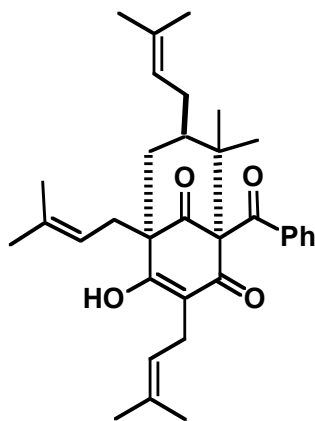


Differentiation of Nonconventional “Carbanions” – The Total Synthesis of Nemorosone and Clusianone

Chihiro Tsukano, Dionicio R. Siegel, and Samuel J. Danishefsky
Angew. Chem. Int. Ed. **2007**, early view

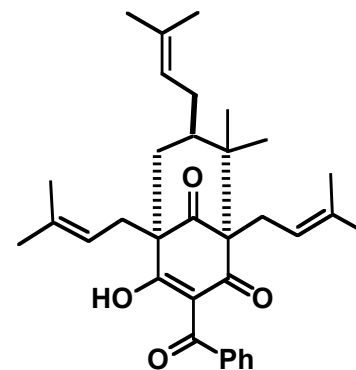
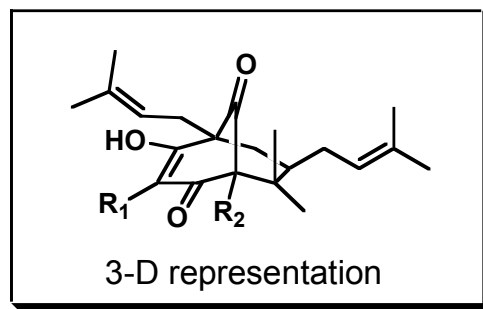
William Paquette
Current Literature – 10/27/07
Wipf Group

Structurally Related Polyprenylated Natural Products



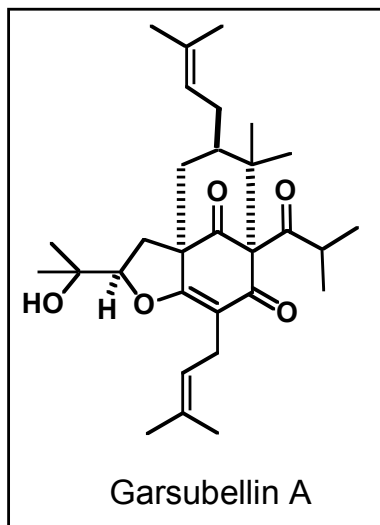
Nemorosone

- Isolated in 2001 from the flowers of *Clusia rosea*
- Telomerase and ERK-1/2 Inhibitor



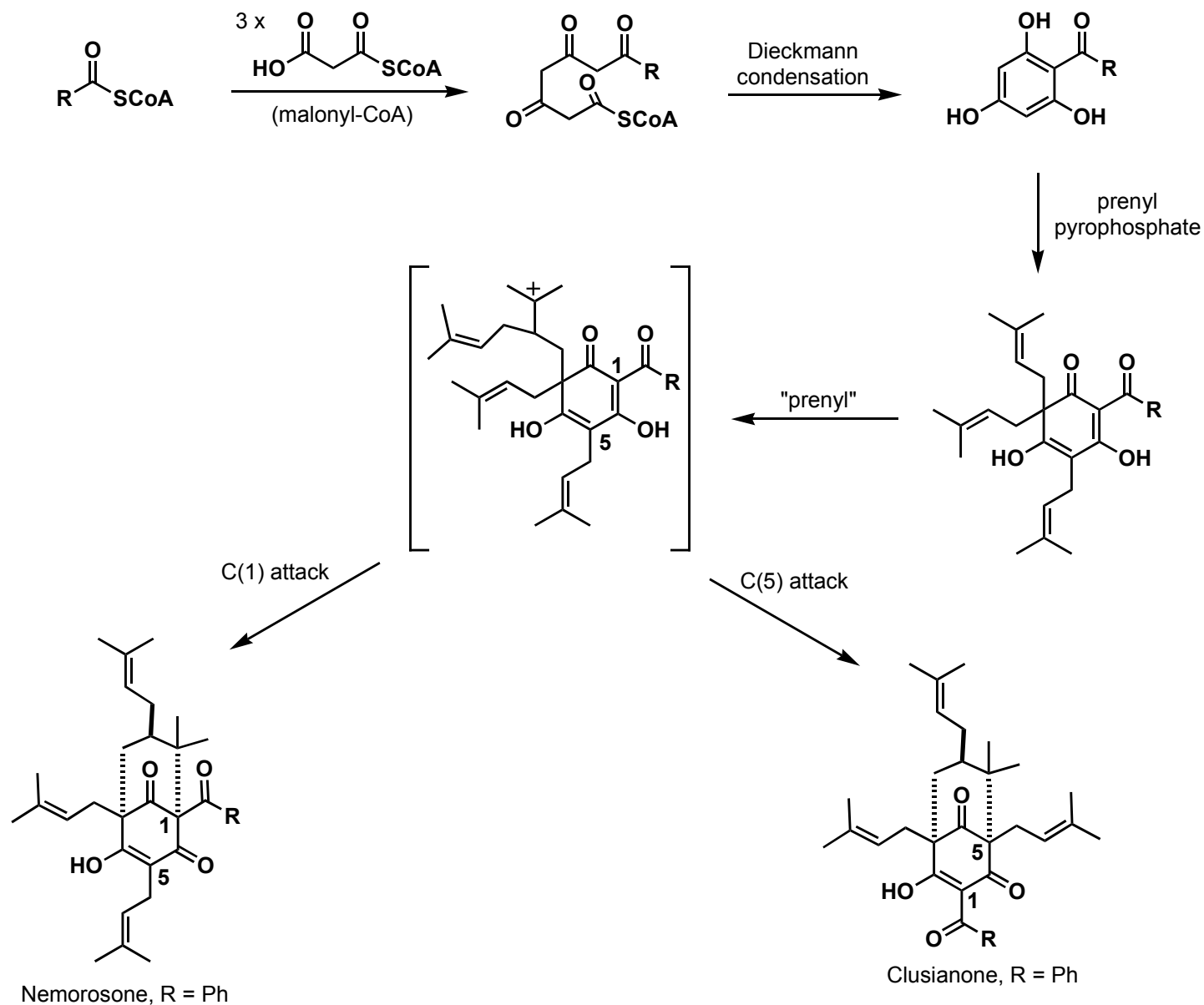
Clusianone

- Isolated in 1976 from the flowers of *Clusia congestiflora*
- Anti-HIV properties



