Institut des Sciences Moléculaires de Marseille
UMR 6263

Synthèse Totale et Réactivité Organique

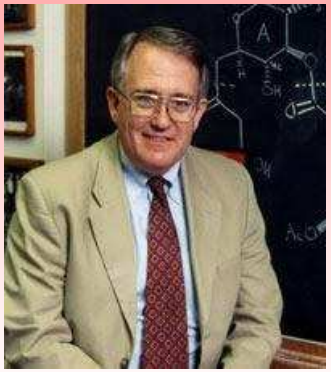
Anion Relay Chemistry (ARC)

An Effective Tactic for Diversity Oriented Synthesis

Marc PRESSET

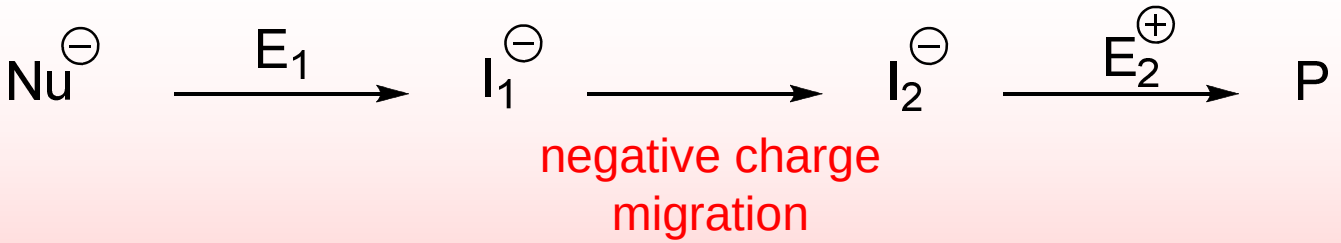
Bibliographical seminar, 09 / 06 / 09

Presentation
History and Definition



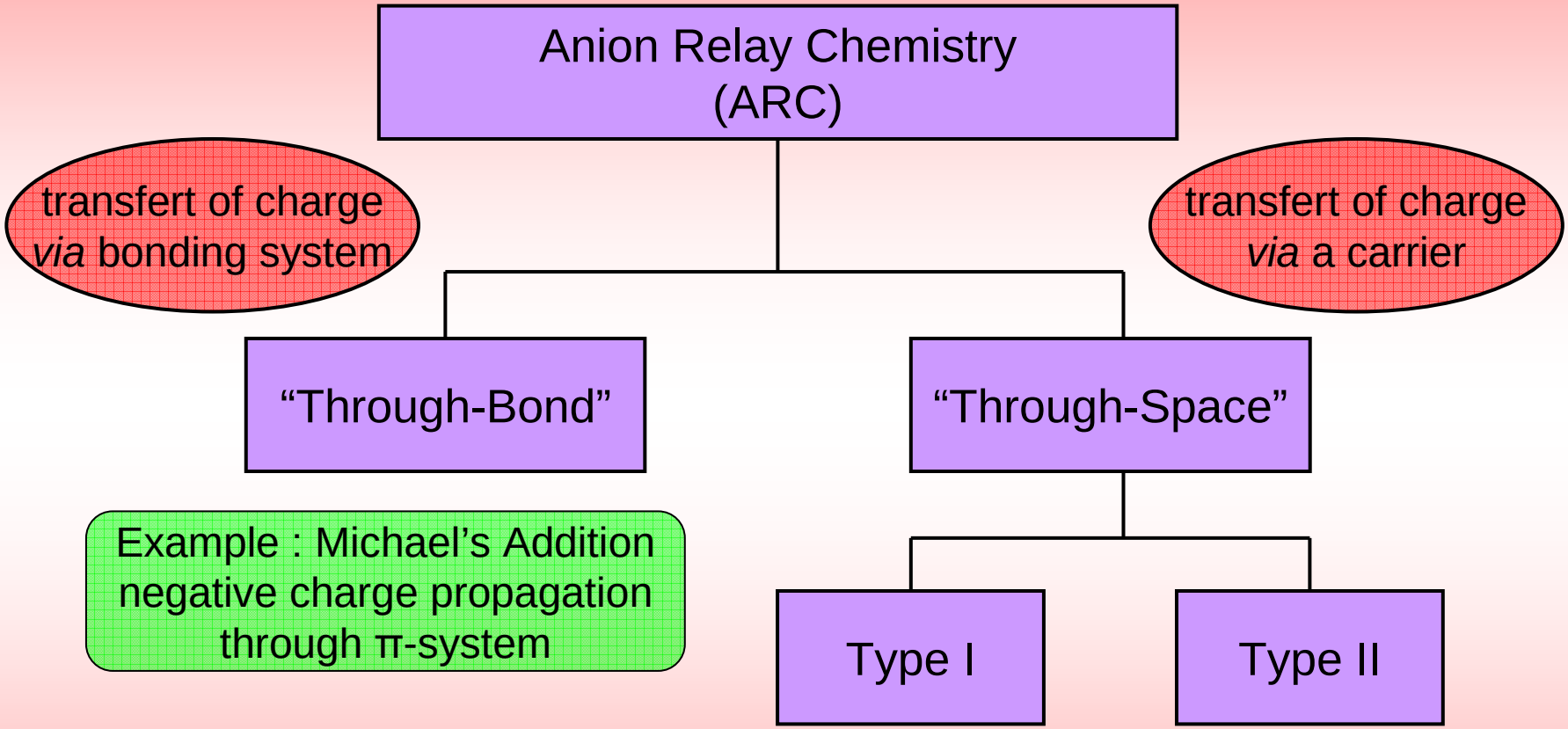
- Well-known chemistry (First example in 1979)
- Concept formalized by B. Smith III in 2006

