Supporting Information

Kinetics of Intramolecular Chemical Exchange by Initial Growth Rates of Spin Saturation Transfer Difference Experiments (SSTD NMR)

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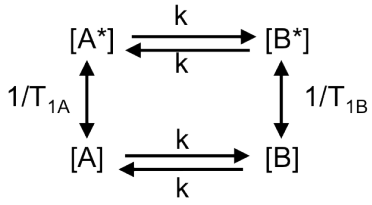
1) Method development: New protocol for determination of the mutual-site exchange rate constant by SSTD NMR build-up curves

A mutual-site exchange kinetics for two spins A and B (two-sites exchange) can be depicted as



where [A] and [A*], as well as [B] and [B*], are the lower and upper spin-state populations of spins A and B, respectively, T_{1A} and T_{1B} are the longitudinal relaxation time constants of spins A and B, and *k* is the mutual-site exchange rate constant.

The rate equation for the magnetization of spin A, taking into account both processes of population exchange, relaxation and chemical exchange, is given by

$$\frac{dM_A}{dt} = -k \cdot (M_A - M_B) + \frac{M_{0A} - M_A}{T_{1A}}$$

Where M_A=[A]-[A*], M_B=[B]-[B*], and M_{0A} is the magnetization of spin A at thermal equilibrium. Selective spin saturation of B, carried out by a selective low power irradiation centred at its chemical shift, leads to disappearance of its ^{1}H NMR signal in the spectrum (M_B=0). Then,

$$\frac{dM_A}{dt} = -k \cdot M_A + \frac{M_{0A} - M_A}{T_{1A}}$$

Multiplying both sides of the equation by $(-1/M_{0A})$:

$$-\frac{1}{M_{0A}} \cdot \frac{dM_A}{dt} = k \cdot \frac{M_A}{M_{0A}} - \frac{1}{T_{1A}} \frac{M_{0A} - M_A}{M_{0A}} = k \cdot \left(1 - \frac{M_{0A} - M_A}{M_{0A}}\right) - \frac{1}{T_{1A}} \frac{M_{0A} - M_A}{M_{0A}}$$

The fraction $\frac{M_{0A}-M_A}{M_{0A}}$ results from the measurement of the intensity of a "difference spectrum" (equilibrium-saturated, $M_{0A} - M_A$) over the intensity of the equilibrium spectrum (M_{0A}). This is similar to the protocol for studying protein-ligand interactions by saturation transfer difference (STD) NMR, and for that reason we have called our method "spin saturation transfer difference (SSTD) NMR", and uses the same pulse sequence as

the standard 1D STD NMR experiment. The main difference between SSTD NMR and STD NMR spectroscopy is that in the first case we directly saturate one of the sites in the mutual-site exchange, and that saturation is transferred exclusively by intramolecular chemical exchange, in contrast to the latter experiment in which, besides the chemical exchange, there must be dipole-dipole interactions between the protein and the ligand protons (protein-ligand intermolecular NOE) to generate saturation in the bound state (the ligand is not directly irradiated), saturation that is further transferred to the free state by chemical exchange.

If we define a new parameter called "spin saturation transfer difference factor" (η_{SSTD}) as:

$$\eta_{SSTD} = \frac{M_{0A} - M_A}{M_{0A}}$$

We arrive to:

$$-\frac{1}{M_{0A}} \cdot \frac{dM_A}{dt} = k \cdot (1 - \eta_{SSTD}) - \frac{1}{T_{1A}} \eta_{SSTD} = k - (k + \frac{1}{T_{1A}}) \cdot \eta_{SSTD}$$

If we consider the derivative of η_{SSTD}:

$$\frac{d\eta_{SSTD}}{dt} = \frac{d}{dt}\left(\frac{M_{0A} - M_A}{M_{0A}}\right) = -\frac{1}{M_{0A}} \cdot \frac{dM_A}{dt}$$

This result matches exactly the left part of the previous equation, so that we can write:

$$\frac{d\eta_{SSTD}}{dt} = k - (k + \frac{1}{T_{1A}}) \cdot \eta_{SSTD}$$

Integration of this differential equation leads to:

$$\eta_{SSTD}(t) = \frac{k}{(1/T_{1A} + k)}(1 - \exp(-(1/T_{1A} + k) \cdot t))$$

The term $(1/T_{1A} + k)$ compiles the two mechanisms affecting the transfer of saturation between the two sites, i.e. the relaxation rate ($R_{1A}=1/T_{1A}$) and the mutual-site exchange rate constant (k). We call this term the "dynamic constant" (δ), so that,

$$\eta_{SSTD}(t) = \frac{k}{\delta}(1 - \exp(-\delta \cdot t))$$

If we determine the derivative and calculate its value at zero saturation time (initial slope):

$$\left.\frac{d\eta_{SSTD}}{dt}\right|_{t=0} = \frac{k}{\delta} \cdot \delta = k$$

That is, the initial slope of the build-up curve is exactly the mutual-site exchange rate constant that we want to determine. The equation for the time evolution of η_{SSTD} and the formula of the initial slope suggest that the way to obtain experimentally the rate constant, *k*, is to carry out SSTD NMR experiments at different saturation times and mathematically fit the experimental curve to the mono-exponential equation:

$$\eta_{SSTD}(t) = A \cdot (1 - \exp(-B \cdot t))$$

The fit will give the parameters A and B, and the initial slope (*k*) can be easily calculated by the product A·B.

$$A \cdot B = k$$

On the other hand, the parameter A correspond to the value of η_{SSTD} at very long saturation times, and we called ${\eta_{SSTD}}^{MAX}$. Taking into account that,

$${\eta_{SSTD}}^{MAX} = \frac{k}{(1/T_{1A} + k)}$$

Once *k* has been determined, it is easy to obtain also T_{1A}.

N. B. On the range of applicability (theoretical limits) of the method. Regarding the upper limit of the rate constant, *k*, the method will not work in two clear cases: (i) when both signals (A and B) of the protons in the two different sites are close enough as to make impossible the saturation of one signal with sufficient selectivity, and (ii) when *k* is extremely high, which in the extreme limit would correspond to a case of free rotation (one single NMR signal). As for the lower limit, clearly the kinetics must be fast enough as to transfer observable magnetization from one site to the other site. If the kinetics rate is much lower than the relaxation rate (R_1) of the spin in that site, there will not be efficient transfer of magnetization between the sites. In the particular case of complex **3** which showed the lowest value of exchange rate of all the studied systems, the rate constant was *k* = 0.085 Hz, at 337 K. As R_1 was 0.71 Hz, in our hands the method is at least applicable up to a low ratio k/R_1 of 0.12.

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2) General experimental details

All reagents were purchased from commercial sources and used without further purification, unless noted otherwise. Deuterated solvents were acquired from Apollo Scientific Limited or Fluorochem and stored over molecular sieves. All the preparative working procedures were carried out under absence of moisture and air under nitrogen atmosphere. Accurate weights were obtained with a Denver Instrument SI-234. ^{1}H and NOE NMR spectra were recorded on a Bruker Avance III 500 MHz NMR spectrometer, fitted with a 5mm broadband observed, BBFO^{plus} Z-gradient SmartProbe^{TM} probe. SSTD NMR experiments were carried out on a Bruker Avance I 500 MHz Inverse Triple Resonance NMR spectrometer, fitted with a 5mm Tx1 Z-gradient probe. Calibration was made using the deuterated solvent residual peak in the case of the ^{1}H NMR (δH = 7.26 ppm for $CDCl_3$, δH = 6.0 ppm for $CDCl_2CDCl_2$, δH = 3.58 ppm for THF-d^8 and δH = 2.90 ppm for Toluene-d^8)[1] and using an internal reference (Na_2PtCl_6 in D_2O) in the case of the ^{195}Pt NMR.[2] Chemical shifts (δ) are given in parts per million (ppm) and coupling constants values (*J*) are given in Hertz (Hz). Abbreviations for multiplicities are as follows: (s) singlet, (d) doublet, (dd) doublet doublet, (t) triplet, (q) quartet, (m) multiplet.

3) Sample preparation and NMR experimental setup

Samples of **1** and **2** were prepared under air dissolving 5 mg of the corresponding compound in 0.6 mL of Toluene-d_8.

Samples of **3** were prepared under air dissolving 3.5 mg of the corresponding compound in 0.55 mL of $CDCl_2CDCl_2$.

A standard 1D STD NMR pulse sequence provided by the manufacturer ("stddiff", Bruker) was used for the experiments. They were carried out on a 11.7 T high-resolution Bruker NMR spectrometer (500 MHz) equipped with an inverse triple resonance (H/C/N) z-gradient probe head. The total saturation time for a given experiment was built by a chain of "n" Gaussian pulses of 50 ms length, with a maximum field strength $\gamma B_1$of 104 Hz, providing a saturation time of "0.05·n" seconds. To avoid relaxation artefacts, all the

1 H. E. Gottlieb, V. Kotlyar and A. Nudelman, *J. Org. Chem.*, 1997**, *62,*** 7512-7515.

2 (a) B. M. Still, P. G. A. Kumar, J. R. Aldrich-Wright and W. S. Price, *Chem. Soc. Rev.* 2007, ***36***, 665-686, and references cited therein. (b) S. J. S. Kerrison and P. J. Sadler, *J. Magn. Reson.*, 1978**, *31,*** 321-325.

experiments within a build-up curve had total duration constant, i.e. the addition of the relaxation delay plus the saturation time and the acquisition time was kept constant (42 s) along the whole set of experiments. On-resonance frequency was selected at the chemical shift of one of the ^{1}H signals of the exchanging sites, and the off-resonance (reference NMR spectrum) frequency was set in all the cases to 40 ppm. For all the SSTD NMR experiments the spectral width was selected to cover the two signals of interest and centred (O1) at the middle frequency between them. Integration of signals was carried out using Topspin 3.1.

4) Analysis of chemical exchange in *N,N*-dimethylacetamide 1

4a) ^{1}H NMR chemical shift assignment: The compound was commercially available.

^{1}H NMR (Toluene-d_8, 500MHz, 25^{o}C): δ (ppm) = 2.60 (s, 3H, CH_3^A), 2.17 (s, 3H, CH_3^B) 1.63 (s, 3H, CH_3CO).

