

SYNLETT Spotlight 343

Danishefsky's Diene

Compiled by Vijay Kumar Das

Vijay Kumar Das was born in 1984 in Nagaon, Assam, India. He received his B.Sc. degree in chemistry from the Gauhati University, India in 2005, and his M.Sc. degree in Applied Chemistry from the Tezpur University, India in 2008. Currently, he is working towards his Ph.D. degree under the supervision of Dr. A. J. Thakur, Associate Professor, at the same university. His current research interests focus on the application of nanoparticles in organic synthesis.

Department of Chemical Sciences, Tezpur University, Napaam, Tezpur 784028, Assam, India
E-mail: vijay@tezu.ernet.in

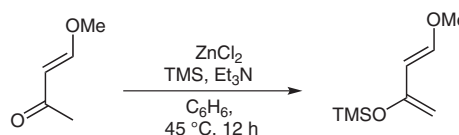


This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Introduction

The Danishefsky's diene, *trans*-1-methoxy-3-trimethylsilyloxy-1,3-butadiene (also known as Kitahara diene), was first introduced by Danishefsky and Kitahara in 1974.¹ Since the diene is very electron-rich it is used as a very reactive reagent in Diels–Alder reactions. The methoxy group accounts for the regioselectivity observed in the Diels–Alder reaction, since the electrophilic carbon to which it is attached will react preferentially with the most nucleophilic atom of the dienophile. The electron-donating nature of this diene confers high reactivity and orientational specificity in its reaction with unsymmetrical dienophiles.

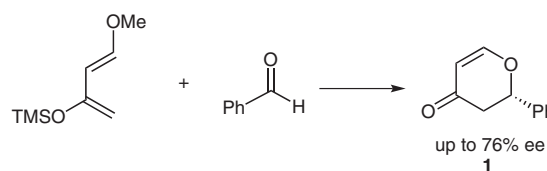
The high reactivity coupled with the easy availability makes 1-methoxy-3-trimethylsilyloxy-1,3-butadiene a potentially very important reagent in organic synthesis. Its first synthesis was reported by Danishefsky and Kitahara starting from 4-methoxy-3-buten-2-one in the presence of trimethylsilyl chloride and zinc chloride (Scheme 1).²



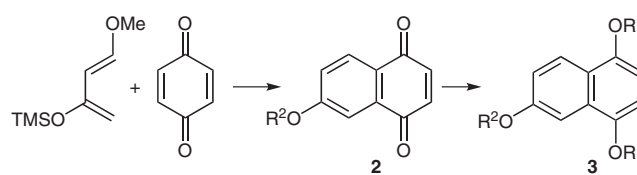
Scheme 1

Abstracts

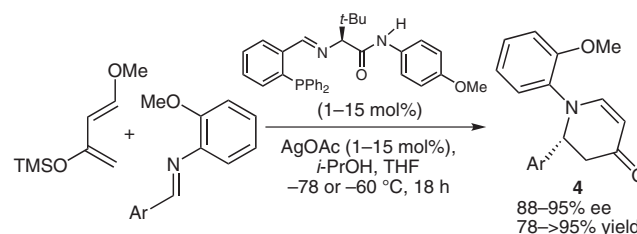
(A) The enantioselective hetero-Diels–Alder reaction of Danishefsky's diene with benzaldehyde has been achieved both experimentally and theoretically, incorporating a series of $\alpha,\alpha,\alpha',\alpha'$ -tetraaryl-1,3-dioxolane-4,5-dimethanol (TADDOL) derivatives as catalysts, affording 2-phenyl-2,3-dihydro-4*H*-pyran-4-one (**1**).³



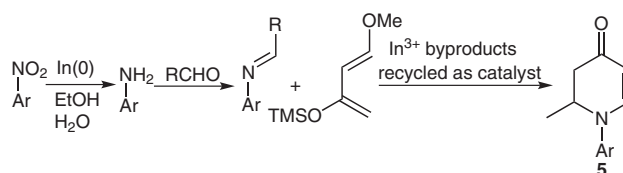
(B) After acetylation, condensation between Danishefsky's diene and benzoquinone afforded a stable methoxytriacetoxydihronaphthalene intermediate **2**, which was subsequently transformed into the regioselective 7-naphthylboronic acid **3** by the Snieckus DOM protocol.⁴