Anion Relay chemistry (ARC) = Multi-Component Coupling Protocol



Different types depending on the nature of the migration

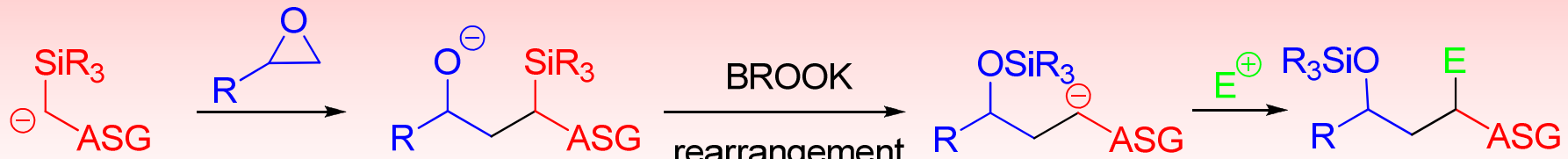
Presentation
Classification



Limitation to Through-Space ARC

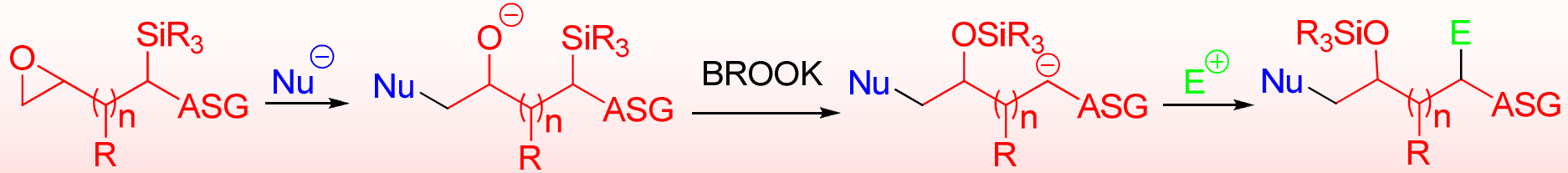
Presentation
Classification

Type I : Relay of negative charge back to its originating locus



bifunctionnal nucleophile linchpin

Type II : Relay of negative charge to a new locus

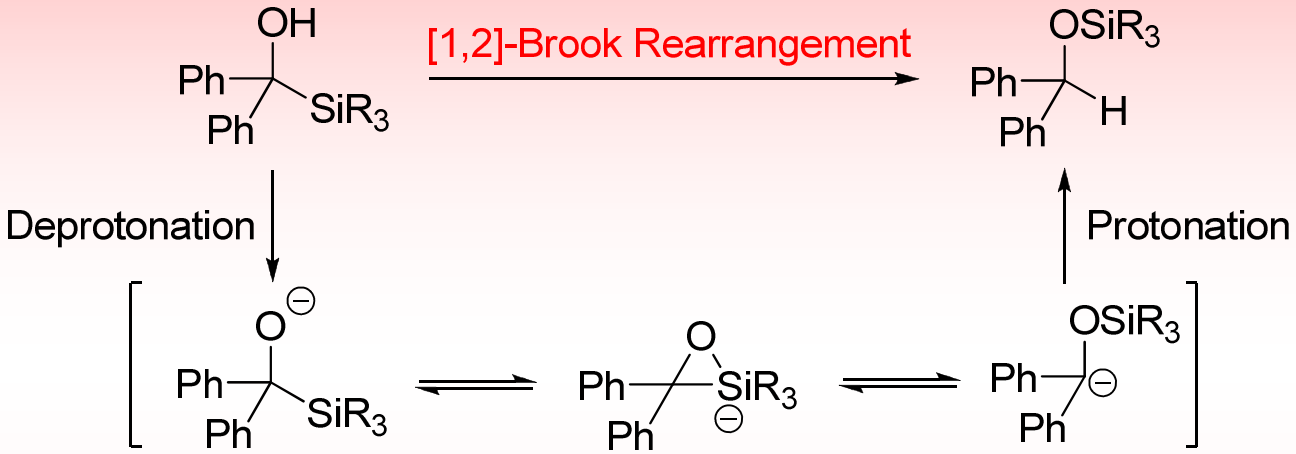


bifunctionnal electrophile linchpin

Importance of Brook rearrangement

Presentation
Brook rearrangement

Brook rearrangement = Reversible migration of a silyl group from C to O

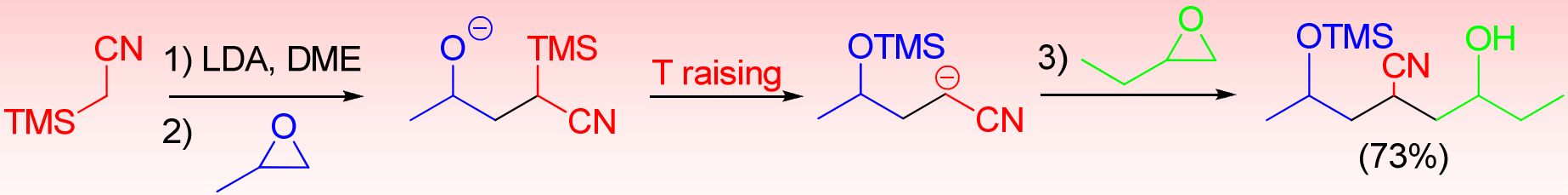


Later studies generalized Brook rearrangement to [1,n] with n=5 [2]

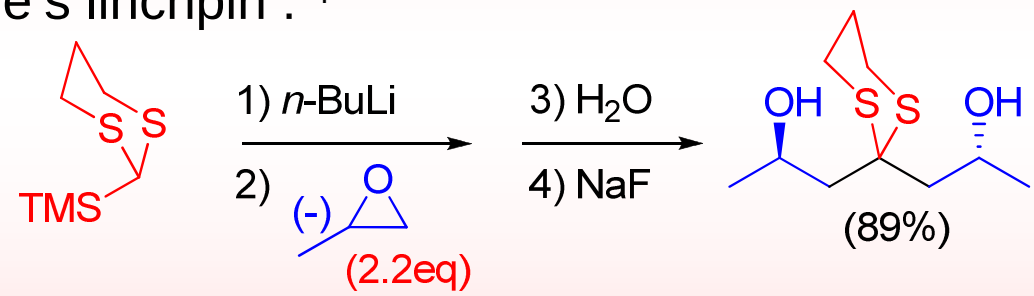
Principal factors governing the equilibrium between oxy and carbanion :
- strengh of the oxygen-metal bond
- anion stabilizing ability of the carbon substituents
- polarity of the solvent

Through-Space Type I ARC
First examples

First example : Matsuda's work [3]

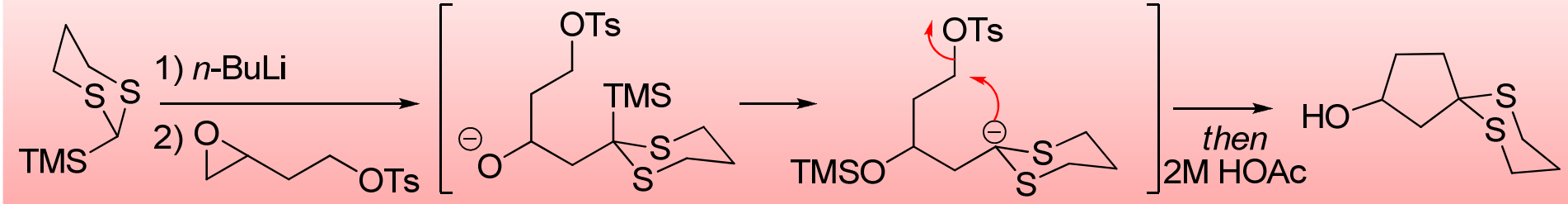


Tietze's linchpin : [4]



Limitation to C_2 symmetric products

Schaumann : dual functional partner [5]

