



A Radical Interdisciplinary Study

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Aim

Promote the teaching of radicals and their reactions

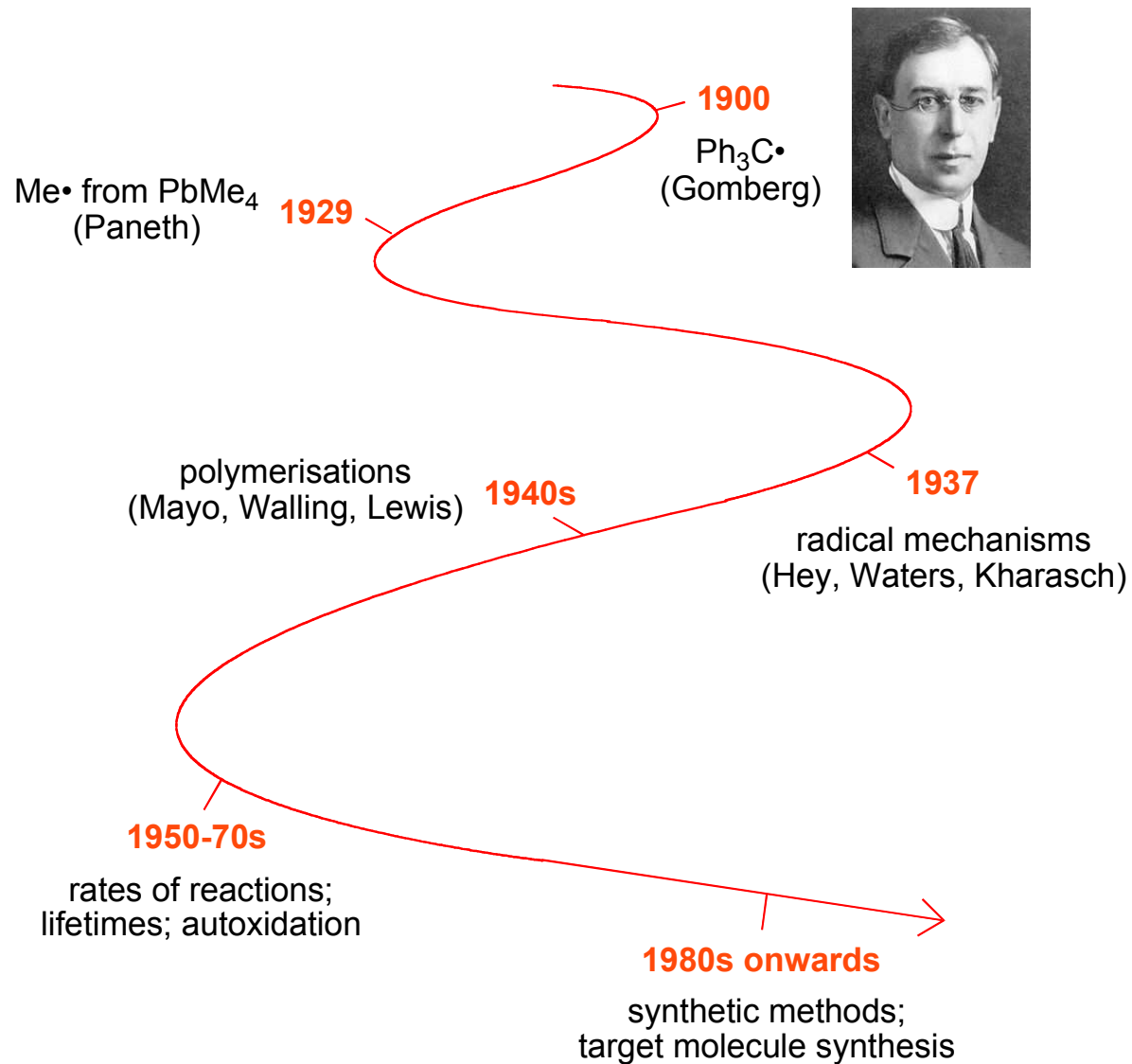
- present ideas for illustrating interdisciplinary research
- to introduce some modern and exciting developments in the area
- use different strategies to introduce the material in an entertaining and fun way

‘How to create memorable lectures’ Mariatte Denman, Stanford University (2005)

‘expressiveness enhances communication and facilitates comprehension’



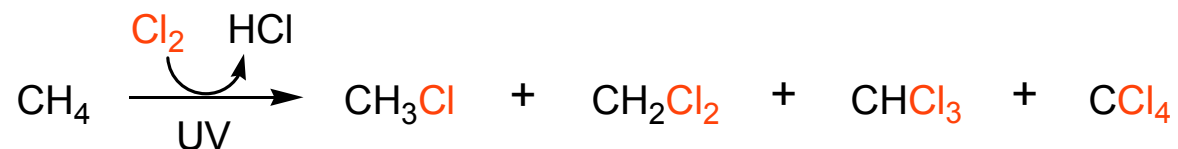
A radical timeline



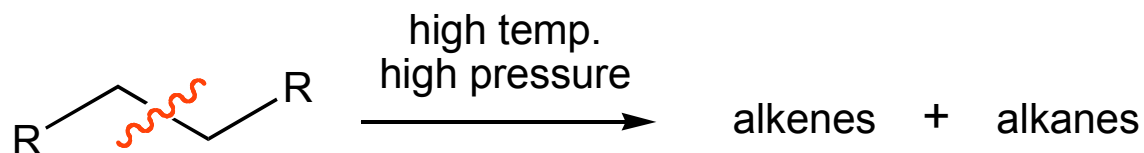


Pre-university – a bad press

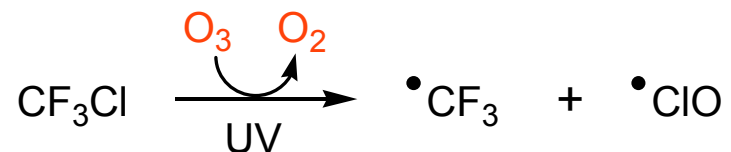
Halogenation of alkanes – unselective



Cracking of alkanes – useful but unselective and harsh conditions



Depletion of the ozone layer – destructive radicals at work (ageing etc)

