Phase Dependence of Conformational Motions in Solids. The *tert*-Butyl Rotation in (1*R**,2*S**,5*R**)-5-*tert*-Butyl-2-hydroxycyclopentanecarboxylic Acid

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Abstract: (1*R**,2*S**,5*R**)-5-*tert*-Butyl-2-hydroxycyclopentanecarboxylic acid exists in several solid phases, two of which are investigated in this report: a first phase (phase I) obtained by crystallization from common solvents and a second phase (phase II) obtained by heating the first phase above ca. 70 °C. The second phase appears to be the stable phase at ambient temperature, and the first phase appears to be a metastable phase. A third phase (phase III), which reverts to phase II on standing at room temperature, is obtained by cooling the melt to room temperature. The rates of rotation of the *tert*-butyl groups in phases I and II have been measured by CP/MAS NMR techniques. The activation parameters for the *tert*-butyl group rotation differ markedly between the two phases: phase I, $\Delta H^{\neq} = 59.0 \pm 2.1$ kJ mol^{-1}, $\Delta S^{\neq} = 51.6 \pm 8.1$ J K^{-1} mol^{-1}; and phase II, $\Delta H^{\neq} = 43.9 \pm 2.5$ kJ mol^{-1}, $\Delta S^{\neq} = 28.3 \pm 9.3$ J K^{-1} mol^{-1}. The structure of phase I has been solved by X-ray diffraction techniques, and this assists in understanding the experimental observations.

Introduction

High-resolution NMR spectroscopy has long been the premier method for the investigation of conformational dynamics of molecules in solution, and an enormous amount of work has been reported in this area. More recently, the utility of solid-state NMR techniques, in particular ^{13}C CP/MAS NMR, for the study of dynamic molecular phenomena in crystalline organic solids has become increasingly recognized. For example, conformational phenomena in solids such as alkyl and aryl group rotations,[1−6] methoxy group rotations,[7] pseudorotations of five-membered rings,[8−10] and dynamic changes in hydrogen-bonding patterns[10] have been observed by CP/MAS techniques.

In general, the environment surrounding a molecule in a crystalline solid is more robust than the solution environment. In addition to the forces that need to be overcome, e.g. for a bond rotation in the free molecule, additional constraints are imposed by the matrix of molecules in the solid. It is harder to deform the environment surrounding such a group in a solid than it is in solution. It is to be expected, therefore, that in solids, conformational processes that show only small volumes of activation or only small overall volume changes are most likely to be observed. That is to say that processes that cause the "least distress" to the crystal structure should be the most readily observable by NMR methods.[1,2] One alkyl group that fulfills these conditions is the *t*-butyl group that has local C_3 symmetry, and we have observed and reported many examples of *tert*-butyl group and related group rotations in the solid state.[1,2,11]

Many of the nuclear interactions that are present in solids are averaged out by rapid isotropic molecular tumbling in solution. This gives a much richer menu of NMR methods from which to choose for studying motions in solids compared with the solution state. Methods using ^{13}C CP/MAS NMR include line-shape analysis,[12] 2D EXSY,[13,14] magnetization transfer,[12] and maximum dipolar broadening.[15] In addition, we have recently shown that $T_{1\varrho}$ measurements in combination with line-shape analysis may be applied to the study of alkyl and aryl group rotations,[1,4,6] notwithstanding the contradictory literature on the matter (for a discussion see refs 16−18). An analysis of the regions in which $T_{1\varrho}$ measurements can give useful dynamic information has been given by Vanderhart and Garroway.[19]

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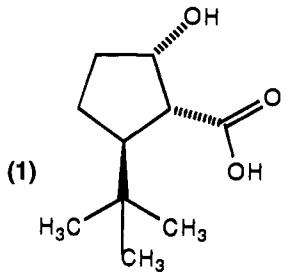
When molecular dynamics are studied in solution, there is only one phase present and, in general, only one dynamic process is under investigation. In the solid state, there are more possibilities. There may be more than one solid phase available. There may be more than one independent molecule in the asymmetric unit. Indeed, both of these possibilities may coexist for the same compound, and these will lead to more than one dynamic process being observable for the same molecule in different phases or in different molecules in the same phase. In both of these cases, the molecular environments of the molecule being studied should vary and so, in principle, the activation parameters for a given molecular motion should differ. We have observed both of these effects,[10] and this paper addresses this issue in the case of a compound for which two solid-state phases are available for study. This paper represents the first experimental observation of differences in activation parameters for the same conformational process in two different solid phases.

Experimental Section

(1*R,2*S**,5*R**)-5-*tert*-Butyl-2-hydroxycyclopentanecarboxylic Acid (1).** To a mixture of 0.05 mol (5.6 g) of freshly prepared potassium *tert*-butoxide in 80 mL of dry toluene was added 0.05 mol (12.9 g) of diethyl 3-*tert*-butyladipate (**2**), and the mixture was stirred and refluxed for 6 h. The cooled solution was acidified with aqueous hydrochloric



acid, and the separated organic layer was washed in turn with $NaHCO_3$ solution and water. After drying and evaporation of the solvent, a mixture of keto esters (**3** and **4**) was obtained, which was dissolved in 100 mL of ethanol. Ten grams of Raney nickel catalyst was added, and reduction was performed in a steel autoclave in a hydrogen atmosphere at 60 atm. After shaking for 10 h at 70 °C, the catalyst was filtered off, the solvent was evaporated off, and the product was fractionated by vacuum distillation at 2 mmHg. The lower-boiling *cis*-enriched ester fraction (3.2 g) was hydrolyzed with 10 mL of 20% aqueous potassium hydroxide for 2 h. The clear solution was extracted with diethyl ether, and the aqueous phase was acidified with hydrochloric acid and extracted with diethyl ether. After drying and evaporation of the solvent, crystalline hydroxy acid was obtained, which was recrystallized several times from a benzene–hexane solvent mixture, resulting in diastereomerically pure hydroxy acid (**1**): mp 94–95 °C; $C_{10}H_{18}O_3$ 186.25; M^+ 186. Anal. Calcd C, 64.49; H, 9.74. Found: C, 64.51; H, 9.96.

