COPPER (I) -CATALYZED DIVERGENT ADDITION REACTIONS OF ENOLDIAZOACETAMIDES WITH NITRONES

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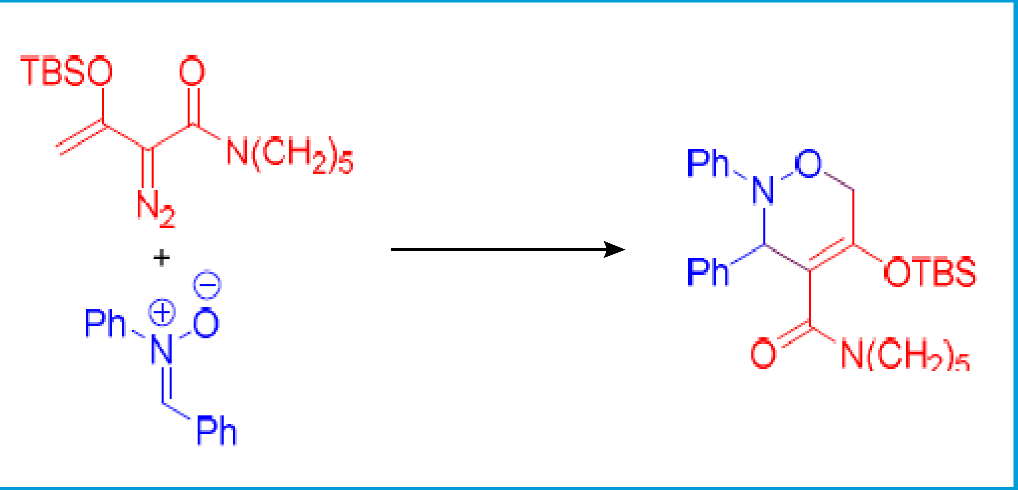
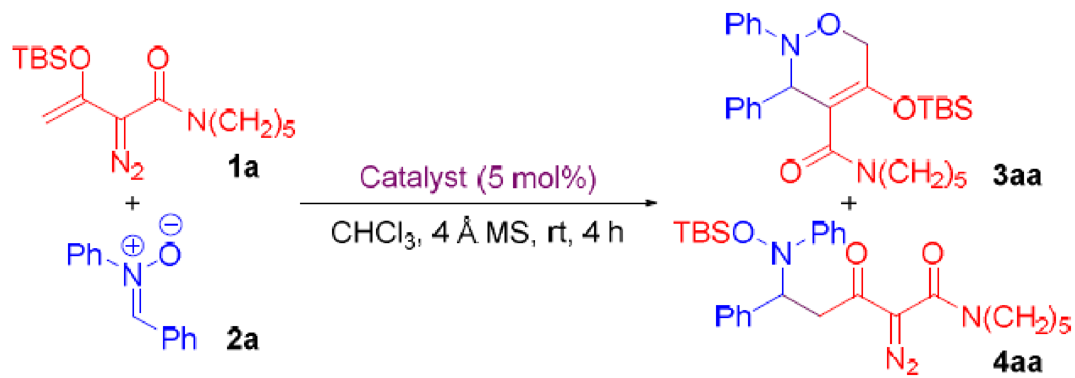
THE INITIAL AIM :

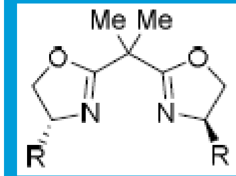
[3 + 3] - CYCLOADDITION REACTION CATALYZED BY Cu(I)



