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Stable Simple Enols. Self-Catalyzed *E*/*Z*-Isomerization of the Sterically Crowded 2-(*m*-Methoxymesityl)-1,2-dimesitylethenol[1]

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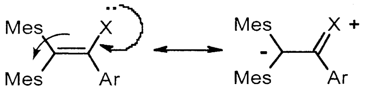
(*E*)-2-(*m*-Methoxymesityl)-1,2-dimesitylethenol (**3a**) isomerizes in the absence of a catalyst in solution to a 1.0:0.9 *E*/*Z* (**3a**/**3b**) equilibrium mixture. In $CDCl_3$, the isomerization is first order in **3a** within a run, but the plot of the rate constant k_{obs} vs the changing $[\mathbf{3a}]_0$ in different runs is a half-parabola, indicating self-catalysis by more than one enol molecule. At 0.09 M enol, the isotope effect $k_{\mathbf{3a}}/k_{\mathbf{3a}-OD} = 2.1$. In the presence of 0.025−0.25 M pyridine-d_5, the k_{obs} vs [pyridine-d_5] plot displays a bell-shaped profile. The change in the shape of the OH signals of the **3a**/**3b** mixture at 295−430 K in $C_6D_5NO_2$ was followed by DNMR. The four signals of the diastereomeric **3a**/**3b** mixture observed at 330 K coalesce at 350 K with barriers of 18.3 and 18.4 kcal mol^{-1} due to the diastereomerization of the vinyl propellers. The resulting two signals observed at >360 K further coalesce at 425 K with a barrier of 22.9 kcal mol^{-1} due either to oxygen-to-oxygen proton exchange or to *E*/*Z* isomerization. The estimated upper limit for the rate of proton exchange of $k_{ex} \le (2-4) \times 10^3$ M^{-1} s^{-1} at 425 K between the enol molecules is sufficiently slow to be a rate-controlling step in the isomerization. A process in which several enol molecules catalyze the isomerization is suggested, and several mechanistic routes are analyzed.

Introduction

An uncatalyzed internal rotation of the double bond in sterically crowded alkenes which leads to $E \rightleftharpoons Z$ isomerization is well-known[2] and usually takes place when the double bond is partially twisted in the ground state. Trimesitylvinyl-X systems **1** (Mes = mesityl) where X is resonatively electron donating, e.g., OR, OAc, OH, are sterically crowded as reflected by different phenomena. (i) They have a propeller conformation in the solid state and in solution[3] with high (>50°) Mes−C=C torsional angles.[4] (ii) They display hindered and correlated rotation around the =C−Ar bonds in solution with activation barriers of 15−27 kcal mol^{-1}.[1,3,5,6] (iii) Their double bond is twisted to a low degree (5−8°).[4] (iv) When X = OH, the enols show high kinetic stability to ketonization.[7] The uncatalyzed rotational barrier around the double bond in these compounds should be lower than that in alkenes due to the contribution of the hybrid form **1a** (eq 1) with the expected longer than normal C1=C2 bond. However, the calculated C=C double bond lengths of vinyl alcohol and of ethylene are almost identical,[8] and



(1)

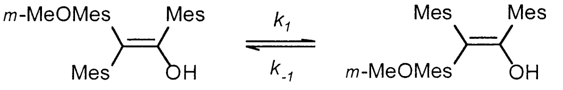
1 **1a**

$R^3R^2C{=}C(OH)R^1$

2a: $R^1{=}R^2{=}H$; $R^3{=}Me$

2b: $R^1{=}R^2{=}H$; $R^3{=}Ph$

2c: $R^1{=}H$; $R^2{=}Ph$; $R^3{=}Mes$



(2)

3a **3b**

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[1] Presented in part in the 59th Meeting of the Israel Chemical Society, Beer Sheva, Israel, Jan 31−Feb 1, 1994, Abstract, p 183, and at the 13th IUPAC Conference on Physical Organic Chemistry, Seoul, Korea, Aug 25−29, 1996 (Rappoport, Z.; Frey, J.; Sigalov, M.; Rochlin, E. *Pure Appl. Chem.* **1997**, *69*, 1933).

