

Dipartimento di Chimica Organica "A. Mangini"
Università di Bologna

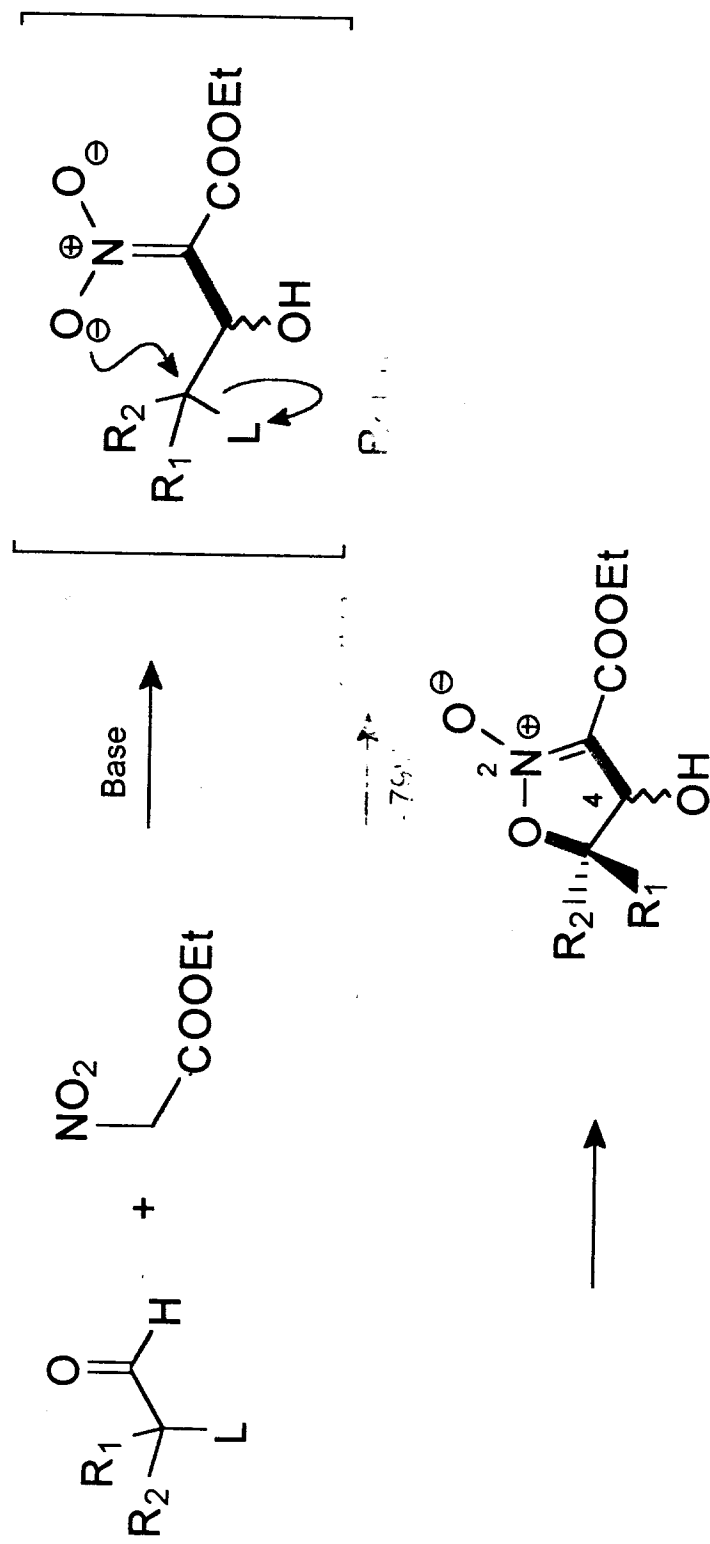
Functionalized Nitroalkanes in the Synthesis of Organic Biomodulators through a Domino Process.