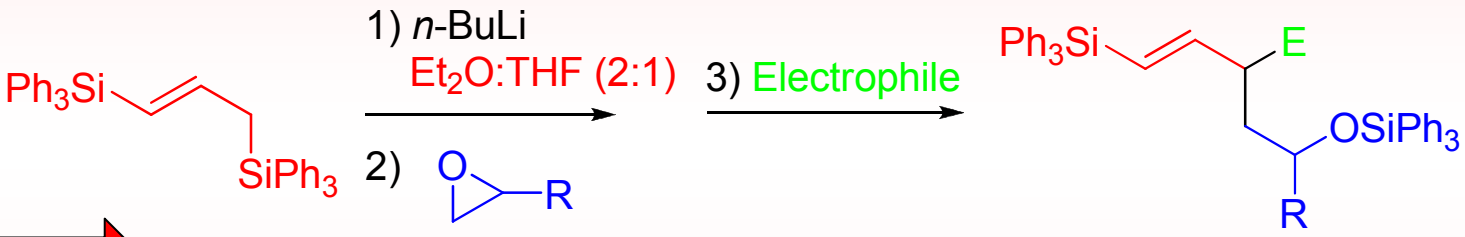


(3) Matsuda, *Perkin Trans. 1*, **1979**, 26
(4) Tietze, *Synlett*, **1994**, 511
(5) Schaumann, *ACIEE*, **1994**, 217

Through-Space Type I ARC
Examples controlling Brook

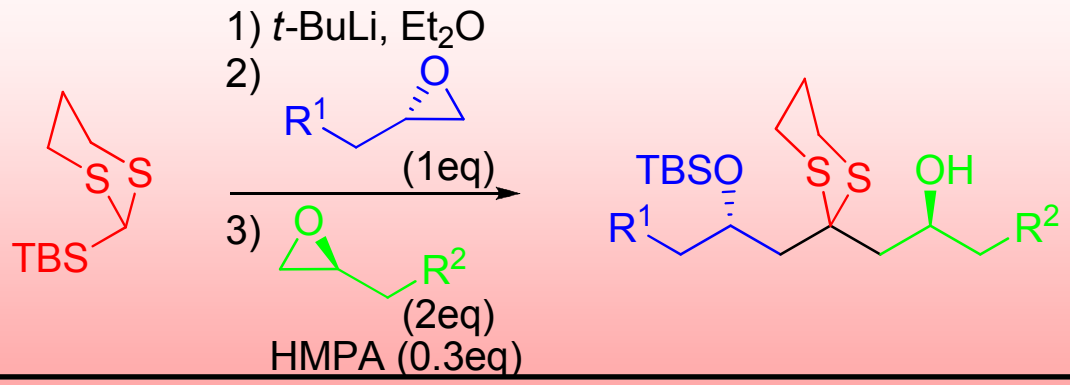
Oshima triggers Brook by additive [6] or solvent : [7]

R=H, X=Cl (80%)
R=Me, X=Cl (68%)
R=Me, X=Br (60%)



R = H, Alk, Ph
E = MeI, PhCHO
(39-52%)

Smith, III uses Tietze's linchpin with solvent-controlled Brook : [8]

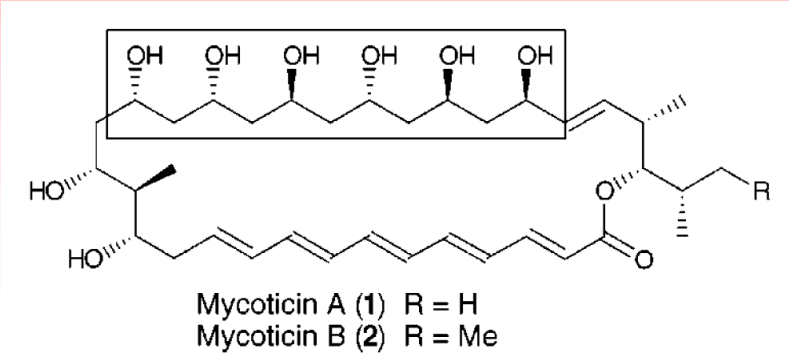


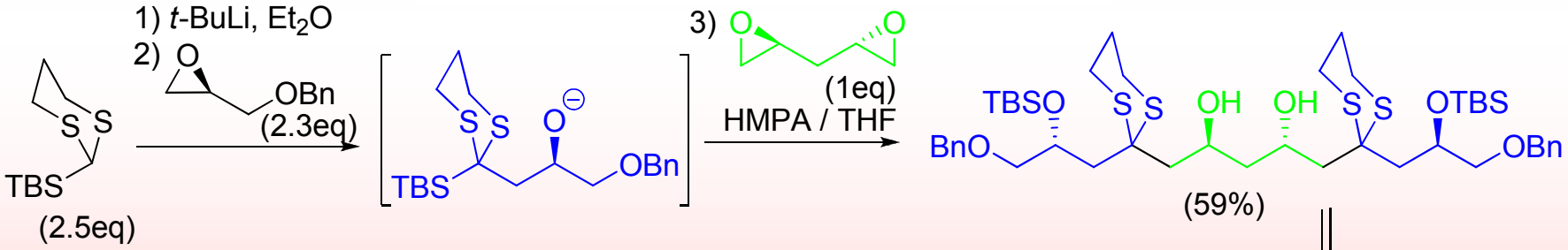
R^1=OBn, alk
R^2=OR, CH_2ODMP
(56-74%)

(6) Oshima, *Tetrahedron*, **1996**, 503
(7) Oshima, *Tetrahedron Lett.*, **1998**, 2575
(8) Smith, III, *JACS*, **1997**, 6925

Through-Space Type I ARC
In Natural Product Synthesis

Smith's formal synthesis of mycoticin : [9]





