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Stopped-Flow NMR: Determining the Kinetics of [*rac*-(C_2H_4(1-indenyl)$_2$)ZrMe][MeB(C_6F_5)$_3$]-Catalyzed Polymerization of 1-Hexene by Direct Observation

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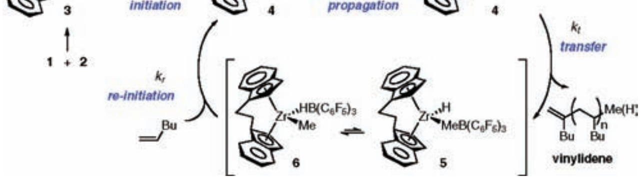
Abstract: Stopped-flow NMR measurements suitable for determination of reaction kinetics on time scales of 100 ms or longer have been achieved by adaptation of a commercial NMR flow probe with a high-efficiency mixer and drive system. Studies of metallocene-catalyzed alkene polymerization at room temperature have been complicated by high rates, imprecise knowledge of the distribution of different catalyst species with time, and the high sensitivity of the catalysts to low concentrations of impurities. Application of the stopped-flow NMR method to the study of the kinetics of 1-hexene polymerization in the presence of (EBI)ZrMe[MeB(C_6F_5)$_3$] demonstrates that NMR spectroscopy provides an efficient method for direct and simultaneous measurement of substrate consumption and catalyst speciation as a function of time. Kinetic modeling of the catalyst and substrate concentration time courses reveal efficient determination of initiation, propagation, and termination rate constants. As first suggested by Collins and co-workers (*Polyhedron* **2005**, *24*, 1234−1249), a kinetic model in which Zr−HB(C_6F_5)$_3$ forms rapidly upon β-hydride elimination but reacts relatively slowly with alkene to reinitiate chain growth is supported by these data.

NMR spectroscopy is arguably the most information-rich spectroscopic method for monitoring organic, biological, and organometallic reactions. However, common NMR probes are limited to monitoring slow reactions (time scale ≥60 s) because of the delay between mixing of the reactants and positioning of the sample in the spectrometer. Techniques such as rapid-injection[1] and stopped-flow[2] NMR spectroscopy, which introduce the reactants in or near the detection region, reduce this time delay, increasing the highest rates studied by several orders of magnitude. We report application of the stopped-flow NMR technique to a challenging but important problem: real-time monitoring of catalyst speciation and monomer consumption for a metallocene-catalyzed alkene polymerization at room temperature.

Highly active catalysts are sought for their practical value but present many mechanistic challenges. Foremost is the determination of catalyst speciation: how much of the catalyst actively produces polymer during the course of the reaction? Previously, we reported the application of rapid quenched-flow[3] (−10 to 50 °C) and low-temperature NMR[4] (−40 to −20 °C) methods to the study of 1-hexene polymerization by *rac*-(C_2H_4(1-indenyl)$_2$)ZrMe$_2$ (**1**) and B(C_6F_5)$_3$ (**2**). These studies led us to conclude that depending on the conditions, ca. 50−90% of the catalyst participates in producing polymer.

Scheme 1. Proposed Mechanism for the Polymerization of 1-Hexene in the Presence of *rac*-(C_2H_4(1-indenyl)$_2$)ZrMe$_2$ (**1**) and B(C_6F_5)$_3$ (**2**)



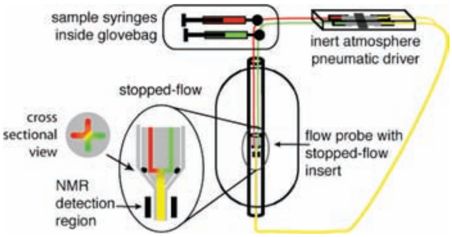


Figure 1. Schematic diagram of the stopped-flow NMR design.

A simplified mechanism for catalytic polymerization is shown in Scheme 1. Rapid activation of **1** by **2** affords **3**, which undergoes an initial alkene insertion (initiation) at a substantially lower rate than for subsequent insertions (propagation). Chain transfer can occur after a 1,2-insertion to afford a vinylidene or a 2,1-misinsertion to form a vinylene end group; here the vinylene pathway is not shown. Catalytic polymerization with metallocenes is fast and exothermic, but the catalysts are sensitive to air and moisture. The challenge is to simultaneously monitor the polymerization and catalyst speciation under approximately authentic bulk polymerization conditions while maintaining the temperature and preventing loss of catalyst to reactions with impurities. As we will demonstrate, stopped-flow NMR experiments enable simultaneous, direct observation of all relevant polymerization steps at room temperature.

The stopped-flow NMR apparatus comprises a custom-made mixer assembly, a pneumatic drive system, and a commercial flow NMR probe modified by replacement of the flow cell (Figure 1).[5] In each kinetic "shot", two reactant streams (200 μL each) flow through a four-jet mixer (cross-sectional view, Figure 1) into the NMR active coil region. At a flow rate of 10 mL/s, complete mixing occurs in less than 5 ms and the solution reaches the end of the detection region in less than 15 ms. The mechanical stop triggers NMR data acquisition, and under optimal conditions, a good spectrum can be obtained 20 ms after the stop, giving a minimum dead time of ca. 35 ms. Because this is a flow system, it is possible to make many kinetic runs in a day, in contrast with rapid-injection NMR studies.

