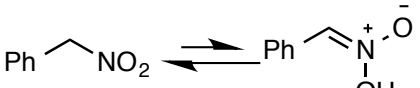
Nitroso and Nitro Compounds

Hai Dao
11/22/2014

Part 1. Introduction

Nitro Compounds



a nitro compound
b.p = 100 °C (8 mm)

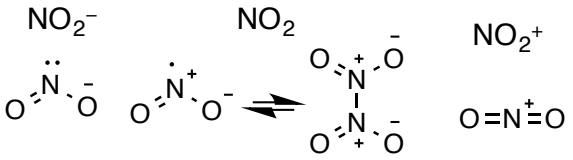
a nitronic acid
m.p = 84 °C
(pKa = 2–6)

	D(Kcal/mol)	d (Å)
CH_3–NO	40	1.48
CH_3–NO_2	57	1.47
CH_3–NH_2	79	1.47
CH_3–I	56	

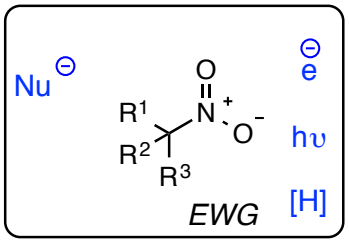
IR: υ(N=O): 1621-1539 cm^{-1}

Nitro group is an EWG (both –I and –M)

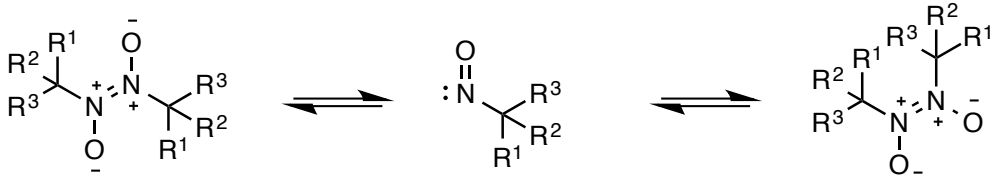
Nitro group is a "sink" of electron



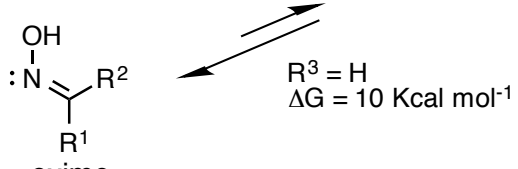
nitrite ion | high temp brown | low temp color less | nitrolium ion



Nitroso Compounds (*C*-Nitroso Compounds)



trans-dimer *colorless* | monomer: *blue color* | *cis*-dimer *colorless*



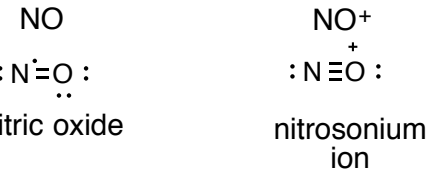
oxime

Blue color: n → π* absorption band 630-790 nm

IR: υ(N=O): 1621-1539 cm^{-1}, dimer υ(N–O): 1300 (*cis*), 1200 (*trans*) cm^{-1}

^{1}H NMR (α-C-H) δ = 4 ppm: nitroso is an EWG

R^3 = H: unstable (favor the oxime form), *in situ* generation



nitric oxide | nitrosonium ion

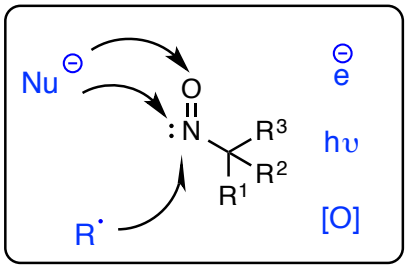
cellular signaling molecule in mammals

Reaction Modes

Nitroso vs. olefin:
- Diels-Alder reaction: as dienophiles
- Ene reaction
- Cope rearrangement

Nitroso vs. carbonyl
- Nucleophilic addition

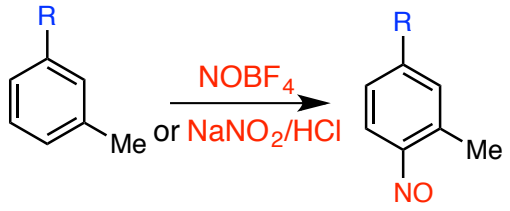
Other reaction modes
- Radical addition
- Redox reaction
- Photochemical reaction



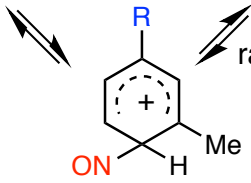
Synthesis of *C*-Nitroso Compounds

With NO+ sources: $NaNO_2$/HCl, $NOBF_4$, NOCl, $NOSbF_6$, RONO...

Substitution



- *R = OH, OMe, Me, NR_2, NHR*
- *para*-selectivity



rate determining step

Wheland intermediate

Kochi *et al. J. Org. Chem.* **1994**, *59*, 5573–5586.
Chem. Rev. **2004**, *104*, 3315–3340.

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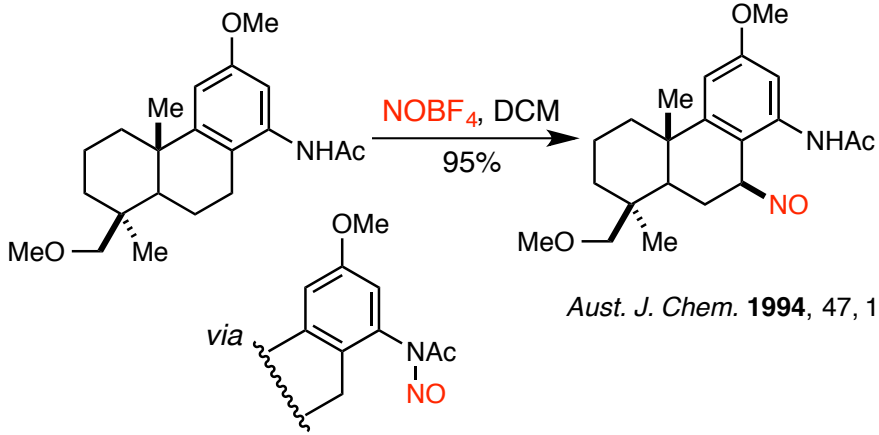
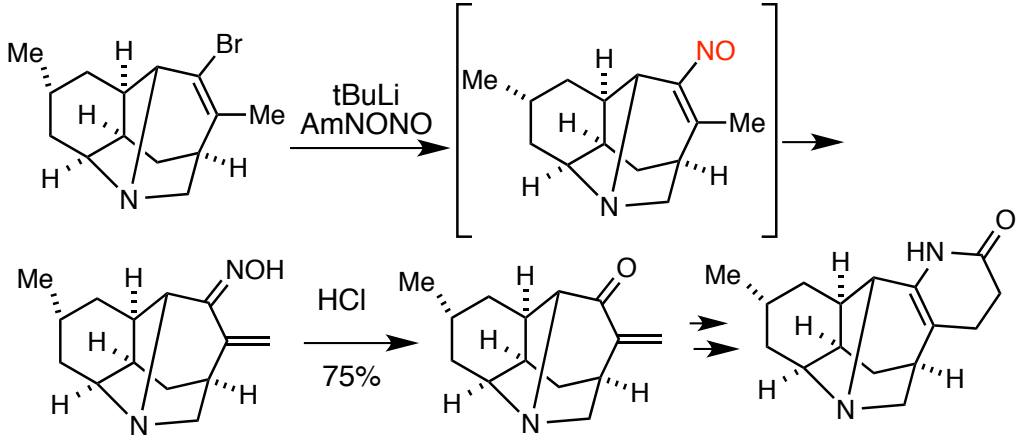
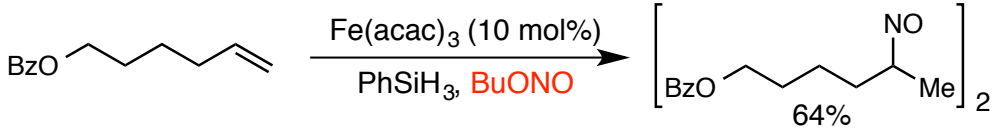


Aust. J. Chem. **1994**, 47, 1483–1508.

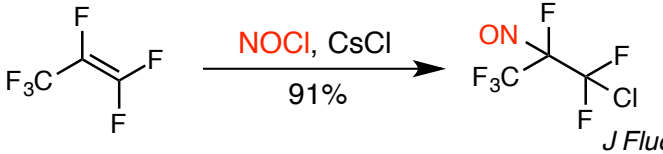


Fukuyama *et al. J. Am. Chem. Soc.* **2013**, *135*, 3243.

***Addition reactions* to C=C double bonds**



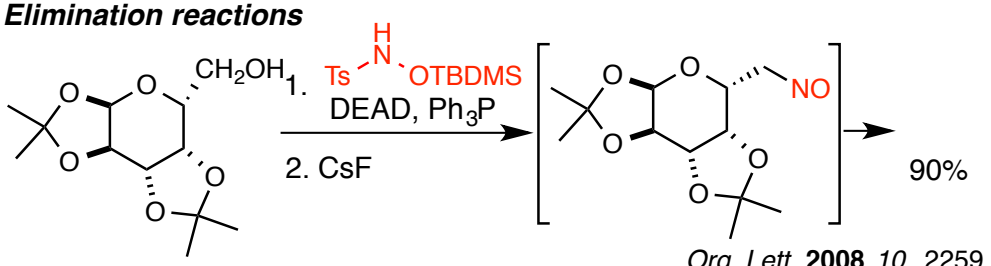
Mukaiyama *et al. Chemistry Letters* **1992**, 1137–1140.



J Fluorine Chem., **1984**, 26, 87.

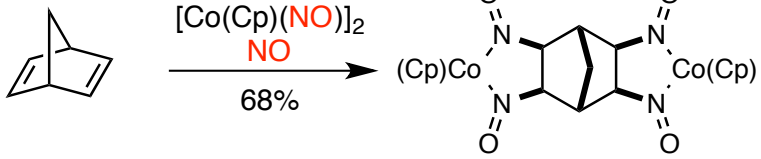
Other external [NO] sources

Elimination reactions



Org. Lett. **2008**, *10*, 2259.

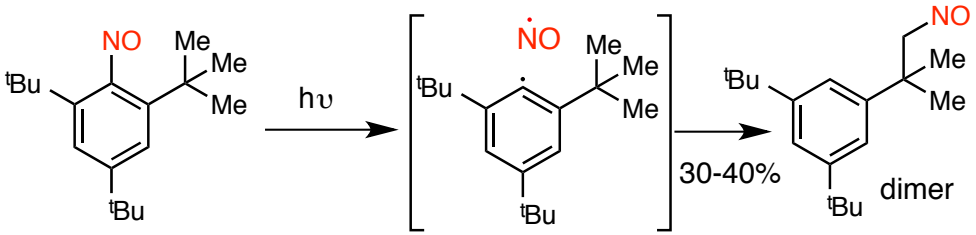
Metal-NO complexes



Organometallics **1983**, *2*, 787.

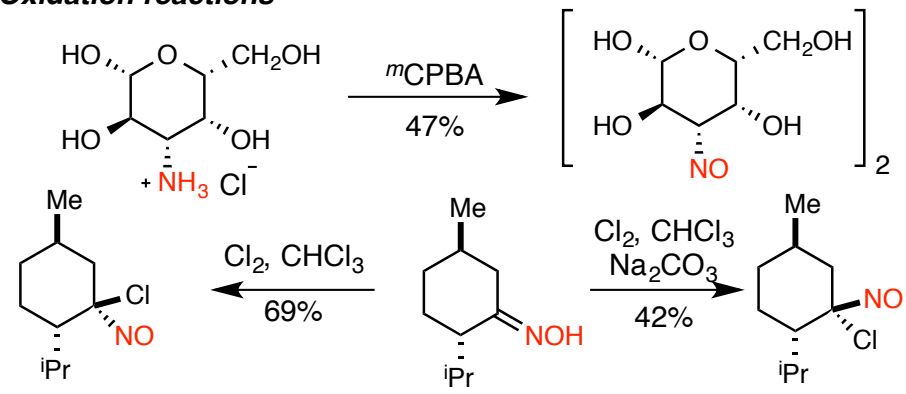
Internal [NO] sources

Barton reaction and other reactions with NO



Can. J. Chem. **1978**, *56*, 2665.

