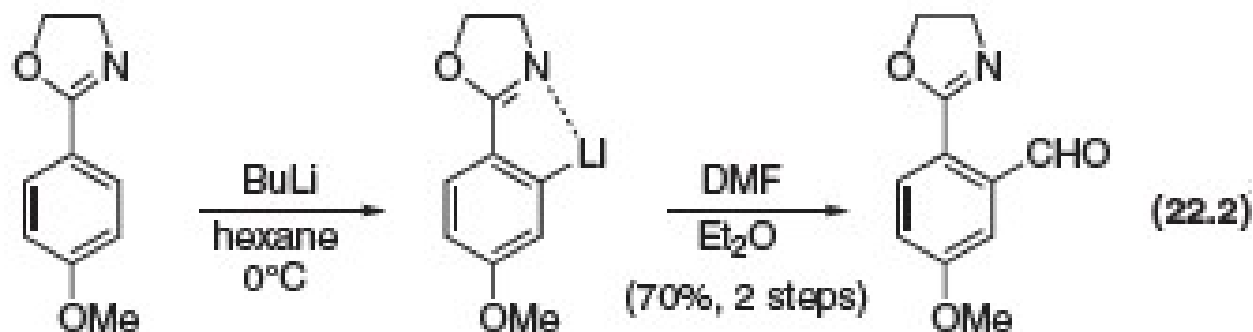
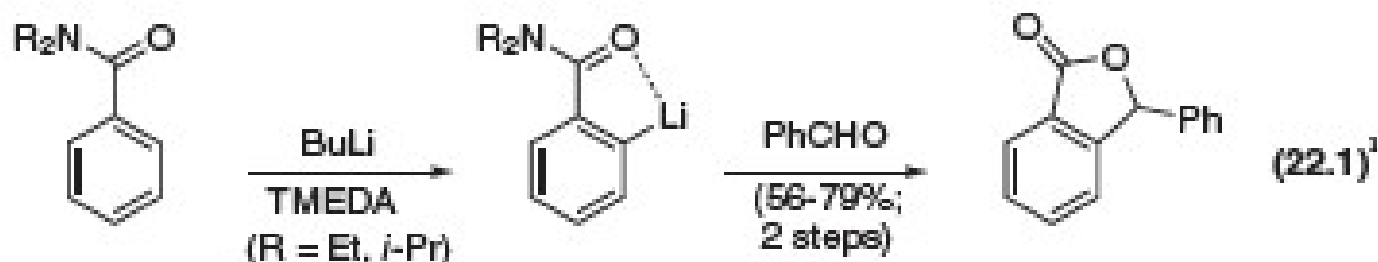


Chapter 22

Directed *ortho* lithiation of arenes



- complexation of lithium with the amide oxygen or the oxazoline nitrogen directs the base to the *ortho* hydrogens

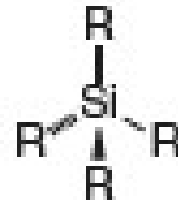
Table 22.1

Electronegativities of Main Group Elements

IIIA	IVA	VA	VIA	VIIA
B	C	N	O	F
2.04	2.55	3.04	3.44	3.98
Al	Si	P	S	Cl
1.61	1.90	2.19	2.58	3.16
Ga	Ge	As	Se	Br
1.81	2.01	2.18	2.55	2.96
In	Sn	Sb	Te	I
1.78	1.96	2.05	2.10	2.66
Tl	Pb	Bi	Po	At
2.04	2.33	2.02	2.00	–

Figure 22.1

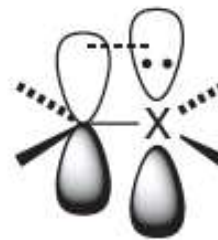
- Stabilization of a carbocation by an atom bearing lone pair (left) and a methyl group carrying a Group IVA substituent (right)



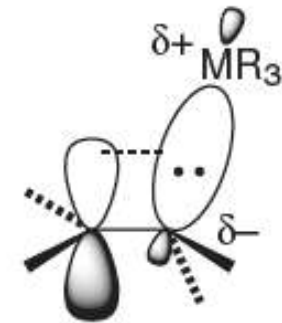
silane



stannane



X = O, N, S, etc.



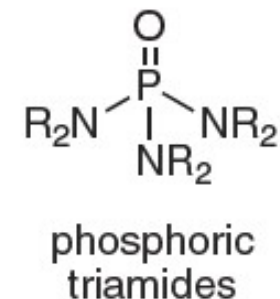
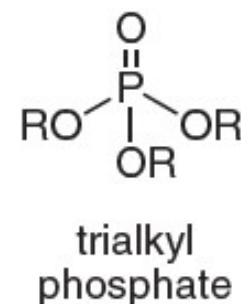
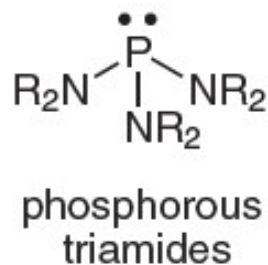
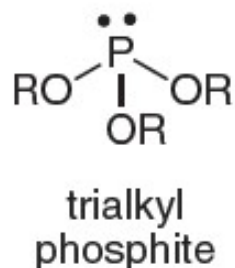
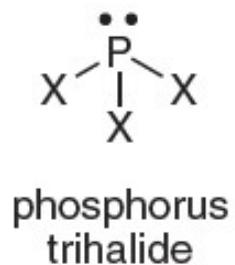
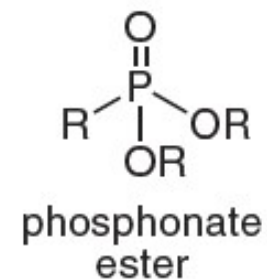
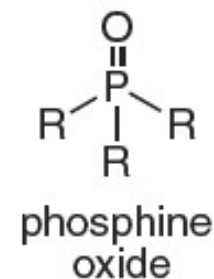
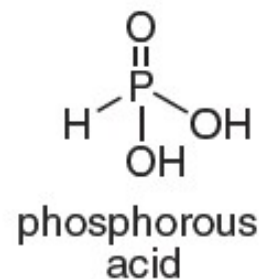
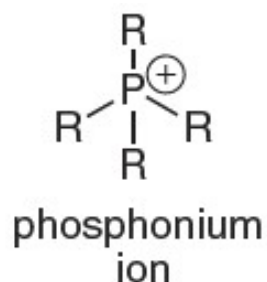
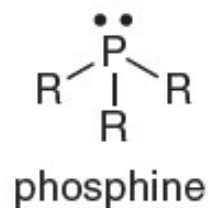
M = Si, Sn [Ge, Pb]

Table 22.2

Bond Energies to Group IVA Elements (kcal mol⁻¹)

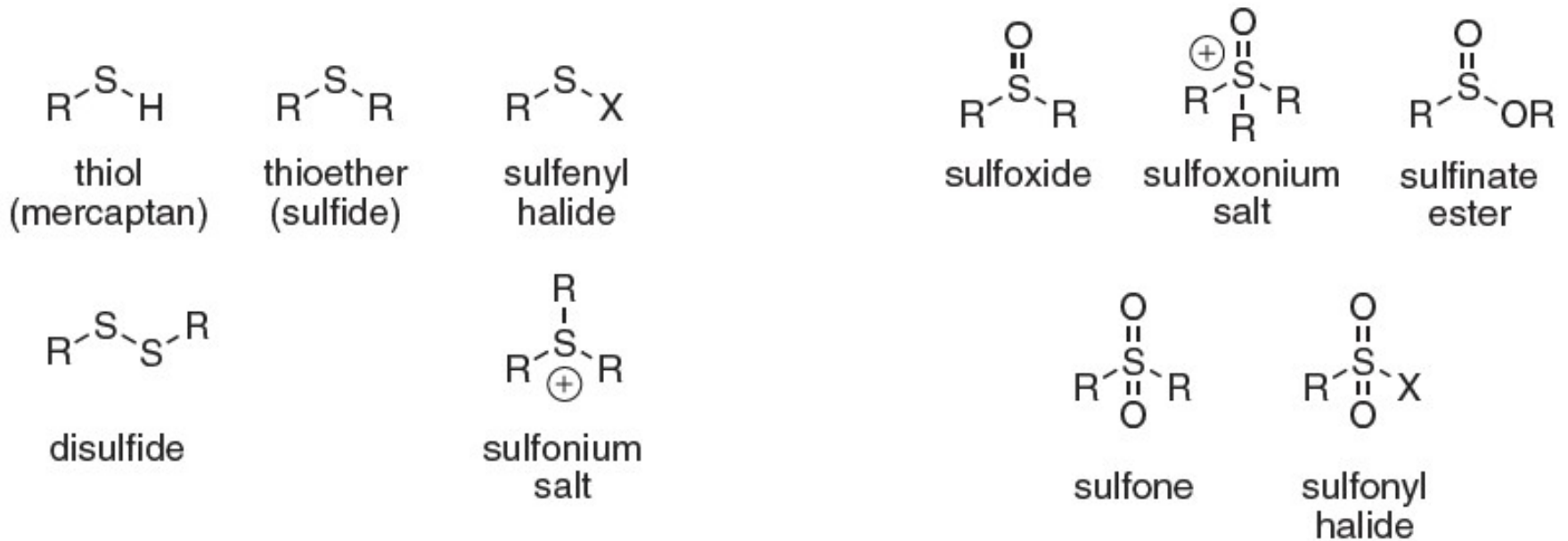
Element	C—X	Si—X	Sn—X
H	88-98	90	60
C	82-88	88-94	46
N	80	100	—
O	80	100-136	95
F	116	139-158	—
Cl	80	109-117	82
Br	64	90-102	65
I	51	71-82	45