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even when the ethylene is substituted by bulky mesityl groups this is not appreciably reflected in bond lengths. The X-ray determined double bond lengths of systems **1**, X = OH, OPr-*i*, are only slightly (by ca. 0.01 Å) longer and those in the corresponding **1**, X = OAc are even shorter than that in ethylene.[4] Furthermore, there is no spontaneous double-bond rotation when X ≠ OH. For example, (*E*)- and (*Z*)-2-*m*-methoxymesityl-1,2-dimesitylvinyl acetates and isopropyl ethers do not undergo a thermal *E*/*Z*-isomerization even when heated in solution up to 150 °C.[6] Likewise, an exchange between the β- and β'-ring protons in the NMR spectra of most trimesitylvinyl systems with identical β- and β'-rings was not observed. However, triarylethenols isomerize relatively rapidly. For example, only (*Z*)-1,2-dimesityl-2-phenylethenol is known,[9] and reactions which should initially give the *E*-isomer, such as hydrolysis of the *E*-acetate, lead only to the *Z*-enol, indicating a rapid *E* → *Z* enol isomerization.[9] Whereas both isomers of simple enols with different β-substituents such as 1-propenol **2a**[10] or 2-phenylethenol **2b**[11] can exist as an *E*/*Z* mixture and their ratio was evaluated for **2b**,[11] they were not separated or isolated and nothing is known about their interconversions. Isomer *Z*-**2c** is more stable than *E*-**2c** but on heating for 5 h in DMSO at 80 °C it isomerizes to an *E*/*Z* mixture richer in *Z*-**2c**.[12]

The first observation pointing to *E*/*Z*-isomerization of the enols was a saturation transfer observation in a pair of β- and β'-*p*-Me groups in the NMR spectrum of 1,2,2-trimesitylethenol (**1**, X = OH).[13] A lower limit of $\Delta G^\ddagger >$ 20.9 kcal mol^{-1} for the exchange barrier of this topomerization was estimated. The MM2-calculated enthalpy of activation for the double-bond rotation in **1** (X = OH) is high ($\Delta H^\ddagger_{\mathrm{rot}} = 51.7$ kcal mol^{-1})[6c] and is reminiscent of the observed $\Delta G^\ddagger > 48.7$ kcal mol^{-1} for rotation around the double bond of a tetramesitylethylene analogue[14] and of the observed values of 36−40 kcal mol^{-1} for similar rotations in other tetraarylethylenes.[15] These values are well above the time scale which enables measurement by NMR. Hence, the observed exchange in trimesitylethenol, as well as the rapid isomerization of an isolated one geometric isomer of 1,2-dimesityl-2-[4-*tert*-butyl-2,6-dimethylphenyl]ethenol[16] to the *E*/*Z* mixture suggest that an efficient catalytic isomerization process is operating.

The mechanism of *E*/*Z* isomerization of ethenols has not been investigated. We recently reported an unusual racemization mechanism of chiral 1-[9′-(2′-fluoroanthryl)]-2,2-dimesitylethenol[17] as compared with its acetate and other crowded **1**, X ≠ OH. It includes the formation of the intermediate 1,2,2-triarylethylcarbenium ion generated by protonation at C1 of the enolic double bond. Such an intermediate should also permit rotation around the C1−C2 bond and hence enable an *E*/*Z* isomerization in an enol with different β-aryl rings which will display similar characteristics to those of the racemization process. The barrier given above for the saturation transfer in **1** leads to a $t_{1/2}$ value which should enable convenient kinetic measurements. A prerequisite for such a study is a pair of *E*/*Z* enol isomers of not too different energies but of sufficiently different and measurable spectral properties. In the present work, we had studied the *E*/*Z* isomerization in the *E*/*Z* pair of 2-(*m*-methoxymesityl)-1,2-dimesitylethenols **3a**/**3b** (eq 2) by a combination of conventional kinetic and DNMR methods in $CDCl_3$ and $C_6D_5NO_2$.

Results and Discussion

Synthesis. A **3a**/**3b** mixture was synthesized by the reaction of MesMgBr with (*m*-methoxymesityl) mesityl ketene. The synthesis of the ketene was described previously.[6a] The pure *E*-isomer **3a** was isolated from the **3a**/**3b** equilibrium mixture by slow crystallization from petroleum ether, and its structure was established by X-ray diffraction.[6a] Unfortunately, we failed to isolate the pure *Z*-isomer **3b** by crystallization from MeOH, which only gave pure **3a**. An attempted LC separation failed due to the fast isomerization on the silica gel column. Fortunately, for routine kinetic measurements either a single isomer or a nonequilibrium mixture of **3a**/**3b** is sufficient.

