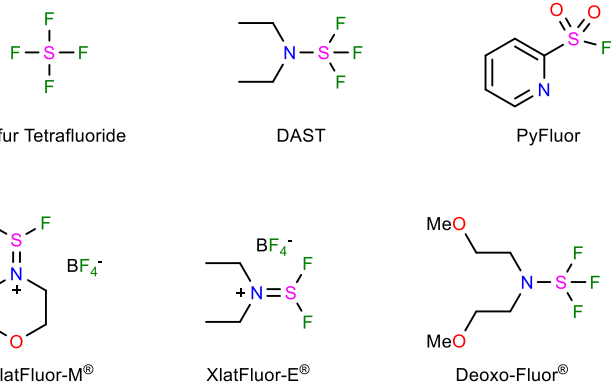
(Diethylamino)sulfur trifluoride (DAST)

Introduction

- DAST offers an easy-to-handle deoxyfluorination reagent compared to SF_4
- DAST is an amber yellow oil, while safer than SF_4 if heated to temperatures above 90 °C it violently decomposes.
- While DAST is widely used there are alternatives that a safer such as Deoxy-Fluor®, XtalFluor-M®, XtalFluor-E®, and PyFluor
- Should be thought of as a nucleophilic source of fluorine in comparison to Selectfluor™ which is an electrophilic source of fluorine



Middleton, W. *J. Org. Chem.* **1975**, 40, 574-578. https://doi.org/10.1021/jo00893a007
Middleton, W. *J. Fluor. Chem.* **1989**, 42, 137-143. https://doi.org/10.1016/S0022-1139(00)83974-3
Bilska-Markowska, M. *Eur. J. Org. Chem.* **2021**, 41, 5585-5604. https://doi.org/10.1002/ejoc.202101027

Deoxyfluorination Original Report

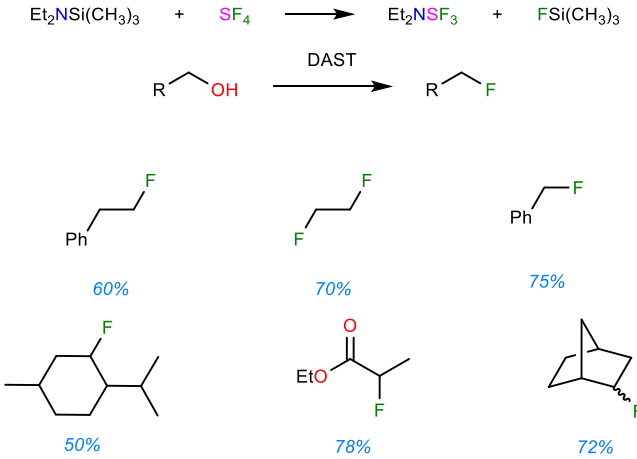
- DAST first reported in 1975 by Middleton while he was a research chemist at DuPont.
- Graduate student at UIUC, under Nelson Leonard
- "…when I was taking my prelimary exams... I had no idea what Teflon® was."
- By 1989 his original paper had over 100 citations, which demonstrates how powerful of a reagent DAST is.

New Fluorinating Reagents. Dialkylaminosulfur Fluorides[1]

William J. Middleton

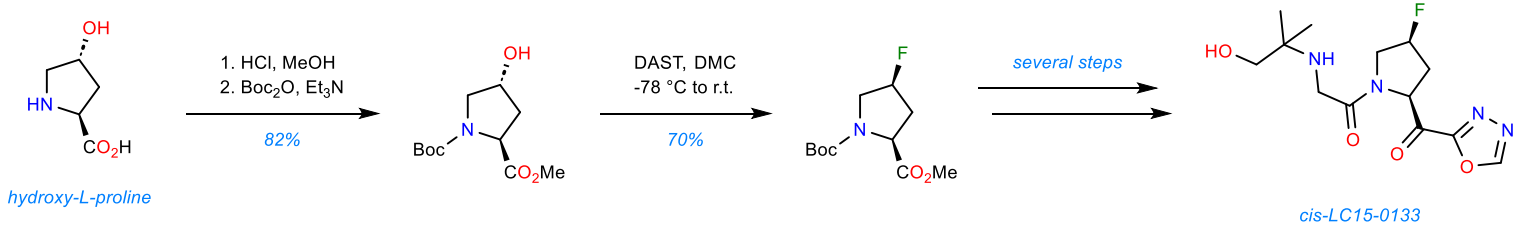
Central Research Department, E. I. du Pont de Nemours and Company, Experimental Station, Wilmington, Delaware 19898