Figures 22.2 and 22.3



- Tricoordinate organophosphorus compounds
- Phosphoryl compounds

Figures 22.4 and 22.5



- Functional groups based on bicoordinate sulfur
- Functional groups containing the thionyl moiety

Table 22.3

Approximate Average Bond Energies of σ Bonds to Group VIA Elements

Bond Energy (kcal mol⁻¹) [kJ mol⁻¹]

Element	H	C	O	S	Se
O	111 [464]	80 [336]	33 [138]	–	–
S	88 [368]	65 [272]	–	63 [264]	–
Se	67 [230]	58 [243]	–	–	44 [184]

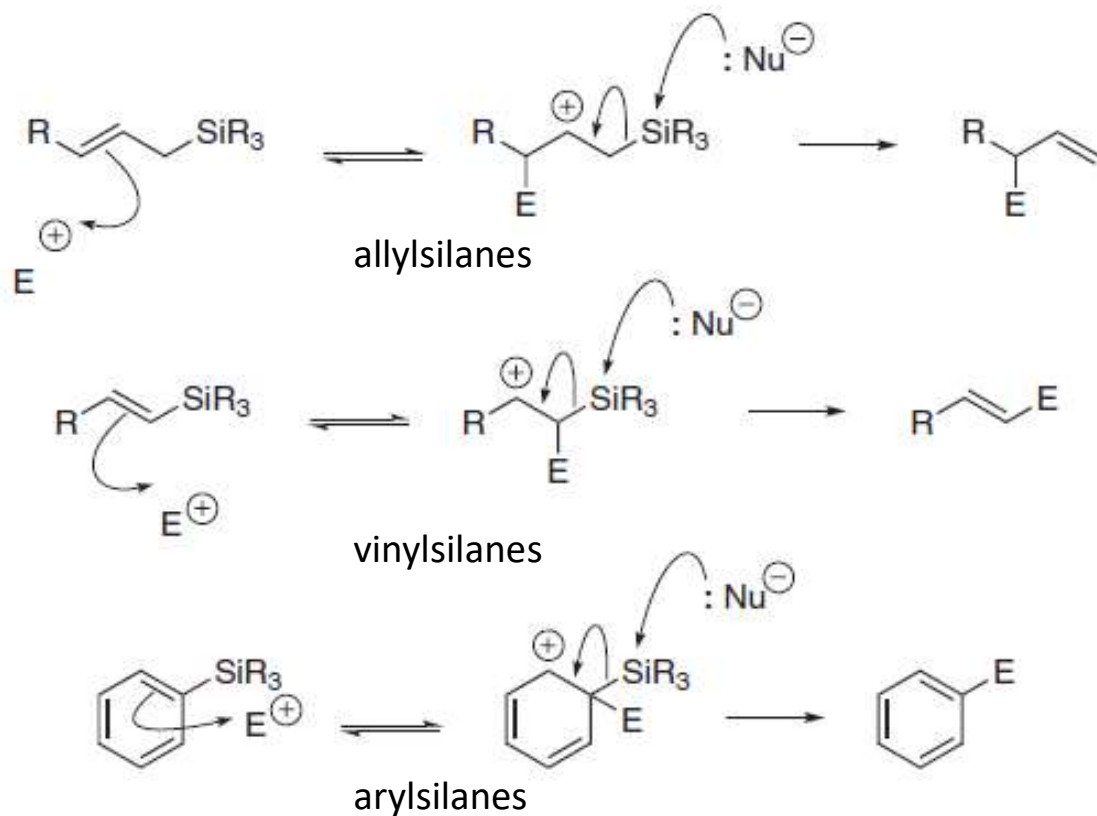
Table 22.4

σ^+ Constants for Silicon- and Tin-containing Substituents

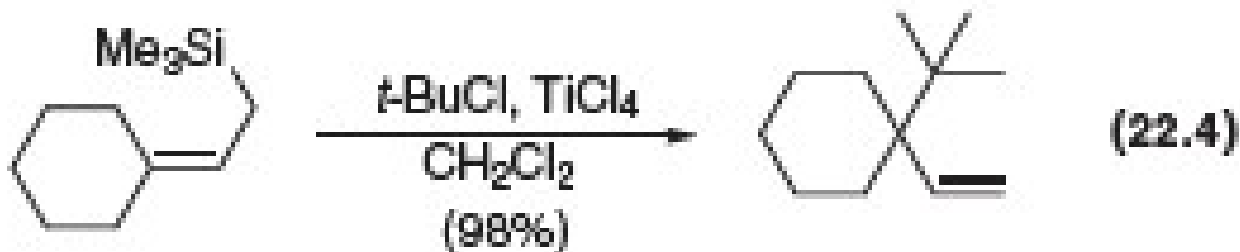
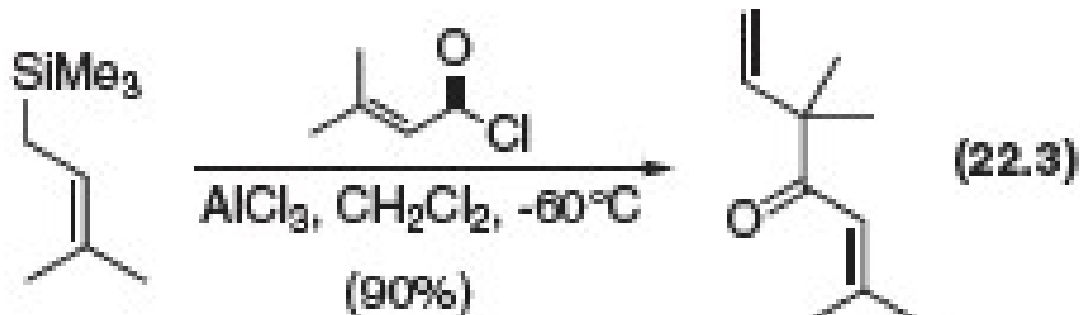
Group	σ^+ constant
—CH ₃	-0.30
—CH ₂ SiPh ₃	-0.4
—CH ₂ SiMe ₃	-0.62
—OCH ₃	-0.78
—CH ₂ SnMe ₃	-0.92
—CH ₂ SnPh ₃	-1.0

Reactions of unsaturated silanes with electrophiles

- allylsilanes react with migration of the double bond
- vinylsilanes react with retention of configuration at carbon
- ipso* displacement in arylsilanes is the most favored reaction