The diastereomerically pure **1** was recrystallized from the following solvents for solid-state NMR investigations: benzene (mp 96–97 °C), hexane (mp 94–95 °C), and diisopropyl ether (mp 97–98 °C). The material from all of these recrystallizations was shown to be identical by CP/MAS NMR and is referred to as phase I. A second phase, referred to here as phase II, was obtained by heating phase I for 20 min close to its melting point (ca. 90 °C). When molten **1** was allowed to cool to ambient temperature over the course of a few minutes, the material obtained showed NMR evidence of the existence of a third phase (phase III) together with phase II. Phase III reverted to phase II on standing at room temperature for a few hours. X-ray structure investigations were performed on phase I crystallized from diisopropyl ether.

NMR Spectra. Solid-state ^{13}C CP/MAS NMR spectra were obtained on a Bruker MSL 500 spectrometer at 125.758 MHz using 4 mm o.d. zirconia rotors in St. Andrews. The following typical conditions were employed: contact time 1 ms, spectral width 30 000 Hz, acquisition time 17.4 ms, spin-locking field frequency ca. 60 kHz, recycle delay 5 s, and spinning speeds 6–8 kHz. Chemical shifts were referenced to the CH_2 resonance in an external adamantane sample at 38.56 ppm. Dipolar-dephased (nonquaternary suppressed (NQS)) spectra were obtained by a standard sequence incorporating a 50 μs dipolar-dephasing delay. $T_{1\varrho}$ measurements were performed as described previously[1] using a standard $T_{1\varrho}$ sequence preceded by cross-polarization. Spin-lock periods of up to 20 ms were employed with a ^{13}C precessional frequency of ca. 60 kHz. Temperatures in the MAS probe were calibrated as described previously using standard samples with known phase changes run under conditions as close to those of the experimental observations as possible.[1]

Solution-state ^1H and ^{13}C NMR spectra were obtained from a $CDCl_3$ solution in a 5 mm tube using the high-resolution probe in the MSL 500 spectrometer or on a Bruker AM 300 spectrometer in St. Andrews.

Errors on the activation parameters quoted in this paper are 95% confidence limits estimated as twice the standard deviation calculated from least-squares linear plots.

Table 1. Crystallographic Data for Phase I of **1**

chemical formula	$C_{10}H_{18}O_3$
formula weight	186.25
habit	monoclinic
lattice type	P
space group	$P2_1/n$
Z	4
a, Å	6.195(3)
b, Å	21.790(6)
c, Å	7.907(2)
β, deg	105.56(3)
V, Å^3	1028.3(7)
ϱ_{calc}, g cm^{-3}	1.203
T, °C	23
μ, cm^{-1}	7.11
λ (Cu Kα, graphite-monochromated), Å	1.54178
R	0.068
R_w	0.064

Structure Determination of Phase I of 1. A crystal of approximate dimensions 0.9 × 0.9 × 0.2 mm^3 recrystallized from diisopropyl ether was found to be monoclinic, crystallizing in space group $P2_1/n$ with cell dimensions a = 6.195(3) Å, b = 21.790(6) Å, c = 7.907(2) Å, β = 105.56(3)°, V = 1028.3(7) Å^3, Z = 4, and d_{calcd} = 1.20 g cm^{-3}. A Rigaku AFC6S diffractometer with graphite monochromator and Cu Kα radiation (λ = 1.541 78 Å) was used for data collection. A total of 2070 unique reflections (h, $\pm k$, $\pm l$; 5° < 2θ < 150.4°) were measured by the ω–2θ technique with a scan range of 1.78 + 0.30-(tan θ) and a scan rate of 8.0° min^{-1} (three rescans). An empirical absorption correction was carried out using the program DIFABS, and the structure was solved using direct methods (SHELXS86 and DIRDIF92). The positions of the hydrogens bonded to oxygens were taken from difference Fourier calculations. All other hydrogens were generated on the basis of geometric information. Convergence was achieved with R = 0.068 and R_w = 0.064. All important data collection, unit cell, and refinement parameters are summarized in Table 1. Full details are available as supplementary material.

Discussion

The cyclopentane derivative (**1**) was prepared by standard synthetic methods[20] (Figure 1). When diethyl 3-*tert*-butyladipate (**2**), obtained from 4-*tert*-butylcyclohexanone by oxidative ring cleavage, was cyclized to ethyl 4-*tert*-butyl-2-oxocyclopentanecarboxylate (**3**) by Dieckmann condensation in the presence of sodium ethoxide, the formation of 4–6% of ethyl 5-*tert*-butyl-2-oxocyclopentanecarboxylate (4) was also observed.[21–23] When the reaction was performed in the presence of potassium

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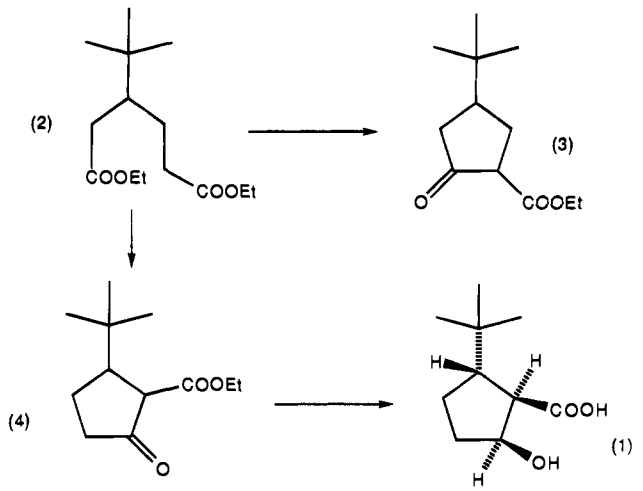


Figure 1. Synthetic route to the title compound (**1**).

