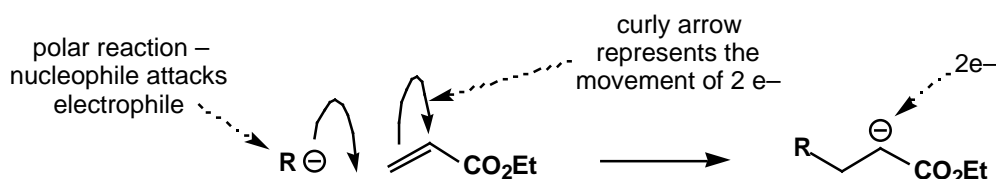
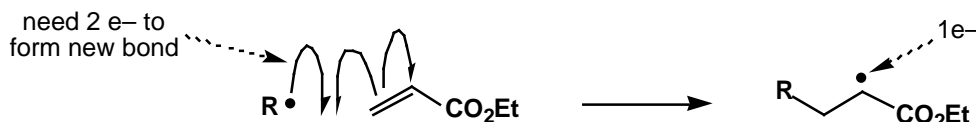


FREE RADICAL REACTIONS IN ORGANIC SYNTHESIS MECHANISM

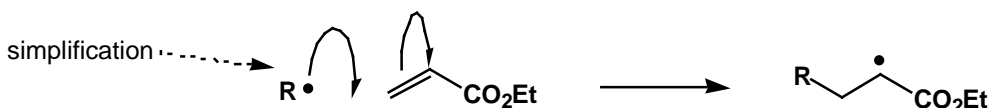
- Before we look at free radical chemistry a quick revision of mechanisms (again)
- You should all be happy with



- Radicals are **one** electron species so we cannot use curly arrows
- Instead use *fish-hooks* – these show the movement of **one** electron



- Diagrams can get quite confusing so they are normally simplified to show electrons only moving in one direction – BUT remember the above is "more accurate"



- Note - we are no longer looking at *proton* removal but *hydrogen* abstraction (it still has its 1 e⁻)

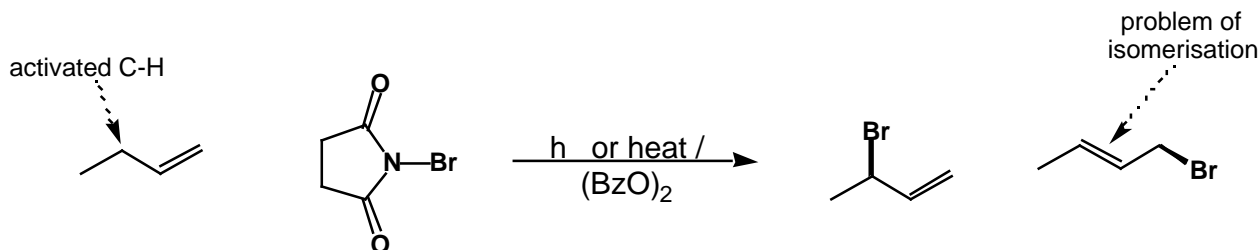


INTRODUCTION

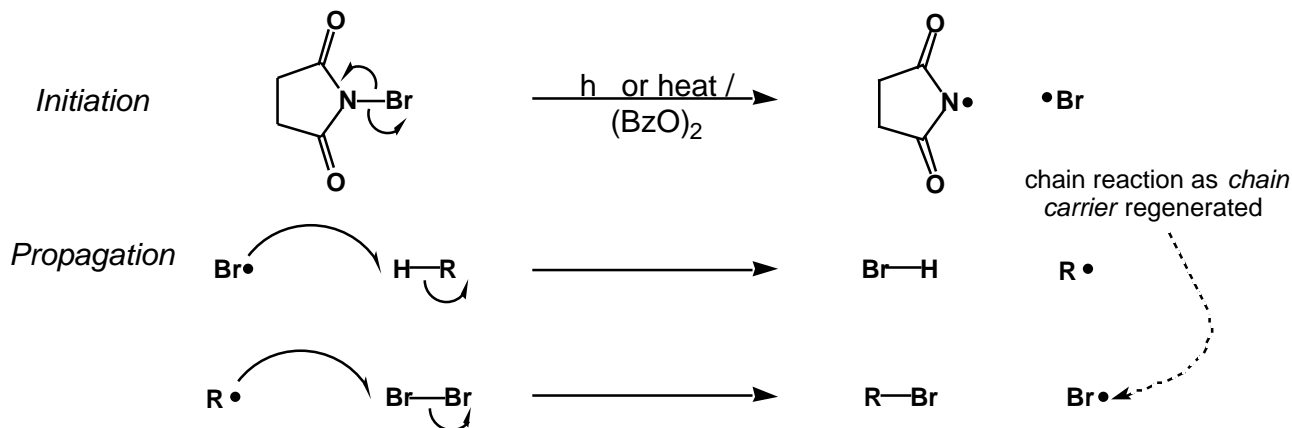
- The last 10–15 years have seen the development of free radical chemistry in organic synthesis
- Major obstacle is the ability of radicals to react with themselves



