CHEM50002: Orbitals in Organic Chemistry - Stereoelectronics

OUTLINE ANSWERS

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1. (i) Compound (2)

(ii) The dispiroketal forms as a single diastereomer as the result of its formation being under thermodynamic control. The product observed is stabilised by four anomeic effects ($\text{n}_\text{O}$→$\sigma^{*}\text{C-OS}$).

\[ \text{HO-CH(OH)(CH(OH))}_2 + \text{CSA (cat.), toluene, 110°C} \rightarrow \text{I (73%)} \]

2. (i & ii) The mechanism and key orbital interactions are indicated below. Any acceptable diagrams showing the shapes of the interacting sigma and sigma star orbitals are OK.

3. 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)].

(i) The mechanism shown below is via a Tiffeneau-Demjanov rearrangement (i.e. semipinacol, where the leaving group is a diazonium salt) and includes the method of formation of the diazonium salt ‘starting material’ (A) given in the question.
(ii) See below. Any acceptable diagram(s) showing the shapes and/or orientation of the interacting sigma and sigma star orbitals is OK.

![Diagram showing the shapes and/or orientation of the interacting sigma and sigma star orbitals.](image)

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

1) $n_0 \rightarrow \sigma^*_{C-C}$ (oxygen lone pair interacts with C-C anti-bond forming C=O bond)
2) $\sigma_{C-C} \rightarrow \sigma^*_{C-N}$ (suprafacial C-C bond migration, & C-N bond cleavage)

The above pathway accounts for the stereochemistry of the product actually obtained in the experiment. However, the reaction may proceed via an alternative pathway involving a Grob fragmentation followed by an aldol reaction. This pathway is consistent with the stereochemical result but does not assure this outcome:

![Diagram showing the Grob fragmentation followed by an aldol reaction.](image)

The orbitals involved are:

![Diagram showing the orbitals involved.](image)

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

1) $n_0 \rightarrow \sigma^*_{C-C}$ (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: