Hydrogen-Bonded Cyclic Dimer Formation in Temperature-Induced Reversal of Tautomerism of Salicylideneanilines

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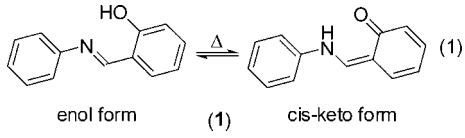
Tautomeric equilibrium of salicylideneanilines is in favor of the enol form in most organic solvents at room temperature. We have previously reported that the equilibrium in saturated hydrocarbon solvents is reversed at low temperature, being totally in favor of the cis-keto form, which is unfavorable at room temperature. Although this stabilization of the cis-keto form has been explained in terms of aggregation of molecules at low temperature, the structure of the aggregate has remained uncharacterized. In this study, we measured UV−vis absorption spectra of salicylideneanilines including those which have *tert*-butyl groups at various positions of the benzene rings. The cis-keto form did not appear at low temperature, when salicylideneanilines have a *tert*-butyl group at a specific position or is restrained to a planar conformation. From these results we propose here that the temperature-induced reversal of the tautomeric equilibrium proceeds through the formation of intermolecular hydrogen-bonded cyclic dimers and the subsequent formation of the higher-order aggregates.

Introduction

Tautomerism is a general phenomenon of organic molecules and plays a vital role in many fields of chemistry[1] and biochemistry.[2] Tautomerization involves an alternation of the π electronic state of the molecules and accordingly accompanies the changes of molecular properties. Such examples can be found in photochromism[3–8] and thermochromism[5–7,9–11] of tautomeric systems. Photochromism occurs when tautomers with different colors mutually exchange through their excited states. Thermochromism takes place when the equilibrium between the tautomers having different colors changes with temperature.

Salicylideneaniline (**1**, abbreviated SA) and its congeners have been known to exhibit photochromism and thermochromism in the solid state.[7–9,11,12] The thermochromism has been explained in terms of the tautomerization between the enol and cis-keto forms having different colors (eq 1).[7,9,11,12] Most SAs exist mainly as the enol form, which is more stable than the cis-keto form, in the solid state and most organic solvents at room temperature. When the temperature is lowered, the population of the enol form increases and that of the cis-keto form decreases, following the Boltzmann distribution law. Thus, the enol form is favored at any temperature.



However, we have found in a previous study that in hydrocarbon solvents, the equilibrium of SAs generally shifts in the opposite direction when the temperature is lowered.[10] As an example, UV−vis absorption spectra of **1** at 297 and 77 K are shown in Figure 1a. At 297 K, there are only the absorption bands assigned to the enol form. At 77 K, in contrast, there are only the absorption bands assigned to the cis-keto form.[13] Thus, the cis-keto form is so much stabilized that it becomes predominant at 77 K. The reversal of the tautomeric equilibrium was observed in many other SAs in hydrocarbon solvents[10] and also reported for related compounds such as tautomeric Schiff bases and azo dyes.[14–17] We have recently found that the reversal of the tautomeric equilibrium also occurs in 7-hydroxyquinolines,[18] the molecular skeleton of which is totally different from SAs. It was also reported that in the hydrocarbon solution of 1-azacarbazole the minor tautomer, which is too unstable to be observed as a monomer at room temperature, was observed as aggregates at low temperature.[19] Therefore, it seems to be a general phenomenon in the tautomeric compounds that the tautomer that is unfavorable at room temperature is stabilized at low temperature.

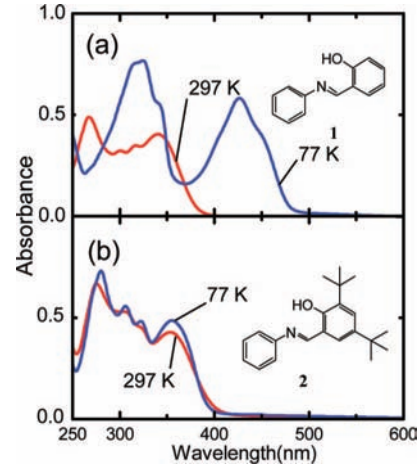


Figure 1. UV−vis absorption spectra of salicylideneaniline (**1**) and *N*-(3,5-di-*tert*-butyl-2-hydroxybenzylidene)aniline (**2**) in the mixture of isopentane and methylcyclohexane (volume ratio = 3:1) at 297 and 77 K, path length 1.0 cm: **1**, 3.6×10^{-5} M; **2**, 4.6×10^{-5} M. The spectra were produced using the data reported in a previous paper.[10]

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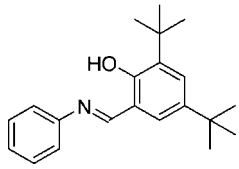
The stabilization of the cis-keto form of SAs at low temperature has been explained in terms of aggregation of the molecules, because it was facilitated in higher concentration solutions.[10] The participation of the aggregation seemed to be confirmed by the spectra of *tert*-butylated salicylideneaniline **2**. In contrast to other SAs including **1**, the spectra of **2** did not show any temperature changes corresponding to the appearance of the cis-keto form (Figure 1b),[10] which was interpreted as due to hindering of the aggregation by the bulky *tert*-butyl groups.