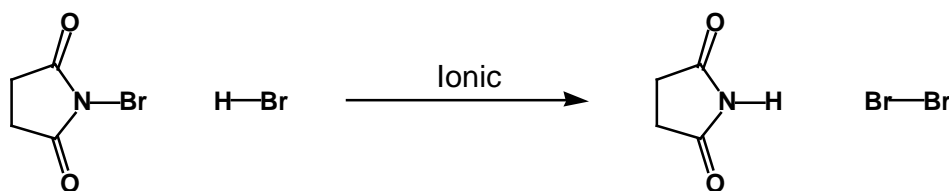
- Overcome by only having a very low concentration of radicals present in a reaction
- Now there are many ways to use these highly reactive species in selective (& synthetically useful) organic reactions
- Good example is the *radical chain process* for allylic halogenation



Radical Chain Mechanism

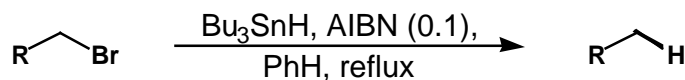


- The use of NBS rather than Br_2 allows controlled formation of Br_2 and provides a mechanism to remove HBr

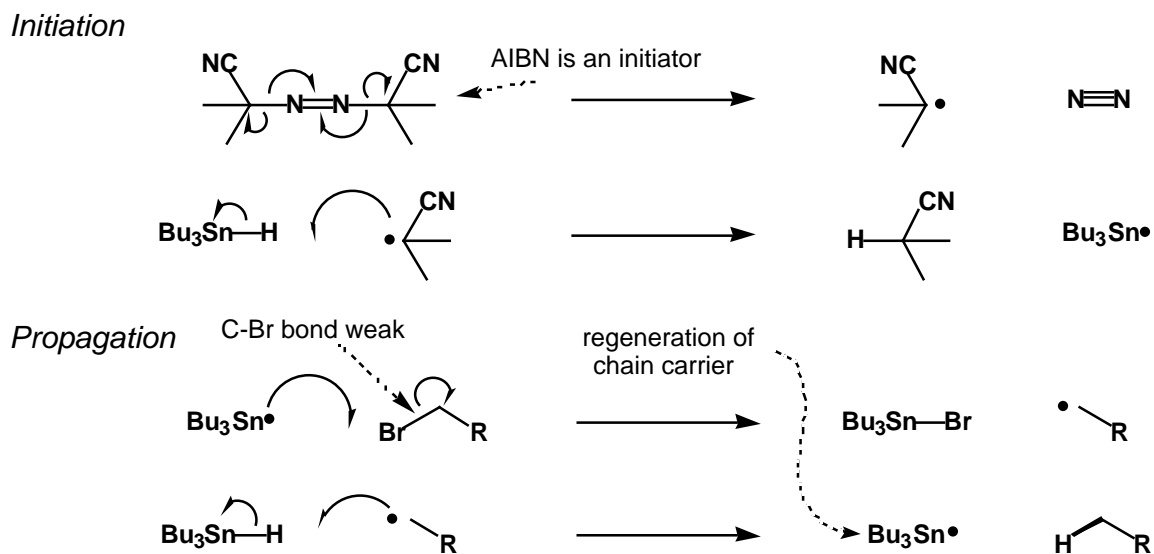


Selectivity in Free Radical Reactions: Tributyltin Hydride Methodology

- C-H bonds very strong so need to be activated
- Strength of bond often prevents chain reaction
- Major problem is often the *selective* activation of a specific C-H bond
- The following reduction reveals a route to overcome this problem