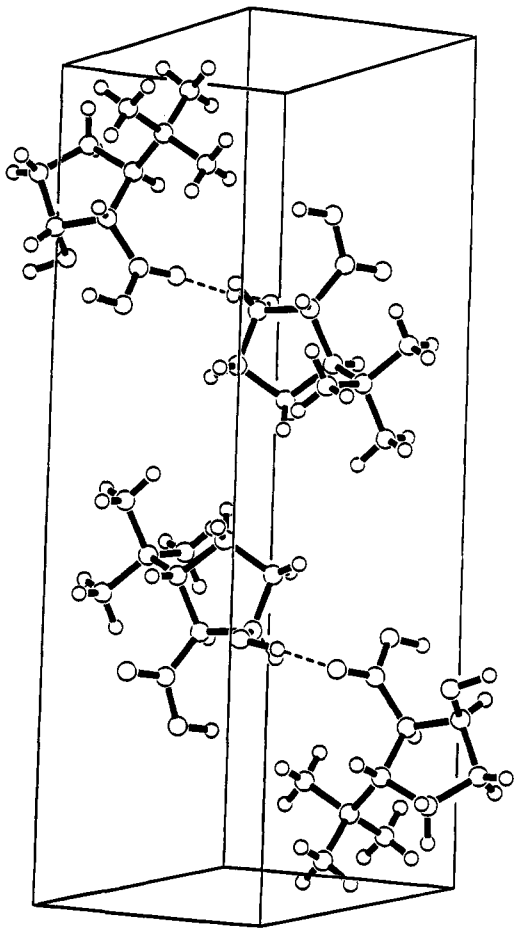


Figure 2. Packing of the molecules of **1** in the unit cell of phase I.

tert-butoxide, the ratio of keto esters **3** and **4** was approximately 1:1. The crude mixture was reduced catalytically, followed by fractional distillation, hydrolysis, and fractional crystallization, which resulted in hydroxy acid **1** in stereohomogeneous form.

A crystal of **1** recrystallized from diisopropyl ether was subject to structural investigation by X-ray diffraction. Relevant data is given in Table 1. The crystal structure is composed of a racemic mixture of the two enatiomers and confirms the relative stereochemistry at the three chiral centers as *RSR* and *SRS*. The packing of the molecules in the unit cell is shown in Figure 2, and the molecular structure is given in Figure 3. The conformation of the five-membered ring can best be described as an envelope because the torsion angle (C1−C5−C4−C3) is close to zero (7.3°). The C2 hydroxyl is in an axial position, the CO_2H is equatorial, and the *tert*-butyl is isoclinal. As

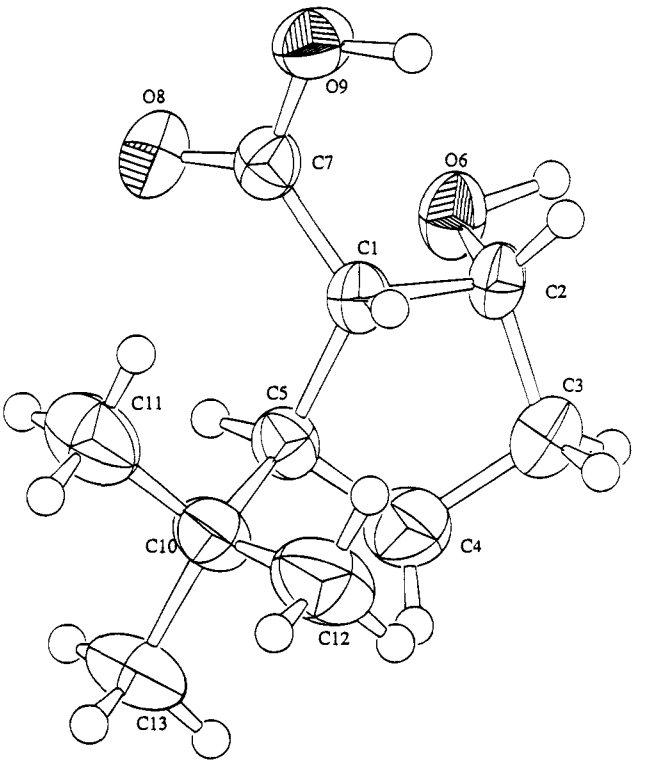


Figure 3. ORTEP diagram of the molecular structure of **1** in phase I.

Table 2. Chemical Shifts in Solution and in the Solid (ppm Relative to TMS)

carbon atom	^1H	^{13}C soln	^{13}C phase I	^{13}C phase II
C1	2.71	50.76	48.99	51.96
C2	4.40	75.64	78.39	75.48
C3	1.79/1.81	34.79	36.95	33.87
C4	1.42/1.82	24.58	25.00	24.24
C5	2.42	51.32	52.96	56.08
C7 (acid)	–	179.68	177.82	180.58
C10 (quaternary)	–	32.73	34.22	32.72
C11,12,13 (methyl)	0.87	27.29	28.59	28.18

expected, the packing of the molecules is primarily determined by the hydrogen-bonding interactions with the hydroxyl group as a donor and the CO_2H group as an acceptor. These atoms form linear chains through the lattice as shown in Figure 4. Interestingly, in view of our measurements of *tert*-butyl group rotations described below, the largest anisotropic displacement parameters are observed for the *tert*-butyl methyl carbons. This is seen well in the ORTEP figure in which the longest axes of the thermal ellipsoids are seen to correspond approximately with the direction of rotation. This is in agreement with the calculations in our earlier paper in which the anisotropic displacement parameters were resolved along the radius for the rotation of the *tert*-butyl groups.[1]

The ^1H spectrum of **1** in $CDCl_3$ solution was obtained at 500 MHz and assigned with the help of a 2D COSY spectrum. The ^{13}C spectrum in $CDCl_3$ solution was obtained at 125.758 MHz and assigned by DEPT and a 2D $^{13}C-^1H$ correlation spectrum (75 MHz). The solution-state ^{13}C spectral assignments were of assistance in assigning the ^{13}C CP/MAS NMR spectra, in particular C3, C4, and C5. Chemical shifts are recorded in Table 2.

The solid-state ^{13}C CP/MAS NMR spectrum of phase I of **1**, recrystallized from a variety of solvents, at ambient temperature (20 °C) is shown in Figure 5a and is in accord with its structure. Dipolar-dephased (NQS) spectra allow for the identification of the carbons of the *tert*-butyl and carboxylate groups. The chemical shifts are identical within less than 3 ppm to those

