



MANGANESE-CATALYZED NUCLEOPHILIC ADDITION OF ALDEHYDES TO CARBONYL COMPOUNDS VIA HYDRAZONE UMPOLUNG ON WATER

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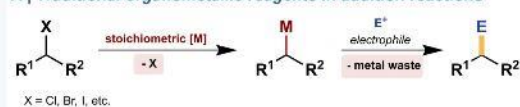
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BACKGROUND

A | Traditional organometallic reagents in addition reactions



B | HOME-chemistry

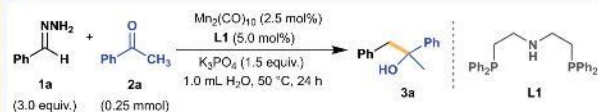


Hydrazones as *OrganoMetallic Equivalents* (HOME-chemistry) still presents **two critical areas of improvement** to showcase its applicability as a greener alternative to classical methods:

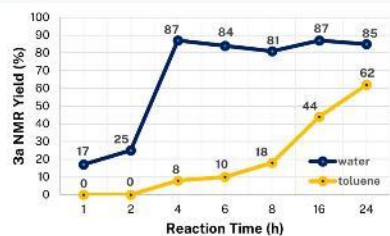
- use non-precious and earth-abundant metals
- develop methods that are operationally simple



REACTION DEVELOPMENT



Entry	Deviation	3a Yield (%)
1	no deviations	84
2	no pre-catalyst	0
3	no ligand	0
4	no pre-catalyst and ligand	0
5	open-air	80
6	1.25 equiv. 1a, 0.2 mL H ₂ O	84
7	3.0 equiv. 1a, neat	82



An increased rate of product **3a** formation was observed when employing on-water versus in toluene.



GREEN METRICS

Comparison of this work (Mn) with other methods for the nucleophilic addition of 1a to 2a via hydrazone umpolung

Benchmark	Ru ^a (ref. 1)	Fe ^b (ref. 2)	Ru ^c (ref. 3)	Mn ^d
earth-abundant metal	X	✓	X	✓
pre-synthesized catalyst	X	✓	X	X
solvent	THF	THF	H ₂ O	H ₂ O / neat
temperature (°C)	45	r.t.	70	50
atmosphere	N ₂	N ₂	Ar	air
additive	CsF	CsF	TBAC	none
yield (%)	94	99	71	84
atom economy (%)	88	88	88	88
reaction mass efficiency (%)	73	80	50	66
process mass efficiency (×10 ³)*	2.8	2.6	4.4	3.4

^a[Ru(*p*-cymene)Cl₂]₂ (0.75 mol%) / dmpe (1.5 mol%)

^b[Ru(*p*-cymene)Cl₂]₂ (1.5 mol%) / PPh₃ (6.0 mol%)

*including purification

^cFe(dmpe)₂Cl₂ (5.0 mol%)

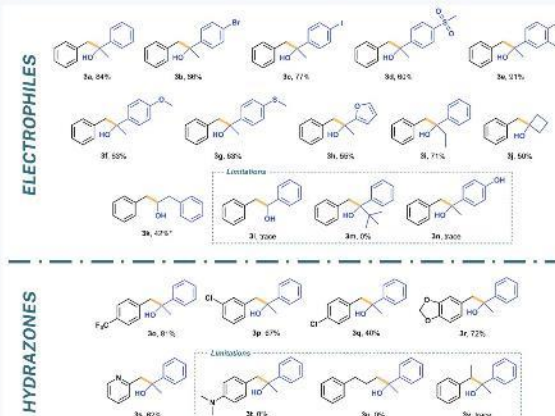
^dMn₂(CO)₁₀ (2.5 mol%) / L1 (5.0 mol%)

Our method (Mn) works:

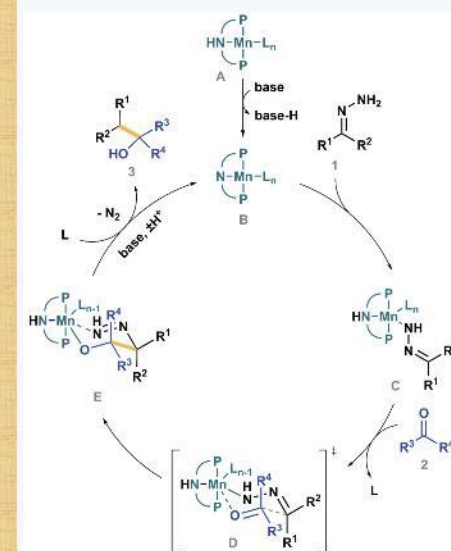
- even under open-air (**operationally simpler**)
- on water or neat (**safer solvent** or even **solventless**)
- even without the use of a phase-transfer catalyst
- with **commercially available** pre-catalyst and ligand



SUBSTRATE SCOPE



PROPOSED MECHANISM



Pre-mixing the ligand, base, & pre-catalyst, is necessary to form the active Mn-amido complex B.

Formation of Zimmerman-Traxler like transition state D.