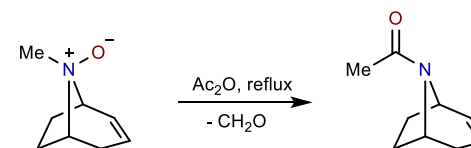


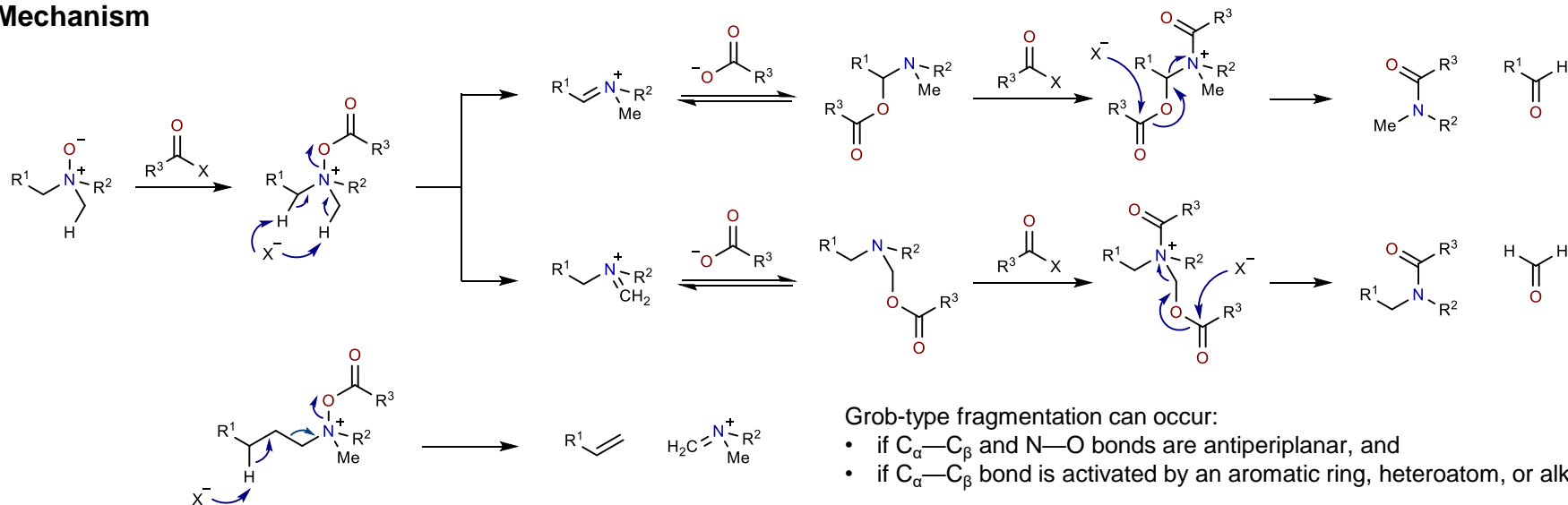
Discovery

- Originally reported in 1927 by Polonovski brothers
- Early uses exclusively for N-demethylation
- Enables a diverse array of fragmentation reactions starting from tertiary amine oxides
- Reaction outcome highly dependent on conditions and substrate



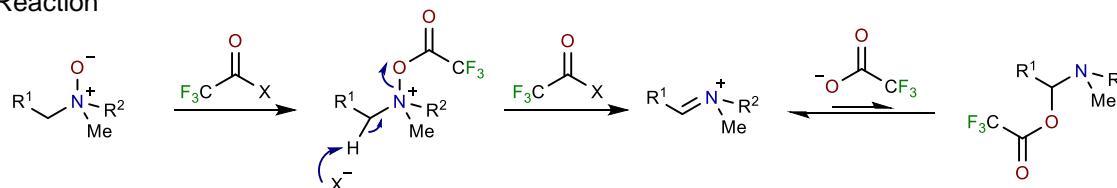
Polonovski, M. *Bull. soc. chim.* **1927**, 1190.