NMR Spectra of 3a and 3a/3b. Solid **3a** is stable under ordinary conditions, while in CCl_4, $CHCl_3$, CH_2Cl_2, C_6H_6, $C_6H_5NO_2$, AcOEt, Me_2CO, DMSO, and MeOH solutions it spontaneously isomerizes within 1−2 h at room temperature to the **3a**/**3b** equilibrium mixture and no byproducts were detected. On a TLC plate, the isomerization is complete within 10−20 min. We use the term "spontaneous" in this work to describe an isomerization in solution which occurs sufficiently rapidly without an added catalyst. Unfortunately, the almost identical UV spectra of **3a** and the **3a**/**3b** mixtures excluded the use of the sensitive UV method for monitoring the isomerization. HPLC analysis was also precluded due to a catalyzed isomerization on the column. In contrast, the ^{1}H NMR spectra of **3a** and **3b** are different. Due to the helicity of the propeller structure and since the *m*-MeO group can lie either above ("up") or below ("down") the plane of the double bond either **3a** or **3b** should exist as two pairs of diastereomers. The four stereoisomers and their inter-relations appear in our earlier papers.[3,6,17] At slow exchange and no accidental signal overlap, each of them will display a maximum of 10 Ar-H, 2 OH, 2 OMe, and 18 Ar-Me signals.

Due to signal overlap, the observed ^{1}H NMR spectrum of **3a** at 200 MHz (Figure 1a) in $CDCl_3$ at 295 K displays fewer signals: 6 broaden Ar-H singlets, 2 OH, 2 OMe, and 15 Ar-Me signals, which is still consistent with the propeller structure. The **3a**/**3b** equilibrium mixture,

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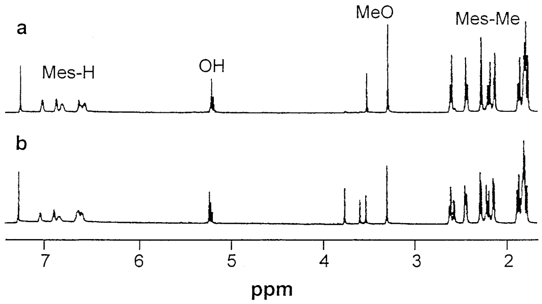

FIGURE 1. ^{1}H NMR spectra of (a) **3a** immediately after dissolution in $CDCl_3$; (b) **3a**/**3b** equilibrium mixture.

which should display at most twice the number of signals of a single isomer, shows under the same conditions a smaller number [6 Ar-H, 3 OH (or 4 OH in the presence of 1 drop of DMSO-d_6), 4 OMe, and 19 Ar-Me signals] (Figure 1b). Due to the overlap, not all the regions of the NMR spectrum are convenient for monitoring the isomerization. However, the remoteness of the four MeO signals of **3a**/**3b** mixture from the other signals and their spread [δ 3.29 (major **3a**), 3.52 (minor **3a**), 3.59 (minor **3b**), 3.75 (major **3b**)] enables ^{1}H NMR monitoring of the E/Z-isomerization at 295 K in $CDCl_3$ by following the decrease and increase of the intensities of the MeO signals of **3a** and **3b**, respectively.

The need for large quantities of the expensive deuteriated solvent for the kinetic investigation limited our study only to the $CDCl_3$ solvent. The use of D_2O or of D_2O-organic media was also precluded due to insolubility of **3a**/**3b** in these media.

Kinetics. Solutions of **3a** (0.09 M) in $CDCl_3$ were first used in the kinetic study, and the decrease in the molar fraction of **3a** with time was followed by using the integrated sum of the MeO signals as an internal standard. In each kinetic run, a reproducible plot for a reversible first-order $E \rightleftharpoons Z$ reaction was obtained by using eq 3, where the P's are the molar fractions of the isomers ($P_{\mathbf{3a}} + P_{\mathbf{3b}} = 1$). An observed first-order rate constant $k_{obs} = k_1 + k_{-1} = (2.8 \pm 0.4) \times 10^{-4}$ s^{-1} was calculated from the slope of the $\ln[[P_{\mathbf{3a}}(K + 1) - 1]/K]$ vs t plot. A $K = k_1/k_{-1}$ value of 0.9 at 295 K was determined thrice at the end of the reaction. By inserting these values into eq 4 where the subscript "eq" indicate the concentrations at equilibrium, we obtained $k_1 = (1.3 \pm 0.2) \times 10^{-4}$ s^{-1} and $k_{-1} = (1.5 \pm 0.2) \times 10^{-4}$ s^{-1}. The k_1 value gives an activation barrier of $\Delta G^{\ddagger}(295\ \text{K}) = 22.4 \pm 0.2$ kcal mol^{-1} for the E/Z isomerization.

$$\ln\{[P_{\mathbf{3a}}(K + 1) - 1]/K\} = -k_{obs}t \qquad (3)$$

$$k_{obs} = k_1 + k_{-1};\ K = k_1/k_{-1} = [\mathbf{3b}]_{eq}/[\mathbf{3a}]_{eq} \qquad (4)$$

To obtain more mechanistic details, we studied briefly the effects of the total enol concentration, of the addition of a base, and of the deuteriation of the enolic OH group on the observed first-order rate constant.

