N-Heterocyclic Carbene-Catalyzed (4 + 2) Cycloaddition/ Decarboxylation of Silyl Dienol Ethers with a,β-Unsaturated Acid Fluorides

Sarah J. Ryan, Lisa Candish, and David W. Lupton*

School of Chemistry, Monash University, Clayton 3800, Victoria, Australia

dx.doi.org/10.1021/ja111067j

David W. Lupton
Lecture?
School of Chemistry
Monash University
Australia

Education:

Sep. 2005 - Jan. 2007 **Postdoctoral Research Fellow, Department of Chemistry** Stanford University, CA, USA. Supervisor: **Professor Barry M. Trots**

June 2001 – Jan. 2005 **Doctorate of Philosophy** Research School of Chemistry, Australian National University, ACT, Australia. Supervisor: Professor **Martin G. Banwell**

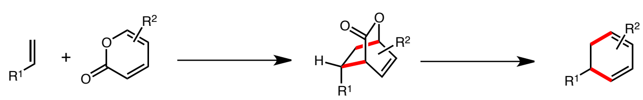
Mar. 2000 – Nov. 2000 **Bachelor of Science (Honours 1st)** University of Adelaide, SA, Australia. Supervisor: Professor **Dennis K. Taylor**

Research Interest:

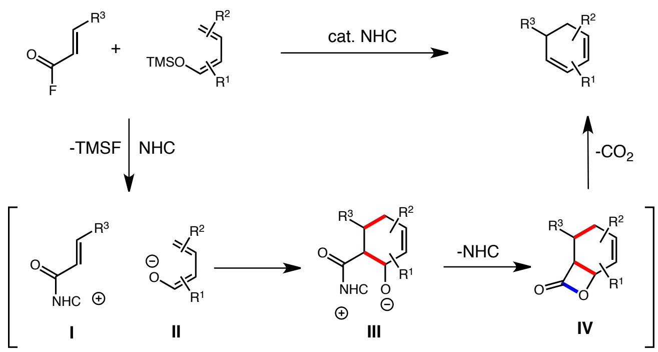
Catalytic Methodologies and Total synthesis

N-Heterocyclic Carbene-Catalyzed Generation of a,b-Unsaturated Acyl Imidazoliums: Synthesis of Dihydropyranones by their Reaction with Enolates Sarah J. Ryan, Lisa Candish, David W. Lupton
J. Am. Chem. Soc., 2009, 131, 14176

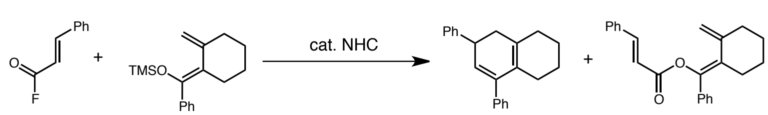
Pyrone Diels-Alder/Decarboxylation



Proposed Transformation in the Paper

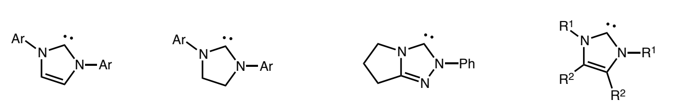


Optimization of reaction conditions



a **b**

Entry	cat. (mol%)	base/solvent	**a**:**b**	yield of **a** (%)
1	**A_1** (20)	KO^{t}Bu/Toluene	3:1	13
2	**A_1** (10)	KO^{t}Bu/THF	>95:5	70
3	**A_1** (10)	THF	77:23	44
4	**A_2** (10)	KO^{t}Bu/THF	3:1	48
5	**B** (10)	KHMDS/THF	-	10
6	**C** (10)	KHMDS/THF	-	trace
7	**D_1** (10)	KHMDS/THF	-	-
8	**D_2** (10)	THF	>95:5	76



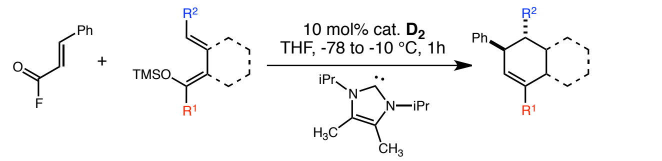
A_1: Ar=2,4,6-$(CH_3)_3C_6H_2$
A_2: Ar=2,6-(i-Pr)$_2C_6H_3$

