FINKELSTEIN REACTION

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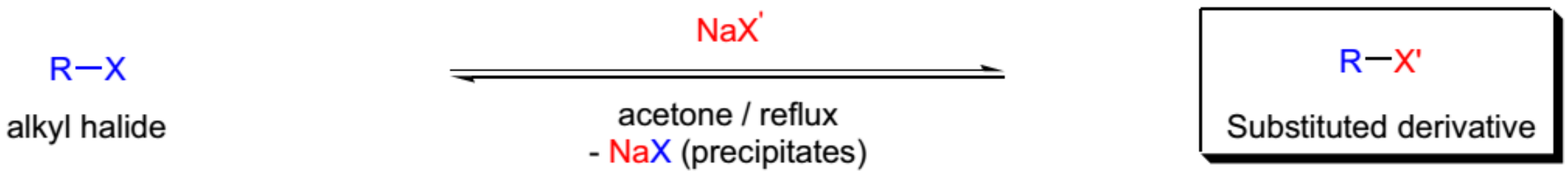
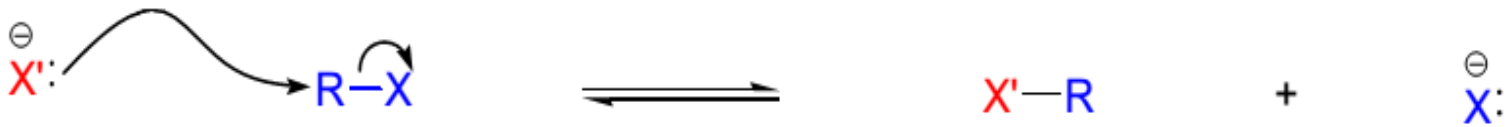
20150512

一、What is Finkelstein reaction

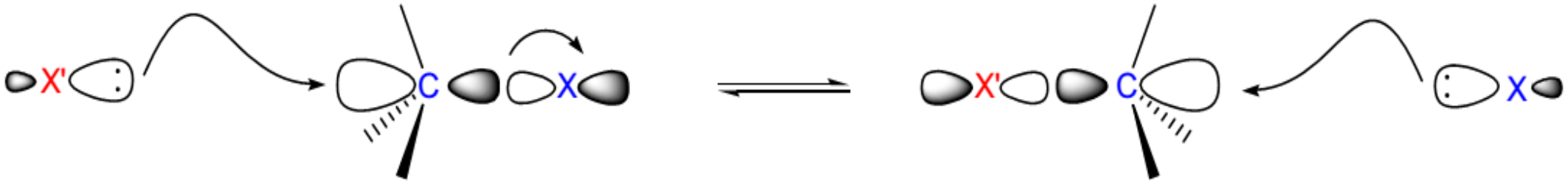


X = Cl, Br, OMs, OTs; R = 1° and 2°alkyl, allyl, benzyl; when X = Cl then X' = Br or I; when X = Br then X' = I

三、 Mechanism of Finkelstein reaction



Description of the process with molecular orbitals:

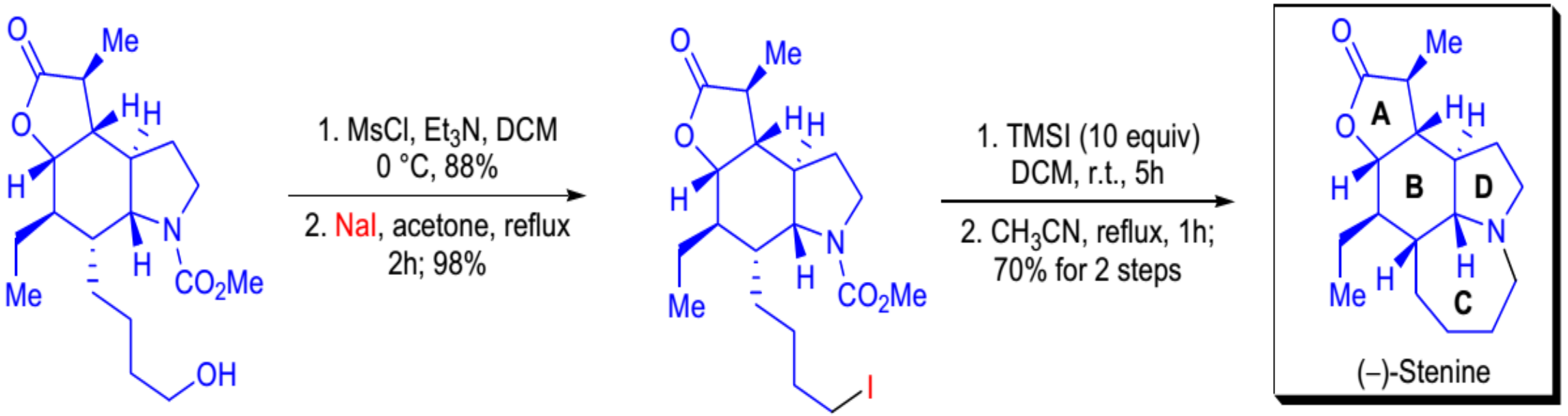


σ* orbital of R-X σ* orbital of R-X'

The driving force for the reaction is the removal of one of the nucleophiles from the equilibrium as an insoluble salt.

