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Acceleration of the reduction of aldehydes and ketones using $Mn(dpm)_3$ catalyst and phenylsilane in the presence of dioxygen

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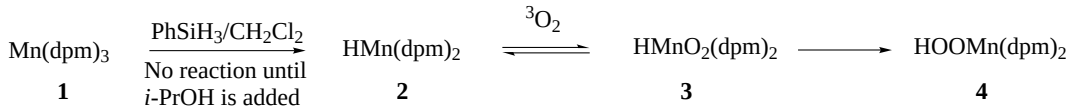
Abstract—Saturated ketones and aldehydes are reduced to alcohols by phenylsilane and $Mn(dpm)_3$(cat) in the presence of dioxygen.

Recently, we reported that tris(dipivaloylmethanato)-manganese(III) **1** (Eq. (1)) [abbreviated to $Mn(dpm)_3$]-(cat), phenylsilane and dioxygen, in 2-propanol at 0°C, converted α,β-unsaturated ketones into α-hydroxy ketones.[1] In the absence of dioxygen, conjugate reduction to the saturated ketone is the major reaction pathway.[2] We observed that **1** reacts with $PhSiH_3$ in the presence of 2-propanol to give a weakly hydridic reducing agent formulated as **2** (or equivalent with $SiPhH_2$ attached to Mn).



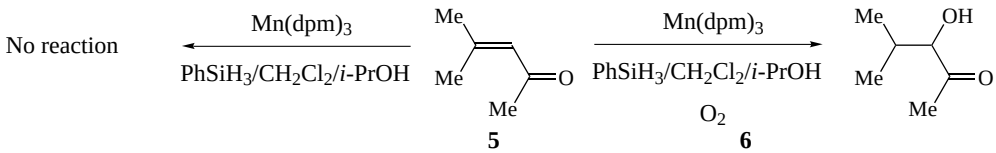
(1)

During the course of this work we observed that in the presence of dioxygen the putative manganese hydride species was more 'hydridic' and was able to conjugatively reduce α,β-unsaturated enones, esters and nitriles that were unreactive when dioxygen was excluded. The uptake of dioxygen that converts **2** into **3** is reversible, and over a period of about 3 h at 25°C **3** is transformed into a non-hydridic species that we suggest is **4**.[3] It was found that **5** was inert to conjugate reduction in the absence of oxygen, whereas in the presence of oxygen, **5** was converted into **6** (Scheme 1).[1]

These observations prompted the interesting notion of whether the hydridic reagent **2** would be unreactive towards saturated carbonyl groups, but when 'activated' by dioxygen (to give **3**) be capable of reducing the carbonyl group to a secondary alcohol.

Treatment of 4-*tert*-butylcyclohexanone (entry 1, Table 1) in 2-propanol/1,2-dichloroethane (DCE) containing $Mn(dpm)_3$ (3 mol%) under an oxygen atmosphere at 25°C with phenylsilane, resulted in rapid (5 min) reduction to the corresponding alcohol as a 14:1 *trans*:*cis* mixture of stereoisomers in 98% yield.[4] Conducting the same procedure, but excluding oxygen, resulted in relatively slow (4 h) conversion into the alcohol (80% conversion, 57% isolated yield).

Table 1 lists a number of substrates that have been exposed to the above reduction conditions. In general entries 2, 3, 4 and 13 show a marked preference for reduction to the more stable equatorial alcohol, in keeping with the Felkin model for cyclic ketones.[5]



Scheme 1.

Keywords: tris(dipivaloylmethanato)manganese(III); dioxygen; hydridic.

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Table 1.

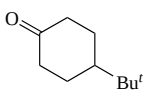
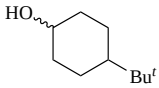
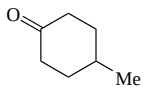
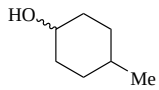
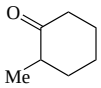
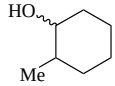
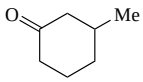
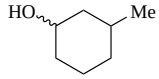
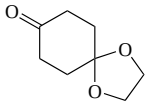
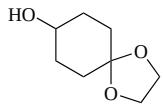
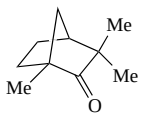
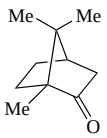
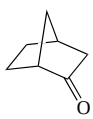
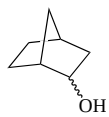
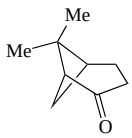
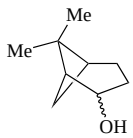
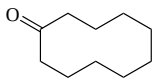
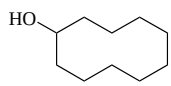
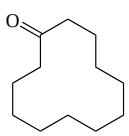
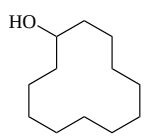
Substrate	Product(s)	Yield (ratio)
1 	 Ref. 7	98% (14:1, *trans*:*cis*)
2 	 Ref. 8	84% (13:1, *trans*:*cis*)
3 	 Ref. 1	87% (2.1:1, *trans*:*cis*)
4 	 Ref. 1	81% (1:9, *trans*:*cis*)
5 		92%
6 		Only trace amounts of reduction was observed by ^{1}H NMR
7 		Only trace amounts of reduction was observed by ^{1}H NMR
8 	 Ref. 9	58% (14:1, *endo*:*exo*) 5% SM
9 	 Ref. 10	53% (1:7, *endo*:*exo*) 31% SM
10 		22%, 75% SM
11 		13%, 85% SM

