

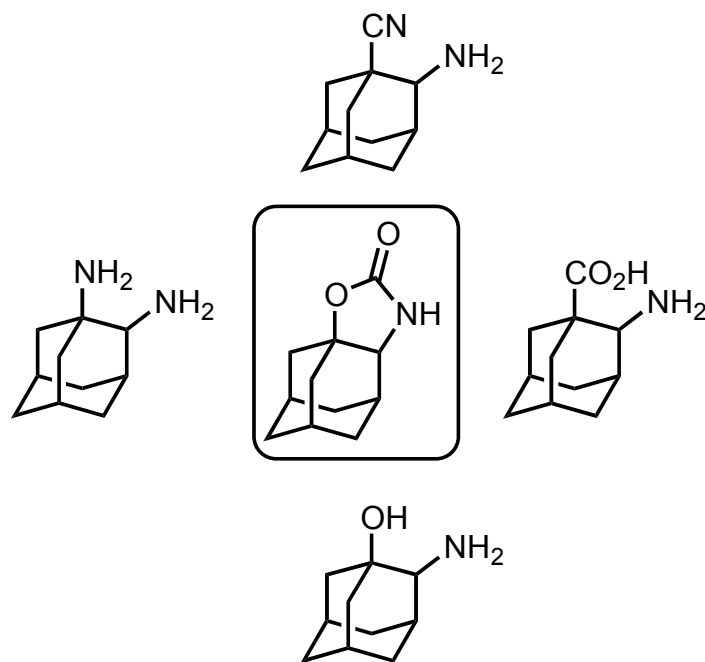
# Reactivity of Adamantane Based Oxazolidinones

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Seminar talk presented by  
**Christian Eschmann**

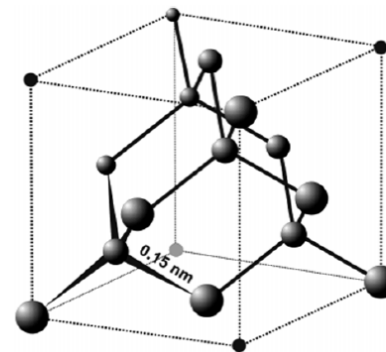
February 19<sup>th</sup>, 2016

*Institute of Organic Chemistry  
Justus-Liebig University Giessen*

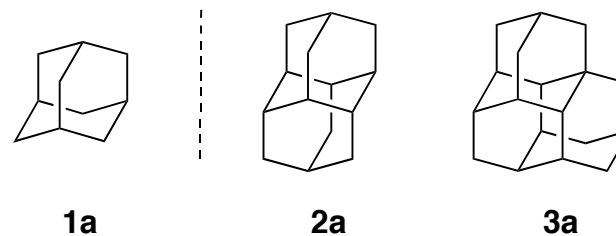




- **Diamond**
- mm range
- $sp^3$
- diamond lattice
- very hard and abrasion-resistant



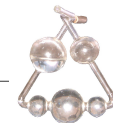
- **Diamondoids**
- diamond structure
- nm range
- very hard
- chemically inert
- can be isolated from mineral oil



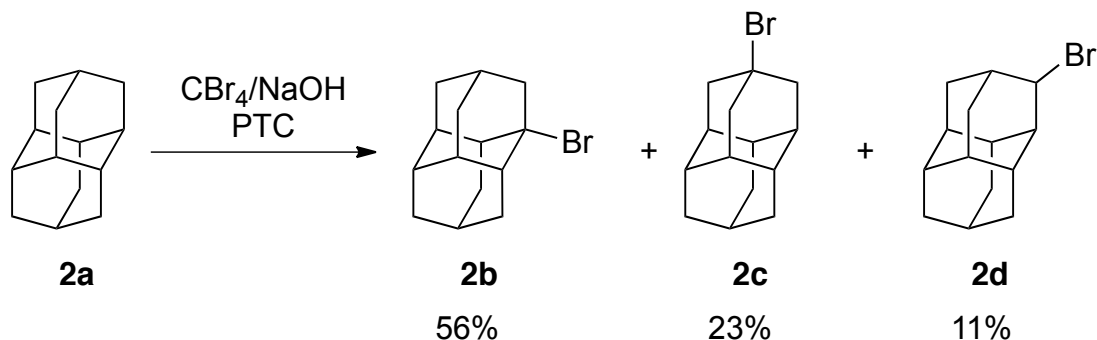
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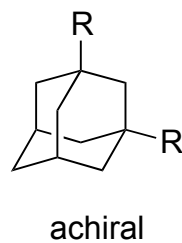
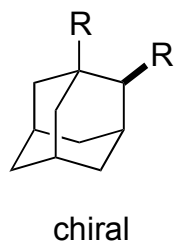
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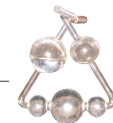
- selective functionalization can be challenging
- mixtures hard to separate



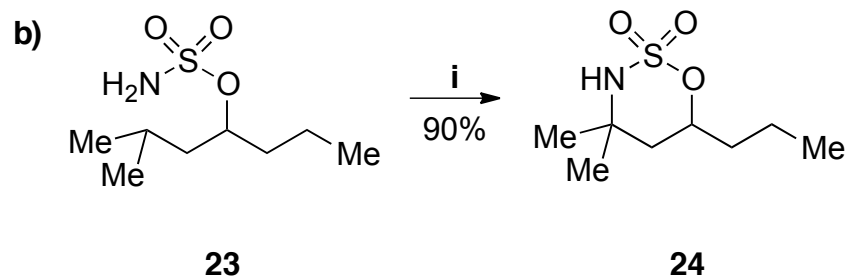
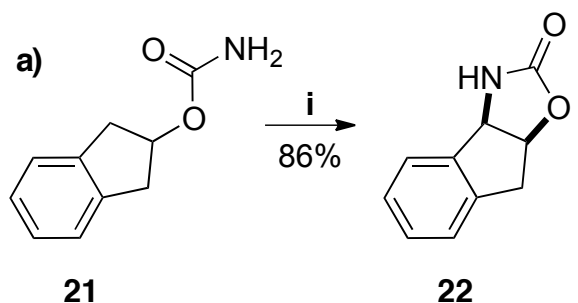
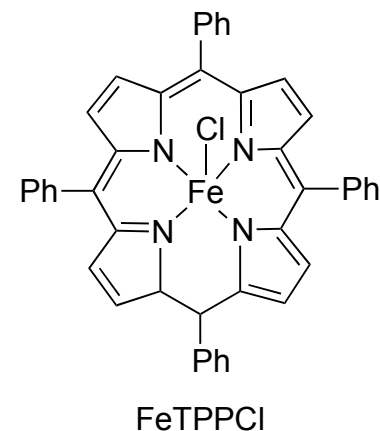
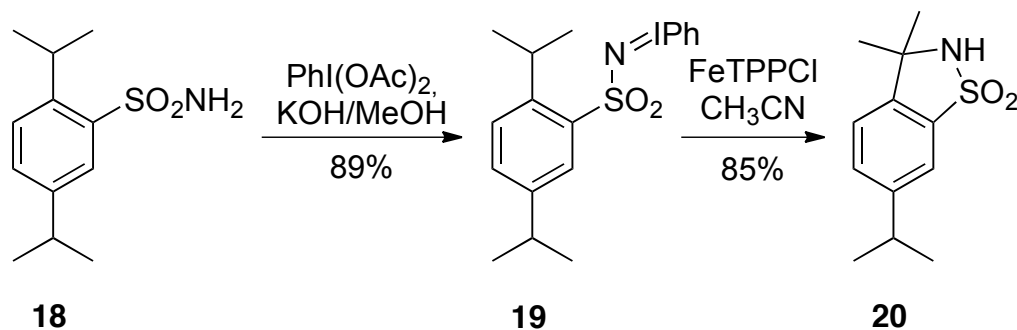
- disubstituted adamantane mostly achiral 1,3 (tertiary positions)
- just few reactions for chiral 1,2-derivatives



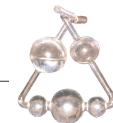




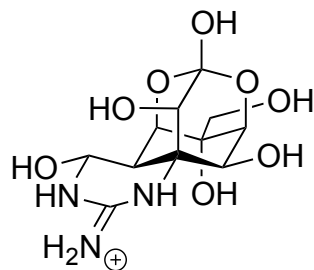
- 1950s first carbene insertions (Yates, Doering)
- 1960s first nitrenes from azides (Lwowski, D.S. Breslow)
- 1967 copper-nitrenoid (Kwart, Kahn)



