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Purpose

To develop a stereoselective method for assembling five- and six-membered cyclic compounds by intramolecular cyclization of $\text{Co}_2(\text{CO})_6$ -complexed propargyl radicals.

Background

Previous studies have shown the most common type of alpha substituent in $\text{Co}_2(\text{CO})_6$ complexed propargyl alcohols have been π -donors². These π -donors can include aromatic rings, oxygen atoms, double bonds, and triple bonds. Their ability to immediately stabilize the propargyl cations greatly accelerated the formation of reactive intermediates. This created extra steps in the synthesis including isolation and subsequent reduction steps. Using σ -donors instead decreases the stability of the requisite cations and requires higher temperatures. This study focuses on the cobalt-mediated intramolecular cyclization as the intermolecular reactions have been studied more in literature. This reaction is biologically significant as the final products are prone to secondary transformations, of immediate relevance to estrogen mimics¹.

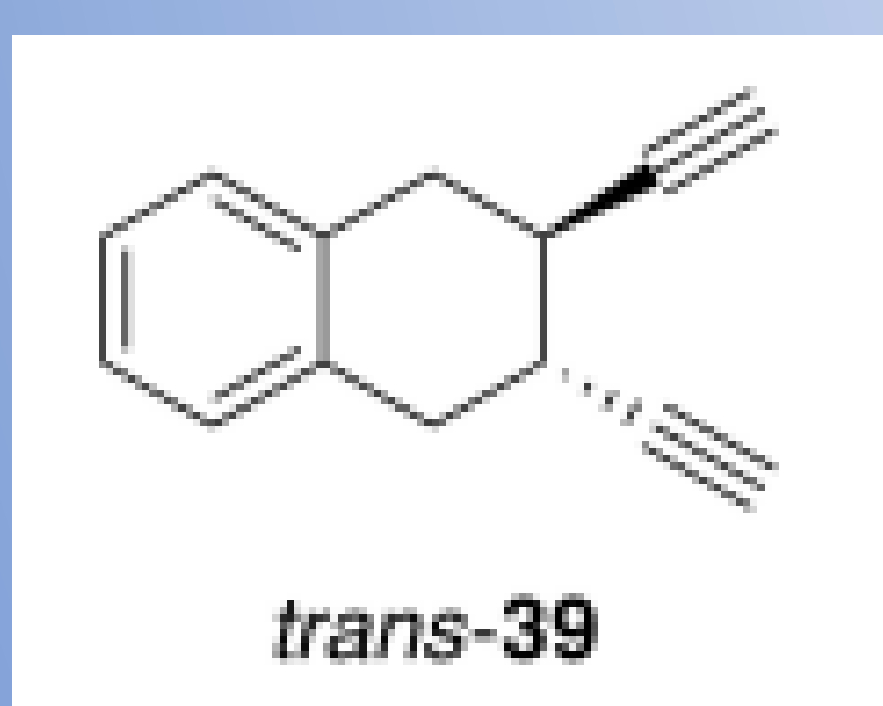


Figure 1. Chemical structure of trans-39¹

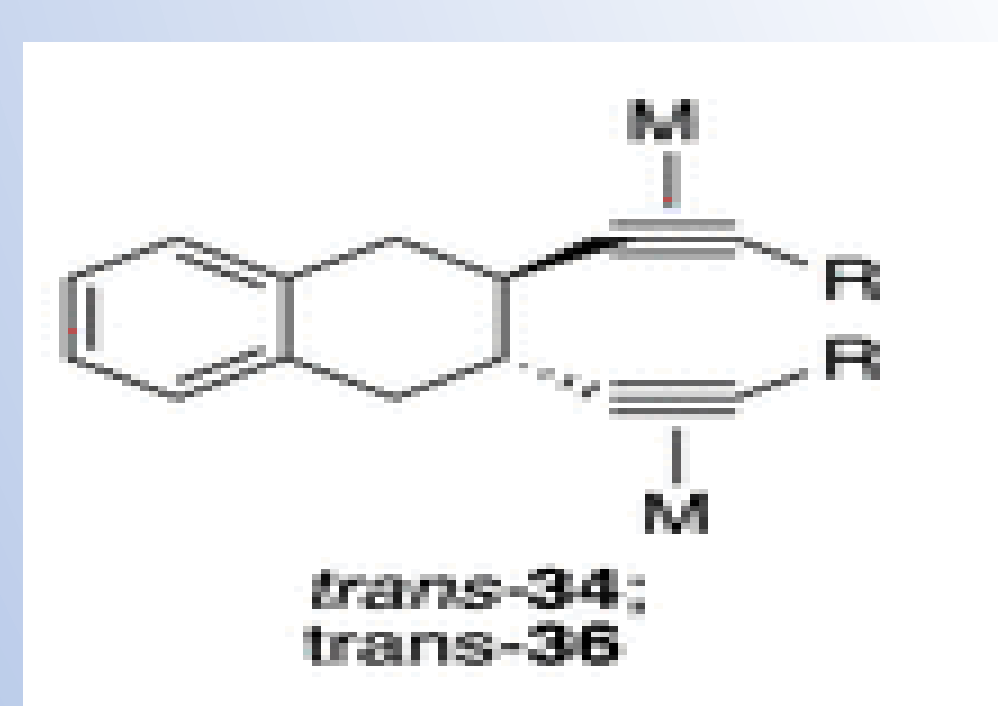


Figure 2. Chemical structure of Trans-36¹

Experimental

- Synthesis of trans-39 was performed under an atmosphere of nitrogen. Trans-36 and Trans-38 were combined with various solvents and reactants at temperature from -20°C to 20°C to afford trans-39.
- Products and intermediates of these reactions were identified using NMR spectroscopy (400MHz), X-ray crystallography analysis and Mass-spectrometry.

Results

- Introducing rigidity into a carbon tether resulted in the formation of trans-tetralins with stereochemistry (trans- 96–100%)