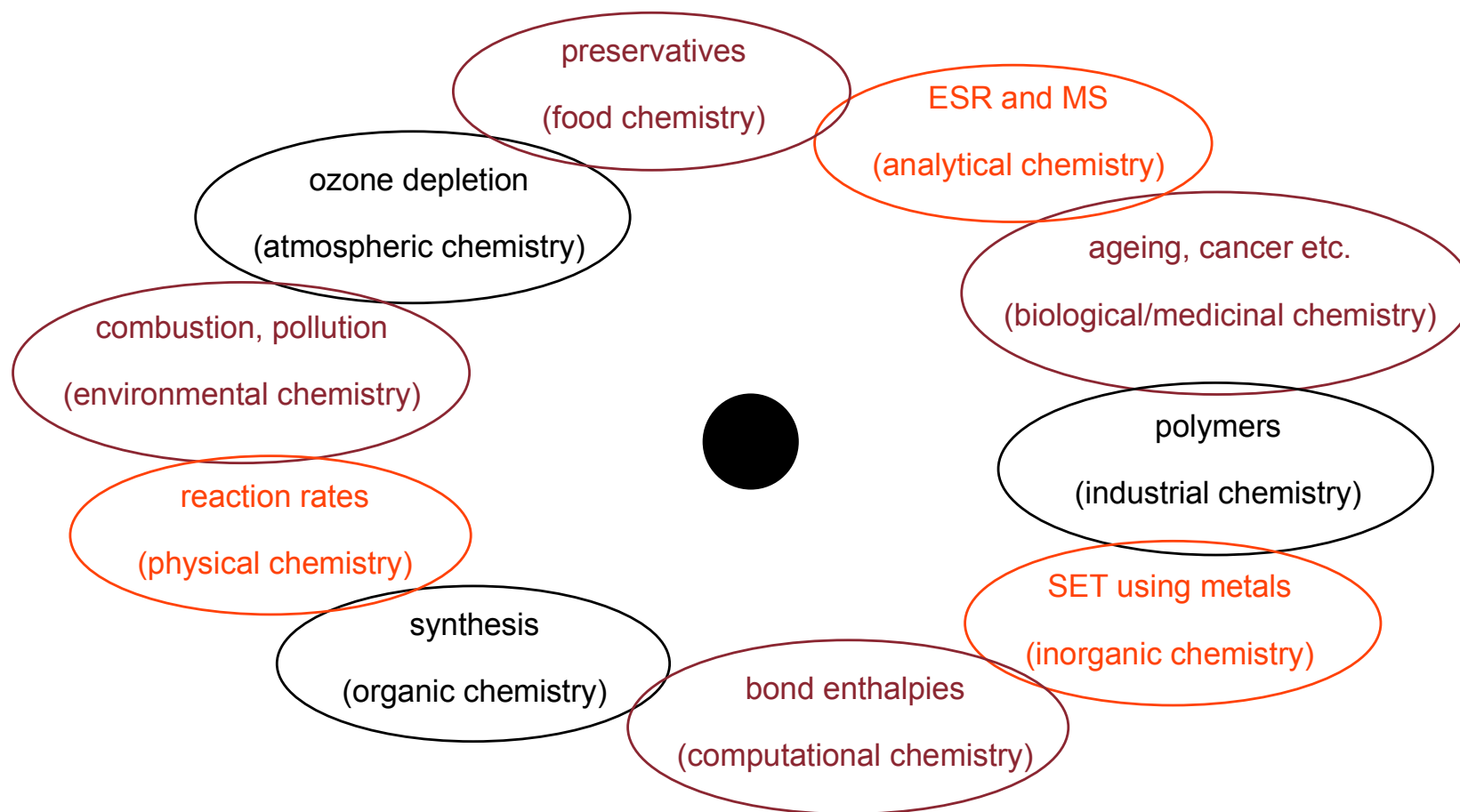


(Polymerisation of alkenes)



A truly interdisciplinary topic

showcases fundamental chemical topics in modern contexts





Contents

Radical structure

Analysis of radical stability

Discuss radical formation

Investigate radical reactions

Consider biomedical/environmental processes

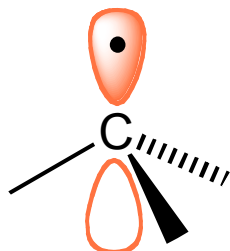
Application in synthesis

Latest developments

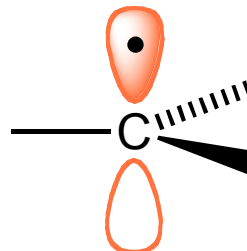


Radical structure

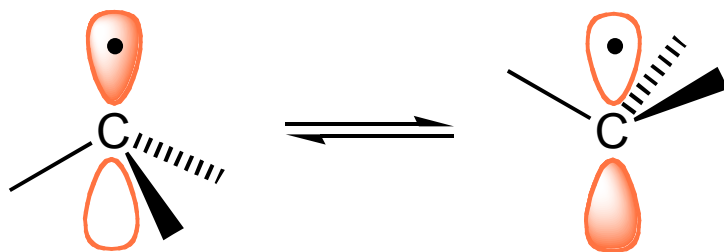
rigid pyramidal



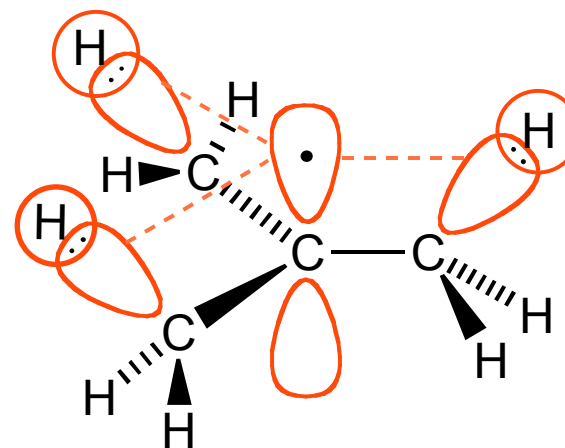
planar



flexible pyramidal



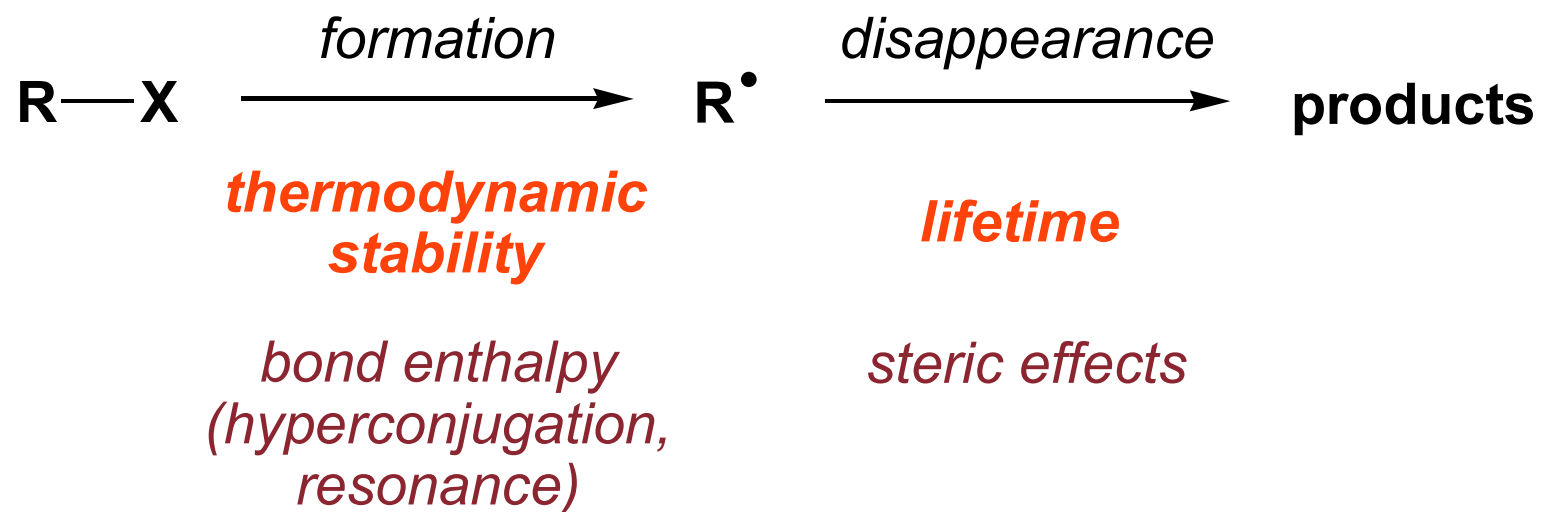
rapid inversion
barrier typically 4–8 kJ mol⁻¹



