times and energies of conformers of cinnamoylmesitylene obtained with the model-free approach method

Carbon atom	τ_M^{298} (ps)	E_{aM} (kcal mol^{-1})	τ_e^{298} (ps)	E_{ae} (kcal mol^{-1})	$\Delta H^{\neq}$ (298) (kcal mol^{-1})	S^2	χ^2
C-2 (5 parameter fit)	55.8	4.16	1.74	6.17	5.6	0.42	0.023
	(±0.61)	(±0.31)	(±0.11)	(±0.26)			
C-2 (3 parameter fit)	2.5	4.00	—	—	—	0.84	0.053
C-7 (5 parameter fit)	36.6	4.42	0.52	6.86	6.6	0.53	0.028
	(±0.28)	(±0.23)	(±0.042)	(±0.43)			
C-7 (3 parameter fit)	0.16	4.30	—	—	—	0.77	0.037

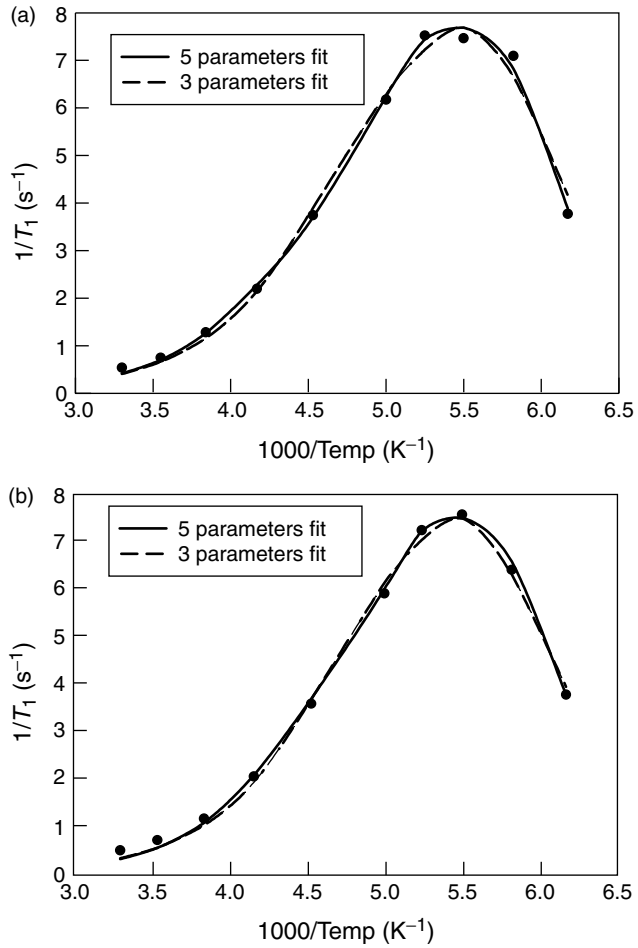

Figure 1. Temperature dependence of relaxation rates for (a) C-2 and (b) C-7. Best simultaneous fit of relaxation and NOE experimental data with full (solid line) and reduced (dashed line) spectral density function.

