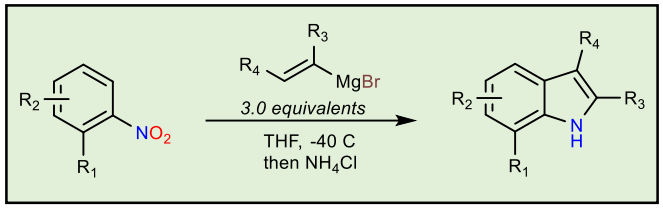
The Bartoli Indole Synthesis

The General Scheme:

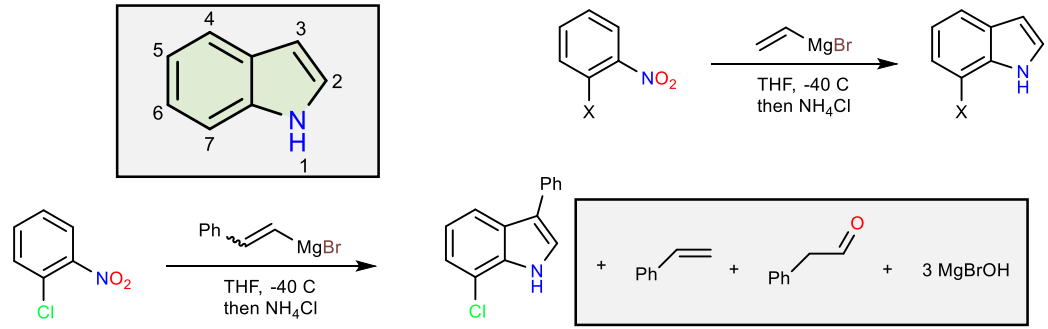


Bartoli, G. *Tetrahedron Lett.* **1989**, *30* (16), 2129–2132. https://doi.org/10.1016/S0040-4039(01)93730-X

Giuseppe Bartoli: *1941-2020*

- Published more than 200 papers in various international journals
- Large contributions to our understanding of organocerium chemistry, Lewis acid catalysis, and most notably providing what is now the most efficient method for the synthesis of 7-substituted indoles.

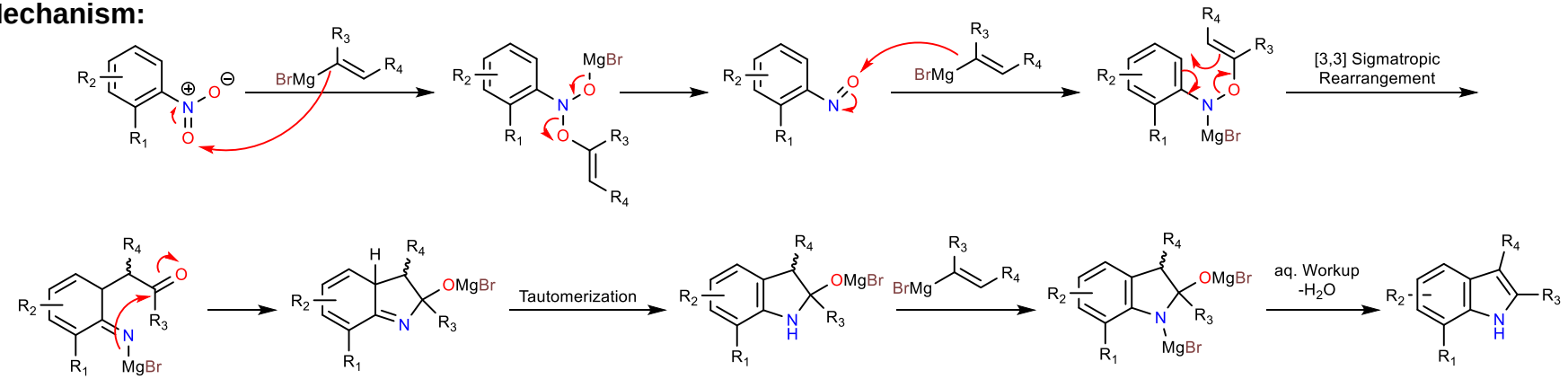
The Discovery:



Bartoli, G. *Tetrahedron Lett.* **1989**, *30* (16), 2129–2132. https://doi.org/10.1016/S0040-4039(01)93730-X

Substrate	Product	Yield (%)
2-Methylnitrobenzene	7-Methylindole	67
2-Bromonitrobenzene	7-Bromoindole	62
2-Chloronitrobenzene	7-Chloroindole	63
2-Trimethylsilyloxynitrobenzene	7-Trimethylsilyloxyindole	41
3-Chloronitrobenzene	4- and 6-Chlroroindole	19
4-Bromonitrobenzene	5-Bromoindole	12
4-Chloronitrobenzene	5-Chloroindole	17
1-Nitronaphthalene	Benzo[g]indole	54
1-nitroacenaphthene	5,6-Dihydroindeno[1,7-fg]indole	59
2-Nitronaphthalene	Benzo[e]indole	17
5-Nitroquinoline	Pyrrolo[2,3-f]quinoline	42

