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Applications of Pulsed Field Gradient Spin−Echo Measurements to the Determination of Molecular Diffusion (and Thus Size) in Organometallic Chemistry

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Pulsed field gradient spin−echo (PGSE) measurements on (a) four arsine complexes of Pd(II), $PdCl_2L_2$ (L = $AsMe_xPh_{3-x}$ (x = 3−0)), (b) three different ferrocene phosphine dendrimers, and (c) a selection of other organometallic complexes of differing molecular weight, are demonstrated to provide a practical alternative to classical methods used in organometallic chemistry for estimating molecular size. PGSE measurements make use of translational and not rotational properties of molecules and will be especially valuable where one cannot isolate an unknown complex and/or where a side product is of especial interest, since one can measure several components of the mixture simultaneously.

Introduction

The determination of molecular size and weight in solution is a frequent problem for organometallic compounds; e.g., in lithium[1] and copper[2] as well as transition-metal carbonyl[3] chemistry, one finds numerous examples of polynuclear species. Several conventional tools can be used to determine the nuclearity of a coordination complex, but none of them are universal. Beyer[4] has summarized several methods which include those based on (a) colligative properties (cryoscopy, ebullioscopy, osmometry, etc.) (b) light scattering, and (c) X-ray diffraction. Methods based on colligative properties are widely used, but these are very sensitive to impurities, whose presence easily lead to wrong conclusions. Light-scattering and solution X-ray diffraction techniques require particle sizes of several nanometers, and they do not readily distinguish between molecules with similar size; moreover, X-ray diffraction techniques require molecules with a high degree of internal structural regularity. Electrospray ionization in mass spectroscopy[5] provides a very important tool in that preexisting ions are transferred from solution to the gas phase where they can be analyzed. However, (a) not all compounds can survive even a mild ionization, and (b) not all metal complexes are stable as ions long enough for the measurement.

NMR methods measuring dipole−dipole relaxation rates,[6] R, provide information on the molecular volume (V). R values, e.g. for a ^{13}C, ^{1}H pair, are given by eq 1,

$$R_{\mathrm{DD}}^{1,2} = \left(\frac{\hbar\gamma_{\mathrm{H}}^{2}\ \gamma_{\mathrm{C}}^{2}}{r_{\mathrm{CH}}^{6}}\right)\left(\frac{\eta V}{kT}\right) = \left(\frac{\hbar\gamma_{\mathrm{H}}^{2}\ \gamma_{\mathrm{C}}^{2}}{r_{\mathrm{CH}}^{6}}\right)\tau_{\mathrm{C}} \qquad (1)$$

where the first quotient contains gyromagnetic ratios and the C−H bond length, r_{CH}. The second term represents the Stokes−Einstein expression for the reorientation correlation time τ_c, which is proportional to the viscosity (η), molecular volume (V), and temperature. Measurements involving relaxation are quite useful; however, (a) internal motions often compete efficiently with overall tumbling and (b) paramagnetic impurities, in particular oxygen, lead to enhanced rates. A promising NMR method involves pulsed field gradient spin−echo (PGSE) sequences,[7,8] which make use of translational and not rotational properties of molecules. PGSE methods have been widely used in the 1970s for determining diffusion coefficients of organic molecules.[7b] In the following decade variants of this technique have been applied to polymer mixtures[7−9] and it is now possible to obtain diffusion data on molecules in various environments, e.g. in porous silica.[7,10] Since there have been very few applications of PGSE methods in organometallic chemistry,[11,12] we present here a detailed report involving a variety of coordination/organometallic com-