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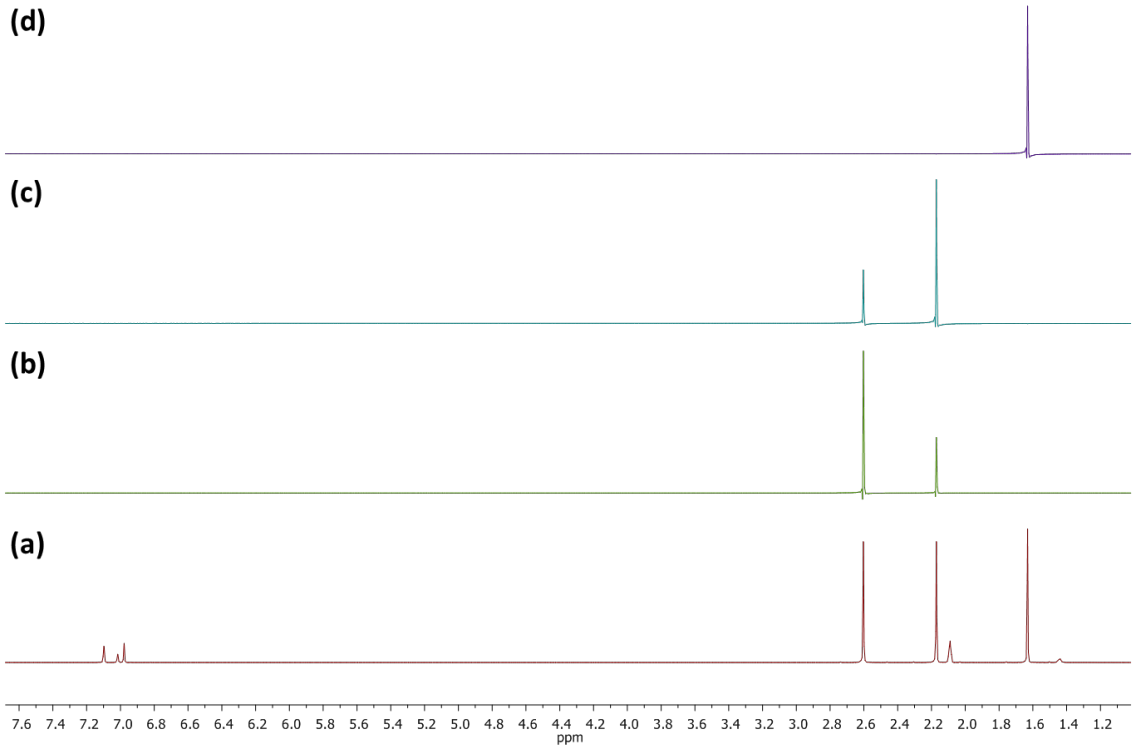
4b) 1D NOE experiments

4b.1) 1D NOE spectra of *N,N*-dimethylacetamide **1** in Toluene-d_8 at room temperature. (a) Full spectra. (b) NOE spectra irradiating signal at 2.60 ppm. (c) NOE spectra irradiating signal at 2.17 ppm. (d) NOE spectra irradiating signal at 1.63 ppm. The positive signals observed in the spectra (b) and (c) are due to the chemical exchange process that takes place in this case at room temperature (NOE effect should appear as negative signals).



4b.2) 1D NOE spectra of *N,N*-dimethylacetamide **1** in Toluene-d_8 at - 40°C. (a) Full spectra. (b) NOE spectra irradiating signal at 2.59 ppm. (c) NOE spectra irradiating signal at 1.95 ppm. (d) NOE spectra irradiating signal at 1.60 ppm. NOE effects were not observed.

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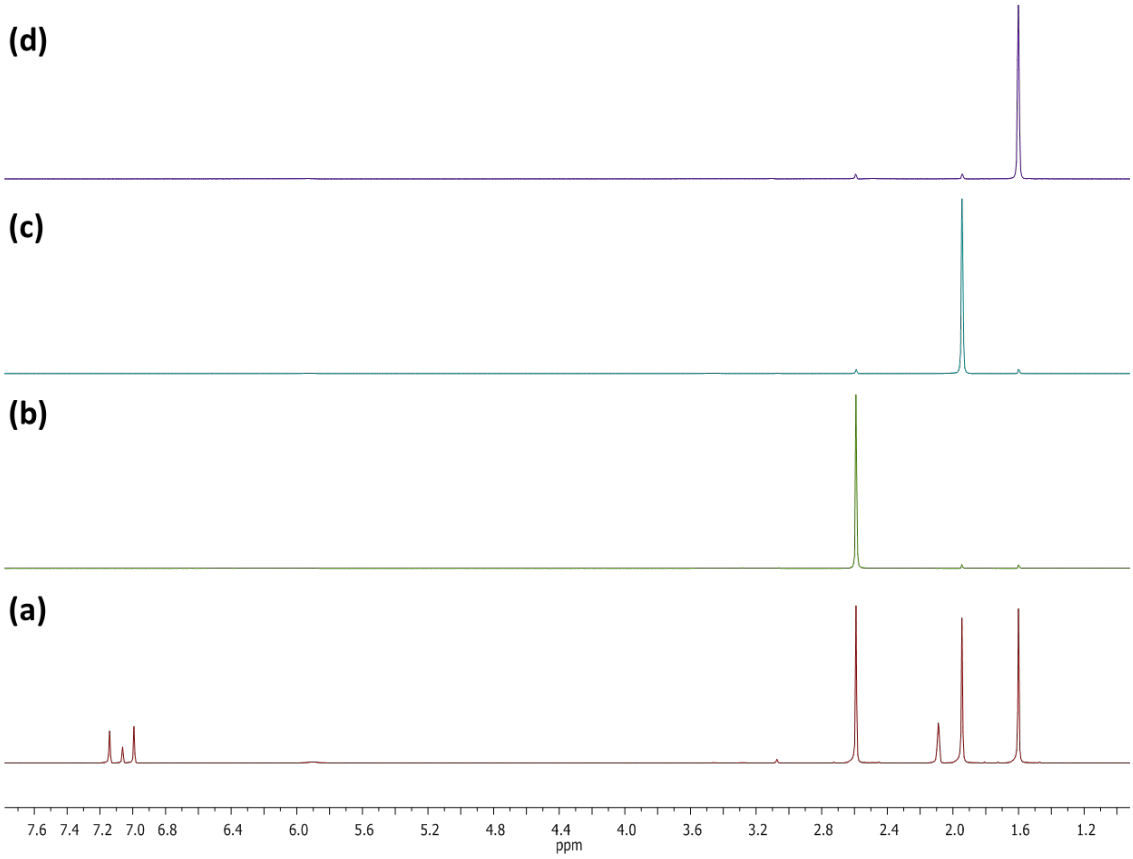

4c) Experimental SSTD build-up curves

The η_{SSTD} factor was calculated from the magnetization transfer observed in the difference spectrum (b) (M_{0A}-M_A) with regard with the spectra before irradiation (a) (M_{0A}).

$$\eta_{SSTD} = \frac{M_{0A} - M_A}{M_{0A}}$$

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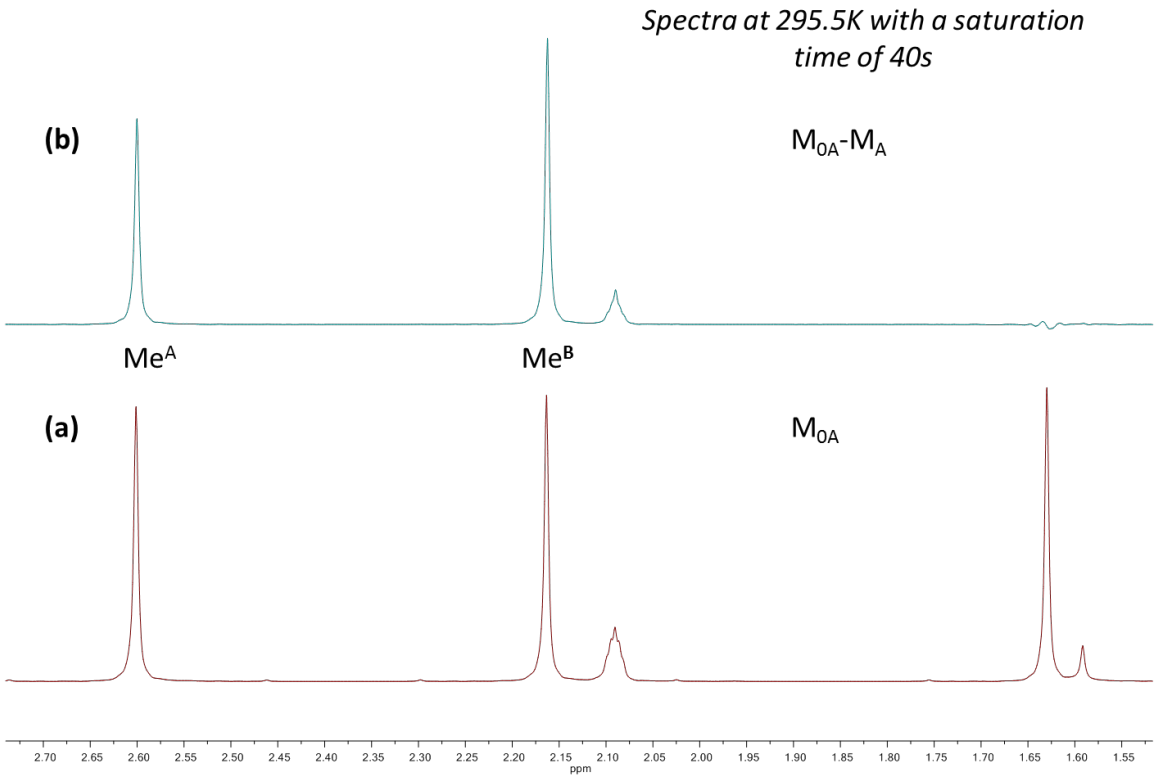

Figure 1S. Example of the ^{1}H NMR expansion of *N,N*-dimethylacetamide **1** in toluene-d_8 before irradiation (a) and "difference spectrum" (b) at 295.5 K with a saturation time of 40 s saturating the signal at 2.16 ppm.