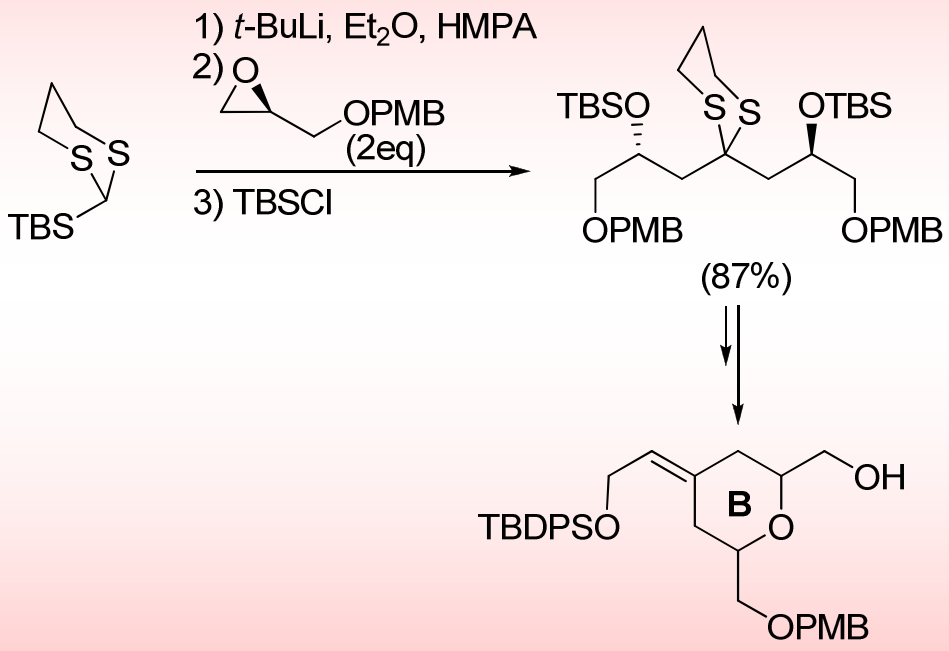
Five-component coupling tactic

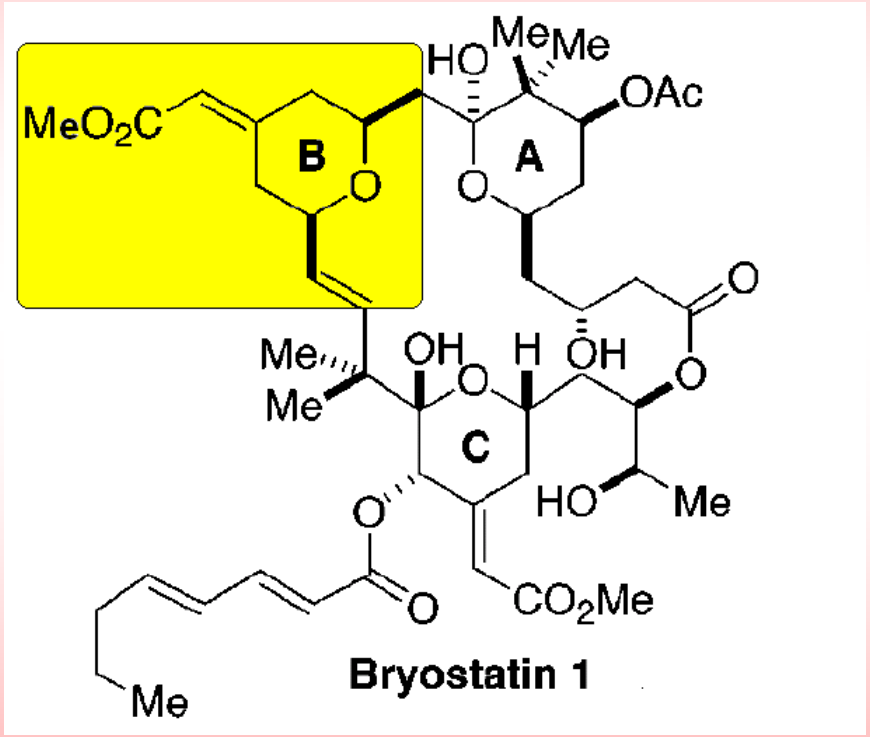
Schreiber's intermediate in 8 steps (five fewer)

(9) Smith, III *Org. Lett.*, **1999**, 2001

Through-Space Type I ARC
In Natural Product Synthesis

Hale's synthesis of ring B of Bryostatin : [10]

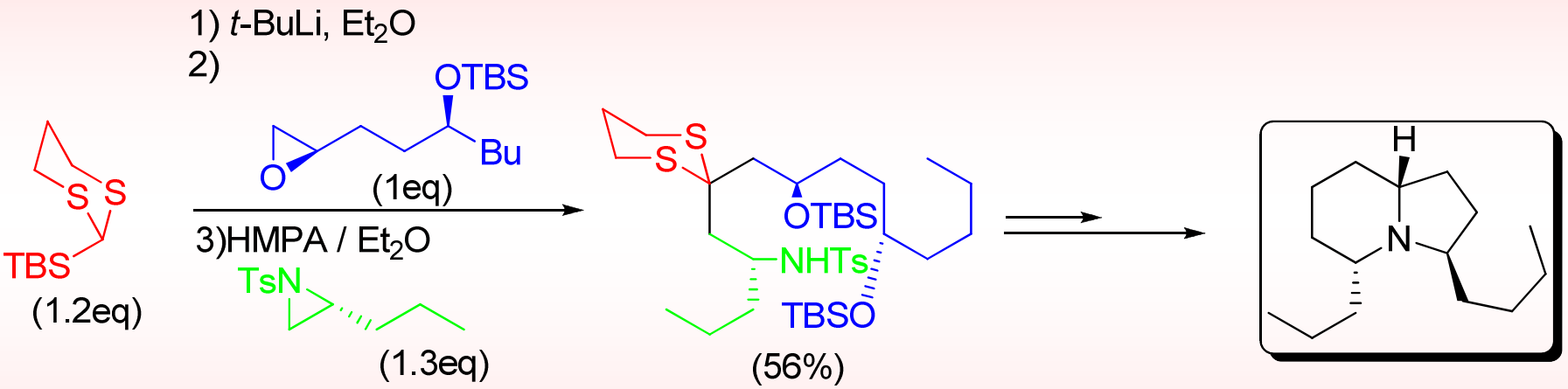




(10) Hale, *Org. Lett.*, **2000**, 2189

Through-Space Type I ARC
In Natural Product Synthesis

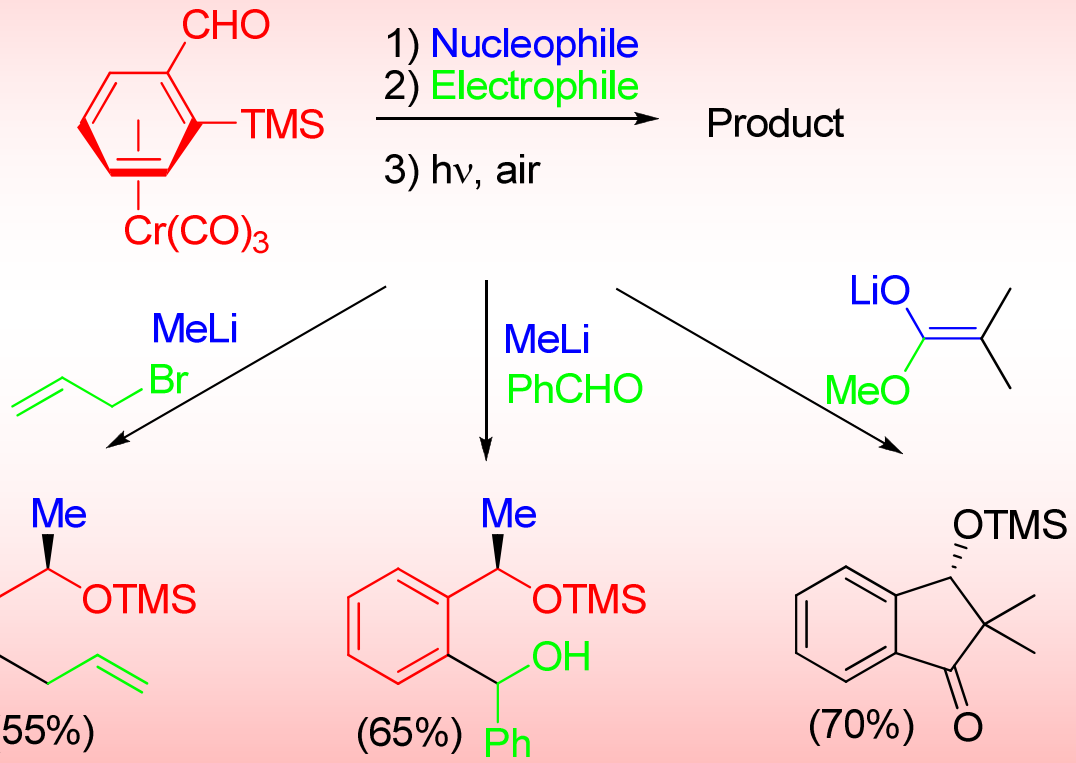
Smith's total synthesis of (-)-indolizidine : [11]



