Basic Problems in *Asymmetric Catalysis*

⟹ **Enantioselectivity**

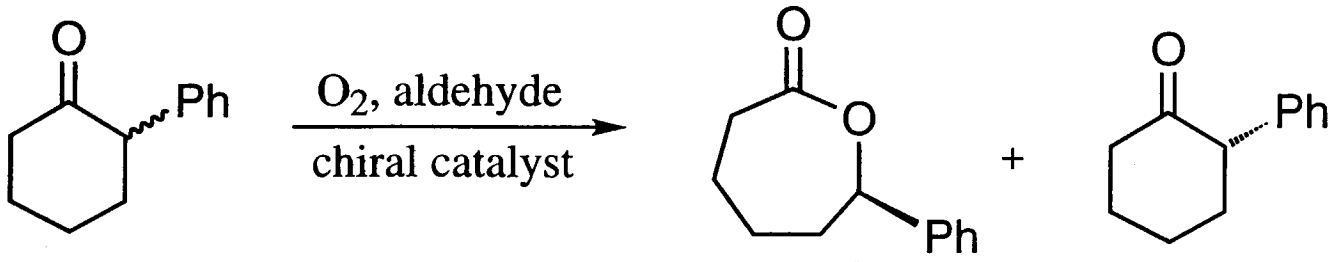
⟹ **Catalyst turnover**

- C-C-bond forming reactions

- reductions

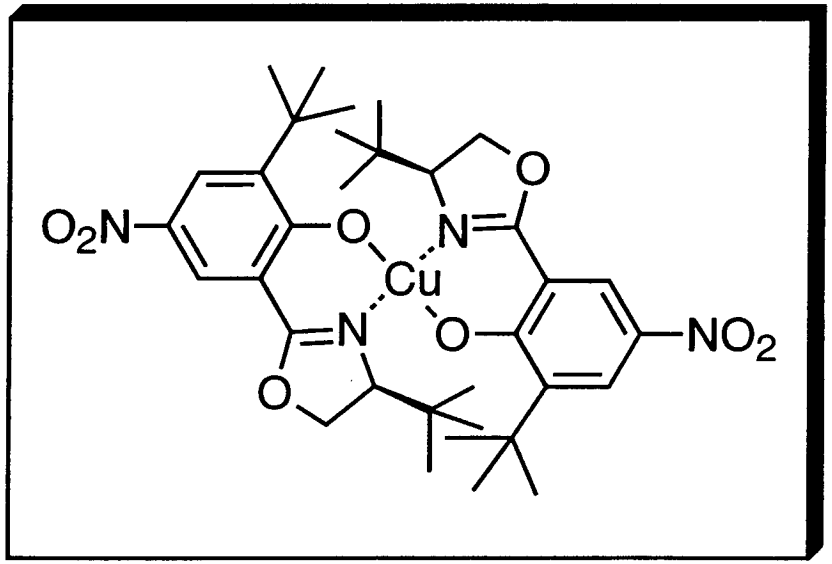
- oxidations

Asymmetric Metal-catalyzed Baeyer-Villiger Oxidation with Oxygen



65% ee

chiral catalyst:

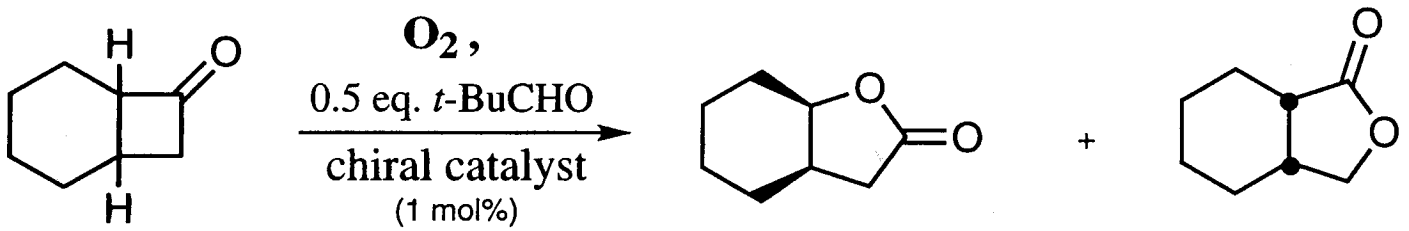


CONDITIONS:

O_2 (1 atm)
1 mol% catalyst
0.5 eq. *t*-BuCHO
benzene (+ water)
room temperature

Bolm, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1848.