Received September 23, 1974



Middleton, W. *Fluor. Chem.* **1999**, 1-2, 207-216. https://doi.org/10.1016/S0022-1139(99)00128-1
Middleton, W. *J. Org. Chem.* **1975**, 40, 574-578. https://doi.org/10.1021/jo00893a007

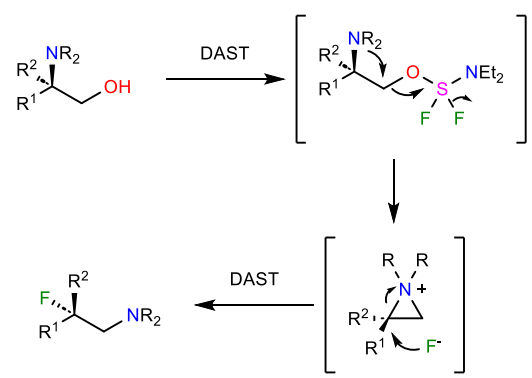
Example

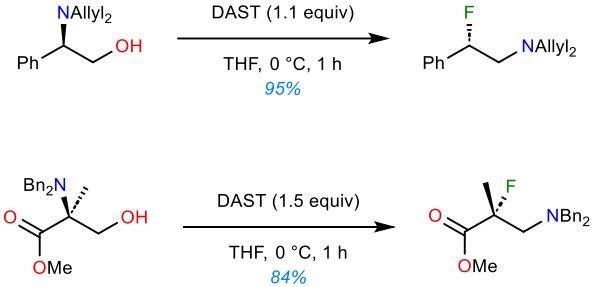


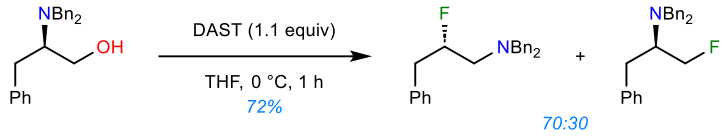
Shin, H. *Org. Process. Res. Dev.* **2008**, 12, 628-631. https://doi.org/10.1021/op800076r

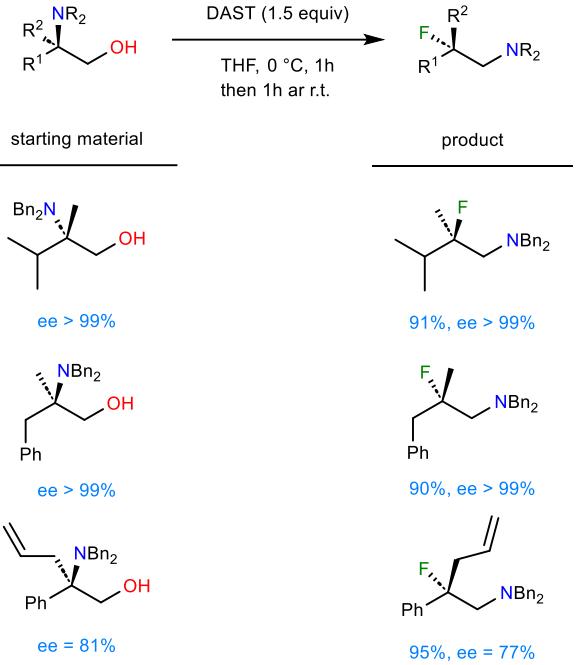
(Diethylamino)sulfur trifluoride (DAST)