In spite of the crucial role of the aggregation in the stabilization of the cis-keto form, any structural information of the aggregates has not been reported. This is mainly because most spectroscopic methods including NMR spectroscopy, which would give valuable information for the structure determination, are difficult to be applied to this case, because of the extremely low concentration of the aggregates as low as 10^{-5} M, the very low temperature as low as 77 K, and the limited solvents (hydrocarbons only).



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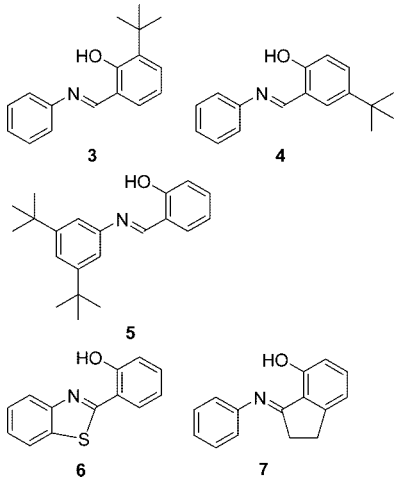
In this study, we measured UV−vis absorption spectra of SAs **3**−**7** in saturated hydrocarbon solvents at 297 and 77 K. We found that whether the reversal of the tautomeric equilibrium takes place or not at low temperature strongly depends on the molecular structure of the compounds. From the examination of their spectra, we propose here that the temperature-induced reversal of the tautomeric equilibrium proceeds through the formation of intermolecular hydrogen-bonded cyclic dimers and the subsequent formation of the higher-order aggregates.



Experimental Section

Materials. Salicylideneanilines with *tert*-butyl groups **3**, **4**, and **5** were prepared according to standard procedures. Compound **6** was purchased from Acros. Compound **7** was prepared according to the procedure described in the literature.[20] All the compounds were recrystallized from methanol.

Characterization data for *N*-(2-hydroxybenzylidene)-3,5-di-*tert*-butylaniline (**5**). Yellow crystals, mp 98.0−98.3 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.36(s, 18H), 6.94(td, 1H), 7.03(dt, 2H), 7.11(d, 1H), 7.35−7.39(m, 2H), 7.42(dd, 1H), 8.63(s, 1H), 13.47(s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 31.44, 35.02. 115.39, 117.21, 118.92, 119.30, 121.08, 132.12, 132.86, 148.01, 152.15, 161.14, 162.09. Anal. Calcd for $C_{21}H_{27}NO$: C, 81.50; H, 8.79; N, 4.53. Found: C, 81.42; H, 8.90; N, 4.39.

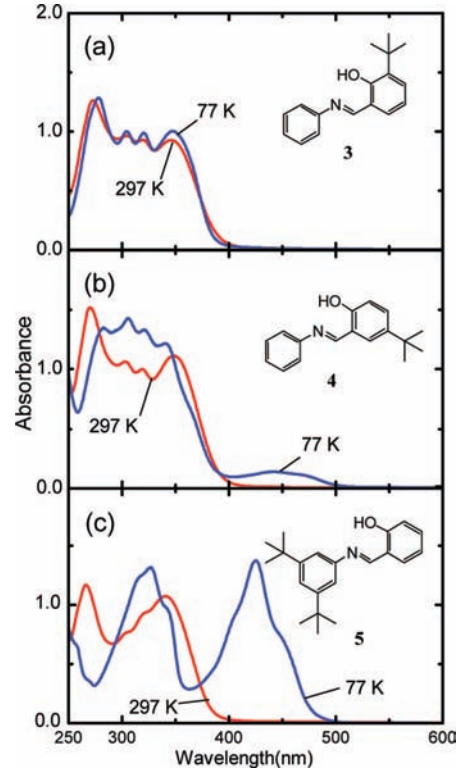


Figure 2. UV−vis absorption spectra of *N*-(3-*tert*-butyl-2-hydroxybenzylidene)aniline (**3**), *N*-(5-*tert*-butyl-2-hydroxybenzylidene)aniline (**4**), and *N*-(2-hydroxybenzylidene)-3,5-di-*tert*-butylaniline (**5**) in the mixture of isopentane and methylcyclohexane (volume ratio = 3:1) at 297 and 77 K, path length 1.0 cm, concentration 7.5×10^{-5} M for each sample.