Asymmetric Baeyer-Villiger Oxidation of Cyclobutanones



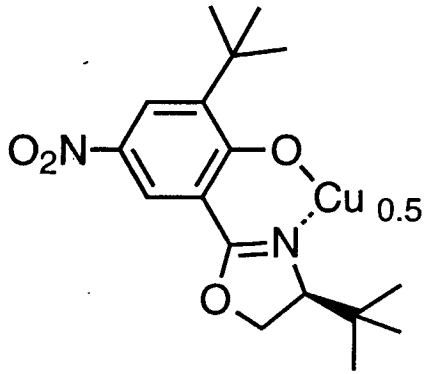
racemic

67% ee
(R,R)-enantiomer

92% ee
(S,R)-enantiomer

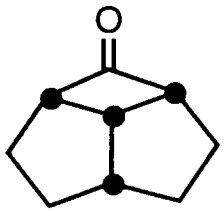
yield: 61% (3 : 1)

chiral catalyst:



Bolm, *J. Chem. Soc., Chem. Commun.* **1995**, 1247.

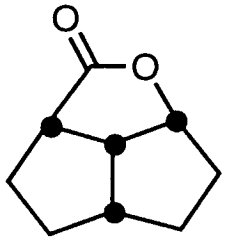
Asymmetric Baeyer-Villiger Oxidation of Kelly's Cyclobutanone



prochiral

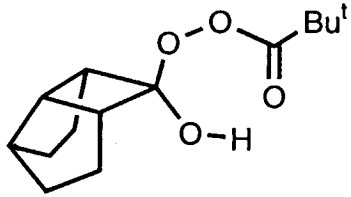
Asymmetric
Baeyer-Villiger
Oxidation

(0.5 eq. *t*-BuCHO)



91% ee

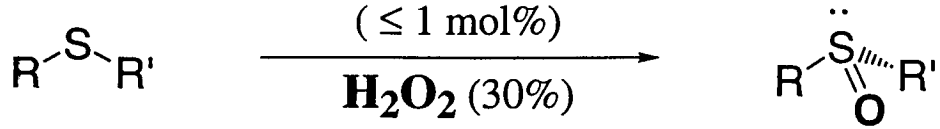
62% yield



Criegee-Intermediate

Bolm , *J. Mol. Cat.* **1997**, *117*, 347.

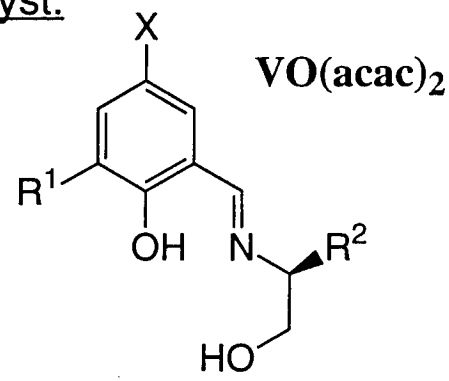
Vanadium-Catalyzed Enantioselective Sulfide Oxidation with H_2O_2



Characteristics:

1. use of H_2O_2 (30%, 1.1 equiv.)
2. simple reaction conditions (open beakers)
3. low catalyst loading (≤1 mol%)
4. simple ligand system (salicylaldehyde/amino alcohol)
5. ligand accelerated catalysis *(LAC)*

