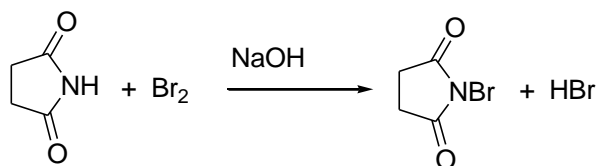


## Module 5                      Reactions with Miscellaneous Reagents

### Lecture 36

#### 5.1 N-Bromosuccinimide (NBS)

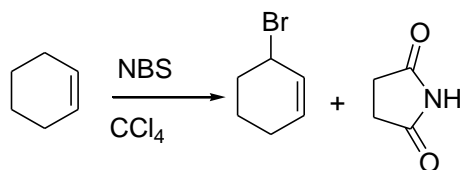
N-Bromosuccinimide (NBS) is a convenient source of bromine for radical substitution as well as electrophilic addition reaction. It is prepared from succinimide and bromine in the presence of NaOH solution. The colourless solid obtained is washed with water and recrystallized from hot water, and stored in a refrigerator and protected from moisture to avoid decomposition. NBS is easier and safer to handle compared to bromine.



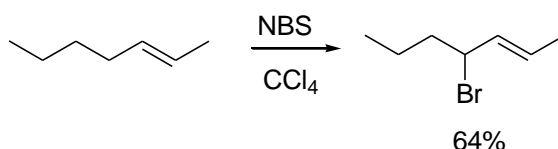
##### 5.1.1 Substitution Reactions

###### Allylic and Benzylic Brominations

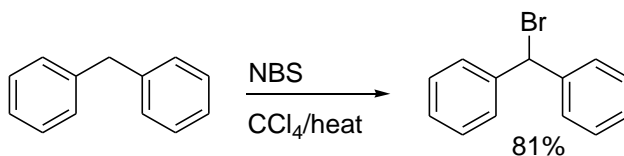
Alkenes react with NBS in dry  $\text{CCl}_4$  under reflux conditions to give allyl bromide. The reaction is initiated by light or peroxide. Although a number of reagents are available for bromination of allylic C-H bond of alkenes, NBS is most commonly used. The reaction is called Wohl-Zigler bromination. For example, cyclohexene reacts with NBS to give 3-bromocyclohexene in the presence of catalytic amount AIBN (radical initiator).



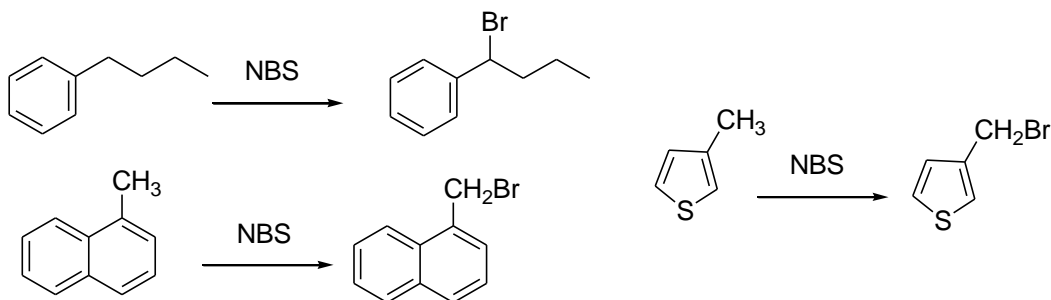
Allylic methylene groups are prone to undergo reaction more readily than allylic methyl group due to stabilization of the radical ( $2 > 1$ ). For example, 2-heptene can be selectively brominated at the secondary allylic carbon compared to the primary carbon.



The reaction conditions are compatible for the bromination of benzylic C-H bonds, which are important from synthetic and mechanistic standpoint. For examples, diphenylmethane reacts with NBS to give bromodiphenylmethane in 81% yield.



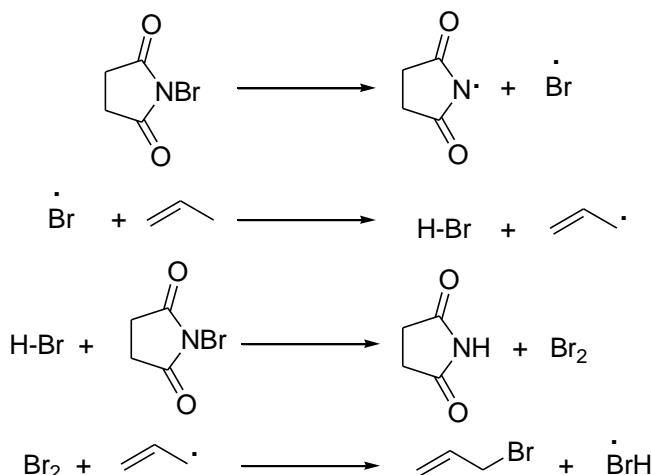
Similarly, 1-phenylbutane, 1-methylnaphthalene and 3-methylthiophene could be reacted with NBS to give the corresponding brominated products (Scheme 1).



Scheme 1

## Mechanism

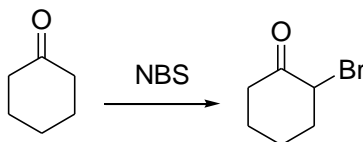
The reaction involves a free radical process (Scheme 2). The reaction is initiated by small amounts of Br radical. The role of NBS is to afford a constant low concentration of molecular bromine. Abstraction of an allylic or benzylic hydrogen by Br radical gives a resonance stabilized allyl or benzyl radical. The selective bromination occurs because the intermediate leading to the product is stabilized by resonance.



Scheme 2

## $\alpha$ -Bromination of Carbonyl Derivatives

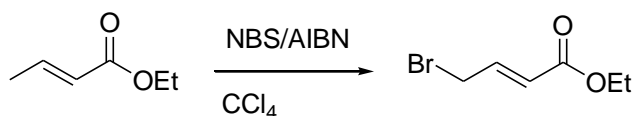
Ketones having enolizable hydrogen can be brominated at the  $\alpha$ -position. The reaction probably involves an addition of  $\text{Br}_2$  to the enol form of the carbonyl derivatives, and elimination of  $\text{HBr}$  generates the  $\alpha$ -bromoketone (Scheme 3).



Scheme 3

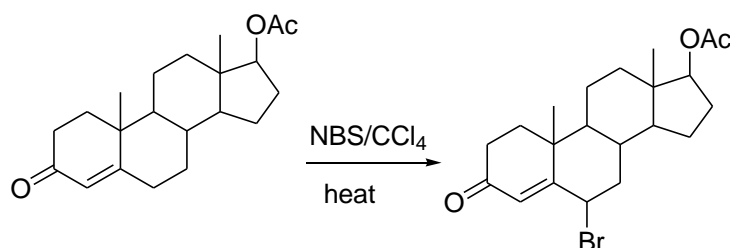
## Allylic Bromination of Unsaturated Acids, Esters, Aldehydes and Ketones

$\alpha,\beta$ -Unsaturated carbonyl compounds undergo reaction with NBS at the allylic C-H bond to give allylic brominated  $\alpha,\beta$ -unsaturated carbonyl compound that can be used in the Reformatsky reaction. For example, ethyl crotonate can be transformed into ethyl 4-bromocrotonate using NBS



Scheme 4

in the presence of catalytic amount of AIBN in CCl<sub>4</sub> under reflux conditions (Scheme 4). Under similar conditions, testosterone acetate can be converted into 6-bromotestosterone acetate in good yield (Scheme 5)



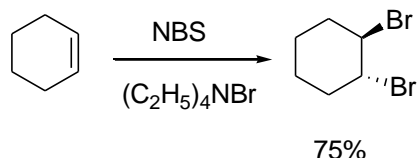
Scheme 5

## Bromination of Aromatic Rings

Aromatic compounds react with NBS under ionic conditions to undergo bromination in the aromatic ring by substitution. In these reactions, the brominating agent could probably be the protonated NBS. Benzene when treated with NBS and a 1:1 mixture of conc. H<sub>2</sub>SO<sub>4</sub> and water gives bromobenzene in 95% yield. Under these conditions, aromatic compounds having highly branched chains also appears to undergo bromination in the aromatic ring with selectivity.

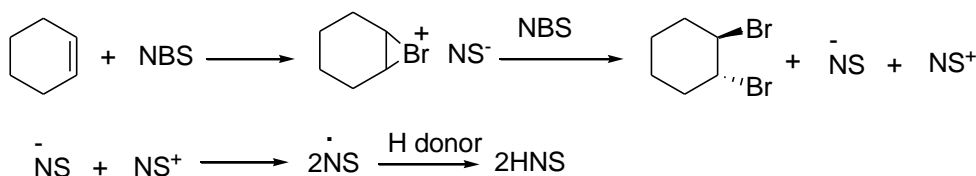
### 5.1.2 Addition Reactions

NBS is often used as the source of electrophilic bromine in polar solvents. For an example, cyclohexene reacts with NBS in the presence of tetraethylammonium bromide to give *trans*-1,2-dibromocyclohexane in good yield (Scheme 6).



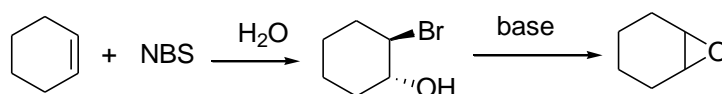
Scheme 6

A possible mechanism is represented in Scheme 7.



Scheme 7

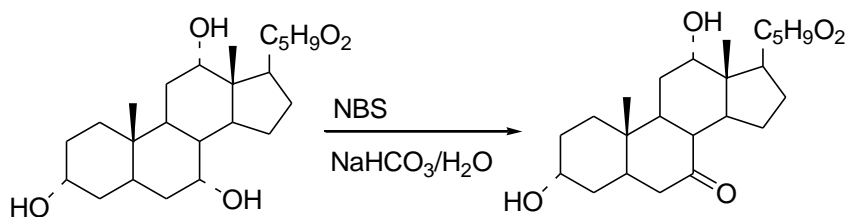
In the presence of excess of water, alkenes undergo reaction with NBS to give bromohydrins that could be converted into epoxides in the presence of base (Scheme 8).



Scheme 8

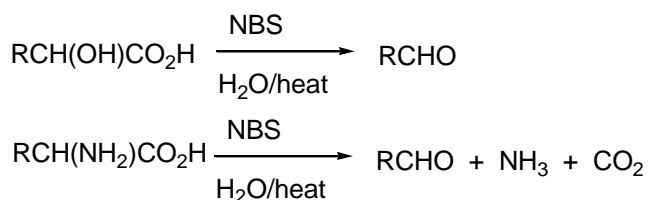
### 5.1.3 Oxidation

Secondary alcohols undergo oxidation to give ketones in the presence of NBS in water. This method has found wide applications in the oxidation of steroidal alcohols. For an example, cholic acid can be selectively oxidized at C-7 using NBS in the presence of water (Scheme 9).



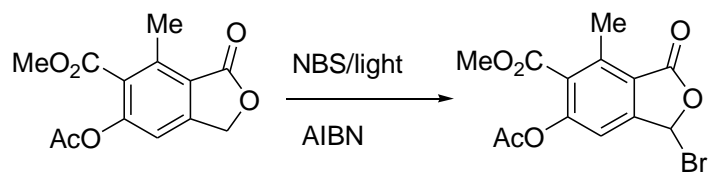
Scheme 9

In hot aqueous solution,  $\alpha$ -hydroxy acids can be oxidized to give aldehydes or ketones with loss of one carbon atom (Scheme 10). For example, glycolic acid, lactic acid and mandelic acid are converted into formaldehyde, acetaldehyde and benzaldehyde. Under these conditions  $\alpha$ -amino acids proceed decarboxylation to give aldehydes.