TABLE 1. Effect of Enol Concentration $[\mathbf{3a}]_0$ and Pyridine Concentration C_{pyr} on the Pseudo-First-Order Rate Constant k_{obs} for the E/Z-Isomerization of 3a at 295 K

$[\mathbf{3a}]_0$, M	$10^4\ k_{obs}$, s^{-1}	C_{pyr}, M ^{a}	$10^4 k_{obs}$, s^{-1}
0.028	0.67	0	2.8
0.049	0.83	0.025	7.0
0.078	1.8	0.050	14.3
0.09	2.8	0.080	32.3
0.104	5.0	0.160	31.7
0.114	6.5	0.175	25.0
		0.200	15.0
		0.225	9.9
		0.25	5.2

^{a} $[\mathbf{3a}]_0 = 0.09$ M.

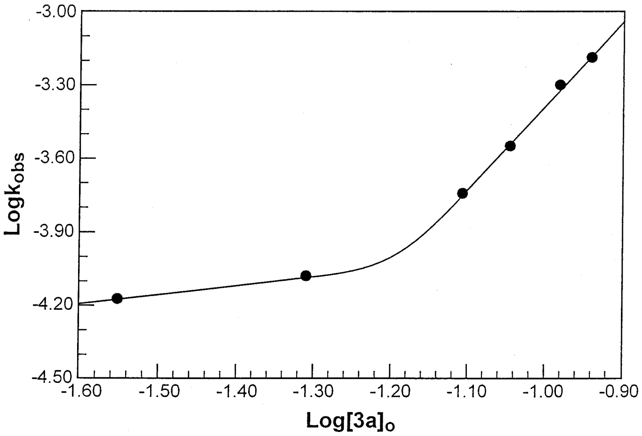

FIGURE 2. Plot of log k_{obs} against log $[\mathbf{3a}]_0$.

On changing the total enol concentration $[\mathbf{3a}]_0$ from 0.02 to 0.114 M, a range convenient for the NMR measurements, the first-order rate constant k_{obs} obtained from eq 3 increases by ca. 10.5-fold (Table 1), suggesting that catalysis by the enol takes place. The k_{obs} vs $[\mathbf{3a}]_0$ plot is a half-parabola-like curve (Figure S1 in the Supporting Information) with a catalytic order larger than one in the enol, although the linearity according to eq 1 is still retained in each run. The reaction does not follow a simple rate law and as seen from Figure 2 the order in the enol is not constant. At low $[\mathbf{3a}]_0$, the overall order in the enol is close to 1, whereas at higher $[\mathbf{3a}]_0$ it is close to 4 indicating a multiple term or complex rate low.[18] The curved dependence of k_{obs} on the total enol concentration means a reaction order higher than two in the enol and that several enol molecules are present in the transition state of the rate controlling step(s), possibly in an associated form. Unfortunately, we know only little about the association of such crowded enols in chloroform and only at low temperature.[19] The pseudo-first-order reaction within a run could be understood if **3a** and **3b** have similar catalytic activities so that k_{obs} is sensitive only to the constant total enol concentration within a kinetic run, and not to the nature of the specific enol. Extrapolation of the k_{obs} vs $[\mathbf{3a}]_0$ plot to zero concentration gives a residual k_{obs} value of ca. 5×10^{-5} s^{-1}, which can be tentatively ascribed either to a monomolecular self-catalyzed reaction or to catalysis by traces of water or impurities in the $CDCl_3$. The higher extent of saturation transfer (vide supra) in a sample that stood for several days in solution than for a freshly dissolved

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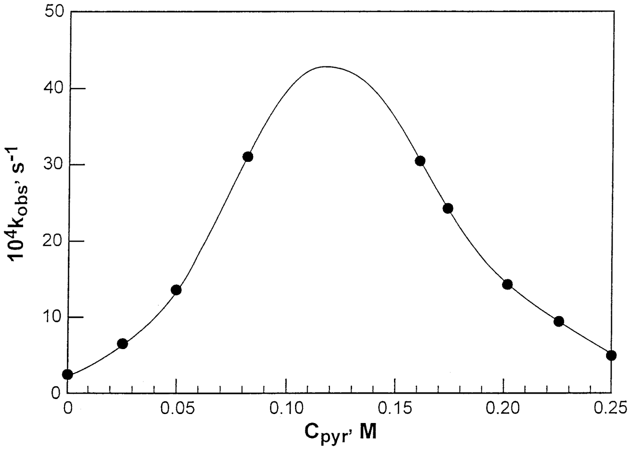

FIGURE 3. Plot of k_{obs} against the pyridine-d_5 concentration C_{pyr}.

sample[13] may reflect the development of catalytic impurities on standing.