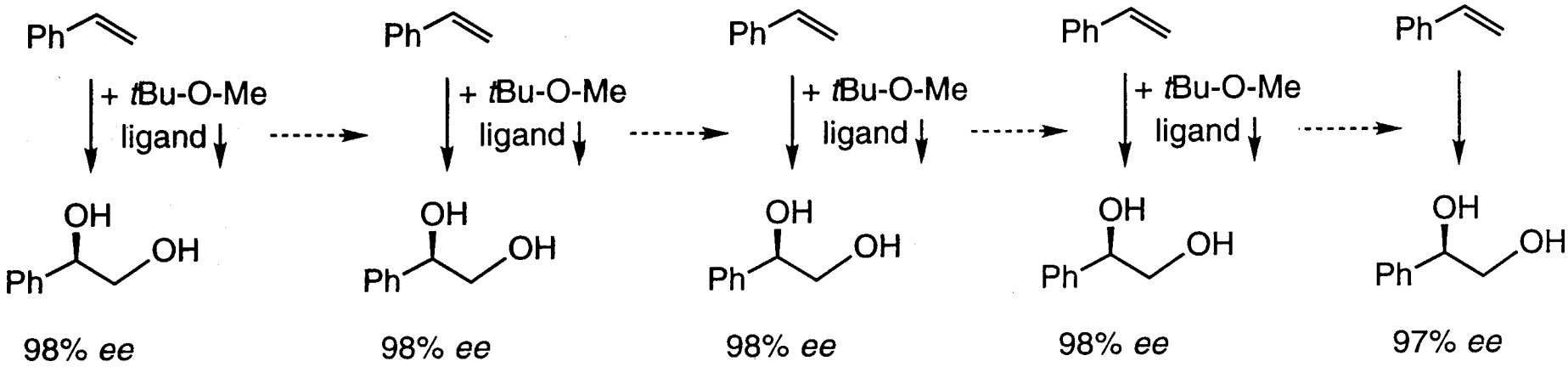
V-catalyst:



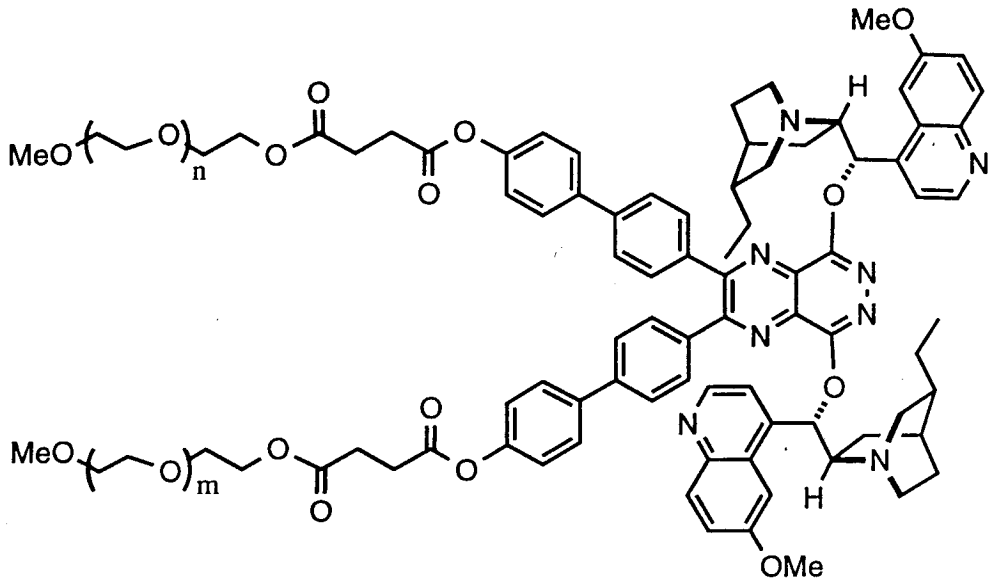
X = H, alkyl, NO_2, ...
R^1 = H, alkyl, aryl, ...
R^2 = alkyl, aryl, ...

Bolm, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2640.