β-Fluoroamines



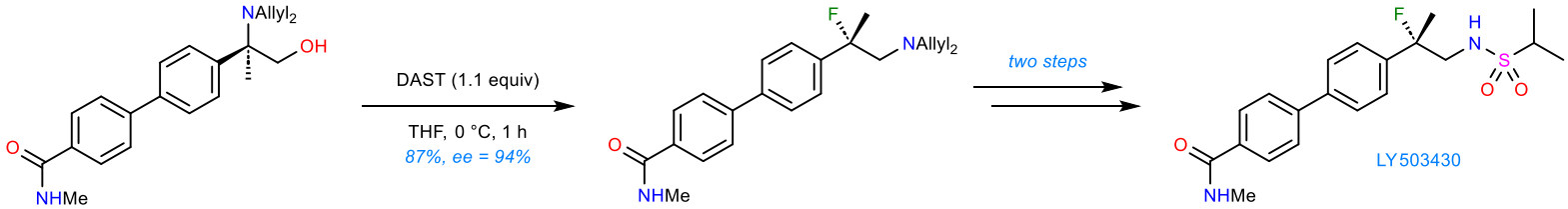




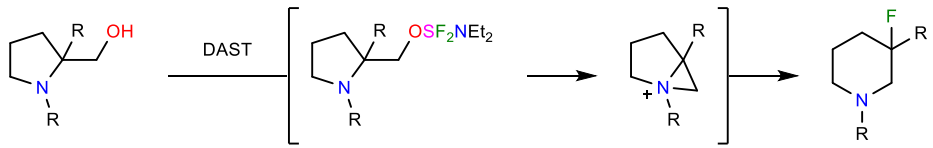


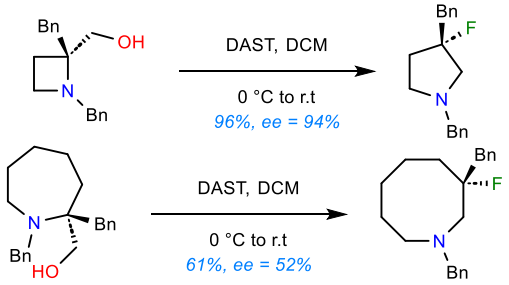
Cossy, J. *Org. Lett.* **2010**, 12, 4620-4623. https://doi.org/10.1021/ol1019579

Example



Ring Expansion



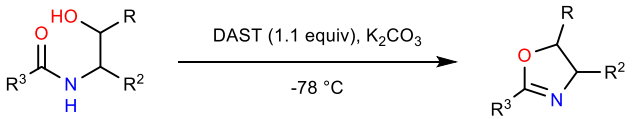


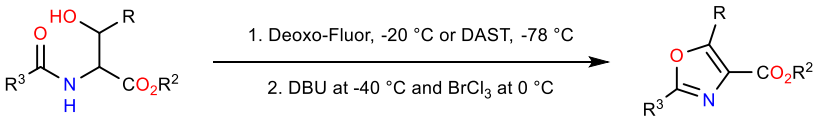
- n=4-7 demonstrated
- *ee* erodes for larger ring sizes

