NMR Temperature-Jump Method for Measuring Reaction Rates: Reaction of Dimethylanthracene with $H_2@C_{60}$

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Received: February 10, 2009; Revised Manuscript Received: March 11, 2009

We show a simple variant on Eigen's familiar temperature-jump method to measure rate constants. The sample is prepared in a sealed NMR tube, which is heated and then abruptly cooled. The NMR spectrum is then taken repeatedly until equilibrium is reestablished at the new temperature. The sample can be used over and over again. We demonstrate the technique on the reversible addition of 9,10-dimethylantracene to C_{60}. The C_{60} contains H_2, and this provides an NMR signal upfield from TMS, well away from the rest of the spectrum. We show that the equilibrium constant for $H_2@C_{60}$ is the same as that for $^3He@C_{60}$.

Introduction

Accurate measurement of reaction kinetics often leads to the development of clever but simple techniques. Manfred Eigen won the 1967 Nobel Prize for his discovery of a series of methods for measuring fast reaction rates. Temperature jump, or T-jump, is the best known of these.[1] A sample at chemical equilibrium is subjected to a rapid change in temperature. As it reacts to go to a new equilibrium, the concentrations are measured, and, ultimately, the rate constants for both the forward and backward reactions are obtained. Aside from its simplicity and elegance, the technique allows one to measure rates for reactions that are rapid compared to how rapidly one can mix the reactants. Furthermore, one can reuse the same sample over and over again. We describe here a variation of T-jump using NMR to measure the concentrations. Conventional NMR is an inherently slow technique, so we cannot measure rates in the microsecond time scale regime, as Eigen could, but we need only the NMR instrumentation found in almost any chemistry department. We apply the technique to a simple association reaction

$$A + B \rightleftharpoons C \qquad (1)$$

In the classic T-jump, the temperature change is small, and we need only the linear terms of the rate law. The return to equilibrium is an exponential decay with one or more relaxation times. Here, we will use a much larger temperature change, and, at least for reaction 1, the nonlinear terms can be included in the equations. Furthermore, we will be able to do the necessary averaging so that the interval for data collection can be comparable to the time scale for the reaction.

For our study we chose the reversible monoaddition of 9,10-dimethylanthracene (DMA) to C_{60}, a reaction that we have studied before.[2] The reaction is a Diels–Alder addition, where the two central carbons of the anthracene (9 and 10) add to one of the hexagon–hexagon double bonds of C_{60}. The [2,4] Diels–Alder addition reaction is one of the most useful in fullerene chemistry. While the addition of unsubstituted anthracene is basically irreversible, the increased steric hindrance of the two methyl groups decreases the exothermicity of the reaction and makes it reversible. Hirsch has used the reaction to add removable templates to C_{60} and thus control the positioning of multiple malonate additions.[3–6] By using C_{60} with a small fraction of the molecules containing ^3He, we have used ^3He NMR spectroscopy to study the thermodynamics of the addition.[2] Each adduct gave a distinct, sharp peak. We found one monoadduct, six bisadducts, eleven trisadducts, and ten tetrakisadducts. By measuring the relative peak heights, we obtained all the equilibrium constants. By repeating the experiment at different temperatures, we also obtained values for ΔH and ΔS for the reaction. More recently, we measured the change in thermodynamics when xenon is put inside C_{60}.[7] Using a mixture of $^3He@C_{60}$, $^{129}Xe@C_{60}$, and DMA, we measured the ratio of peak areas for the monoadduct and for the unreacted $X@C_{60}$ for both He and Xe. The ratio of these ratios is $K_{eq}(Xe)/K_{eq}(He)$, since the concentration of free DMA cancels out. We found that $^3He@C_{60}$ is more reactive below 35 °C, but $^{129}Xe@C_{60}$ is more reactive above. Putting xenon inside C_{60} changes both ΔH and ΔS for the reaction.