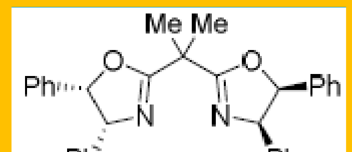
SCREENING OF CATALYSTS



entry	catalyst	recovery of **2a** (%)[b,c]	**3aa** yield (%)[d]	**3aa** ee (%)[e]	**4aa** yield (%)[c,d]
1	$Cu(OTf)_2$	n.d.	12	--	75
2	*$CuOTf\cdot Tol_{1/2}$*	*n.d.*	*trace*	--	*88*
3	$Cu(MeCN)_4PF_6$	20	33	--	33
4	$Cu(MeCN)_4BF_4$	26	61	--	n.d.
5[f]	$Cu(MeCN)_4BF_4$/**5a**	18	70	78	n.d.
6[f]	$Cu(MeCN)_4BF_4$/**5b**	81	10	rac.	n.d.
7[f]	$Cu(MeCN)_4BF_4$/**5c**	20	69	74	n.d.
8[f]	$Cu(MeCN)_4BF_4$/**5d**	n.d.	93	94	n.d.
9[f]	*$Cu(MeCN)_4BF_4$/**6***	*n.d.*	*96*	*98*	*n.d.*
10	$Rh_2(OAc)_4$	73	19	--	n.d.



5a, R = ^{i}Pr
5b, R = ^{t}Bu
5c, R = Bn
5d, R = Ph



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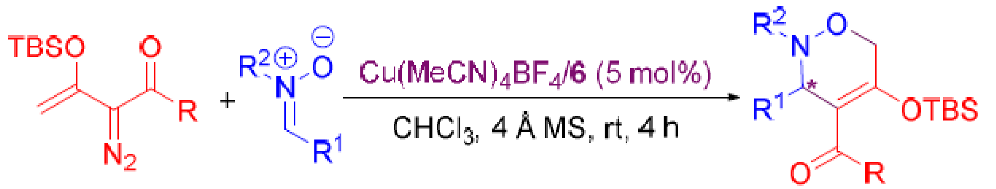
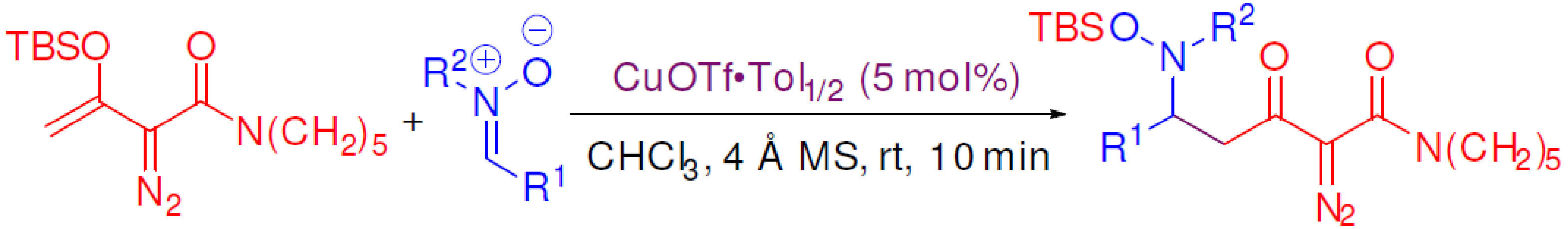
SCOPE OF [3 + 3] - CYCLOADDITION REACTION



entry	2	R¹, R²	3	yield (%)[b]	ee (%)[c]
1	**2a**	Ph, Ph	**3aa**	96	98
2	**2b**	4-ClC_6H_4, Ph	**3ab**	94	98 (*S*)
3	**2c**	4-MeC_6H_4, Ph	**3ac**	96	96
4	**2d**	4-$MeOC_6H_4$, Ph	**3ad**	95	96
5	**2e**	3-ClC_6H_4, Ph	**3ae**	90	96
6	**2f**	2-naphthyl, Ph	**3af**	94	97
7	**2g**	2-furyl, Ph	**3ag**	91	98
8	**2h**	Ph, 4-$(EtO_2C)C_6H_4$	**3ah**	92	93
9	**2i**	Ph, 3-Br-4-MeC_6H_3	**3ai**	96	94
10[d]	**2j**	cyclohexyl, Bn	**3aj**	93	94
11[e]	**2a**	Ph, Ph	**3ba**	96	96

