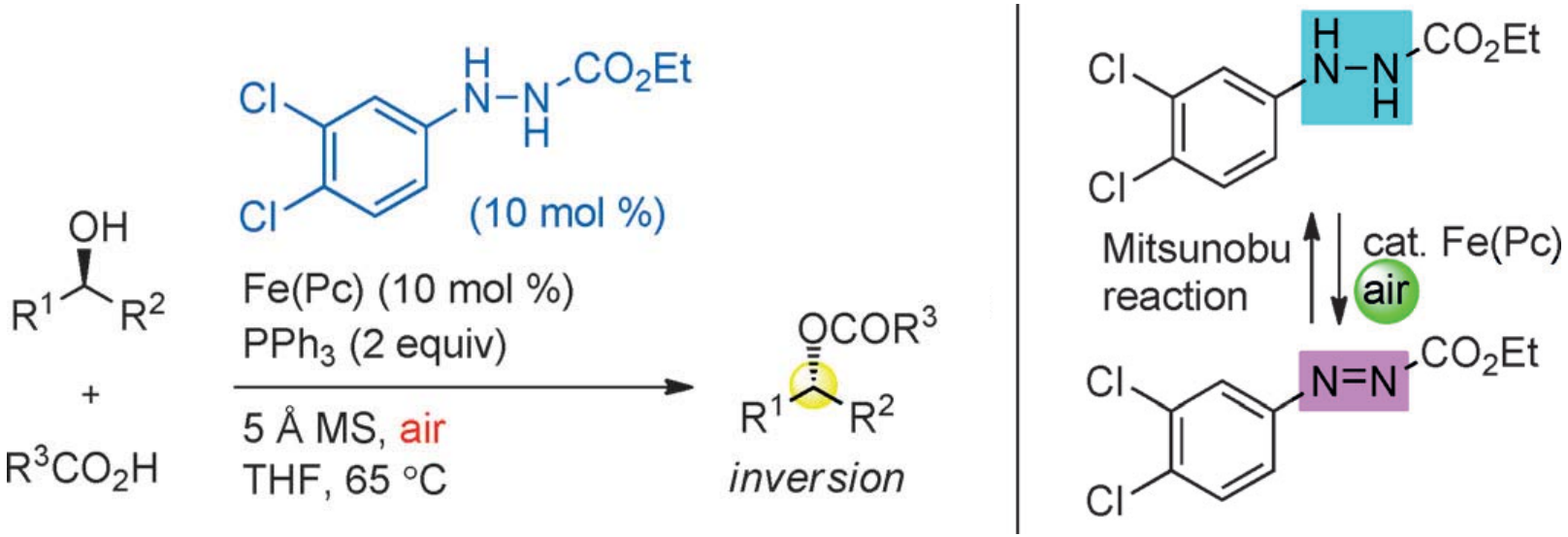
Recyclable Mitsunobu Reagents:

Catalytic Mitsunobu Reactions with an Iron Catalyst and Atmospheric Oxygen

T.Taniguchi et. *al*., *Angew. Chem. Int. Ed*. 2013, *52*, 1 – 6

Recyclable Mitsunobu Reagents: Catalytic Mitsunobu Reactions with an Iron Catalyst and Atmospheric Oxygen



T.Taniguchi et. *al*., *Angew. Chem. Int. Ed*. 2013, *52*, 1 – 6

Literature precedent and background

❖ 1967

$EtO_2C-N=N-CO_2Et$

DEAD = Diethyl azodicarboxylate

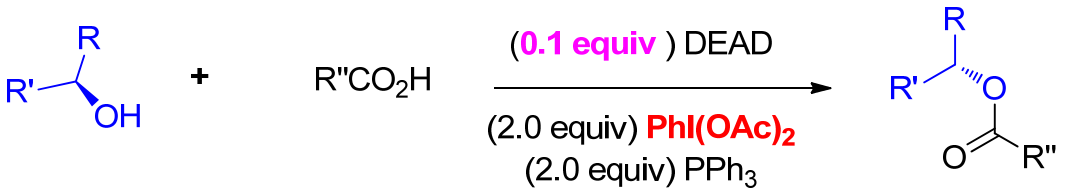
hydrazine byproduct

Oyo Mitsunobu

O. Mitsunobu, Y. Yamada, *Bull. Chem. Soc. Jap.* **1967**, *40*, 2380–2382.

✓ Natural products synthesis : Tedanolide, spongidepsin .....

