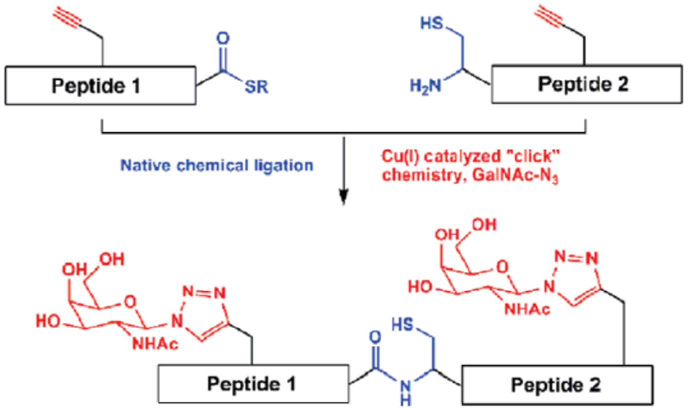
Literature Presentation

Pablo García-Reynaga

11/13/2009

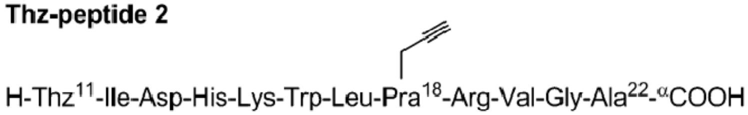
A One-Pot Approach to Neoglycopeptides using Orthogonal Native Chemical Ligation and Click Chemistry



Peptide-thioester 1

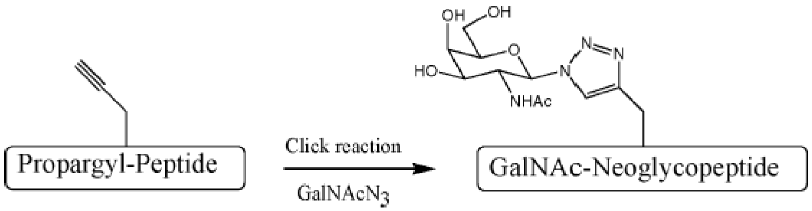

H$_2$N-Phe^{1}-Tyr-Pro-Asn-Gln-Thr-Met-Glu-Pra^{9}-Ser^{10}-$^{\alpha}$COSCH$_2$CH$_2$Ala

Thz-peptide 2


H-Thz^{11}-Ile-Asp-His-Lys-Trp-Leu-Pra^{18}-Arg-Val-Gly-Ala^{22}-$^{\alpha}$COOH

Cys-peptide 3


H$_2$N-Cys^{11}-Ile-Asp-Cys^{14}(Acm)-His-Lys-Trp-Leu-Pra^{19}-Arg-Val-Gly-Ala^{23}-$^{\alpha}$COOH



entry	peptide[a]	catalyst	solvent	temperature	time	product yield (%)[b]
1	3	20 mM CuI/30 mM DIEA	DMF	25 °C	>12 h	<40
2	3	20 mM CuSO$_4$/30 mM NaAsc	MeCN/H$_2$O 1:1	25 °C	4 h	>85
3	3	20 mM CuSO$_4$/30 mM TCEP	6 M GnHCl/0.2 M Na$_2$HPO$_4$, pH 7	25 °C	3 h	>95
4	1	20 mM CuSO$_4$/30 mM NaAsc	MeCN/H$_2$O 1:1	35 °C[c]	7 h	>85
5	1	20 mM CuSO$_4$/30 mM TCEP	6 M GnHCl/0.2 M Na$_2$HPO$_4$, pH 7	35 °C[c]	5 h	>95

[a] Reactions were performed on 3 mM concentration of peptide using GalNAc-N$_3$ (5 mM). [b] Based on integration of HPLC traces, not isolated. [c] No reaction was observed after 1 h at 25 °C, at which point the temperature was increased to 35 °C.