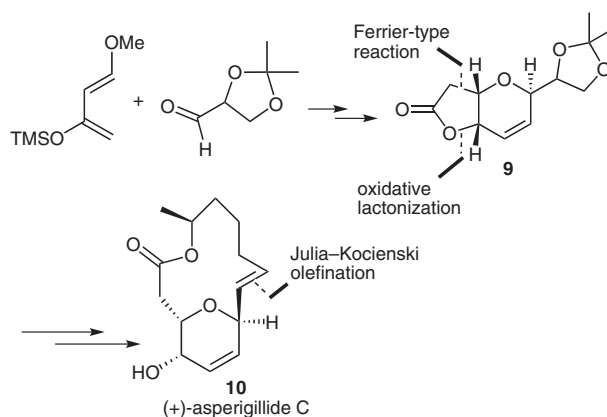
(C) Mandai and co-workers delineated the reaction of Danishefsky's diene with aryl/alkyl-substituted aldimine catalyzed by silver in the presence of a ligand leading to the formation of pyridinone **4**.⁵



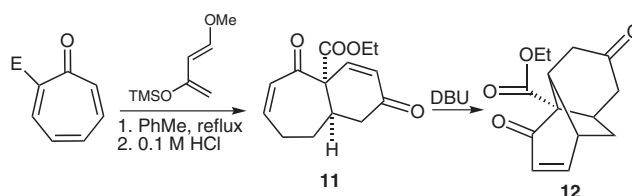
(D) Alaimo and co-workers have designed domino reactions where the nitroarene reduction by indium(0) generates an amine to which addition of an aldehyde followed by Danishefsky's diene provides access to dihydropyridin-4-ones **5**. The yields are comparable or superior to the reported stepwise reactions.⁶



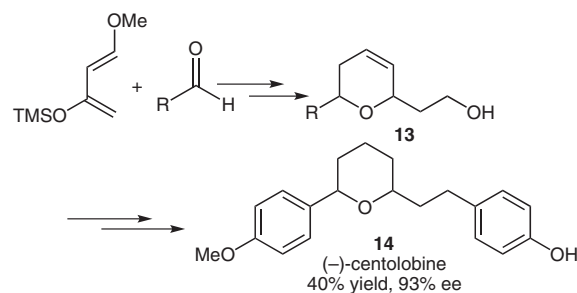
(E) The hetero-Diels–Alder reaction between glyceraldehyde acetonide and the Danishefsky's diene formed one of the key steps in the enantioselective formal total synthesis of the cytotoxic macrolide (+)-aspergillide C (**10**).⁷



(F) Tropones reacting with Danishefsky's diene served one of the important steps in a multistep synthesis of polycyclic compounds **12**.⁸



(G) Chaładaj et al. presented a simple and efficient synthetic route to chiral *cis*-6-substituted 2-(2-hydroxyethyl)-5,6-dihydro-2*H*-pyrans, a versatile chiral building block, by performing three key transformations: enantioselective hetero-Diels–Alder reaction of an aldehyde with Danishefsky's diene, selective reduction of the carbonyl function, and Claisen or related rearrangement. The synthetic utility of this methodology was illustrated by the total synthesis of antibiotic (–)-centolobine **14**.⁹



References

- (1) Danishefsky, S.; Kitahara, T. *J. Am. Chem. Soc.* **1974**, *96*, 7807.
- (2) (a) Danishefsky, S.; Kitahara, T.; Schuda, P. F. *Org. Synth., Coll. Vol.* **1990**, *7*, 312. (b) Danishefsky, S.; Kitahara, T.; Schuda, P. F. *Org. Synth., Coll. Vol.* **1983**, *61*, 147.
- (3) Zhang, X.; Du, H.; Wang, Z.; Wu, Y. D.; Ding, K. *J. Org. Chem.* **2006**, *71*, 2862.
- (4) Ameer, F.; Green, I. R.; Krohn, K.; Sitoza, M. *Synth. Commun.* **2007**, *37*, 3041.
- (5) Mandai, H.; Mandai, K.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2008**, *130*, 17961.
- (6) Alaimo, P. J.; Brien, R.; Johnson, A. W.; Slauson, S. R.; Brien, J. M.; Tyson, E. L.; Marshall, A. L.; Ottinger, C. E.; Chacon, J. G.; Wallace, L.; Paulino, C. Y.; Connell, S. *Org. Lett.* **2008**, *10*, 5111.
- (7) Panarese, J. D.; Waters, S. P. *Org. Lett.* **2009**, *11*, 5086.
- (8) Yeo, J. E.; Bae, S. H.; Do, Y. S.; Sun, R.; Kim, H. J.; Koo, S. *J. Org. Chem.* **2009**, *74*, 917.
- (9) Chaładaj, W.; Kowalczyk, R.; Jurczak, J. *J. Org. Chem.* **2010**, *75*, 1740.