The basic experiment is quite simple. We made $H_2@C_{60}$ following the synthesis reported by the Komatsu group.[8–10] $H_2@C_{60}$ is preferable to $^3He@C_{60}$ for several reasons. We can make it with an incorporation fraction of about 50% as compared to ~1% for $^3He@C_{60}$. Since there are two hydrogen atoms in $H_2@C_{60}$ as compared to one ^3He atom and since proton NMR is more sensitive than ^3He NMR, we have an increase in sensitivity of more than 2 orders of magnitude. The resonances for the endohedral hydrogen all occur well upfield from TMS and are thus well separated from the rest of the spectrum. Finally, we can measure the proton resonances for the methyl groups for the bound and free DMA and thus measure its concentration. Even with these advantages, NMR measurement times are still comparable to the reaction rate. Below, we reformulate the rate equations to account for this.

We put a solution of $H_2@C_{60}$ and DMA dissolved in *o*-dichlorobenzene (ODCB) in an NMR tube, evacuate it, and seal it under vacuum. This protects the DMA from air oxidation and eliminates solvent evaporation. The tube is then heated to 75 °C. At this temperature the DMA complex is almost completely dissociated. The reaction is fast, so the required heating time is only a few minutes. The tube is then rapidly cooled to the desired temperature and placed in the spectrometer, and the spectrum is taken repeatedly until equilibrium is established at the new temperature. From the peak intensities,

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10.1021/jp901230y CCC: $40.75

we can then get the rate constants for the association and dissociation reactions. First, we had to verify that equilibrium data collected using $^3He@C_{60}$ is valid for $H_2@C_{60}$.

Experimental Details

Preparation of Labeled Fullerenes. $^3He@C_{60}$ was prepared as described previously.[11] Briefly, C_{60} and KCN were ground to a fine powder in a ball mill. The sample was sealed in a copper tube with ∼3 atm of ^3He gas. Two tubes were placed in a high-pressure vessel and heated to 650 °C and 3000 atm for 8 h. The soluble portion of the product was extracted and contained ∼1% ^3He. $H_2@C_{60}$ was prepared by the Komatsu method.[8−10] A series of additions to C_{60} produces an adduct with a hole, a 13-membered ring. This was heated to 200 °C in a high-pressure vessel directly connected to a hydrogen cylinder without a reducing valve, giving a final pressure of ∼150 atm. After cooling, a second set of reactions closes the hole to produce C_{60}, with H_2 inside about 45% of the molecules.

$H_2@C_{60}$/$^3He@C_{60}$ Competition. In an NMR tube, 4 mg of 1% enriched $^3He@C_{60}$ was mixed with 0.33 mg of $H_2@C_{60}$ and dissolved in 650 μL of 99% *o*-dichlorobenzene-d_4. Also, 2 mg of $Cr(acac)_3$ was added to increase the T_1 relaxation rate of the ^3He nucleus. Finally, 1.04 mg of DMA was added and allowed to react overnight. In two subsequent measurements, the amount of DMA was increased by 0.5 mg each time.

$H_2@C_{60}$ T-Jump Sample. Approximately 1 mg of $H_2@C_{60}$ was dissolved in 375 μL of *o*-dichlorobenzene (ODCB) and 50 μL of benzene-d_6 in a 5 mm NMR tube. One-half molar equivalence of DMA was added via 12 μL of a 10 mg/mL ODCB stock solution (∼120 μg). The solvent was degassed and the tube pumped down (<1 torr) and sealed. This sample was used for all low-temperature data points (−17 to 29 °C). An additional half-equivalent of DMA was added for higher temperatures.

^3He NMR Spectroscopy. The NMR spectra were taken on a Bruker Avance 500 MHz spectrometer running at a ^3He frequency of 380.9 MHz. Typically, 400 pulses were used with a width of 7 μs and a recycling delay of 2 s. All chemical shifts were relative to the known resonance of ^3He dissolved in solution. Line broadening of up to 2 Hz was used to improve the signal-to-noise ratio.

^1H NMR Spectroscopy. The proton NMR spectra were taken on the same 500 MHz Bruker Avance spectrometer. A solvent-gating pulse sequence was chosen to eliminate a large signal from the ring protons on the nondeuterated solvent molecules. Large solvent signals reduce the automatic gain setting on the instrument, limiting sensitivity for smaller ones. For the competition reaction, 256 scans were collected with a 3 s acquisition time and a 2 s recycling delay, and 5 Hz of line broadening was applied.