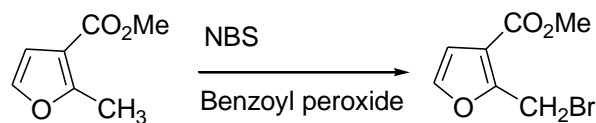


Scheme 10

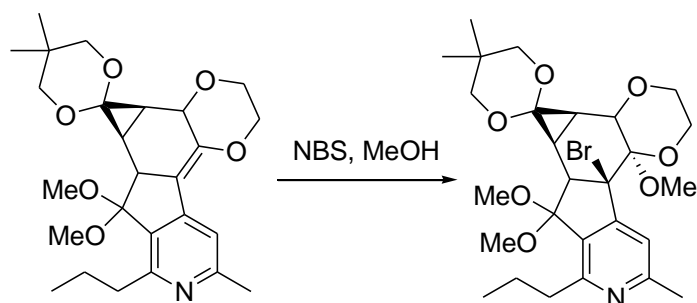
**Examples:**



T. R. Kelly, D. Xu, G. Martinez, H. Wang, *Org. Lett.* **2002**, 4, 1527.



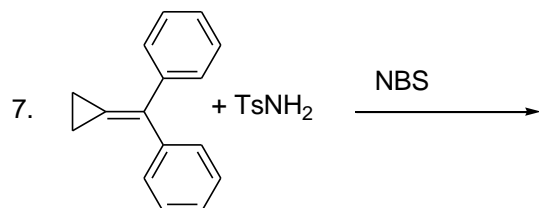
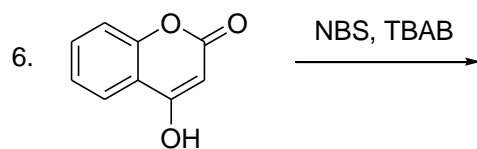
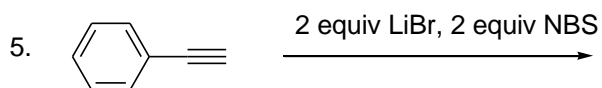
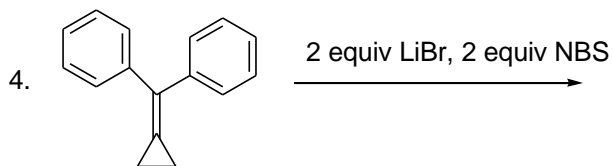
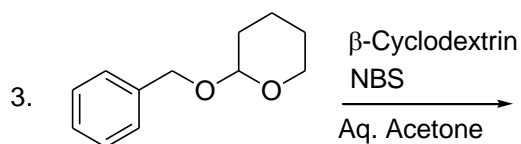
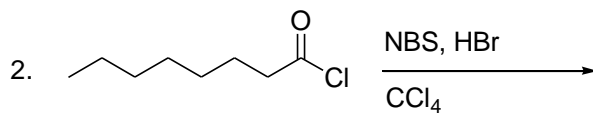
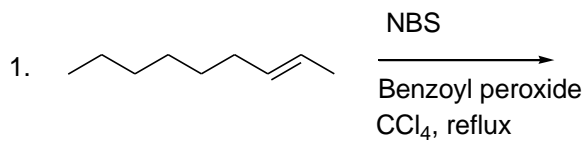
H. Khatuya, *Tetrahedron Lett.* **2002**, 42, 2643.



D. L. Boger, S. Ichikawa, H. Jiang, *J. Am. Chem. Soc.* **2000**, 122, 12169.

**Problems:**

A. Find out the major products in the following reactions.





## Text Books

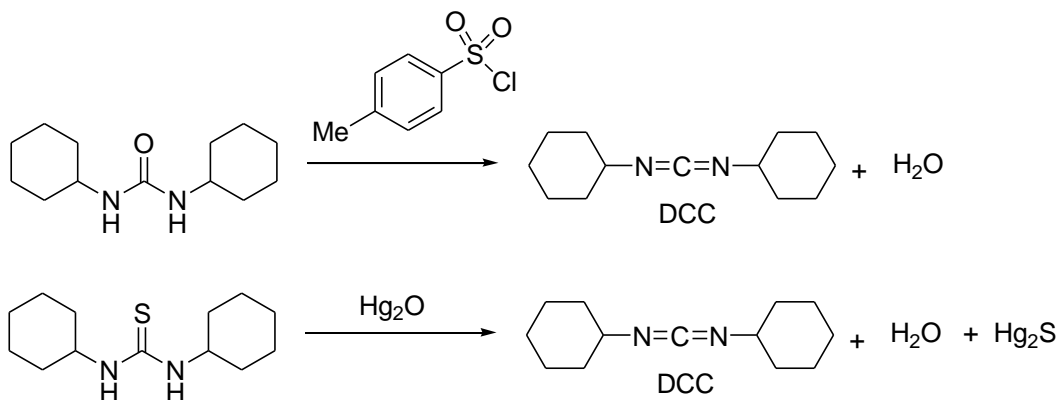
M. B. Smith, *Organic Synthesis*, 2<sup>nd</sup> Ed., McGraw Hill, Singapore, 2004.

V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms*, Narosa Publishing House, New Delhi, 2002.

## Lecture 37

### 5.2 N,N-Dicyclohexylcarbodiimide (DCC)

*N,N*-Dicyclohexylcarbodiimide (DCC) is a dehydrating agent often used to form esters, amides or anhydrides. It is commercially available as a waxy low-melting solid (34-35 °C). It can also be prepared by oxidation of dicyclohexylurea with *p*-toluenesulfonyl chloride in hot pyridine or by heating dicyclohexylthiourea with yellow mercuric oxide (Scheme 1). The section covers some important applications in organic synthesis.

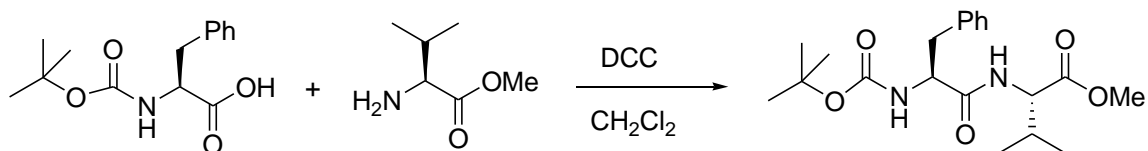


Scheme 1

J.S. Albert, A. D. Hamilton, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 1751.

### 5.2.1 Synthesis of Peptides

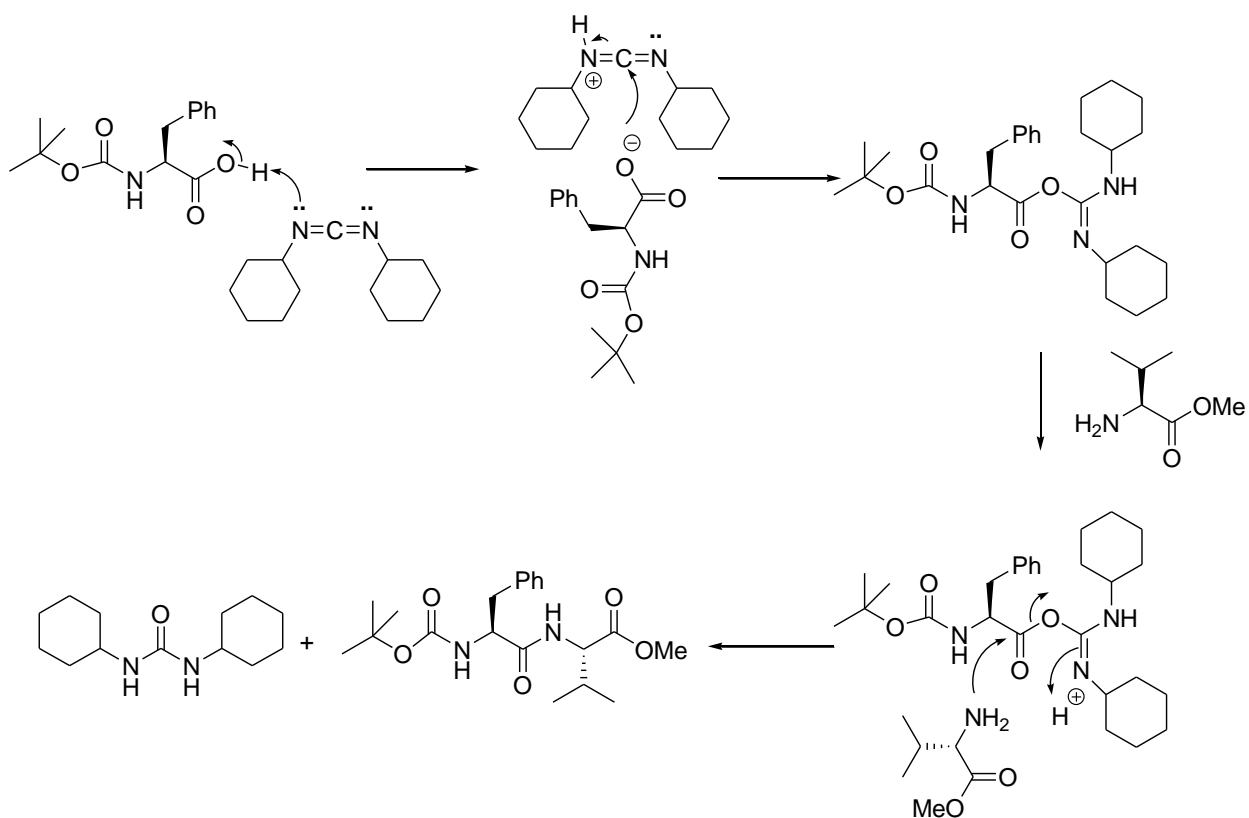
DCC is useful for the coupling of amino acids *via* amide C-N bonds. The amino acid monomers should be such that the ends to be available and other reactive groups protected. For example, for the synthesis of dipeptide between two  $\alpha$ -amino acids, the amino group of one of the amino acids and the carboxylic group of the other must be protected before the two amino acids are brought together in the presence of DCC (Scheme 2).



Scheme 2

#### Mechanism

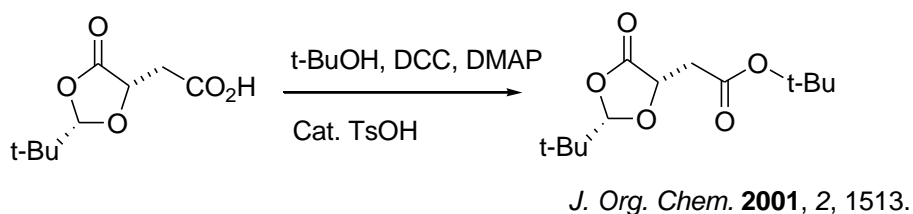
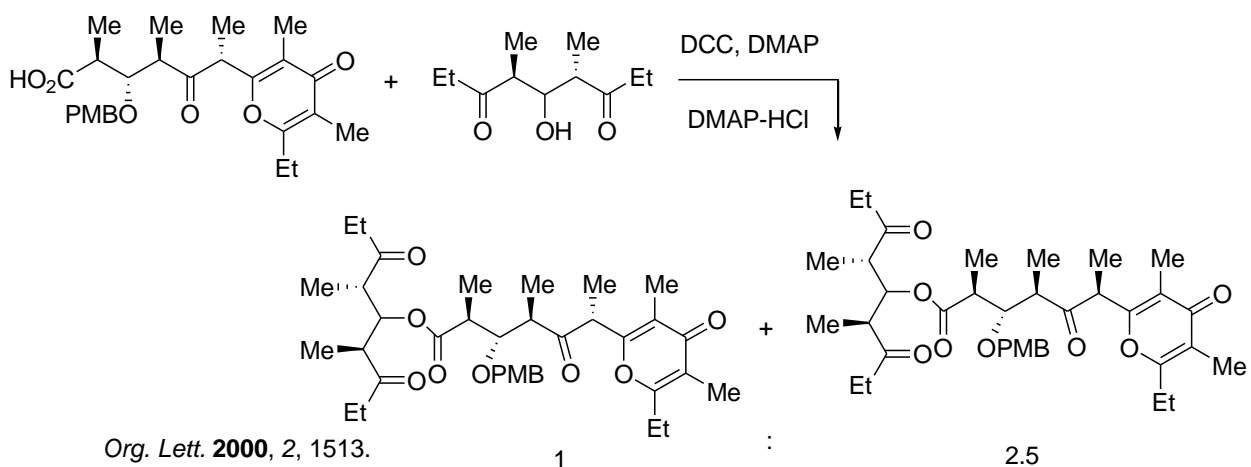
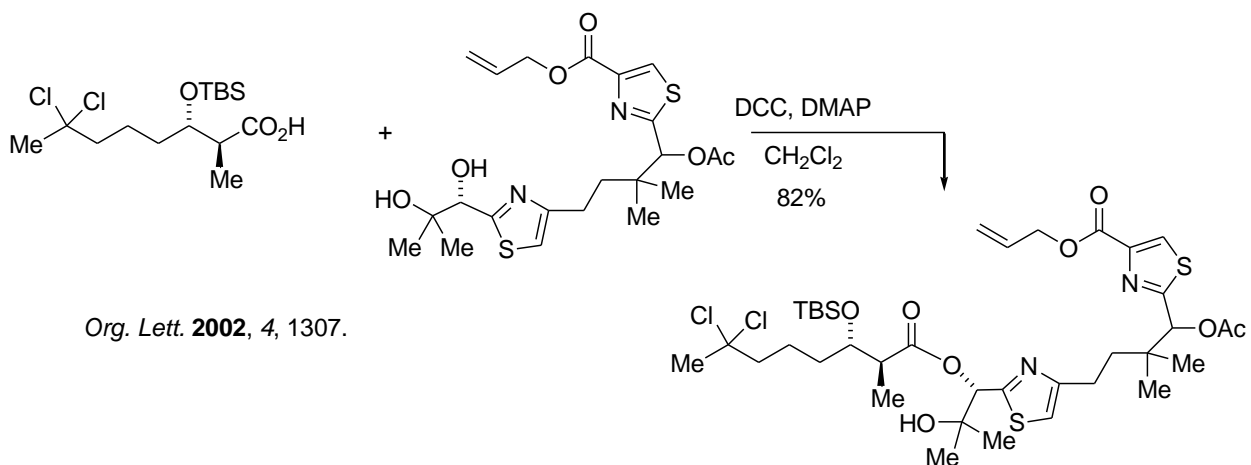
DCC reacts with the carboxyl group of amino protected acid to give activated acylating agent that undergoes reaction with amino group of other amino acid to form of a new amide bond (Scheme 3).