The isomerization of **3a**-OD was studied under the same conditions (295 K, $[\mathbf{3a}]_0 = 0.09$ M), and the kinetic isotope effect (KIE) on k_{obs} is $k_H/k_D = 2.1$. Consequently, a proton transfer is definitely involved in the rate-determining step(s) of the isomerization. From the k_{obs} vs $[\mathbf{3a}]_0$ plot, the proton transfer in the absence of added acids or bases probably takes place in a transition state containing several enol molecules. A third-order term was reported for several reactions subject to general acid (base) catalysis, such as enolization of ketones[20] and mutarotation of tetramethylglucose.[21] It was ascribed to a concerted mechanism in which two catalyst molecules—one a proton donor and one a proton acceptor—are present in the transition state. Bell suggested that in low dielectric constant solvents such mechanism might be preferable over the stepwise route.[21] Self-catalysis by the substrate, resulting in a second order in the substrate, was recently observed for the enolization of malonate anion.[22]

We were unable to quantitatively study the acid/base catalysis in the *E*/*Z*-isomerization since our enols are insoluble in D_2O or aqueous–organic media, and hence, the use of buffer solutions was precluded. Consequently, we studied only the effect of 0.025–0.25 M pyridine-d_5 on the isomerization rate in $CDCl_3$. Due to deviations from the first order plots at several pyridine concentrations we used only the intercepts of the plots in the first 50–70% reaction in our qualitative analysis. A plot of k_{obs} vs [pyridine-d_5] displays a bell-shaped profile (Figure 3): At the lower [pyridine-d_5] of 0–0.1 M, k_{obs} increases and reaches a maximum at ca. 0.1–0.12 M and it then decreases almost to its initial "uncatalyzed" value at ca. 0.25 M pyridine.

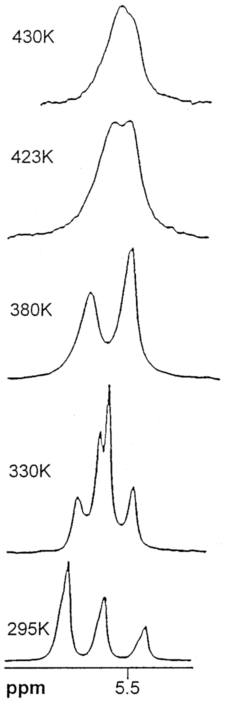

FIGURE 4. Temperature-dependent ^{1}H NMR spectrum of the OH region of **3a**/**3b** equilibrium mixture in $C_6D_5NO_2$.

DNMR Study. The proton exchange between two enol molecules could be monitored by a dynamic NMR technique using as probes the four well-resolved OH singlets in the NMR spectrum of the **3a**/**3b** equilibrium mixture. Since temperatures above the boiling point of $CDCl_3$ are required in order to follow the exchange of the OH protons, the exchange was studied in $C_6D_5NO_2$ at $[\mathbf{3a}]_0 = 0.03$ M. The temperature dependent changes of the OH signals at 295–430 K are shown in Figure 4. Whereas at 295 K only three OH signals are observed at 5.54, 5.515, and 5.49 ppm, due to their slight shift upfield on raising the temperature all four singlets belonging to the two diastereomeric pairs of **3a**/**3b** are observed at 330 K. Broadening takes place on further temperature increase, and each pair coalesces at 350 K, giving barriers of 18.4 ± 0.2 and 18.3 ± 0.2 kcal mol^{-1}. These values resemble the barriers of 18.8 and 18.3 kcal mol^{-1} for the 3-ring flip diastereomerization process obtained earlier for **3a**/**3b** from the coalescence of the MeO signals[6a] and identify the observed processes as the diastereomerizations of **3a** and **3b**. Two signals, one belonging to **3a** and one to **3b**, then start to appear at 360 K, and they remain relatively sharp and separate with $\Delta\nu = 5.8$ Hz at the 380–400 K region (Figure 4). They then coalesce at 425 K, giving a barrier of $\Delta G_c^‡ = 22.9 \pm 0.1$ kcal mol^{-1} which is surprisingly close to the isomerization barrier derived above from k_{obs} at 295 K in $CDCl_3$ from the kinetic study. Consequently, the barrier for proton exchange between **3a** and **3b** is ≥ 22.9 kcal mol^{-1} regardless whether the coalescence is due to a chemical exchange or to an *E*/*Z* isomerization process. This barrier corresponds to a first-order rate constant of $k_c \leq 13$ s^{-1} at $T_c = 425$ K. When equilibrium enol concentrations $[\mathbf{3a}] \approx [\mathbf{3b}] \approx [\mathbf{3a}]_0/2$ of ca. 0.01–0.02 M are used to estimate a second-order proton exchange rate constant (k_{ex}) for **3a**/**3b**, a value of $k_{ex} \leq 6.5–13 \times 10^2$ M^{-1} s^{-1} is obtained. The effective proton exchange rate constant in **3a**/**3b** solution will be ca. 3 times larger, i.e., $k_{ex} \leq (2–4) \times 10^3$ M^{-1} s^{-1}, since **3a**/**3a** and **3b**/**3b** exchanges also occur but they are unobservable by NMR. This value is unusually low for

