Asymmetric Baeyer-Villiger Oxidations

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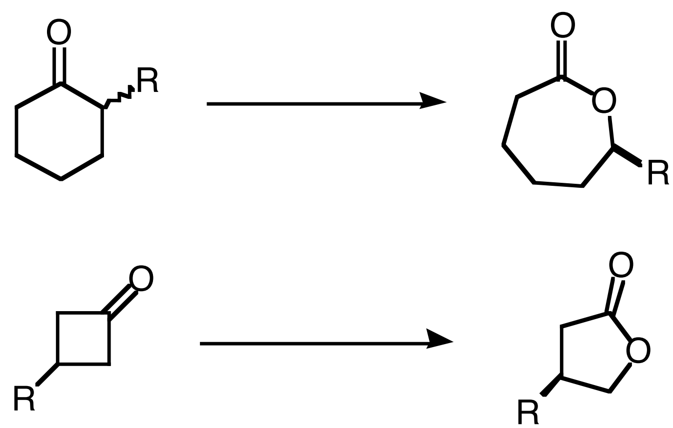
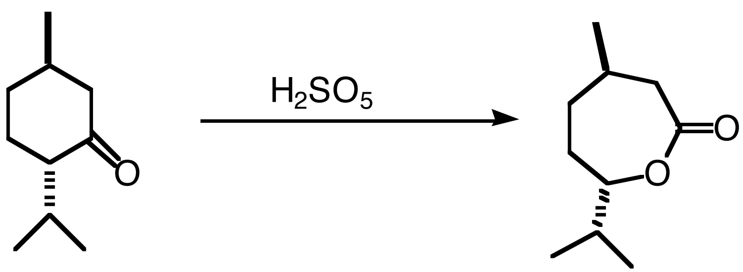


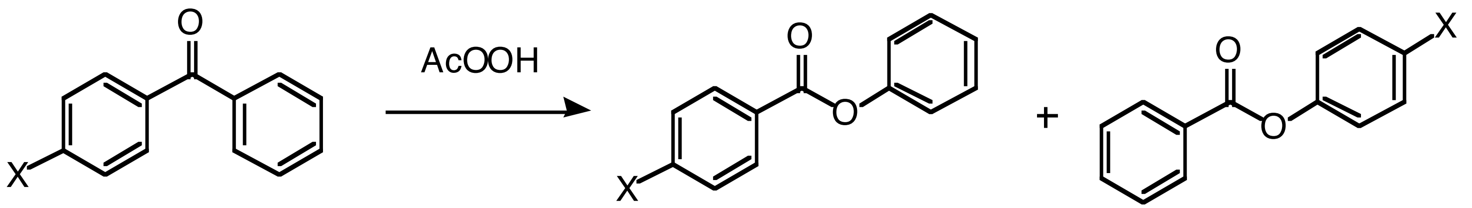
Baeyer and Villiger

- First demonstrated in 1899 in oxidation of menthone



A. Baeyer, V. Villiger, *Ber. Dtsch. Chem. Ges.* **1899,** *32*, 3625

Early Studies: Migration



•Competition experiments demonstrated preferential migration when X is electron donating.

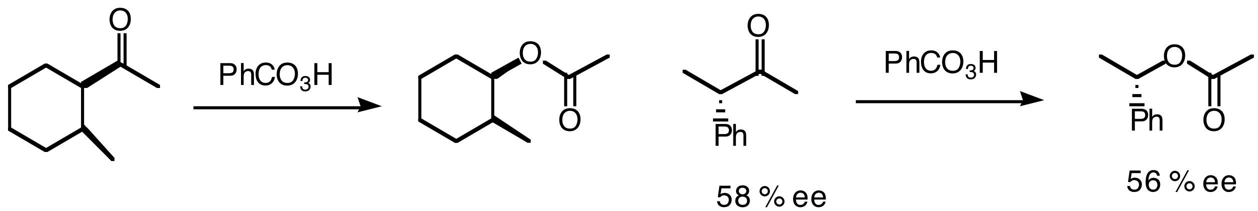
•Migratory aptitude: 3^0 > cyclohexyl > 2^0 > benzyl > phenyl >1^0 > cyclopentyl > methyl.

