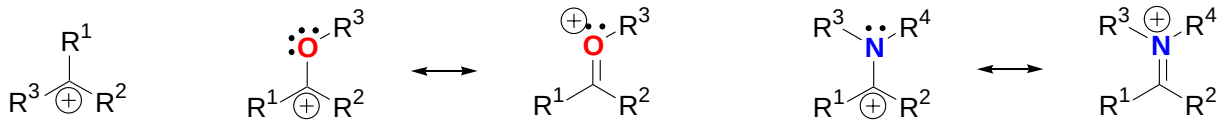
Carbocations



C-substituted carbocation ***O-substituted carbocation*** ***N-substituted carbocation***

increasing stability ⟶

Hydride ion affinities (kcal/mol)

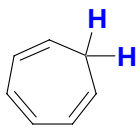
H_3C^+	314
$MeCH_2^+$	276
Me_2CH^+	249
Me_3C^+	231
$H_2C{=}CH^+$	287
$H{-}C{\equiv}C^+$	386
$PhCH_2^+$	239

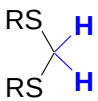
Carbocation generation

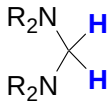
a) Hydride abstraction

$R_3C\text{-}H$ + Lewis acid ⟶ $R_3C^{\oplus}$

e.g.







+ BF_3, $Ph_3C^{\oplus}\ BF_4^{\ominus}$ etc

b) Halide/alkoxide abstraction

$R_3C\text{-}X$ + Lewis acid ⟶ $R_3C^{\oplus}$

X = F, Cl, Br, I, OR

Lewis acid: Ag^+, $AlCl_3$, $SnCl_4$, $SbCl_5$, SbF_5, AsF_5, BF_3, $ZnCl_2$, $POCl_3$ etc.

c) Protic acid-catalyzed ROH removal

$R^1{}_3C\text{-}OR^2$ + HA ⟶ $R_3C^{\oplus}$

R^1 = Aryl, any other cation-stabilizing substituent

R^2 = H, alkyl

HA = H_2SO_4, $HClO_4$, $HOSO_2CF_3$ (HOTf)

d) S_N1 / E1 dissociation

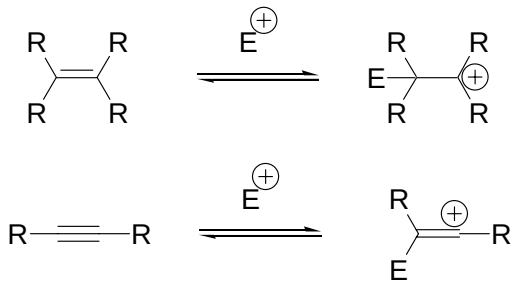
$R^1{}_3C\text{-}X$ ⟶ $R_3C^{\oplus}$ + $X^{\ominus}$

X = $N_2^+ > OSO_2R^2 > OPO(OR^2)_2 > I$ ...

note: solvation of the cation

Carbocation generation

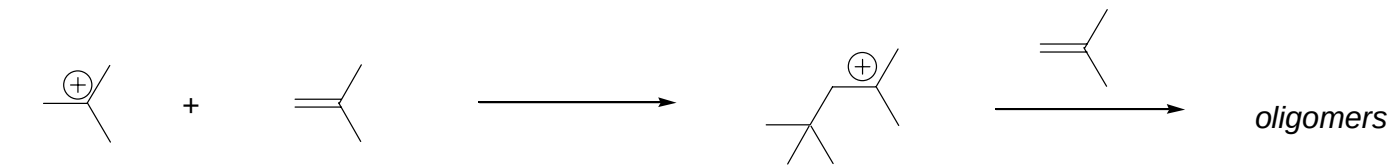
e) Addition of electrophiles to alkenes/alkynes



basis of important C-C bond forming reactions

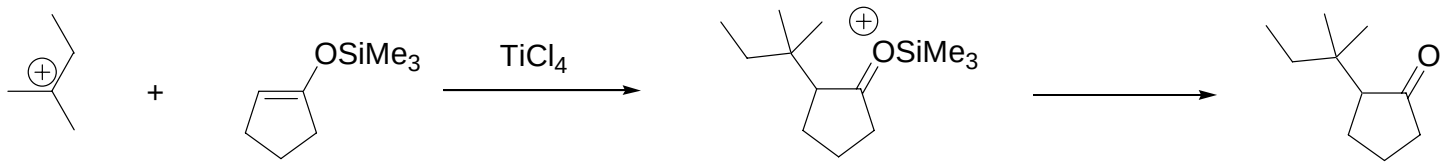
C-C bond formation using carbocations

Dimerization of isobutene



electrophile *nucleophile*

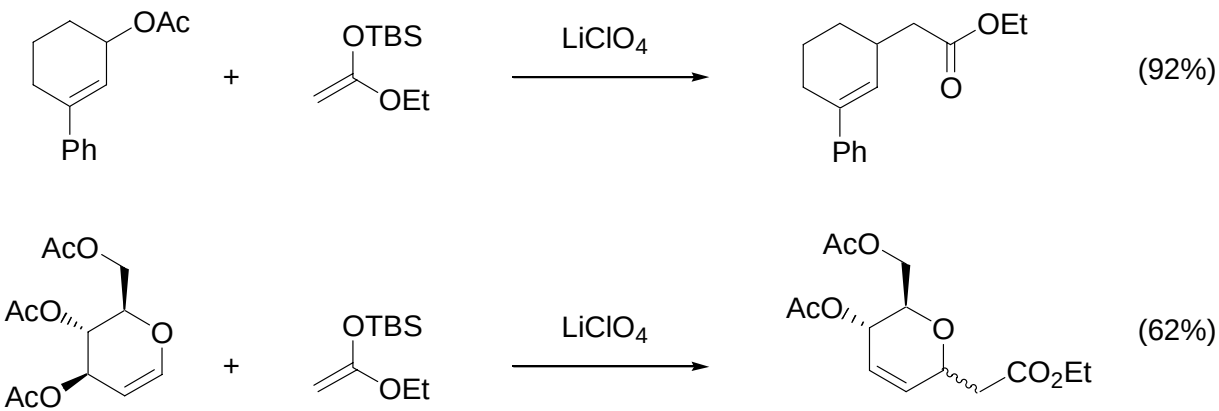
Termination by silyl enol ethers



electrophile *nucleophile*

Reetz, THL **1979**, 1427.