The Progress of an Idea towards Amino Polyols

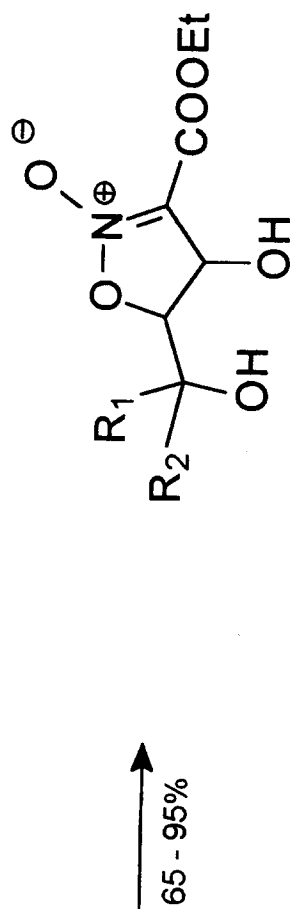
Goffredo Rosini

Ischia Advanced School of Organic Chemistry

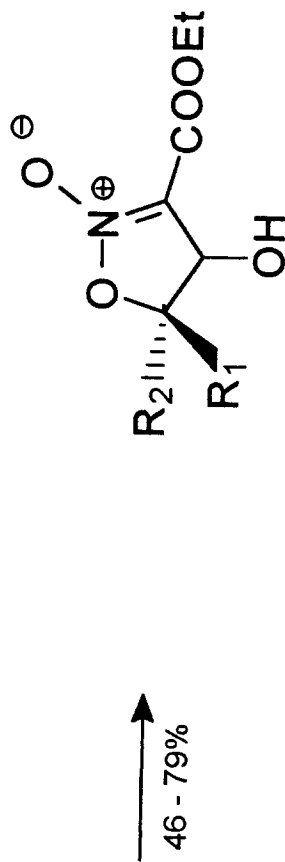
A stereoselective tandem process



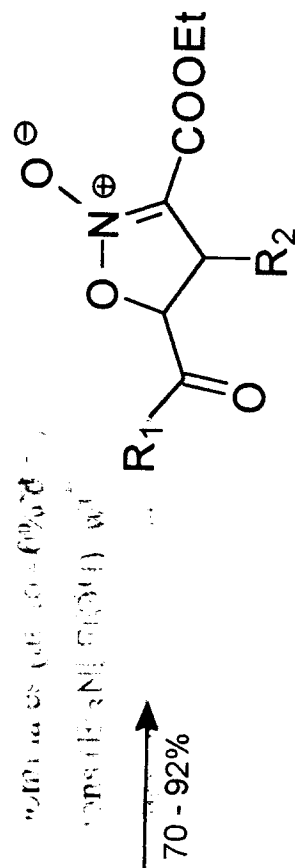
A general reaction



J. Org. Chem. 1990 , 55, 781.

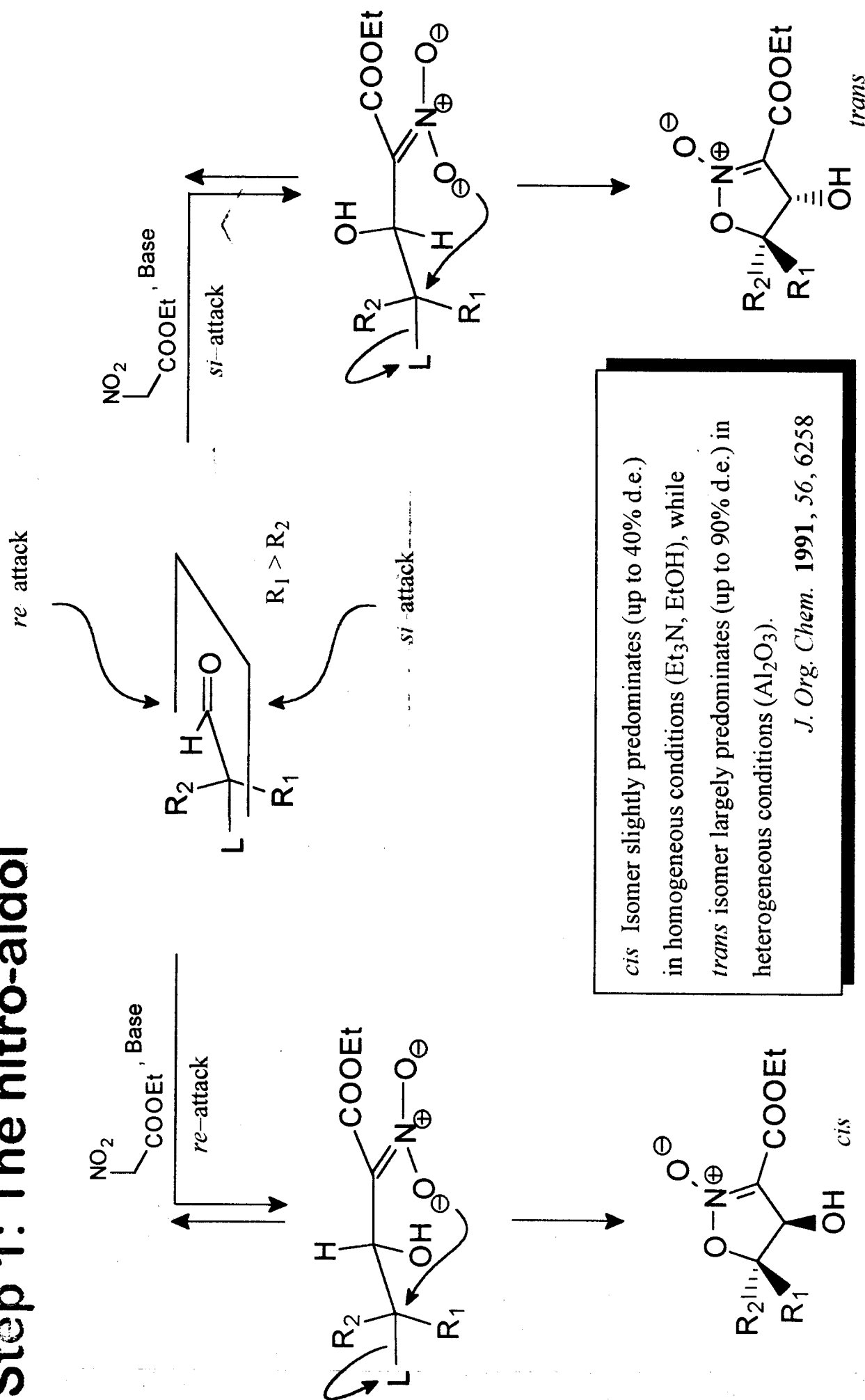


J. Org. Chem. 1991 , 56, 6258.

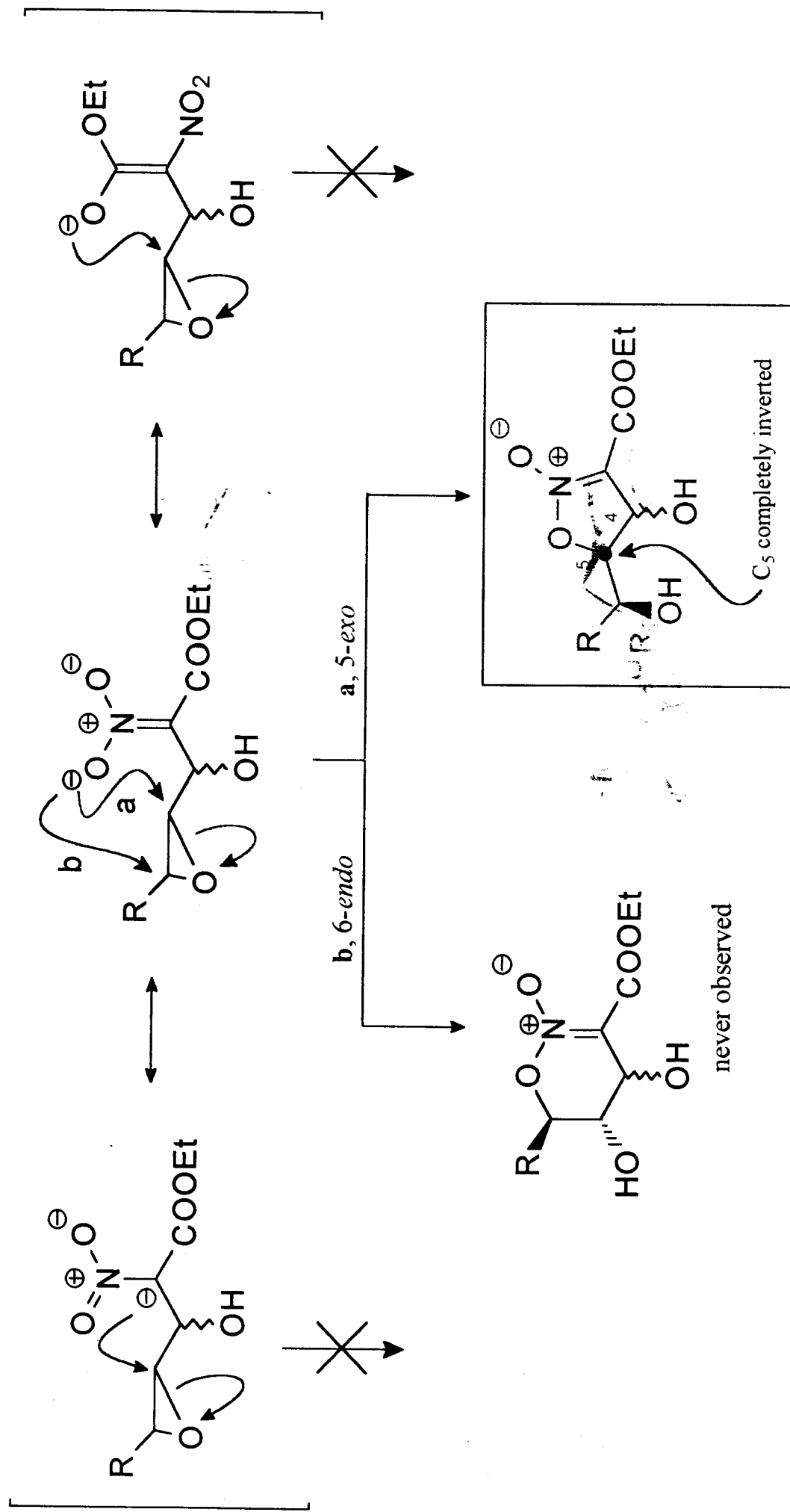