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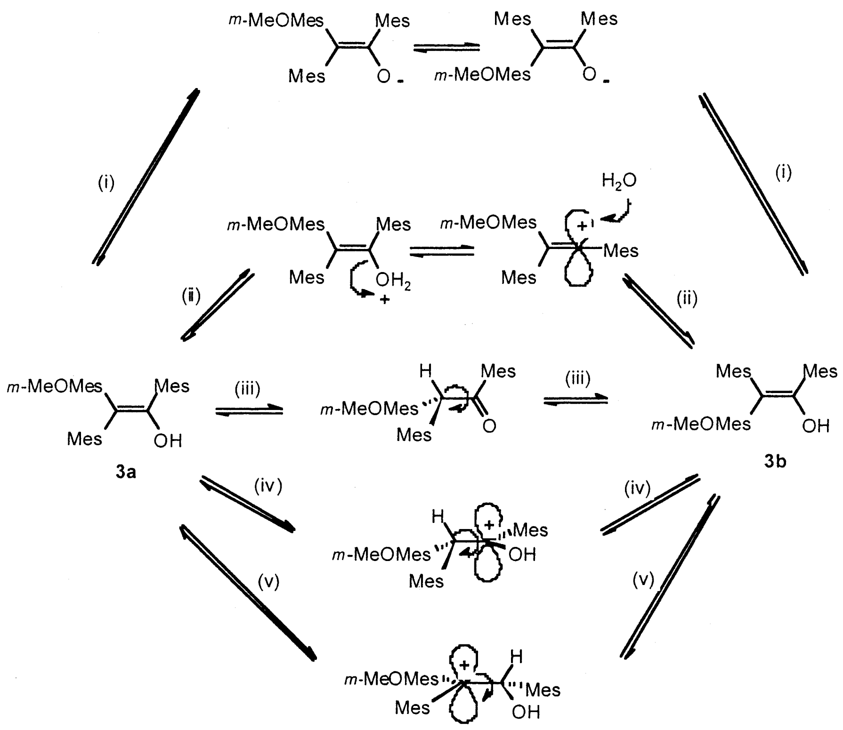
SCHEME 1



exchange of OH protons at such high temperature, and it resembles exchange rate constants for CH-acids.[23] In contrast, the isotope exchange between the OH group of **3a**/**3b** and D_2O in $CDCl_3$ is fast and is complete before the NMR spectrum is immediately taken. Consequently, the slow proton exchange is ascribed to a steric inhibition to mutual approach of two enol molecules, especially in the low dielectric aprotic medium. A similar steric hindrance for hydrogen bonding of 2,2-[24] and 1,2-diarylethenols[25] was previously suggested.

C═C Bond Rotation in the Enolate Anion. Force field calculation showed that the C═C bond rotation in the enolate anion of **1** (X = OH) has an activation enthalpy of $\Delta H^{\ddagger}_{\text{rot}} = 39.8$ kcal mol^{-1}. Although the value is 12 kcal mol^{-1} lower than $\Delta H^{\ddagger}_{\text{rot}} = 51.7$ kcal mol^{-1} in **1** (X = OH),[6c] it is still too high to account for the spontaneous *E*/*Z* isomerization. Consequently, we studied briefly the dynamic behavior of Na-**3a**/**3b** enolates in $(CD_3)_2SO$ solution. The enolates were obtained by treating the **3a**/**3b** equilibrium mixture with sodium hydride in $(CD_3)_2SO$.