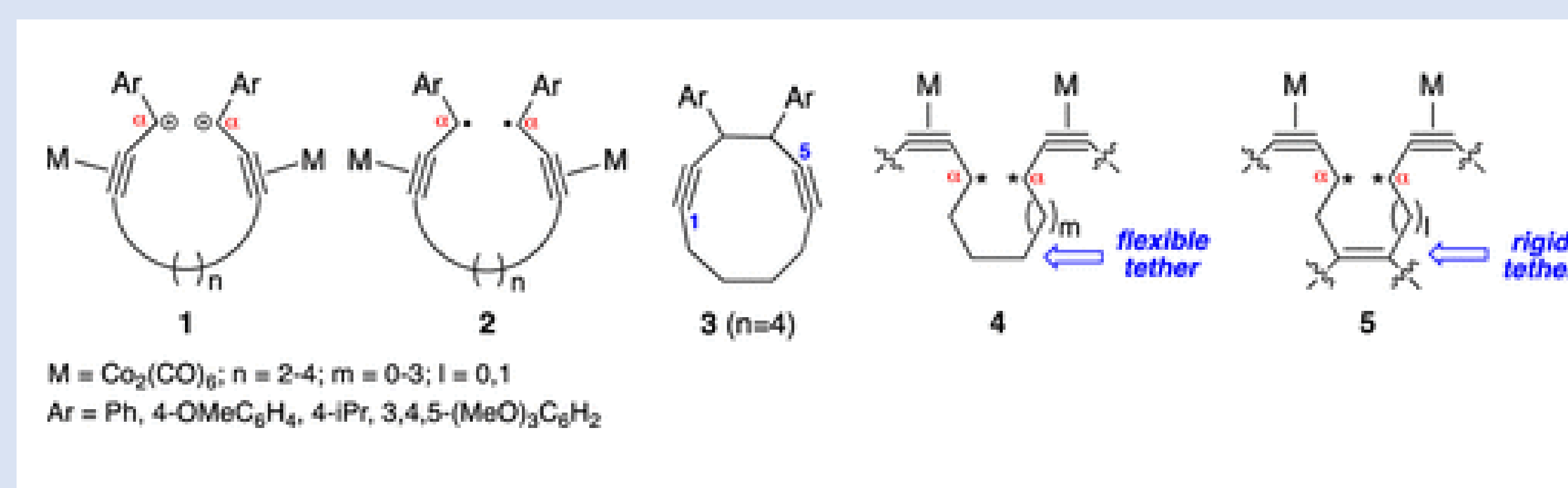


Figure 3. Radical Cyclization mechanism comparing tether rigidity¹

- NMR spectra of the desired tetralin product

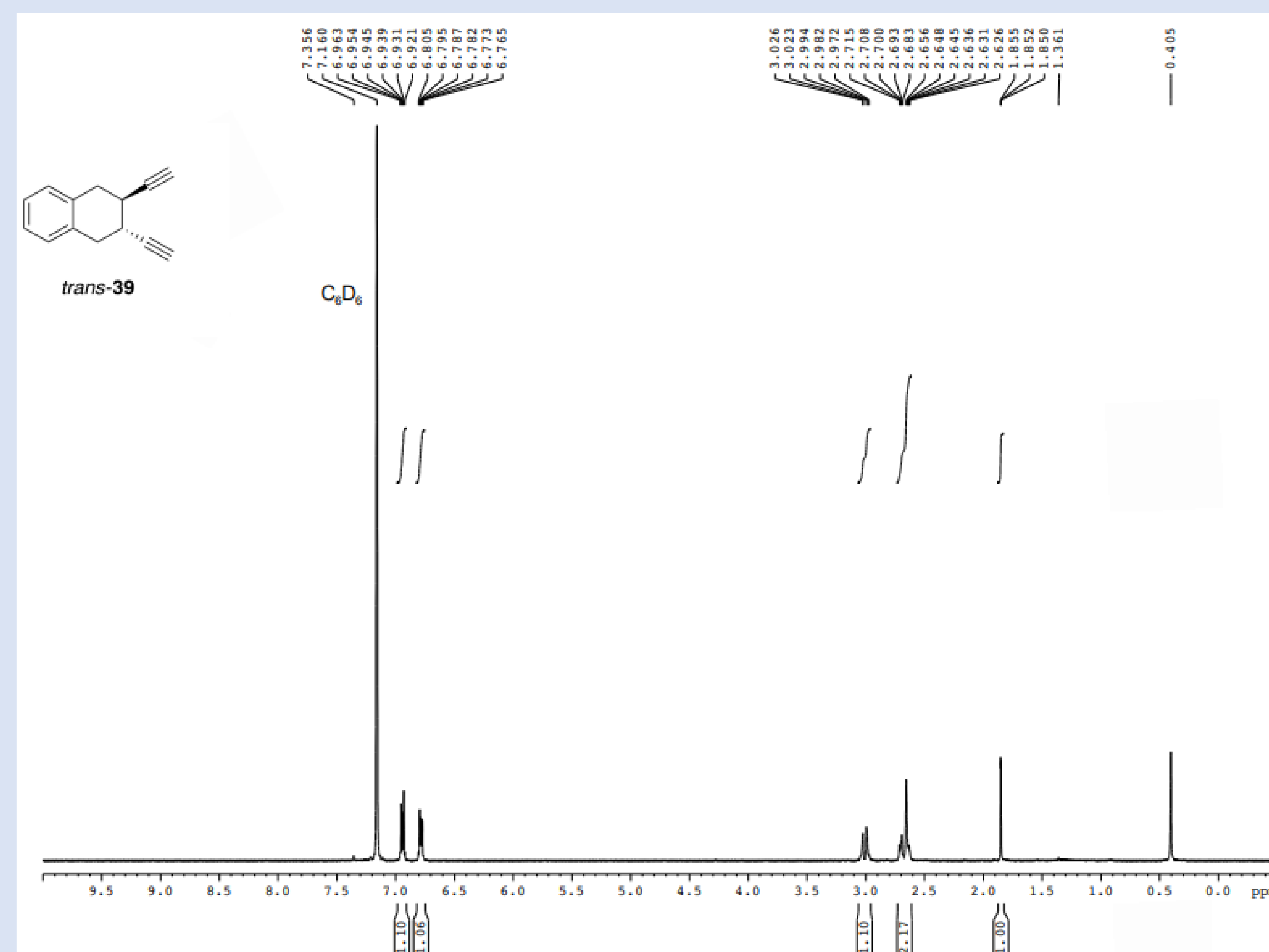


