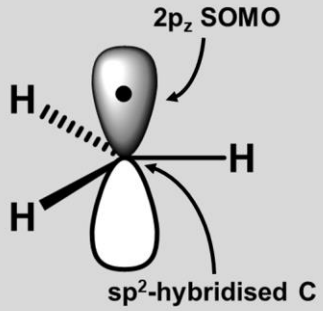
# *Radical Reactions for C-C Bond Formation*

Models/Topics Covered: Bond Dissociation Energies, Sterics, HSAB, FMO Theory, Resonance, Hybridisation, Mechanisms

The following questions are drawn mainly from the matter in Chapter 37 of Clayden, Greeves, and Warren's 'Organic Chemistry' (2nd ed.) **Ref[1]**. They focus on fundamental underlying concepts relevant to organic radical chemistry – primarily aspects of stability and selectivity – and examples of useful organic transformations using radicals.



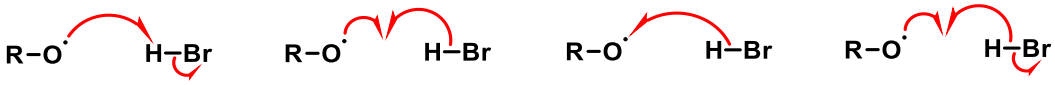

| Bond X–Y | $\Delta G$ for X–Y → X$^\bullet$ + Y$^\bullet$, kJ mol$^{-1}$ | Bond X–Y | $\Delta G$ for X–Y → X$^\bullet$ + Y$^\bullet$, kJ mol$^{-1}$ |
|---|---|---|---|
| H–OH | 498 | $CH_3$–Br | 293 |
| $H_3C$–H | 435 | $CH_3$–I | 234 |
| $H_3C$–OH | 383 | Cl–Cl | 243 |
| $H_3C$–$CH_3$ | 368 | Br–Br | 192 |
| H–Cl | 431 | I–I | 151 |
| H–Br | 366 | HO–OH | 213 |
| H–I | 298 | MeO–OMe | 151 |
| $CH_3$–Cl | 349 | | |

| Bond | Representative bond energy, kJ mol$^{-1}$ |
|---|---|
| C–Br | 280 |
| Sn–H | 308 |
| C–H | 418 |
| Sn–Br | 552 |

*(Left) Methyl radical. (Right) Bond Dissociation Energies. Reproduced from Ref[1].*

## Question 1 (Quick-fire Radical Knowledge)

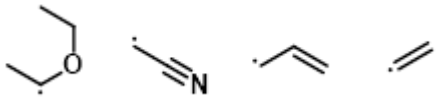
(i). Which of the following is the correct way of drawing a radical mechanism?

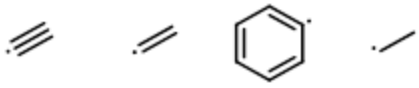



(ii). For each of the following lists of radicals, indicate the order of stability.

(a) $\cdot CH_3$ $\cdot NH_2$ $\cdot OH$ $\cdot F$

(b) F· Cl· Br· I·

(c) 

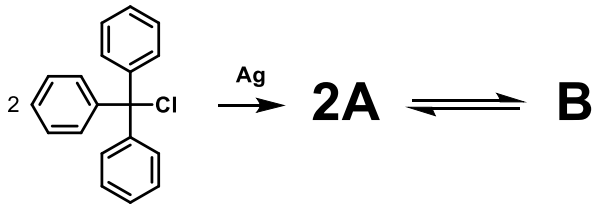
(d) 

(e) $\cdot CH_3$ 

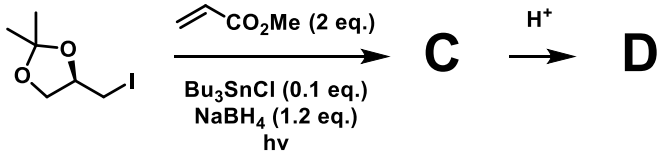
(f) $\cdot CH_3$ $\cdot CH_2F$ $\cdot CHF_2$ $\cdot CF_3$

## Question 2 (Selectivity in Radical Chain Reactions for C-C Bond Formation)

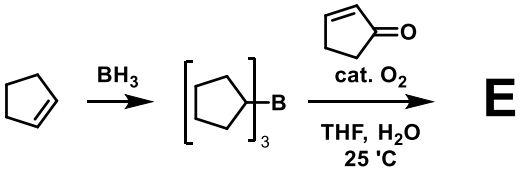
The following reactions are all examples of radical cascade reactions. Provide the products (**A**-**H**), mechanisms, and comment on the selectivity in each case. For mechanisms, radical generation and propagation are of interest. Termination may be ignored as radical concentration is usually low enough that the termination by-products may be assumed to occur with negligible yield.