Mechanism: Another radical chain reaction

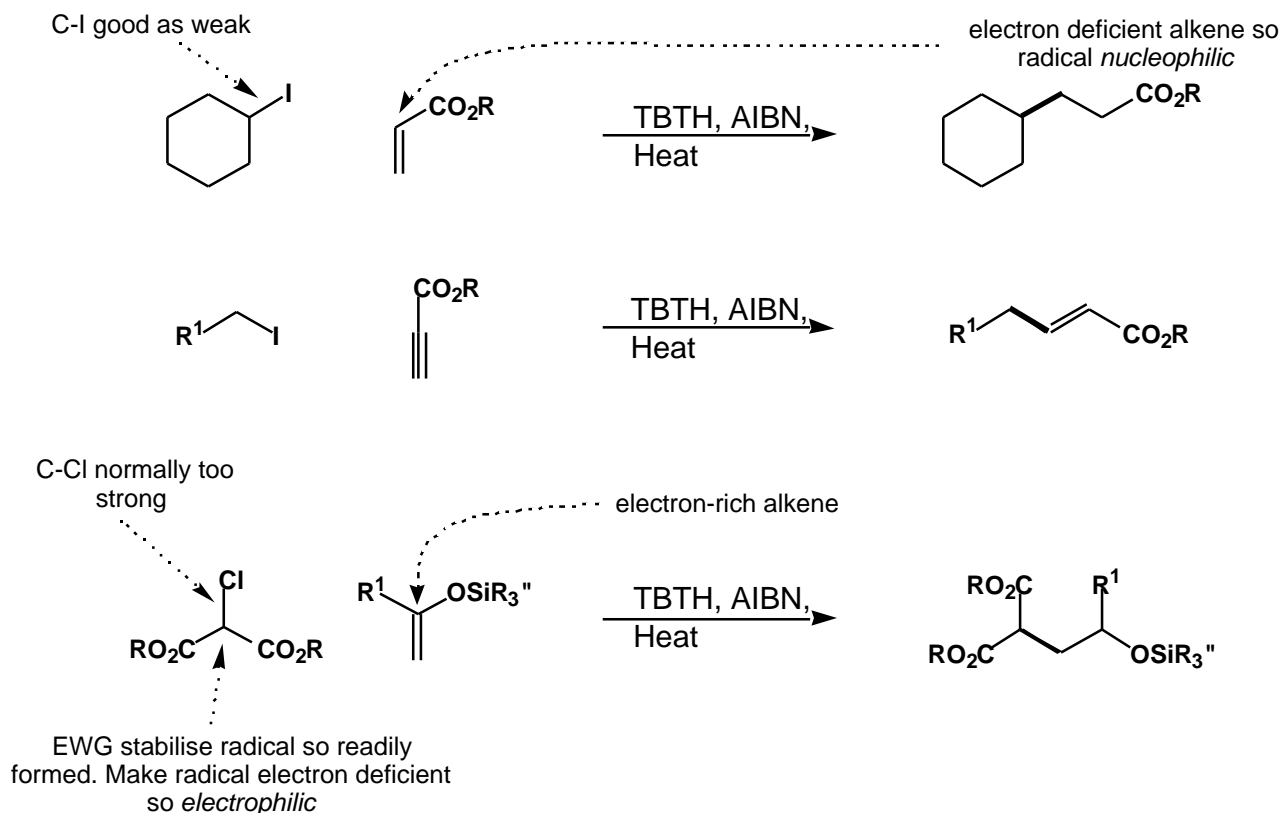


- Chain termination by variety of processes
- Relative rates of each process allow selective formation of carbon centred radical
- Tributyltin (TBT) propagates chain

