Electronic Supporting Information

The Precise Molecular Location of Gadolinium Atoms has a Significant Influence on the Efficacy of Nanoparticulate MRI Positive Contrast Agents

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Part 1: Polymer characterizations

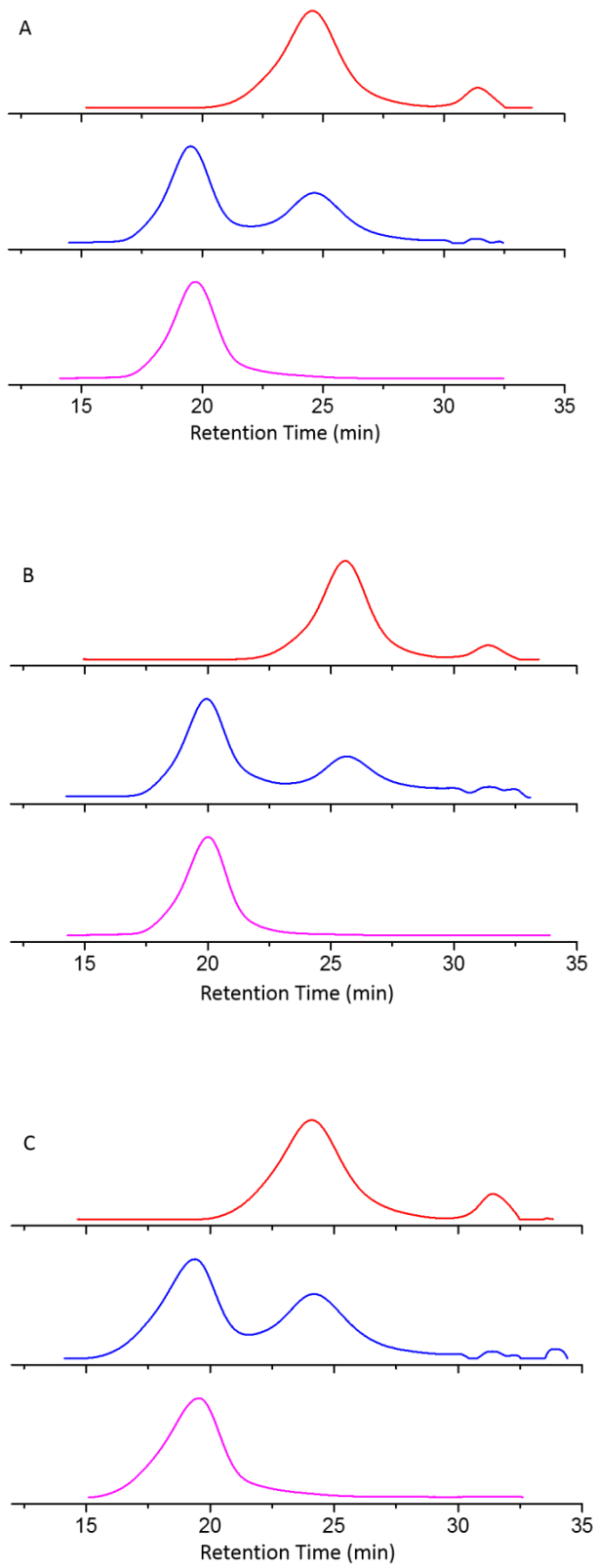


Figure S1. SEC traces (—star arm linear polymer; —crude star polymer; —star polymer after purification) of different star polymers used in this study. A) CCS-A; B) CCS-B and C) CCS-C.

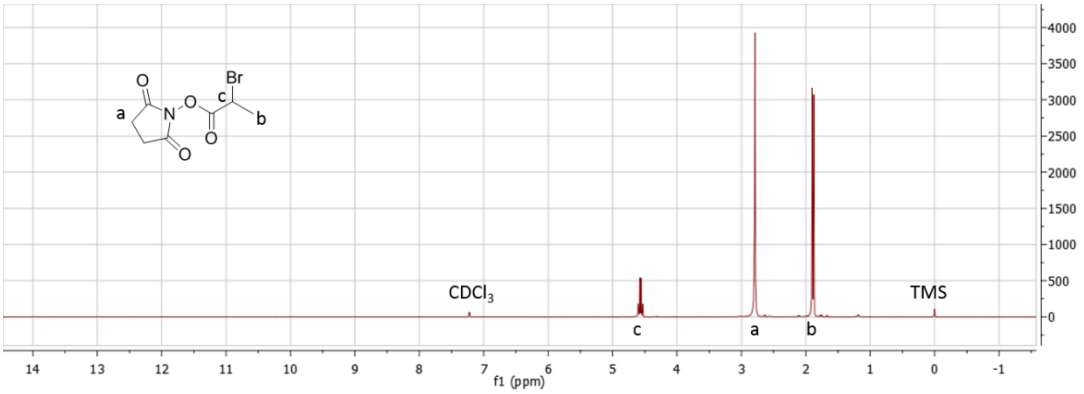


Figure S2. ^{1}H NMR spectrum of N-succinimidyl bromoacetate recorded in $CDCl_3$

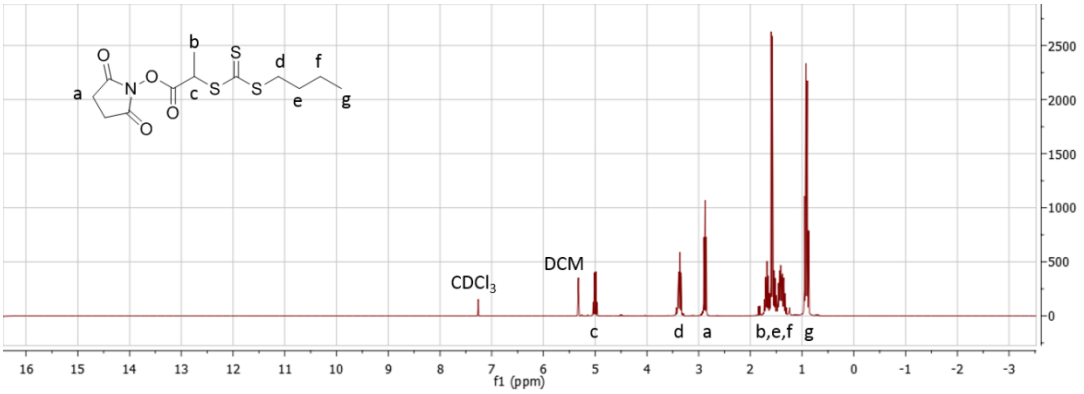


Figure S3. ^{1}H NMR spectrum of 2,5-dioxopyrrolidin-1-yl 2-(((butylthio) carbonothioyl) thio) propanoate (DPBP) recorded in $CDCl_3$