Oxidation reactions



synthesis **2006**, 3819.

Reduction from Nitro group

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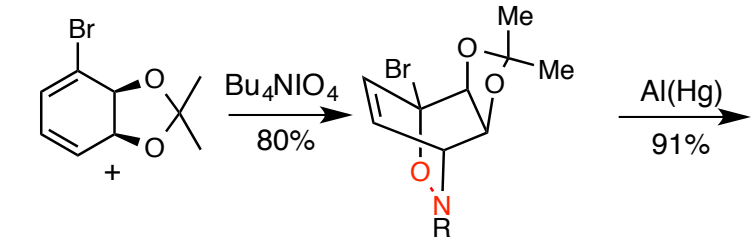
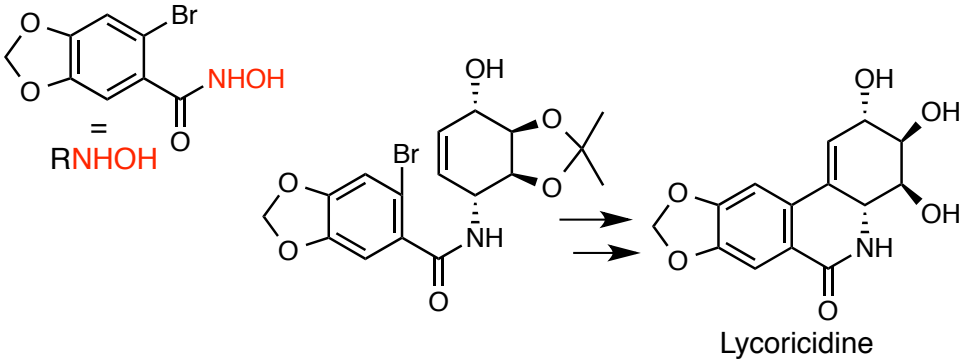
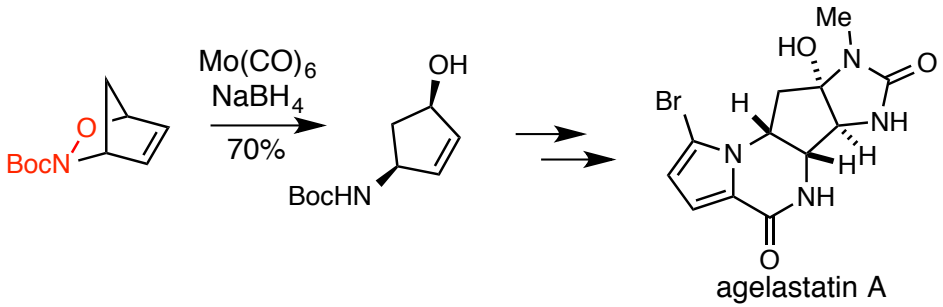
Reaction of *C*-Nitroso Compounds

Hetero Diels-Alder reaction

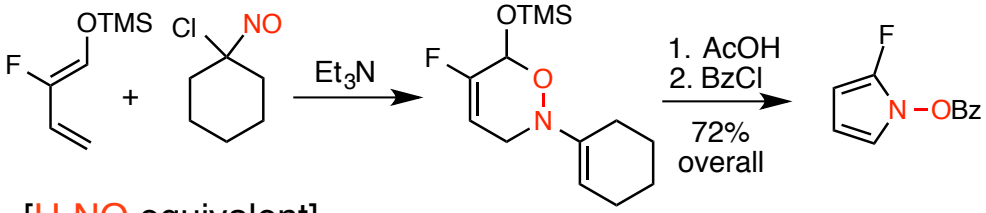




Hudlicky, *et al. J. Am. Chem. Soc.* **1992**, *114*, 9694–9696.

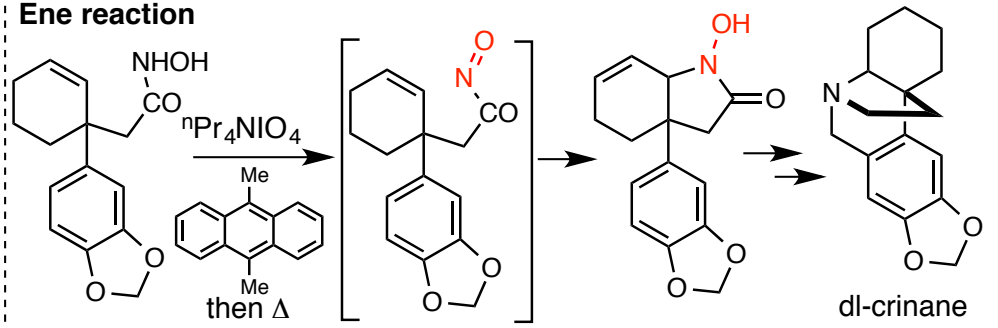


Tanaka *et al. Org. Lett.* **2008**, *10*, 5457–5460.

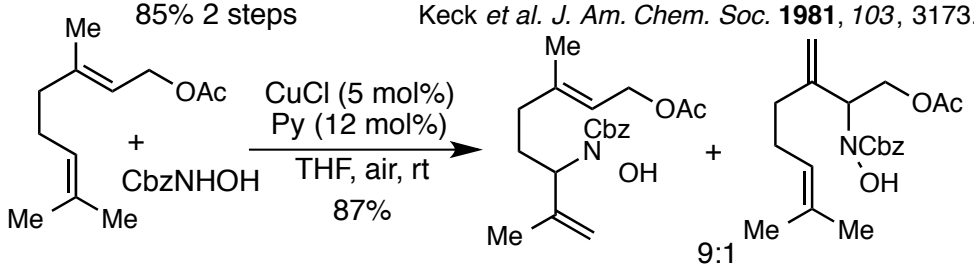


Schlosser, *et al. Tetrahedron* **1993**, *49*, 1445.