(11) Smith, III, *Org. Lett.*, **2004**, 1493

Through-Space Type II ARC
First examples

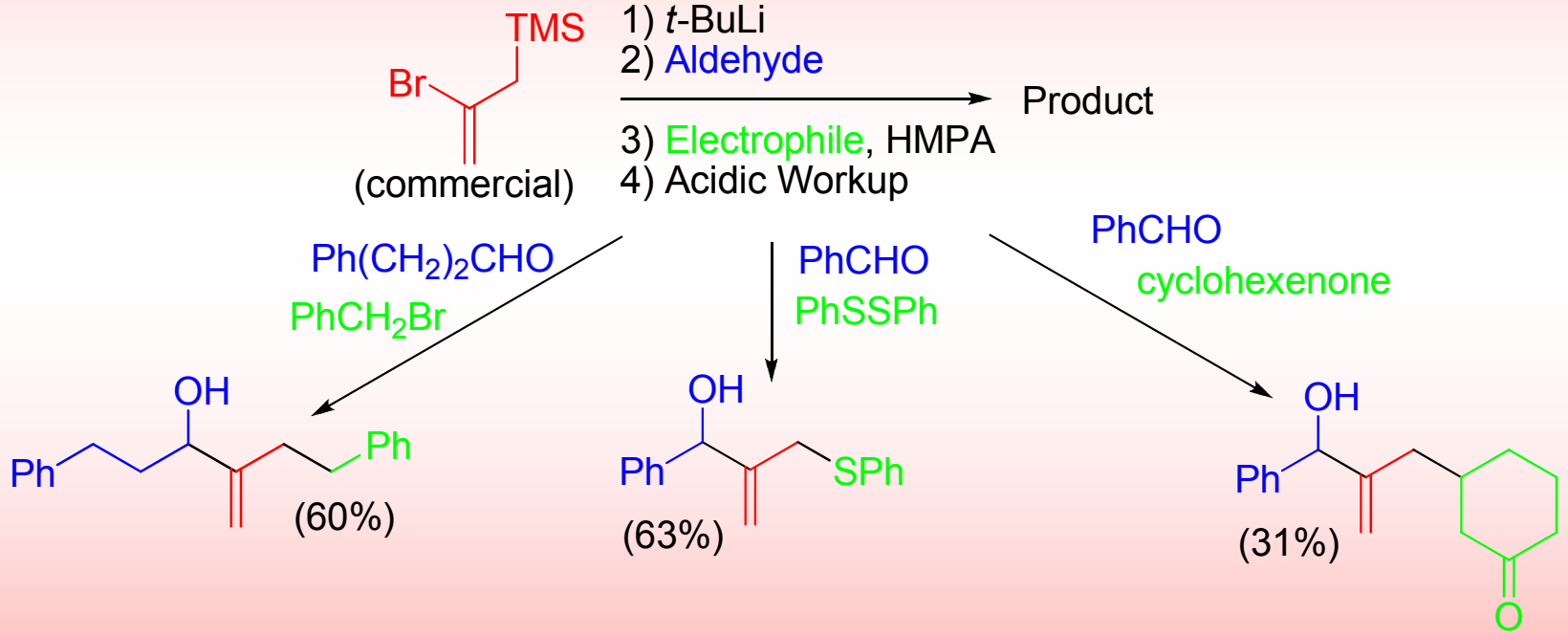
Moser's complex : [12, 13]



(12) Moser, *Org. Lett.*, **2000**, 717
(13) Moser, *Org. Lett.*, **2002**, 1981

Through-Space Type II ARC
Others linchpins

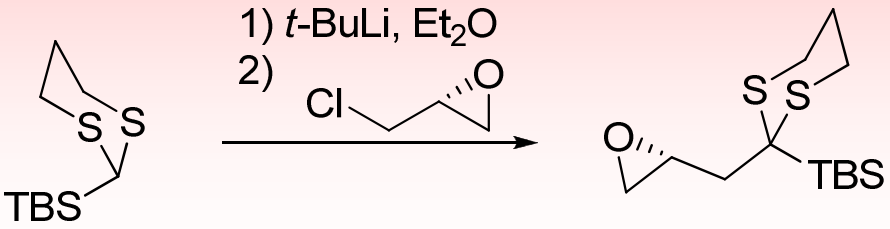
Smith's linchpin (Dianion synthon) : [14]

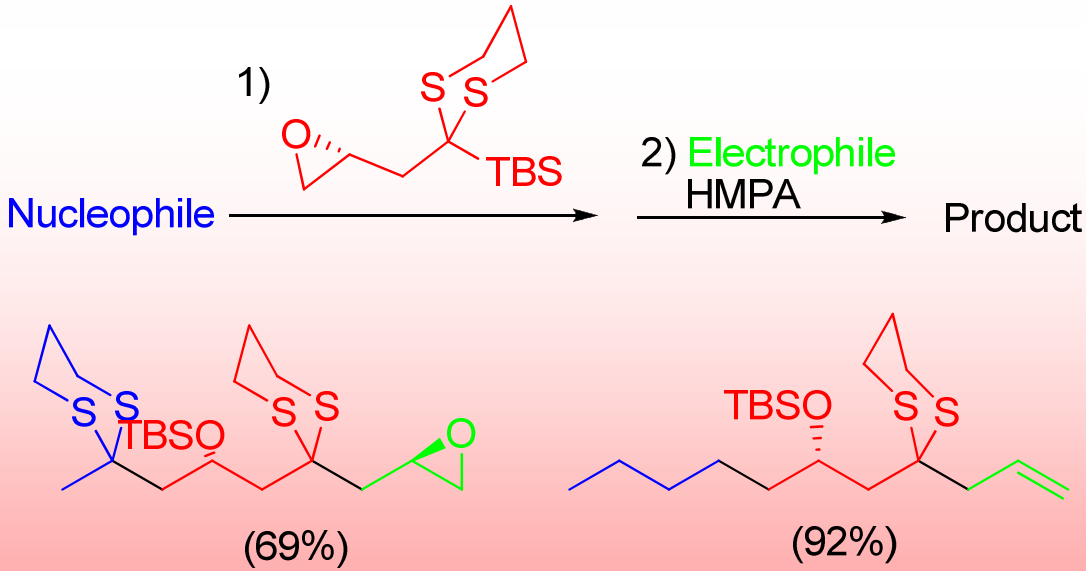


(14) Smith, III, *Synlett*, **2004**, 1363

Through-Space Type II ARC
Others linchpins

Smith's design of new linchpin (Cation/Anion synthon) : [15]