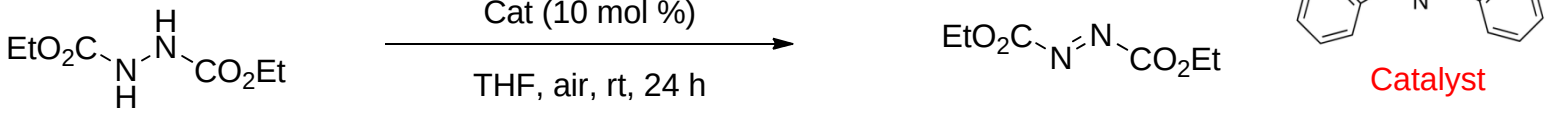
❖ 2006



T. Y. S. But, P. H. Toy, *J. Am. Chem. Soc.*, **2006**, *128*, 9636-9637.

Optimization of the new catalytic approach

❖ Aerobic oxidation of hydrazines



diethyl 1,2-hydrazinedicarboxylate

DEAD = Diethyl azodicarboxylate

Catalyst

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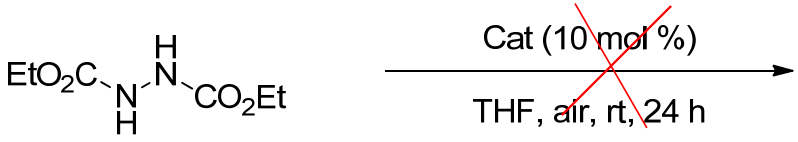
Optimization of the new catalytic approach

