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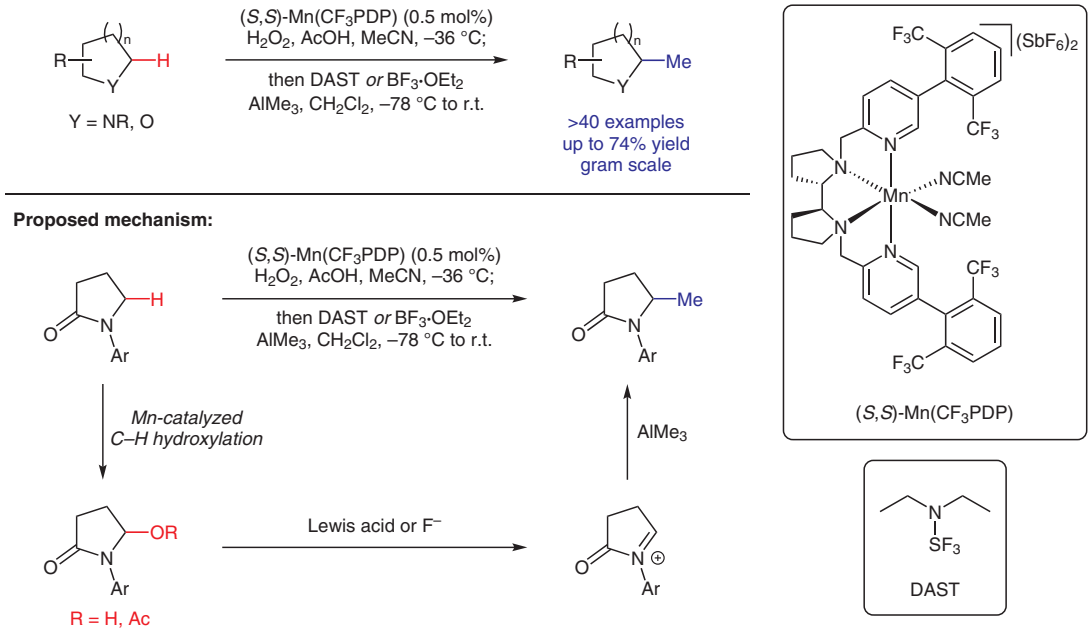
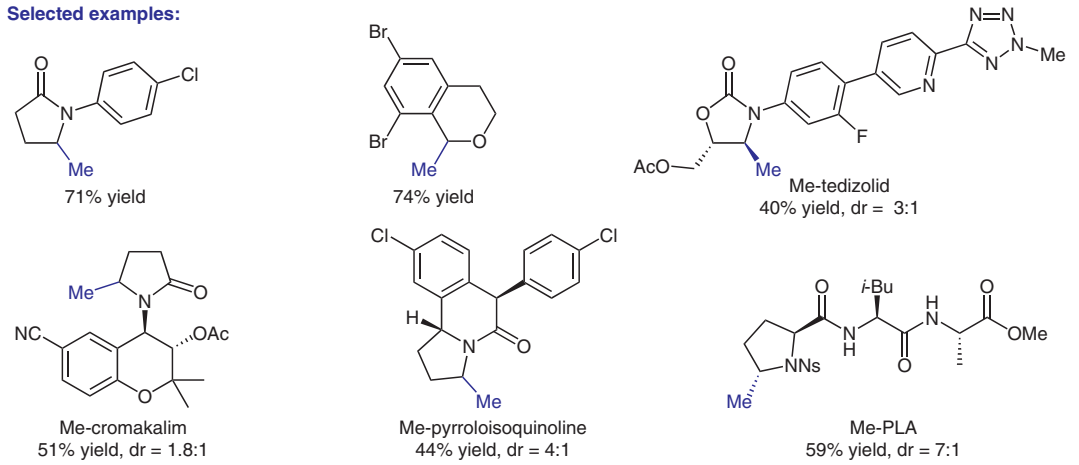
Late-Stage Oxidative C(sp^3)–H Methylation
Nature **2020**, *580*, 621–627.

Manganese-Catalyzed Methylation of C(sp^3)–H Bonds α to Heteroatoms





Significance: White and co-workers report a chemoselective C(sp^3)–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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Category
Metals in Synthesis

Key words
C–H functionalization
methylation
late-stage diversification
manganese catalysis
C–C bond formation

Synfact of the Month

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