•Doering also observed catalysis by sulfuric acid.

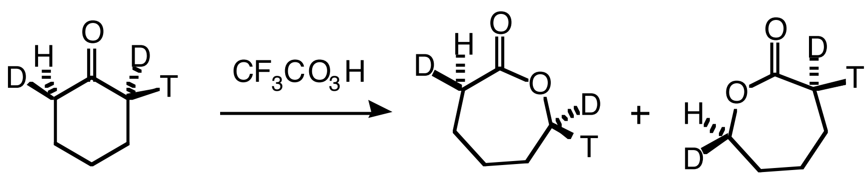
•Result consistant with electron-deficient intermediate in mechanism.

W. E. Doering; L. Speers, *J. Am. Chem. Soc.* **1950**, *72*, 5515.
M. Renz; B Meunier, *Eur. J. Org. Chem.* **1999**, 737.

Stereochemistry of Migration



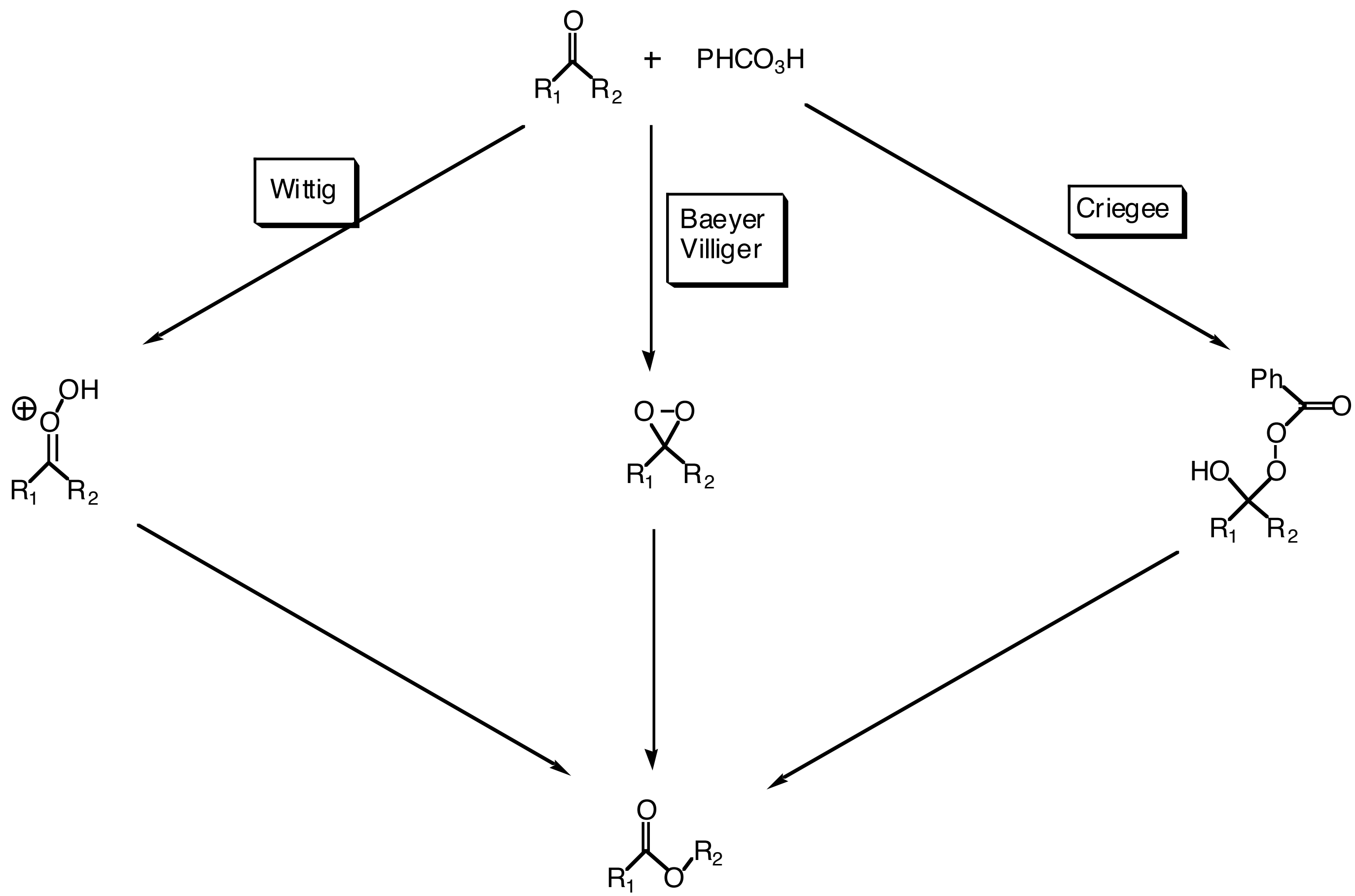
R. Turner. *J. Am. Chem. Soc.* **1950**, *72*, 878.
K. Mislow; J. Benner, *J. Am. Chem. Soc.* **1953**, *75*, 2318