三、Synthetic applications(1)

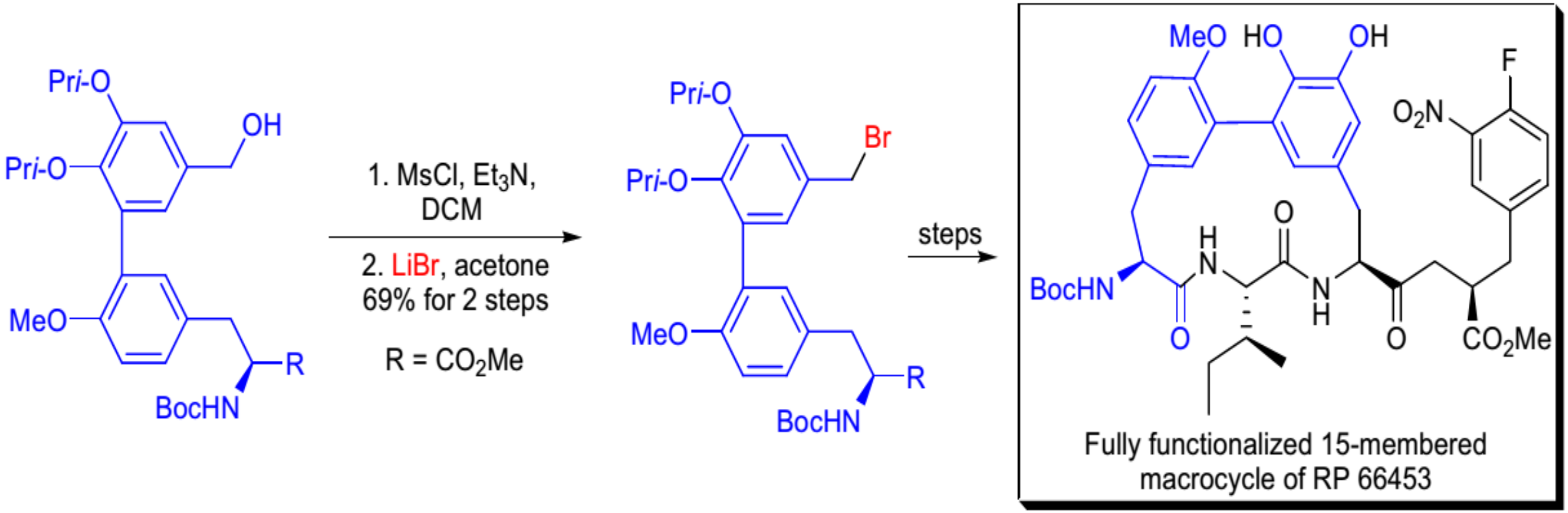
During the endgame of the total synthesis of the stemona alkaloid (–)-stenine, Y. Morimoto and co-workers utilized the *Finkelstein reaction* to prepare a primary alkyl iodide from a primary alkyl mesylate.[28] The mesylate was prepared from the corresponding primary alcohol with $MsCl/Et_3N$. The resulting primary alkyl iodide was used in the subsequent *intramolecular N-alkylation* to construct the final perhydroazepine C-ring of the natural product.