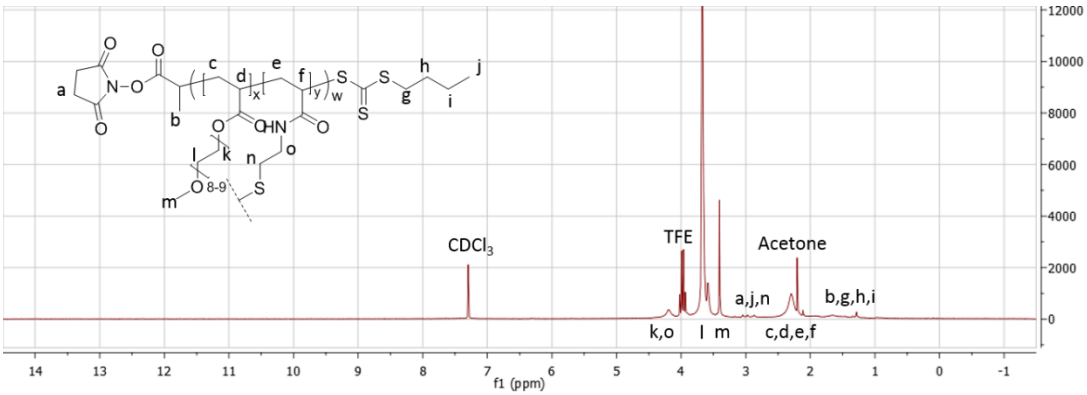


Figure S4. ^{1}H NMR spectrum of CCS-A recorded in $CDCl_3$

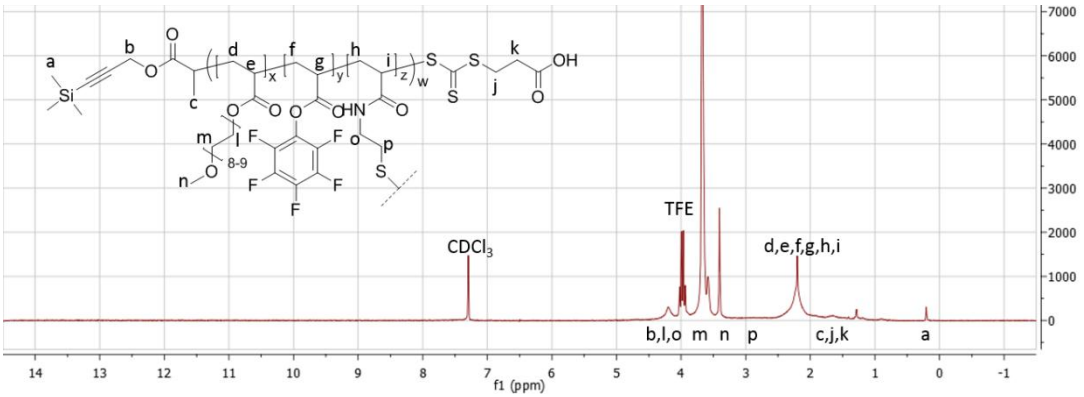


Figure S5. ^{1}H NMR spectrum of CCS-B recorded in $CDCl_3$

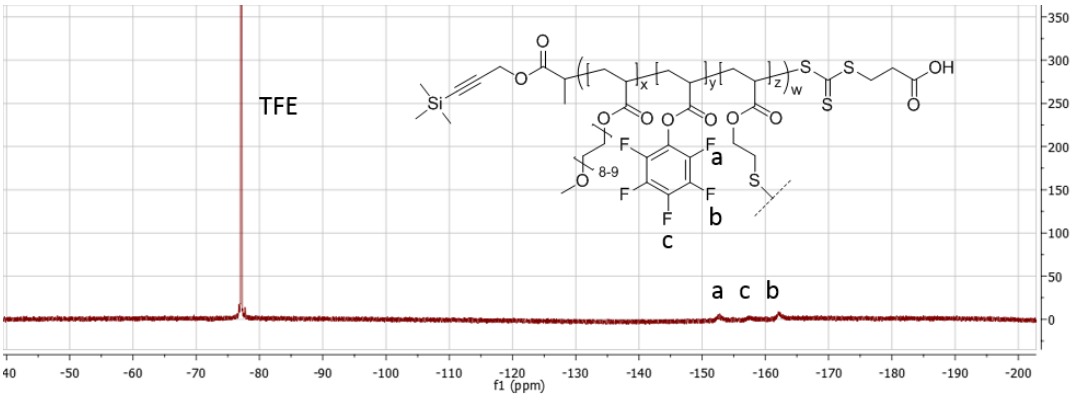


Figure S6. ^{19}F NMR spectrum of CCS-B recorded in $CDCl_3$

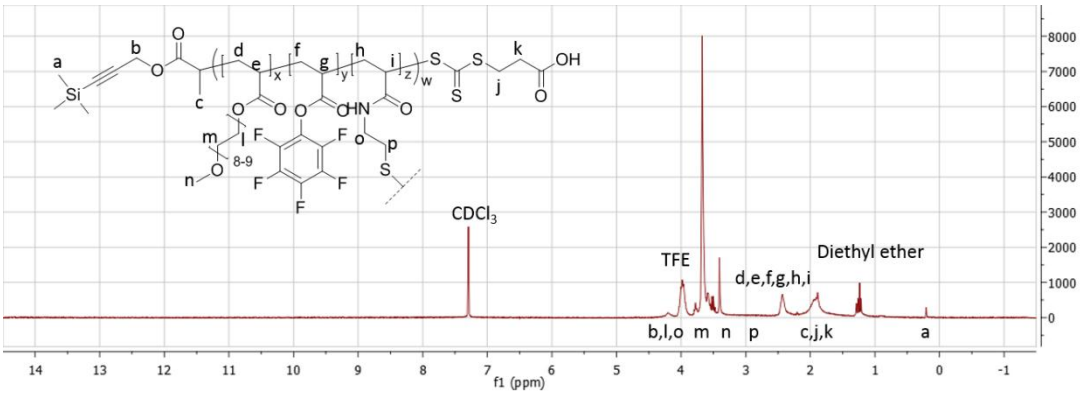


Figure S7. ^{1}H NMR spectrum of CCS-C recorded in $CDCl_3$

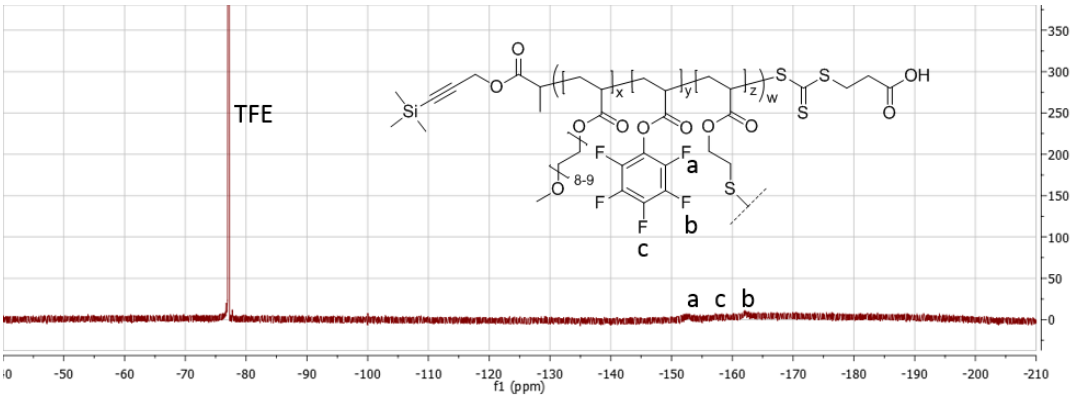


Figure S8. ^{19}F NMR spectrum of CCS-C recorded in $CDCl_3$

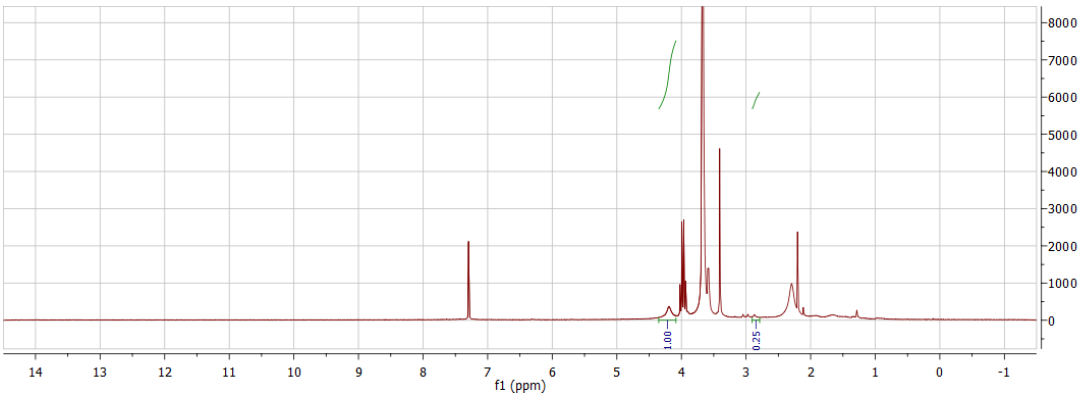


Figure S9. ^{1}H NMR spectrum of CCS-A recorded in $CDCl_3$

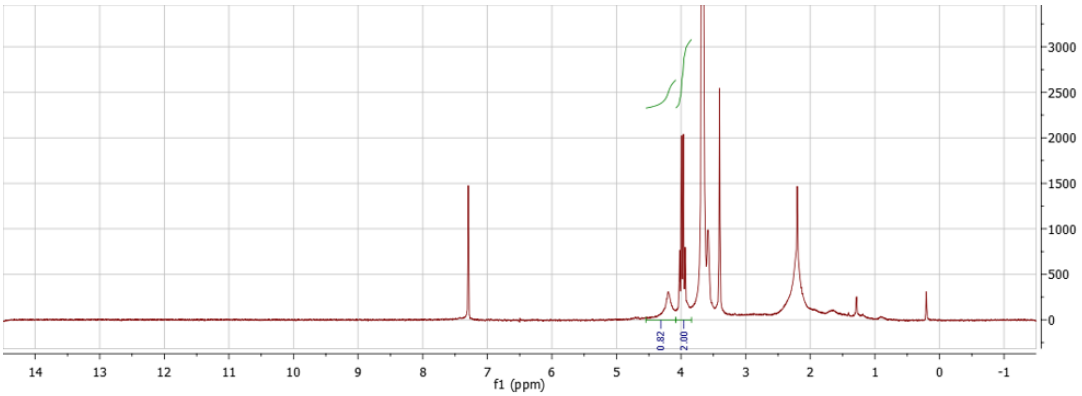


Figure S10. ^{1}H NMR spectrum of CCS-B recorded in $CDCl_3$

