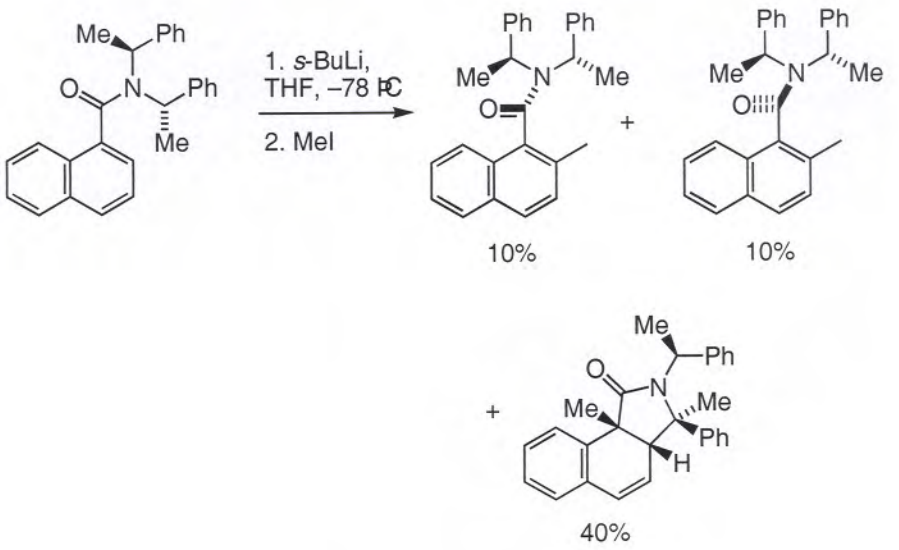
Synthesis Using Dearomatising Cyclisations

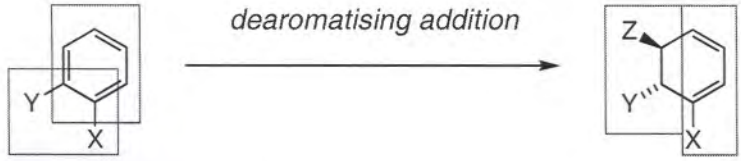
Jonathan Clayden

http://clor2.ch.man.ac.uk/home.htm

THE UNIVERSITY
of MANCHESTER



Chris Beech, Anjum Ahmed



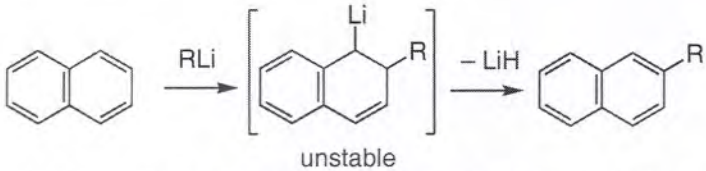
simple aromatic starting materials	versatile synthetic intermediates
regiochemistry readily controlled (electrophilic substitution; orthometallation)	stereochemistry introduced
limited reactivity	wide range of possible reactivity

methods...

Mander: *Synlett* 1991, 134; Bach, *Angew Chemie.* 1996, **35**, 729

- reduction (Birch)
- oxidation (phenols, *Pseudomonas putida...)*
- [hydrogenation]
- [radical or electrophilic addition]
- carbenes and carbenoids
- nucleophilic addition

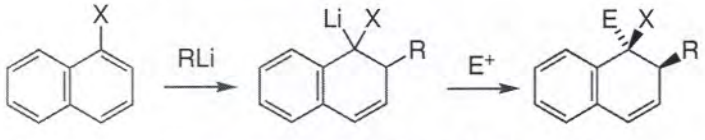
naphthalenes:



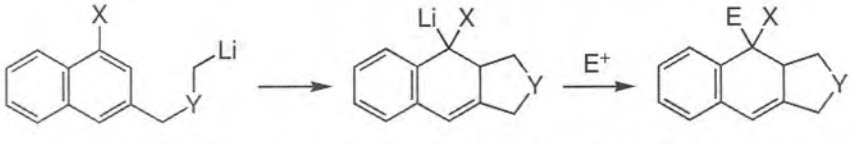
unstable

J. A. Dixon, D. H. Fishman, R. S. Dudinyak, *Tetrahedron Lett.*, 1964, 613

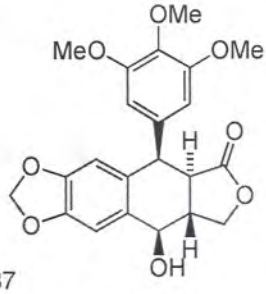
activated naphthalenes:



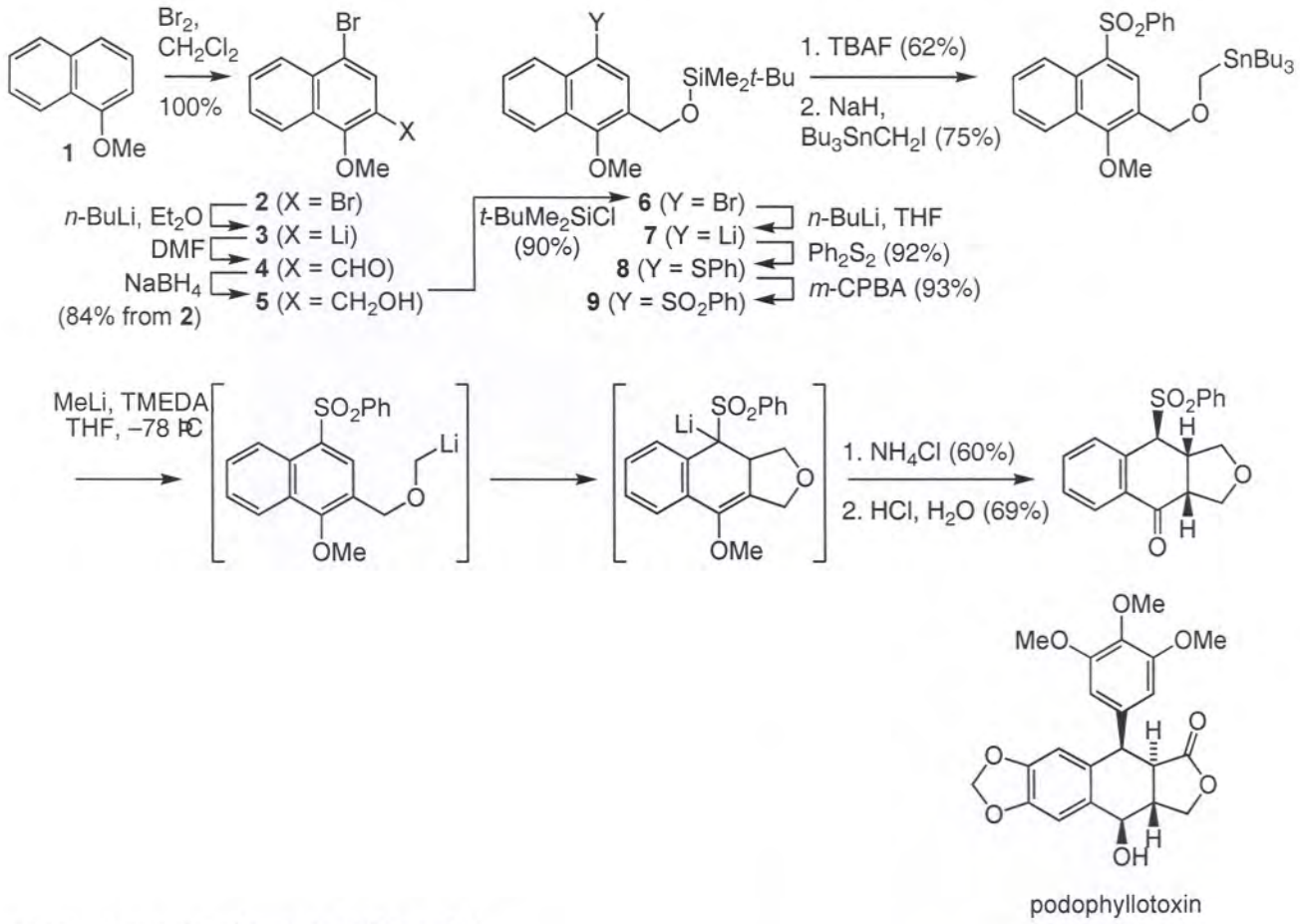
X = sulfone: Stoyanovich, *Tetrahedron* 1971, **27**, 433
oxazoline: Meyers, *Tetrahedron* 1985, **41**, 837; *Tetrahedron* 1994, 5**0**, 2297
imine: Meyers, *Tetrahedron Lett.* 1987, **28**, 5279
carboxylate: Mortier, *J. Org. Chem.* 1996, **61**, 5206
hindered ester: Tomioka, *Tetrahedron* 1999, **55**, 4955