Scheme 3

### 5.2.2 Synthesis of Esters

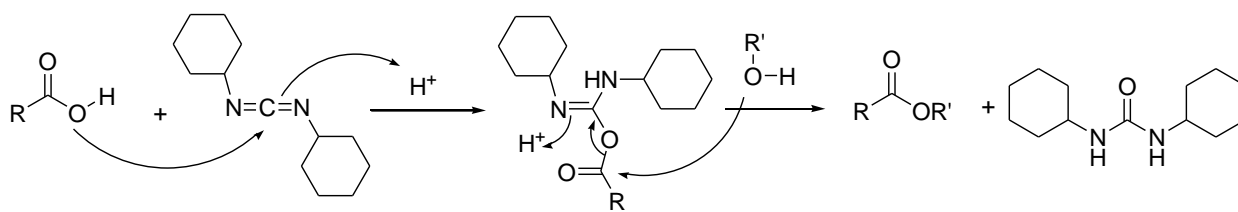
The synthesis of esters from carboxylic acids and alcohols can be accomplished in the presence of DCC in  $\text{CH}_2\text{Cl}_2$  solvent at ambient conditions. This reaction is called Steglich esterification and usually for the sterically hindered substrates (Scheme 4).



Scheme 4

## Mechanism

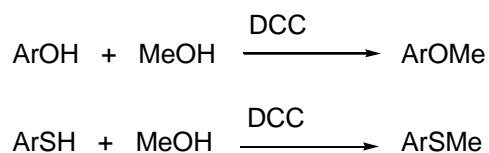
The carboxylic acid proceeds reaction with DCC to afford activated acylating agent that undergoes reaction with the alcohol (Scheme 5).



Scheme 5

### 5.2.3 Synthesis of Ethers and Thioethers

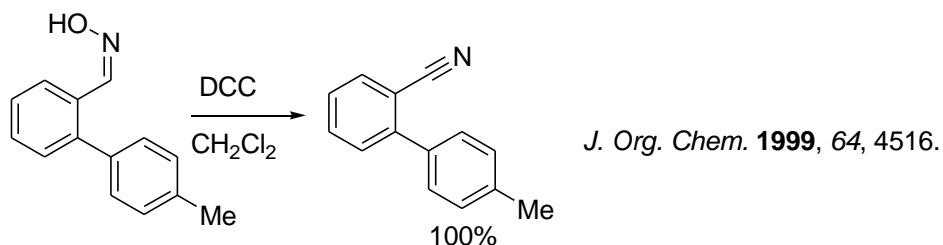
Phenols and thiophenols can be reacted with alcohols to give ethers in the presence of DCC (Scheme 5).



Scheme 5

### 5.2.4 Synthesis of Nitrile

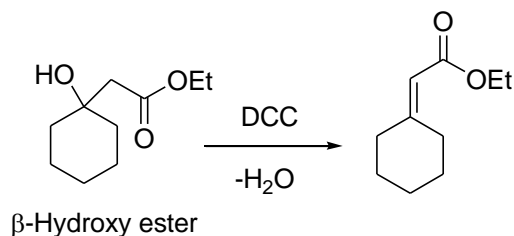
The readily accessible oximes from aldehydes and hydroxyl amine readily undergo dehydration in the presence of DCC to nitriles in quantitative yields (Scheme 6).



Scheme 6

### 5.2.5 Synthesis of $\alpha,\beta$ -Unsaturated Esters

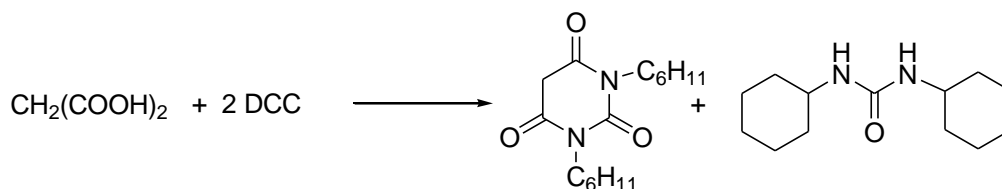
The dehydration of  $\beta$ -hydroxy esters can be efficiently carried out using DCC to give  $\alpha,\beta$ -unsaturated ester (Scheme 7).



Scheme 7

### 5.2.6 Heterocyclization Reactions

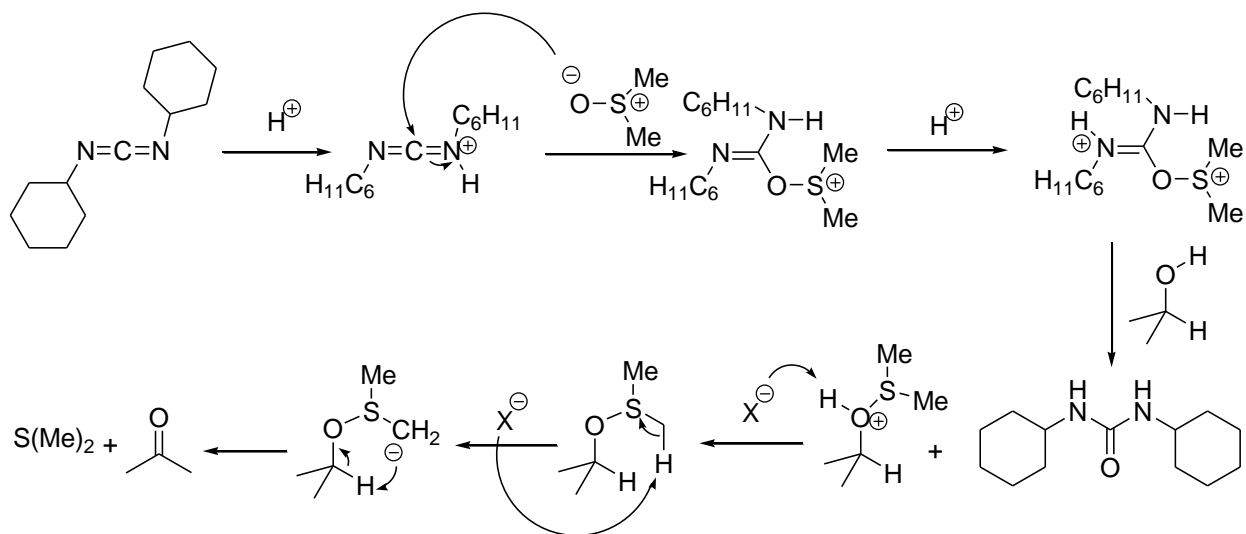
DCC is used as reactant as well as reagent in heterocyclization reactions. For an example, barbituric acid and its derivatives can be prepared by the reaction of malonic acid with DCC (Scheme 8).



Scheme 8

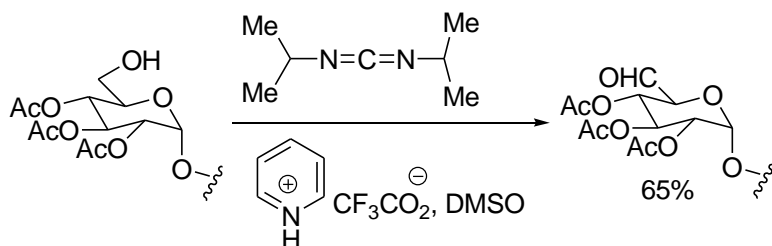
### 5.2.7 Heterocyclization Reactions

A mixture of DCC and DMSO catalyzes the oxidation of alcohols to aldehydes or ketones in the presence of acid catalyst. The reaction is called Pfitzner-Moffatt oxidation. A sulfur ylide is formed with base abstracts the  $\alpha$ -proton, generating dimethyl sulfide and the aldehyde or ketone (Scheme 9).

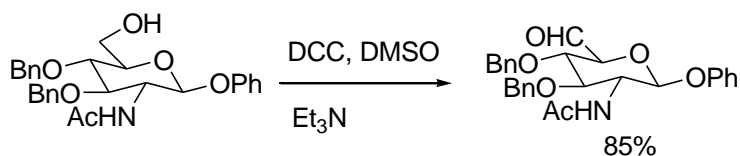


Scheme 9

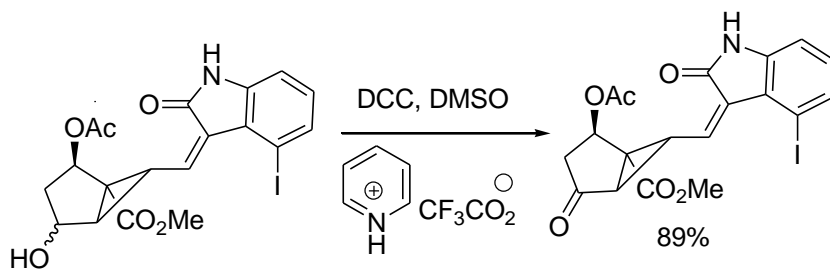
### Examples:



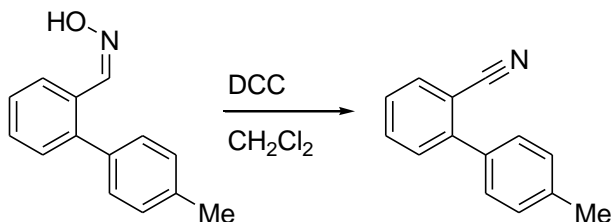
B. Sauerbrei, J. Niggemann, S. Grisger, S. Lee, H. G. Floss, *Carbohydrate Research* **1996**, **280**, 223.



R. Schworer, R. R. Schmidt, *J. Am. Chem. Soc.* **2002**, **124**, 1632.



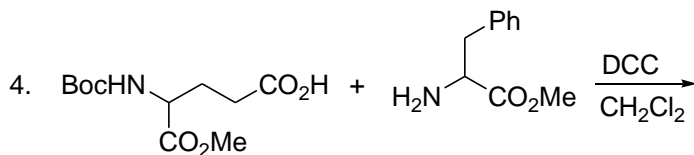
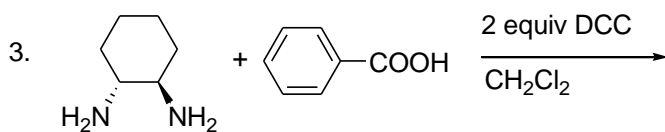
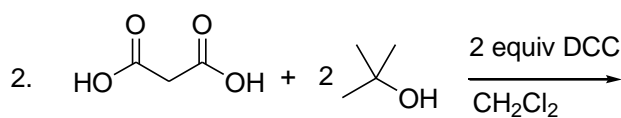
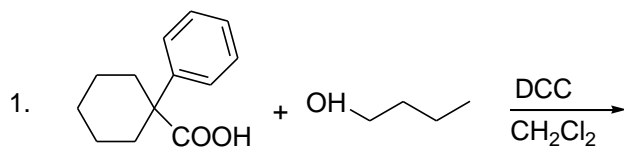
R. Schworer, R. R. Schmidt, *J. Am. Chem. Soc.* **2002**, 124, 1632.



D. Goubet, P. Meric, J.-R. Dormoy, P. Moreau, *J. Org. Chem.* **1999**, 64, 4516.

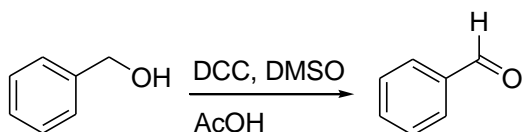
### Problems:

A. What products would you expect from the following reactions?



B. Rationalize the following reaction.





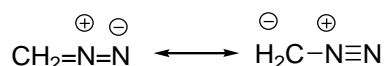
### Text Book

M. B. Smith, *Organic Synthesis*, 2<sup>nd</sup> Ed., McGraw Hill, Singapore, 2004.

## Lecture 38

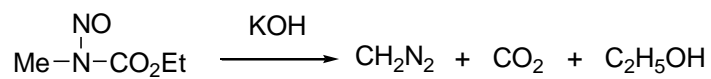
### 5.3 Diazomethane ( $\text{CH}_2\text{N}_2$ )

Diazomethane is yellow, toxic and reactive gas which is soluble in ether. Liquid diazomethane is explosive but may be handled safely in ethereal solution. It is prepared immediately prior to use and represented by the following resonance hybrid structures.

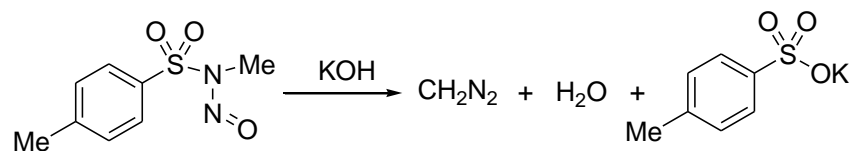


T. Sammakia, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1512.

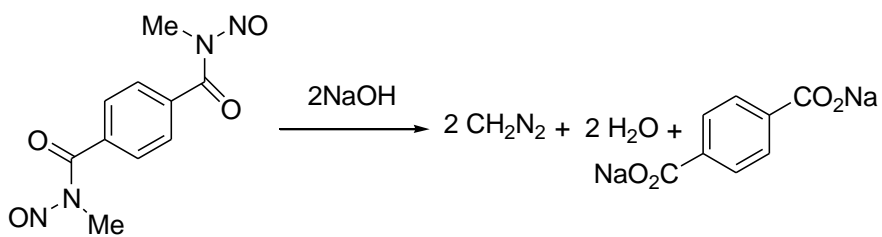
Major sources for the preparation of diazomethane are the basic hydrolysis of *N*-methyl-*N*-nitrosocompounds (Scheme 1-3).