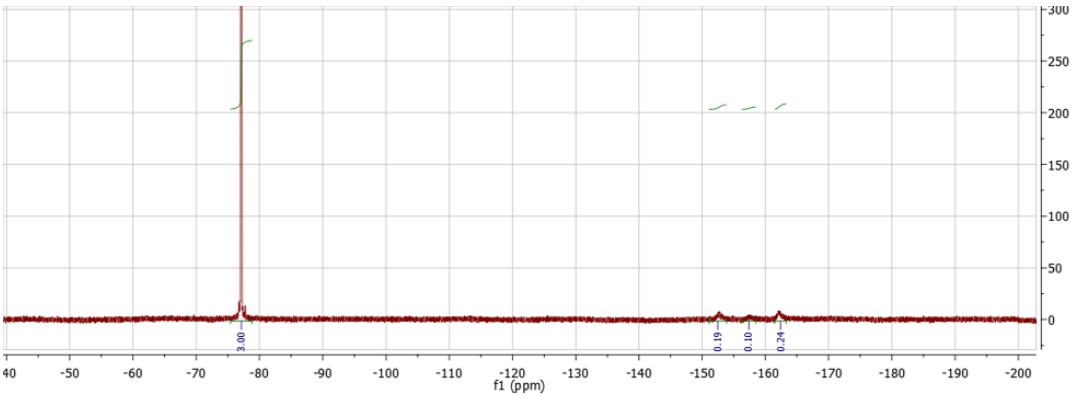


Figure S11. ^{19}F NMR spectrum of CCS-B recorded in $CDCl_3$

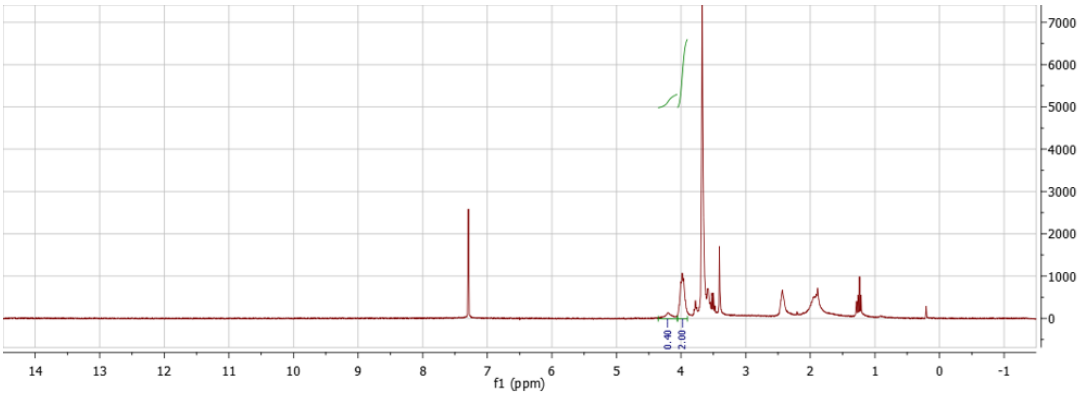


Figure S12. ^{1}H NMR spectrum of CCS-C recorded in $CDCl_3$

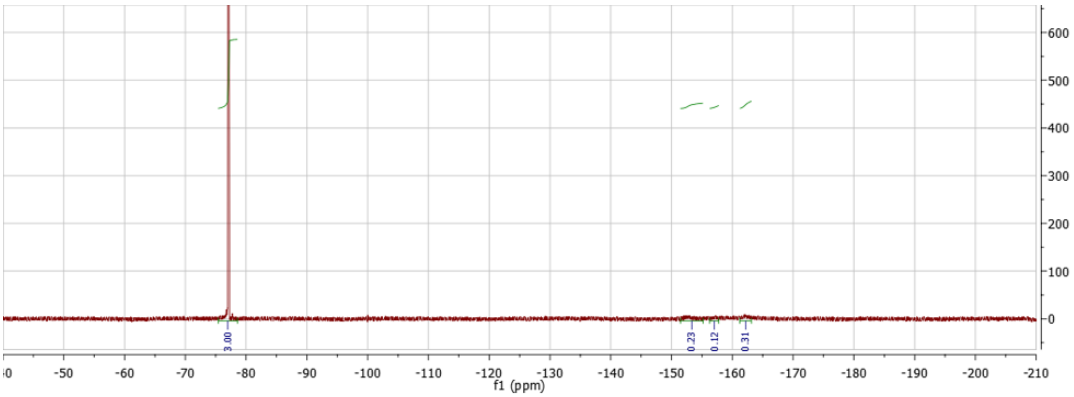


Figure S13. ^{19}F NMR spectrum of CCS-C recorded in $CDCl_3$

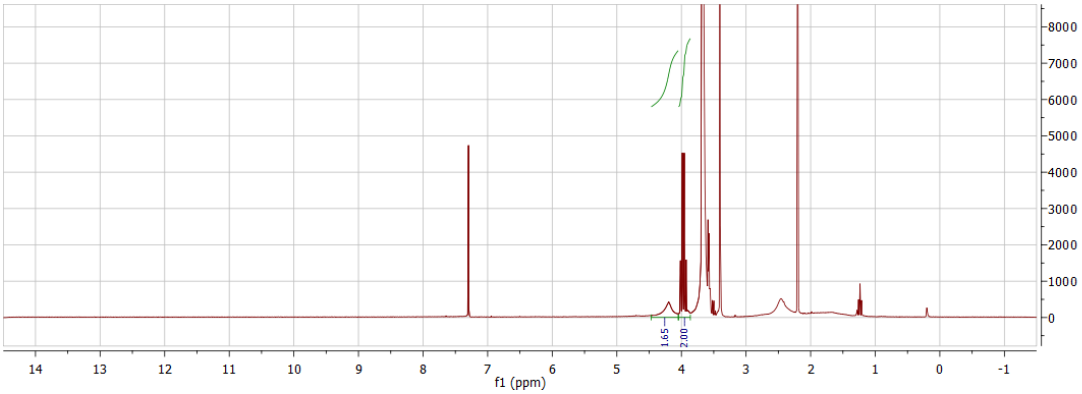


Figure S14. ^{1}H NMR spectrum of HBP-D recorded in $CDCl_3$

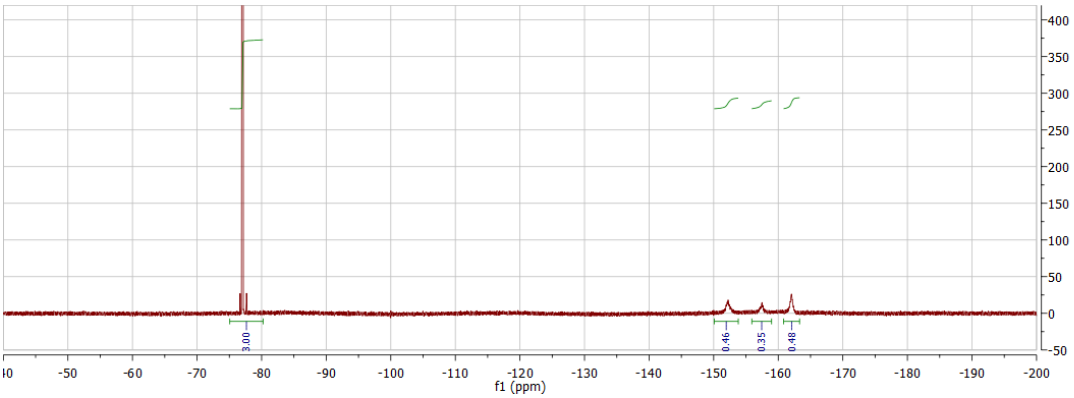


Figure S15. ^{19}F NMR spectrum of HBP-D recorded in $CDCl_3$

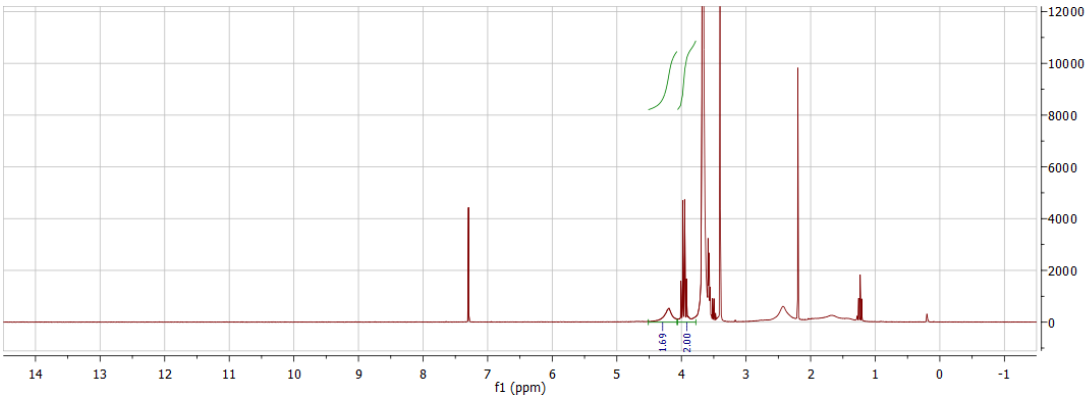


Figure S16. ^{1}H NMR spectrum of HBP-E recorded in $CDCl_3$

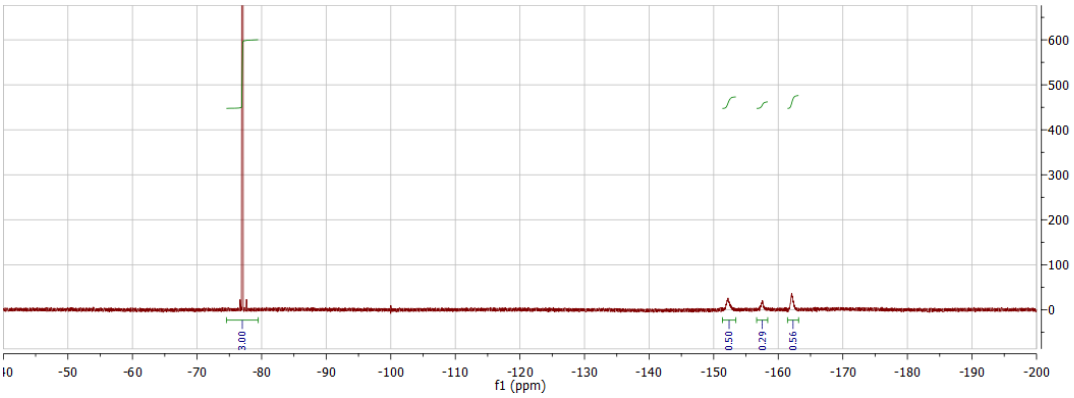


Figure S17. ^{19}F NMR spectrum of HBP-E recorded in $CDCl_3$