Ene reaction



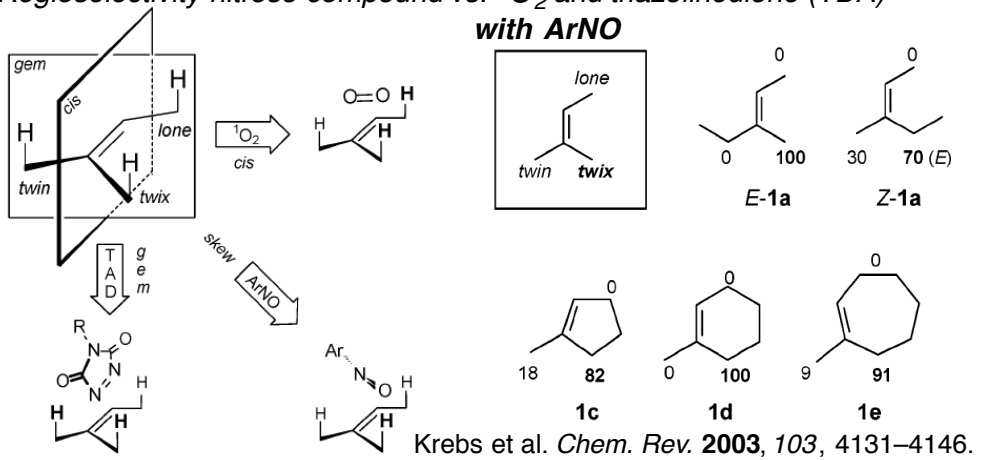
Keck *et al. J. Am. Chem. Soc.* **1981**, *103*, 3173.



J. Read de Alaniz, *J. Am. Chem. Soc.* **2011**, *133*, 10430–10433.

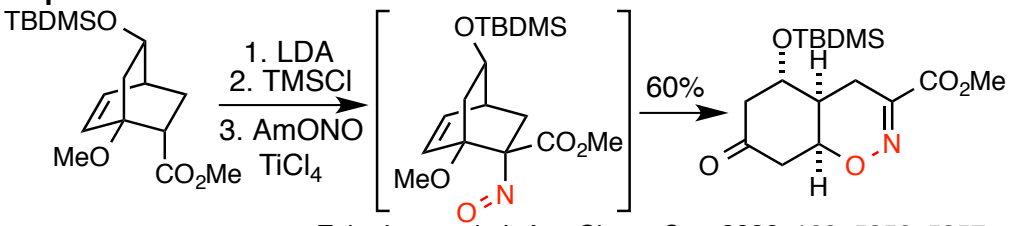
Regioselectivity nitroso compound vs. $^1O_2$ and triazolinedione (TDA)

with ArNO



Krebs et al. *Chem. Rev.* **2003**, *103*, 4131–4146.

Cope reaction



Zakarian *et al. J. Am. Chem. Soc.* **2006**, *128*, 5356–5357.

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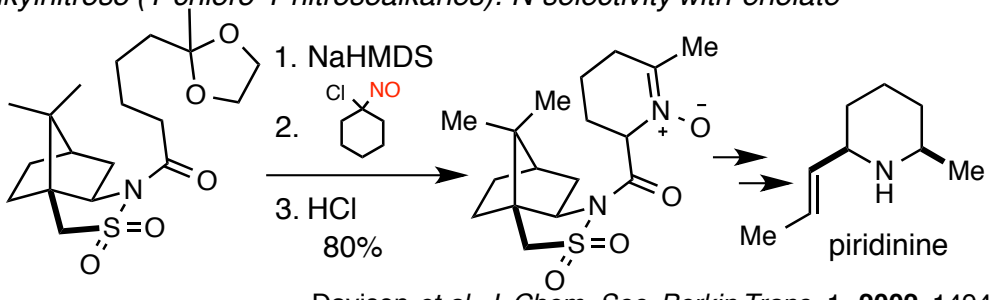
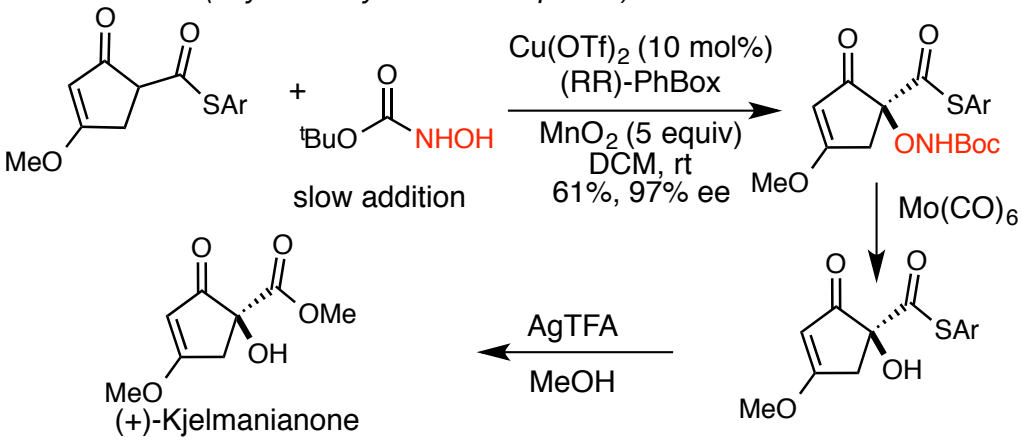
O-Nitroso aldol vs. *N*-nitroso aldol reaction

alkylnitroso (1-chloro-1-nitrosoalkanes): N selectivity with enolate

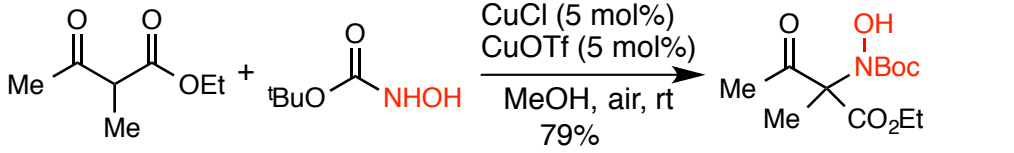


Davison *et al. J. Chem. Soc. Perkin Trans.* 1, **2002**, 1494.