The values of η_{SSTD} were obtained for different saturation times at each temperature and their plot versus saturation time gave exponential curves in which a plateau was reached at long saturation times and which exponential fit allowed us to obtain the values of the rate constants of the process at the different temperatures.

$$\eta_{SSTD}(t) = \frac{k}{(1/T_{1A} + k)}(1 - \exp(-(1/T_{1A} + k) \cdot t))$$

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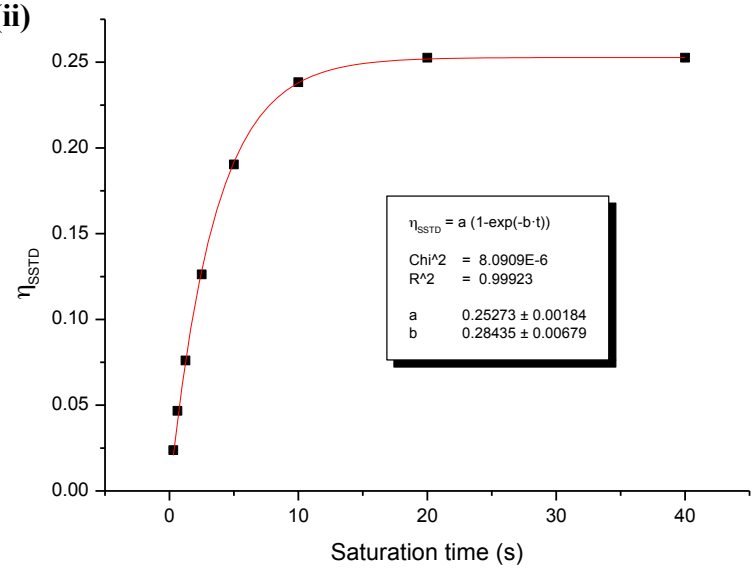
4c.1) (i) Values of η_{SSTD} obtained at different saturation times for *N,N*-dimethylacetamide **1** at 278 K. (ii) Plot of η_{SSTD} versus saturation times with the exponential fit. (iii) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.2526
20	0.2526
10	0.2383
5	0.1904
2.5	0.1263
1.25	0.0761
0.625	0.0467
0.3	0.0238

(ii)



(iii) $k = 0.072\ (\pm 0.002)\ s^{-1}$

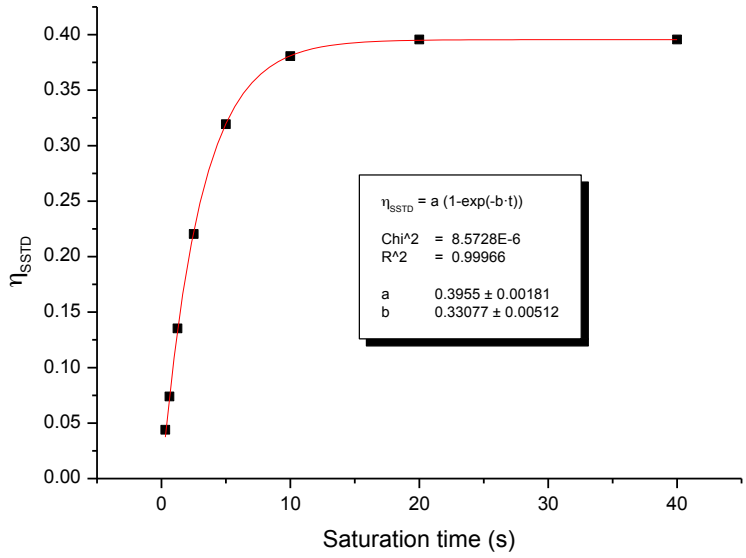
$T_{1A} = 4.71\ (\pm 0.01)$ s

4c.2) (i) Values of η_{SSTD} obtained at different saturation times for *N,N*-dimethylacetamide **1** at 283 K. (ii) Plot of η_{SSTD} versus saturation times with the exponential fit. (iii) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.3957
20	0.3957
10	0.3806
5	0.3193
2.5	0.2204
1.25	0.1353
0.625	0.0739
0.3	0.044

(ii)



(iii) $k = 0.131\ (\pm 0.003)\ s^{-1}$

$T_{1A} = 5.000\ (\pm 0.008)$ s

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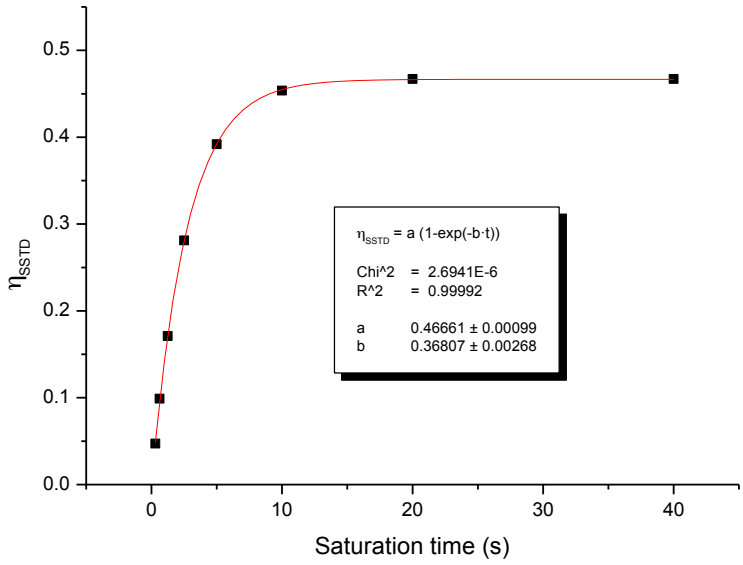
4c.3) (i) Values of η_{SSTD} obtained at different saturation times for *N,N*-dimethylacetamide **1** at 285.5 K. (ii) Plot of η_{SSTD} versus saturation times with the exponential fit. (iii) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.4671
20	0.4671
10	0.4537
5	0.3919
2.5	0.2812
1.25	0.171
0.625	0.099
0.3	0.0472

(ii)



(iii) $k = 0.172\ (\pm 0.002)\ s^{-1}$

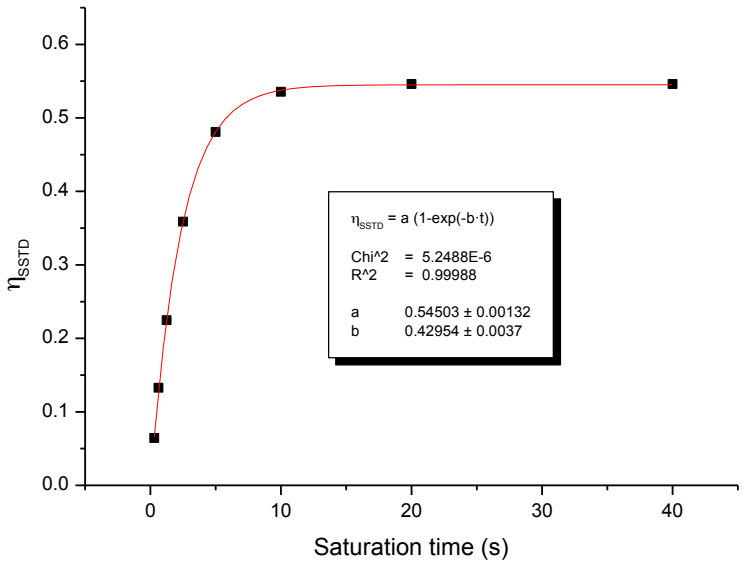
$T_{1A} = 5.094\ (\pm 0.005)$ s

4c.4) (i) Values of η_{SSTD} obtained at different saturation times for *N,N*-dimethylacetamide **1** at 288 K. (ii) Plot of η_{SSTD} versus saturation times with the exponential fit. (iii) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.5461
20	0.5461
10	0.5355
5	0.481
2.5	0.3589
1.25	0.2247
0.625	0.1327
0.3	0.0644

(ii)



(iii) $k = 0.234\ (\pm 0.003)\ s^{-1}$

$T_{1A} = 5.117\ (\pm 0.007)$ s

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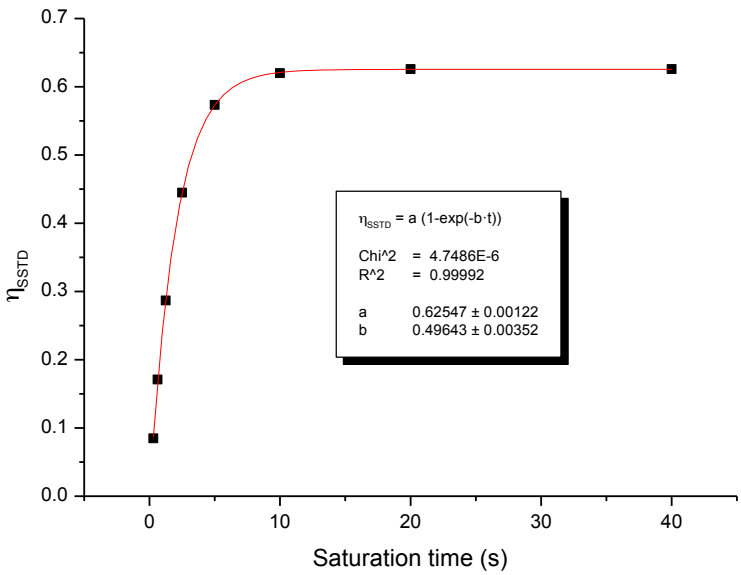
4c.5) (i) Values of η_{SSTD} obtained at different saturation times for *N,N*-dimethylacetamide **1** at 290.5 K. (ii) Plot of η_{SSTD} versus saturation times with the exponential fit. (iii) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.626
20	0.626
10	0.6199
5	0.5734
2.5	0.4449
1.25	0.2868
0.625	0.171
0.3	0.0847

(ii)



(iii) $k = 0.311\ (\pm 0.003)\ s^{-1}$

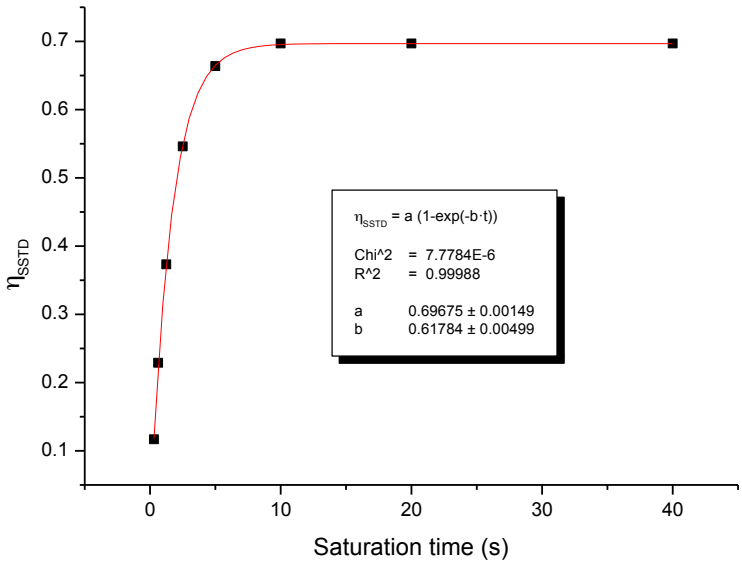
$T_{1A} = 5.378\ (\pm 0.007)$ s

4c.6) (i) Values of η_{SSTD} obtained at different saturation times for *N,N*-dimethylacetamide **1** at 293 K. (ii) Plot of η_{SSTD} versus saturation times with the exponential fit. (iii) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.6969
20	0.6969
10	0.6969
5	0.6638
2.5	0.5461
1.25	0.3732
0.625	0.2291
0.3	0.1169

(ii)