J. Org. Chem. 1995 , 60, 6624.

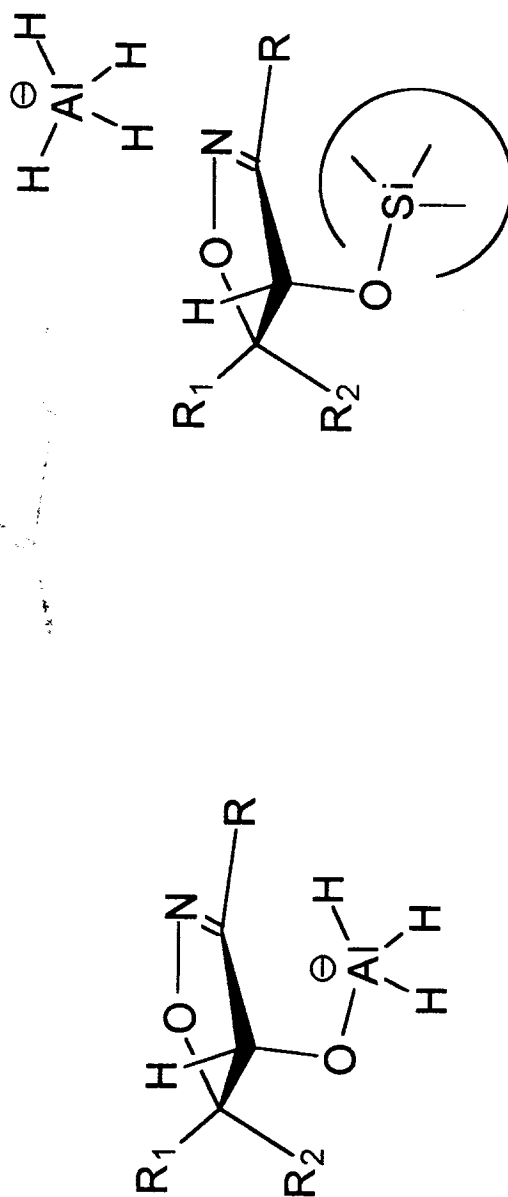
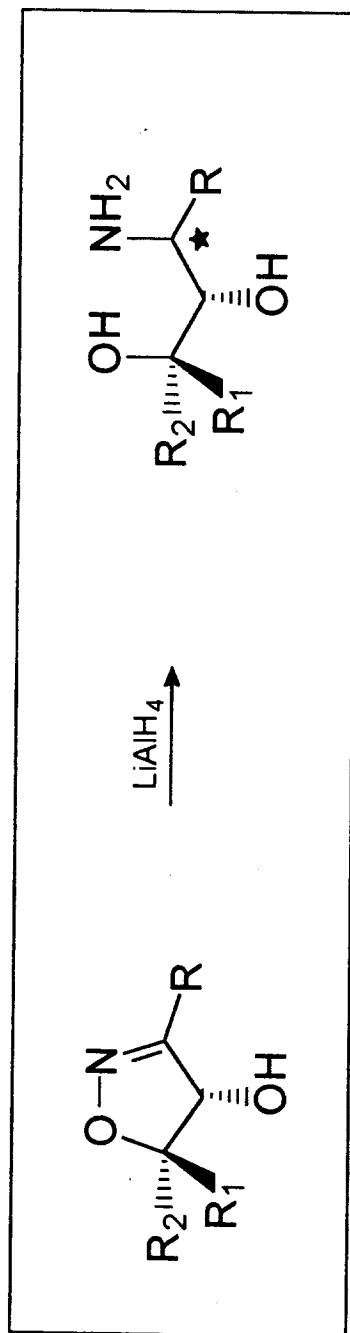
Step 1: The nitro-aldol



Step 2: The intramolecular ring closure

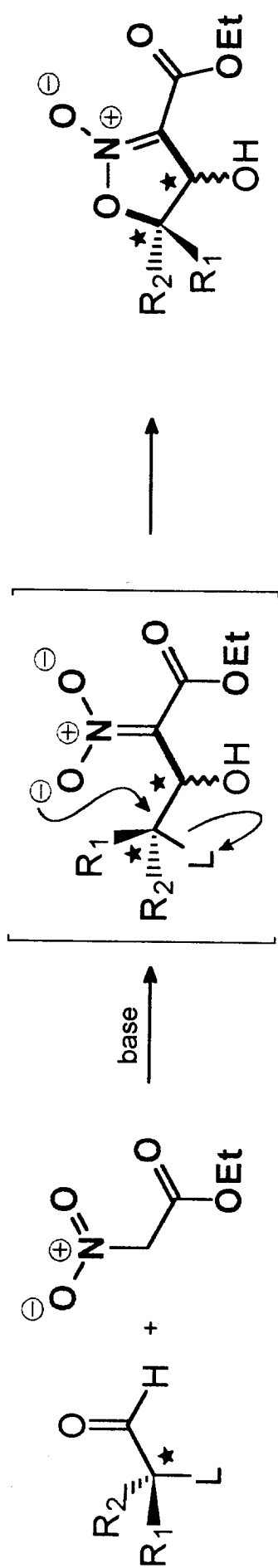


Stereoselective reductive ring-opening of 2-isoxazolines

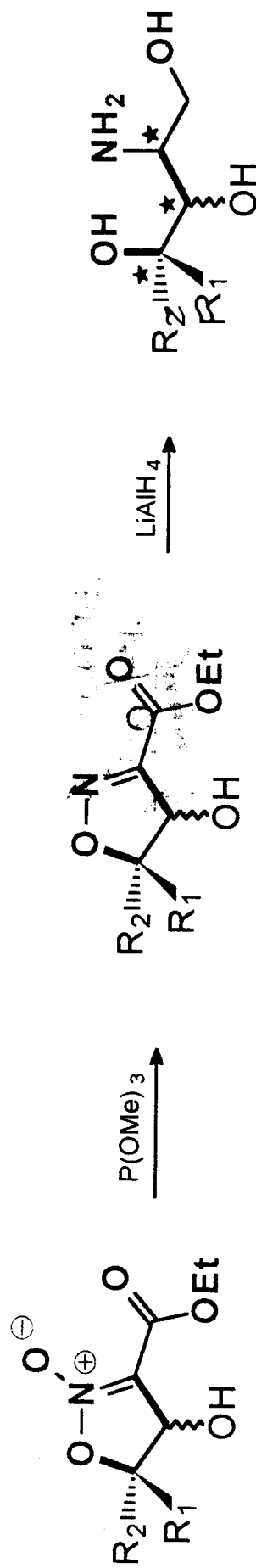


Jäger, V. et al. *Angew. Chem., Int. Ed. Engl.* **1981**, 20, 601.

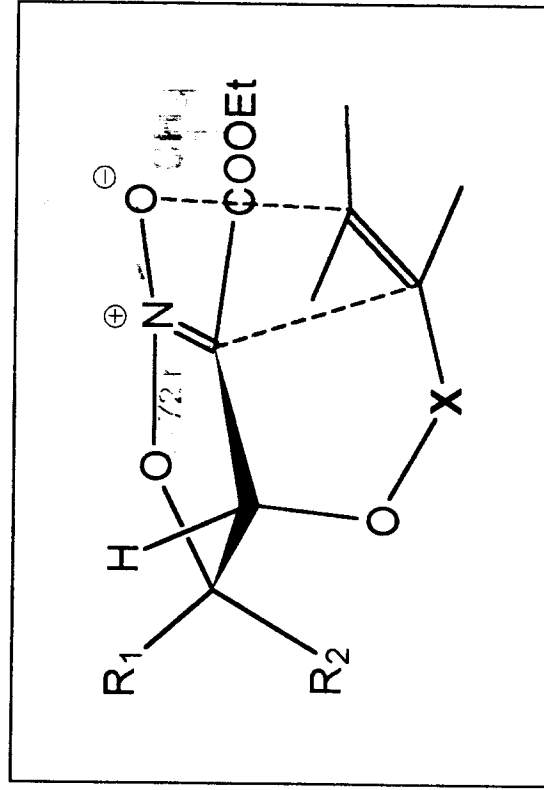
“Folding”