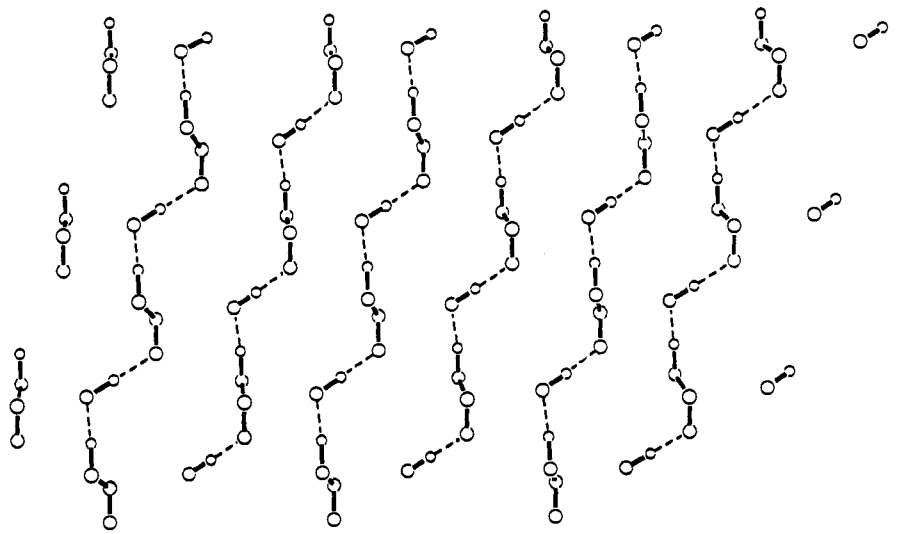


Figure 4. Chains of hydrogen bonding in the crystal structure of **1** in phase I. Any atoms not involved in the chains are ignored for clarity.

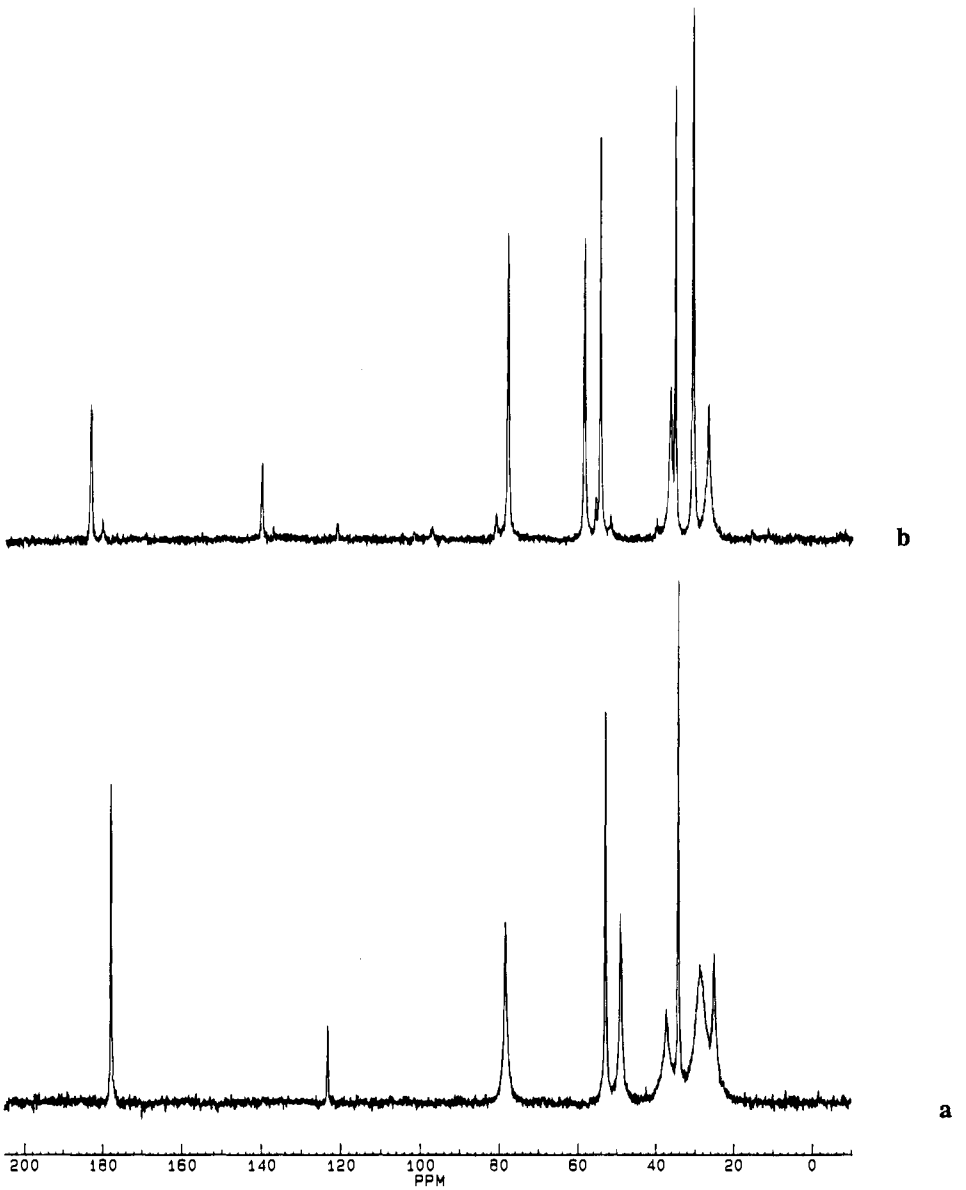


Figure 5. (a) ^{13}C CP/MAS spectrum of **1** as crystallized from the common solvents described in the text (phase I). (b) ^{13}C CP/MAS spectrum of **1** after phase modification by heating to 80 °C for about 2 h (phase II). Small traces of phase I are still visible. The peaks of moderate intensity at 120−140 ppm in both spectra are spinning side bands on the carboxyl ^{13}C resonance.

obtained for the same material in $CDCl_3$ solution. The CH_3 resonance of the *tert*-butyl group is a broadened singlet of lower than expected intensity. The reduction in intensity arises from poor cross-polarization due to a reduction in $T_{1\varrho}$ associated with

Table 3. $T_{1\varrho}$ and Rate Data for Phase I[a]

temp, K	$T_{1\varrho}$, ms[b]	k, s^{-1}[c]
248	–	8.0×10^2
252	–	1.6×10^3
255	–	2.2×10^3
259	–	3.5×10^3
263	–	5.0×10^3
266	–	8.0×10^3
270	–	1.2×10^4
273	–	1.6×10^4
295	8.56	1.20×10^5
298	7.68	1.34×10^5
302	5.75	1.80×10^5
306	3.69	2.94×10^5
310	3.50	3.11×10^5
313	3.18	3.48×10^5
317	2.74	4.21×10^5
320	2.02	6.85×10^5
324	1.79	1.13×10^6
328	2.06	1.95×10^6
331	2.13	2.07×10^6