Sequential Use of MeO-PEG-Enlarged Ligands

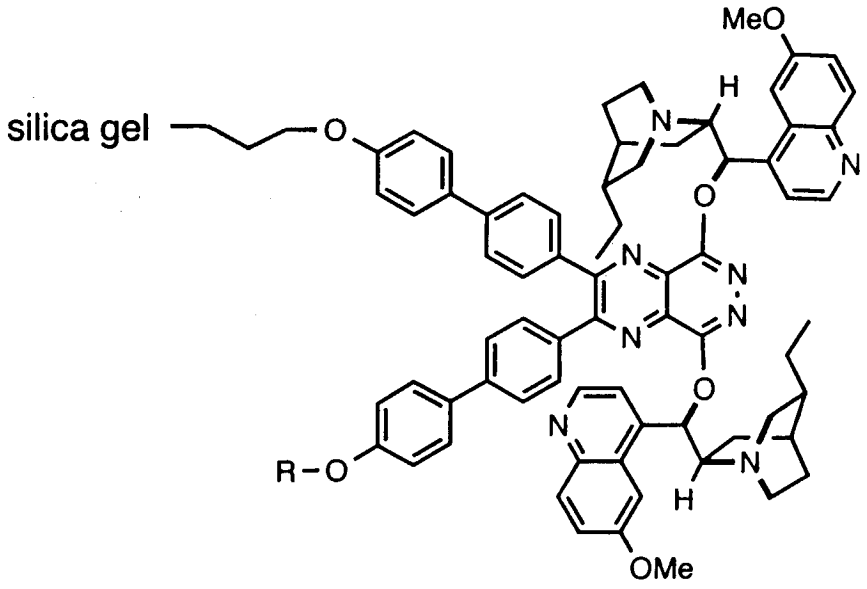


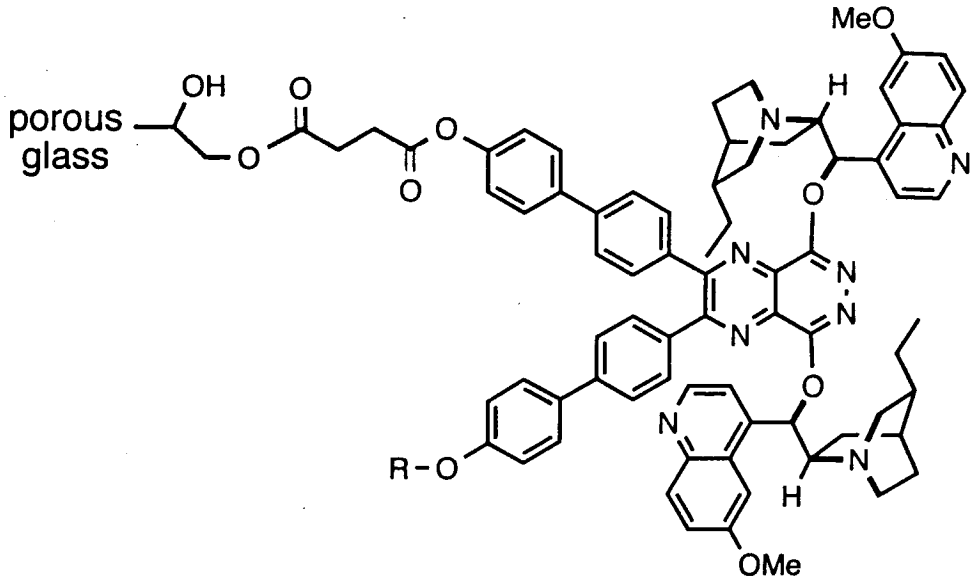
ligand =

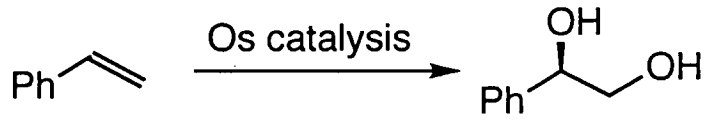


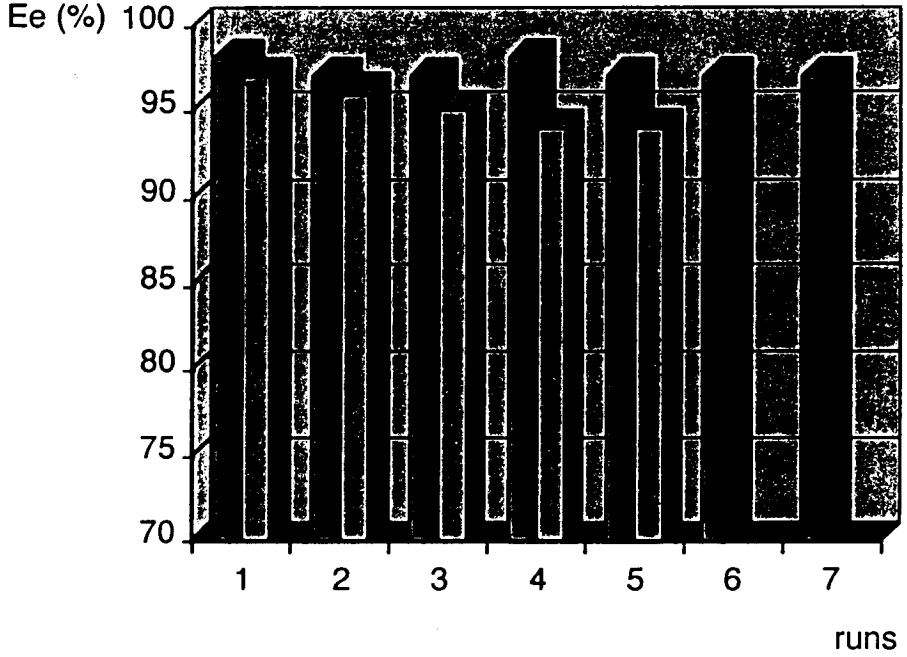
Review:
Bolm, *Eur. J. Org. Chem.* **1998**, 21.