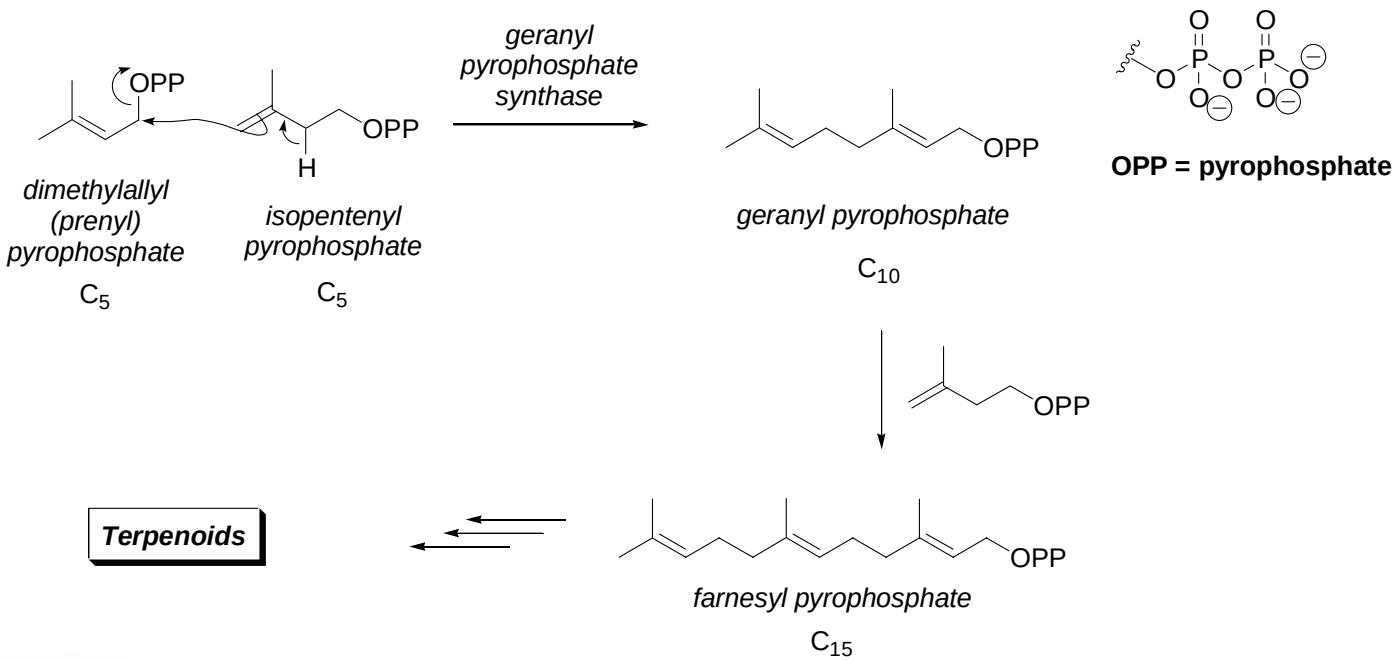
Alkylations by allylic cations



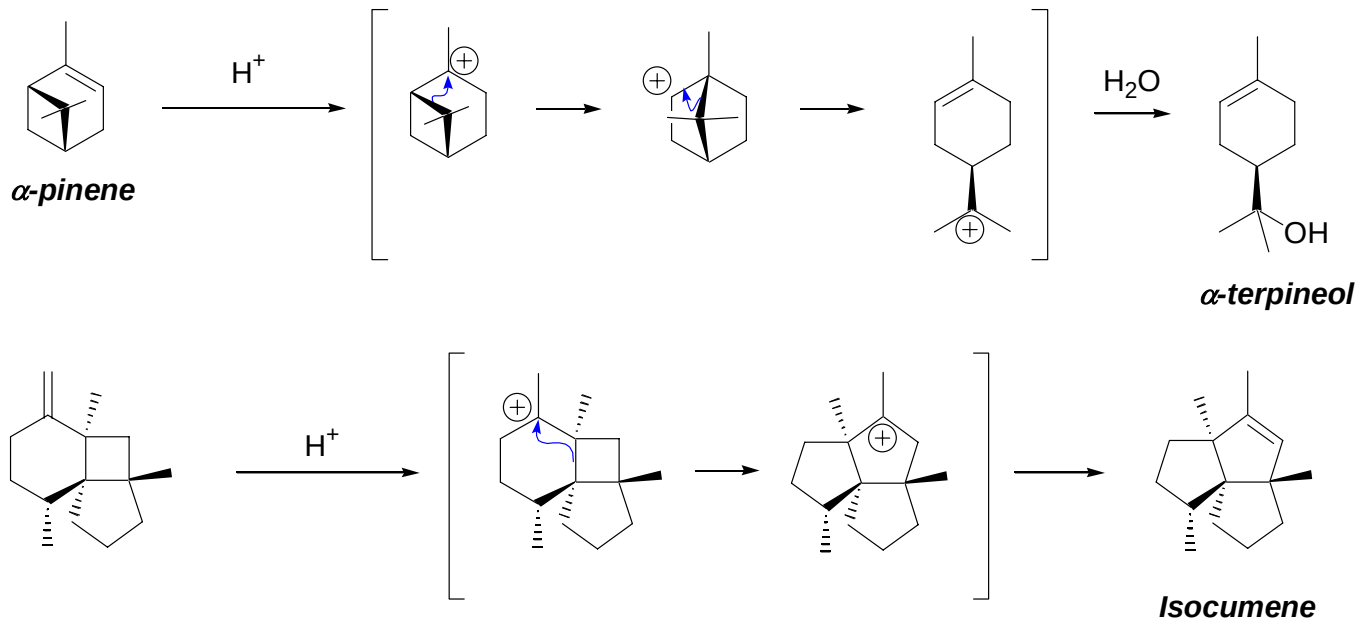
3:1 diastereoselection (α:β)

Pearson & Schkeryantz, *JOC* **1992**, *57*, 2986.