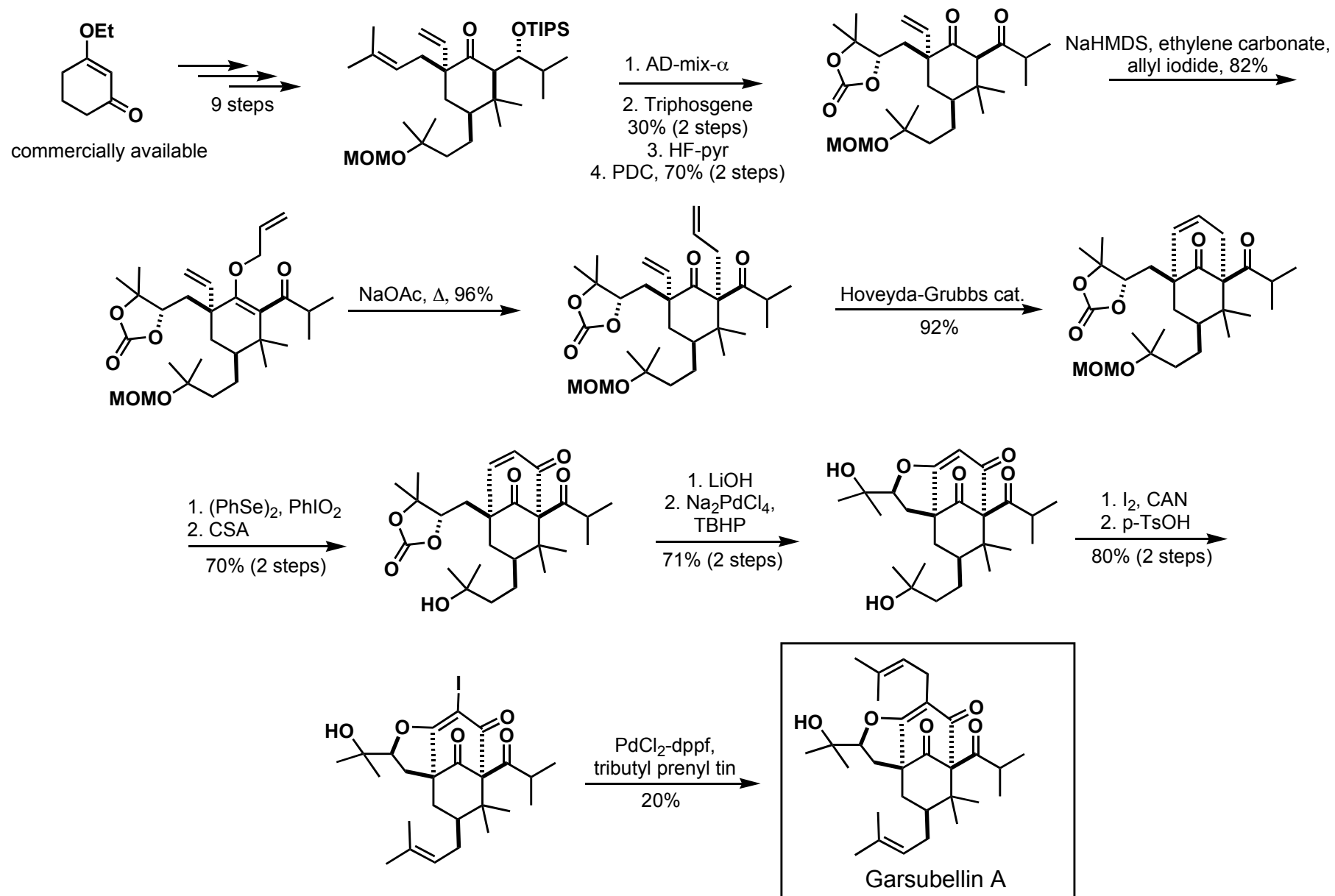
Garsubellin A

Biosynthesis of Polyprenylated Natural Products



Ciochina, R. and Grossman, R. B. *Chem. Rev.* **2006**, *106*, 3963-3986.

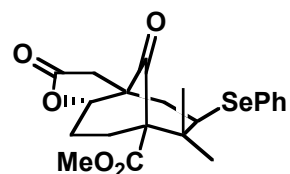
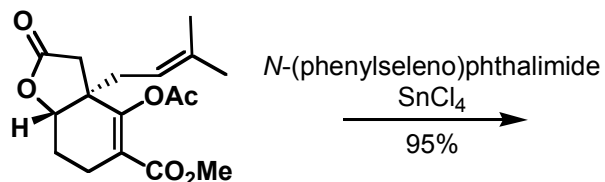
First Total Synthesis of (\pm)-Garsubellin A



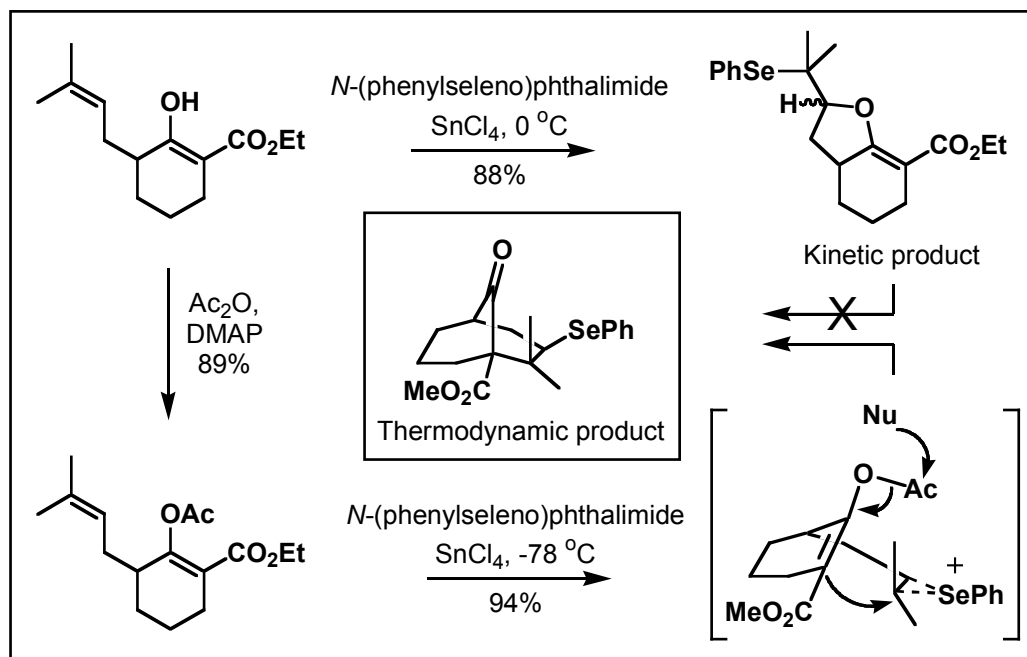
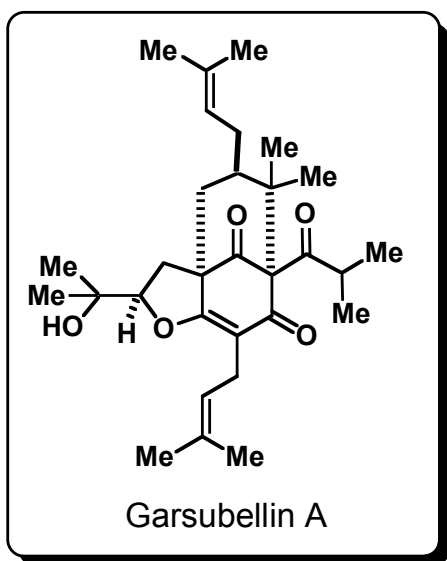
M. Shibasaki, et. al. *J. Am. Chem. Soc.* **2005**, *127*, 14200-14201.