N-Methyl-N-nitrosourethane

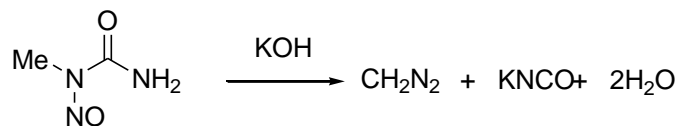


N-Methyl-N-nitroso-*p*-toluenesulfonamide

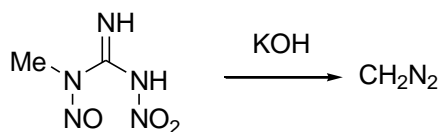


*N,N'*-Dimethyl-*N,N'*-dinitroterephthalamide

Scheme 1



N-Methyl-N-nitrosourea

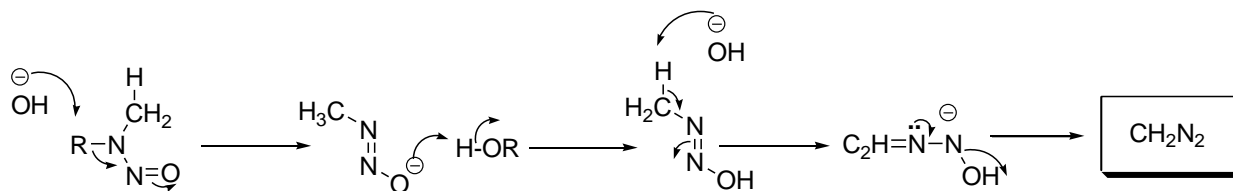


N-Methyl-*N'*-nitrosoguanidine

Scheme 2

## Mechanism

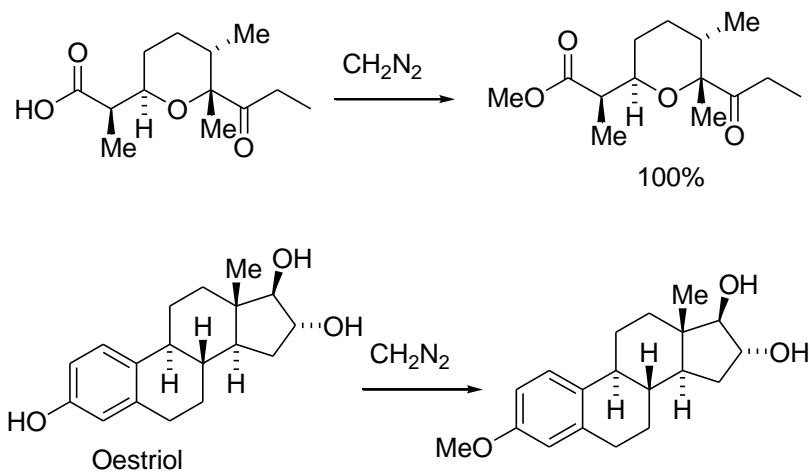
The key step is base-catalyzed elimination.



Scheme 3

### 5.3.1 Methylation

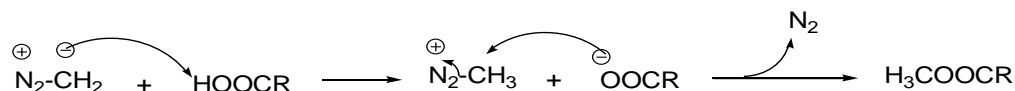
Diazomethane methylates acidic hydroxyl groups, carboxylic acids, sulfonic acids, phenols and enols. Conditions are mild and the products are obtained in high yield (Scheme 5).



Scheme 5

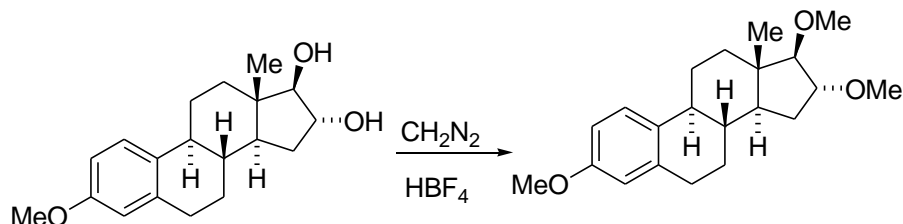
## Mechanism

Diazomethane is a powerful methylating agent, particularly useful for mild preparation of methyl esters of acids (Scheme 6).



Scheme 6

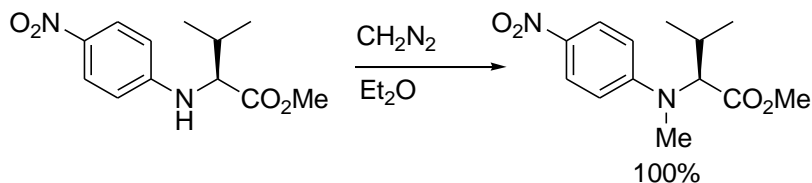
The reactions aliphatic alcohols require catalyst because of the low acidity of the hydroxyl hydrogen.  $\text{AlCl}_3$  and  $\text{BF}_3\cdot\text{OEt}_2$  are generally employed for this purpose (Scheme 7).



Scheme 7

Similarly, the reactions of aliphatic amines with diazomethane are also effective in the presence of catalysts such as  $\text{BF}_3\cdot\text{OEt}_2$  and cuprous cyanide. However, the methylation of aromatic amines can be accomplished without the Lewis acid catalyst.

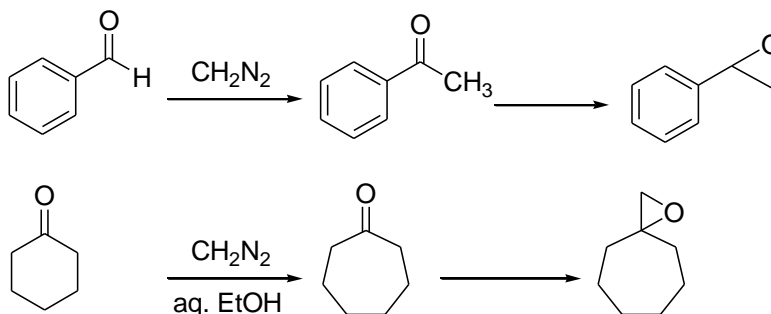
### Example:



M. L. Di Gioia, A. Leggio, A. Le Pera, A. Liguori, A. Napoli, C. Siciliano, G. Sindona, *J. Org. Chem.* **2003**, 68, 7416.

### 5.3.2 Homologations

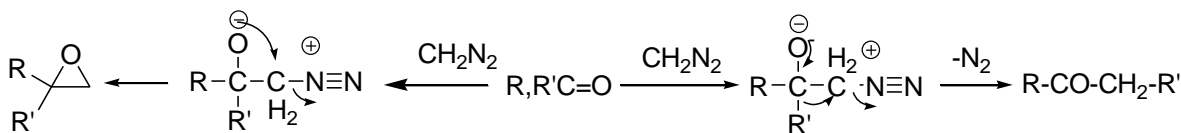
Diazomethane reacts with aldehydes to afford methyl ketones and ketones can be converted into higher homologues (Scheme 8). In both the cases the yields are moderate due to the formation of epoxides as by-product.



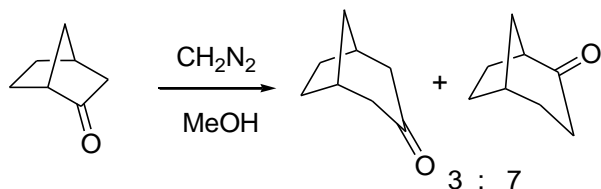
Scheme 8

#### Mechanism

The addition of diazomethane to the carbonyl group of the aldehydes or ketone can give betain, which could lose nitrogen and lead rearrangement to yield higher ketone or can cyclize to afford epoxides (Scheme 9).



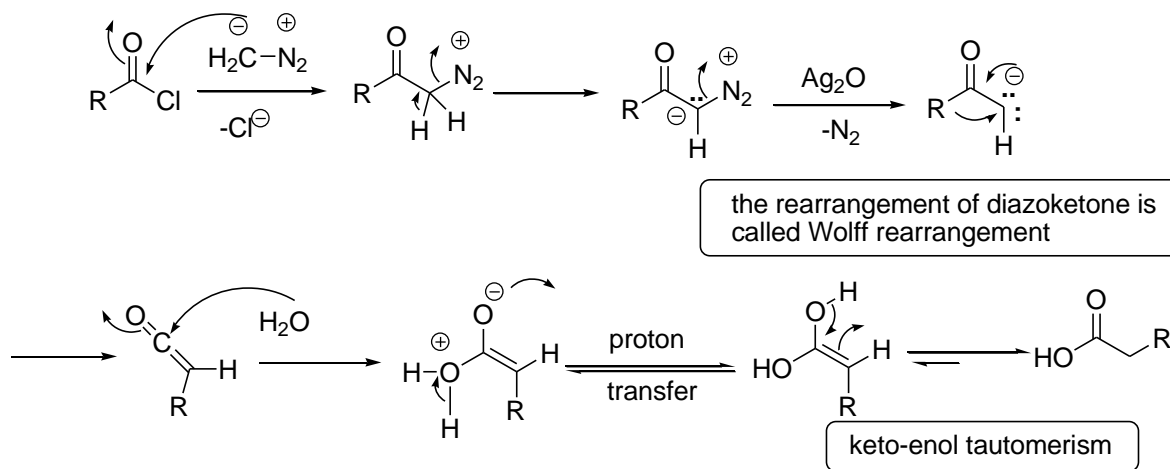
Scheme 9

**Example:**

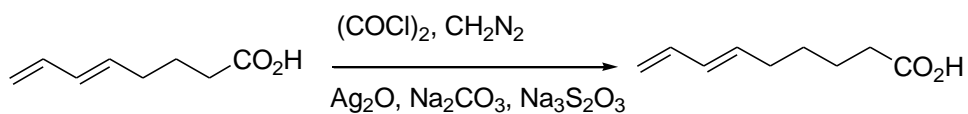
Y. Auberson, R. Mampuya, Bimwala, P. Vogel, *Tetrahedron Lett.* **1991**, 32, 1637.

**Arndt-Eistert Homologation Reaction**

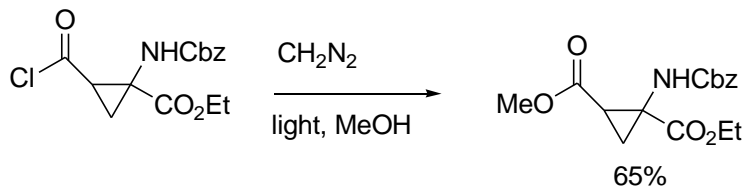
The reaction of acid chloride with diazomethane gives  $\alpha$ -diazoketone, which rearranges with loss of nitrogen to provide ketene in the presence of colloidal silver. The ketene is subsequently transformed into carboxylic acid (Scheme 10). It is called Arndt-Eistert Homologation reaction.



Scheme 10

**Example:**

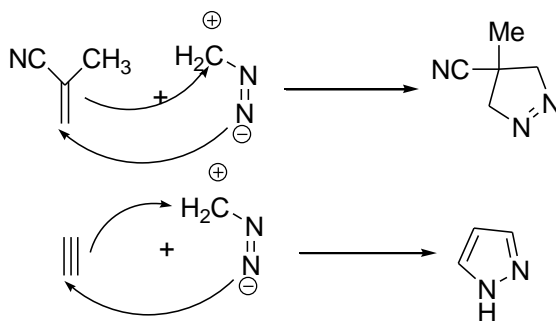
T. Hudlicky, J. P. Sheth, *Tetrahedron Lett.* **1979**, 29, 2667.



J. M. Jimenez, R. M. Ortuno, *Tetrahedron: Asymmetry* **1996**, 7, 3203.

**5.3.3 Addition Reactions**

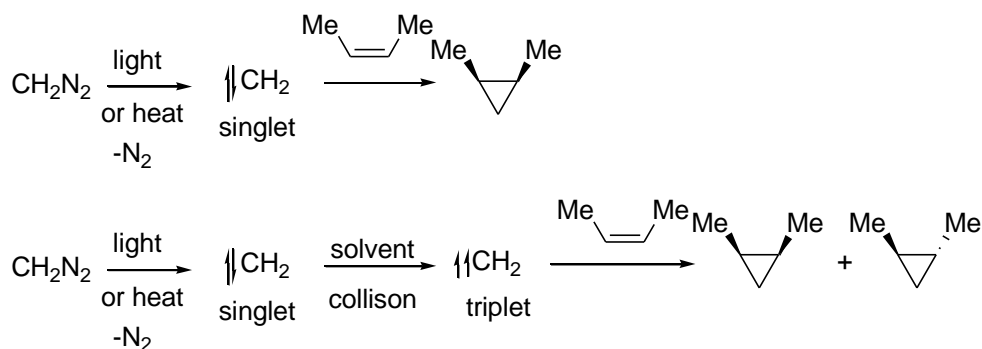
The 1,3-dipolar addition of reaction of diazomethane with a variety of compounds having ethylenic and acetylenic bonds afford heterocyclic compounds (Scheme 11).



Scheme 11

### 5.3.4 Cycloaddition

Heat as well as light produces carbene from diazomethane through loss of nitrogen that can add to alkenes to give cyclopropane derivatives (Scheme 12). If the reaction is diluted with a large amount of an inert solvent, the carbene undergoes more collisions before it reacts and so the chances of flipping singlet to triplet carbene are increased. Addition to alkenes is then less stereospecific.

