Catalytic Enantioselective Oxidative Cyclization by Cooperative Catalysis

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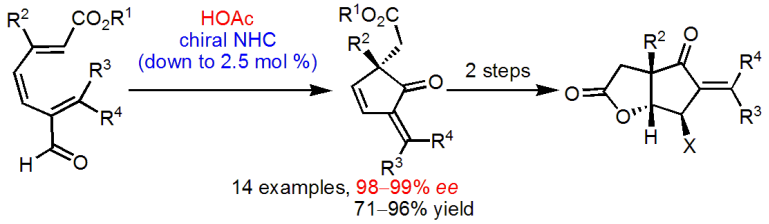
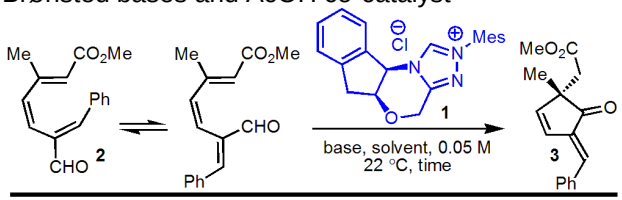


Densely functionalized cyclopentenones are useful synthetic intermediates. We report herein a new method to synthesize this important class of compounds through a highly enantioselective (98–> 99% *ee*) triene cyclization that is co-catalyzed by acetic acid and a chiral NHC. We discovered that not only could acetic acid co-exist with NHCs, but it could also greatly stabilize the active catalyst, which enables a long-lived catalyst with high reactivity and selectivity.

Table 1. Correlation of NHC reactivity with Brønsted bases and AcOH co-catalyst



entry	base (equiv)	solvent	**1** (equiv)	time (h)	yield[a] (%)	final yield[b] (%)	*ee*[c] (%)
1	KHMDS (0.2)	THF	0.2	7	0	16	95
2	KO*t*-Bu (0.2)	THF	0.2	7	<5	17	98
3	DBU (0.2)	THF	0.2	7	0	0	NA
4	(*i*-Pr)$_2$EtN (0.2)	THF	0.2	7	0	0	NA
5	Et$_3$N (0.2)	THF	0.2	7	0	0	NA
6	K$_2$CO$_3$ (0.2)	THF	0.2	7	15	52	95
7	NaOAc (0.2)	THF	0.2	5	85	85	97
8	NaOBz (0.2)	THF	0.2	7	52	83	97
9	NaOAc (0.1)	THF	0.1	7	44	79	97
10	NaOAc (0.5)	THF	0.1	7	62	84	97
11	NaOAc (1.0)	THF	0.1	7	88	88	97
12	NaOAc (1.0)	ether	0.1	2.5	96	96	98
13[d]	NaOAc (0.5)	ether	0.05	4.0	96	96	99
14[d]	NaOAc (0.25)	ether	0.025	7.5	96	96	99

a Yields refer to isolated yields after column chromatography.
b Final yields are obtained after 48 h, when there is no further conversion.

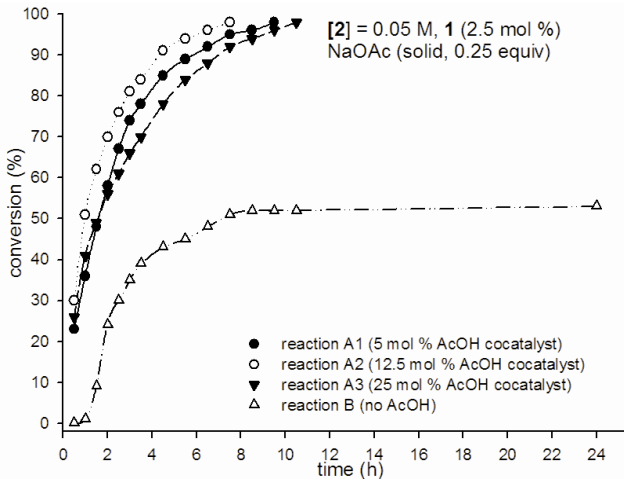
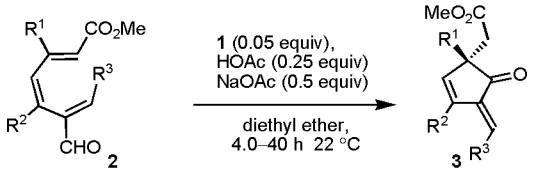


Figure 1. Kinetic studies to reveal the crucial role of AcOH to stabilize the active catalyst.

Table 2. Substrate scope of the cyclization reaction



entry	R^1	R^2	R^3	yield (%)[a]	*ee* of **3** (%)[b]
1	Me	H	Ph	96	99
2	Me	H	*p*-Br-Ph	92	99
3	Me	H	*p*-Cl-Ph	93	98
4	Me	H	*p*-Me-Ph	95	99
5[c]	Me	H	*p*-OMe-Ph	75	99
6	Me	H	*m*-Cl-Ph	94	99
7	Me	H	*O*-CH$_2$-*O*-Ph	87	>99
8	Me	Me	Ph	80	>99
9	Me	Me	*p*-Br-Ph	94	>99
10	Me	Me	*m*-Cl-Ph	94	>99
11[c]	Ph	H	Ph	80	99
12[c]	Ph	H	*p*-Cl-Ph	82	>99
13[c]	Ph	H	*p*-Br-Ph	71	99
14[c]	Ph	H	*m*-Cl-Ph	74	>99

[a]Yields refer to isolated yields after column chromatography.
[b] *ee* was determined by chiral HPLC. [c] 10 mol % of **1** was applied.