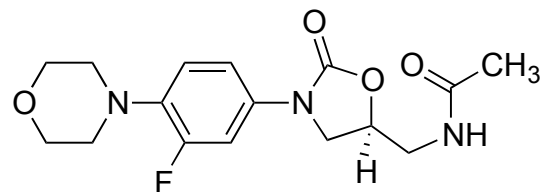
i:  $\text{PhI(OAc)}_2$ ,  $\text{MgO}$ , 5 mol%  $\text{Rh}_2(\text{OAc})_4$ ,  $\text{CH}_2\text{Cl}_2$ ,  $40^\circ\text{C}$



- natural products
- antibiotics

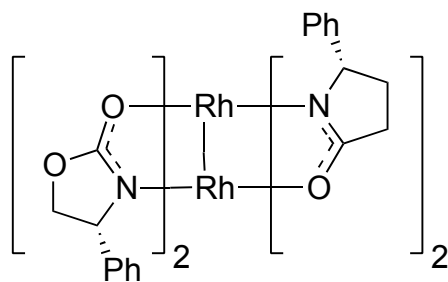


Tetrodotoxin

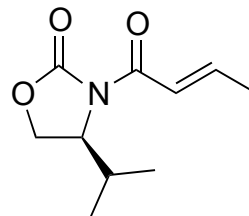


Linezolid

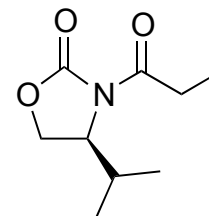
- ligands for Doyle's catalysts **34**
- auxiliaries in Evans chemistry



**34**



**32**



**33**

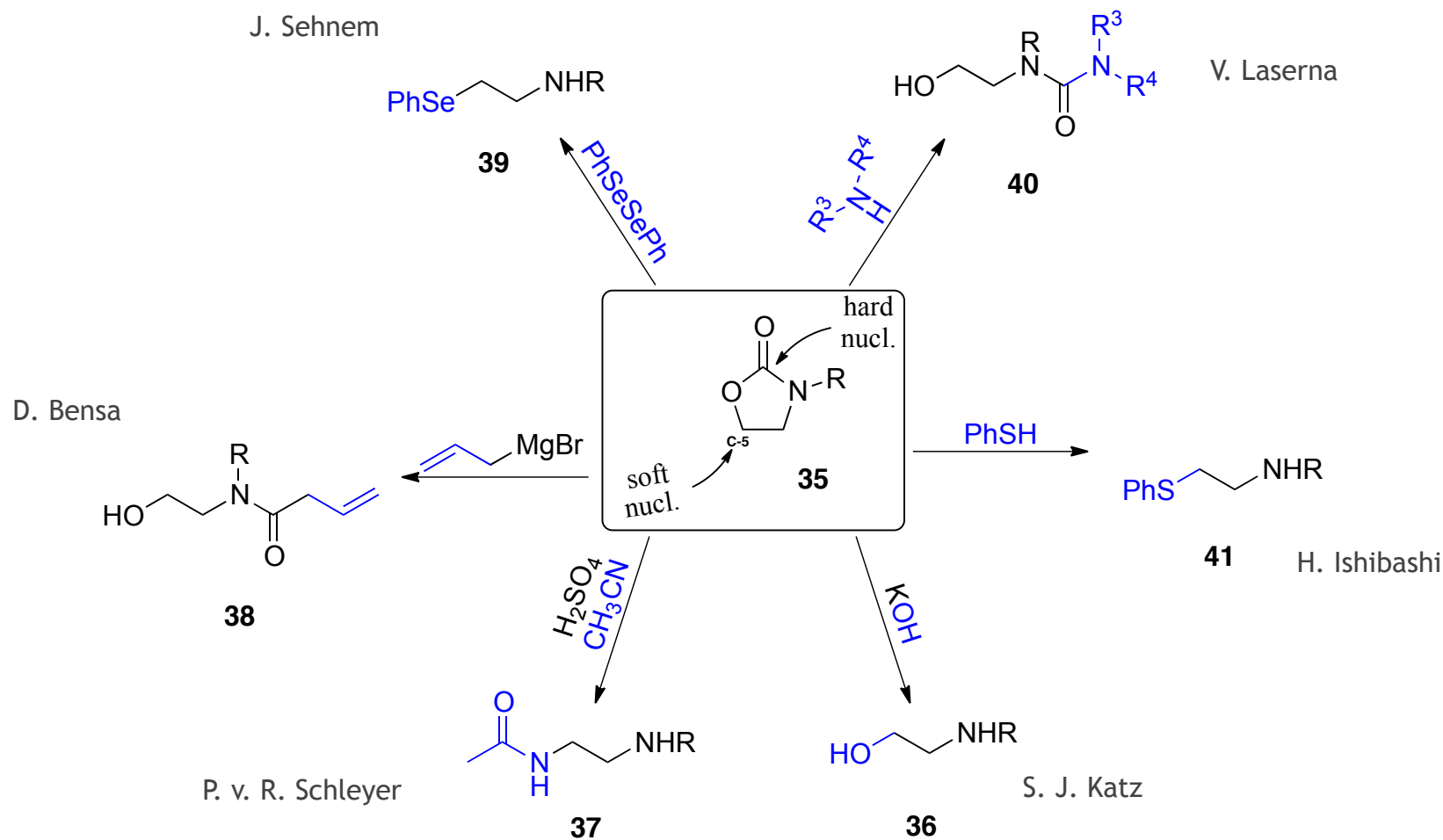
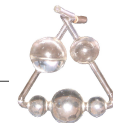
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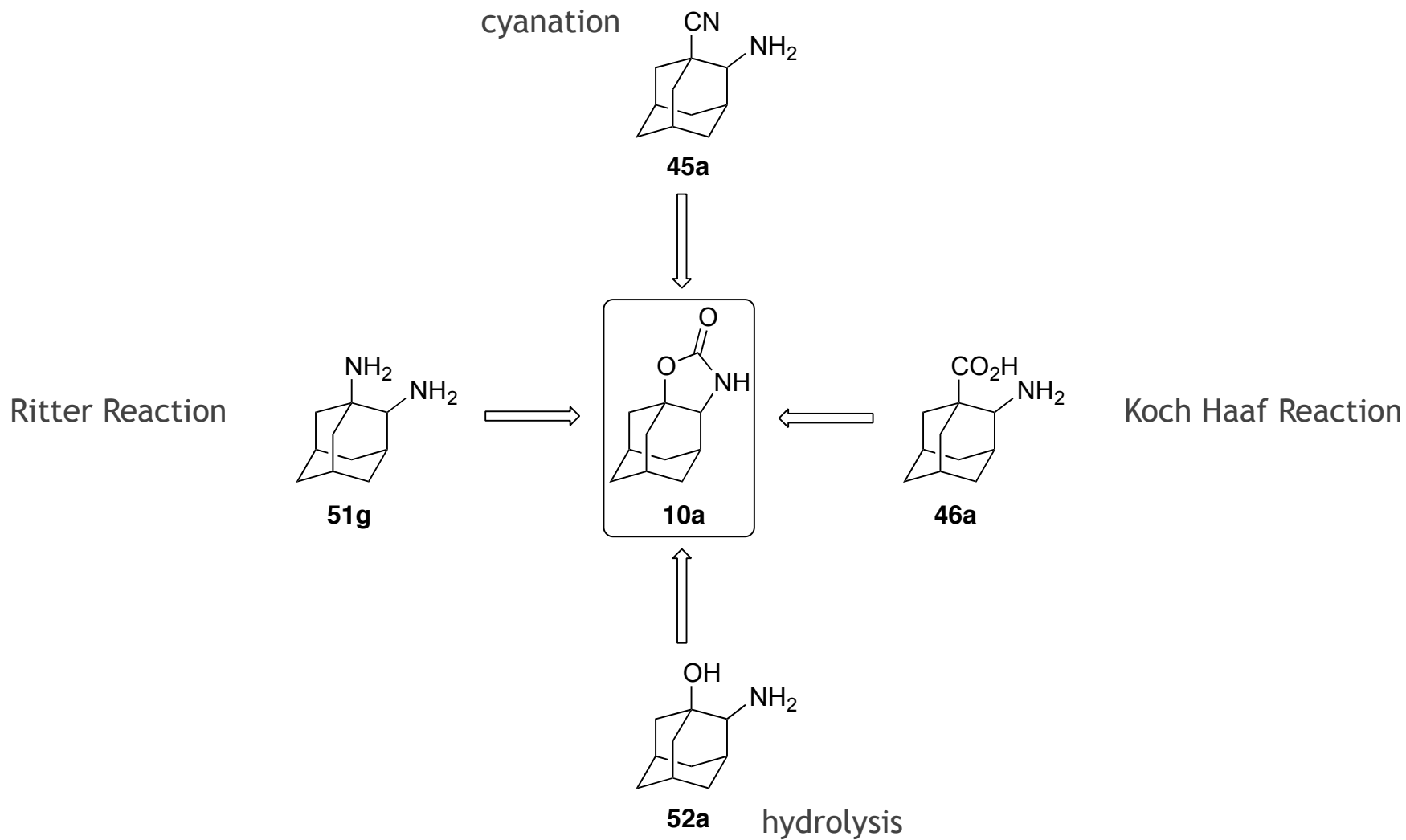
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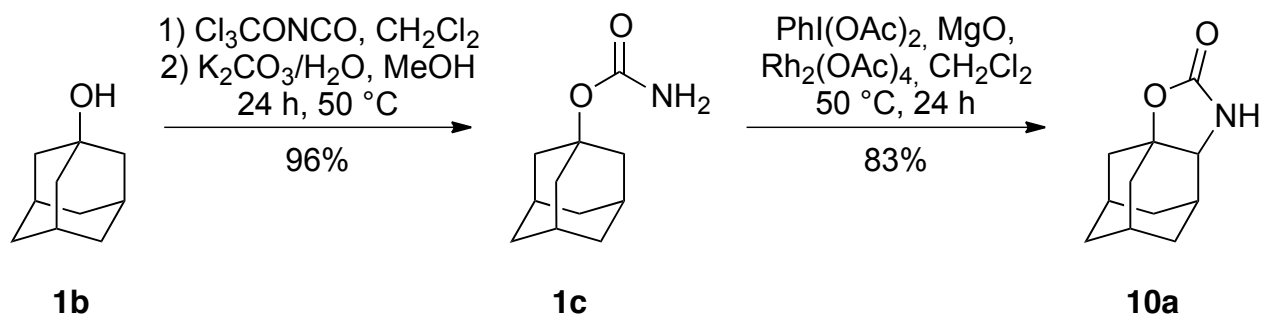
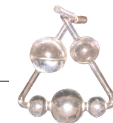
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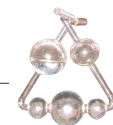




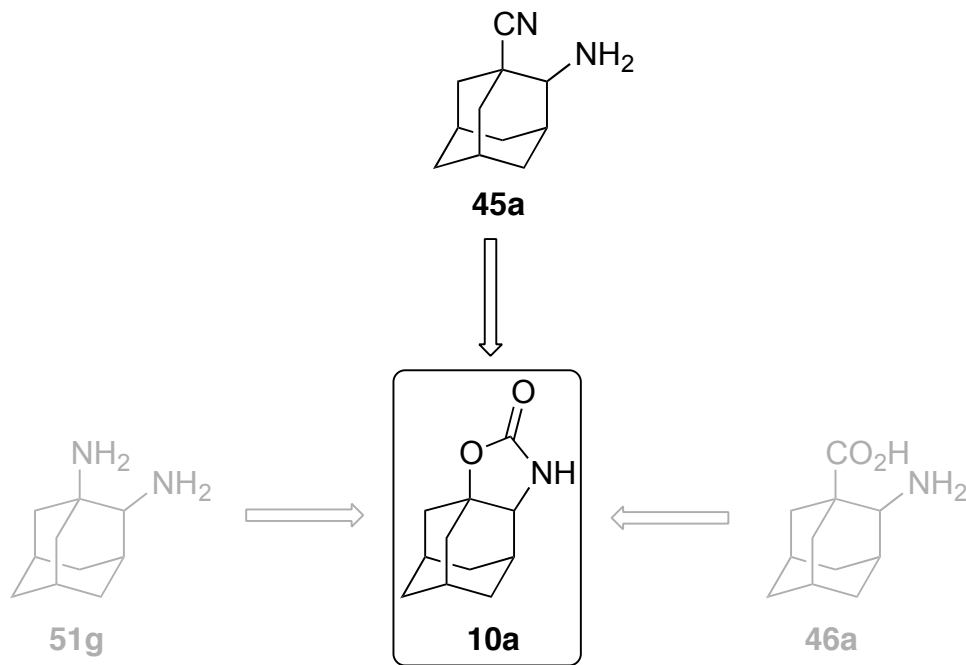
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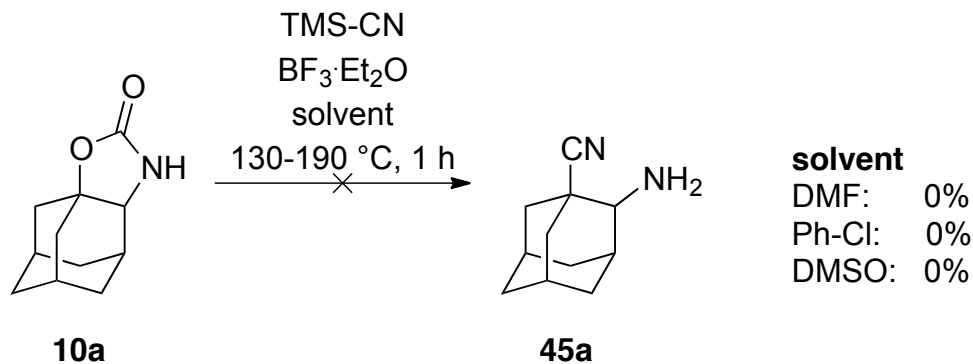


- cyanation
- microwave
- lewis acid

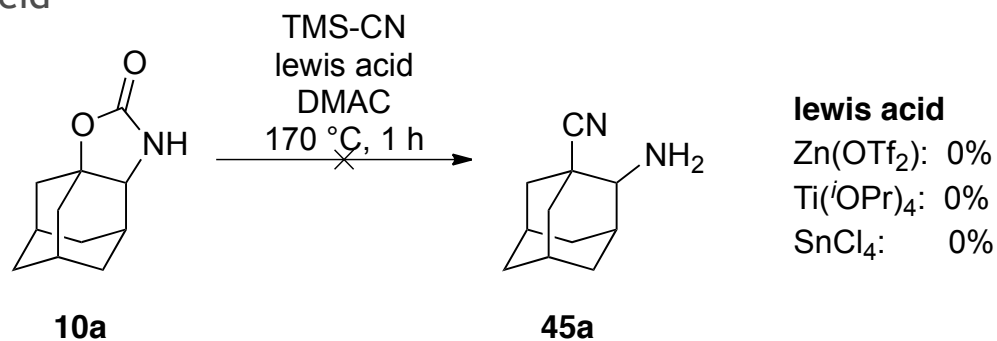


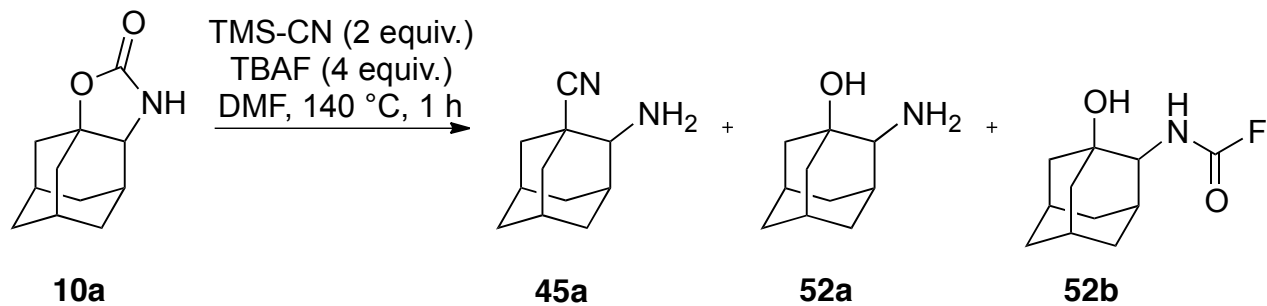
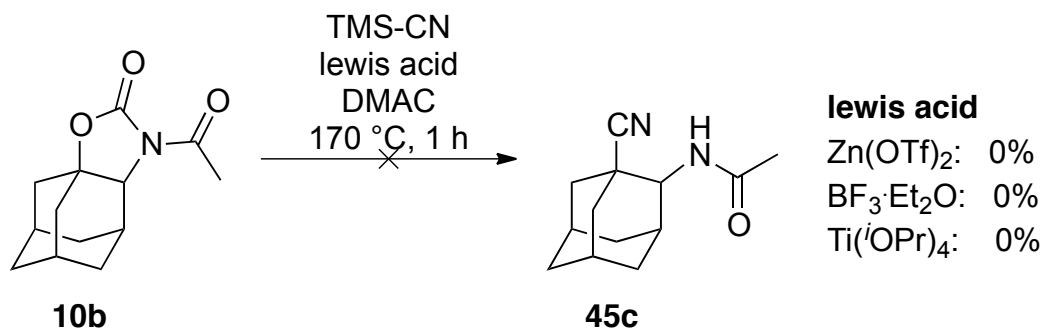
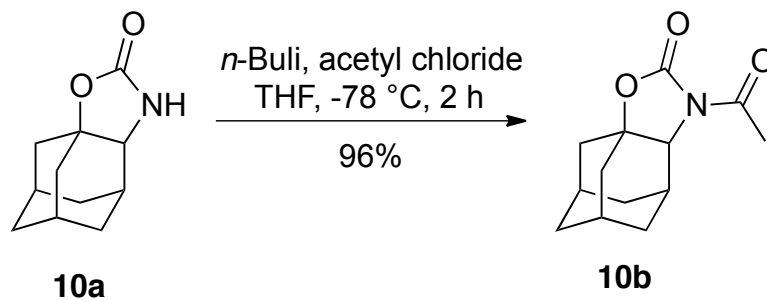
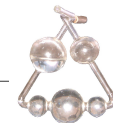