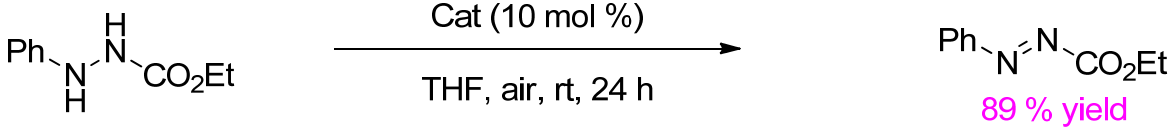
❖ Aerobic oxidation of hydrazines

Catalyst



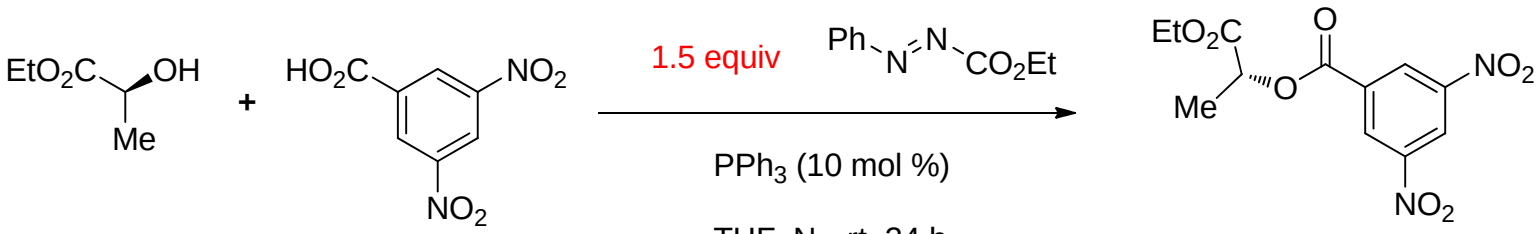
diethyl 1,2-hydrazinedicarboxylate

DEAD = Diethyl azodicarboxylate



89 % yield

❖ Evalutation in the Mitsunobu reaction

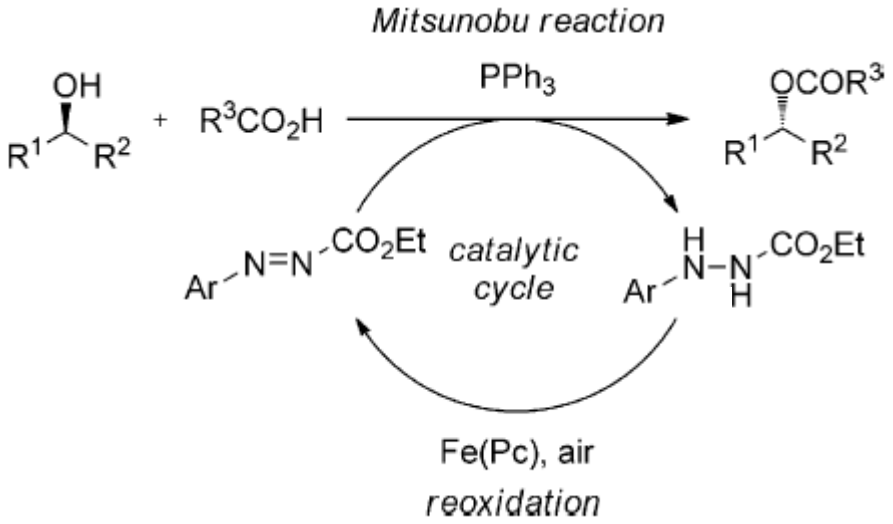


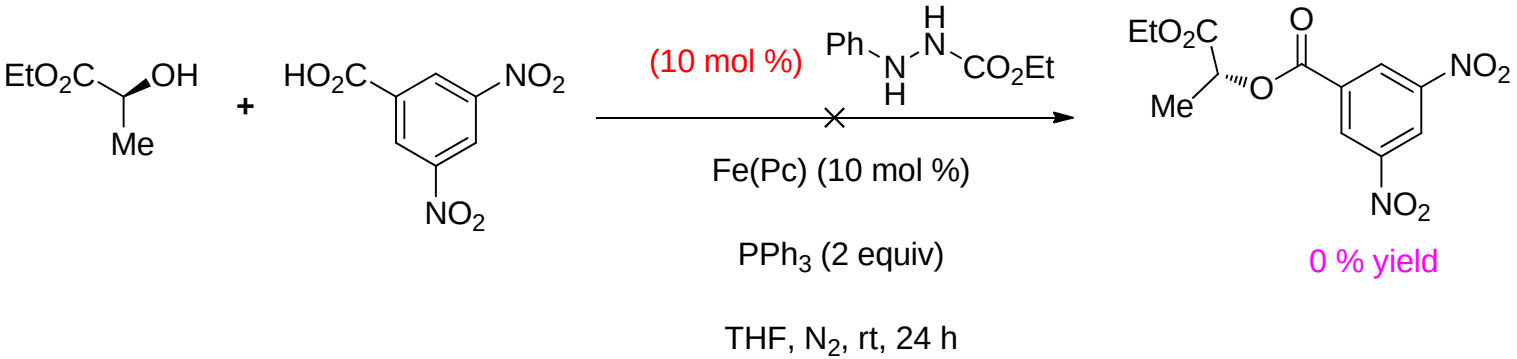
50 % yield

99 : 1 er

Optimization of the new catalytic approach

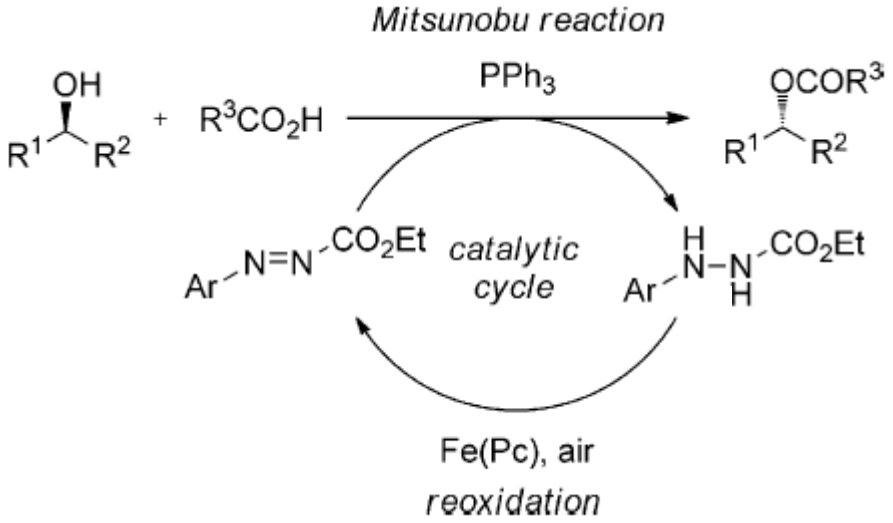
❖ Concept for a catalytic Mitsunobu reaction