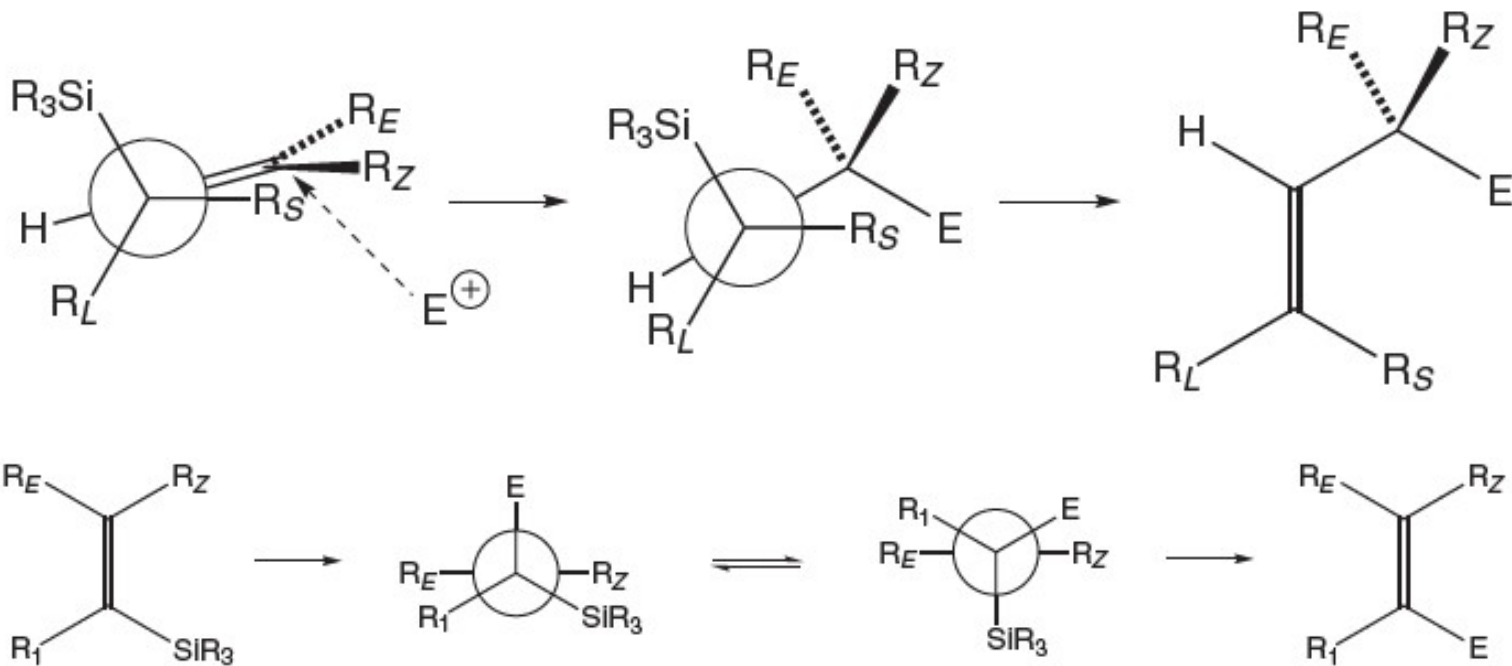


Representative electrophilic substitutions of allylsilanes



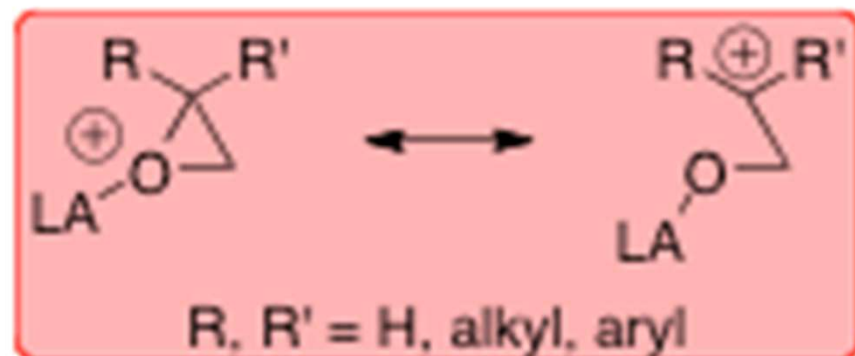
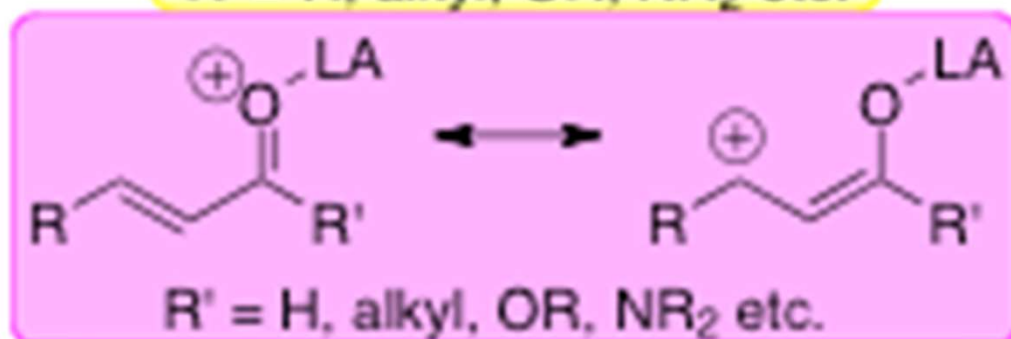
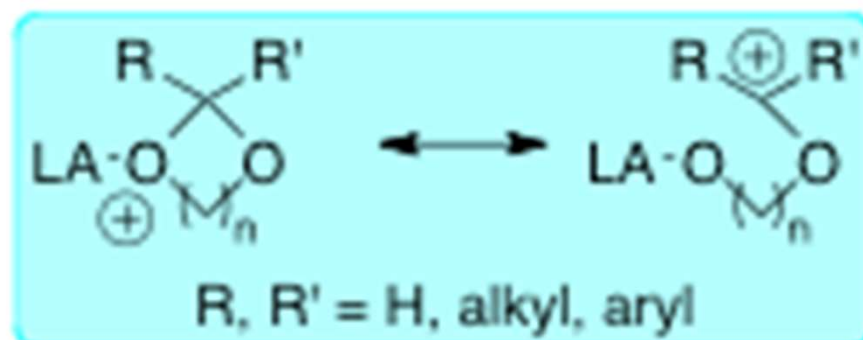
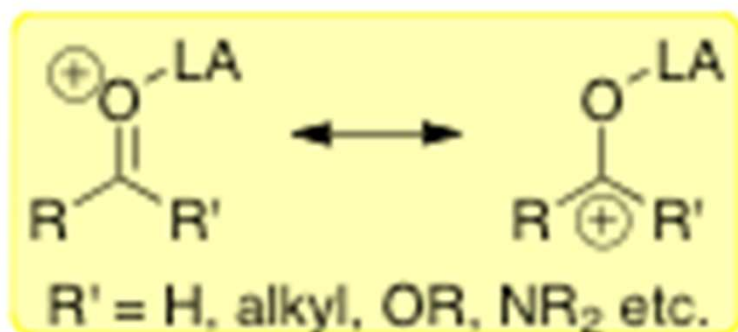
- addition of electrophile gives the β -silyl cation in preference to other regioisomeric cations
- this permits the formation of very hindered molecules

Figures 22.7 and 22.8



- The stereochemistry of the reaction between an allylsilane and an electrophile. R_S is the smaller substituent; R_L is the larger substituent
- The stereochemistry of the reaction of a vinylsilane with an electrophile

Electrophiles for the Hosomi-Sakurai reaction



$\text{LA} = \text{TiCl}_4, \text{AlCl}_3, \text{Et}_2\text{AlCl}, \text{BF}_3, \text{ etc.}$

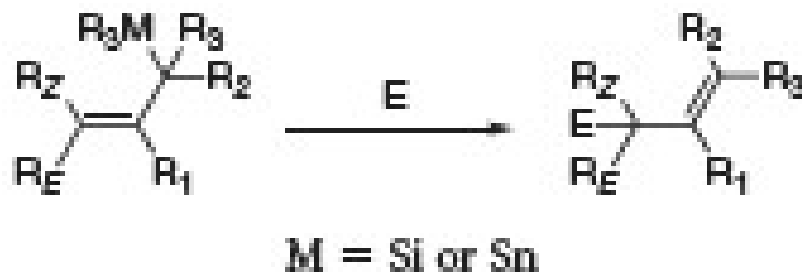
(22.5)

Reaction synopses: Electrophilic substitution of vinylsilanes



Reagents: H_3O^+ ; etc.;
or $\text{Br}_2, \text{CH}_2\text{Cl}_2; \text{Br}_2, \text{H}_2\text{O}$; etc.
or $\text{RCOCl}, \text{AlCl}_3; \text{RCOCl}, \text{AlCl}_3; \text{RCOCl}, \text{TiCl}_4$; etc.;
or $\text{RCHO}, \text{SnCl}_4; \text{R}_2\text{CO}, \text{TiCl}_4;$
 $\text{RCH}(\text{OR}')_2, \text{TiCl}_4$; etc.
or $\text{RCH}=\text{CHCOR}, \text{Et}_2\text{AlCl}$; etc.
or epoxide, SnCl_4 ; etc.

Reaction synopses: Hosomi-Sakurai reaction



Reaction occurs with allylic rearrangement; chirality transfer occurs with chiral allylsilanes and allylstannanes

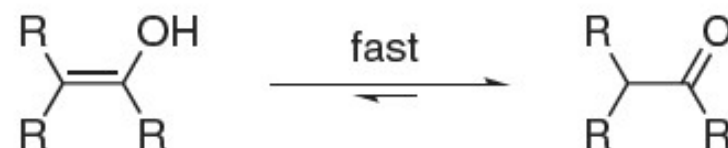
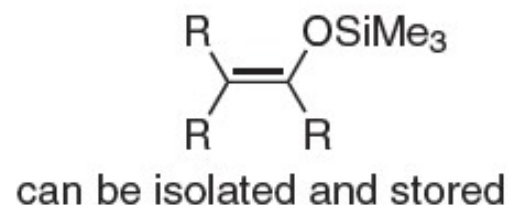
Reagents: H_3O^+ ; etc.;
 or $\text{Br}_2, \text{CH}_2\text{Cl}_2; \text{Br}_2, \text{H}_2\text{O}$; etc.
 or $\text{RCl}, \text{AlCl}_3; \text{RCOCl}, \text{AlCl}_3; \text{RCOCl}, \text{TiCl}_4$; etc.;
 or $\text{RCHO}, \text{SnCl}_4; \text{R}_2\text{CO}, \text{TiCl}_4; \text{RCH}(\text{OR}')_2, \text{TiCl}_4$; etc.
 or $\text{RCH}=\text{CHCOR}, \text{Et}_2\text{AlCl}$; etc.
 or epoxide, SnCl_4 ; etc.

Figure 22.9

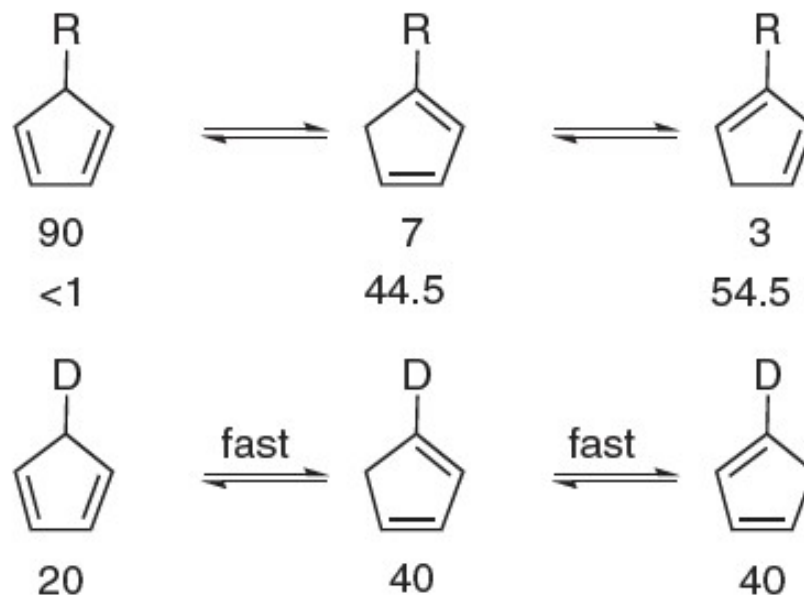
Effects of replacing hydrogen by trimethylsilyl on reactivity and stability of compounds