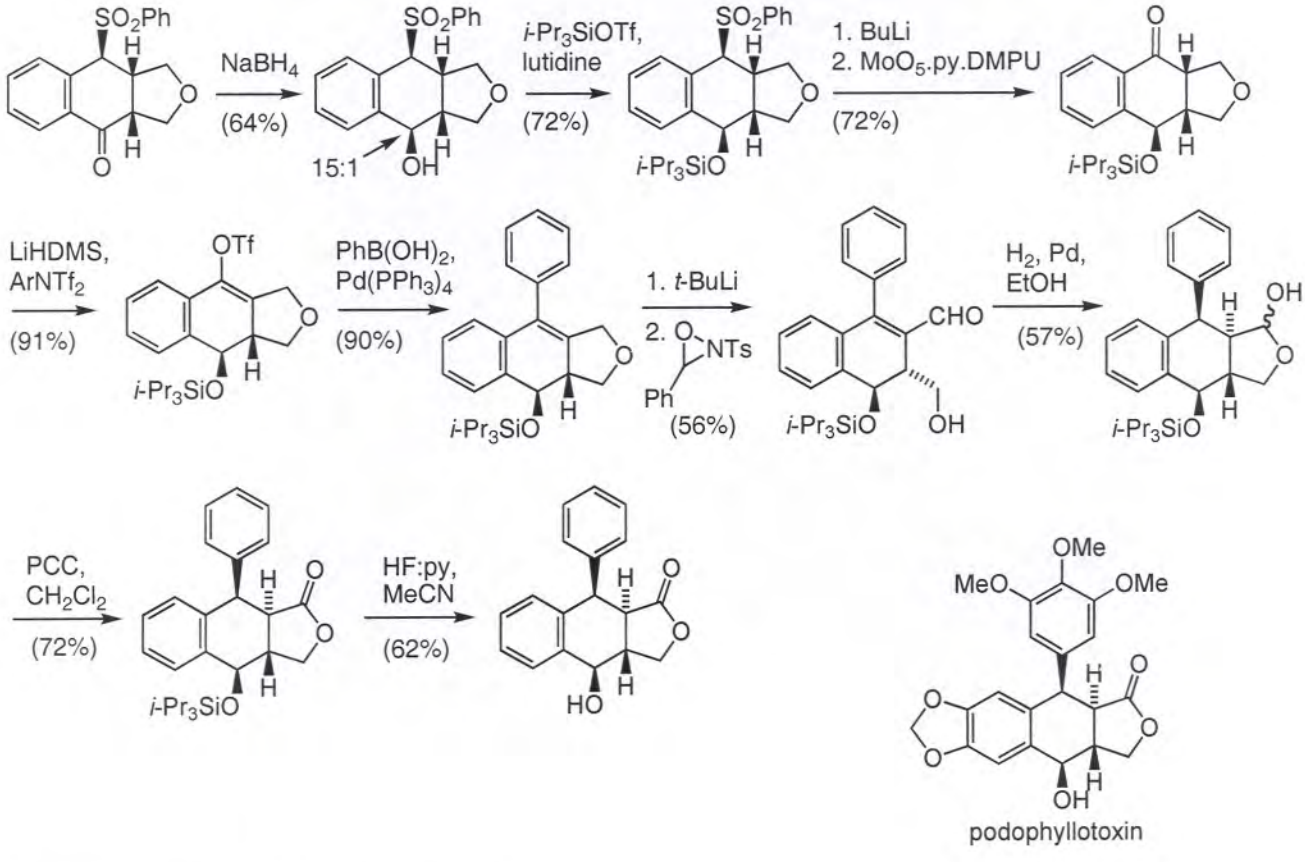
X = amide, oxazoline, sulfone: J. Clayden and M. N. Kenworthy, *Org. Lett.*, 2002, **4**, 787



podophyllotoxin

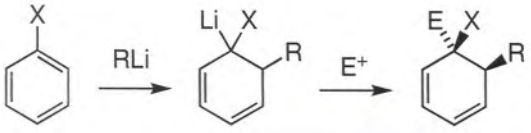


Martin Kenworthy, *Org. Lett.*, 2003, **5**, 831

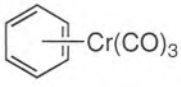


Martin Kenworthy, *Org. Lett.*, 2003, **5**, 831

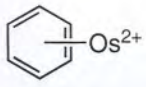
activated benzene derivatives:



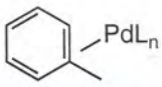
X = hindered ester: Miyano, *Tetrahedron Lett.* 1995, **36**, 4821
C=O Al complex: Yamamoto, *JACS* 1995, **117**, 9091



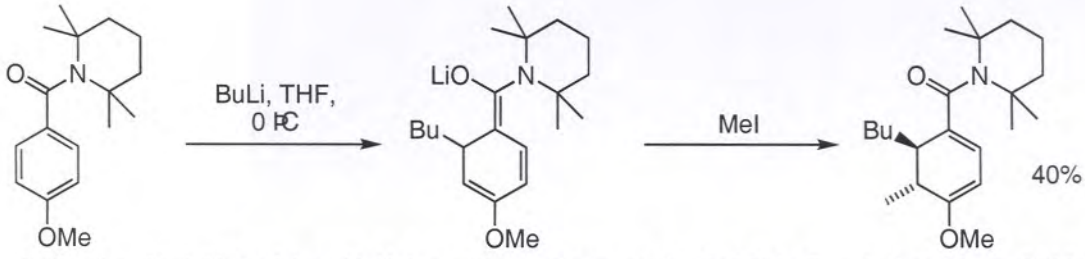
Kündig:
Synthesis 2001, 2040



Harman:
Coord. Chem. Rev. 2000, **206**, 3

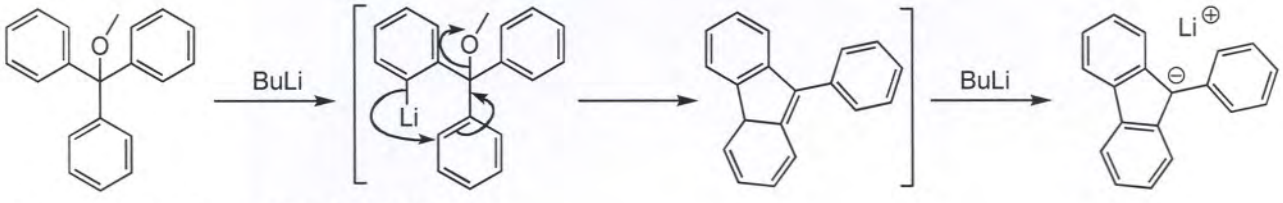


Yamamoto:
JACS 2001, **123,** 759

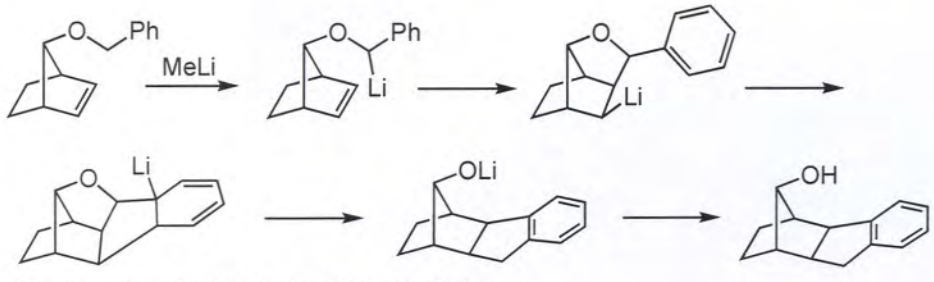


J. Clayden, Y. J. Y. Foricher, H. K. Lam *Chem. Commun.* 2002, 2138; *Eur. J. Org. Chem.* 2002, 3558

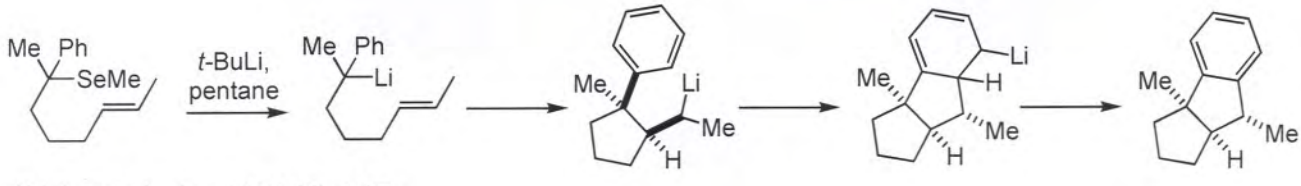
organolithium cyclisation onto unactivated benzene derivatives:



Gilman: *J. Am. Chem. Soc.* 1952, **74**, 6282

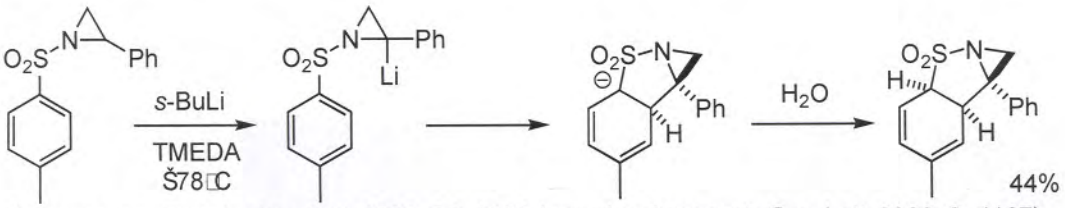


Klumpp: *Tetrahedron Lett.* 1974, **15**, 2911

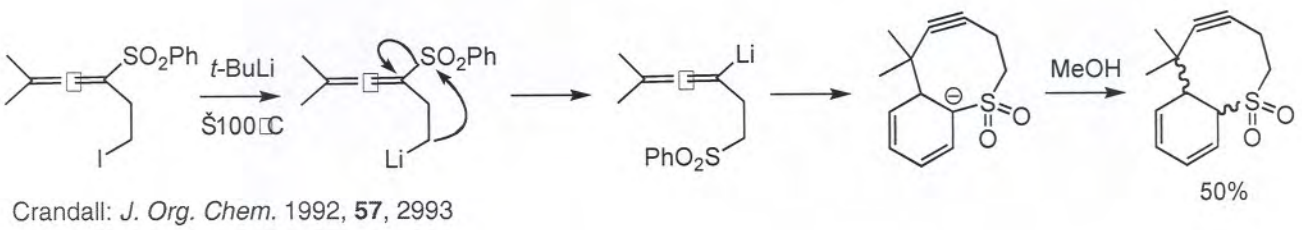


Krief: *Tetrahedron* 1994, **50**, 7177

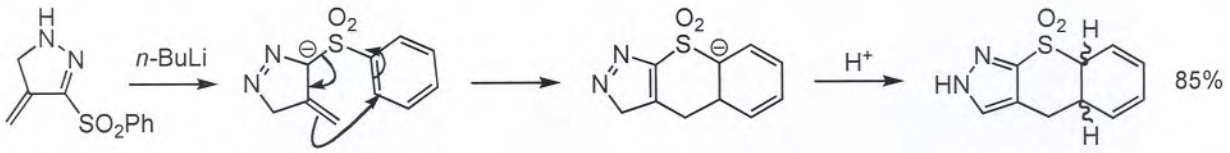
organolithium cyclisation onto activated benzene derivatives:



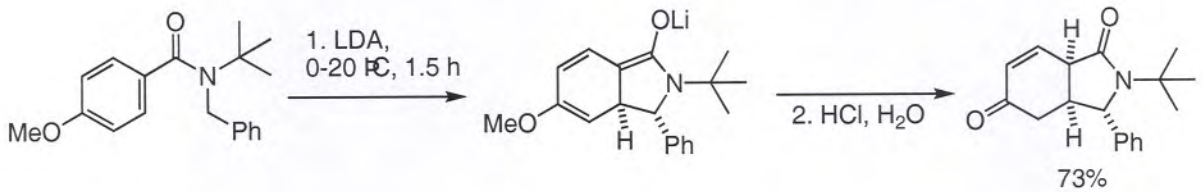
Schaumann: *Tetrahedron Lett.* 1991, **32**, 1299 (see also Aggarwal: *Org. Lett.* 2000, **2**, 4107)