The dynamic behavior of the Na-**3a**/**3b** enolates in $(CD_3)_2SO$ at 295−380 K qualitatively resembles that of the **3a**/**3b** equilibrium mixture in $C_6D_5NO_2$.[7a] At 295 K and 400 MHz, the spectrum is consistent with the propeller structure; i.e., both geometric isomers exist as pairs of helicity diastereomers displaying 9 Ar-H, 4 MeO, and 24 Mes-Me signals out of the possible maximum of 20, 4, and 36 signals, respectively. On raising the temperature, many signals broaden and several coalescence processes take place above 320 K due first to the threshold 3-ring flip process[16] and then probably to higher energy 2-ring flip processes.[6a,b] The important feature for our study is that two separate MeO signals and six separate *p*-Me signals are observed above 380 K. The *p*-Me signals are still sharp above 420 K, and no broadening occurs up to 444 K (Figure 5). Other signals, i.e., *o*-Me and Mes-H, remain broad. Furthermore, saturation transfer was neither observed between any of the six *p*-Me nor between the two MeO signals, indicating that *E*/*Z*-isomerization of the enolate is very slow on NMR time-scale even at 444 K. This conclusion was strengthened by monitoring the MeO signals of Na-**3a** enolate prepared by rapid dissolution of **3a** in $(CD_3)_2SO$ containing a nearly stoichiometric amount of sodium hydride. At 295 K, the Na-**3b** MeO signals were not observed even after 48 h. Assuming that the C═C bond rotation in the enolate is not strongly solvent dependent, this observation exclude intermediacy of the enolate in the spontaneous *E*/*Z*-isomerization of the parent enol.

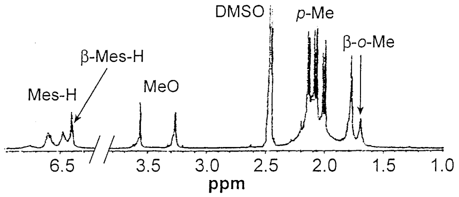


FIGURE 5. ^{1}H NMR spectrum of Na-**3a**/**3b** enolates in $(CD_3)_2SO$ at 444 K.

Possible Mechanisms. The experimental data excludes the possibility of a spontaneous *E*/*Z*-isomerization in **3a** by a C═C bond rotation in the neutral enol molecule. Five routes involving proton transfer that may lead to the isomerization of **3a** are known from the literature and were discussed previously[16,17] (Scheme 1): (i) ionization to the enolate ion → rotation → neutralization; (ii) protonation of the OH group → ionization to a linear vinyl cation → capture by water from both

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(23) Reference 21, Chapter 7.

(24) Rappoport, Z.; Nugiel, D. A.; Biali, S. E. *J. Org. Chem.* **1988**, *53*, 4814.

(25) Nadler, E. B.; Rappoport, Z. *J. Am. Chem. Soc.* **1989**, *111*, 213.

sides of the empty p-orbital → deprotonation; (iii) ketonization → rotation → re-enolization; (iv) protonation at C2; or (v) at C1 of the double bond → rotation → deprotonation.

Route (i) is unlikely since the isomerization of the Na-**3a** enolate in the $(CD_3)_2SO$ was much slower than that of the neutral enol. It is also inconsistent with the bell shape profile of the pyridine catalysis in $CDCl_3$ since for an isomerization involving an enol ⇌ enolate preequilibrium the rate must increase on increasing the [pyridine-d_5].

Route (ii) is also excluded. First, vinyl cation formation by initial protonation of the enolic OH group have no precedent[26] and it is highly likely that formation of the ion will be slower than the observed isomerization. Second, its rate should decrease consistently on increasing the base concentration, in contrast with observation.

Concerning route (iii), we note that the ketone (*m*-MeOMes)MesCHCOMes **4** was not detected in our reaction mixtures by NMR or TLC neither at room temperature in $CDCl_3$ nor at 430 K in $C_6D_5NO_2$. In the closely related 1,2,2-trimesitylethenol/1,2,2-trimesitylethanone system the equilibrium percentage of the ketone is 1.2% in hexane at 353.6 K,[27] and by analogy, we expect formation of detectable concentration of **4** during the isomerization. Although **4** may still be an "unstable intermediate" in the *E*/*Z*-isomerization with lower than equilibrium content in the mixture, the half-life for the TFA-catalyzed ketonization of **1** in hexane at 353.6K is several hours,[27] much longer than the half-life for the spontaneous isomerization of the structurally similar **3** at room temperature.

Route (iv) involves protonation at C2, which should be rate determining for the ketonization and hence is also excluded. Although C2 protonation may be electronically favored over C1 protonation, the approach of a proton to the sterically crowded C2 is slow, as deduced from the slow protonation of a structurally related enol[28] and the protonation rate is likely to be slower than the isomerization rate.