(iii) $k = 0.430\ (\pm 0.004)\ s^{-1}$

$T_{1A} = 5.35\ (\pm 0.01)$ s

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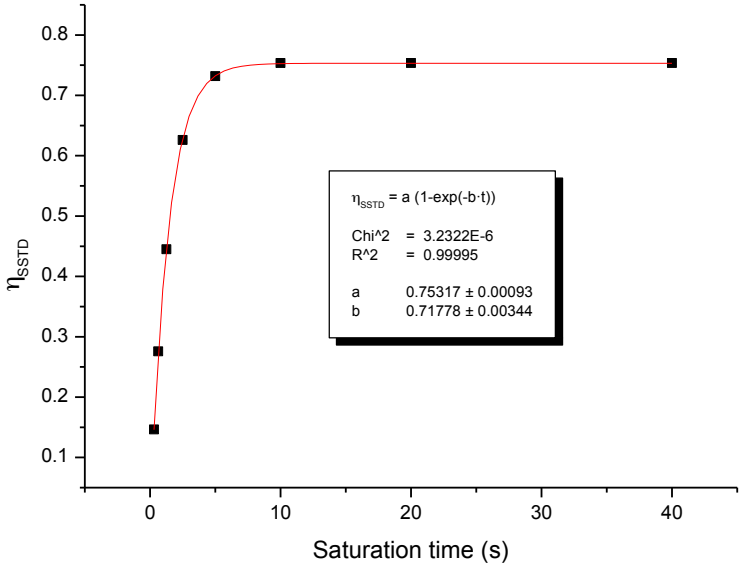
4c.7) (i) Values of η_{SSTD} obtained at different saturation times for *N,N*-dimethylacetamide **1** at 295.5 K. (ii) Plot of η_{SSTD} versus saturation times with the exponential fit. (iii) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.7535
20	0.7535
10	0.7535
5	0.7318
2.5	0.626
1.25	0.4449
0.625	0.2758
0.3	0.1463

(ii)



(iii) $k = 0.541\ (\pm 0.003)\ s^{-1}$

$T_{1A} = 5.656\ (\pm 0.006)\ s$

4d) Eyring plot for *N,N*-dimethylacetamide **1**. Slope and intercept values were used to calculate the enthalpy and entropy of activation, respectively.

T (K)	***k*** **(s^{-1})**	**Ln(*k*/T)**	**1/T**
278	0.072	-8.25871	0.0036
283	0.131	-7.678	0.00353
285.5	0.172	-7.4145	0.0035
288	0.234	-7.11539	0.00347
290.5	0.311	-6.83957	0.00344
293	0.43	-6.52414	0.00341
295.5	0.541	-6.303	0.00338

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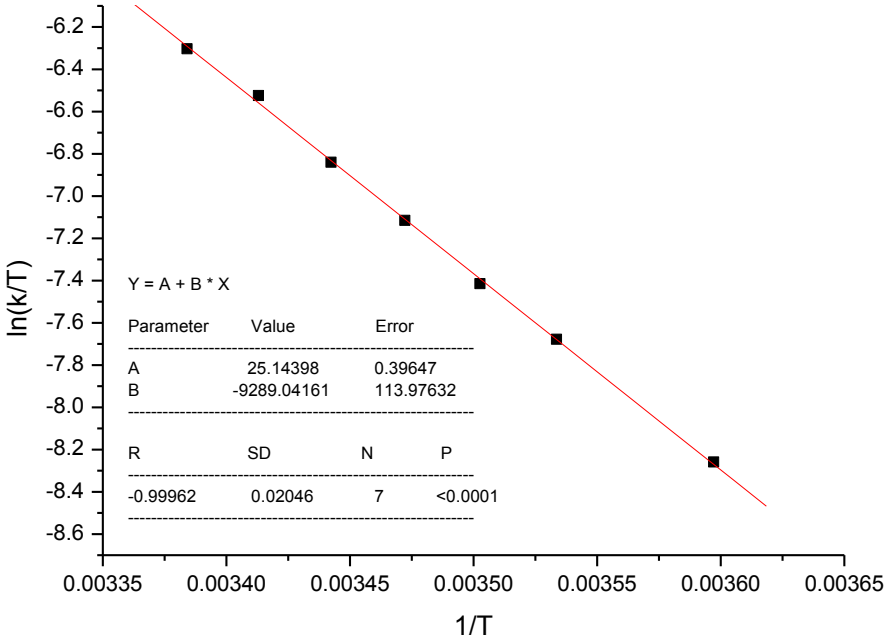

$$\ln\left(\frac{k}{T}\right) = \ln\left(\frac{k_B}{h}\right) - \frac{\Delta H^{\ddagger}}{RT} + \frac{\Delta S^{\ddagger}}{R}$$

$$\Delta S^{\ddagger} = 11.5 \pm 0.4 Jmol^{-1}K^{-1}$$

$$\Delta H^{\ddagger} = 77.23 \pm 0.11 KJmol^{-1}K^{-1}$$

$$E_{A(298)} = \Delta H^{\ddagger} + RT = 79.71 \pm 0.11 KJmol^{-1}K^{-1}$$

$$\Delta G^{\ddagger}_{(298)} = \Delta H^{\ddagger} - T\Delta S^{\ddagger} = 73.80 \pm 0.11 KJmol^{-1}K^{-1}$$

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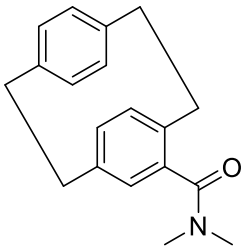
5) Analysis of chemical exchange in 4-*N*,*N*-dimethylamido[2.2]paracyclophane 2

5a) ^{1}H NMR chemical shift assignment: A sample of this compound was kindly donated by the research group of Dr C. Richards (UEA).[3]



^{1}H NMR (Toluene-d_8, 500MHz, 25^{o}C): δ (ppm) = 7.48 (d, *J* = 7.8 Hz, 1H, Ar), 6.40 (s, 2H, Ar), 6.31 – 6.37 (m, 2H, Ar), 6.26 (d, *J* = 7.7 Hz, 1H, Ar), 6.19 (d, *J* = 7.7 Hz, 1H, Ar), 3.39 – 3.31 (m, 1H, C*H*H), 3.25 – 3.17 (m, 1H, CH*H*), 2.76 – 2.98 (m, 3H, CH_2+C*H*H), 2.80 (s, 3H, CH_3^A), 2.75 – 2.58 (m, 3H, CH_2+CH*H*), 2.19 (s, 3H, CH_3^B).

5b) 1D NOE experiments

5b.1) 1D NOE experiment of 4-*N,N*-dimethylamido[2.2]paracyclophane **2** in Toluene-d_8 at room temperature. (a) Full spectra. (b) NOE spectra irradiating signal at 2.19 ppm. The positive signals observed in the spectra (b) and (c) are due to the chemical exchange process that takes place in this case at room temperature (NOE effect should appear as negative signals).

3 N. Dendele, F. Bisaro, A.-C. Gaumont, S. Perrio and C. J. Richards, *Chem. Commun.* 2012**,** ***48,*** 1991-1993.

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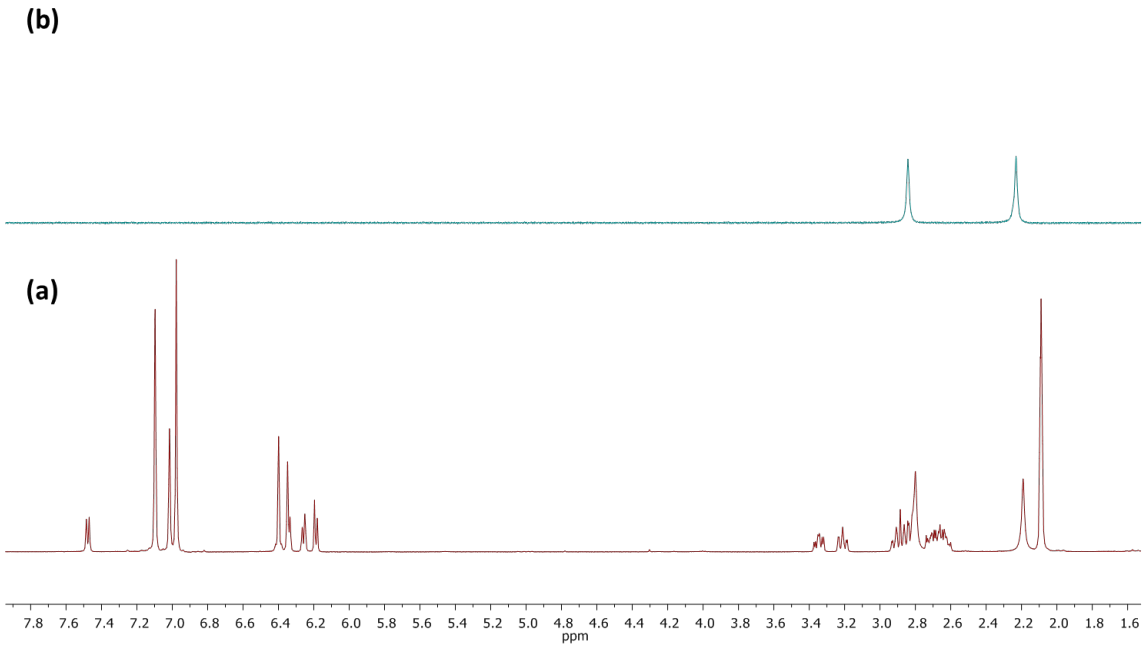
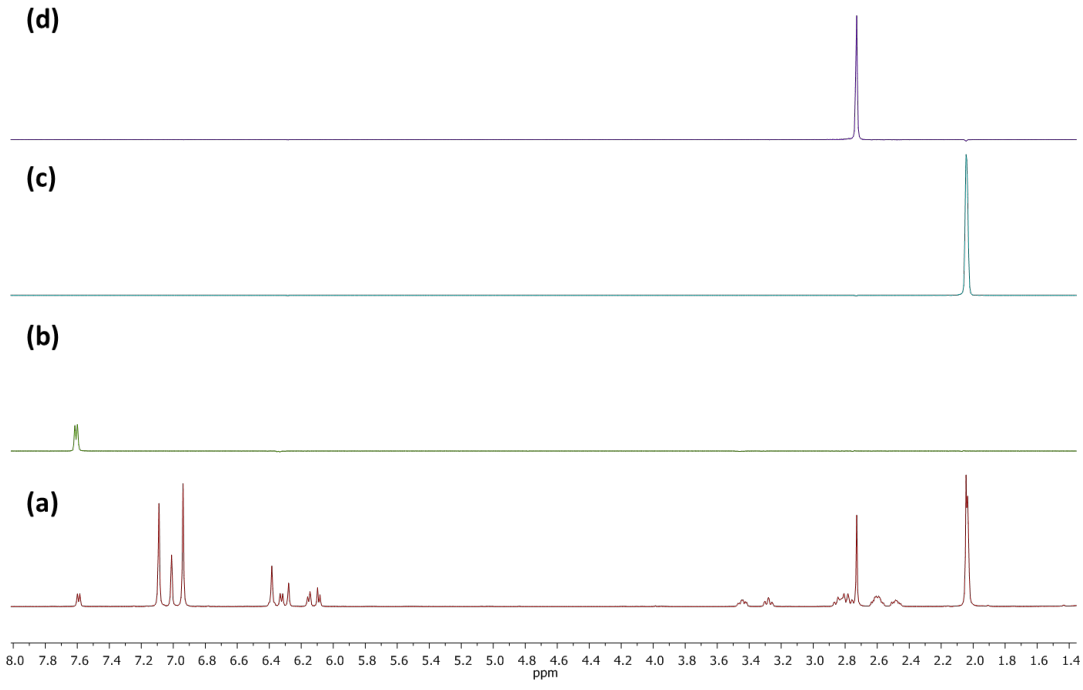


5b.1) NOE experiment of 4-*N,N*-dimethylamido[2.2]paracyclophane **2** in Toluene-d_8 at -40°C. (a) Full spectra. (b) NOE spectra irradiating signal at 7.63 ppm. (c) NOE spectra irradiating signal at 2.77 ppm. (d) NOE spectra irradiating signal at 2.08 ppm. NOE effects were not observed.



