CHEM60001:
An Introduction to Reaction Stereoelectronics

LECTURE 7 *Problem Class Answers*

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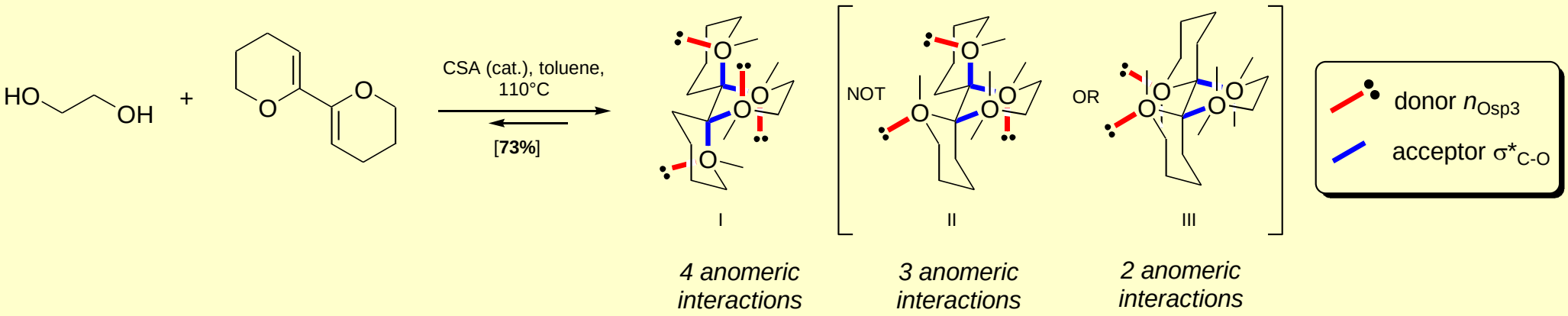
Question 1 (parts i & ii)

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 ($n_O \rightarrow \sigma_{CO}$).



4 anomeric interactions

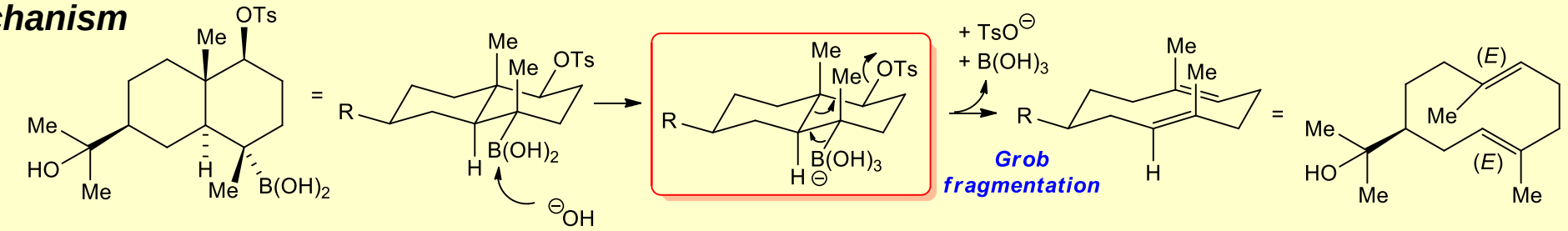
3 anomeric interactions

2 anomeric interactions

Question 2 (parts I & ii)

