# ELECTROPHILIC A AMINATION REACTION OF B KETO ESTER USING N HYDROXY CARBAMATES –MERGING AEROBIC OXIDATION AND LEWIS ACID CATALYSIS

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ABSTRACT

The power of nitrosocarbonyl chemistry and demonstrate their potential as new viable electrophilic source of nitrogen in α- functionalization reaction.Nitroso carbonyls as an alternative to aryl nitroso compoundsprovidetheproductswithasynthetically easily manipulated N—carbonyl bond.we present the development of the first N-selective nitrosoaldol reaction utilizing nitrosoformate esters, generated in situ, astheelectrophilicsourceofnitrogen Asymmetric *a*-amination of carbonyl compounds is ofconsiderablesignificanceinorganicsynthesis.The chiral *a*-amino carbonyl products are versatile build- ing blocks, and they can be easily transformed into new valuable functional compounds, such as *a*-aminoacids,*a*-aminoaldehydes,and*b*-aminoalco- hols.

KEYWORDS:Nitroso carbonyls,nitrosoaldol methods,*N*-hydroxycarbamates

Anestablishedstrategyistheuseofstablearyl nitroso compounds as N electrophiles to construct the enantioenriched*a*-amino carbonyls with chiral transitionmetals[1]ororganocatalysts.[2]Ho wever,the application of these *a*-amino carbonyl products is synthetically limited owing to difficulties associated with cleaving the

N—arylbond Asymmetric *a*-amination of carbonyl compounds is ofconsiderablesignificanceinorganicsynthesis.Anestablishedstrategyistheuseofstablearyl



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nitroso compounds as N electrophiles to construct the enantioenriched*a*-amino carbonyls with chiral transitionmetals[1]ororganocatalysts.[2]

Nitroso carbonyls as an alternative to aryl nitroso compoundsprovidetheproductswithasynthetically easily manipulated N—carbonyl bond. As a result of their high reactivity and instability, nitroso carbonyls are generally in situ generated through theoxidation of precursors of *N*-hydroxycarbamates.[3]Yamamoto and co-workers reported the first example of the copper(II) trifluoromethanesulfonate[$Cu(OTf)_2$]-catalyzed asymmetric *a*-aminoxylation of *a*-substituted *b*-keto esters through the in situ generation of nitro- socarbonyls from the $MnO_2$-mediated oxidation of thecorresponding*N*-hydroxycarbamates.[4]Almostat the same time, Read deAlaniz discovered the CuCl-and$Cu(OTf)_2$-catalyzed*a*-hydroxyaminationof*a*-sub- stituted*b*-keto esters. Nevertheless, attempts at anasymmetric versionfailedbecausethechiralligandsmade theni- trosoaldol reaction O selective.[6] .Thestudy showed that oxidants of this type played a crucial role in the regioselectivity(e.g., N- versus O-nitrosoaldol reaction). All other screened oxidants such as $Cu^I$/pyridine with $O_2$, $MnO_2$, and$PhI(OAc)_2$preferredOselectivity.Furthermore,veryrecent- ly, Maruoka[8] and Yamamoto[9] independently developed elegantstrategiesfortheasymmetric*a*-hydroxyaminationofaldehydesbyusing$MnO_2$astheoxidantandchiral(*R*)2-triphenylmethylpyrrolidine(2)and(*S*)-proline–tetrazole3asrespective catalyststoachievehighNselectivity.Theamino-oxylation reaction to afford α-oxygenatedcarbonylcompounds hasbeenextensivelydevelopedandnowrepresentsaversatilemethod to gain access to the α-xycarbonylsynthon(Figure1a).[4]

Notably absent from nitrosoaldol methods are examples with nitrosocarbonyl intermediates, which can easily be modified and would represent a desirable alternative to arylnitrosocompounds in electrophilic amination. In this communication, we present the development of the first N-selective nitrosoaldol reaction utilizing nitrosoformate esters, generated in situ, astheelectrophilicsourceofnitrogen(Figure1c


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).[7]Thisnew process is highly N-selective, uses an operationally convenient procedure, air, as the sole oxidant, and provides direct entry intoα-aminocarbonylderivativeswithfunctionalgroupsthat are easy tomanipulate. wefocused onaseriesoffunctionalgroupmanipulationsthathighlightthe utility of using a nitrosoformate intermediate as the electrophilic source of nitrogen. For example, hydrogenation ofthe Cbz-group with 5 mol% Pd/C or an acid catalyzed deprotectionofBoc-groupleadstoα-hydroxylamineproduct