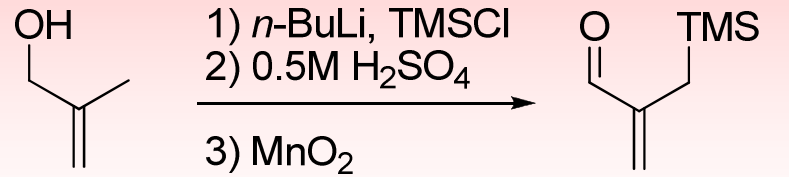


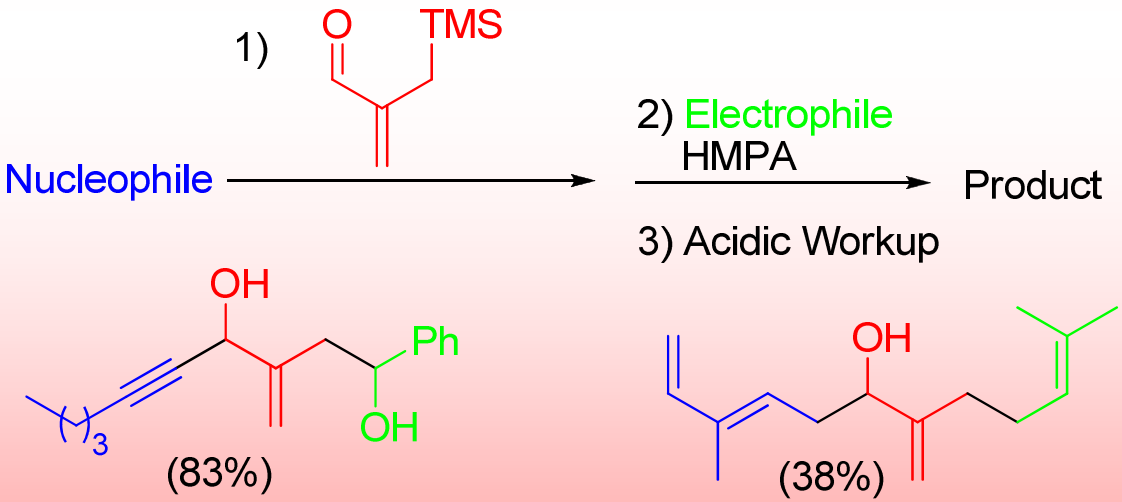


(15) Smith, III, *JACS*, **2006**, 66

Through-Space Type II ARC
Others linchpins

Smith's design of new linchpin (Cation/Anion synthon) : [16]

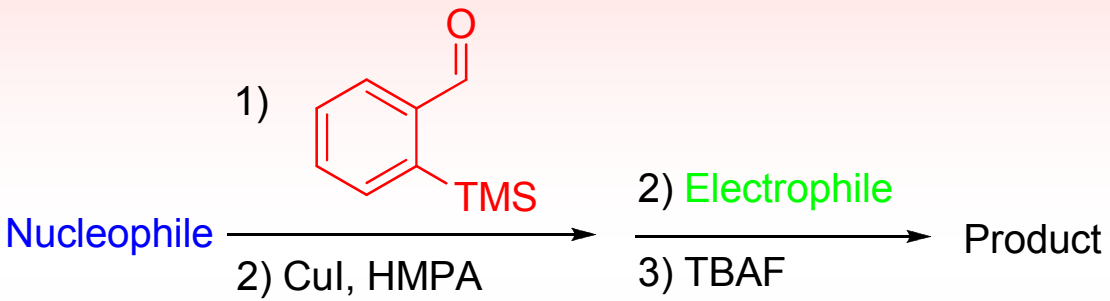


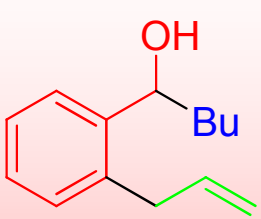


(16) Smith, III, *Org. Lett.*, **2007**, 3307

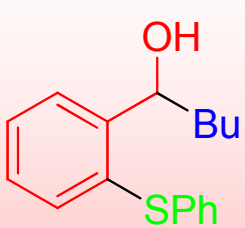
Through-Space Type II ARC
Others linchpins

Smith's design of new linchpin (Cation/Anion synthon) : [17]

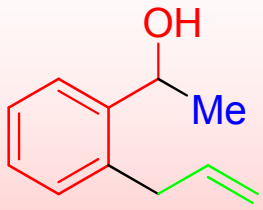




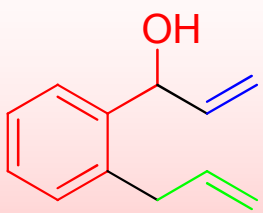
(69%)



(69%)



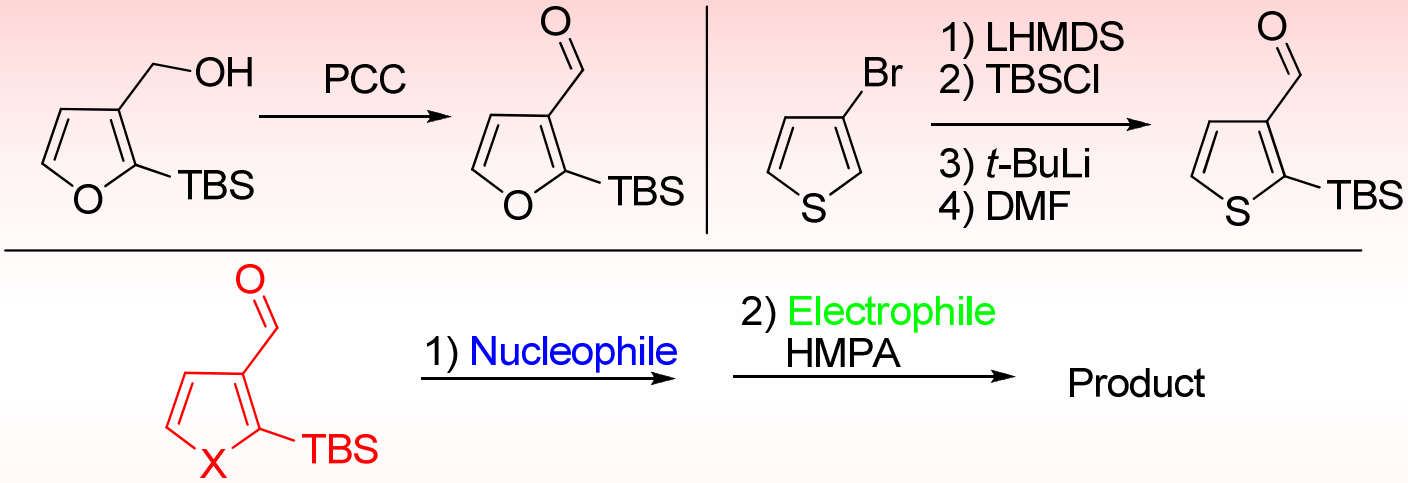
(68%)