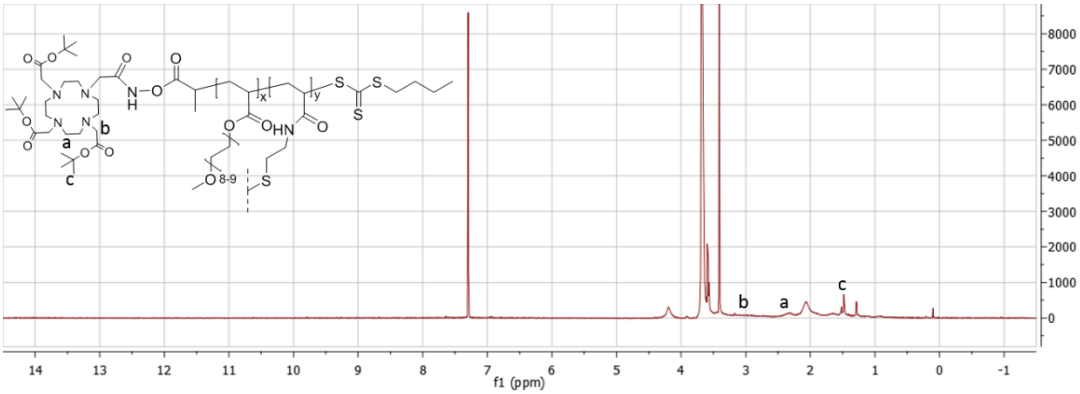


Figure S18. ^{1}H NMR spectrum of CCS-A-DO3A recorded in $CDCl_3$

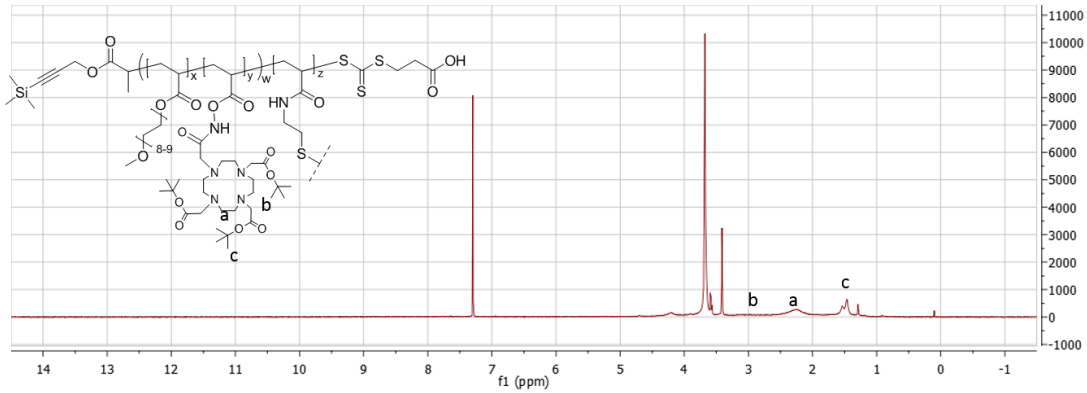


Figure S19. ^{1}H NMR spectrum of CCS-B-DO3A recorded in $CDCl_3$

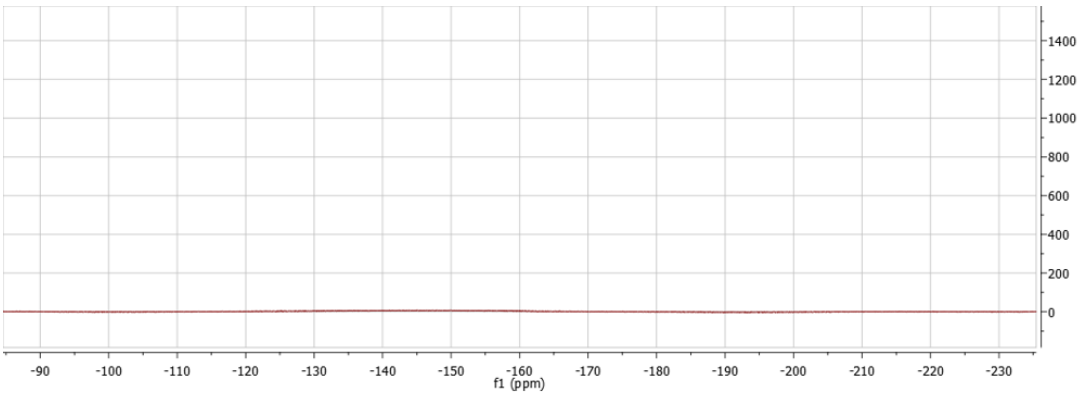


Figure S20. ^{19}F NMR spectrum of CCS-B-DO3A recorded in $CDCl_3$

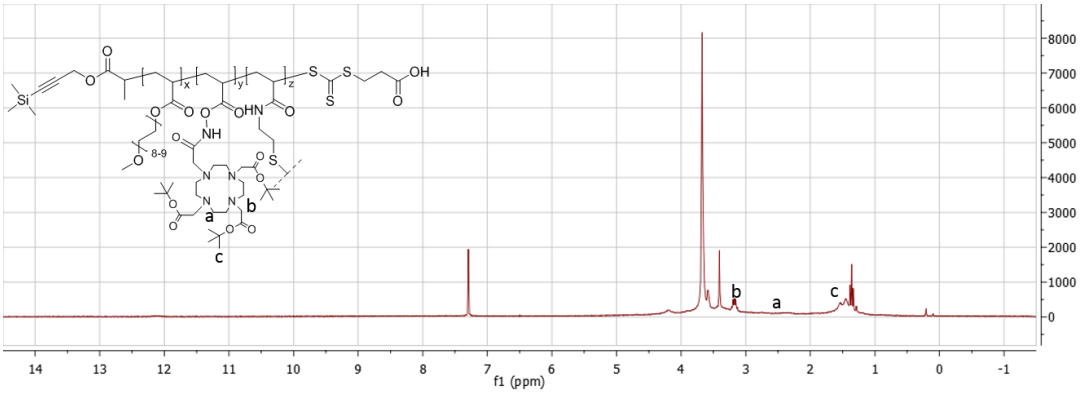


Figure S21. ^{1}H NMR spectrum of CCS-C-DO3A recorded in $CDCl_3$

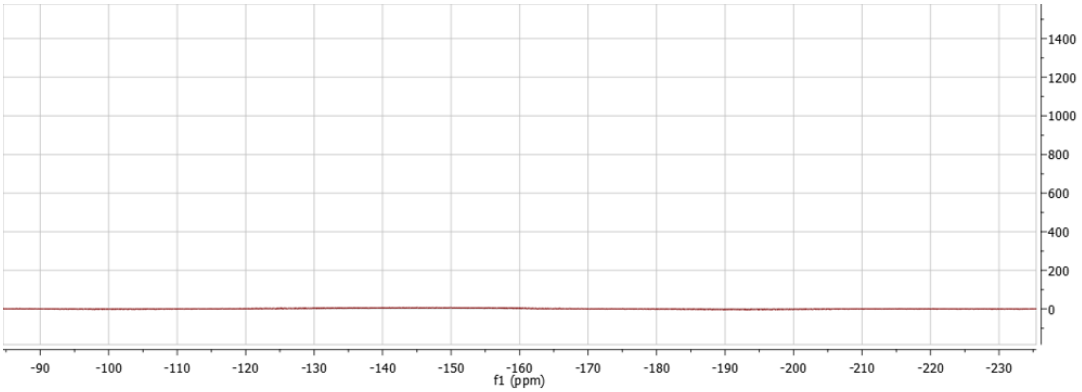


Figure S22. ^{19}F NMR spectrum of CCS-C-DO3A recorded in $CDCl_3$

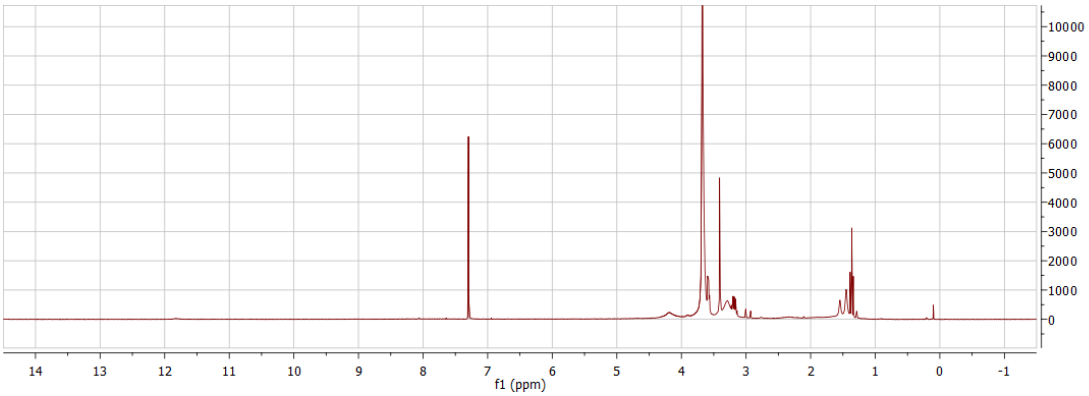


Figure S23. ^{1}H NMR spectrum of HBP-D-DO3A recorded in $CDCl_3$

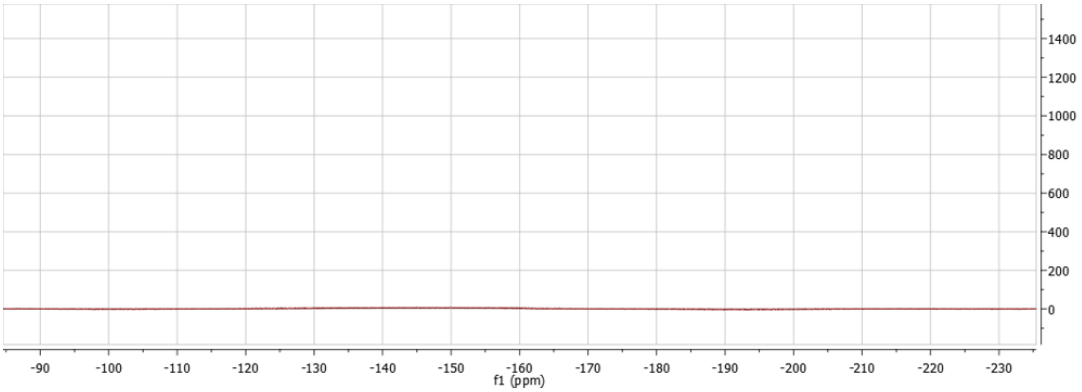