Aldol reaction (acyl and arylnitroso compound): steric and electronic factors

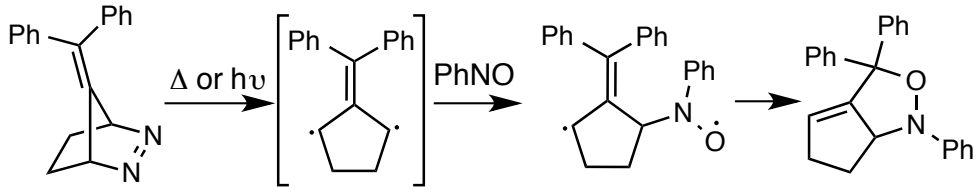


Yamamoto *et al. J. Am. Chem. Soc.* **2012**, *134*, 18566.



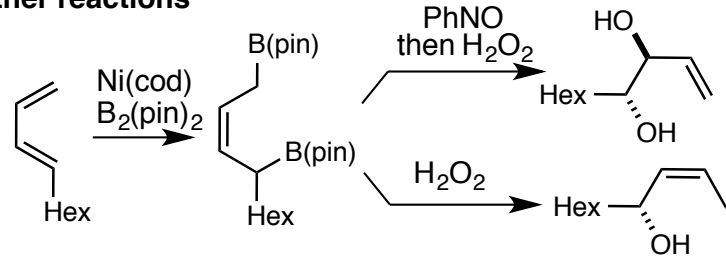
Read de Alaniz, et al. *J. Am. Chem. Soc.* **2012**, *134*, 18948–18951.

Reaction with radical

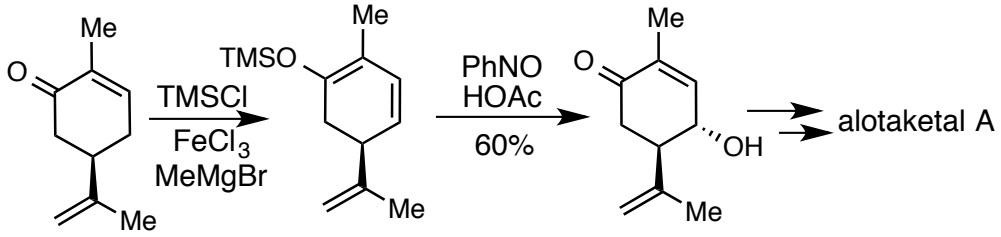


Adam *et al. Tetrahedron Letters* **1991**, *32*, 4283.

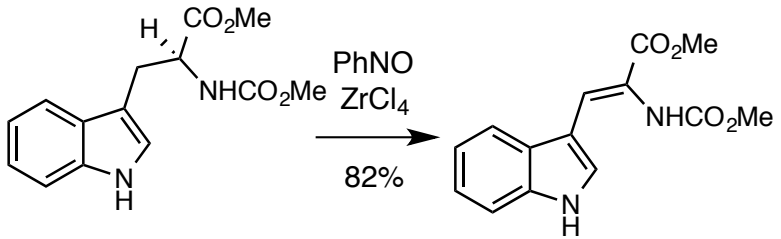
Other reactions



Morken *et al. Org. Lett.* **2010**, *12*, 3796.



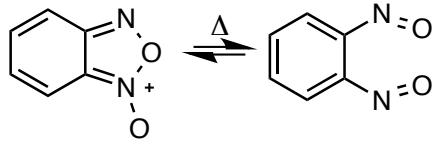
Yang *et al. Org. Lett* **2010**, *12*, 5072–5074.



Baran *et al. J. Am. Chem. Soc.* **2006**, *128*, 8678–8693.

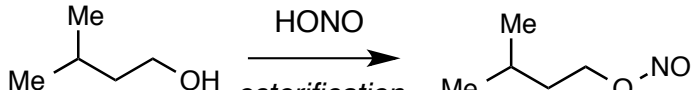
Other nitroso compounds

Furoxans



furoxan

O-Nitroso compounds (nitrite compounds)



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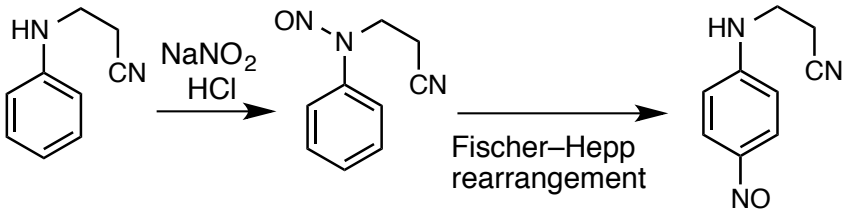
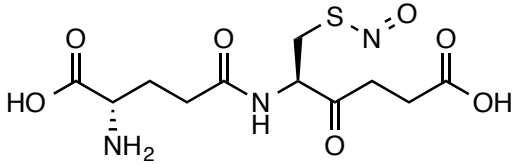
N-Nitrosoamine (secondary amine derivatives)



D'Amico *et al. J. Am. Chem. Soc.* **1959**, *81*, 5957–5963.

S-Nitrosothiols (thionitrites)

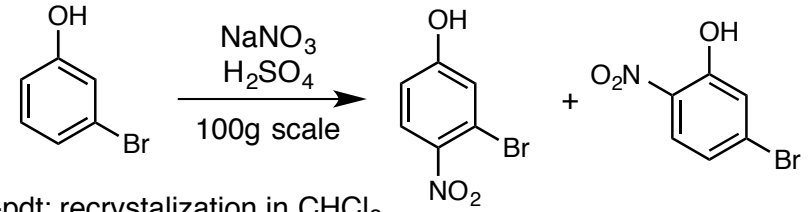


S-Nitrosoglutathione (GSNO)

- NO is an important cellular signaling molecule
- GSNO: endogenous NO carriers and donors