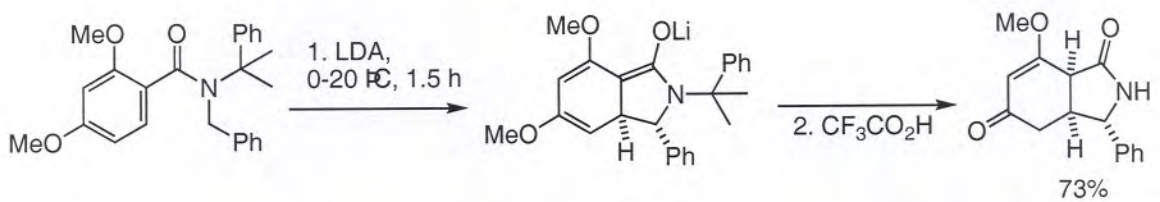


Crandall: *J. Org. Chem.* 1992, **57**, 2993

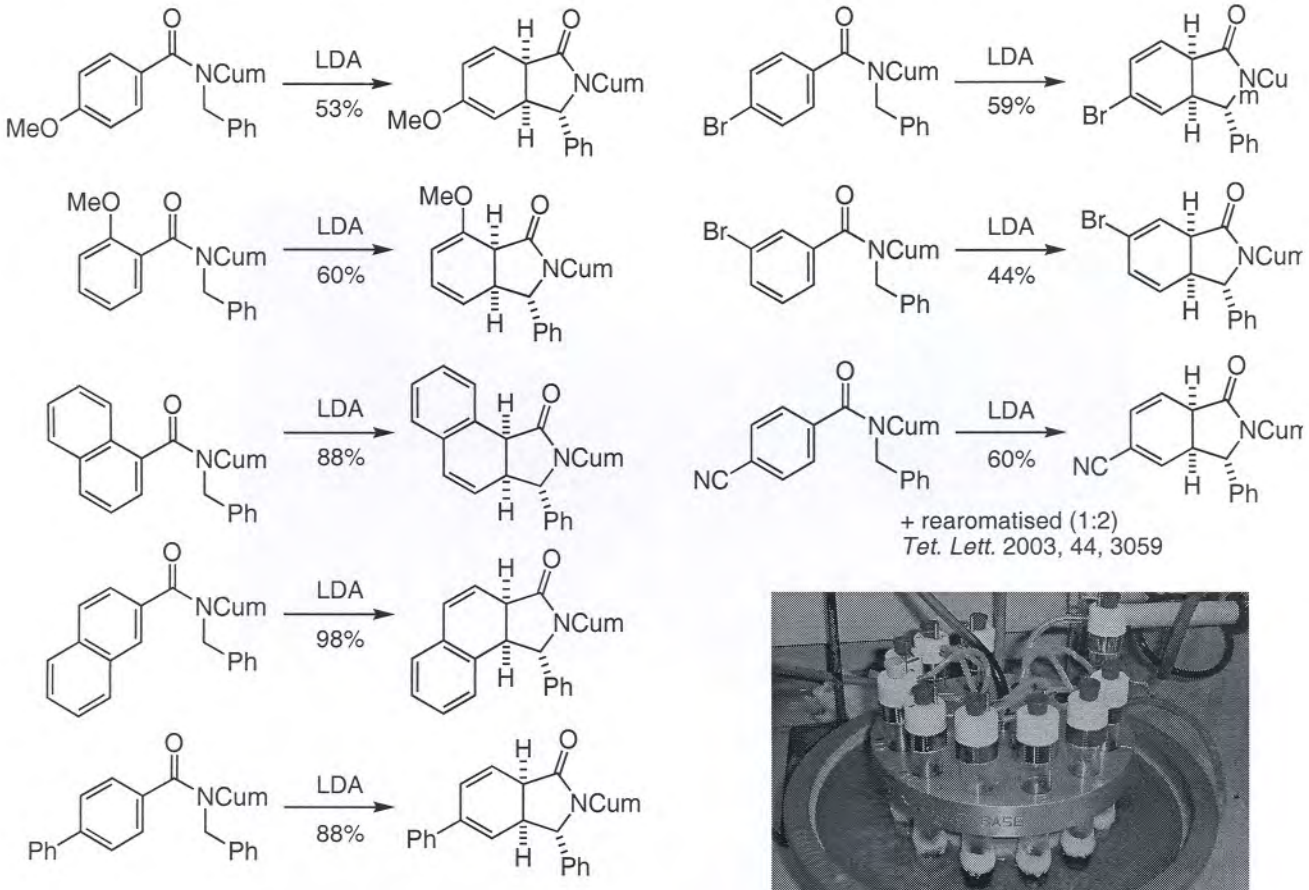


Padwa: *J. Org. Chem.* 1993, **58**, 2061



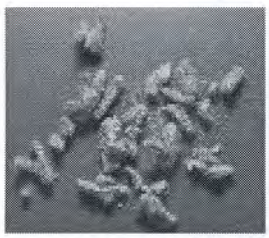


Samreen Yasin, *Synlett* 2001, 302
Christel Menet; *Org. Lett.* 2000, **2**, 4229



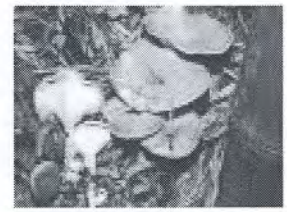
Christel Menet; *Org. Lett.* 2000, **2**, 4229

