Third Year Reactive Intermediates: Radicals, Arynes, Carbenes etc.

Radicals

References:
Moody and Whitham "Reactive Intermediates," Oxford Chemistry Primer 8; Carey and Sundberg "Advanced Organic Chemistry" Part A, Chapter 12 and Part B, Chapter 10; March "Advanced Organic Chemistry" 4th ed., Chapters 5, 7 + 14;

Notes:
Augment your notes from 2nd/3rd year lectures to ensure they include the following:
1. Radical Generation: Thermolysis of weak bonds; Photolysis of weak bonds; 1-electron redox chemistry; Chain processes; Selectivity and reactivity; Polar effects (nucleophilic and electrophilic radicals) and "polarity matching"
2. Synthesis with radicals: Reactions between radicals and non-radicals; Reactions between radicals and other radicals; Types of reactions (addition, substitution, elimination, rearrangement, electron transfer ($S_{RN}1$); Use in making C-C, C-H and C-Hal bonds; Stereochemical effects; Cyclisations and Baldwin's Rules.
3. Specific Topics: Bu_3SnH reductions; Barton-thiohydroxamic esters; Barton-remote functionalisation (nitrite ester photolysis); Radicals in aromatic substitution e.g. diazonium salts + Cu(I); Kolbe synthesis; Hunsdiecker reaction; Fremy's salt; Birch reduction, acyloin reaction and reductive dimerisation of ketones.

Other Reactive Intermediates

Reading: Lecture Notes (for reference when you have them); "Reactive Intermediates", Moody and Whitham, OCP no 8; "Polar Rearrangements", L. M. Harwood, OCP no 5

Carbocations and Carbanions

Structure and Reactivity a) Basics; susceptibility to nucleophiles / electrophiles, e- rich or poor species etc. b) Pyramidal inversion for C- and exceptions, planarity of C+. c) Evidence ego C+ - kinetics of S_N1, solvent and substituent effects (Hammet plots), crystal structures i.e. bond lengths and hyperconjugation, stable C+. d) Formation e.g. C- - S_E1, Li-halogen exchange, deprotonation etc.
Reactions a) Rearrangements: concerted vs stepwise arguments (both C+ and C-). b) C- as nucleophiles, bases, reducing agents (via SET).

Carbenes

Structure and Reactivity
a) singlet and triplet states
b) substituent effects on reactivity
c) evidence for structures i.e. matrix isolation, ESR etc

Generation
a) Diazo Compounds - stabilisation by carbenoid formation with TM complexes
b) Tosylhydrazones - Bamford Stevens Reaction
c) Ketenes - tendency to polymerise
d) Strained Rings - eqm driven by relief of ring strain

e) Ylides - formal equivalents ie carbene transfer reagents
f) Strained Alkenes - only if sterically unfavourable
g) Heterocycles - if provides stable fragment but needs high T
h) a - Elimination - note ease of elimination I > Br > Cl > F
i) Simmons Smith Reaction – stereospecificity

Reactions
a) Cycloadditions - Skell Hypothesis - ring enlargement with aromatic compounds
b) Insertion into C-H - stereochemical consequence of singlet / triplet – chemoselectivity - substituent effects
c) Insertion into X-H
d) Rearrangements i) facile process due to electrophilic nature; ii)Wolff rearrangement (use in Arndt Eistert Rxn); iii) Skattebol Rearrangement
e) With Nucleophiles - Ylid formation and Riemer Tiemann Rxn of phenoxides.

Nitrenes - note similarity to carbenes
Structure and Reactivity
a) singlet and triplet states
b) substituent effects on reactivity
c) evidence - low T matrix isolation studies, ESR etc...

Generation
a) Azides
b) Isocyanates - hν only
c) Oxidation of hydrazines - with Pb(IV), MnO2 etc
d) Ylides
e) Small rings - hν on oxaziridines
f) Heterocycles - if stable fragment formed
g) Elimination - base mediated h) Reduction - of nitro / nitroso groups with P(III)

Reactions
a) Cycloadditions i. aziridine formation; ii. ring expansion with aromatics
b) Insertion - selectivity of C-H
c) Rearrangements - possible involvement in rearrangement to electron deficient N => Hofmann, Lossen and Curtius rearrangements
d) With nucleophiles - ylid formation

Arynes
Structure and Reactivity
a) possibility of o- / m- / p- derivatives
b) evidence for structures
c) stabilisation by complexation