hyperconjugation



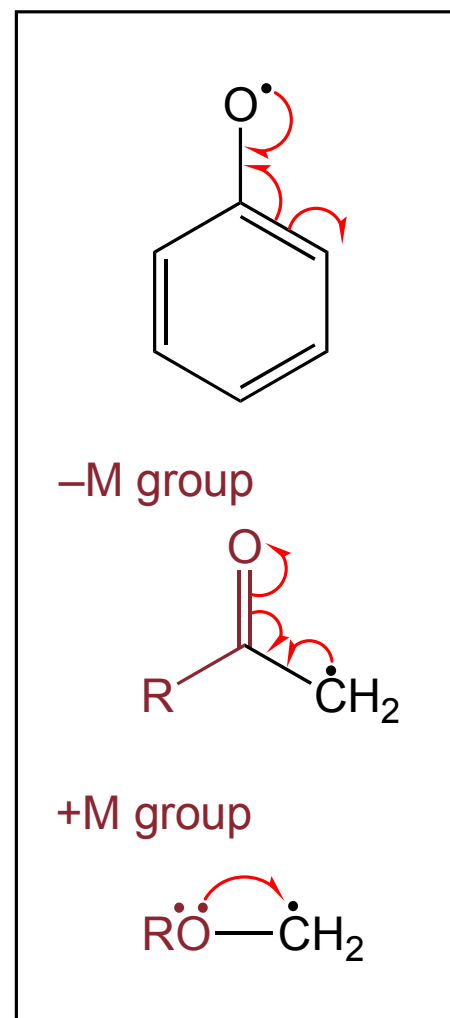
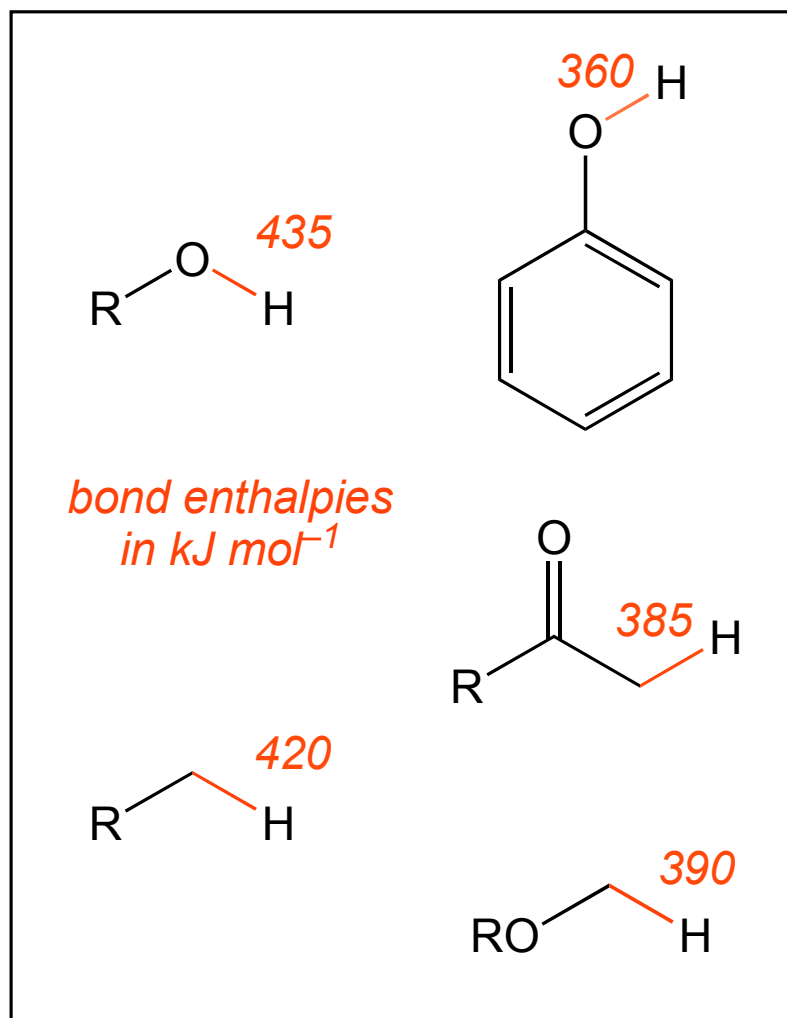
Analysis of radical stability





Analysis of radical stability

bond enthalpy and resonance

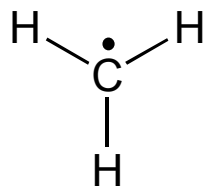




Analysis of radical stability

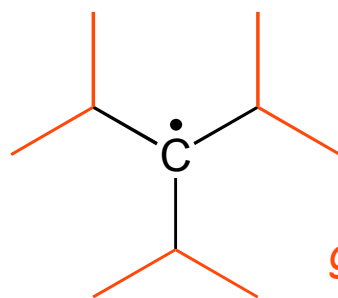
steric effects - size matters

lifetime (ESR)



$\sim 0.2 \times 10^{-3}$ seconds

(at 10^{-6} mol dm $^{-3}$)

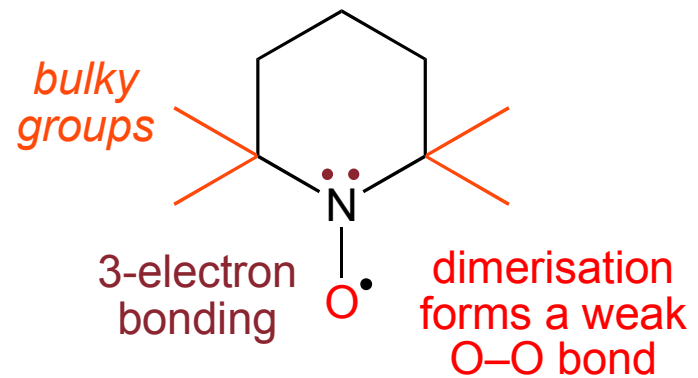


bulky groups

~ 21 hours

persistent radicals

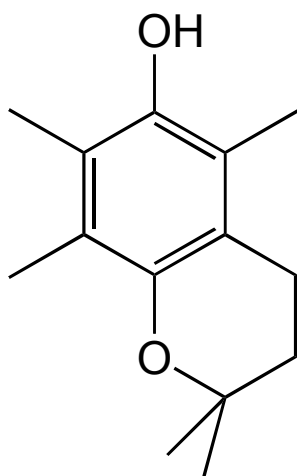
TEMPO – a stable solid



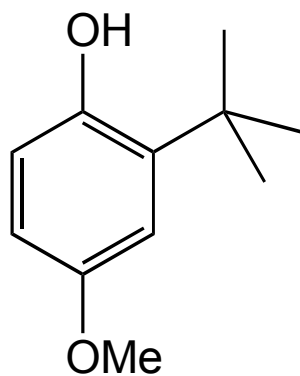


Analysis of radical stability: you are the judge

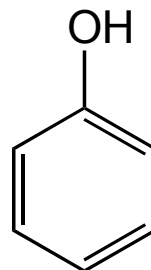
Which of the following phenols has the weakest O–H bond?



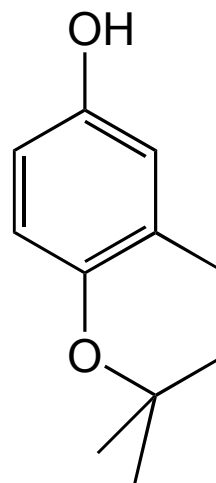
A



B



C



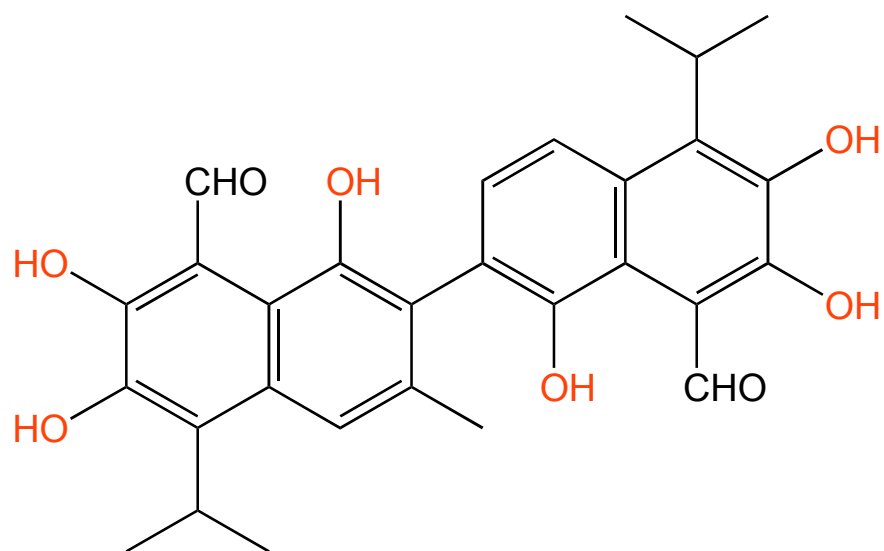
D

α -tocopherol: a natural antioxidant in Vitamin E



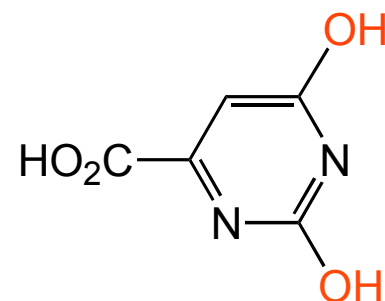
Analysis of radical stability: an aside

Gossypol (antioxidant from the cotton plant)



Once used as a male contraceptive in China but its effects were permanent in up to 20% of patients!

Erotic acid

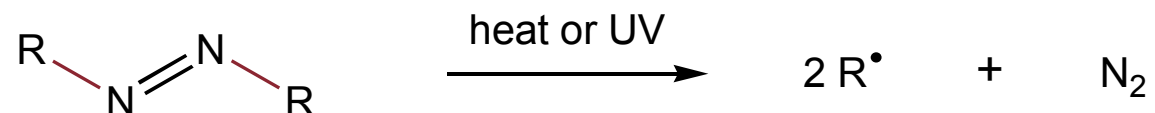


This is orotic acid (vitamin B13) but it has been misspelt so often it is also known as erotic acid. If you add another carbon to it, it becomes homo-erotic acid

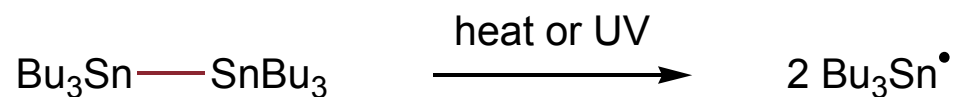


Discuss radical formation

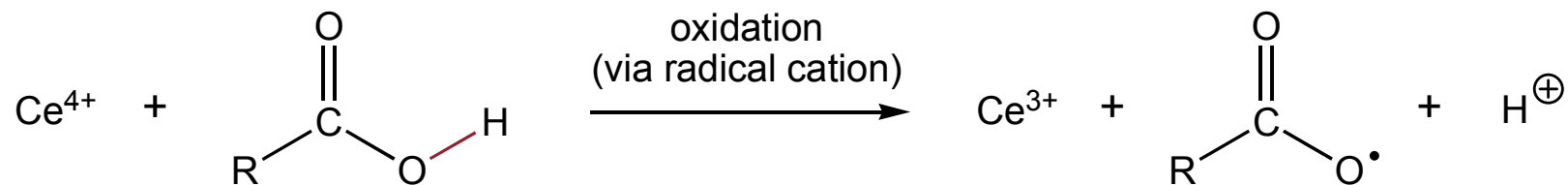
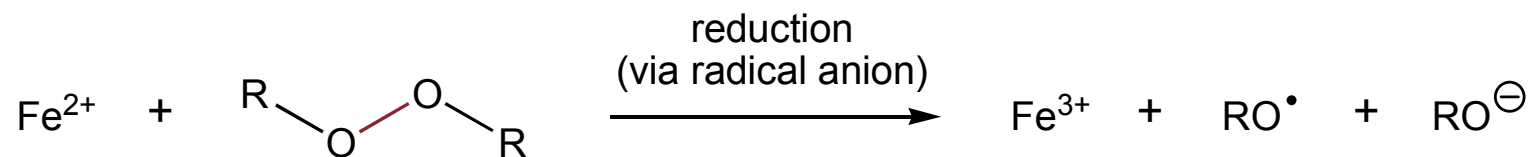
organics (azo compounds, peroxides etc)



organometallics (M-M or M-C bonds)



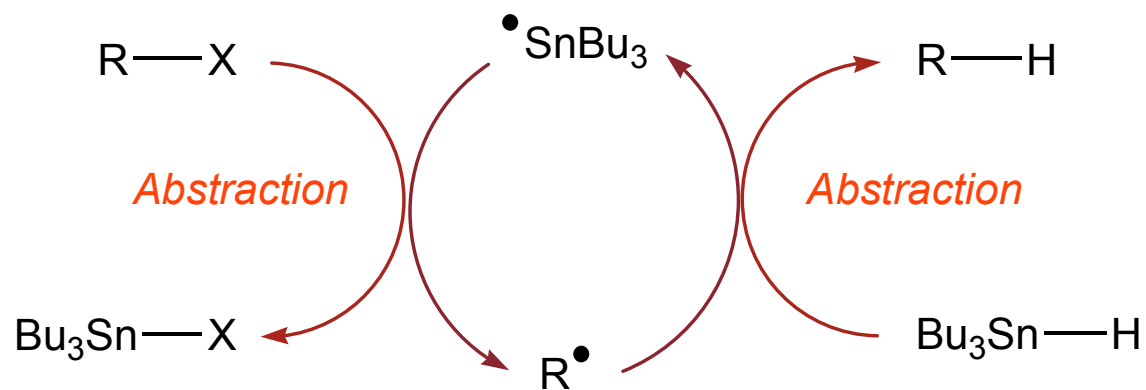
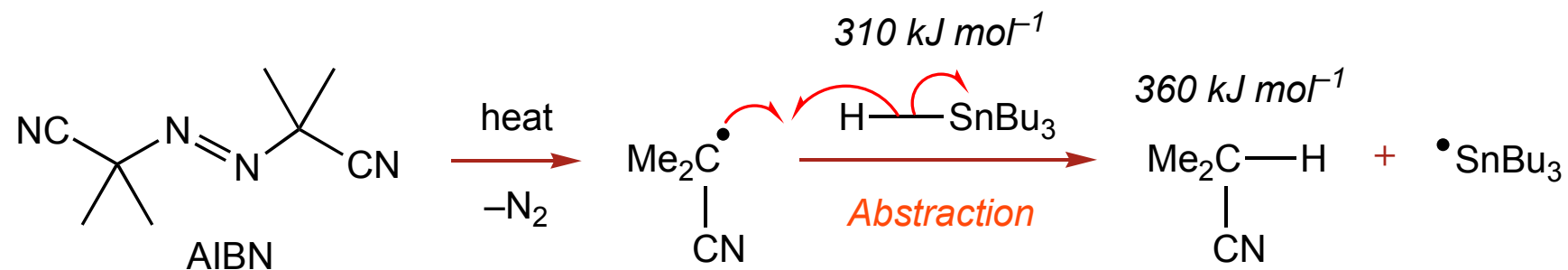
metals (single electron transfer)



electrolysis (Kolbe); mass spectrometry (EI)



