J. Am. Chem. Soc. **1993**, *115*, 9747-9749 9747

Tautomeric Proton Transfer of Tropolone Included in α- and β-Cyclodextrins

K. Takegoshi* and Kunio Hikichi

Contribution from the Department of Polymer Science, Faculty of Science, Hokkaido University, Sapporo 060, Japan

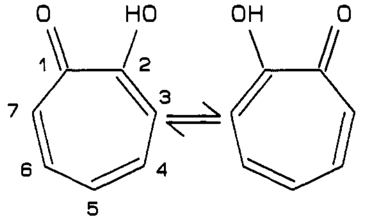
Received May 5, 1993[⊗]

Abstract: ^{13}C MAS NMR spectra of tropolone included in α- and β-cyclodextrins are observed at various temperatures in order to study tautomeric proton transfer. The activation energy for tautomeric proton transfer is <39 and 50.5 kJ/mol for tropolone in α- and β-cyclodextrins, respectively. Kinetic solid-state effects on the tautomeric proton transfer in tropolone are examined.

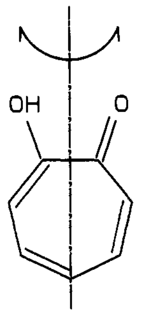
Introduction

The tautomeric proton transfer of tropolone in the solid state has been studied by one- and two-dimensional ^{13}C MAS NMR. It has been reported that the proton transfer in the solid state is a slow process with an activation energy of 109 kJ/mol.[1] In solution, the proton transfer is so fast that two signals of the two tautomeric forms are averaged into a singlet. The slow tautomeric proton transfer in the solid state suggests that tautomeric proton transfer involves not only proton transfer (Scheme I) but also concomitant π-flip (Scheme II) to keep tropolone at a proper lattice position. Since the proton transfer occurs with a small activation energy, the whole process is limited mainly by the π-flip associated with a high activation energy. Such an intermolecular effect on intramolecular kinetics has been widely appreciated and termed the kinetic solid-state effect (KSSE).[2] In this work, we investigate the tautometric proton transfer of tropolone that is included in α- and β-cyclodextrins (α-CDx and β-CDx). We attempt to isolate a tropolone molecule from surrounding tropolones by inclusion in CDx. We intend to investigate the tautomeric process without a KSSE.

Scheme I



Scheme II



Experimental Section

Tropolone was obtained from Tokyo Kasei Co. On the basis of UV titration experiments, Takeshita et al. indicated that α-CDx includes one tropolone molecule, while β-CDx includes two.[3] Tropolone was mixed with α- and β-CDx in 1:1 and 2:1 molar ratios, respectively, in aqueous solution. The colorless fine needles that formed were collected by filtration and dried over silica gel.

NMR measurements were made using a JEOL GX-270 spectrometer operating at frequencies of 67 MHz for ^{13}C and 270 MHz for ^{1}H. High-resolution solid-state ^{13}C NMR spectra were obtained by the combined use of high-power proton decoupling (DD) and magic-angle sample spinning (MAS). The contact time for the cross-polarization (CP) signal enhancement was 2 ms, and the repetition time of accumulation was 4 s. When the CP efficiency was low because of short $T_{1\rho}$, the conventional 90° pulse method was employed. The radio-frequency (rf) field strength for both ^{1}H and ^{13}C was about 55.6 kHz. The ^{1}H decoupling frequency was chosen to be 3 ppm downfield from $(CH_3)_4Si$ (TMS). A double-bearing aluminum oxide rotor was used at a spinning frequency of 6 kHz at temperatures above 310 K and mostly 5.5 kHz below 310 K. The setting of the magic angle was monitored by the ^{79}Br NMR spectrum of KBr incorporated into the rotor. The ^{13}C chemical shift was calibrated in ppm relative to TMS by taking the methine carbon of solid adamantane (29.50 ppm) as an external reference standard. Variable-temperature measurements were accomplished using a JEOL MVT temperature controller. Temperature calibration was done by the conventional methanol method; methanol is shielded in a glass tube and fitted into a rotor spinning at about 5.5 kHz. Signal accumulation was in most cases started 20 min after the desired temperature was achieved.