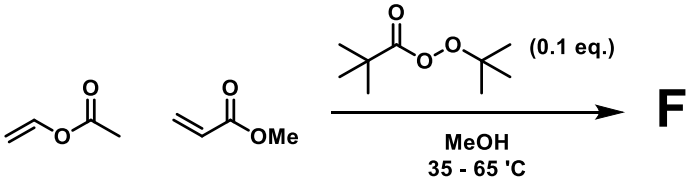

*First example of a radical; identified by Gomberg in 1900.*



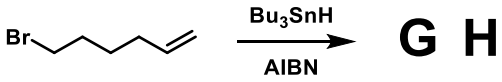

*C-C bond formation reaction using a variation of a common tin reagent.*




*C-C bond formation reaction with an interesting method of radical generation using B as a non-toxic alternative to Sn.*



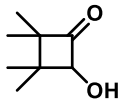
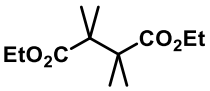
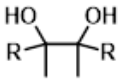
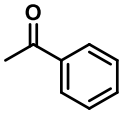

*Extension of radical C-C bond formation to a useful materials application.*




*Example of an intramolecular C-C bond formation.*

## Question 3 (Ketyl Radical Dimerisation)

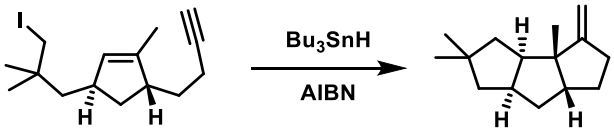
Match the following Named Reactions with the exemplar starting material, conditions, and products, and the usage of the reaction. Two blank entries are included to add an extra challenge.

| Named Reaction | Starting Material | Conditions | Products | Usage Notes |
|---|---|---|---|---|
| **Pinacol Reaction** | | $TiCl_3$, Zn/Cu, THF |  | Uncommon. Better alternatives exist. |
| **Bouveault-Blanc Reduction** |  | i) Na, EtOH<br>ii) $H^+$ |  | Carbocyclic rings of size >3. |
| **McMurry Reaction** |  | i) Na, $Me_3SiCl$, PhMe<br>ii) HCl, $H_2O$, THF | | Symmetric diols. |
| **Acyloin Reaction** |  | i) Mg, benzene<br>ii) $H^+$ |  | Symmetric tetra-substituted alkenes. Formation of cyclic alkenes of size >8. |

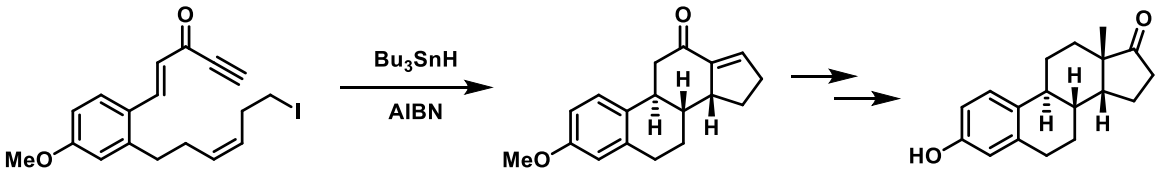
## Question 4 (Use in Total Synthesis)

Below are two examples of radical cascade-style reactions applied to the synthesis of biological relevant molecules. Provide a mechanism for each, rationalising the choice of regioselectivity at each stage.

(i). (±)-Hirsutene




(ii). *Epi*-Oestrone





[1] Clayden, Greeves, Warren. 2012. *Organic Chemistry.* 2nd ed. Oxford, UK: Oxford University Press.
[2] Gomberg 'An instance of trivalent carbon: Triphenylmethyl' *J. Am. Chem. Soc.* 1900, **22**(11), 757 (DOI: 10.1021/ja02049a006)
[3] Ashenhurst. *Radical Reactions*. MasterOrganicChemistry. [Online]. Accessed 5th July 2022. Section starting from: https://www.masterorganicchemistry.com/2010/06/25/bond-dissociation-energies-homolytic-cleavage/
[4] Zhang 'Radical Substituent Effects of α-F and α-$CF_3$ Groups' *J. Org. Chem.* 1998, **63**(11), 3590 (DOI: 10.1021/jo9722313)
[5] Wysocki, Teles, Dehn, Trapp, Schafer, Schaub 'Photoinduced Direct Conversion of Cyclohexane into Cyclohexanone Oxime using LEDs' *ChemPhotoChem* 2018, **2**, 22 (DOI: 10.1002/cptc.201700151)
[6] Marten, Famili, Mohanty. 1988. *Copolymers of vinyl acetate and acrylates*. EP 0 275 900 A2.
[7] Itsuno. 'Bouveault-Blanc Reduction' in: *Comprehensive Organic Name Reactions and Reagents*. Wang (ed.), 2010 (DOI: 10.1002/9780470638859.conrr109)
[8] Romero, Galliher, Pratt, Stephenson 'Radicals in natural product synthesis' *Chem. Soc. Rev.* 2018, **47**, 7851 (DOI: 10.1039/C8CS00379C)
[9] Pattenden, Stoker, Thomson 'Cascade radical-mediated cyclisations with conjugated ynone electrophores. An approach to the synthesis of steroids and other novel ring-fused polycyclic carbocycles' *Org. Biomol. Chem.* 2007, **5**, 1776 (DOI: 10.1039/B703373G)