Figure S24. ^{19}F NMR spectrum of HBP-D-DO3A recorded in $CDCl_3$

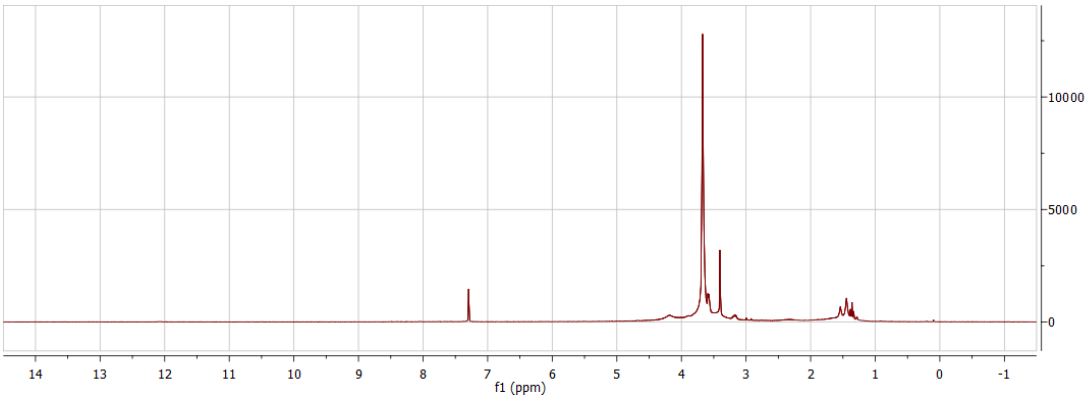


Figure S25. ^{1}H NMR spectrum of HBP-E-DO3A recorded in $CDCl_3$

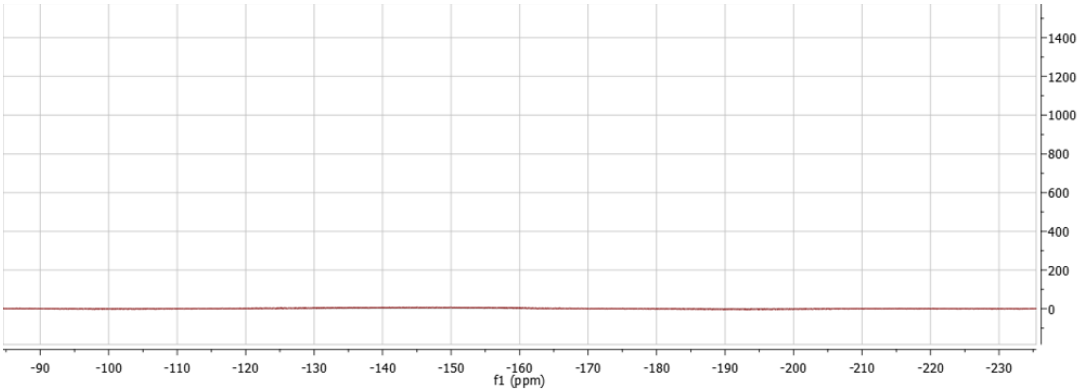


Figure S26. ^{19}F NMR spectrum of HBP-E-DO3A recorded in $CDCl_3$

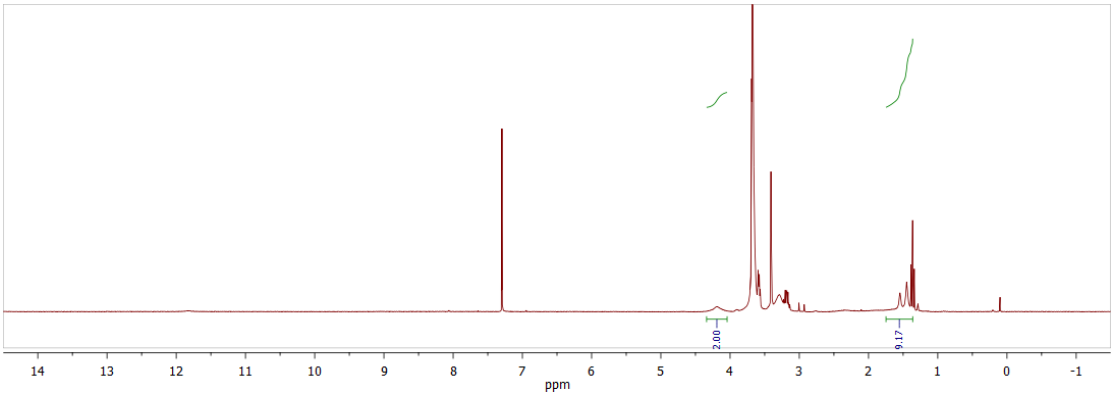


Figure S27. ^{1}H NMR spectrum of HBP-D recorded in $CDCl_3$

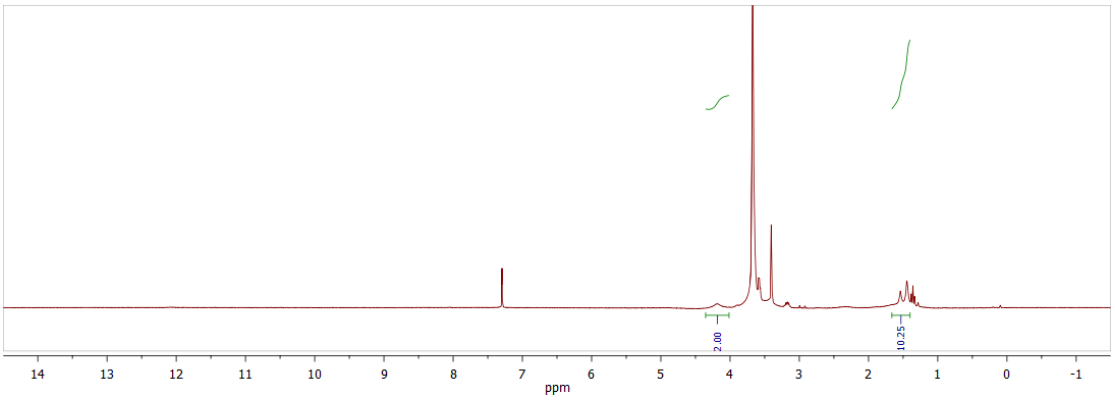


Figure S28. ^{1}H NMR spectrum of HBP-E recorded in $CDCl_3$

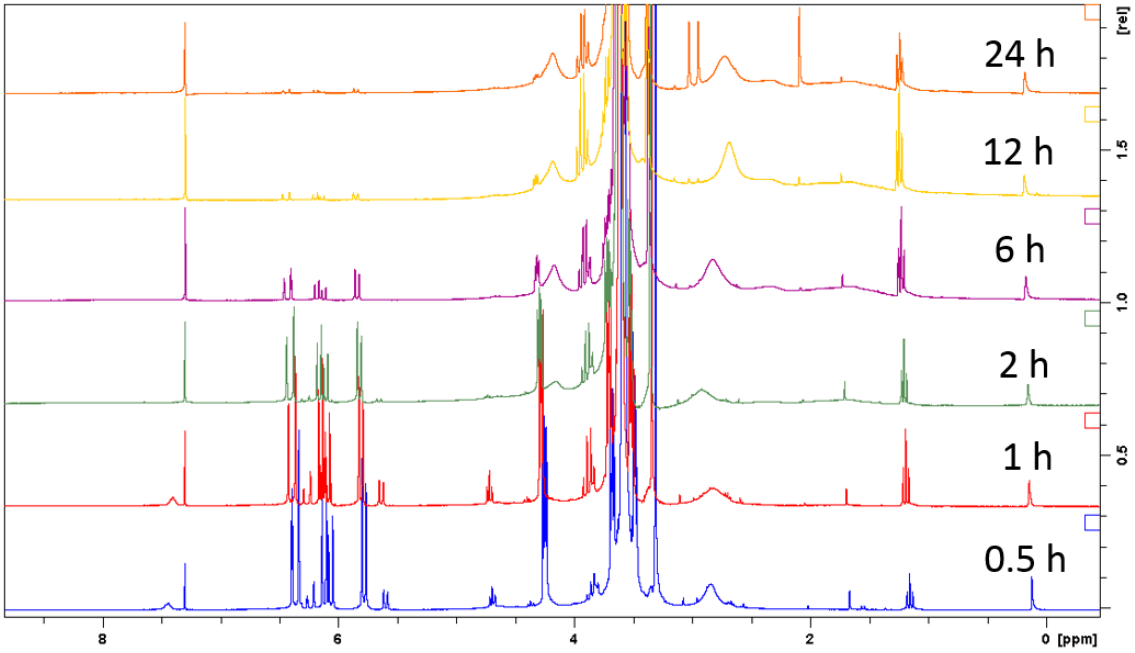


Figure S29. ^{1}H NMR spectrum of the kinetic study of HBP-D. (Recorded in $CDCl_3$)

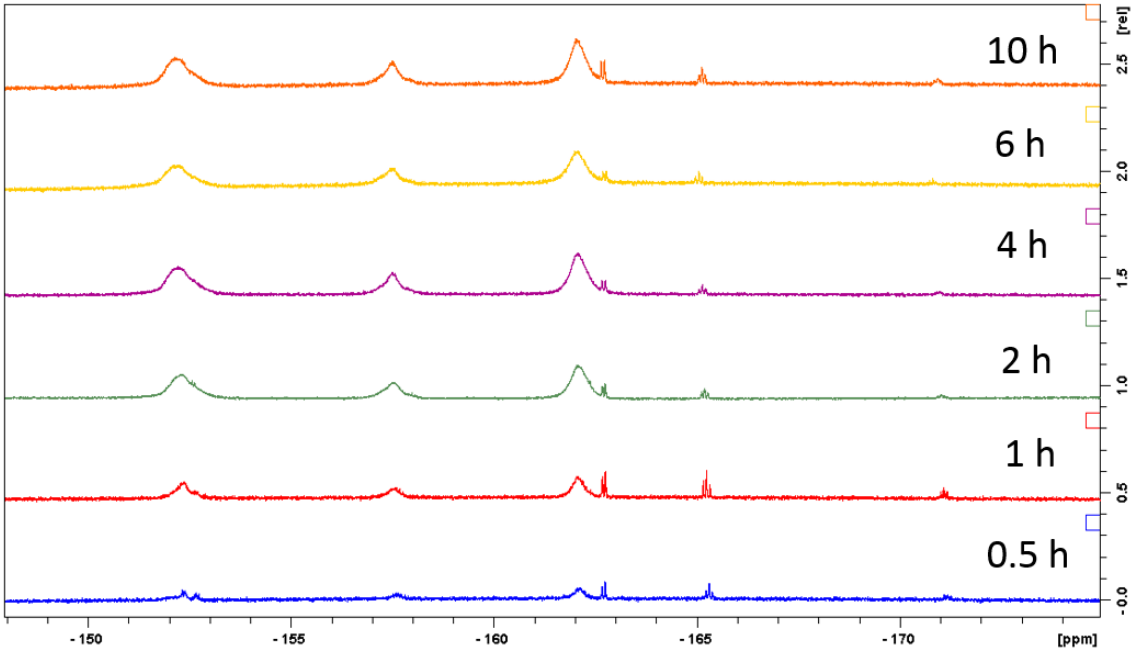


Figure S30. ^{19}F NMR spectrum of the kinetic study of HBP-D. (Recorded in $CDCl_3$)