SCOPE OF MUKAIYAMA-MANNICH REACTION



1a

2a, R^1 = Ph, R^2 = Ph — **4aa**, 88% yield

2b, R^1 = 4-ClC_6H_4, R^2 = Ph — **4ab**, 84% yield

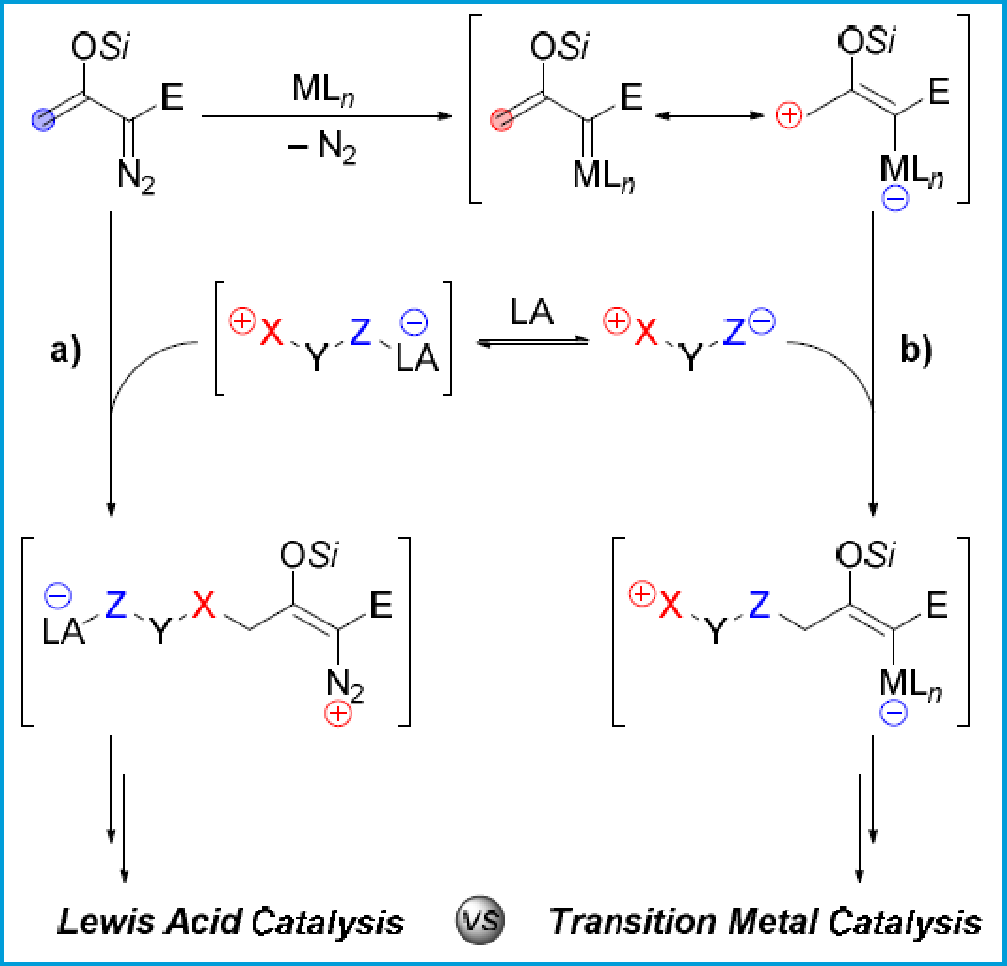
2f, R^1 = 2-naphthyl, R^2 = Ph — **4af**, 86% yield