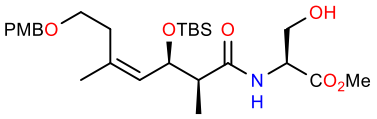
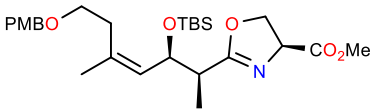
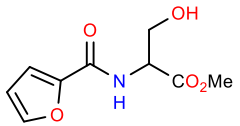
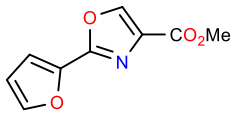
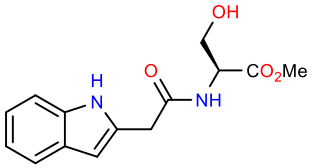
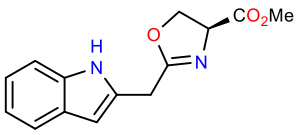
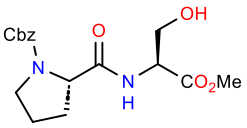
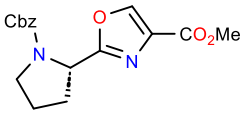
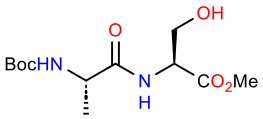
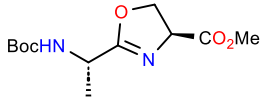
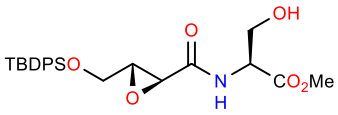
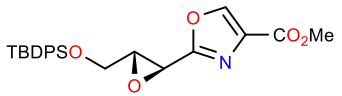
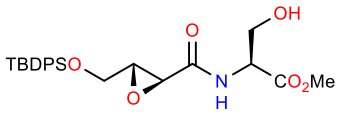
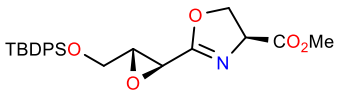
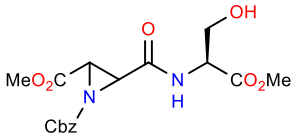
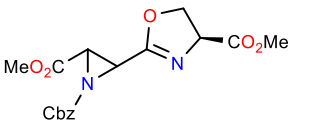
Cossy, J. *Org. Lett.* **2012**, 77, 6087-6099 https://doi.org/10.1021/jo300887u

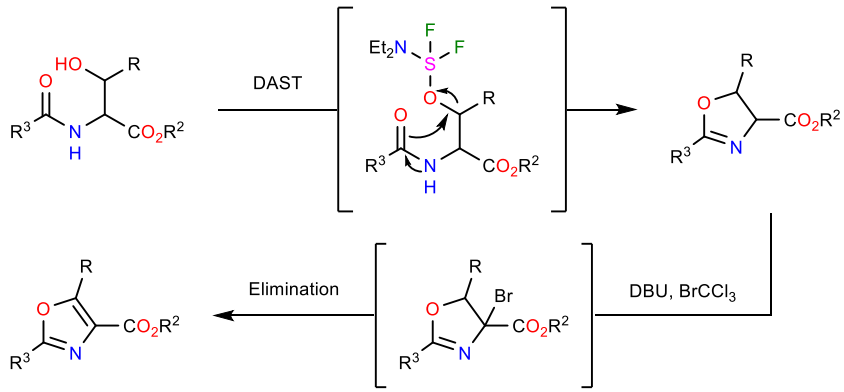
(Diethylamino)sulfur trifluoride (DAST)

Heterocycle Synthesis





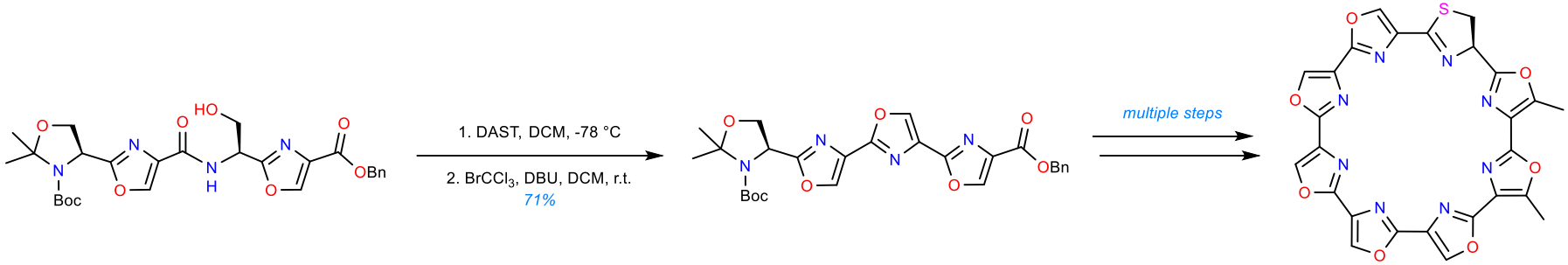
starting material	product		starting material	product	
		80%			67%
		88%			65%
		71%			54%
		73%			
		90%			