T-Jump Procedure. The sample was placed in a water bath at 75 °C until the color changed from chestnut brown to purple, as $C_{60}\cdot$DMA dissociated to form C_{60}, typically 3−5 min. The tube was then plunged into a water or freezing-point bath of desired temperature until equilibrated, about 30 s. It was quickly placed into the spectrometer, already cooled or heated to the correct temperature. All proton spectra were acquired using the same conditions as above, except scan times. Scan times were varied at each temperature, ranging from 1 min for the higher temperatures to 5 min for lower ones.

Theory

Referring to reaction 1, we will let A be C_{60}, B be DMA, and C be $C_{60}\cdot$DMA. Then

$$\frac{d[A]}{dt} = -k_f[A][B] + k_r[C] \tag{2}$$

where k_f and k_r are the forward and reverse rate constants. We note that $k_f/k_r = K_{eq}$, the equilibrium constant. Let $[A]_{eq}$, $[B]_{eq}$, and $[C]_{eq}$ be the final equilibrium concentrations at $t = \infty$. Let $[A] = [A]_{eq} + x$. Then, by stoichiometry, $[B] = [B]_{eq} + x$ and $[C] = [C]_{eq} - x$. Then

$$\frac{d[A]}{dt} = \frac{dx}{dt} = \{-k_f[A]_{eq}[B]_{eq} + k_r[C]_{eq}\} - \{k_f[A]_{eq} + k_f[B]_{eq} + k_r\}x - k_f x^2 \tag{3}$$

The first set of brackets is zero, since it is the net rate of reaction at equilibrium. We define the relaxation time

$$\tau = \frac{1}{k_f[A]_{eq} + k_f[B]_{eq} + k_r} \tag{4}$$

Then

$$dt = -\frac{dx}{x/\tau + k_f x^2} \tag{5}$$

In the usual T-jump, the term in x^2 is neglected. We cannot do that here, since the change in concentrations is too large. Integrating both sides of the equation gives

$$t = C + \tau \ln\left|1 + \frac{1}{k_f \tau x}\right| \tag{6}$$

Taking the exponential and rearranging gives

$$x = \frac{1}{k_f \tau (A e^{t/\tau} - 1)} \tag{7}$$

If we let x_0 be the value of x at $t = 0$, then

$$x = \frac{x_0 e^{-t/\tau}}{1 + k_f \tau x_0 (1 - e^{-t/\tau})} \tag{8}$$

In the usual T-jump case, the second term in the denominator is neglected, so that x has a simple exponential dependence on t. Equation 8 can easily be differentiated to give eq 5.

At high temperatures, where the reaction is fast, the concentrations may change appreciably during the acquisition time for the NMR. We must then integrate eq 8 over the time interval (t_1, t_2)

$$\int_{t_1}^{t_2} x\, dt = \frac{1}{k_f} \ln\left\{\frac{1 + k_f \tau x_0[1 - \exp(-t_2/\tau)]}{1 + k_f \tau x_0[1 - \exp(-t_1/\tau)]}\right\} \tag{9}$$

Results and Discussion

Comparison of $^3He@C_{60}$ and $H_2@C_{60}$. We dissolved $^3He@C_{60}$, $H_2@C_{60}$, and varying amounts of DMA in ODCB-d_4 and took the NMR spectra. Figure 1 shows a representative spectrum. The top panel shows the proton spectrum and the bottom panel the ^3He spectrum. The proton spectrum is referenced to TMS, while the ^3He spectrum is referenced to dissolved ^3He gas. However, the difference in chemical shift between the monoadduct and the unreacted C_{60} is −3.53 ppm in both cases. This contrasts with $^{129}Xe@C_{60}$ where the difference is +10.9 ppm. The ratio of peak areas for the monoadduct to the unreacted C_{60} is proportional to K_1, the equilibrium constant for the first addition. The ratio of these two ratios is equal to the ratio of the two equilibrium constants

$$\frac{K_1(^3\mathrm{He})}{K_1(\mathrm{H_2})} = 1.05 \pm 0.10 \tag{10}$$

since the concentration of free DMA cancels out. This, again contrasts with ^{129}Xe, where the ratio of equilibrium constants is as high as 3.2 at 10 °C and is strongly dependent on temperature. In the case of the bis- and higher adducts, there are very small differences in the chemical shifts between the ^{3}He and H_2 cases. The ratio of K_2 for the equilibrium between mono- and bisadducts is also 1.05 ± 0.1. The Supporting Information shows ^{3}He and proton NMR spectra showing the mono- and bisadducts. In both cases we conclude that the endohedral molecule is basically rattling around inside the C_{60} cage without causing any significant perturbation in the electrons of C_{60}. There is a very weak van der Waals attraction between the carbon cage and the molecule inside plus a repulsive force as the molecule gets close to the cage. We can then safely assume that the equilibrium constants of both endohedral fullerenes are the same as those of empty C_{60}.