- microwave
- variation of solvent



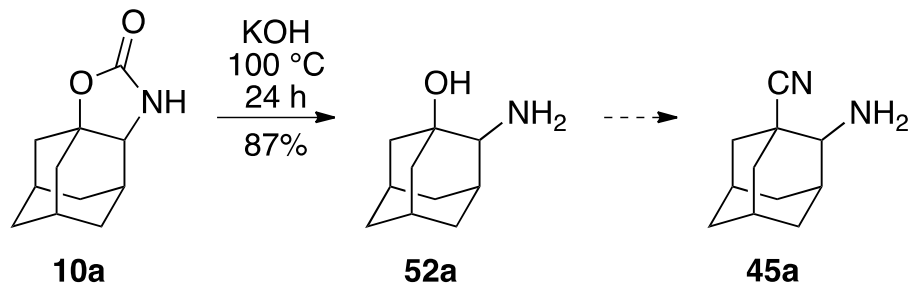
- variation of lewis acid



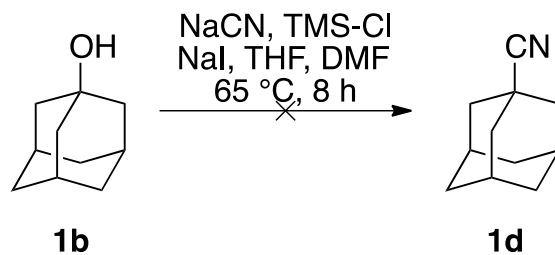




- hydrolysis to corresponding amino alcohol **52a**
- substitution of **52a** via known procedures

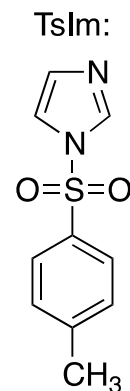
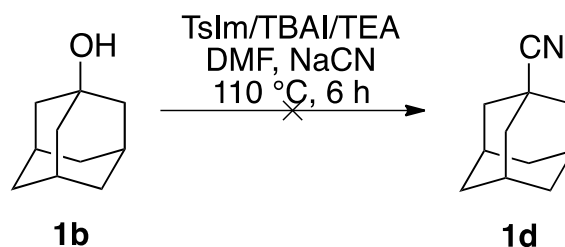


- Davis *et al.*



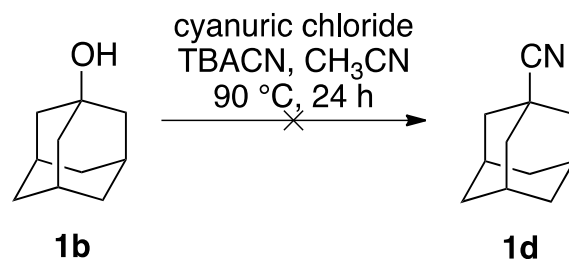


- Soltani *et al.*

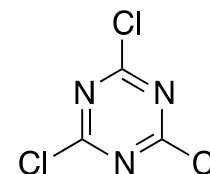


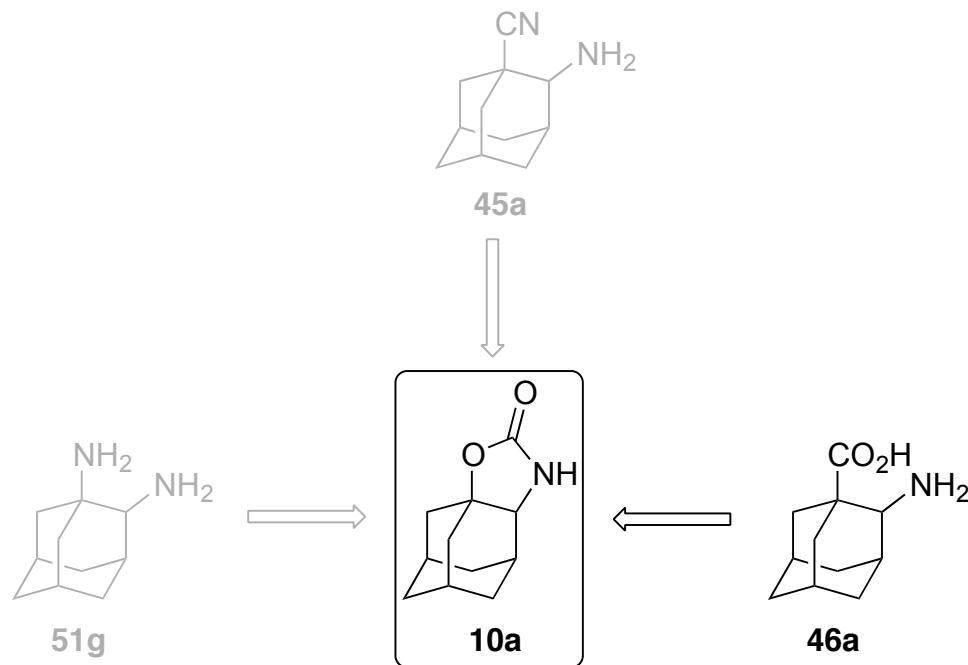
Tslm: 1-(*p*-Toluenesulfonyl)imidazole

- Akhlaghinia *et al.*

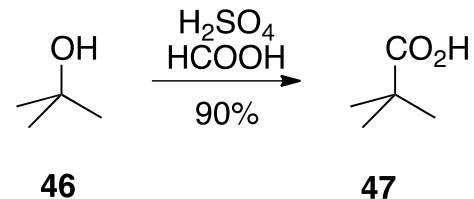


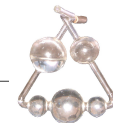
cyanuric chloride



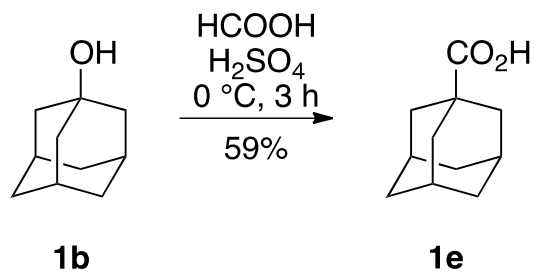


- Herbert Koch & Wolfgang Haaf
- Substrates: alcohols, alkenes, alkyl chlorides
- $S_N1$
- CO as nucleophile
- exothermic