Measurements. The UV−vis absorption spectra were measured on a Jasco Ubest V-560 spectrometer equipped with a liquid nitrogen bath cryostat Oxford DN1704 or OptistatDN. The temperature of the cryostat was controlled within ±0.1 K. A spectroscopic grade isopentane from Merck (UVASOL) and a spectroscopic grade methylcyclohexane from Aldrich were used as received. The path length was 1.0 cm. An apparent increase in absorbance due to the contraction of the solvent at low temperatures was corrected using the method described in the literature.[21]

Calculations. Ab initio calculations were performed at the MP2/6−31G* and HF/6−31G** levels using the Gaussian 98 program.[22] The structures of the cyclic dimers of the enol forms and the cis-keto forms were optimized imposing centrosymmetric constraints. For the energy calculation of the dimers, basis set superposition error (BSSE) was corrected using the counterpoise method.[23] At the HF/6−31G** level, the cyclic dimer structures were confirmed to be at energy minima by vibrational frequency calculations that gave no imaginary frequency. Frequency calculations could not be carried out at the MP2/6−31G* level due to the limitation of computer resources.

Results and Discussion

As mentioned in the previous section, the cis-keto form of most SAs becomes predominant in hydrocarbon solvents at low temperature. However, it is not the case in **2**, which has *tert*-

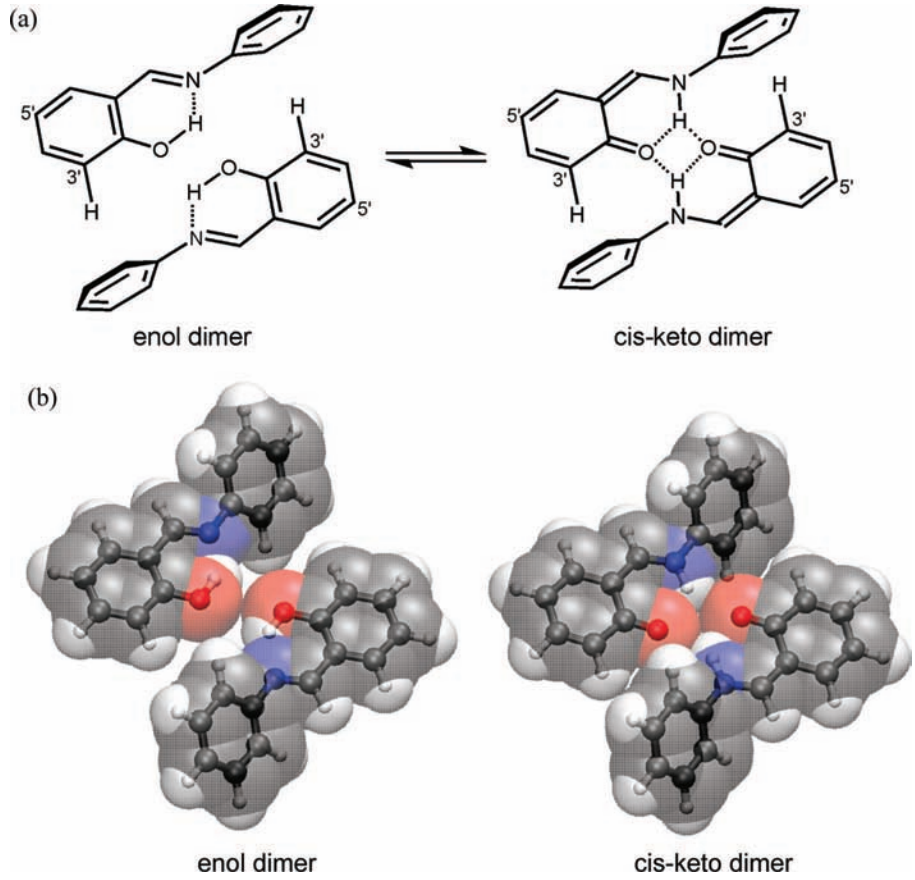


Figure 3. Intermolecular hydrogen-bonded cyclic dimers of the enol and cis-keto forms of **1**. (a) Schematic presentation and (b) molecular models obtained from the geometry optimization by quantum mechanical calculations using HF/6−31G**.

butyl groups on a benzene ring. The nonappearance of the cis-keto form in **2** was interpreted as due to hindering of aggregation by the bulky *tert*-butyl groups.

