Key Elements in Organic Synthesis: Recent Advances in p-Block Chemistry

Recent Advances in Sulfur Chemistry

4th December 2009

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University of London

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Talk Overview

1) Sulfur containing Natural Products

Epidithiodiketopiperazines (ETPs)

2) Sulfur-Carbon Bond Formation

Formation of aryl-S bonds
Benzothiazoles/ Benzothiophenes
Sulfur Electrophiles with Alkynes
Sulfur Radical Chemistry

3) Sulfur Mediated C-C, Bond Formation

Pummerer and Pummerer-type reactions
Ramberg Bäcklund reaction
Sulfoxide directed *ortho*-lithiation

4) Chiral Sulfur Ligands and Catalysts

Ellman type sulfonylimines

5) Rearrangements

Sulfur Natural Products

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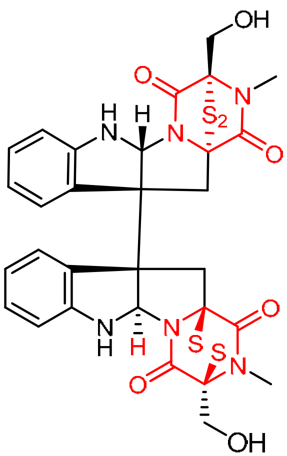
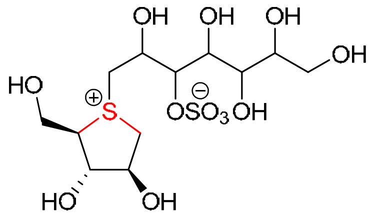
Sulfur Natural Products

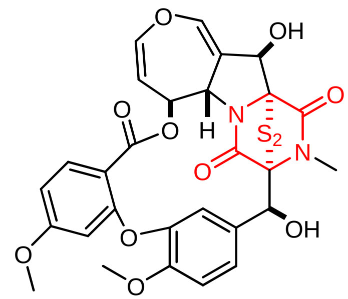


Chaetocin
anti-myeloma

<2007Blood2579>

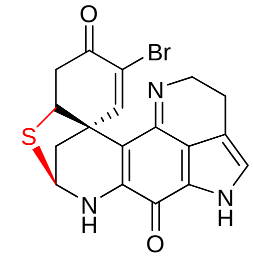


Kotolanol
Glycosidase Inhibitor
<2009JACS5621>



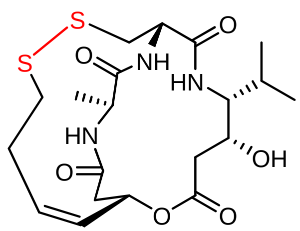
MPC1001
Anticancer

<2009JOC513>



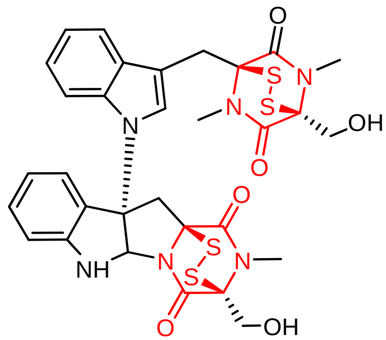
Discorhabin A
Cytotoxic

<2009OL4048>

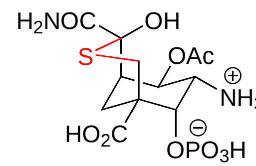


Spiruchostatin A
HDAC inhibitor

<2009TL2970>

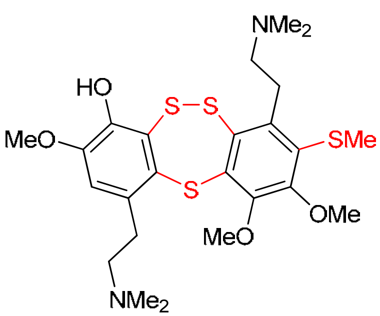


Chetomin
HIF-1 Anti-cancer
50-60 nM
<2004Cancer Cell 33>
<2009JBC26831>

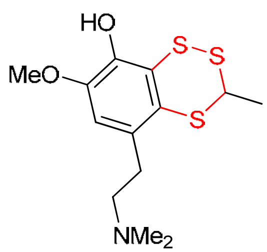


Tagetitoxin
Proposed Structure
Inhibitor of RNA polymerase

<2008OL5477>

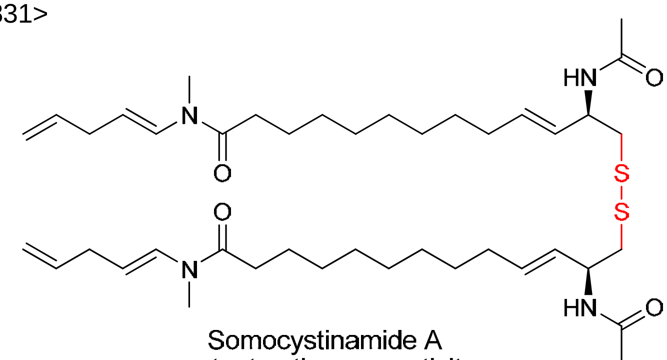


Lissoclibadin 5
1μM against L1210 Leukemia
cell lines



Lissoclibadin 13
2.2μM against L1210 Leukemia
cell lines

<2009T9598>



Somocystinamide A
potent anticancer activity

<2008OL4449>
<2009PNAS2313>

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Epidithiodiketopiperazines

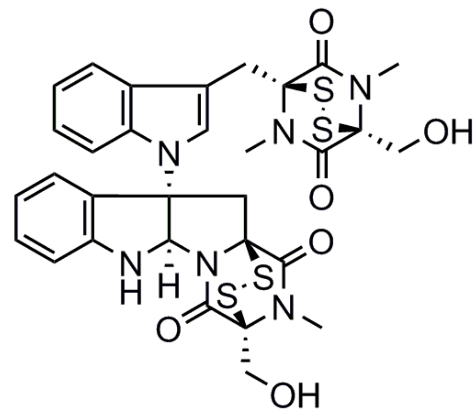
– **2004. Kung et al. identified chetomin from a screen of ~600,000 compounds as the only compound that showed inhibition of HIF-1α/p300 binding**

– **Viable drug target**

– **Chetomin effective *in vitro* and *in vivo,***

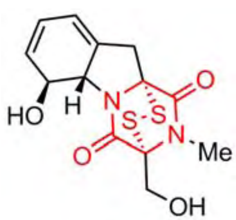
  – ↓ HIF mediated gene expression

  – ↓ tumor size in mouse xenograft models



Properties

•Antitumor, antiviral and antibacterial activity.
•Inhibitor of transcription factor NFκB,
•Inhibitors of farnesyl transferase and HIF.
•catalytic .



Gliotoxin

Recent mechanism of action studies of ETP core and Chetomin
Schofield <2009JBC26831>

Kung <2000Nature Medicine 1335>
Kung <2004 Cancer Cell 33>

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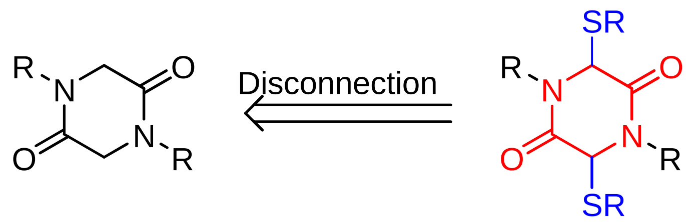
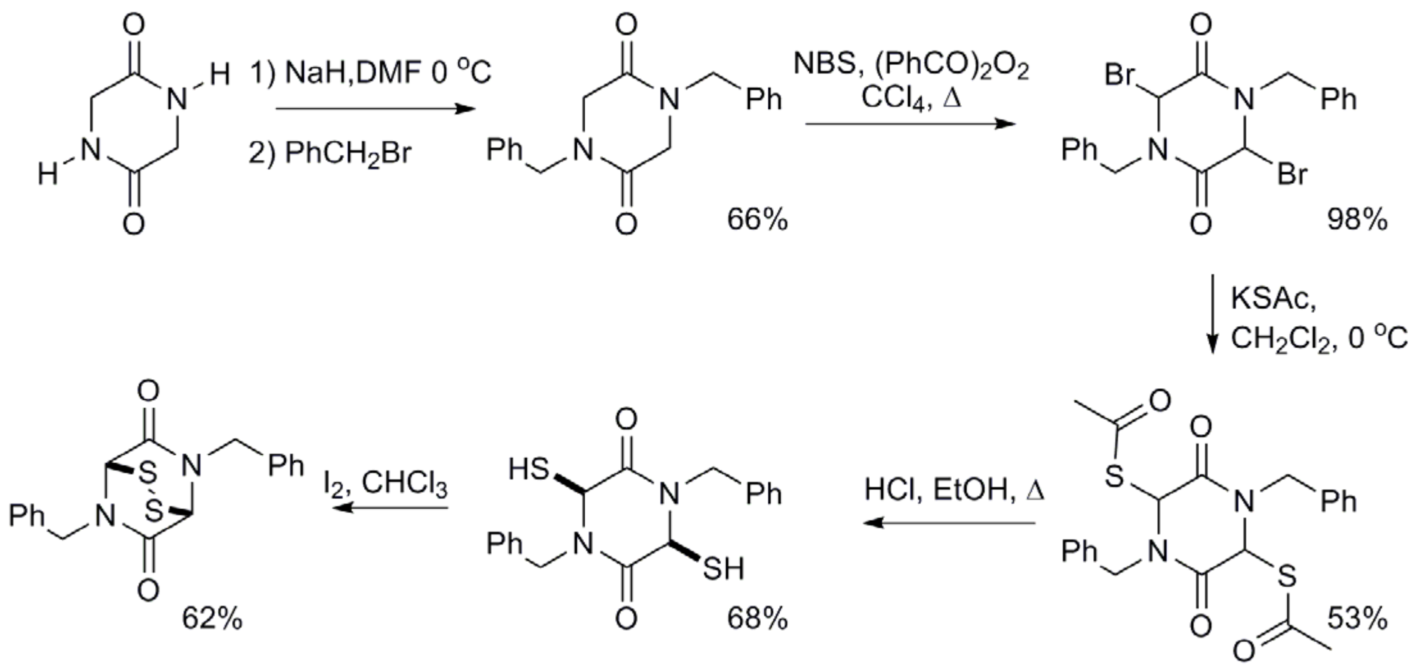
ETP Core Synthesis





Kishi<1981T2045>

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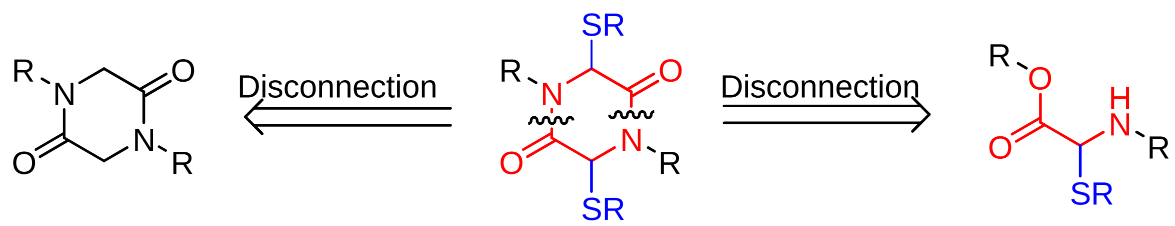
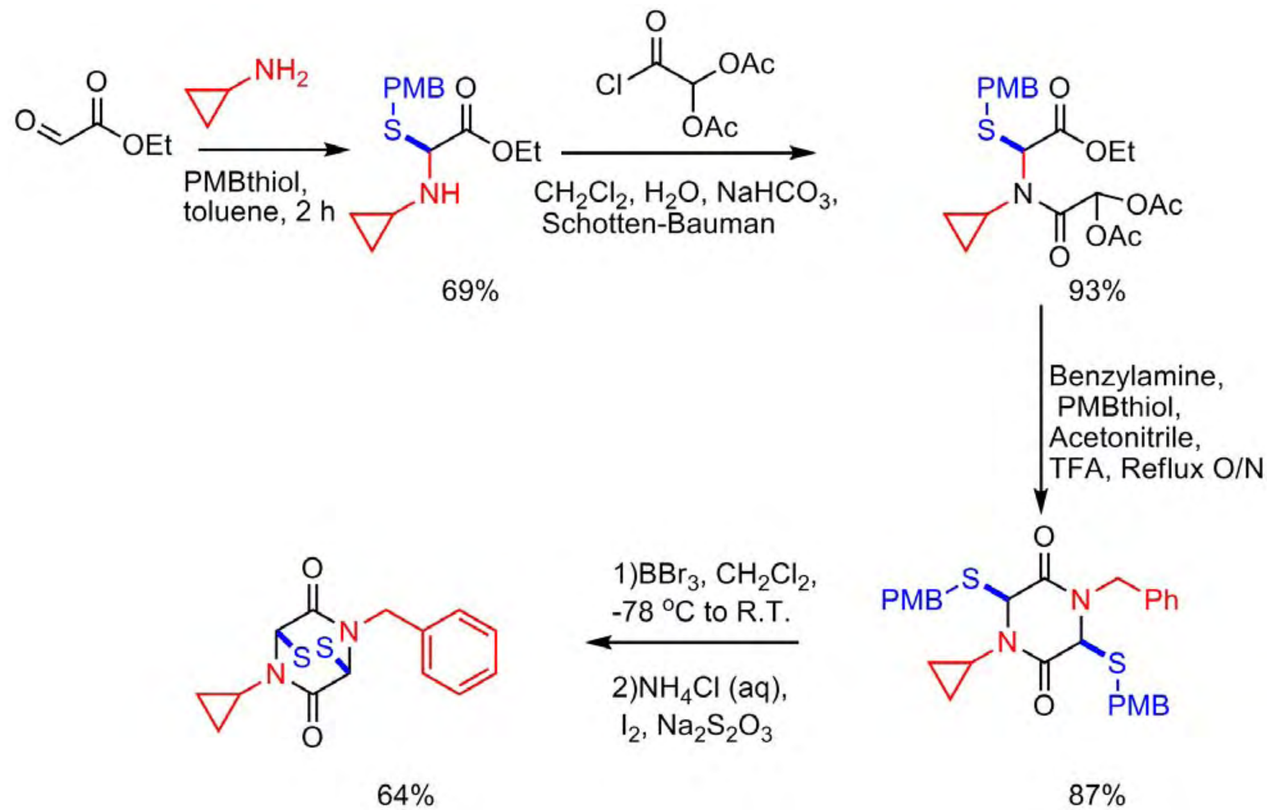
ETP Core Synthesis





Hilton/Motherwell<2006TL2387>

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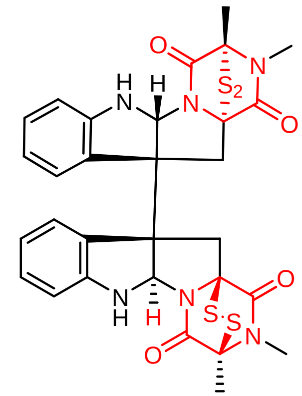
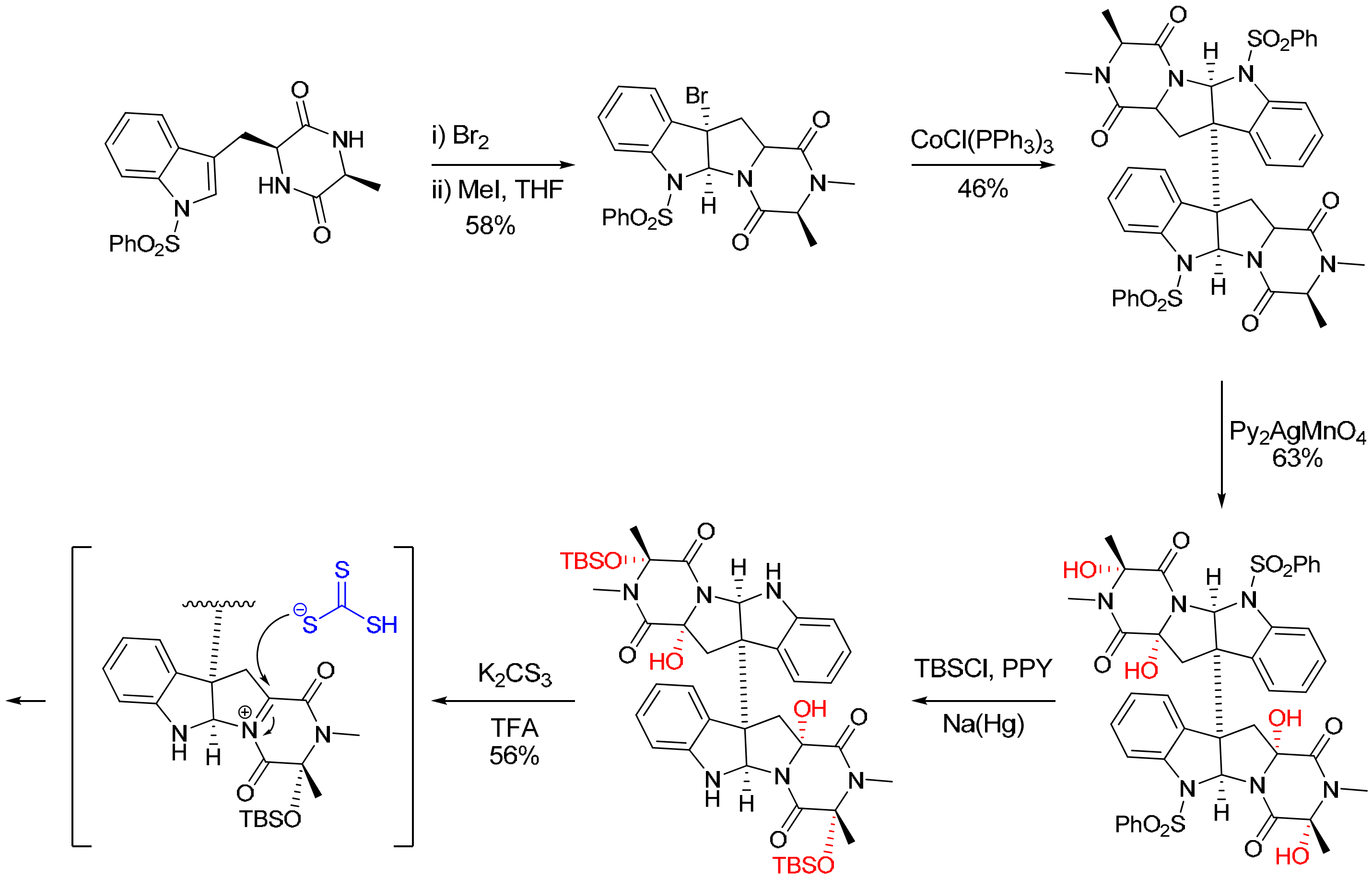
ETP Synthesis