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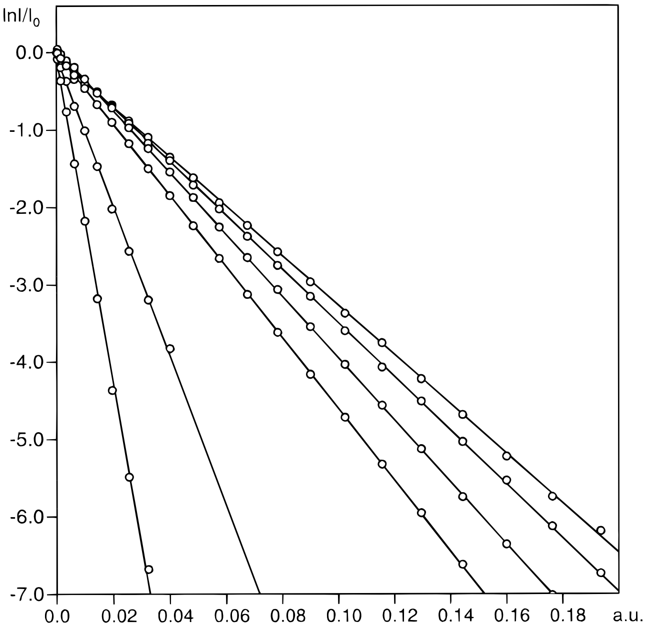

Figure 1. Plot of $\ln(I/I_0)$ vs arbitrary units proportional to the square of the gradient amplitude. The slopes of the lines are related to the diffusion coefficients, D. The six lines stem from water, $CHCl_3$, and the four Pd−arsine complexes $PdCl_2L_2$ ($L = AsMe_xPh_{3-x}$ ($x = 3-0$)) (increasing molecular weight from left to right). The absolute value of the slope decreases with increasing molecular weight.

plexes and suggest that this method provides a valid alternative to those described above. The PGSE tool provides several clear advantages: (a) impurities are not a problem because the evaluation is done selectively for the individual NMR signals,[13] (b) internal movements do not influence the diffusion process, (c) one can take data on mixtures of isomers (or diastereomers) which may not readily crystallize, and (d) one can determine individual diffusion coefficients for several species (including those of a reference) simultaneously.

Results and Discussion

A description of the basic idea behind this NMR methodology is given in the Appendix, whereas Figures 1 and 2 demonstrate the potential of PGSE methods. In Figure 1, the results (from left to right) for water, $CHCl_3$, and four arsine complexes of Pd(II),[14] $PdCl_2L_2$ ($L = AsMe_xPh_{3-x}$ ($x = 3-0$)) are reported, while in Figure 2 the results for three different ferrocene phosphine dendrimers[15] (see Chart 1) are shown.

The graphs reflect the decreasing signal intensities $\ln(I/I_0)$ (I/I_0 = (observed spin−echo intensity)/(intensity without gradients)) as a function of a constant waiting time (during which the molecules move) and a varied gradient strength. The latter is given along the x axis in arbitrary units proportional to the square of the gradient amplitude. The slopes of the lines are related to the diffusion coefficients, D, as given in eq 2, where

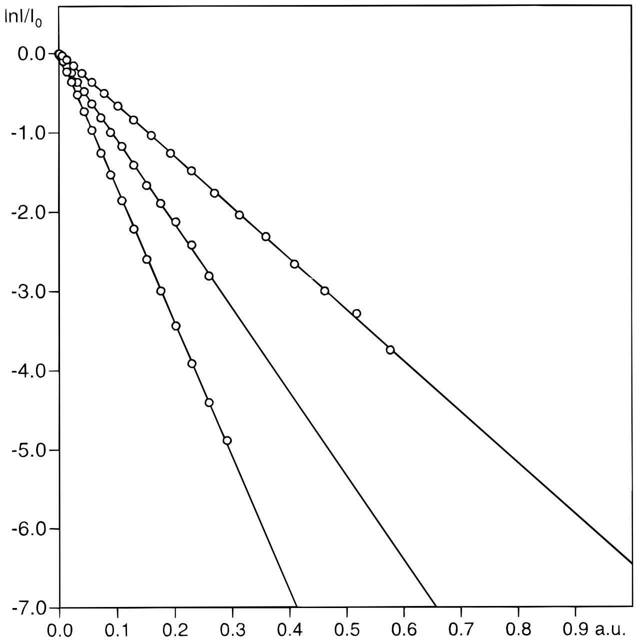

Figure 2. Plot of $\ln(I/I_0)$ vs arbitrary units proportional to the square of the gradient amplitude for the three ferrocene dendrimers of Chart 1. The largest compound has the smallest slope.

$$\ln\left(\frac{I}{I_0}\right) = -\gamma\delta^2G^2\left(\Delta - \frac{\delta}{3}\right)D \qquad (2)$$

G = gradient strength, Δ = delay between the midpoints of the gradients, D = diffusion coefficient, and δ = length of the gradient pulse.