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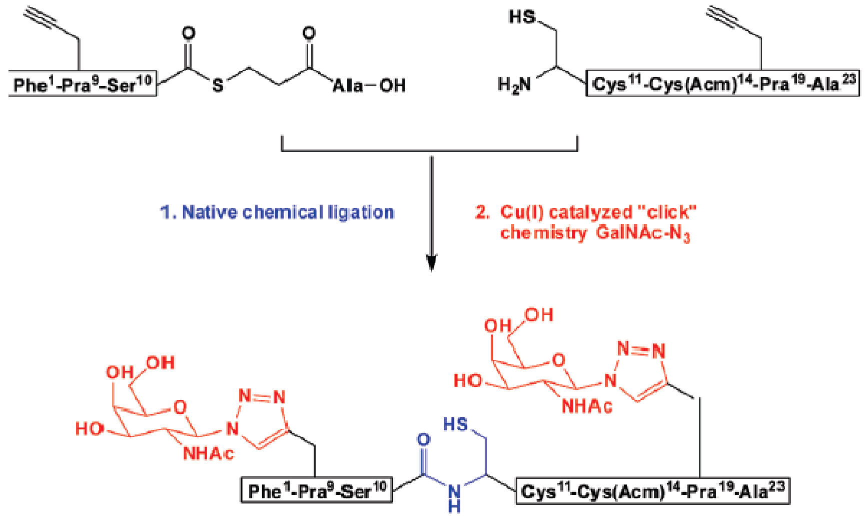
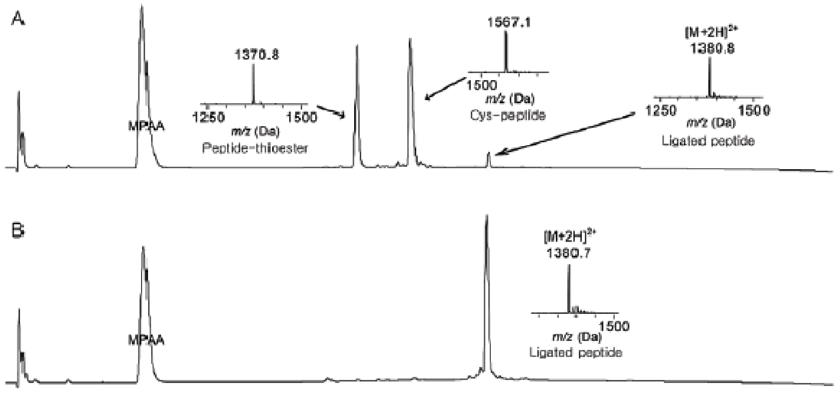
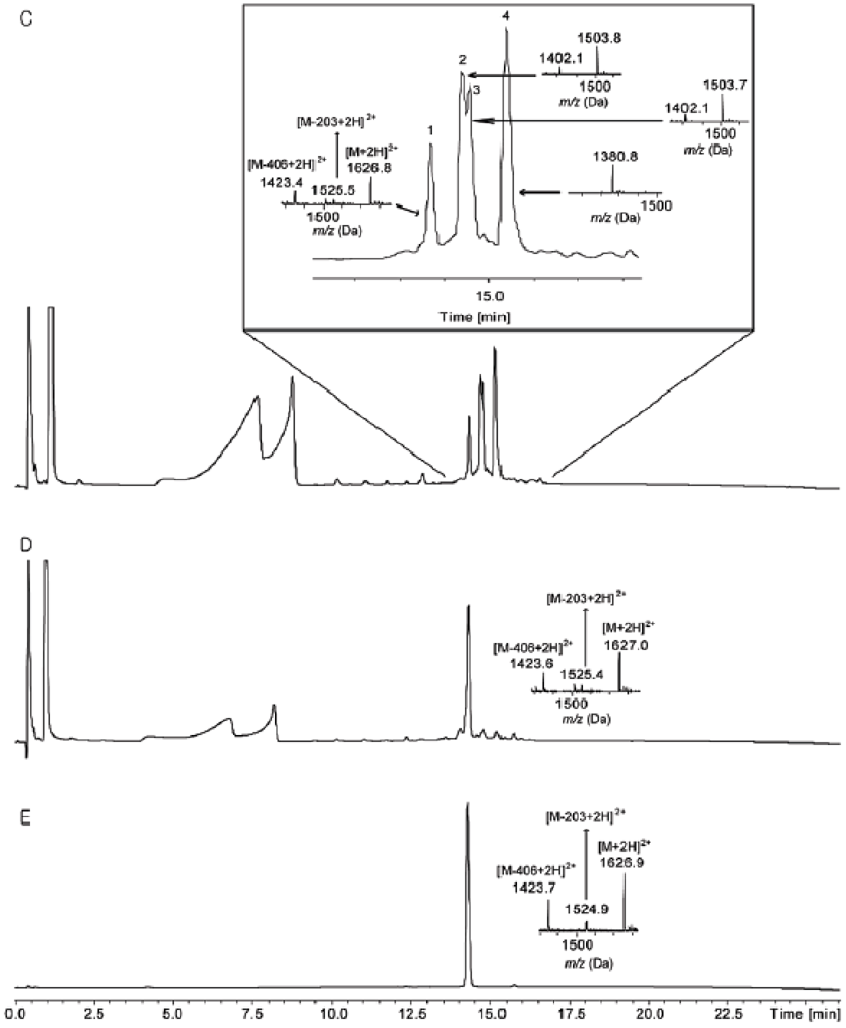


One-pot NCL and "Click" Chemistry





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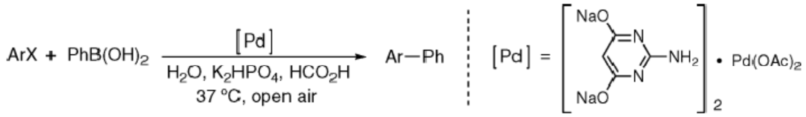
A Convenient Catalyst for Aqueous and Protein Suzuki–Miyaura Cross-Coupling

Table 1. Model Cross-Couplings with Pd-pyrimidine Catalyst[a]



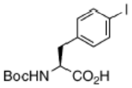
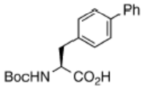
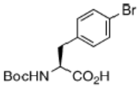
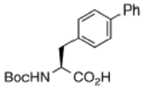
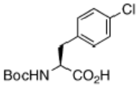
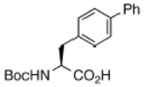
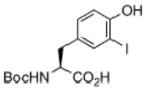
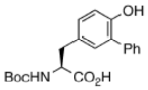
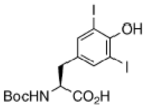
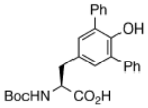
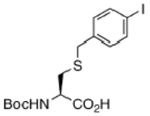
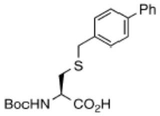
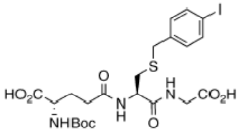
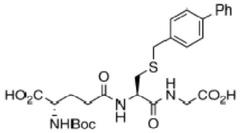
Entry	ArX	Pd Loading	Conditions	Coupling Product	Yield (%)
1		1%	37 °C, 4 h		95
2		1%	37 °C, 4 h		98
3		1%	37 °C, 4 h		0
4		1%	37 °C, 4 h		94
5		2%	37 °C, 4 h		95
6		1%–10%	37 °C, 6 h		0
7		4%	37 °C, 6 h		92

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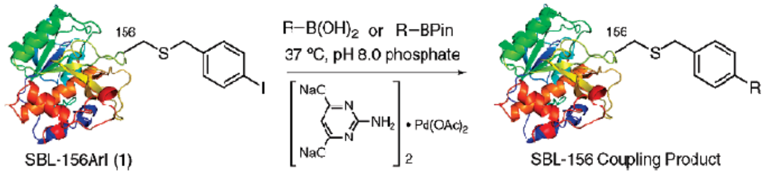
Table 2. Suzuki–Miyaura Cross-Coupling on a Protein Surface



