

## 8.1: Road Maps in Total Synthesis of Natural Products

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Topics required for successful completion are listed under each link.

[Abyssomicin, Sorensen, 2006](#)

alkene addition  
carbonyl addition  
carboxylic substitution  
nucleophilic substitution  
oxidation of alcohols  
pericyclics

[Amphilectolide, Trauner, 2014](#)

carbonyl addition  
carbonyl reduction  
"Claisen condensation"-type carboxylic substitution  
cuprate addition  
ester reduction  
nitrile hydrolysis

[Annamoxic Acid, Corey, 2004](#)

*alkene addition*  
*carbonyl addition*  
*elimination*  
*pericyclics*

[Anominine, Nicolaou, 2012](#)

*aldol reaction*  
*aliphatic nucleophilic substitution*  
*carbonyl addition*  
*carboxyl substitution*  
*elimination*  
*oxidation of alcohols*  
*radicals*

[Aplykurodinone, Danishefsky, 2010](#)

*aliphatic nucleophilic substitution*  
*carbonyl addition*  
*carboxylic substitution*  
*elimination*

## | oxidation of alcohols

[Atisine, Fukumoto, 1990](#)

esterification & amidification

Michael addition

reduction of esters

Wittig & Horner-Wadsworth-Emmons reactions

[Aurantioclavine, Ellman, 2010](#)

aliphatic nucleophilic substitution

carbonyl addition

carboxylic substitution

[Aza-epothilone B, Danishefsky, 2000](#)

*with bioassay study*

aliphatic nucleophilic substitution

carbonyl addition

carboxylic substitution

[Brevenal, Crimmins, 2010](#)

(partial synthesis)

carbonyl addition, anionic & semianionic nucleophiles

carbonyl addition, aldols

carbonyl addition, ylides

[Brevetoxin, Crimmins, 2009](#)

aliphatic nucleophilic substitution

electrophilic addition to alkenes

carbonyl addition

[Briarellin, Crimmins, 2011](#)

nucleophilic addition to epoxide

aliphatic nucleophilic substitution

silyl protecting groups

carboxylic substitution

carbonyl addition

electrophilic addition to alkenes

ylide addition

oxidation of alcohols

[Bryostatin, Burke, 2004](#)

dihydroxylation

Horner-Wadsworth-Emmons or Wittig reaction

hydroboration - oxidation

oxidation of alcohols

reduction of esters and ketones

ring-closing olefin metathesis

[Callipeltoside, MacMillan, 2008](#)

*aliphatic nucleophilic substitution*

*electrophilic addition to alkenes*

*carbonyl addition*

*carboxylic substitution*

*oxidation of alcohols*

[Cassiol, Stoltz, 2008](#)

*aliphatic nucleophilic substitution*

*carbonyl addition*

*carboxylic substitution*

[Cavicularin, Beaudry, 2013](#)

*Diels Alder*

*etherification*

*palladium coupling*

*Wittig or Tebbe reactions*

[Clavolonine, Fujioka, 2011](#)

aliphatic nucleophilic substitution and elimination

[Deoxytetracycline, Stork, 1996](#)

*carbonyl addition (anionic and neutral nucleophiles)*

*carboxylic substitution*

*conjugate addition*

[Dedihydrosemofalin, Overman, 2003](#)

alpha-alkylation

aza-Cope rearrangement

catalytic hydrogenation

Diels Alder

iminium ion formation

oxidation of alcohols

ozonolysis

reduction of esters

silylation of alcohols

silylation of enolates

silyl ether cleavage

Wittig & Horner-Wadsworth-Emmons reactions

[Dendrobine, Carreira, 2012](#)

*carbonyl addition*

*carboxylic substitution*

[Doliculide, Ghosh, 2001](#)