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5c) Experimental SSTD build-up curves

The η_{SSTD} factor was calculated from the magnetization transfer observed in the difference spectrum (b) (M_{0A}-M_A) with regard with the spectra before irradiation (a) (M_{0A}).

$$\eta_{SSTD} = \frac{M_{0A} - M_A}{M_{0A}}$$

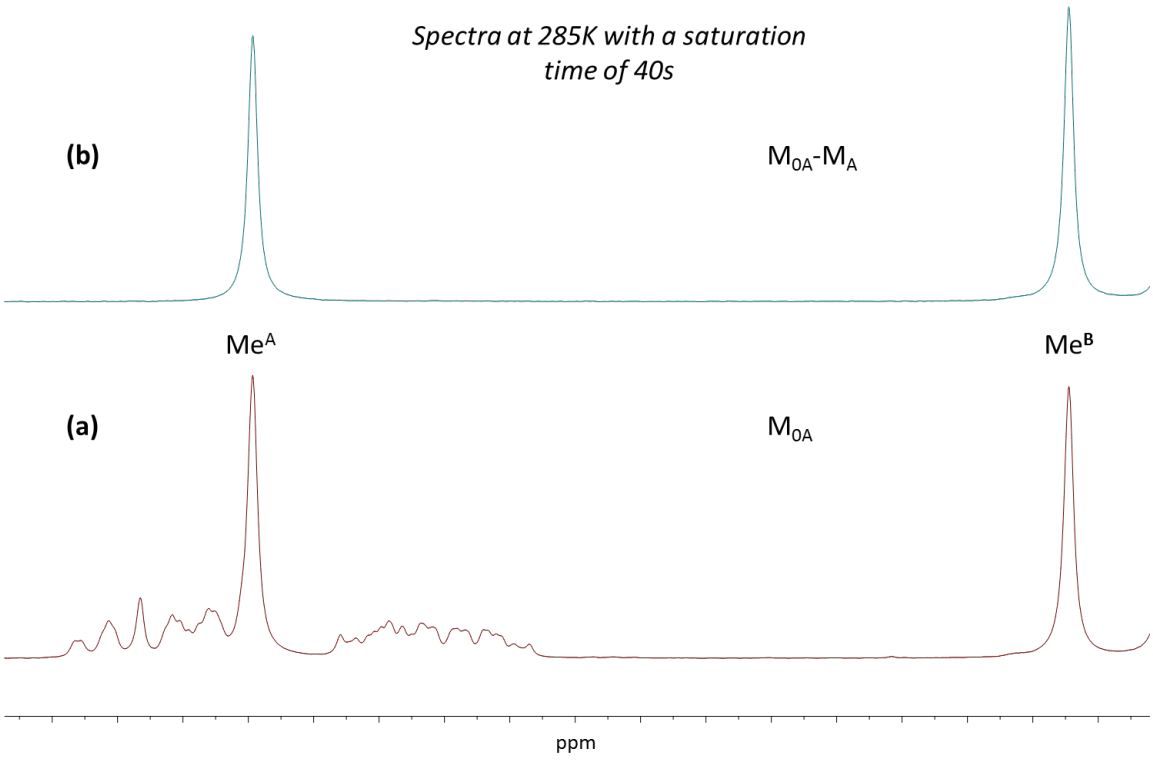


Figure 2S. Example of the ^{1}H NMR expansion of 4-*N,N*-dimethylamido[2.2]paracyclophane **2** in Toluene-d_8 before irradiation (a) and "difference spectrum" (b) at 285 K with a saturation time of 40 s saturating the signal at 2.17 ppm.

The values of η_{SSTD} were obtained for different saturation times at each temperature and their plot versus saturation time gave exponential curves in which a plateau was reached at long saturation times and which exponential fit allowed us to obtain the values of the rate constants of the process at the different temperatures.

$$\eta_{SSTD}(t) = \frac{k}{(1/T_{1A} + k)}(1 - \exp(-(1/T_{1A} + k) \cdot t))$$

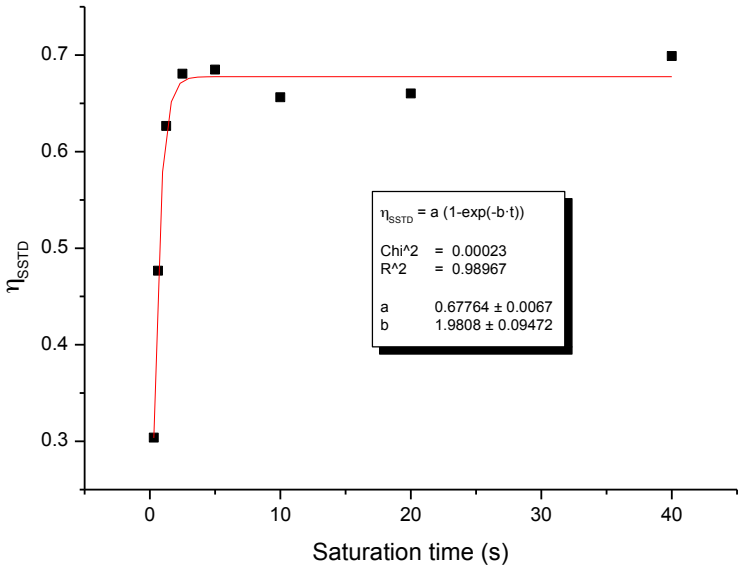
Supporting Information

5c.1) (i) Values of η_{SSTD} obtained at different saturation times for 4-*N,N*-dimethylamido[2.2]paracyclophane **2** at 273 K. (ii) Plot of η_{SSTD} versus saturation times with the exponential fit. (iii) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.69895
20	0.66023
10	0.65628
5	0.68496
2.5	0.68062
1.25	0.62658
0.625	0.4767
0.3	0.30389

(ii)



(iii) $k = 1.34\ (\pm 0.08)\ s^{-1}$

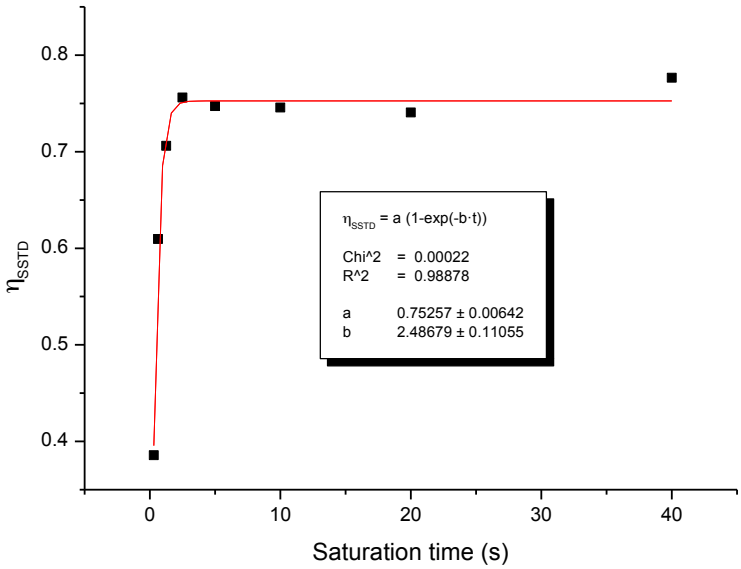
$T_{1A} = 1.6\ (\pm 0.2)$ s

5c.2) (i) Values of η_{SSTD} obtained at different saturation times for 4-*N,N*-dimethylamido[2.2]paracyclophane **2** at 276 K. (ii) Plot of η_{SSTD} versus saturation times with the exponential fit. (iii) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.77664
20	0.7406
10	0.74577
5	0.74716
2.5	0.75608
1.25	0.70615
0.625	0.60954
0.3	0.38565

(ii)



(iii) $k = 1.87\ (\pm 0.09)\ s^{-1}$

$T_{1A} = 1.6\ (\pm 0.2)$ s

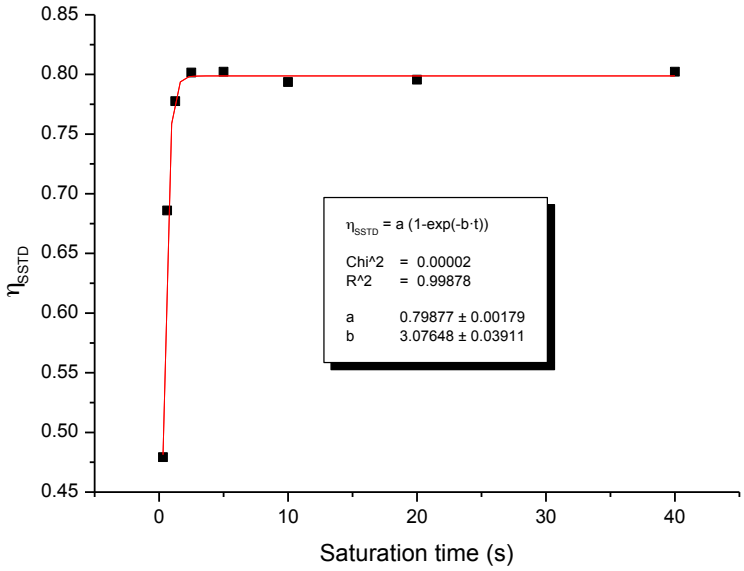
Supporting Information

5c.3) (i) Values of η_{SSTD} obtained at different saturation times for 4-*N,N*-dimethylamido[2.2]paracyclophane **2** at 279 K. (ii) Plot of η_{SSTD} versus saturation times with the exponential fit. (iii) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.8023
20	0.7956
10	0.7936
5	0.8023
2.5	0.8016
1.25	0.7776
0.625	0.686
0.3	0.4792