[3.3.1] Bicycles

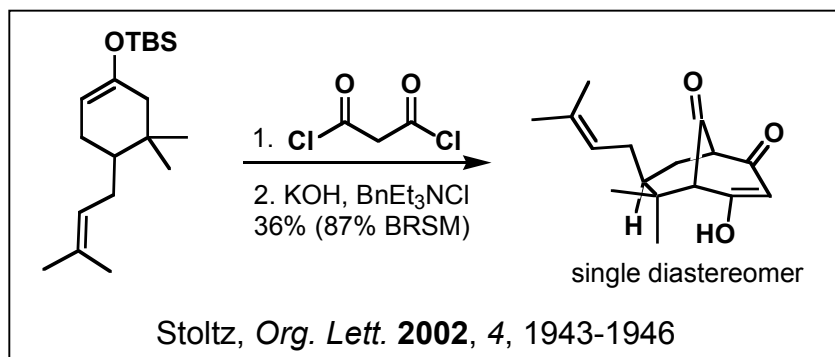
Facile Construction Toward Polyprenylated Compounds



Nicolaou, *J. Am. Chem. Soc.* **1999**, 121, 4724-4725

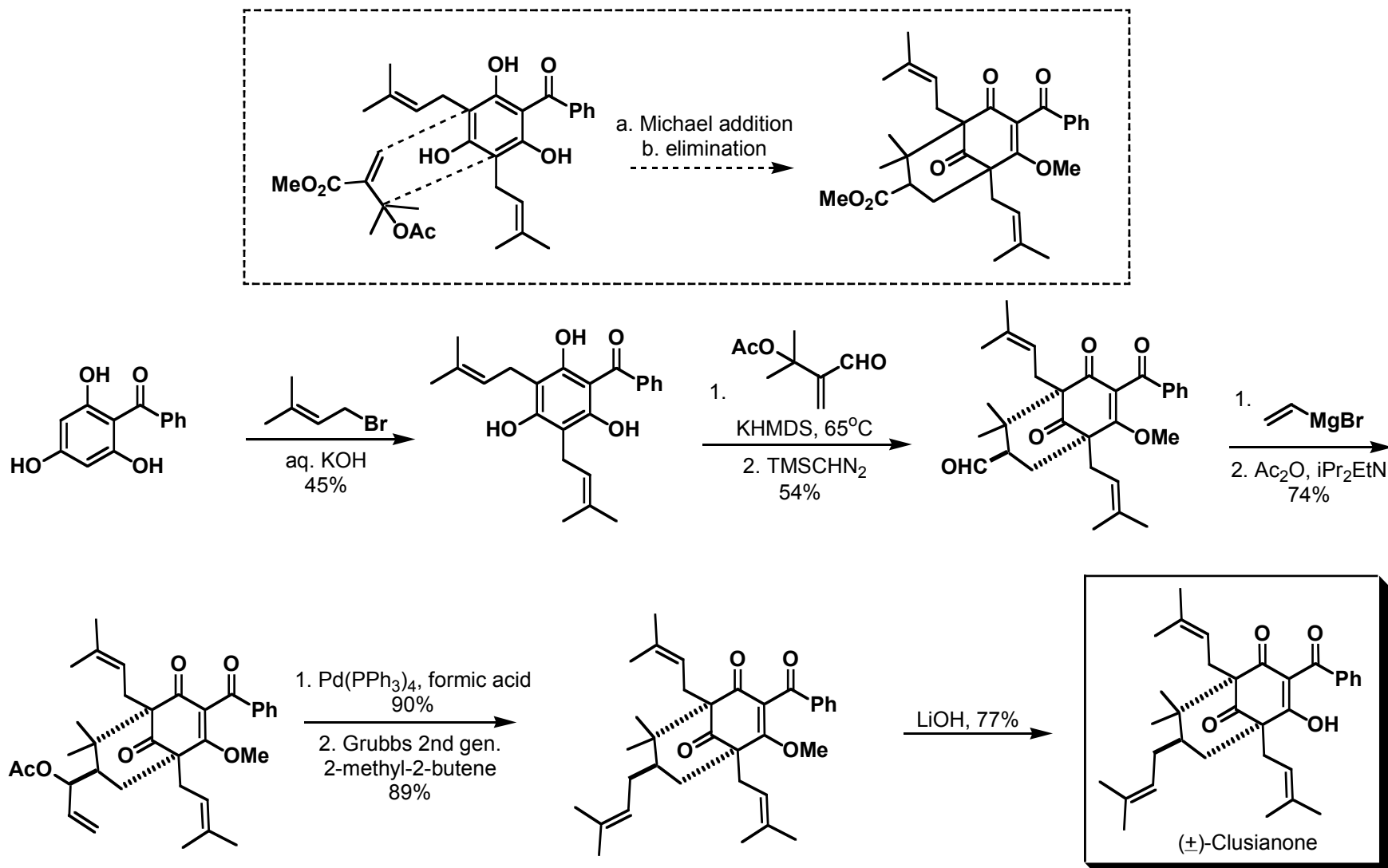


Nicolaou, *Org. Lett.* **1999**, 1, 807-810



Stoltz, *Org. Lett.* **2002**, 4, 1943-1946

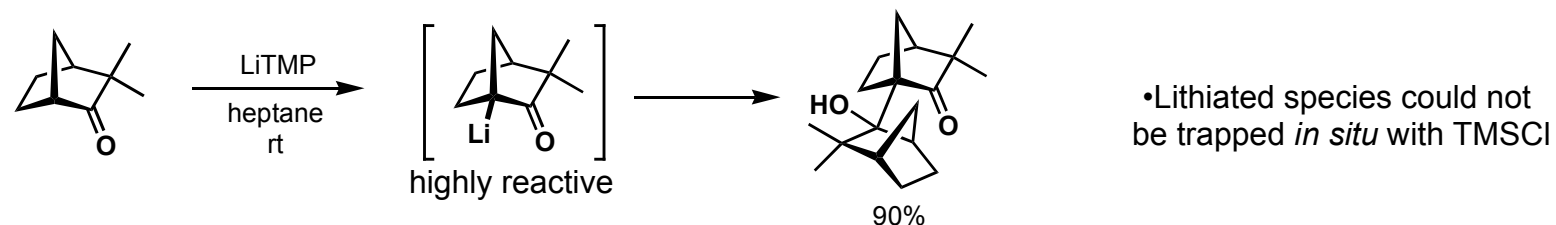
Expedient Synthesis of (\pm)Clusianone



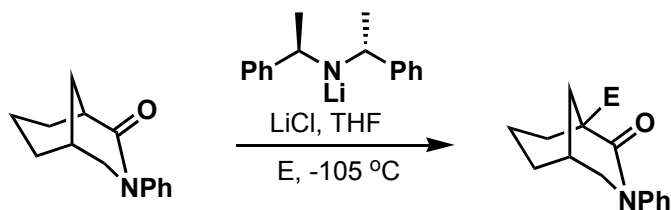
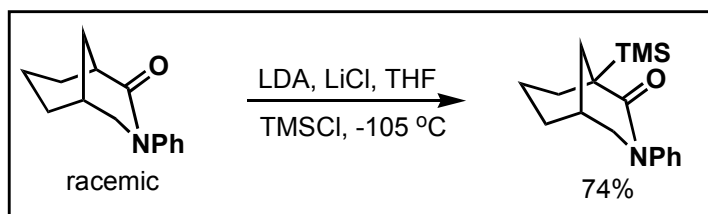
J. Qi and J. A. Porco, Jr. *J. Am. Chem. Soc.* **2007**, *129*, 12682-12683