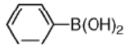
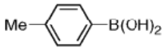
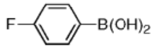
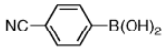
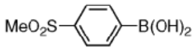
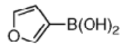
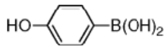
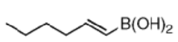
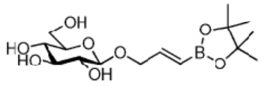
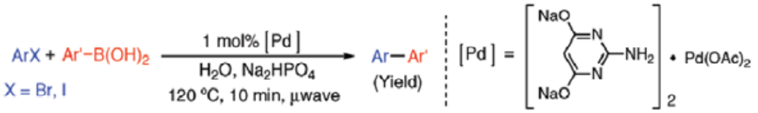
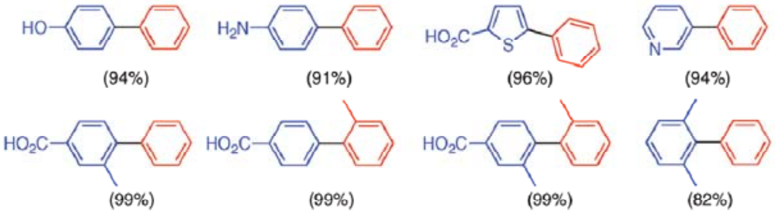
Entry	R-B(OH)$_2$ / R-BPin	Time	Mass Calculated	Mass Observed	Conversion
1		30 min	27035	27035	> 95%
2		30 min	27049	27049	> 95%
3		30 min	27053	27053	> 95%
4		30 min	27060	27060	> 95%
5		30 min	27113	27113	> 95%
6		30 min	27025	27025	> 95%
7		30 min	27051	27052	> 95%
8		30 min	27041	27041	> 95%
9		60 min	27177	27176	> 95%

Table 3. Pd-Pyrimidine Catalyst in Aqueous Biaryl Synthesis[a]





(94%) (91%) (96%) (94%)

(99%) (99%) (99%) (82%)

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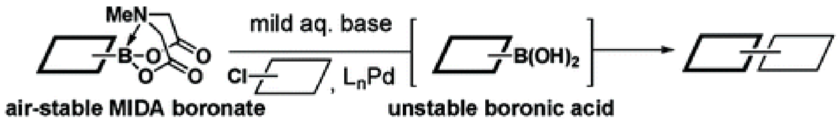
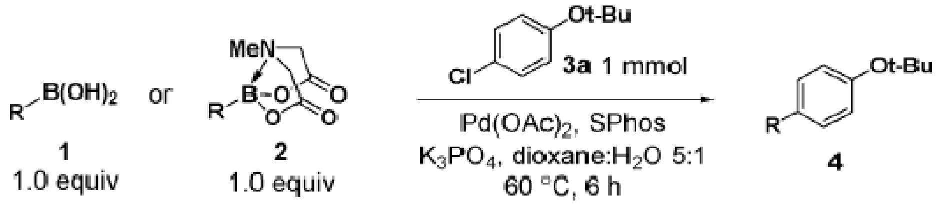
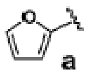
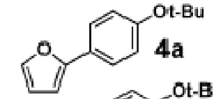
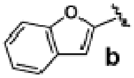
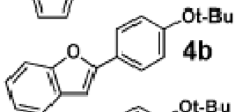
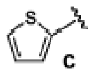
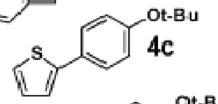
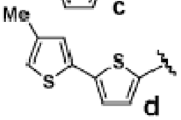
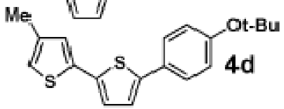
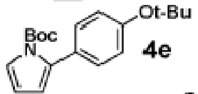
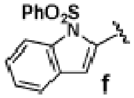
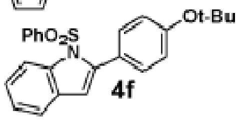
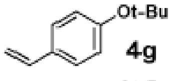
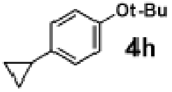




entry	R	% remaining after benchtop storage under air[a]		4	% isolated yield from cross-coupling[c]	
		1 (15 days)	2 (60 days)		1	2
1	 a	7	>95[b]	 4a	68	**94**
2	 b	88	>95	 4b	50	**92**
3	 c	80	>95	 4c	37	**94**
4	 d	80	>95[b]	 4d	45	**96**
5	 e	<5	>95	 4e	61	**90**
6	 f	<5	>95	 4f	14	**93**
7[d]	 g	5	>95[b]	 4g	79	**98**
8[d]	 h	31	>95	 4h	95	**96**

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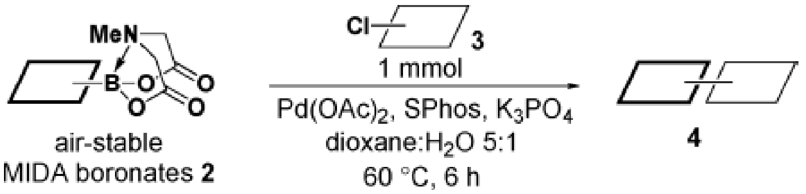


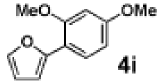
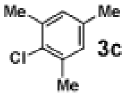
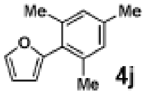
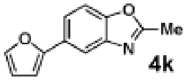
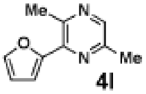
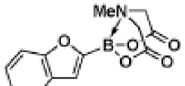
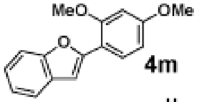
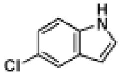
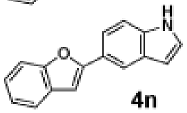
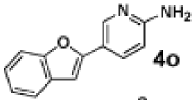
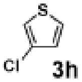
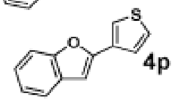
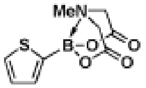
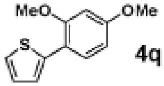
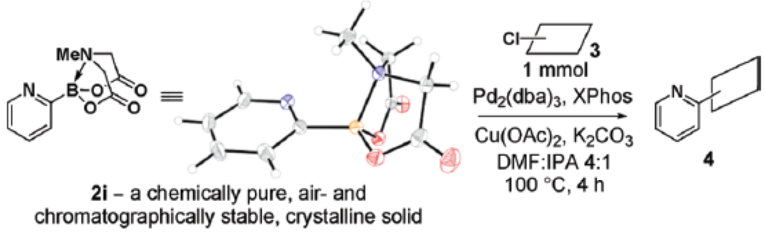
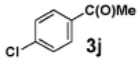
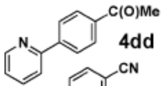
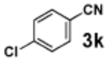
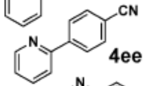
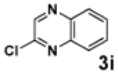
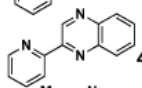
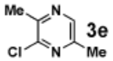
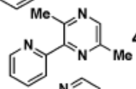
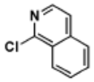
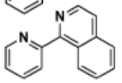
entry	2	3	4	% isolated yield
1	 **2a**	 **3b**	 **4i**	99
2	**2a**	 **3c**	 **4j**	97
3	**2a**	 **3d**	 **4k**	99
4	**2a**	 **3e**	 **4l**	91
5	 **2b**	**3b**	 **4m**	94
6	**2b**	 **3f**	 **4n**	94
7[b]	**2b**	 **3g**	 **4o**	85
8[b]	**2b**	 **3h**	 **4p**	85
9	 **2c**	**3b**	 **4q**	98