(ii)



(iii) $k = 2.46\ (\pm 0.04)\ s^{-1}$

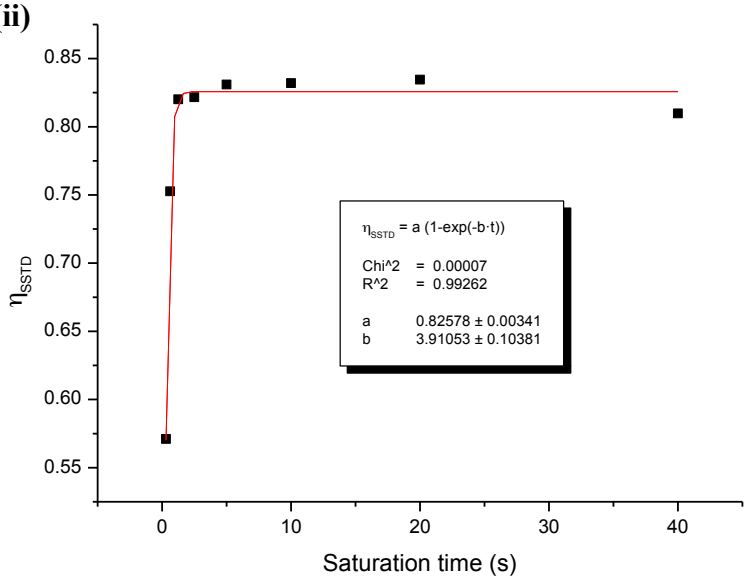
$T_{1A} = 1.62\ (\pm 0.08)$ s

5c.4) (i) Values of η_{SSTD} obtained at different saturation times for 4-*N,N*-dimethylamido[2.2]paracyclophane **2** at 282 K. (ii) Plot of η_{SSTD} versus saturation times with the exponential fit. (iii) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.80979
20	0.8346
10	0.83205
5	0.83097
2.5	0.82168
1.25	0.8201
0.625	0.75267
0.3	0.57108

(ii)



(c) $k = 3.2\ (\pm 0.2)\ s^{-1}$

$T_{1A} = 1.4\ (\pm 0.3)$ s

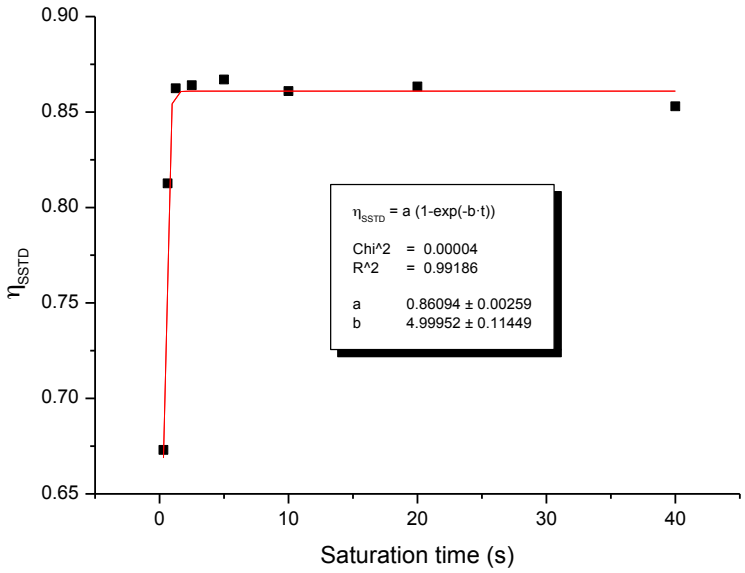
Supporting Information

5c.5) (i) Values of η_{SSTD} obtained at different saturation times for 4-*N,N*-dimethylamido[2.2]paracyclophane **2** at 285 K. (ii) Plot of η_{SSTD} versus saturation times with the exponential fit. (iii) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.853
20	0.8634
10	0.86096
5	0.867
2.5	0.864
1.25	0.8624
0.625	0.81259
0.3	0.673

(ii)



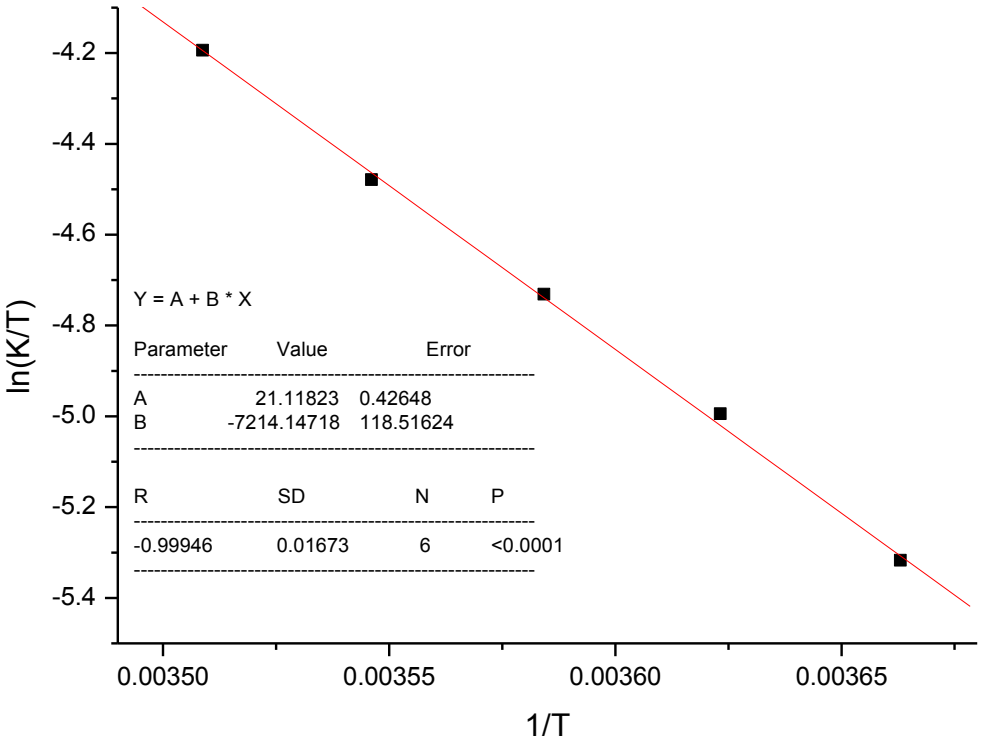
(iii) $k = 4.3\ (\pm 0.1)\ s^{-1}$

$T_1 = 1.4\ (\pm 0.2)$ s

5d) Eyring plot for 4-*N,N*-dimethylamido[2.2] **2**. Slope and intercept values were used to calculate the enthalpy and entropy of activation, respectively.

T (K)	***k*** **(s^{-1})**	**Ln(*k*/T)**	**1/T**
273	1.34 (±0.08)	-5.3168	0.00366
276	1.87 (±0.09)	-4.99446	0.00362
279	2.46 (±0.04)	-4.73105	0.00358
282	3.2 (±0.2)	-4.47876	0.00355
285	4.3 (±0.1)	-4.19387	0.00351

Supporting Information



$$\ln\left(\frac{k}{T}\right) = \ln\left(\frac{k_B}{h}\right) - \frac{\Delta H^{\ddagger}}{RT} + \frac{\Delta S^{\ddagger}}{R}$$

$$\Delta S^{\ddagger} = -22.0 \pm 0.4 Jmol^{-1}K^{-1}$$

$$\Delta H^{\ddagger} = 59.98 \pm 0.12 KJmol^{-1}K^{-1}$$

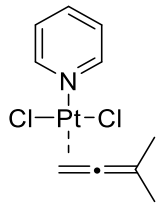
$$E_{A(298)} = \Delta H^{\ddagger} + RT = 62.46 \pm 0.12 KJmol^{-1}K^{-1}$$

$$\Delta G^{\ddagger}_{(298)} = \Delta H^{\ddagger} - T\Delta S^{\ddagger} = 66.54 \pm 0.12\ KJmol^{-1}K^{-1}$$

Supporting Information

6) Analysis of chemical exchange in $PtCl_2$(dimethylallene)(pyridine) 3

6a) ^{1}H NMR chemical shift assignment: This compound was prepared according to reported procedures.[4]



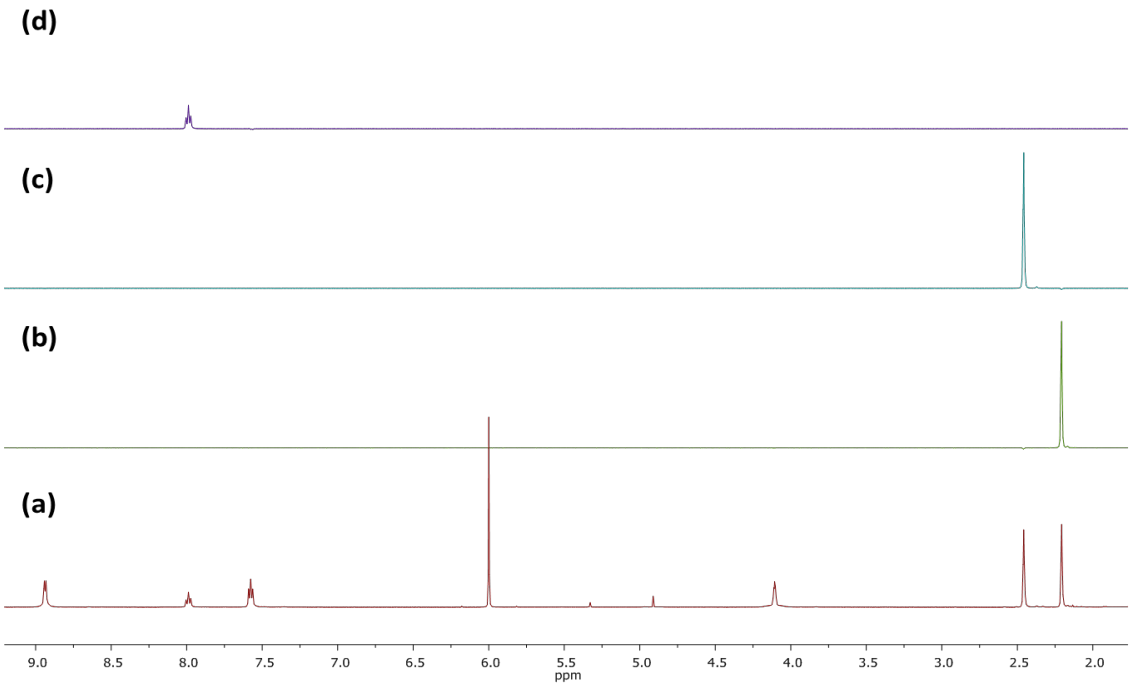
^{1}H NMR (500 MHz, $CDCl_2CDCl_2$, 25 ^{o}C) δ (ppm) = 8.94 (d, J = 5.2 Hz, 2H, py), 7.99 (t, J = 7.7 Hz, 1H, py), 7.58 (t, J = 6.9 Hz, 2H, py), 4.17 – 4.04 (m, 2H, =$=CH_2$), 2.46 (s, 3H, CH_3^B), 2.21 (s, 3H, CH_3^A); ^{195}Pt NMR (107.2 MHz, $CDCl_3$, 25 ^{o}C) δ (ppm) = 2254.24.