Substitutions of Bridged Carbonyl Compounds

Reactivity of "anti-Bredt" Carbanions

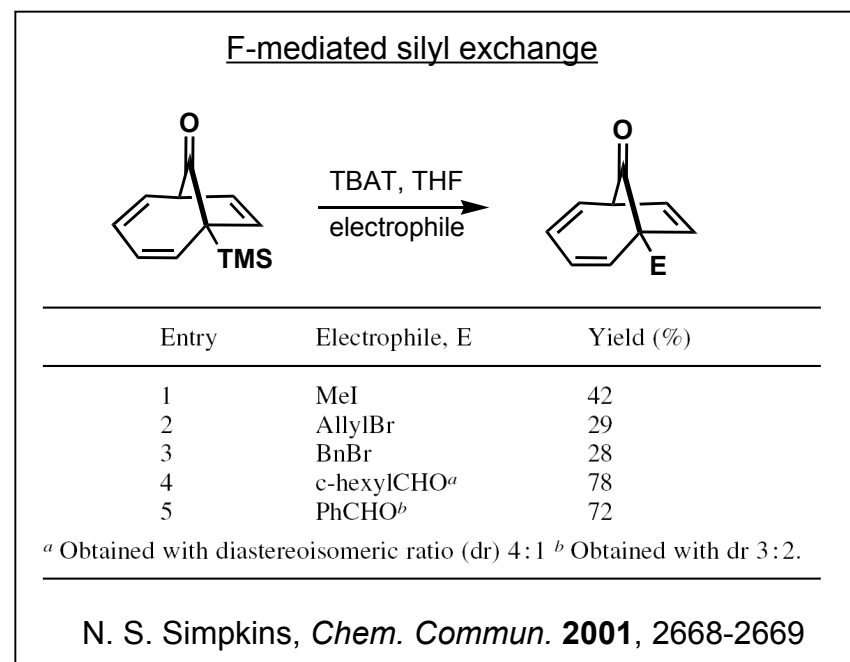


C. Shiner, *J. Am. Chem. Soc.* **1988**, *110*, 957-958



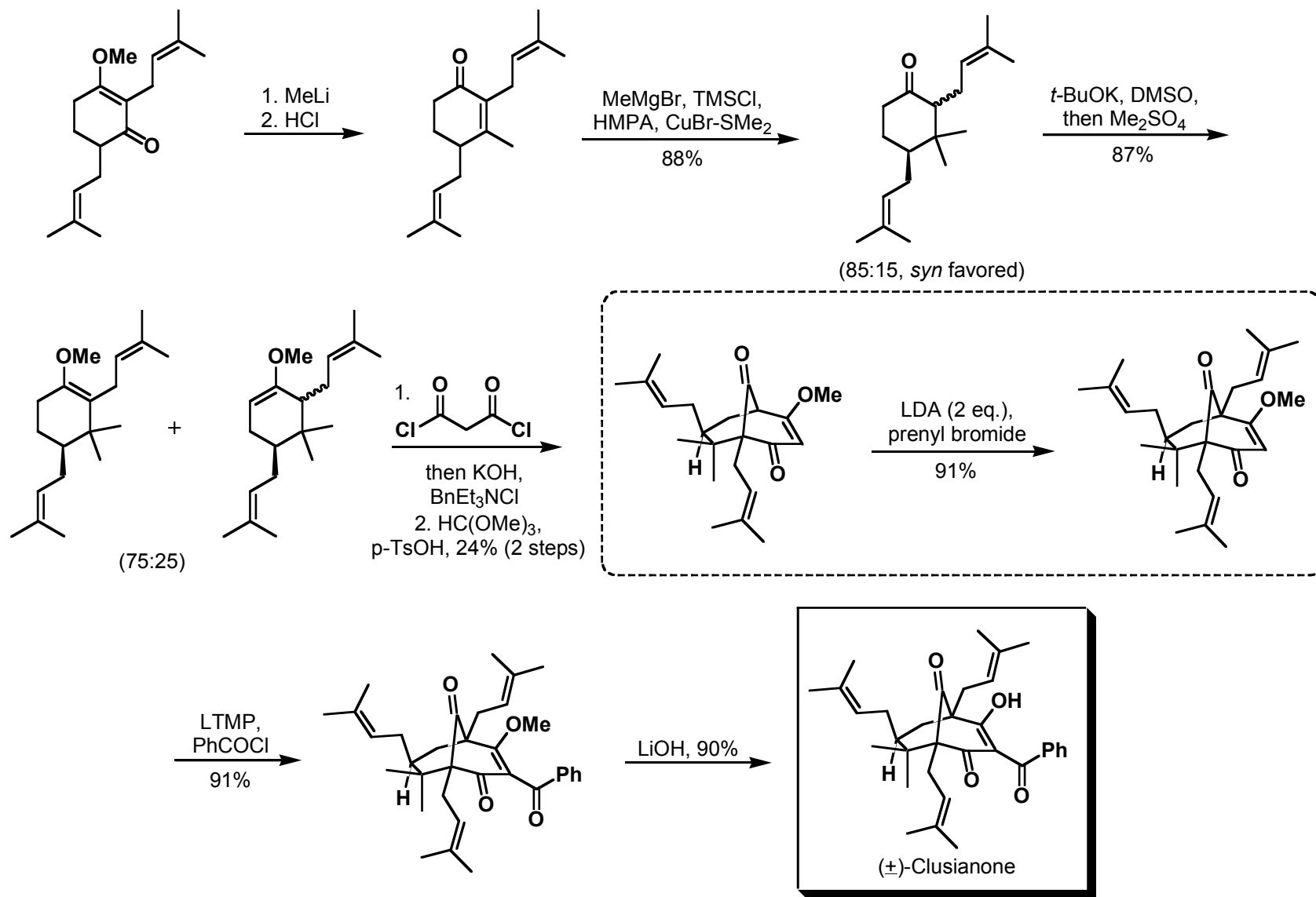
product	electrophile	E	yield (%)	ee (%)
(-)- 22	methyl iodide	Me	57	97
(-)- 23	allyl bromide	CH ₂ CH=CH ₂	42	95
(-)- 24	prenyl bromide	CH ₂ CH=C(Me) ₂	50	98
(-)- 25	benzyl bromide	CH ₂ Ph	52	95
(-)- 26	pivaloyl chloride	CO ^t Bu	56	98

N. S. Simpkins, *Org. Lett.* **2003**, *5*, 1673-1675



Racemic Clusianone Synthesis

Bridgehead Functionalization of the [3.3.1] Ring

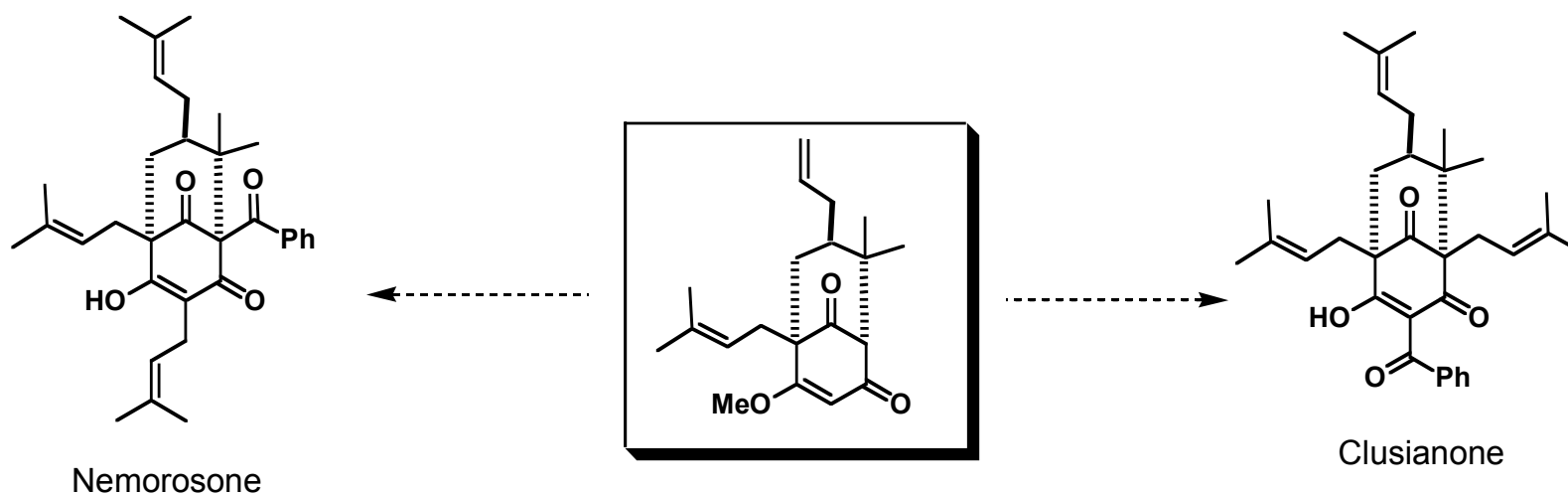


Rodeschini, V.; Ahmad, N. M.; Simpkins, N. S. *Org. Lett.* **2006**, *8*, 5283-5285