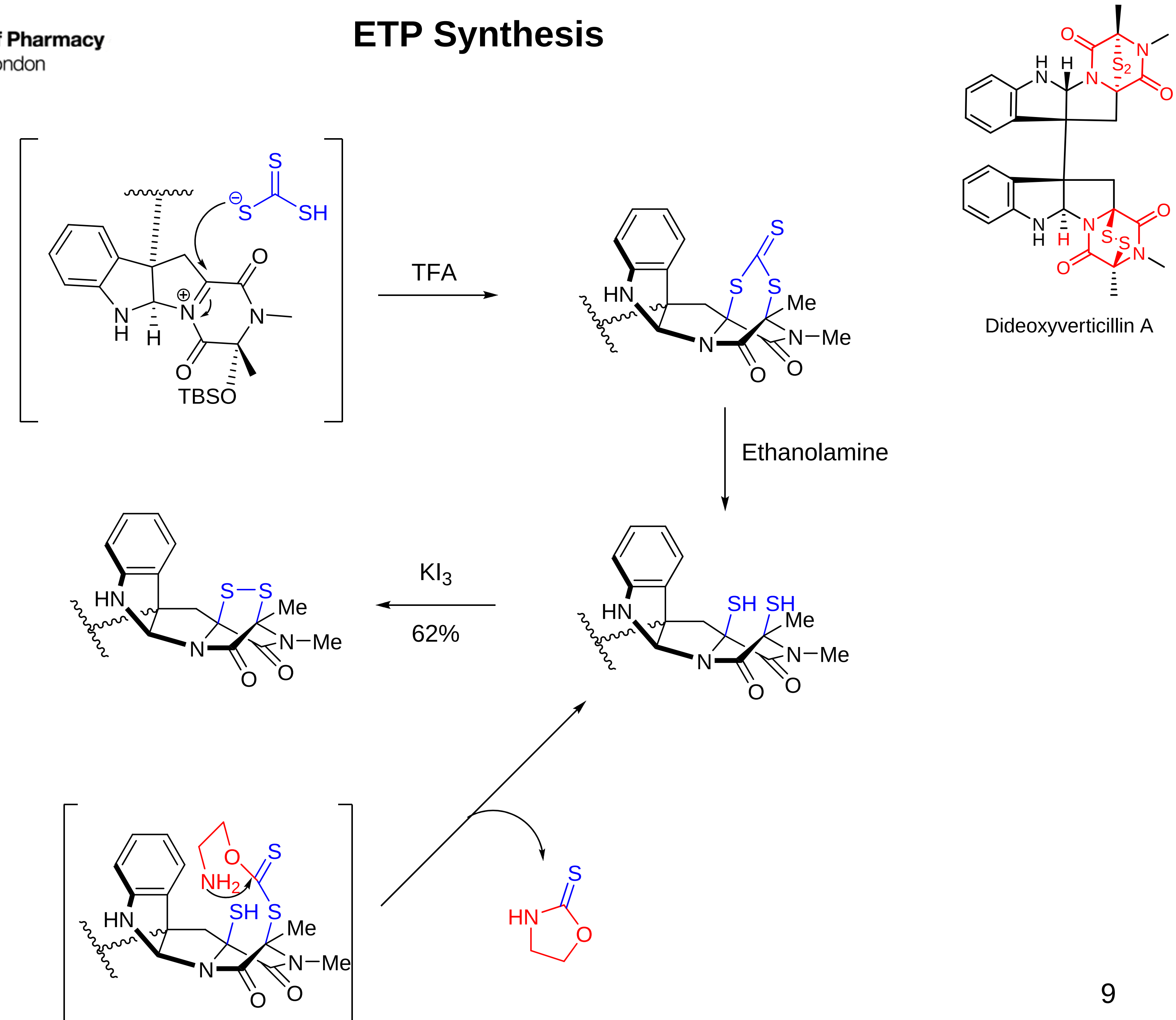


Dideoxyverticillin A



Movassaghi <2009Science238>

ETP Synthesis



Movassaghi <2009Science238>

Sulfur-Carbon Bond Formation

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Formation of Aryl-S bonds

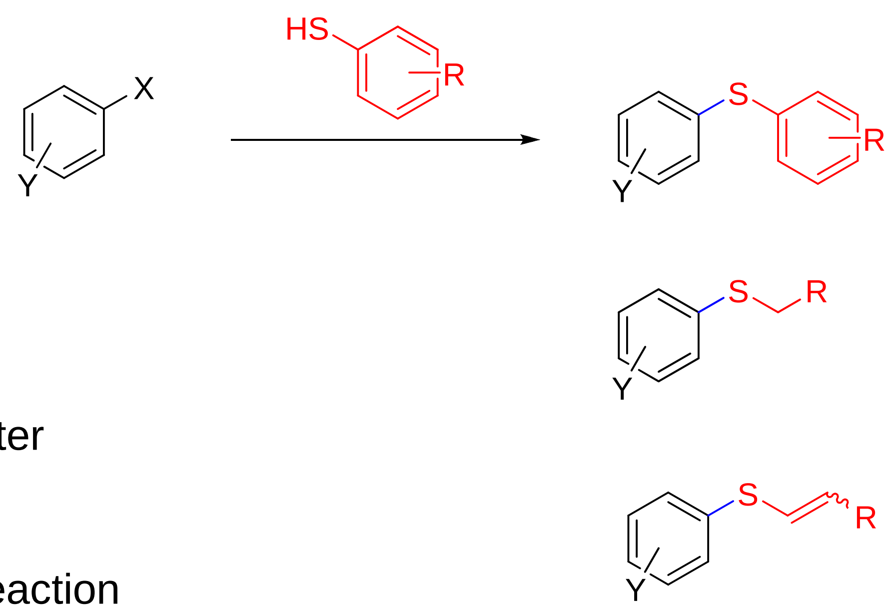
Increasing interest in formation of aryl C-S bond due to increasing prevalence in areas of therapeutic interest, such as Cancer, HIV and Alzheimers disease

Previous work on metal catalysed aryl C-S bond formation has been limited due to the view that metal catalysts would be deactivated by thio-compounds.

C-H activation has more recently been investigated for the formation of C-S bonds

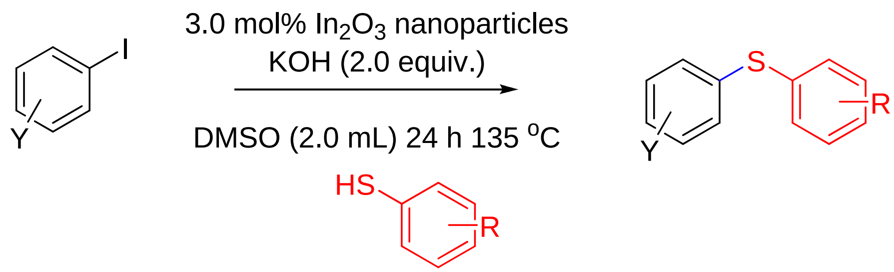
For recent papers, see the following:

<2009OL1697>
<2008OL5147>
<2009JOC4005>
<2009JOC1663>
<2009JOC459>
<2009Green Chemistry326> Reaction in water
<2009JOC4005>
<2009JACS7852>
<2009TL3661> - Microwave Ullmann type reaction
Ma<2009OL – ASAP article> Aryl iodide, CuI, Sulfur powder



Formation of Aryl-S bonds

Cross-Coupling of Thiols with Aryl halides under Ligand free Conditions

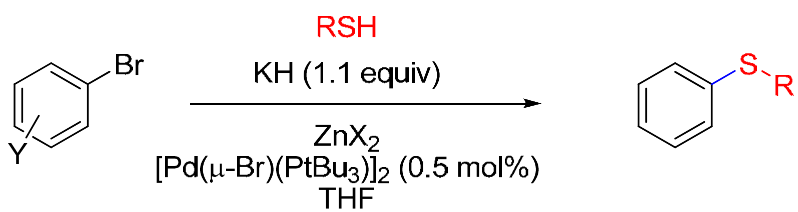


Yields 60-91%

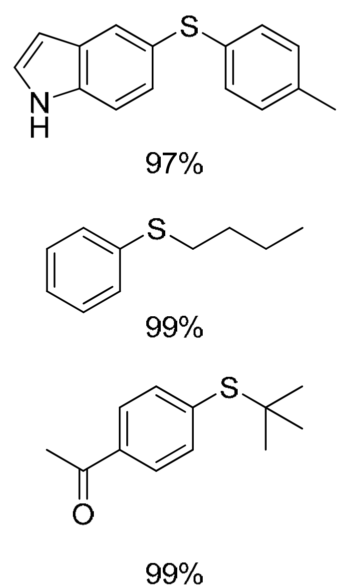
Aryl thiols only

Rao<2009OL1697>

Zinc-Mediated Pd-catalysed C-S bond formation



Yields 70-99%
monodentate phosphine ligand

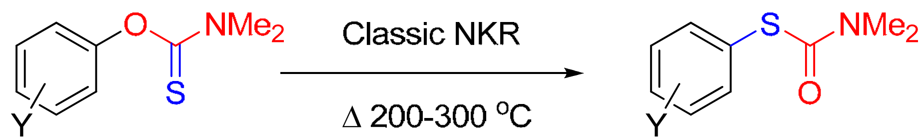


See also Hartwig<2009JOC1663>
Bisphosphine ligand -
alkyl and aryl thiols tolerated. Yields >80%
Cat loading 0.01-0.5%

Stambuli<2009JOC4005>

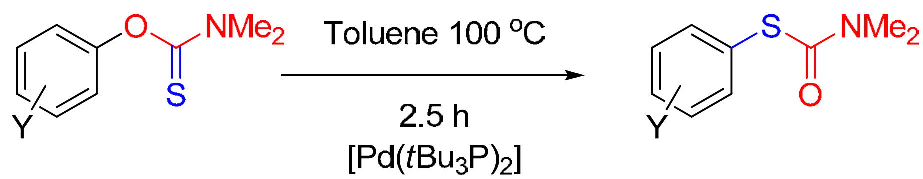
Formation of Aryl-S bonds

Newman-Kwart Rearrangement of *O*-Aryl Thiocarbamates



Kappe<2009EJOC1321>
<2009OPRD321>.

NKR in flow and microwave chemistry

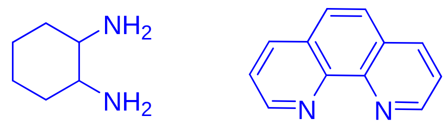


Proposed Pd-Sulfur complex

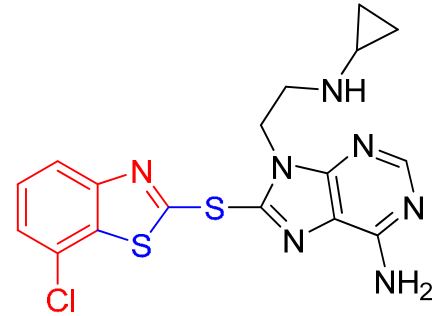
Entry	Ar	Time	Conv. (%)	Temp.
1	*p*-$NO_2C_6H_4$	2.5 h	>99	180 °C
2	*p*-$MeOC_6H_4$	14 h	92	>295 °C

Lloyd-Jones<2009ACIE1>

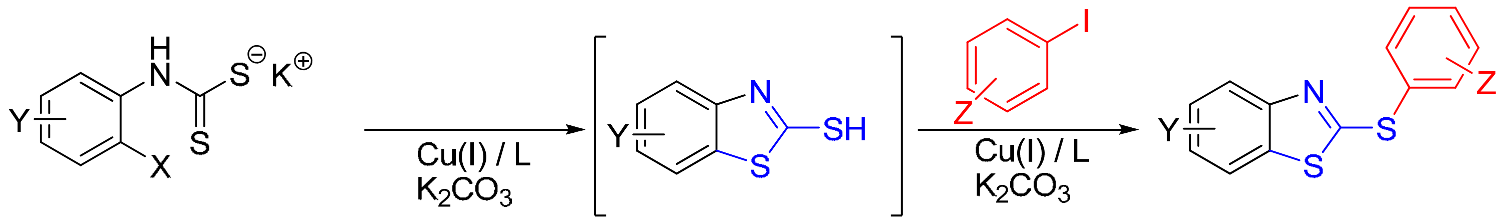
Arylthiobenzothiazoles and Benzothiazoles



Optimum Ligands



HSP 90 Inhibitor

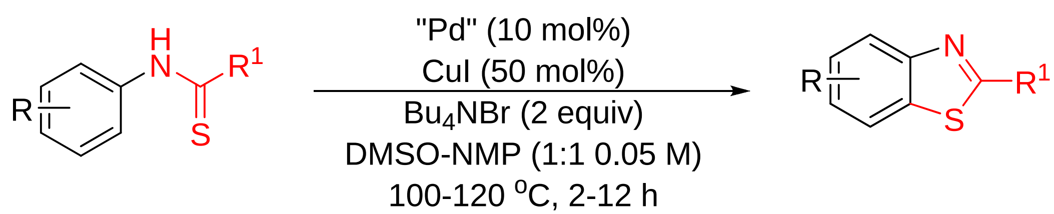


Optimum Ratio = dithicarbamate:aryl iodide:CuI:ligand:base
1:1:0.05:0.1:1.3

Yields 56-90%

Patel<2009OL4254>

Benzothiazoles *via* C-H activation



Catalysts: $PdCl_2$, $PdCl_2(cod)_2$, $PdBr_2$

Inamato & Doi<2008OL5147>

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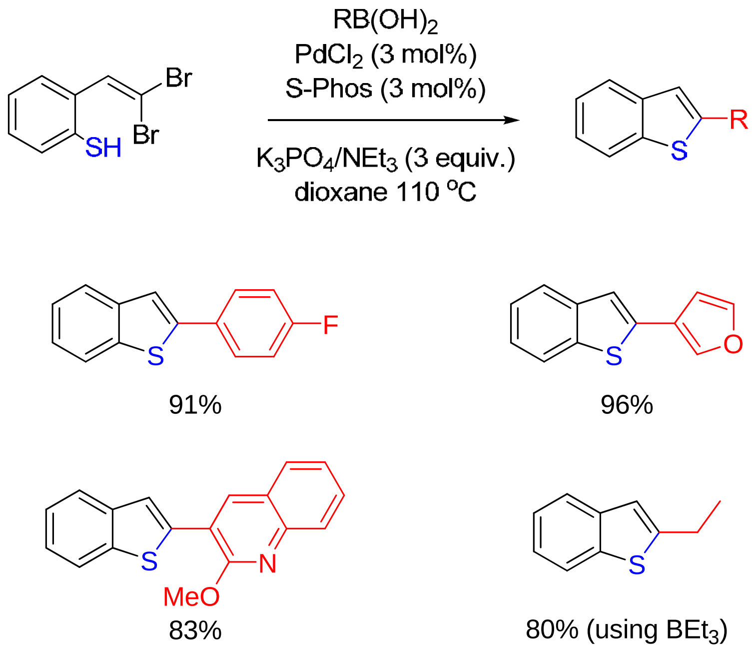
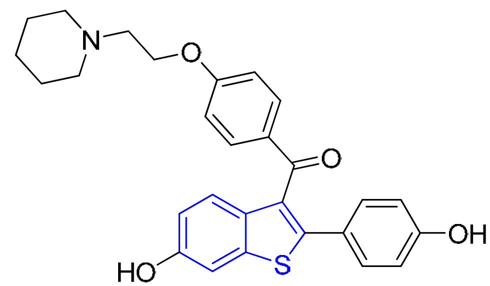
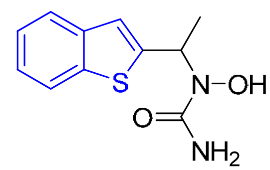
Benzothiophenes *via* Pd-Catalysed C-S Coupling

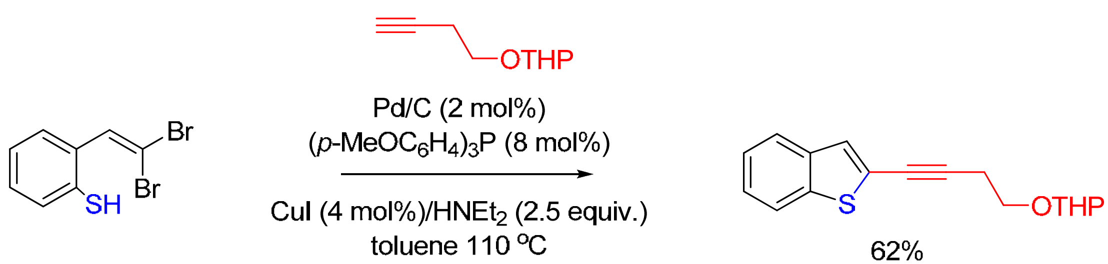




Raloxifene



Zileuton



Note: reaction catalysed by Pd/C

Lautens<2009ACIE7064>

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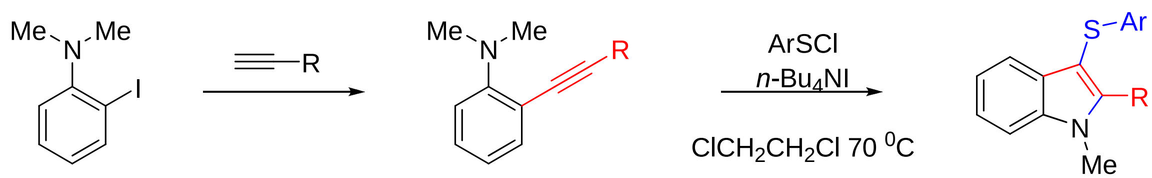
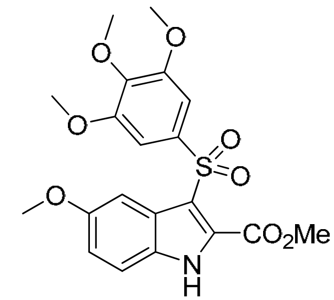
Reaction of Sulfur Electrophiles With Alkynes

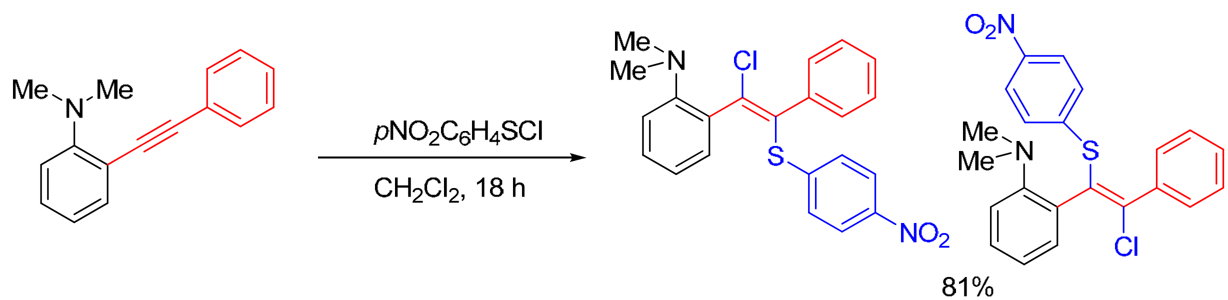
Synthesis of 3-sulfenylindoles

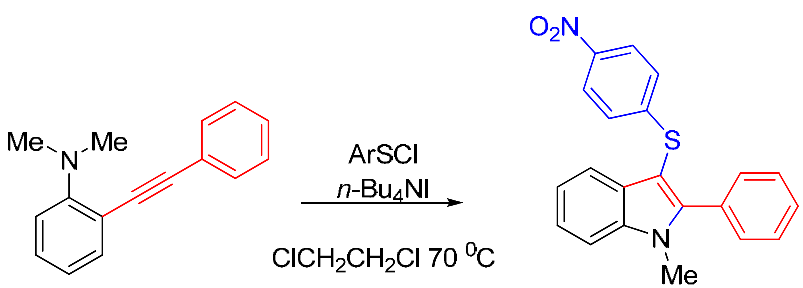




L-737,126
Anti-HIV

Reaction in absence of TBAI





Entry	Additive	Solvent	ºC	Time	Yield (%)
1	TBAI (1.0 eq.)	DCM	rt	60 h	86
2	TBAI (1.0 eq.)	1,2-DCE	70	5 h	90

For the synthesis of indoles and 3,1-benzoxazines, dihydrobezofurans, see: <2007T8250>

Larock<2009JOC6802>

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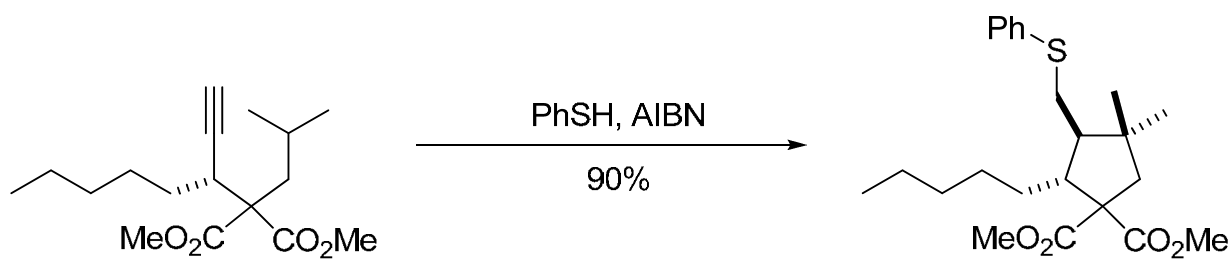
Thiol Mediated Radical Cyclisations

Reaction traditionally carried out with Bu_3SnH or derivatives
Drawbacks: toxicity, purification, cost.