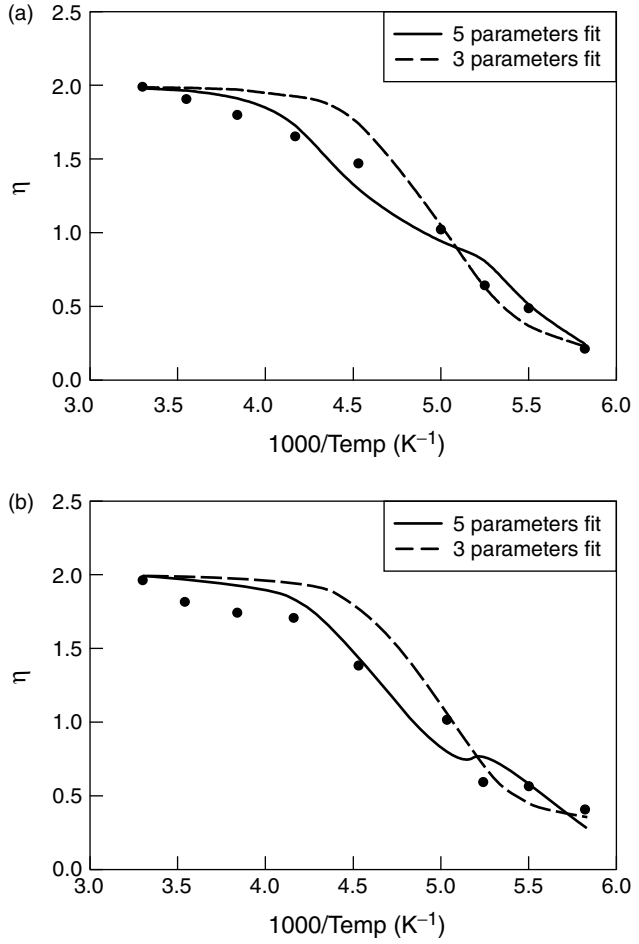

Figure 2. Temperature dependence of NOE data for (a) C-2 and (b) C-7. Best simultaneous fit of relaxation and NOE experimental data with full (solid line) and reduced (dashed line) spectral density function.

Table 2. Theoretical relative energies of conformers of cinnamoylmesitylene ($\Delta H^{\neq}$ in kcal mol^{-1}) according to Scheme 1

θ_1 (°)	θ_2 (°)	3–21G	6–31G*	MP2/6–31G*
0	0	0.0	0.0	0.0
0	60	6.9		
0	90	10.3	8.4	7.5
0	180	1.1	−0.3	−0.9
90	0	4.5		
Methyl rotation		1.1		

obtained from the theoretical calculations decrease with improvement of the theoretical level and approach the NMR results. The difference of <2 kcal mol^{-1} (1 kcal = 4.184 kJ) in $\Delta H^{\neq}$ between values calculated on the basis of NMR data and the *ab initio* values is well within the range of precision of theoretical MO calculations. The tendency for a decrease in the calculated values of $\Delta H^{\neq}$ with improvement of the theoretical level is well defined. In this respect, there is good agreement between the NMR and the theoretical results.

Whereas the 3–21G basis RHF calculations predict the global conformational minimum of **1** at $\theta_2 = 0°$, s-*trans*, 6–31G* and MP2/6–31G* indicate the global minimum at $\theta_2 = 180°$, s-*cis*, even though the calculated energy difference between the two 'planar' conformers is <1 kcal mol^{-1}. The strong steric repulsion between the H-2 proton and the mesityl fragment in the s-*trans* conformation can explain the higher ground-state energy of the latter conformer. The steric strain is partially relieved by twisting the mesityl fragment to 90°, out of the molecular plane. The s-*cis* ($\theta_2 = 180°$) conformer is more stable, since the steric interactions are less pronounced.

The pre-exponential factors τ_{c0} in the Arrhenius equation [Eqn (7)] for overall and intramolecular motion, τ_{M0} and τ_{e0}, were also determined. Their values can be interpreted as rate constants in the absence of the activation energy constraint for the respective motion. In other words, if E_a were zero or T infinite, then $k_M = (\tau_{M0})^{-1}$ for overall and $k_e = (\tau_{e0})^{-1}$ for the internal motion. The pre-exponential factors can be used to calculate the entropy of activation, $\Delta S^{\neq}$, using the following relation:

$$\frac{1}{\tau_{c_0}} = \frac{k_B T_e}{h} e^{\Delta S^{\neq}/R} \tag{10}$$

where again indices c ≡ M or e apply for overall or internal motions, respectively; k_B is the Boltzmann constant, h is

Planck's constant and T_e is the mean absolute temperature of the range over which the rate constants were determined.