C-C bond formation: alkylation of alkenes

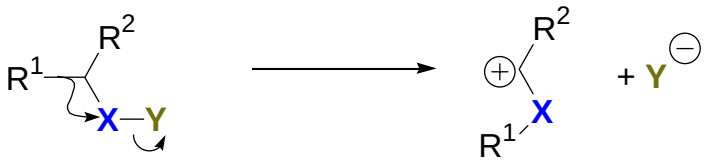


Carbocation rearrangements

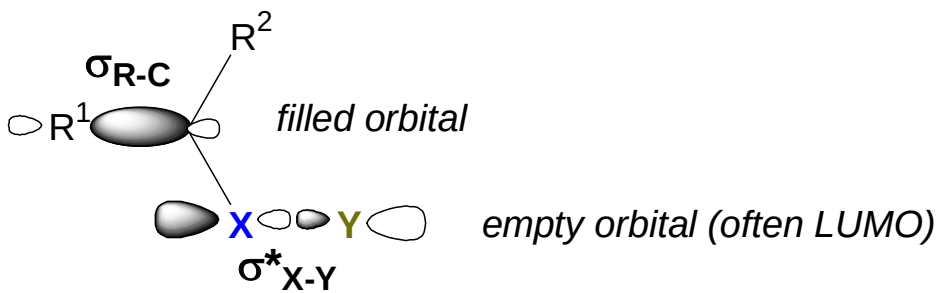


Pirrung, *JACS* **1979**, *101*, 7130

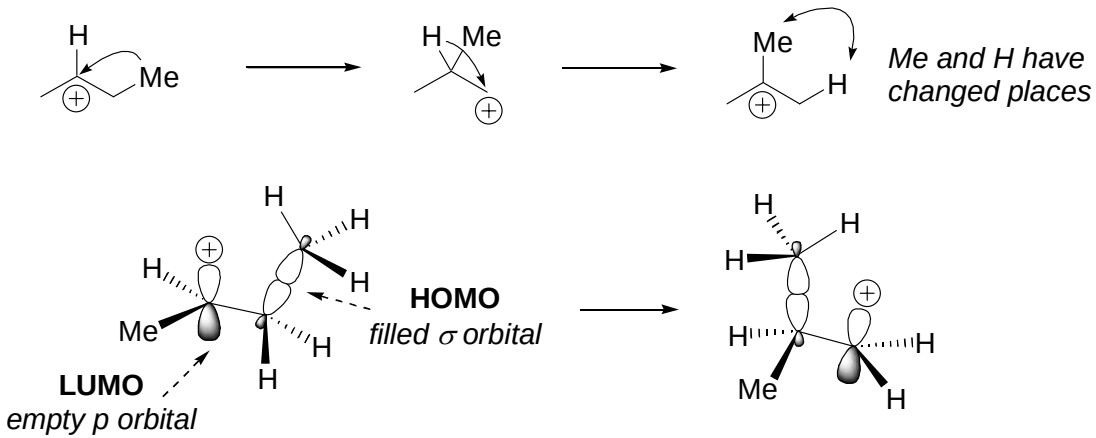
Migrations



Y = good
leaving group
R^1 = a group
capable of stabilizing
positive charge



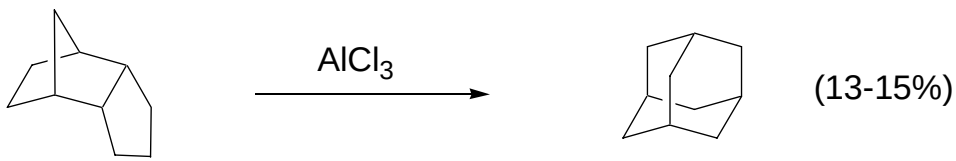
The migrating groups migrate with their pairs of electrons



- Rearrangements (Wagner-Meerwein shifts) occur very easily with carbocations
- Groups hop back and forth until the most stable carbocation is reached
- Thermodynamic control!

When following through a carbocationic rearrangements, **number the carbon atoms in the starting material and the product before you try to work out the mechanism.**

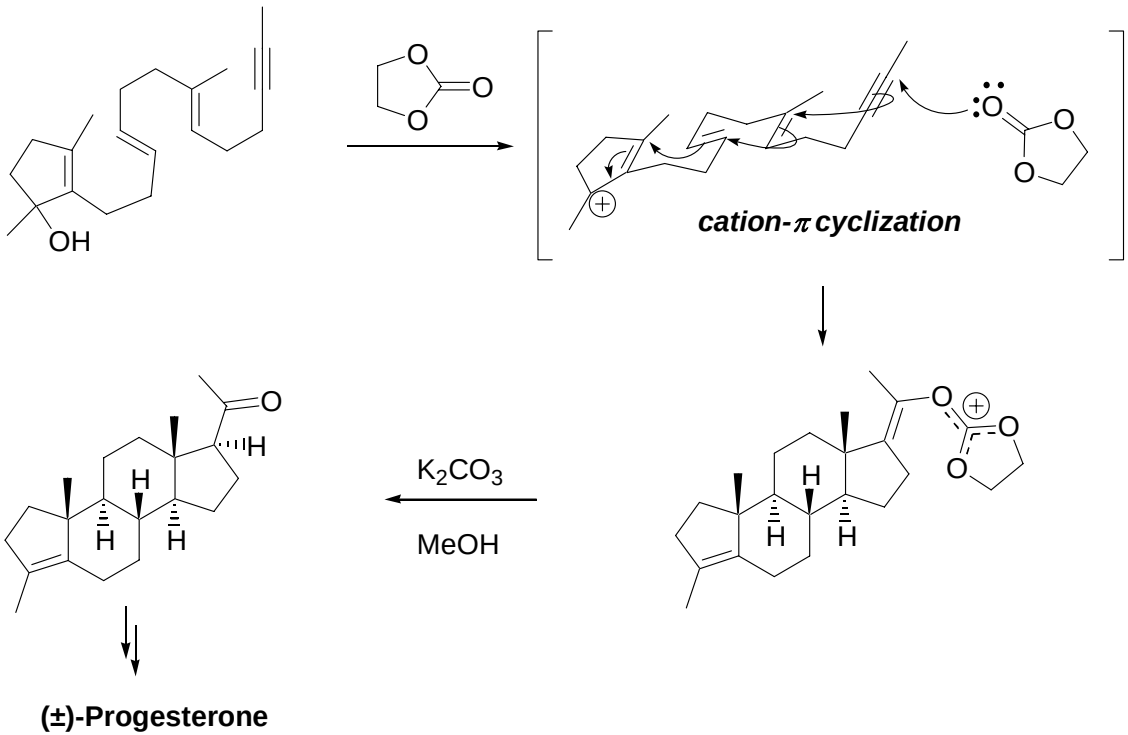
Cationic rearrangements: adamantane



"the upper layer, a brown mush of adamantane and other products, is decanted carefully from the lower black tarry layer..."

