

An azide-containing initiator for the cationic ring-opening-polymerization of 2-oxazolines

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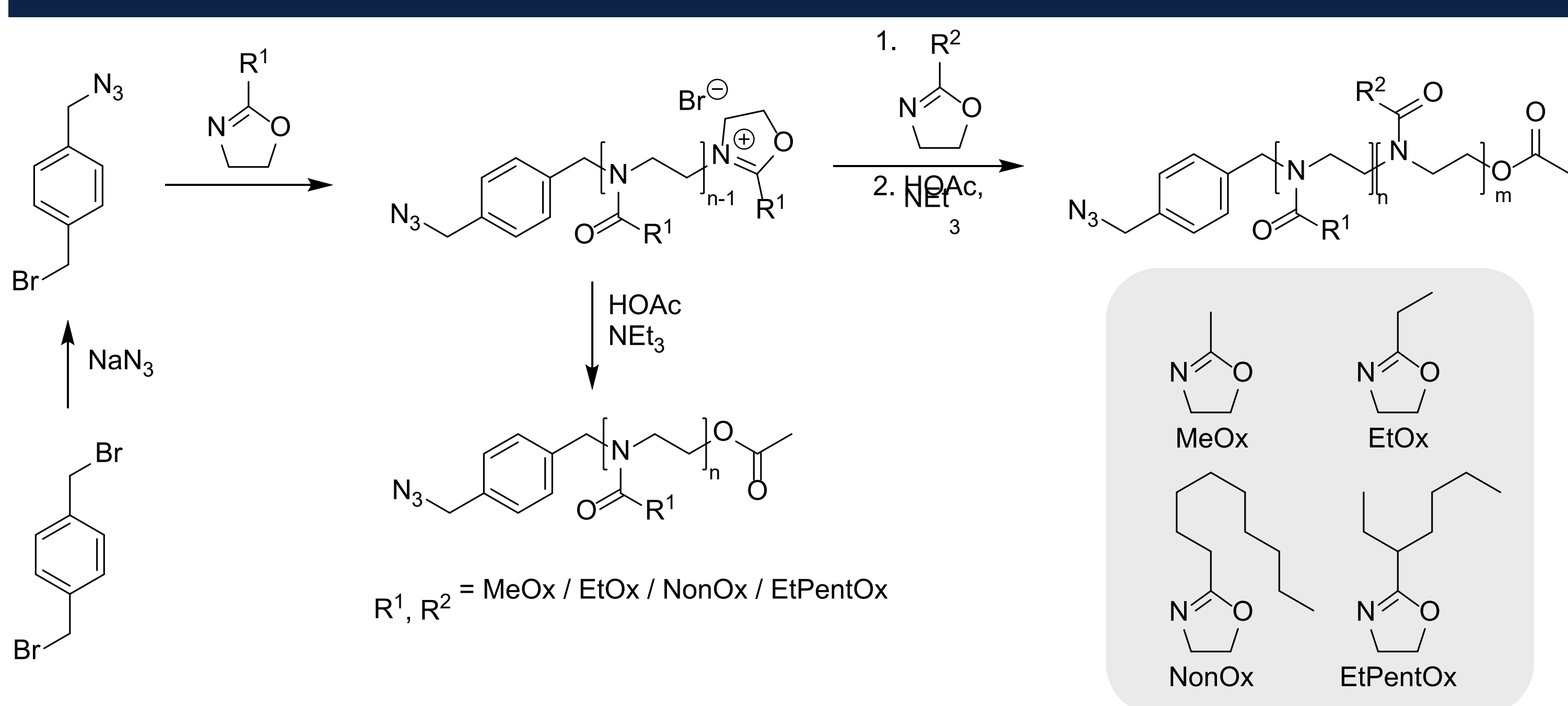
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Introduction

Poly(2-oxazoline)s (POx) represent a versatile class of polymers synthesized *via* a living cationic ring-opening polymerization (CROP). This living nature allows for precise control over molar mass, dispersity, and end-group functionality. One common method for end-capping the CROP is through termination with nucleophiles such as sodium azide, which introduces an azide end-group suitable for further click chemistry modifications.^[1-3] However, the functionalization of, in particular, hydrophobic POx with azide end groups for bioconjugation has posed significant synthetic challenges. Herein, we report the development of a novel initiator system for the CROP of 2-oxazolines that enables the direct incorporation of azide functionality at the α -terminus of various POx derivatives. This approach overcomes previous limitations in quenching reactions of hydrophobic POx variants and provides consistently high end group fidelity across a spectrum of POx hydrophilicity. Polymers with an azide end group exhibited excellent reactivity in azide-alkyne cycloaddition reactions.