Wipf, P. *Org. Lett.* **2000**, 2, 1165-1168. https://doi.org/10.1021/ol005777b

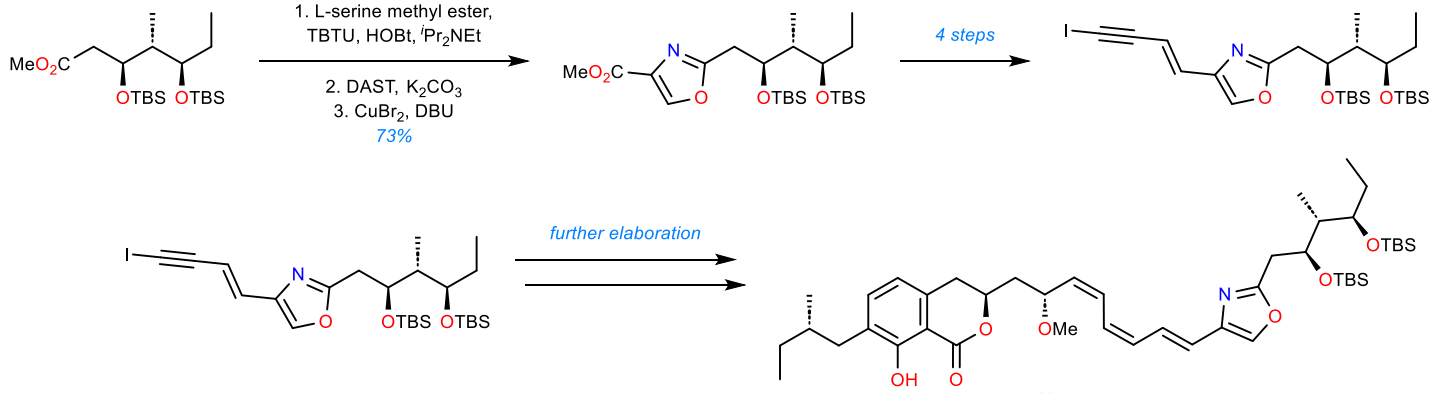
(Diethylamino)sulfur trifluoride (DAST)

Examples in Total Synthesis



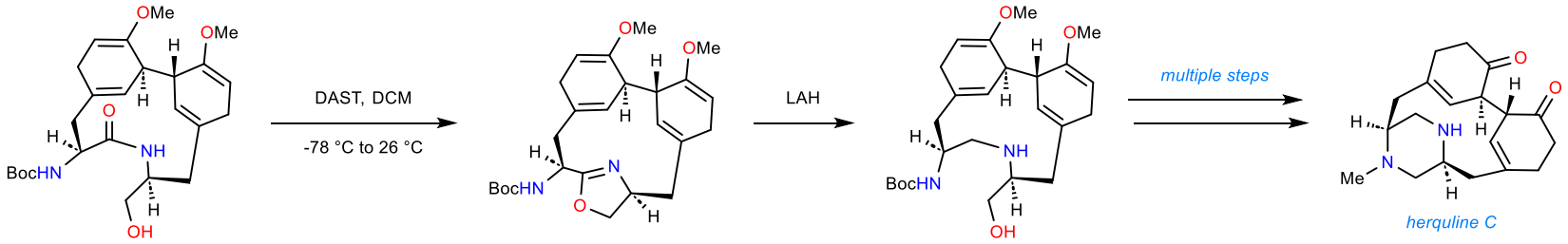
Takahashi, T. *Org. Lett.* **2006**, 8, 4165-4167. https://doi.org/10.1021/ol061793i

(R)-telomestatin



Rizzacasa, M. *Org. Lett.* **2024**, 26, 1062-1066. https://doi.org/10.1021/acs.orglett.3c04268

(-)-Icumazole A



Wood, J. *J. Am. Chem. Soc.* **2019**, 141, 25-28. https://doi.org/10.1021/jacs.8b10212

herquline C