Results and Discussion

Figures 1 and 2 show CP/MAS spectra of tropolone in α- and β-CDx, respectively, at various temperatures. At temperatures higher than 320 K, tropolone in β-CDx undergoes an irreversible spectral change caused probably by dehydration; new peaks appear at 174.3, 133.0, 139.5, and 127.5 ppm. In this work, we discuss the results below 320 K. Chemical shift values of tropolone signals in α-CDx and those in β-CDx observed at 311 and 222 K are collated in Table I together with those of pure solids and those in deuterated dimethyl sulfoxide (DMSO-d_6) solution.[4] The chemical shift values of tropolone in α-CDx are independent of temperature and are very similar to those in solution. The line width shows an apparent temperature dependence. For tropolone in β-CDx, the chemical shift values at 222 K are similar to those of the pure solid. On the other hand, the chemical shift values at 311 K are very similar to those found for tropolones in solution.

For tropolone in β-CDx, the observed temperature dependence of the spectra is characteristic of the two-site jump associated with tautomeric proton transfer. The rate of tautomeric proton

---

* To whom correspondence should be addressed at the Department of Chemistry, Faculty of Science, Kyoto University, Kyoto 606, Japan.

⊗ Abstract published in *Advance ACS Abstracts*, October 1, 1993.

(1) (a) Szeverenyi, N. M.; Bax, A.; Maciel, G. E. *J. Am. Chem. Soc.* **1983**, *105*, 2579–2582. (b) Titman, J. T.; Luz, Z.; Spiess, H. W. *J. Am. Chem. Soc.* **1992**, *114*, 3756–3765.

(2) Limbach, H. H.; Hening, J.; Kendrick, R.; Yannoni, C. S. *J. Am. Chem. Soc.* **1984**, *106*, 4059–4060.

(3) Takeshita, H.; Kumamoto, M.; Kouno, I. *Bull. Chem. Soc. Jpn.* **1960**, *53*, 1006–1009.

(4) Imashiro, F.; Maeda, S.; Takegoshi, K.; Terao, T.; Saika, A. *Chem. Phys. Lett.* **1982**, *92*, 642–645.

0002-7863/93/1515-9747$04.00/0

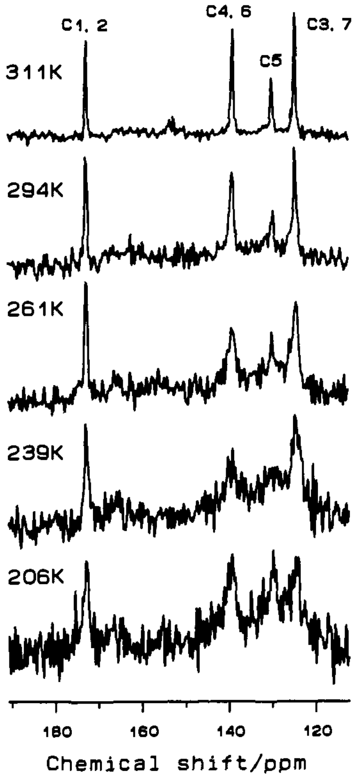


Figure 1. ^{13}C CP/MAS spectra of the tropolone/α-CDx inclusion complex at various temperatures. Only tropolone signals are observed in this region (110–190 ppm).

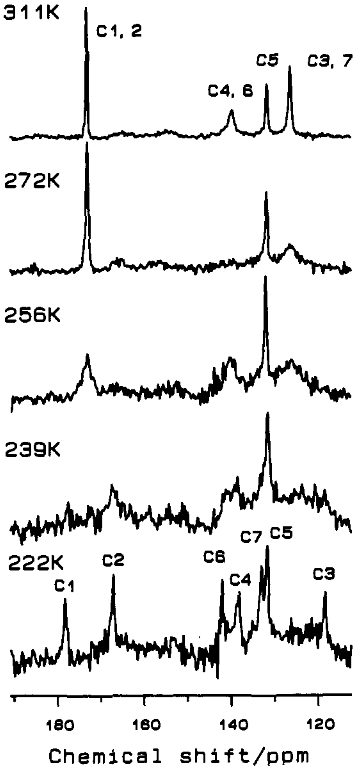


Figure 2. ^{13}C CP/MAS spectra of the tropolone/β-CDx inclusion complex at various temperatures. Only tropolone signals are observed in this region (110–190 ppm).