Synthesis



Scheme 1: Schematic representation of the synthesis of the azide containing initiator and the polymerization of 2-oxazolines using the initiator.

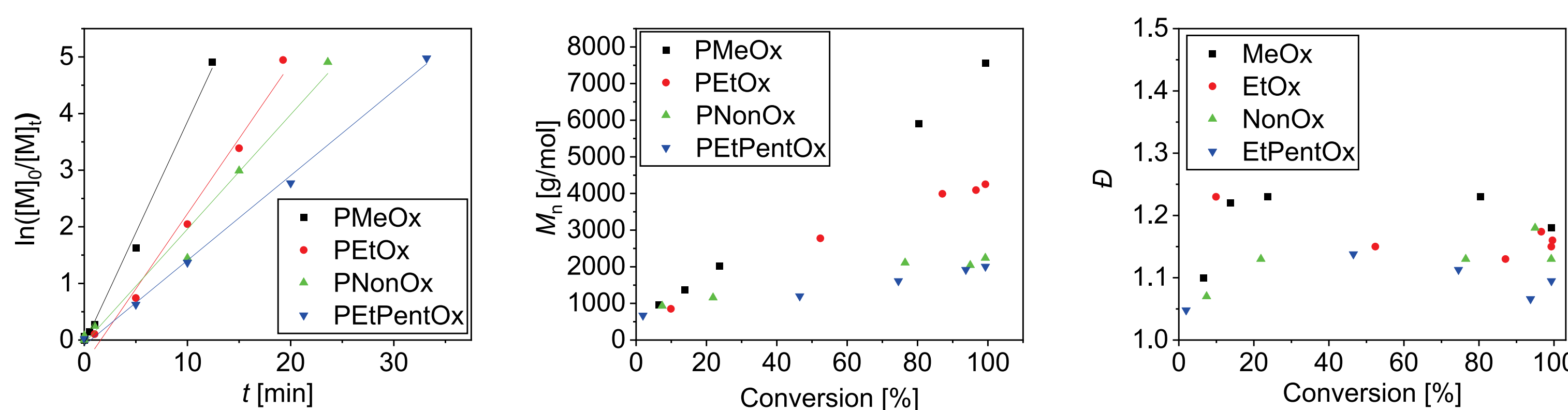


Figure 1: Kinetic studies of the CROP of 2-oxazolines with the azide initiator ($[M]/[I] = 40$ for the hydrophilic and 10 for the hydrophobic monomers) at 140 °C. k_p (MeOx) = $6.58 \cdot 10^{-2}$ L/(mol·s), k_p (EtOx) = $4.42 \cdot 10^{-2}$ L/(mol·s), k_p (NonOx) = $3.39 \cdot 10^{-2}$ L/(mol·s), k_p (EtPentOx) = $2.50 \cdot 10^{-2}$ L/(mol·s).

