CHEM60001: An Introduction to Reaction Stereoelectronics

LECTURE 7 Problem Class Answers

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Ley dispiroketal formation – the product forms as a single diastereomer as the result of its formation being under thermodynamic control. The product observed is stabilised by four anomeric effects ($n_O \rightarrow \sigma_{CO}$).
Question 2 (parts I & ii)

**Grob fragmentation**

**Mechanism**

Interacting orbitals:

\[
\begin{align*}
\text{initiation} & : \text{RB(OH)}_2 \rightarrow \text{RB(OH)}_3^6 \\
\sigma_{C-B} & \rightarrow \sigma^*_{C-B} \\
& \text{(better donor, higher energy)}
\end{align*}
\]

**NB.** bold bonds are all anti-periplanar with respect to each other. The blue pathway is followed because it leads to the more substituted alkene products - i.e. the sigma conjugation that stabilises the more substituted alkene products is also important in the transition state(s) for this rearrangement

1) \( \sigma_0 \rightarrow \sigma^*_{\text{C-B}} \) (OH- attacks boronic acid)
2) \( 3\times \sigma_0 \rightarrow \sigma^*_{\text{C-B}} \)
3) \( \sigma_{\text{C-B}} \rightarrow \sigma^*_{\text{C-C}} \) (C-B bond cleavage, C=C bond formation, & C-C bond cleavage)
4) \( \sigma_{\text{C-C}} \rightarrow \sigma^*_{\text{C-O}} \) (C=C bond formation and C-O bond cleavage)
Question 3 (parts i & ii)

This reaction was reported by R.B. Woodward as part of his classic synthesis of prostaglandin F2α [Woodward J. Am. Chem. Soc. 1973, 95, 6853 (DOI)].

Mechanism & stereochemistry: Tiffaneau-Demyanov semi-pinacol rearrangement?

Interacting orbitals:

NB. bold bonds are all anti-periplanar with respect to each other

1) n₀ → σ∗_C-C (oxygen lone pair interacts with C-C anti-bond forming C=O bond)
2) σ₀_C-C → σ∗_C,N (suprafacial C-C bond migration, & C-N bond cleavage)
OR...Grob fragmentation-aldol reaction?

Mechanism & stereochemistry:

Interacting orbitals:

1) \( n_O \rightarrow \sigma^*_{C-C} \) (oxygen lone pair interacts with C-C anti-bond forming C=O bond)
2) \( \sigma_{C-C} \rightarrow \sigma^*_{C-N} \) (C-C bond cleavage & C=C bond formation)

**NB.** Prof Henry Rzepa has performed some density functional calculations and at the B3LYP/6-31G(d) level and the Tiffeneau-Demjanov pathway is lower in energy by ~ 5.6 kcal/mol: see: