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DFT Analysis of Catalytic Urethanation

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Reaction profiles for catalytic urethanation are analyzed by DFT calculations. A well-known basic catalyst 1,4-diazabicyclo[2.2.2]octane (DABCO) activates alcohol molecules and accelerates the direct addition toward isocyanates. Self-catalysis by alcohols is also characterized as an accelerated direct addition.

Urethane compounds are derived from isocyanates and alcohols. They are important ingredients for thermosetting resins such as polyurethanes. The modern polymer industry owes a great deal to urethanes in coatings, adhesives, and foams. Mechanisms of urethane formation (urethanation) have attracted many chemists. Despite many studies,[1–8] determination of the reaction mechanism is still an open question, because the rate of reaction is quite complex. In general, the apparent rate of reaction is first order with respect to isocyanate, and second order with respect to alcohol.[3,5,6] The rate of reaction also depends on concentration of basic catalysts,[1,2,7,8] such as 1,4-diazabicyclo[2.2.2]octane (DABCO).[7,8] Thus, early workers concluded that the reaction causes a transition state including one isocyanate and two alcohols.[3,5,6] It has been suggested that isocyanate–alcohol complex is formed by fast pre-equilibrium reaction, and reacts with another alcohol in the rate-determining step.[3] For a long time, the resultant second-order alcoholic mechanism was widely believed,[3,5] because the rate is apparently well reproduced. On the other hand, less attention has been paid to one-to-one direct addition between isocyanate and alcohol molecules, except for some recent studies.[9–13]

In the previous work,[11] direct addition of alcohols to isocyanates was theoretically suggested as a dominant mechanism in urethane formation by means of semiempirical IRC (intrinsic reaction coordinate) analysis.[11] That is, the reaction is caused by one isocyanate and one alcohol, and thus, the rate is essentially first order with respect to both molecules. Recently, Çoban and Konuklar also showed preference for the direct addition mechanism.[12] They showed that addition of alcohol molecules occurs toward N=C rather than C=O bonds. As an analogous reaction, Lee et al. observed direct addition of allylic ethers toward chlorosulfonyl isocyanate.[13] The direct addition of substrates toward isocyanate is reasonable in that rate constants of urethanation are subject to less isotope effects by deuterium substitution of active hydrogens, and reverse reaction (decomposition of urethane) is often observed even in rigid polyurethane without alcohols.[11] In the forward reaction, however, another alcohol molecule may serve as a self catalyst. Then, the apparent rate of reaction will be probably enhanced, relative to the purely direct addition.

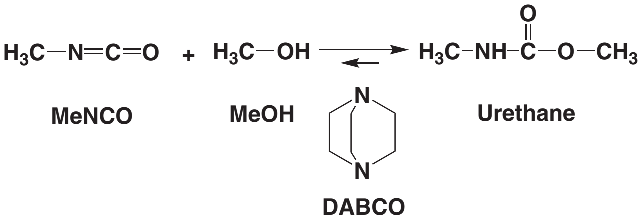

Figure 1. The simplest urethanation between methylisocyanate and methanol.

The direct addition mechanism is considered to be a fundamental reaction in organic chemistry, and worth analyzing by means of modern calculations including DFT (density functional theory). Mechanism for catalytic urethanation is also interesting in that some basic catalysts enhance the rate of reaction to a great extent. In this article, DFT analysis on urethanation is presented at B3LYP/3-21G level of theory, including the typical catalyst DABCO. As the simplest model, reaction between methylisocyanate (MeNCO) and methanol (MeOH) is analyzed, as shown in Figure 1. From MeNCO and MeOH, noncatalytic urethanation requires ca. 11 kcal mol^{-1} of activation energy, which is comparable with experimental results. The transition state is characterized as a hopping process of the active hydrogen in the –NHOC– four-membered ring. DABCO activates alcohol molecules, and accelerates the hydrogen transfer. Then, the activation energy is drastically reduced to 5.6 kcal mol^{-1}.

The calculations were done under B3LYP/3-21G level of theory by using GAMESS.[14–17] For the noncatalytic process, more accurate calculations are possible in principle with basis sets such as 6-31G(d). For the catalytic process however, large basis sets above 3-21G level could not be applied due to the size of the systems and convergence problems. Nevertheless, qualitative description for relative comparison of reactivity is probably well obtained at 3-21G basis sets, because transition states with very large interatomic distances are not present in the energy surface, as shown later.