Table I. ^{13}C NMR Chemical Shifts for Tropolones in the Solid State and in DMSO-d_6[a]

	C1,2	C3,7	C4,6	C5
in DMSO-d_6[b]	171.7	124.3	137.3	127.9
in α-CDx at 311 K	172.5	124.1	138.5	129.4
in β-CDx at 311 K	173.0	125.7	139.3	131.1

	C1	C2	C3	C4	C5	C6	C7
as pure solid[a]	178.1	165.9	116.7	134.4	131.5	142.4	134.4
in β-CDx at 222 K	178.1	167.1	117.9	137.7	138.4	141.8	132.6

[a] Chemical shifts in ppm. [b] Reference 4.

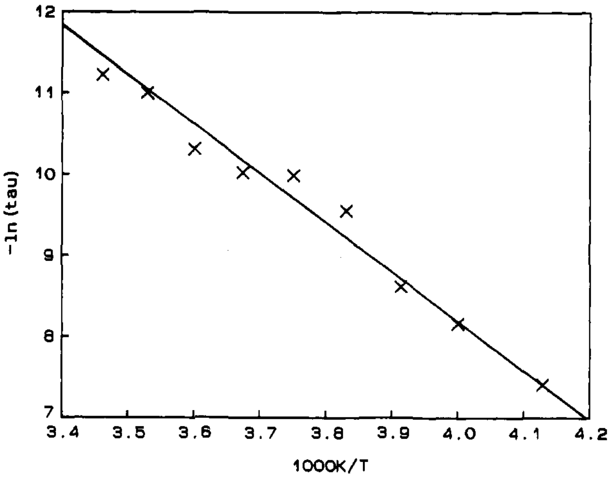


Figure 3. Temperature dependence of correlation time τ of the two-site jump motion deduced from the signals of C1,2 of tropolone in β-CDx. The solid curve is the "best fit" one.

transfer is fast at 311 K but slow at 222 K. Since the C5 signal does not show any significant line broadening or narrowing, the C5 motion is not appreciable. We conclude that the tropolone molecules does not undergo an overall motion in β-CDx. We analyzed the observed temperature-dependent line shapes of C1,2 to obtain the tautomeric proton-transfer rate by assuming an exchange between two equally populated sites and the same line width for the two signals.[5] The rate obtained is plotted in Figure 3. We regarded the C5 line width at each temperature as the static line width. The straight line in Figure 3 is the best fitted line, assuming an Arrhenius temperature dependence. The activation energy is estimated to be 50.5 ± 2.0 kJ/mol, and the correlation time at infinite temperature is $(8 \pm 8) \times 10^{-15}$ s (error is σ). The rate determined from C1,2 can reproduce well the spectra of C3,7 but not those of C4,6. The observed C4,6 signal at 311 K is much broader than expected. Presumably, tautomeric proton transfer at these temperatures is still too slow to achieve a perfect C_2 symmetry for tropolone, and displacement from an ideal conformation is larger for C4 and C6 than for the other carbons. Or there may be a disorder in the position of tropolone in β-CDx and large local variations in the vicinity of C4 and C6. The obtained activation energy for the tautomeric proton transfer of tropolone in β-CDx (50.5 kJ/mol) is smaller than that obtained for pure tropolone (109 kJ/mol).

For tropolone in α-CDx, tautomeric proton transfer is fast even at 206 K, the lowest temperature attained by our NMR probe. The proton-transfer rate must be more than 2000 Hz at 206 K. If we assume τ_0 to be 8×10^{-15} s, the highest possible activation energy is calculatd to be 39 kJ/mol. If we consider this value as an activation energy of proton transfer free from KSSE, the activation energy for the π-flip in the pure tropolone crystal is estimated to be 70 kJ/mol.