[a] ^{13}C spin-locking field ca. 60 kHz. [b] The $T_{1\varrho}$ data give a value of 4.2×10^8 s^{-2} for B^2. [c] These rate data give $\Delta H^{\neq} = 59.0 \pm 2.5$ kJ mol^{-1} and $\Delta S^{\neq} = 51.6 \pm 8.1$ J K^{-1} mol^{-1}.

the *tert*-butyl group rotation being similar to the precessional frequency of the nuclei in the spin-locking field during cross-polarization. The *tert*-butyl methyl resonance sharpens on warming, broadens further, and splits into three lines on cooling. $T_{1\varrho}$ values were obtained for the ^{13}C of the *tert*-butyl methyl carbons and the central quaternary carbon atom over the temperature range 295−331 K from which rate constants for the rotation of the *tert*-butyl group were calculated by previously described methods.[1] The $T_{1\varrho}$ values for the methyl carbons and the derived values for the rate constants and the dipolar $^{13}C-^{1}H$ interaction are listed in Table 3. The rates from the $T_{1\varrho}$ measurements on the central quaternary carbon atom were consistent with those from the methyls. Rate constants for the rotation of the *tert*-butyl group were also obtained from the line-shape changes at lower temperatures. These rates are also listed in Table 3 and the observed line-shape changes for the methyl resonances obtained by means of an NQS sequence to eliminate CH and CH_2 resonances are shown in Figure 6.

On heating to ca. 70 °C, the spectrum changes slowly. The changes are more rapid at higher temperature and correspond to a phase change of the solid from phase I into phase II. The phase-transformed solid gives a ^{1}H NMR spectrum in $CDCl_3$ solution identical to that of the non-phase-transformed material, confirming that the changes are not the result of a solid-state chemical reaction. The ^{13}C CP/MAS NMR spectrum of phase II containing a very small residual amount of phase I is shown in Figure 5b. This material showed no signs of reverting to phase I after standing at 20 °C for more than 6 months.

If molten **1** is allowed to cool to room temperature over the course of a few minutes, the spectrum of the solid obtained shows evidence of a third phase (phase III) together with very small amounts of phase II (Figure 7a). This material reverts slowly to phase II at room temperature and more rapidly on warming. Figure 7b shows the spectrum of phase III after

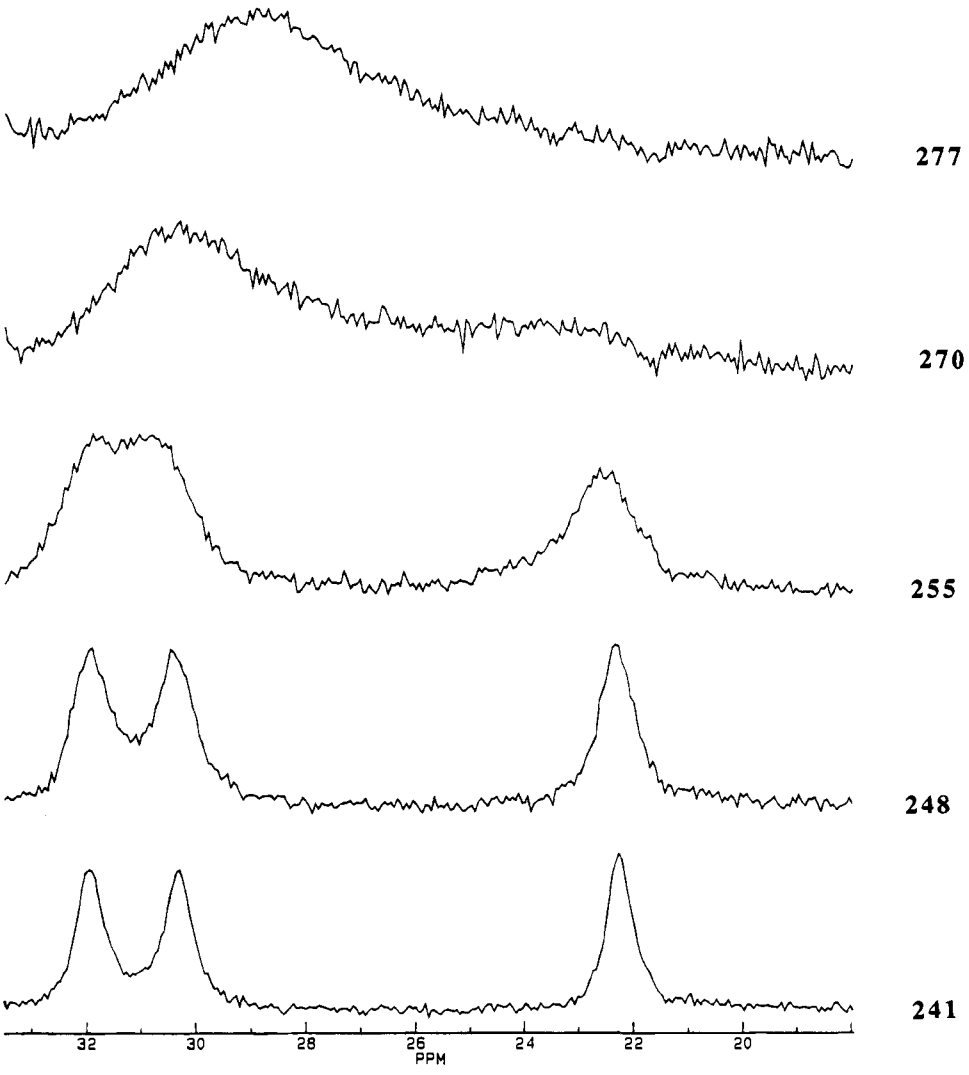


Figure 6. Line shape of the *tert*-butyl resonance of phase I at different temperatures.