6b) 1D NOE experiments

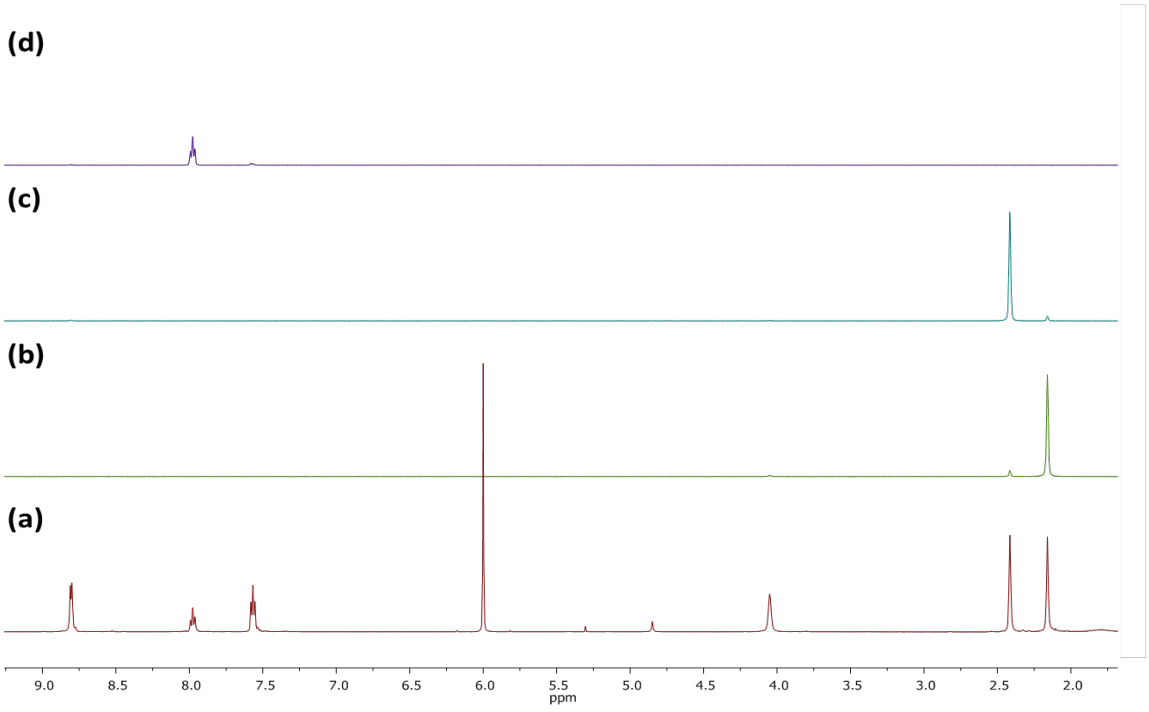
6b.1) 1D NOE spectra of $PtCl_2$(dimethylallene)(pyridine) **3** in $CDCl_2CDCl_2$ at room temperature. (a) Full spectra. (b) NOE spectra irradiating signal at 2.21 ppm. (c) NOE spectra irradiating signal at 2.46 ppm. (d) NOE spectra irradiating signal at 7.99 ppm. NOE effects were not observed.

4 K. Vrieze, H. C. Volger and A. P. Praat, *J. Organometal. Chem.,* 1970, ***21,*** 467-475.

Supporting Information



6b.2) 1D NOE experiment of $PtCl_2$(dimethylallene)(pyridine) **3** in $CDCl_2CDCl_2$ at -40°C. (a) Full spectra. (b) NOE spectra irradiating signal at 7.98 ppm. (c) NOE spectra irradiating signal at 2.42 ppm. (d) NOE spectra irradiating signal at 2.16 ppm. NOE effects were not observed.



Supporting Information

6c) Experimental SSTD build-up curves

The η_{SSTD} factor was calculated from the magnetization transfer observed in the difference spectrum (b) (M_{0A}-M_A) with regard with the spectra before irradiation (a) (M_{0A}).

$$\eta_{SSTD} = \frac{M_{0A} - M_A}{M_{0A}}$$

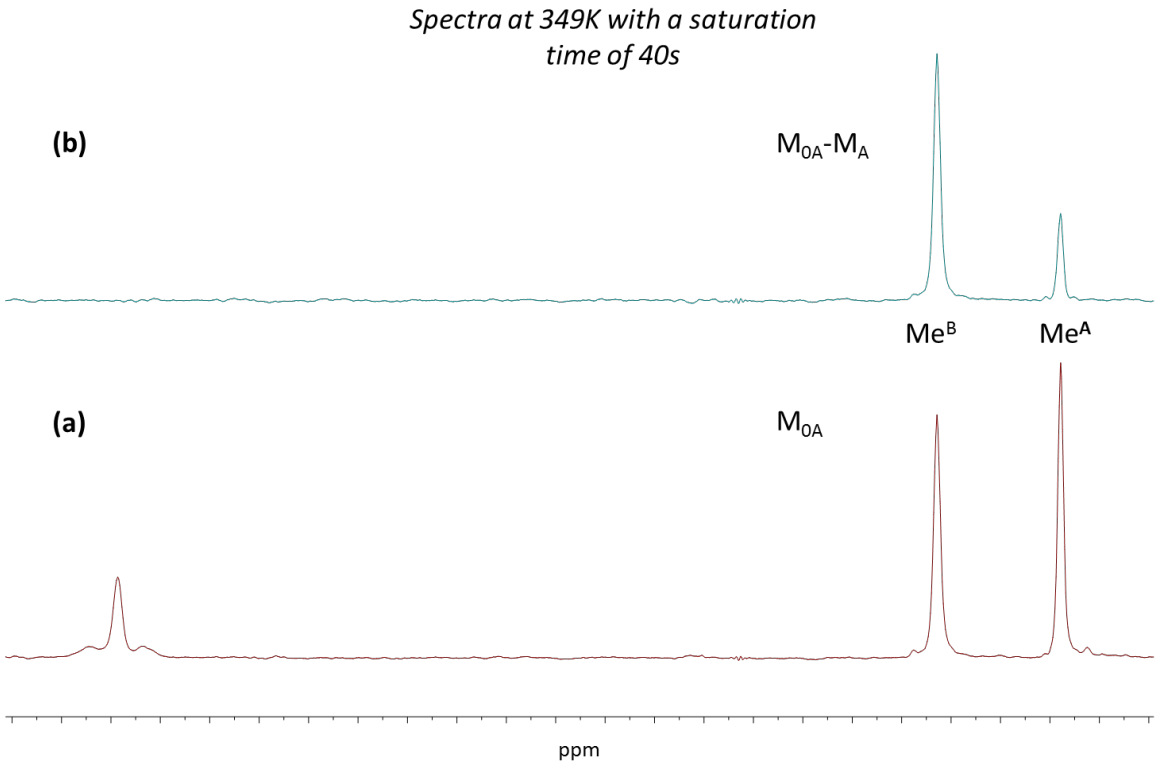


Figure 3S. Example of the ^{1}H NMR expansion of $PtCl_2$(dimethylallene)(pyridine) **3** in $CDCl_2CDCl_2$ before irradiation (a) and "difference spectrum" (b) at 349 K with a saturation time of 40 s saturating the signal at 2.48 ppm.

The values of η_{SSTD} were obtained for different saturation times at each temperature and their plot versus saturation time gave exponential curves in which a plateau was reached at long saturation times and which exponential fit allowed us to obtain the values of the rate constants of the process at the different temperatures.

$$\eta_{SSTD}(t) = \frac{k}{(1/T_{1A} + k)}(1 - \exp(-(1/T_{1A} + k) \cdot t))$$

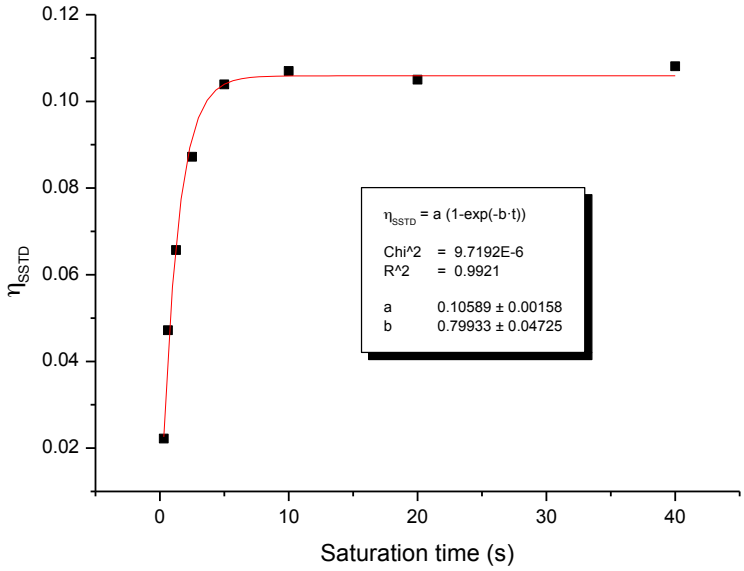
Supporting Information

6c.1) (i) Values of η_{SSTD} obtained at different saturation times for $PtCl_2$(dimethylallene)(pyridine) **3** at 337 K. (b) Plot of η_{SSTD} versus saturation times with the exponential fit. (c) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.1081
20	0.105
10	0.107
5	0.1039
2.5	0.0872
1.25	0.0657
0.625	0.0472
0.3	0.0222

(ii)