Table 1. (*Continued*)

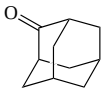
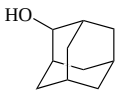
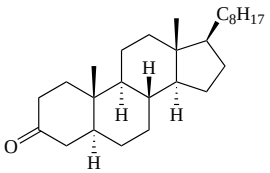
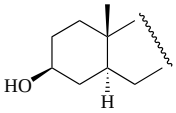
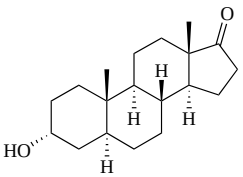
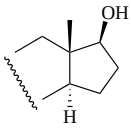
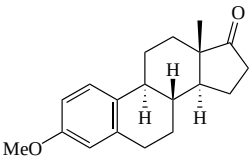
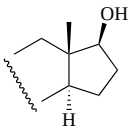
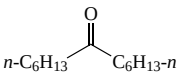
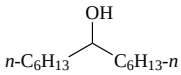
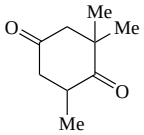
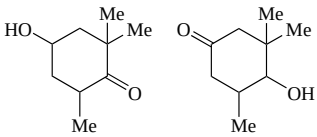
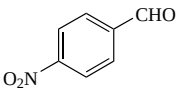
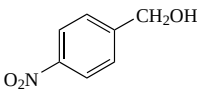
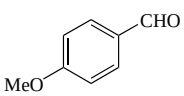
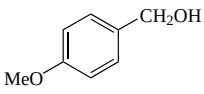
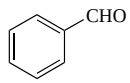
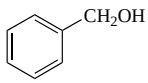
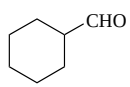
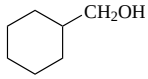
Substrate	Product(s)	Yield (ratio)
12 	 Ref. 11	99%
13 	 Ref. 12	92%, (35:1, 3β:3α)
14 	 Ref. 13	47%, 37% SM, and some *O*-silylated product. (mass balance)
15 	 Ref. 14	61%, 20% SM, and some *O*-silylated product (mass balance)
16 		43%, and some *O*-silylated product (mass balance)
17 	 Ref. 15	85%, both products shown, and diols
18 		24%, by ^{1}H NMR
19 		NR
20 		80%
21 		56%

Table 1. (*Continued*)

Substrate	Product(s)	Yield (ratio)
22 		68%
23 		92%

The yields refer to isolated products unless otherwise stated. All reactions were run under the same conditions except entry 15, where a 1:1 ratio of 2-propanol:1,2-dichloroethane was employed to dissolve the substrate.

Semmelhack has also reported that $Et_3SiH/Ru(II)/AgOCOCF_3$ reduces 4-*tert*-butylcyclohexanone to give the equatorial alcohol as the major stereoisomer (95:5).[6]

Hindered ketones (entries 6, 7, 8, 9, 14, 15 and 16) are less reactive, and where stereoselectivity issues arise the major alcohol results from reduction from the least encumbered face of the carbonyl group. Medium ring ketones (entries 10 and 11) are also less reactive. Carbonyl groups conjugated with an aromatic ring are only slowly reduced, and aromatic aldehydes (entries 20, 21 and 22) were surprisingly (relative to entry 23) slow to reduce.

Representative procedure: Phenylsilane (348 μL, 0.4 equiv.) was added dropwise to a stirred solution of the substrate (2 mmol) and $Mn(dpm)_3$ (36 mg, 3 mol%) in 2-propanol (2 mL)/1,2-dichloroethane (100 μL) under an oxygen atmosphere (1 Atm) at 23°C. On completion of the reaction (TLC), the mixture was evaporated to dryness and the residue purified by chromatography over silica gel eluting with EtOAc/pentane mixtures to give the corresponding alcohol.

In summary, the above reduction procedure provides a mild method that does not need exclusion of air or moisture.

Acknowledgements

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