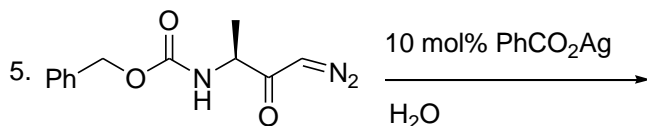
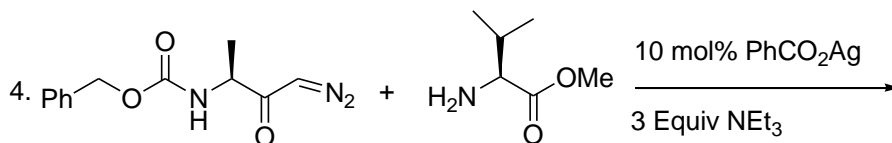
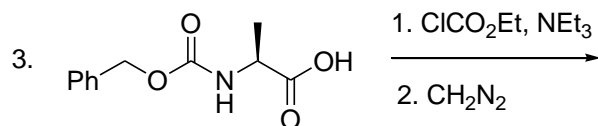
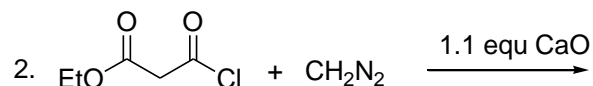
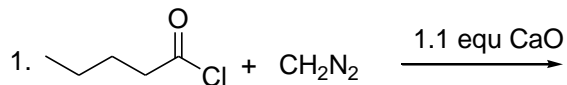


Scheme 12

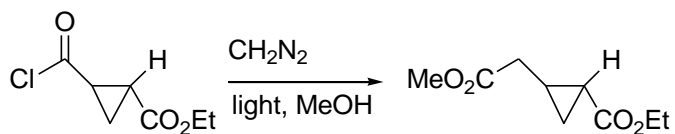


**Problems:**

A. Complete the following reactions.



B. Rationalize the following reaction.

**Text Book**M. B. Smith, *Organic Synthesis*, 2<sup>nd</sup> Ed., McGraw Hill, Singapore, 2004.

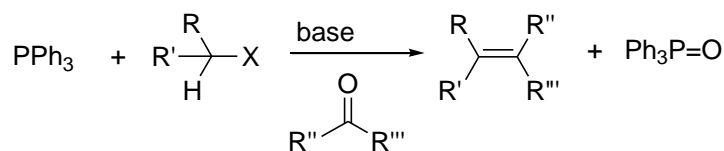
## Lecture 39

### 5.4 Phosphorus Reagents

Phosphorus based compounds are extensively used in organic synthesis as reagents as well as ligands for metal-catalyzed reactions. This section covers some of the important applications as reagents.

#### 5.4.1 Wittig Reaction

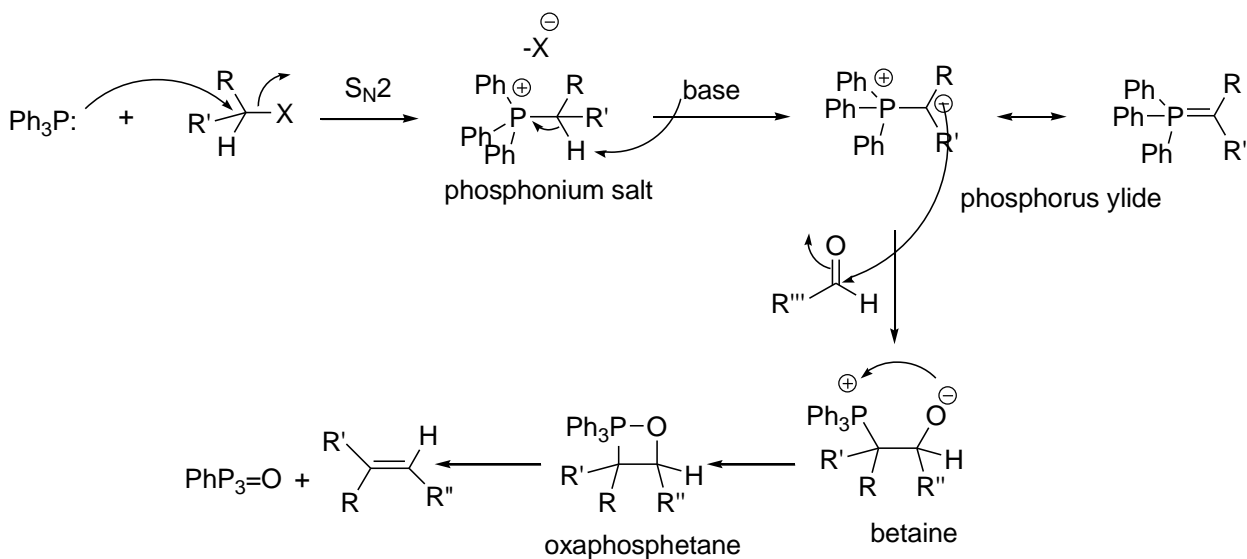
The reactions of alkyl halides with aldehydes or ketones in the presence of triphenylphosphine and base give alkenes in high yield (Scheme 1). The reaction is known as Wittig reaction and was awarded Nobel prize in 1979. The reaction is versatile and affords powerful tool for the construction of alkenes with excellent stereoselectivity.



Scheme 1

#### Mechanism

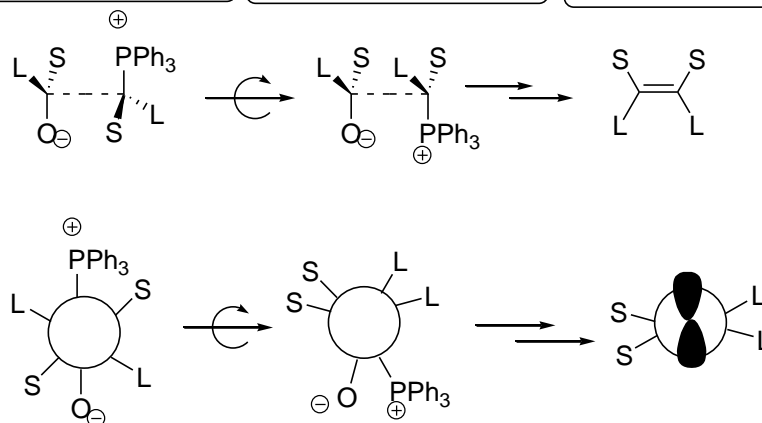
$\text{PPh}_3$  reacts with alkyl halide to give phosphonium salt *via* the nucleophilic displacement ( $\text{S}_{\text{N}}2$ ) of halide by the nucleophilic phosphorus atom of triphenylphosphine (Scheme 2). The acidic hydrogen of the phosphonium salt can be removed by strong base to give phosphorus ylides (commonly known as Wittig reagent). These phosphorus ylides carry a positive and a negative charge on adjacent atoms can be represented as double bonded species, called phosphoranes. Phosphorus ylides are strong nucleophiles and add to aldehydes or ketones to form betain that collapses to a four membered ring called oxaphosphetane, which can decompose to give the alkene and triphenylphosphine oxide.



Preferred anti attack of ylide,  
minimizing steric interactions

bond rotation follows  
to form the betaine

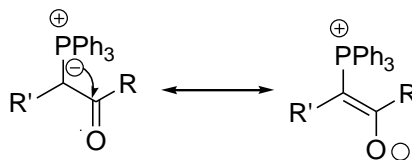
The reaction gives  
the cis alkene



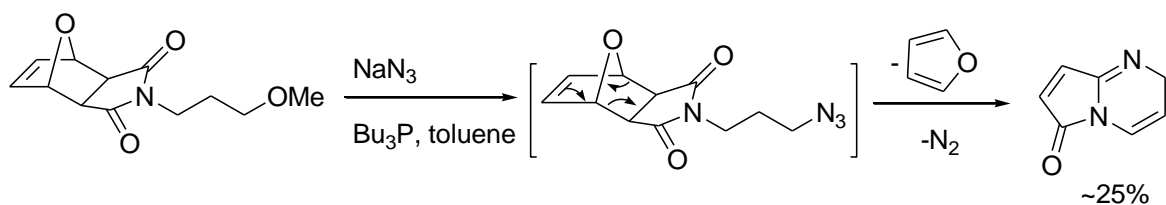
Scheme 2

Other phosphines may be used for the reaction. But they should not contain a proton that could be abstracted as is the proton on the halide coupling partner, as a mixture of desired and undesired ylides would be formed.

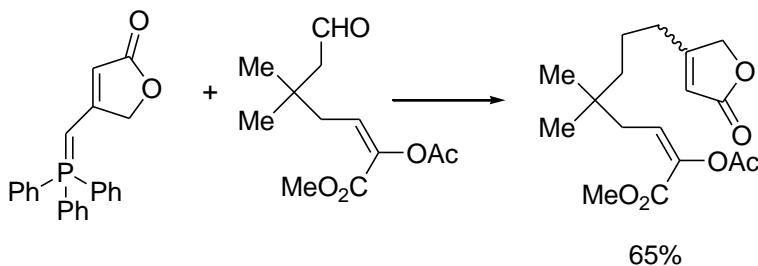
If the halide contains an electron withdrawing group, the negative charges in the ylide is delocalized, decreasing its nucleophilicity and reactivity. Aldehydes may still react, but ketones likely will not.



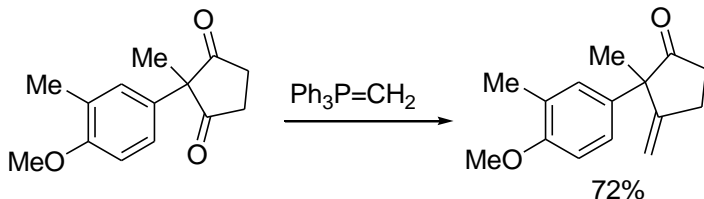
### Examples:



B. J. Neubert, B. B. Snider, *Org. Lett.* **2003**, 5, 765.



R. K. Boeckman, Jr., T. R. Aless, *J. Am. Chem. Soc.* **1982**, 104, 3216.

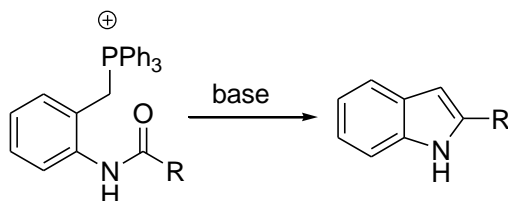


S. P. Chavan, R. K. Kharul, R. R. Kale, D. A. Khobragade, *Tetrahedron* **2003**, 59, 2737.

### 5.4.2 Wittig Indole Synthesis

Indoles are important structural unit and found in numerous natural product and biologically important compounds. Thus, the construction of the indole structural framework remains in organic synthesis. Anilides having methylphosphonium

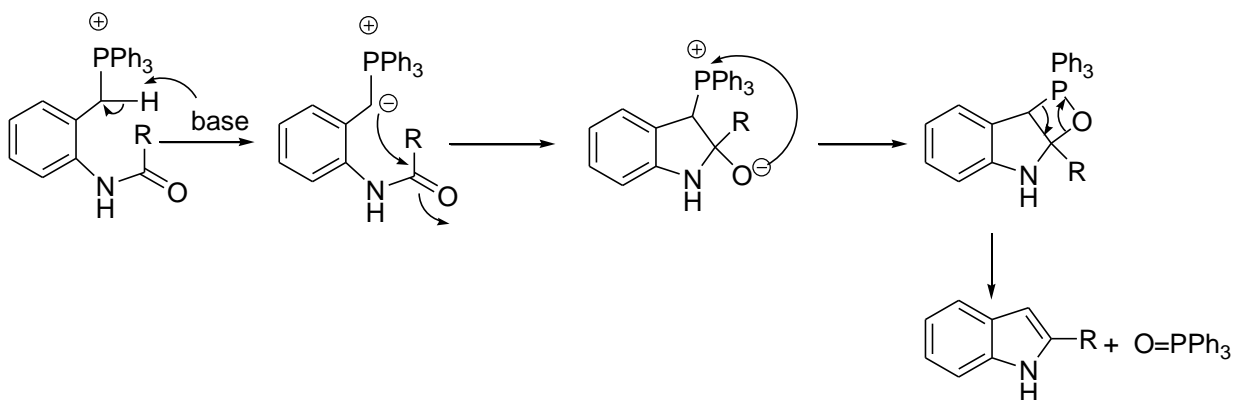
salt at their *ortho* position can be converted into indoles in the presence of base (Scheme 3). The reaction is called Wittig indole synthesis.



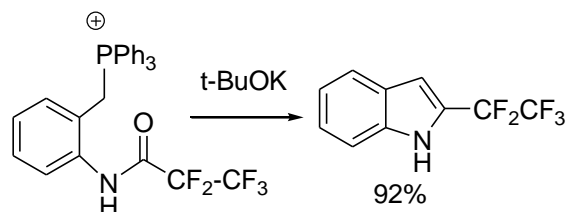
Scheme 3

### Mechanism

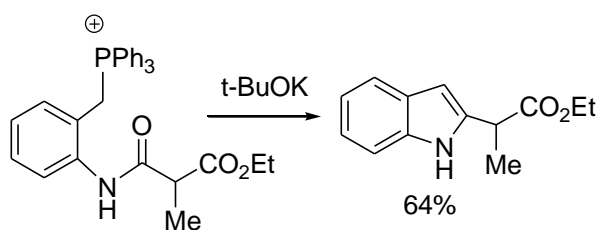
An intramolecular nucleophilic addition of phosphorus yield to carbonyl group of amide can give four membered ring oxaphosphetane that can decompose to give the target heterocycle (Scheme 4).