*aliphatic nucleophilic substitution*

*electrophilic addition to alkenes*

[Dynemicin, Danishefsky, 1996](#)

aliphatic nucleophilic substitution

alkene oxidation

carbonyl addition

carboxylic substitution

elimination

oxidation of alcohols

pericyclics

[Echinopine, Nicolaou, 2010](#)

aliphatic nucleophilic substitution

carbonyl addition

carboxylic substitution

[Epothilone, Altmann, 2008](#)

aldol reaction

alpha deprotonation

Grignard reactions

Wittig and Horner-Wadsworth-Emmons reactions

[Fischerindole, Baran, 2008](#)

aliphatic nucleophilic substitution

carbonyl addition,

carboxylic substitution,

electrophilic addition to alkenes

oxidation of alcohols

radicals

[Ginkgolide, Corey, 1988](#)

aliphatic nucleophilic substitution

carbonyl addition

carboxylic substitution

conjugate addition

electrophilic addition to alkenes

enolates

rearrangements

radicals

[Glucosylceramide, Overkleeft, 2007](#)

*contains a bioassay exercise*

*aliphatic nucleophilic substitution*

*carbonyl addition*

*carboxylic substitution*

*elimination*

*oxidation of alcohols*

[Juvenile Hormone 1, Corey, 1968](#)

aliphatic nucleophilic substitution

carbonyl addition

carboxylic substitution

cuprate addition

electrophilic addition to alkenes

oxidation of alcohols

Wittig reaction

[Lepistine, Yokoshima & Fukuyama, 2014](#)

aliphatic nucleophilic substitution

elimination

[Longifolene, Corey, 1961](#)

*aliphatic nucleophilic substitution*

*alkene oxidation*

*carbonyl addition*

*carboxylic substitution*

*elimination*

*oxidation of alcohols*

[Lycopladiene, Weinreb, 2015](#)

acetal/ketal cleavage

acetal/ketal formation

catalytic hydroformylation of alkenes

Grignard reactions

reductive amination

[Manzacidin A, Kawabata, 2013](#)

carboxylic substitution: esterification and amidification

conjugate addition

[Nahuoic Acid, Smith, 2017](#)

acetal / ketal formation

alkene reduction

carbonyl reduction

cuprate addition

Diels Alder reaction

epoxide opening (organometallic)

ester hydrolysis

keto-enol tautomerism

methoxymethyl ether formation

olefin metathesis

silyl ether formation & cleavage

syn dihydroxylation

thioacetal / thioketal cleavage

[Nakadomarin, Kerr, 2007](#)

aliphatic nucleophilic substitution

carbonyl addition

carboxylic substitution

conjugate addition

elimination

oxidation of alcohols

[Norzoanthamine, Theodorakis, 2011](#)

Robinson annulation

conjugate addition

anionic addition to carbonyls

carboxylic substitution

[Octalactin, Buszek, 1994](#)

alkene reduction

epoxidation

hydroboration / oxidation

Lindlar's catalyst

silyl ether cleavage

[Okilactomycin, Smith, 2007](#)

aldol condensation

aliphatic nucleophilic substitution

carbonyl addition

carboxylic substitution

elimination

oxidation of alcohols

pericyclics

[Perhydrohistrionicotoxin, Corey, 1975](#)

aliphatic nucleophilic substitution

carbonyl addition

carboxylic substitution

conjugate addition

elimination

enolates

oxidation of alcohols

radicals

[Periplanone, Still, 1979](#)

*aldol condensation*

*aliphatic nucleophilic substitution*

*carbonyl addition*

*carboxylic substitution,*

*elimination*

*oxidation of alcohols*

*pericyclics*

[Platensimicin, Ghosh, 2009](#)

*aliphatic nucleophilic substitution*

*electrophilic addition to alkenes*

[Polyanthellin, Johnson, 2009](#)

*electrophilic addition to alkenes: halogenation, hydroboration, oxymercuration, epoxidation, cyclopropanation*

*aliphatic nucleophilic substitution*

[Polycavernoside, Sasaki, 2017](#)

*epoxidation*

*epoxide ring-opening*

*esterification*

*oxidation of alcohols*

*silyl ether cleavage*

[Prostaglandin A2, Corey, 1972](#)