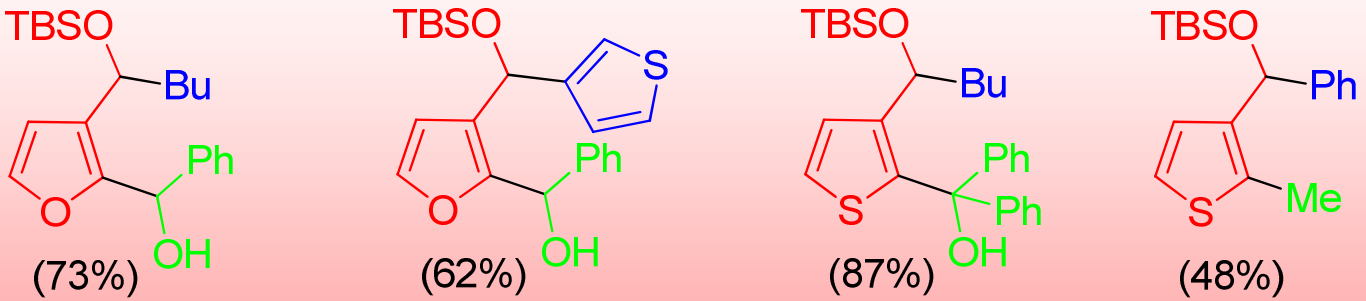


(66%)

Through-Space Type II ARC
Others linchpins

Xian's design of new linchpin (Cation/Anion synthon) : [18]