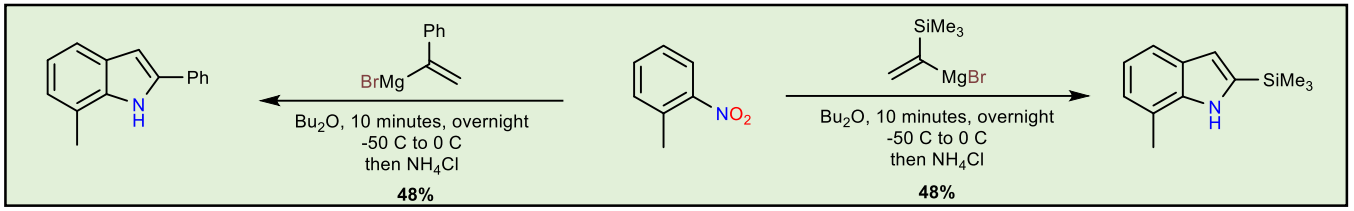
The Mechanism:



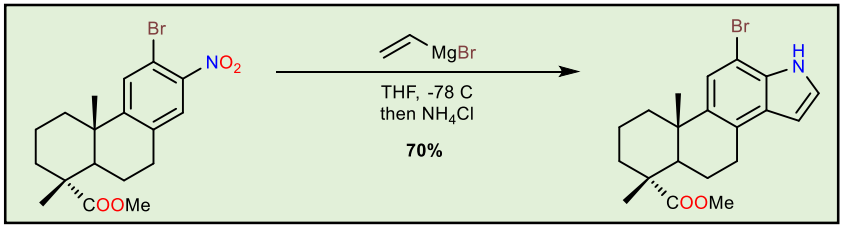
Bosco M, J. Chem. Soc., Perkin Trans. 2, **1991**, *657-663* https://doi.org/10.1039/P29910000657

The Bartoli Indole Synthesis

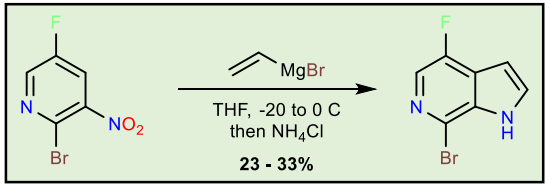
Substrate Scope:



Bartoli, G. J. Chem. Soc., Perkin Trans. 1, ***1991****, 2757-2761* https://doi.org/10.1039/P19910002757



Fonseca, T. Bioorg. Med. Chem., ***2004****, 12, 103–112* http://doi.org/10.1016/j.bmc.2003.10.013



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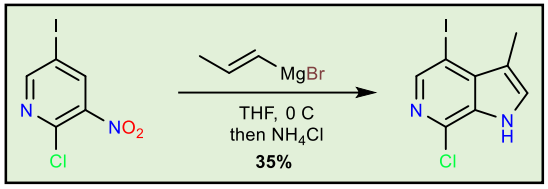
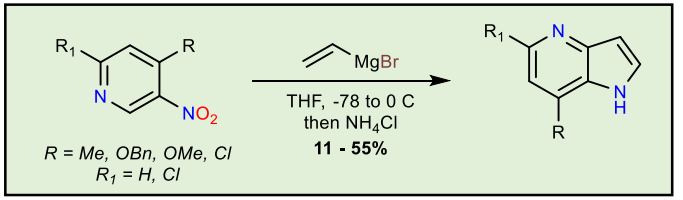


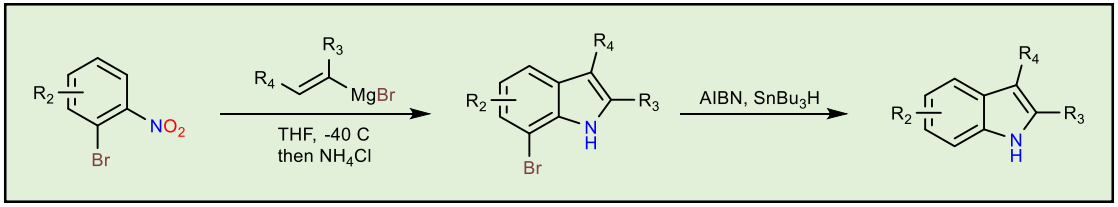
Giblin, A J. Med. Chem., ***2009****, 52, 5785–5788.* https://doi.org/10.1021/jm9009857



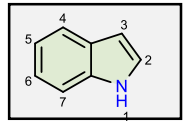
Zhang, X. J. Org. Chem., ***2002****, 67, 2345–2347* https://doi.org/10.1021/jo0111614

Dobbs Modification:

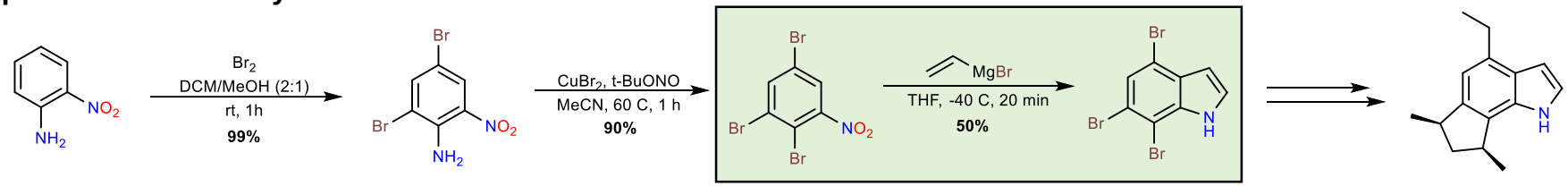
- Allows for the powerful regioselectivity of the Bartoli Indole Synthesis by utilizing Br as an ortho-directing group which can later be cleaved, thus circumventing the need for functionality at position 7.



Dobbs A, J. Org. Chem. ***2001****, 66, 638-641* https://doi.org/10.1021%2Fjo0057396

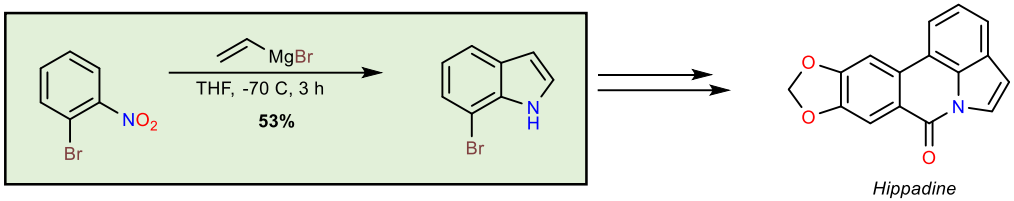


Applications in Total Synthesis:



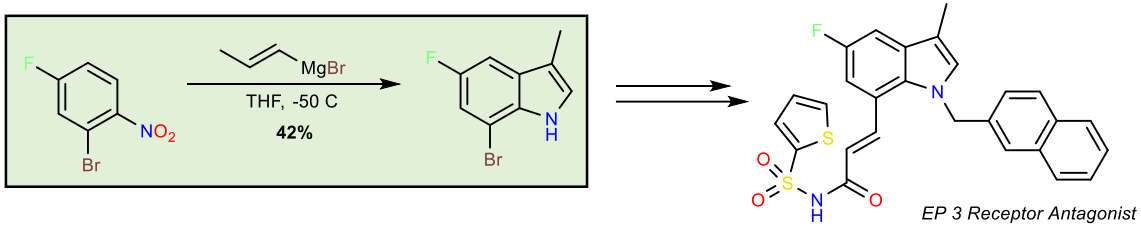
cis-trikentrin A

Brown, N. Tetrahedron Lett. ***2009****, (50) 7113-7115* https://doi.org/10.1016/j.tetlet.2009.09.083



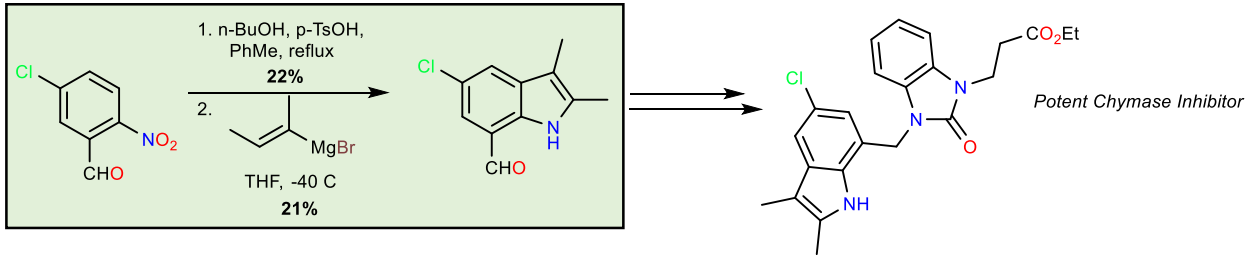
Hippadine

Harrowven D. Synthesis ***1999****, No. 8, 1300–1302* https://doi.org/10.1055/S-1999-3556



EP 3 Receptor Antagonist

Singh, J, J. Med. Chem. ***2010****, 53, 18-36* https://doi.org/10.1021/jm9005912



Potent Chymase Inhibitor

Lo H. Bioorganic & Medicinal Chemistry Letters, ***2011,*** *21 (15), 4533-4539,* https://doi.org/10.1016/j.bmcl.2011.05.126.