Heterogeneous AD with Silica Anchored Ligands in Consecutive Reactions



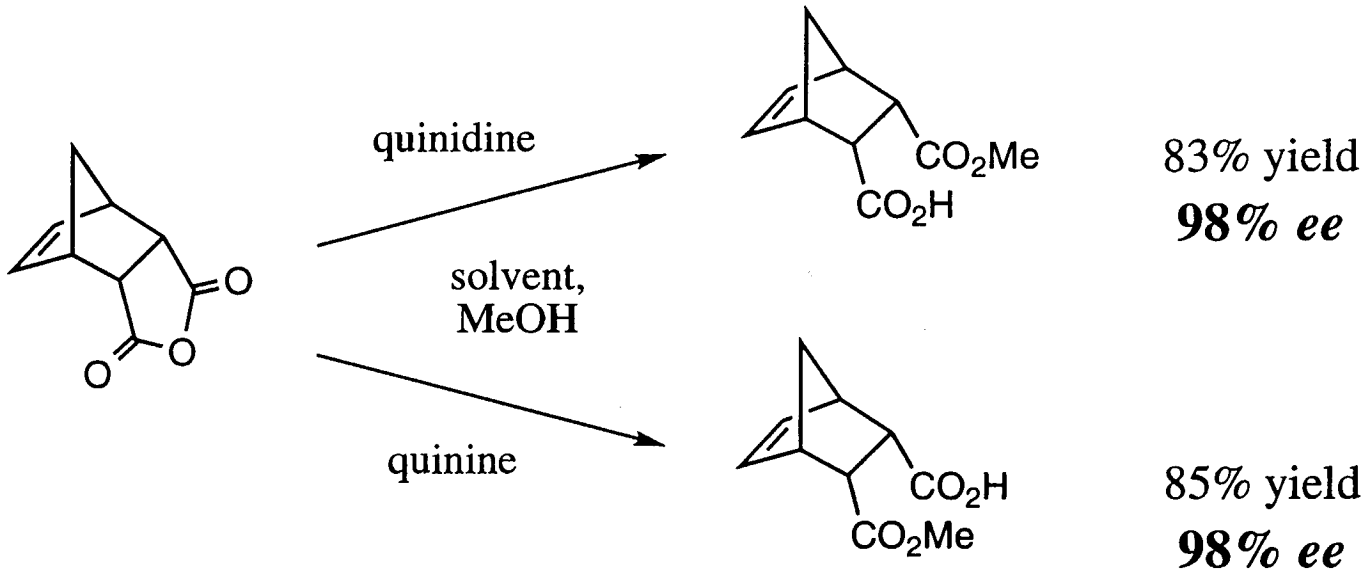






1st run	2nd run	3rd run
98% *ee*	98% *ee*	95% *ee*
93% yield	50% yield	34% yield

Optimization of the Asymmetric Anhydride Opening

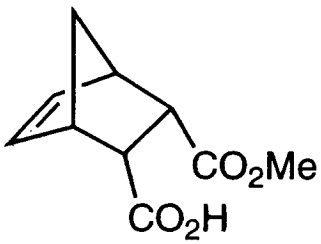


conditions:

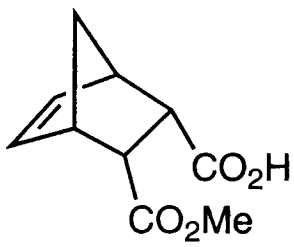
1.1 equiv. of alkaloid

toluene / CCl_4, -50°C, 36h

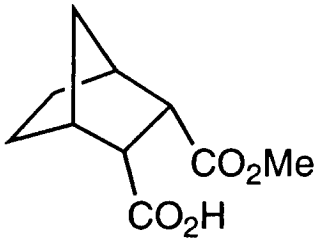
Use of the Asymmetric Anhydride Opening



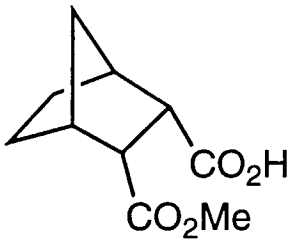
83% yield
98% *ee*



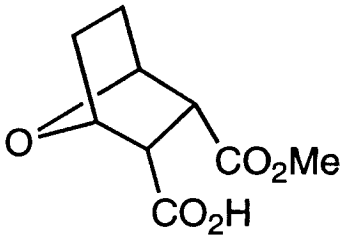
85% yield
98% *ee*



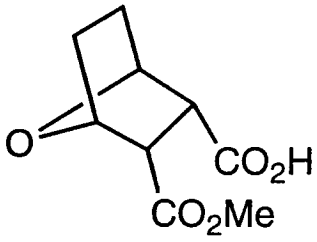
84% yield
94% *ee*



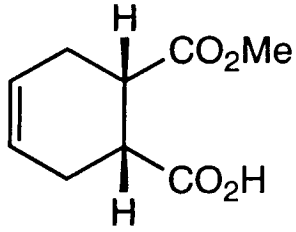
86% yield
94% *ee*



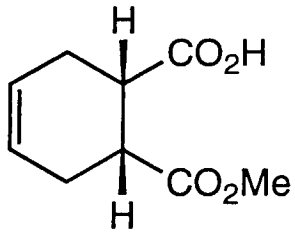
69% yield
94% *ee*



79% yield
93% *ee*

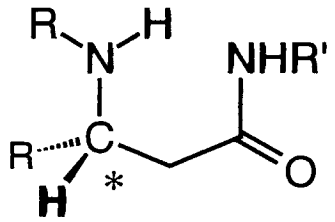


93% yield
95% *ee*

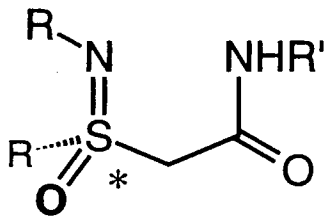


99% yield
93% *ee*

Sulfoximines ≙ β-Amino Acids ?

