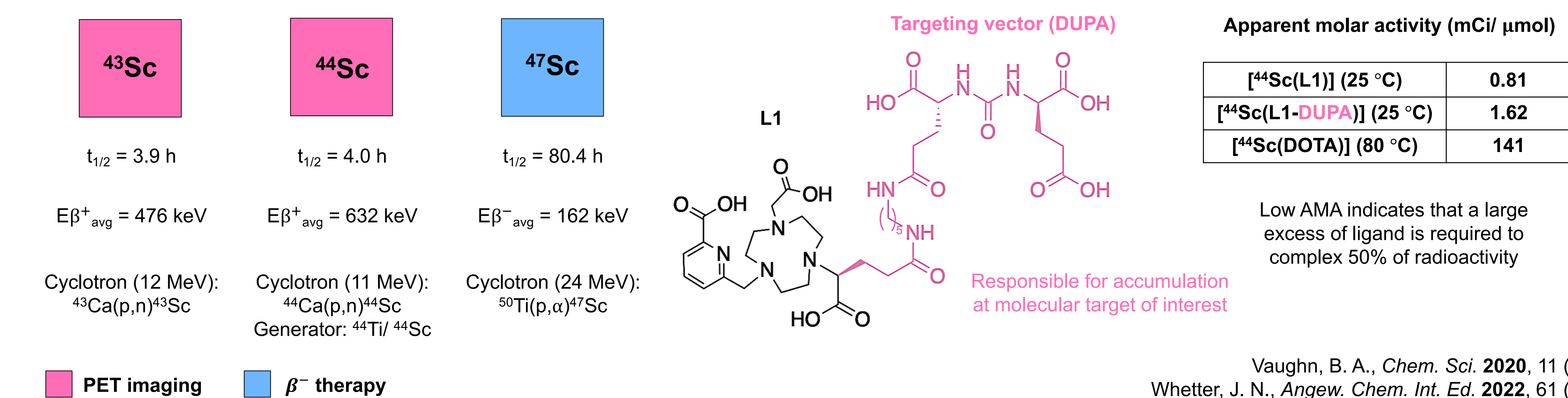


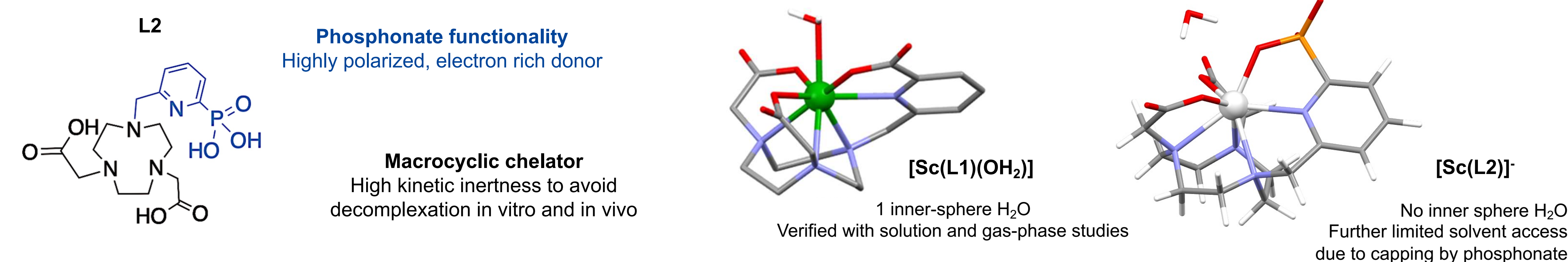
The challenge: Can we further improve chelator properties for Sc isotopes?