This interpretation was supported by the UV−vis spectra of **3**, which has a *tert*-butyl group on a benzene ring (Figure 2a). Compound **3** exhibited only the absorption bands of the enol form both at 297 and 77 K, indicating that the tautomeric equilibrium of **3** did not shift to the cis-keto form at 77 K. However, in the spectra of **4** and **5**, which also have *tert*-butyl groups, the absorption bands of the cis-keto form appeared at 77 K (Figure 2b,c). This spectral change shows that the equilibrium of **4** and **5** shifted to the cis-keto form at 77 K despite that they have *tert*-butyl groups. These results demonstrate that the *tert*-butyl groups do not necessarily inhibit the aggregation and the resultant stabilization of the cis-keto form.

To rationalize the strong compound-dependence of the spectral changes, we propose here a working hypothesis that the aggregation at low temperature occurs by way of the formation of intermolecular hydrogen-bonded cyclic dimers shown in Figure 3. The compound-dependent spectral changes can be explained by whether or not the molecule is able to form the cyclic dimers.

The structures of the cyclic dimers of the enol and cis-keto forms of SA (**1**) were optimized by quantum mechanical calculations (Figure 3b). In the cyclic dimers, two SA molecules are aligned in an antiparallel fashion through intermolecular hydrogen bonding. The intermolecular hydrogen bonds of the enol dimer are geometrically much less favorable than those of the cis-keto dimer. The torsion angles N═C(H)−C−C(O) of the enol form or N−C(H)═C−C(═O) of the cis-keto form is nearly 0 deg due to the intramolecular O−H···N or O···H−N hydrogen bonding, as in the monomers of SAs.[7,24] On the other hand, the N−Ph bond of either form is substantially twisted to avoid the steric repulsion between the H atom at the C3′ position and the benzene ring facing it. If the H atom is replaced with a bulky substituent such as a *tert*-butyl group, the steric repulsion would be too severe to form the cyclic dimers. Accordingly, the formation of the cyclic dimers is not possible for **2** and **3** because of their *tert*-butyl group at C3′ position but possible for **4** and **5** because of the absence of any substituents at their C3′ position.

Our hypothesis on the cyclic dimer formation was substantiated by the quite contrasting results of **6** and **7**. The UV−vis spectra of **6**, which is restrained to a planar conformation by the sulfur bridge, showed only the absorption band of the enol form at 297 and 77 K (Figure 4a). The absence of the temperature-induced change of the spectra of **6** can be interpreted that no cyclic dimer is formed in **6** because the N−Ph bond cannot twist to avoid the steric repulsion between the H atom at C3′ and the benzene ring facing it. In contrast, compound **7**, in which the twisting of the C−Ph bond is inhibited but that of the N−Ph bond is not limited, showed a pronounced spectral change (Figure 4b). Only the absorption bands of the enol form were observed at 297 K, but the prominent bands of the cis-keto form appeared at 77 K. All the above results lead to conclude that the formation of the intermolecular hydrogen-bonded cyclic dimers is essential for the temperature-induced reversal of the tautomerism of SAs.

Intermolecular hydrogen bonding has been known to stabilize the tautomers that are less stable as isolated molecules. For example, some SAs exist mainly as the cis-keto form with intermolecular hydrogen bonding in crystals, in contrast to in

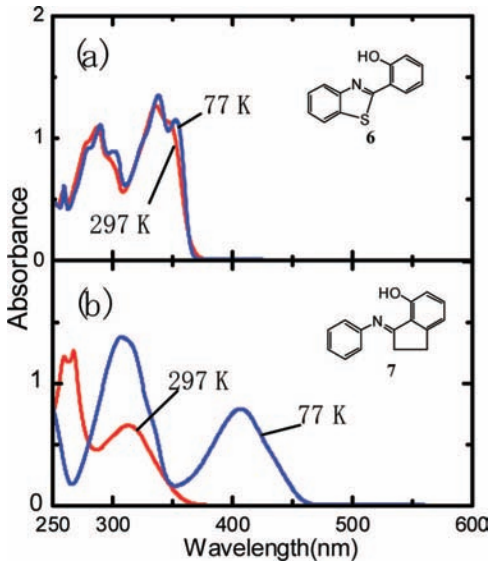


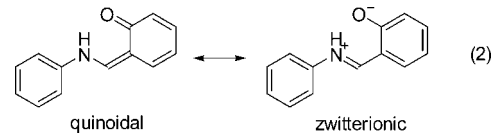
Figure 4. UV−vis absorption spectra of 2-(2-hydroxyphenyl)benzothiazole (**6**) and 2,3-dihydro-3-(phenylimino)-1H-inden-4-ol (**7**) in the mixture of isopentane and methylcyclohexane (volume ratio = 3:1) at 297 and 77 K, path length 1.0 cm, concentration 7.5×10^{-5} M for each sample.