Investigate radical reactions: a chain reaction

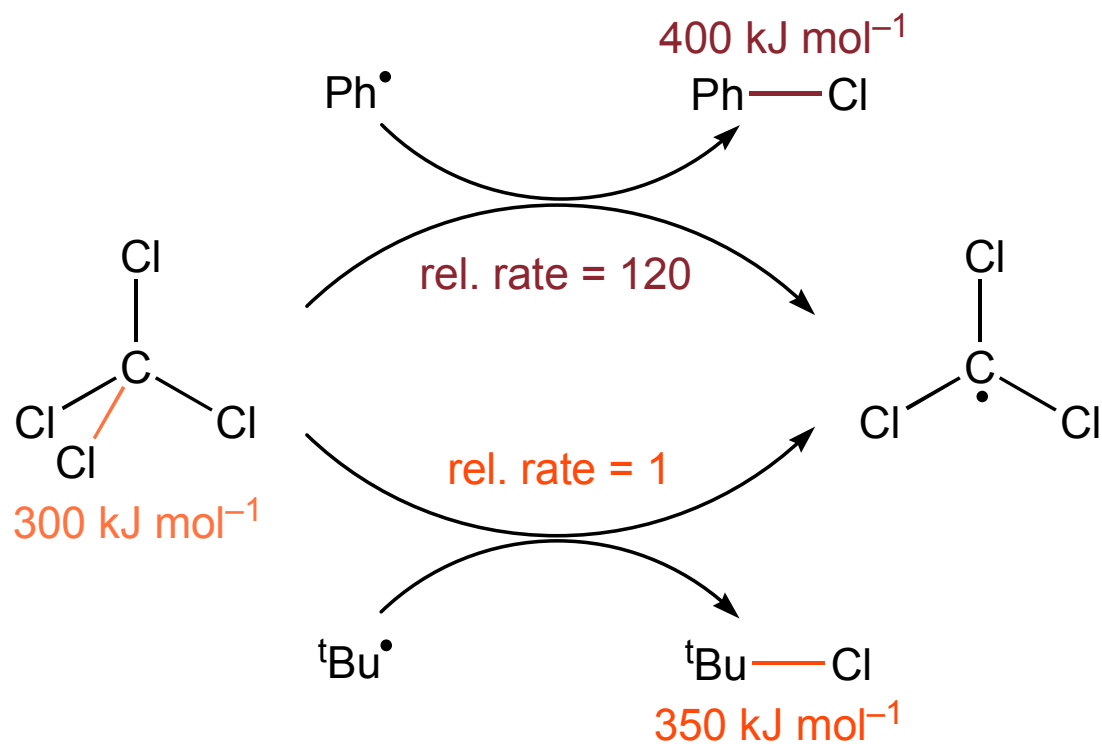




Investigate radical reactions

Predicting selectivity – bond enthalpies

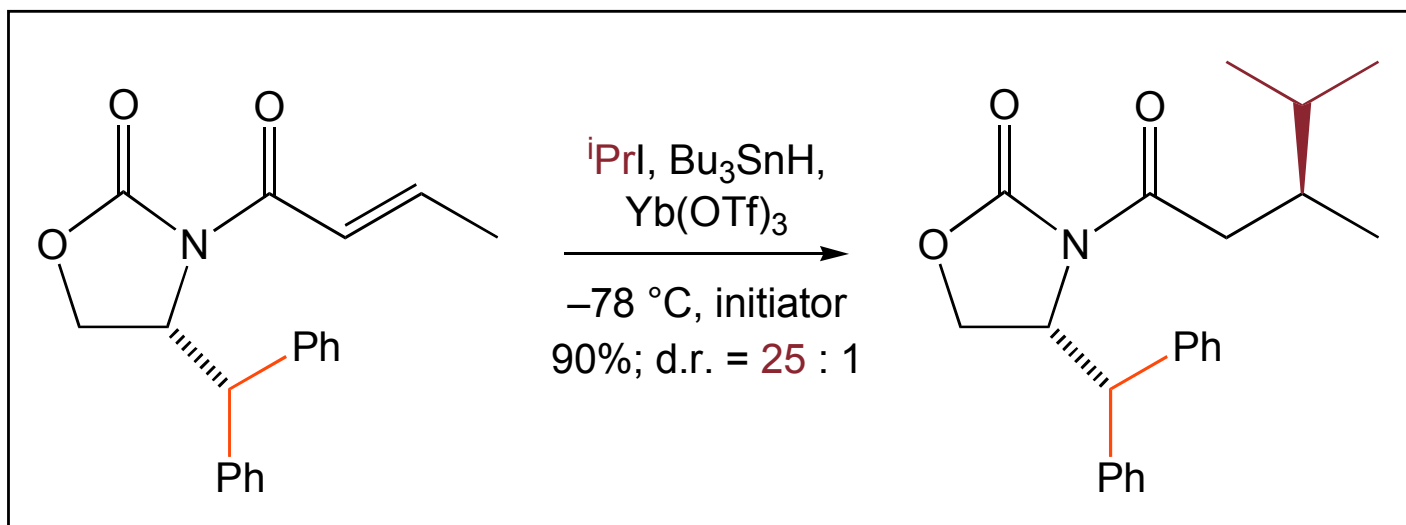
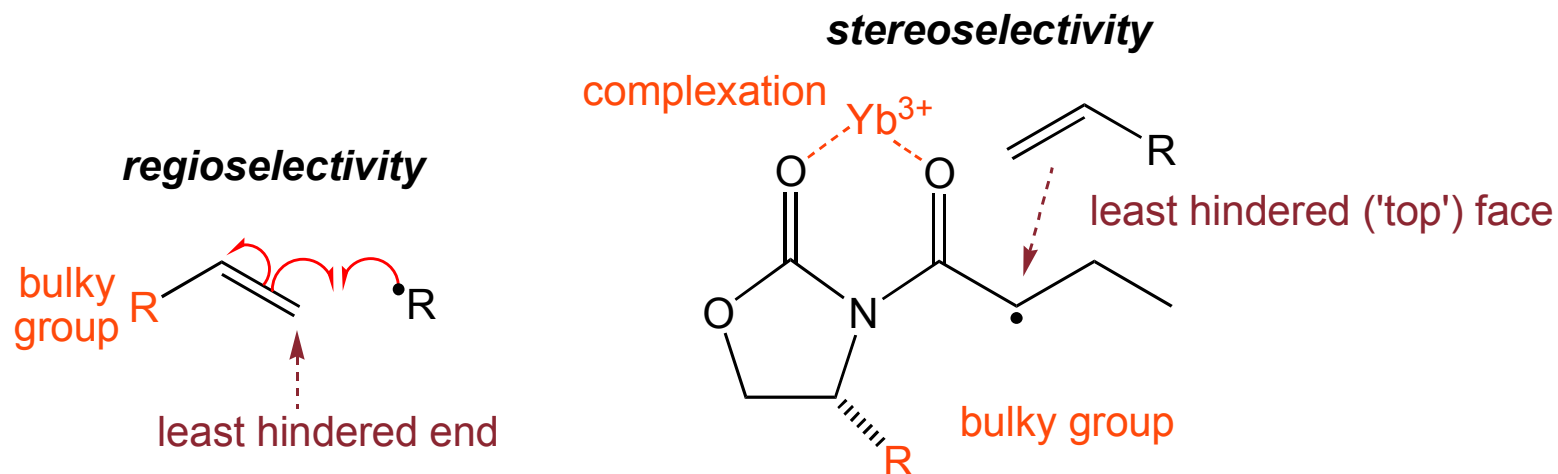
break weak bonds, make stronger bonds (a guide)





Investigate radical reactions

Predicting selectivity – steric effects

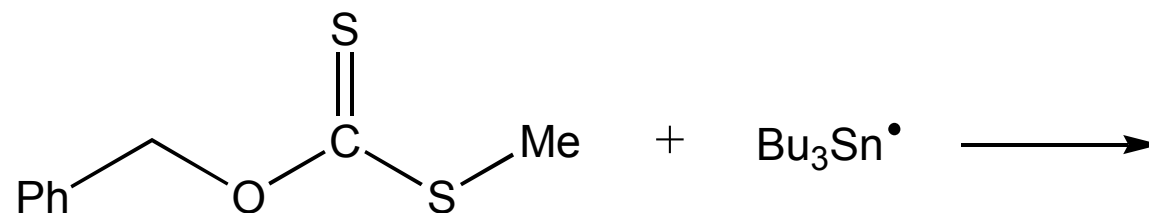




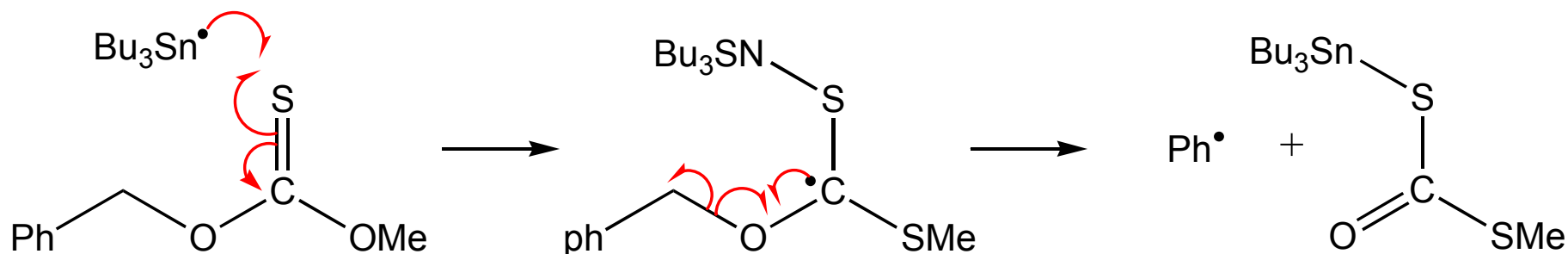
Investigate radical reactions: you are the judge

Examination question

Write a mechanism and the organic product(s) from the following reaction. (3 marks)



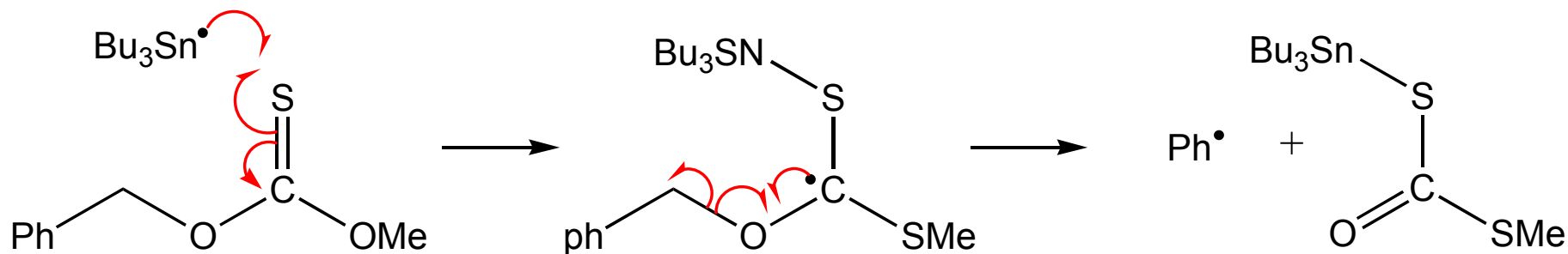
Answer by I.M. Unsure. How many marks would you give out of 3?