The polymerization of 1-hexene in toluene-d_8 at room temperature (ca. 24 °C) was repeated using different concentrations of 1-hexene (100−250 mM), **1** (4.4−11.1 mM), and **2** (4.9−12.3 mM).

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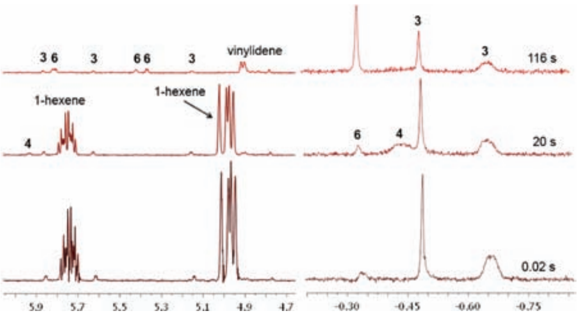

Figure 2. Stopped-flow NMR spectra acquired at 0.02, 20, and 116 s following the mechanical stop during the polymerization of 1-hexene (201 mM) using **1** (11.1 mM) and **2** (12.3 mM) in toluene-d_8 at ambient temperature (ca. 24 °C).

In a typical experiment,[5] separate solutions of the catalyst precursors [**1**, **2**, and 1,4-bis(trimethylsilyl)benzene as the internal standard] and the monomer were placed simultaneously into two reactant lines. Each stopped-flow shot was followed by NMR acquisition of a series of single-scan spectra using a 30° pulses and 4 s interpulse delays. By repeating the experiment with different post-stop delays, the reaction time course was sampled evenly throughout complete monomer consumption. Representative stopped-flow NMR spectra are shown in Figure 2.

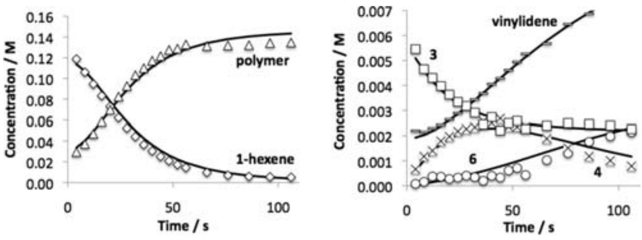

Figure 3. Plots of concentration vs time for the polymerization of 1-hexene (161 mM) using **1** (8.84 mM) and **2** (9.86 mM) in toluene-d_8 at ca. 24 °C. The solid lines were obtained from the kinetic model using rate constant values that best fit all shots.

Stopped-flow NMR analysis provides unusually detailed kinetic information. One can quantitatively monitor polymerization of monomer and the transformation $\mathbf{3} \rightarrow \mathbf{4}$, which previously had been detected only at low temperatures (e.g., −40 °C).[4a] Most notably, the spectra reveal a slow accumulation of hydridoborate **6** prior to complete consumption of 1-hexene. This result and kinetic modeling (see below) indicate that **6** reacts with 1-hexene much more slowly than **4** ($k_r < k_p$); qualitatively similar results were reported by Collins and co-workers.[6]

Concentrations calculated from spectral integrations referenced to the internal standard were fitted to the kinetic model using COPASI[7] (Figure 3) to determine the rates of initiation, propagation, chain transfer, and reinitiation (Table 1).

In comparison with results obtained using the rapid quenched-flow (RQF) method (see the "RQF (25 °C)" entry in Table 1), direct observation using the stopped-flow NMR technique afforded similar rates of initiation but 2-fold higher rates of propagation and chain transfer. Perhaps coincidently, kinetic modeling studies carried out by Abu-Omar and co-workers (see the "0 °C" entries in Table 1) on RQF results led them to propose that an unknown polymerization event renders a significant portion (43%) of the catalyst inactive and to predict similar rates of initiation but higher rates of propagation and chain termination.[8] The origin of the discrepancy is unclear, but one should bear in mind that the apparent values of catalytic rate constants critically rely on knowing the concentration of active catalyst. The stopped-flow NMR technique uniquely allows direct, quantitative observation of the monomer, polymer, and catalyst species present throughout the reaction. The NMR spectra did not reveal evidence of any Zr species other than **3**, **4**, and **6** during the reaction, and the total Zr concentration remained constant. However, it is possible that new Zr species have resonances coincident with those of the identified species.