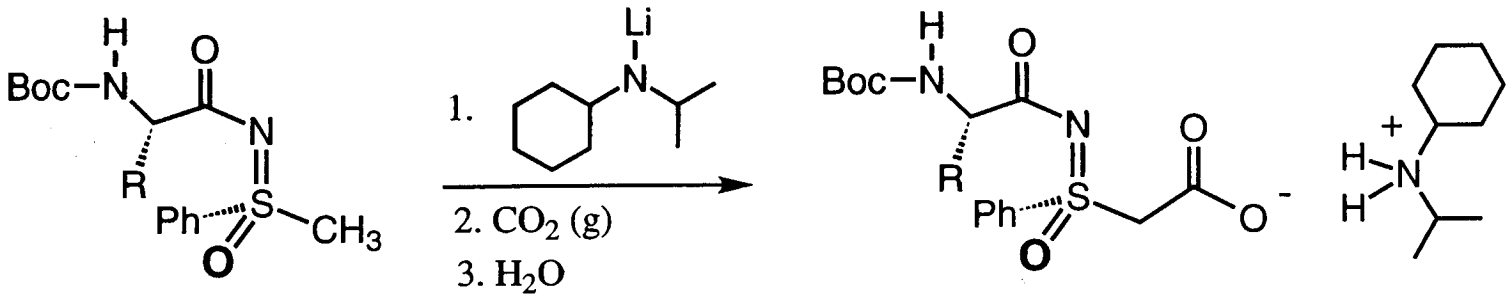


β-Amino Acid

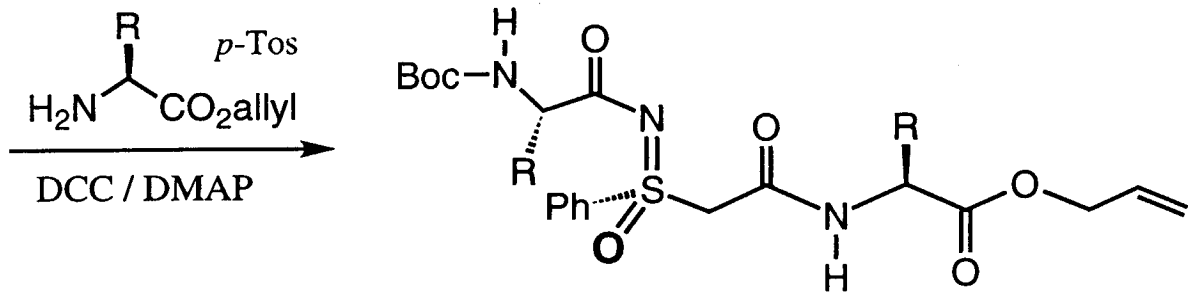


Sulfoximine

Sulfoximines in Pseudopeptides

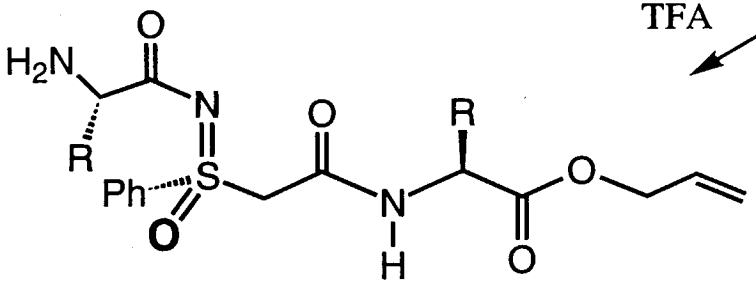


R = *i*-Pr (82%)
R = *i*-Bu (77%)
R = *s*-Bu (70%)



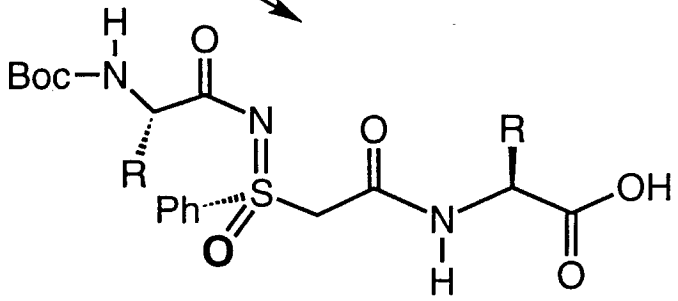
R = *i*-Pr (82%)
R = *i*-Bu (76%)
R = *s*-Bu (68%)

CH_2Cl_2, 0°C
TFA



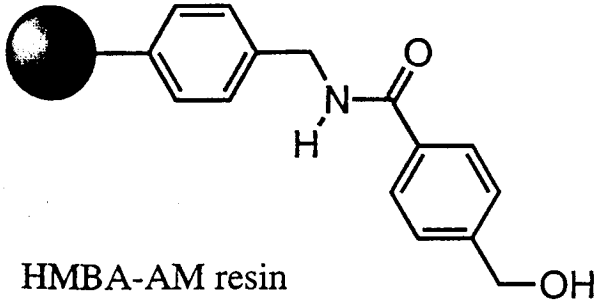
R = *i*-Pr (97%)
R = *i*-Bu (93%)
R = *s*-Bu (93%)

Pd-catalysis



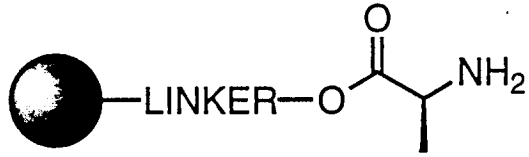
problem: Pd(0)!

Solid-Phase Synthesis of Pseudopeptides with Sulfoximines

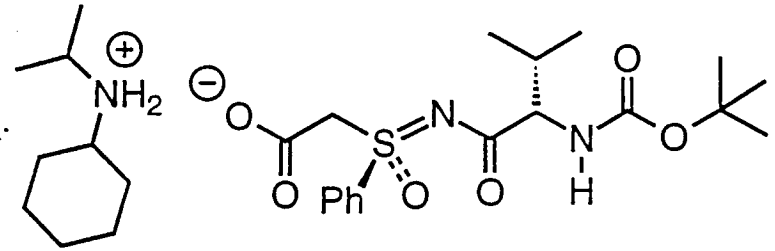


HMBA-AM resin
(1.03 mmol/g)