The Kainoids



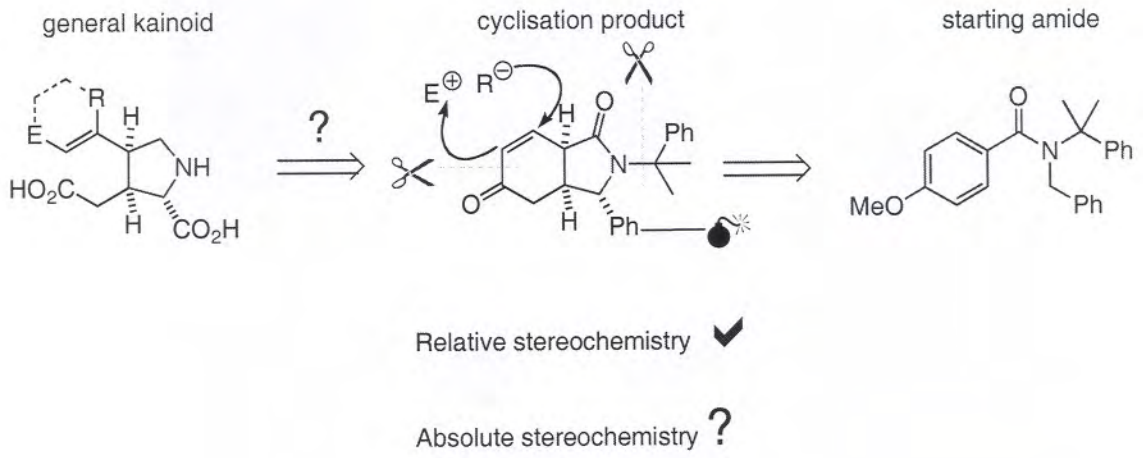
Digenea simplex

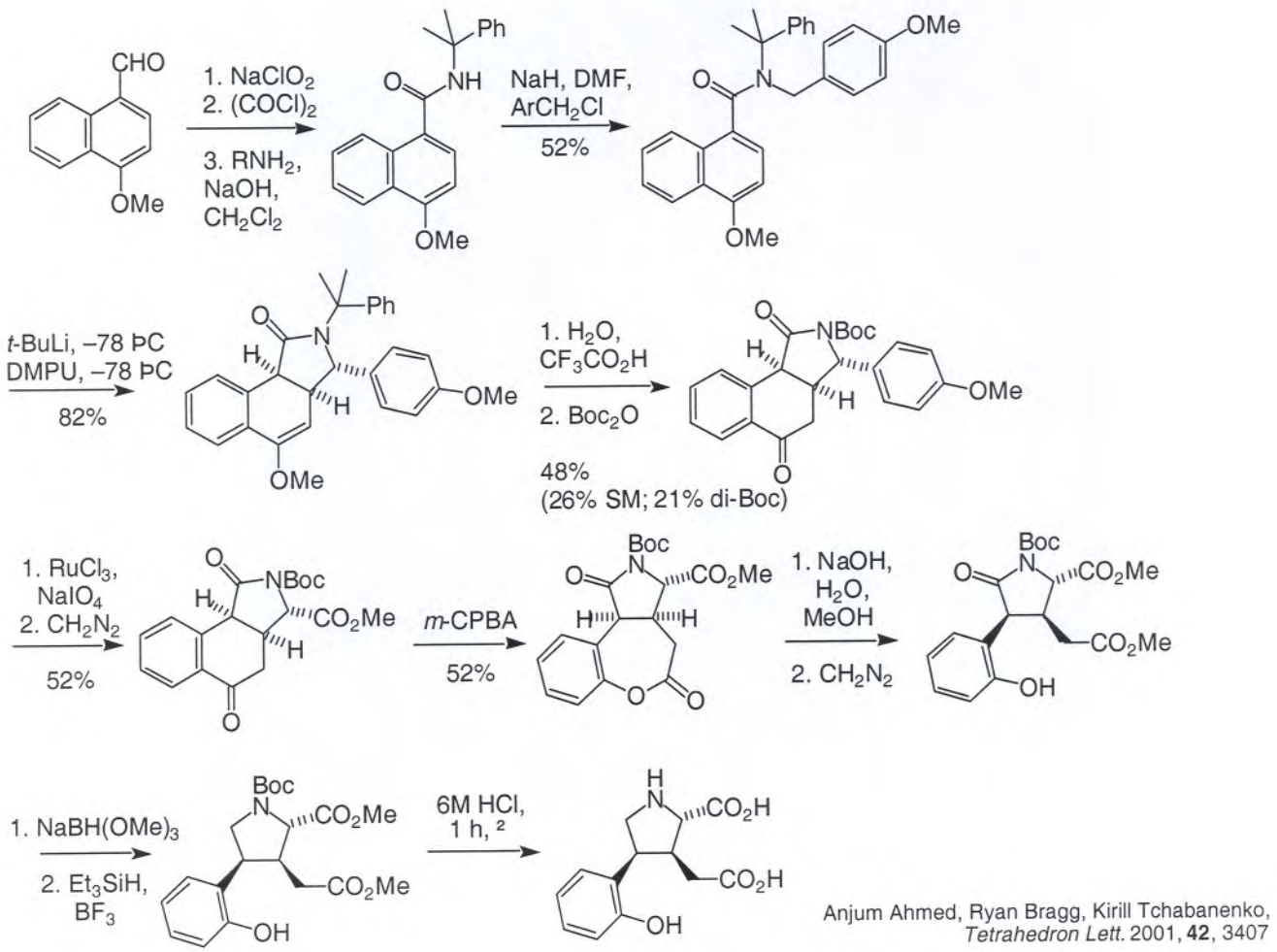
Pseudonitzschia pungens



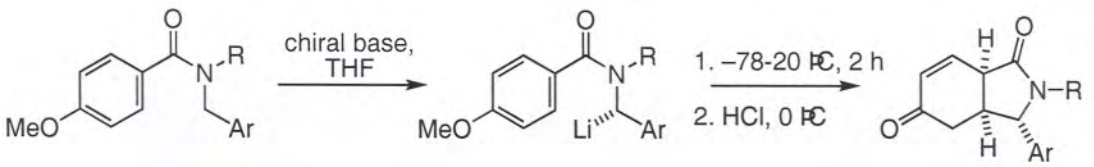
Clitocybe acromelalga

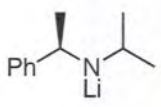
Review: A. Parsons, *Tetrahedron* 1996, **52**, 4149

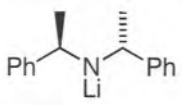




Anjum Ahmed, Ryan Bragg, Kirill Tchabanenko,
Tetrahedron Lett. 2001, **42**, 3407

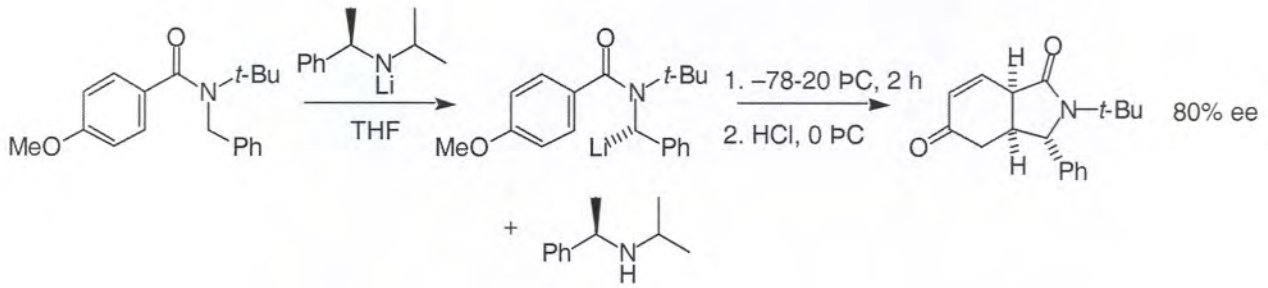


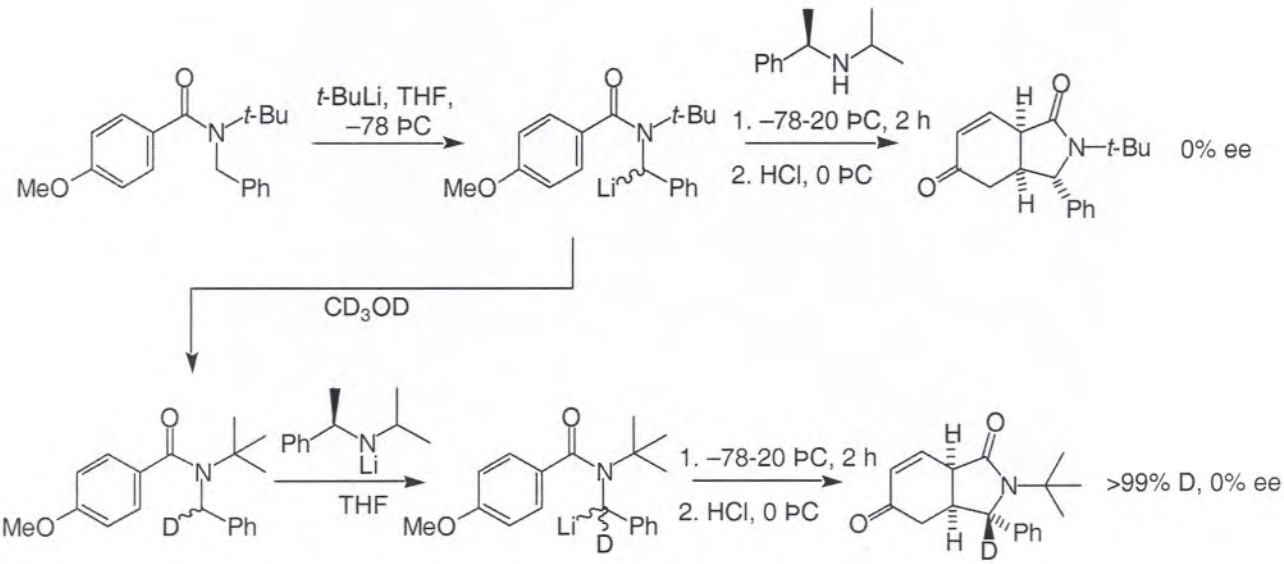




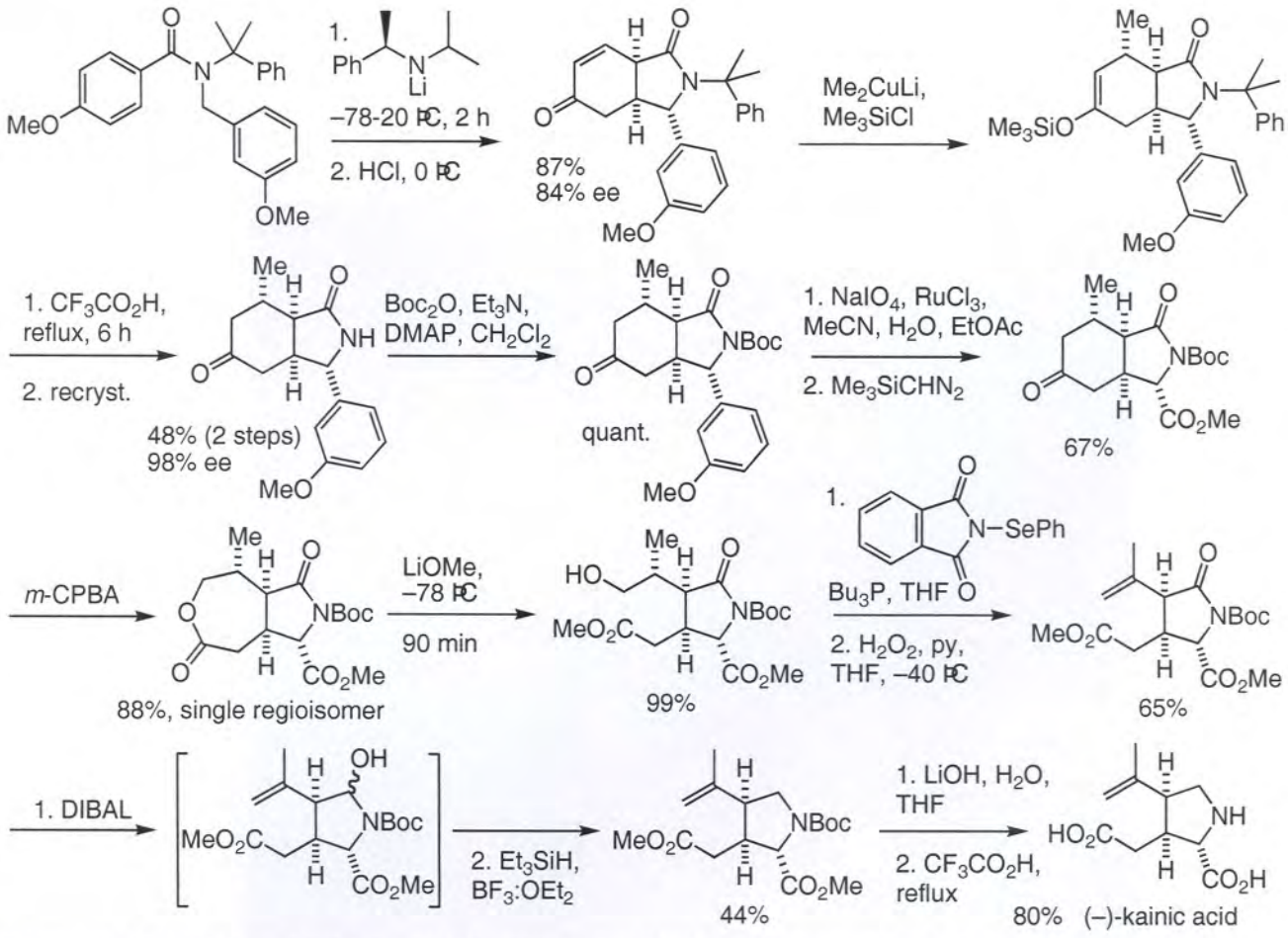
R =	Ar =	yield (%)	ee (%)		
t-Bu	Ph	72	80	recryst.	>99%
	m-$MeOC_6H_4$	–	–		
cumyl	Ph	60	81	recryst.	>99%
	m-$MeOC_6H_4$	87	84		
t-Bu	Ph	73	80	recryst.	>99%
	m-$MeOC_6H_4$	59	73		
cumyl	Ph	64	75	recryst.	>99%
	m-$MeOC_6H_4$	low	–		