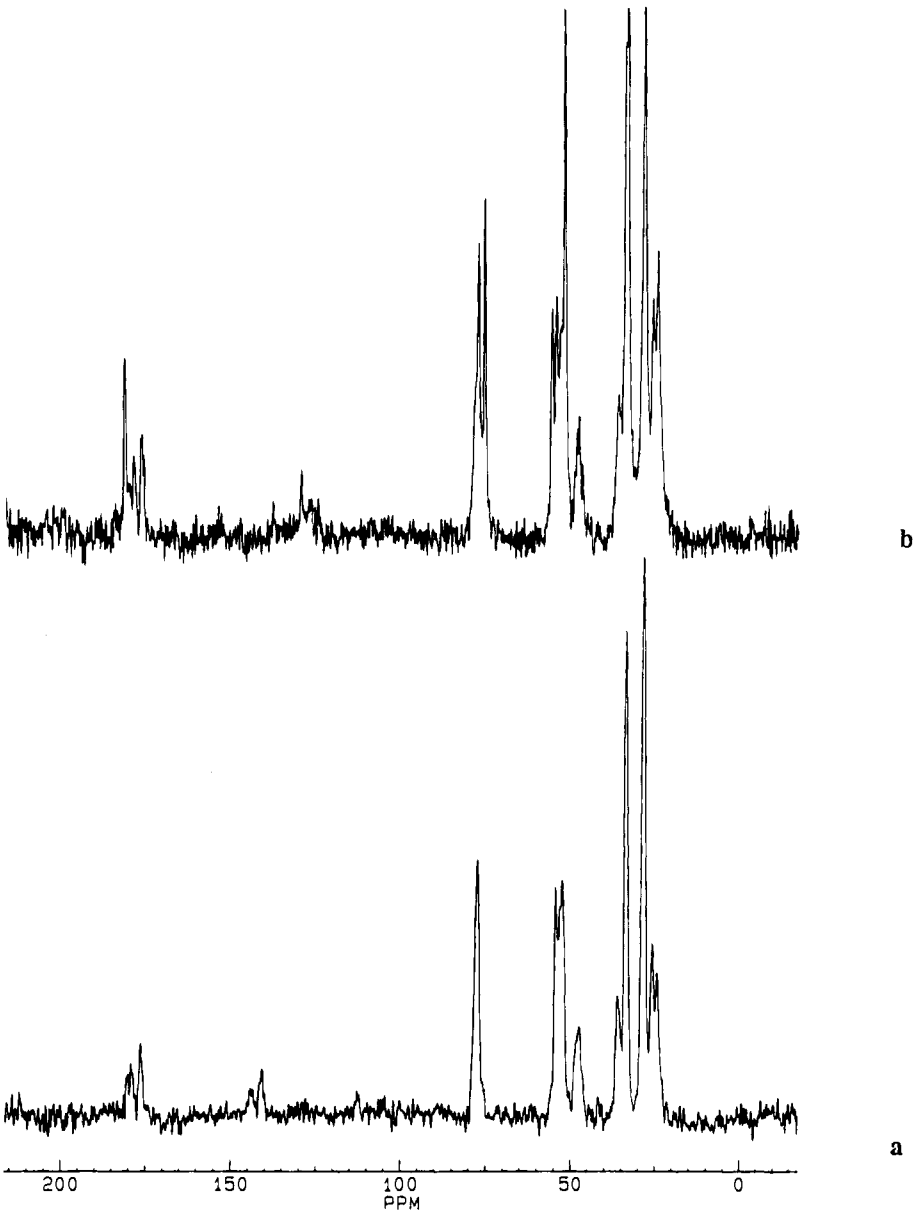


Figure 7. (a) ^{13}C CP/MAS spectrum of **1** immediately after solidification of the melt at room temperature (phase III). (b) ^{13}C CP/MAS spectrum of phase III after standing for 4 h at ca. 20 °C showing evidence of substantial conversion to phase II. The small peaks at ca. 130−150 ppm are spinning side bands on the carboxyl ^{13}C resonances.

standing for 4 h at ca. 20 °C. There is evidence of substantial conversion to phase II. Phase III has broader lines than phases I or II, indicative of disorder in the solid-state structure. There is also evidence of lines being split, e.g. the carbonyl resonance contains at least two lines, suggesting either that more than one molecule exists in the asymmetric unit or that phase III consists of more than a single phase.

These observations are consistent with phases I and III being metastable phases that show transitions to phase II which appears to be the stable phase under ambient conditions. The existence of multiple phases of this material may be associated with different hydrogen-bonding patterns in the different solid phases. The crystallization of **1** from all common solvents is, therefore, a kinetically controlled process, possibly due to hydrogen-bond association patterns in solution, and does not give the thermodynamically most stable solid phase. Analogously, crystallization of **1** from the melt is a kinetically controlled process, presumably dominated by different hydrogen-bonding patterns in the melt. These ideas are supported by the importance of the hydrogen-bonding patterns seen in the crystal structure of phase I.

The ^{13}C chemical shifts in the CP/MAS NMR spectrum of phase II are closer to those of the $CDCl_3$ solution than those of phase I. The NQS spectrum allowed for the identification of the resonances from the carboxyl and *tert*-butyl carbons. The *tert*-butyl methyl singlet of phase II at ambient temperature is considerably sharper and of greater relative intensity than that of phase I, implying that the *tert*-butyl group is rotating more rapidly in the former. Dynamic line-shape changes are observed over the temperature range ca. 220−240 K from which rate constants for the *tert*-butyl group rotation were obtained. As for phase I, ^{13}C $T_{1\varrho}$ values were obtained for the *tert*-butyl methyl carbons and the central quaternary carbon atom over the temperature range 255−320K from which rate constants for the rotation of the *tert*-butyl group were calculated by previously described methods.[1] The $T_{1\varrho}$ values, the rate constants from the $T_{1\varrho}$ measurements and the line-shape changes, and the calculated value of the dipolar $^{13}C-^{1}H$ interaction (B^2) are listed in Table 4. The line shapes for the *tert*-butyl methyl resonances obtained at different temperatures by means of an NQS sequence to eliminate the CH and CH_2 resonances are shown in Figure 8.

Table 4. $T_{1\varrho}$ and Rate Data for Phase II[a]

temp, K	$T_{1\varrho}$, ms[b]	k, s^{-1}[c]
223	–	6.0×10^3
226	–	1.1×10^4
230	–	1.5×10^4
234	–	2.2×10^4
237	–	3.0×10^4
255	6.22	2.13×10^5
263	3.46	4.18×10^5
270	2.90	5.38×10^5
277	2.80	5.69×10^5
284	2.25	1.13×10^6
288	3.68	3.32×10^6
292	3.93	3.60×10^6
299	4.65	4.32×10^6
306	5.51	5.30×10^6
313	8.87	8.77×10^6
320	10.9	1.08×10^7

[a] ^{13}C spin-locking field ca. 60 kHz. [b] The $T_{1\varrho}$ data give a value of 3.4×10^8 s^{-2} for B^2. [c] These rate data give $\Delta H^{\neq} = 43.9 \pm 2.5$ kJmol^{-1} and $\Delta S^{\neq} = 28.3 \pm 9.3$ J K^{-1} mol^{-1}.

