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Molecular Weight Determination of Coordination and Organometallic Oligomers by T_1 and NOE Constant Measurements : Concepts and Challenges

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Summary: This paper describes how to determine molecular weights of coordination and organometallic polymers (or rather oligomers) in solution using spin-lattice relaxation time (T_1) and Nuclear Overhauser Enhancement constant (η_{NOE}) measurements. The methodology is explained using simple organometallic complexes such as $M(CN\text{-}t\text{-}Bu)_4^+$ complexes (M = Cu, Ag). Very good results are obtained for oligomers that exhibit a rigid structure. Conversely, very poor results are extracted when the materials show flexible chains in the backbone. The typical examples for rigid and flexible oligomers are the $\{Ag(dmb)_2^+\}_n$ (dmb = 1,8-diisocyano-p-menthane), and $\{Pd_2(dmb)_2(diphos)^{2+}\}_n$ (diphos = dppa, dppb, dpppent, and dpph) as well as $\{Pd_2(diphos)_2(dmb)^{2+}\}_n$ (diphos = dppe, dppr, and dppp**R**; **R** = $O(CH_2)_2O$-naphthyl), respectively.

Keywords: molecular dynamics; molecular weight measurements; Nuclear Overhauser Enhancement; spin-lattice relaxation times

Introduction

The molecular weight (M_n or M_w) and molecular weight distribution (also called the polydispersity constant) are two of the fundamental properties of macromolecules. In the area of coordination and organometallic polymers, a particularly challenging problem occurs when the polymeric materials turn out to be oligomeric in solution. The problem is the accurate estimation of smaller molecular dimension polymers (i.e. M_n or M_w). Techniques such as light scattering, osmometric and intrinsic viscosity measurements are three methods commonly used to determine these properties. However, a limitation of 5 000-10 000 exists for these methods, making the investigations of oligomers difficult. In addition, the relatively weak solubility that some materials may exhibit represents another important challenge for the techniques mentioned above.

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On the other hand, techniques such as Fast Atom Bombardments (FAB), Matrix-Assisted-Laser-Desorption-Ionisation-Time-of-Flight (MALDI-TOF), and electron spray mass spectrometry are also common characterization techniques for materials with molecular weight exceeding 1 000-1 300 mass units. Because of the relative fragility of the coordination bond or the fact that some species are already charged like in poly-cationic polymers, there is no guarantee of success in such measurements.

Because of all these common problems encountered by our group, another methodology that overcomes solubility and molecular dimension challenges has been used. This method is particularly suitable for oligomers, and is based on NMR techniques called spin-lattice relaxation time and Overhauser Nuclear Enhancement constant (η_{NOE}), which seeks to evaluate the dimension of the tumbling molecule from the knowledge of the correlation time (τ_c). This paper describes the concept and methodology, and some examples where this method does and does not apply.

Concept

According to theory, the volume (V) of a spherical molecule tumbling in solution can be calculated by using the Stokes-Einstein-Debye equation (1):

$$\tau_c = V\ \eta_{visc} / k\ T \qquad (1)$$

where η_{visc} is the viscosity of the medium, k is the Boltzman constant, and T is the temperature. For non-spherical molecules, this equation becomes more complex and involves a decomposition of the molecular motions according to the various axes of the molecule (normally x, y, and z, for ellipsoid-shaped molecules), and as a consequence, three correlation times must be obtained. Because the T_1 measurements provide an average value, it is inadequate to attempt to decompose the problem along the three axes. In such a case, this method is an approximation.

The measurement of the dipole-dipole relaxation time (T_1^{DD} = a spin relaxation due to interactions with the surrounding nuclei), one can extract τ_c according to the general Equation 2 (for this equation the considered dipole-dipole interactions are those generated by the ^1H and ^{13}C nuclei generally encountered in ^{13}C NMR for instance):

$$1/T_1^{DD} = \Sigma(\hbar^2\gamma_H^2\gamma_C^2/10r_{CH}^6)\bullet\{\tau_c/[1+(\omega_H-\omega_C)^2\tau_c^2]+ 3\tau_c/[1+\omega_C^2\tau_c^2] + 6\tau_c/[1+(\omega_H+\omega_C)^2\tau_c^2]\} \quad (2)$$

where $\hbar$ ($h/2\pi$) is the Plank constant, γ is the magnetogyric ratio for a given nuclei, and r_{CH} is the distance between the two interacting nuclei. In the extreme narrowing limit, where molecular motions are very fast (i.e. small molecules, $\omega\tau_c << 1$), Equation 2 becomes:

$$1/ T_1^{DD} = \Sigma\ [(\hbar^2\ \gamma_H^2\ \gamma_C^2) / (r_{CH}^6)] \bullet \tau_c \qquad (3)$$