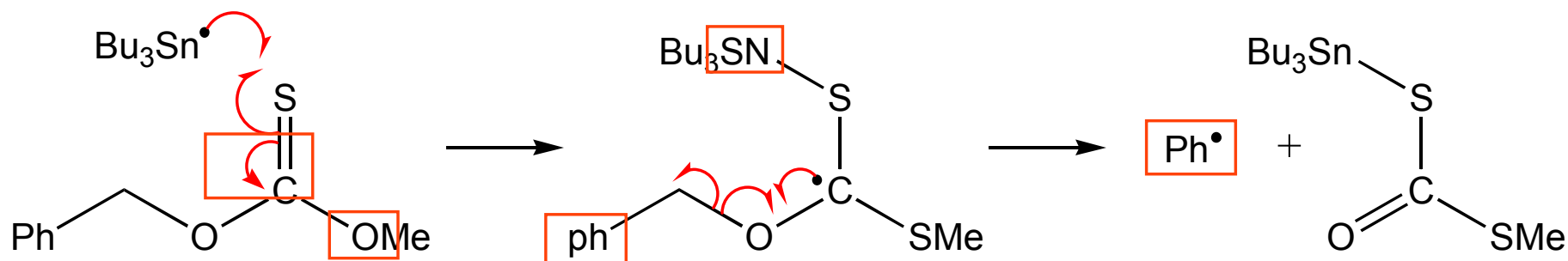
(a) 0 (b) 0.5 (c) 1 (d) 1.5 (e) 2 (f) 2.5 (g) 3.0



Investigate radical reactions: you are the judge



There are five major errors

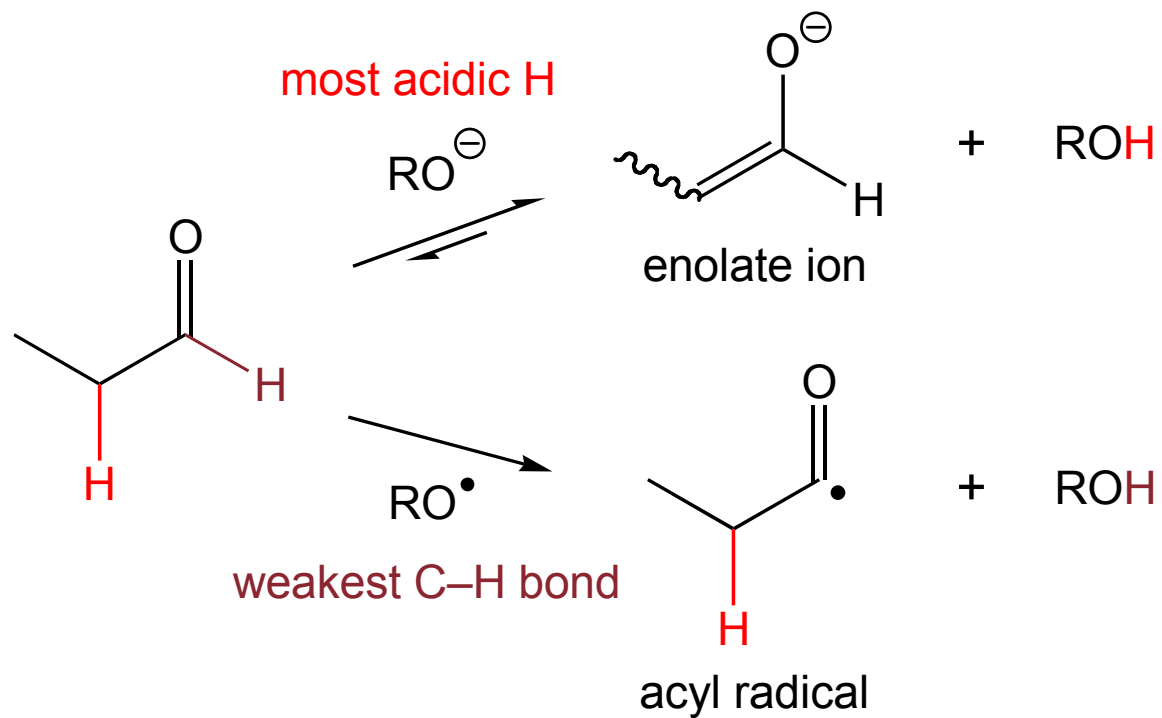


(a) 0 (b) 0.5 (c) 1 (d) 1.5 (e) 2 (f) 2.5 (g) 3.0



Investigate radical reactions

contrasting selectivity – radicals vs ions





Consider biomedical/environmental processes

Nitrogen monoxide, nitric oxide ($\bullet\text{NO}$)

**analysis –
detect surface radicals
on polymers (XPS)**

**pollutant –
ozone depletion
and acid rain (HNO_3)**

**synthesis –
intermediate in
the Barton reaction**

increase blood flow in the body
e.g. Viagra enhances the
effects of NO; nitroglycerin,
reduces the pain of angina by
generating NO