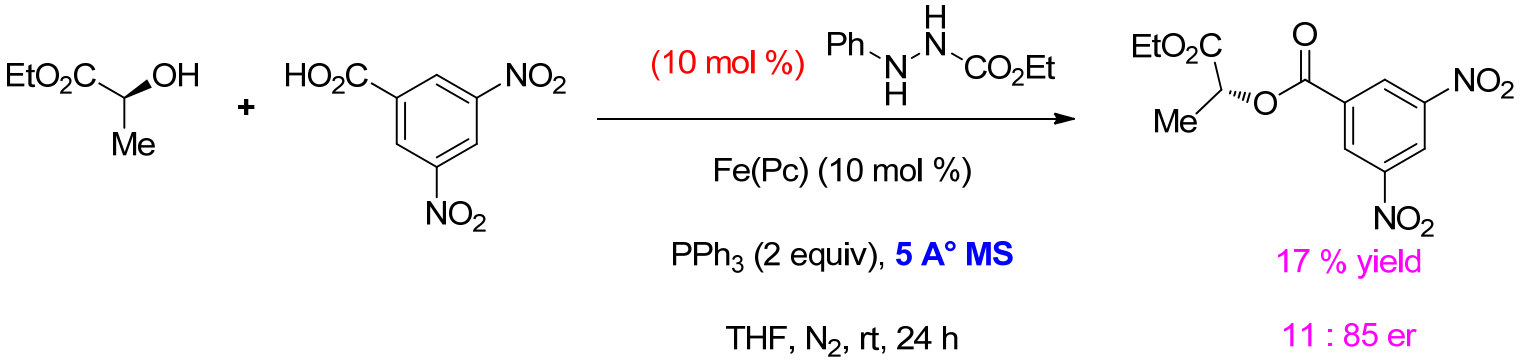




Optimization of the new catalytic approach

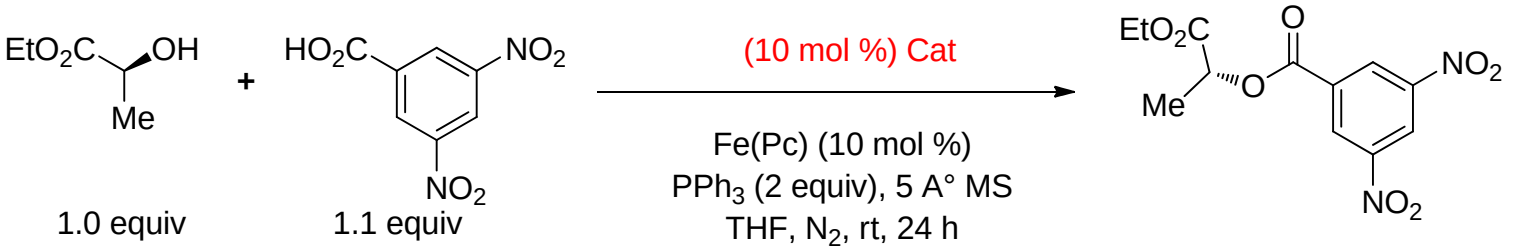
❖ Concept for a catalytic Mitsunobu reaction

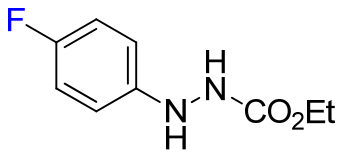




Optimization of the new catalytic approach

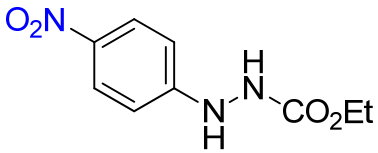
❖ Optimization of the hydrazines catalyst