To verify if the extreme narrowing limit applies, one has to check if T_1 varies with the magnetic field strength (H_o). If it does not apply, then Equation 2 must be used. Experimentally, the measured T_1 represents the sum of all contributions to spin-lattice relaxations, so that T_1^{DD} must be extracted from:

$$1/ T_1 = \Sigma\ 1/ T_1^i = 1/ T_1^{DD} + 1/ T_1^{SR} + 1/ T_1^{CSA} + 1/ T_1^{SC} + 1/ T_1^{exc} + 1/ T_1^{Q} + 1/ T_1^{para} \qquad (4)$$

where SR, SCA, SC, exc, and para designate relaxations operating via spin-rotation, chemical shift anisotropy, scalar, chemical exchange, quadrupolar, and the presence of paramagnetic electrons (details for the description of these different mechanisms to relaxation are given in ref.[1] and ref.[2]. In the extreme narrowing limit, T_1^{DD} is field independent and can be extracted at the intercept of the graph $1/T_1$ vs H_o. For such a method, accuracy can only be obtained if many spectrometers with different fields are available, which is rarely the case. Instead, the measurements of the NOE effect (the experimentally observed enhancement of the ^{13}C signal, for instance, during coupled vs uncoupled experiments) give access to η_{NOE}:

$$NOE = 1 + \eta_{NOE} = 1 + (\gamma_H/2\gamma_C) \qquad (5)$$

where η_{NOE} is the fractional NOE constant. Hence one can more confidently obtain T_1^{DD}:

$$1 / T_1^{DD} = (\eta_{NOE})/(T_1 \bullet \eta_{max}) \tag{6}$$

where η_{max} is the maximum NOE effect one can get for two given nuclei in the extreme narrowing limit. For ^1H and ^{13}C interactions, $\eta_{max} = \gamma_H/2\gamma_C = 1.988$, while for ^1H and ^{31}P, for example, $\eta_{max} = \gamma_H/2\gamma_P = 1.235$, where the ^{13}C and ^{31}P are the probed nuclei (i.e. for which the T_1 are measured).

For example, the tetracoordinated cations $M(CN\text{-}t\text{-}Bu)_4^+$ (M= Cu, Ag) have recently been investigated as models for the repetitive unit in the polycationic coordination polymer $\{Ag(dmb)_2^+\}_n$.[3, 4] Table 1 compares the T_1 data for the various salts.

Table 1. T_1 data for $[M(CN\text{-}t\text{-}Bu)_4](X)$ salts for the 63-64 ppm signal $(-^{13}C(CH_3)_4)$[a]

M	X	T_1
		s
Ag	BF_4^-	37.5
Ag	ClO_4^-	37.1
Ag	NO_3^-	36.0
Cu	BF_4^-	34.2
Cu	ClO_4^-	32.6
Cu	NO_3^-	33.5

[a] At 298 K in d_3-acetonitrile on a 300 MHz instrument.

There is very little influence of the counter-anion on T_1, indicating that the dragging of the counter-ion during tumbling could be neglected. Similarly, the close resemblance of T_1(Cu) and T_1(Ag) indicates that both nuclei have a similar influence on T_1 for this specific nuclei. The η_{NOE} data are also about constant ($\eta_{NOE} = 1.31 \pm 0.03$). For $[Ag(CN\text{-}t\text{-}Bu)_4]BF_4$ as an example, equation 6 computes $T_1^{DD} = 57.0$ s, and τ_c (from equation 3) is 2.11×10^{-10} s. The "hydrodynamic" volume that takes into account the dragging of solvent molecules (and counter-ions) during tumbling is 2.37×10^{-27} m^3 (or 2370 Å^3) according to the Stokes-Einstein-Debye equation. The use of this relation is justified by the fact that the tetrahedral structure of the cation resembles that of a sphere. The value for V is very large when compared to X-ray data of related complex Fe(CN-t-Bu)$_5$ (in the order of 750 Å^3)[5] (since no structure exists for the [M(CN-t-Bu)$_4$](X) complexes discussed above). This difference not only shows the importance of the solvent dragging, but also the potentially large inaccuracy that one may experience.

In order to overcome this problem, one can extract the dimension of an unknown molecule using another molecule for comparison (i.e. a standard). This molecule must have some important characteristics to be adequate. The existence of an X-ray structure is preferable in order to obtain information about the volume. To the contrary, computer modeling is sufficient. The standard should also bear the same charge as the unknown, as well as the same ligands. These properties confirm that the dragging of the counter-ion and solvent molecules during tumbling in solution are the same. Hence, by combining Equation 1, 3 and 6, one obtains:

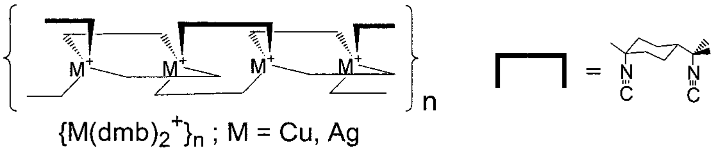
$$\frac{T_1(\mathrm{sam})}{T_1(\mathrm{sta})} = \frac{\eta_{CH}(\mathrm{sam})}{\eta_{CH}(\mathrm{sta})} \bullet \frac{V(\mathrm{sta})}{V(\mathrm{sam})} \bullet \frac{\Sigma\ 1/r^6{}_{CH}(\mathrm{sta})}{\Sigma\ 1/r^6{}_{CH}(\mathrm{sam})} \qquad (7)$$

where sta and sam stand for standard and sample, respectively, and η_{CH} is η_{NOE} (applied to ^{13}C-^{1}H interactions as an example). By using exactly the same probe on the same ligand in the standard and the sample, the term [$\Sigma\ 1/r^6{}_{CH}$(sam)]/ [$\Sigma\ 1/r^6{}_{CH}$(sta)] becomes unity. Hence, to extract V(sam), one measures T_1(sam), T_1(sta), η_{CH}(sam), and η_{CH}(sta), and uses X-ray data or computations for V(sta), again if the extreme narrowing limit applies. For organometallic or coordination polymers, by using a standard that closely resembles a repetitive unit of the polymer, the ratio V(sam)/V(sta) can give a very good estimate of the number of units in the polymeric chain.

Two problems exist; 1) the use of the Stoke-Einstein-Debye equation is an approximation in this methodology, and 2) the standard does not always perfectly mimic the solute-solvent interactions as the polymer chain does, for simple geometry reasons. Despite these problems, the estimation of the molecular dimension is still valuable information, when no other technique can be applied.

The $\{Ag(dmb)_2^+\}_n$ Case

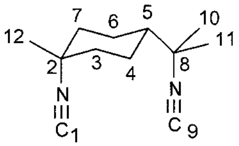
Since the discovery of this polymer in 1992 (Scheme 1)[6] and its Cu analogue,[7] many new related polymers such as $\{Pt_4(dmb)_4(diphos)_2^+\}_n$,[8] (diphos = $Ph_2P(CH_2)_mPPh_2$ (m = 4-6), $\{Pd_4(dmb)_4(dmb)^{2+}\}_n$,[9] mixed-metal $\{Cu_xAg_{1-x}(dmb)_2^+\}_n$,[10] mixed-ligand $\{M(dmb)\text{-}(dppm)^+\}_n$ (M = Cu, Ag; dppm= $Ph_2PCH_2PPh_2$),[10] and mixed-conformation[11] have been prepared and confidently characterized from X-ray crystallography or, on rare occasions, molecular weight determination.