2h, R^1 = Ph, R^2 = 4-$(EtO_2C)C_6H_4$ — **4ah**, 92% yield

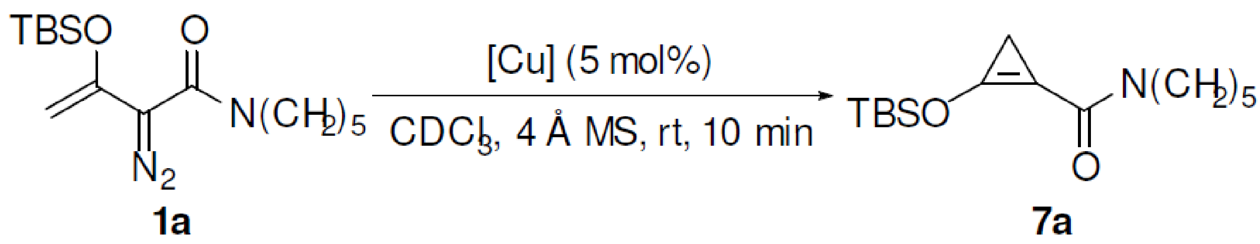
BUT
WHAT IS THE MECHANISM OF THIS REACTION
?

Experimental studies

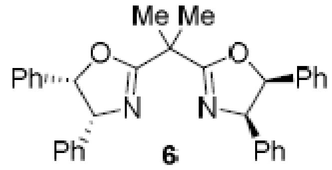
RECALL ABOUT POSSIBLE MECANISMS