SYNTHETIC APPLICATION OF CARBON CENTRED RADICALS

Intermolecular Addition Reactions

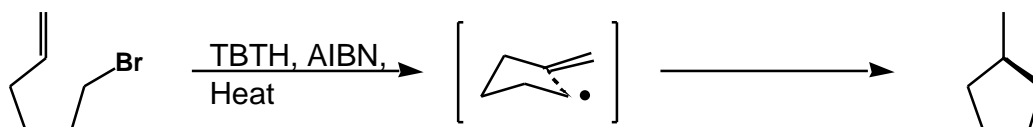
- TBT generates synthetically useful radicals
- Addition reactions



- NOTE: radicals can be both *nucleophilic* and *electrophilic*

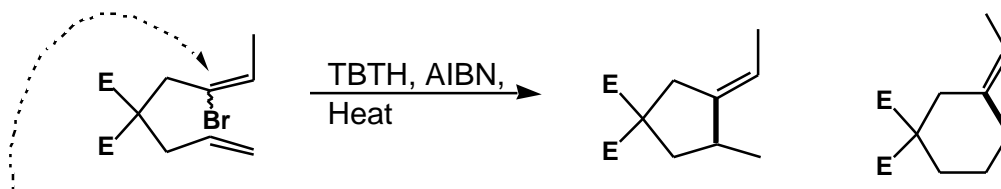
Intramolecular Addition: Radical Based Ring-Formation Reactions

- Free radicals are very useful for the preparation of rings
- Radical reactions readily form 5 membered rings
- Formation of 5-ring takes place under *kinetic* control (energy of transition state for the formation of 5-ring lower than that for 6-ring)



Vinyl Radicals

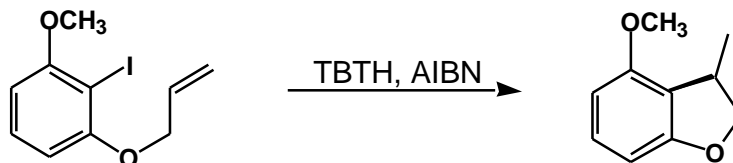
- More reactive (less stable) than alkyl radicals
- Generate by the normal methodology (TBTH, AIBN)
- Normally only used in *intramolecular* reactions (problems of dimerisation with intermolecular)