J. Rozzell; S. Benner. *J. Org. Chem.* **1983**, *48*, 1190.

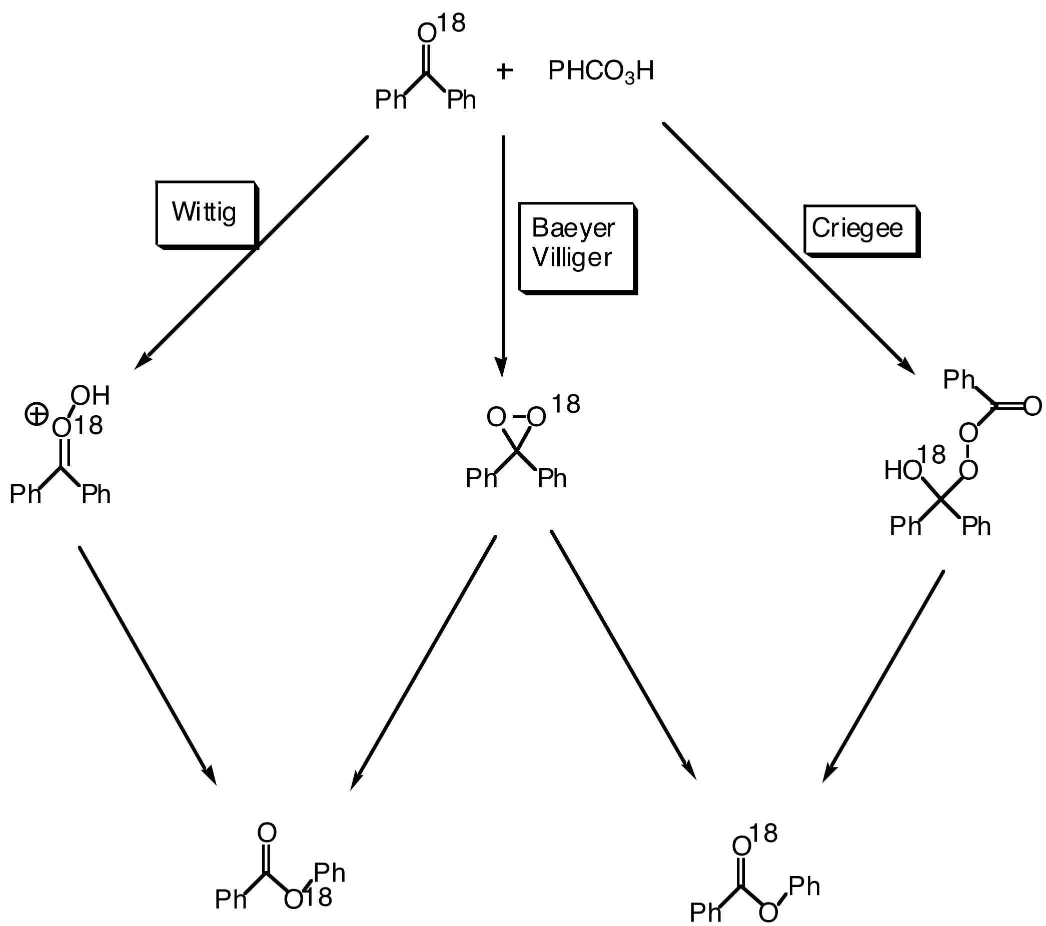
- Retention of configuration at migrating carbon.