- Sc³⁺ isotopes exhibit ideal properties for diagnostic imaging and therapy, well-matched to the pharmacokinetics of small biologics
- Yet, development of clinically applicable radiopharmaceuticals is impeded by poorly understood aqueous Sc³⁺ coordination chemistry
- The gold standard chelator, DOTA, and our first-generation platform, L1, exhibit low apparent molar activity at room temperature



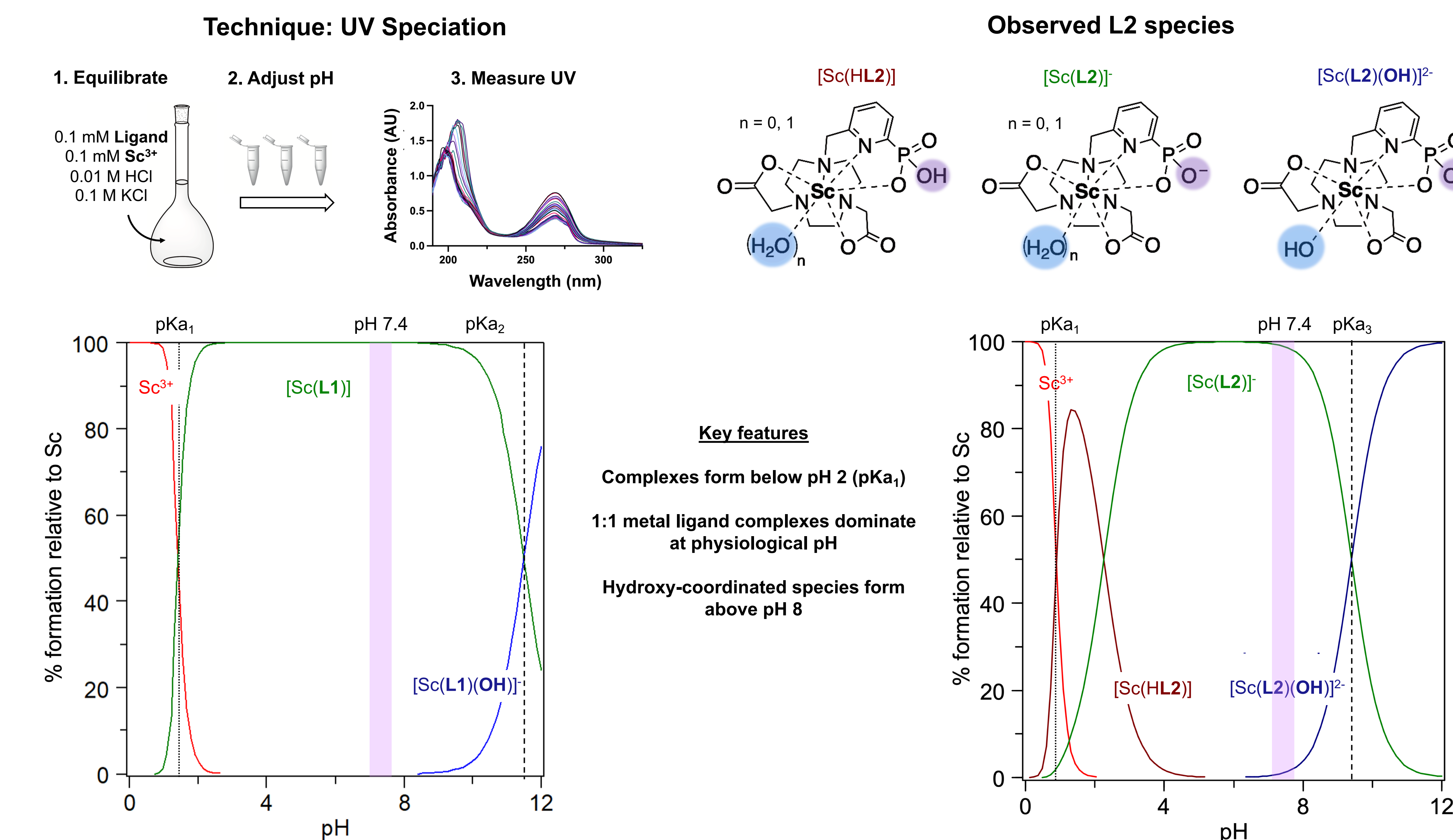
To harness Sc isotopes for radiolabeling of thermally-sensitive biologics, we seek high apparent molar activity at 25 °C.