Note: geometry of vinyl halide unimportant as radical can invert

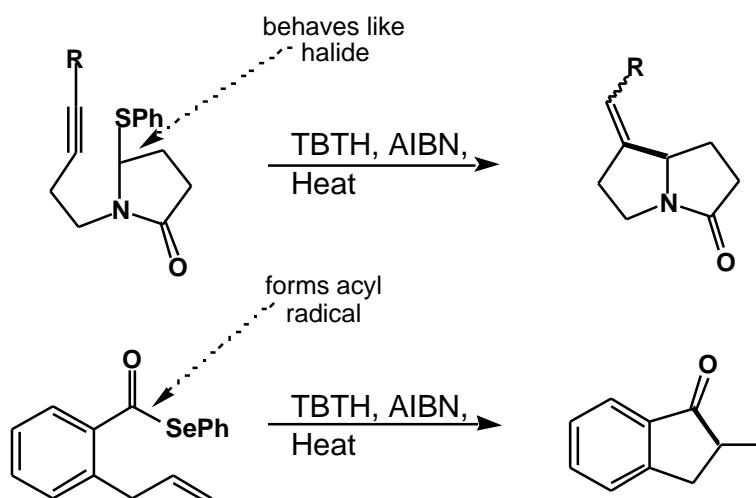
Aryl Radicals

- Aryl radicals are very reactive



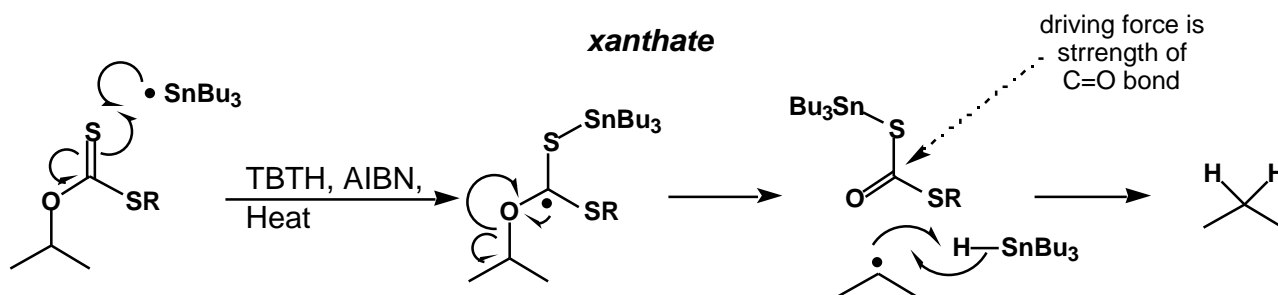
Other Precursors: Sulfides and Selenides

- Just as useful as halides (and frequently give better yields)



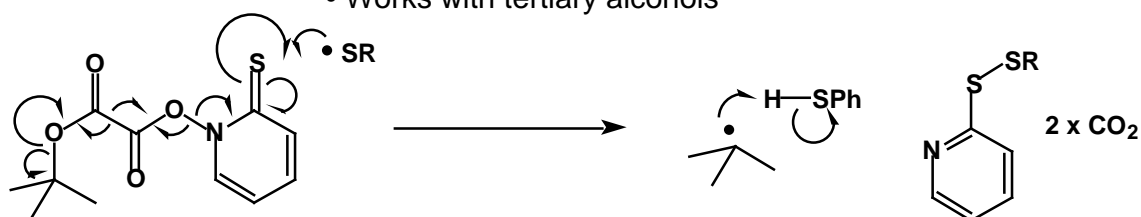
Other Precursors: Alcohol Derivatives

- Deoxygenation of alcohols a good method for preparing carbon-centred radicals
- Good for primary and secondary alcohols but not for tertiary (3° radicals less stable)



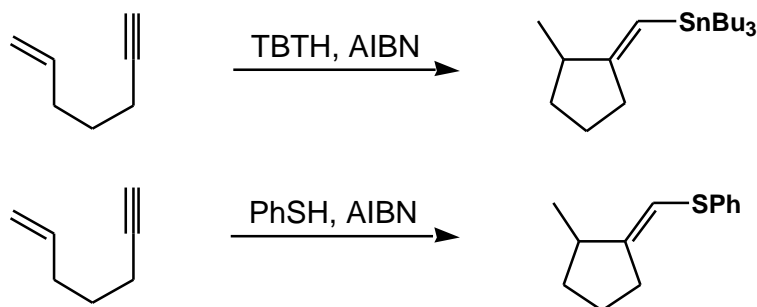
oxalate

- Works with tertiary alcohols



Other Precursors: Multiple Bonds

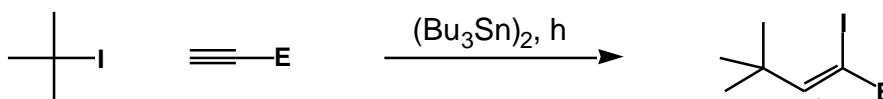
- Utilise the addition of a radical to a multiple bond as the *propagating* step (also incorporates further functionality into the molecule)



EFFICIENCY IN RADICAL REACTIONS

- Normally chain propagation step is the abstraction of H from TBTH
- Waste of a radical as reduced C-X to C-H
- So *chain transfer reactions* developed