Thiol mediated cyclisations avoid these problems

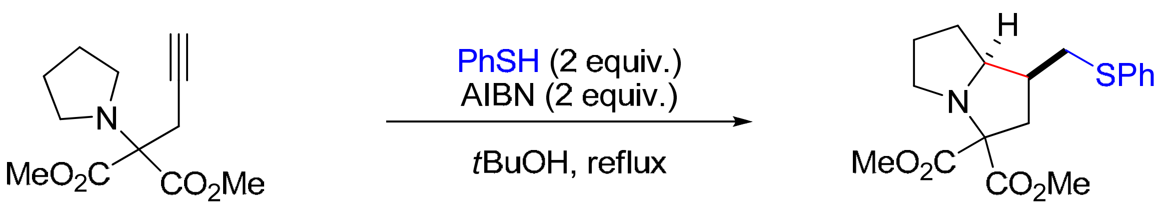


Renaud<2004OL2563>

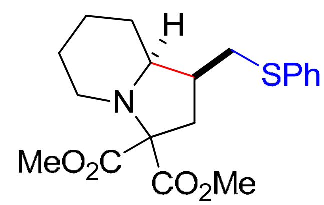
For recent papers:
<2008T9799> Review – Majumdar
<2007OL1061>
<2007TL9124>
<2009TL228>
<2007OL4375> - Renaud
<2009OL2651>
<2007TL5265>
<2007TL7031>
<2009OL3298> - Initiator Free
<2008CSR1603> Review N-centred radicals, Xanthate - Zard

Thiol Mediated Radical Cyclisations

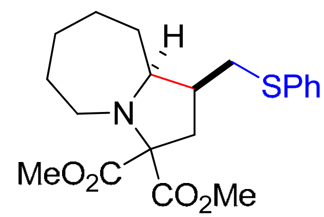
Thiophenol-mediated 1,5-hydrogen transfer for the synthesis of indolizidenes and related compounds



55%

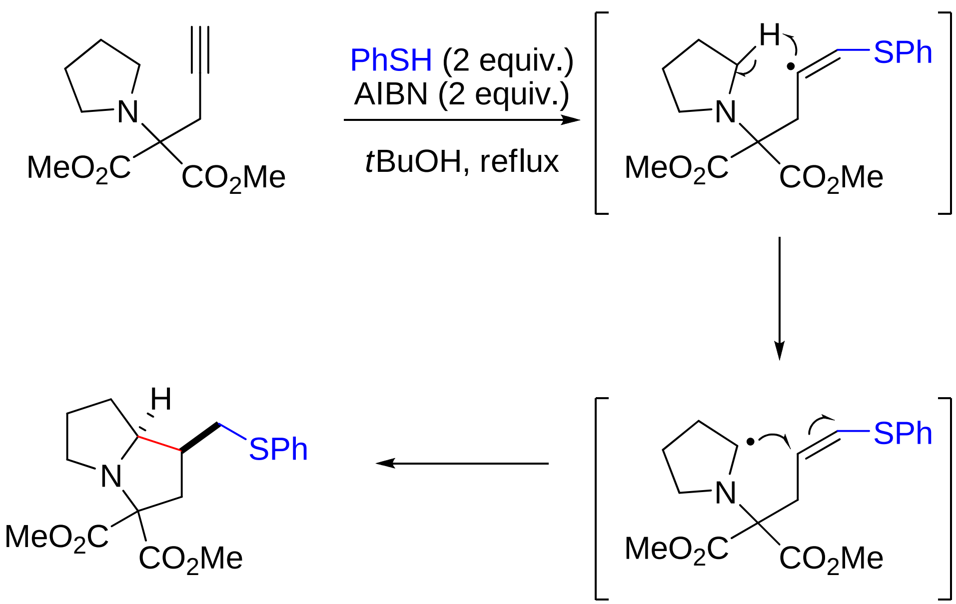


90%



92%

Mechanism of cyclisation



Renaud<2007OL4375>

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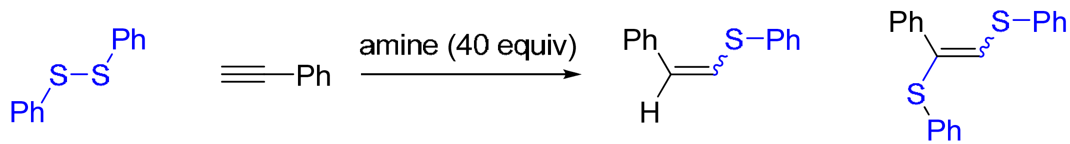
Thiol Mediated Radical Cyclisations

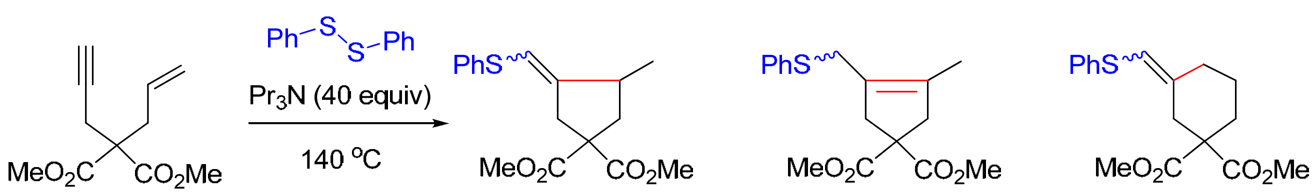
Amine-mediated single electron transfer



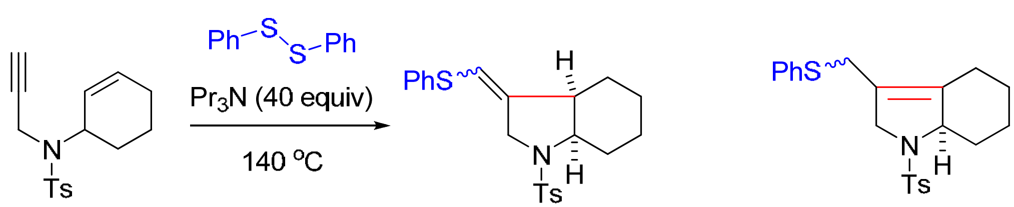
Minor

Entry	amine	Time	Temp.	Yield (%)
1	NEt_3	8 h	90 ºC	74
2	Pr_3N	3 h	140 ºC	83
3	Pyridine	24 h	115 ºC	No reaction
4	*i*$PrNEt_2$	4.5 h	125 ºC	69

Addition of 2 equiv. water increases yield



Yield = 80%, Ratio 56:17:27



Yield = 61%, Ratio 89:11

Ishibashi<2009OL3298>

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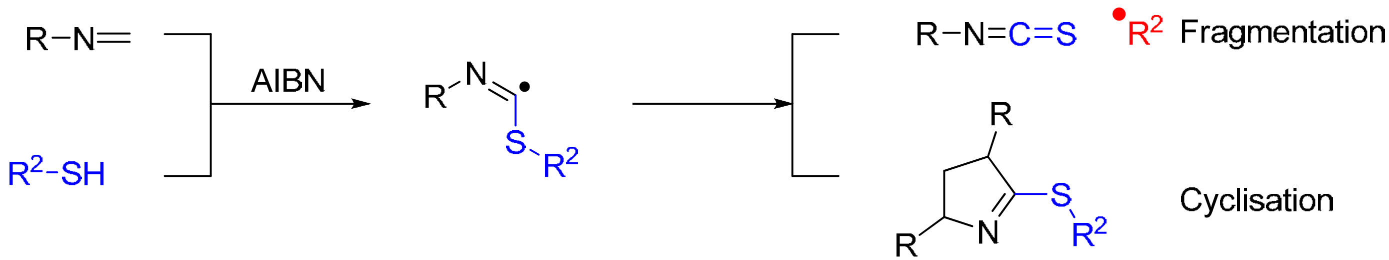
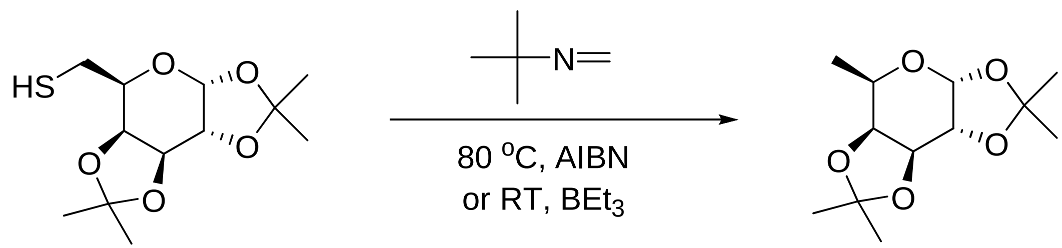
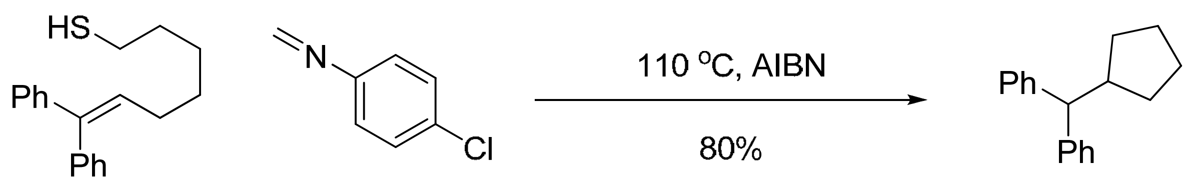
Thiol Radicals and Isocyanides



Barton-McCombie-type reaction

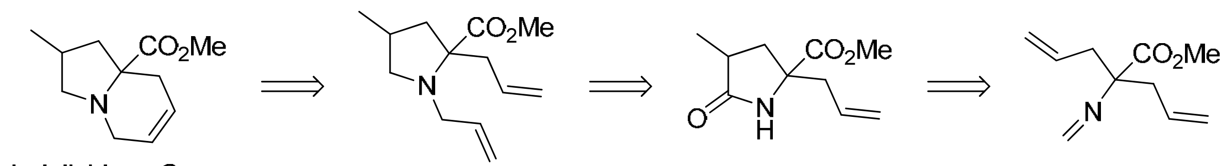


>95%

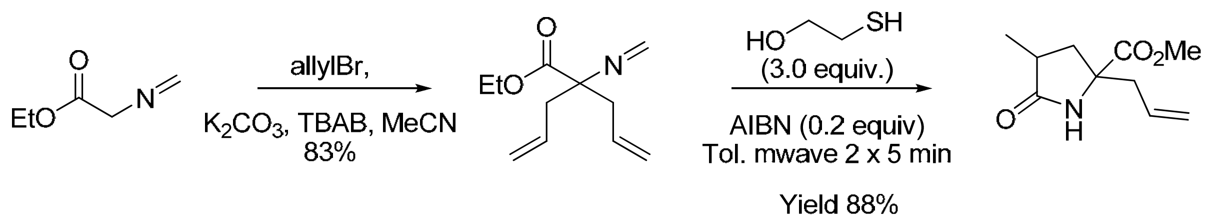


Minozzi<2004ACIE3598>

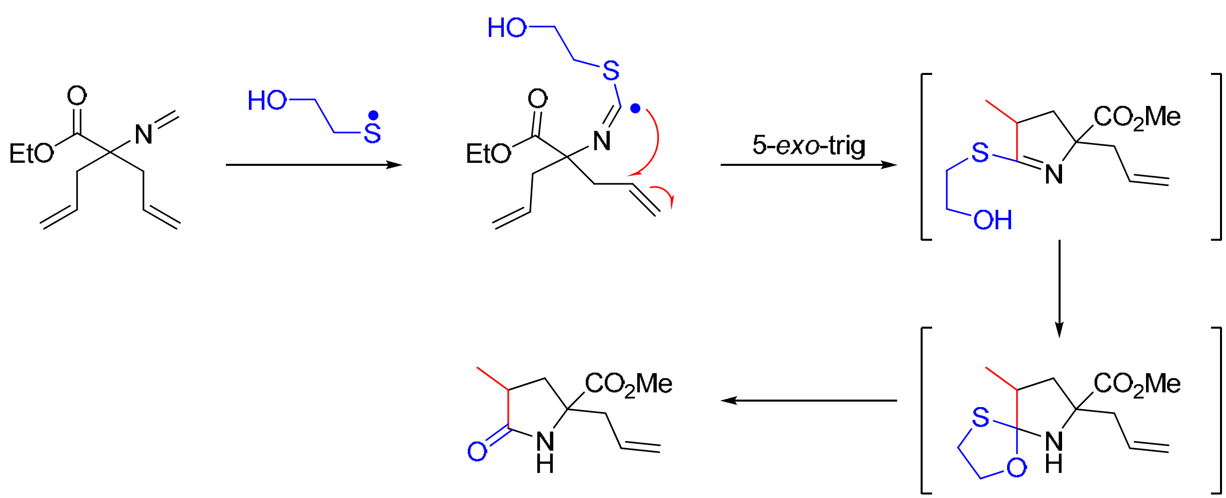
Thiol Radicals and Isocyanides



Indolizidene Core



Can also be carried out on a solid support: <2004TL8541>



Kilburn<2008TL6364><2003TL1347>

Sulfur Mediated C-C bond Formation

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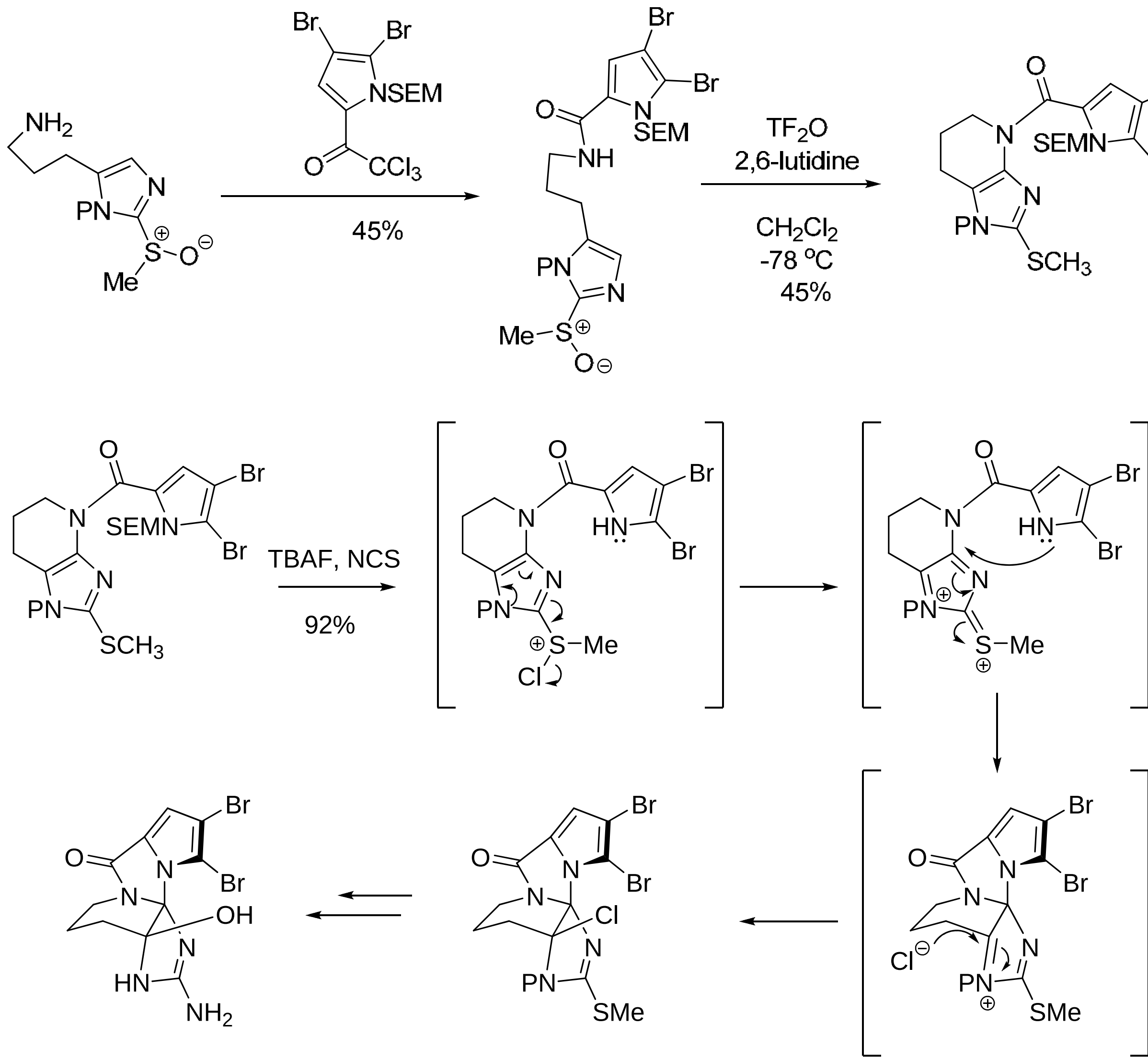
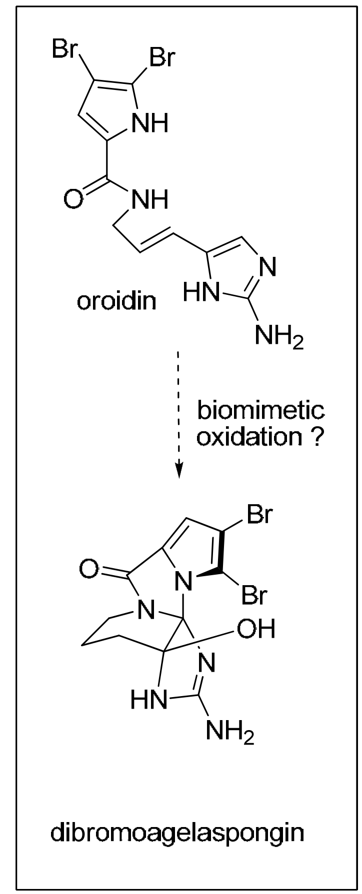
Pummerer and Pummerer-type Reactions

Reviews: Feldman<2006T5003> see also Pellissier<2006T1619>





Feldman<2008JACS14964><2009JOC3449>

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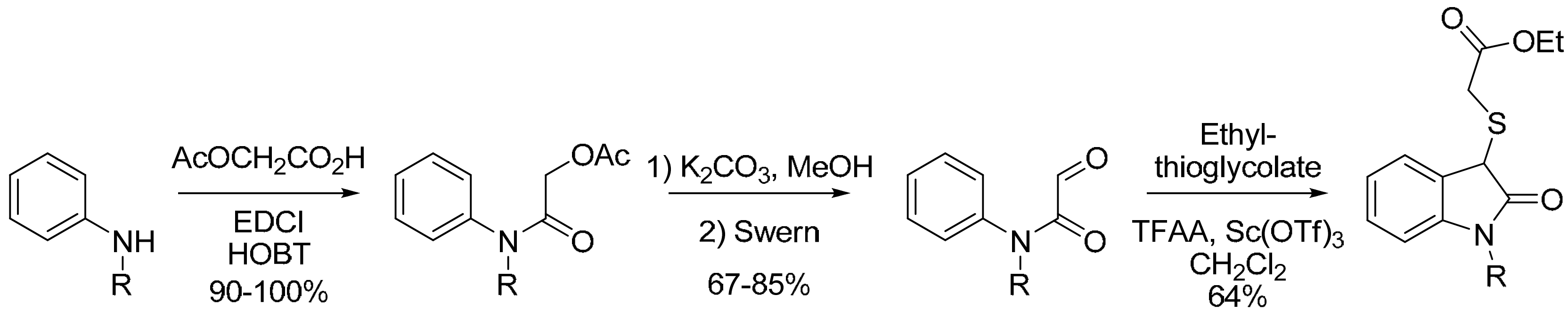
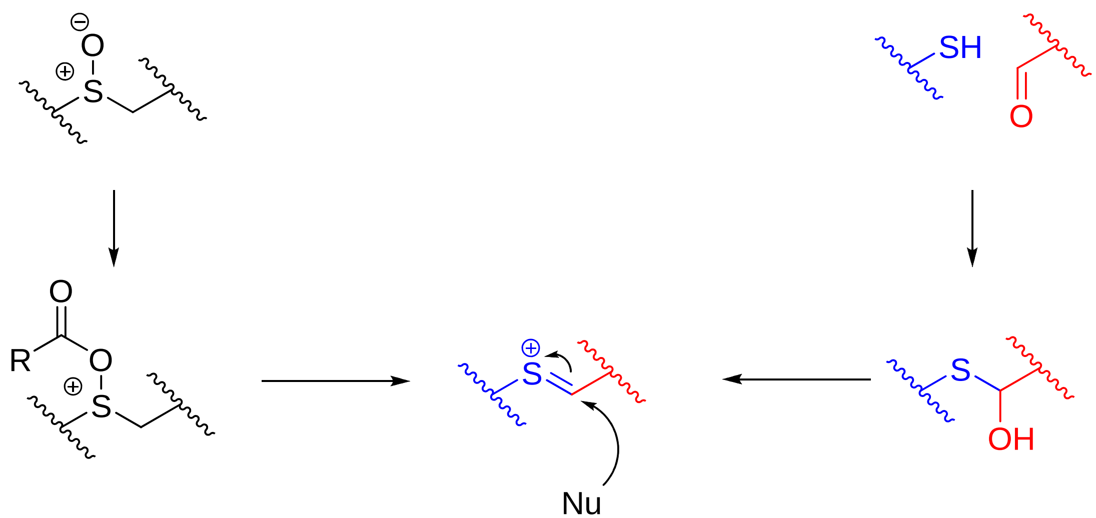
Pummerer and Pummerer-type Reactions