(iii) $k = 0.085\ (\pm 0.006)\ s^{-1}$

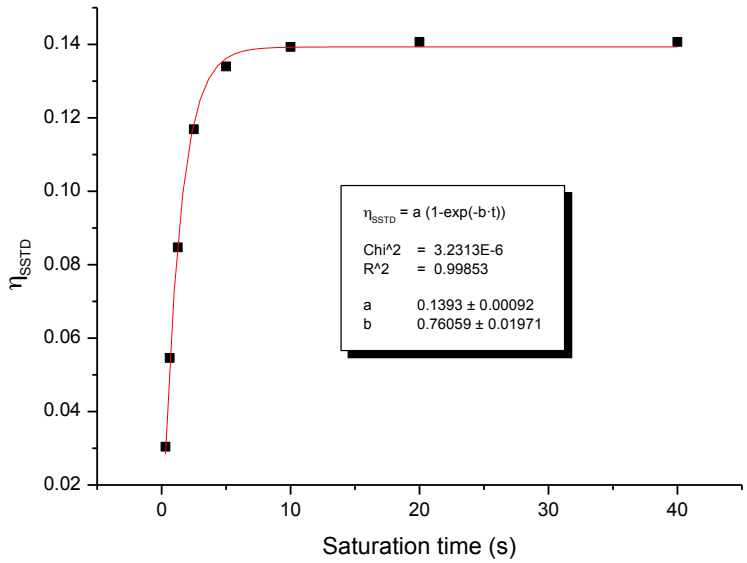
$T_{1A} = 1.40\ (\pm 0.06)$ s

6c.2) (i) Values of η_{SSTD} obtained at different saturation times for $PtCl_2$(dimethylallene)(pyridine) **3** at 340 K. (b) Plot of η_{SSTD} versus saturation times with the exponential fit. (c) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.1407
20	0.1407
10	0.1393
5	0.134
2.5	0.1169
1.25	0.0847
0.625	0.0546
0.3	0.0304

(ii)



(iii) $k = 0.106\ (\pm 0.003)\ s^{-1}$

$T_{1A} = 1.53\ (\pm 0.02)$ s

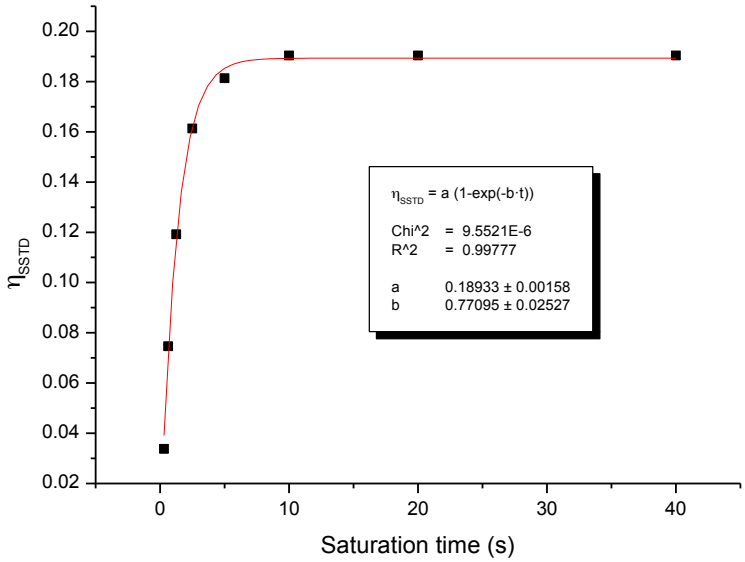
Supporting Information

6c.3) (i) Values of η_{SSTD} obtained at different saturation times for $PtCl_2$(dimethylallene)(pyridine) **3** at 343 K. (ii) Plot of η_{SSTD} versus saturation times with the exponential fit. (iii) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.1904
20	0.1904
10	0.1904
5	0.1813
2.5	0.1613
1.25	0.1192
0.625	0.0746
0.3	0.0338

(ii)



(iii) $k = 0.146\ (\pm 0.006)\ s^{-1}$

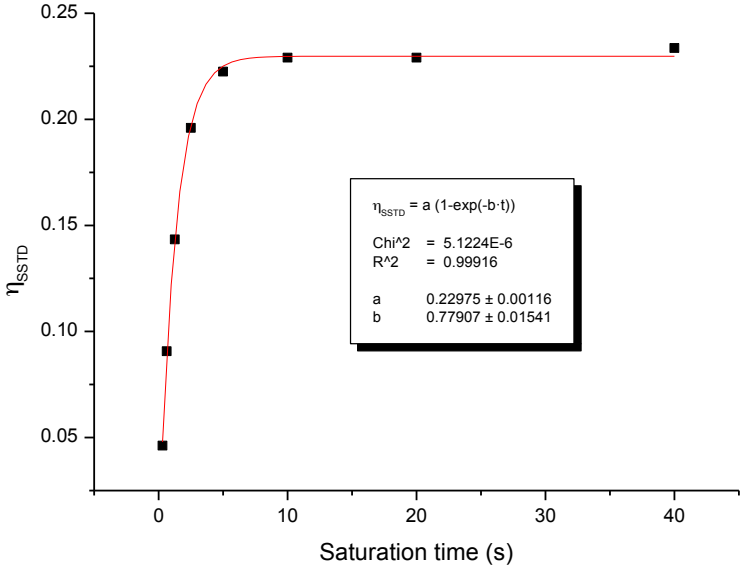
$T_{1A} = 1.60\ (\pm 0.04)$ s

6c.4) (i) Values of η_{SSTD} obtained at different saturation times for $PtCl_2$(dimethylallene)(pyridine) **3** at 346 K. (ii) Plot of η_{SSTD} versus saturation times with the exponential fit. (iii) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.2336
20	0.2291
10	0.2291
5	0.2225
2.5	0.196
1.25	0.1434
0.625	0.0907
0.3	0.0462

(ii)



(iii) $k = 0.179\ (\pm 0.004)\ s^{-1}$

$T_{1A} = 1.67\ (\pm 0.01)$ s

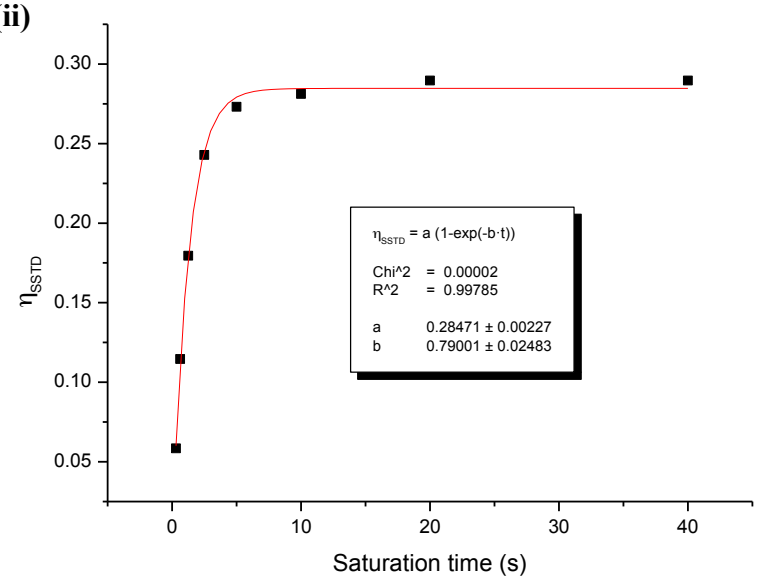
Supporting Information

6c.5) (i) Values of η_{SSTD} obtained at different saturation times for $PtCl_2$(dimethylallene)(pyridine) **3** at 349 K. (ii) Plot of η_{SSTD} versus saturation times with the exponential fit. (iii) Values of the rate constant (k) and relaxation times (T_{1A}).

(i)

t_{sat} (s)	η_{SSTD}
40	0.2896
20	0.2896
10	0.2812
5	0.2731
2.5	0.2429
1.25	0.1795
0.625	0.1146
0.3	0.0584

(ii)



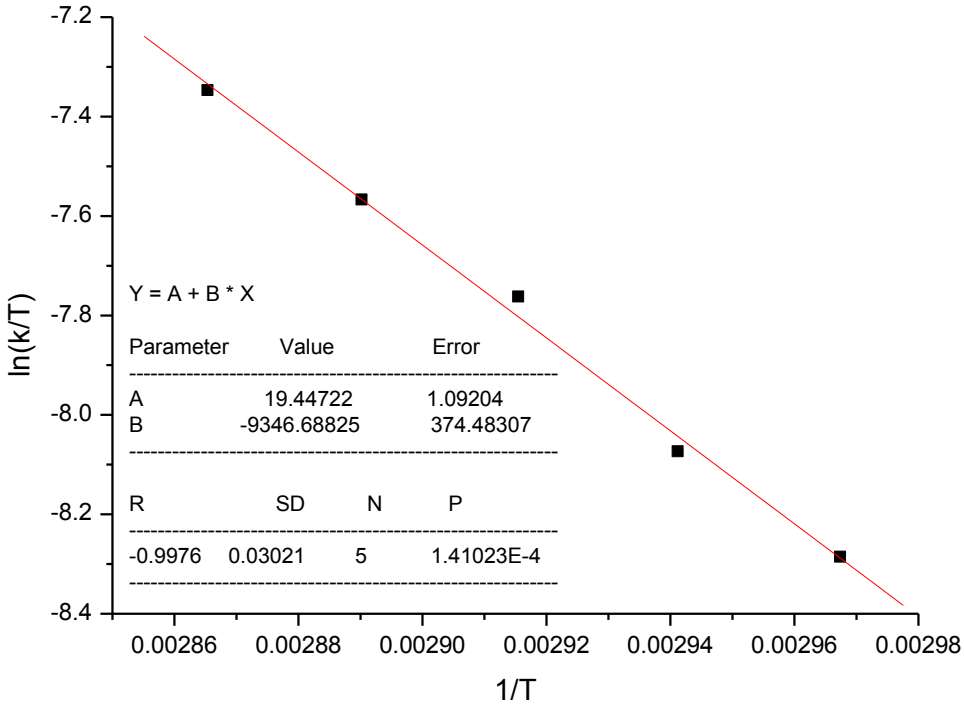
(iii) $k = 0.225\ (\pm 0.009)\ s^{-1}$

$T_{1A} = 1.77\ (\pm 0.03)$ s

6d) Eyring plot for $PtCl_2$(dimethylallene)(pyridine) **3**. Slope and intercept values were used to calculate the enthalpy and entropy of activation, respectively.

T (K)	***k*** **(s^{-1})**	**Ln(*k*/T)**	**1/T**
337	0.085	-8.28519	0.00297
340	0.106	-8.07326	0.00294
343	0.146	-7.76188	0.00292
346	0.179	-7.56681	0.00289
349	0.225	-7.34673	0.00287

Supporting Information



$$\ln\left(\frac{k}{T}\right) = \ln\left(\frac{k_B}{h}\right) - \frac{\Delta H^{\ddagger}}{RT} + \frac{\Delta S^{\ddagger}}{R}$$

$$\Delta S^{\ddagger} = -35.9 \pm 1 Jmol^{-1}K^{-1}$$

$$\Delta H^{\ddagger} = 77.7 \pm 0.4 KJmol^{-1}K^{-1}$$

$$E_{A(298)} = \Delta H^{\ddagger} + RT = 80.2 \pm 0.4\ KJmol^{-1}K^{-1}$$

$$\Delta G^{\ddagger}_{(298)} = \Delta H^{\ddagger} - T\Delta S^{\ddagger} = 88.4 \pm 0.4\ KJmol^{-1}K^{-1}$$