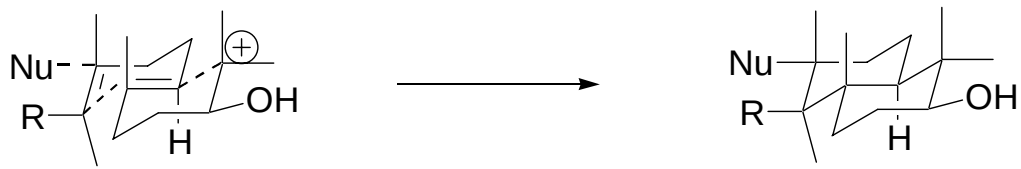
Schleyer, P. v. R.; Donaldson, M. M.; Nicholas, R. D.; Cupas, C. *Org. Synth. Coll. Vol. V,* **1973**, 16-19.

Cationic cyclizations: progesterone

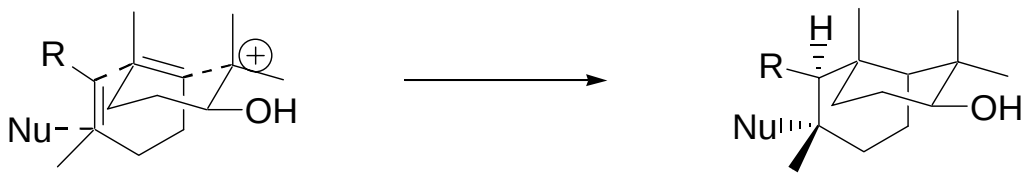


Johnson, W. S.; Gravestock, M. B.; McCarry, B. E. *J. Am. Chem. Soc.* **1971**, *93*, 4332.