$\text{Me}_3\text{Si}-\text{N}_3$
distillable

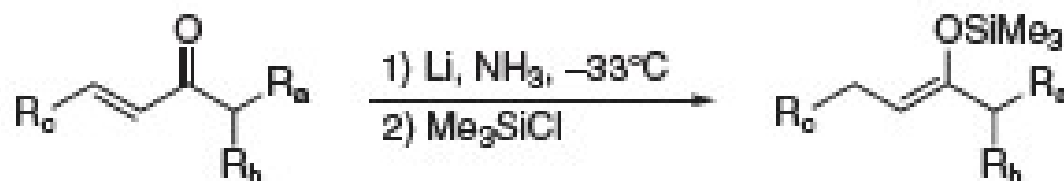
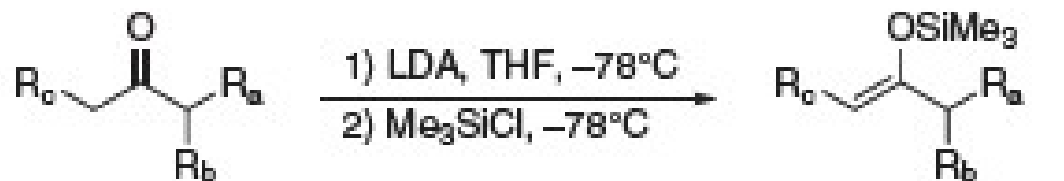
$\text{H}-\text{N}_3$
explosive



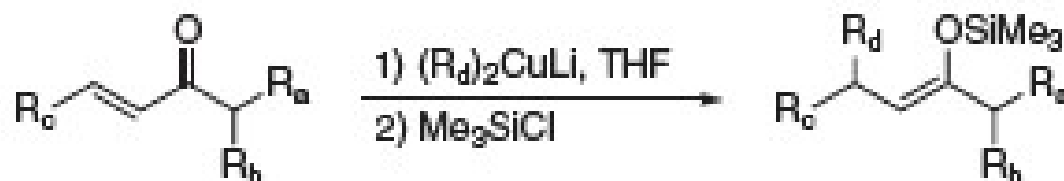
R = SiMe_3
R = Me



Methods for forming enol trimethylsilyl ethers

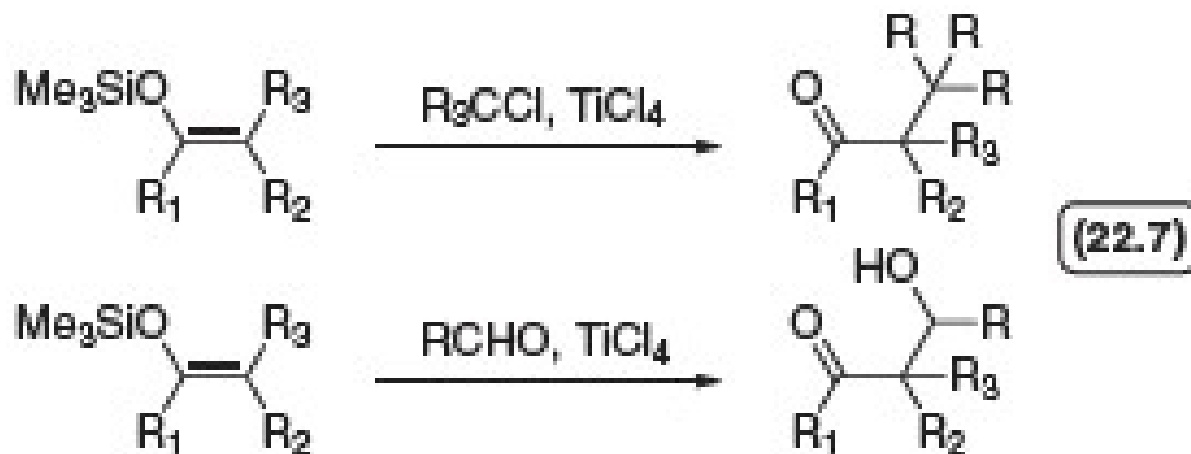


(22.6)



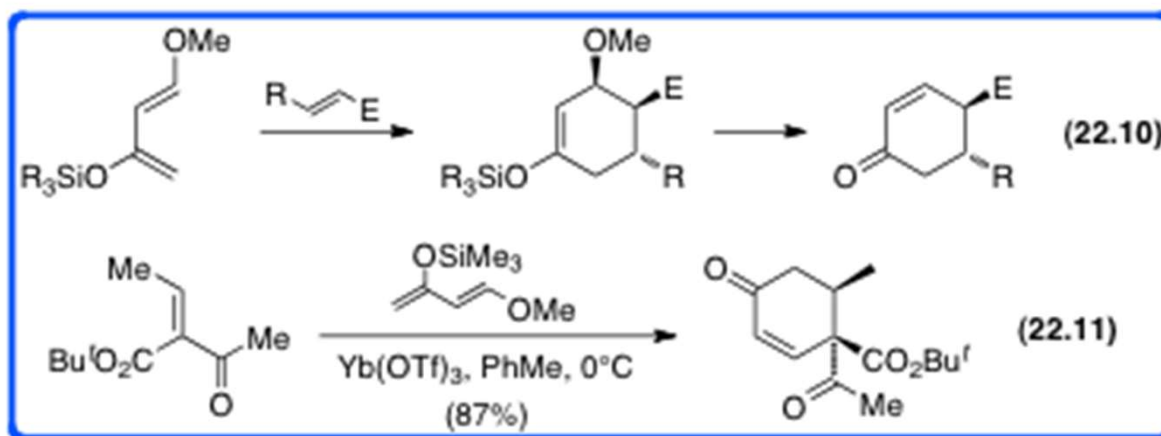
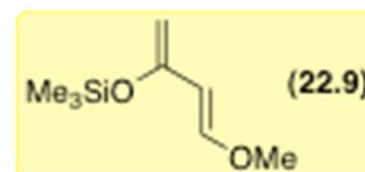
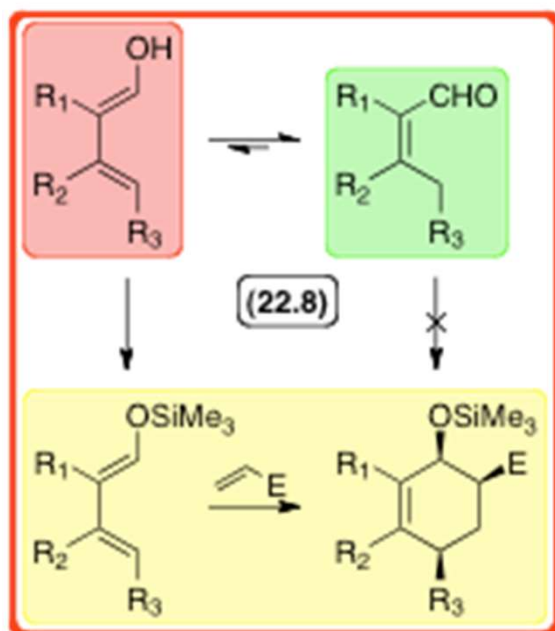
- deprotonation of the carbonyl compound and trapping with Me_3SiCl
- Birch reduction of a conjugated enone in the absence of a proton source and trapping with Me_3SiCl
- conjugate addition of a cuprate to a conjugated carbonyl compound and trapping with Me_3SiCl

Mukaiyama alkylation and aldol reactions



- the enol trimethylsilyl ether allows these reactions to be carried out in the absence of a strong base
- this permits, for example, the incorporation of a tertiary alkyl group at the α carbon of a ketone; using the enolate anion would result in E2 elimination from the alkyl halide

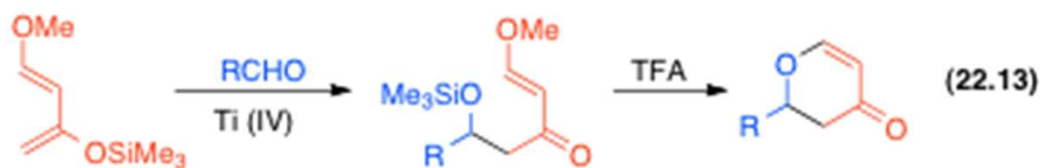
Silyloxy dienes: Danishefsky's diene



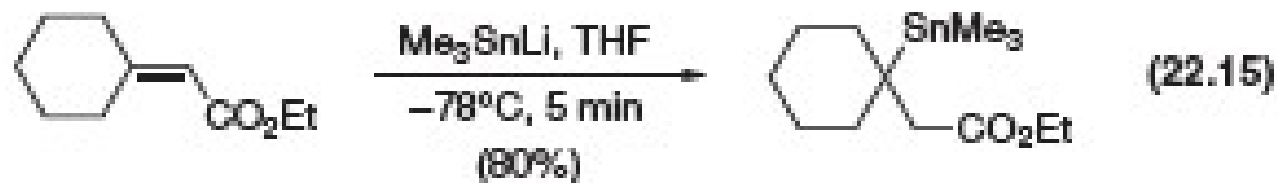
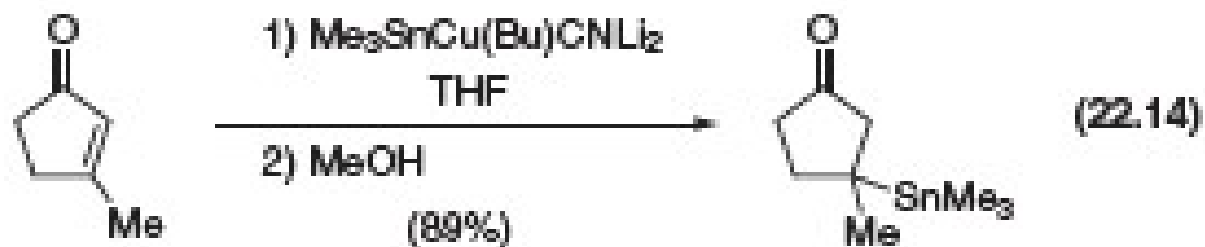
- 1-hydroxydienes extremely rapidly tautomerize to the conjugated aldehyde (22.8)
- the aldehyde cannot be used as a diene in a Diels-Alder reaction
- trapping the dienol as the silyl ether permits isolation of the silyl surrogate for the dienol
- the best known example of a silyloxydiene is Danishefsky's diene (22.9), which is an excellent diene in normal electron demand Diels-Alder cycloadditions (22.10, 22.11)

Other reactions of Danishefsky's diene

- in the presence of a suitable Lewis acid catalyst, the diene will react with an aldehyde in a formal [4+2] cycloaddition to give a pyran derivative; the reaction can be made asymmetric with an appropriate chiral catalyst
- the diene reacts with the Lewis acid complex of an aldehyde to give the product of a Mukaiyama aldol addition



Conjugate additions of stannyl nucleophiles



- stannylolithiums and stannylcuprates add to conjugated systems to give the conjugate addition product exclusively
- the long C—Sn bond means that these additions are much less susceptible to steric hindrance than conjugate additions of carbon nucleophiles
- silyllithiums often give the competing 1,2-addition product as the major product of the reaction.