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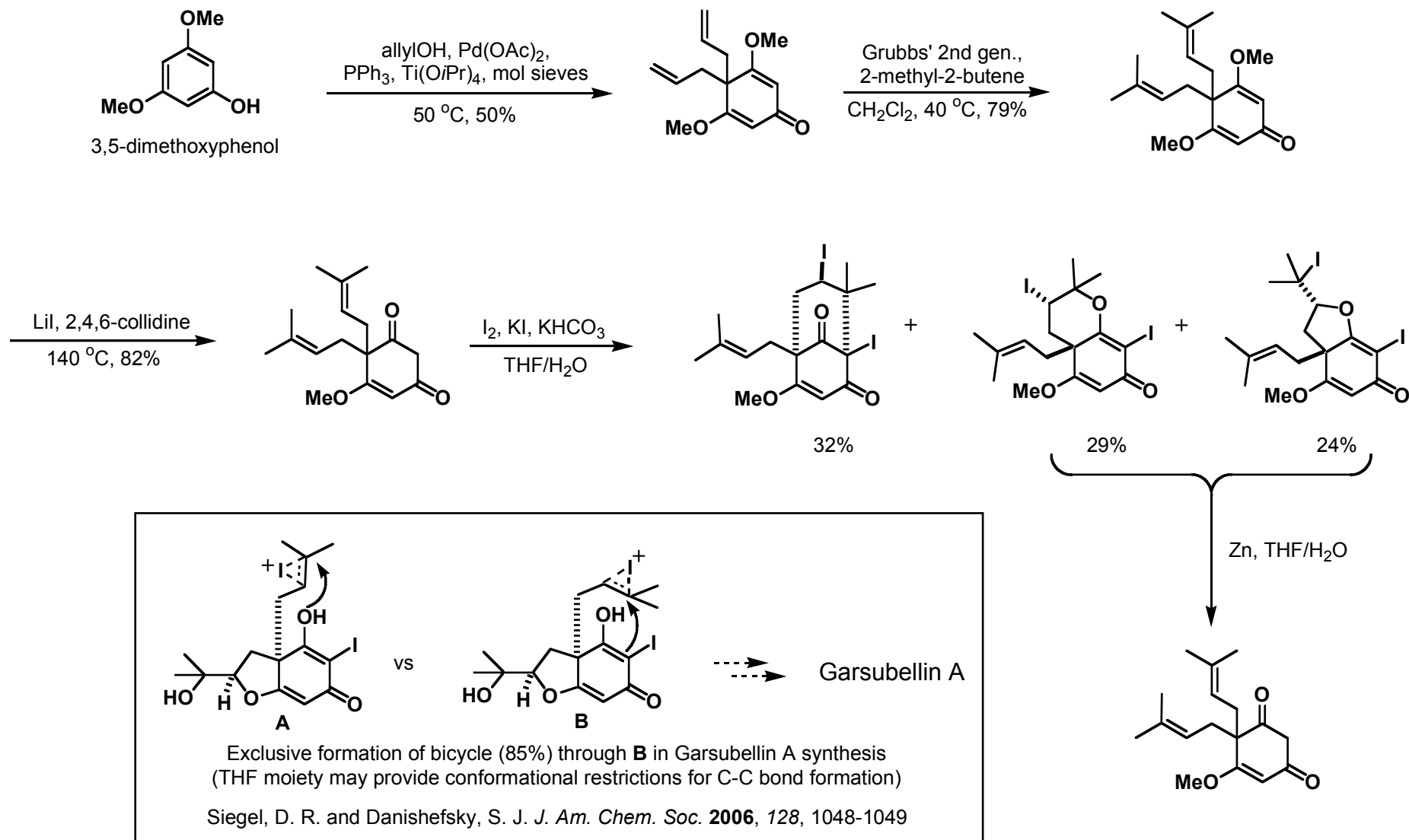
Title Paper

Chihiro Tsukano, Dionicio R. Siegel, and Samuel J. Danishefsky