Reaction proceeds *via* a Pummerer-type reaction of the hemithioacetal

Pummerer Reaction

Connective Pummerer-type Reaction

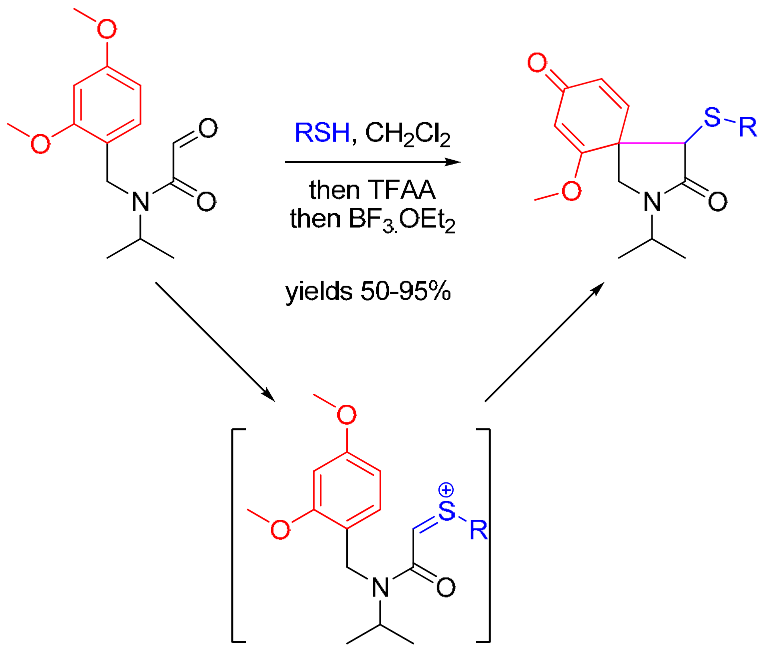


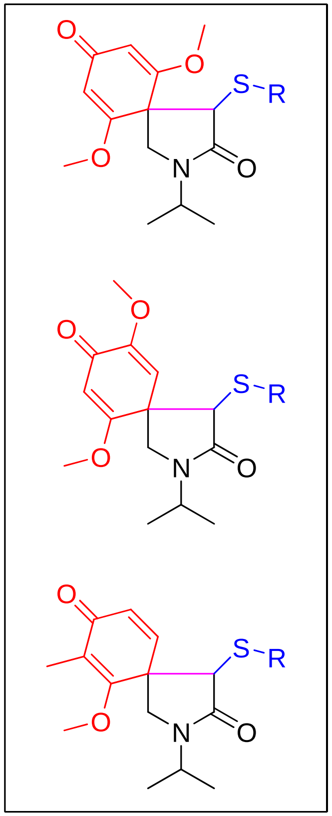
Proctor<2009OBC589>

Pummerer and Pummerer-type Reactions

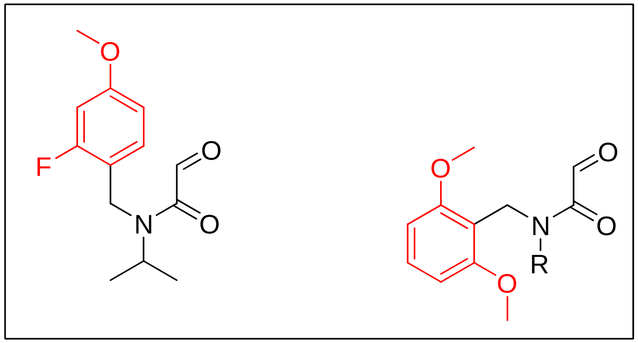
Synthesis of Azospirocyclic cyclohexadienones

Reaction proceeds *via* the same Pummerer-type reaction of the hemithioacetal





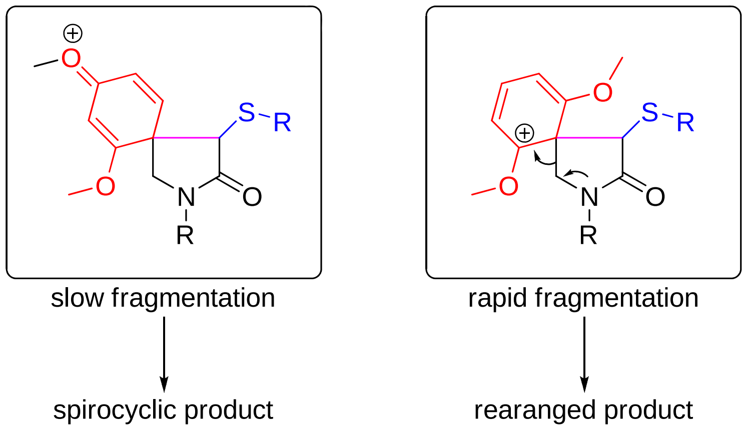
However, reaction does not work for all benzylic substrates:

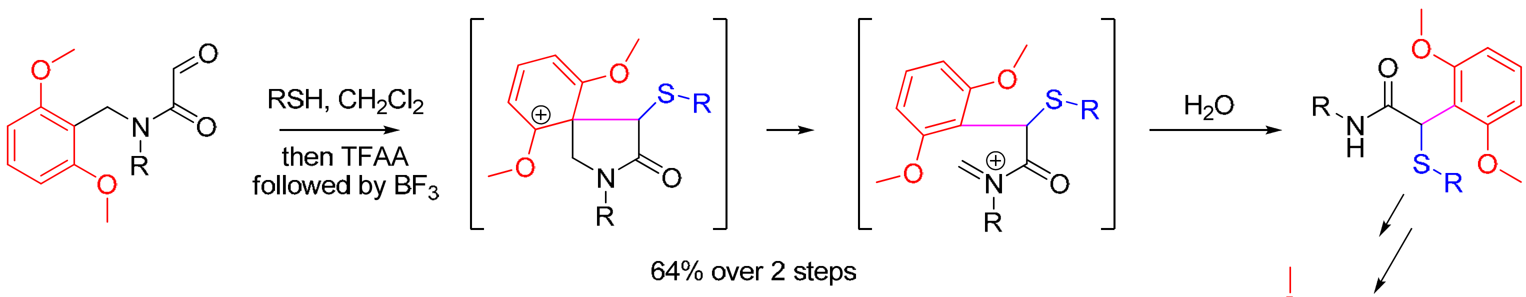


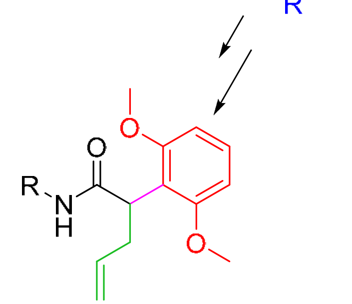
Proctor<2008OL1441>

Pummerer and Pummerer-type Reactions

Reaction proceeds *via* the same Pummerer-type reaction of the hemithioacetal. However, the outcome of the reaction depends heavily on the intermediate:







Sulfur nucleophiles can incorporate a fluorous tag.
Used to synthesise a range of substituted α-aryl acetamides.

Proctor<2009CC3101>

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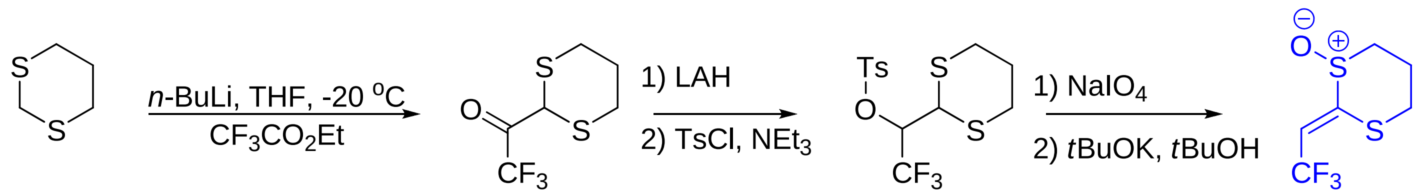
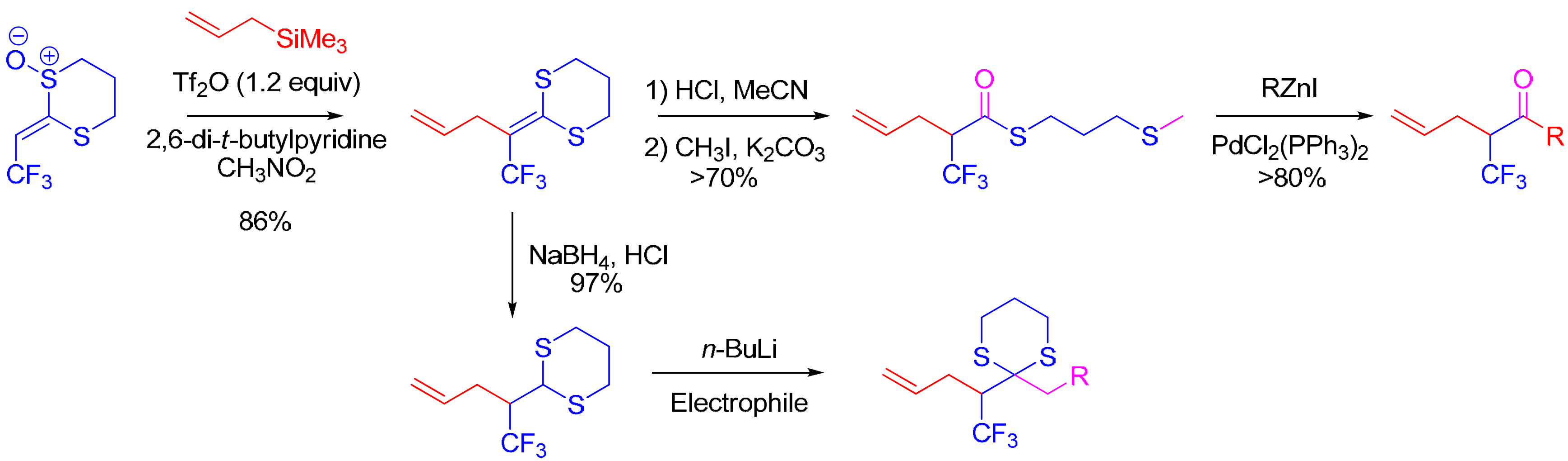
Pummerer and Pummerer-type reactions
Trifluoromethylation

Dithianes as trifluoromethylketene equivalents:
provides for a facile way to introduce the CF_3 group

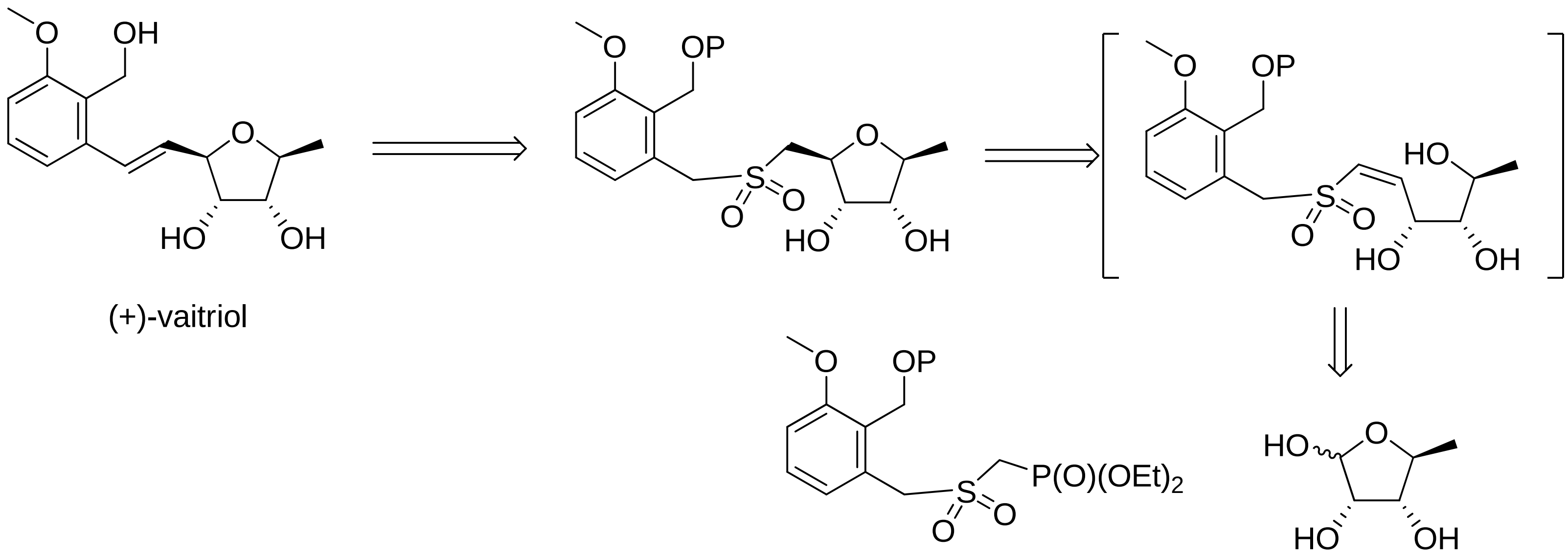


Products are versatile and make use of the dithiane



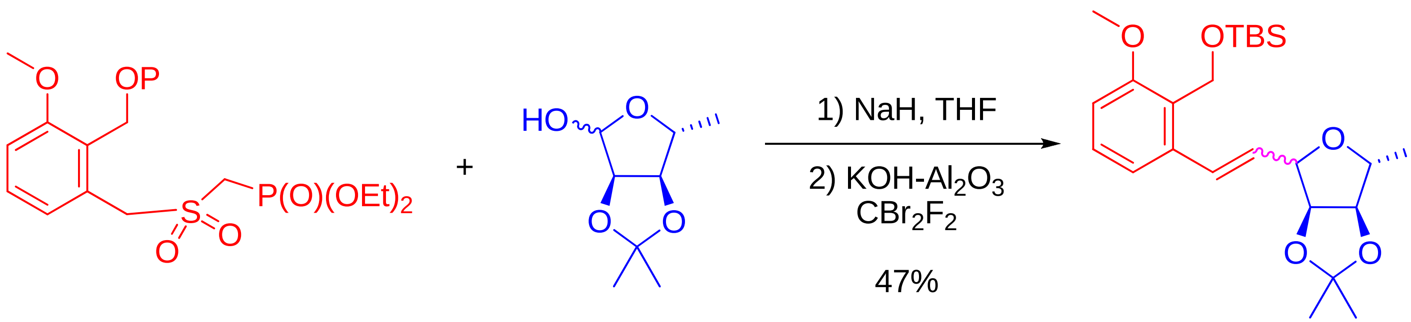
Oshima<2009OL2185>

Ramberg-Bäcklund Reaction



(+)-vaitriol

Utilising a domino HWE/conjugate addition/Ramberg-Bäcklund sequence



See also <2009JOC2271>

Taylor<2007T12123>

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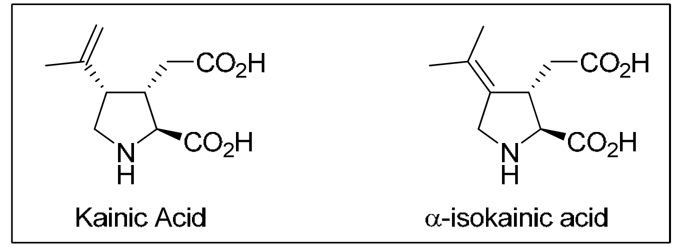
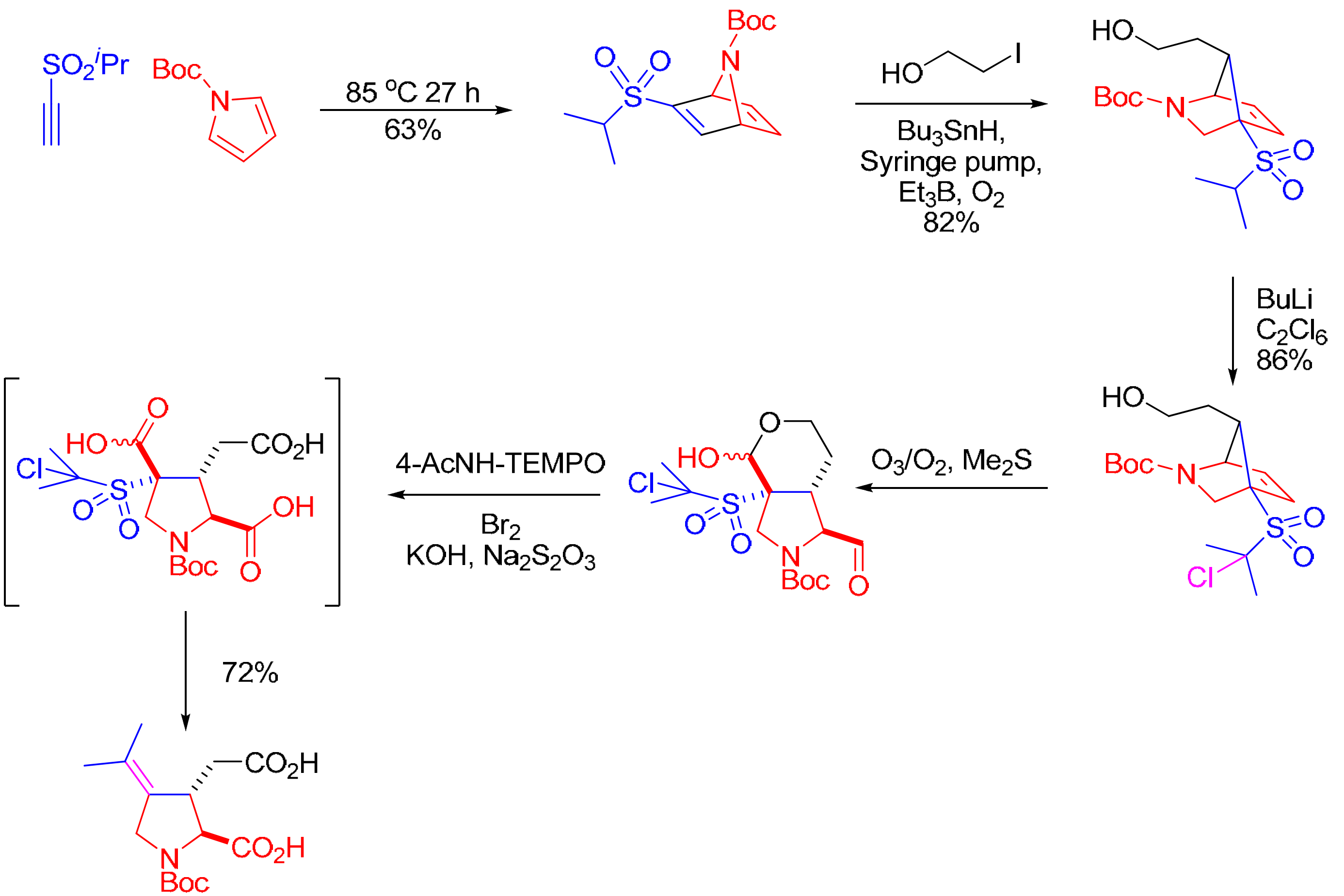
Ramberg-Bäcklund Reaction

Decarboxylative Ramberg-Bäcklund sequence



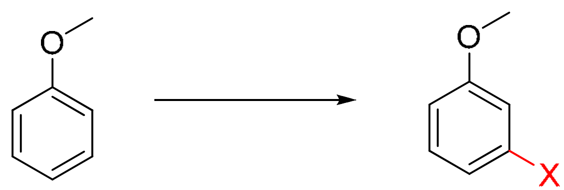


Hodgson<2005SL1267>

Sulfoxide Directed *ortho*-Lithiation

Method for *meta*-substitution of arenes

Synthesis of substituted arenes and heterocycles using sulfoxides as directing groups for lithiation and also as removable auxiliaries



For directed *ortho*-metallation see also:
<2004ACIE888>, <2007JOC3199>

Brown<2008OBC1215>

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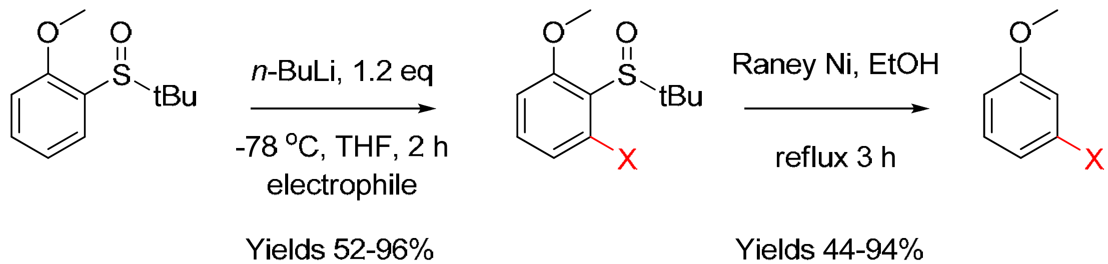
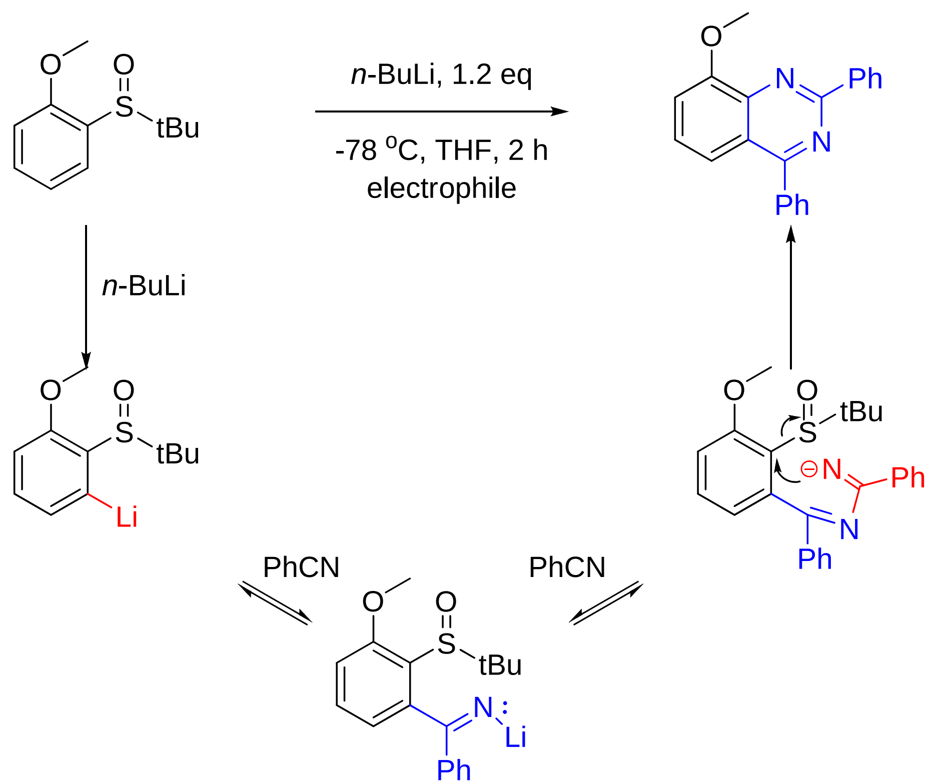
Sulfoxide Directed *ortho*-Lithiation