Table 3. Slow-Release Cross-Coupling of Air-Stable 2-Pyridyl MIDA Boronate **2i** with Aryl and Heteroaryl Chlorides[a]



entry	3	4	% isolated yield
1	 **3j**	 **4dd**	72
2	 **3k**	 **4ee**	60
3	 **3i**	 **4ff**	79
4	 **3e**	 **4gg**	52
5	 **3l**	 **4hh**	74

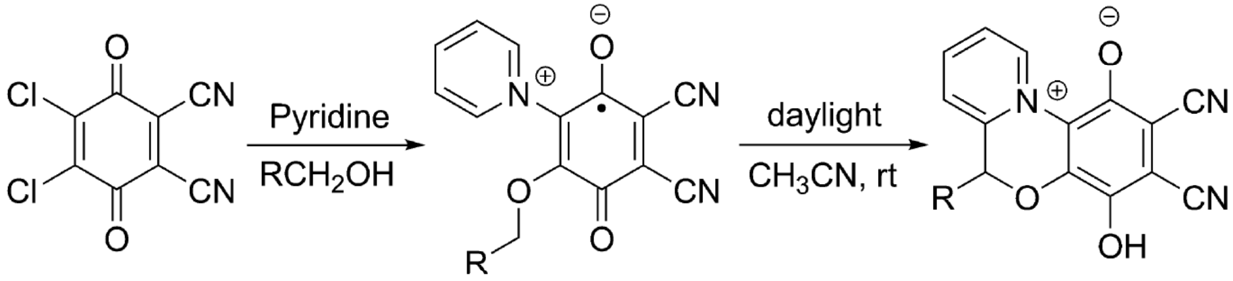
Burke et. al. *J. Am. Chem. Soc.*, **2009**, *131* (20), pp 6961–6963

Literature Presentation

Seth Carmody

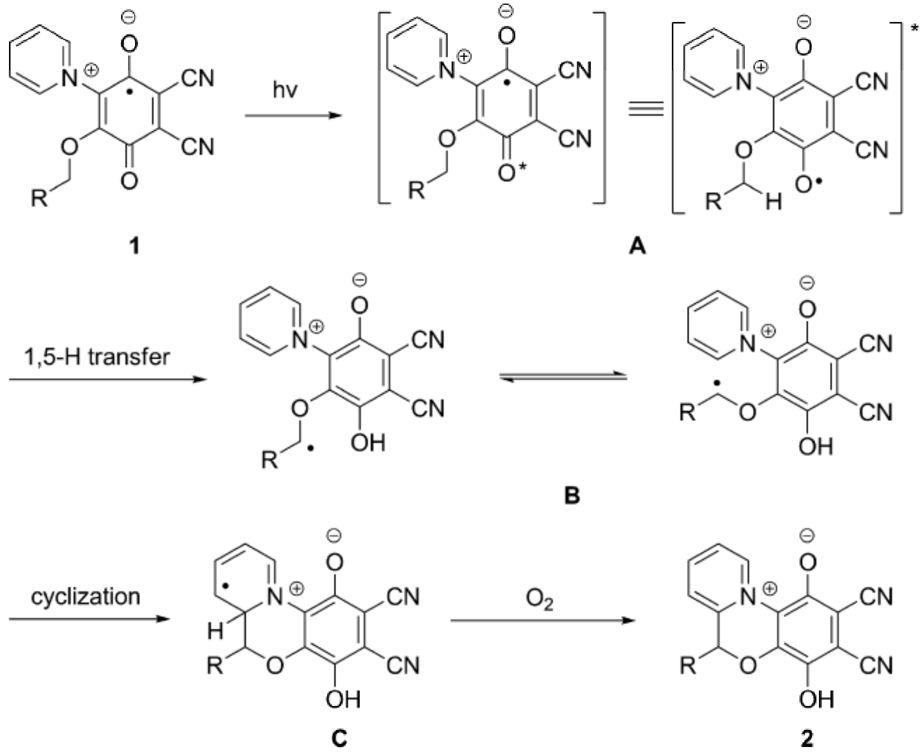
11/13/2009

Zwitterionic Hydroquinone-Fused [1,4]Oxazinium Derivatives



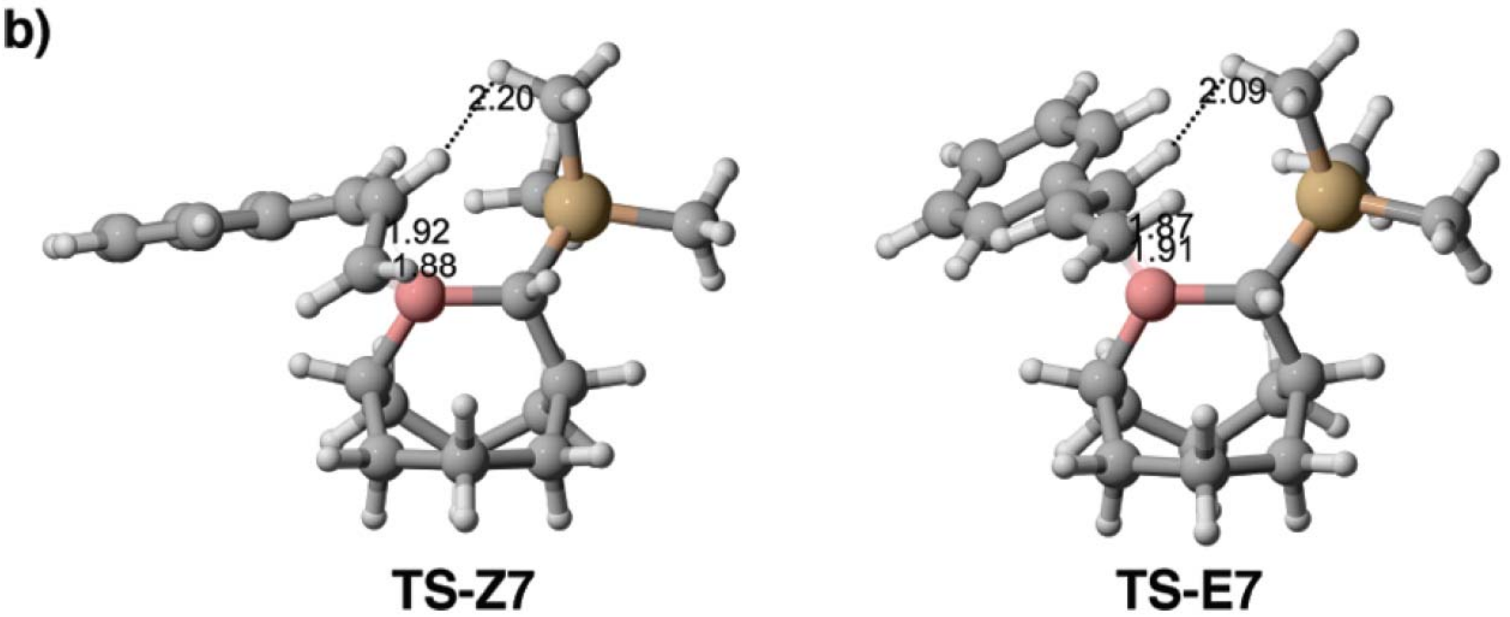
1a R = H, 45%
1b R = Me, 41%
1c R = Et, 28%
1d R = $MeOCH_2$, 44%