Click reaction

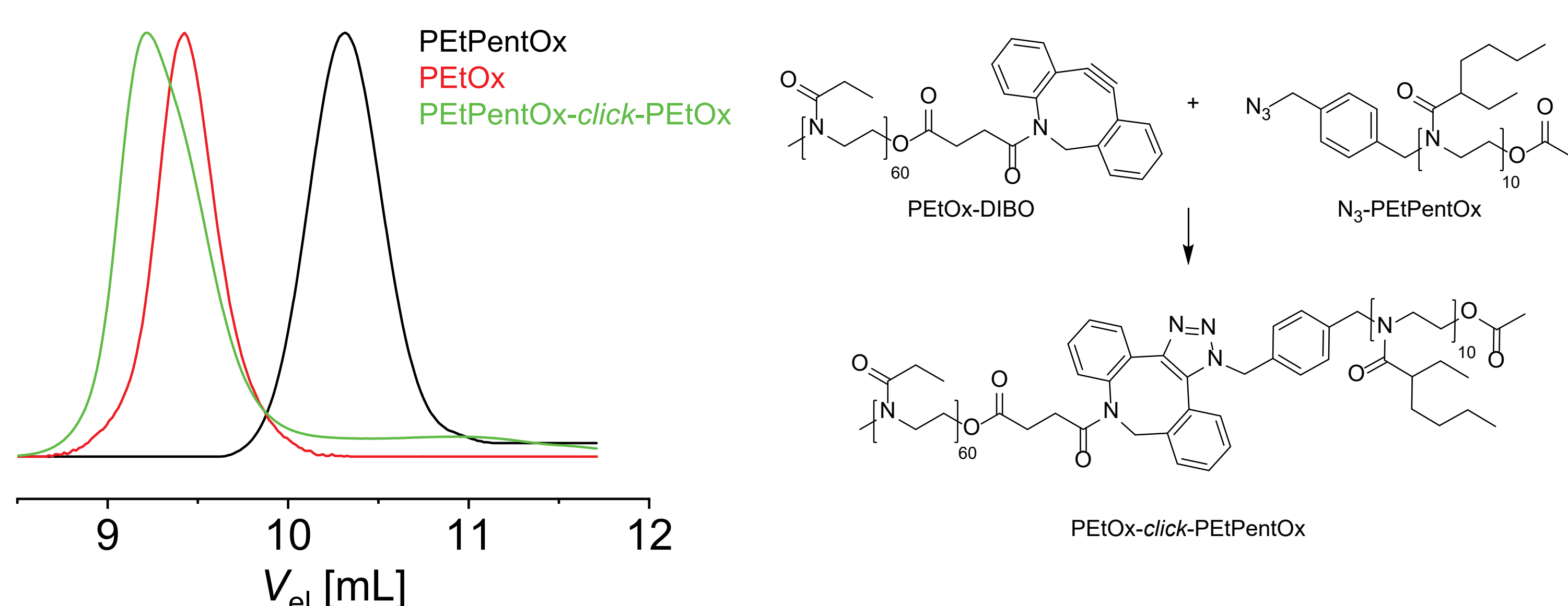


Figure 2: Overlay of SEC elutograms (CHCl₃, RID) of PEtOx-DIBO, N₃-PEtPentOx and PEtPentOx-click-PEtOx.