Further examination of the experimental spectra of tropolone in α-CDx reveals that line widths of all carbon signals show temperature dependence due to motional broadening or narrowing. The line width of each peak was obtained by fitting the whole tropolone signal to the sum of four Lorentz-type lines. Since the CP efficiency is very low at temperatures of 206–239 K owing to short ^{1}H and ^{13}C $T_{1\rho}$'s, the rate of molecular motion at these temperatures is probably comparable to the decoupling frequency.

---

(5) Martin, M. L.; Martin, G. L.; Delpuech, J.-J. *Practical NMR Spectroscopy*; Hyden: London, 1980; Chapter 8.

The broadening is therefore attributed to interference between the proton decoupling and the molecular motion. The temperature dependence of line width δ may be described as[6]

$$\delta(T) = \delta_0 + A(X/(1 + X^2)) \qquad (1)$$

with

$$X = \omega_1\tau_0 \exp(E_a/RT)$$

The first term in eq 1 represents the intrinsic static line broadening, which is assumed to be 20 Hz. The second represents the interference term. ω_1 is the intensity (in rad·s^{-1}) of the decoupling field, and A decribes the ^{1}H–^{13}C dipolar interaction. With A, τ_0, and E_a taken as adjusting parameters, the observed line width vs temperature data for C4,6 are least-squares-fitted to eqs 1 and 2 (Figure 4). The "best fit" parameters are $A = 528 \pm 230$ Hz, $\tau_0 = (3 \pm 3) \times 10^{-11}$ s, and $E_a = 21.2 \pm 5.3$ kJ/mol (error is σ). By using the same values of τ_0 and E_a, the line widths of C1,2 are reproduced with $A = 160$ Hz. A reason for the smaller A value is that there are no directly-bonded ^{1}H for C1,2; the dipolar interaction is weak as compared to that of C4,6. Since the temperature dependence of all carbon line widths can be described by the same activation parameters (τ_0 and E_a), we concluded that tropolone in α-CDx undergoes overall motion concomitant with a fast tautomeric proton transfer.

Figure 5 shows the spectra in a range of 50–110 ppm, in which signals of α- and β-CDx appear. The two spectra of α-CDx are almost the same; the tropolone molecule undergoes slow motion at 217 K (Figure 5a) and rapid motion at 311 K (Figure 5b). This suggests that the change in the motional state of tropolone does not give rise to any significant structural changes in α-CDx. On the other hand, the spectrum of β-CDx at 222 K (Figure 5c) is remarkably different from that at 311 K (Figure 5d); the proton transfer is slow at 222 K and fast at 311 K. Concomitant with the slowing of proton transfer, the signal of β-CDx shows additional splitting. This indicates that the slowing of the proton transfer causes structural changes in β-CDx. The energy required for such structural changes is included in the activation energy for the proton transfer (50.5 kJ/mol). Taking into account an activation energy of less than 39 kJ/mol for tropolone in α-CDx, the energy for structural changes in β-CDx is estimated to be about 11.5 kJ/mol.

It is important to discuss whether the proton transfer occurs within one tropolone molecule or within several tropolones. It is possible for coordinated water molecules or OH groups of CDx to participate in the process. The contribution of the latter is unlikely because OH groups do not exist inside of the CDx cavity.[7] Since tropolone in α-CDx undergoes fast overall motion, it is difficult to form intermolecular hydrogen bonds. Thus, the proton transfer occurs within one tropolone molecule in α-CDx. Since there are two tropolones in one β-CDx, it is possible that the proton transfer occurs between two tropolone molecules in β-CDx. More detailed structural information is needed for further discussion. Unfortunately, several attempts to grow a single crystal tolerable for X-ray crystallography have failed.