2a R = H, 70%
2b R = Me, 72%
2c R = Et, 68%
2d R = $MeOCH_2$, 61%

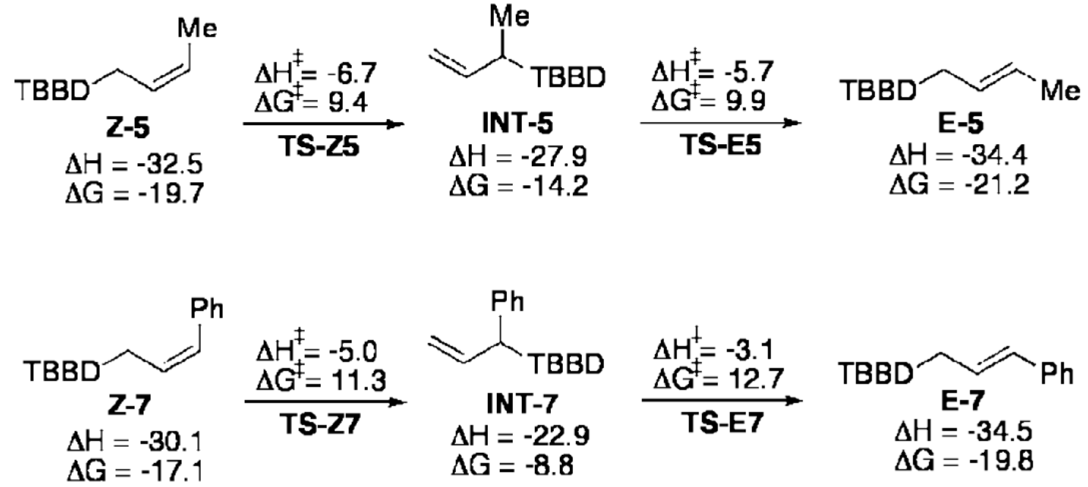


Decurtins, S.*et al. Org. Lett.* 2009 ASAP

Thermodynamic vs. Kinetic Control of Allene Hydroboration



b) Boratropic Shift



Roush, W.R. *et al. Org. Lett.* 2009 ASAP

Copper(II)-Accelerated Azide-Alkyne Cycloaddition

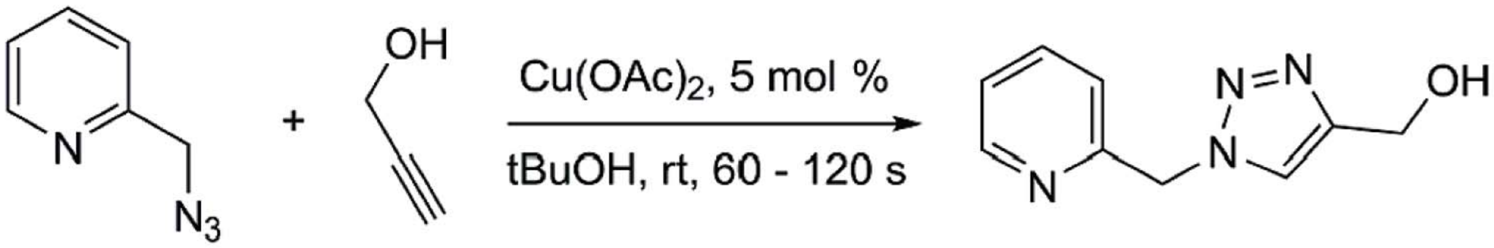
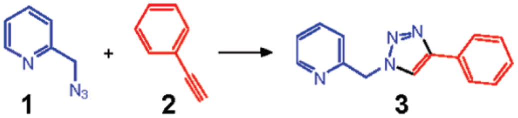


Table 1. Effects of Copper Source and Solvent on Reaction Yield After 18 h at rt[a]

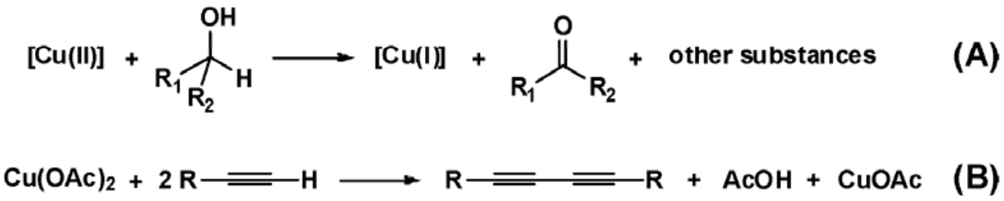


1 2 3

entry	copper source	copper loading	solvent	yield
1	$CuCl_2$	5 mol %	tBuOH	ND[b]
2	$CuCl_2$	5 mol %	iPrOH	4%
3	$CuCl_2$	5 mol %	EtOH	17%
4	$CuCl_2$	5 mol %	MeOH	79%
5	$CuSO_4$	5 mol %	MeOH	81%
6	$CuSO_4$	5 mol %	tBuOH	6%
7	$Cu(OAc)_2$	5 mol %	MeOH	90%
8	$Cu(OAc)_2$	5 mol %	tBuOH	>95%
9	$CuCl_2$ + NaOAc	5 mol %	tBuOH	88%

[a] 0.2−0.25 mmol of **1** and 0.3 mmol of **2** in 0.5 mL of solvent. [b] ND: Not detected by thin-layer chromatography (TLC).