To our disappointment, multiple attempts to obtain a crystalline sample of phase II for X-ray diffraction study failed. These included attempts at crystallization from toluene at 100 °C (above phase transition temperature) and crystallization from strongly hydrogen-bonding solvents such as water and acetic acid. X-ray powder diffraction was attempted to solve the structure of phase II, but there were insufficient lines in the diffraction pattern to allow any reasonable structure to be extracted.

Activation plots for the rotation of the *tert*-butyl groups in phases I and II are shown in Figure 9. The rates of rotation obtained from two independent but complementary NMR techniques fall satisfyingly onto the same straight lines for both phases. The experimentally determined values for the C–H dipolar interaction (B^2) in the *tert*-butyl methyl groups are satisfactorily in agreement with those determined by one of us in an earlier paper both by experiment and by calculation.[1] Phase II has the higher rates of rotation and the lower activation energy. The temperature range over which the rates were measured for both phases (nearly 100 K) and the rate range studied ($>10^3$ in both cases) give confidence in the derived activation parameters. The enthalpies and entropies of activation for the two phases differ substantially: phase I, $\Delta H^{\neq} = 59.0 \pm 2.1$ kJ mol^{-1}, $\Delta S^{\neq} = +51.6 \pm 8.1$ J K^{-1} mol^{-1}; phase II, $\Delta H^{\neq} = 43.9 \pm 2.5$ kJ mol^{-1}, $\Delta S^{\neq} = +28.3 \pm 9.3$ J K^{-1} mol^{-1}.

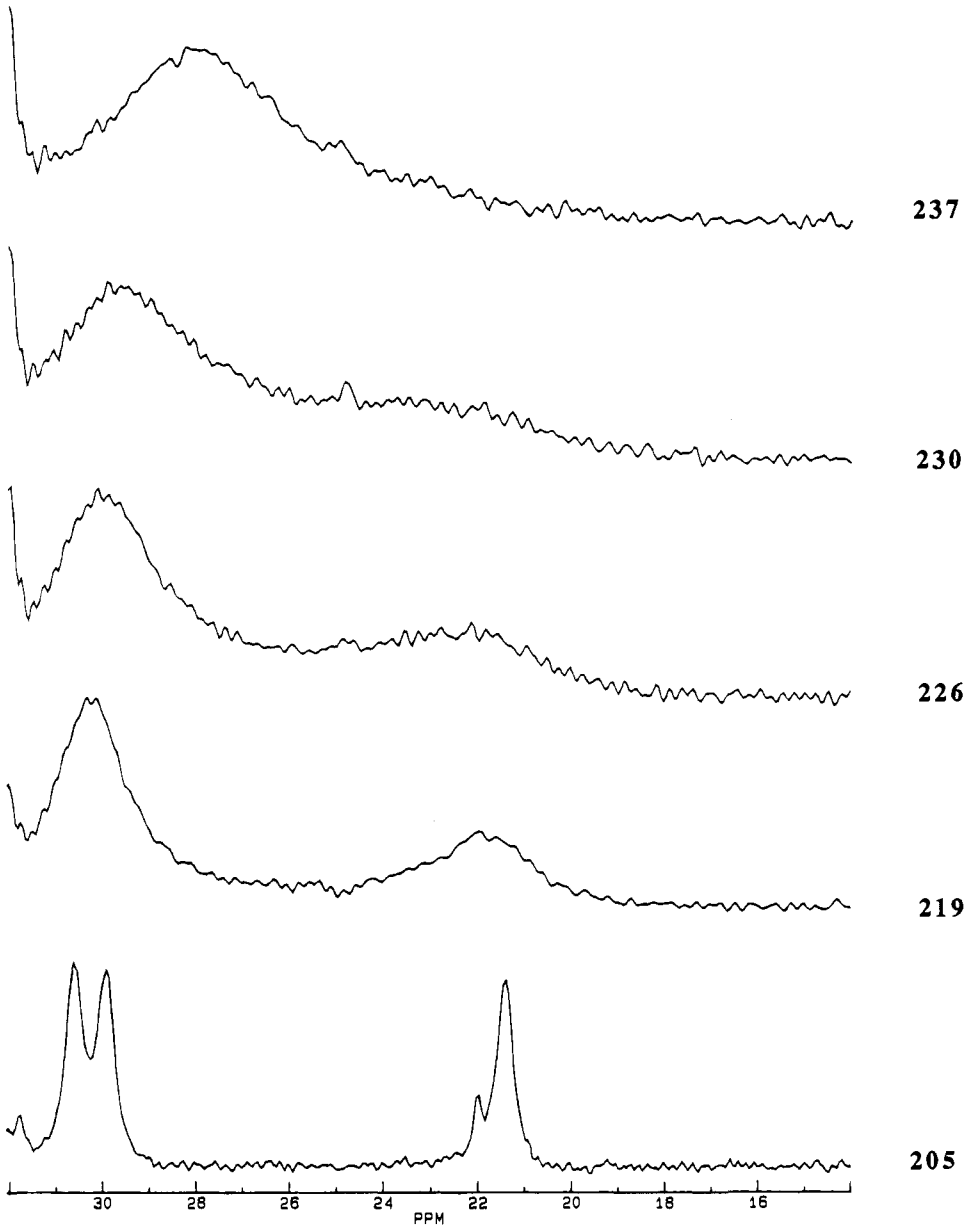


Figure 8. Line shape of the *tert*-butyl resonance of phase II at different temperatures.