Angew. Chem. Int. Ed. **2007**, early view

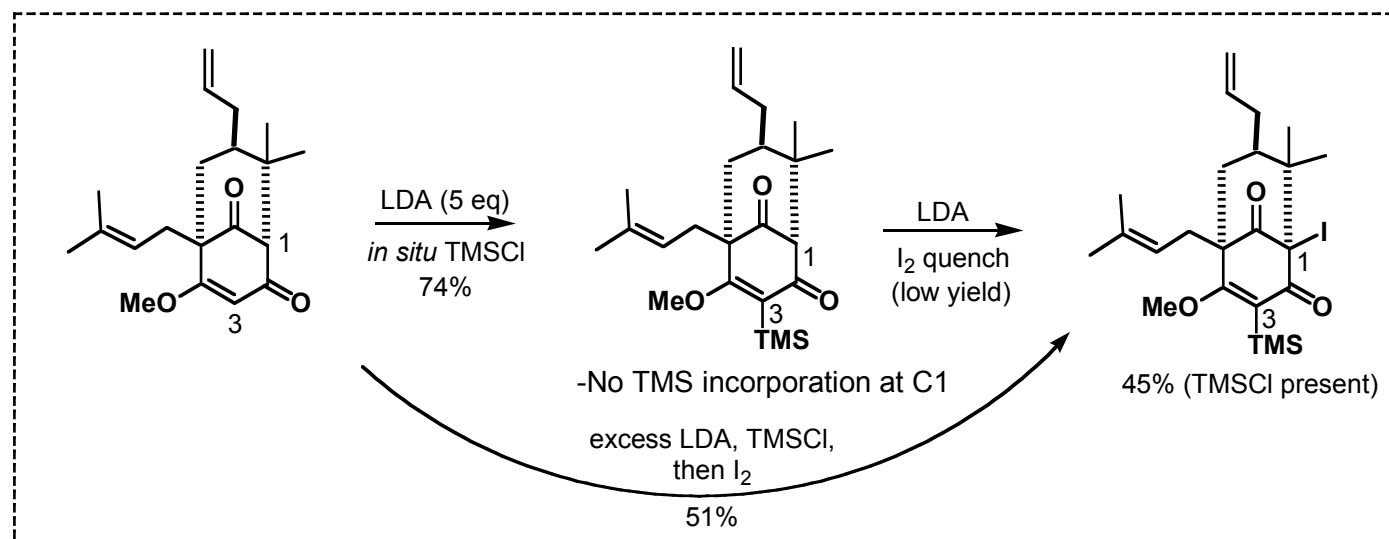
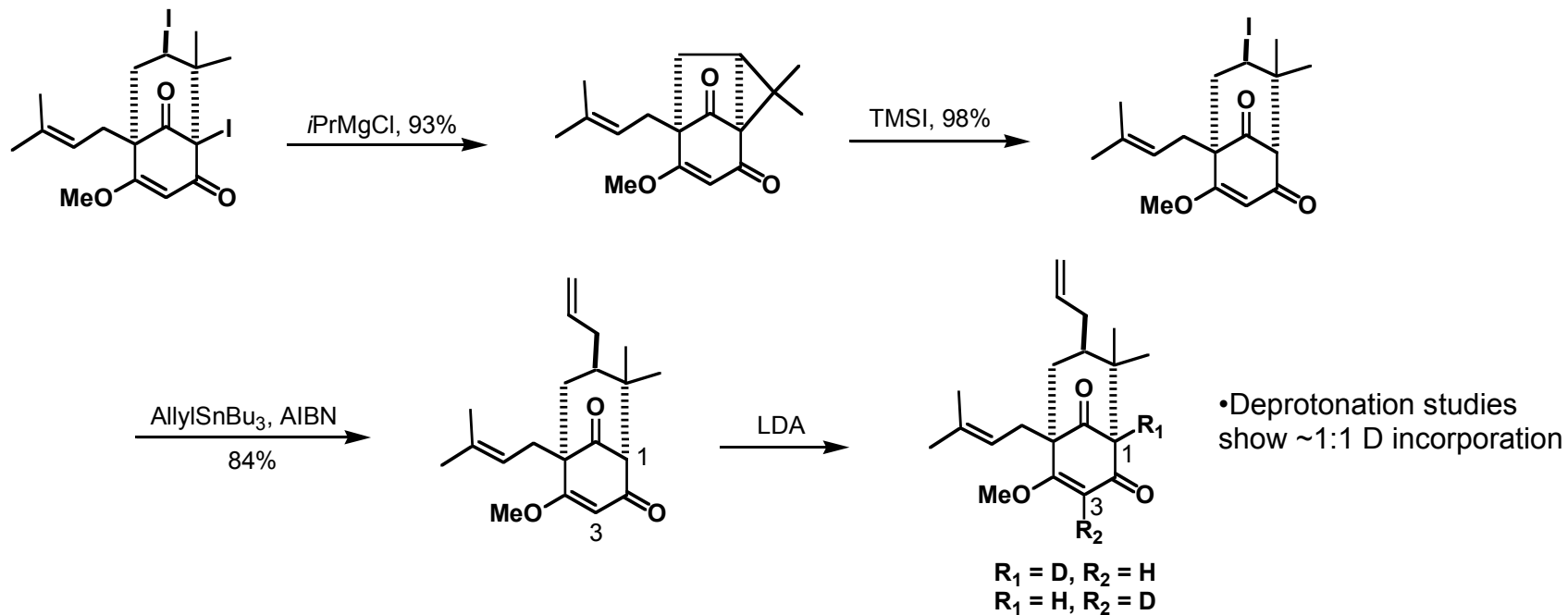