Synthesis of nitro compounds

Nitration with NO_2^+

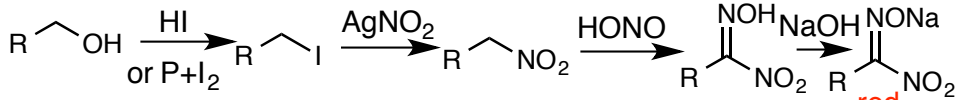


p-pdt: recrystalization in $CHCl_3$

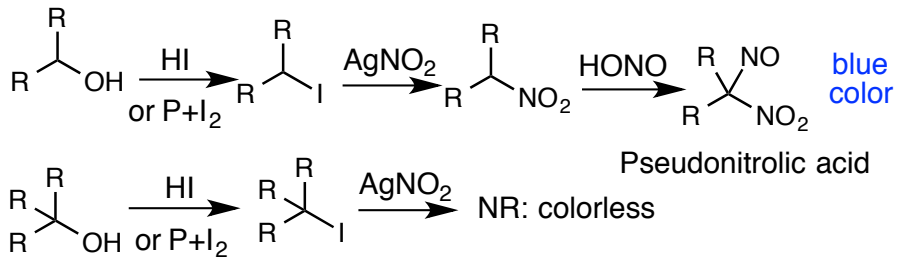
Nitration with NO_2^-

$AgNO_2$: Victor-Meyer reaction, $NaNO_2$: Kornblum reaction, KNO_2

Victor-Meyer test (primary vs. secondary vs. tertiary alcohol)



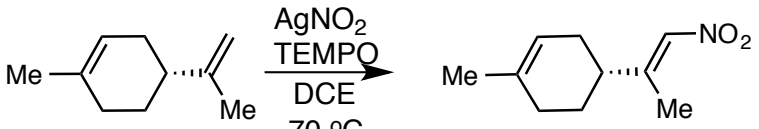
nitrolic acid



Pseudonitrolic acid

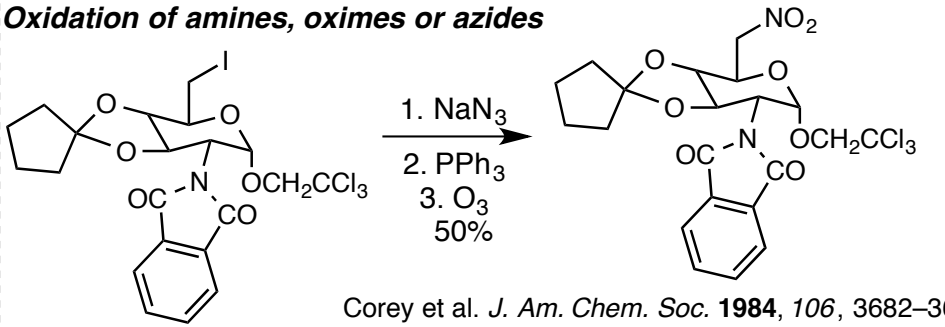
NR: colorless

Nitration with nitro radical



Maiti *et al. J. Am. Chem. Soc.* **2013**, *135*, 3355

Oxidation of amines, oximes or azides



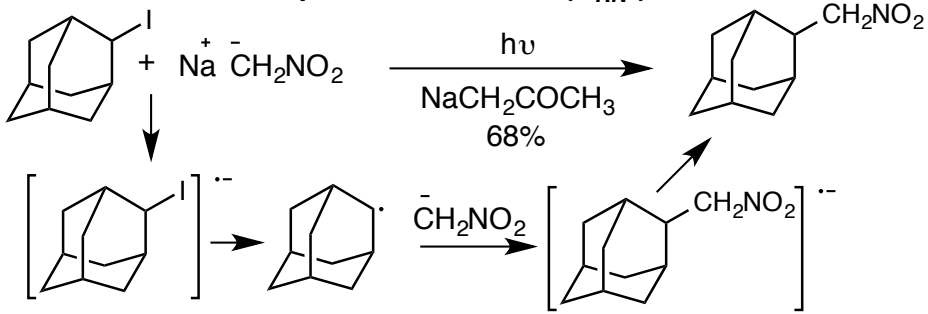
Corey et al. *J. Am. Chem. Soc.* **1984**, *106*, 3682–3683.

Reaction of nitro compounds

Henry reaction, Michael reaction: see ref

Nef reaction, reduction: see ref

Radical chain nucleophilic substitution ($S_{RN}1$)



Rossi *et al. J. Org. Chem.* **1999**, *64*, 5826.

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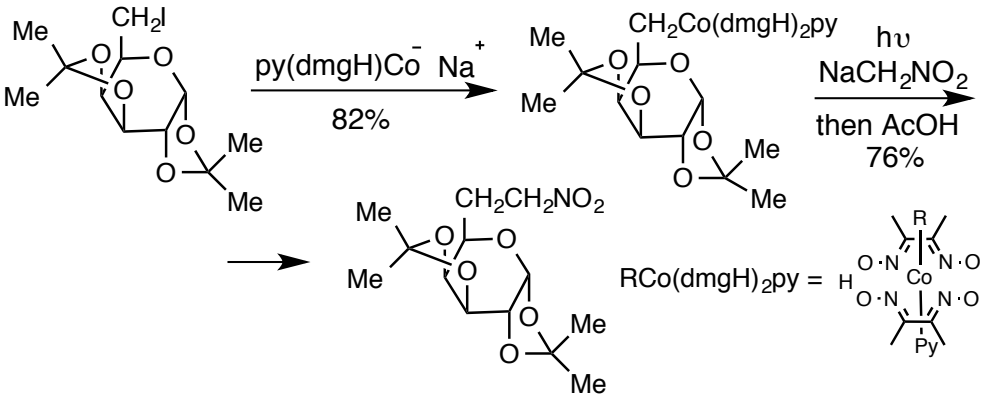
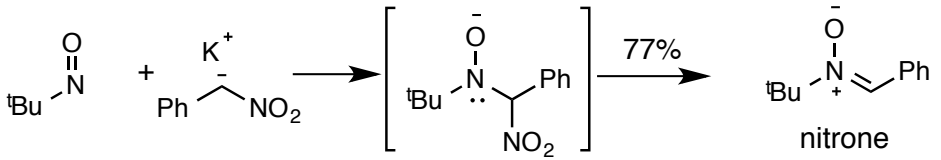


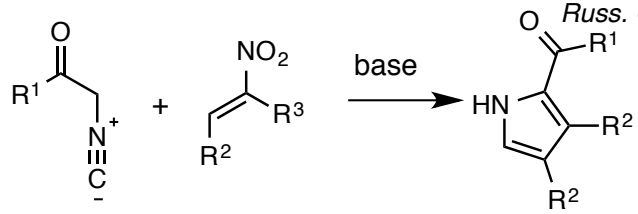
Branchaud *et al. Tetrahedron Letters* **1991**, *32*, 3639.