From Figure 1, one can see that the smaller $AsMe_3$ complex moves faster than the analogous $AsMe_2Ph$, which is then faster than the heavier analogues, and all four of these are slower than water and solvent, which move relatively quickly. This basic idea is even clearer from Figure 2, in that with increasing dendrimer size, one observes decreasing (absolute values) of the slopes and thus markedly different diffusion coefficients.

We are beginning to develop a small reference library based on our PGSE measurements, and Table 1 shows measured values of the ratio $m/(\Delta - \delta/3)$, for a series of Pd(II) complexes **1**−**6** with different ligands. The parameter m represents the slope of the line, and this ratio is directly proportional to the diffusion coefficient, D. The data in the table were obtained from experiments using different values of the diffusion time (Δ) in order to show that (a) we can readily reproduce our D values, (b) there is a crude correlation with what one would expect with respect to molecular size (smaller absolute values are indicative of slower motions), and (c) there is no additional time-dependent variable in eq 1, other than Δ. This last point implies that the molecular translation movements in $CDCl_3$ are due only to diffusion and not to other processes, e.g. convection. We have also used other solvents, e.g. THF, and those with a viscosity equal to—or larger than—the viscosity of chloroform

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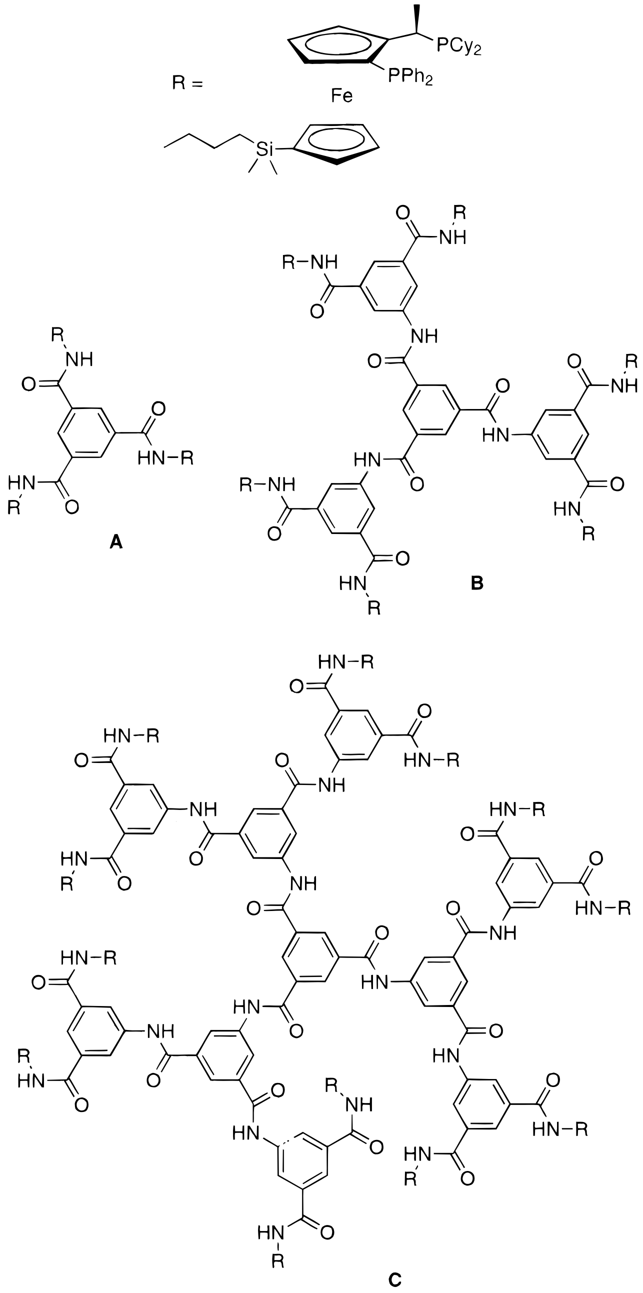
[15] We thank Prof. A. Togni and co-workers for the gift of these dendrimers: Köllner, C.; Pugin, B.; Togni, A. *J. Am. Chem. Soc.* **1998**, *39*, 10274.