Method for *meta*-substitution of arenes



Formation of quinazolines



Brown<2008OBC1215>

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Chiral Sulfur Ligands and Catalysts

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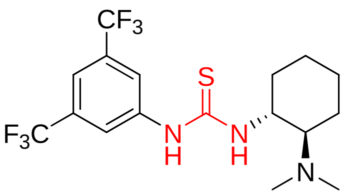
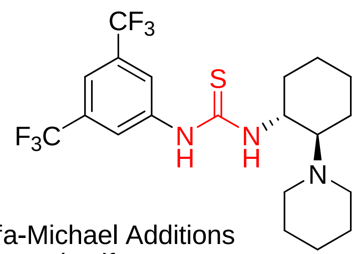
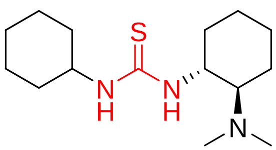
Chiral Sulfur Ligands and Catalysts

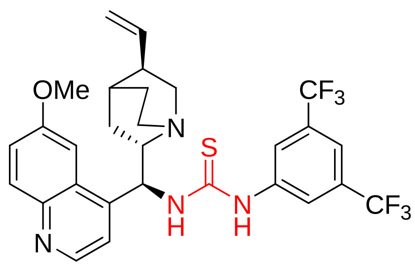
Reviews: Schulz<2007CR5133> see also Pellissier<2007T1297>,
Sone<2008Current Organic Synthesis305>
Aggarwal<2007CR5841>





Asymmetric Sulfa-Michael Additions
to α,β-unsaturated sulfonates

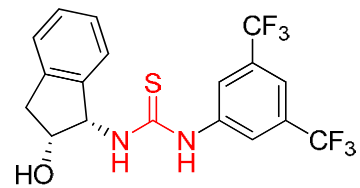




Enders<2009EJOC1665>

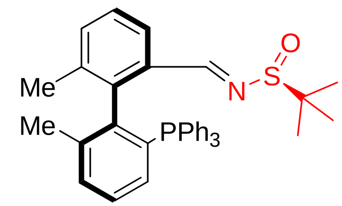
Dixon<2008OL1389>
Enantioselective Michael addition

Enantioselective addition
of indoles to nitroalkenes



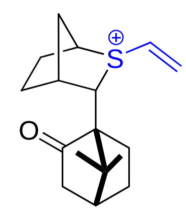
Seidel<2008JACS16464>

Ligand in Palladium-catalysed
addition to *N*-benzylisatin



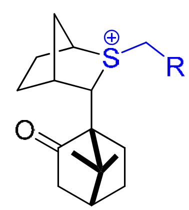
Qin<2009JOC283>

Epoxy-Annulations
of α-amido ketones



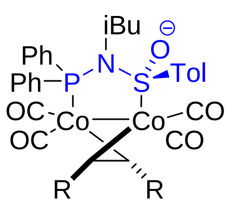
Aggarwal<2008OL1501>

Epoxidation/Cyclopropanation
Aziridination
Reaction with Boranes <2007JACS14632>



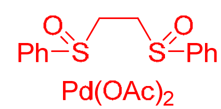
Aggarwal<2008OBC1185>
<2008CC120>, <2006CEJ568>
<2006T11297>
Substituted pyrrolidines /
piperidines <2006CC2156>

Asymmetric Pauson-Khand Reaction



Verdaguer<2009OL4346>
<2007ACIE5020>

Intramolecular
C-H oxidation



White<2009NC547>

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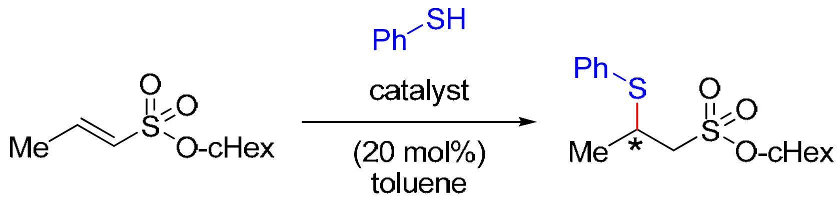
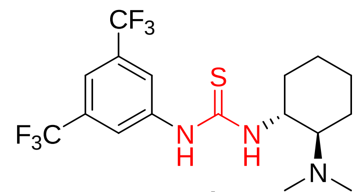
Chiral Sulfur Ligands and Catalysts

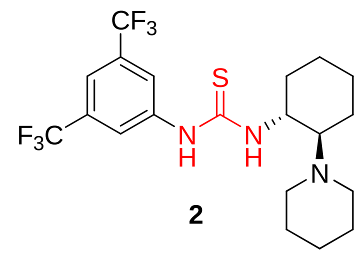


Enders<2009EJOC1665>

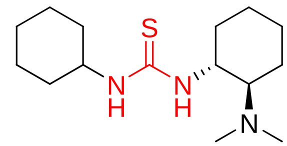
Catalyst 4 (Takemoto<2003JACS12675>)
yields 40-94% ee's of 31-64%



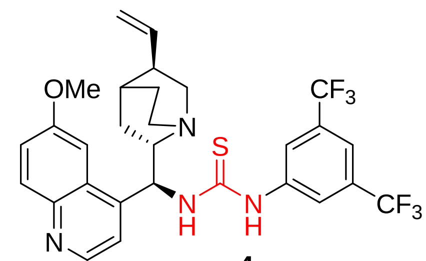
1



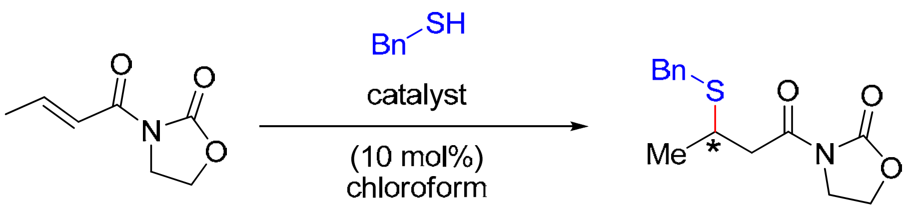
2



3

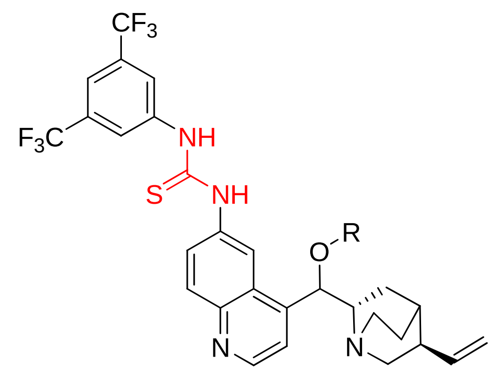


4



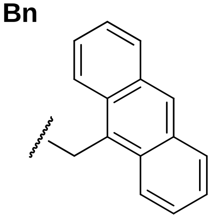
Entry	Catalyst	Time	Conv. (%)	ee (%)
1	4	24 h	95	45
2	5	5 h	>99	68
3	6	5 h	>99	85

Yields 84-99%, ee's 85-96%



5, R = Bn

6, R =



Deng<2009JACS418>

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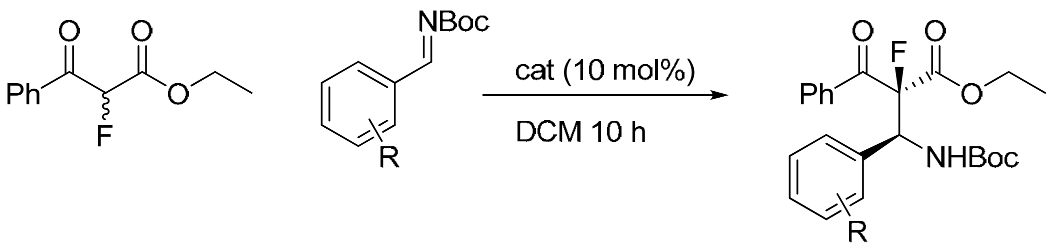
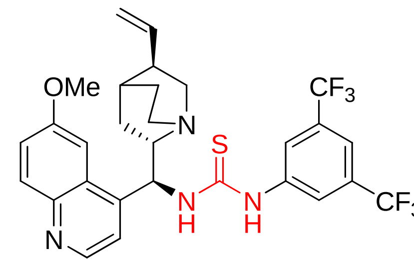
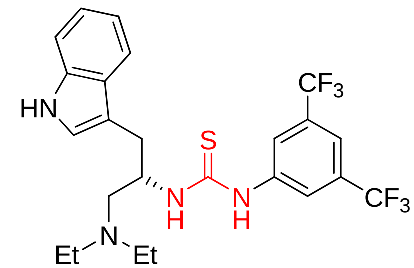
Chiral Sulfur Ligands and Catalysts





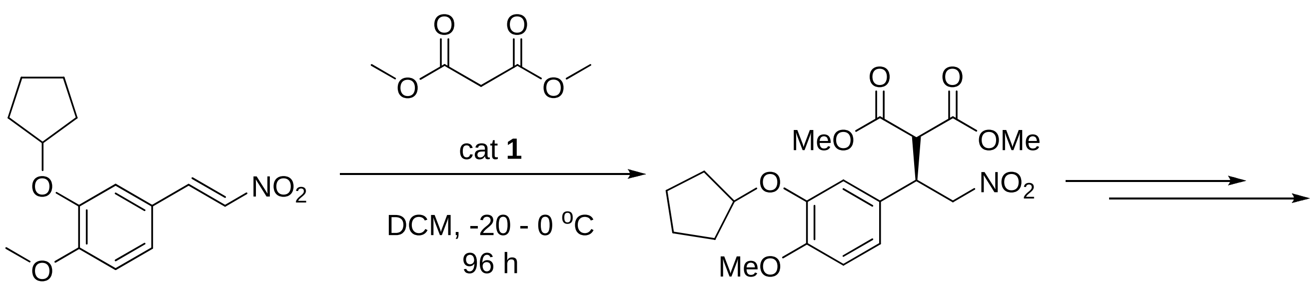
1



2

Catalyst 2 gave best ee's and yield
Yields 70-96%
ee's 81-97%

Lu<2009ACIE7604>



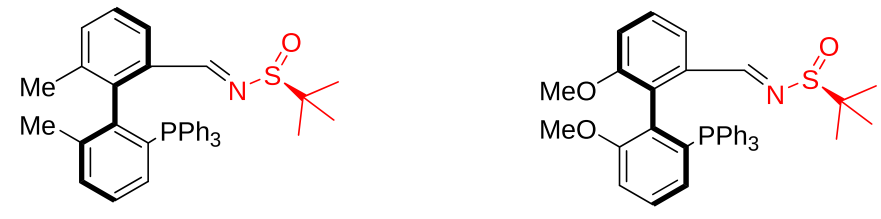
96% yield, 94% ee
(recrystallised to >99%, 87% yield)

Antidepressant
(*R*)-rolipram, >99% ee
63% yield/ 6 steps

See also Ellman<2009JACS8754> for similar additions to nitroalkenes
and Seidel<2008JACS16464>

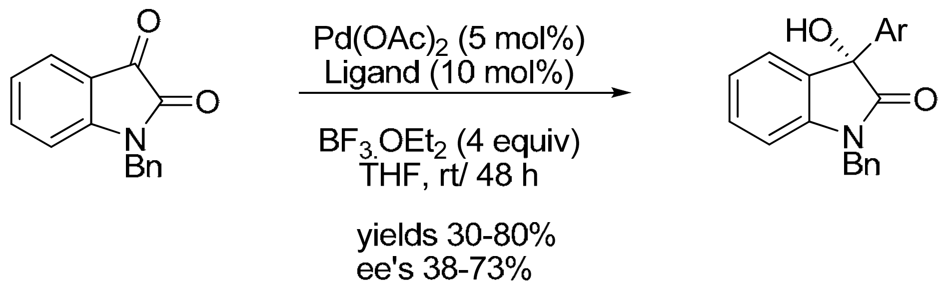
Dixon<2008OL1389>

Chiral Sulfur Ligands and Catalysts



(Ra,S) **1**

(Ra,S) **2**



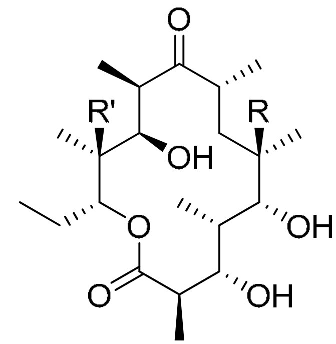
Entry	Ligand	Product	Yield (%)	ee (%)
1	(R_a,*S*) **1**	R = Ph	63	67 (*S*)
2	(S_a, *S*) **1**	R = Ph	48	62 (*R*)
3	(R_a,*S*) **2**	R = Ph	40	60 (*S*)
4	(S_a, *S*) **2**	R = Ph	30	57 (*R*)

Ligands are related to those of Ellman<2003OL545>

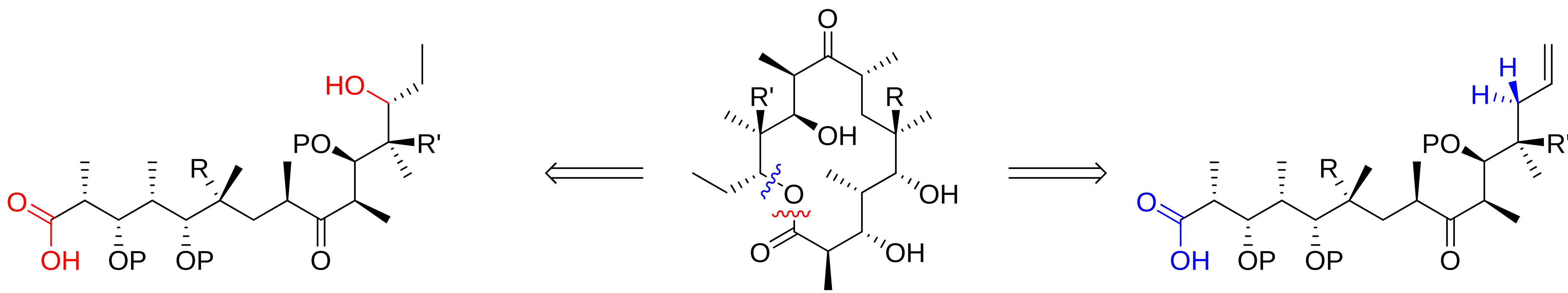
Qin<2009JOC283>

Chiral Sulfur Ligands and Catalysts

Polyketide macrolides present a number of synthetic challenges including: stereocontrol, and macrocyclisation



6-Deoxyerythronolide B, R = R' = H
Erythronolide B, R = OH, R' = H
Erythronolide A, R = R' = OH



Stereochemically defined

Stereochemically versatile

White<2009NC547>

Chiral Sulfur Ligands and Catalysts

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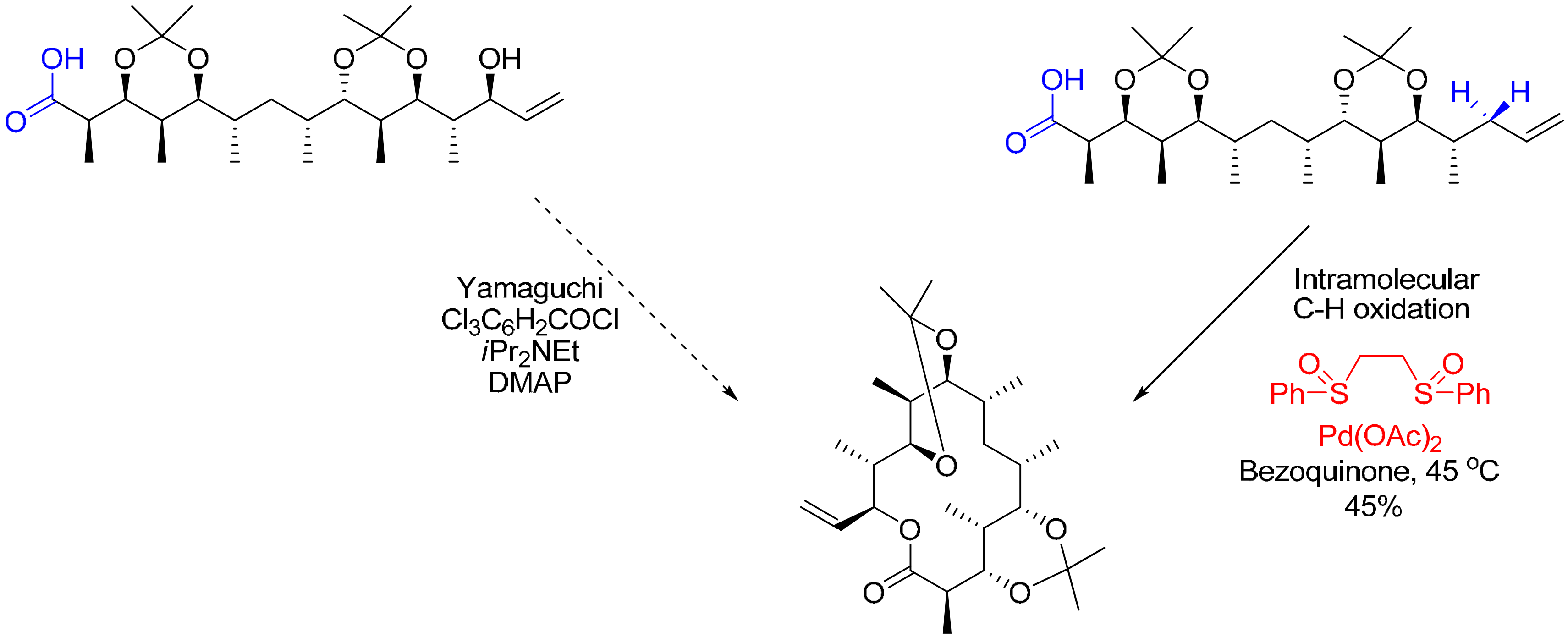

Yamaguchi macrolactonisation failed to produce the macrolide. Use of C-H oxidation leads to activation with the palladium catalyst facilitating selective ring formation

White<2009NC547>

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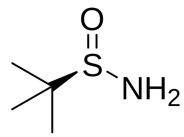
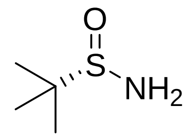
Ellman Type Sulfonylimines





tert-butanesulfimines - chiral amnie equivalents
-related to Davis' *para*-toluenesulfimines <2006JOC8993><1998CSR13>

For reviews of the Ellman reaction see: Ellman<2002ACR984>, Chemla<2009CSR1162>, Lin<2009ACR831>, Stockman<2006T8869>.

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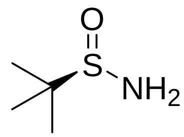
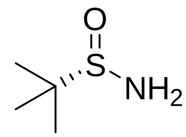
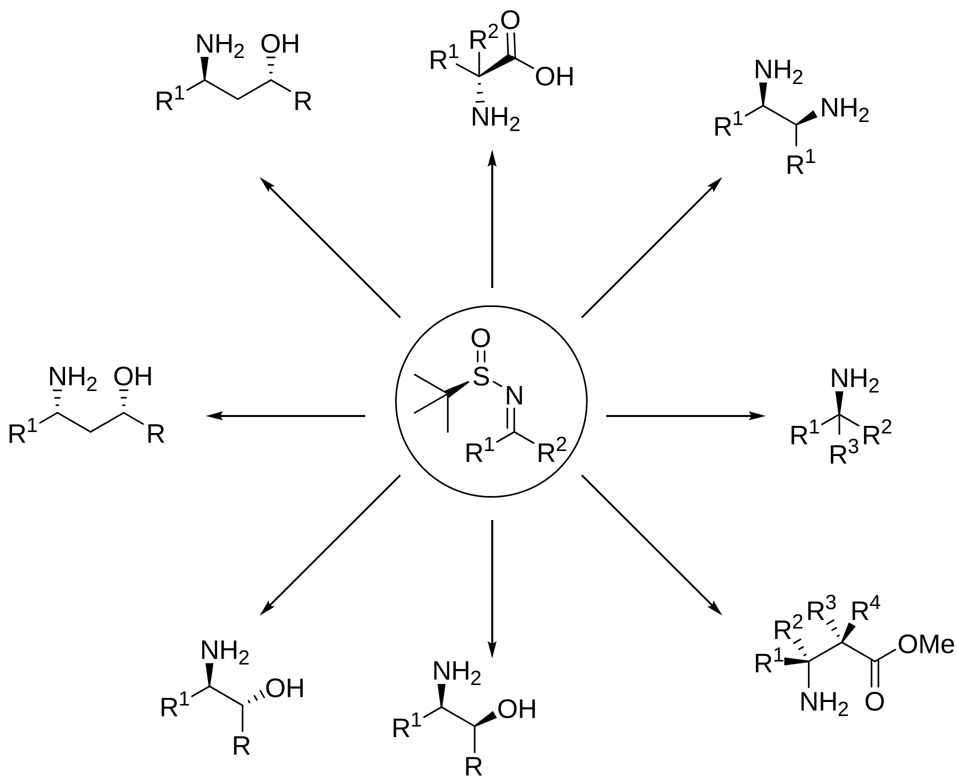
Ellman Type Sulfonylimines

tert-butanesulfimines - chiral amnie equivalents
-related to Davis' *para*-toluenesulfimines <2006JOC8993><1998CSR13>



For reviews of Ellman sulfonylimines see: Ellman<2002ACR984>, Chemla<2009CSR1162>, Lin<2009ACR831>, Stockman<2006T8869>.