Scheme 1. Two Processes by Which Catalytic Cu(I) Species Might Have Been Generated



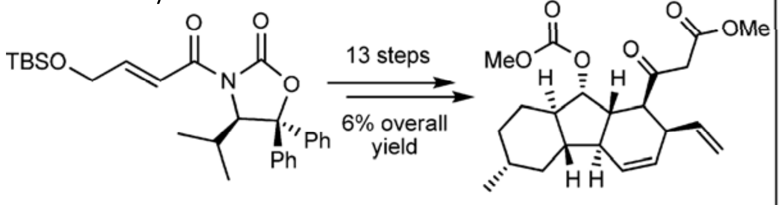
Zhu, L. *et al.* *Org. Lett.* 2009 ASAP

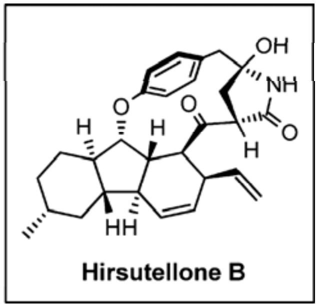
Literature Presentation

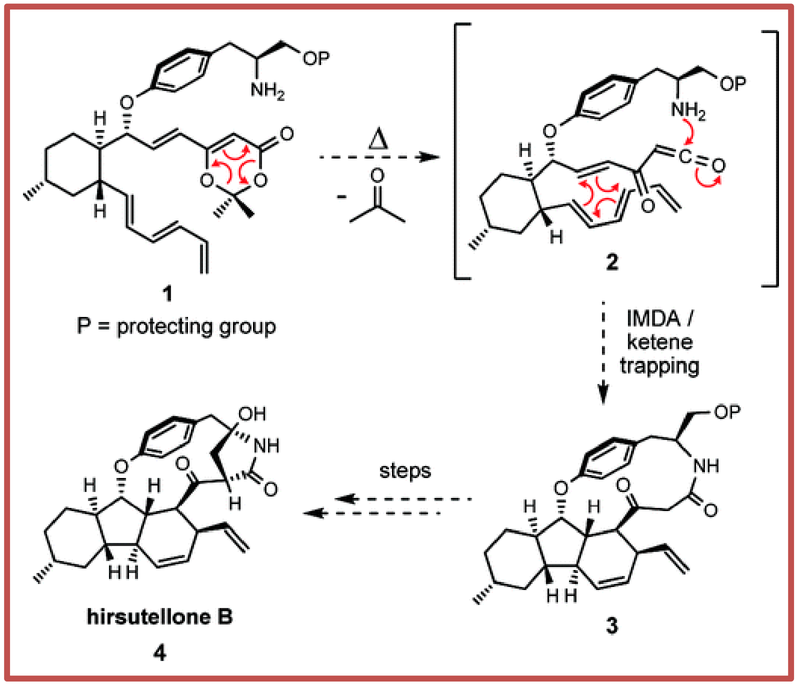
Angela K. Carrillo Alocén
11/13/2009

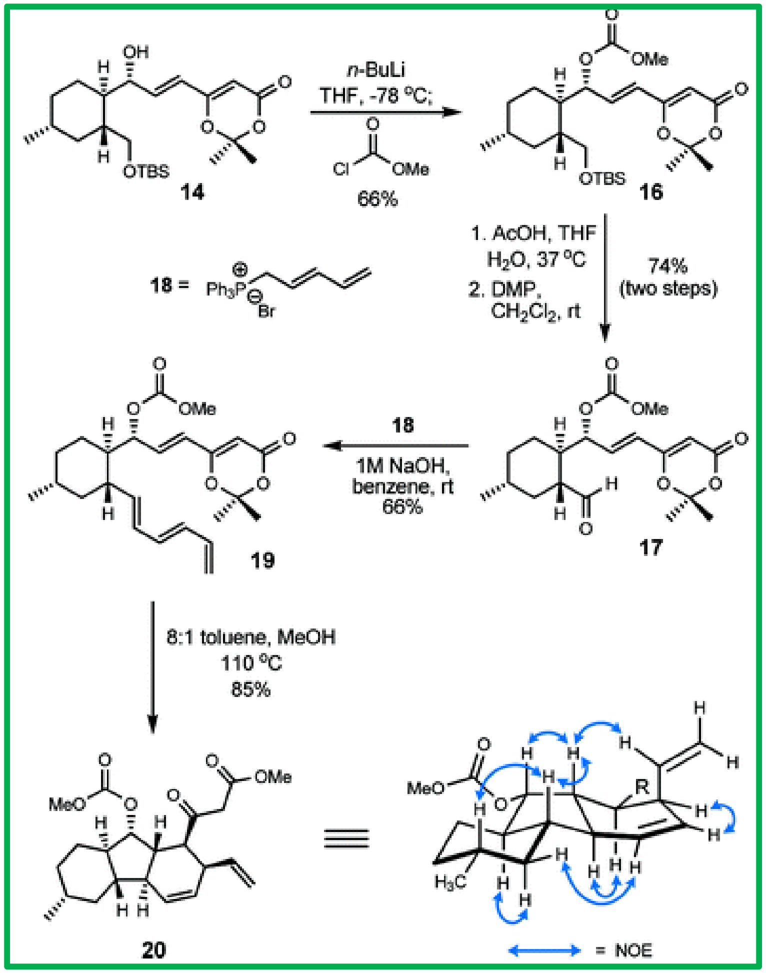
A Rapid, Asymmetric Synthesis of the Decahydrofluorene Core of the Hirsutellones