Mechanism



Variants

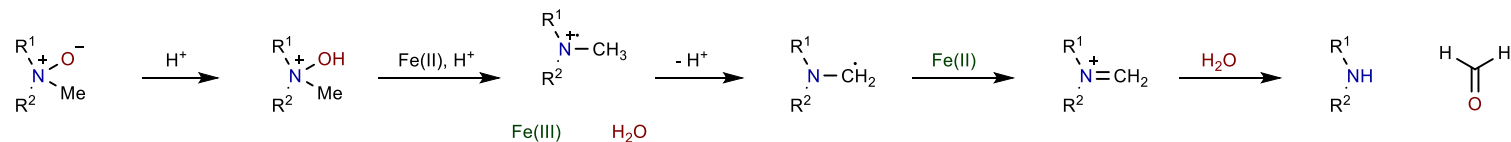
- Polonovski-Potier Reaction



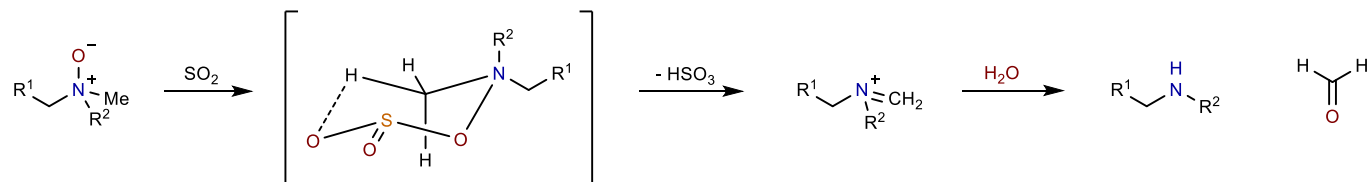
- The use of trifluoroacetic anhydride (TFAA) shifts equilibrium, favors iminium
- Allows trapping of iminium

Grierson, D. *Org. React.* **1990**, 39, 85. <https://doi.org/10.1002/0471264180.or039.02>

- Iron (II) Activation

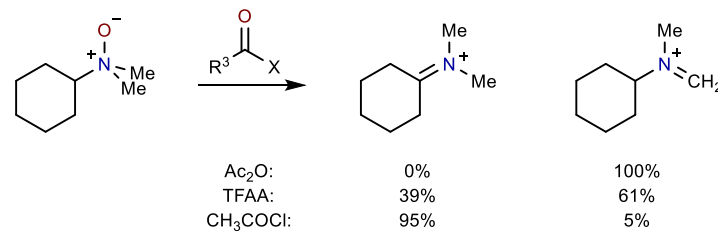


- SO₂ Activation

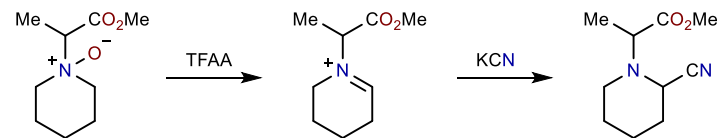


Selectivity

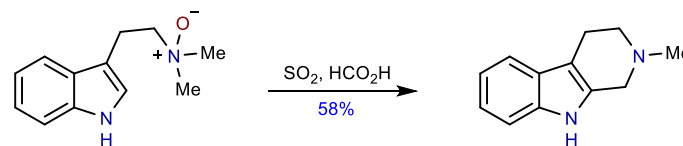
- TFAA** gives more **thermodynamically** stable iminium
- Acetic anhydride** deprotonates the more **kinetically** acidic alpha proton



- Electron withdrawing groups can increase selectivity



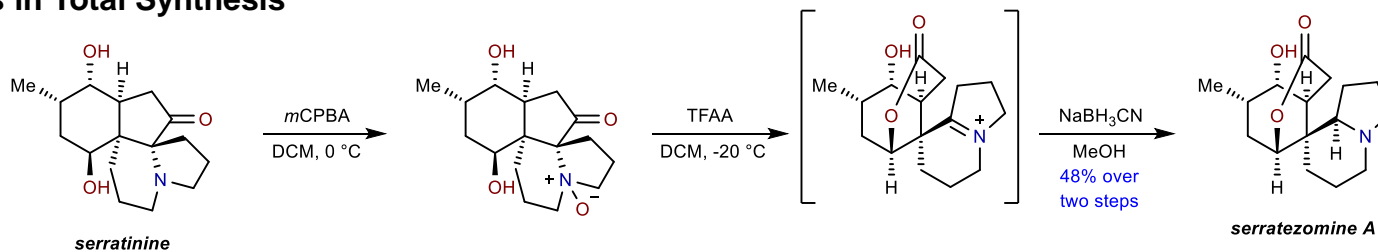
- Endocyclic iminium ions are favored over exocyclic iminiums