Thiolate anions and the cleavage of methyl esters and ethers

- thiolate anions in HMPA are powerful nucleophiles that react with methyl esters and methyl aryl ethers by the S_N2 mechanism to give the carboxylate anion or the phenoxide anion
- alkylselenide anions also cleave methyl esters and methyl aryl ethers

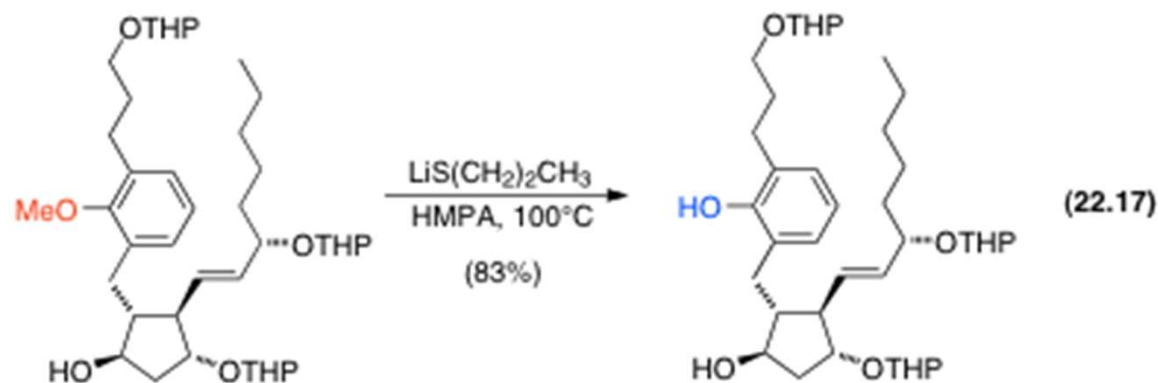
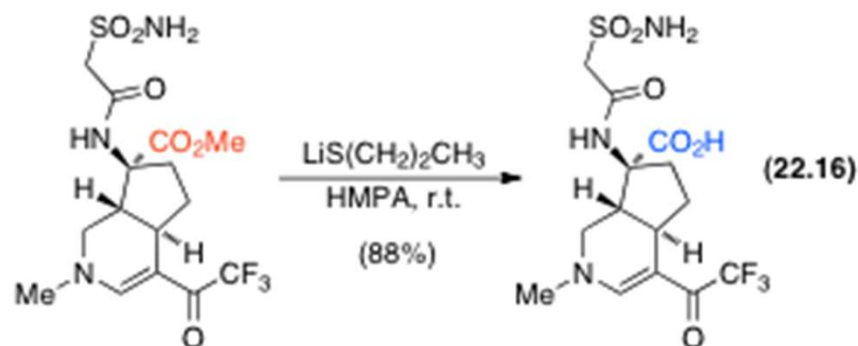
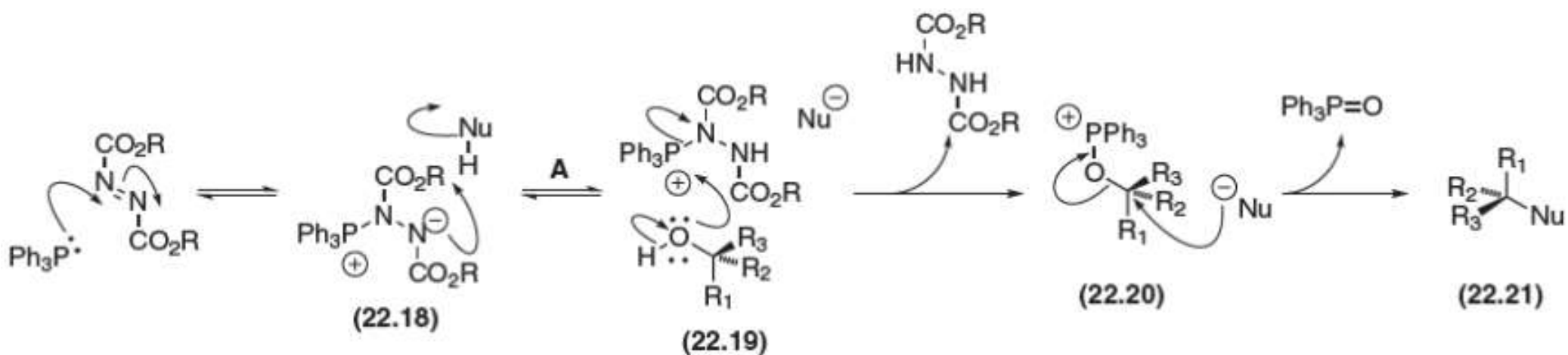
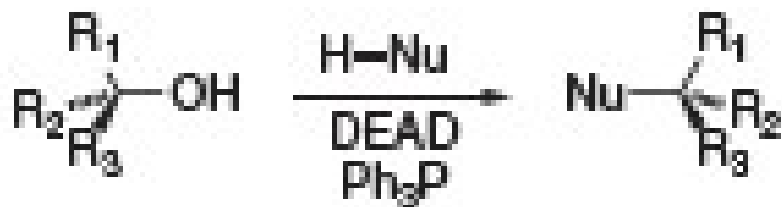


Figure 22.10



The mechanism of the Mitsunobu reaction. The position of the equilibrium marked as A depends on the pK_a value of $H-Nu$.

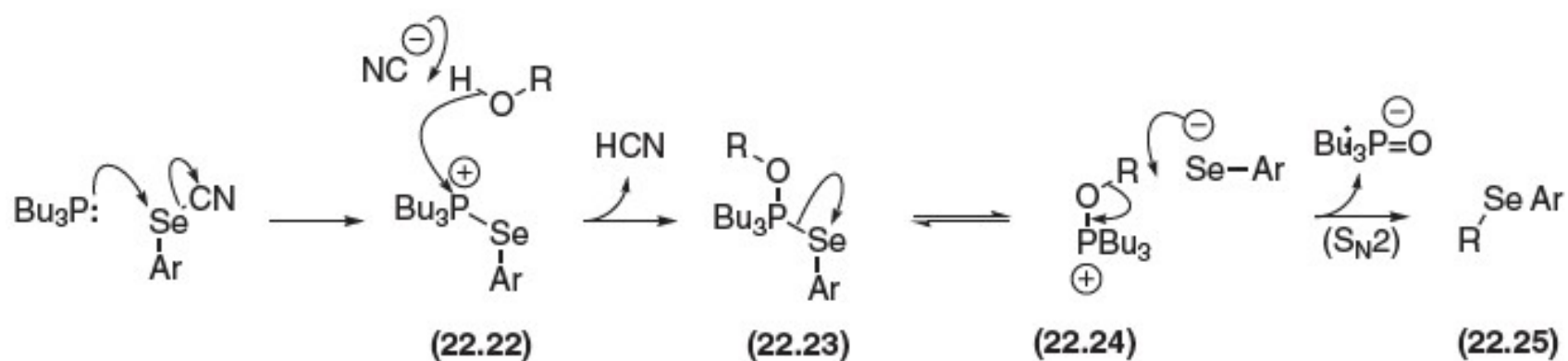
Reaction synopses: Mitsunobu reaction



H—Nu: RCO₂H; phthalimide; RSO₂NH₂; ArOH; etc.
DEAD may be replaced by the methyl
(DMAD) or isopropyl (DIAD) analogues