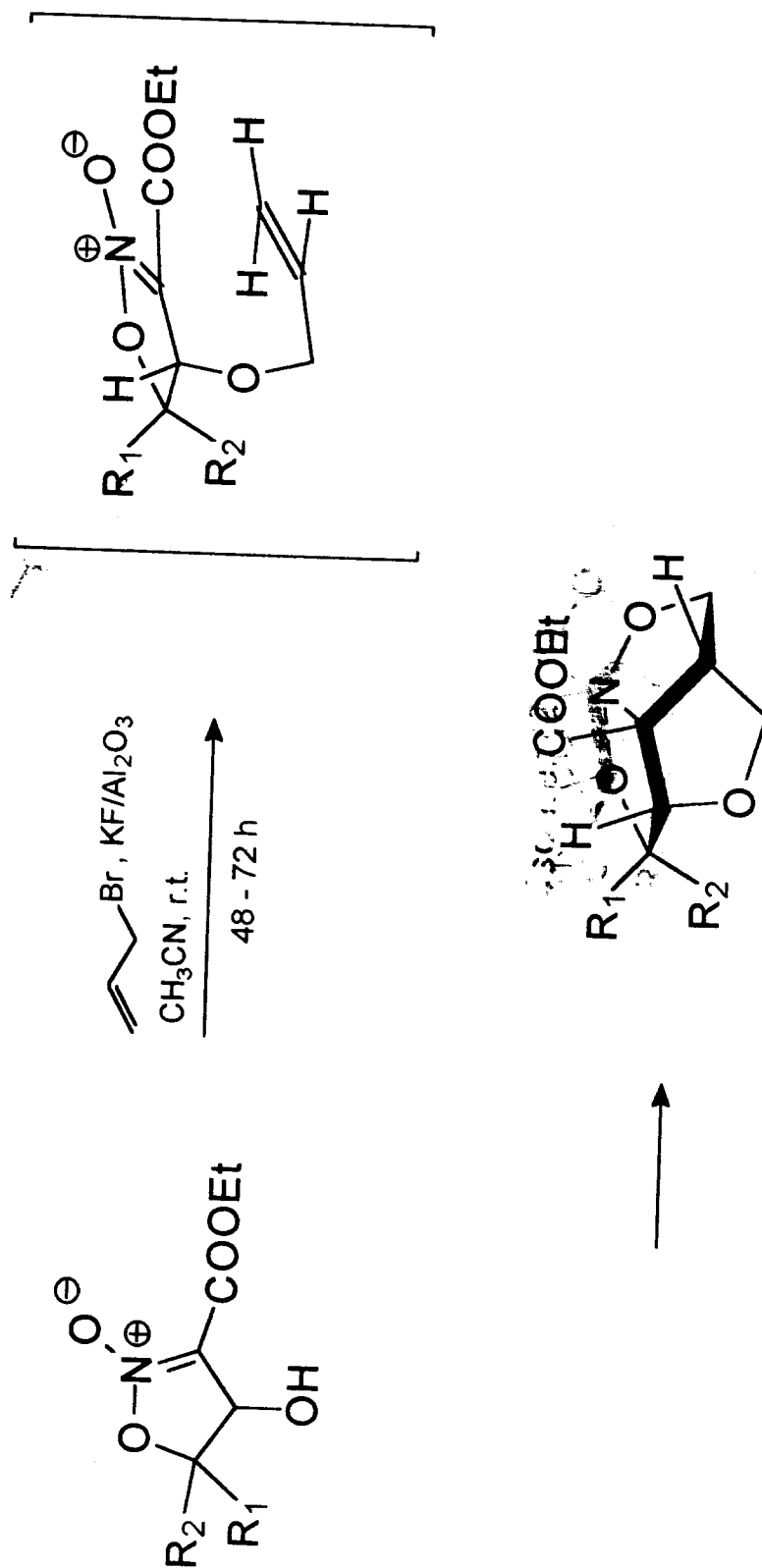
“Unfolding”

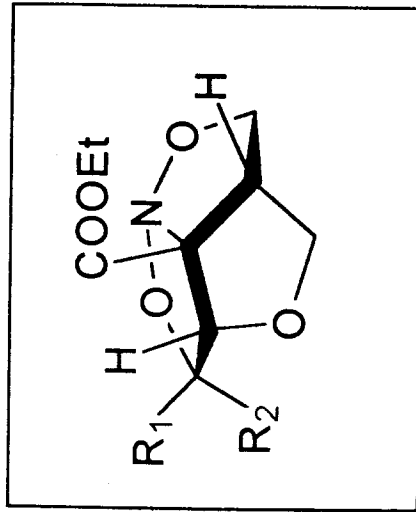


An intramolecular 1,3-dipolar cycloaddition



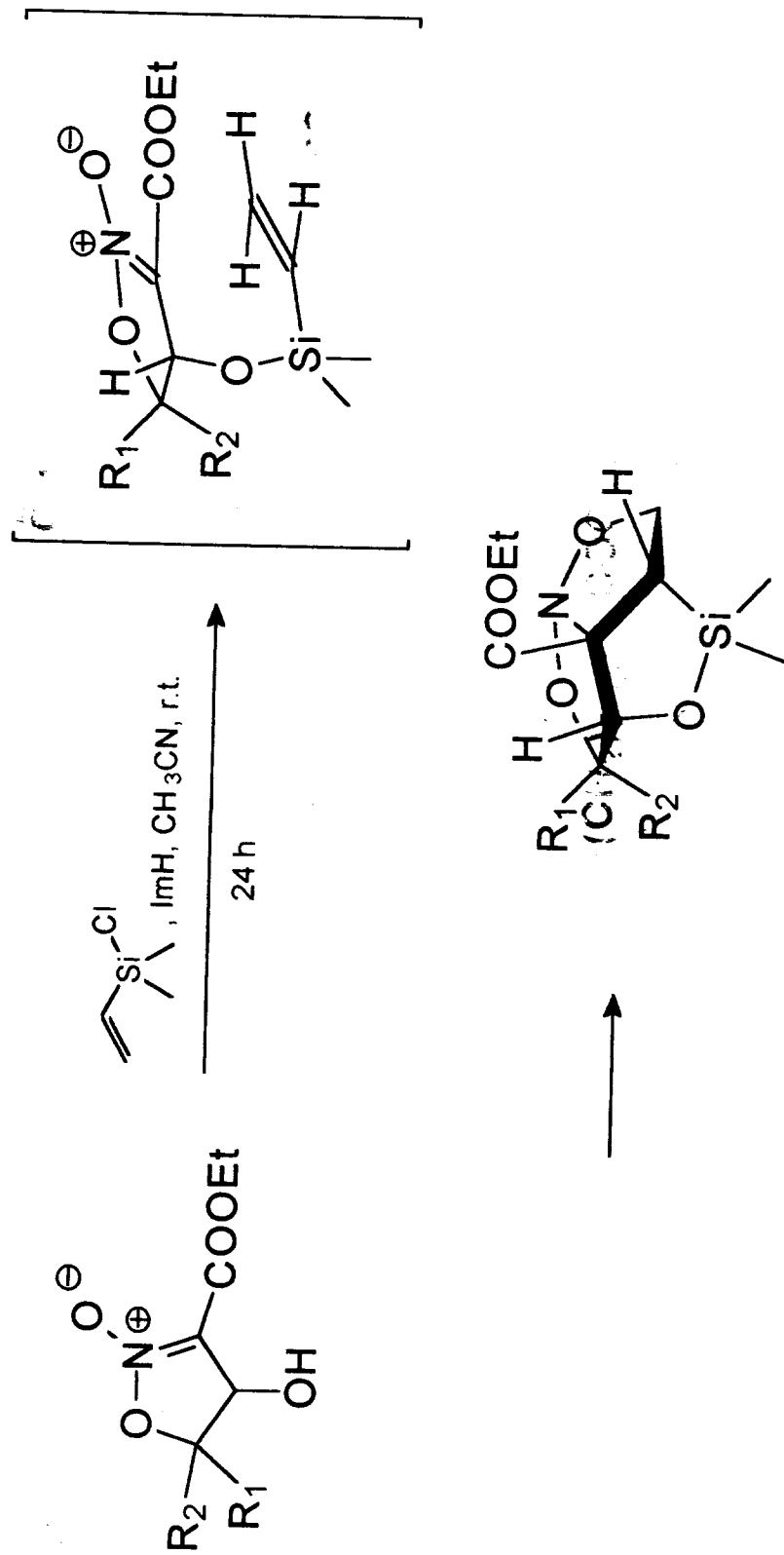
A new tandem process

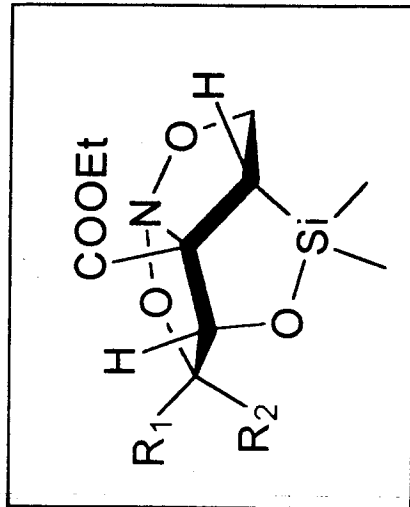




R ₁	R ₂	Yield (%)
H		62
Ph		66
<i>n</i> -C ₁₂ H ₂₅ + <i>cis</i> isomer (2 : 1)	H	84
	—(CH ₂) ₅ —	74
CH ₃	CH ₃	91