Measurement of the Equilibrium Constant. Wang et al.[2] measured the equilibrium constant for the monoaddition of DMA to C_{60} at four different temperatures. This gave

$$\ln K_{\mathrm{eq}} = -30.8 + 11\,500/T \tag{11}$$

where K_{eq} is in L/mol. This corresponds to

$$\Delta H = -95.8\ \mathrm{kJ/mol} = -22.9\ \mathrm{kcal/mol} \tag{12}$$

$$\Delta S = -256\ \mathrm{J/mol\ K} = -61.2\ \mathrm{cal/mol\ K} \tag{13}$$

As we show above, the equilibrium constants for $^3He@C_{60}$ and $H_2@C_{60}$ are the same within experimental error. We remeasured K_{eq} at 22 °C and got agreement with Wang et al. Under the conditions of our experiment at lower T, the concentration of free DMA is so low that we cannot measure it accurately, so we calculated it using eq 11.

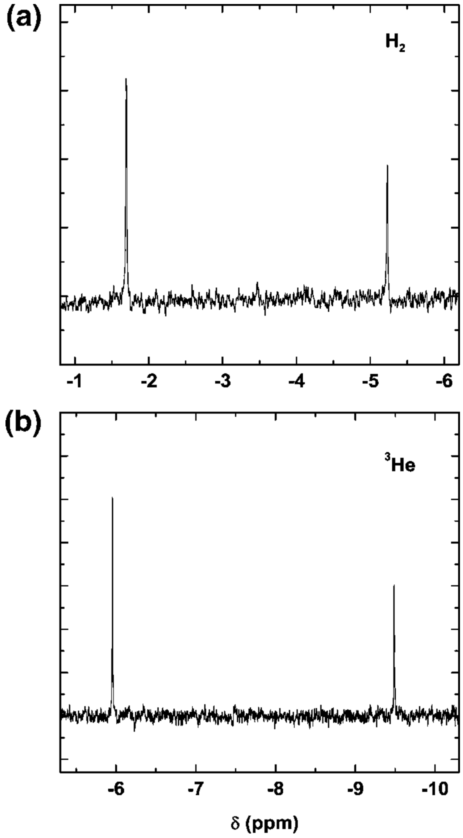

Figure 1. NMR spectra for $X@C_{60}$ and $X@C_{60}{\cdot}DMA$. The left peak is due to $X@C_{60}$ and the right peak to $X@C_{60}{\cdot}DMA$. Top panel, X = H_2; bottom panel, X = ^{3}He.

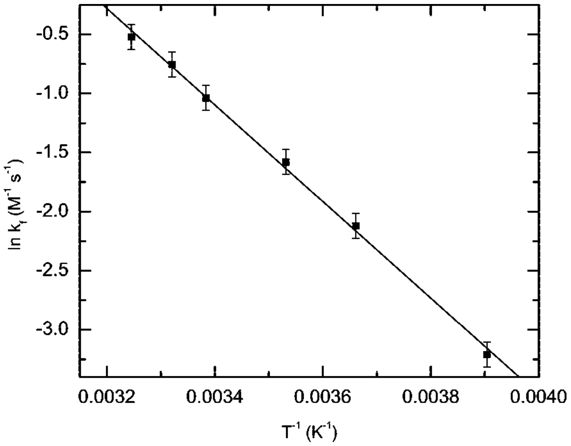

Figure 2. Arrhenius plot of the forward rate constant for C_{60} + DMA. The temperature range is −17 to 35 °C.