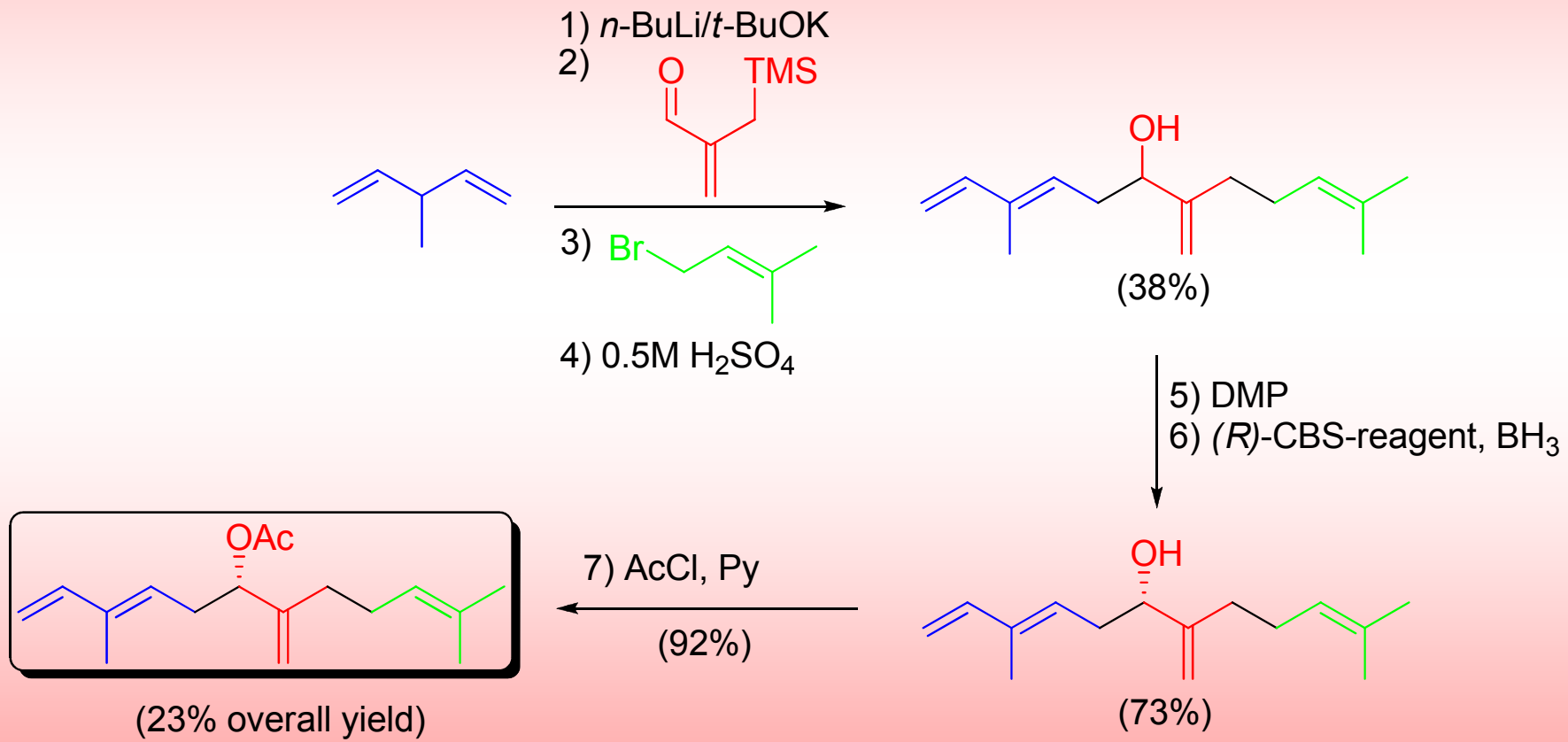




(18) Xian, *Org. Lett.*, **2009**, 1861

Through-Space Type II ARC
In Natural Product Synthesis

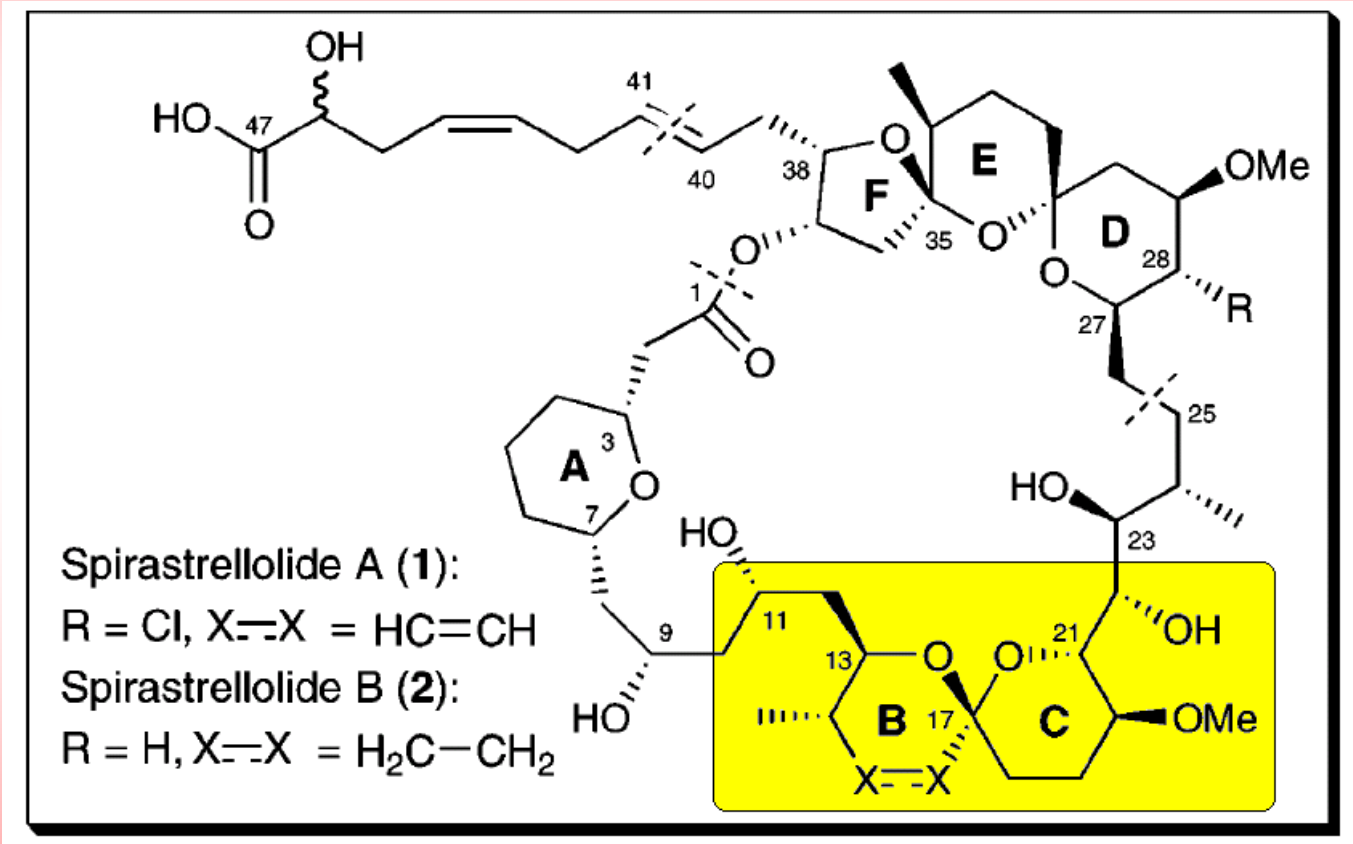
Smith's total synthesis of a gorgonian sesquiterpene : [19]



(19) Smith,III, *Org. Lett.*, **2007**, 3307

Through-Space Type II ARC
In Natural Product Synthesis

Smith's synthesis of BC-spiroketal unit of spirastrellolides : [20]



(20) Smith,III, *Org. Lett.*, **2007**, 3307

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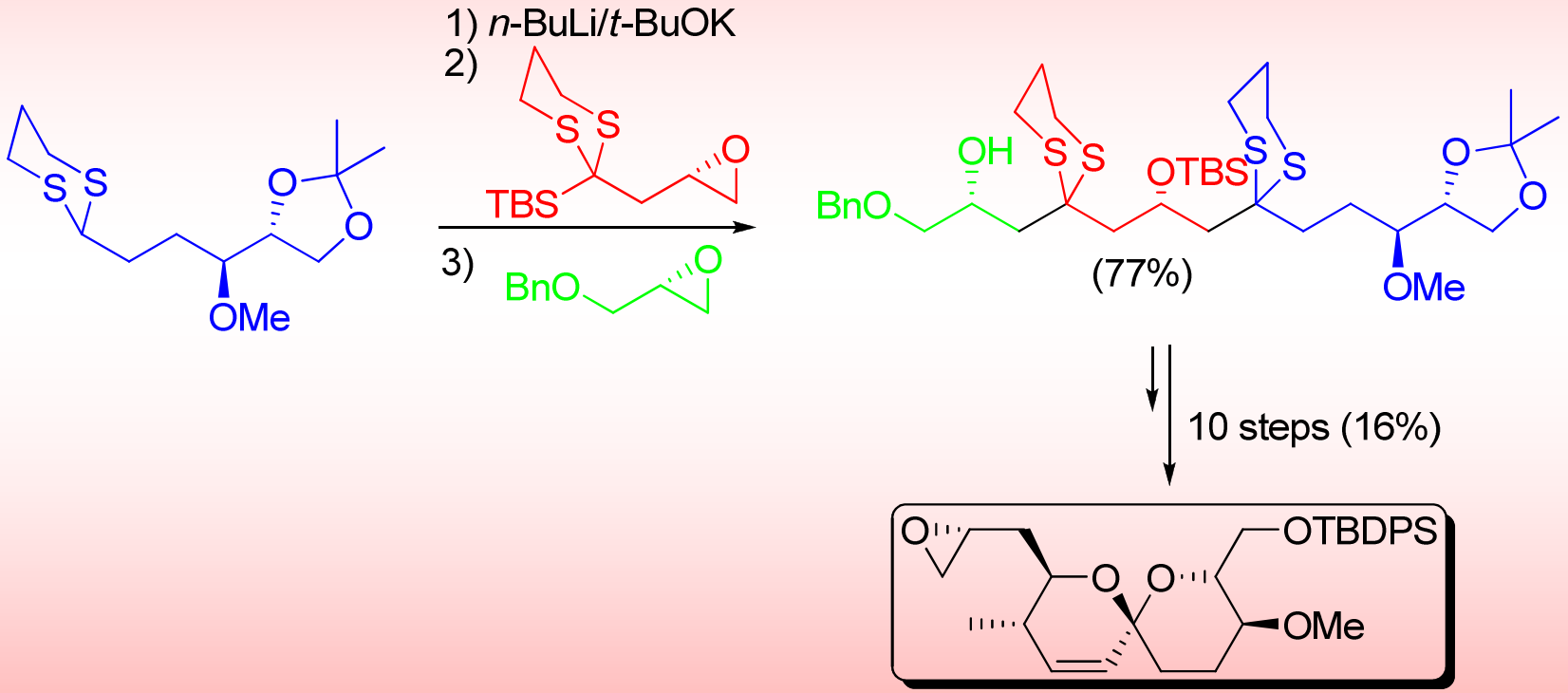

(20) Smith,III, *Org. Lett.*, **2007**, 3307

Conclusion

- Numerous linchpins
- Applications in natural products total synthesis

- Limited to Brook rearrangement
- Good yields but not excellent