S. David Tilley, Keith P. Reber and Erik J. Sorensen; *Org. Lett.* **2009,** 11, 701-703.





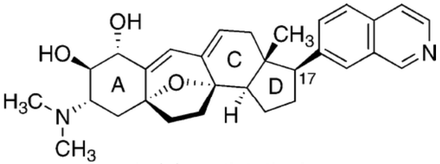




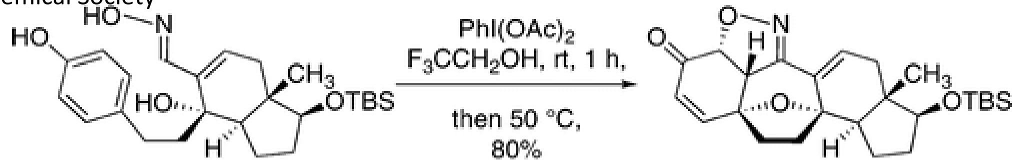
November 13th 2009, Angela K. Carrillo Alocén

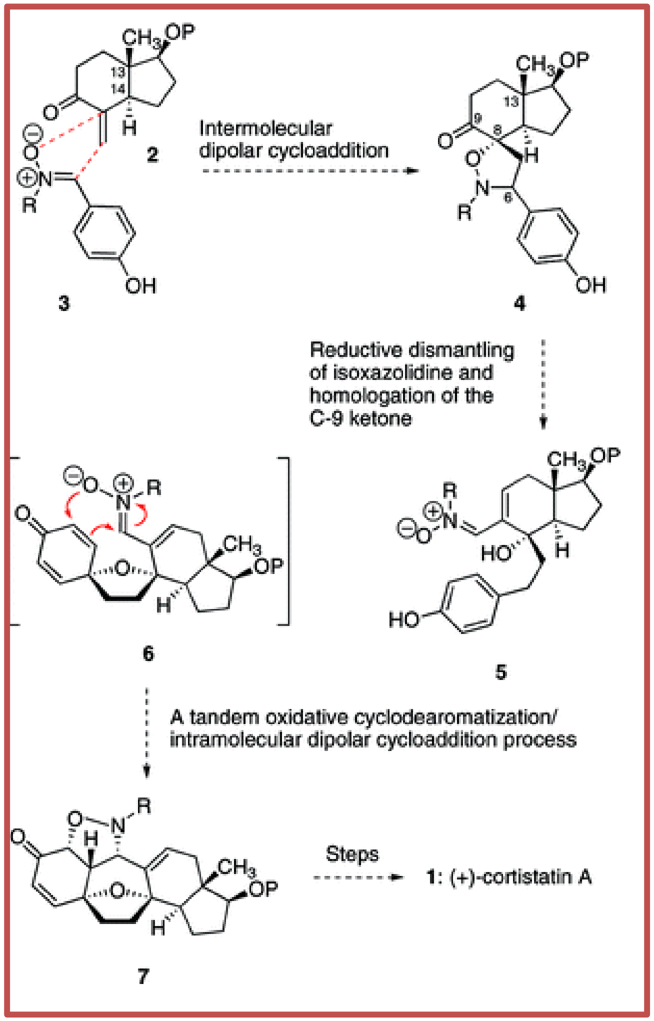
A Hypervalent Iodine-Induced Double Annulation Enables a Concise Synthesis of the Pentacyclic Core Structure of the Cortistatins

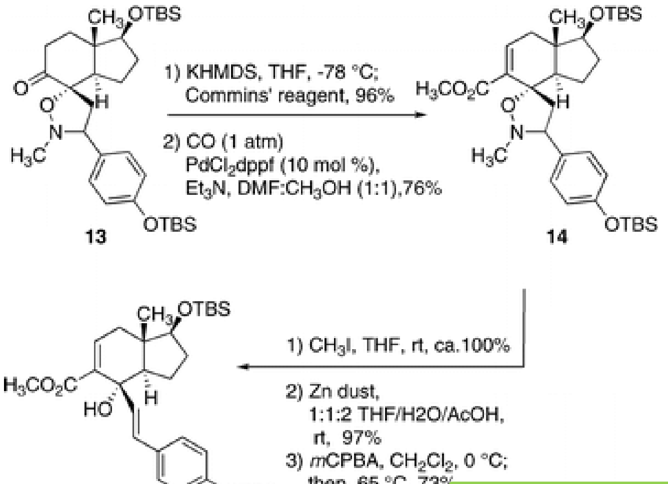
Jessica L. Frie, Christopher S. Jeffrey and Erik J. Sorensen; *Org. Lett.* **2009,** ASAP

