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A Facile Method for the Conversion of Oximes to Ketones and Aldehydes By the Use of Activated MnO_2

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Abstract Activated manganese dioxide (MnO_2) was found to be an efficient oxidant in the conversion of oximes to carbonyl compounds. The utility of this method in synthesis was demonstrated by the conversion of galactose to its acyclic aldose derivative **5**.

Oximes are easily obtained from carbonyl compounds, and have great potential as intermediates in organic synthesis.[1] Furthermore, oximes have served for the protection of carbonyl groups as exemplified in the syntheses of erythromycin derivatives[2a] and perhydrohistrionicotoxin.[2b] However, only a limited number of methods is available for the conversion of oximes to the corresponding carbonyl compounds under mild reaction conditions.[2c-e] We report here a facile method for the conversion of oximes to ketones and aldehydes, by the use of activated MnO_2.[3]

The conversion was carried out by treatment of oximes with commercially available activated MnO_2[4] in an aprotic solvent such as hexane or CH_2Cl_2 at room temperature. These results are characterized as follows (Table 1):

(1) This methodology was applicable to ketoximes and aldoximes and both gave the corresponding carbonyl compounds in excellent yields (entries 1-7).

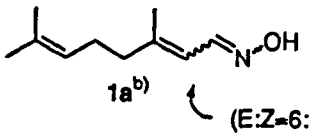
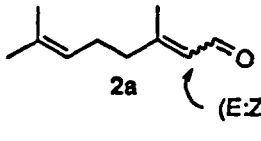
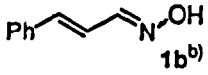
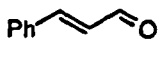
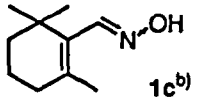
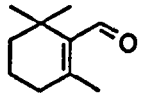
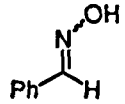
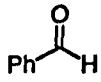
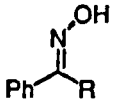
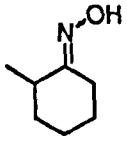
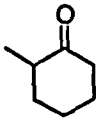
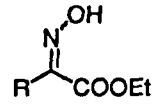
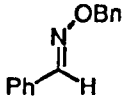
(2) Both *syn*- and *anti*-oximes were also smoothly transformed (entries 1, 2, 5, and 7).

(3) Isomerization of the olefinic double bond geometry of α,β-unsaturated oximes was not observed in the reaction (entries 1 and 2).

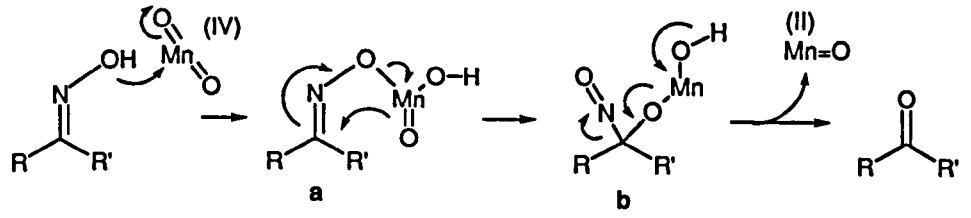
(4) Benzyloxime and the oximes derived from α-ketoesters were unreactive to MnO_2 (entries 8 and 9).

A proposed reaction mechanism is shown in Scheme 1. An intermediate **b** is formed through nucleophilic addition of the hydroxyl group of oxime to MnO_2, followed by the [2,3]-sigmatropic rearrangement of **a**. The intermediate **b** undergoes decomposition to give the carbonyl compound (Scheme 1).

Table 1. Conversion of Oximes to Ketones and Aldehydes with MnO_2

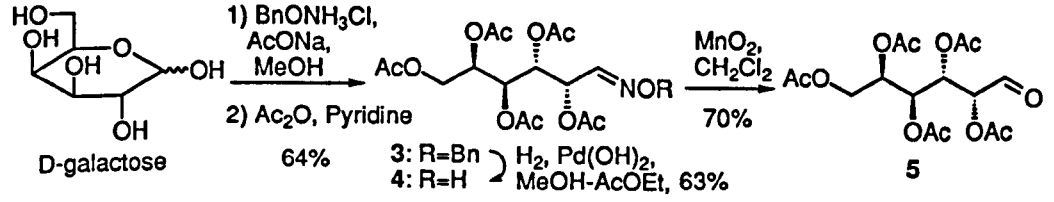
Entry	Oxime[a]	Aldehyde and Ketone	Yield (%)[c]
1	 **1a**[b] (E:Z=6:4)	 **2a** (E:Z=6:4)	83
2	 **1b**[b]	 **2b**	87
3	 **1c**[b]	 **2c**	91
4	 **1d**	 **2d**	84
5	 **1e**[b]	$C_{11}H_{23}CHO$ **2e**	78
6	 **1f**[b]; R=Me **1g**; R=Ph	 **2f**; R=Me **2g**; R=Ph	84 91
7	 **1h**[b]	 **2h**	92
8	 **1i**; R=Me **1j**; R=COOEt	no reaction no reaction	----- -----
9	 **1k**	no reaction	-----

a) Oximes **1a-k** were synthesized by treatment of carbonyl compounds with hydroxylamine hydrochloride or benzyloxyamine hydrochloride (1.2 eq) in the presence of AcONa (1.2 eq) in MeOH at room temperature. Oximes **1c,d, f, l, j** and **k** were obtained as a single isomer. The other oximes **1a, b, e, and h** were obtained as a mixture of *syn*- and *anti*-isomers. b) A mixture of *syn*- and *anti*- isomers was used. c) Isolated yield