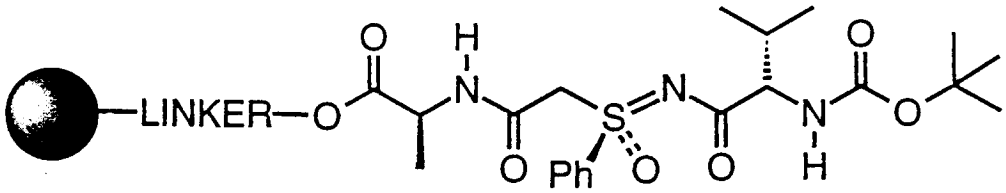
1. Boc-Ala-OH, DIC, HOBt, CH_2Cl_2
2. TFA, CH_2Cl_2



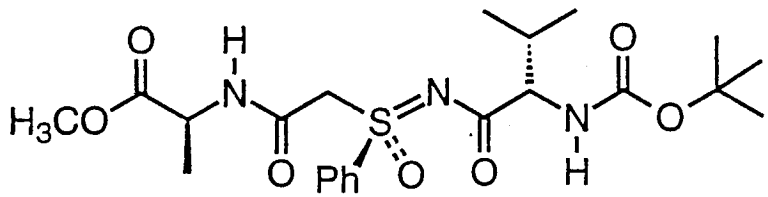
1. *p*-TsOH, CH_2Cl_2 / DMF
2. 3 eq.



Boc-Val-Sulf-O^- NR_4^+



MeOH, NEt_3

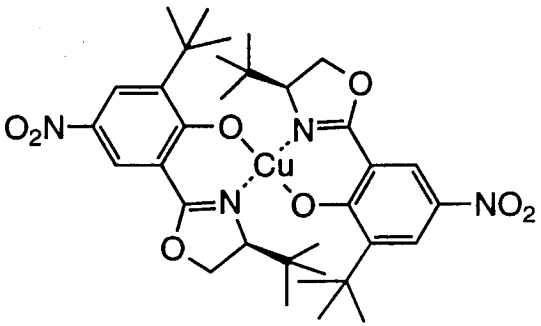


Boc-Val-Sulf-Ala-OMe

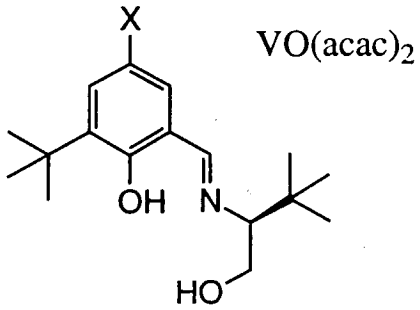
yield: 45% (based on initial resin loading)
purity: >95% (by NMR)

Summary

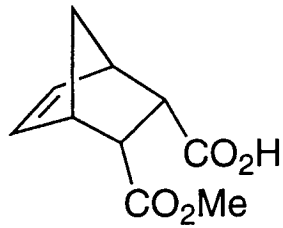
- **Baeyer-Villiger Oxidation**



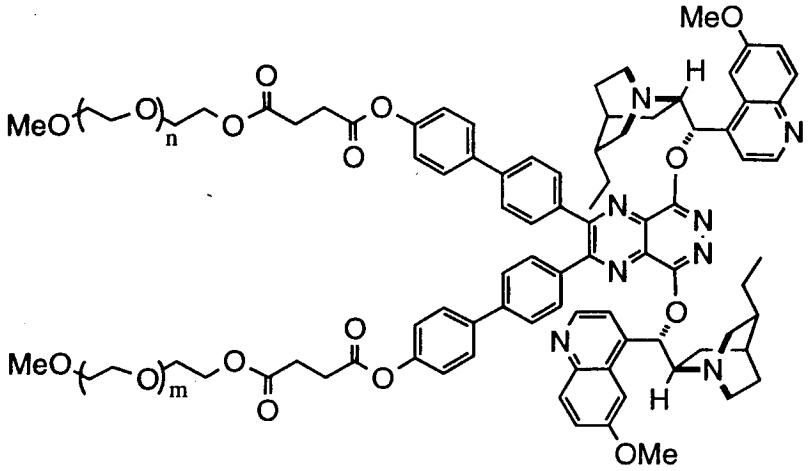
- **Sulfide Oxidation**



- **Anhydride Openings**



- **Supported Dihydroxylations**



- **Pseudopeptides**