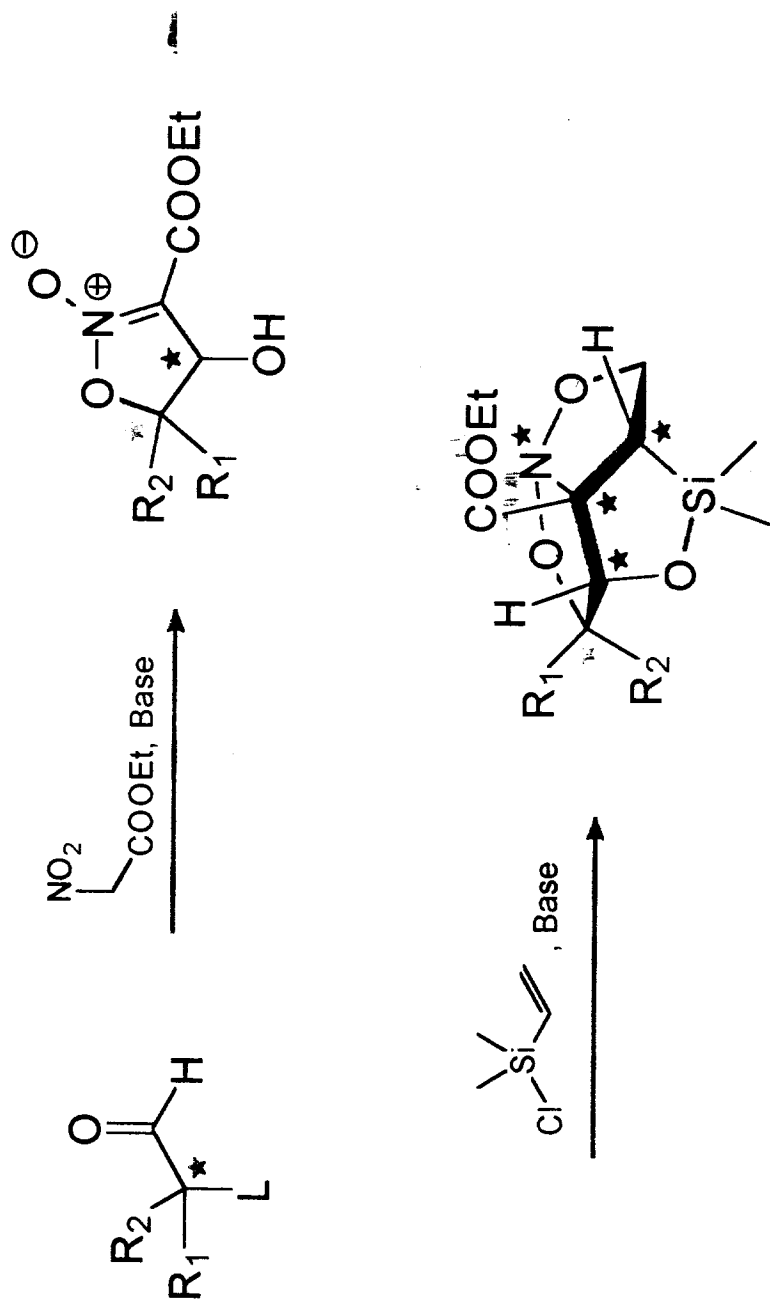
The first silicon-tethered 1,3-dipolar cycloaddition



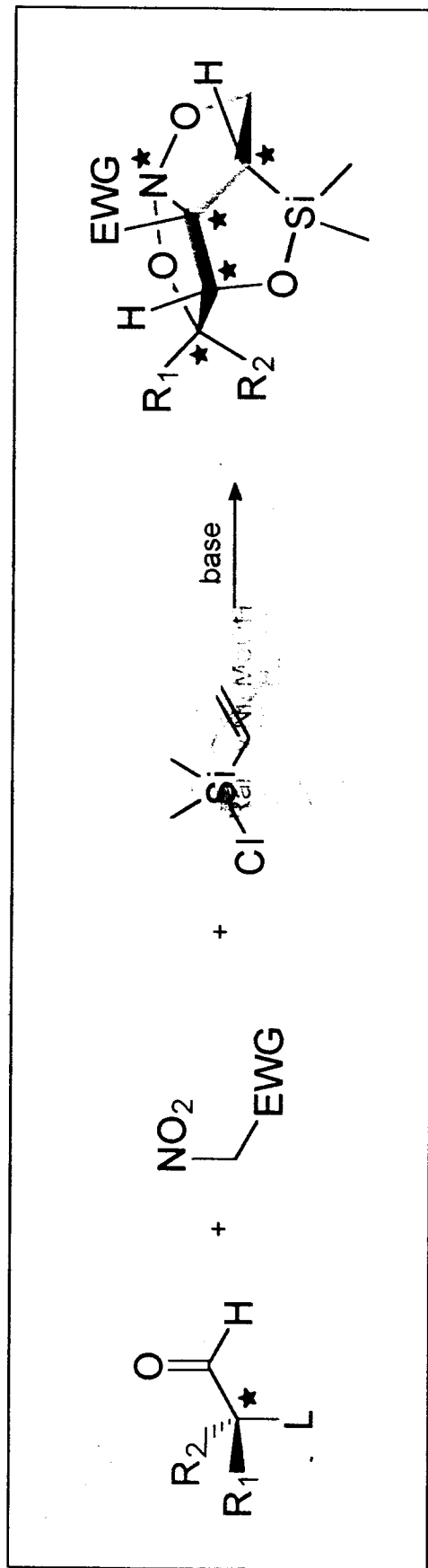


R ₁	R ₂	Yield (%)
H		95
	H	>99
Ph		99
<i>n</i> -C ₁₂ H ₂₅ + <i>cis</i> isomer (2 : 1)	H	79
—(CH ₂) ₅ —		>99
CH ₃	CH ₃	96
CH ₃ CH ₂	CH ₃ CH ₂	95
Bu + <i>cis</i> isomer (5 : 1)	H	97

Two consecutive and mild tandem processes

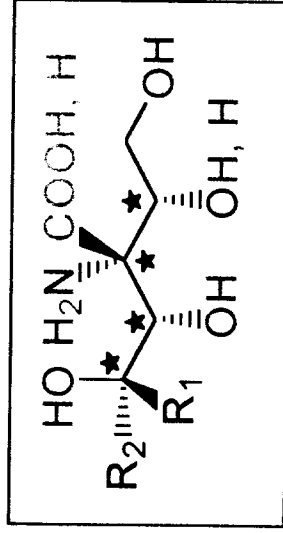
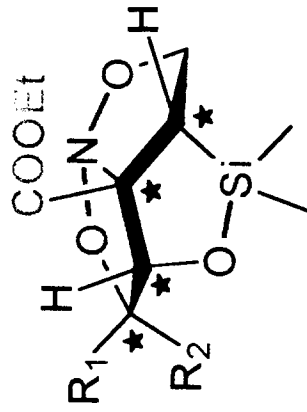