solution, where they exist mainly as the enol form.[9,25] According to quantum mechanical calculations of **1**, the cis-keto form is less stable than the enol form as a monomer by 8.7 kcal mol^{-1} at the MP2/6−31G* level (8.8 kcal mol^{-1} at the HF/6−31G** level). As the cyclic dimer, the energy difference is decreased to 6.7 kcal mol^{-1} at the MP2/6−31G* level (7.2 kcal mol^{-1} at the HF/6−31G** level). The decrease of the energy difference can be explained in terms of stronger intermolecular hydrogen bonds in the cis-keto dimer than that in the enol dimer, which results in the larger interaction energy in the cis-keto dimer.[26] The calculations show that the cis-keto form is still less stable than the enol form. The formation of the intermolecular hydrogen-bonded cyclic dimer is, therefore, not sufficient for the reversal of the tautomeric equilibrium in **1**, in contrast to a salicylidenealkylamine[27] and 2-hydroxypyridines,[28] where their tautomerisms are reversed when they crystallize from solution by the formation of the intermolecular hydrogen-bonded cyclic dimers. This is most likely due to the much larger energy difference between the tautomers in **1** compared with those in salicylidenealkylamines and 2-hydroxypyridines.

The fact that the cyclic dimer formation is essential but insufficient for the reversal of the tautomeric equilibrium in **1** suggests that another intermolecular interaction is necessary to further stabilize the cis-keto form. Such an interaction would be caused by aggregation of the cyclic dimers. We have reported in a previous paper that the temperature-induced reversal of the tautomeric equilibrium of 7-hydroxyquinolines requires the formation of the higher order aggregates of hydrogen-bonded aggregates.[18] Accordingly we propose here a similar explanation that the formation of the higher order aggregates of the intermolecular hydrogen-bonded cyclic dimers is also essential for the predominance of the cis-keto form of SAs at low temperature. Thus, when the temperature is lowered, the enol monomers first form the enol cyclic dimer. The cis-keto cyclic dimer is in equilibrium with the enol cyclic dimer but is too unstable to detect. The enol cyclic dimers further form the higher order aggregates of the enol form. In the higher order aggregates, the enol form is in equilibrium with the cis-keto form, which is much more stable than the enol form. As a result, the higher order aggregates of the cis-keto form become predominant at low temperature.

The essential role of the higher-order aggregates for the stabilization of the cis-keto form is supported by the UV−vis spectra of **4**, which is, according to molecular modeling, able to form the intermolecular hydrogen-bonded cyclic dimers despite the presence of the *tert*-butyl group at the C5′ position. The spectra exhibited the absorption band of the cis-keto form in the 400−500 nm range at 77 K with a much lower intensity than that of **1** and **5** (Figure 2b), indicating the smaller population of the cis-keto form in **4** than in **1** and **5** at 77 K. These results can be therefore interpreted that the cis-keto form is not sufficiently stabilized in **4** because the further aggregation of the cyclic dimers is somewhat hindered by the bulky *tert*-butyl group at the 5′ position.

The stabilization of the cis-keto form in the higher-order aggregates is likely due to electrostatic interactions. We have previously shown that the cis-keto form is substantially stabilized in crystals because of its zwitterionic character (eq 2).[9,29] The cis-keto form in the higher-order aggregates would be, therefore, also zwitterionic as in crystals and consequently stabilized by electrostatic interactions.



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Concluding Remarks

We propose here that the temperature-induced reversal of the tautomeric equilibrium of salicylideneanilines in saturated hydrocarbon solvents at low temperature proceeds through the formation of intermolecular hydrogen-bonded cyclic dimers and the subsequent formation of the higher-order aggregates that have the intermolecular hydrogen-bonded cyclic dimer of the cis-keto form as a basic structural unit. Formation of intermolecular hydrogen bonding and further aggregation of the hydrogen-bonded aggregates might be commonly involved in a variety of tautomeric compounds as the cause for the temperature-induced shift to the tautomer that is less stable as an isolated molecule.

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(26) The weak interaction in the enol dimer can explain the fact that the formation of the dimer as an intermediate species was not clearly observed in the UV−vis spectra.[10] This is mainly because the spectral changes corresponding to the dimer formation are not large due to the weak intermolecular interaction. This makes a sharp contrast to 7-hydroxyquinolines, where the formation of the enol dimer is driven by the formation of intermolecular hydrogen bonds, which leads to significant spectral changes at intermediate stages.

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