Generation
a) Aryl anions - isotopic labelling experiments, directing substituents
b) Zwitterions
c) Thermal / photochemical fragmentation - if form thermally stable fragment
d) Oxidative Fragmentation
e) Bergmann Cyclisation of 1, 3 enediynes

Reactions

a) Cycloaddition – only if generated in the absence of a nucleophile; Diels Alder, Ene, [2+2] reactions etc 1,3 dipolar additions, trimerisation reaction etc
b) Nucleophilic addition i. order of reactivity; ii. with amines / phosphines etc; iii. steric / electronic substituent effects

2000 Q4. Give mechanisms for **FIVE** of the following reactions which proceed by radical intermediates:

[5 x 4 marks]

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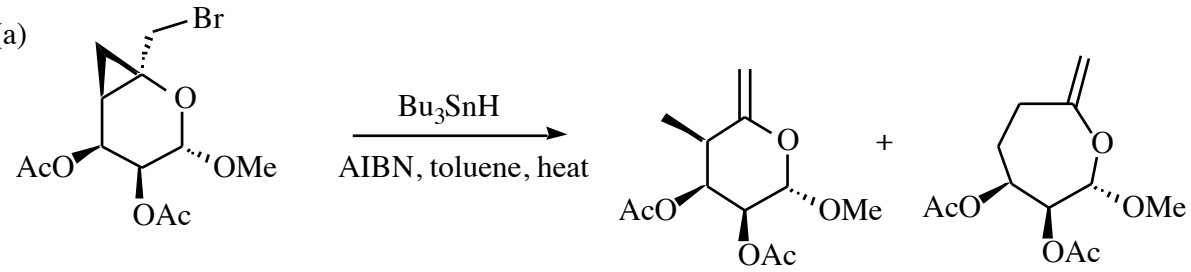

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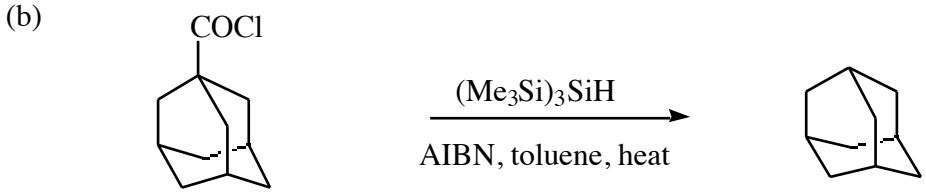

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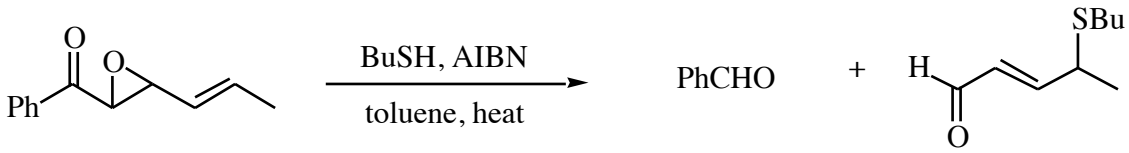

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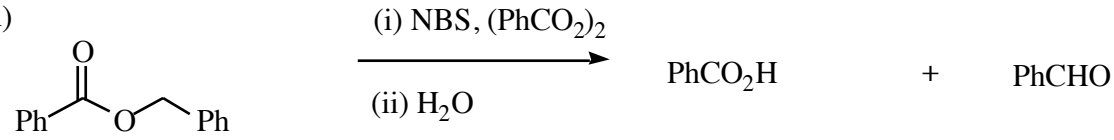

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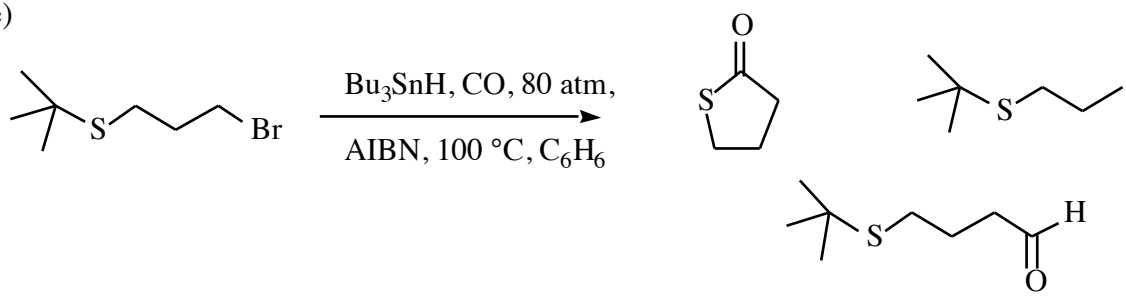