Stereoelectronic effects in cationic cyclizations

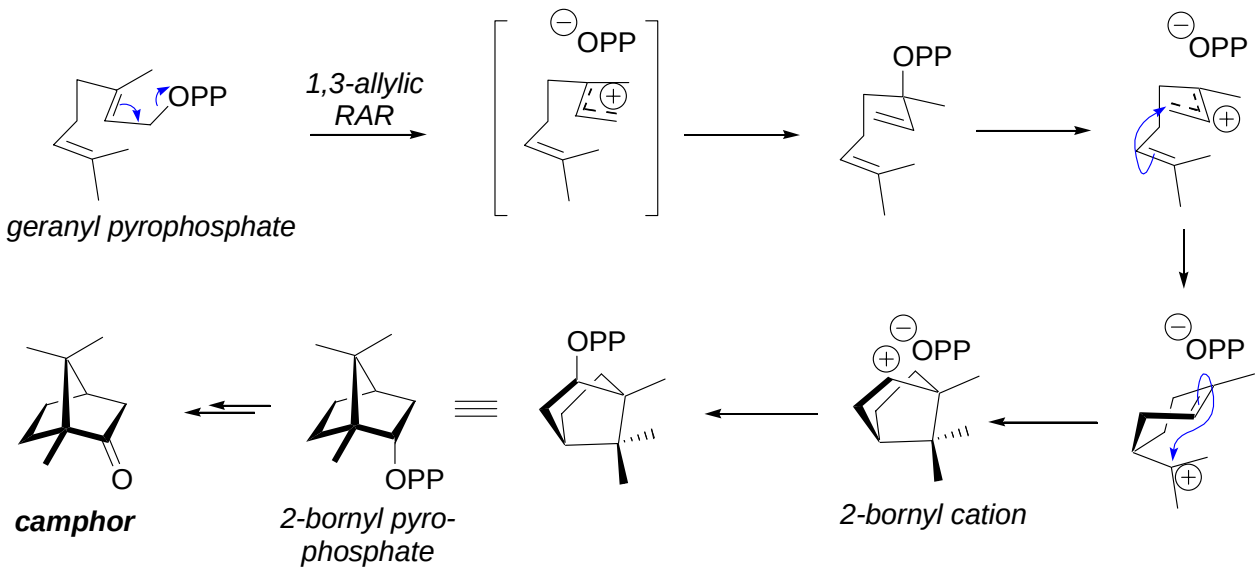


trans alkene

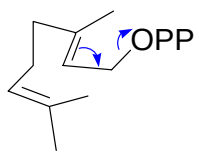


cis alkene

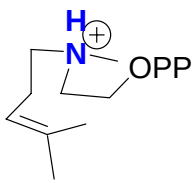
How camphor gets its shape



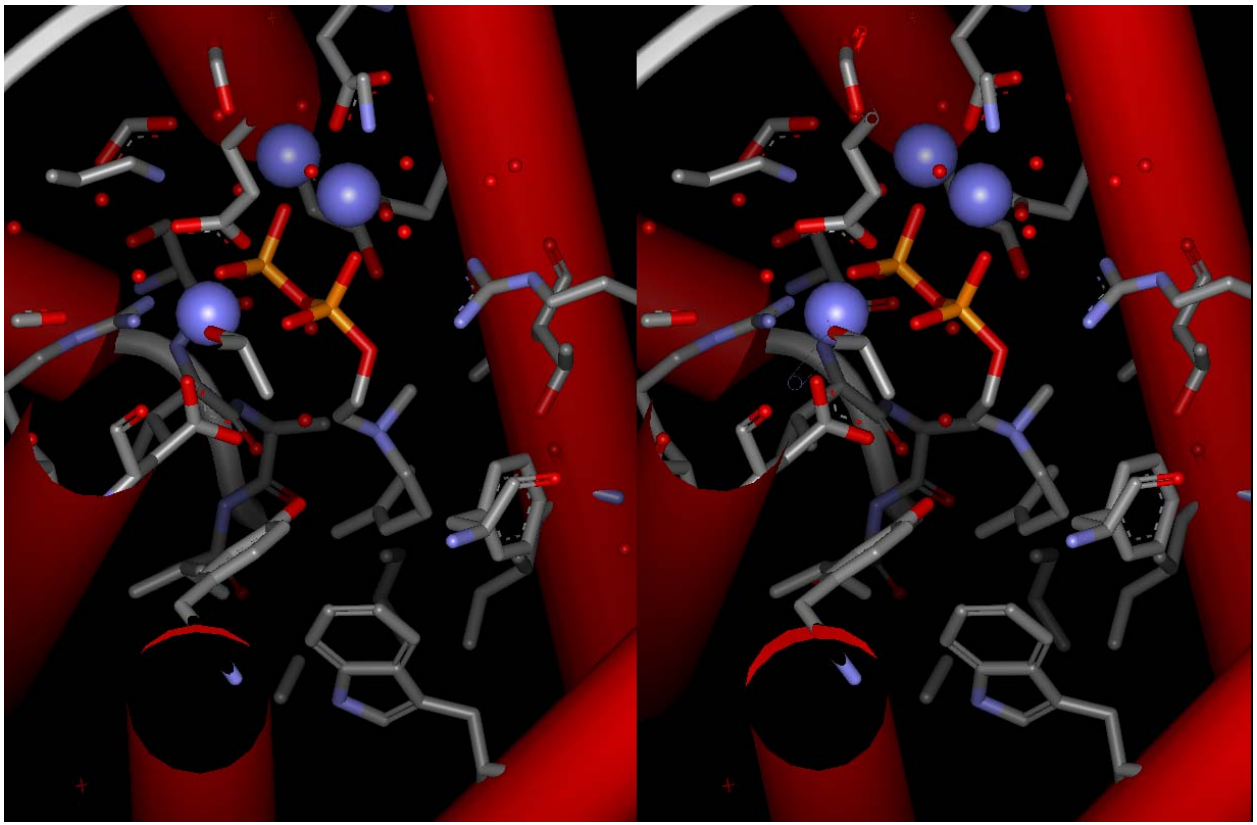
Bornyl pyrophosphate synthase caught in the act



geranyl-OPP

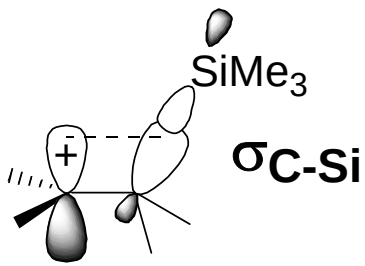


aza analog



Whittington, D. A.; Wise, M. L.; Urbansky, M.; Coates, R. M.; Croteau, R. B.; Christianson, D. W. *Proc. Acad. Natl. Sci. USA* **2002**, *99*, 15375-15380.

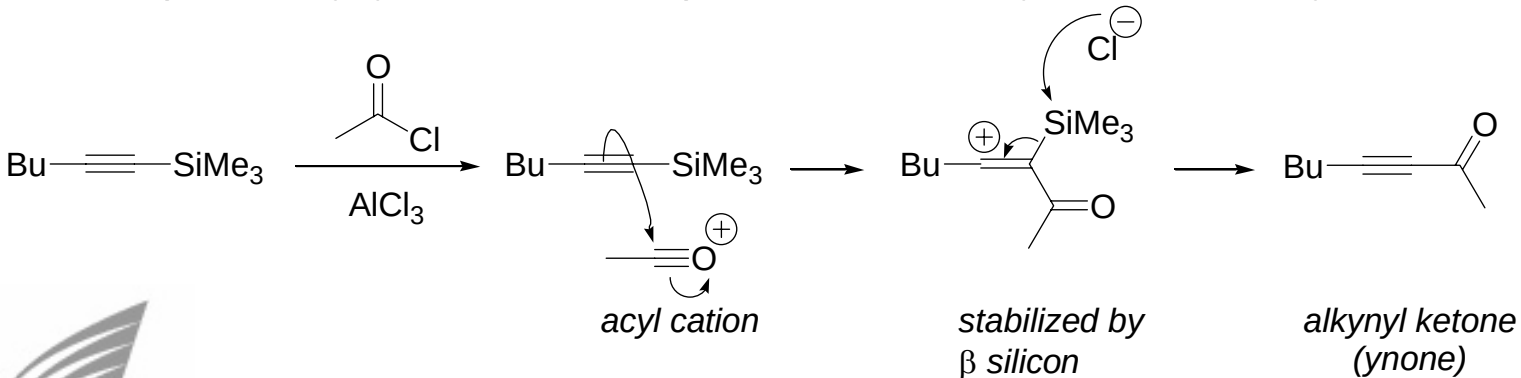
Silicon stabilizes positive charge on the β carbon



The C-Si bond is polarized towards the more electronegative atom, C.

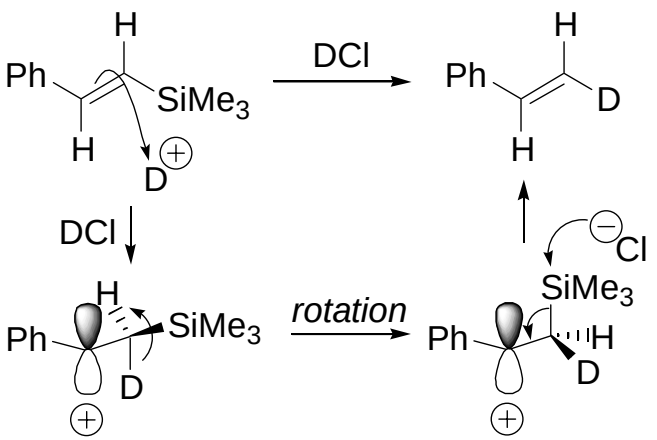
The $\sigma_{C\text{-}Si}$ orbital is biased towards C and can easily donate electron density to the neighboring carbocation (by overlapping with the empty p orbital).