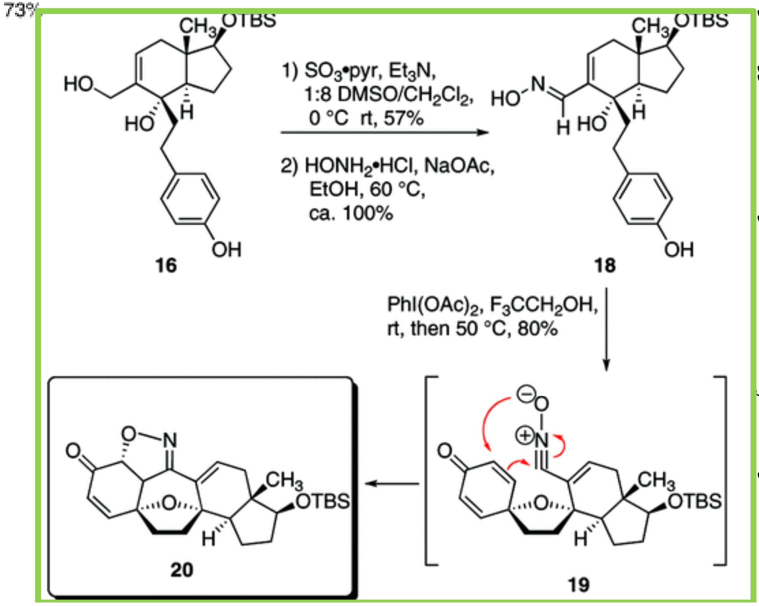


1: (+)-cortistatin A





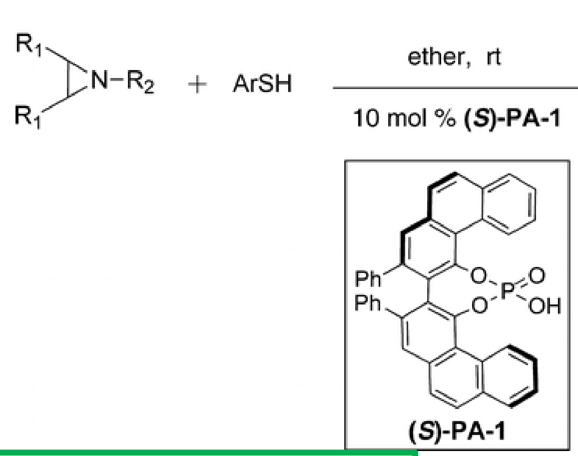




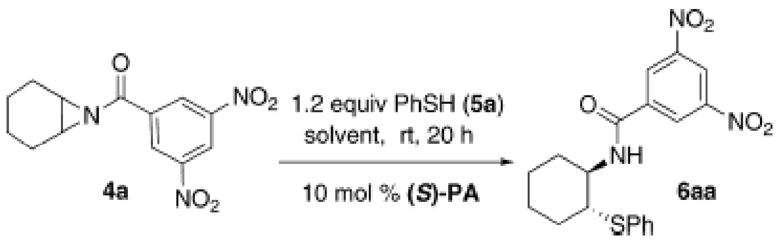
November 13th 2009, *Angela K, Carrillo Alocén*

Chiral Phosphoric Acid-Catalyzed Desymmetrization of *meso-Aziridines* with Functionalized Mercaptans

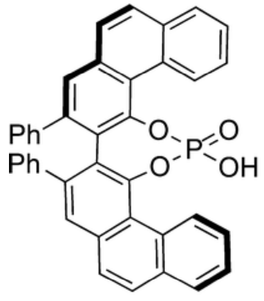
Shawn E. Larson, Juan C. Baso, Guilong Li and Jon C. Antilla; *Org. Lett.*, **2009**, 11 (22), pp 5186–5189



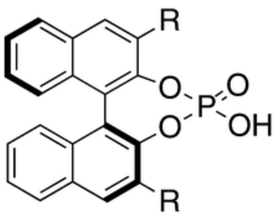
25+ highly enantioselective examples



entry	catalyst (*S*)	solvent	yield,[a] %	ee,[b] %
1	PA-1	toluene	74	70
2	PA-1	DCM	91	86
3	PA-1	EtOAc	89	31
4	PA-1	MeCN	82	40
5	PA-1	THF	95	12
6	PA-1	MTBE	99	96
7	PA-1[c]	ether	95	97
8	PA-2	ether	78	0
9	PA-3	ether	64	11
10	PA-1[d]	ether	65	89



(*S*)-PA-1



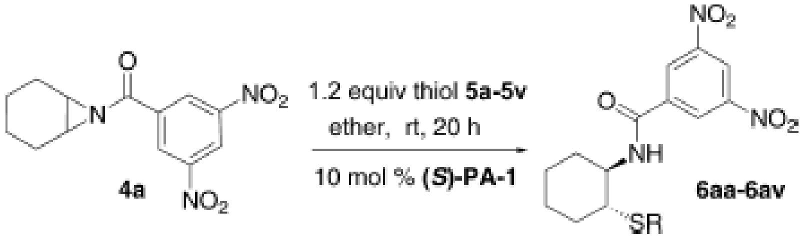
(*S*)-PA-2 R = SiPh$_3$

(*S*)-PA-3 R = 9-Anthryl

November 13th 2009, Angela K. Carrillo Alocén

Chiral Phosphoric Acid-Catalyzed Desymmetrization of *meso-Aziridines* with Functionalized Mercaptans

Shawn E. Larson, Juan C. Baso, Guilong Li and Jon C. Antilla; *Org. Lett.*, **2009**, 11 (22), pp 5186–5189



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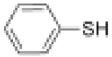
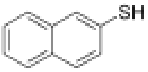
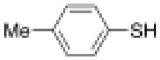
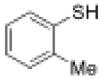
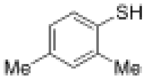
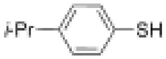
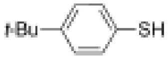
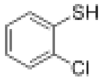
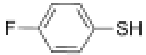
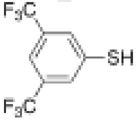
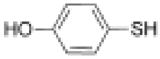
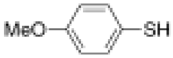
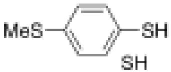
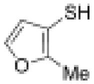
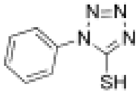
1		97	96
2		99	95
3		94	93
4		88	94
5		85	93
6		99	93
7		96	93
8		87	96
9		89	98
10		85	91
11		70	84
12		81	89
13		99	>99
14		78	90
15		72	74
16		75	55
17		71	82
18		78	61
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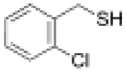
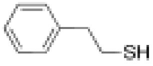
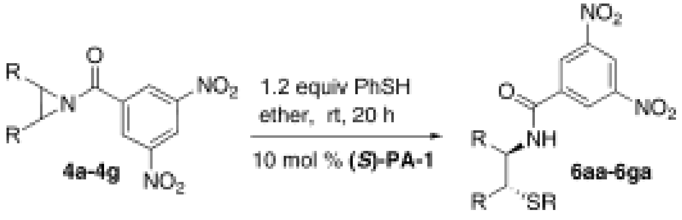
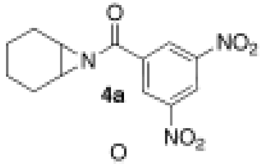
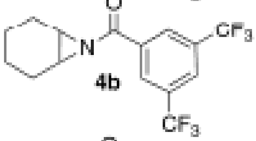
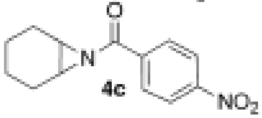
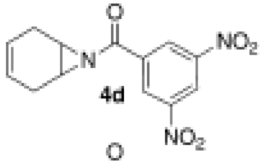
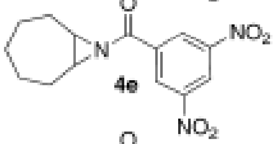
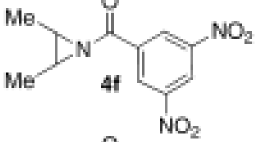
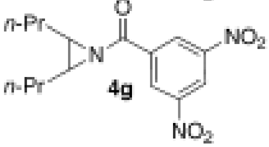
20		42	62
21		40	32
22	HS−*n*-hexyl	15	18



entry	aziridine	yield, %[a]	ee, %[b]
1		95	97
2		97	43
3		63	6
4		99	95
5		95	96
6		97	95
7		94	87

November 13th 2009, Angela K, Carrillo Alocén