Stereochemistry: inversion of configuration

Figure 22.11



The mechanism of the one-step S_N2 conversion of alcohols to selenides

Reaction synopses: Grieco selenylation

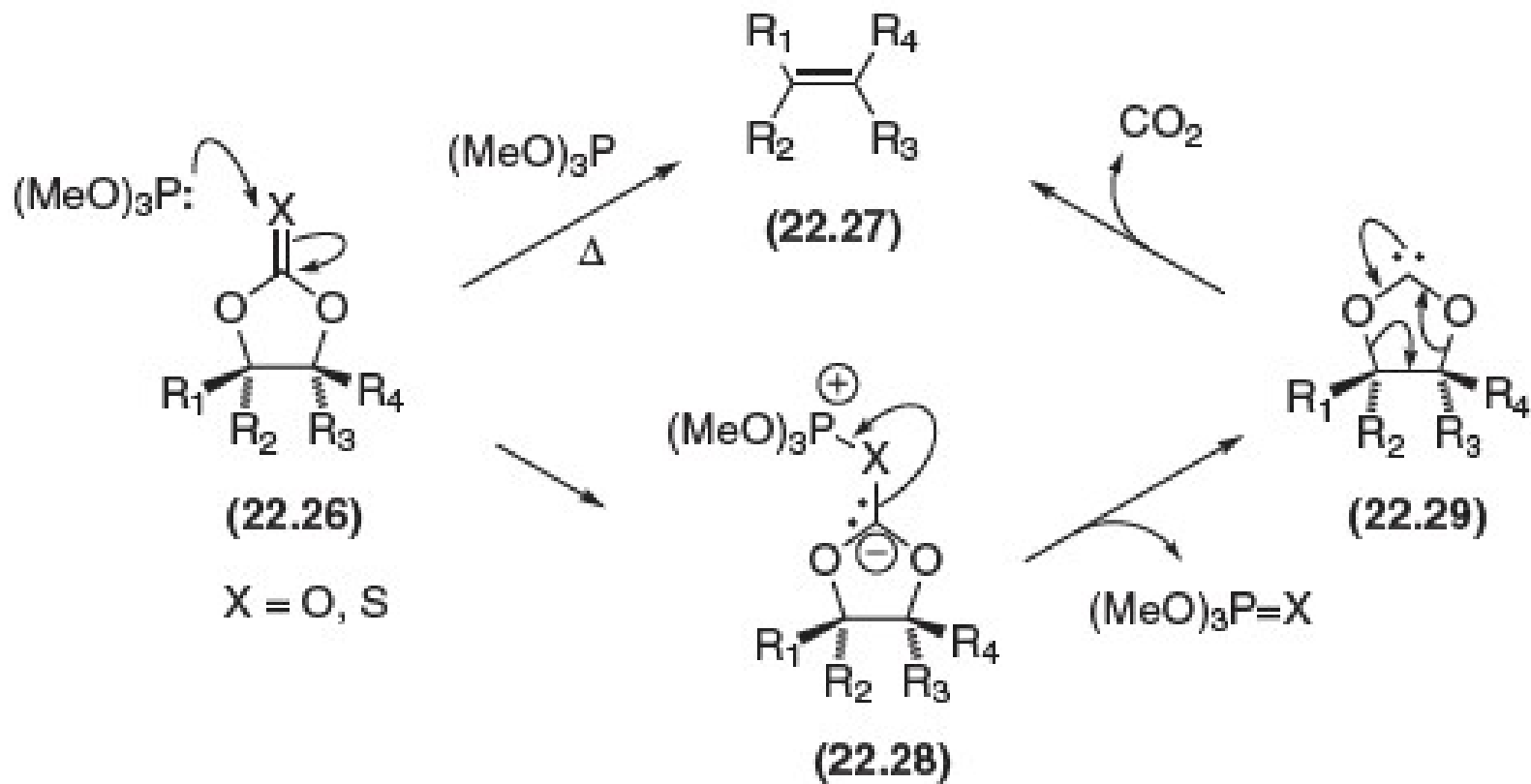


Reagents: PhSeCN, Bu₃P, PhMe;
o-O₂NC₆H₄SeCN, Bu₃P, PhMe; etc.

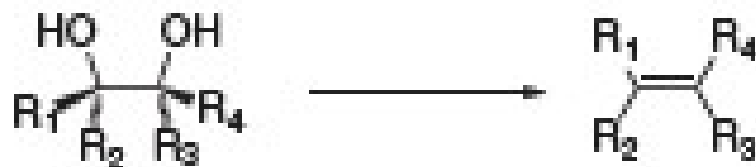
Stereochemistry: inversion of configuration at carbon

Figure 22.12

- The Corey-Winter elimination



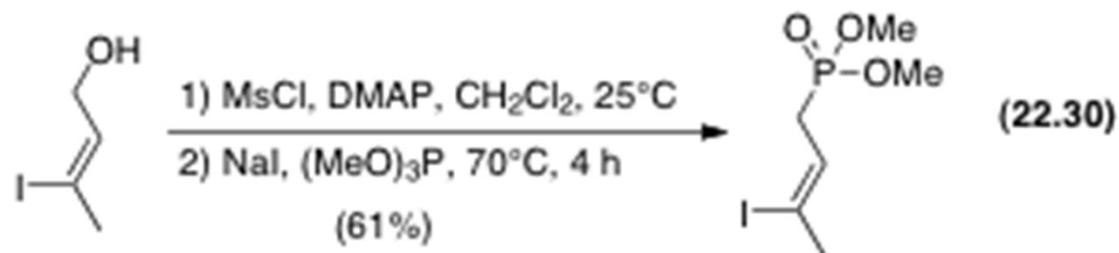
Reaction synopses: Corey-Winter reaction



Reagents: 1) Cl₂C=X, py; 2) (MeO)₃P, Δ (X=O, S);
or 1) Im₂C=X, CH₂Cl₂; 2) (MeO)₃P, Δ (X=O, S).

Stereochemistry: *syn* elimination through a cyclic carbene

Figure 22.13



The mechanism of the
Michaelis-Arbuzov
rearrangement

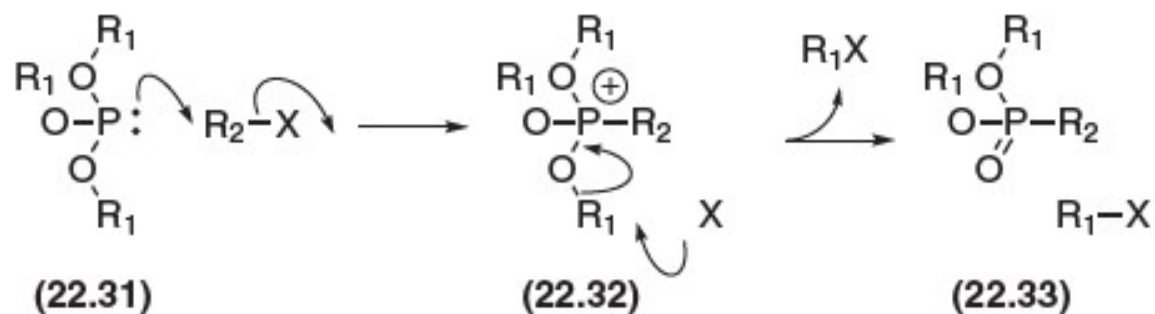
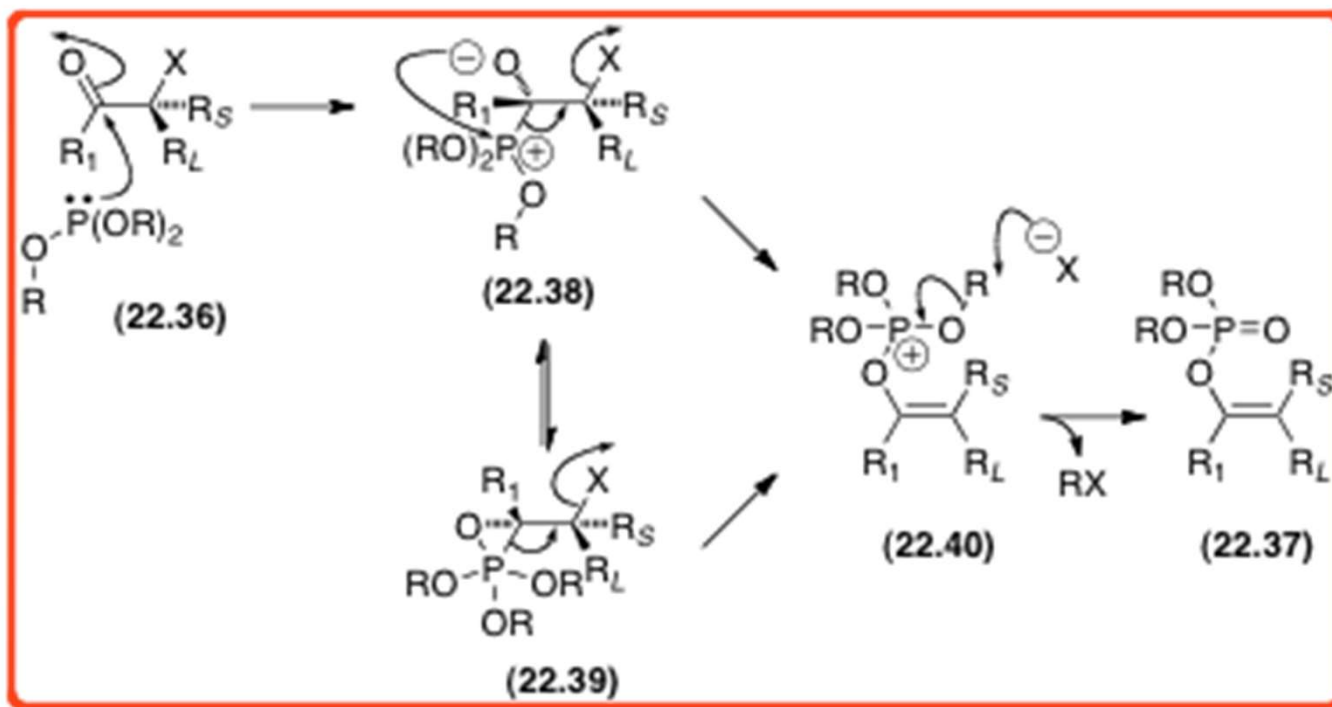


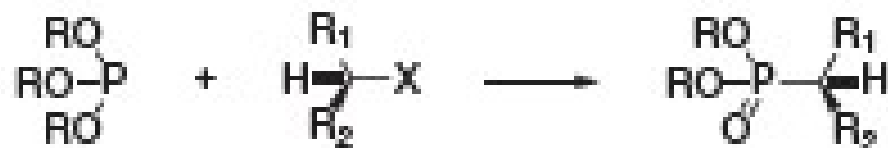
Figure 22.14



The mechanism of the Perchow reaction. R_L is the sterically more demanding substituent, and R_S is the sterically less demanding substituent at the α carbon.