Christel Menet; *Chem. Commun. 2002, 38*

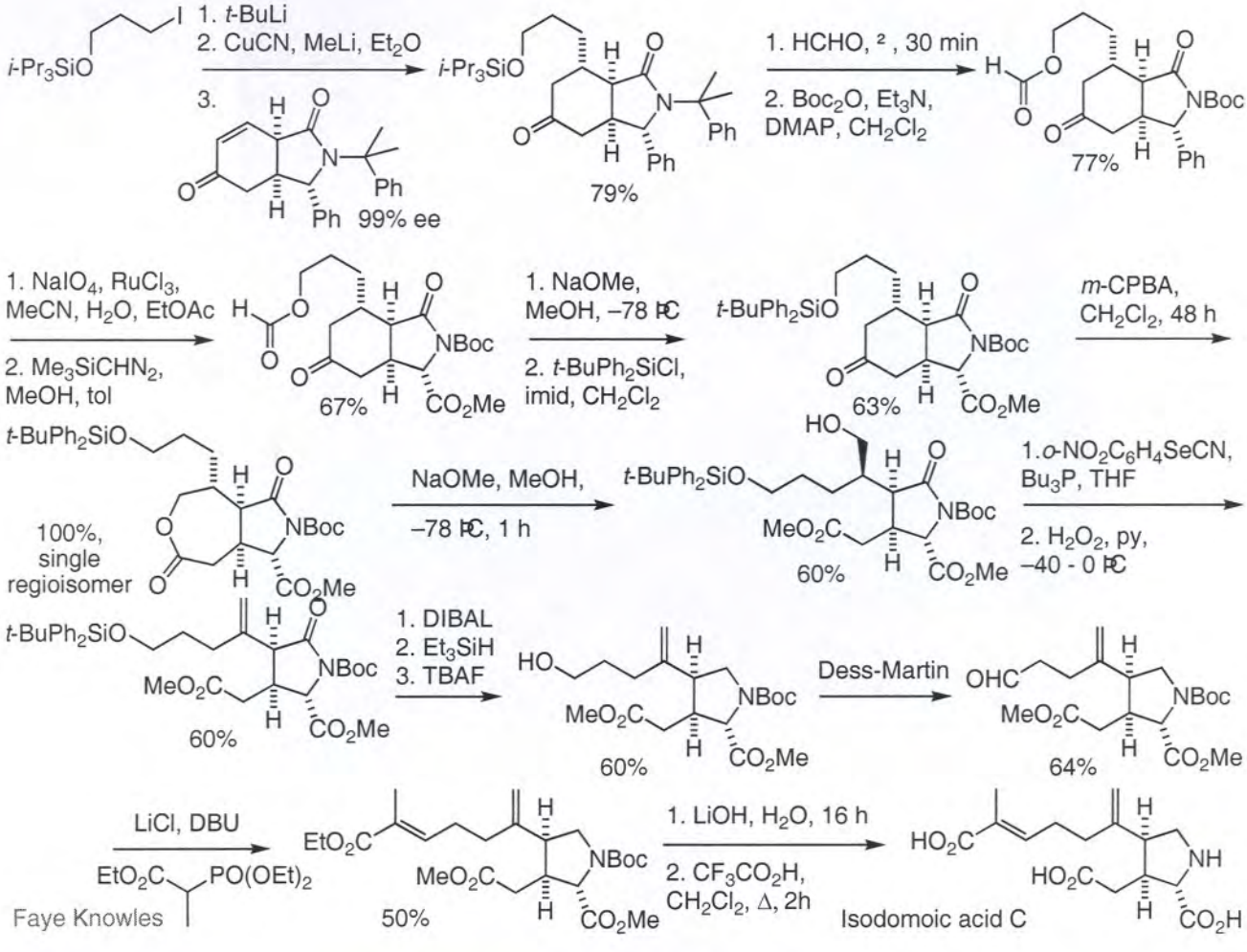


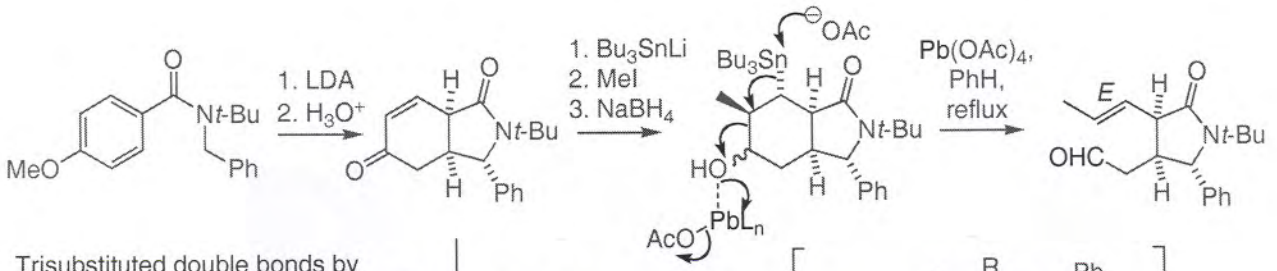


Christel Menet; *Chem. Commun. 2002, 38*



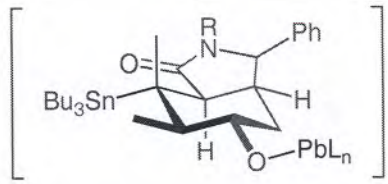
(–)-synthesis: Christel Menet *Tetrahedron* 2002, **58**, 4727; (±)-synthesis: Kirill Tchabanenko *Chem. Comm.* 2000, 317





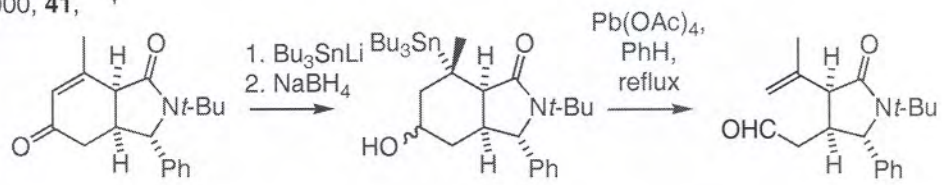
Trisubstituted double bonds by fragmentation: see Syntex synthesis of Cecropia Juvenile Hormone:

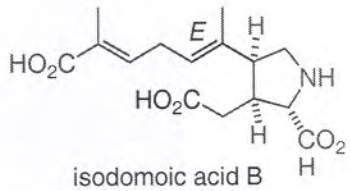
JACS 1968, **90**, 6224



Pb-promoted fragmentation:

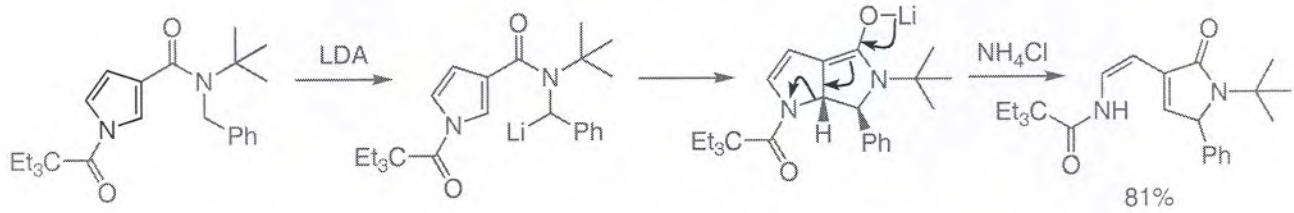
Posner, *Tetrahedron Lett.* 2000, **41**, 9655