Elimination of NO_2^-

NO_2^- is a good leaving group

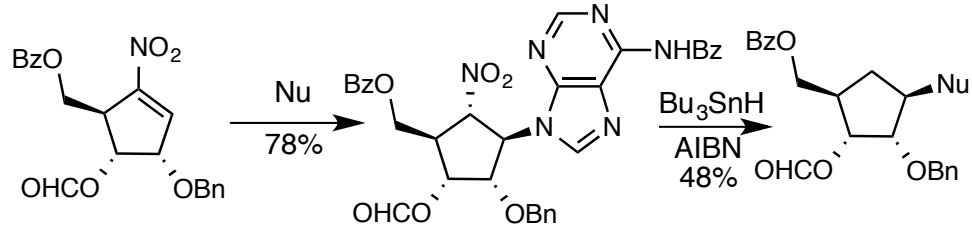


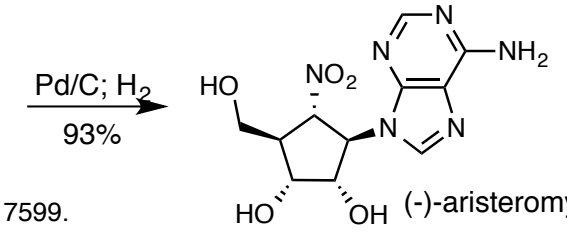
Russ. Chem. Bull. **1996**, *45*, 856.



Barton-Zard pyrrole synthesis

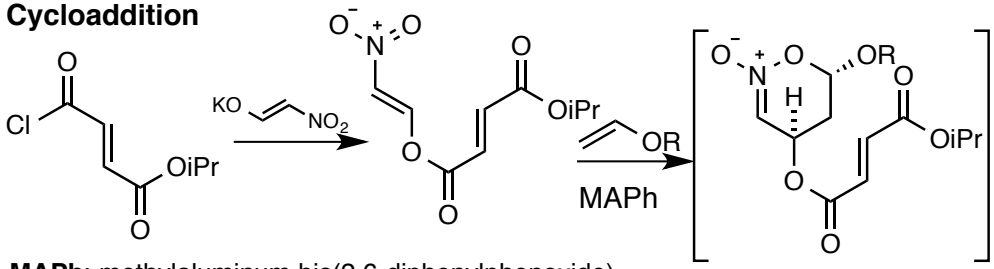
removal of NO_2 under radical conditions



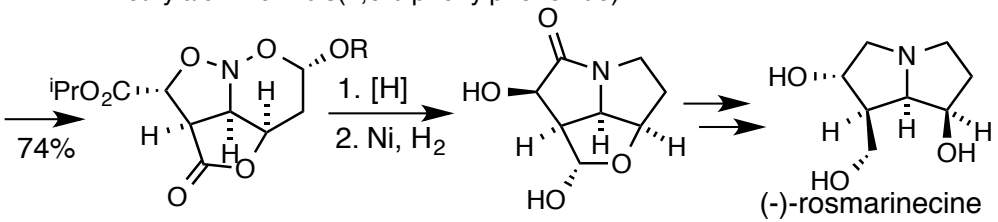


Zanirato *et al.*
Tetrahedron Letters **1996**, *37*, 7599.

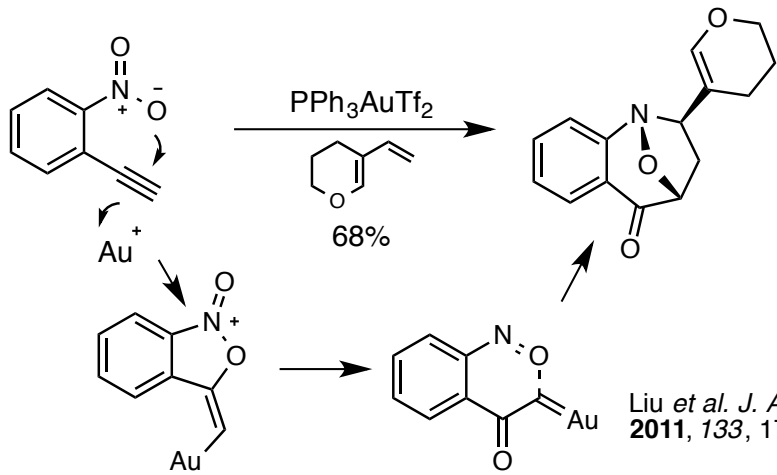
Cycloaddition



MAPh: methylaluminum bis(2,6-diphenylphenoxide)



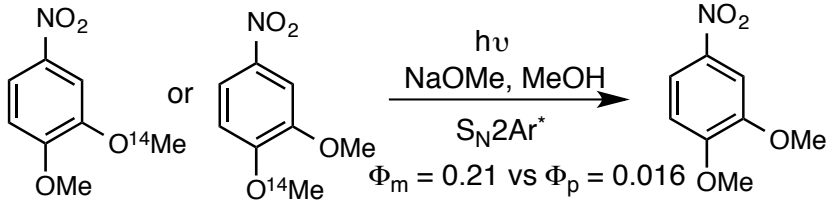
Denmark *et al. J. Am. Chem. Soc.* **1996**, *118*, 8266.



Liu *et al. J. Am. Chem. Soc.* **2011**, *133*, 1769.