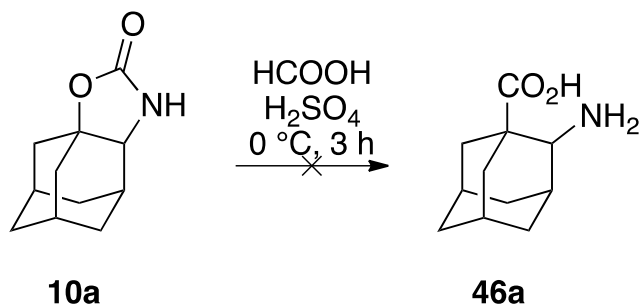


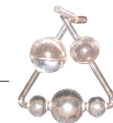


- Koch Haaf Reaction with adamantan-1-ol **1b**

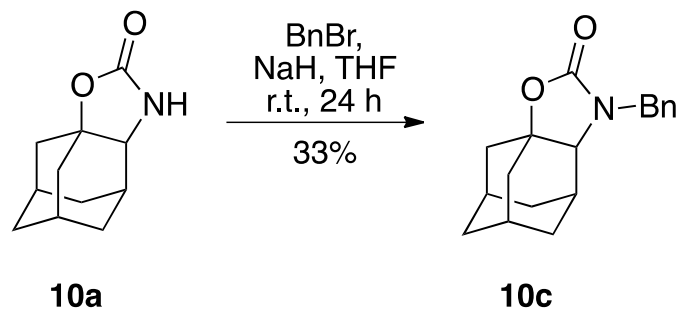


- transfer to adamantinoxazolidin-2-on **10a**
- complex mixture

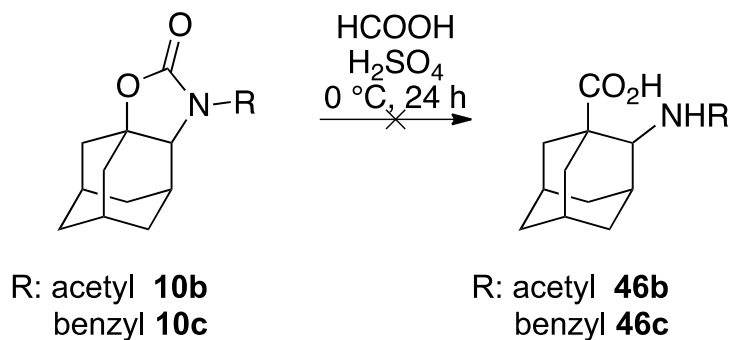


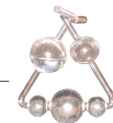


- *N*-substitution with EDG & EWG

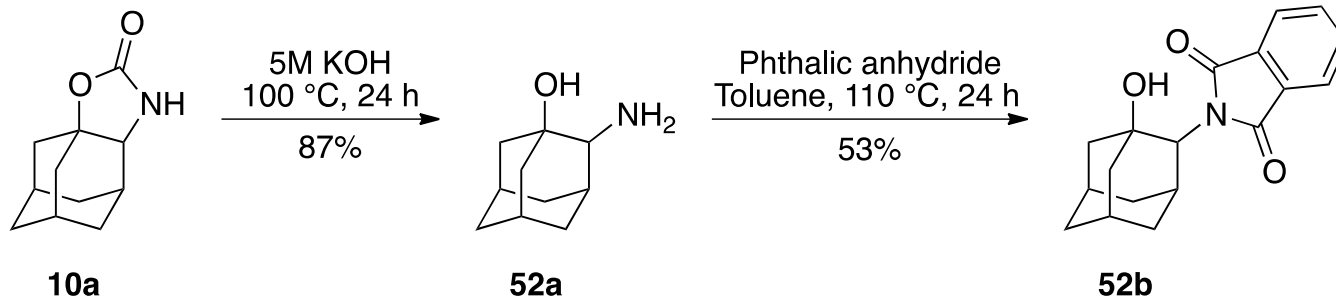


- starting material isolated
- decarboxylation problematic

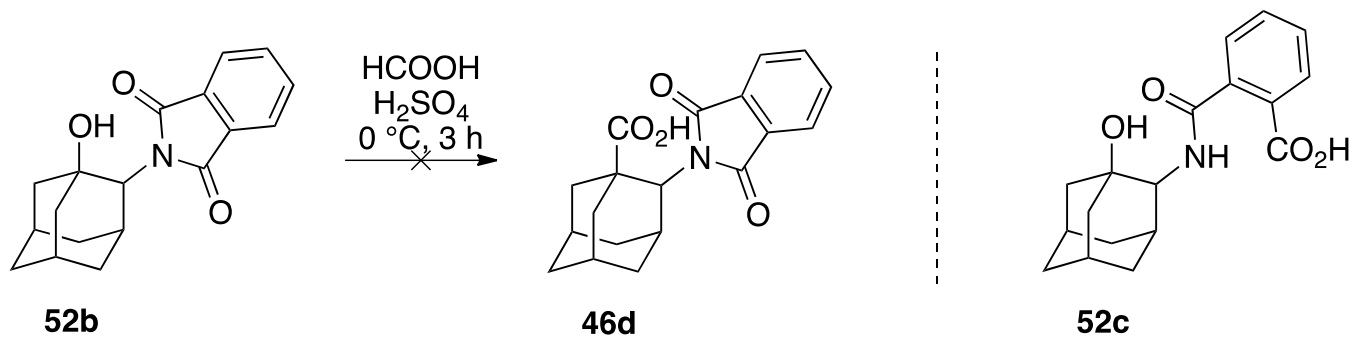


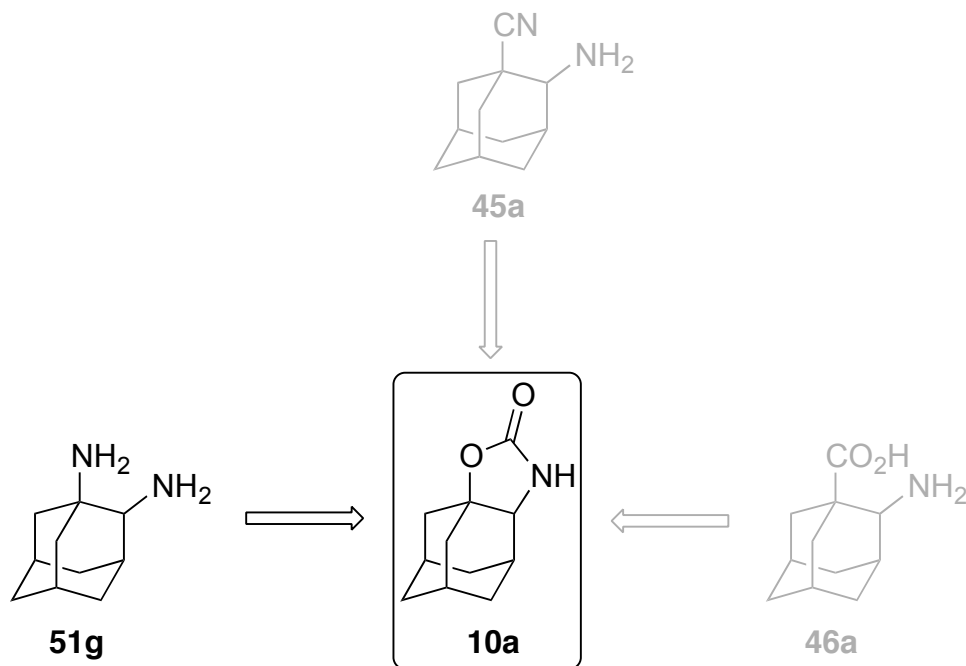


- first hydrolysis to corresponding amino alcohol **52a**
- Koch Haaf Reaction with amino alcohol
- protecting group to avoid side reactions / zwitterionic character

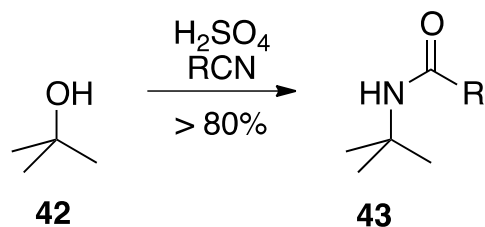


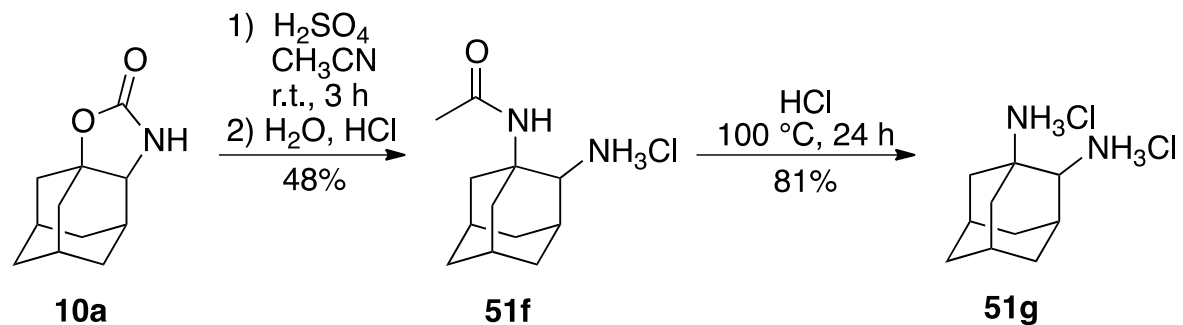
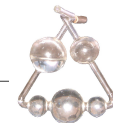
- phthalimide not stable under Koch Haaf conditions



