Appendix 2

Evaluation of *ee* by chiral GC and by ^{1}H NMR with the chiral shift reagent Eu(hfc)$_3$.

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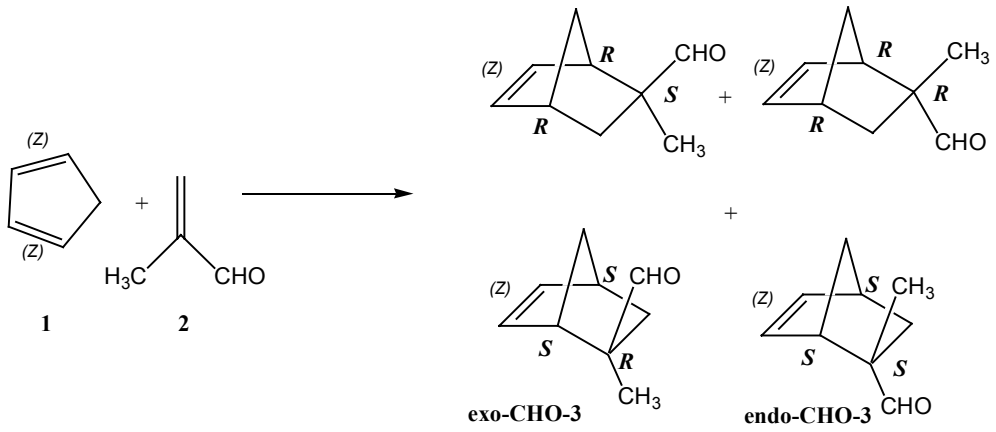
A. Chiral GC.

A cycloaddition of cyclopentadiene to methacrolein, in principle, yields four norbornene adducts: two diastereoisomers, namely **exo-CHO-3** and **endo-CHO-3**, and two enantiomers, ***R*** and ***S*** for each diastereomer..

An achiral cycloaddition (no catalyst or an achiral Lewis acid) yields more ***exo*** diastereoisomer than ***endo*** (see the Table at the bottom of ***Fig. 1***). Each diastereoisomer is a racemic mixture (50% ***R***+50% ***S***).

A chiral catalyzed cycloaddition preserves and enhances substantially the amount of the **exo** norbornene derivative, but also favors one enantiomer over the other.



catalyst	solvent	temp	time	exo:endo	R	S
no	THF	RT	8h	5.6:1	50%	50%
BLn* (L-Tartaric acid)	CH_2Cl_2	-78 C	24 h	94 : 6	92.4%	7.6%
BLn* (D-Tartaric acid)	CH_2Cl_2	-78 C	24 h	92 : 8	11%	89%

Fig. 1. Cycloaddition of cyclopentadiene to methacrolein under uncatalyzed and chiral catalyzed conditions.

The chiral (Supelco ALPHADEX120[2]; oven temperature isotherm of 65 °C) GC traces for a crude sample resulted from the uncatalyzed (***Fig.2***) and Lewis acid chiral

[1] Send your comments to mircea@mit.edu.

[2] **Cyclodextrin (CD) is a chiral component in the stationary phase of a DEX capillary column. Cyclodextrins are cyclic oligomers of six or more molecules of D(+)-glucose linked through α(1-4) glycosidic bonds. In**

boron catalyzed cycloaddition of cyclopentadiene to methacrolein (***Fig. 3*** and ***Fig. 4***)[3] are:

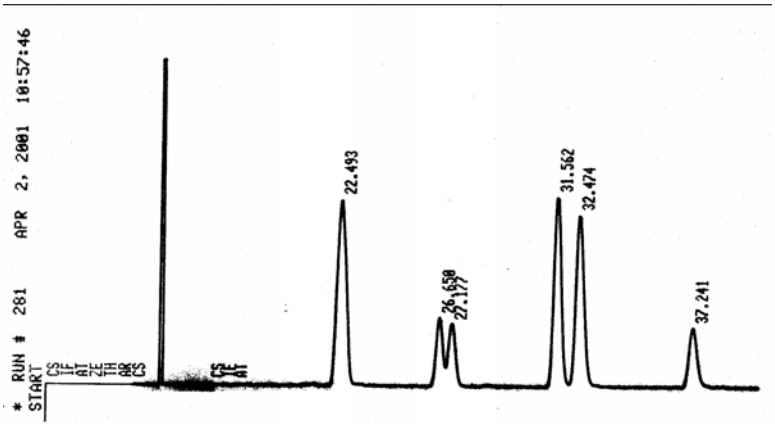


Fig. 2. **Chiral GC trace of the crude product mixture resulted from cyclopentadiene cycloaddition to methacrolein.**

