Planar Chiral Sulfinyl Diene Iron(0) Tricarbonyl Complexes as a Platform for Diastereoselective Synthesis of Spiroketals

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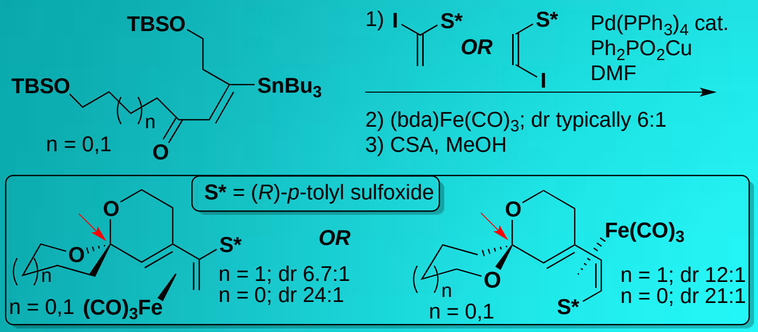
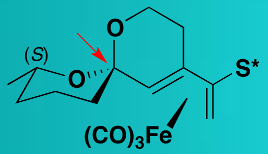
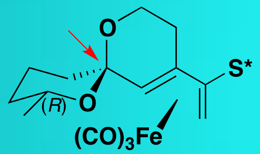


There is significant interest in the synthesis of spiroketals, as these are privileged pharmacophores and are present in numerous natural products. We have demonstrated that an element of planar chirality (an iron(0) tricarbonyl diene unit) can influence the absolute stereochemistry of a spiroketal stereocenter. We are seeking to expand the scope of this chemical transfomation and to determine if the selectivity (diastereomeric ratio, dr) can be maintained or improved.

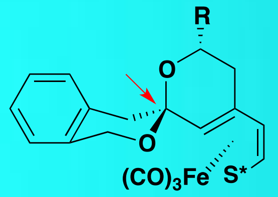


46:1 (matched)
O atom *anti* to $Fe(CO)_3$



1:9 (mismatched)
O atom *syn* to $Fe(CO)_3$

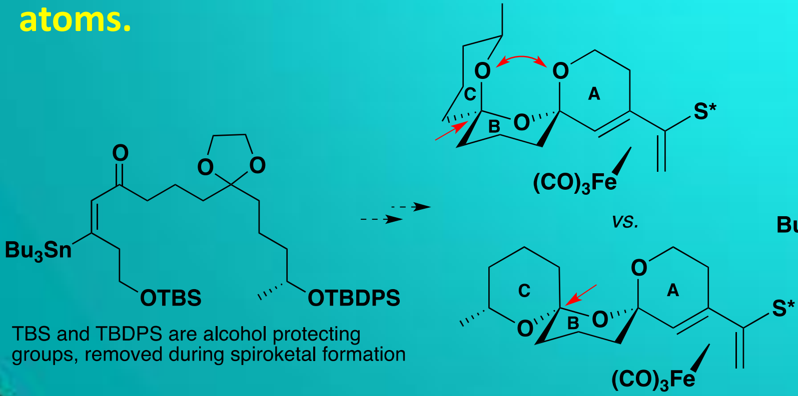
The addition of a stereocenter can enhance the selectivity directed by the planar chirality or it can overwhelm it. The added methyl prefers to be equatorial.



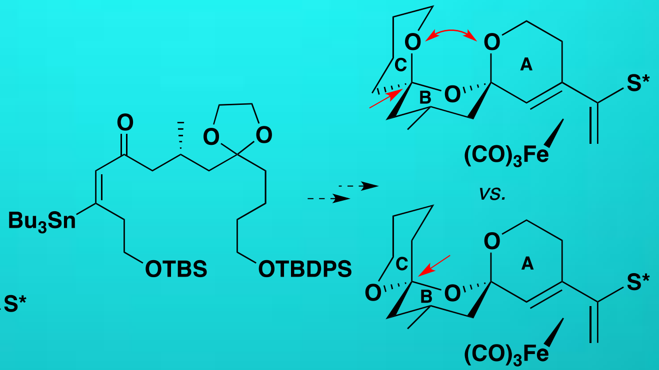
R = **H**; dr 5.5:1
R = **CH_3**; dr > 40:1

With an aromatic fused to the spiroketal precursor the ideal ring conformation is distorted, and selectivity Is diminished. But addition of a single stereocenter (when R = methyl) restores selectivity.

Making bisspiroketals selectively Is a greater challenge. Replusion between the A-ring and C-ring oxygen atoms can reduce the likelihood that the B and C rings are arranged in the otherwise preferred orientation with mutually axial O atoms.



TBS and TBDPS are alcohol protecting groups, removed during spiroketal formation



We hope to learn about The relative impact of these influences by applying lessons learned in the simpler cases by adding a stereocenter in order to bias the selectivity.