**signalling
molecule in
biology**

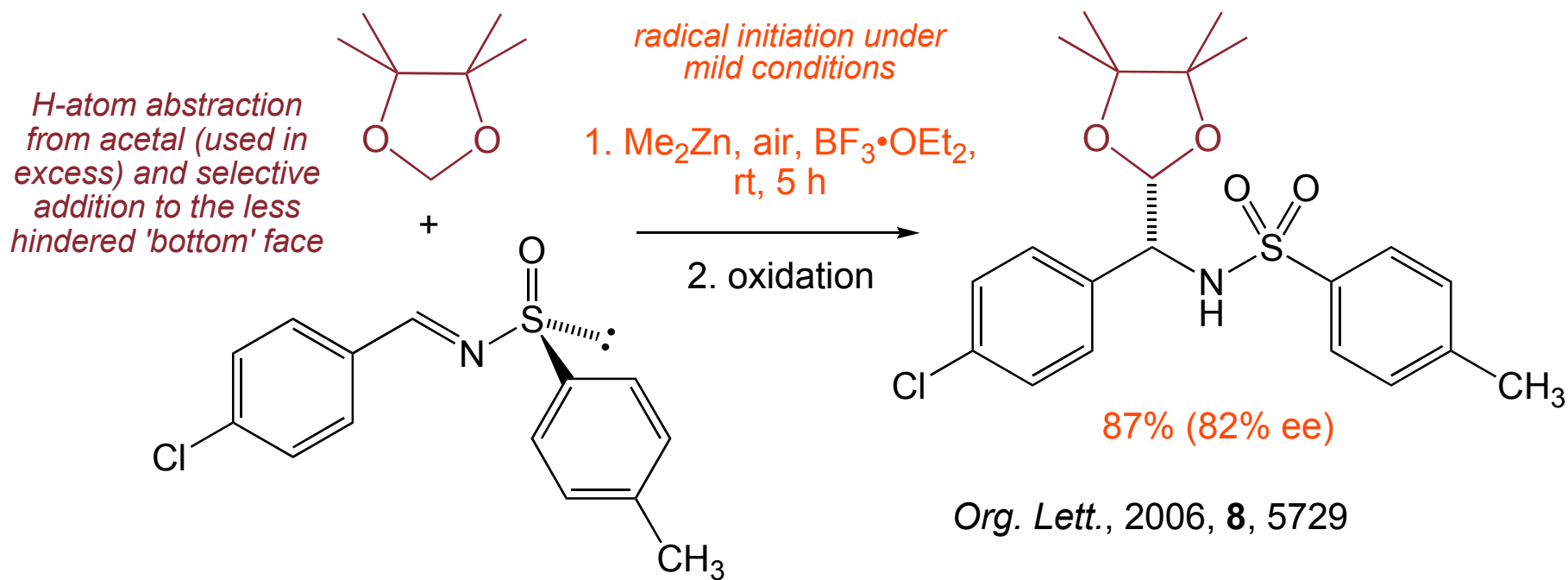
plant pollination
and flowering

fire flies and
luminescence



Application in synthesis

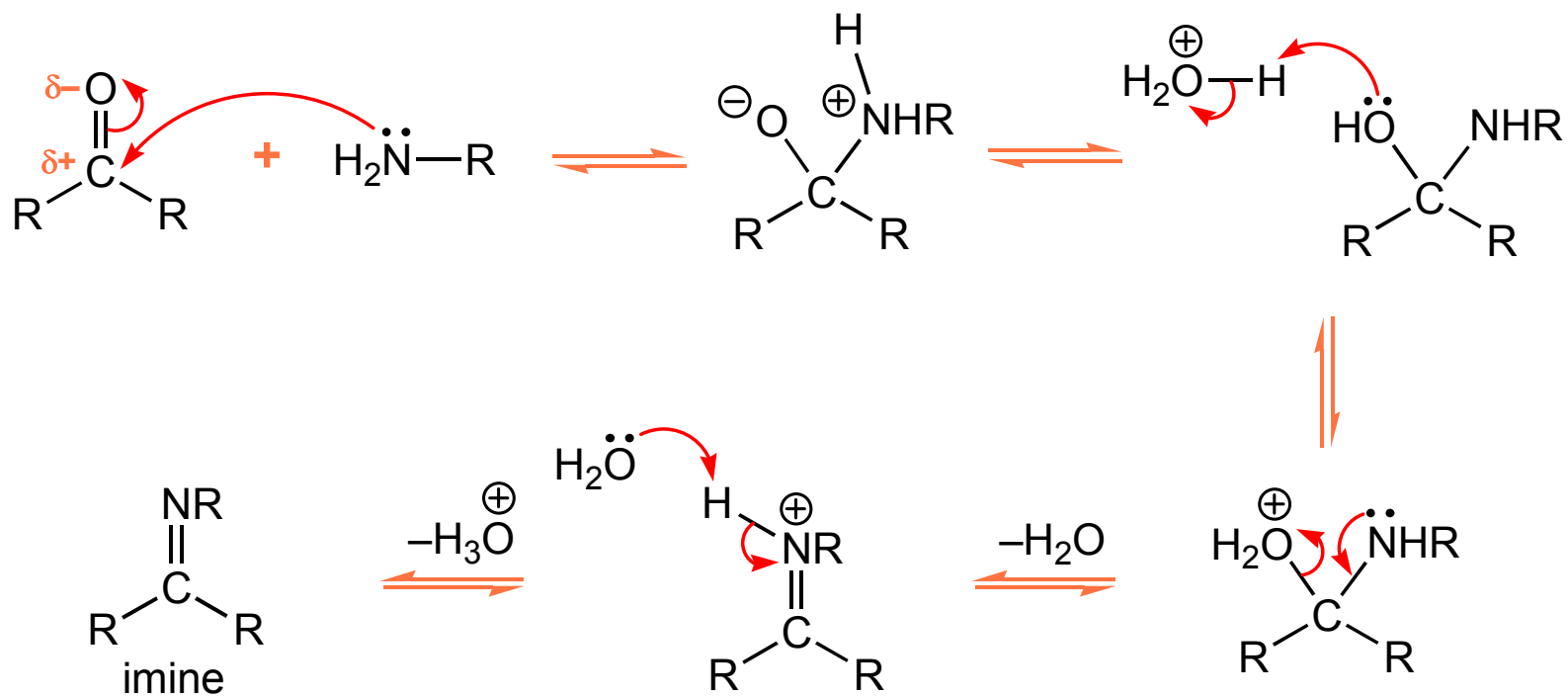
'synthetic radical reactions are unselective, require high temperatures or specialised UV equipment, benzene as solvent and toxic chain carriers'