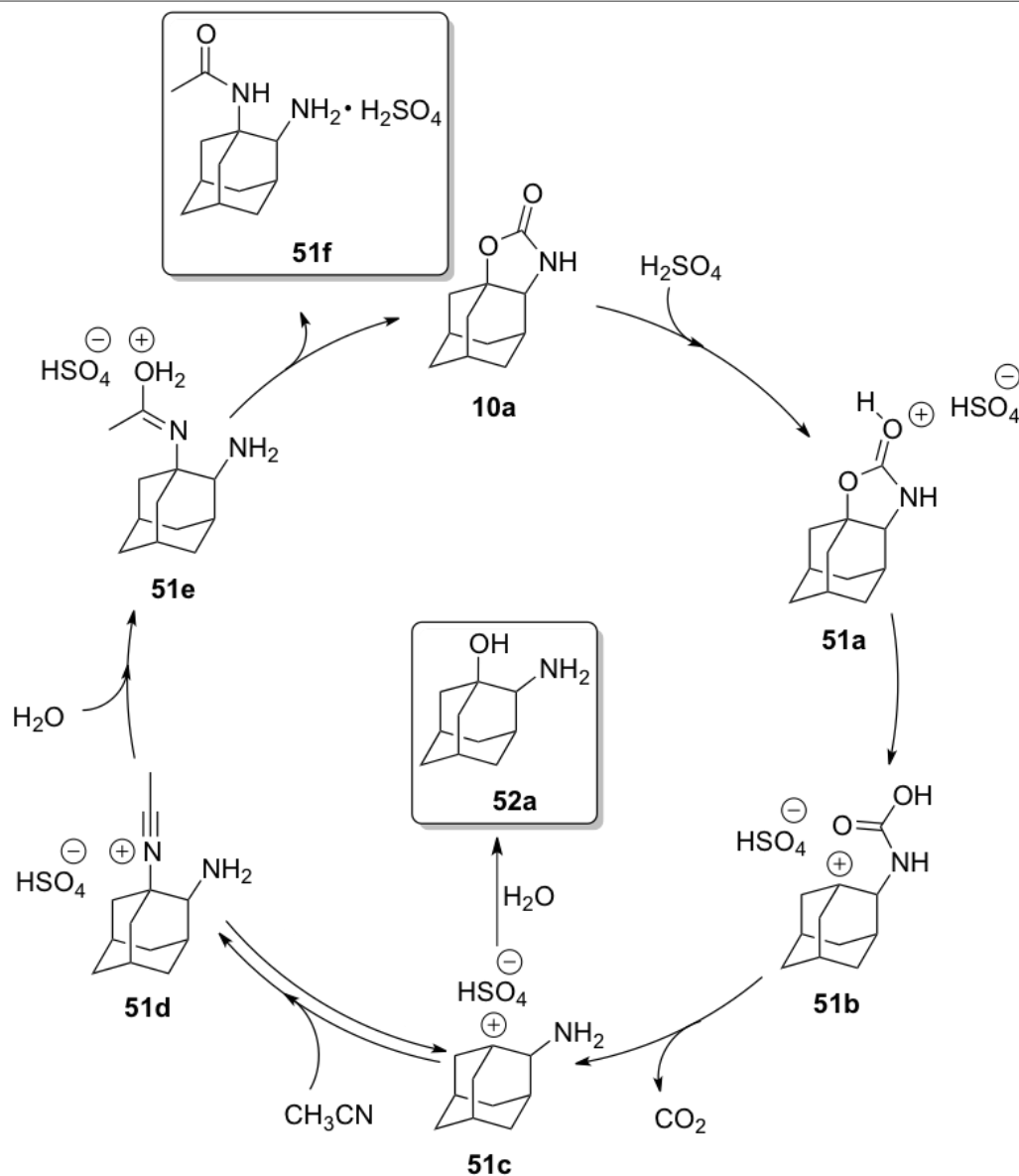
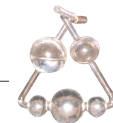


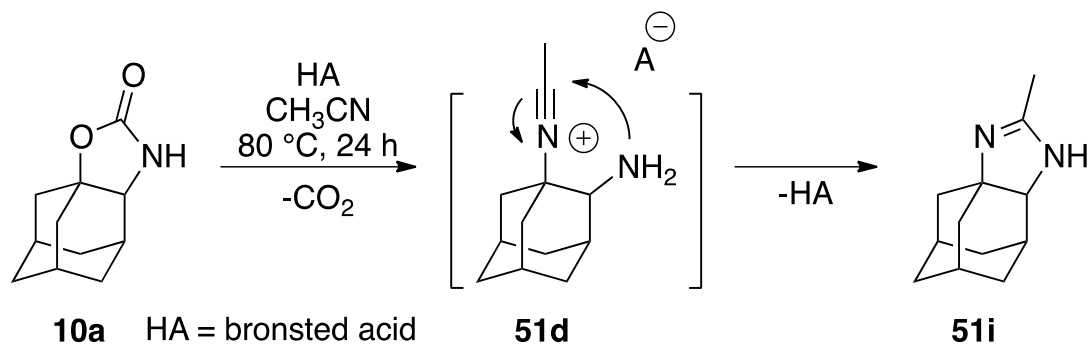
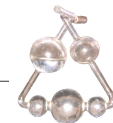
- John J. Ritter
- Substrates: alcohols, alkenes
- $S_N1$
- strong acid



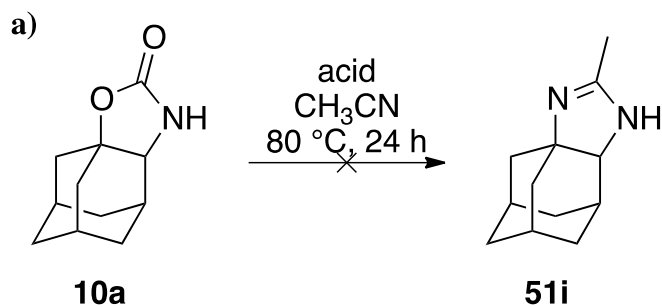
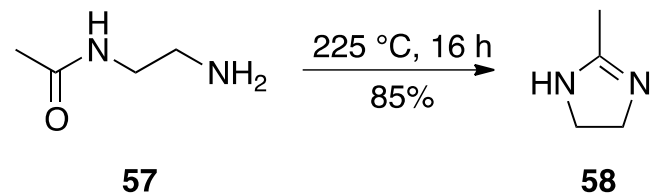


- Schleyer 1971
- reproduced
- variation of reaction parameters
- yield increased ( < 50%)

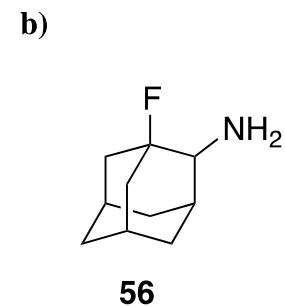


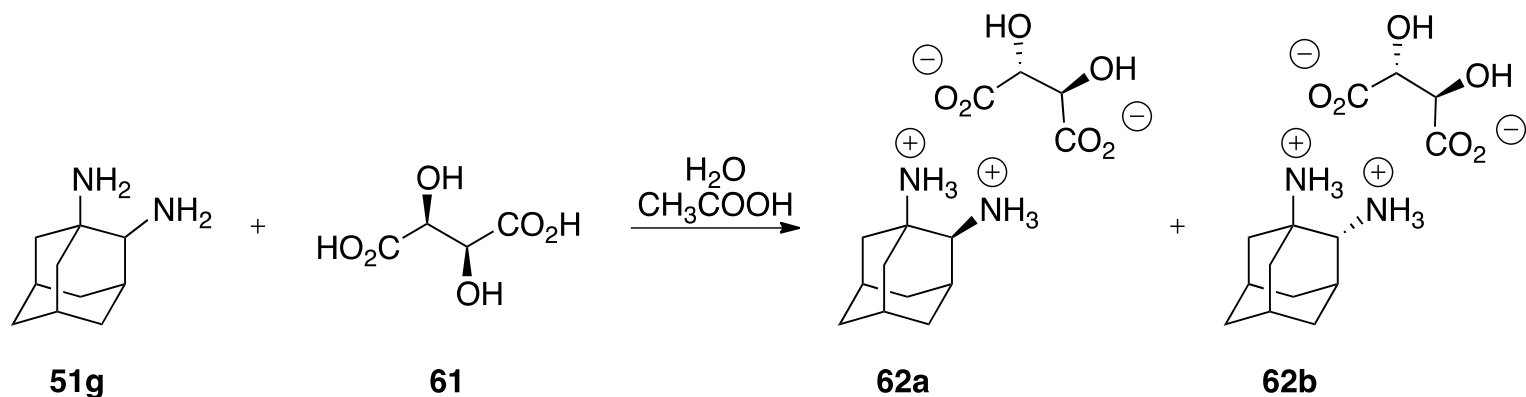


- intramolecular ring closure to imidazoline
- Baldwin rules: allowed (*5-endo-dig*)