Chart 1. Ferrocene Dendrimers A−C



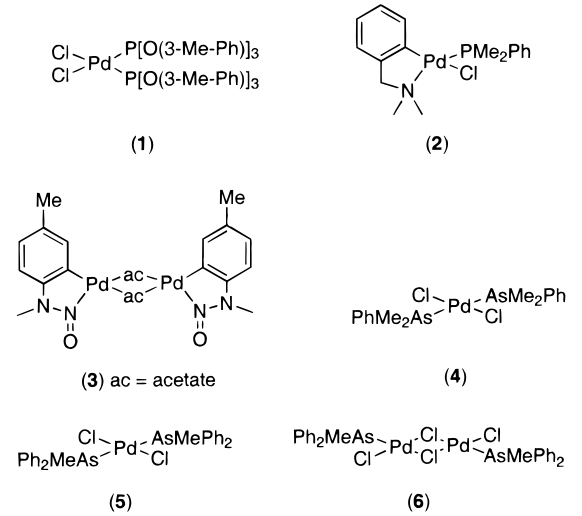
afford constant values of $m/(\Delta - \delta/3)$. With methylene chloride, a lower viscosity solvent, the $m/(\Delta - \delta/3)$ ratios were often not as constant, perhaps due to convection.

Since we do not measure the molecular size of our complexes directly, but a translational property, i.e., their diffusion coefficients, we need to relate these to a molecular property: e.g., the hydrodynamic radii, r_H. This can be achieved via the Stokes−Einstein equation (eq 3, where r_H = radius and η = viscosity), which allows

$$D = \frac{kT}{6\pi\eta r_H} \tag{3}$$

us to use measured D values to estimate r_H. As a check on our results, we estimated several r_H values for a selection of neutral organometallic complexes, or closely related analogues, for which the crystal structures are known. In several cases, **8**−**10** (see Table 2 and Chart 2), the X-ray data were taken from studies carried out in our laboratory.[19−21] Using the crystallographic data from their unit cells and assuming the molecules to be "spherical" [24] affords the results shown in the table. Figure 3 shows a plot of the r_H values from the PGSE measurements vs the radii obtained from the crystallographic data. The agreement is acceptable (perhaps

Table 1. $-m/(\Delta - \delta/3)$ and D in $CDCl_3$ Values for 1−6



compd	Δ (ms)	$-m/(\Delta - \delta/3)$	D (10^{-10} m^2 s^{-1})
1	45	0.0319	6.26
	65	0.0317	6.21
	85	0.0319	6.26
2	45	0.0429	8.41
	65	0.0432	8.47
	85	0.0429	8.41
3	65	0.0374	7.33
	85	0.0375	7.35
	105	0.0376	7.37
	125	0.0379	7.43
4	75	0.0428	8.37
	85	0.0426	8.35
	95	0.0428	8.39
	115	0.0422	8.27
5	65	0.0376	7.37
	85	0.0378	7.41
	95	0.0372	7.29
	105	0.0373	7.31
6	65	0.0346	6.78
	85	0.0346	6.78
	95	0.0348	6.82
	105	0.0347	6.80
	125	0.0347	6.74