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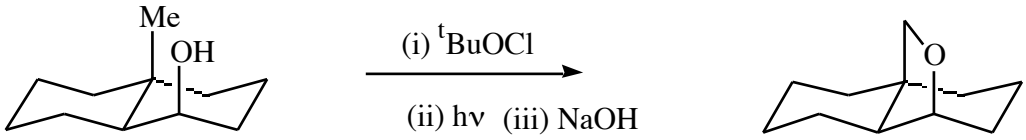

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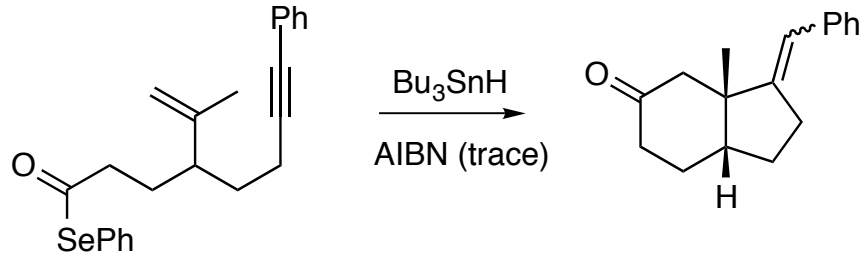
2001 Q4. Provide mechanisms for **FOUR** of the following. **[4 x 5]**

(a)



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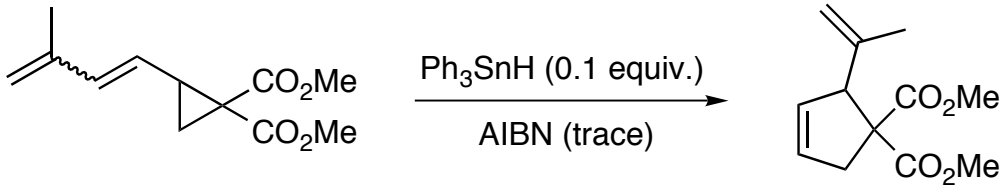

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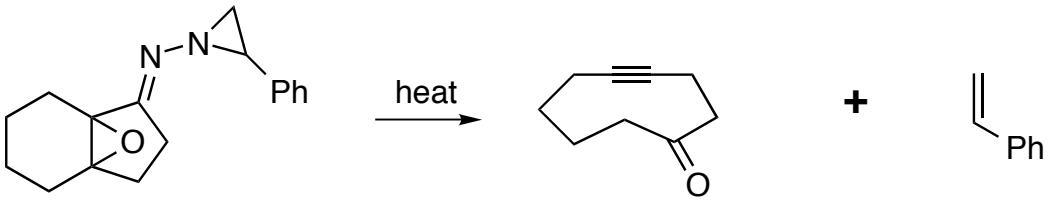

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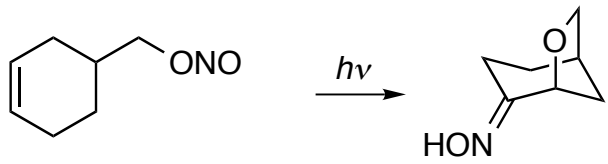

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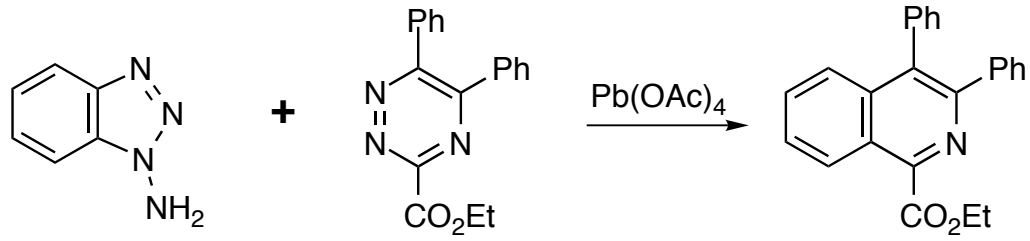

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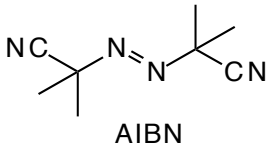
2002 Q2. Answer ***both*** part **A** and part **B**.