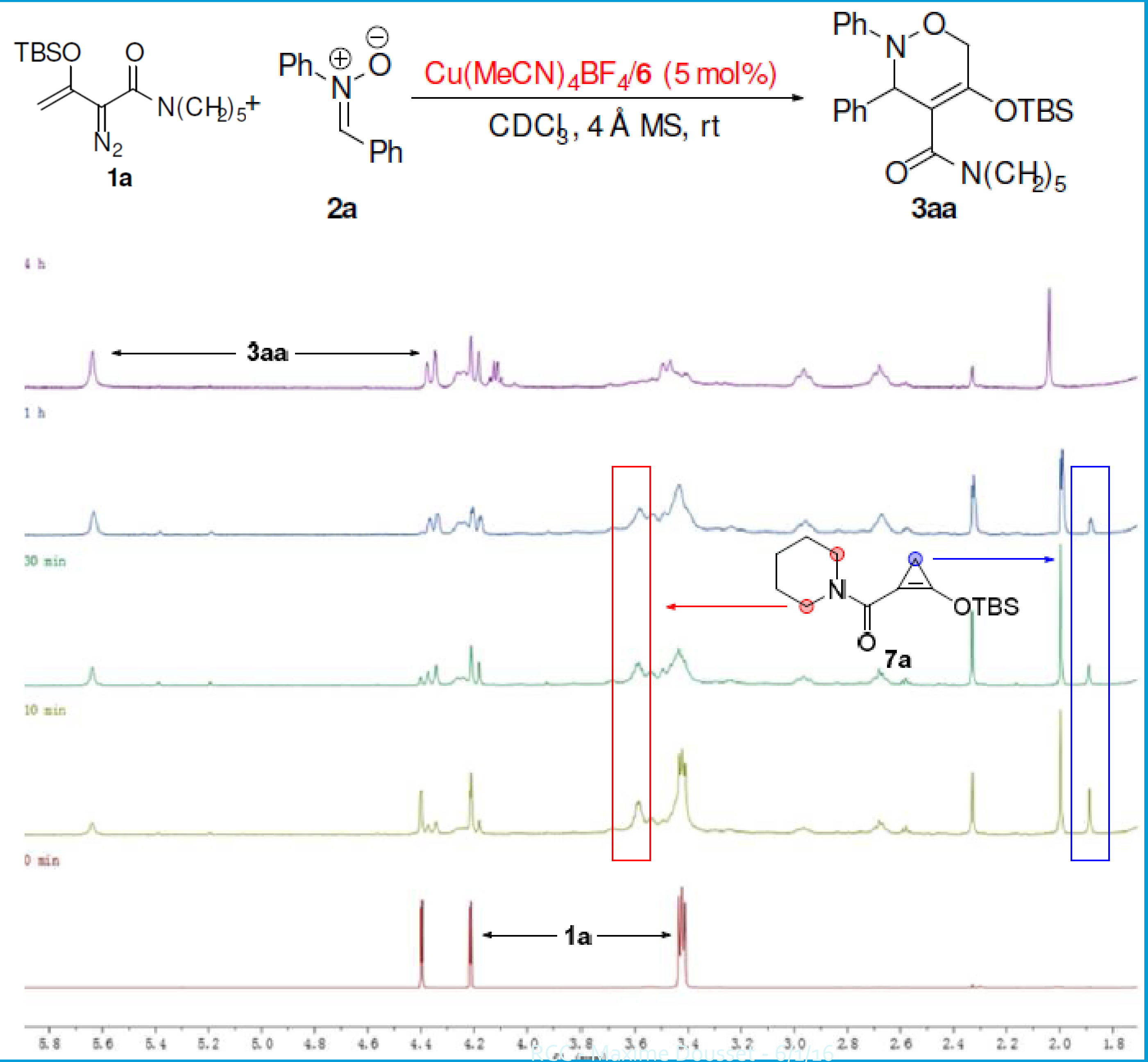
THE AIM OF THE STUDIE, FIND AN INTERMEDIATE OF THE REACTION



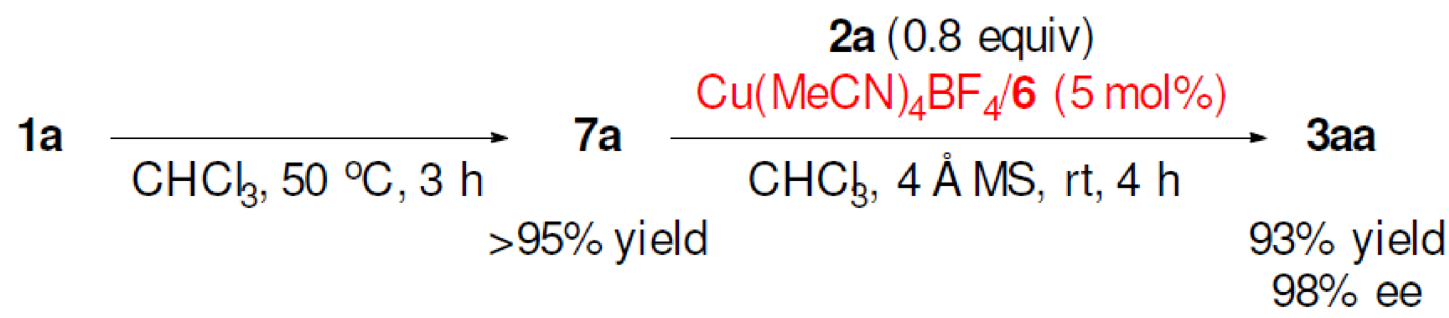
[Cu]	conversion of **1a**	**7a**
$Cu(MeCN)_4BF_4$/**6**	>95%	observed by ^1H NMR
$CuOTf{\cdot}Tol_{1/2}$	12%	not detectable