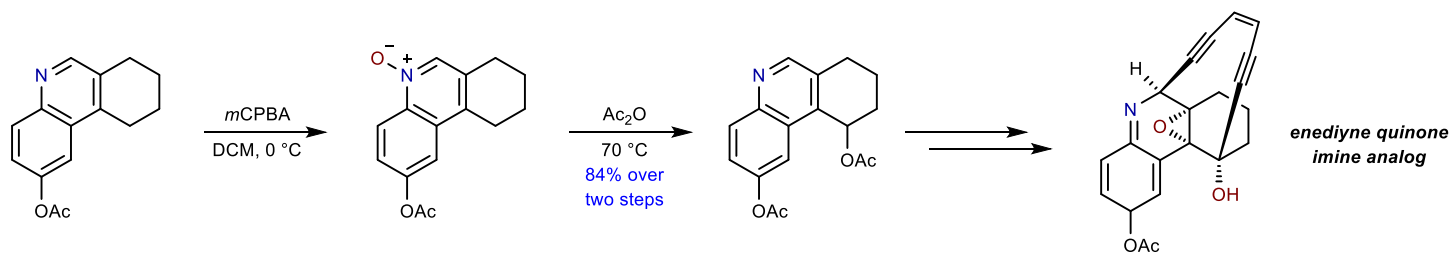
- FeSO₄ and SO₂ are much more sensitive to sterics and are used primarily for demethylation

Grierson, D. *Org. React.* **1990**, 39, 85. <https://doi.org/10.1002/0471264180.or039.02>

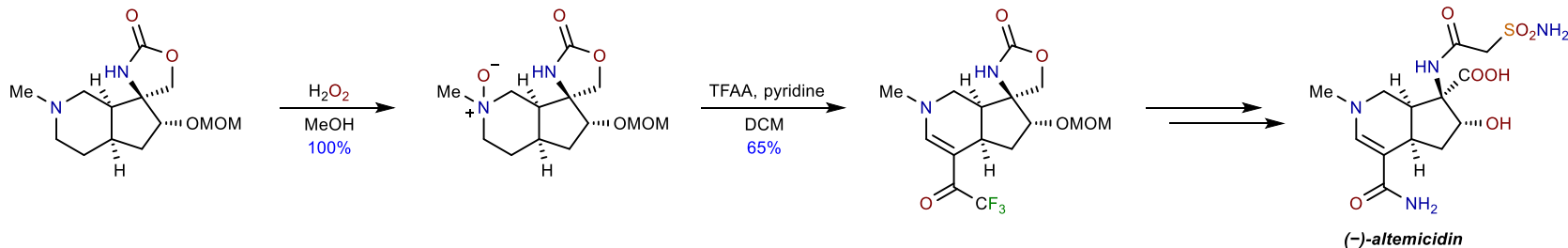
Applications in Total Synthesis



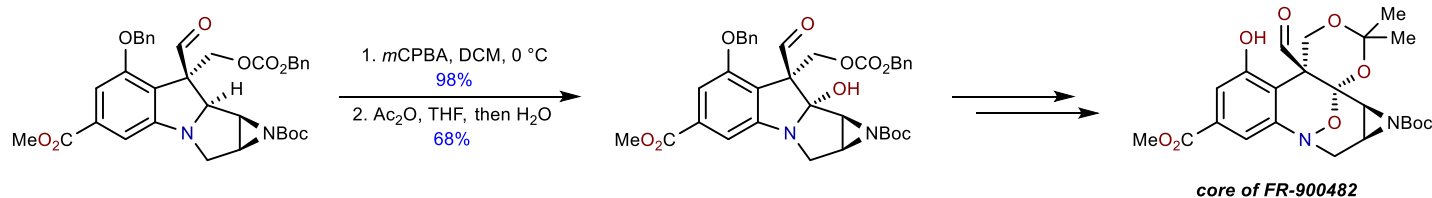
Kobayashi, J. *J. Org. Chem.* **2002**, 67, 5378. <https://doi.org/10.1021/jo025821w>