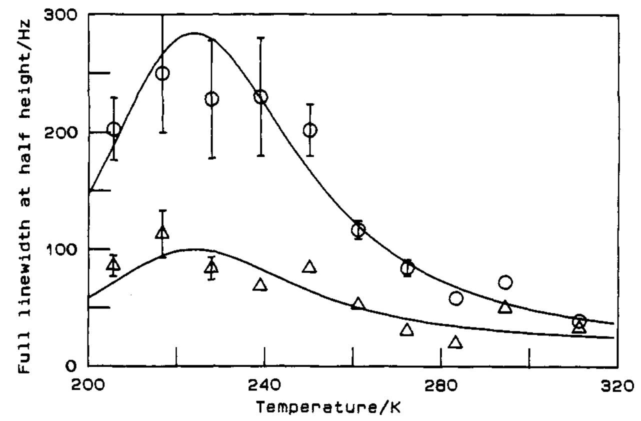


Figure 4. Temperature dependence of the line widths of C4,6 (○) and C1,2 (△) of tropolone in α-CDx. The solid curves are the "best fit" ones.

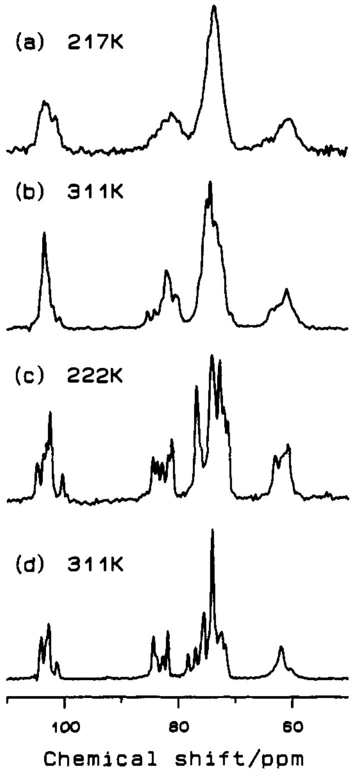


Figure 5. ^{13}C CP/MAS spectra of tropolone/α- and β-CDx inclusion complexes. Only CDx signals are observed in this region (50–110 ppm): (a, b) α-CDx; (c, d) β-CDx.

The activation energy for the proton transfer of tropolone is reduced significantly when it is included in CDx. The requirement for its lattice to maintain crystallographic symmetry (KSSE) is weak or absent for the tautomeric process of proton transfer of tropolone in α- and β-CDx. This suggests that the tropolone molecules in CDx are disordered; the two orientations of a tropolone molecule which arise from the tautomeric proton transfer have the same steric energy and co-exist in CDx. Such a disorder of a guest molecule in inclusion complexes is widely observed. For example, a single-crystal neutron diffraction study of partially deuterated β-CDx ethanol octahydrate shows that the ethanol hydroxyl orientation and the water orientations are disordered.[7] Furthermore, X-ray crystallography of a pure tropolone solid shows that tropolone forms a dimer, and intermolecular hydrogen bonding is indicated.[8] The KSSE is more stringent when such strong intermolecular hydrogen bonding is present because the tautomeric proton transfer involves breaking of hydrogen bonds. On the other hand, such intermolecular interaction is less prominent for the tropolones included in CDx. Since restoration of the crystallographic symmetry is not required, and since tropolone in CDx is rather isolated from other tropolones, we could observe the tautomeric proton transfer of tropolone without significant KSSE.

Acknowledgment. We thank Prof. I. Tanaka and his students for their efforts in attempting to grow single crystals. This work was supported by a Grant-in-Aid for Scientific Research (02554014) from the Ministry of Education, Science and Culture of Japan.

---

[6] (a) VanderHart, D. L.; Earl, W. L.; Garroway, A. N. *J. Magn. Reson.* **1981**, *44*, 361–401. (b) Rothwell, W. P.; Waugh, J. S. *J. Chem. Phys.* **1981**, *74*, 2721–2732.

[7] Steiner, T.; Mason, S. A.; Saenger, W. *J. Am. Chem. Soc.* **1991**, *113*, 5676–5687 and references therein.

[8] Shimanouchi, H.; Sasada, Y. *Acta Crystallogr., Sect. B* **1973**, *B29*, 81–90.