Application in synthesis: revision

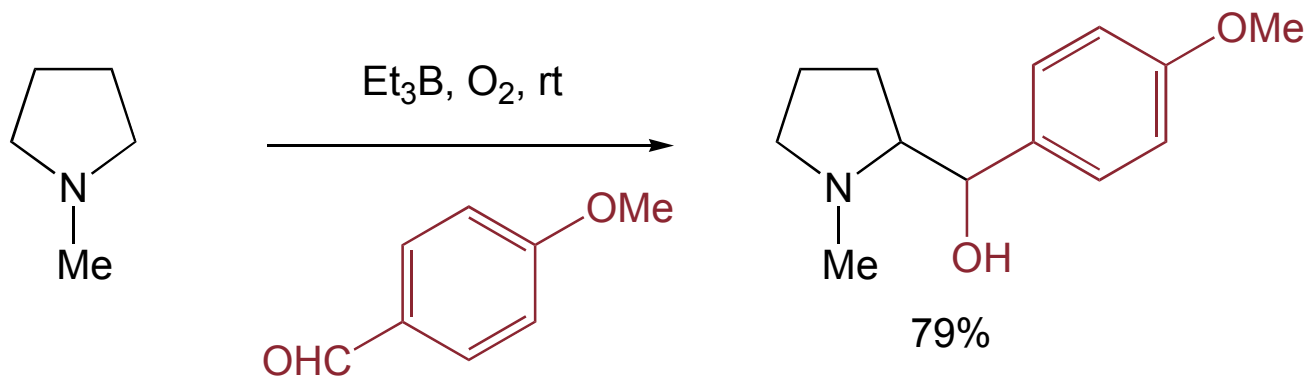
imine formation



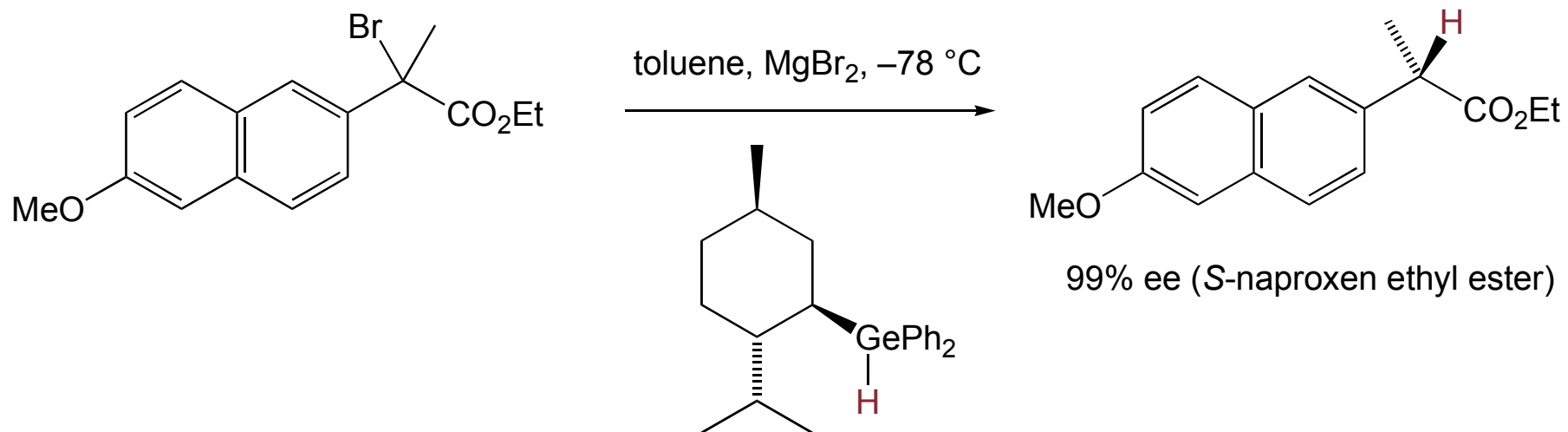


Latest developments

technically clean methods

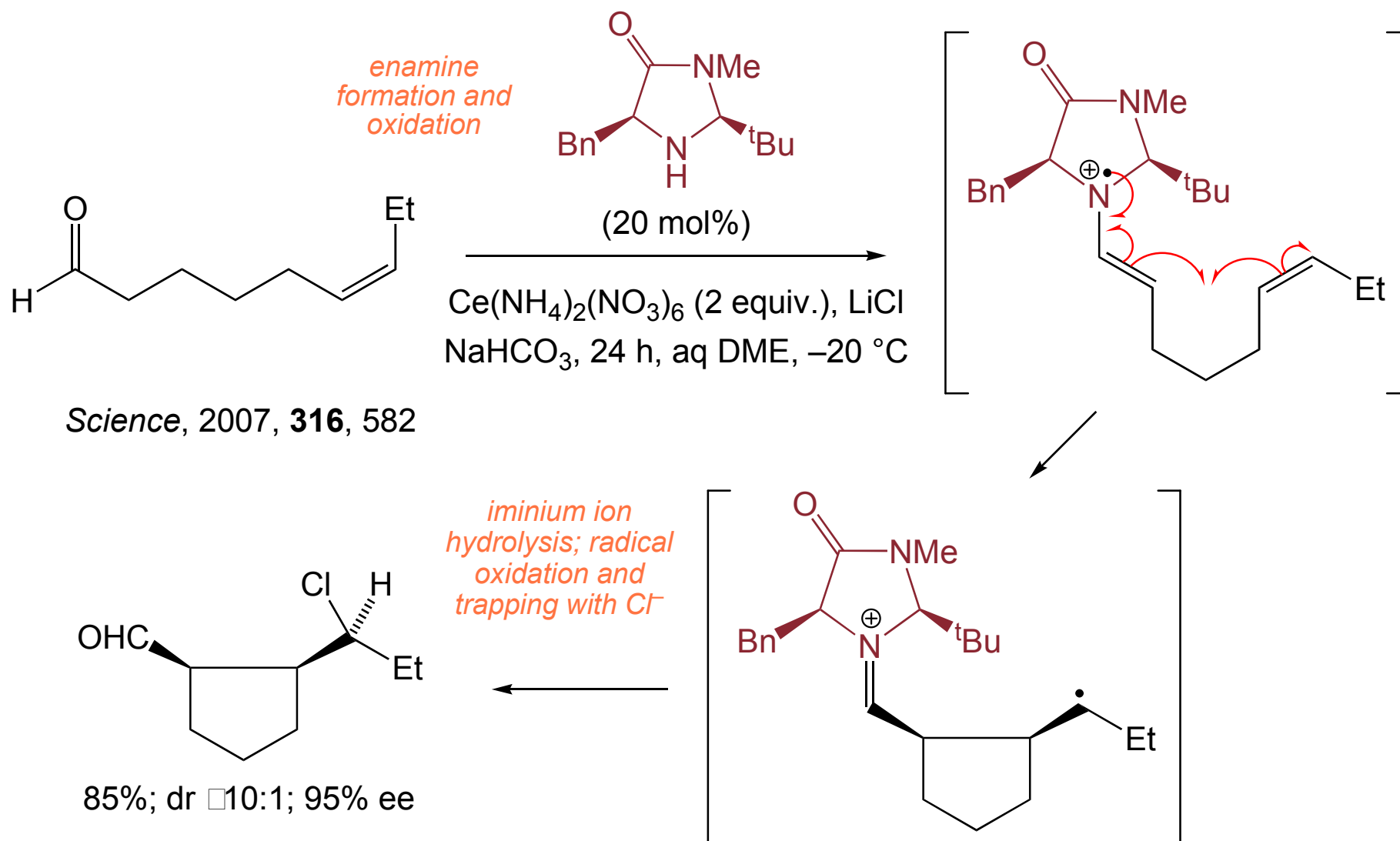


enantioselective methods





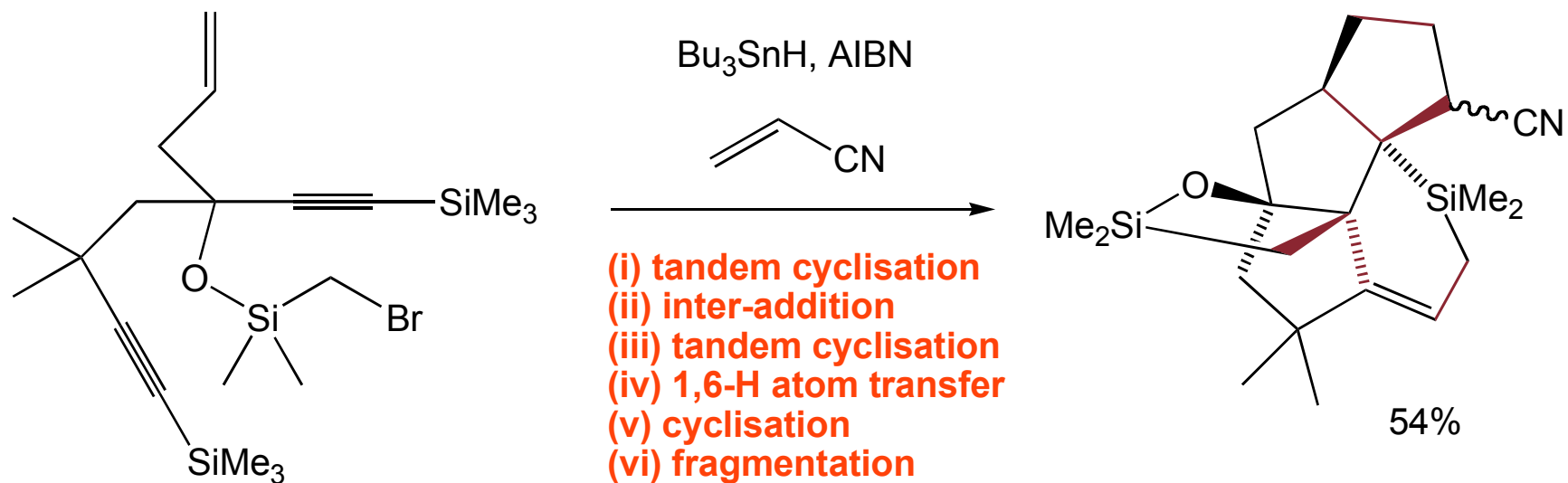
Latest developments: enantioselective organocatalysis





Latest developments

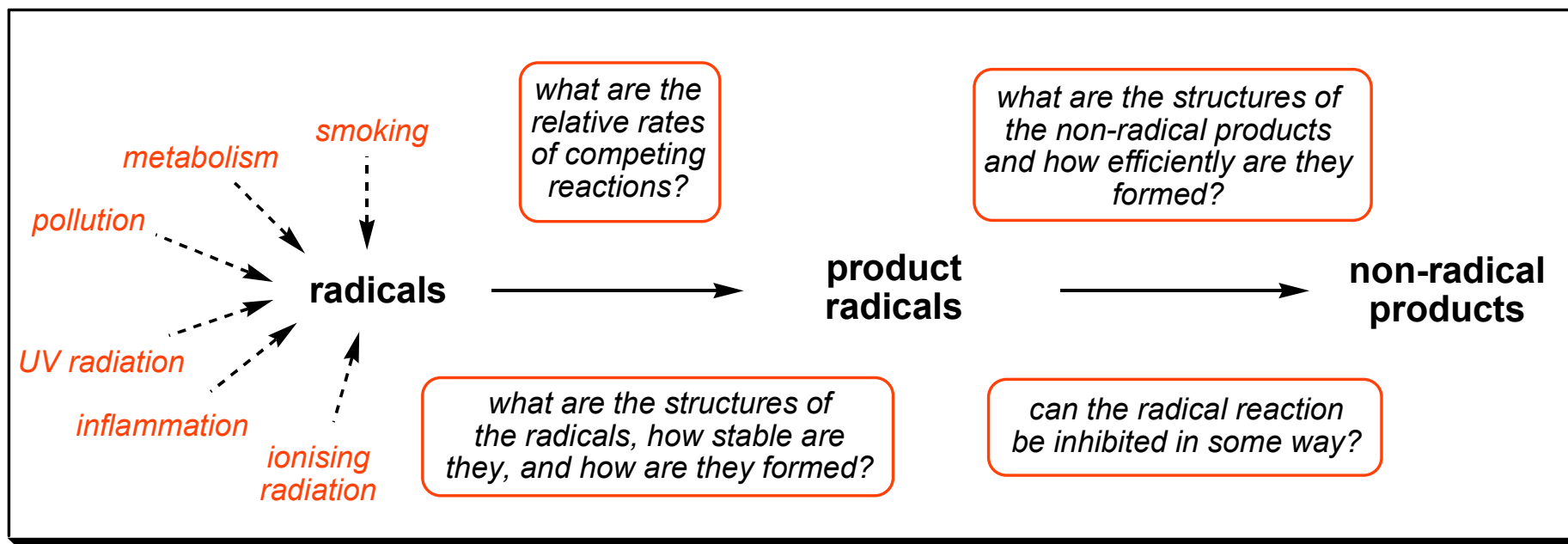
cascades – the ultimate in control





Conclusion

Radicals and their reactions are an interdisciplinary topic that showcases fundamental chemical topics in modern contexts





Oh, My ketone!

Oh, my ketone! Oh, my ketone!
And my primary amine.
You reacted, lost some water and
You formed a new imine.

Now the lone pair on the N then
Bonds with carbonyl C.
Pi electrons go to O, a
Proton shifts fast as can be.

Now the O is feeling greedy
Grabs an H from OH₃.
Free electrons from the N then
Form a pi bond, water leaves.

Now the N is protonated
And a plus charge can be seen.
So the water yanks the H off
And we've formed a new imine.

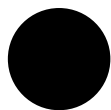
Oh, my ketone! Oh, my ketone!
And my primary amine.
Your reacted, lost some water and
You formed a new imine.



Radical reduction – acting it out



tin radical



RX



arrow



tin halide



radical



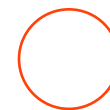
tin hydride



arrow



RH



tin radical