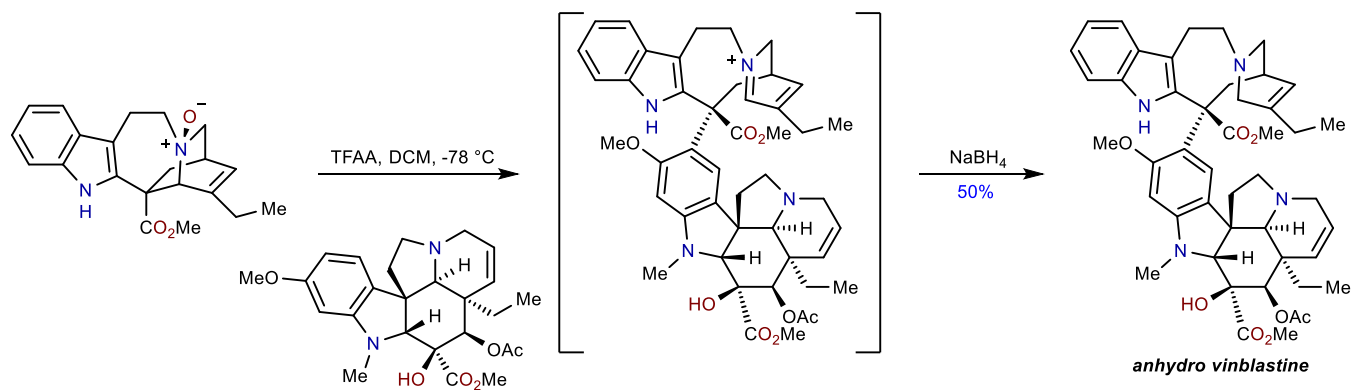
Danishefsky, S. J. *J. Am. Chem. Soc.* **1996**, 118, 9509. <https://doi.org/10.1021/ja960040w>



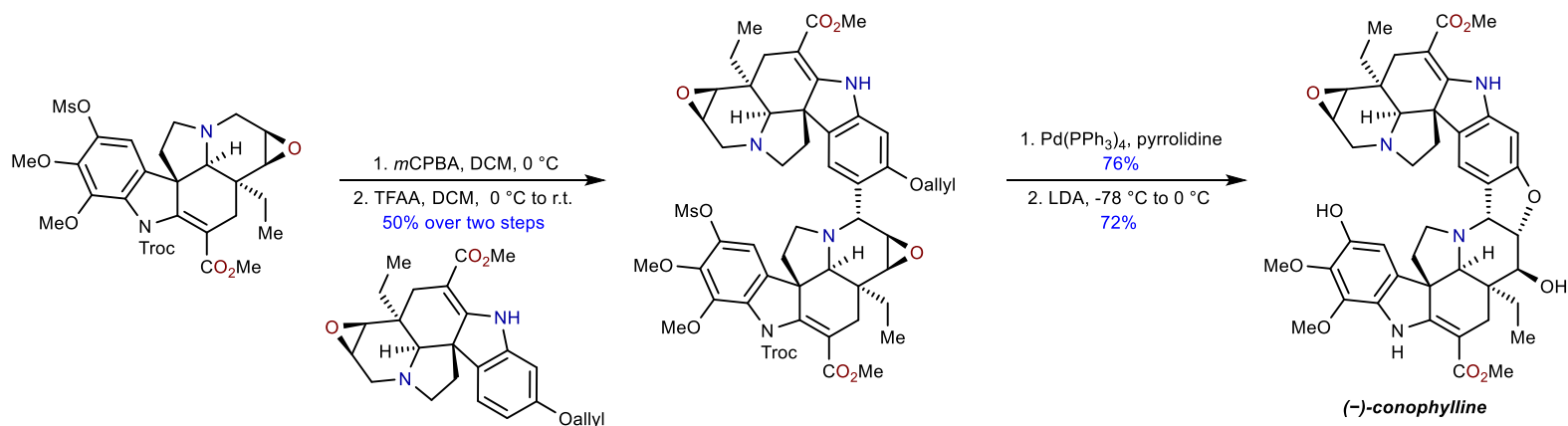
Kende, A. S. *J. Am. Chem. Soc.* **1995**, 117, 10597. <https://doi.org/10.1021/ja00147a032>



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Fukuyama, T. *Angew. Chem. Int. Ed.* **2011**, *50*, 4884. <https://doi.org/10.1002/anie.201100981>