Figure 2 shows the reaction profile for urethanation without any catalyst. The activation energy $\Delta E^{\ddagger}$ for the forward reaction is 11.4 kcal mol^{-1}, which is the same order as experimental data (ca. 8–9 kcal mol^{-1}).[7] However, the experimental data probably consists of an average between purely direct addition and an alcohol-catalytic process, as shown later. This reaction itself is highly exothermic, as observed under usual conditions. In the present calculation, the heat of reaction ΔE was estimated to be -36.6 kcal mol^{-1}, which is comparable with those of PM3 (ca. -19 kcal mol^{-1})[11] and HF/STO-3G (-49.7 kcal mol^{-1})[9] calculations. Typical heats of reactions in urethanations (experimentally observed by decomposition of phenylurethanes) are ca. -13–-21 kcal mol^{-1}.[18] At B3LYP/6-31G(d) level of theory, theoretical heat of reaction ΔE was improved to -28.4 kcal mol^{-1}, but the activation energy for the forward reaction became 27.0 kcal mol^{-1}. In this system, effects of polarization functions are probably large. At least, the

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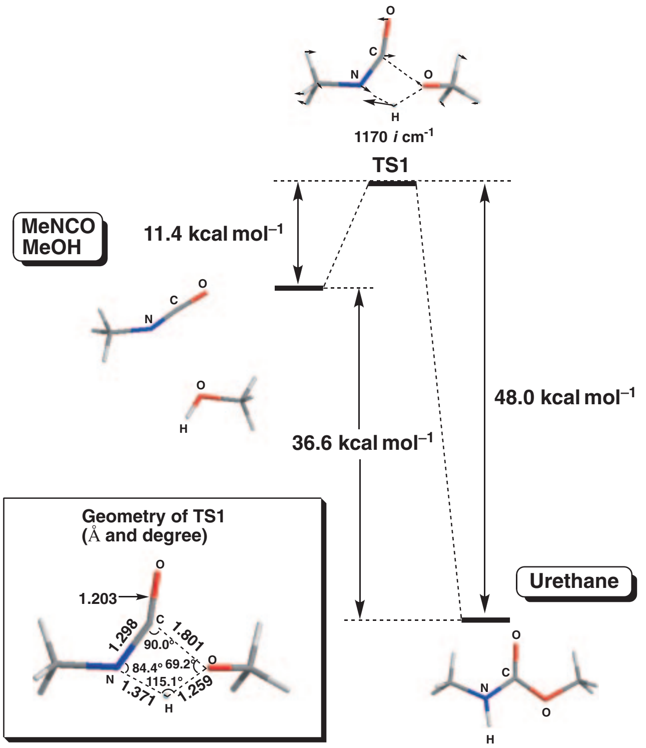

Figure 2. Energy diagram for noncatalytic urethanation at B3LYP/3-21G level of theory.

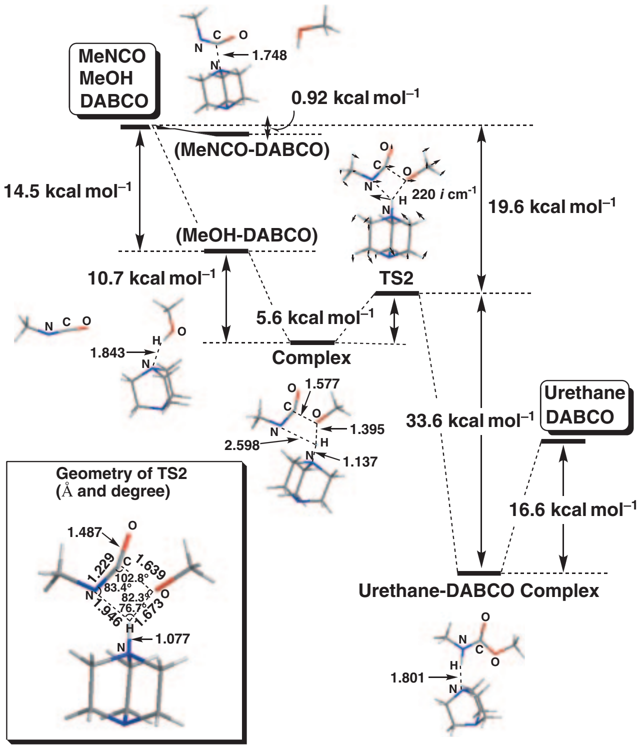

Figure 3. Energy diagram for DABCO-catalytic urethanation at B3LYP/3-21G level of theory.

activation energy for the reverse reaction (48.0 kcal mol^{-1}) is overestimated to a great extent.