A Domino Process

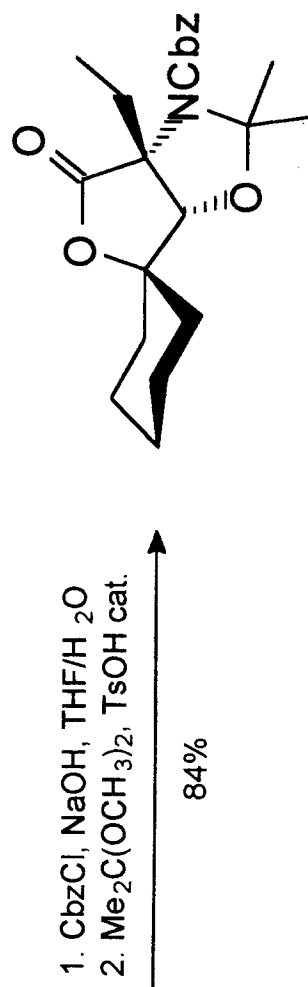
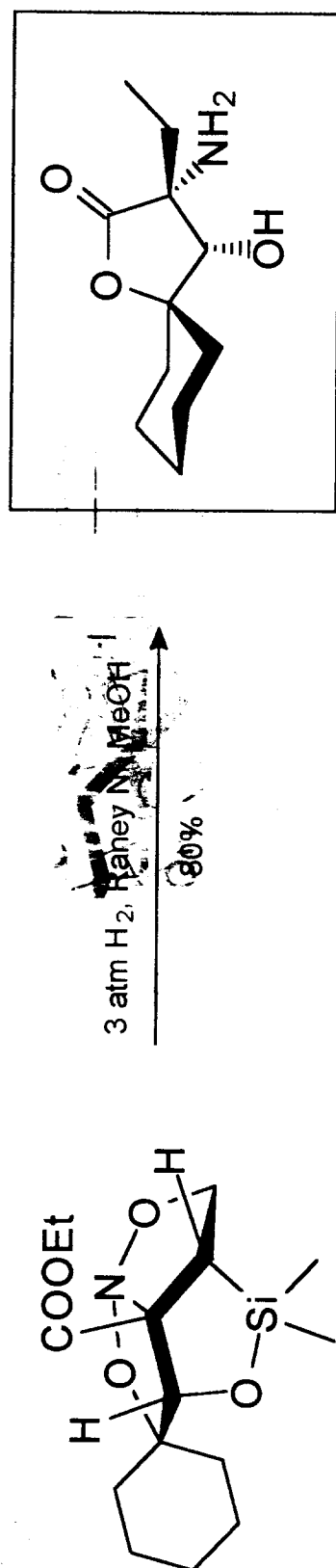


R ₁	R ₂	L	EWG	Yield (%)
C ₁₂ H ₂₅	H	Br	COOEt	61
+ enantiomer				
CH ₃	H	OTs	COOEt	66
CH ₃	H	OTs	SO ₂ Ph	76

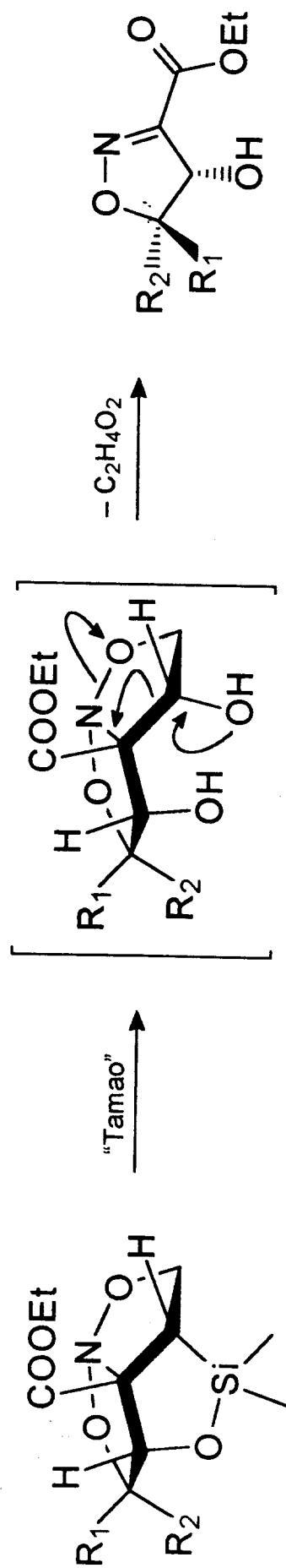
The unfolding of the tricycle



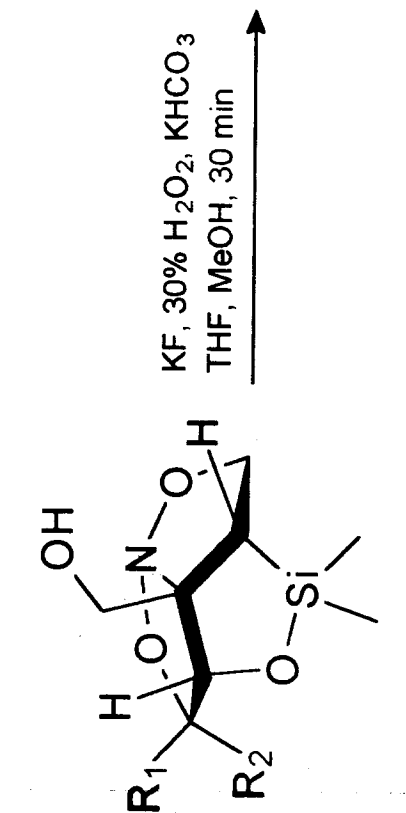
The first attempt of unfolding



Tamao oxidation of the tricyclic system



R_1	R_2	Yield
Me	Me	82
$-(CH_2)_5-$		89
Bu	H	77
H	Bu	70



Yield (%)