Part A. Give mechanisms to explain how ***two*** of the following reagents initiate free radical reactions. **[2 × 2]**

(a) 

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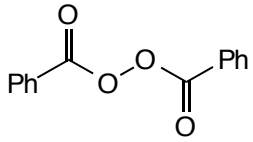
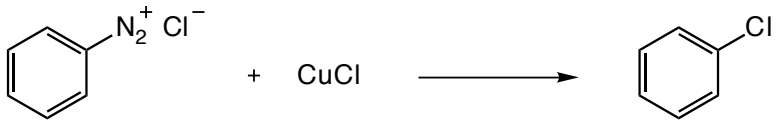
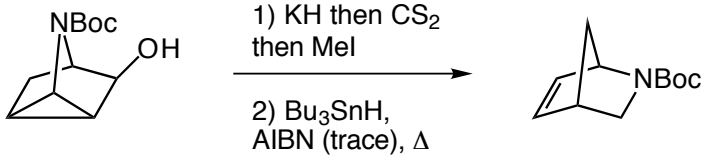
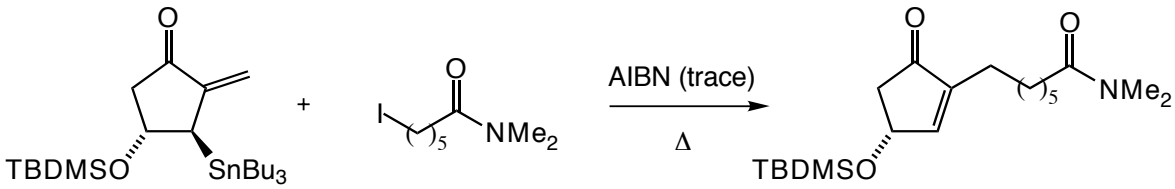
(b) 

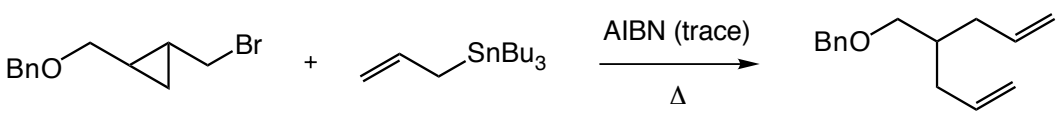
(c) H_2O_2 / Fe^{2+}

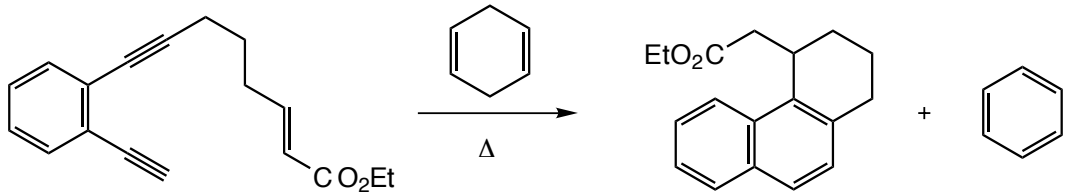
Part B. Explain the chemistry in ***four*** of the following. **[4 × 4]**

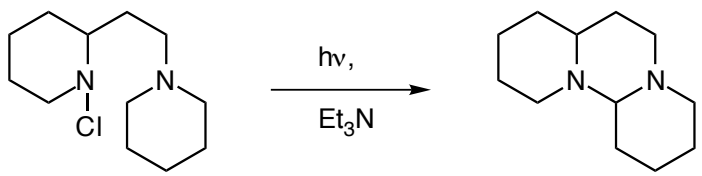
(a) 

(b) 

(c) 

(d) 

(e) 

(f) 

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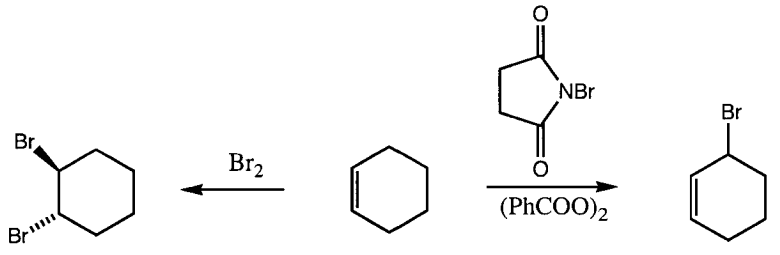
7. Answer ***BOTH*** parts **A and B** of this question.