Scheme 1

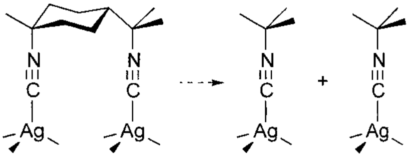
For the title polymer, light scattering and osmometric measurements indicate that M_w and M_n cannot be measured by these methods, which place the upper limit to 10 000. Similarly, both FAB mass and MALDI-TOF spectra exhibit fragment peaks of about 3 units (1100-1300).[5] The measurements of the intrinsic viscosity exhibit a delay of barely 0.5 s, which make this method far too inaccurate for any meaningful use.

For the $\{[Ag(dmb)_2]X\}_n$ polymers (X = BF_4^-, ClO_4^-, NO_3^-), the probe nuclei is the sp^3-hybridized quaternary carbon #2, more particularly ^{13}C located in the dmb-cyclohexyl ring (see Scheme 2). This nuclei is selected for the following reasons. The rigidity of the M-C≡N-^{13}C unit allows one to measure a T_1 process that is less influenced by intramolecular motions such as spin-rotation relaxation known for methyl groups for instance, and motion of alkyl chains. In addition a quaternary ^{13}C relaxes more slowly than others, because of the absence of close $^1H\cdots{}^{13}C$ dipole-dipole interactions which are known to induce efficient relaxation of the ^{13}C nuclei. As a result the larger time scale provides an opportunity to gain accuracy. The δ value for this ^{13}C is 63.3 ppm (CD_3CN).



Scheme 2

Table 2 summarizes the NMR results for various salts of $\{[Ag(dmb)_2]X\}_n$ (X = BF_4^-, ClO_4^-, NO_3^-). The average η_{NOE} in these cases is 1.75 ± 0.03, expectedly different from that found for the corresponding ^{13}C nuclei in the $[Ag(CN\text{-}t\text{-}Bu)_4](X)$ salts used as standards due to the great similarity between two Bu-t-NC ligands and one dmb (Scheme 3).



Scheme 3

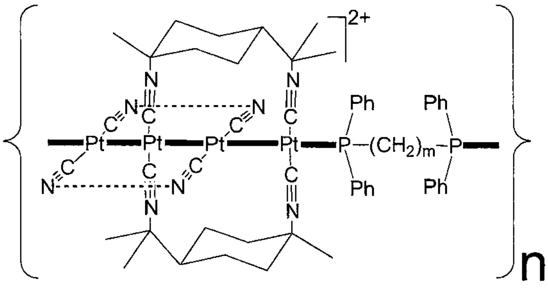
The V(sta) is the hydrodynamic volume estimated above, and it is assumed that $V(Ag(CN\text{-}t\text{-}Bu)_4^+) \sim V(Ag(dmb)_2^+)$. The number of units ranges from 7 to 9 giving M_n of 4 000-5 000, which is exactly where it was predicted to be (see above). These oligomers correspond to small "rigid rods" of about 43-50 Å (or 4.5 – 5 nm) in lenght.

Table 2. Selected data for the $\{[Ag(dmb)_2]X\}_n$ materials.

	NO_3^-	BF_4^-	ClO_4^-
T_1 (± 0.20 s)	6.90	7.53	7.93
T_1^{DD}(± 0.20 s)	7.84	8.55	9.77
τ_c (x 10-9 s ± 3%)	1.97	1.81	1.58
V ($Å^3$)	22000	203000	17700
Number of units	~9	~8	~7

Larger Polymers

The corresponding $\{[Cu(dmb)_2]BF_4\}_n$ polymer, M_w of 160 000[7] and M_n of 133 000[12] (about 300 units) are obtained from light scattering and osmometric measurements, respectively. On the basis of T_1, one can predict that as T_1 decreases, the molecular dimension increases. This is well exemplified by the series $\{Ag(dmb)_2^+\}_n$ (T_1 = 6.90-7.93 s; number of units = 8 ± 1 above), $\{Ag_{0.27}Cu_{0.73}(dmb)_2^+\}_n$ (T_1 = 6.35 s),[4] and $\{Cu(dmb)_2^+\}_n$ (T_1 = 2.63 s; ~300 units). The change of T_1 vs the number of units is not linear, as one would anticipate from Equation 2, which in fact exhibits a V-shaped curve. As T_1 decreases, the method becomes more inaccurate due to the lack of sensitivity of T_1 vs M_n (or τ_c). This phenomena is also well demonstrated in the cases of the $\{Pt_4(dmb)_4(diphos)_2^+\}_n$ (diphos = $Ph_2P(CH_2)_mPPh_2$ (m = 4-6; Scheme 4, Table 3) polymers for which M_n was obtained from the intrinsic viscosity measurements,[8] reported earlier. The η_{NOE} values were not measured, so the comparison between the number of units measured from the intrinsic viscosity properties and from the T_1/NOE method could not be performed.