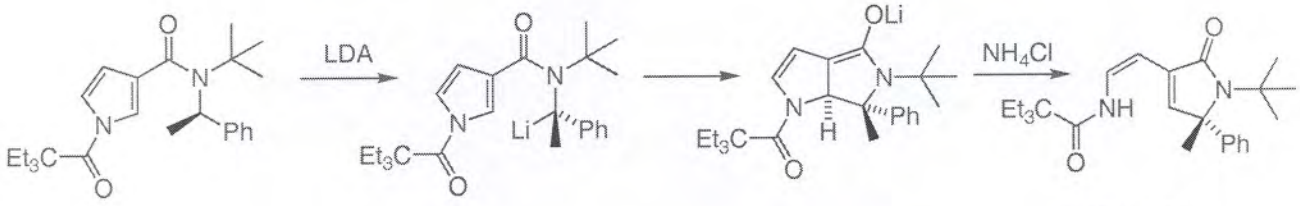




Katherine Hebditch

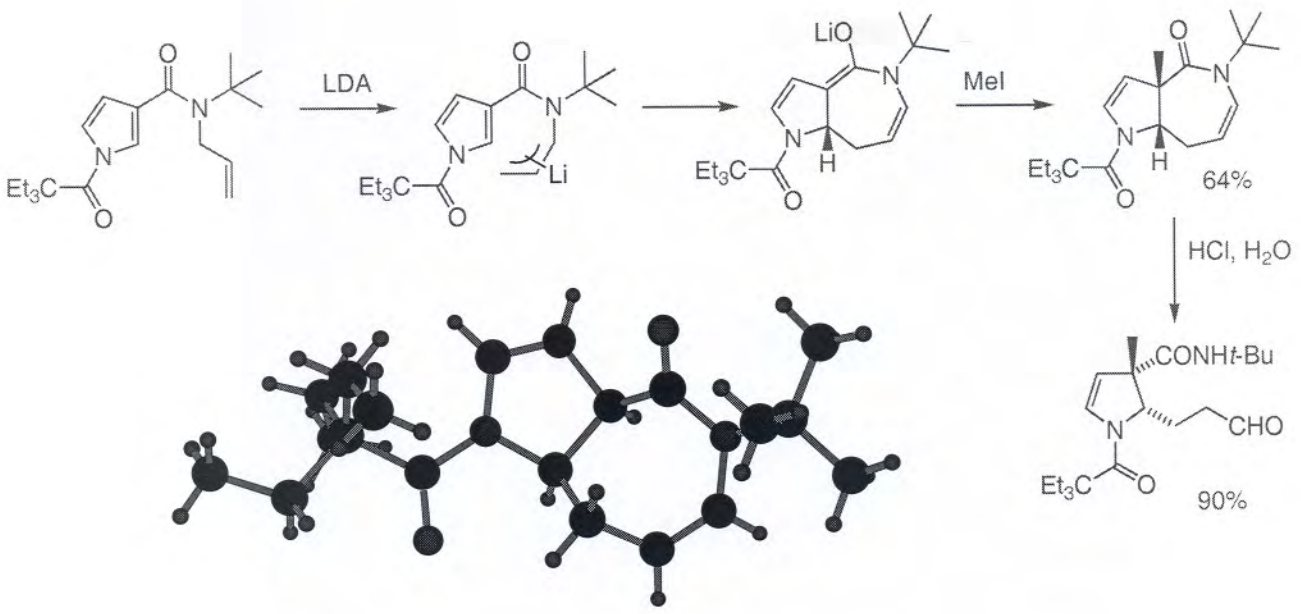
isodomoic acid B



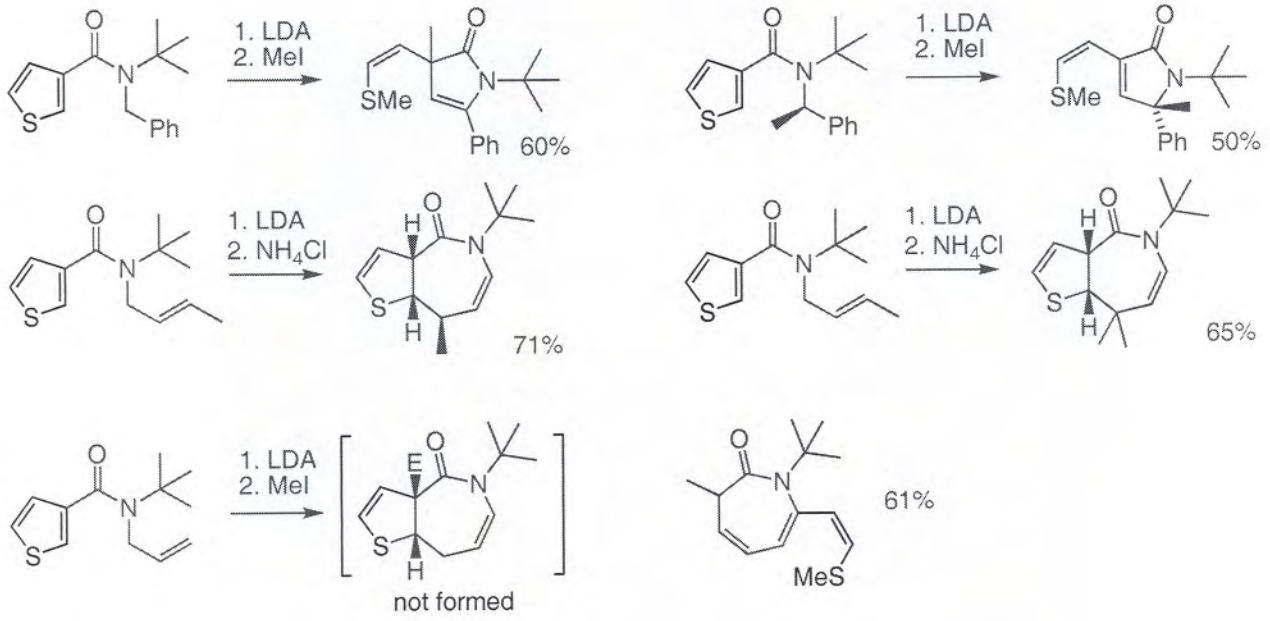


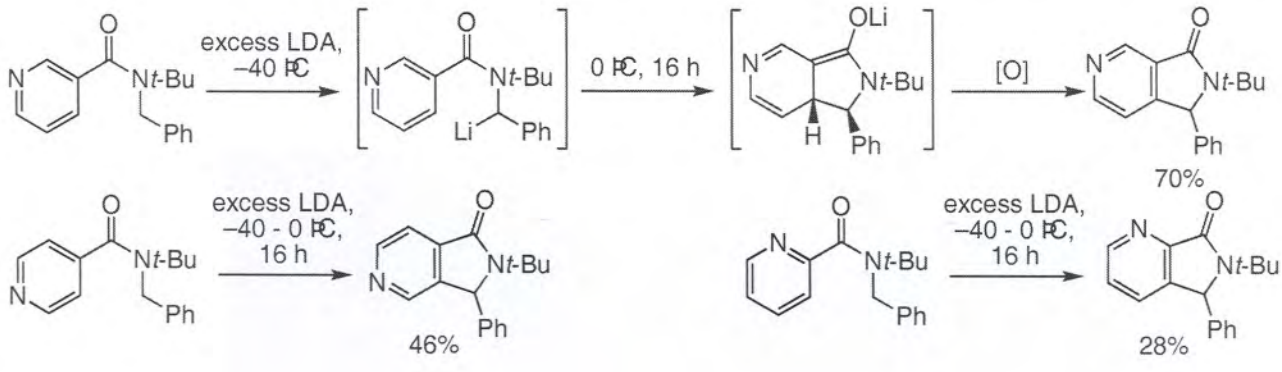
87%; >99% ee

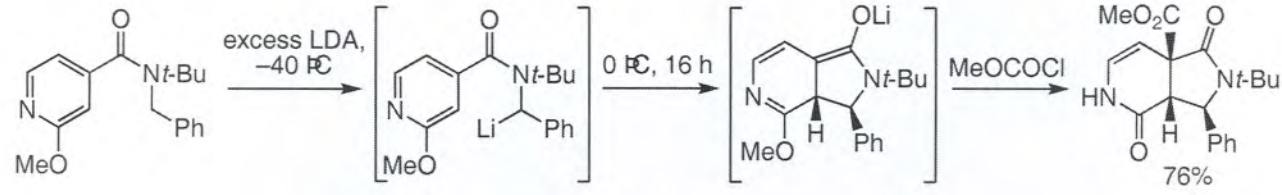
Rachel Turnbull, *Org. Lett.* 2004, **6**, 609



Rachel Turnbull, *Org. Lett.* 2004, **6**, 609







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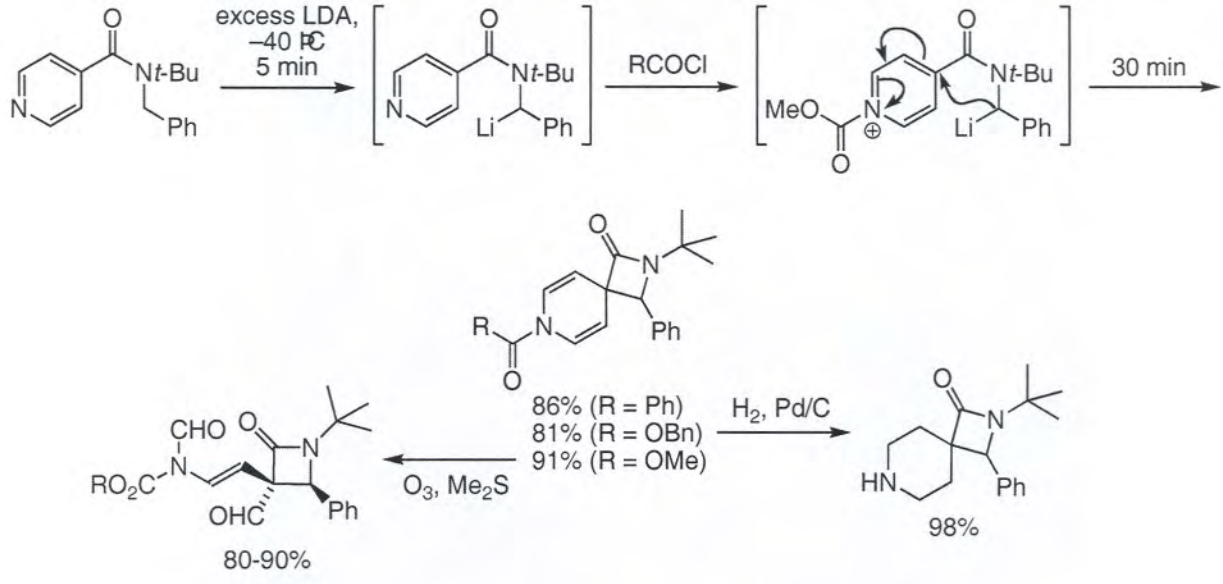