Analytical data

Homopolymers

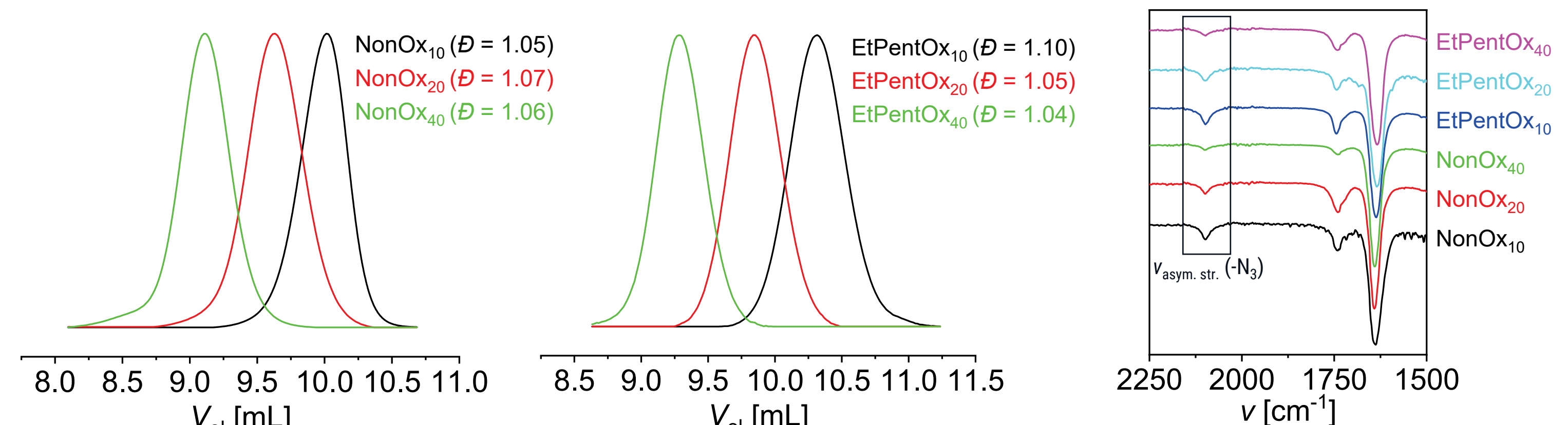


Figure 3: Overlay of SEC elutograms (CHCl₃, RID) and IR spectra of the azide initiated homopolymers (PNonOx and PEtPentOx).