Construct from a common intermediate

Construction of the Requisite Bicycle

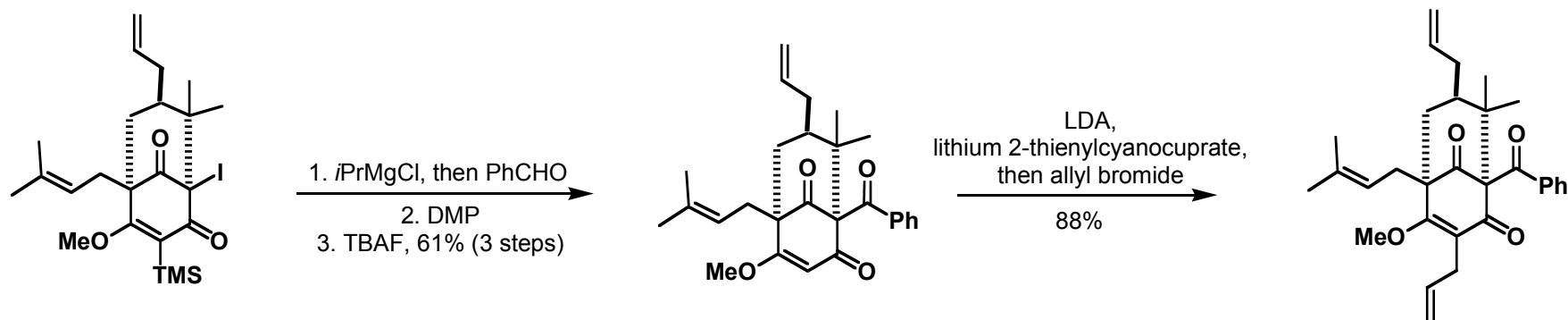


Selective Quenching of the [3.3.1] System

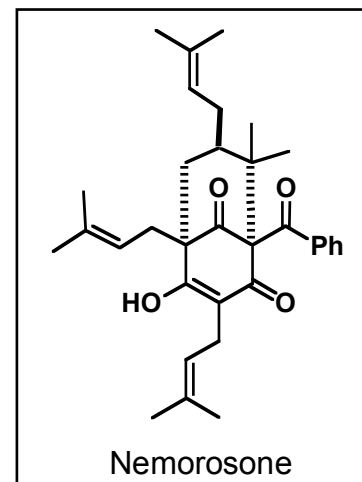
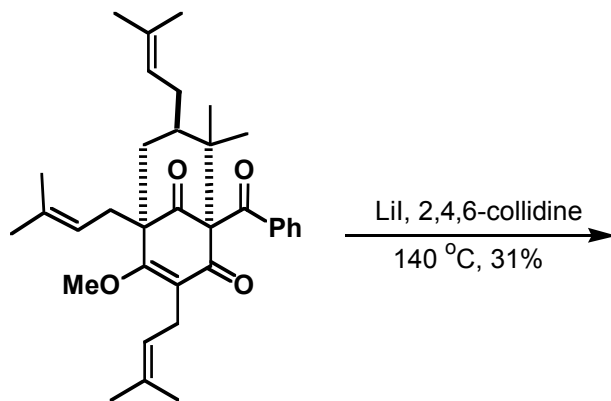