A. Rationalise the following *THREE* pairs of reactions. **[3 x 4]**

(i)



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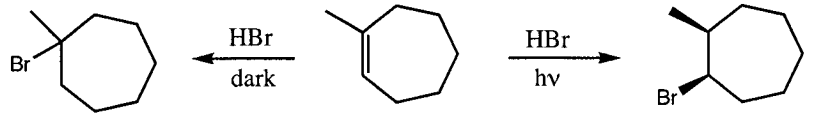

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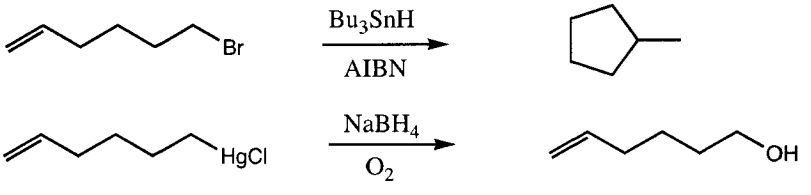
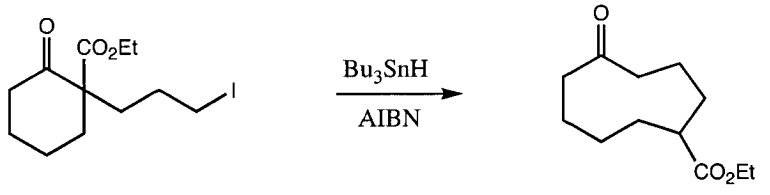


B. Suggest mechanisms for *TWO* of the following reactions. **[2 x 4]**

(i)



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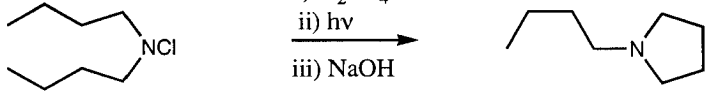

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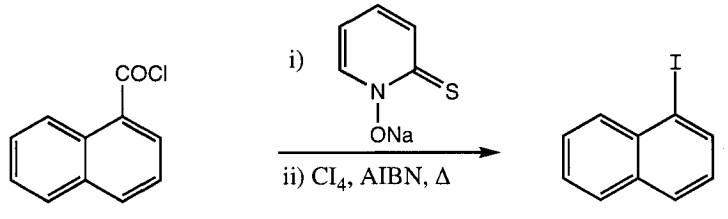
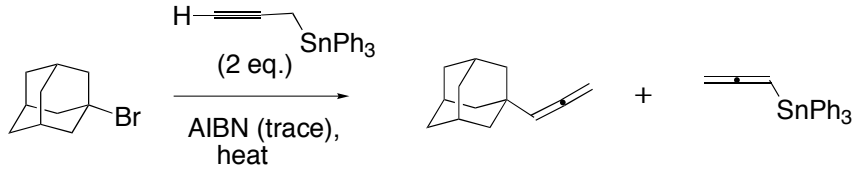


2005 Q6. Give mechanisms for ***five*** of the following processes, and comment on those factors which lead to the observed product outcome.

[5 × 4]

(a)



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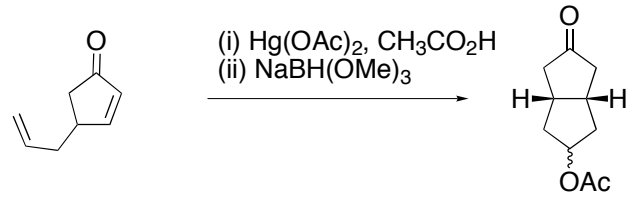

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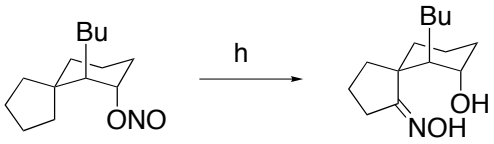

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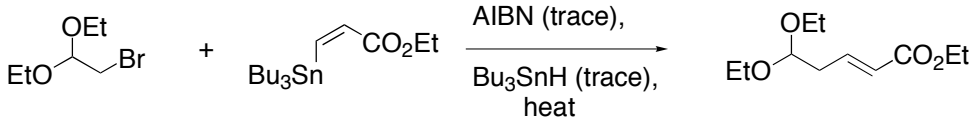