Our solution: Adapted ligand design

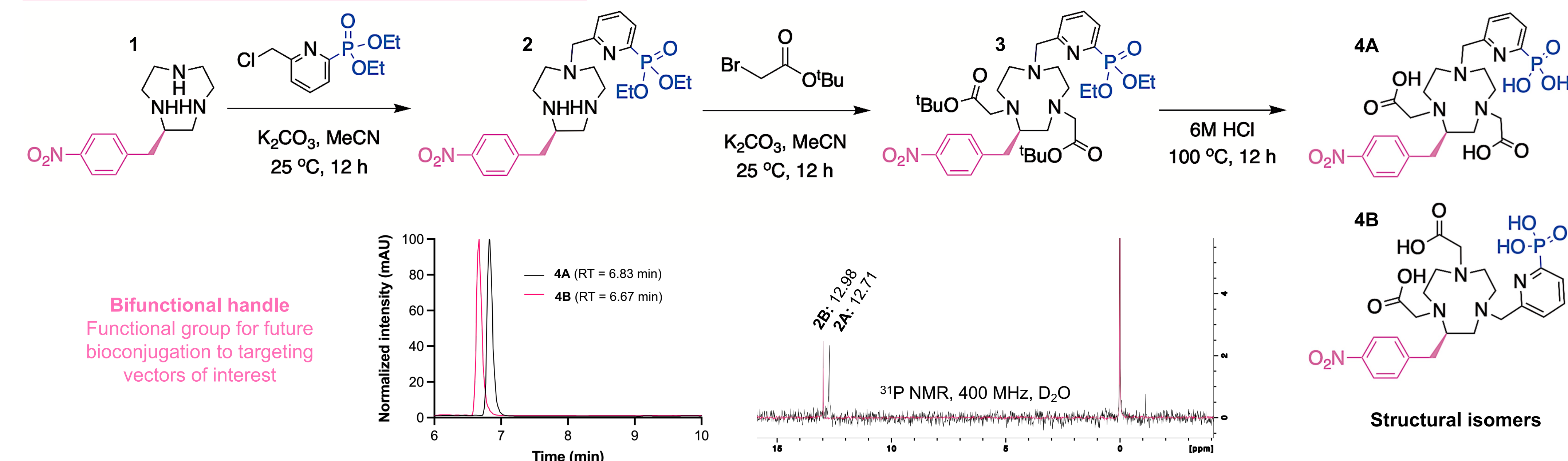


We hypothesize that introduction of phosphonate functionality will impart rapid chelation kinetics with scandium.

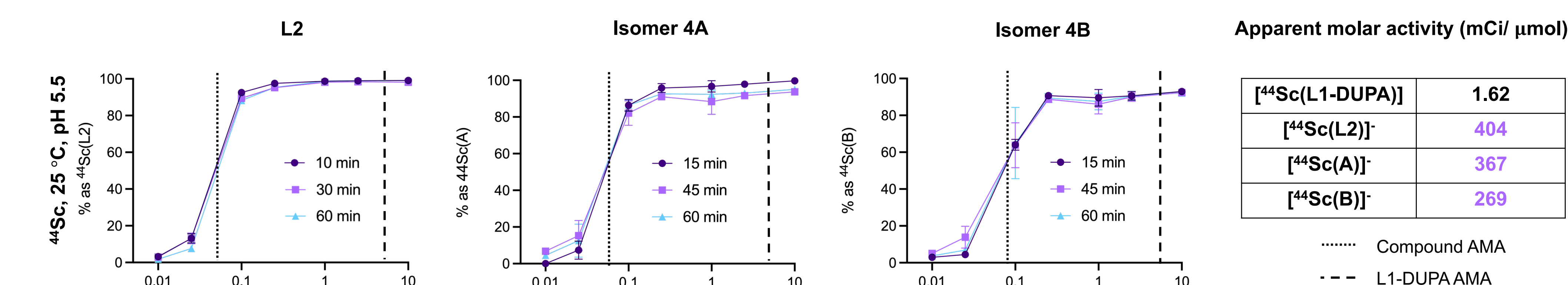
Solution thermodynamics: What species are present under relevant pH conditions?



