DI-FUNCTIONALIZATION OF ALKENES USING AN OXIDANT GENERATED FROM MANGANESE(II) CHLORIDE UNDER OXYGEN: SYNTHESIS OF γ-LACTONES†

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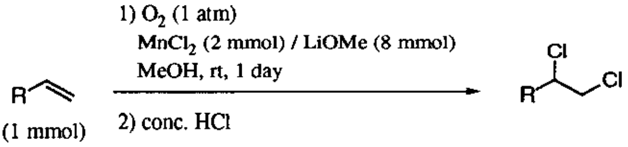
Abstract - Alkenes are oxidatively dichlorinated by stirring with manganese(II) chloride-lithium methoxide under oxygen atmosphere, followed by treatment with conc. hydrochloric acid. This di-functionalization of alkenes can be applied to the chlorolactonization of lithium 4-pentenoates.

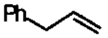
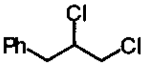
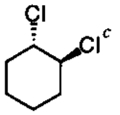
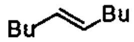
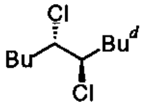
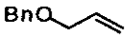
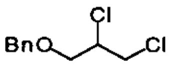
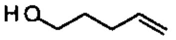
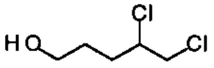
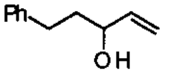
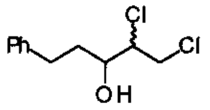
Oxidation is the essential subject in organic synthesis especially as the functionalization of molecules. In the course of our investigation on manganese ate complexes,[1] we incidentally found the oxidative dichlorination of alkenes[2] using a manganese(II) salt[3-5] under oxygen atmosphere (Scheme 1). Here we wish to report the reaction and its application to the synthesis of γ-lactones.

Scheme 1



A representative procedure for the dichlorination of allylbenzene is as follows. To a flask containing 5 mL of methanol, a solution of butyllithium in hexane (1.64 M, 4.9 mL, 8 mmol) was added *under argon*, and then $MnCl_2$ (252 mg, 2 mmol) was added under flashing argon. After the flask was *purged with oxygen*, the brown mixture was stirred for 2 h at room temperature. Allylbenzene (118 mg, 1 mmol) was introduced and the mixture was stirred for 1 day at room temperature. To the mixture, conc. HCl was added. The resultant mixture was passed through a short column (silica gel) with Et_2O as an eluent. After evaporation of solvents, a crude product was obtained. This material was further purified by column chromatography on silica gel, and pure 1,2-dichloro-3-phenylpropane was obtained (126 mg, 0.67 mmol, 67%). Selected examples of the oxidation are listed in Table 1. As can be seen in the Table, the present reaction is quite general. For reactions of internal olefins, the yields were marginal, but in the cases, *trans*-dichlorination proceeded selectively (Entries 2[6] and 3[8]). Ether-function tolerated under the reaction conditions (Entry 3) and, more interestingly, even hydroxy-compounds could be adapted to this reaction, where an intramolecular hydroxy group, to some extent, seemed to enhance the reactivity (Entries 4 and 5).

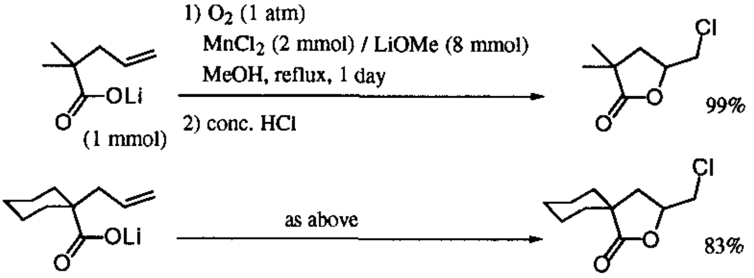
Table 1. Dichlorination of Alkenes[a]

Entry	Alkene	Product	Yield/%[b]
1			67
2			56
3			53
4			67
5			75
6			92[e]

[a] Reaction was carried out using an alkene (1 mmol), $MnCl_2$ (2 mmol), and LiOMe (8 mmol) in MeOH (5 mL) at rt for 1 day under oxygen (1 atm). [b] Isolated yield by column chromatography on silica gel. [c] Only an *anti*-isomer was detected. See, ref. 6. [d] Alkene (18%) was recovered. See, ref. 8. [e] A mixture of diastereomers was obtained in the ratio of 53/47.