Example: in alkynyl silanes, electrophiles attack the silyl end exclusively:



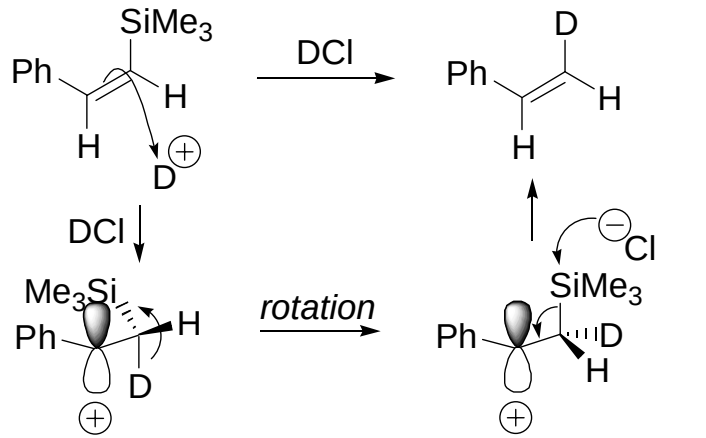
Protodesilylation: retention of alkene configuration

(*E*)-vinyl silane

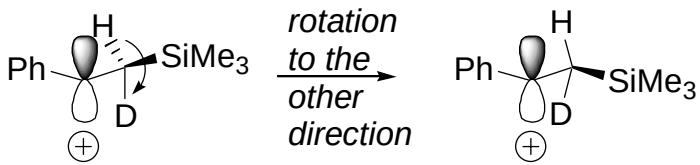


correctly aligned for stabilization by Si

(Z)-vinyl silane

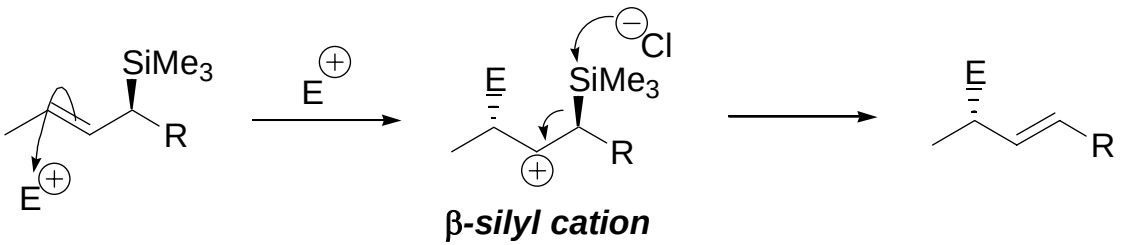


correctly aligned for stabilization by Si

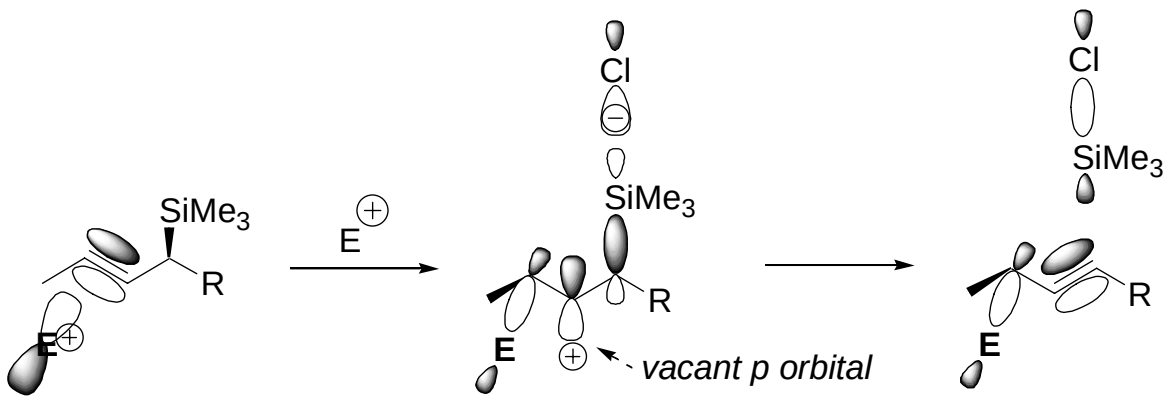


high-energy conformation: C-Si σ parallel to p orbital

Allyl silanes also react through β-silyl cations



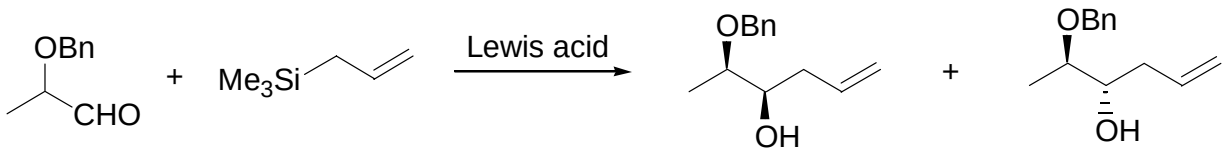
β-*silyl cation*



β-*silyl cation*

Allyl silanes are much more reactive than vinyl silanes towards electrophiles

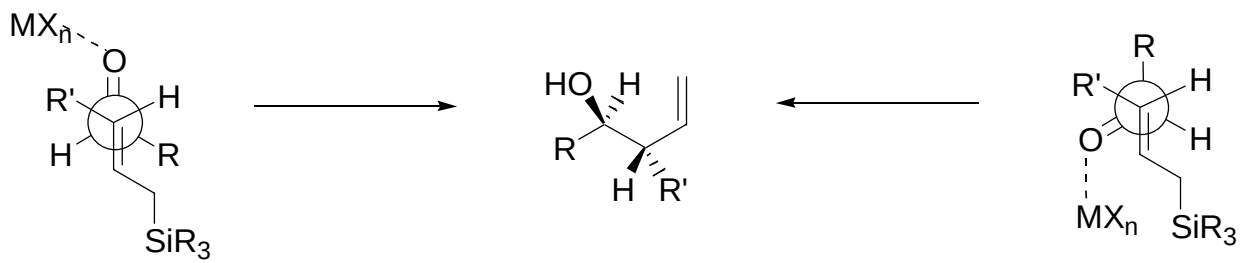
Addition of allylsilanes to C=O: the Sakurai-Hosomi reaction



$SnCl_4$	97	:	3 (chelation control)
$BF_3{\cdot}Et_2O$	40	:	60 (Felkin control)

Heathcock, C. H.; Kiyooka, S.; Blumenkopf, T. A. *J. Org. Chem.* **1984,** *49*, 4214.