The best-fit values calculated from data sets for C-2 and C-7, using the full correlation time function, are τ_{e0} (C-2) = 5.2×10^{-17} s, τ_{M0} (C-2) = 5.0×10^{-14} s, τ_{e0} (C-7) = 0.5×10^{-17} s and τ_{M0} (C-7) = 2×10^{-14} s. These values were used to calculate the activation entropy for the overall ($\Delta S_M^{\neq}$) and internal ($\Delta S_e^{\neq}$) motions, according to Eqn (10). We obtained the following results: $\Delta S_M^{\neq}$ (C-2) = 3.0 cal K^{-1} mol^{-1}, $\Delta S_e^{\neq}$ (C-2) = 16.8 cal K^{-1} mol^{-1}, $\Delta S_M^{\neq}$ (C-7) = 4.8 cal K^{-1} mol^{-1} and $\Delta S_e^{\neq}$ (C-7) = 19.8 cal K^{-1} mol^{-1}.

The interpretation of the physical significance of entropy of activation is not straightforward and we discuss its value only in general terms.

The $\Delta S_e^{\neq}$ values calculated from the two data sets are high and almost identical. We assume that the restricted rotation in the ground state can be regarded as more like a libration. In this respect, the ground state has less internal rotational degrees of freedom and its entropy is relatively low. On the other hand, the transition state for the internal rotation is less mechanically restricted in comparison with the ground state. The relatively 'loose' structure corresponding to the energy maximum of internal rotation, is associated with a higher amplitude of librations, which implies a lower vibrational frequency and consequently higher entropy. The strongly positive activation entropy of internal motion, $\Delta S_e^{\neq}$, can be explained by the gain in entropy due to increased motional freedom during the structural transition through the internal motion energy maximum. The activation entropy of internal motion about a single bond of one part of the molecule with respect to the other, that is hindered in some way, may be considered in terms of vibrational contributions to the partition function, as the contribution of a single low-frequency libration. An approximate estimation of the lower and upper limits of $\Delta S_e^{\neq}$ can be made on the basis of the order of magnitude of the partition functions for different types of internal molecular motion found in the literature.[33,34] Assuming a simplified mechanistic model with restricted motion in the energy minimum and liberated motion in the maximum we can estimate $\Delta S_e^{\neq}$ to be in the range 5–20 cal K^{-1} mol^{-1}. The calculated values for the examined system fall in this range. The relatively high values of $\Delta S_e^{\neq}$ indicate that the interconversion between the two rotamers has an appreciable rate. These results confirm the experimental observations that the examined process is fast relative to the NMR chemical shift time-scale.

The $\Delta S_M^{\neq}$ values calculated from both data sets are low and almost identical. The relatively low activation entropy for the overall molecular reorientation implies that no appreciable change in entropy is associated with this process. These results are generally in agreement with the typical values for a monomolecular first-order reaction, associated with overall molecular reorientation where the molecule can be considered as a rigid rotator.

The theoretical results at the 3–21G level indicate that the phenyl rotation about the θ_1 angle has a low barrier (see the last entry in Table 2), which would be difficult to detect within the usual temperature range of the NMR studies. The same calculations of the threefold rotational barrier of methyl groups in the mesityl fragment give an energy barrier of roughly 1 kcal mol^{-1}, which seems hardly amenable to NMR studies.

CONCLUSION

The Lipari–Szabo model-free approach was successfully used to investigate the molecular dynamics of cinnamoylmesitylene (**1**). Simultaneous analysis of both heteronuclear spin–lattice relaxation times and NOE data, taken at different temperatures, allows one to determine the correlation times of overall and internal molecular motions and the generalized order parameter which are measures of the molecular mobility. The rotation around the C-3—C-4 bond was found to be relatively restricted and the activation energy for this rotation was calculated. We found that the application of a full correlation time function gives better results than the reduced equation.

The $\Delta S^{\neq}$ results corroborate our findings for the dynamic behavior of the studied compound and confirm the adequacy and applicability of the model-free approach for the examination of fast but relatively hindered internal motion in low molecular weight systems.

The *ab initio* MO calculations were performed to verify the experimental results. The agreement between the NMR and theoretical results is good.

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