Rate Measurement. Since absolute intensity measurements in NMR are not reliable, we measured

$$z = \frac{[C_{60}\cdot \mathrm{DMA}]}{[C_{60}] + [C_{60}\cdot \mathrm{DMA}]} = \frac{[C_{60}\cdot \mathrm{DMA}]_{\mathrm{eq}} - x}{[C_{60}]_{\mathrm{t}}} \tag{14}$$

where $[C_{60}]_t = [C_{60}] + [C_{60}{\cdot}DMA]$ is the total concentration of C_{60}, which we know from making up the solution. The fit to eq 9 is a nonlinear least-squares fit with four unknown parameters: τ, x_0, $[C_{60}{\cdot}DMA]_{eq}$, and k_f. However, the parameters are not all independent, since k_f can be obtained from τ and K_{eq}. A nonlinear fit is an iterative procedure that requires an initial guess for each parameter. It may not converge. Furthermore, the fit for this reaction is very insensitive to k_f. Therefore, we first fit the data to a simple exponential to get τ and $[C_{60}{\cdot}DMA]_{eq}$. This gave approximate values of k_f and k_r. These parameters were then used as the starting guesses for the full nonlinear fit, which then rapidly converged to give a final value for τ. From this we get the final values of k_f and k_r. The Supporting Information gives a plot of z vs time for two temperatures along with the fitted curves.

Figure 2 shows an Arrhenius plot of ln k_f vs $1/T$. The linear fit to the Arrhenius data gives

$$E_a = 34\ \mathrm{kJ/mol} = 8.1\ \mathrm{kcal/mol} \tag{15}$$

$$A = 3.6 \times 10^5\ \mathrm{M^{-1}\ s^{-1}} \tag{16}$$

Wang et al.[2] measured $\Delta H = -96$ kJ/mol. Therefore, E_a for the reverse reaction is 130 kJ/mol. Sarova et al.[12] measured the rates for the Diels−Alder addition of anthracene and tetracene to C_{60}. These reactions are irreversible and very much slower than the reaction with DMA. The reactions take days rather than hours. The activation energies are E_a = 59 kJ/mol for anthracene and E_a = 49 kJ/mol for tetracene. The A parameters are roughly the same as for DMA.

Summary

We show here a very simple variation on the T-jump method for measuring the rate constants for a reaction that goes to equilibrium. It requires only an NMR spectrometer capable of doing variable-temperature measurements. We applied the method to the Diels−Alder addition of 9,10-dimethylanthracene to C_{60}.

Supporting Information Available: A plot of the fit of the concentration z vs time for two temperatures, along with the fitted nonlinear curves. ^{3}He and proton NMR spectra showing the mono- and bisadducts for the addition of DMA to C_{60}. The information is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Houston, P. L. *Chemical Kinetics and Reaction Dynamics*; McGraw-Hill: New York, 2001.

(2) Wang, G. W.; Saunders, M.; Cross, R. J. *J. Am. Chem. Soc.* **2001**, *123* (2), 256–259.

(3) Hirsch, A.; Vostrowsky, O. *Eur. J. Org. Chem.* **2001**, (5), 829–848.

(4) Lamparth, I.; Herzog, A.; Hirsch, A. *Tetrahedron* **1996**, *52* (14), 5065–5075.

(5) Lamparth, I.; Maichle-Mössmer, C.; Hirsch, A. *Angew. Chem., Int. Ed. Engl.* **1995**, *34* (15), 1607–1609.

(6) Hirsch, A.; Brettreich, M. *Fullerenes: Chemistry and Reactions*; Wiley: Weinheim, 2005.

(7) Frunzi, M.; Cross, R. J.; Saunders, M. *J. Am. Chem. Soc.* **2007**, *129* (43), 13343–13346.

(8) Murata, Y.; Murata, M.; Komatsu, K. *Chem.—Eur. J.* **2003**, *9* (7), 1600–1609.

(9) Murata, M.; Murata, Y.; Komatsu, K. *J. Am. Chem. Soc.* **2006**, *128* (24), 8024–8033.

(10) Komatsu, K.; Murata, M.; Murata, Y. *Science* **2005**, *307* (5707), 238–240.

(11) Cross, R. J.; Khong, A.; Saunders, M. *J. Org. Chem.* **2003**, *68* (21), 8281–8283.

(12) Sarova, G. H.; Berberan-Santos, M. N. *Chem. Phys. Lett.* **2004**, *397* (4−6), 402–407.

JP901230Y