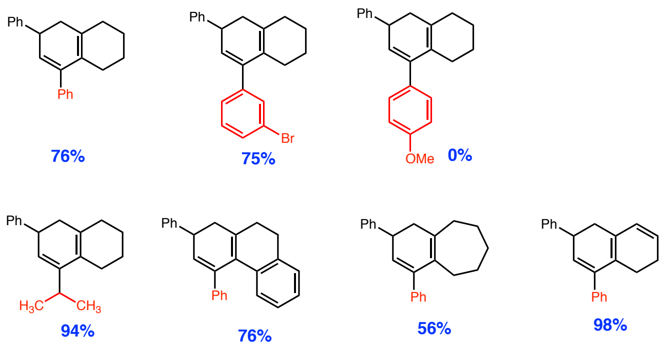
B: Ar=2,4,6-$(CH_3)_3C_6H_2$

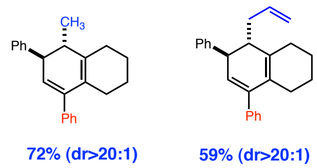
C

D_1: R_1=CH_3, R_2=-$(CH)_4$-
D_2: R_1=i-Pr, R_2=CH_3

Substrate scope in regard to silyl dienol ether:

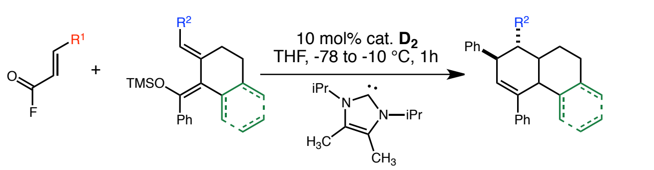


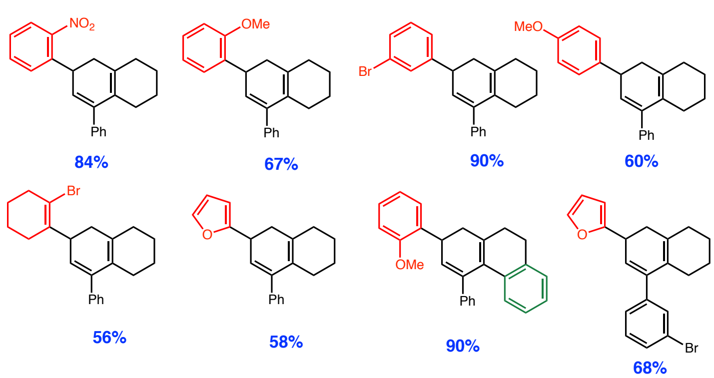


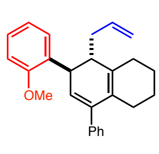


good yields when R^1 = Electron-poor Ar, alkyl groups
poor substrates when R^1 = Electron-rich Ar, acyclic dienolates
Alkyl groups at R^2 gave high diastereoselectivities

Substrate scope in regard to acyl fluoride:

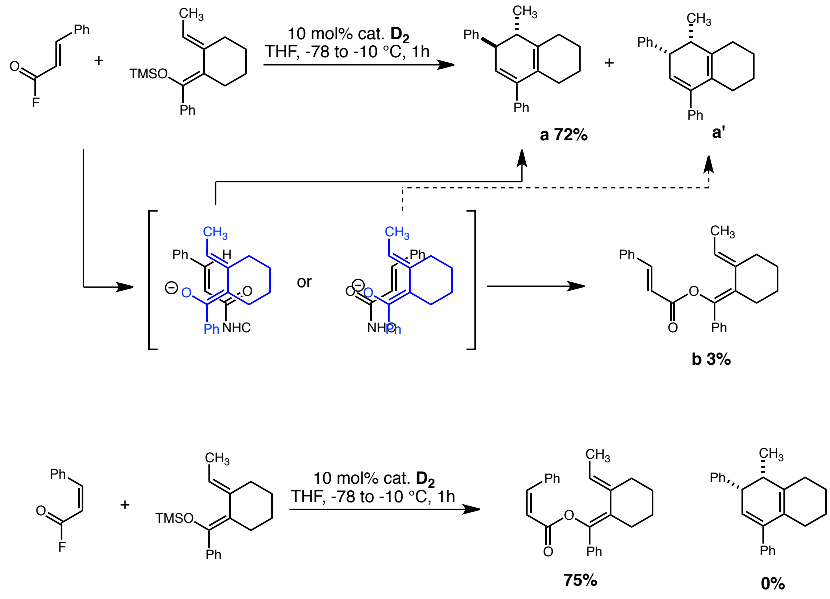






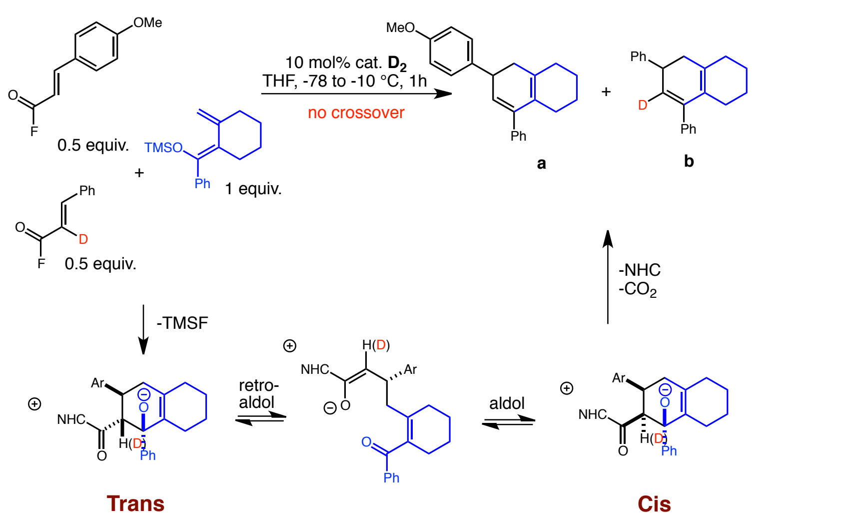
Good for electron-rich, electron-poor aromatic, and olefinic groups

Mechanistic rationale: **endo selective 4+2 cycloaddition**



KIE analysis indicates a concerted reaction mechanism

Crossover Studies: **an intermolecular proton transfer process or retro-aldol/aldol sequence?**



Answer: **no scrambling of the deuterium-----> retro-aldol/aldol sequence**

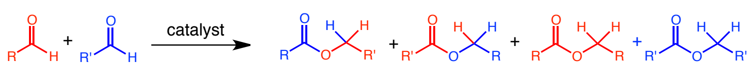
Nickel-Catalyzed Selective Conversion of Two Different Aldehydes to Cross-Coupled Esters

Yoichi Hoshimoto,† Masato Ohashi,†,‡ and Sensuke Ogoshi*,†

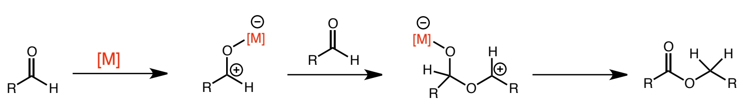
Department of Applied Chemistry, Faculty of Engineering, and ‡Center for Atomic and Molecular Technologies, Osaka University, Suita, Osaka 565-0871, Japan

dx.doi.org/10.1021/ja109908x

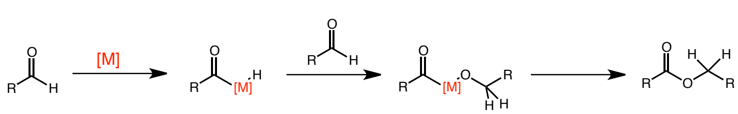
Tishchenko reaction



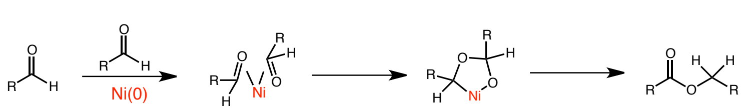
Lewis acid catalyzed reaction via oxygen-metal interaction



Transition metal catalyzed hydroacylation of aldehyde via carbon-hydrogen bond activation

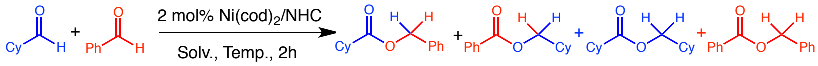


Nickel catalyzed reaction vis η2 coordination of two aldehydes at the same time



Homocoupling of aliphatic aldehydes is faster than that of aryl aldehydes------>
Selective crossed Tishchenko reation ???

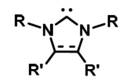
Optimization of reaction conditions



A^1 **B^1** **A^{1}B^1** **B^{1}A^1** **A^{1}A^1** **B^{1}B^1**

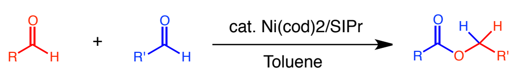
Entry	NHC	Solv.	Temp. (°C)	A^{1}B^1 (%)	B^{1}A^1 (%)	A^{1}A^1 (%)	B^{1}B^1 (%)	Selectivity
1	IPrCl	Benzene	60	58	4	12	18	0.63
2	SIPr	Benzene	60	87	< 1	6	7	0.87
3	IPr	Toluene	60	86	< 1	6	7	0.86
4	IMes	Benzene	60	79	2	9	9	0.79
5[a]	ICy	Benzene	60	complicated mixture				-
6	SIPr	Toluene	23 (28 h)	80	< 1	6	8	0.85
7	SIPr	Toluene	40 (4 h)	94	< 1	2	4	0.94
8	SIPr	Toluene	50	90	< 1	3	7	0.90
9	SIPr	Toluene	80	78	< 1	6	11	0.82
10	SIPr	THF	50	88	< 1	6	6	0.88
11[b]	SIPr	1,4-Dioxane	50	37	< 1	1	4	0.88
12[b]	SIPr	EtOAc	50	8	-	< 1	2	0.80
13[b]	SIPr	Hexane	50	23	-	1	3	0.85
14[b]	SIPr	*o*-Xylene	50	13	-	< 1	2	0.87