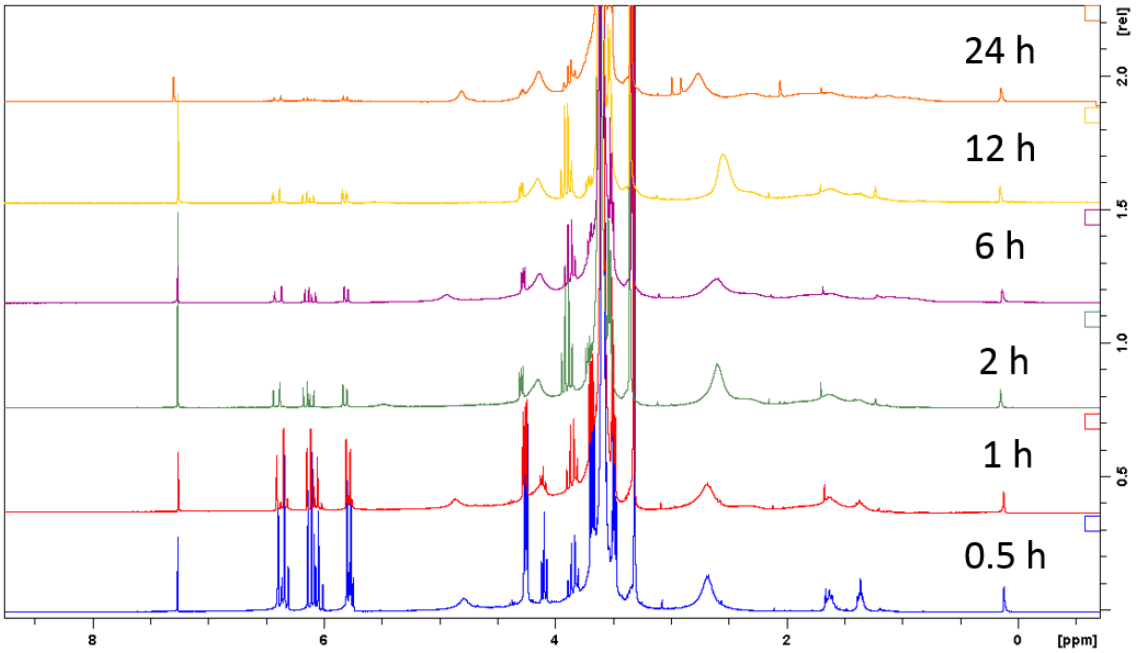


Figure S31. ^{1}H NMR spectrum of the kinetic study of HBP-E. (Recorded in $CDCl_3$)

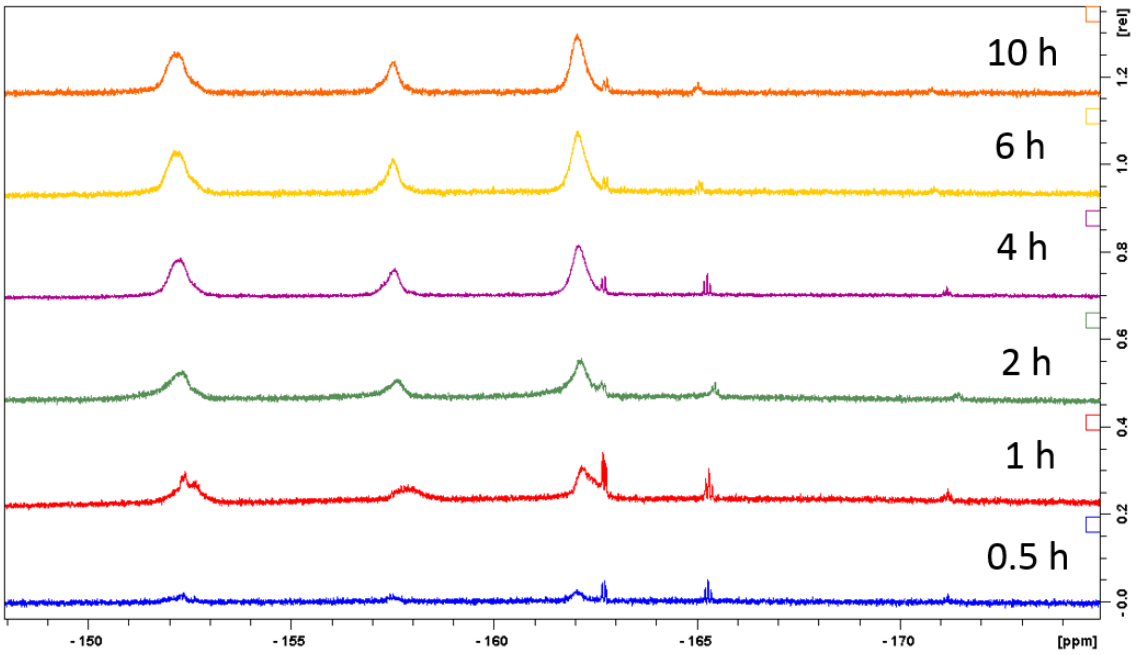
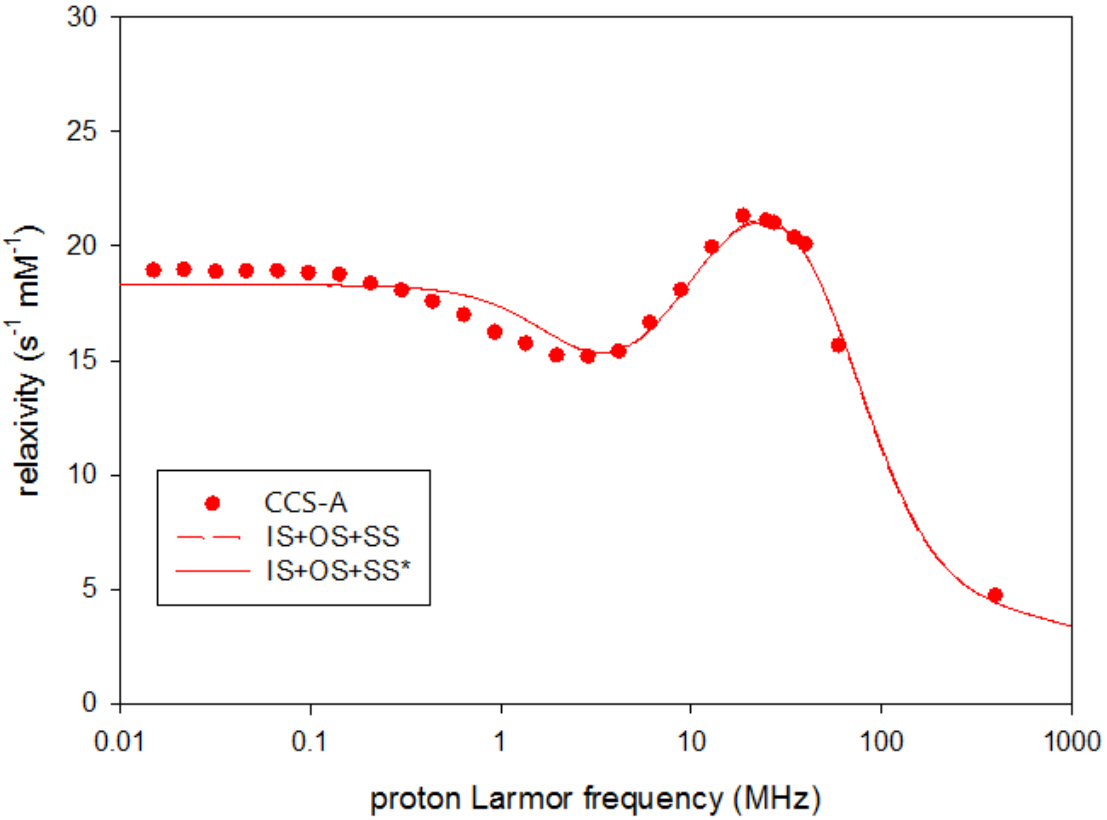
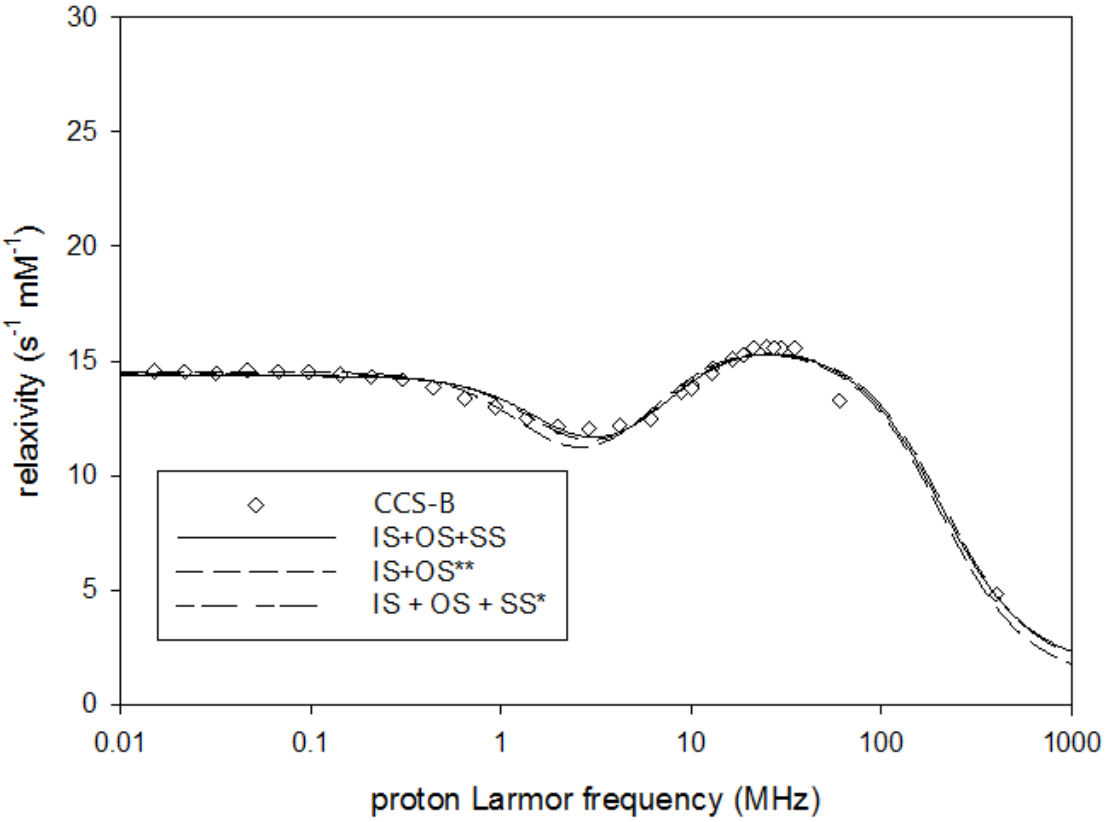
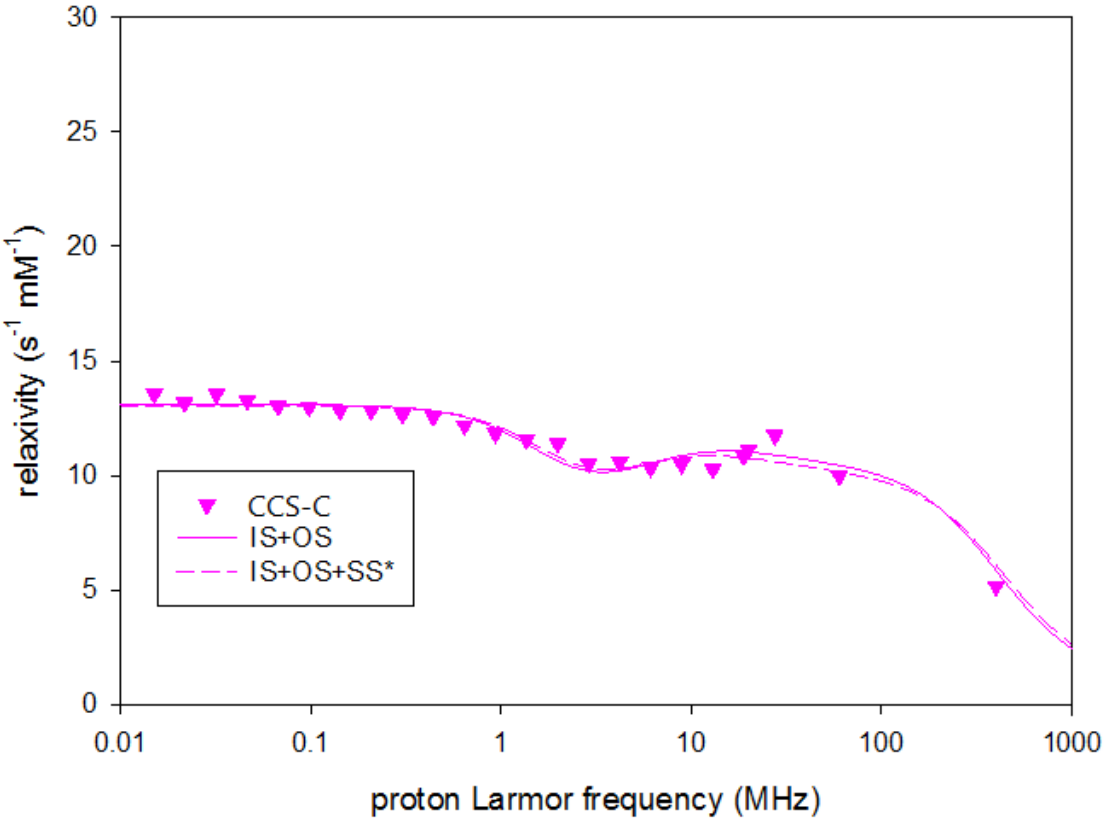
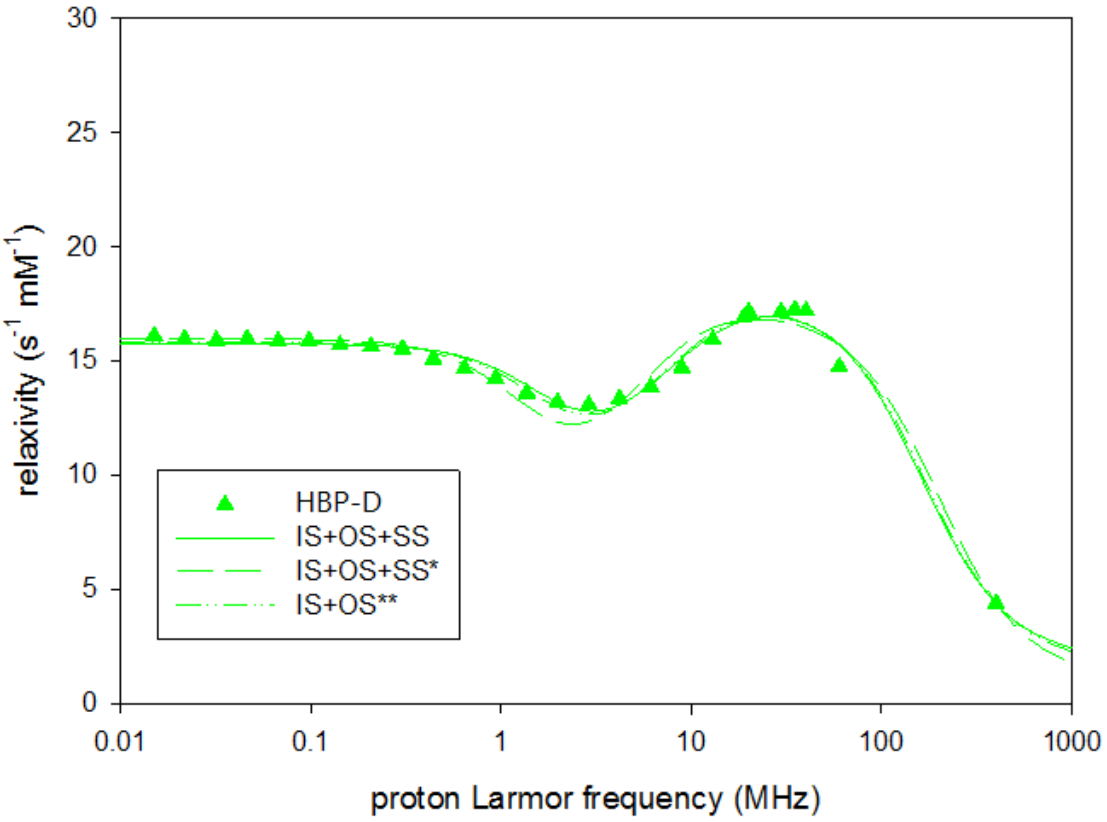