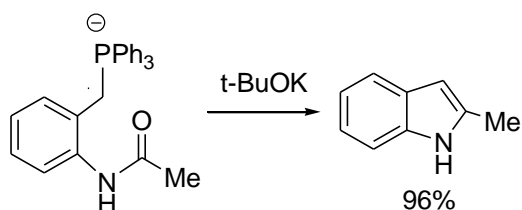
Scheme 4

**Examples:**

K. Miyashita, K. Kondoh, K. Tsuchiya, H. Miyabe, T. Imanishi, *J. Chem. Soc. Perkin Trans 1*, **1996**, 1261.



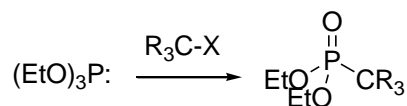
B. Danieli, G. Lesma, G. Palmisano, D. Passarella, A. Silvani, *Tetrahedron* **1994**, 50, 6941.



M. Le Corre, Y. Le Stane, A. Hercouet, H. Le Brown, *Tetrahedron* **1985**, 41, 5313.

**5.4.3 Michaelis-Arbuzov Reaction**

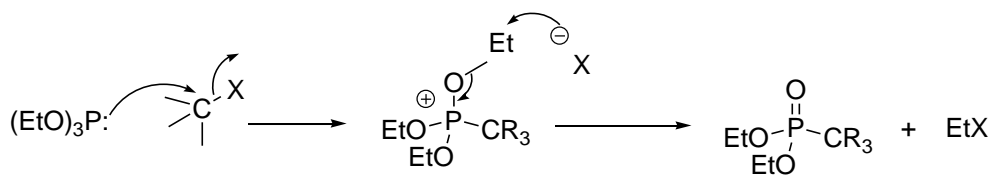
Several modifications of the Wittig reaction have been made to improve the reactivity of the ylides. The reaction of alkyl halides with triethylphosphite gives phosphonate esters (Scheme 7). This reaction is called Michaelis-Arbuzov reaction. The phosphonate esters are the precursor for the synthesis of more reactive ylides.



Scheme 5

### Mechanism

The rearrangement takes place *via* S<sub>N</sub>2 reaction (Scheme 8).

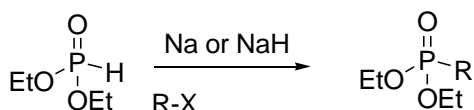


Scheme 6

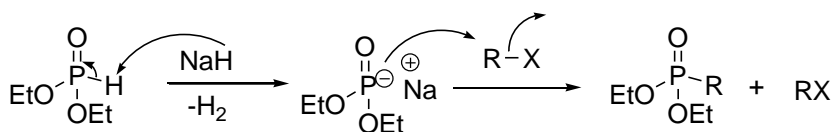
**For Related Reactions on Phosphonate Ester Synthesis, see:**

### Michaelis-Becker Reaction

Hydrogen phosphonate reacts with alkyl halide in the presence of base to give an alkyl phosphonate. However, the yield is often lower than the corresponding Michaelis-Arbuzov reaction.

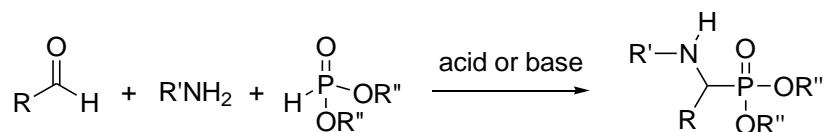


### Mechanism



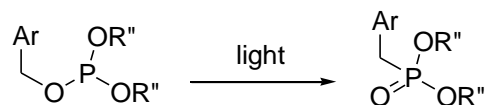
### Kabachnik-Fields Reaction

The three-component coupling of a carbonyl compound, an amine and a hydrogen phosphonate leads to α-aminophosphonates. This has been an important method in drug discovery research for generating peptidomimetic compounds.

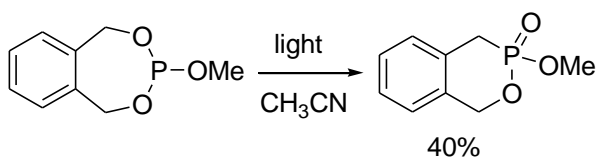


### The Photo-Arbuzov Reaction

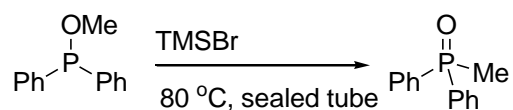
Irradiation of benzyl phosphate leads to rearrangement to give benzyl phosphonate.



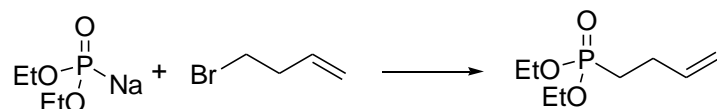
### Examples:



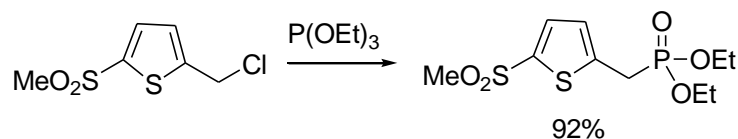
M. S. Landis, N. J. Turro, W. Bhanthumnavin, W. G. Bentrude, *J. Organometallic Chem.* **2002**, 646, 239.



P. –Y. Renard, P. Vayron, C. Mioskowski, *Org. Lett.* **2003**, 5, 1661.

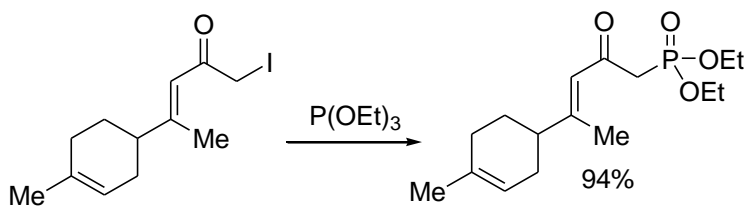


I. Pergment, M. Srebink, *Org. Lett.* **2001**, 3, 217.

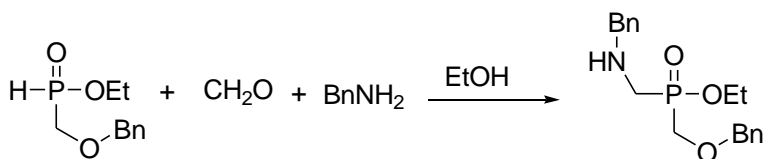


S.-S. Chou, D.-J. Sun, J.-Y. Huang, P.-K. Yang, H.-C. Lin, *Tetrahedron Lett.* **1996**, 37, 7279.





R. W. Driesen, M. Blouin, *J. Org. Chem.* **1996**, 61, 7202.



H.-J. Cristan, A. Herve, D. Virieus, *Tetrahedron* **2004**, 60, 877.

#### 5.4.4 Vilsmeier-Haack Reaction

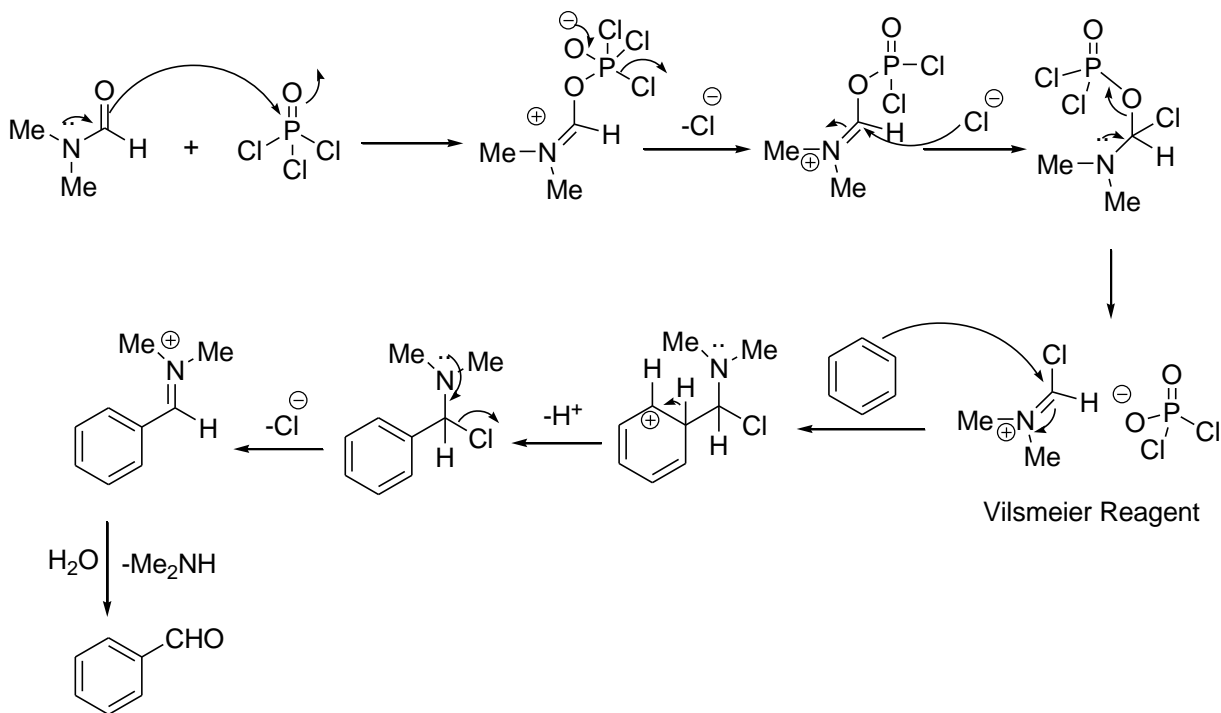
Activated alkenes as well as aromatic compounds react with disubstituted formamides and  $\text{POCl}_3$  to give aldehydes (Scheme 7). The reaction is called Vilsmeier reaction.



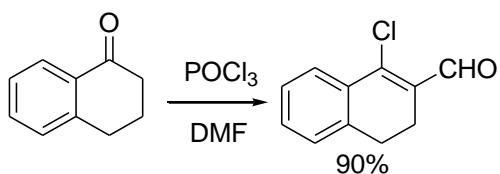
Scheme 7

**Mechanism**

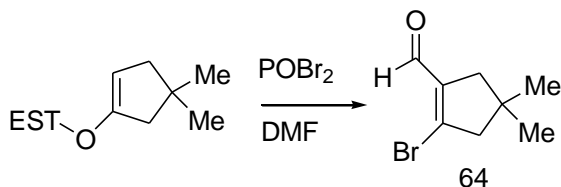
*N,N*-Dimethylformamide reacts with  $\text{POCl}_3$  to afford the reactive species that reacts with organic substrates to give the aldehydes (Scheme 8).



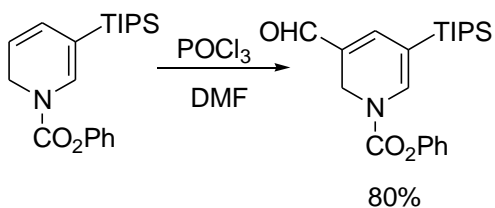
Scheme 8

**Examples:**

S. Hesse, G. Kirsch, *Tetrahedron Lett.* **2002**, 43, 1213.



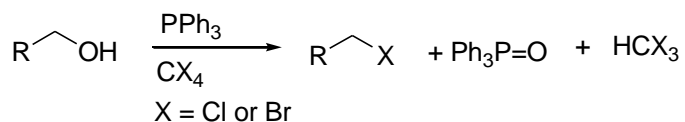
R. A. Aungst, Jr., C. Chan, R. L. Funk, *Org. Lett.* **2001**, 3, 2611.



D. L. Comins, A. L. Williams, *Org. Lett.* **2001**, 3, 3217.

### 5.4.5 Appel Reaction

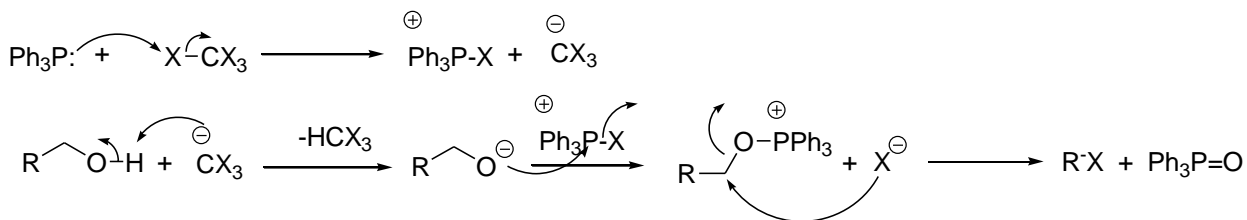
Alcohols react with  $\text{CCl}_4$  or  $\text{CBr}_4$  in the presence of  $\text{PPh}_3$  to give alkyl halide (Scheme 9). The process is known as Appel reaction. The method is straight forward and the products are obtained in moderate to good yield.