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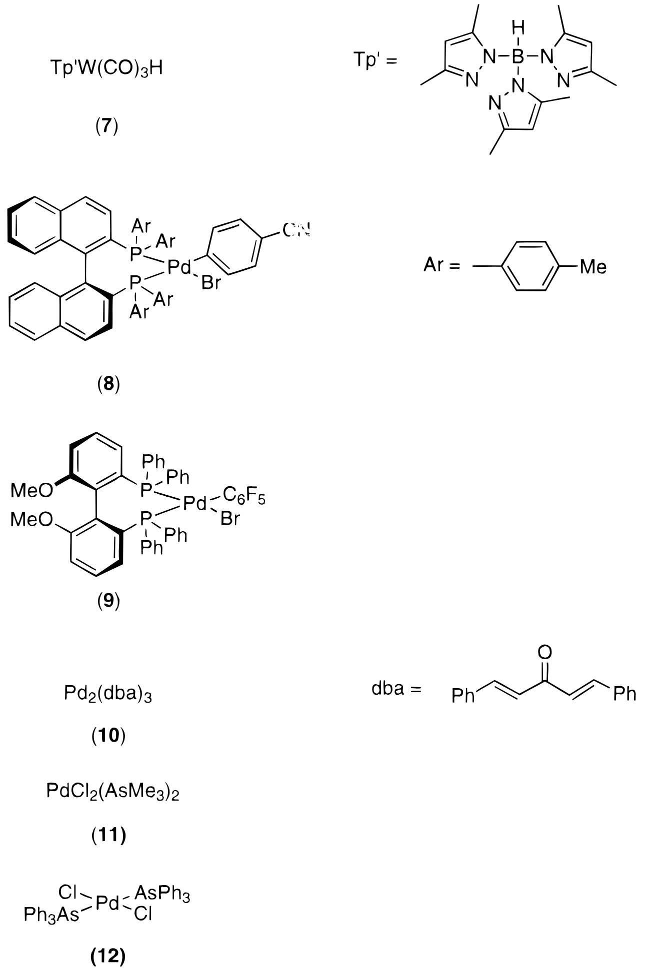
(24) In principle, one should consider the molecules as oblate or prolate in shape instead of just spherical.

Table 2. Estimated Hydrodynamic Radii, r_H

compd[a]	hydrodynamic radius	radius from X-ray
4	4.8	4.8[b,16]
5	5.4	5.4[c,17]
7	4.6	5.0[18]
8	7.1	6.8[19]
9	6.0	6.2[20]
10	6.2	6.3[21]
11	4.2	4.1[d,22]
12	5.8	5.8[e,23]

[a] For compounds **4**, **5**, **11**, and **12** the radii in the solid state were estimated using reported structures for closely related phosphine, instead of arsine complexes. [b] *trans*-$PdCl_2(PMe_2Ph)_2$. [c] *cis*-$PdCl_2(PMePh_2)_2$. [d] *cis*-$PdCl_2(PMe_3)_2$ [e] *trans*-$PdCl_2(PPh_3)_2$.

Chart 2



too good given the crude approximations) and suggests a legitimacy to our approach.

On the basis of our brief survey, which includes a variety of metals and molecular weights, we conclude that pulsed field gradient spin–echo techniques provide a practical alternative to classical methods of estimating molecular size. These methods will be especially valuable where one cannot isolate an unknown complex and/or where a side product is of especial interest, since one can measure several components of the mixture simultaneously.

Experimental Section

All the measurements were performed on a Bruker AVANCE 400 spectrometer equipped with a microprocessor-controlled gradient unit and a multinuclear probe with an actively shielded *Z*-gradient coil. The complexes were dissolved in distilled $CDCl_3$ and measured at 296 K without spinning. The shape of the gradients was rectangular, their length was 5 ms, and the strength was varied in the course of the experiment. The diffusion coefficients reported in Table 1 were estimated using the diffusion coefficient of HDO in D_2O[25] as a reference. Measuring the latter and the complexes under the same conditions, such as temperature, length, and shape of the gradients, allows one to use the simple relationship (4) to

$$\left(\frac{m_{\mathrm{HDO}}}{m_{\mathrm{compl}}}\right) = \left[\frac{m_{\mathrm{HDO}}/(\Delta - \delta/3)}{m_{\mathrm{compl}}/(\Delta - \delta/3)}\right] = \frac{D_{\mathrm{HDO}}}{D_{\mathrm{compl}}} \qquad (4)$$

obtain the *D* value of the complex. The hydrodynamic radii, reported in Table 2, were calculated from the values of the experimental diffusion coefficients using the Stokes–Einstein relationship.

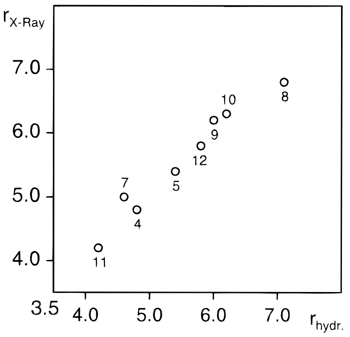


Figure 3. Plot of the hydrodynamic radii vs the radii calculated from the crystallographic data. For compounds **4**, **5**, **11**, and **12**, the radii in the solid state were estimated using reported structures for the analogous phosphine, instead of arsine.

