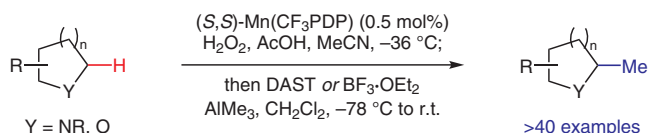
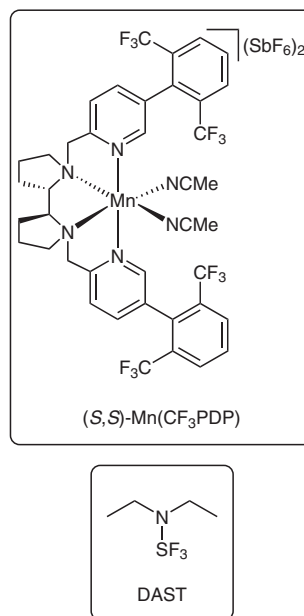
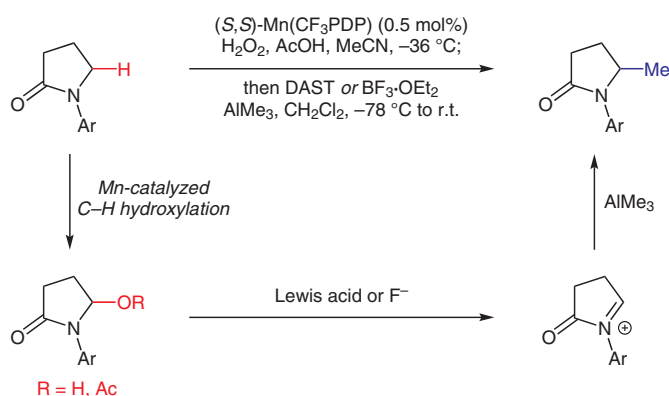


K. FENG, R. E. QUEVEDO, J. T. KOHRT, M. S. ODERINDE, U. REILLY, M. C. WHITE*
(UNIVERSITY OF ILLINOIS, URBANA, USA)
Late-Stage Oxidative C(sp³)-H Methylation
Nature 2020, 580, 621–627.

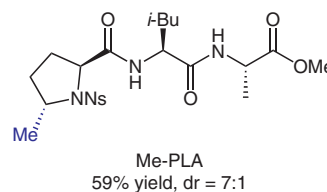
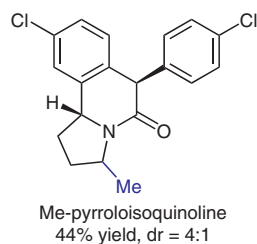
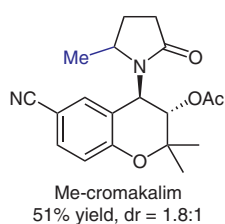
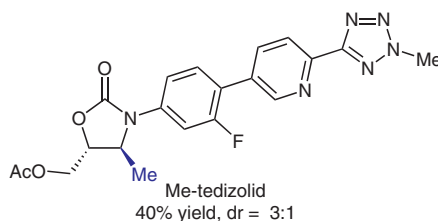
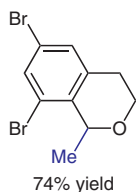
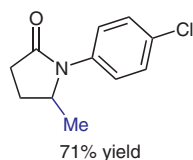
Manganese-Catalyzed Methylation of C(sp³)-H Bonds α to Heteroatoms



Proposed mechanism:



Selected examples:



Significance: White and co-workers report a chemoselective C(sp³)-H methylation of heterocycles by using a three-step protocol. The method was applied to a broad substrate scope, including drug molecules, peptides, and natural products. The ability to introduce a ‘magic methyl’ group in certain pharmacologically relevant compounds has been shown to significantly improve their bioactivity.

Comment: The authors combined a manganese-catalyzed methylene hydroxylation with subsequent iminium/oxonium formation and methylation to achieve the functionalization of various heterocyclic cores α to the heteroatom. The transformation proceeds at low catalyst loading with remarkable chemoselectivity and moderate to good overall yields.

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Synfacts 2020, 16(06), 0663 Published online: 15.05.2020
DOI: 10.1055/s-0040-1707804; Reg-No.: L05620SF