Figure 4. H-¹NMR spectra of compound Trans-39¹

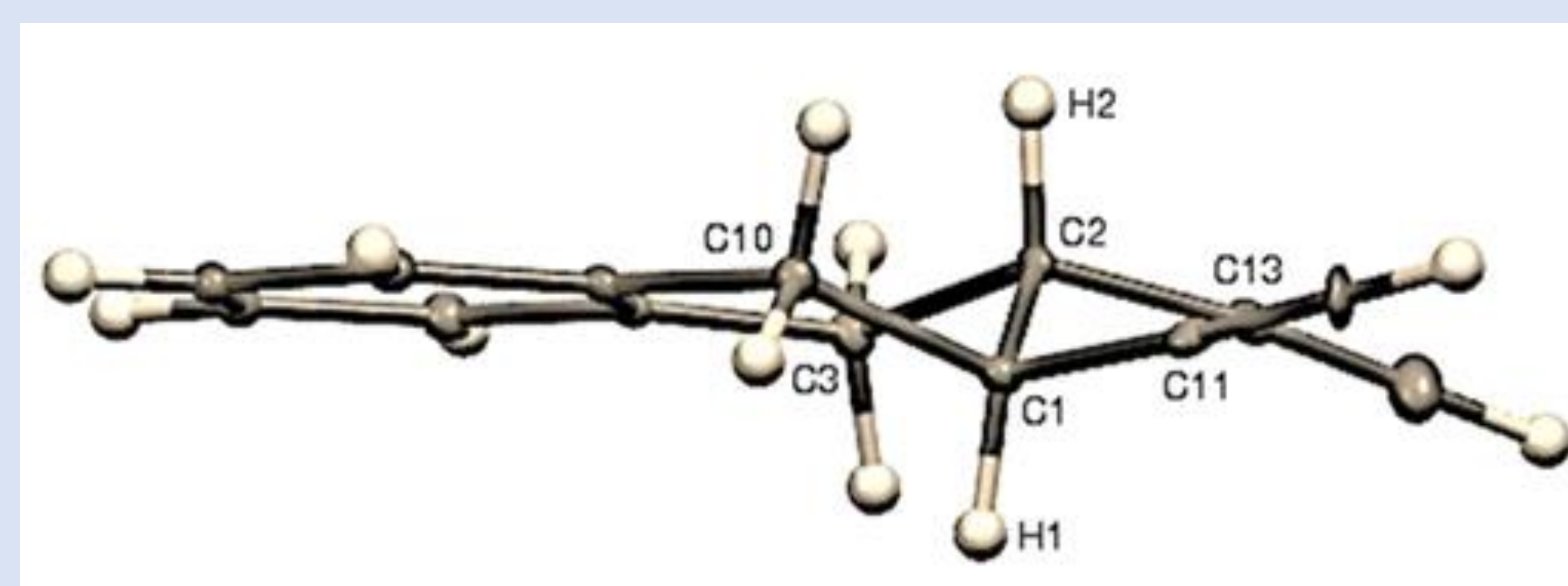


Figure 5. X-ray crystallography image of the trans-39 product¹

Results Cont.