Scheme 1

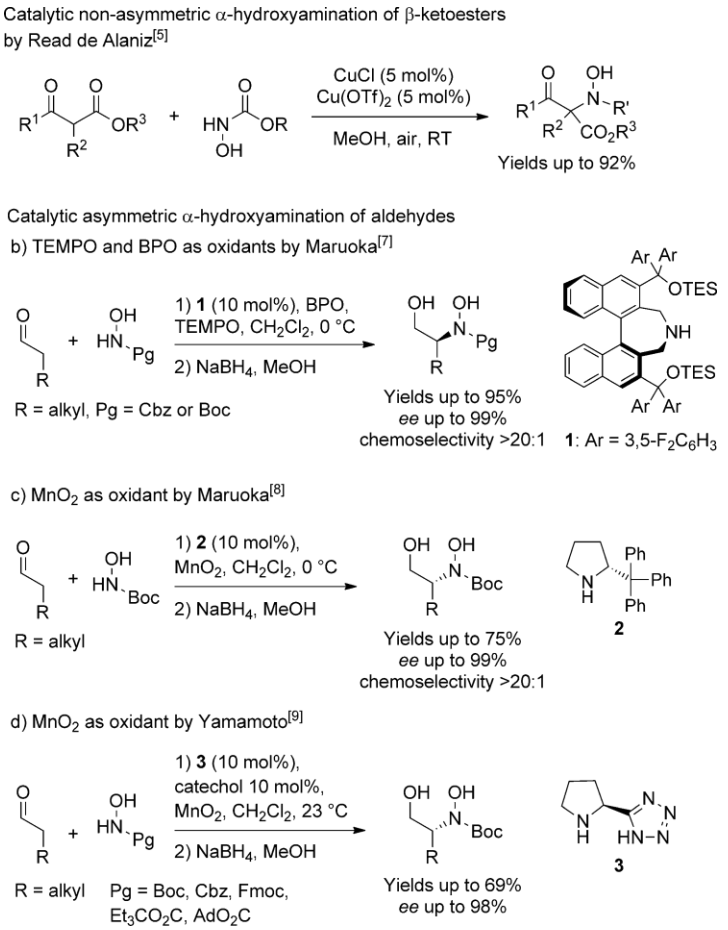


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Table2.SubstrateScopeStudiesfortheNitrosoformateα-AminationReaction[a,b]


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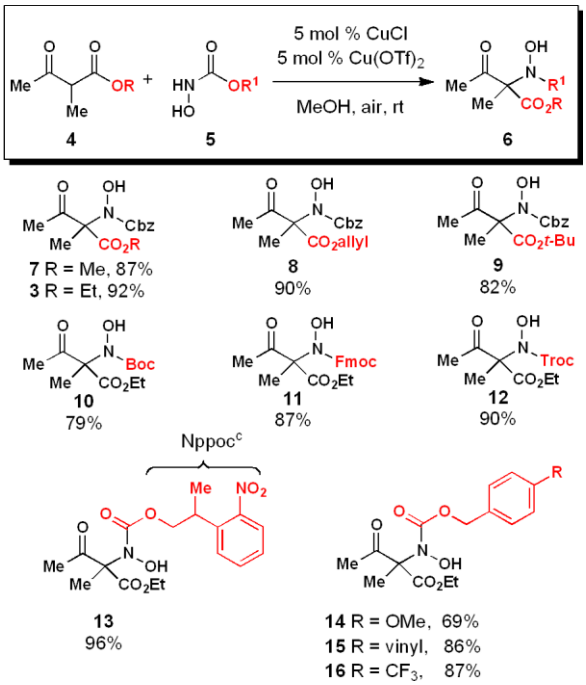


[a]Allreactionswereperformedwithreagent-gradeMeOH,using1.2 equivof4and1equivof5.[b]Yieldsarereported asisolatedyieldsof theN-regioisomer.

Thenewmethod- ology harnesses the power of nitrosocarbonyl chemistry and demonstratestheirpotentialasanewviableelectr ophilicsource ofnitrogeninα-functionalizationreactions.

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