R₂

R₁

94

Me

Ph

88

Et

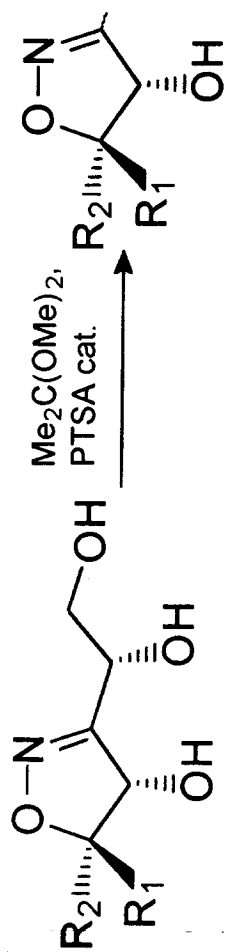
Et

95

H

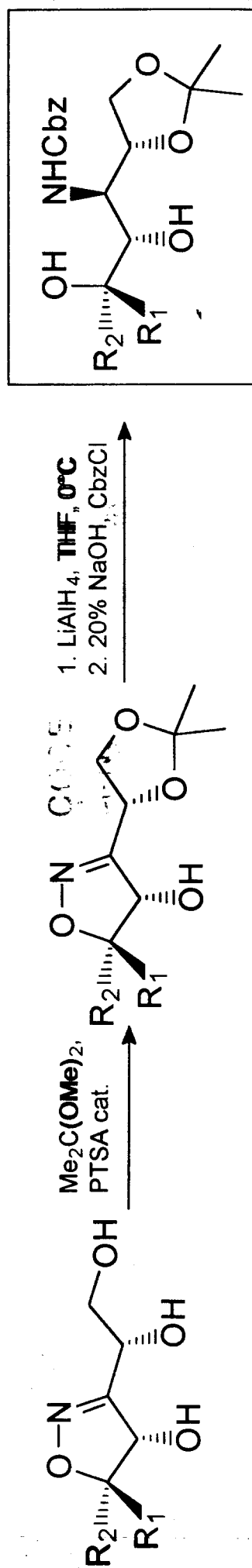
n-C₁₂H₂₅

Synthesis of amino pol

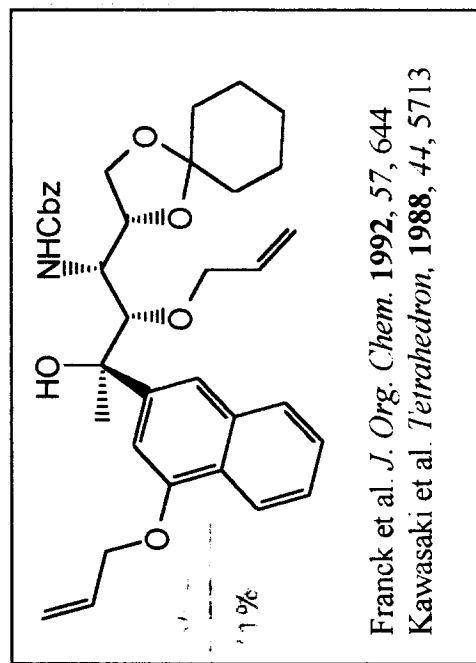


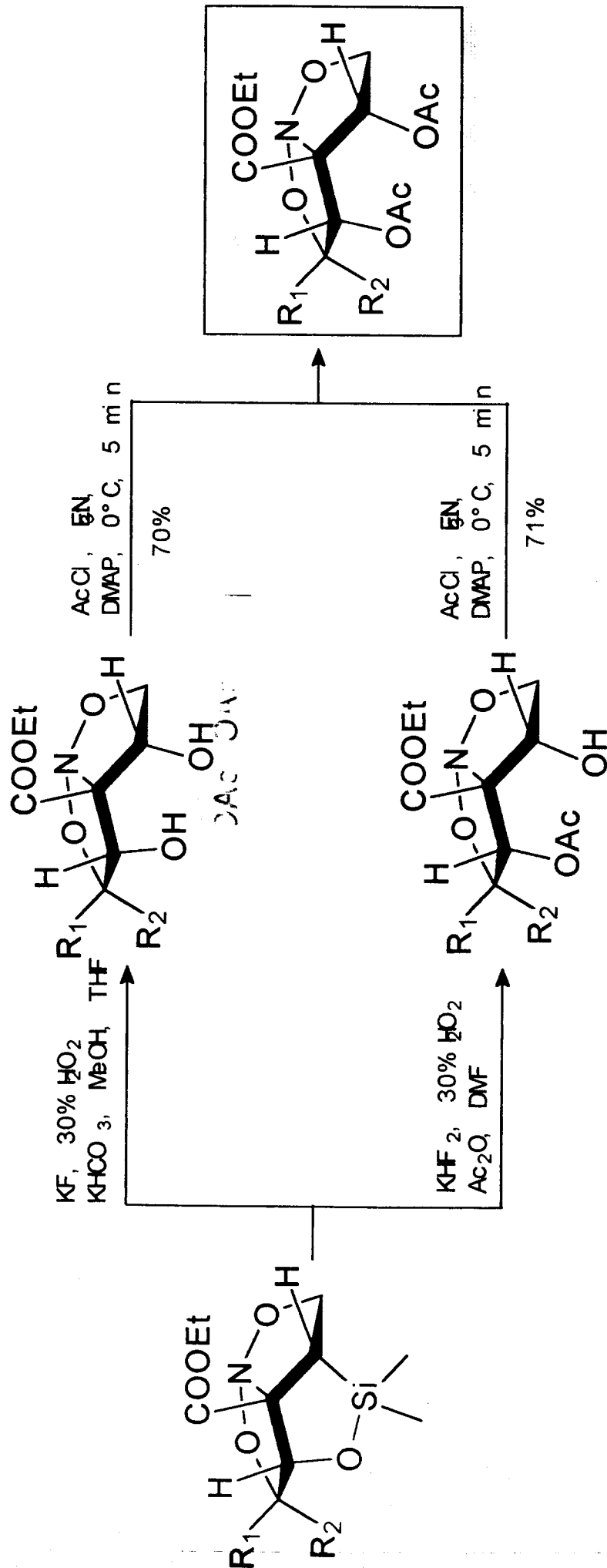
R ₁	R ₂	Time (h)	Yield (%)
Ph	Me	1	71
Et	Et	0.75	72
n-C ₁₂ H ₂₅	H	1	74

Synthesis of amino polyhydroxylated compounds

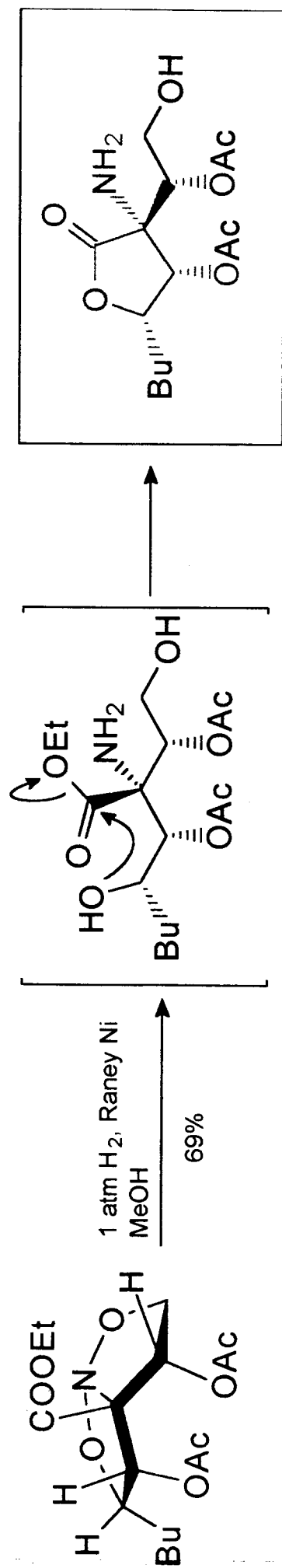


R_1	R_2	Time (h)	Yield (%)
Ph	Me	1	71
Et	Et	0.75	72
$n\text{-C}_{12}\text{H}_{25}$	H	1	74