Scheme 1

The present method was successfully applied to the synthesis of the acyclic galactose pentaacetate which was conventionally achieved by the conversion of D-galactose into its dithioacetal derivative, followed by the deprotection after chemical manipulation of the hydroxyl groups.[5] Ring opening of D-galactose with benzyloxyamine, followed by acetylation of the hydroxyl groups gave the acyclic benzyloxime 3.[6] Removal of the benzyl group of 3 afforded 4,[7] which was subjected to our method to provide 2,3,4,5,6-*O*-pentaacetyl-D-galactose 5[8] (Scheme 2).



Scheme 2

In conclusion, we have developed a facile method for the conversion of oximes to the corresponding carbonyl compounds. The present procedure has several advantages: (a) simple reaction procedure; (b) easy availability of activated MnO_2; (c) high yields from both aldoximes and ketoximes; (d) wide applicability to highly functionalized oximes.

Typical procedure for the conversion of oximes to the corresponding carbonyl compounds:

To a solution of oxime **1d** 80 mg (0.38 mmol) in hexane (8 mL) was added activated MnO_2 [2 g, (Eastman Kodak Company, Chem #50193)]. The suspension was vigorously stirred for 15 min and filtered through Celite. The filtrate was concentrated and purified by silica gel column chromatography (hexane/Et_2O=95:5) to give benzaldehyde as a pale yellow oil (59 mg, 84%).

Acknowledgment: We thank Dr. Terumi Nakajima, Director, for his encouragement.

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5. Wolfrom, M. L. *J. Am. Chem. Soc.* **1930**, *52*, 2464-2473.
6. Benzyloxime **3** was obtained as a single isomer. **3**: colorless crystals (mp; 131-132 °C, Hexane-AcOEt). $[\alpha]_D^{27}$ +40° (*c*=1.1, $CHCl_3$). ^{1}H-NMR (400 MHz, $CDCl_3$);δ 7.33-7.26 (5H, m), 7.23 (1H, d, *J*=5.6 Hz), 5.54 (1H, dd, *J*=5.2, 2 Hz), 5.41 (1H, dd, *J*=9.6, 2 Hz), 5.39 (1H, dd, *J*=9.6, 2 Hz), 5.29 (1H, ddd, *J*=7.2, 5.2, 2 Hz), 5.07 (2H, s), 4.26 (1H, dd, *J*=12, 5.2 Hz), 3,87 (1H, dd, *J*=12, 7.2 Hz), 2.99, 2.92, 2.08, 2.02, and 2.00 (each 3H, s). HRMS (FABS, *m/z*); Calcd for $C_{23}H_{30}O_{11}N$ $(M+H)^+$; 496.1821, Found 496.1819.
7. A 1:5 geometrical mixture of **4** was obtained as colorless crystals. ^{1}H-NMR (400 MHz, $CDCl_3$); δ 7.24 (5/6H, d, *J*=5.2 Hz), 6.53 (1/6H, d, *J*=5.2 Hz), 6.03 (1/6H, dd, *J*=5.2, 2.4 Hz), 5.70 (1/6H, dd,*J*=10, 2.4 Hz), 5.43 (5/6H, dd, *J*=10, 2 Hz), 5.45-5.40 (2/6H, m), 5.40 (5/6H, dd, *J*=10, 2.4 Hz), 5.31 (5/6H, ddd, *J*=7.2, 4.8, 2 Hz), 5.30 (1/6H, m), 4.29 (1/6H, dd, *J*=11.2, 2 Hz), 4.27 (5/6H, dd, *J*=11.6, 4.8 Hz), 3.87 (5/6H, dd, *J*=11.2, 7.2 Hz), 3.86 (1/6H, dd, *J*=11.2, 8 Hz), 2.13 and 2.12 (each 3/6H, s), 2.114 (15/6H, s), 2.113 (3/6H, s), 2.11 (15/6H, s), 2.09 (15/6H, s), 2.08 (3H, s), 2.07 (3/6H, s), 2.03 (15/6H, s). HRMS (FABMS, *m/z*); calcd for $C_{16}H_{24}O_{11}N$ $(M+H)^+$ 406.1349. Found 406.1346.
8. **5**: colorless crystals. mp 118-119°C (toluene) [Lit.[5] mp 120-121°C (toluene)]. ^{1}H-NMR (400 MHz, $CDCl_3$);δ 9.45 (1H, s), 5.64 (1H, dd, *J*=9.6, 2Hz), 5.47 (1H, dd, *J*=9.6, 2 Hz), 5.36 (1H, ddd, *J*=7.2, 4.8, 2 Hz), 5.25 (1H, d, *J*=2 Hz), 4.28 (1H, dd, *J*=11.6, 4.8 Hz), 3.91 (1H, dd, *J*=11.6, 7.2 Hz), 2.21, 2.11, 2.10, 2.04, and 2.03 (each 3H, s). HRMS (FABMS, *m/z*); Calcd for $C_{16}H_{22}O_{10}$ $(M+H)^+$; 391.1240. Found 391.1268.

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