Scheme 9

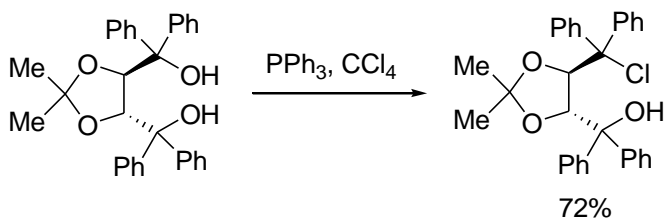
#### Mechanism

The reaction takes place *via*  $\text{S}_{\text{N}}2$  process (Scheme 10).

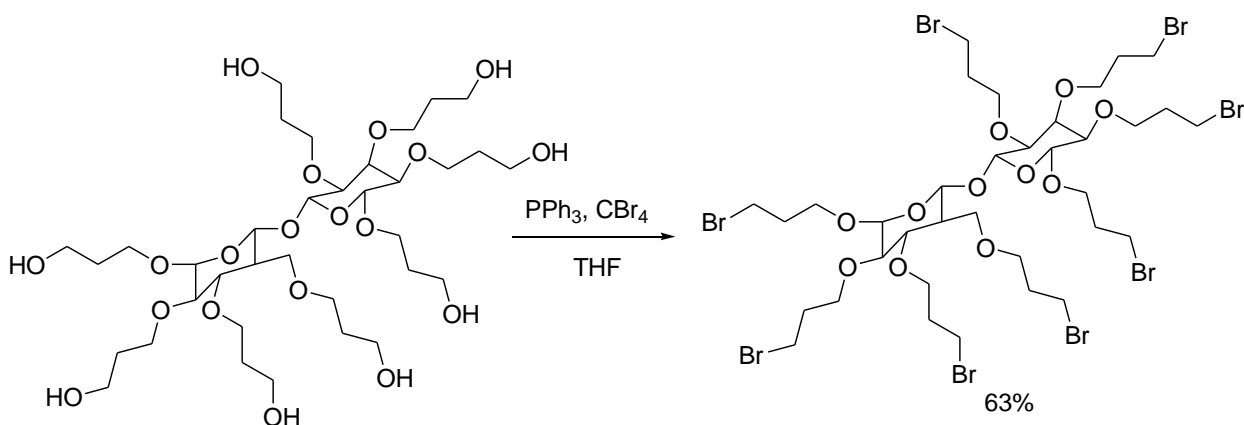


Scheme 10

**Examples:**



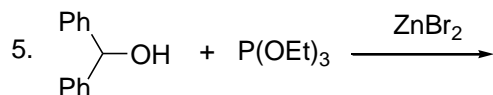
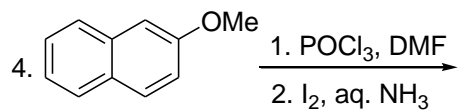
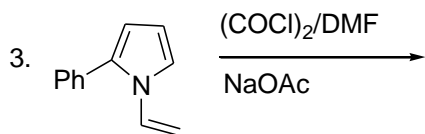
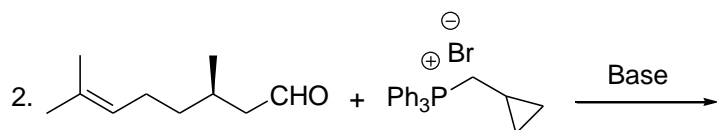
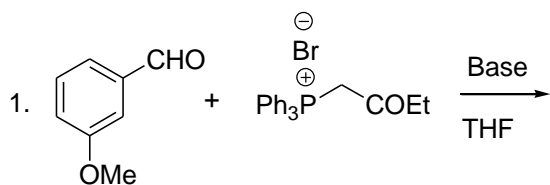
D. Seebach, A. Pichota, A. K. Beck, A. B. Pinkerton, T. Litz, J. Karjalainen, V. Gramlich, *Org. Lett.* **1999**, 1, 55.



M. Dubber, T. K. Lindhorst, *Org. Lett.* **2001**, 3, 4019.

**Problems:**

Write the major products for the following reactions.

**Text Book**

M. B. Smith, *Organic Synthesis*, 2<sup>nd</sup> Ed., McGraw Hill, Singapore, 2004.

## Lecture 40

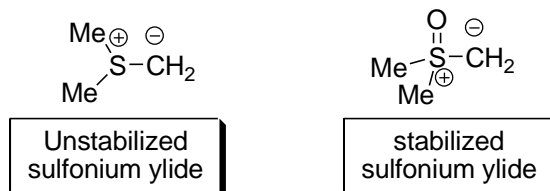
### 5.5 Sulfur, Selenium and Tellurium Compounds

#### 5.5.1 Sulfur Compounds

Organosulfur compounds find wide applications in organic synthesis. Following are the some of the important applications.

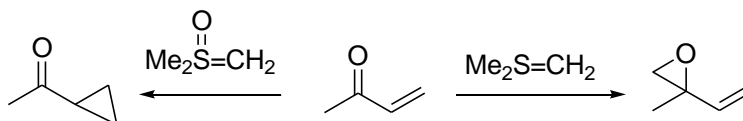
##### 5.5.1.1 Sulfur Ylides

Sulfur ylides have numerous applications in organic synthesis. Among them, diemthylsulfonium methyllide (unstabilized) and dimethyloxosulfonium methyllide (stabilized) are extensively used in organic synthesis. These reagents are called Corey-Chaykovsky reagents.



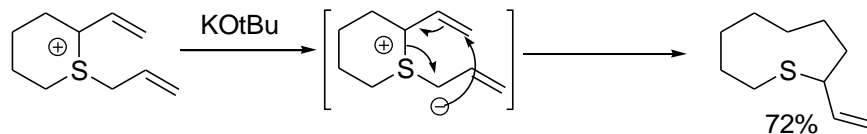
J. S. Ng, C. Liu, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **7**, 5335.

They exhibit different reactions with  $\alpha,\beta$ -unsaturated carbonyl compounds. The former afford epoxides and the latter give cyclopropanes (Scheme 1). In the absence of double bond, both give epoxides. The epoxide formation is kinetically favourable while the formation of cyclopropane is the thermodynamic product.



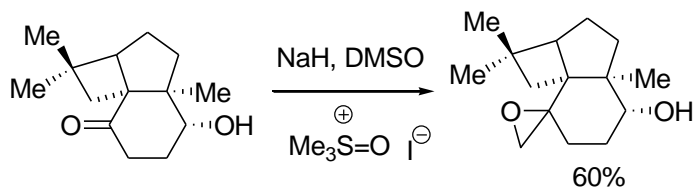
Scheme 1

Sulfur ylides undergo rearrangements to give valuable products (Scheme 2).

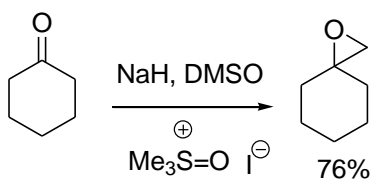


Scheme 2

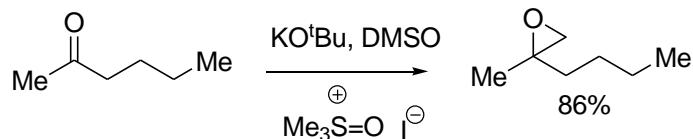
### Examples:



C. F. D. Amigo, I. G. Collado, J. R. Hanson, R. Hernandez-Galan, P. B. Hitchcock, A. J. Macias-Sanchez, D. J. Mobbs, *J. Org. Chem.* **2001**, 66, 4327.



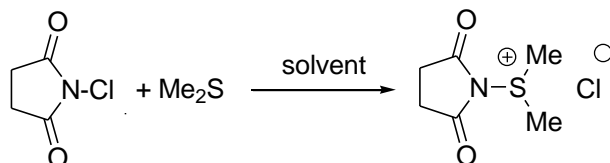
E. J. Corey, M. Chaykovsky, *Org. Synth.* CV5, 755.



J. S. Nag, *Synth. Commun.* **1990**, 20, 1193.

### 5.5.1.2 Oxidation

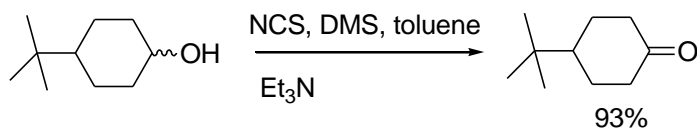
N-Chlorosuccinimide-dimethyl sulfide, prepared *in situ* from NCS and DMS, is used as mild oxidizing reagent in organic synthesis (Scheme 3). This reagent is called Corey-Kim reagent.



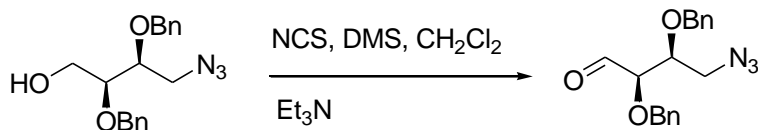
Scheme 3

R. C. Kelly, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1208.

### Examples:



E. J. Corey, C. U. Kim, P. F. Misco, *Org. Synth.* CV 6, 220.

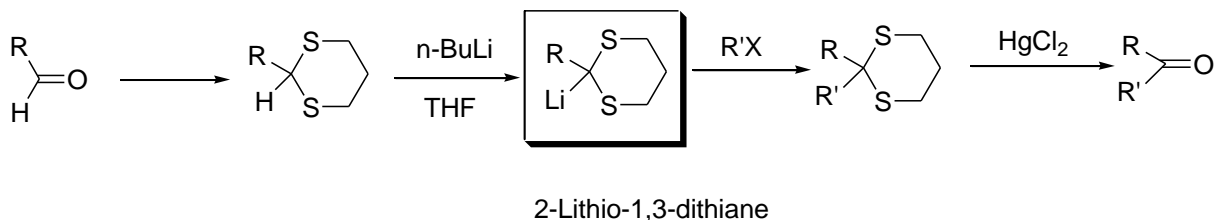


J. Z. Ho, R. M. Mohareb, J. H. Ahn, T. B. Sim, H. Rapoport, *J. Org. Chem.* **2003**, **68**, 109.

### 5.5.1.3 C-C Bond Formation



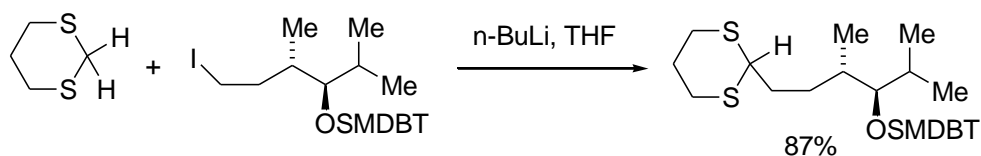
2-Lithio-1,3-dithiane is widely used in organic synthesis as “umpolung” reagent (Scheme 4). It is also called Corey-Seebach reagent.



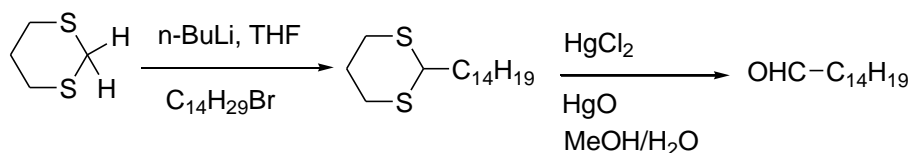
Scheme 4

M. *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 2953.

### Examples:



P. G. Steel, E. J. Thomas, *J. Chem. Soc., Perkin, Trans 1*, **1997**, 371.



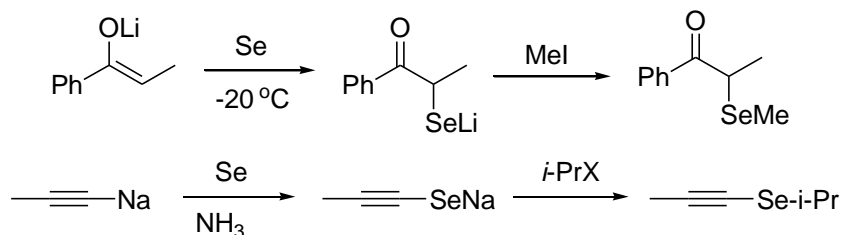
D. Seebach, A. K. Beck, *Org. Synth.* CV6, 869.

## 5.5.2 Selenium Compounds

The study of organoselenium compounds has received considerable attention because of their interesting properties. In this section, we will cover some of the important applications of Se and SeO<sub>2</sub> in organic synthesis.

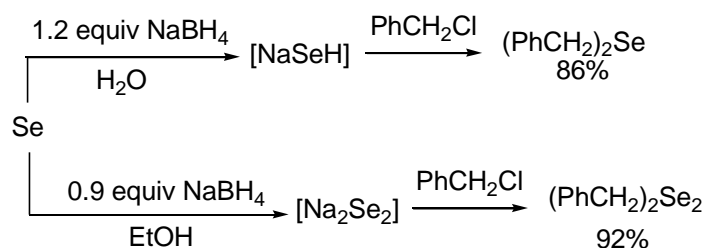
### 5.5.2.1 Selenium

Selenium reacts with organolithium, -sodium and -magnesium to provide metal selenolates that afford selenides by the reaction with electrophiles (Scheme 1), diselenides by oxidation, and selenols by acidification.



