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SUBSTITUENT DIRECTED OXIDATIVE CYCLIZATION WITH CETYLTRIMETHYLAMMONIUM PERMANGANATE: A GENERAL APPROACH TO THE SYNTHESIS OF γ- AND δ-LACTONES

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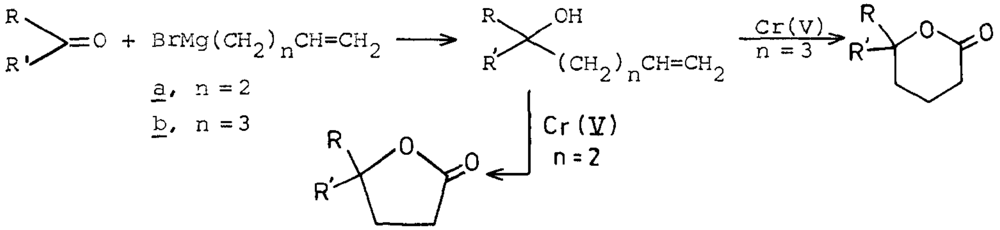
Summary. Treatment of primary, secondary or tertiary γ- and δ-hydroxy-olefins with cetyltrimethylammonium permanganate gives good yields of γ- and δ-lactones by oxidative cyclization, with loss of one carbon.

Earlier work from our laboratories has shown that treatment of tertiary-γ- and δ-hydroxy olefins with pentavalent chromium reagent, $(BiPyH_2)CrOCl_5$[1] affords very good yields of the corresponding γ- and δ-lactones.[2] A number of spiro and bicyclic lactones have been synthesized using this methodology (Scheme 1). Schlecht and Kim[3] reported a similar transformation of hydroxyolefins to lactones with chromium trioxide in acetic acid/acetic anhydride.

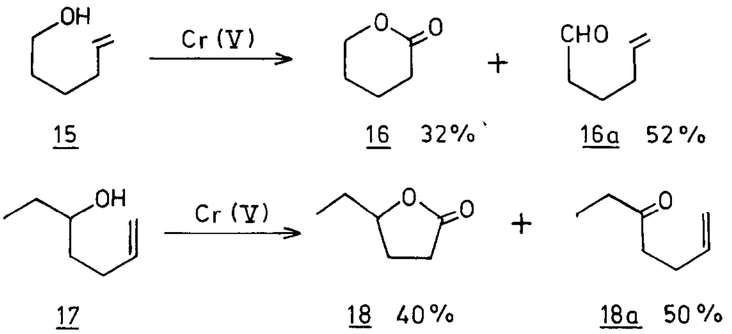
Scheme 1



Although both methodologies mentioned above[2,3] work well in the case of tertiary hydroxyolefins, they are not synthetically useful for oxidative cyclization of primary or secondary γ- and δ-hydroxyolefins. For example, oxidation of 15 and 17 with chromium(V) reagent gives only poor yield of the lactones 16 and 18, respectively, the major product being the corresponding carbonyl compounds 16a and 18a (Scheme 2).

It was felt that if the oxidative cyclization methodology can be applied to the synthesis of γ- and δ-lactones in good yield from primary or secondary hydroxyolefins this would prove to be extremely useful. In this communication we report our results on such a methodology using cetyltrimethylammonium perman-

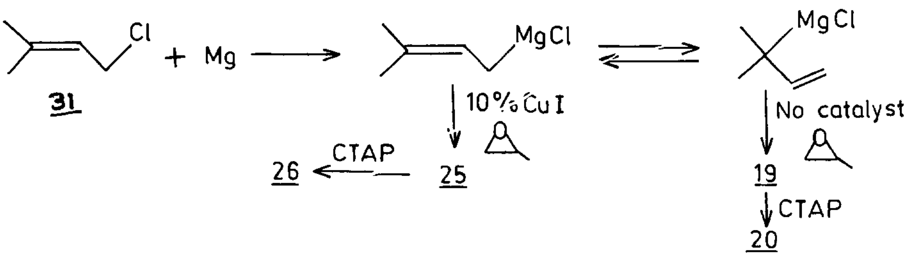
Scheme 2



ganate (CTAP) as the oxidizing agent. Earlier we have successfully employed this reagent for cis-hydroxylation of olefins[4] and for selective oxidation of benzylic alcohols.[5] Here we have taken advantage of the fact that unlike other permanganate derived reagents, cetyltrimethylammonium permanganate (CTAP) does not oxidise primary and secondary alcohols to the respective carbonyl compounds.[4,5]

When treated with two molar equivalents of CTAP in CH_2Cl_2 or $CHCl_3$ (25-50°) we find that primary, secondary and tertiary γ- and δ-hydroxyolefins undergo oxidative cyclization to give γ- and δ-lactones, respectively in good yields. The scope of this methodology can be easily gauged from the variety of substrates indicated in the Table. The oxidation of compounds 19 and 25 (Table) is particularly interesting since they are derived from the same allyl chloride 31 via Grignard reaction under different conditions[6] and lead to two different lactones 20 and 26, respectively (Scheme 3).