Path to bifunctional model derivatives of L2



Radiochemical synthesis: Does our second-generation chelator platform exhibit improved properties with ⁴⁴Sc?



Yes, L2 and its derivatives exhibit drastically higher apparent molar activity at room temperature than L1-DUPA.

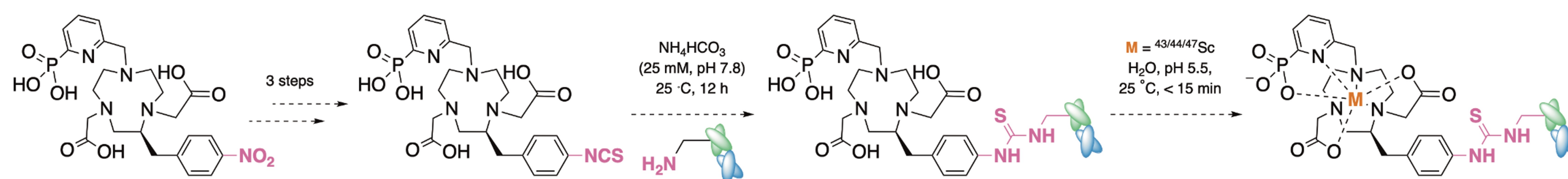
Conclusions:

Our second-generation phosphonate-based chelator platform, L2:

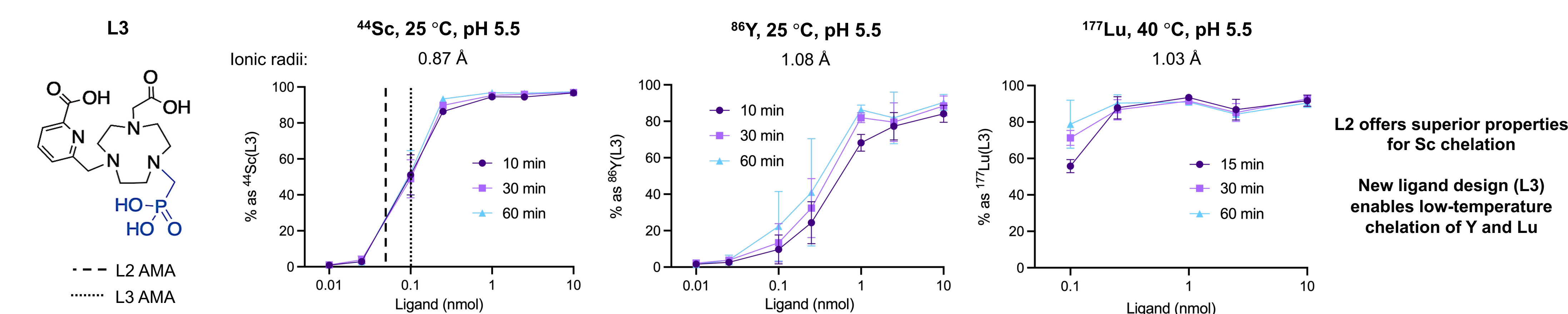
- Successfully stabilizes Sc³⁺ under conditions relevant for radiochemical synthesis and biological applications
- Affords ⁴⁴Sc complexes with improved apparent molar activity (AMA) under conditions compatible with thermally-sensitive biologics

Future outlook:

1. Path to bioconjugation of thermally-sensitive biologics



2. Toward chelation of small, rare earth radiometals (scandium, yttrium, and lutetium) for theranostic applications



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