Figure S32. ^{19}F NMR spectrum of the kinetic study of HBP-E. (Recorded in $CDCl_3$)









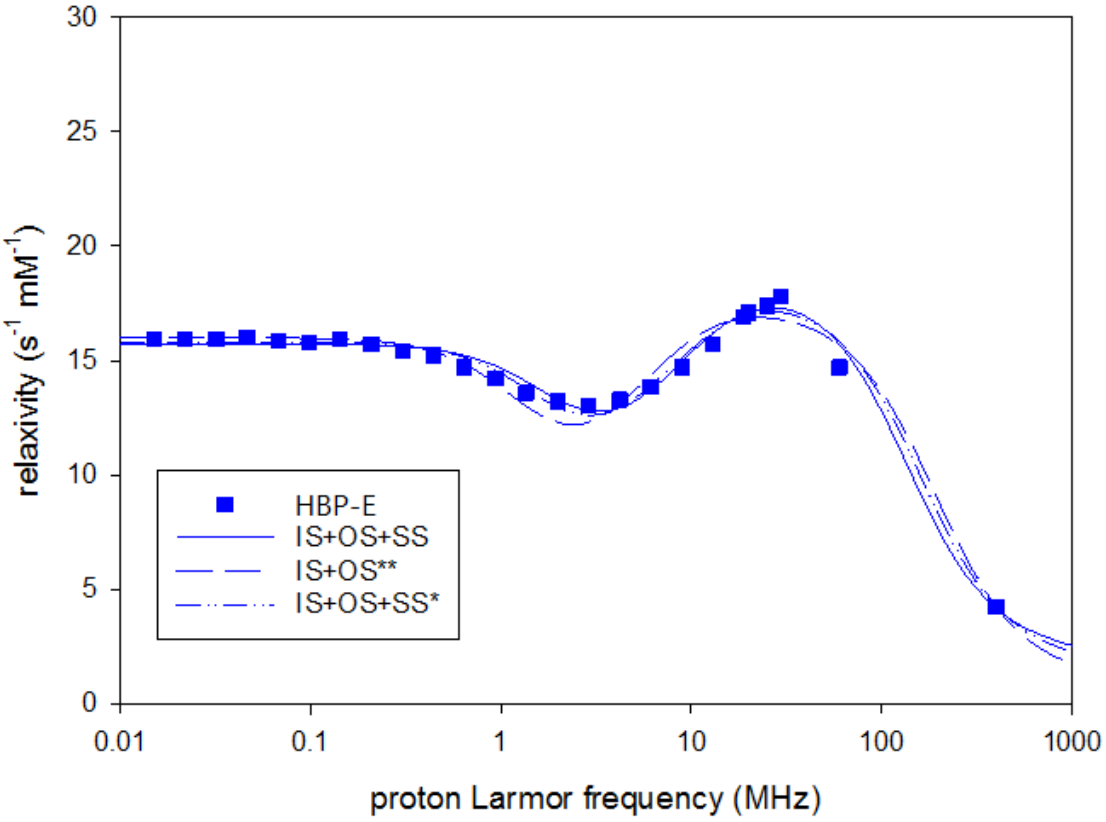


Figure S33. ^{1}H NMRD profiles of CCS-A, CCS-B, CCS-C, HBP-D and HBP-E. *range of τ_M fixed between 750 and 900 ns during the fitting (IS + OS + SS). ** range of τ_M fixed between 750 and 900 ns during the fitting (IS + OS).