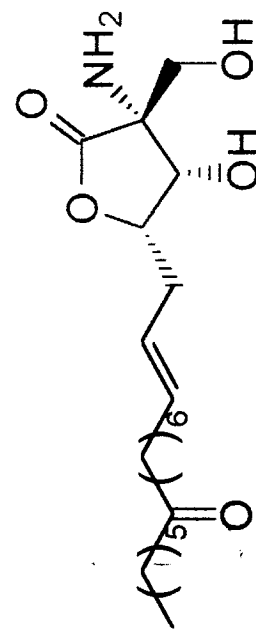




Synthesis of polyhydroxylated aminoacid derivatives



J. Am. Chem. Soc. **1996**, 118, 0000

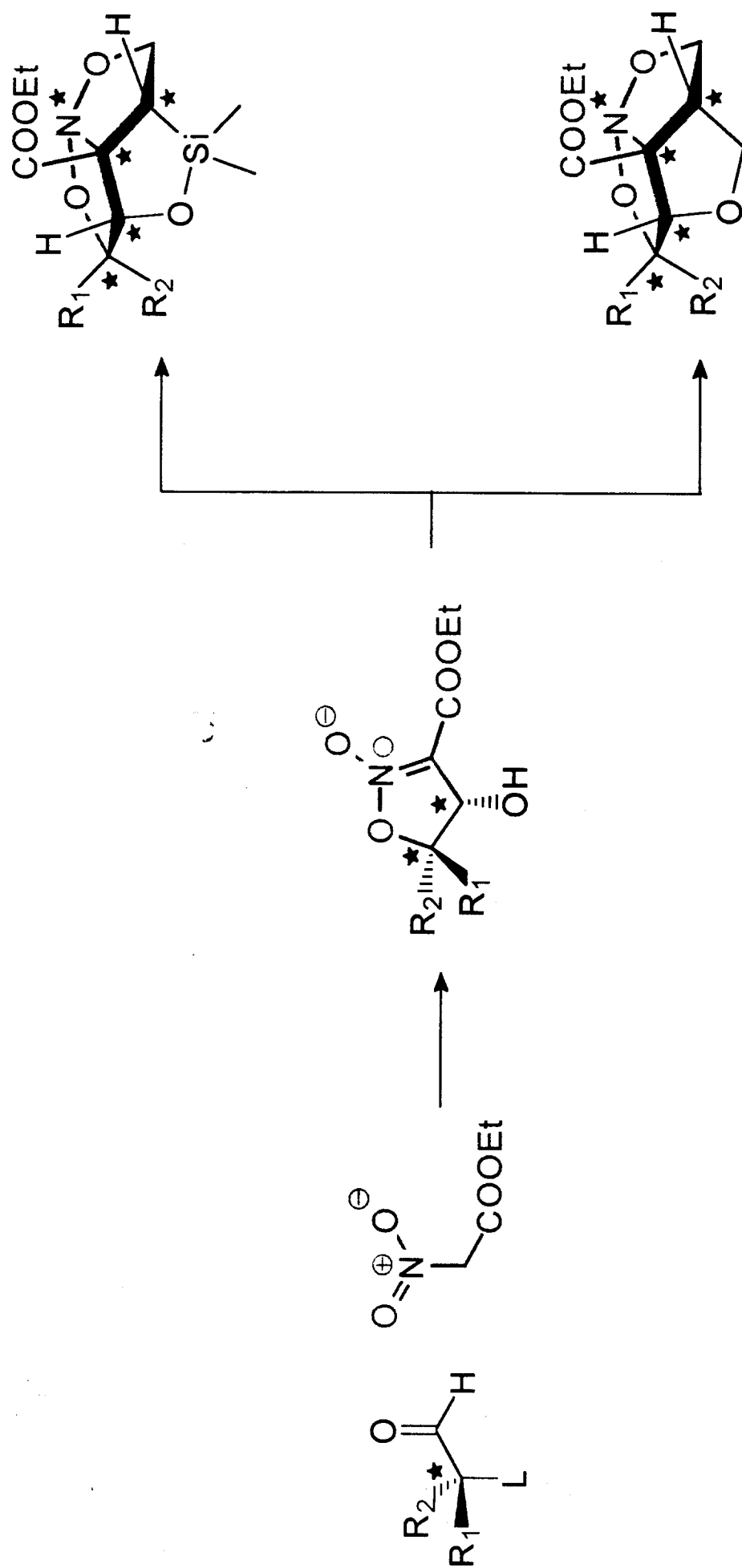


Myriocin γ -lactone: a potent immunosuppressant

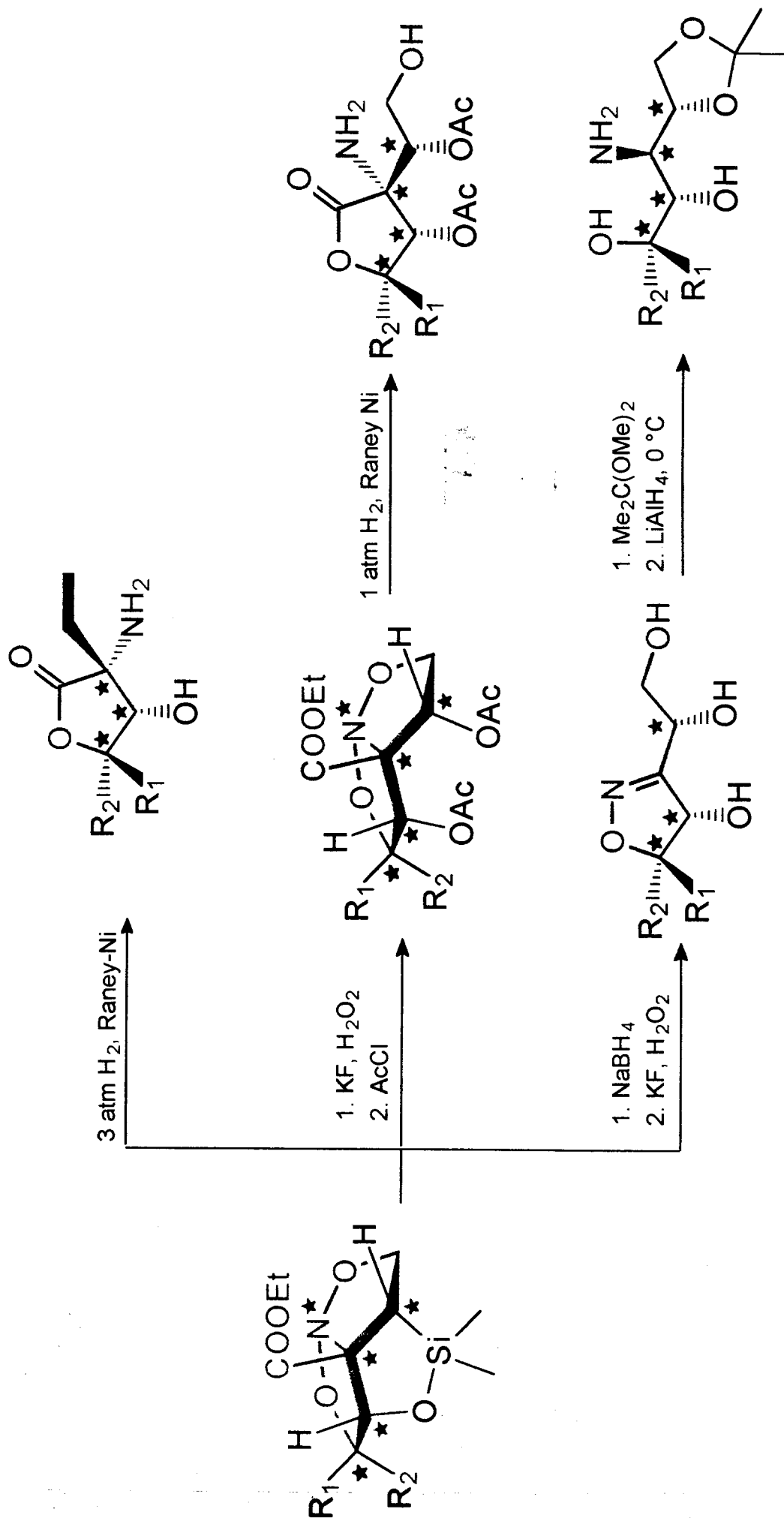
Yoshikawa et al. *Tetrahedron* **1995**, 51, 6209

Nagao et al. *Tetrahedron Lett.* **1995**, 36, 2097

The "folding"



The "unfolding"



Acknowledgements

Dr. Emanuela Marotta, Dr. Paolo Righi

Synthesis of 2-Isoxazolines 2-Oxides:

- from α,β -epoxy aldehydes (1990-1992)

Dr. Roberta Galarini

Dr. Giuseppe Martelli

Dr. Andrea Tasso

from 2-bromo aldehydes (1990-1991)

Dr. Jean-Paul Seerden

from 2-bromo enones (1994)

Dr. Carmela Galli

from α -hydroxy aldehydes (1996)

Luigi Maini

Folding of the Tricyclic Compounds (1995-1996)

Dr. Andrea Landuzzi

Paolo Francesco Campo

Unfolding of the Tricyclic Compounds (1996-)

Dr. Camillo Tartaglia



Alma Mater Studiorum
Università di Bologna



This work was supported by research grants from the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (MURST), Italy, the Consiglio Nazionale delle Ricerche (CNR), Italy and by the University of Bologna (Progetto d'Ateneo: Biomodulatori Organici: Sintesi, Proprietà ed Applicazioni).