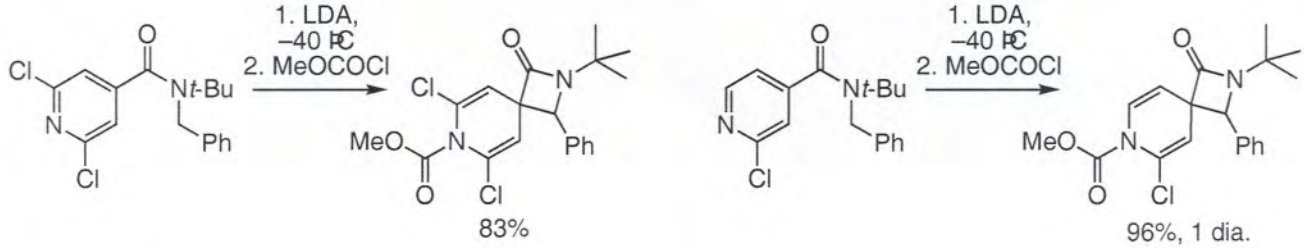

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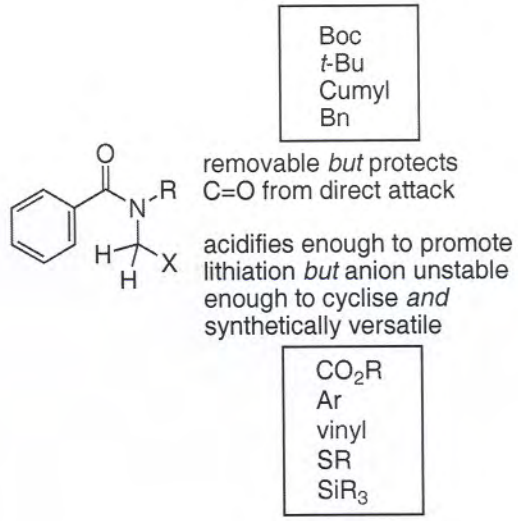
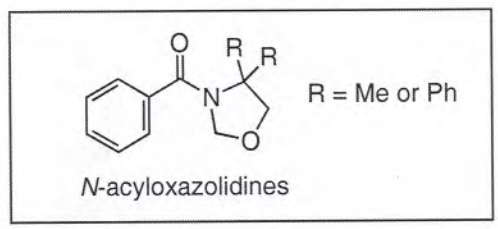
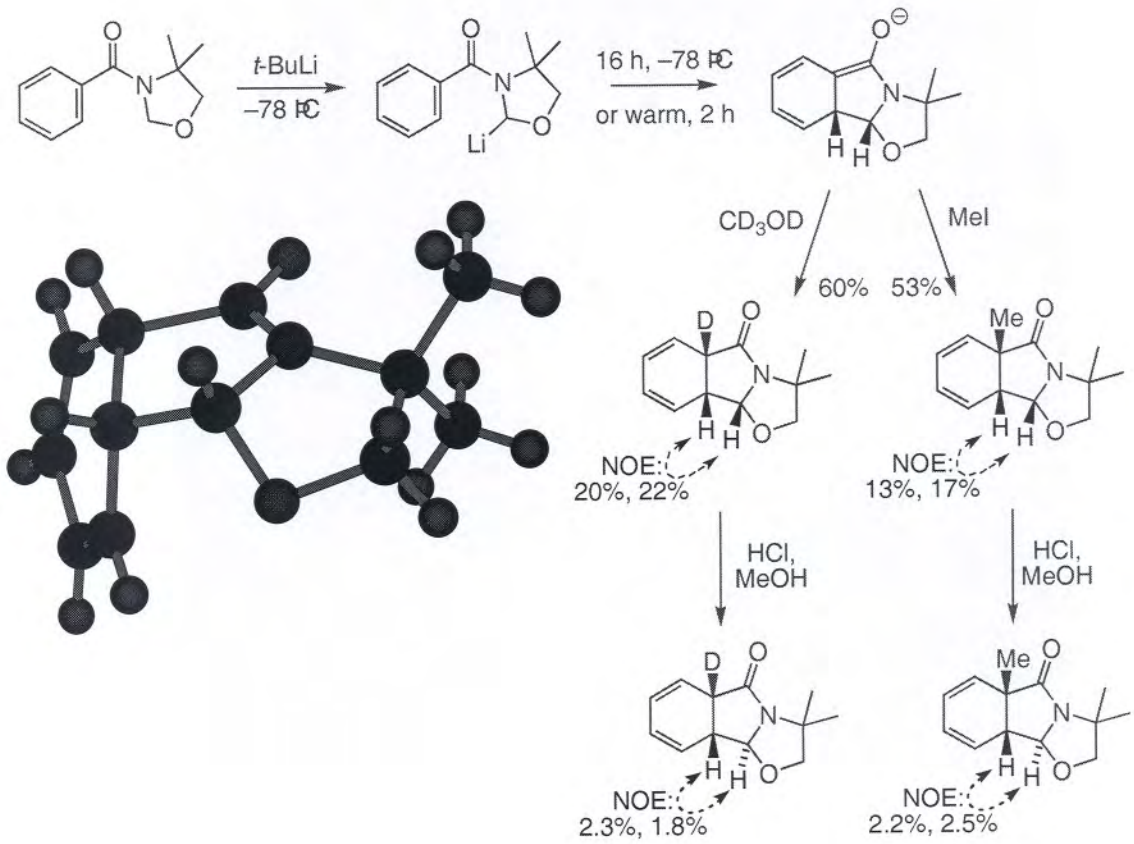
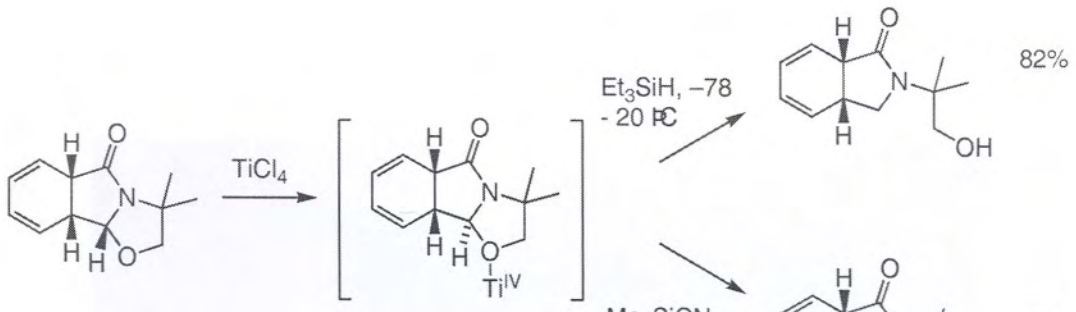
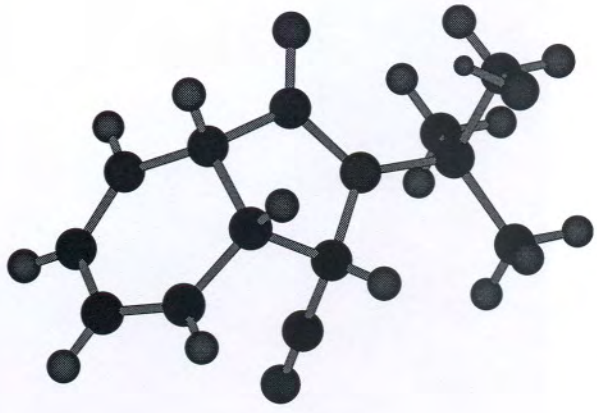






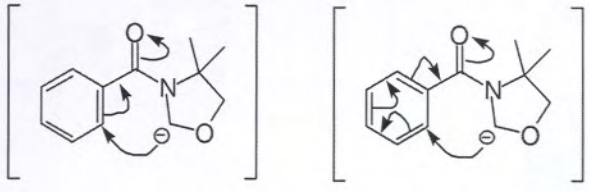
Jonathan Clayden, Savroop Purewal, Madeleine Helliwell and Simon J. Mantell, *Angew. Chemie. Int. Ed.*, 2002, **41**, 1091