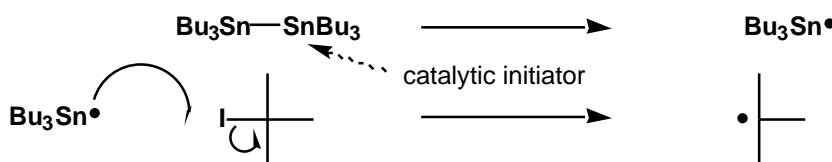
Group or Atom Transfer: Halogen



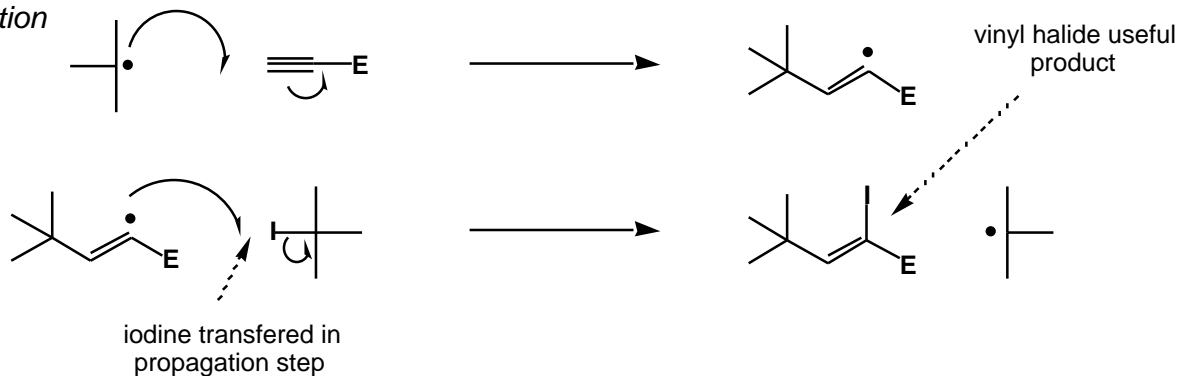
Note: all atoms in SM are in product

Mechanism

Initiation

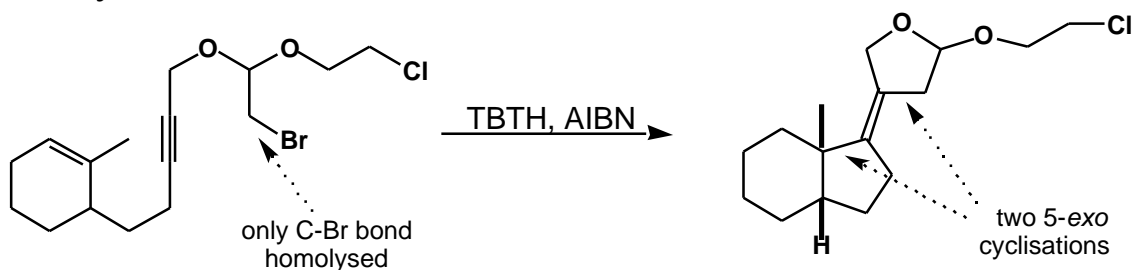


Propagation

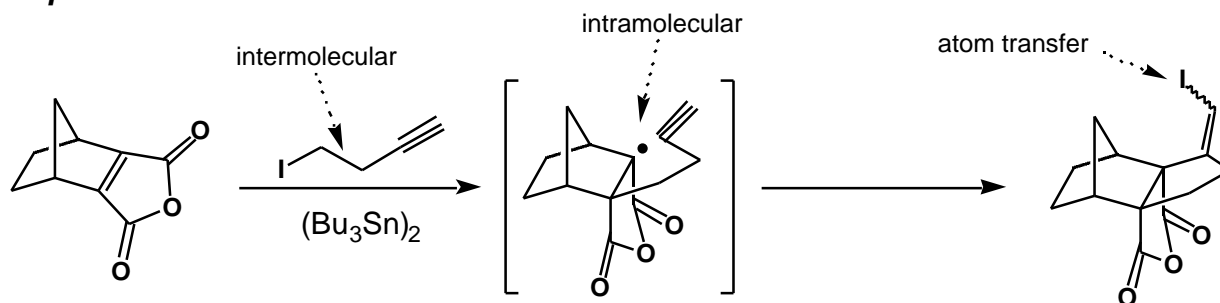


Radical Based Sequences: Multiple Bond Formation

- Radicals readily lend themselves to the formation of a number of bonds in one step
- **Tandem Cyclisations**



- **Sequenced Reactions**



What have we learnt?

- Radical reactions very versatile
- Can be very efficient
- Good for ring formation
- Atom transfer allow functional group incorporation
- Readily used to form a number of bonds in one step