Photochemistry

***meta*-activation**

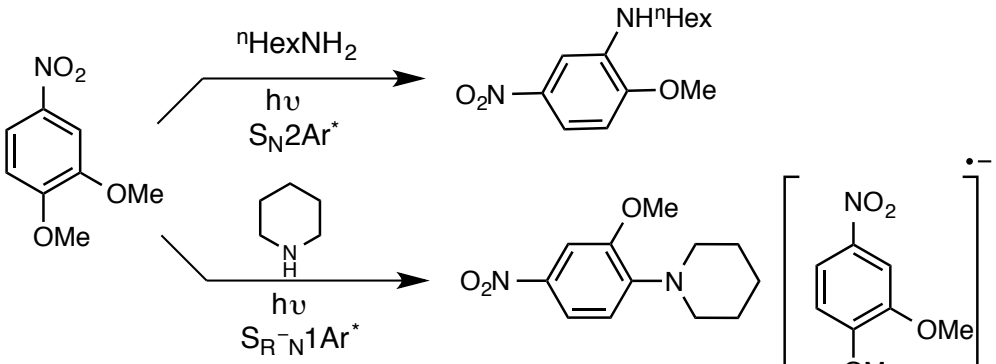


- direct substitution of the triplet state: *meta*-activation vs. S_NAr
- depend on: nucleophiles, solvent system

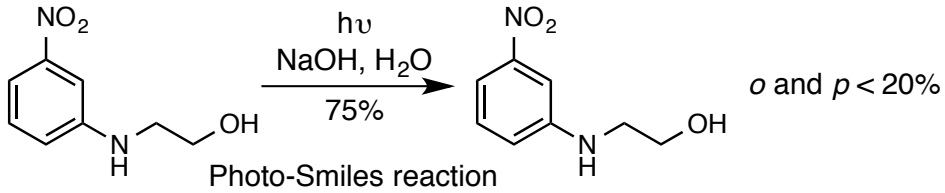
Havinga *et al. J. Am. Chem. Soc.* **1981**, *103*, 7257–7262.

Nitroso and Nitro Compounds

Hai Dao
11/22/2014



$S_{R}^{-}{}_{N}1Ar^{*}$: radical ion pair *via* ET from amine to nitro

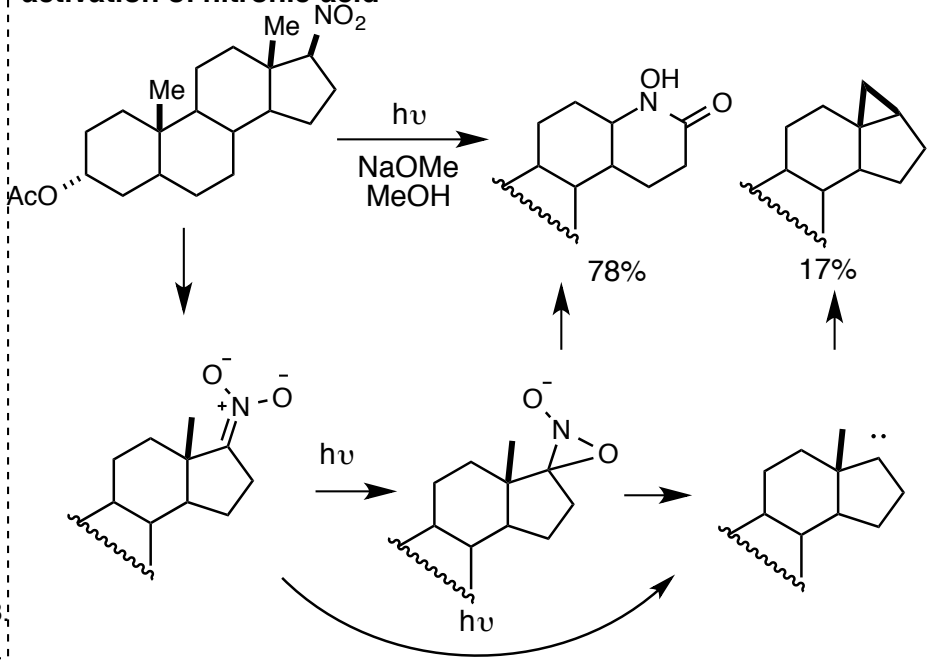


o and *p* < 20%

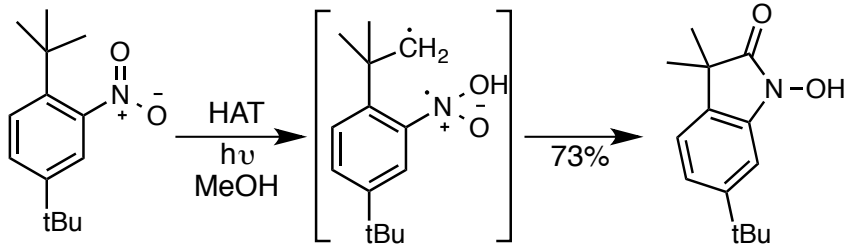
Photo-Smiles reaction

Oxman *et al. J. Am. Chem. Soc.* **1980**, *102*, 4848.

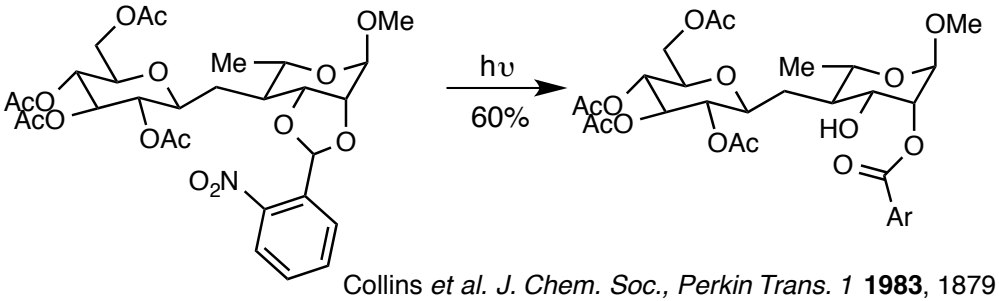
activation of nitronic acid



Activation of nitro group



Döpp *et al. Eur. J. Org. Chem.* **1979**, *1979*, 554–563.



Collins *et al. J. Chem. Soc., Perkin Trans. 1* **1983**, 1879