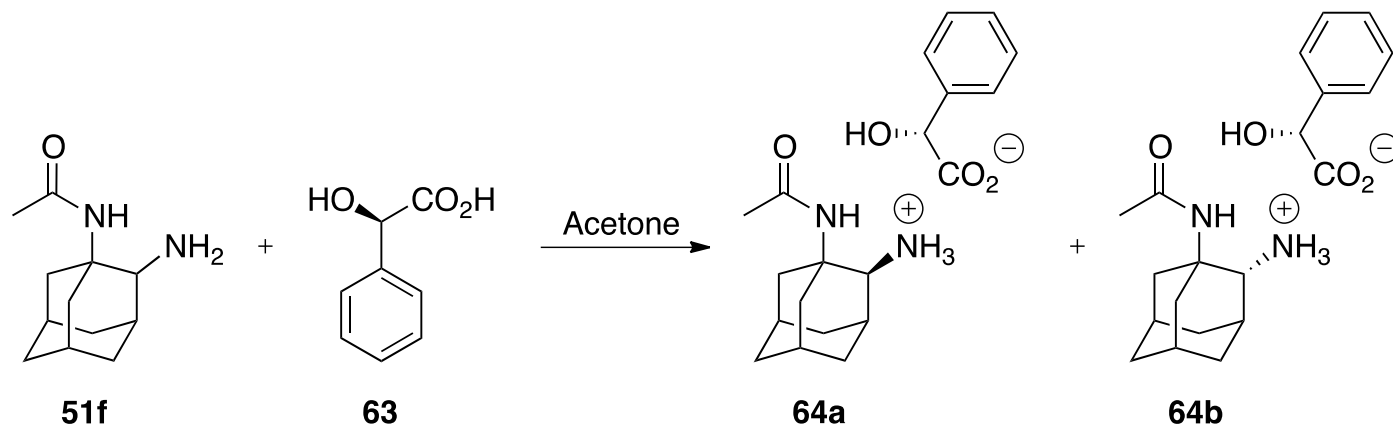


**acid**  
 pTSA  
 TFA  
 NH<sub>2</sub>-NH<sub>2</sub>·H<sub>2</sub>SO<sub>4</sub>  
 HBF<sub>4</sub>·Et<sub>2</sub>O  
 TfOH

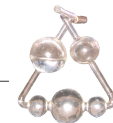




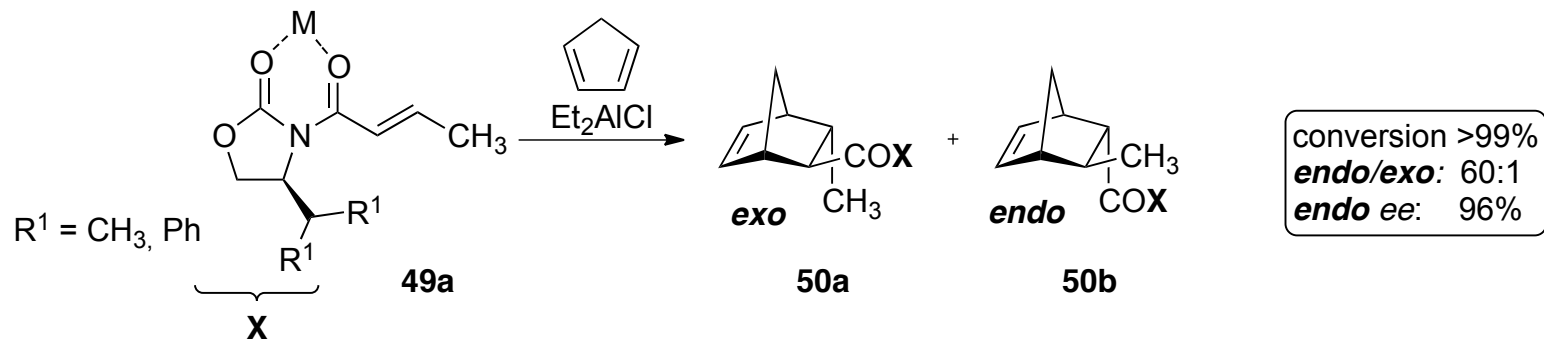
- diamine and L-tartaric acid
- no crystallization in acetone, EE, H<sub>2</sub>O (+ acetic acid)



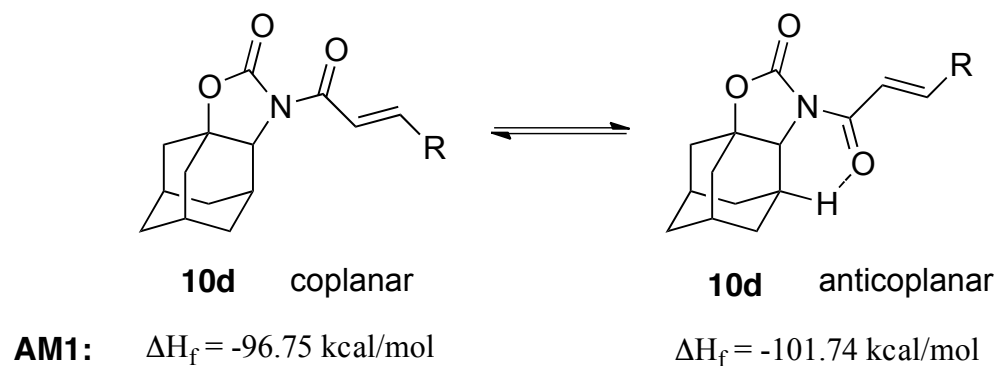
- *N*-acetyladamantane-1,2-diamine and D-mandelic acid
- solvents: acetone, ethanol, EE, DCM
- crystallization just in acetone
- two times crystallization = 10% *ee*