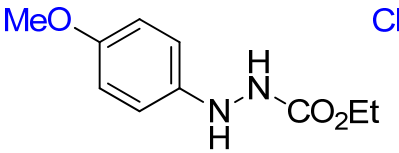
20 %

11 : 89 er



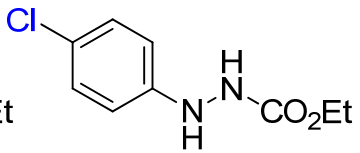
30 %

87 : 13 er



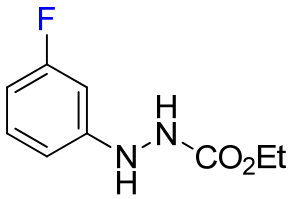
19 %

8 : 92 er



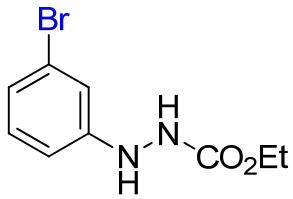
37 %

80 : 20 er



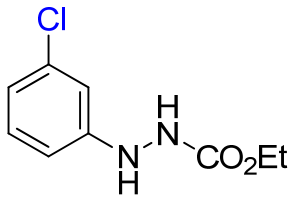
25 %

94 : 6 er



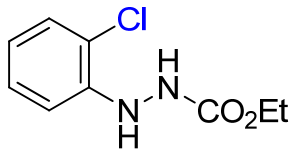
48 %

92 : 8 er



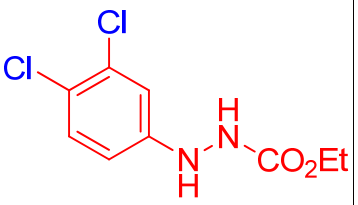
53 %

94 : 6 er



23 %

85 : 15 er

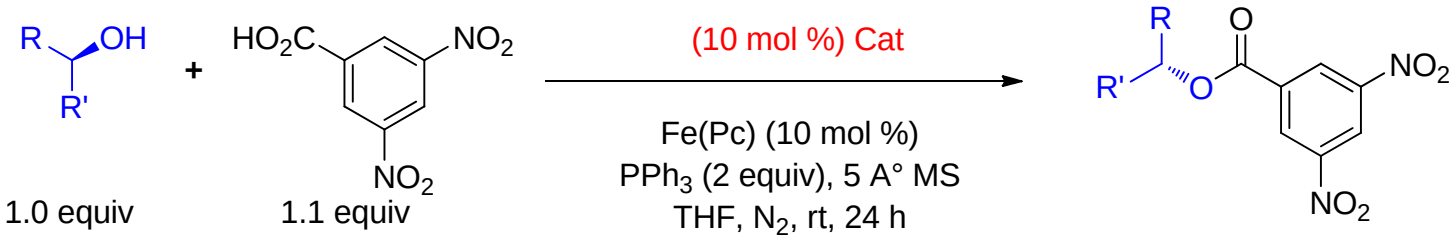


79 %

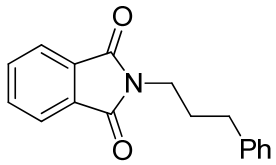
98 : 2 er

Good yield and good enantiomeric ratio

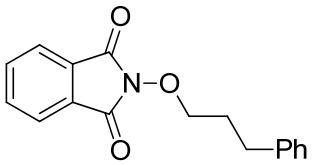
Scope of the new catalytic Mitsunobu reaction



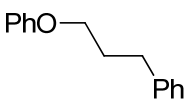
1.0 equiv 1.1 equiv



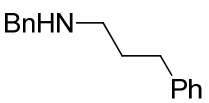
65 %



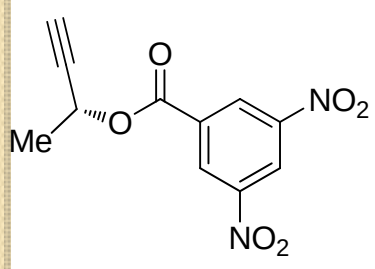
64 %



54 %

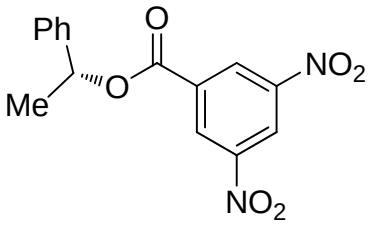


51 %



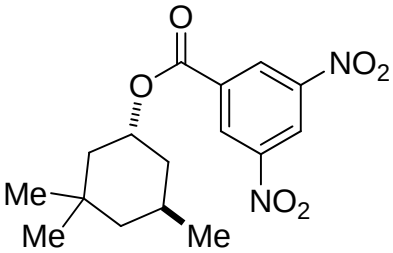
91 %

97 : 3 er



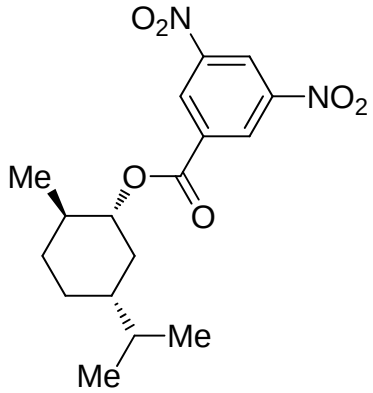
73 %

97 : 3 er



57 %

92 : 8 dr



28 %

25 : 75 dr

✓ With inversion of configuration

Selected examples

Conclusion

- Innovative catalytic Mitsunobu reaction
- Inexpensive and nontoxic iron phthalocyanine
- Hydrazine catalyst easily prepared and fully recovered
- Limitation: Moderate reactivity and low yields

  Further improvement need to be done