N------N = dmb; m = 4, 5, 6

Scheme 4

Table 3. Dimension of the $\{Pt_4(dmb)_4(Ph_2P(CH_2)_mPPh_2)\}_n$ polymers.[a]

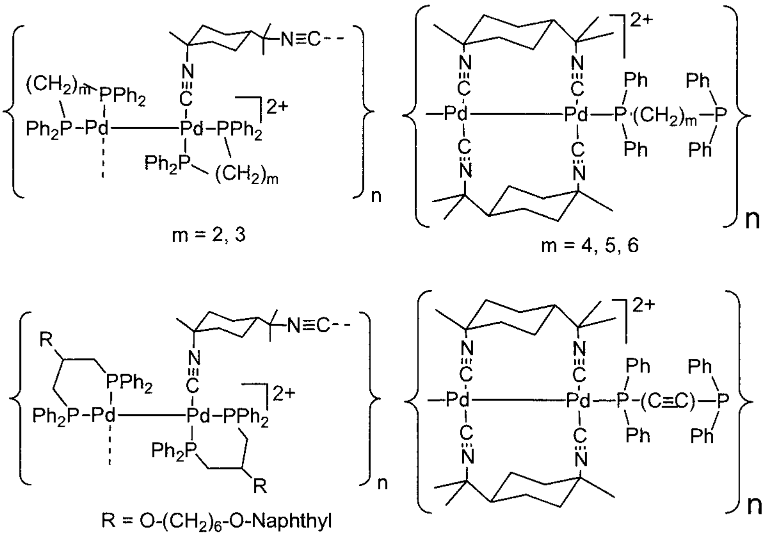
Polymers	[η] cm³/g	T_1 ^{13}C s	M_n	numbers of units
$Pt_4(dmb)_4(PPh_3)_2^{2+}$	_	3.76	2000	1
$\{Pt_4(dmb)_4(Ph_2P(CH_2)_4PPh_2)^{2+}\}_n$	3.66	2.19	203000	100
$\{Pt_4(dmb)_4(Ph_2P(CH_2)_5PPh_2)^{2+}\}_n$	4.78	1.69	307000	150
$\{Pt_4(dmb)_4(Ph_2P(CH_2)_6PPh_2)^{2+}\}_n$	2.06	2.24	84000	40

[a]The same dmb-peak at 63 ppm is probed. The solvent is CD_3CN at room temperature.

In conclusion, this methodology is better suited for small oligomers, which is very convenient here, since reliable methods for small molecules and larger polymers already exist.

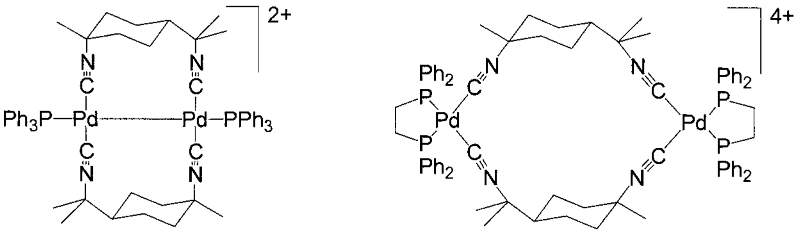
Molecular Dynamics

As stated above, the comparison between the number of units obtained from the intrinsic viscosity properties and from the T_1/NOE method could not be performed for this earlier work, but was recently performed in our laboratory.[13] Indeed, two series of organometallic polymers have been prepared (Scheme 5): 1) $\{Pd_2(diphos)_2(dmb)^{2+}\}_n$ (diphos = dppe, dpppr, dpppR (R = O-$(CH_2)_6$-O-Naphthyl)), and 2) $\{Pd_2(dmb)_2(diphos')^{2+}\}_n$ (diphos = dppb, dpppent, dpph, dppa). Because the ligand environment about the Pd_2-bonded fragment is different, the color of the materials is different. These are respectively, yellow and red, and are found to be amorphous according to XRD patterns. Both series exhibit the dmb ligand, which can act as a bridging ligand between two Pd_2 units, or the Pd-Pd bond.