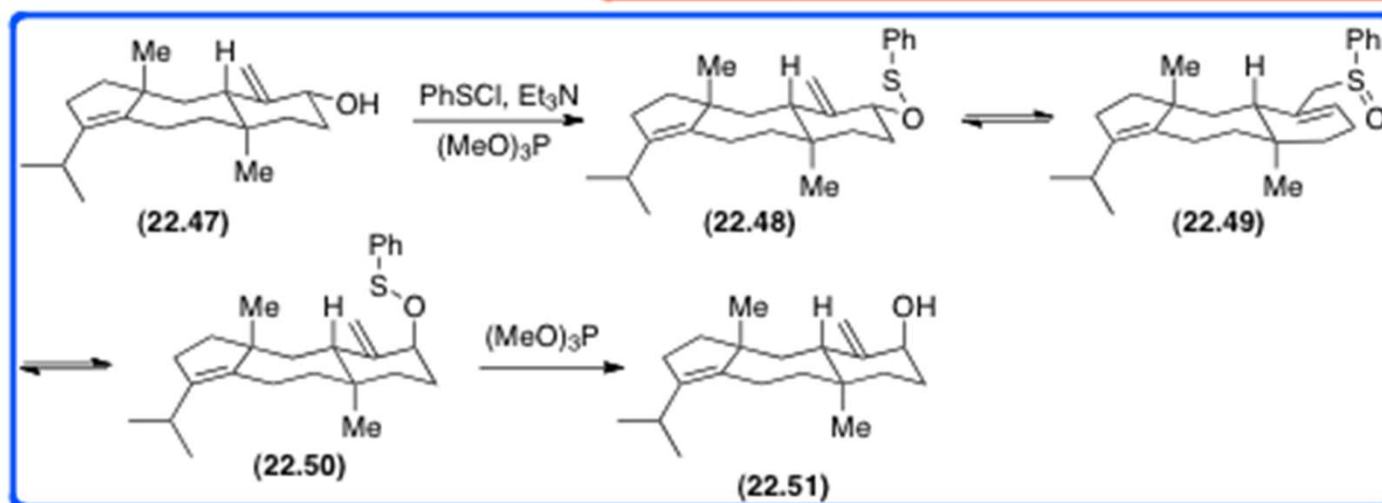
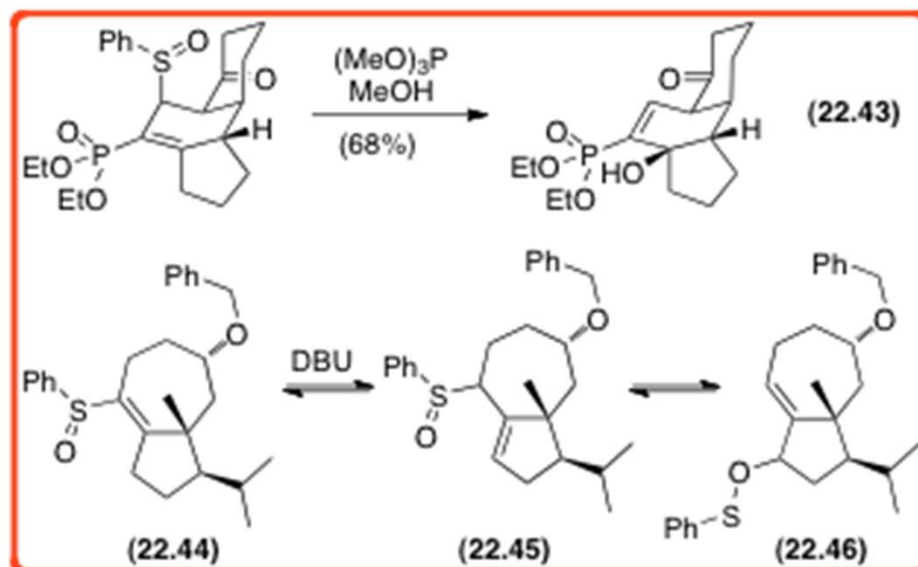
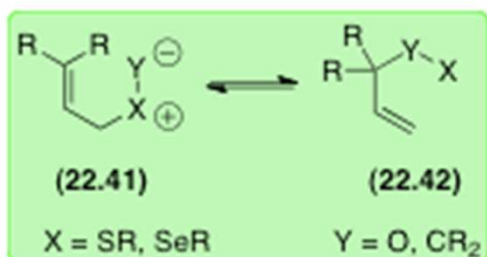


Reaction synopses: Arbuzov (Michaelis-Arbuzov) rearrangement

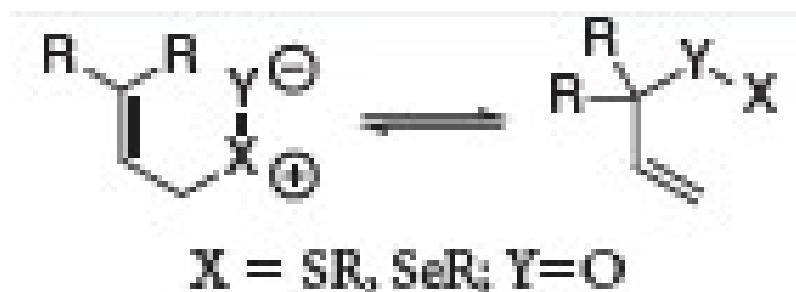


Stereochemistry: Inversion of configuration in alkyl halide

[2,3]-Rearrangements of sulfoxides, selenoxides, and sulfur ylides



Reaction synopses: Mislow-Evans rearrangement



Reaction may be extended to sulfonium ylides ($Y=CR_2$), as well as sulfilimines ($Y=NR$).

Figure 22.15

Exo and *endo* transition states for the concerted [2,3]-sigmatropic rearrangements of chiral sulfoxides (X=S) and selenoxides (X=Se)