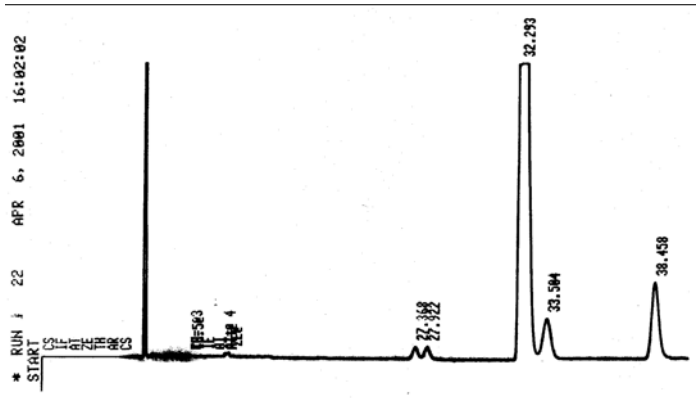


Fig. 2. **Chiral GC trace of the crude product mixture resulted from the cyclopentadiene cycloaddition to methacrolein in** the **presence of the chiral boron catalyst synthesized from the L-tartaric acid precursor.**

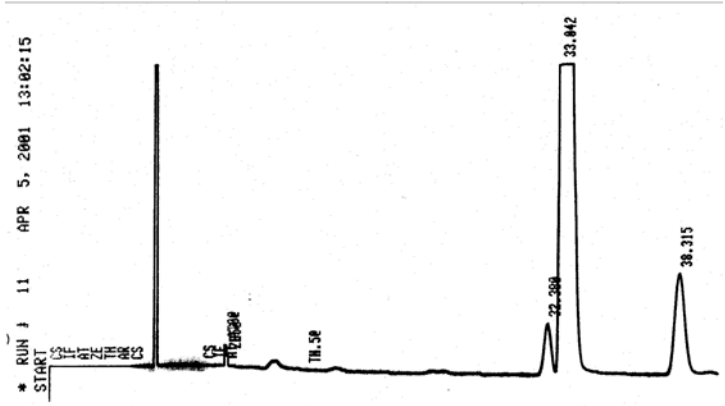


Fig. 3. **Chiral GC trace of the crude product mixture resulted from the cyclopentadiene cycloaddition to methacrolein in the presence of the chiral boron catalyst synthesized from the D-tartaric acid precursor.**

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particular, α-CD contains six residues of glucose. The size of the torus-shaped cavity is 4.7-5.2 Å. The stationary phase of the ALPHADEX120 is formed from 20% permethylated α-CD in poly(35% phenyl / 65% dimethylsiloxane).

[3] **Samples provided by Emilie, Michelle, Jeremy, Elisa, Kathryn (5.32-2002).**

GC peak identification.

- GC/MS peaks at **RT: 31.562, 32.474 and 37.141 min** are due to **exo-** and **endo-CHO-3**, respectively, because all display in GC/MS a molecular ion at 136. Based on the relative peak intensities of CHO signals in ^{1}H NMR, it is clear that the major diastereoisomer is **exo-CHO-3.** Therefore, the peaks corresponding to **RT 31.562 min and 32.474 min are due to *R*** and ***S* exo-CHO-3**, respectively.
- The earlier two peaks (26.650 min and 27.177 min) are due to the enantiomers of the cyclopentadiene dimer (molecular ion 132)!
- The peak at 22.493 min is due to the methacrolein dimer (molecular ion 140).

Asymmetric cycloadditions:

The enantiomeric excess (***ee***) is defined as follows:

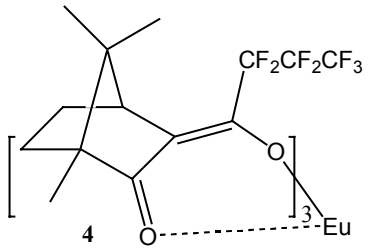
$$ee(\%) = \frac{|I_R - I_S|}{I_R + I_S} x100$$

I_R (or I_S) is the intensity (%) of the respective peak in the GC output. The Table from the bottom of ***Fig. 1***, provides the actual ***ee*** values calculated for the cycloadditions carried out with the chiral boron catalyst resulted from the precursors of tartaric acids enantiomers.

When the chiral catalyst precursor is derived from the (2***R***,3***R***)-tartaric acid (natural), the Diels-Alder adduct **exo-CHO-3** has the ***R*** configuration. The ***S*** enantiomer of the **exo-CHO-3** is formed when the catalyst is derived from (2***S***,3***S***)-tartaric acid.