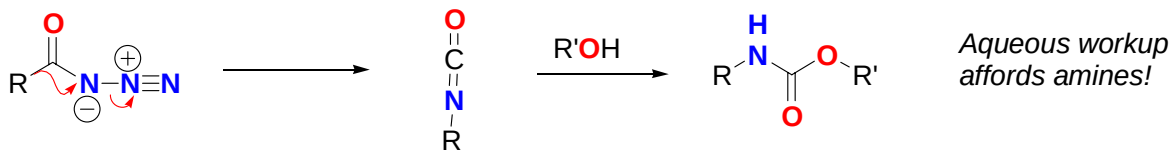
The reaction usually takes place *via* an open transition state, e.g.



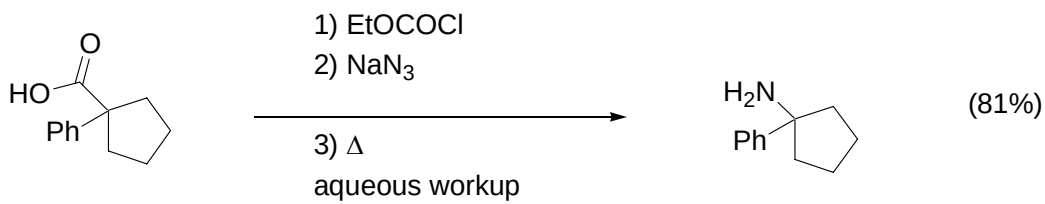
antiperiplanar TS *anti* *synclinal TS*

Reviews: a) Sakurai, H. *Pure Appl. Chem.* **1982**, *54*, 1. b) Masse, C.; Panek, J. *Chem. Rev.* **1995***, 95*, 1293**.**

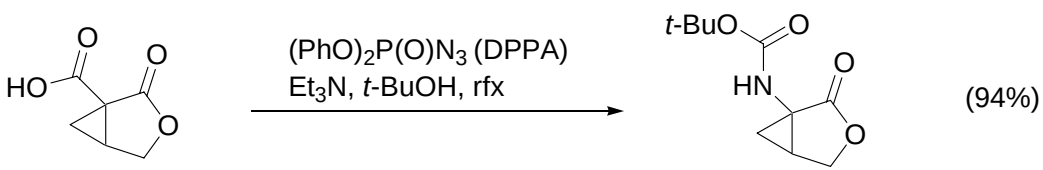
Migration to electron-deficient N: Curtius RAR



acyl azide ***isocyanate*** *(can be isolated)* *carbamate*

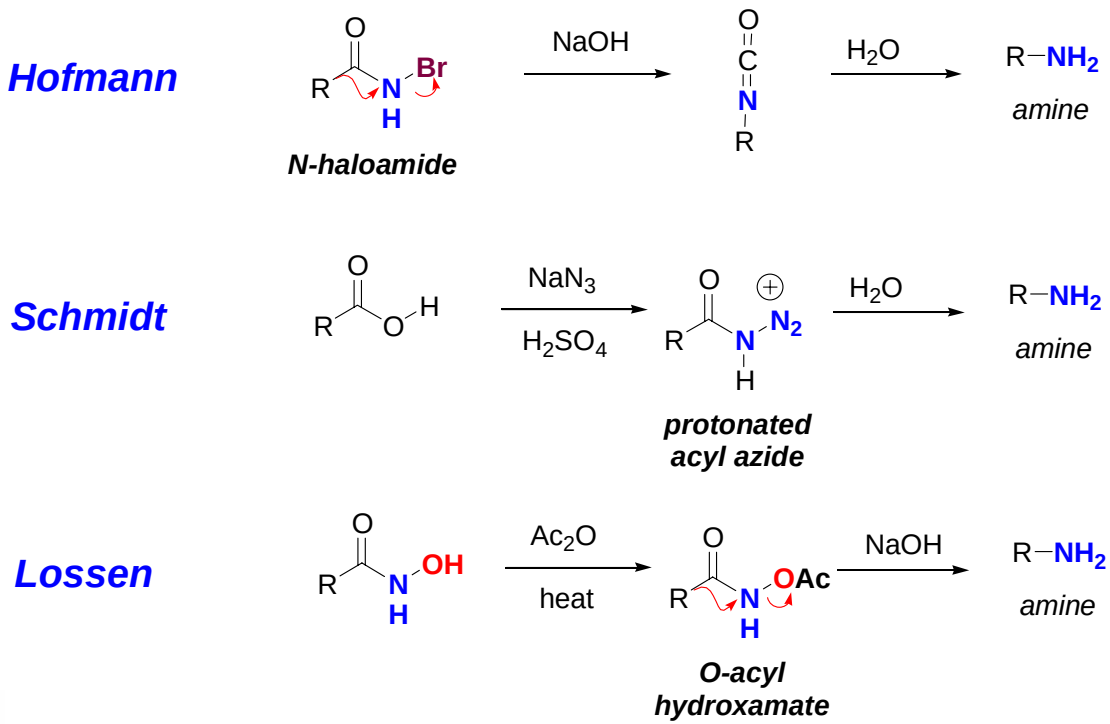


Kaiser & Weinstock, *Org. Synth.* **1971**, *51*, 48.



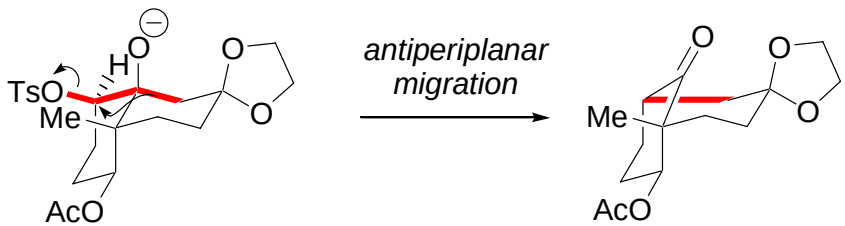
Koskinen & Muñoz, *JOC* **1993**, *58*, 879.