- lewis acids account for high conversion and selectivity



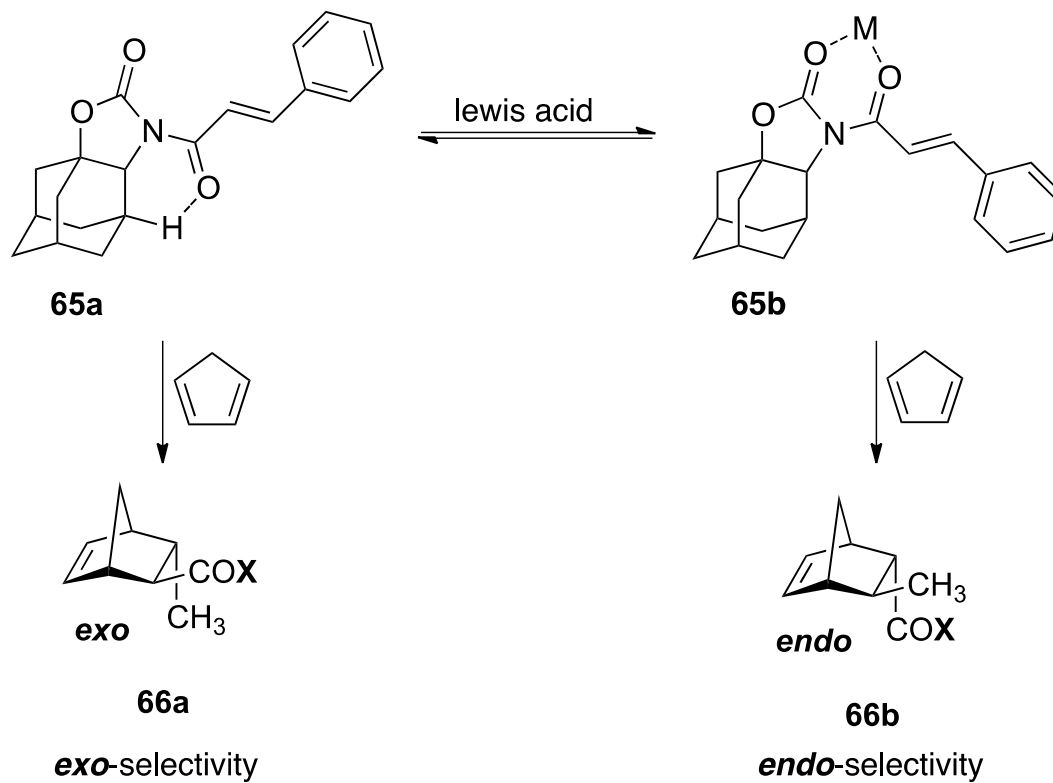
- anticoplanar conformation favored

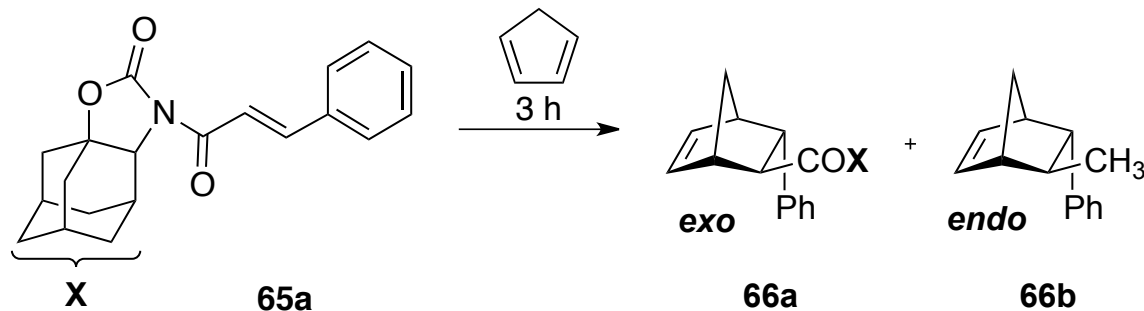
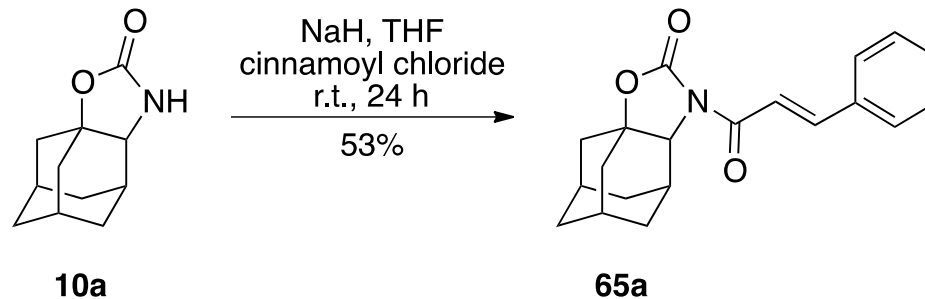
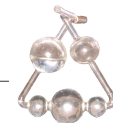


$$\Delta\Delta H_f = 4.99 \text{ kcal/mol}$$



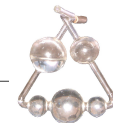
- control of selectivity?



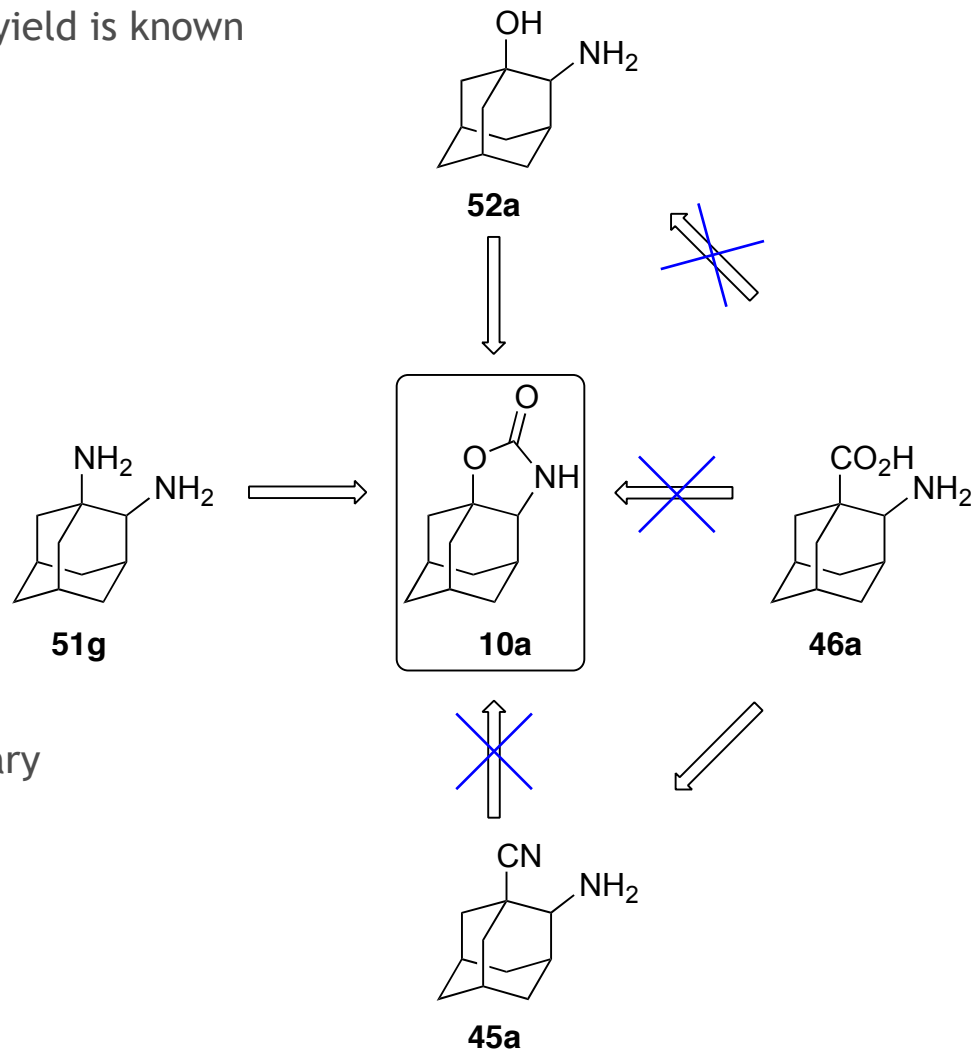


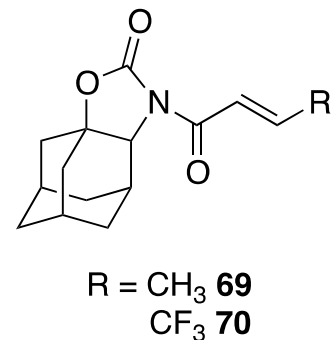
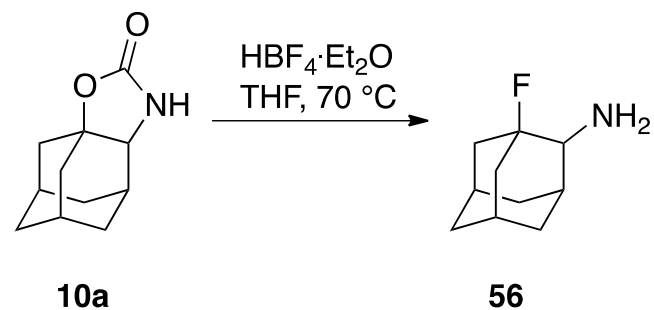
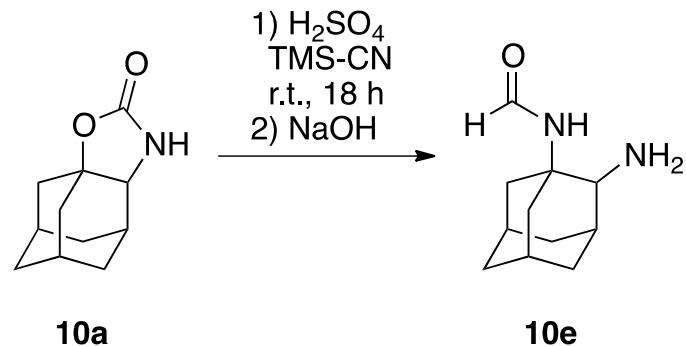
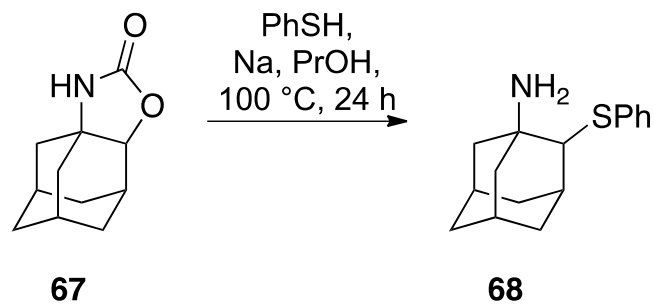
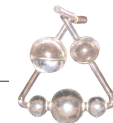
entry	lewis acid	temperature	conversion <sup>a</sup>
1	-	-20 °C	0%
2	-	21 °C	0%
3	SnCl <sub>4</sub> (1.5 eq.)	21 °C	20%

a: conversion determined by NMR



- hydrolysis to amino alcohol **52a** in good yield is known
- $S_N1$  cyanation to **45a** did not work
- Koch Haaf strategy to **46a** did not work (decarboxylation problematic)
- Ritter Reaction to **51g** successfully reproduced
- racemic resolution by crystallization has to be optimized
- anhydrous Ritter Reaction to imidazoline failed
- Adamantanoxazolidin-2-on **10a** as auxiliary in Diels Alder Reactions
- cinnamoyl oxazolidinone less reactive





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- Lab B205 (Jan-Philipp Berndt, Dominik Niedek, Jan Schümann)
- Analytical department
- the whole group!