- Proposed reaction mechanism pathway of trans-39

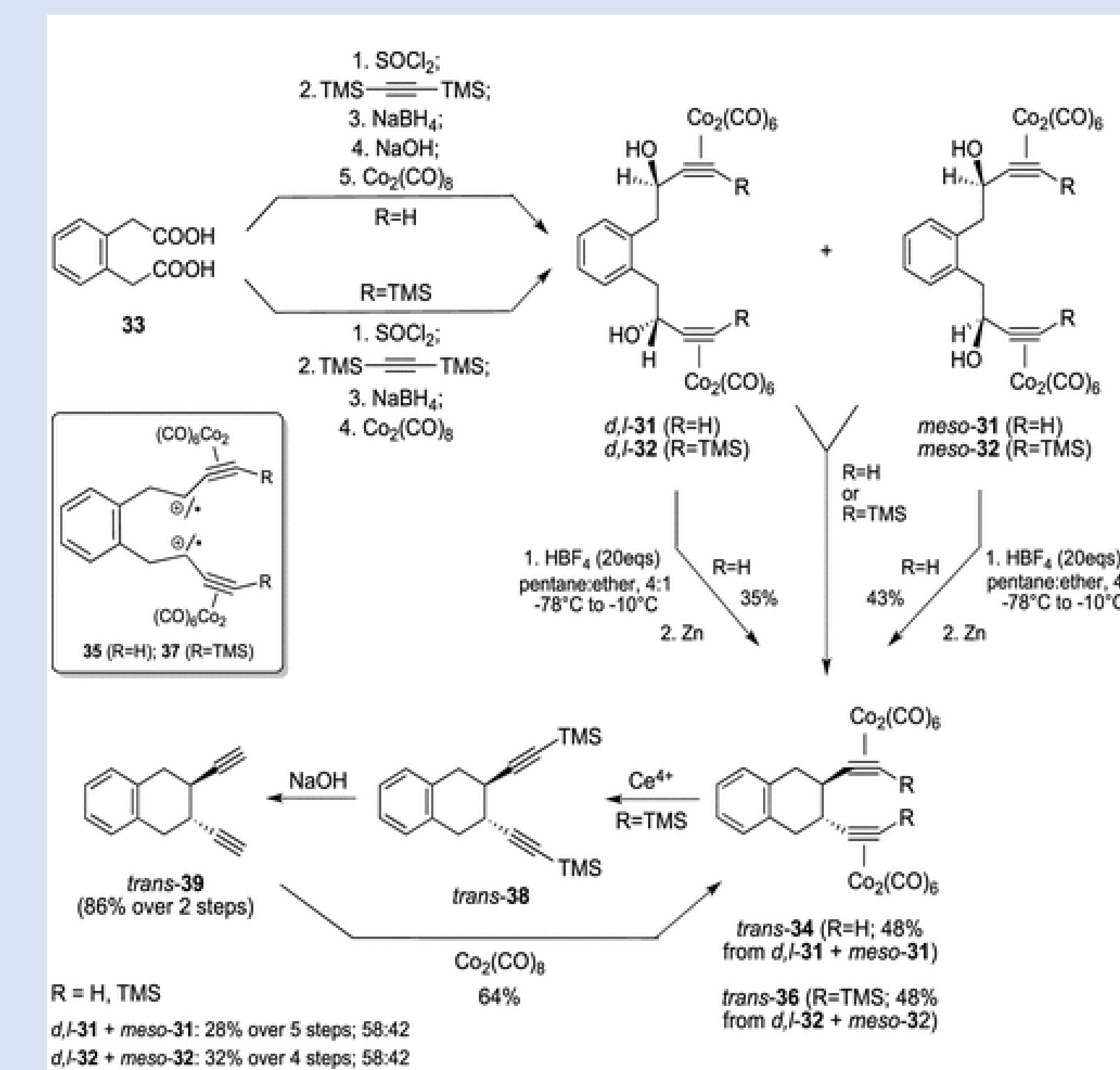


Figure 6. Proposed reaction mechanism for the formation of a tetralin¹

Conclusion

Overall, within intramolecular cobalt-mediated radical cyclization reactions, four main items were determined.

- The tethers rigidity (flexible vs rigid)
- Tethers length (C3 vs C4)
- Configuration of propargyl diols (meso vs D,L)
- Degree of substitution of the acetylenic moieties (terminal vs internal)

Future Work

- Future work includes further investigation into the industrial applications of intramolecular cobalt mediated cyclization's.

References

- Melikyan, G. *Organomet. Chem.* **2023**, *42*, 547-564
- Melikyan, G. *Organomet. Chem.* **2023**, *33*, 1, 69-83