Grob fragmentation

Mechanism

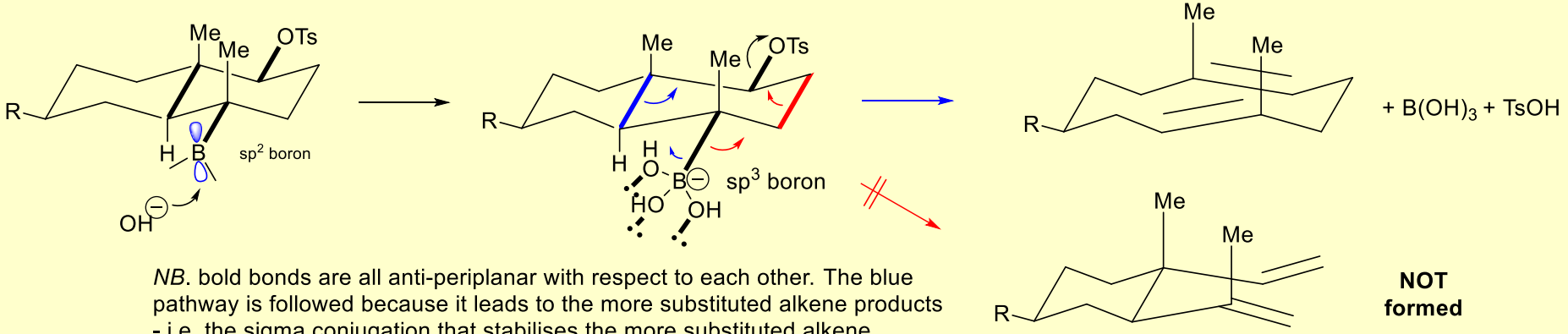


'initiation' *RB(OH)$_2$ -> RB(OH)$_3^{\ominus}$*

$\sigma_{C\text{-}B}$ becomes $\sigma_{C\text{-}B}^{\ominus}$

(better donor, higher energy)

Interacting orbitals:



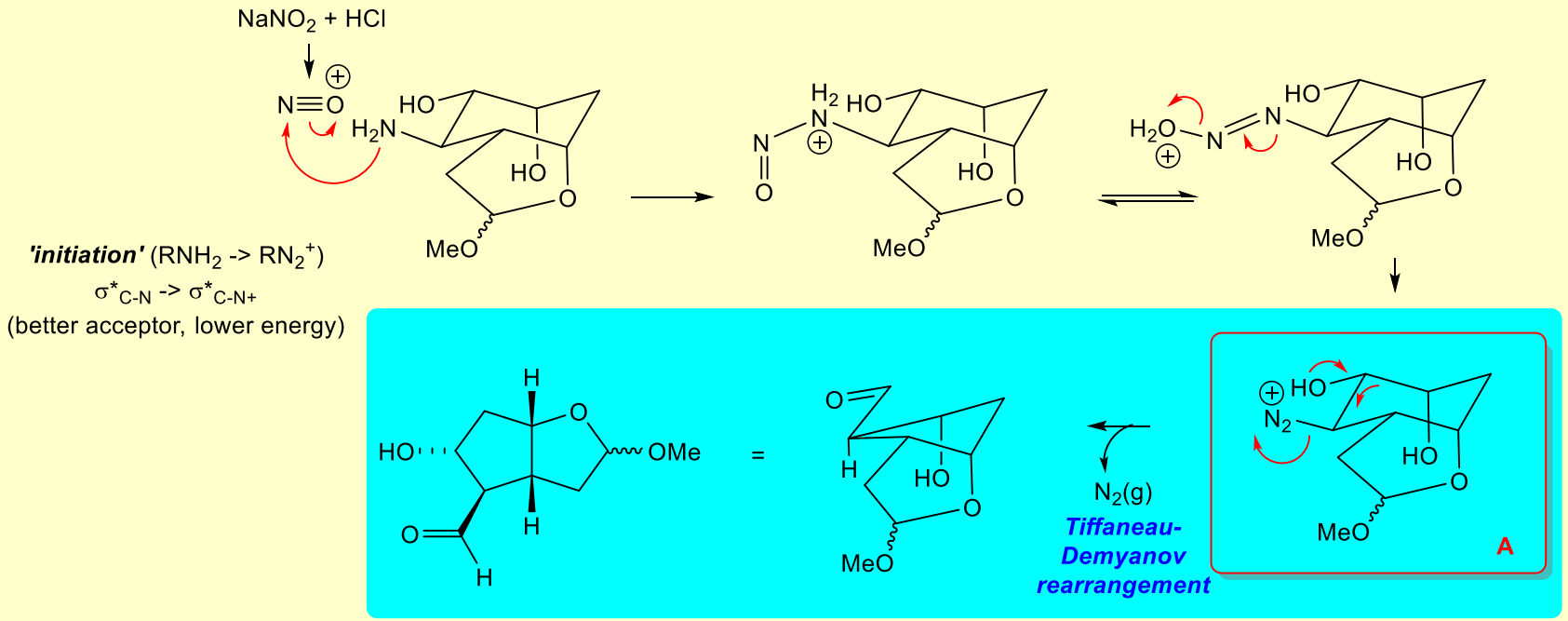
NB. bold bonds are all anti-periplanar with respect to each other. The blue pathway is followed because it leads to the more substituted alkene products - i.e. the sigma conjugation that stabilises the more substituted alkene products is also important in the transition state(s) for this rearrangemnt