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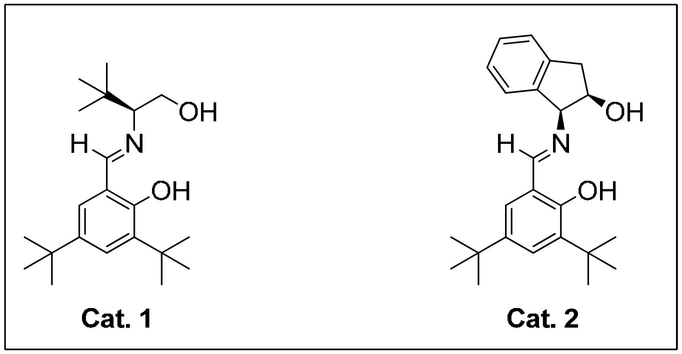
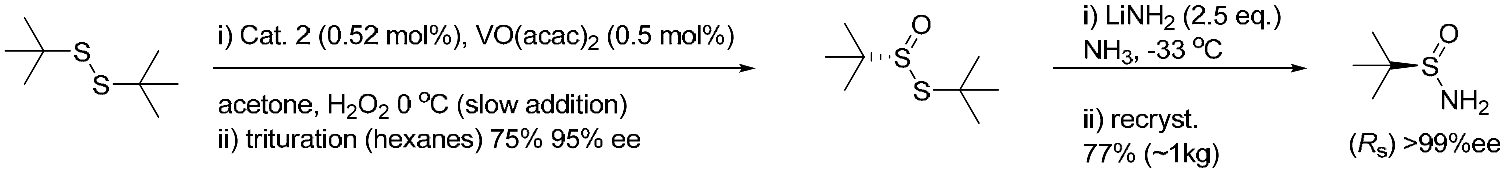
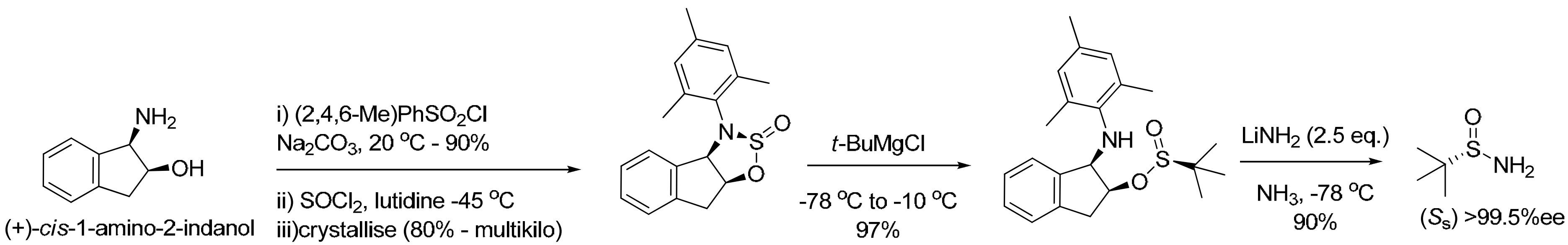
Ellman Type Sulfonylimines





Ellman<2005OS157>



Senanayake<2005ACA93>

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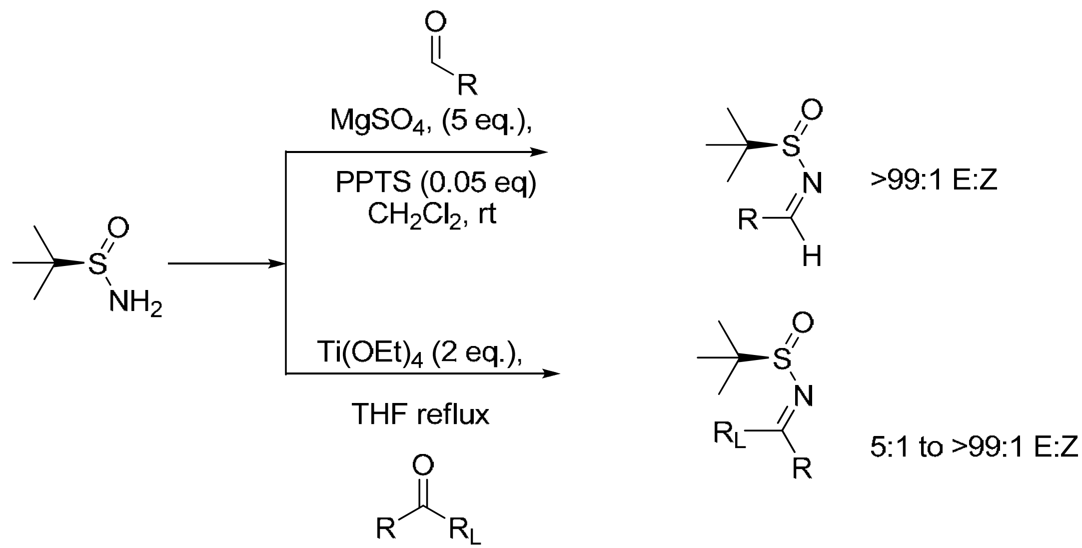
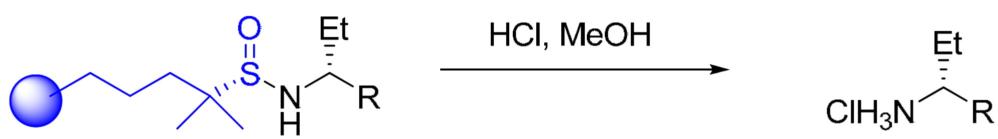
Ellman Type Sulfonylimines

Formation of aldimines and ketimines



Deprotection is straightforward under acidic conditions:



Recycling of *tert*-butanesulfinyl group: Ellman<2009JOC2646>, Aggarwal <2009TL3482>

Ellman<2001JACS10127>

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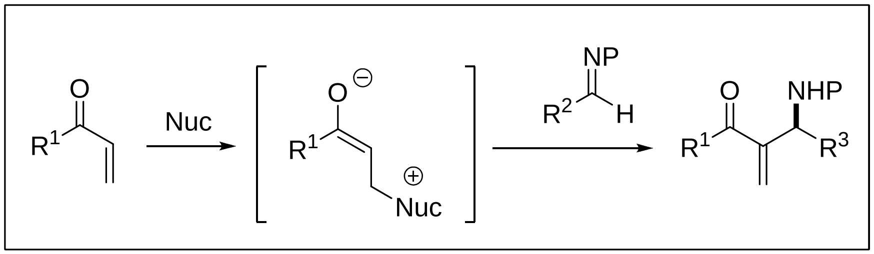
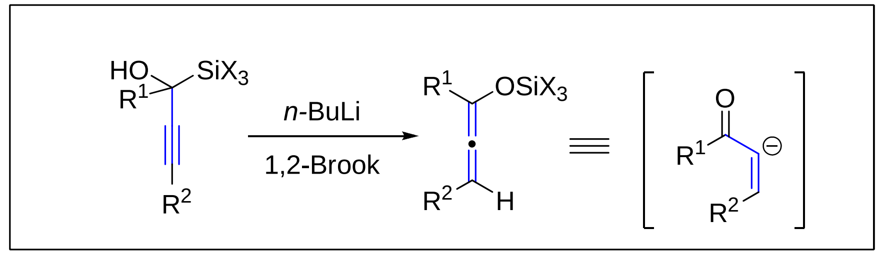
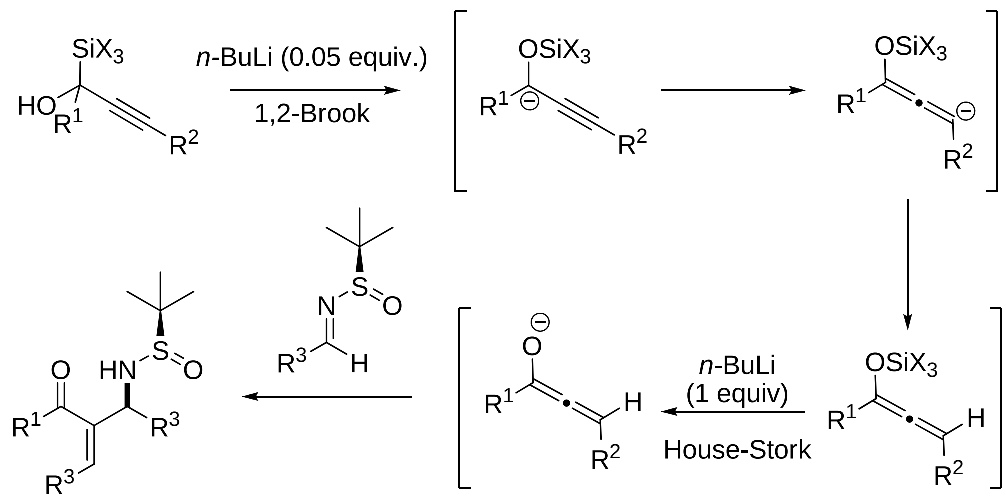
Ellman Type Sulfonylimines

aza-Morita-Baylis-Hillman reaction

Analogous use of lithium allenolates– synthesised *in-situ via* initial Brook rearrangement







yields 70-94%
d.r. 8:1 to 20:1

See also Chemla <2009OL931> and Viso <2008OL4775> for related reactions

Scheidt<2008OL5227>

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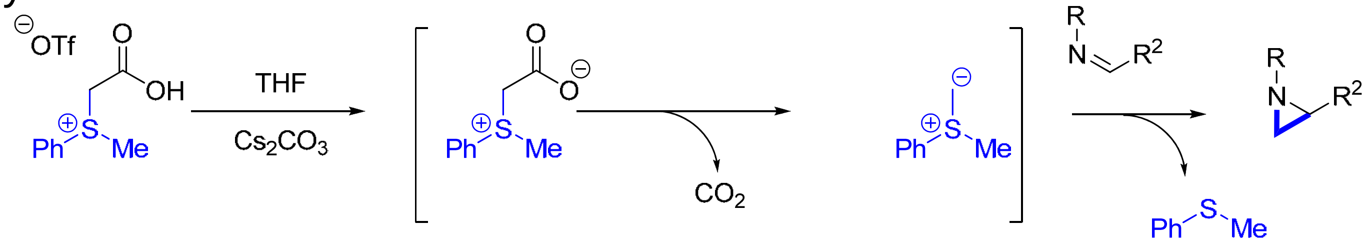
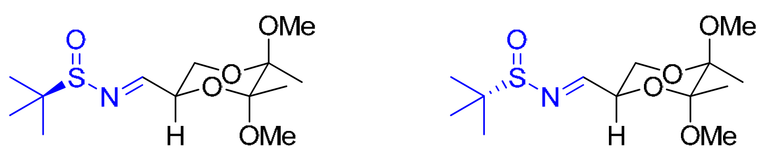
Ellman Type Sulfonylimines
Aziridine Formation

Sulfur ylide formation



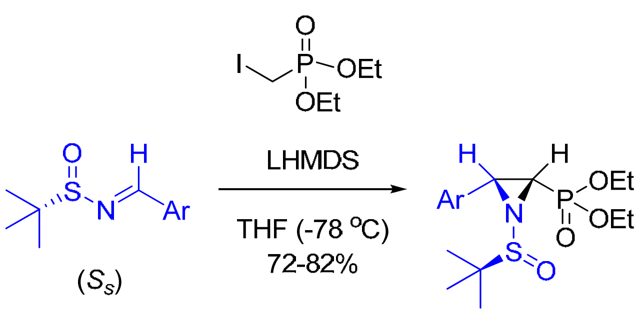
Combined Ellman reagent with Ley butanediacetal to synthesise aziridines



Yield 92% dr >95:5

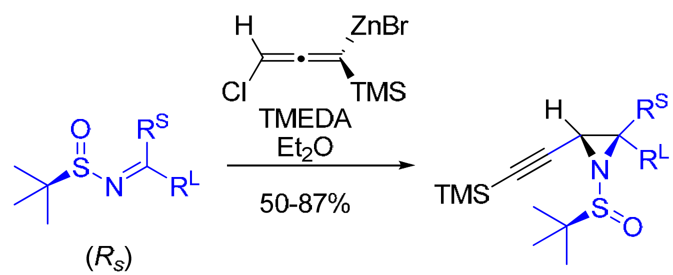
Yield 88% dr >78:22

Forbes<2009CC1882>



(S_s)

single isomer



(R_s)

>98:2 dr

Davis<2006JOC6894>

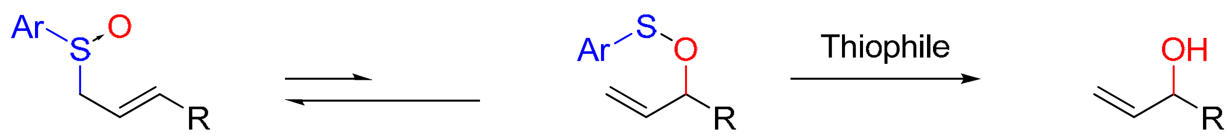
Chemla<2004JOC8244>

For additional examples: Sweeney<2009EJOC4911>

Rearrangements

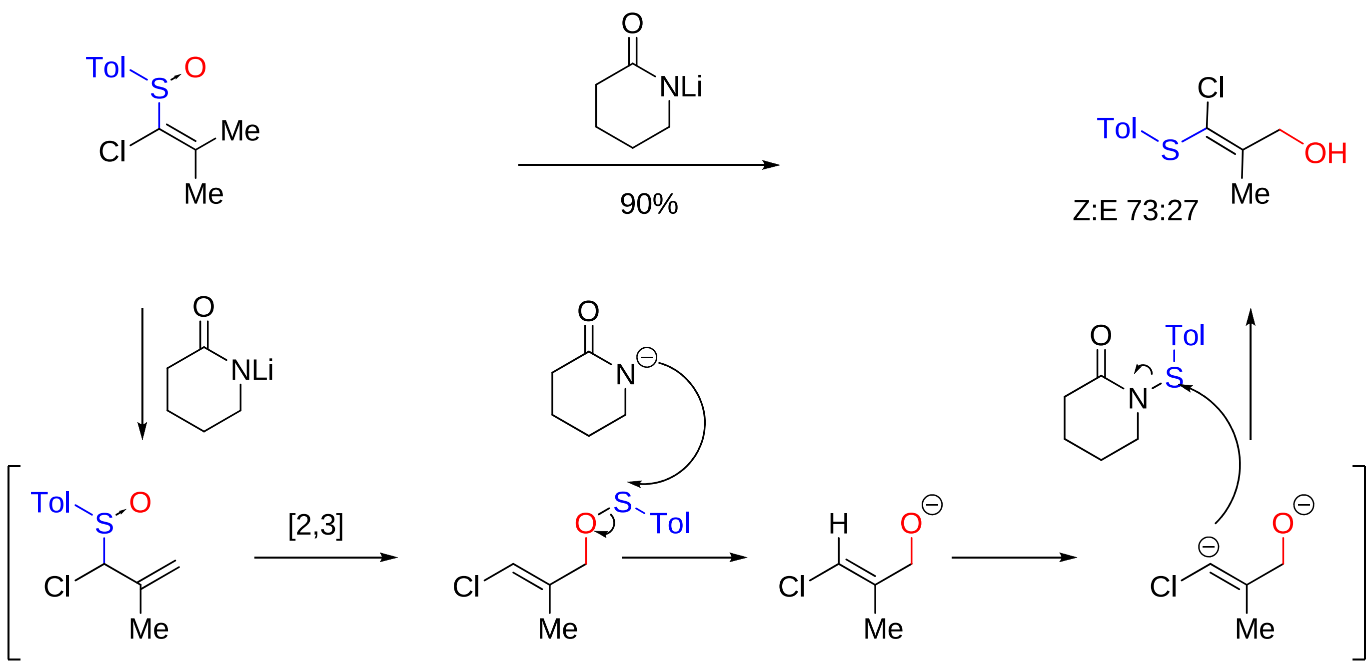
Rearrangements
[2,3] Mislow-Braverman-Evans Rearrangement

Classical [2,3] Mislow-Braverman-Evans rearrangements results in formation of an alcohol with loss of sulfur



Satoh's approach results in retention of the sulfur atom on the original carbon

Satoh<2006TL1981>



Reaction was carried out with 5 equivalents of base (LDA produced complex mixtures)

Rearrangements
[2,3] Thia-Sommelet-Hauser

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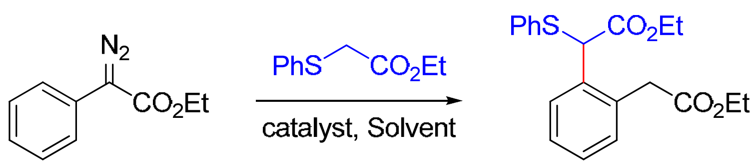
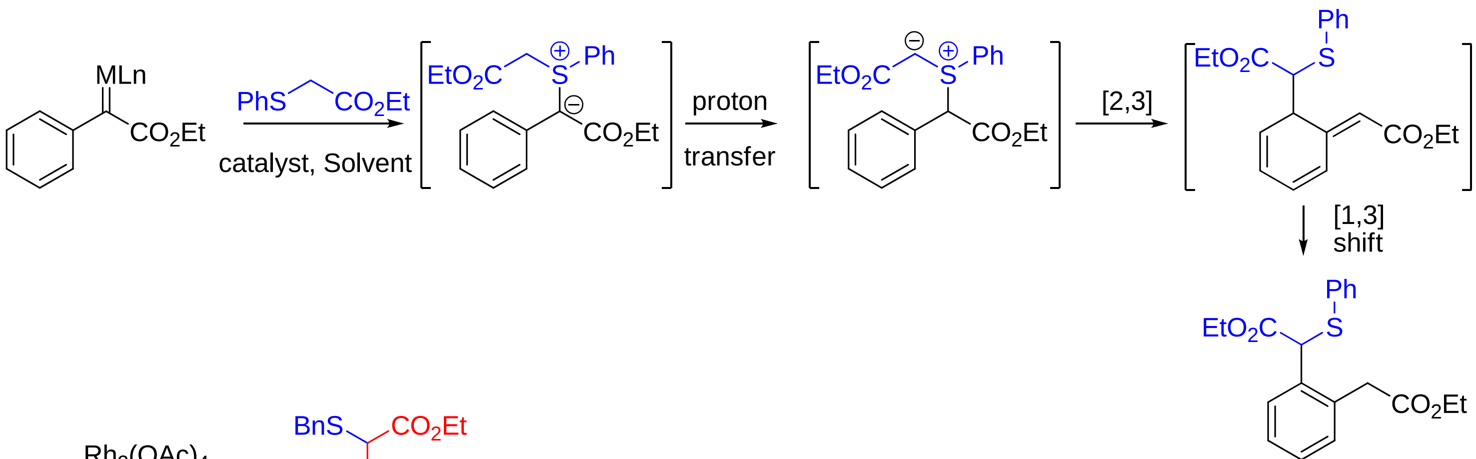
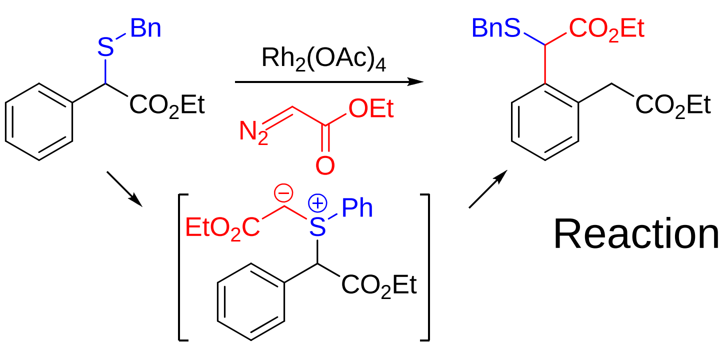
Synthesis of substituted arenes