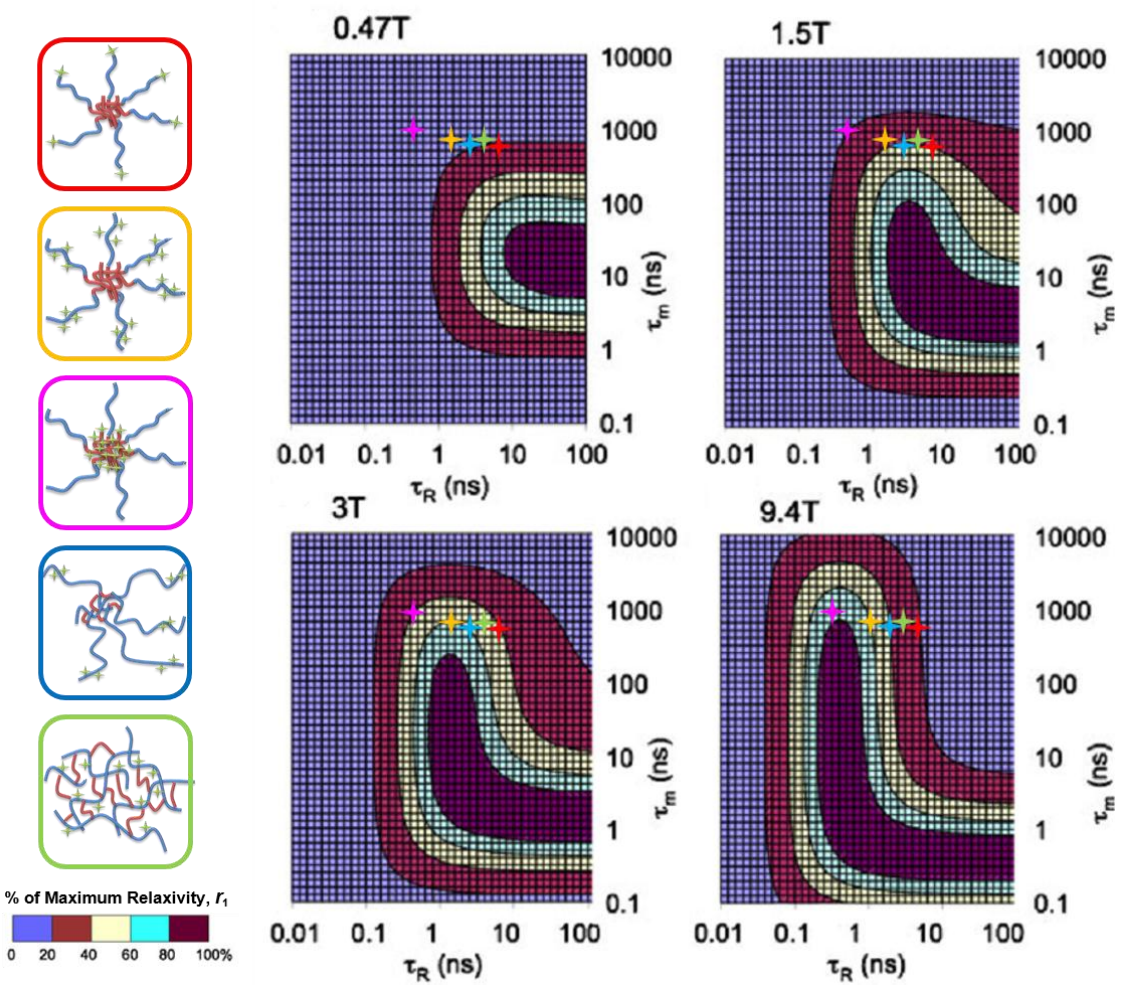


Figure S34. 2D simulation of interplay between water residency time (τ_m) and rotational motion (τ_R) on maximum achievable r_1.

Part 2: Determination of Polymer Composition

The composition of OEGA and NHS ester moieties was calculated using ^{1}H NMR according to the following equations:

$$f_{OEGA} = \int_{4.5ppm}^{4.1ppm}/2 \,/\, (\int_{4.5ppm}^{4.1ppm}/2 \; + \; \int_{2.95ppm}^{2.75ppm}/4\,)$$

$$f_{NHS} = \int_{2.95ppm}^{2.75ppm}/4 \,/\, (\int_{4.5ppm}^{4.1ppm}/2 \; + \; \int_{2.95ppm}^{2.75ppm}/4\,)$$

Where $\int_{4.5ppm}^{4.1ppm}$ corresponds to the CH_2 protons of OEGA and $\int_{2.95ppm}^{2.75ppm}$ is the integral of the signal of CH_2-CH_2 from the NHS ester.

The composition of OEGA and PFPA moieties was calculated using 2,2,2-Trifluoroethanol (TFE) as a reference in ^{1}H NMR and ^{19}F NMR according to the following equations:

In the ^{1}H NMR:

$$f_{TFE} = \int_{4.06ppm}^{3.86ppm}/2 \,/(\int_{4.06ppm}^{3.86ppm} \,/2 + \int_{4.5ppm}^{4.1ppm}/2\,)$$

$$f_{OEGA} = \int_{4.5ppm}^{4.1ppm}/2 \,/(\int_{4.06ppm}^{3.86ppm} \,/2 + \int_{4.5ppm}^{4.1ppm}/2\,)$$

Where $\int_{4.06ppm}^{3.86ppm}$ corresponds to the CH_2 protons of TFE and $\int_{4.5ppm}^{4.1ppm}$ is the integral of the signal of CH_2 from the OEGA.

In the ^{19}F NMR

$$f_{TFE} = \int_{-79.75ppm}^{-76.04ppm}/3 \,/\, [\int_{-79.75ppm}^{-76.04ppm}/3 + (\int_{-154.50ppm}^{-153.17ppm} + \int_{-160.94ppm}^{-159.01ppm} + \int_{-165.07ppm}^{-163.61ppm}\,)/5]$$

$$f_{PFPA} = (\int_{-154.50ppm}^{-153.17ppm} + \int_{-160.94ppm}^{-159.01ppm} + \int_{-165.07ppm}^{-163.61ppm}\,)/5 \,/\, [\int_{-79.75ppm}^{-76.04ppm}/3 + (\int_{-154.50ppm}^{-153.17ppm} + \int_{-160.94ppm}^{-159.01ppm} + \int_{-165.07ppm}^{-163.61ppm}\,)/5]$$

Where $\int_{-79.75ppm}^{-76.04ppm}$ is the integrals from signals attributed to the ^{19}F from TFE and $(\int_{-154.50ppm}^{-153.17ppm} + \int_{-160.94ppm}^{-159.01ppm} + \int_{-165.07}^{-163.61}\,)$ represent the ^{19}F signal of PFPA.

If the f_{TFE} in the last two equations give the same value, the polymer composition will be the following equation:

$$f_{OEGA} = \int_{4.5ppm}^{4.1ppm}/2 \,/\, [\, \int_{4.5ppm}^{4.1ppm}/2 \; + \; (\int_{-154.50ppm}^{-153.17ppm} + \int_{-160.94ppm}^{-159.01ppm} + \int_{-165.07ppm}^{-163.61ppm}\,)\,/5]$$

$$f_{PFPA} = (\int_{-154.50ppm}^{-153.17ppm} + \int_{-160.94ppm}^{-159.01ppm} + \int_{-165.07ppm}^{-163.61ppm}\,)\,/5 \,/\, [\int_{4.5ppm}^{4.1ppm}/2 \; + \; (\int_{-154.50ppm}^{-153.17ppm} + \int_{-160.94ppm}^{-159.01ppm} + \int_{-165.07ppm}^{-163.61ppm}\,)\,/5]$$

The composition of OEGA and DO3A moieties was calculated using ^{1}H NMR according to the following equations:

$$f_{OEGA} = \int_{4.5ppm}^{4.1ppm}/2 \;/\, (\int_{4.5ppm}^{4.1ppm}/2 \; + \; \int_{1.7ppm}^{1.4ppm}/27)$$

$$f_{DO3A} = \int_{1.7ppm}^{1.4ppm}/27 \,/\, (\int_{4.5ppm}^{4.1ppm}/2 \; + \; \int_{1.7ppm}^{1.4ppm}/27)$$

Where $\int_{4.5ppm}^{4.1ppm}$ corresponds to the CH_2 protons of OEGA and $\int_{1.7ppm}^{1.4ppm}$ is the integral of the signal of CH_3 from the *tert*-butyl group of DO3A.

Part 3: Determination of monomer conversion

Monomer conversions (α) are calculated as followed:

In the equation, subscript "0" and "t" corresponding to time 0 and different reaction times (0.5-24 hours), respectively.

$$\alpha_{\text{OEGA}} = 1 - \frac{(\text{F}_{\text{OEGA}})_t/(\text{F}_{\text{TMS}})_t}{(\text{F}_{\text{OEGA}})_0/(\text{F}_{\text{TMS}})_0}$$

$$\alpha_{\textit{N,N'}\text{-methylenebisacrylamide}} = 1 - \frac{(\text{F}_{\textit{N,N'}-\text{methylenebisacrylamide}})_t/(\text{F}_{\text{TMS}})_t}{(\text{F}_{\textit{N,N'}-\text{methylenebisacrylamide}})_0/(\text{F}_{\text{TMS}})_0}$$

$$\alpha_{\text{1,6-hexanediol diacrylate}} = 1 - \frac{(\text{F}_{\text{1,6-hexanediol diacrylate}})_t/(\text{F}_{\text{TMS}})_t}{(\text{F}_{\text{1,6-hexanediol diacrylate}})_0/(\text{F}_{\text{TMS}})_0}$$

$$\alpha_{\text{PFPA}} = \frac{(\text{F}_{\text{PFPA}})_t}{(\text{F}_{\text{PFPA}})_n + (\text{F}_{\text{PFPA Monomer}})_t}$$

Using ^{1}H NMR, f_{TMS}, f_{OEGA}, $f_{\textit{N,N'}\text{-methylenebisacrylamide}}$ and $f_{\text{1,6-hexanediol diacrylate}}$ are defined:

$$f_{\text{TMS}} = \int_{0.5ppm}^{0ppm}/9$$

$$f_{\text{OEGA}} = \int_{5.8ppm}^{5.7ppm}$$

$$f_{\textit{N,N'}\text{-methylenebisacrylamide}} = \int_{5.6ppm}^{5.5ppm}$$

$$f_{\text{1,6-hexanediol diacrylate}} = \int_{6.4ppm}^{6.3ppm}$$

Using ^{19}F NMR, f_{PFPA} and $f_{\text{PFPA Monomer}}$ are defined:

$$f_{\text{PFPA}} = \left(\int_{-154.50ppm}^{-153.17ppm} + \int_{-160.94ppm}^{-159.01ppm} + \int_{-165.07ppm}^{-163.61ppm}\right)$$

$$f_{\text{PFPA Monomer}} = \left(\int_{-163.0ppm}^{-162.5ppm} + \int_{-165.5ppm}^{-165.0ppm} + \int_{-171.5ppm}^{-171.0ppm}\right)$$