Scheme 3

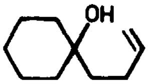
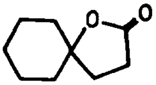
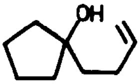
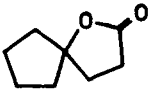
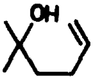
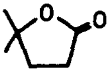
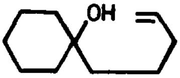
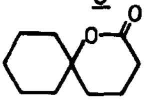
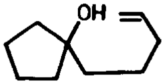
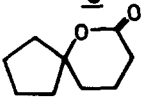
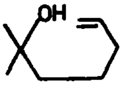
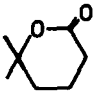
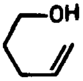
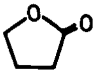
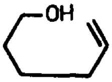
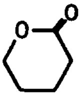
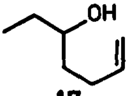
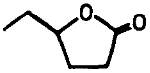
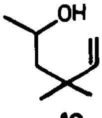
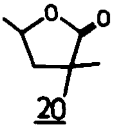
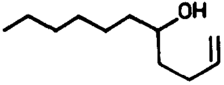
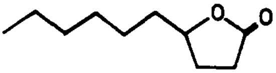


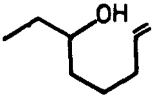
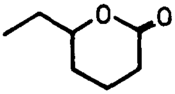
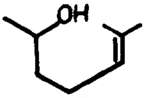
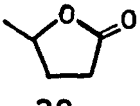
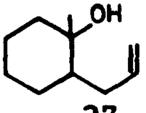
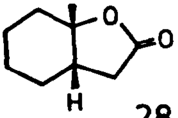
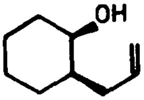
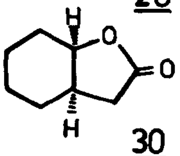
This simple two step methodology using oxidative cyclization with CTAP is quite general and is clearly a substituent directed oxidation where the hydroxyl group plays a key role in bringing about this unusual reaction with loss of one carbon. Mechanistic studies of this reaction and its application to the synthesis of natural products are currently in progress.

A typical procedure for oxidative cyclization is given below:

A solution of CTAP (0.808 g, 2 mmol) in dichloromethane (8 ml) was added

Table : Oxidation of hydroxyolefins to lactones with CTAP[a]

Entry	Substrate[b]	Reaction Time (h)	Temp. °C/ Solvent	Product[c]	Yield[d] %
1	 1	6.0	50°/ $CHCl_3$	 2	76
2	 3	6.5	50°/ $CHCl_3$	 4	71
3	 5	8.0	25°/ CH_2Cl_2	 6	68
4	 7	3.0	50°/ $CHCl_3$	 8	52
5	 9	3.0	50°/ $CHCl_3$	 10	54
6	 11	3.0	50°/ $CHCl_3$	 12	54
7	 13	4.5	25°/ $CHCl_3$	 14	65
8	 15	3.0	25°/ $CHCl_3$	 16	50
9	 17	4.0	25°/ $CHCl_3$	 18	69
10	 19	3.5	25°/ CH_2Cl_2	 20	78
11	 21	5.0	25°/ $CHCl_3$	 22	66

12	 23	3.0	25°/ $CHCl_3$	 24	51
13	 25	3.5	25°/ CH_2Cl_2	 26	70
14	 27	6.0	25°/ CH_2Cl_2	 28	55
15	 29	4.0	25°/ CH_2Cl_2	 30	74

a) All reactions were carried out using two molar equivalents of CTAP in chloroform or dichloromethane; b) Most of the substrates were prepared by the reaction of appropriate carbonyl compounds with Grignard reagents; c) All the products gave satisfactory spectral and elemental analysis; d) Yields refer to pure, isolated products.

dropwise to a stirred solution of 25 (0.128 g, 1 mmol) in dichloromethane (5 ml) at 25°C. Stirring was continued for 3.5 hr and then the mixture was concentrated to half its volume under reduced pressure. The residual solution was diluted with ether (60 ml) and filtered through a pad of Celite and anhyd. $MgSO_4$. The filtrate was concentrated in the rotatory evaporator and the product was purified by column chromatography (silica gel) and eluted with ether-petroleum ether (1:1) to afford lactone 26 as an oil (0.070 g, 70%). IR ($CHCl_3$): 1775 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.4 (d, 3H), 1.8-2.4 (m, 4H), 4.6 (m, 1H); M^+ = 100.

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