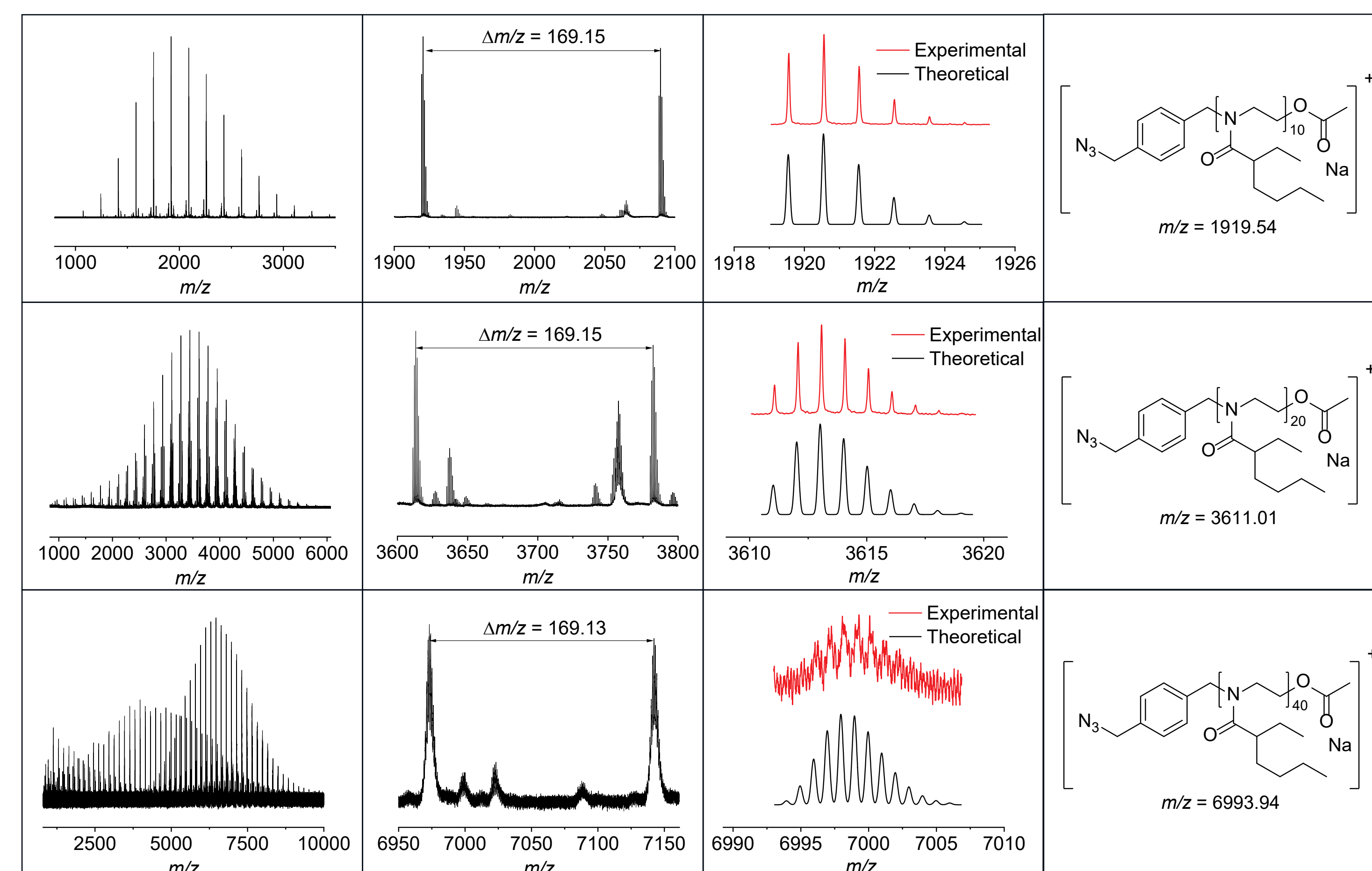


Figure 4: MALDI-TOF mass spectra (Dithranol + NaTFA) of the PEtPentOx with varying DP. From left to right: Full spectra, zoom into an m/z region displaying the PEtPentOx repeating units, and overlay of the measured and calculated isotopic pattern of the most abundant species. All identified m/z species were found as sodium adducts.

Block copolymers

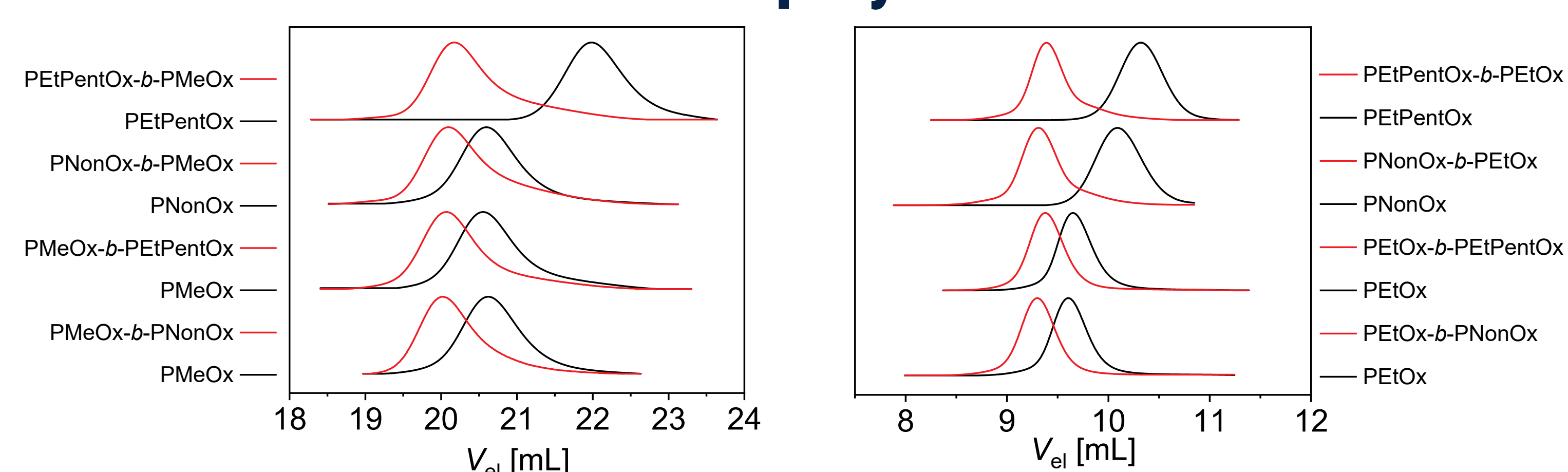


Figure 5: Overlay of SEC elutograms of azide containing amphiphilic block copolymers (left: DMAc, RID, right: CHCl₃ RID).

Conclusion

A novel CROP initiator for the polymerization of 2-oxazolines enabled the synthesis of hydrophobic homopolymers and amphiphilic block copolymers featuring an α -azide end group. MALDI-TOF-MS analysis confirmed the presence of this azide group in the polymers. This functionality was successfully utilized in click reactions with a hydrophilic PEtOx demonstrating its utility for post-polymerization modification.

Acknowledgments

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 [2] K. Kempe, R. Hoogenboom, M. Jäger, U. S. Schubert, *Macromolecules* **2011**, 44, 6424-6432.
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