stemona alkaloid：百部生物碱，具有治疗咳嗽、抵抗病原微生物等功效。

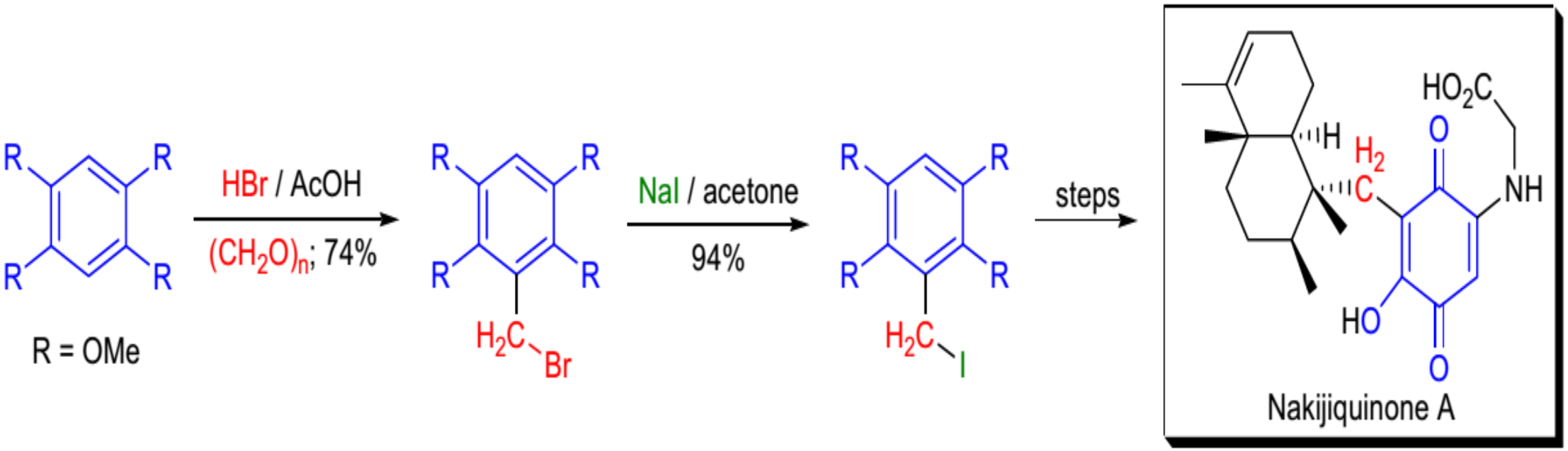
Synthetic applications(2)

In the laboratory of J. Zhu, the synthesis of the fully functionalized 15-membered biaryl-containing macrocycle of RP 66453 was accomplished.[29] One of the key steps in their approach was *Corey's enantioselective alkylation of a glycine template* with a structurally complex biaryl benzyl bromide. This benzyl bromide was prepared from the corresponding benzyl mesylate *via* the *Finkelstein reaction* using lithium bromide in acetone.



Synthetic applications(3)

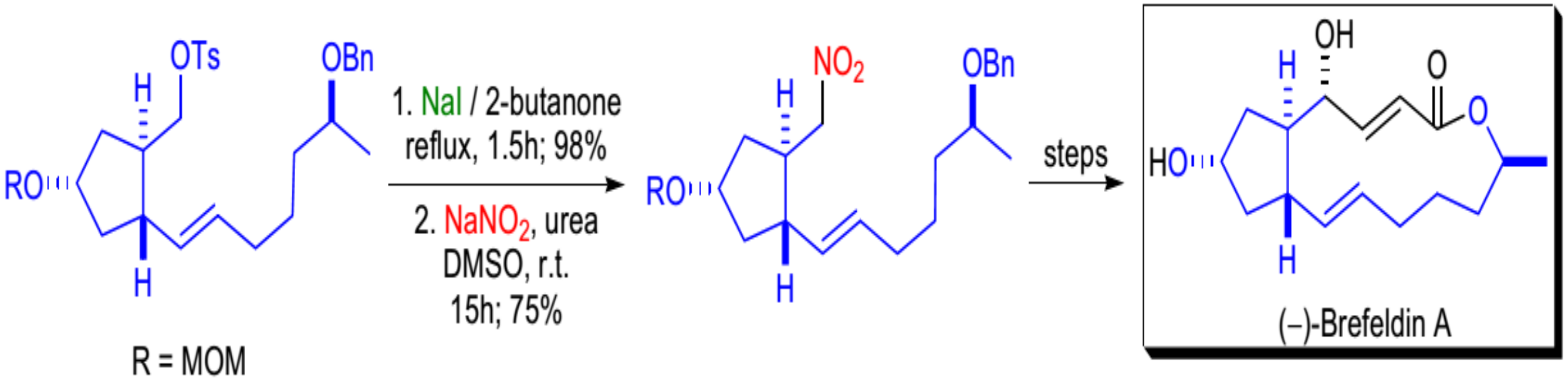
The marine sesquiterpene nakijiquinones were synthesized and biologically evaluated by H. Waldmann et al.[30] The core structure of the natural product was assembled *via* a *reductive alkylation* of a bicyclic enone with tetramethoxybenzyl iodide. This aryl iodide was obtained in a two-step procedure: treatment of the corresponding 1,2,4,5-tetramethoxybenzene with HBr/paraformaldehyde/AcOH followed by the *Finkelstein reaction* to replace the bromide with iodide.



sesquiterpene 倍半萜烯，多用作香料

Synthetic applications(4)

The key step in D. Kim's total synthesis of (–)-brefeldin A was an *intramolecular nitrile-oxide cycloaddition*.[31] In order to prepare the substrate for this cycloaddition, a *double Finkelstein reaction* was performed; first an alkyl tosylate was replaced with iodide; then the iodide was exchanged with a nitrite ion to afford the desired alkyl nitro compound.



(–)-brefeldin A:布雷菲德菌素A,具有抗真菌、抗病毒、抗有丝分裂、抗肿瘤等生物学活性。