As for basis-set impact on the heat of reaction, Cysewski et al. systematically calculated the thermodynamic quantity in detail.[19] They reported B3LYP calculations on heats of the same reaction by using large basis sets up to 6-311+G(d,3p). To our knowledge, their results ($\Delta E = -26$–-20 kcal mol^{-1} for *trans*-peptide urethane) are probably the most reliable theoretical data in noncatalytic urethanation. The absolute value of heat of reaction decreases with increase in the size of basis set. From the experimental results of equilibrium constant (ca. 10^2–10^3 order based on the forward reaction),[18] change of Gibbs energy in this reaction should be ca. -4–-3 kcal mol^{-1} at room temperature. In general, change of entropy in urethanation is very large. Considering the change of entropy (ca. -40 cal mol^{-1} K^{-1})[7] and zero-point energy calibration (ca. $+3$–4 kcal mol^{-1}), accurate heat of reaction ΔE should be ca. -20 kcal mol^{-1}. Cysewski et al. well reproduced the change of enthalpy and Gibbs free energy at quite large basis set over 6-311+G(d,p).[19]

The geometry and vibration mode of the transition state (TS1) is also shown in Figure 2. Hereinafter, the geometry parameters in all the figures are shown in units of Å and degree. It can be seen from the largest vibration vector that the active hydrogen hops from the alcohol oxygen to isocyanate nitrogen. This is consistent with the PM3[11] and HF/STO-3G[9] results. While in MeOH Mulliken charge of the active hydrogen is +0.332, in TS1, the charge becomes +0.395, which shows increase in "acidity." This suggests basic-catalyst process of urethanation, as expected from stabilization of the transition state. It is well known that tertiary amines are powerful catalysts for urethanation.[8] In particular, DABCO is one of the most active catalysts. Baker et al. proposed that urethanation under tertiary-amine catalysts is triggered by complexation between isocyanates and catalysts, and the resultant complex reacts with alcohols to afford urethanes.[1–3] However, as shown below, this mechanism is perhaps invalid, because the relative stability of isocyanate–amine complex is much smaller than that of alcohol–amine complex.

Figure 3 shows the reaction profile of the same urethanation under DABCO. We first examined complexation energies for MeNCO–DABCO and MeOH–DABCO. While the former is very small as estimated to be 0.92 kcal mol^{-1}, the latter is quite large, as estimated to be 14.5 kcal mol^{-1}. Thus, we can roughly guess that the catalytic process is initiated by activation of alcohol molecules under DABCO. Strictly speaking, there should be small activation energies for the complexations, but the accurate calculations on these two-body problems are not important theoretically or experimentally. Geometry of MeOH–DABCO complex is shown in Figure 3. One of the lone pairs in DABCO coordinates with the active hydrogen in MeOH. This is consistent with IR spectra of alcohol–amine complex, which was observed by earlier workers in relation to the base-catalytic urethanation.[4] MeNCO–DABCO complex cannot be dominant in the reaction path due to the instability. The transition state (TS2) was found as a saddle point by usual procedure. TS2 is also characterized by an –NHOC– four-membered ring, in which the active hydrogen transfers between oxygen of alcohol and nitrogen of isocyanate. The Mulliken charge of the active hydrogen is +0.459, which suggests acidic character of TS2. IRC calculation toward the reverse direction leads to a three-body complex consisting MeNCO, MeOH, and DABCO, as shown in the center of Figure 3. For the forward direction, TS2 leads to a urethane–DABCO complex. The activation energy from the three-body complex to TS2 is 5.6 kcal mol^{-1}.