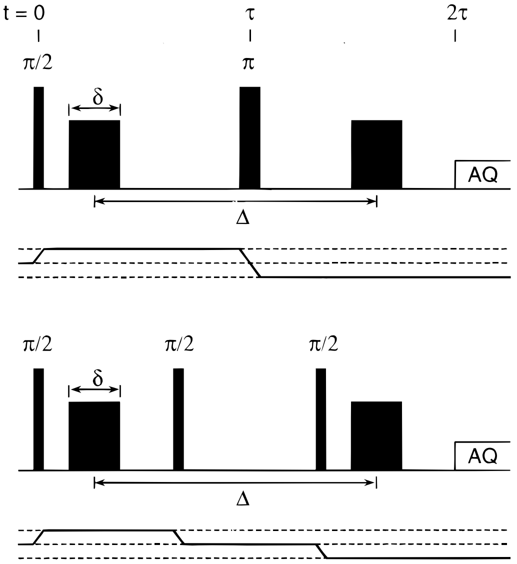


Figure 4. Pulse sequences used for the PGSE measurements with their corresponding coherence level diagrams.

Appendix. The basic element of any NMR diffusion measurement consists of an echo sequence, such as the classical Hahn spin echo method, in combination with the application of static or pulsed field gradients. The two sequences we employed are shown in Figure 4.

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Spin−Echo Method.[7] In the Stejskal−Tanner experiment (Figure 4 (top)), transverse magnetization is generated by the initial $\pi/2$ pulse which, in the absence of the static or pulsed field gradient, dephases due to chemical shift, hetero- and homonuclear coupling evolution, and spin−spin (T_2) relaxation. After application of an intermediate π pulse at $t = \tau$, the magnetization refocuses, generating an echo at $t = 2\tau$, at which point the sampling (intensity measurement) of the echo decay starts. Fourier transformation of this signal results in a conventional NMR spectrum, in which the signal amplitudes are weighted by their individual T_2's and the signal phases of the multiplets are distorted by the product $2J\tau\pi$. Both effects are present in the diffusion experiment but due to the fixed timing are kept constant within the experiment.

The application of the first pulsed linear field gradient at time t ($0 < t < \tau$) results in an additional (strong) dephasing of the magnetization with a phase angle proportional to the length (δ) and the amplitude (G) of the gradient. Because the strength of the gradient varies linearly along, for example, the z axis, only spins contained within a narrow slice of the sample have the same phase angle; in other words, the spins (and therefore the molecules in which they reside) are phase-encoded in the one-dimensional space. The second gradient pulse, which must be exactly equal to the first, acts on the −1 coherence order and reverses the respective phases and the echo forms in the usual way. If, however, spins move out of their slice into neighboring slices via Brownian motion, the phase they acquire in the refocusing gradient will not be the one they experienced in the preparation step. This leads to incomplete refocusing, as in the T_2 dephasing, and thus to an attenuation of the echo amplitude. As smaller molecules move faster, they translate during the time interval Δ into slices further apart from the original, thus giving rise to smaller echo intensities and steeper slopes, m.

Stimulated Echo Method.[7] The second experiment shown in Figure 4 (bottom) works quite the same, with the difference that the phase angles which encode the position of the spin are stored along the z axis in the rotating frame of reference by the action of the second $\pi/2$ pulse. Transverse magnetization and the respective phases are restored by the third $\pi/2$ pulse. This method has the advantage that, in the longest part of Δ, T_1 as opposed to T_2 is the effective relaxation path. Since $T_1 > T_2$, normally a better signal/noise ratio is expected. Furthermore, dephasing in multiplets due to homonuclear coupling is attenuated.

Technically, the experiment is performed by repeating the sequence while systematically changing one of its crucial parameters, which is the time allowed for diffusion (Δ), the length (δ), or the strength (G) of the gradient. We followed the last approach. Typical measuring times for high-quality data are usually less than 2 h.

Mathematically, the diffusion part of the echo amplitude can be expressed by eq 2, which implies that the data are best presented in the semilogarithmic way of giving $\ln(I/I_0)$ vs Δ, $\delta^2(\Delta - \delta/3)$, or G^2. The diffusion coefficient D is then proportional to the slope of the regression line.

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