1) n_O -> $p_{vac\ on\ B}$ (OH- attacks boronic acid)
2) 3x n_O -> $\sigma^*_{C\text{-}B}$
3) $\sigma_{C\text{-}B}$ -> $\sigma^*_{C\text{-}C}$ (C-B bond cleavage, C=C bond formation, & C-C bond cleavage)
4) σC-C -> σ*C-O (C=C bond formation and C-O bond cleavage)

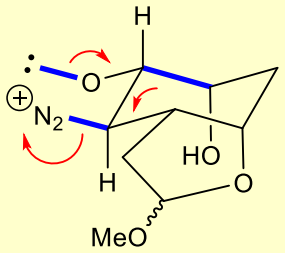
Question 3 (parts i &ii)

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:



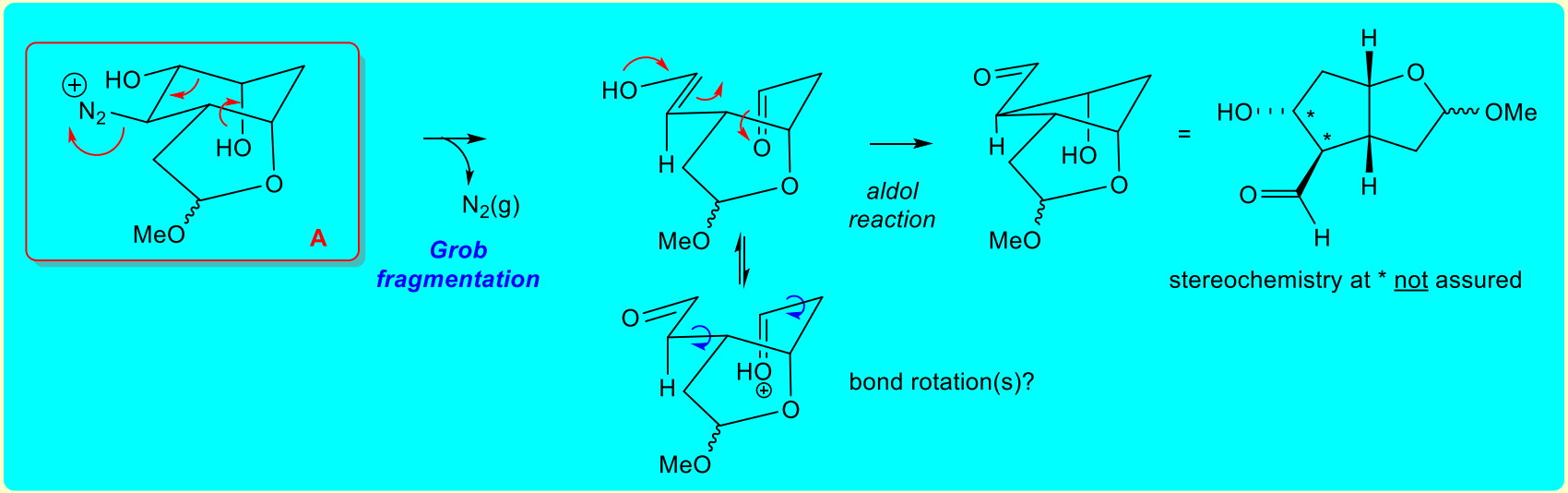
NB. bold bonds are all anti-periplanar with respect to each other

1) n_O -> $\sigma^*_{C\text{-}C}$ (oxygen lone pair interacts with C-C anti-bond forming C=O bond)
2) $\sigma_{C\text{-}C}$ -> $\sigma^*_{C\text{-}N}$ (suprafacial C-C bond migration, & C-N bond cleavage)

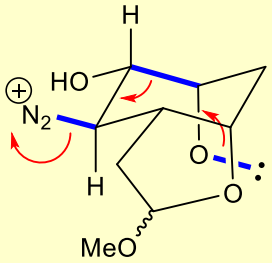
Question 3 cont.

OR...Grob fragmentation-aldol reaction?

Mechanism & stereochemistry:



Interacting orbitals:



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

1) n_O -> $\sigma^*_{C\text{-}C}$ (oxygen lone pair interacts with C-C anti-bond forming C=O bond)
2) $\sigma_{C\text{-}C}$ -> $\sigma^*_{C\text{-}N}$ (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:***
- **http://www.ch.ic.ac.uk/local/organic/tutorial/synoptic/q2a.html**