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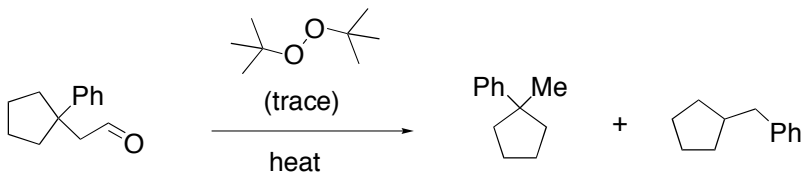

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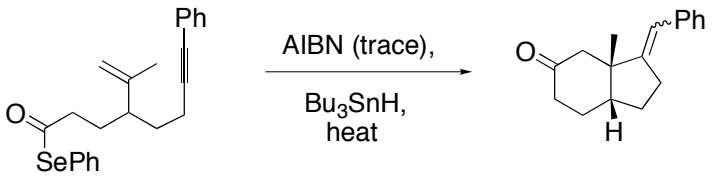


2006 Q5. Answer *both* Parts **A** and **B** of this question.

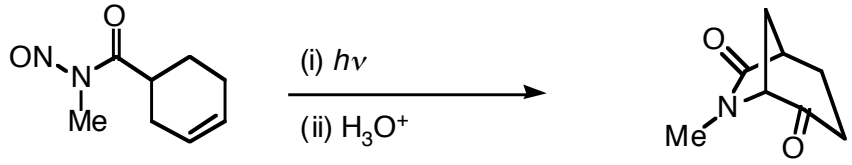
Part A.

Outline the relevance of (i) steric, (ii) resonance and (iii) hybridisation effects upon the stability of carbon based radical intermediates. **[4]**

Part B.

Give mechanisms to rationalise the observed product outcome for ***four*** of the following reactions. **[4 × 4]**

(a)



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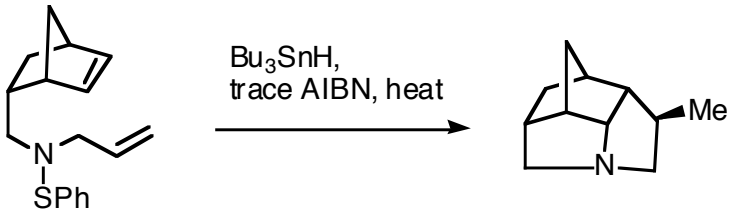

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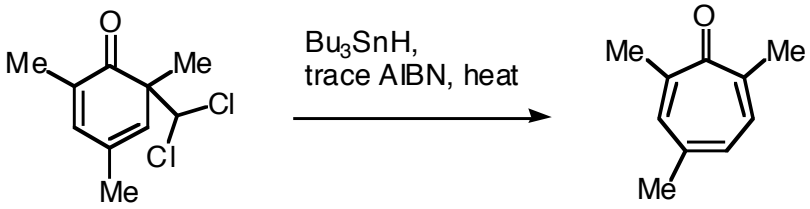

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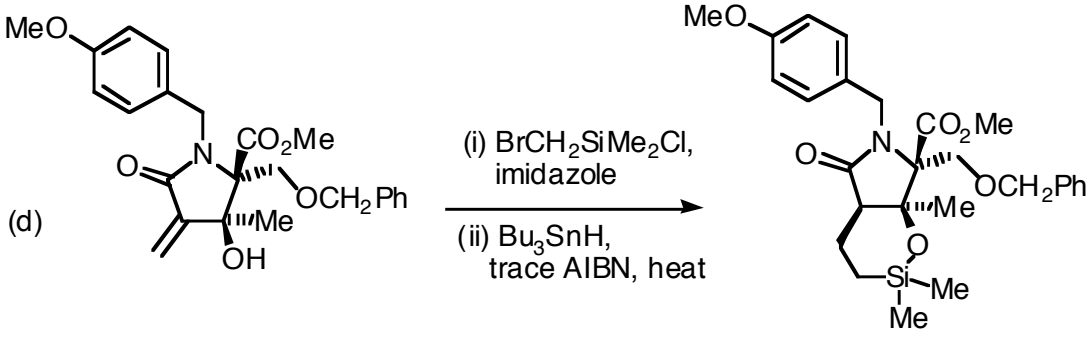

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