B. NMR with shift reagents[4].

Enantiomers are not differentiated in the NMR spectrum: the probe is isotropic. However, diastereoisomers display different chemical shifts. Diastereoisomer complexes are formed by mixing the chiral shift reagent Eu(hfc)$_3$ (**4**), with a mixture of enantiomers of **exo-** and **endo-CHO-3** (in $CDCl_3$ solution). Because the shift reagent **4** is a Lewis



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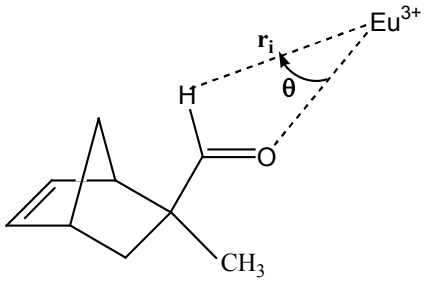
Europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate]
Eu(hfc)$_3$
very hygroscopic

[4] *Lanthanide Shift Reagents in Stereochemical Analysis*, Morril, T. C., Ed., VCH Publishers: New York, 1986.

acid, the Eu^{3+} coordinates[5] at the oxygen of C**H**O. Eu^{3+} induces a spreading of the chemical shifts over a wider range of the spectrum according to the McConnell-Robertson[6] equation: $\Delta = \mathbf{K}\frac{3\cos\vartheta - 1}{\mathbf{r}_i^3}$. Δ is the "pseudocontact shift", r_i and θ are defined in the figure:



Since the proton from the C**H**O is very close to Eu^{3+}, it is anticipated to experience a large pseudocontact shift, shown by the arrows in ***Fig. 5.*** There are two H NMRs presented in this figure. In the right, the undopped H NMR, in which the larger singlet at 9.69 ppm is assigned to **exo-CHO** and the smaller singlet at 9.40 ppm that is assigned to **endo-CHO**. After adding $Eu(hfc)_3$,all the **CHO** moved downfield and became split in a 1:1 ratio.

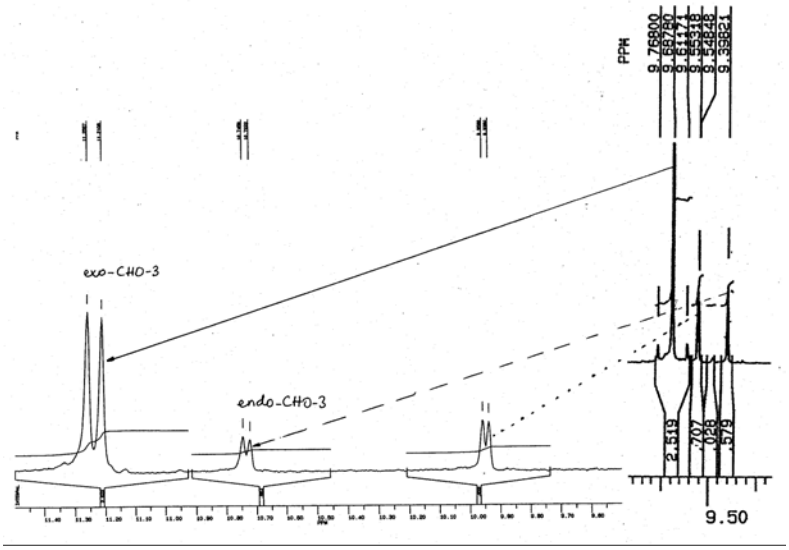


Fig. 5. The displacement and split of **CHO** signals as result of added $Eu(hfc)_3$ to crude **exo-CHO-3** and **endo-CHO-3** resulted in the uncatalyzed cycloaddition of cyclopentadiene to methacrolein.

At this time, there are no available Lanthanide Induced Shift (LIS)-H NMR data from catalyzed experiments. We hope to get these results from the work done by the third rotation. As for the chiral GC, the enantiomeric excess results according to the

[5] Eu^{3+} is paramagnetic ($4f^6$) and has short electron-spin relaxation time ($<10^{-12}$ s). Therefore, it induces H NMR shifts without appreciable line broadening.
[6] McConnell, H. M.; Robertson, R. E. *J. Chem. Phys.*, **1958**, *29*, 1361.

equation: $\boldsymbol{ee} = \frac{|\mathbf{I_R} - \mathbf{I_S}|}{\mathbf{I_R} + \mathbf{I_S}} \mathbf{x}100\mathbf{(\%)}$. I_R and I_S are the magnitude of the integrals of LIS induced aldehyde proton signals (for enantiomer ***R*** and ***S***).