Site-selective Functionalization using Orthogonal Groups

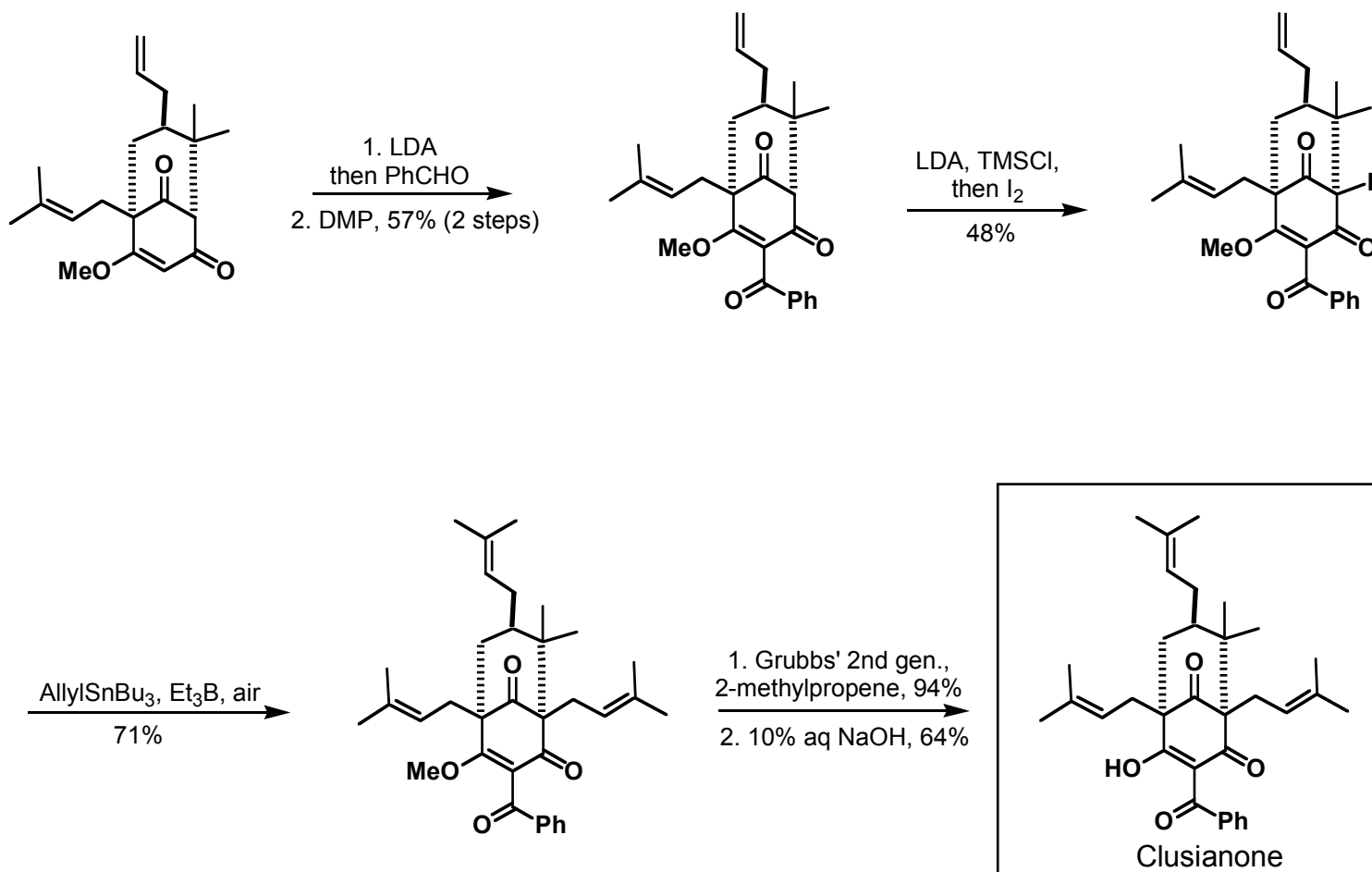
Completion of Nemorosone



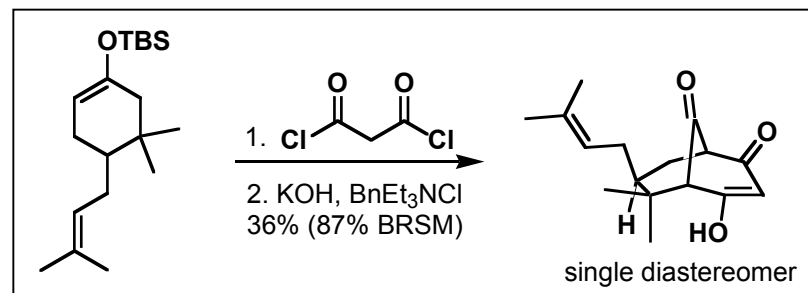
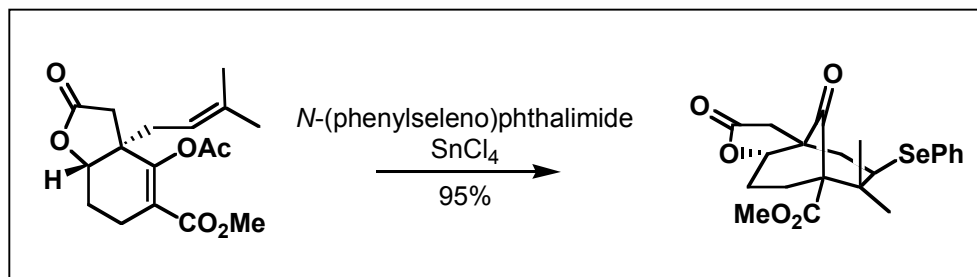
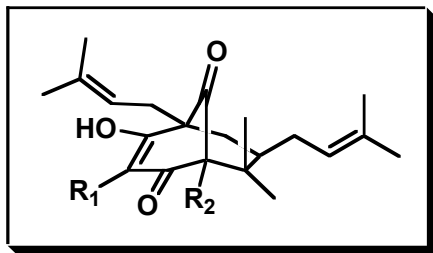
Grubbs' 2nd gen.,
2-methylpropene
CH₂Cl₂, 40 °C, 91%



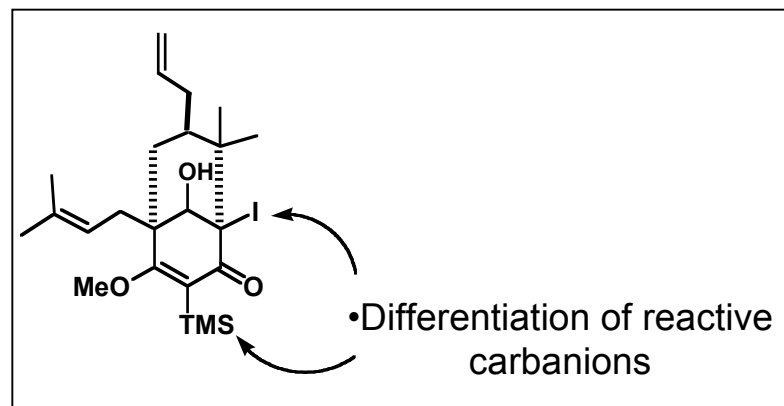
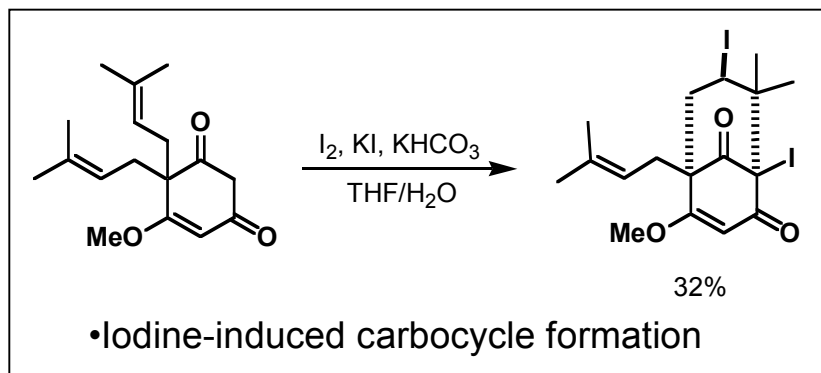
Completion of Clusianone



Summary and Conclusions



•Bicyclo[3.3.1] ring systems can be constructed rapidly from relatively simple structures



••Concise syntheses of nemorosone, clusianone, and related natural products offer good starting points for potential structure-activity profiling