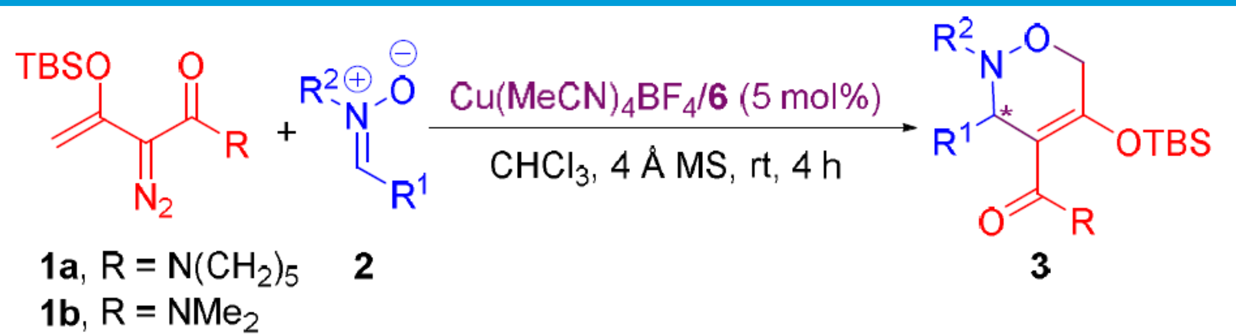
NMR MONITORING



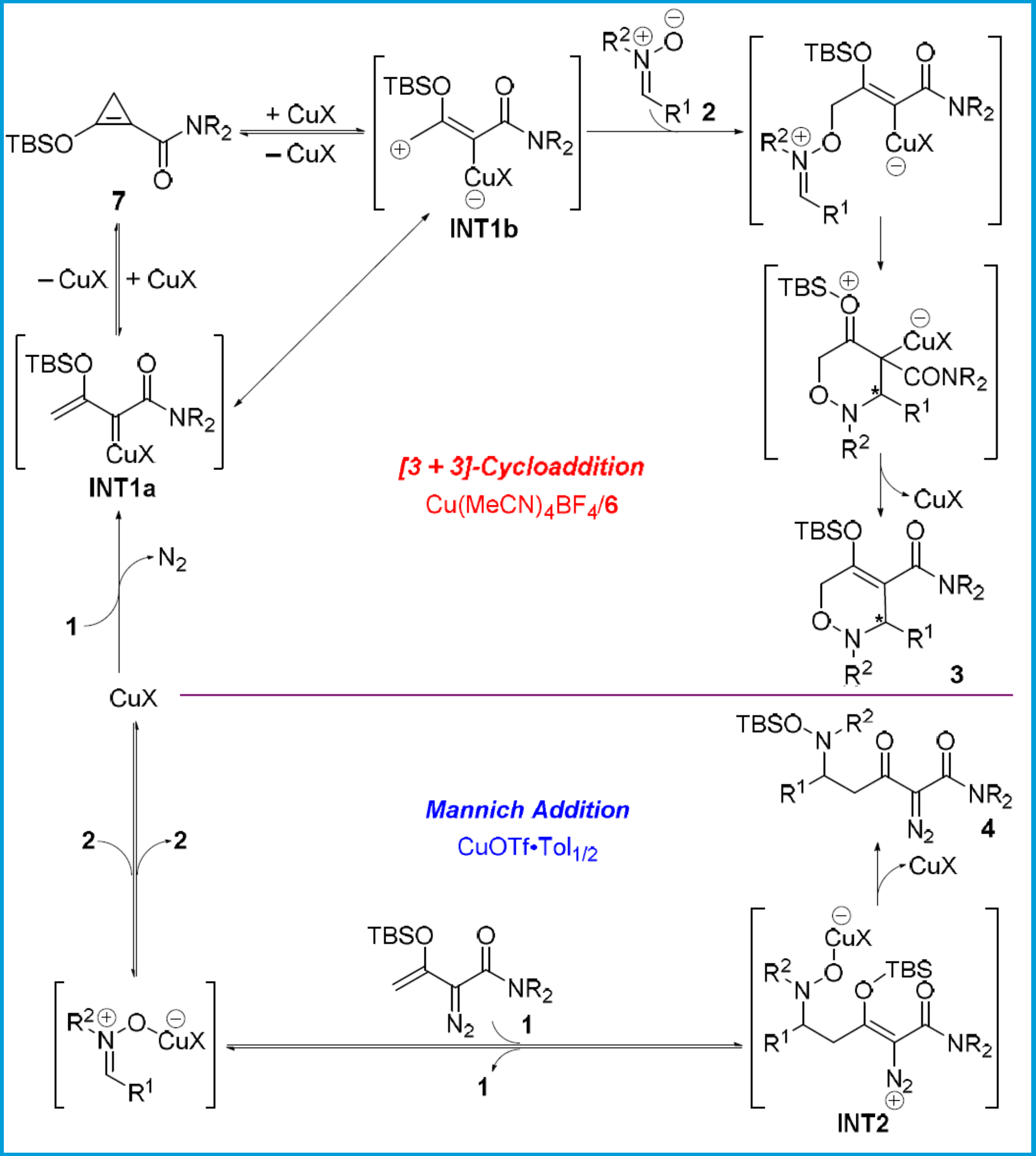
With the intermediate 7a (cyclopropene)