(v) A protonation at the sterically more accessible C1 by a second enol molecule, which generates a stabilized tertiary diarylmethyl carbenium ion (route v) and is slower than the subsequent C1−C2 bond rotation in the carbenium ion is consistent with both the self-catalysis and with the KIE. The higher order than 2 in the enol is ascribed either to a contribution of a concerted route in which one enol protonates and another deprotonates the isomerizing enol molecule or as due to a reaction of a cluster of several enol molecules preceding the protonation-deprotonation step(s). The bell shape catalysis by pyridine could also be consistent with this route. At low [pyridine-d_5] a pyridine molecule may catalyze the reaction by serving as a deprotonating species in a concerted transition state. At higher [pyridine-d_5], deprotonation of the enol species reduces the rate by lowering the concentration of the protonating species. The relatively low KIE is attributed to a composite rate constant, where the proton transfer step is not fully rate controlling. The DNMR experiment shows that at 425 K the oxygen-to-oxygen and hence more so the oxygen-to-carbon proton transfer between the enol molecules is sufficiently slow to be the rate controlling step. We regard our explanation as tentative which requires further experimental support.

Conclusions. The main outcome of this study is that *E*/*Z*-isomerization in sterically crowded 2-(*m*-methoxymesityl)-1,2-dimesitylethenol **3** in $CDCl_3$ does not proceed via a C=C bond rotation in the neutral enol but includes a proton-transfer step(s) as deduced from the k_H/k_D value of 2.1 and the bell-shaped catalysis by pyridine-d_5. In the absence of added catalysts the reaction is self-catalyzed by the enol as deduced from the curved k_{obs} vs $[\mathbf{3a}]_0$ dependence, which suggests higher than second order terms in the enol. The apparently conflicting pseudo-first-order dependence on [**3a**] within a run is ascribed to a similar catalytic activities of **3a** and **3b**. A DNMR study involving the OH signals of **3a**/**3b** mixture in $C_6D_5NO_2$ gave an upper limit estimate at 425 K of $k_{ex} \leq (2-4) \times 10^3\ M^{-1}\ s^{-1}$ for the rate constant of oxygen-to-oxygen proton exchange between the enol molecules. This unusually low value for an oxygen acid is ascribed to a steric inhibition to a mutual approach of two enol molecules. The enolate anion is excluded as an isomerization intermediate since no saturation transfer was observed between the six *p*-Me signals of Na-**3a**/**3b** enolates in $(CD_3)_2SO$ at 444 K and isomerization in a fresh solution of Na-**3a** enolate was not observed. The most likely (but still tentative) route for the isomerization is an internal rotation in the C1-protonated carbenium ion intermediate formed from the enol.

Experimental Section

Materials. **3a** and mixtures of **3a**/**3b** were prepared as described previously.[6a] The **3a**-OD was prepared as follows: 50 mg of **3a** was dissolved in 10 mL of $CHCl_3$, and after the solution was shaken for 1−2 min with 1 mL of D_2O, the phases were quickly separated, the organic phase was filtered through a sintered glass with ca. 5 mm layer of anhydrous oven-activated $MgSO_4$ and rapidly evaporated in vacuo, dried and kept in a desiccator. Its ^1H NMR spectrum was identical with that of **3a** except for the absence of OH signals. Since solutions of Na-**3a**/**3b** enolates in $(CD_3)_2SO$ are sensitive to oxygen, the oxygen was removed by a stream of dry nitrogen and the studies were conducted under argon. The deuteriated solvents were the best available commercial grades and were used without further purification. Commercial $CDCl_3$ was stored over Mg turnings before use.

Kinetics. In a typical run an 0.02−0.114 M solution of the enol in 5.0 mL of $CDCl_3$ was prepared and 0.5 mL aliquots were transferred into the NMR tube and thermostated in the probe of the spectrometer at 295 ± 0.2 K for 5 min. Acquisitions of 16 pulses were done automatically at a predetermined times (1, 5, 10, 15, 20, 30, 45, 60, 75, and 90 min). The integrated sum of the MeO signals served as an internal standard. The equilibrium constant $K = [\mathbf{3b}]/[\mathbf{3a}]$ for the first-order reversible isomerization reaction was measured after several hours and several days for the same sample and the values were identical within the experimental error ($K = 0.9 \pm 0.05$). In the pyridine-catalyzed kinetics, 1−40 μL of pyridine-d_5 was added to 0.09 M solution of **3a** in $CDCl_3$.

The DNMR experiments were conducted similarly to those described previously.[6a,b]

Supporting Information Available: Figure S1: k_{obs} vs the enol concentration [**3a**]. This material is available free of charge via the Internet at http://pubs.acs.org.

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[26] *Dicoordinated Carbocations*; Rappoport, Z., Stang, P. J., Eds.; Wiley: Chichester, 1997.

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[28] Nadler, E. B.; Rappoport, Z. *J. Org. Chem.* **1990**, *55*, 2673.