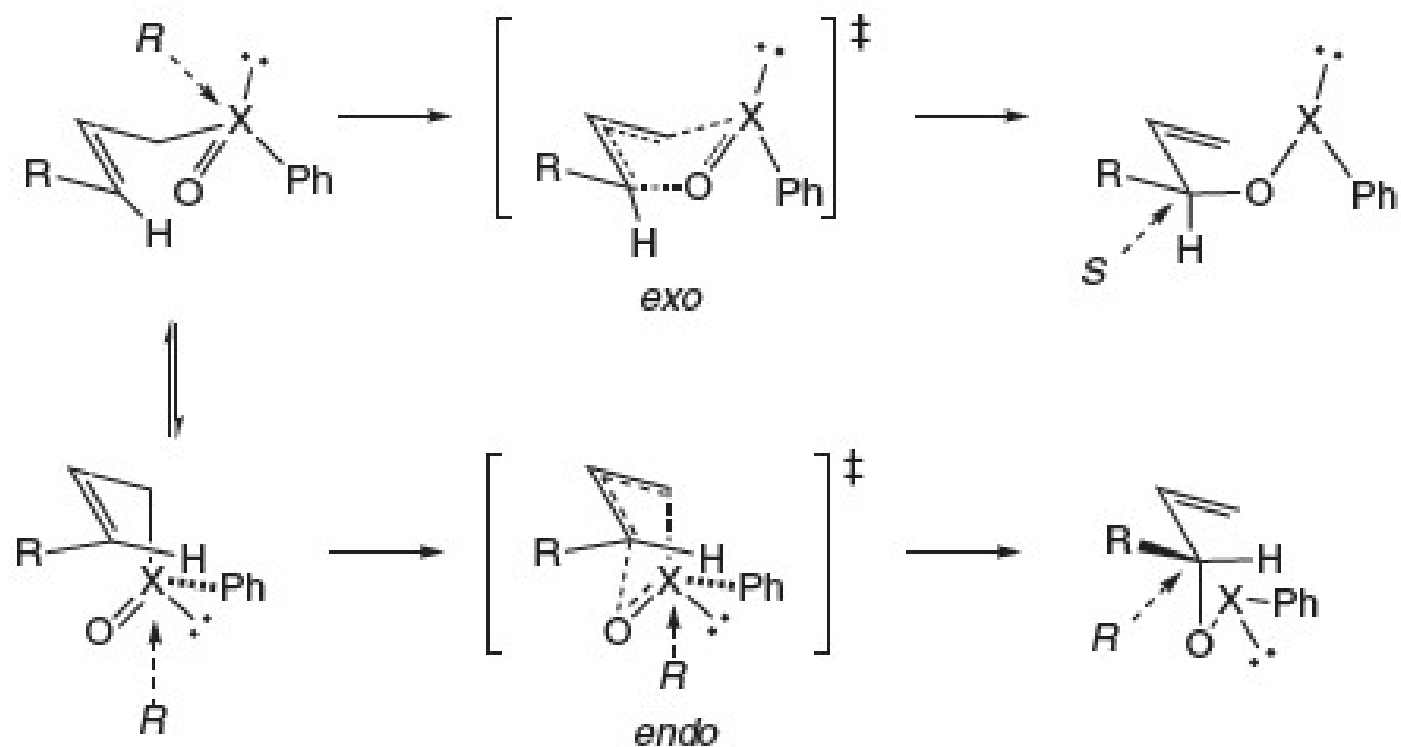
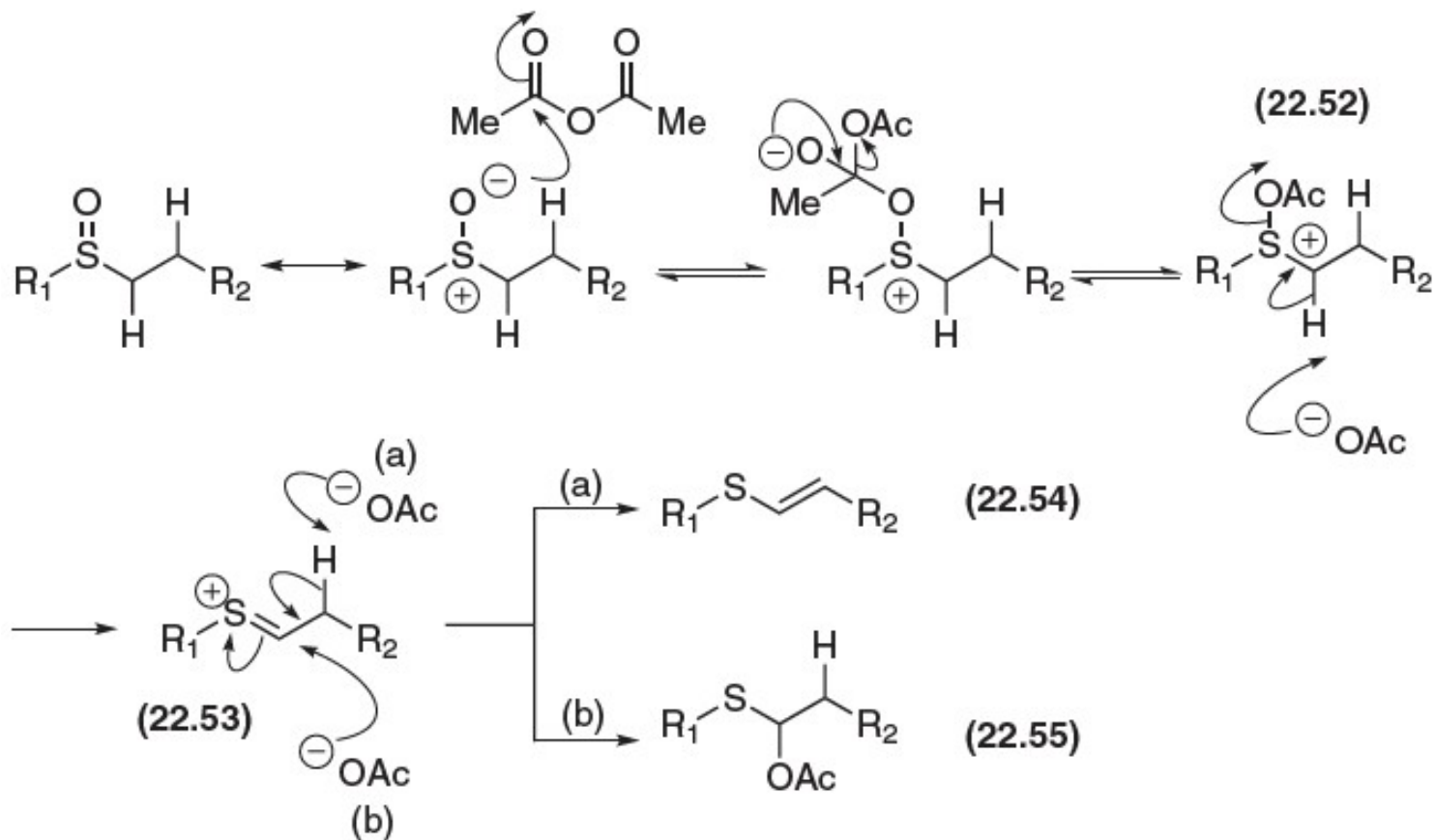
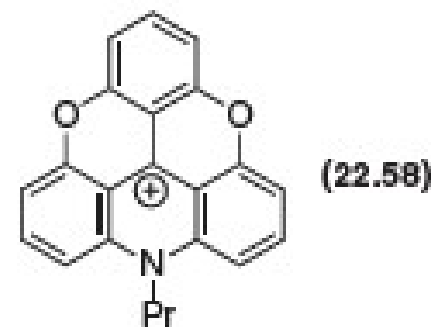
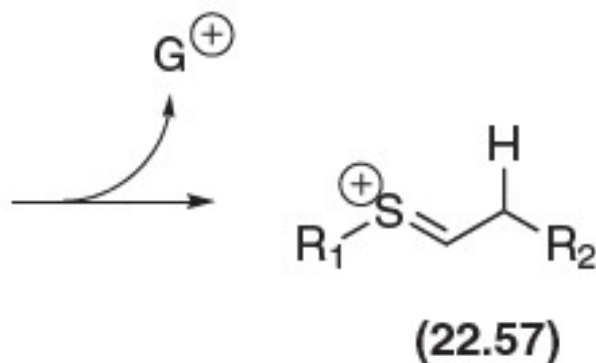
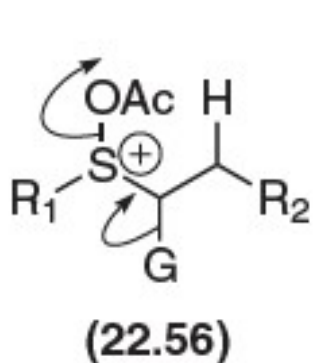


Figure 22.16



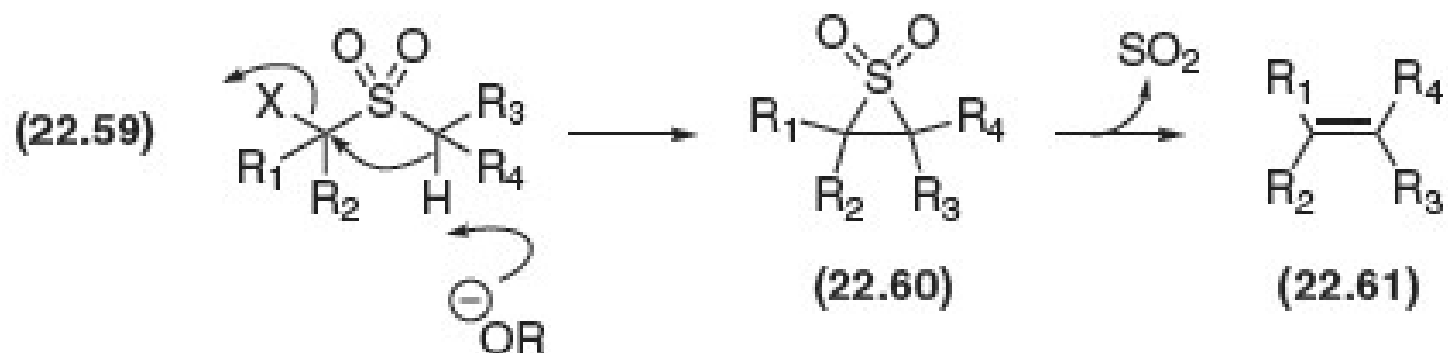
The currently accepted mechanism of the Pummerer rearrangement.

Figure 22.17

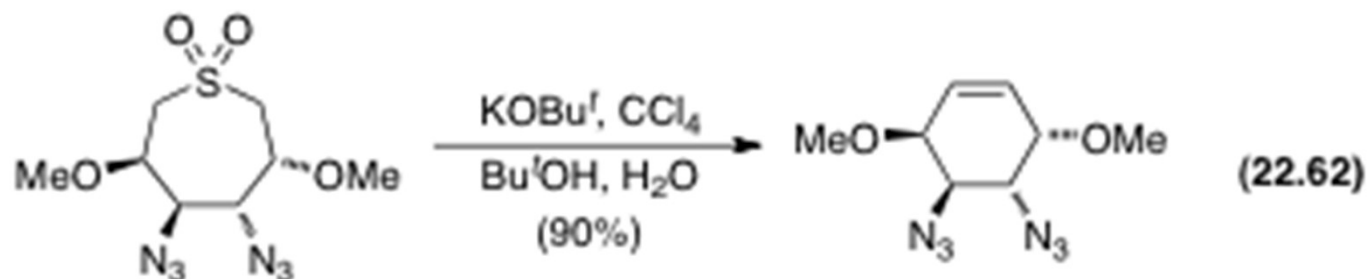


- The key step of the Pummerer fragmentation
- this reaction occurs when the group G can be lost as a very stable cation

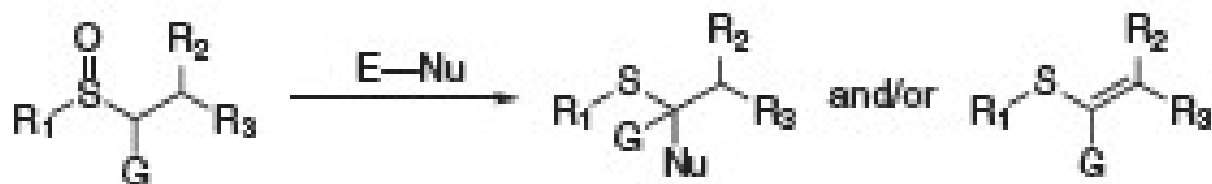
Figure 22.18



The mechanism of the Ramberg-Bäcklund reaction



Reaction synopses: Pummerer rearrangement



Reagents: Ac_2O , Δ ; Ph-N=C=O ; H^+ ; etc.

If group G can leave as a highly stable cation, the Pummerer fragmentation may dominate the reaction.

Reaction synopses: Ramberg-Bäcklund reaction



Reagents:
or

$KOBu'$, THF; KOH , Me_2SO ; etc.
 $KOBu'$, $t-BuOH-H_2O$, CCl_4 ; etc.