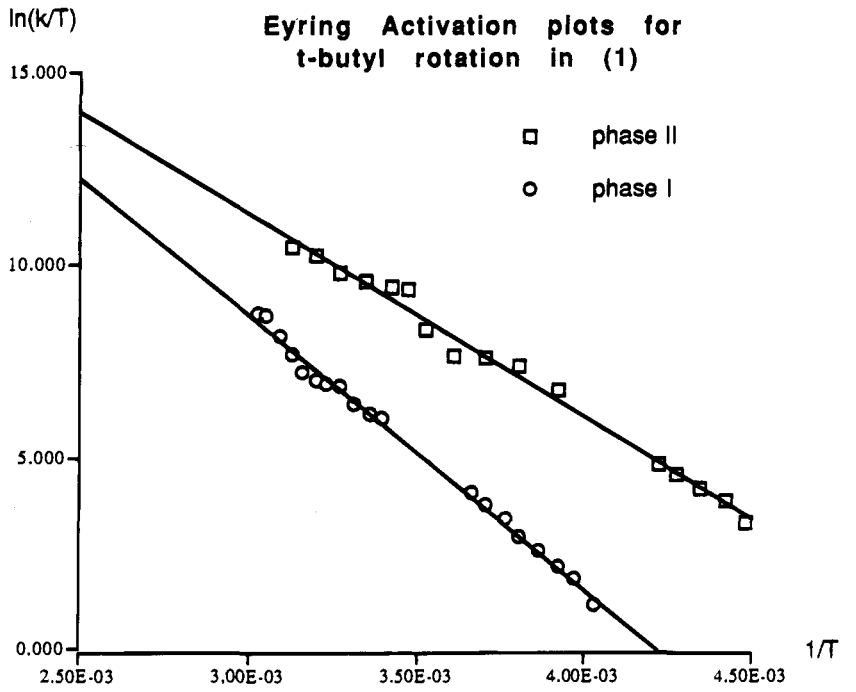


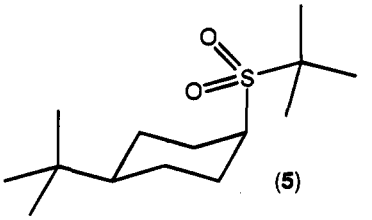
Figure 9. Eyring activation plots for the *tert*-butyl group rotations in phases I and II of **1**. Rate constants from the $T_{1\rho}$ values to the left are separated by small gaps from the rate constants from the line-shape analysis on the right.

The enthalpies of activation for the two phases differ by more than 3 times the sum of the 95% confidence limits on the values. Phase II has both faster rotation rates for the *tert*-butyl group than phase I at the same temperature in the temperature range studied and a lower enthalpy of activation. The data show that the entropies of activation for the two phases are substantially positive. They differ by 50% more than the sum of their 95% confidence limits, suggesting strongly that they are indeed different and that phase I has a greater entropy of activation than phase II. Thus, the proposal that we made at the outset of this paper, that the activation parameters for a molecular motion for the same molecule in two differing crystal phases should be different, has been confirmed.

Within a molecular mechanics (MM) framework, the concepts of enthalpy and entropy of activation are intuitively obvious for conformational motions in an isolated molecule in the gas phase. For a group rotation in an isolated molecule, the enthalpy of activation can be regarded as the work done by the molecule in overcoming intramolecular resistance to the motion when reaching the transition state and the entropy of activation can be regarded as arising from the redistribution of the internal energy of the molecule amongst its various vibrational modes. These MM concepts become more clouded in solution because solvent molecules can, in principle, be regarded as involved, and, in the case of hydrogen bonding, certainly are involved as in, for example, nitrogen inversion.[24] Interestingly, where entropies of activation have been determined reliably for conformational processes in the gas phase and in solution, they are generally small. What do these MM concepts mean in a solid, and how do experimentally determined values for solids compare with those in solution?

The enthalpy of activation for a group rotation in a solid can be regarded as the work done during the rotation to arrive at the transition state against both intramolecular resistance and the resistance provided by adjacent molecules in the lattice. Vibrational modes in solids have to be regarded as of the entire lattice and not of individual molecules. Therefore, the entropy of activation arises from a redistribution of vibrational energy throughout the entire crystal lattice and not just inside a single molecule. Enthalpies and entropies of activation in solids, therefore, do not refer to the properties of individual molecules. In this respect, a high (and positive) entropy of activation indicates a more random distribution of energy throughout the lattice in the transition state than in the ground state. The lower the entropy of activation, the less the disorder in the distribution of energy amongst the vibrationally allowed states of the lattice at the the transition state. In this conceptual framework, a cooperative or cogwheeling rotation of a group in a solid should lower the activation entropy.

The entropies of activation that we have determined are considerably larger than those generally found for conformational processes in solution. The entropies of activation are also larger than those we reported earlier for both *tert*-butyl groups in **5**[1] but are smaller than some others that we have measured recently.[11] The large entropy of activation for phase I ($\Delta S^{\neq}$ =



(5)

51.6 ± 8.1 J K^{-1} mol^{-1}) suggests strongly that there is no interaction between the *tert*-butyl groups during their rotations. This is borne out by the X-ray diffraction study in which the *tert*-butyl groups are seen to be some distance apart. To understand the meanings of activation parameters for solids such as those, we have determined it will be advantageous to perform molecular-modeling studies on ensembles of molecules resembling crystal lattices.

Conclusions

(1*R**,2*S**,5*R**)-5-*tert*-Butyl-2-hydroxycyclopentanecarboxylic acid (**1**) exists in several solid phases. Crystallization from common solvents gives a metastable phase I which changes on heating to a stable phase II. A third metastable phase (phase III) is obtained by cooling the melt. The importance of

(24) Riddell, F. G.; Lehn, J. M.; Wagner, J. *Chem. Commun.* **1968**, 1403.

hydrogen-bonding in the structure of phase I determined by X-ray diffraction suggests that hydrogen bonding interactions are important in determining the differences between the phases and the kinetics of crystallization both from solution and from the melt. The *tert*-butyl group rotations in phases I and II occur at different rates and with different activation parameters. The faster rotating *tert*-butyl (phase II) has the lower enthalpy of activation. The entropies of activation for the *tert*-butyl rotations are substantial and positive in contrast with some earlier observations. Cogwheeling of the *tert*-butyl groups in phase I is unlikely. The concepts of activation parameters for conformational processes in solids are less intuitive than those of free molecules or those of molecules in solution. Molecular-modeling studies to interpret the meanings of these parameters in solids are needed.

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Supplementary Material Available: A listing of the X-ray diffraction determination data (15 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal and can be ordered from the ACS; and can be downloaded from the Internet; see any current masthead page for ordering information and Internet acess instructions.

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