Proposed Mechanisms



Criegee, *Angew. Chem.* **1948**, *560*, 127
A. Baeyer; V. Villiger. *Ber. Dtsch. Chem. Ges.* **1900**, *33*, 124.
G. Wittig. *Ber. Dtsch. Chem. Ges.* **1940**, *73,* 295.

Labeling Studies



- O^{18} label observed only in carbonyl.
- Results support formation of Criegee intermediate.

W. E. Doering; E. Dorfman. *J. Am. Chem. Soc.* **1953**, *75*, 5595.

Enzymatic Transformations

Recombinant Baker's yeast oxidations give good yields and excellent ee's.

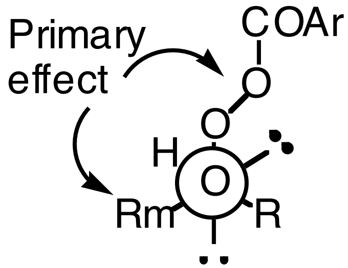
J. Stewart et al. *J. Am. Chem. Soc.* **1998.** *120*, 3541.

Oxygen as Terminal Oxidant

Molecular oxygen with metal catalysts give oxidation products in good yield.

T. Mukaiyama et al. *Chem*. *Lett*. **1991.** 641.
S. Murahashi; Y. Oda; T. Naota. *Tetrahedron Lett*. **1992.** *33*, 7557.

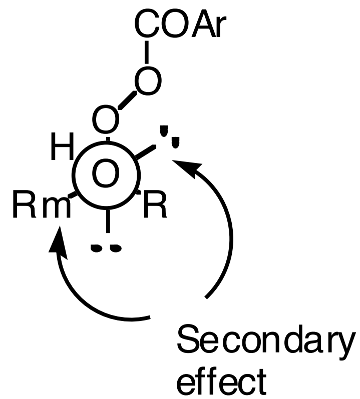
Primary Stereoelectronic Effect



Migrating group must be antiperiplanar to O-O bond of the leaving group.

C. Crudden; A. Chen; L. Calhoun. *Angew. Chem. Int. Ed.* **2000**, *39*, 2851.

Secondary Stereoelectronic Effect



Lone pair on oxygen must be antiperiplanar to migrating group.

R. Noyori; H. Kobayashi; T. Sato. *Tetrahedron Lett.* **1980.** *21*, 2573.

System Comparison

System	Prochiral yields	Prochiral ee's	Racemate yields	Racemate ee's	Chiral substrate loading
Cu	77-92 %	26-47 %	21-65 %	47-69 %	1 mol %
Pt	-	-	Under 25 %	Up to 45 %	1 mol %
Sharpless	64%	40 %	7-40 %	37-75 %	1.5 equiv.
Acetal	quant.	Up to 89 %	-	-	1.0 equiv.
Zr	quant.	Up to 31 %	quant.	Major up to 35% Minor up to 84 %	1.0 equiv.
Mg	quant.	Up to 65 %	-	-	25-50 mol %
$ZnEt_2$	60's to 80's	Up to 40 %	-	-	1.2 equiv.
Co-salen	72 %	77 %	-	-	5 mol %
Al	quant.	60's to 70's	quant.	~70% for both products	15 mol %

Conclusion

- Asymmetric Baeyer-Villiger systems have made significant progress over the past decade.
- Currents systems are limited in scope.
- Yields and ee's still too low.
- Enzymatic and traditional methods still superior.
- Asymmetric Baeyer-Villiger shows promise for future study and synthetic utility.