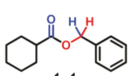
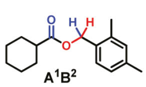
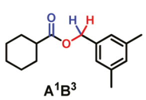
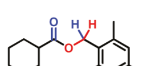
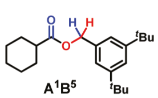
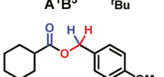
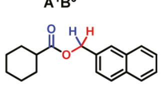
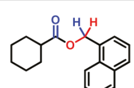
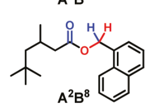
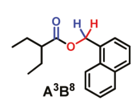
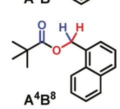
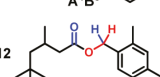
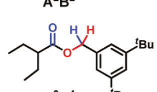
[a]Unidentified products were detected by GC.
[b]Benzoin condensation of B^1 proceeded.



IPrCl; R = 2,6-diisopropylphenyl, R' = Cl
SIPr; R = 2,6-diisopropylphenyl, R' = H_2 (saturated)
IPr; R = 2,6-diisopropylphenyl, R' = H
IMes; R = 2,4,6-trimethylphenyl, R' = H
ICy; R = cyclohexyl, R' = H

Exploration of substrate scope



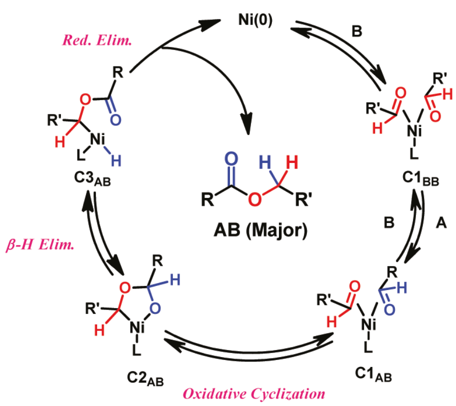
Entry	AB	Condition[b]	Conv. of B[c] (%)	Yield[d] (%)	Selectivity[c]
1	 A^{1}B^1	2/40/4	> 99	94(84)	0.94
2	 A^{1}B^2	4/40/4	> 99	92(88)	0.92
3	 A^{1}B^3	2/40/4	> 99	94(85)	0.94
4	 A^{1}B^4	4/40/4	89	57	0.64
5	 A^{1}B^5	2/40/4	> 99	89(81)	0.89
6	 A^{1}B^6	2/40/4	> 99	87(82)	0.87
7	 A^{1}B^7	4/50/2	98	92(83)	0.94
8	 A^{1}B^8	2/50/2	66	64(47)	0.98
9	 A^{2}B^8	4/50/2	61	61(66)	> 0.99
10[e]	 A^{3}B^8	10/23/12	81	75(65)	0.93
11[f]	 A^{4}B^8	10/23/12	83	73(65)	0.94
12	 A^{2}B^2	4/40/4	90	82(66)	0.94
13	 A^{3}B^4	4/40/4	> 99	88(83)	0.88

Trend: Aliphatic aldehyde be the carboxylic acid part, and the aryl aldehyde be the alcohol part
No crosscoupling were observed with p-Cl and p-NO2 substituted benzaldehydes.

Plausible mechanisms for the nickel-catalyzed crossed Tishchenko reaction

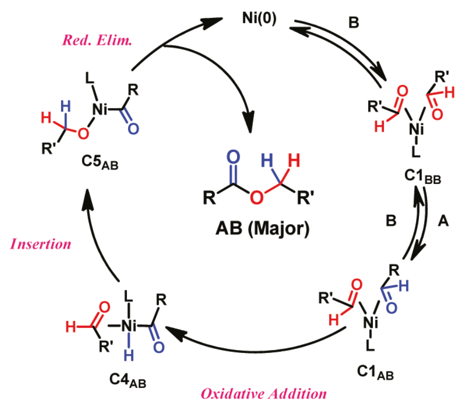
Electron-poor component coordinate to nickel(0) more efficiently due to backbonding

Path 2A



Supported by measurement of rate constant and KIE analysis

Path 2B



No decarbonylation was observed