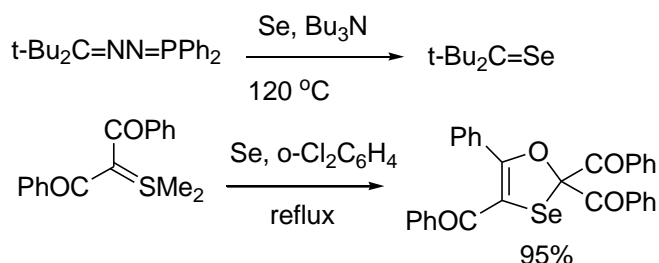
Scheme 1

Selenium is reduced to metal salts of hydrogen selenide or diselenide that are useful precursor of selenides and diselenides, respectively. For example,  $\text{NaBH}_4$  reduces Se into  $\text{NaSeH}$  or  $\text{Na}_2\text{Se}_2$  depending on the reaction conditions that could be readily reactive with benzyl chloride to give dibenzyl diselenide in high yield (Scheme 2).

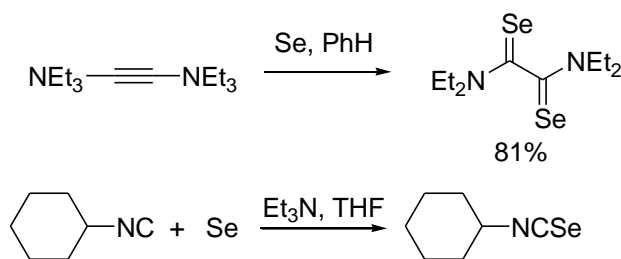


Scheme 2

Reaction of Se with hydrazones, sulfonium or phosphonium ylides and  $\alpha$ -halo carbonions gives selones. Sterically hindered selones can be isolated, whereas the less hindered selones can be reacted in situ with ylides (Scheme 3).



Reaction of Se with diaminoalkyne and isocyanide gives a diselenoamide and isoselenocyanate, respectively (Scheme 4).

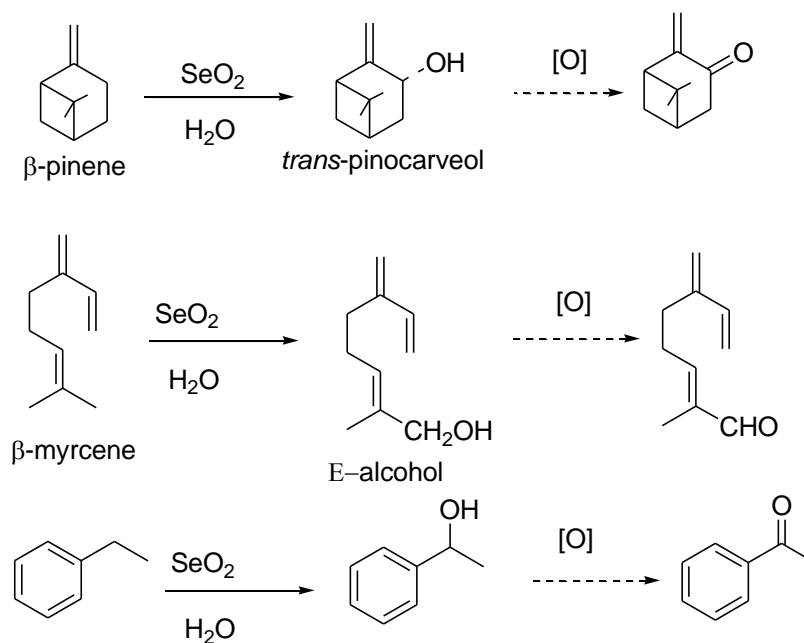


Scheme 4

### 5.5.2.2 Selenium Dioxide

Selenium dioxide ( $\text{SeO}_2$ ) is useful for the oxidation of allylic and benzylic C-H bonds to give alcohols or ketones (Scheme 5). The order of ease of oxidation is  $\text{CH}_2 > \text{CH}_3 > \text{CH}$ . The oxidation takes place at the more substituted end of the double bond.

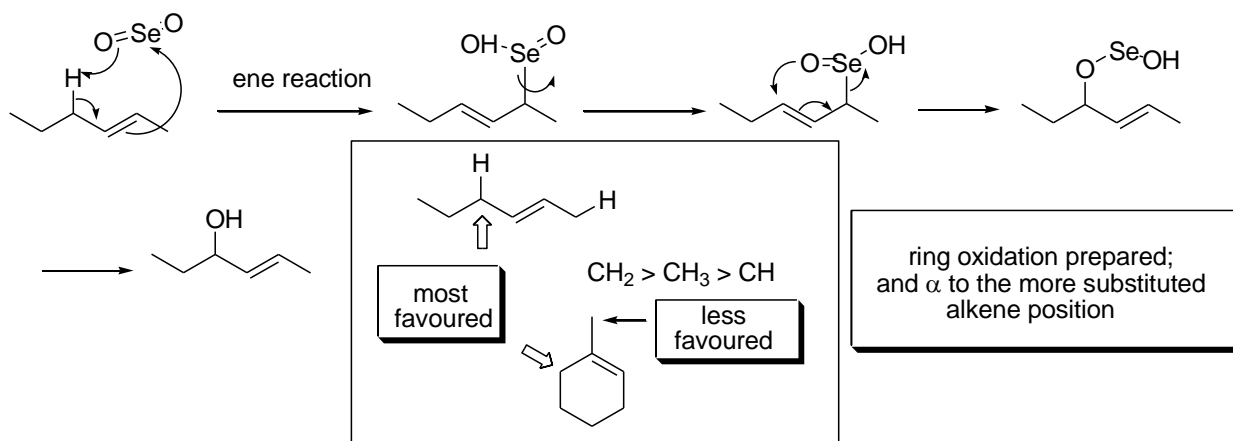
W. J. Hoekstra, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4437.



Scheme 5

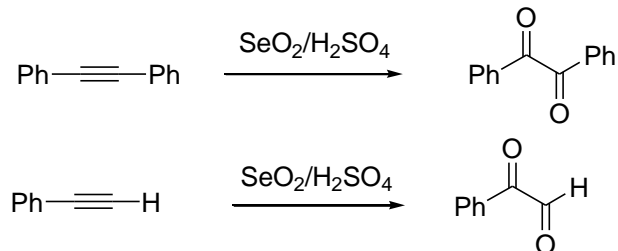
### Mechanism

The reaction takes place *via* ene reaction. In the absence of hydrolysis, alkenes can be converted into carbonyl compounds (Scheme 6).



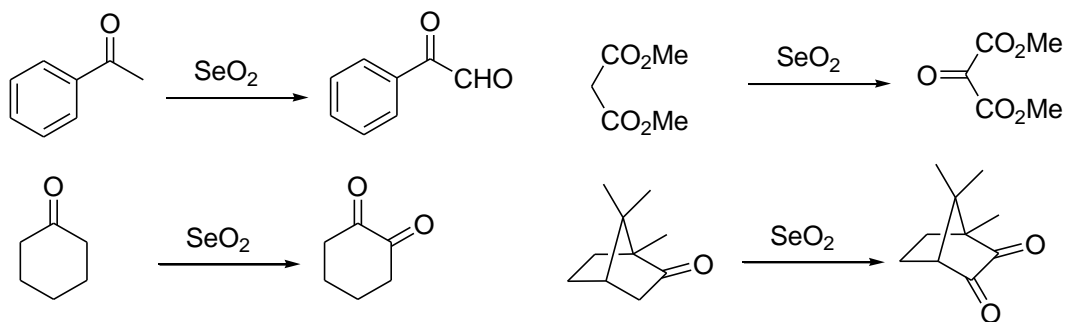
Scheme 6

SeO<sub>2</sub> oxidizes alkynes into 1,2-dicarbonyl compounds in the presence of small amount of H<sub>2</sub>SO<sub>4</sub> with high yield (Scheme 7).

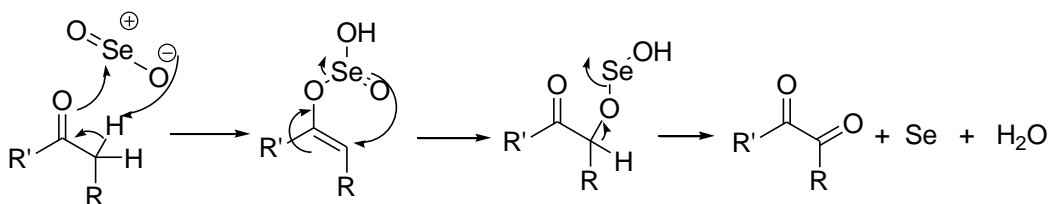


Scheme 7

SeO<sub>2</sub> is useful reagent for the oxidation of methyl or methylene group adjacent to the carbonyl group to give 1,2-dicarbonyl compounds (Scheme 8). The reaction is called Riley oxidation.

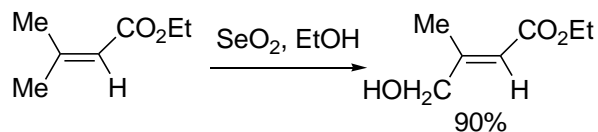


The reaction takes place *via* the intermediate  $\beta$ -ketoseleninic acid.

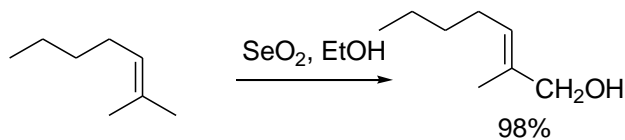


Scheme 8

### Examples:



R. W. Curley, Jr., C. J. Ticorras, *J. Org. Chem.* **1986**, 51, 256.

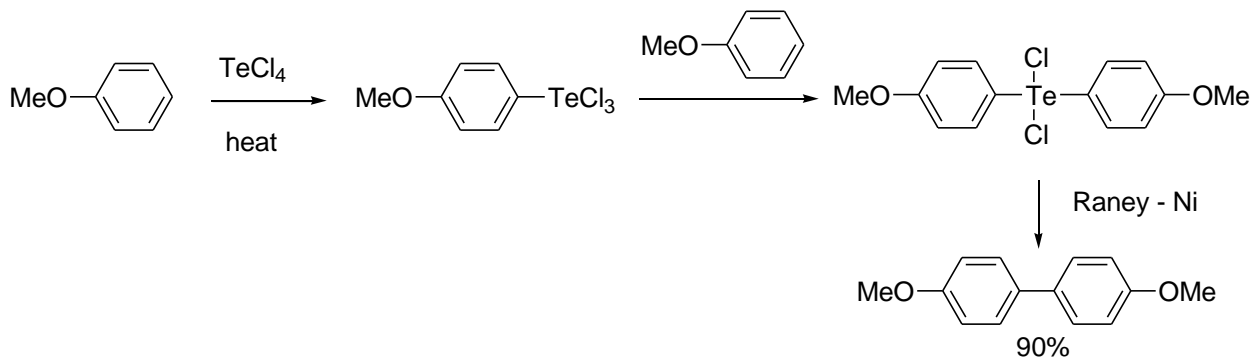


H. Rapoport, U. T. Bhalerao, *J. Am. Chem. Soc.* **1971**, 93, 4835.

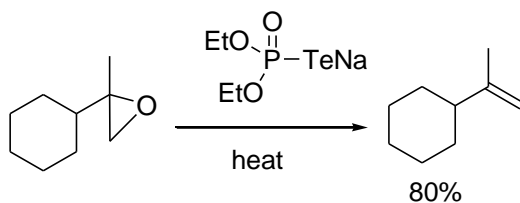
### 5.5.3 Tellurium Compounds

Organotellurium compounds have been used in a number of organic transformations. The following are some of the important applications.

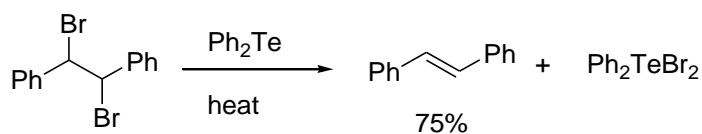
#### Synthesis of Biaryls



#### Deoxygenation of Epoxides

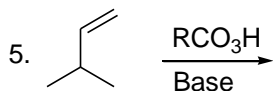
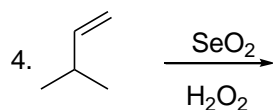
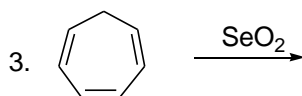
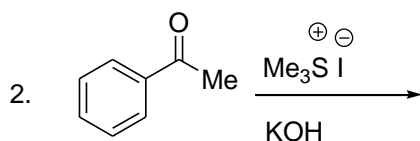
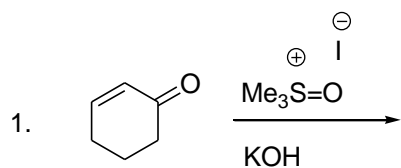


#### Vicinal Dibromination

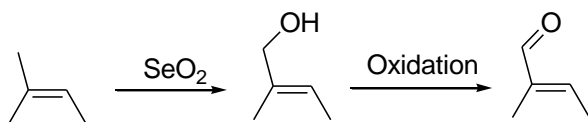


**Problems:**

A. What product would you expect from the following reactions?



B. Rationalize the following reaction.

**Text Book**M. B. Smith, *Organic Synthesis*, 2<sup>nd</sup> Ed., McGraw Hill, Singapore, 2004.