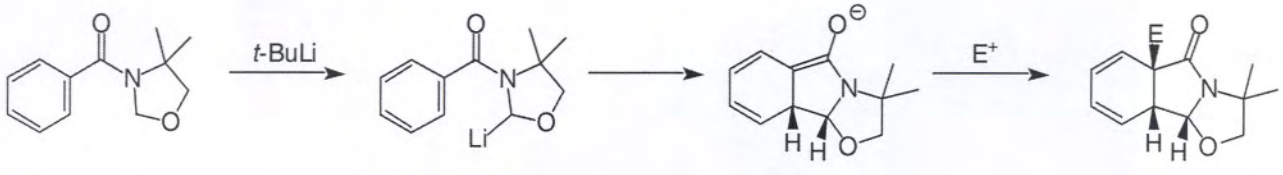


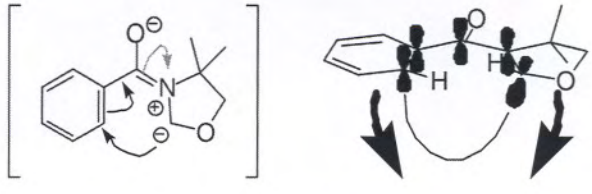


Savroop Purewal

5 endo (exo) trig



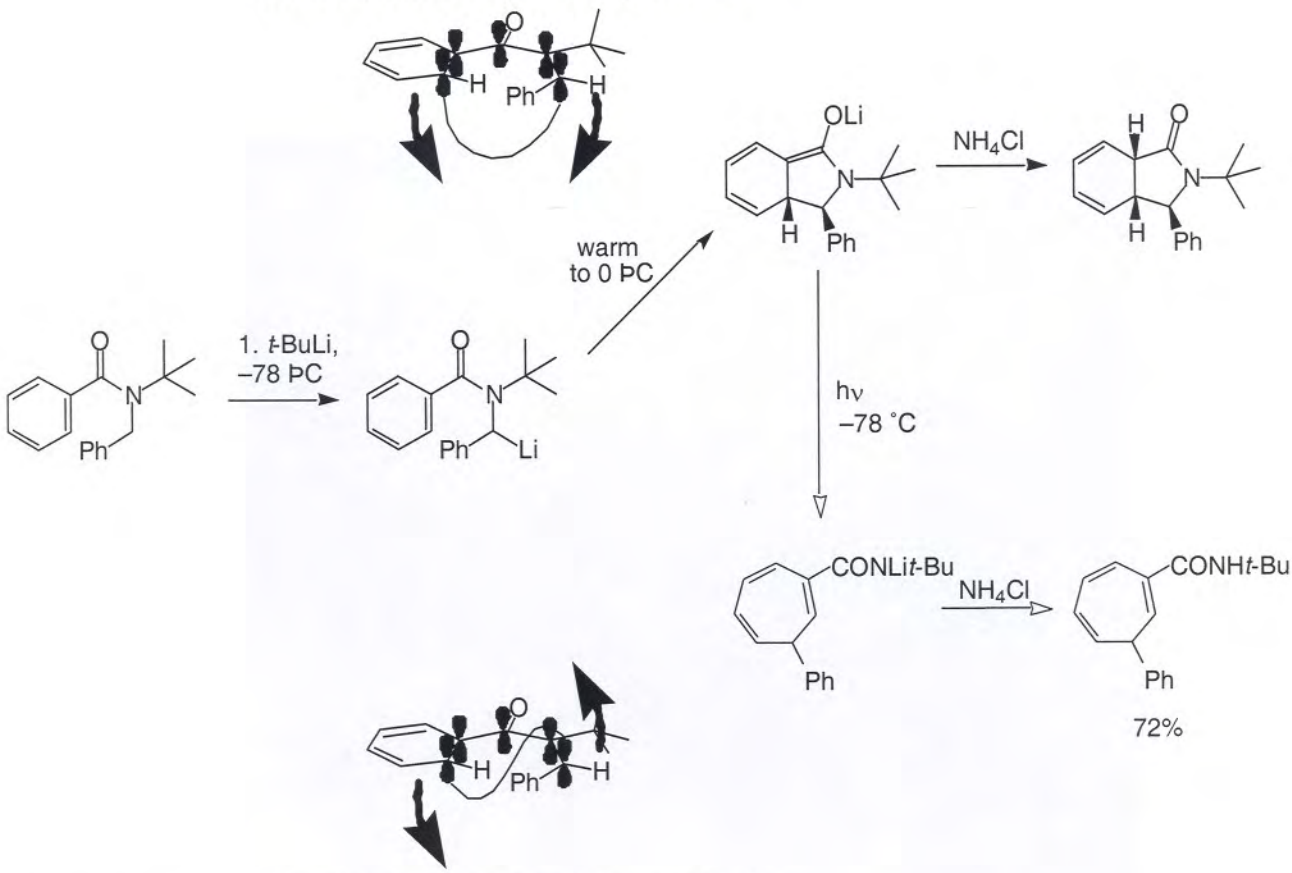




6 electron disrotatory electrocyclisation

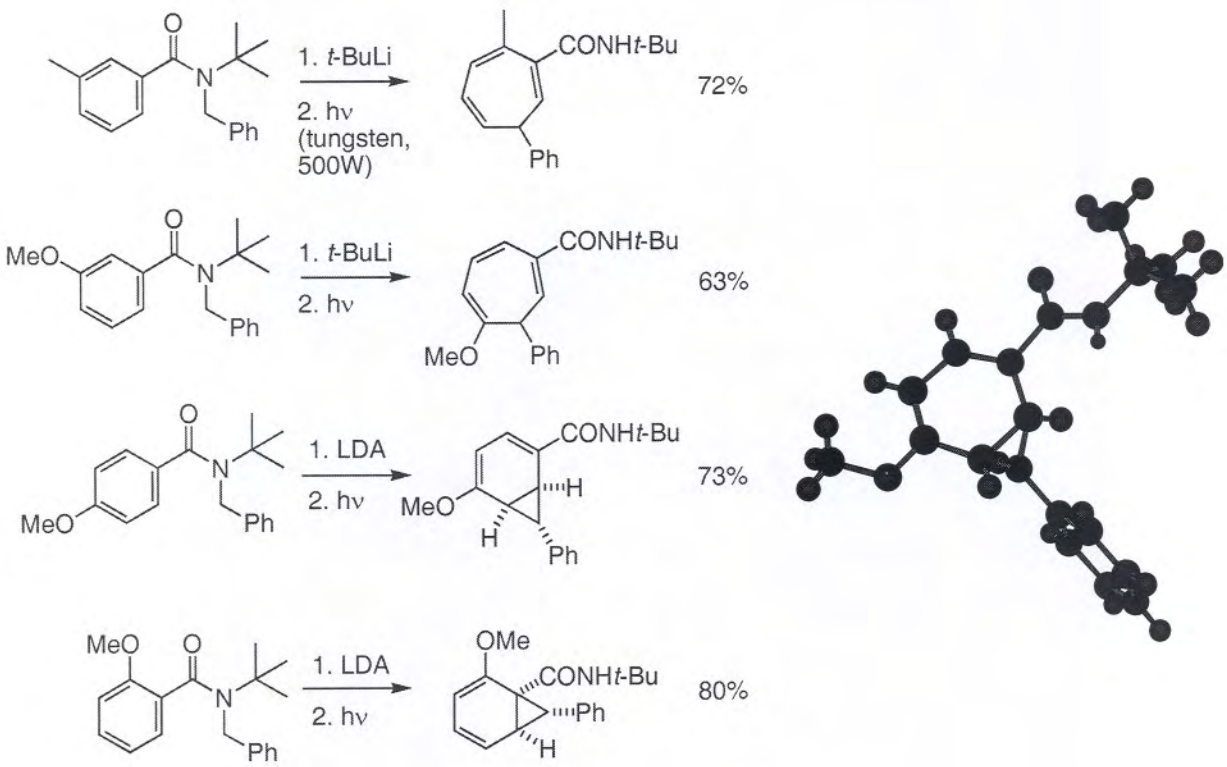
Savroop Purewal

6 electron disrotatory electrocyclisation

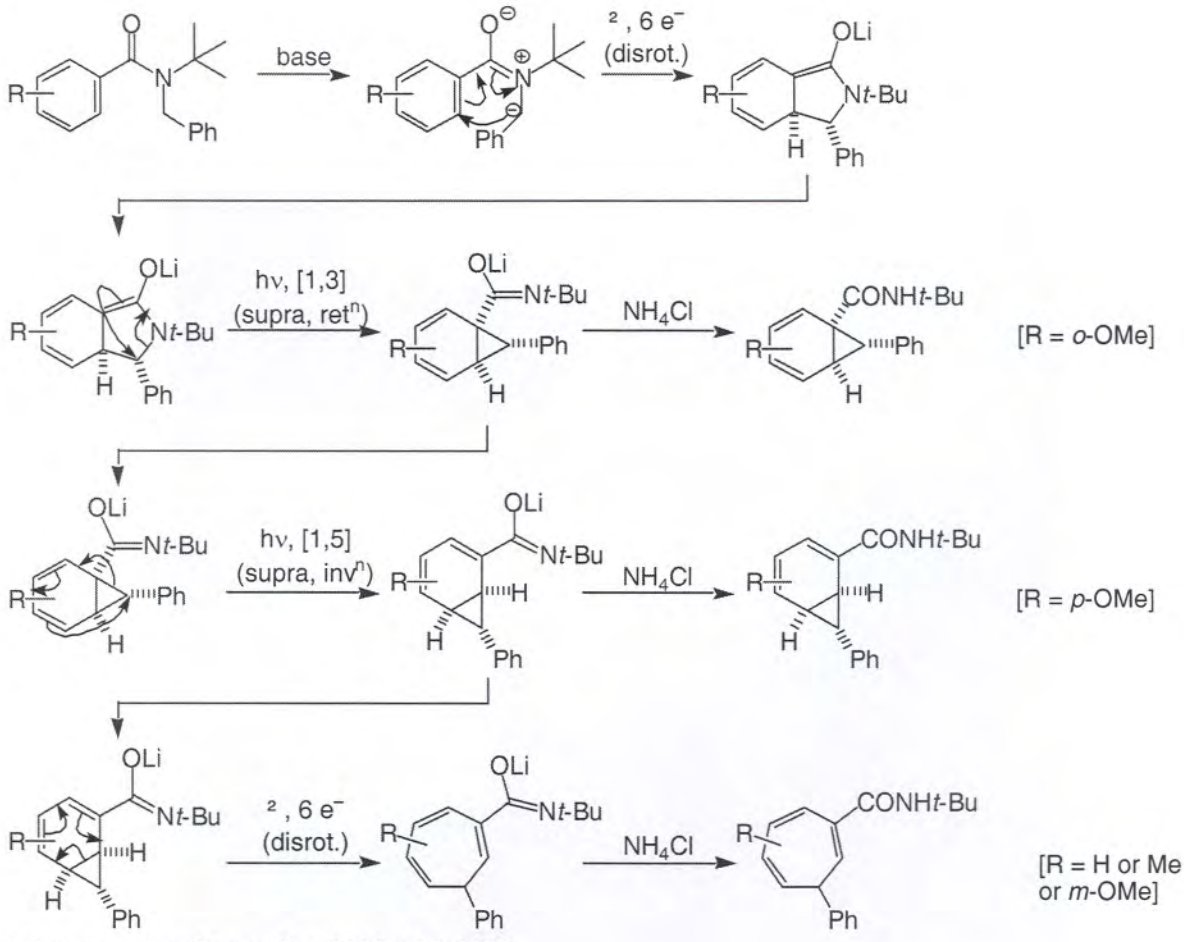


6 electron conrotatory electrocyclisation?

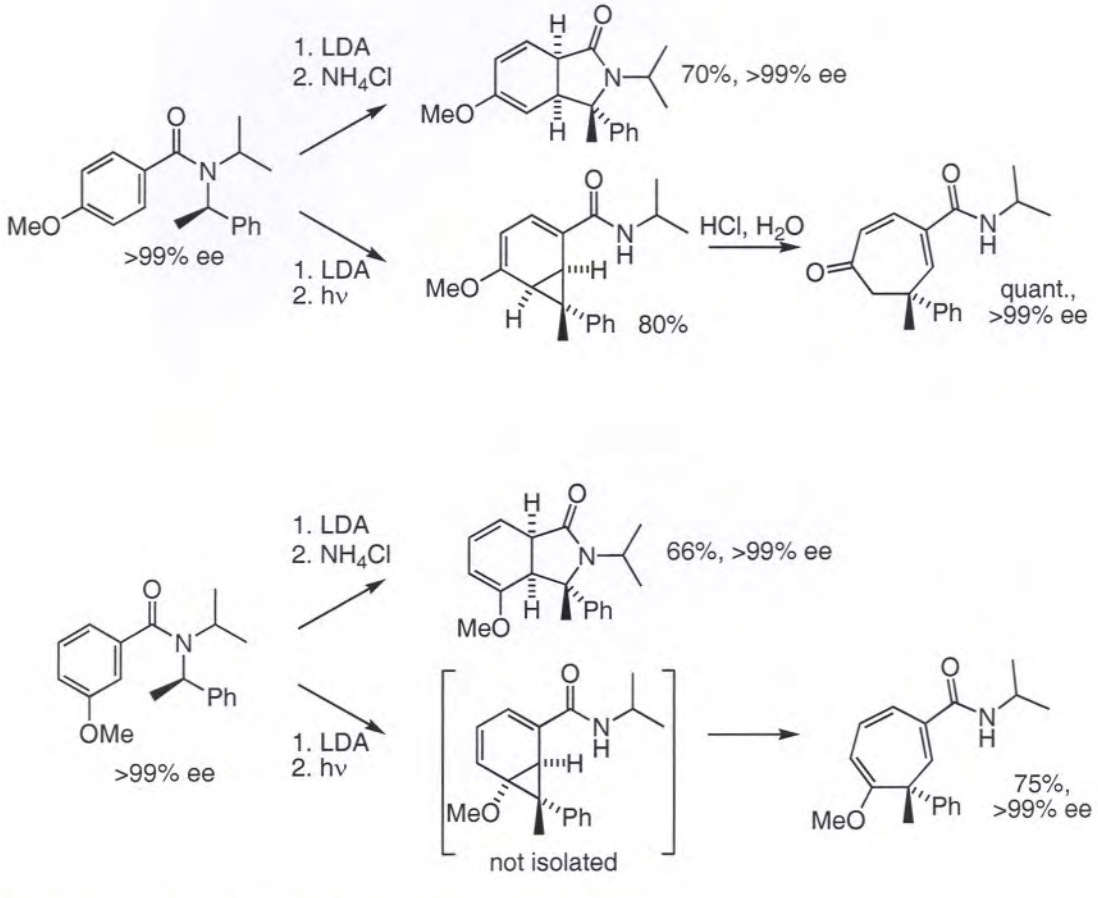
Christel Menet



Christel Menet; *J. Am. Chem. Soc.* 2003, **125**, 9278



Christel Menet; *J. Am. Chem. Soc.* 2003, **125**, 9278



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