Entry	Catalyst	Solvent	Time	Yield (%)
1	$Rh_2(OAc)_4$	DCM	2 h	51
2	$Rh_2(OAc)_4$	Tol.	2 h	67
3	$Rh_2(O_2CCF_3)_4$	Tol.	0.5 h	87





Reaction can easily be carried out in "reverse" with ethyl diazoacetate

Wang<2008OL693>

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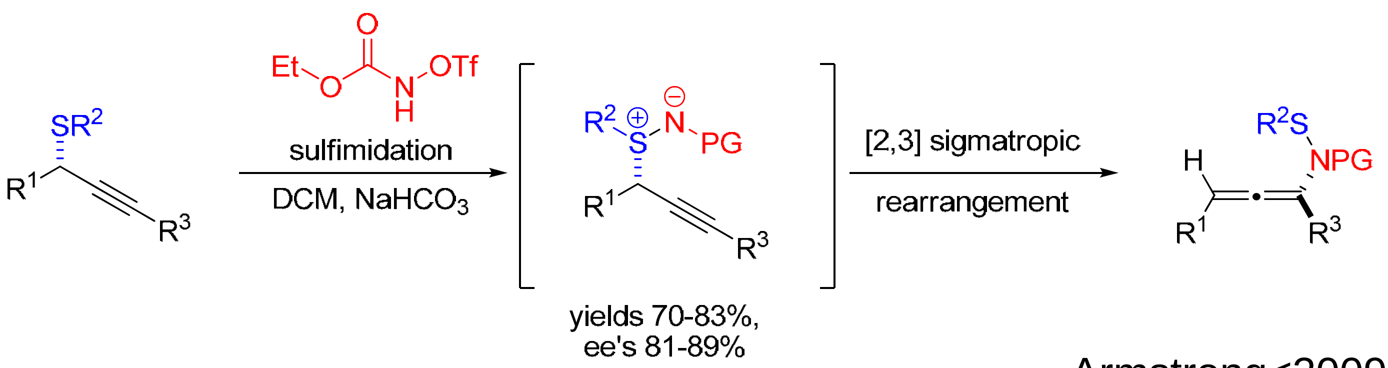
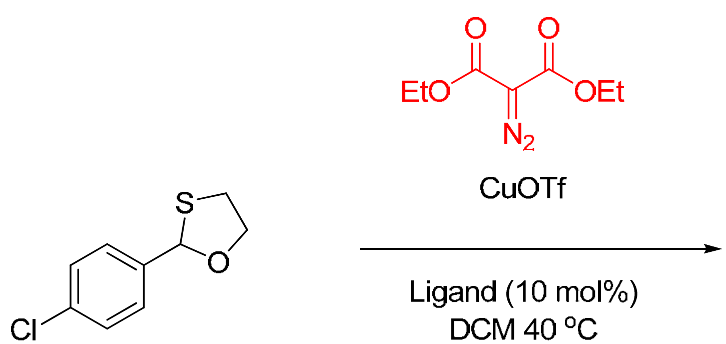
Rearrangements
[1,2] Stevens and sulfimide [2,3] rearrangements

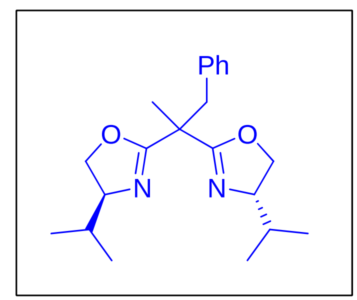
Synthesis of Allenamides *via* sulfimide [2,3]-sigmatropic rearrangement



Armstrong<2009OL1547>

Asymmetric [1,2]-Stevens Rearrangement of Sulfur Ylides

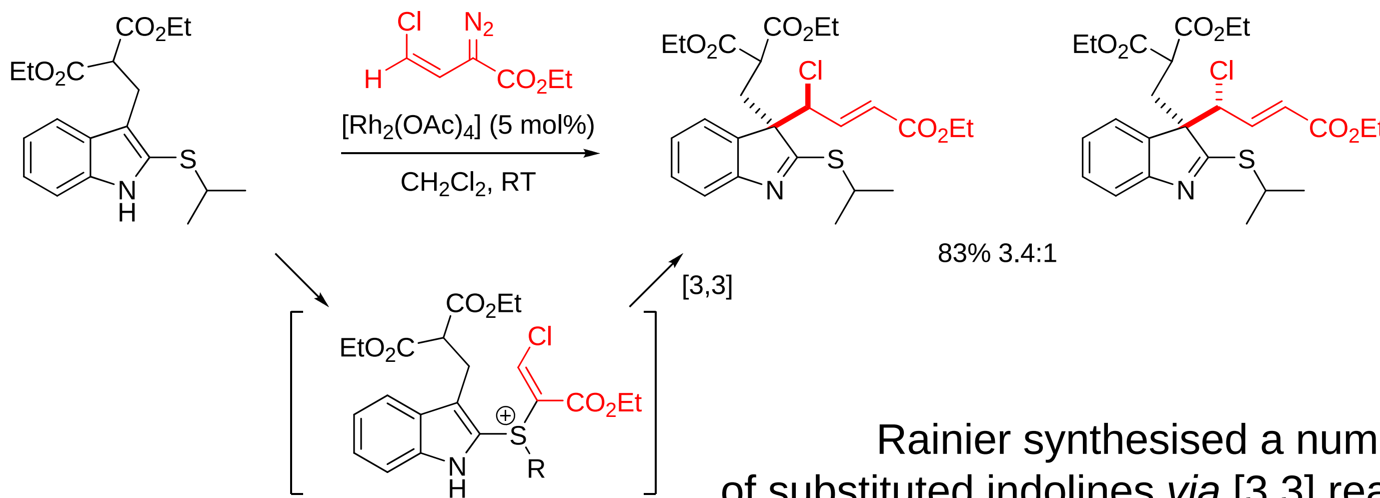




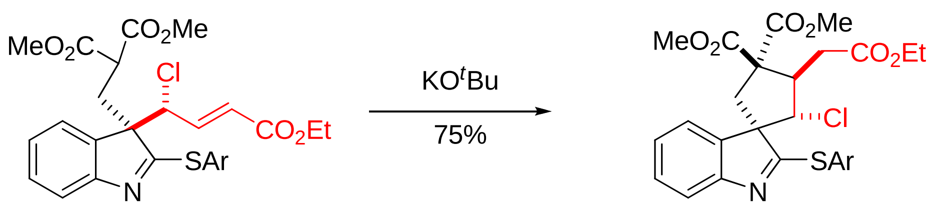
Tang and co-workers investigated a range of bisoxazoline ligands
Yields 60-98% ee's 50-90%

Tang<2009ASC309>

Rearrangements
[3,3] Sulfonium Ylide rearrangements



Rainier synthesised a number of substituted indolines *via* [3,3] rearrangement



Products are readily converted to spirocyclopentanes

Rainier<2008ACIE5374>

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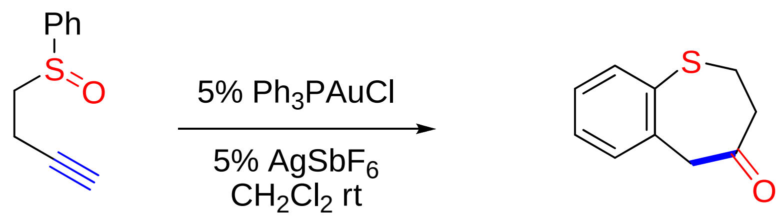
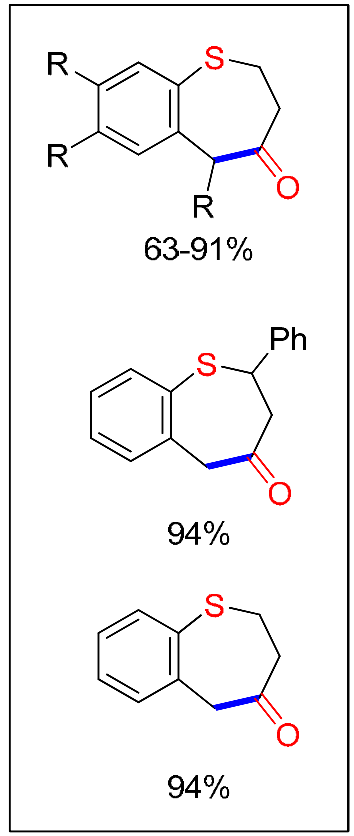
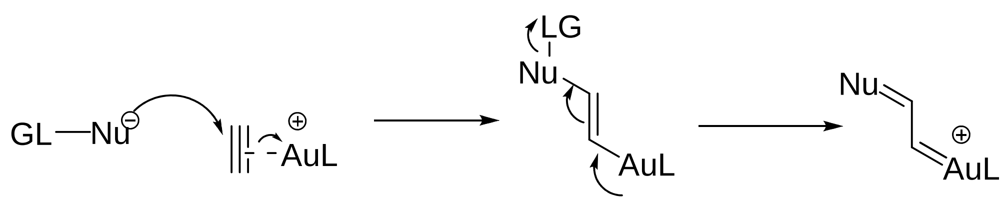
Rearrangements of Alkynyl Sulfoxides Catalysed by Gold (I) Complexes

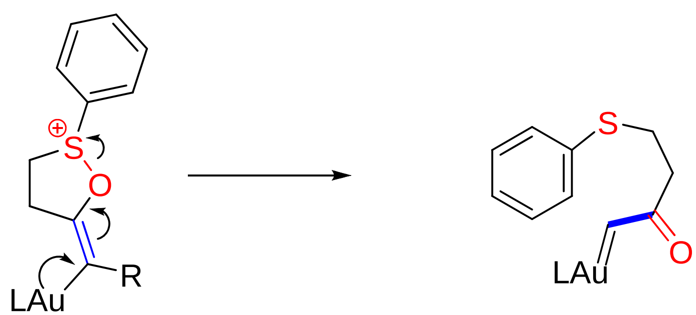
Reaction of sulfoxides with gold-carbenoid species:





Reaction proceeds via rearrangement and reaction of the metal carbenoid:





For related reactions see also Zhang<2007ACIE5156>
and reactions of allenes Krause<2006ACIE1897>

Toste<2007JACS4160>

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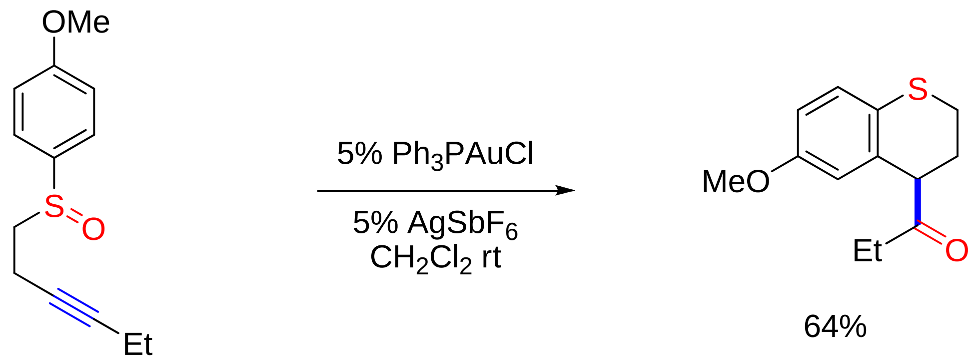
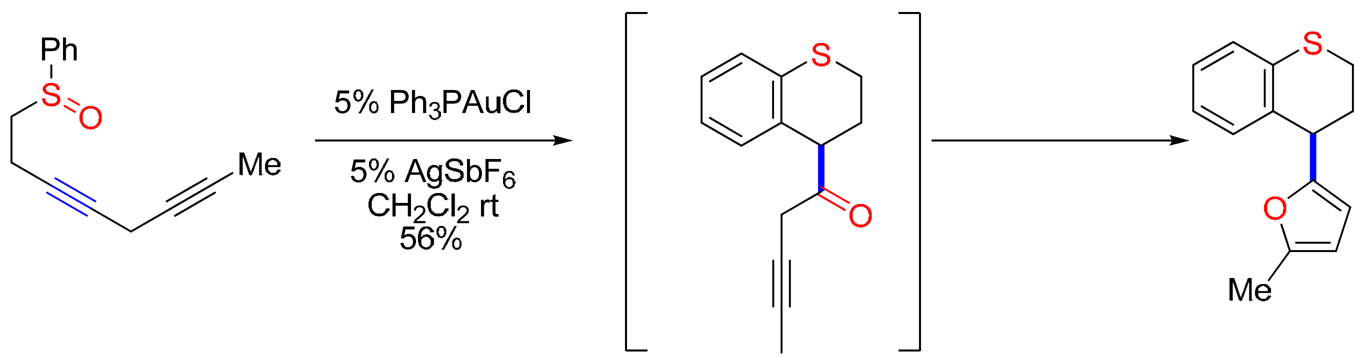
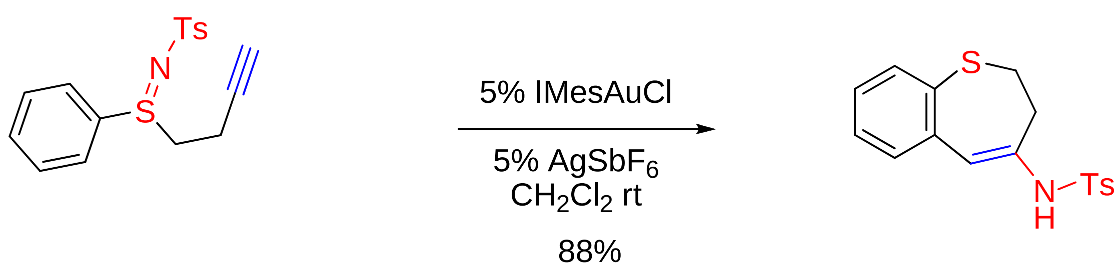
Rearrangements of Alkynyl Sulfoxides Catalysed by Gold (I) Complexes

Reaction of sulfoxides with gold-carbenoid species:





Reaction also works with sulfimines:



Toste<2007JACS4160>

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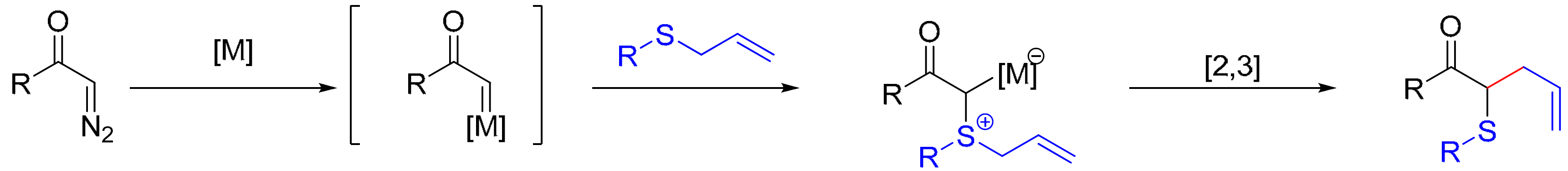
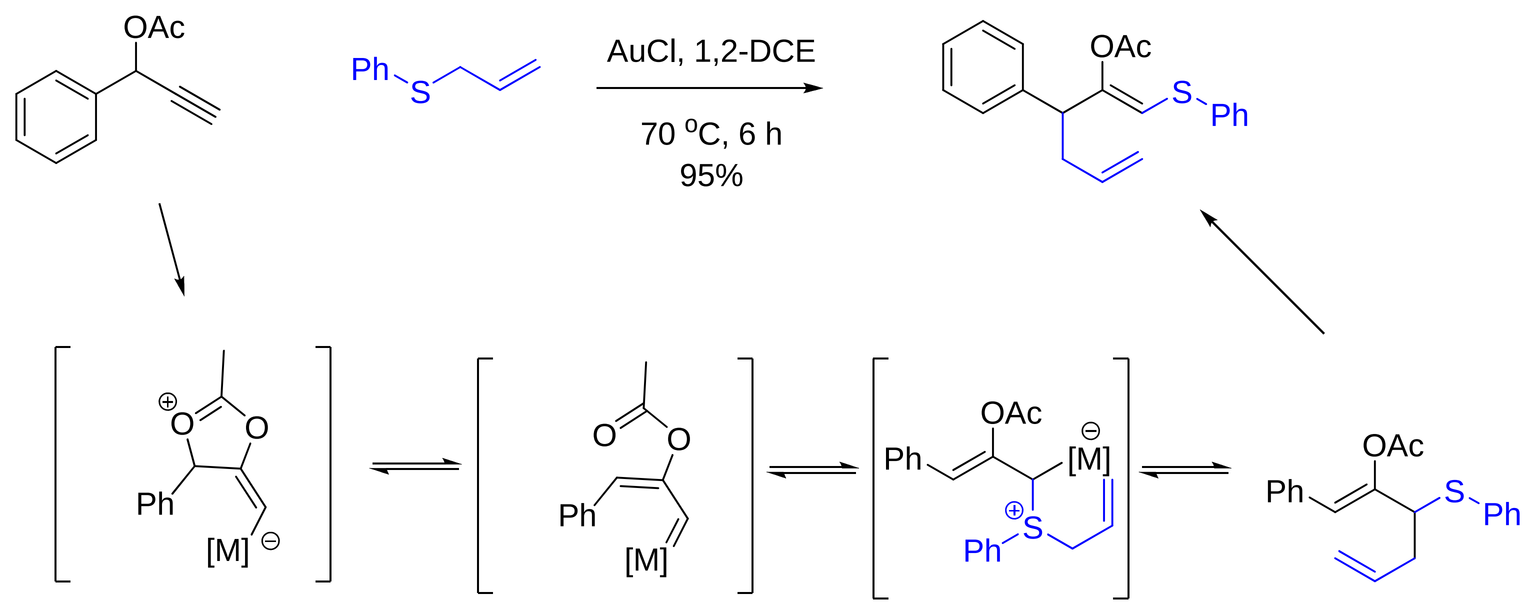
Rearrangements of Alkynyl Sulfoxides Catalysed by Gold (I) Complexes

Reaction of allyl sulfides with gold-carbenoid species:



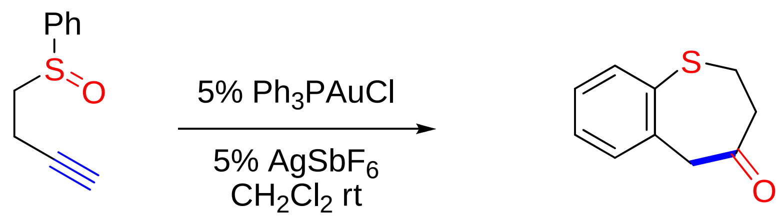
Doyle-Kirmse reaction – anticipated product:



Davies<2008CC238>

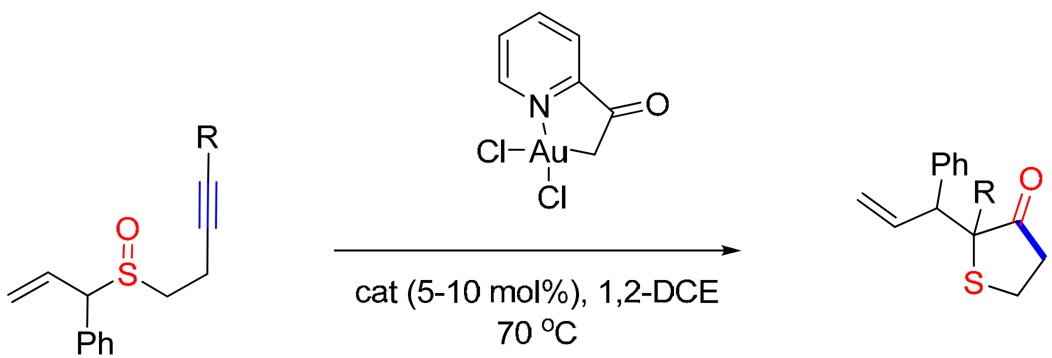
Rearrangements of Alkynyl Sulfoxides Catalysed by Gold (I) Complexes

Reaction of sulfoxides with gold-carbenoid species:

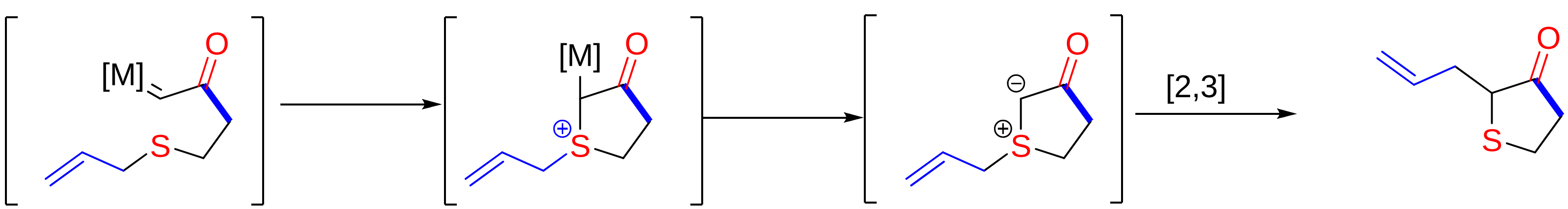


Reaction of sulfur with the metal carbenoid:

Toste<2007JACS4160>



Yields 40-85%



Davies<2009ACIE8372>

Thanks

Thanks to the organising Committee

Thank you for listening

Journal Abbreviations

ACA	Aldrichimica Acta
ASC	Advanced Synthesis and Catalysis
ACIE	Angewandte Chemie International Edition
ACR	Accounts of Chemical Research
CC	Chemical Communications
CR	Chemical Reviews
CSR	Chemical Society Reviews
EJOC	European Journal of Organic Chemistry
JACS	Journal of the American Chemical Society
JBC	Journal of Biological Chemistry
JOC	Journal of Organic Chemistry
NC	Nature Chemistry
OBC	Organic and Biomolecular Chemistry
OL	Organic Letters
OPRD	Organic Process Research and Development
OS	Organic Syntheses
PNAS	Proceedings of the Natural Academy of Sciences
SL	Synlett
T	Tetrahedron
TL	Tetrahedron Letters

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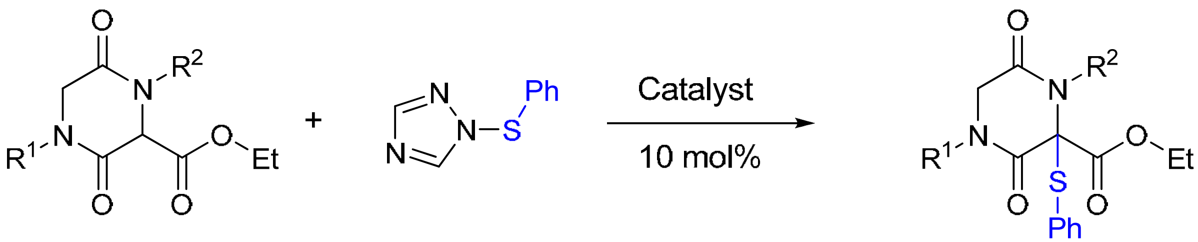
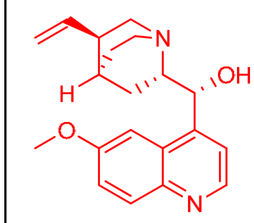
Additional Slides

ETP Core Synthesis

Stable sulfur electrophile instead of sulfenyl chloride





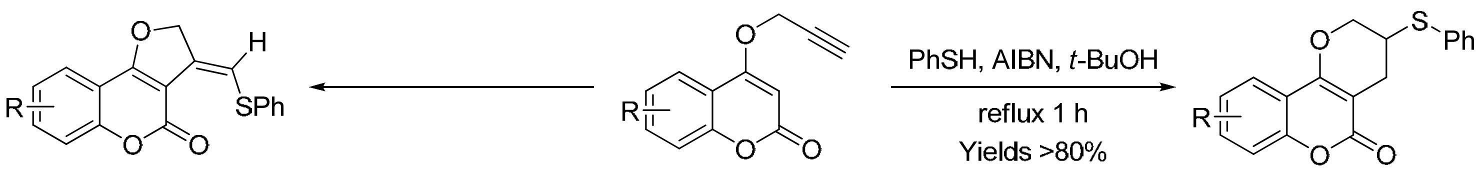
Quinine

R_1	R_2	Solvent	Temp.	Equiv.	Time	Yield (%)
Et	Et	Tol.	Rt	3.0	60 h	77
Et	Et	Tol.	Rt	8.0	48 h	77
Bn	Bn	Tol.	Rt	3.0	60 h	75

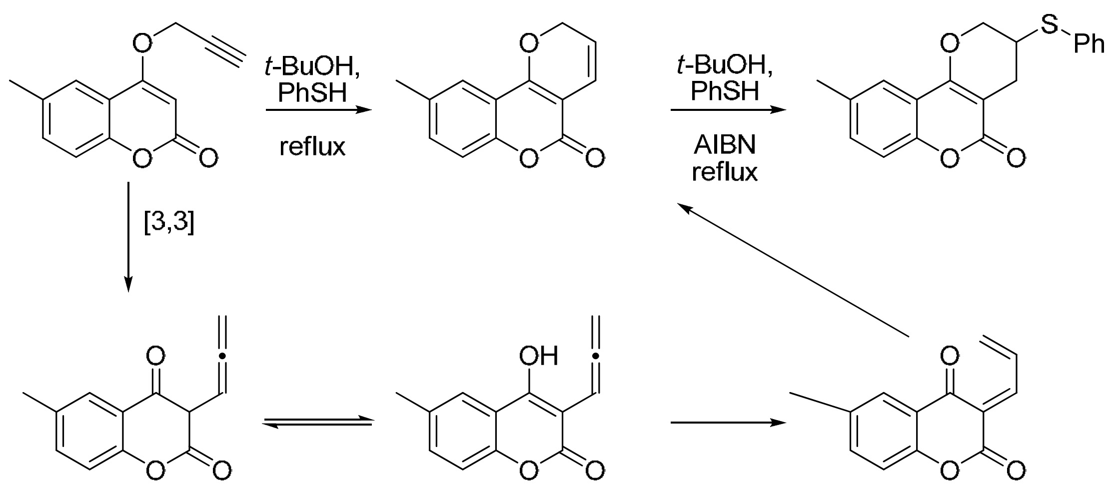
Olenyuk <2009TL4310>

Thiol Radicals and Rearrangements

Thiophenol catalysed Claisen rearrangement of coumarin derivatives



In absence of Thiophenol no rearrangement takes place

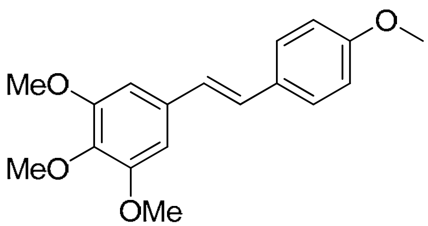


Similar reaction observed with indole annulated sulfur heterocycles <2007TL7031>

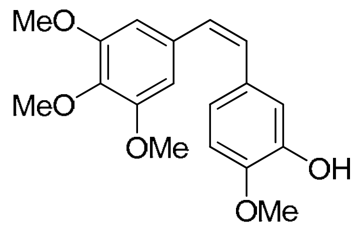
Majumdar<2007TL5265>

Ramberg-Bäcklund Reaction

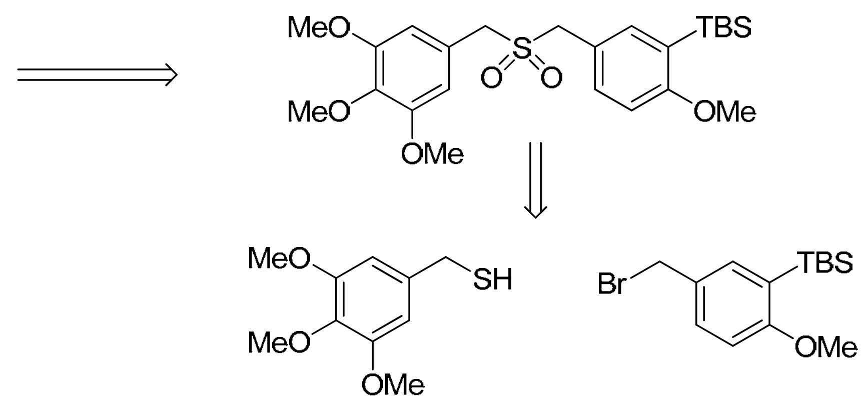
Synthesis of stilbenoid anti-cancer agents combrestatin A-4 and DMU-212

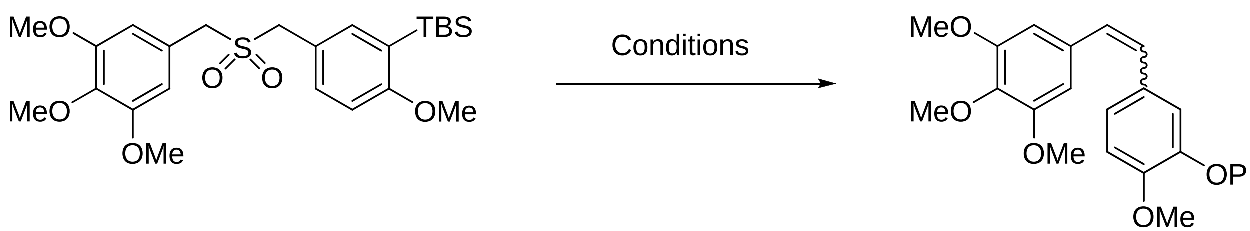


DMU-212



Combrestatin A-4



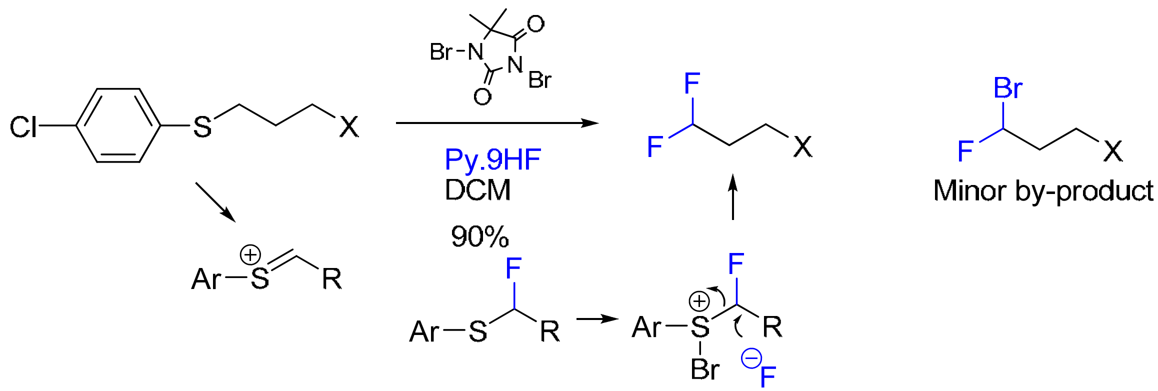


Entry	Conditions	*E:Z*	Yield (%)	Conditions
1	CF_2Br_2, *t*BuOH, KOH-Al_2O_3, 0 ^oC to rt 12 h	90:10	81	Chan 1994CC1771
2	$C_2F_4Br_2$, *t*BuOH, KOH-Al_2O_3, reflux12 h	85:15	72	Franck 1999OL2149
3	CCl_4, *t*BuOH, KOH, H_2O	47:53	69	Meyers 1969JACS7510

Taylor<2007CC1617>

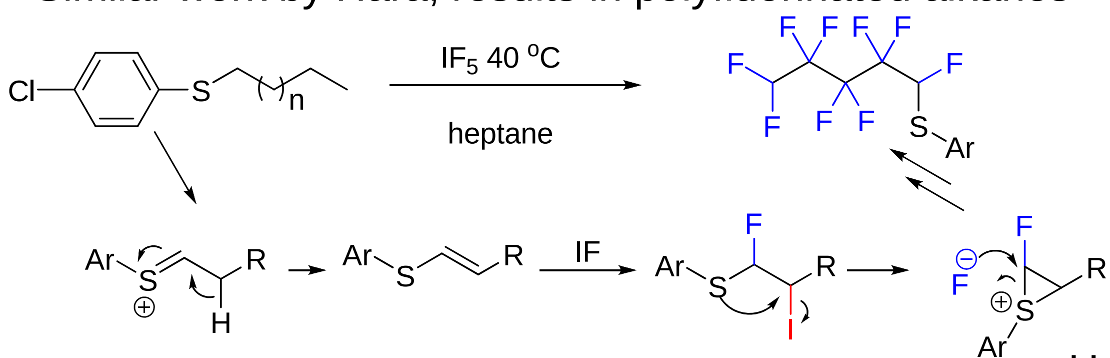
Pummerer and Pummerer-type reactions
Fluorination

Oxidative desulfurisation procedure to produce geminal 1,1-difluoroalkanes



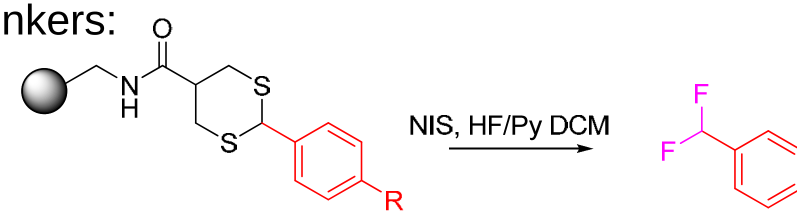
Haufe<2008SL106>

Similar work by Hara, results in polyfluorinated alkanes



Hara<2004T11445>

See also fluorinating cleavage of solid phase linkers:
<2008ACIE8120>



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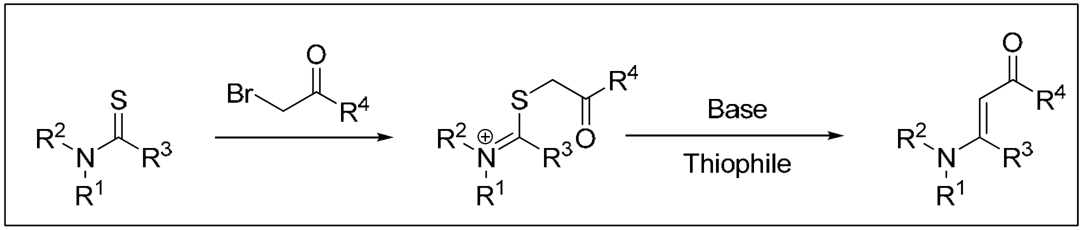
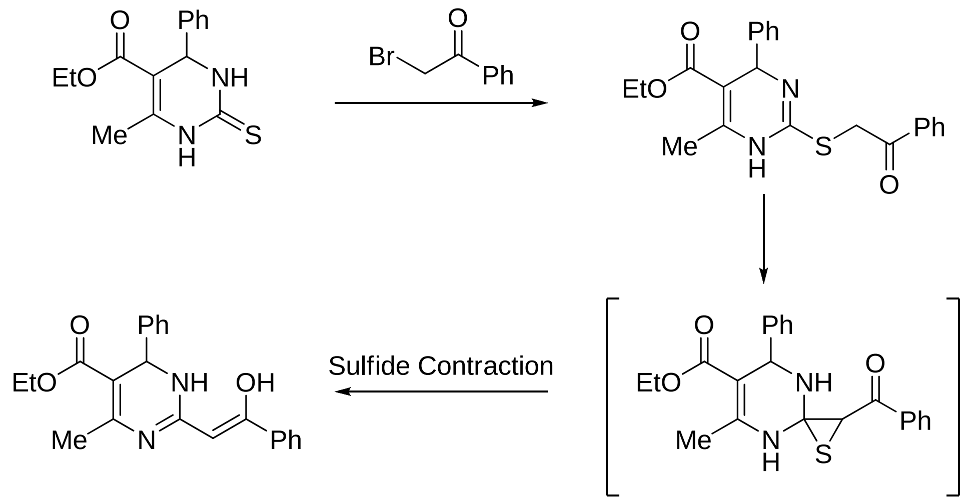
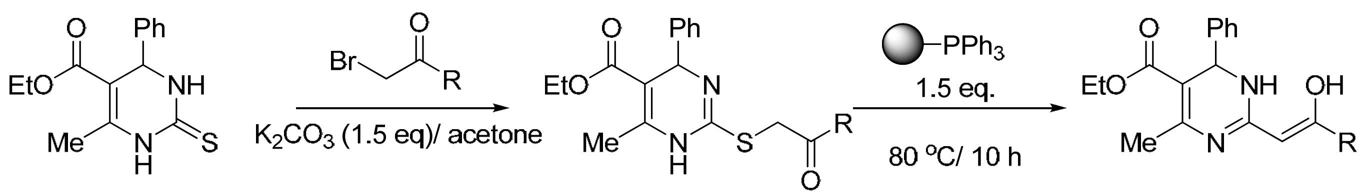
Eschenmoser Coupling reaction







One-pot, two step procedure

<2009TL1838>

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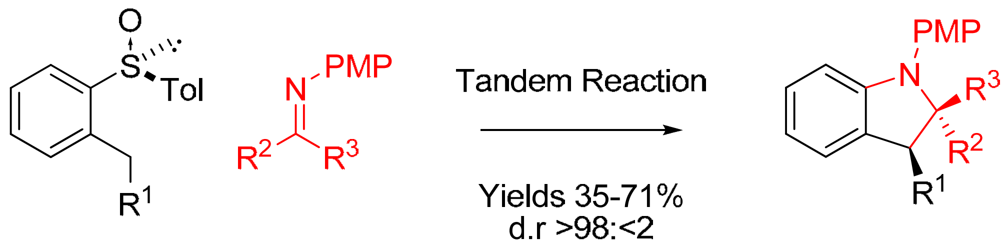
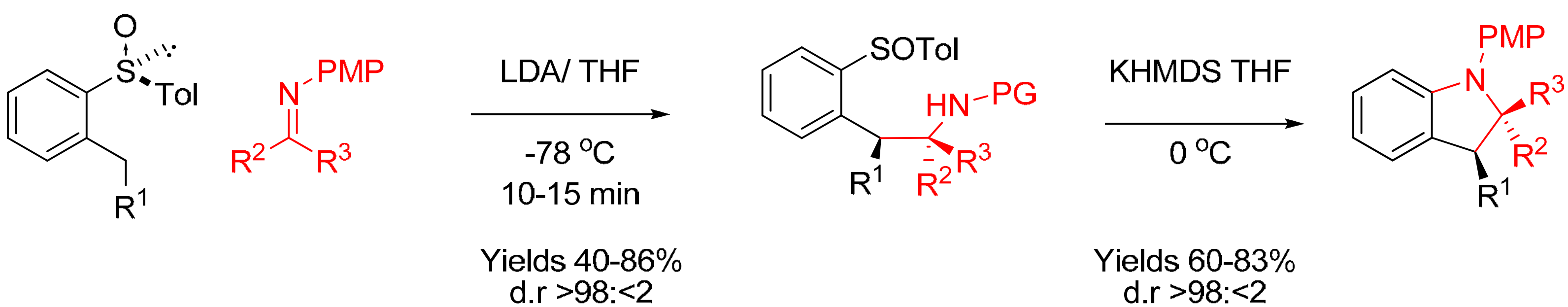
Ellman-type reaction

Optically pure Indolines from chiral tolyl-sulfinylalkylbenzenes



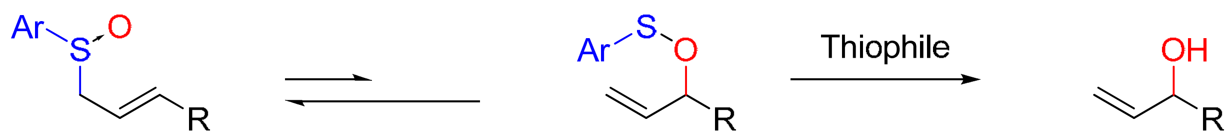
Tandem process proceeds at room temperature



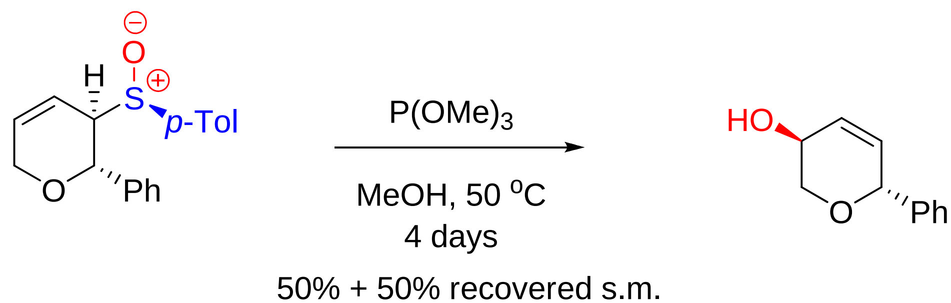
Fustero<2008ACIE7941>

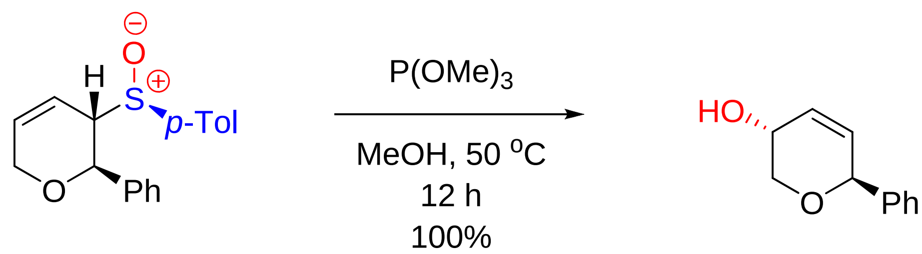
Rearrangements
[2,3] Mislow-Braverman-Evans Rearrangement

Classical [2,3] Mislow-Braverman-Evans rearrangements results in formation of analcohol with loss of sulfur



Satoh<2006TL1981>





Detailed investigation into the effects of substituents on the pyran ring and how they affect the rearrangement outcome.

Pradilla<2008JOC8929>