Variants of Curtius: Hofmann, Schmidt, Lossen

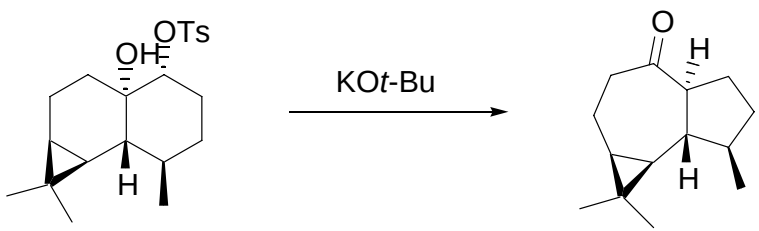


Semipinacol rearrangements

If one of the OH groups is converted into a good leaving group, this controls the regiochemistry of the rearrangement:

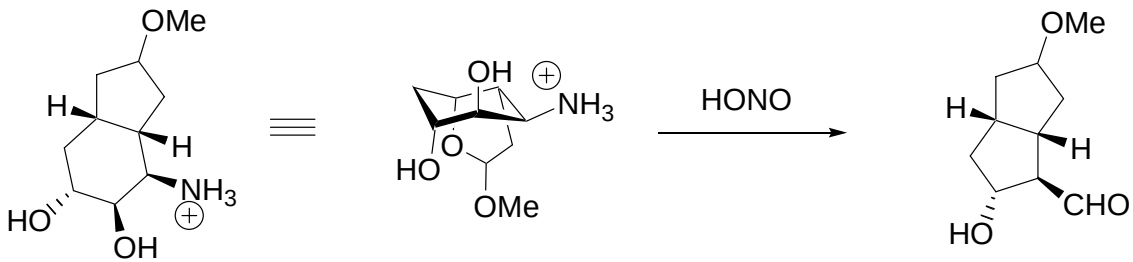


Heathcock, C. H.; Del Mar, E. G.; Graham, S. L. *J. Am. Chem. Soc.* **1982**, *104*, 1907.



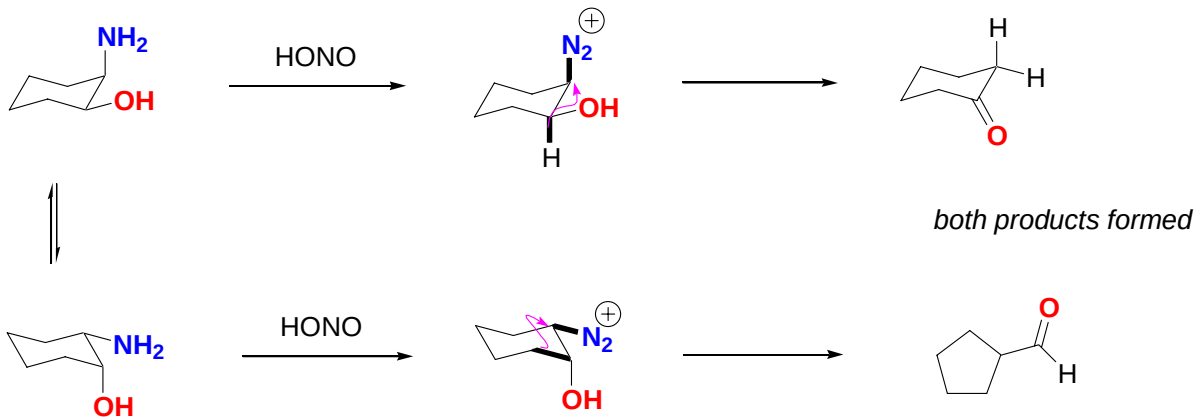
Büchi, G.; Hofheinz, W, Paukstelis, J. V. *J. Am. Chem. Soc.* **1966**, *88*, 4113.

Demjanov-Tiffeneau

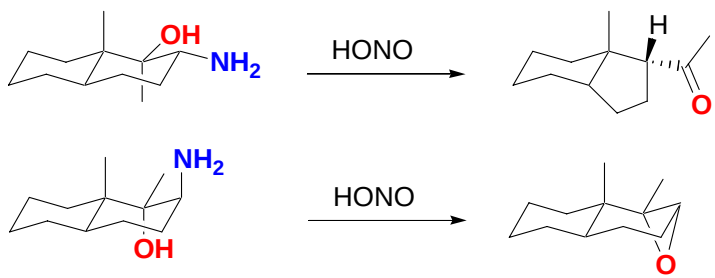


Woodward et al. *JACS* **1973**, *95*, 6853.

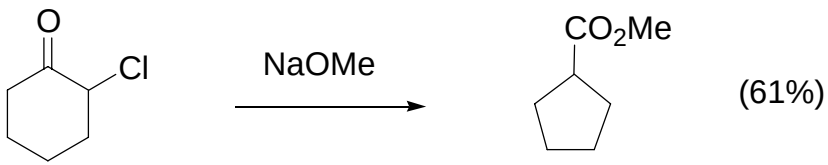
Demjanov-Tiffeneau RAR



Explain the following:

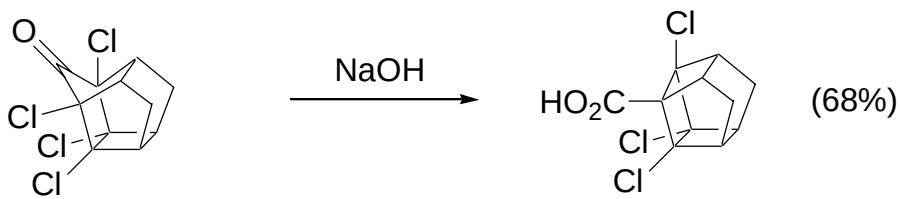


Favorskii RAR



(61%)

Goheen and Vaughan, *Org. Synth. Coll. Vol. IV,* **1963**, 594.



(68%)

Stedman, Miller, Davis & Hoover, *JOC* **1970**, *35*, 4169.