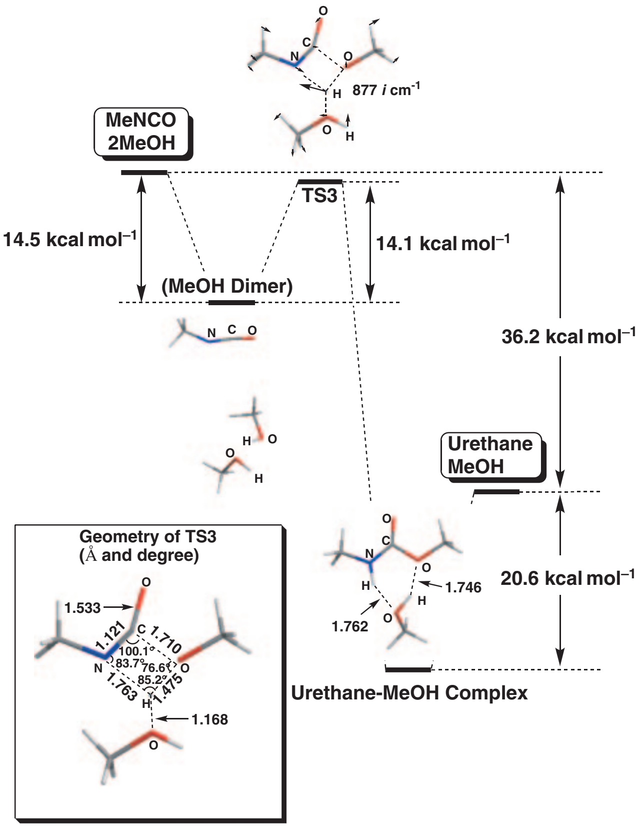

Figure 4. Energy diagram for alcohol-catalytic urethanation at B3LYP/3-21G level of theory.

Compared with that without DABCO, the activation energy is drastically reduced. Since the precomplexation is thought to be caused by very small activation energy, if any, the rate-determining step of the whole catalytic process lies around TS2. TS2 decomposes into urethane–DABCO complex, which is 16.6 kcal mol^{-1} lower than completely dissociated urethane and DABCO. The complexation energy is lower than that of the whole stability of the three-body complex, and thus, DABCO is recycled continuously. In the reverse reaction, the activation energy for the rate-determining step becomes 33.6 kcal mol^{-1}. This is also much less than that of the noncatalytic process. The reverse reaction can be applied to recycling process of polyurethane,[20] one-pot coatings[21] and so on.

In the catalytic process, the rate-determining step lies in the reaction between alcohol–DABCO complex and MeNCO. The rate should be essentially first order with respect to the alcohol. In the noncatalytic process, however, particularly in nonpolar or weakly polar solvents, two alcohol molecules may participate in the rate-determining step due to the hydrogen bonding.[6] Another alcohol molecule may serve as a self catalyst, and the whole rate constant may deviate from the first order. Though Raspoet et al. proposed transition states including triply associated alcohols,[22] this probably occurs under limited conditions due to the large entropy change. Figure 4 shows an energy diagram for the alcohol-catalytic process, in which addition of MeOH toward MeNCO is supported by another MeOH molecule. First, two MeOH molecules associate to form a dimer 14.5 kcal mol^{-1} below the separated molecules. Based on the dimeric system, the activation energy for the forward reaction is 14.1 kcal mol^{-1}, which is the same order as that of noncatalytic reaction. However, this is much larger than that of DABCO-catalytic process, which is probably due to the weak basicity of alcohols. The transition state TS3 is also characterized as a hopping of the active hydrogen with Mulliken charge +0.461. We note that the active hydrogen and oxygen atoms are supplied from the same alcohol molecule, similar to the DABCO-catalytic process. TS3 results in a urethane–MeOH complex, which lies 20.6 kcal mol^{-1} below separated urethane and MeOH. Therefore, when the complexation is lifted by reactants or solvents, the apparent rate of reaction deviates from first order to second order with respect to the alcohol concentration.

In summary, catalytic urethanation is characterized as accelerated direct addition between isocyanates and alcohols. Basicity of catalysts highly influences on the stability of the transition states, and self-catalyzed process by alcohols is also plausible as an analogous mechanism.

Supporting Information

Optimized coordinates for TS1, TS2, and TS3. This material is available free of charge on the web at http://www.csj.jp/journals/bcsj/.

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