Scheme 5

The two T₁/NOE standards used for the two series are the complexes $Pd_2(dmb)_2(PPh_3)_2^{2+}$ and $Pd_2(dppe)_2(dmb)_2^{4+}$ (Scheme 6) for the "red" and "yellow" series, respectively.



$Pd_2(dmb)_2(PPh_3)_2^{2+}$ $Pd_2(dppe)_2(dmb)_2^{4+}$

Scheme 6

The data in Table 4 summarizes the M_n data obtained from the measurements of the intrinsic viscosity, and the corresponding number of units. The "yellow" series, $\{Pd_2(diphos)_2\text{-}(dmb)^{2+}\}_n$ (diphos = dppe, dpppr, dpppR), are found to be a little shorter (~7-8) than that of the "red" series, $\{Pd_2(dmb)_2(diphos')^{2+}\}_n$ (diphos = dppb, dpppent, dpph, dppa) (12-16 units). These materials are oligomers when dissolved in solution (which does not necessarily reflect the nature of the materials in the solid state).

Table 4. Comparison between T_1/NOE and intrinsic viscosity data

	M_n	Nb. of units (intr. visc.)	Nb. of units (T_1/NOE)
$\{Pd_2(dmb)_2(dppb)^{2+}\}_n$	17 800	~14	~ 4
$\{Pd_2(dmb)_2(dpppen)^{2+}\}_n$	18 400	~14	~ 4
$\{Pd_2(dmb)_2(dpph)^{2+}\}_n$	16 100	~12	~ 4
$\{Pd_2(dmb)_2(dpa)^{2+}\}_n$	19 500	~16	~ 5
$\{Pd_2(dppe)_2(dmb)^{2+}\}_n$	11 800	~ 8	~ 2
$\{Pd_2(dppp)_2(dmb)^{2+}\}_n$	12 100	~ 8	~ 2
$\{Pd_2(dppp\mathbf{R})_2(dmb)^{2+}\}_n$	13 600	~ 7	~ 2

Even more interesting, the number of units evaluated from the T_1/NOE method is systematically 3 – 4 times smaller than that measured from the intrinsic viscosity properties. This discrepancy is due to the presence of chain flexibility, which allows "local" molecular motions. The probe ^{13}C nuclei senses motions that are the equivalent to 4-5 units for the "red" series, and about only 2 for the "yellow" series (dmb being sufficiently flexible for that). In support of this explanation, this method was recently applied to unambiguously confirmed mass data that suggested dimeric structures for a series of rhodium(I) complexes of diphosphinated-calix[4]arenes.[14] Molecular modeling showed very rigid dimers due to the presence of slightly encumbered rings. In these cases, and the $\{Ag(dmb)_2^+\}_n$ cases presented above, the rigidity of the molecular structures allowed the accurate estimation of the molecular dimension by T_1/NOE.

Coming back to molecular dynamics, by changing the flexible alkyl chain for a more rigid group (from $-(CH_2)_m-$ to $-C{\equiv}C-$), or by adding large lateral chains to the backbone ($O-(CH_2)_6.O-$Naphthyl), no sensitive effect is observed on the estimated number of units by T_1/NOE. These results indicate that the presence of lateral chains do not affect the molecular motions about the ^{13}C probe, and that the $-C{\equiv}C-$ group is still fairly flexible due to the absence of an important barrier to rotation.

Conclusion

The T_1/NOE method is not new. Ironically, it was used long ago for the estimation of the molecular weight of proteins. The dimensions of proteins are generally so large that the slow narrowing limit must apply ($\omega\tau_c >> 1$), and the more complex Equation 2 must be used. In addition, accuracy is best achieved when a comparison with a known standard is made. Finally, chain flexibility represents an important problem in the application of this method. Considering these facts, some earlier studies may need to be revisited. For this research program, the application of this method works best for oligomers, which exhibit M_n that are often a problem for most techniques in polymer science. The low solubility of some materials can also be overcome by simply accumulating data for a longer period of time.

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