This oxidative difunctionalization of alkenes can be applied to the chlorolactonization of lithium 4-pentenoates (Scheme 2).[9]

Scheme 2



Although it is premature to discuss active species and the mechanism of reactions presented here, higher valent manganese chloride seems to be an actual chlorinating agent. Control experiments showed the final addition of HCl is essential.[10] Therefore a manganese(II) ate complex coordinated by the methoxide may be possibly oxidized to the corresponding high-valent manganese(III or IV) complex under oxygen, which subsequently reacts with HCl to form manganese chloride of higher valency as a dichlorination and oxychlorination agent.

Finally, the present oxidative chlorination using $MnCl_2$ is interesting in comparison with previously reported the *trans*-dichlorination of alkenes with high-valent manganese chloride generated *in situ* from manganese(III, IV, and VII) salts such as $[Mn_3O(OAc)_7HOAc]$[3], MnO_2[4] and $KMnO_4$.[5] The scope and limitation of the reaction and further applications to organic synthesis are now under active investigations.

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REFERENCES AND NOTES

[†] The paper is dedicated to the celebration of the 75th birthday of Professor Koji Nakanishi, Columbia University.

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2. For the dichlorination of alkenes, see *e.g.* with SO_2Cl_2, M. S. Kharasch and H. C. Brown, *J. Am. Chem. Soc.*, 1939, **61**, 3432; with SO_2Cl_2, Cl_2 or PCl_5, L. Spiegler and J. M. Tinker, *J. Am. Chem. Soc.*, 1939, **61**, 940; with Cl_2, H. J. Lucas and C. W. Gould, Jr., *J. Am. Chem. Soc.*, 1941, **63**, 2541; M. C. Hoff, K. W. Greenlee, and C. E. Boord, *J. Am. Chem. Soc.*, 1951, **73**, 3329; with HCl and NCS, C. H. Robinson, L. Finckenor, E. P. Oliveto, and D. Gould, *J. Am. Chem. Soc.*, 1959, **81**, 2191; with HCl, $CaCl_2$, and H_2O_2, T.-L. Ho, B. G. B. Gupta, and G. A. Olah, *Synthesis*, 1977, 676; with polymer-supported Cl_2, A. Bongini, G. Cainelli, M. Contento, and F. Manescalchi, *J. Chem. Soc., Chem. Commun.*, 1980, 1278.

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6. The stereochemistry of the product was determined in comparison with the authentic samples for *syn*- and *anti*-isomers that were independently prepared according to ref. 7 and ref. 4, respectively.

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8. Essentially the same ^{1}H NMR spectrum of the crude product as that of the product produced under the reaction conditions reported by Markó *et al.*[5] was obtained, showing the *anti*-addition proceeds predominantly. On the other hand, Markó *et al.* reported that the reagent was unstable at >-35 °C. This suggests that the active species are different from those in the reaction presented here. The starting material was completely consumed and the yield of the *anti*-addition product was increased up to 77% when 3.0 equiv of $MnCl_2$ and 12 equiv of LiOMe were employed.

9. For the chlorolactonization, see *e.g.* D. G. Garratt, M. D. Ryan, and P. L. Beaulieu, *J. Org. Chem.*, 1980, **45**, 839; Y. Tamaru, M. Mizutani, Y. Furukawa, S. Kawamura, Z. Yoshida, K. Yanagi, and M. Minobe, *J. Am. Chem. Soc.*, 1984, **106**, 1079.

10. Without the addition of conc. HCl, the starting alkene was recovered.

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