One pot reaction



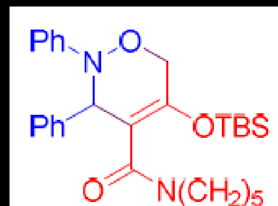
entry	2	R^1, R^2	3	yield (%)[b]	ee (%)[c]
1	**2a**	Ph, Ph	**3aa**	96	98


[3 + 3]-Cycloaddition
Cu(MeCN)4BF4/6
Mannich Addition
CuOTf•Tol1/2
INT1a
INT1b
INT2
+ CuX
− CuX
N2

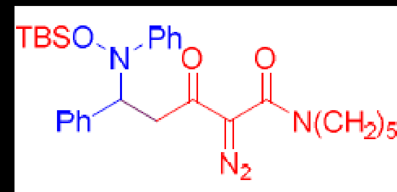
❑ THEY DEVELOPED A SWITCHING REACTION PATHWAY

[3+3] cycloaddition

Mukaiyama-Mannich

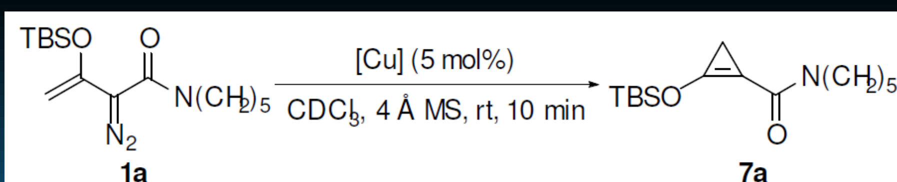


Yield : 91 - 96 %
ee : 93-98



Yield : 84 - 92 %

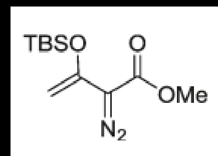
❑ THEY FOUND AND ISOLATED AN INTERMEDIATE



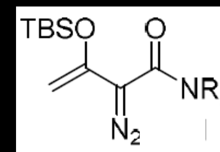
[Cu]	conversion of **1a**	**7a**
$Cu(MeCN)_4BF_4$/**6**	>95%	observed by ^1H NMR

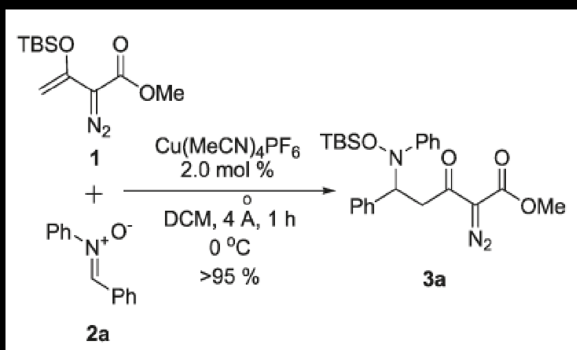
❑ THEY HIGHLIGHT A DIFFERENT OF REACTIVITY

ENOLDIAZOACETATE

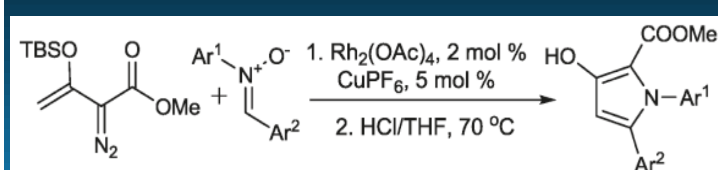


ENOLDIAZOACETAMIDE





VS



VS