TRANSITION METAL-CATALYZED METHODOLOGIES FOR THE SYNTHESIS OF COMPLEX AMIDE BUILDING BLOCKS

Thesis by

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For Jessie

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ABSTRACT

Amides are ubiquitous functional groups that play a critical role in the composition and function of many biologically active molecules. Herein, this thesis presents three novel methodologies toward the construction of small molecules bearing amide functionality. In the first chapter, a convergent Ni-catalyzed N–N cross-coupling for the synthesis of hydrazides is described. This reaction constitutes the first example of a transition metal-catalyzed N–N bond forming reaction compatible with a wide array of aliphatic amine nucleophiles. In the second chapter, an enantioselective α-vinylation of γ-lactams is presented. In the third chapter, a novel, enantioselective spirocyclization of Pd-enolates intercepted under decarboxylative allylic alkylation conditions is disclosed. Finally, in the last appendices, we present a revised and expedient route toward the bis-THIQ natural product scaffold and describe the synthesis of some non-natural analogs.

PUBLISHED CONTENT AND CONTRIBUTIONS

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LIST OF ABBREVIATIONS

$[\alpha]_D$	specific rotation at wavelength of sodium D line
ºC	degrees Celsius
Å	Angstrom
Aq	aqueous
Ar	aryl
atm	atmosphere
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
bp	boiling point
br	broad
Bz	benzoyl
c	concentration for specific rotation measurements
calc'd	calculated
cm^{-1}	wavenumer(s)
d	doublet
D	deuterium
dba	dibenzylideneacetone
DMF	*N,N*-dimethylformamide
dr	diastereomeric ratio
ee	enantiomeric excess
equiv	equivalent(s)

ESI	electrospray ionization
Et	ethyl
EtOAc	ethyl acetate
G	grams
GC	gas chromatography
h	hours
HPLC	high-performance liquid chromatography
HRMS	high-resolution mass spectrometry
Hz	hertz
IPA	isopropanol
IR	infrared (spectroscopy)
J	coupling constant (NMR), exchange coupling constant (diradicals)
kcal	kilocalorie
KHMDS	potassium hexamethyldisilazide
L	liter; ligand
LDA	lithium diisopropylamide
m/z	mass to charge ratio
Me	methyl
mg	milligram(s)
MHz	megahertz
min	minutes
mol	mole(s)
n-Bu	*n*-butyl

NHC	*N*-heterocyclic carbene
NMR	nuclear magnetic resonance
Pd/C	palladium on carbon
Ph	phenyl
PHOX	phosphinooxazoline
ppm	parts per million
R	generic for any atom or functional groups
SCF	self-consistent field
SFC	supercritical fluid chromatography
THIQ	tetrahydroisoquinoline