Table 1. Rate Constants for Initiation (k_i), Propagation (k_p), Chain Transfer (k_t), and Reinitiation (k_r) of 1-Hexene Polymerization Catalyzed by **3** in Toluene-d_8 at Ambient Temperature (ca. 24 °C) Fitted Using COPASI.[7]

entry	k_i/M^{-1} s^{-1}	k_p/M^{-1} s^{-1}	k_t/s^{-1}	k_r/M^{-1} s^{-1}
1[a]	0.224(2)	13.2(1)	0.0317(4)	2.70(7)
2[a]	0.218(2)	18.6(2)	0.0345(4)	4.12(6)
3[a]	0.255(1)	18.3(1)	0.0303(3)	2.56(3)
4[a]	0.222(3)	17.8(2)	0.0264(5)	1.62(5)
5[a]	0.314(3)	21.8(2)	0.0369(6)	2.33(7)
6[a]	0.215(2)	15.2(1)	0.0339(4)	1.80(3)
global fit	0.2353(6)	16.83(6)	0.0323(2)	2.06(2)
RQF (25 °C)[b]	0.25	8.1	0.0132	$>10k_p$[c]
RQF (0 °C)[b]	0.033	2.2	0.00066	$>10k_p$[c]
MP (0 °C)[d]	0.031	3.7	0.0024	10^3k_p[c]

[a] Experiments were carried out using different concentrations of 1-hexene (101−250 mM), **1** (4.4−11.1 mM), and **2** (4.9−12.3 mM).[5] Temperature changes during the reaction are not known; however, model studies suggested that the maximum temperature rise under the above reaction conditions was ≤3 °C.[5] [b] Results from rapid quenched-flow experiments[3b] using 1-hexene (500−1500 mM), **1** (0.83 mM), and **2** (0.83 mM). [c] Reinitiation was previously assumed to occur very rapidly and assigned a value >10-fold larger than k_p. [d] Rate constants predicted from kinetic modeling as reported by Abu-Omar and co-workers.[8]

In summary, a commercial flow probe has been modified for stopped-flow NMR analysis and applied to the kinetic study of 1-hexene polymerization (**3**, toluene-d_8, ca. 24 °C). The technique enables incisive, efficient, and time-resolved quantitation of reactants, products, and all observable catalytic species under ambient conditions. These data are sufficiently complete to determine all of the rate constants from a single set of stopped-flow runs. Such analyses reveal that hydridoborate **6** does not undergo immediate reinitiation in the presence of 1-hexene, as we previously assumed.

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Supporting Information Available: NMR probe modification, assembly of the fluid drive system, experimental details, and analysis of results. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) (a) McGarrity, J. F.; Prodolliet, J.; Smyth, T. *Org. Magn. Reson.* **1981**, *17*, 59–65. (b) Ogle, C. A.; Johnson, H. C.; Wang, X. L.; Strickler, F. H.; Bucca, D.; Gordon, B. *Macromolecules* **1995**, *28*, 5184–5194. (c) Perrin, C. L.; Rivero, I. A. *Rev. Sci. Instrum.* **1999**, *70*, 2173–2174. (d) Jones, A. C.; Sanders, A. W.; Bevan, M. J.; Reich, H. J. *J. Am. Chem. Soc.* **2007**, *129*, 3492–3493.

(2) (a) Kühne, R. O.; Schaffhauser, T.; Wokaun, A.; Ernst, R. R. *J. Magn. Reson.* **1979**, *35*, 39–67. (b) Gomez-Hens, A.; Perez-Bendito, D. *Anal. Chim. Acta* **1991**, *242*, 147–177. (c) Green, D. B.; Lane, J.; Wing, R. M. *Appl. Spectrosc.* **1987**, *41*, 847–851.

(3) (a) Liu, Z.; Somsook, E.; Landis, C. R. *J. Am. Chem. Soc.* **2001**, *123*, 2915–2916. (b) Liu, Z.; Somsook, E.; White, C. B.; Rosaaen, K. A.; Landis, C. R. *J. Am. Chem. Soc.* **2001**, *123*, 11193–11207.

(4) (a) Landis, C. R.; Rosaaen, K. A.; Sillars, D. R. *J. Am. Chem. Soc.* **2003**, *125*, 1710–1711. (b) Sillars, D. R.; Landis, C. R. *J. Am. Chem. Soc.* **2003**, *125*, 9894–9895. (c) Landis, C. R.; Sillars, D. R.; Batterton, J. M. *J. Am. Chem. Soc.* **2004**, *126*, 8890–8891.

(5) Full details of the NMR probe modifications, stopped-flow operation, and experimental procedures are provided in the Supporting Information.

(6) Al-Humydi, A.; Garrison, J. C.; Mohammed, M.; Youngs, W. J.; Collins, S. *Polyhedron* **2005**, *24*, 1234–1249.

(7) COPASI (Complex Pathway Simulator): Hoops, S.; Sahle, S.; Gauges, R.; Lee, C.; Pahle, J.; Simus, N.; Singhal, M.; Xu, L.; Mendes, P.; Kummer, U. *Bioinformatics* **2006**, *22*, 3067–3074.

(8) Novstrup, K. A.; Travia, N. E.; Medvedev, G. A.; Stanciu, C.; Switzer, J. M.; Thomson, K. T.; Delgass, W. N.; Abu-Omar, M. M.; Caruthers, J. M. *J. Am. Chem. Soc.* **2010**, *132*, 558–566.

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