- aliphatic nucleophilic substitution*
- carbonyl addition*
- carboxylic substitution*
- elimination*
- oxidation of alcohols*

[Quinine, Stork, 2001](#)

- aliphatic nucleophilic substitution*
- carbonyl addition*
- carboxylic substitution*

[Quinocarcin, Stoltz, 2008](#)

- carbonyl addition*
- carboxylic substitution*

[Salvileucalin, Reisman, 2011](#)

- carbonyl addition*
- carboxylic substitution*

[Saxitoxin, Du Bois, 2006](#)

- Contains a bioassay exercise.*
- aliphatic nucleophilic substitution*
- carbonyl addition*
- carboxylic substitution*
- electrophilic addition to alkenes*
- oxidation of alcohols*

[Scholarisine, Smith, 2012](#)

- aliphatic nucleophilic substitution*
- carbonyl addition*
- carboxylic substitution,*

[Serotobenine, Fukuyama & Kan, 2008](#)

- aliphatic nucleophilic substitution*
- alkene oxidation*
- carbonyl addition*
- carboxylic substitution*



*elimination*

*oxidation of alcohols*

*pericyclics*

[Solamine, Stark, 2006](#)

*aliphatic nucleophilic substitution*

*alkene oxidation*

*carbonyl addition*

*carboxylic substitution*

*elimination*

*oxidation of alcohols*

[Spongidepsin, Cossy, 2006](#)

*activation of carboxylic acids*

*esterification & amidification*

*Grignard reactions*

*hydrolysis of amides*

*reduction of esters*

*Wittig & Horner-Wadsworth-Emmons reactions*

[Strychnine, Overman, 1993](#)

*aliphatic nucleophilic substitution*

*alkene oxidation*

*carbonyl addition*

*carboxylic substitution*

*conjugate addition*

*elimination*

*enolates*

Exercise: [catalytic cycles in transition metal organometallics](#).

[Taiwaniaquinol, Fillion, 2005](#)

*aldol condensation*

*alpha alkylation*

*conjugate addition*

*electrophilic aromatic substitution*

*etherification*

*palladium coupling*

[Taxol, Nicolaou, 1994](#)

*aliphatic nucleophilic substitution*

alkene oxidation

carbonyl addition

carboxylic substitution

elimination

oxidation of alcohols

pericyclics

radicals

[Tetrodotoxin, Kishi, 1972](#)

aliphatic nucleophilic substitution

alkene oxidation

carbonyl addition

carboxylic substitution

electrophilic addition to alkenes

oxidation of alcohols

pericyclics

rearrangements

[Tubingensin, Li, 2012](#)

carbonyl addition

carboxylic substitution, aldol

[Tulearin, Cossy, 2009](#)

carbonyl addition, anionic & semianionic nucleophiles

carbonyl addition, aldols

carbonyl addition, ylides

[Vermiculine, Corey, 1975](#)

carbonyl addition

carboxylic substitution

[Vibsanin, Takeo, 2015](#)

addition to carbonyl (organometallic)

allylic substitution

ester hydrolysis

ester reduction

esterification

ether formation

Mitsunobu reaction

silyl ether formation and cleavage

Wittig / Horner-Wadsworth-Emmons

[Vinigrol, Berriault, 2005](#)

acetals & ketals

Claisen rearrangement

Diels Alder

*syn*-dihydroxylations

esterification

Grignard reagents

hydride additions

oxidation of alcohols

silyl ethers

[Vittatalactone, Breit, 2010](#)

Aliphatic nucleophilic substitution

[Zaragozic acid, Nicolaou, 1994](#)

aliphatic nucleophilic substitution

alkene oxidation

carbonyl addition

carboxylic substitution

organo-transition metal reactions

oxidation of alcohols

radicals

sulfur ylides

[Zincophorin, Hsung, 2007](#)

aliphatic nucleophilic substitution

electrophilic addition to alkenes

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