

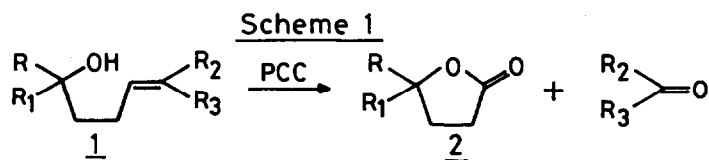
OXIDATION OF TETRAHYDROFURAN METHANOL DERIVATIVES WITH PYRIDINIUM CHLOROCHROMATE: A FACILE SYNTHESIS OF γ -BUTYROLACTONES

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Abstract: Treatment of a number of tetrahydrofuran methanol derivatives with pyridinium chlorochromate led to the formation of the corresponding γ -butyrolactones with the loss of one or more carbon atoms in good yields under mild reaction conditions.

Earlier we reported a substituent directed oxidative cyclization of γ -hydroxy olefins 1 to the corresponding γ -lactones 2 mediated by pyridinium chlorochromate (PCC) (Scheme-1).^{1,2} In the course of studying this transformation further from a synthetic and mechanistic point of view, we encountered some interesting oxidative transformations of tetrahydrofuran methanol derivatives with PCC.

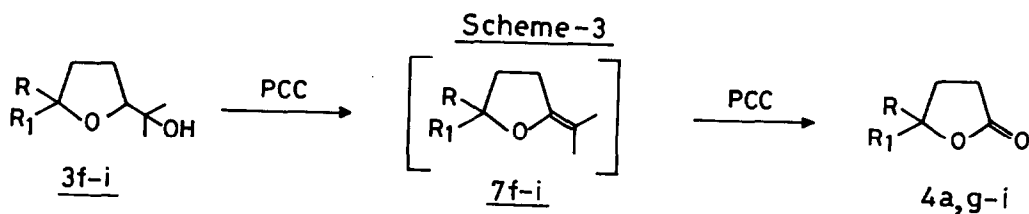
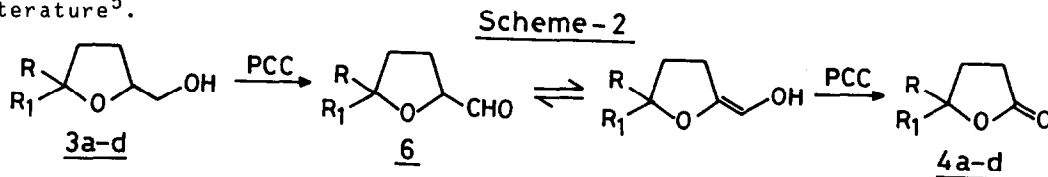


$R, R_1 = \text{alkyl or aryl}; R_2, R_3 = \text{H, alkyl, aryl.}$

A number of tetrahydrofuran methanol derivatives 3 were prepared from the corresponding γ -hydroxy olefins 1³ by reaction with *m*-chloroperbenzoic acid at 0°C.⁴ When tetrahydrofuran methanols 3a-i were treated with pyridinium chlorochromate (PCC) (4 mole equiv) and molecular sieves 3A⁰ in dichloromethane under reflux (3-8 h) the corresponding γ -butyrolactone derivatives 4a-i were obtained in high yields. The results of such an oxidative transformation are listed in the Table. There are some interesting observations in the order of reactivity and overall yield of the products which are dependent on the structure of the tetrahydrofuran methanol 3. Compounds 3a-d having primary hydroxyl group take longer (7-8 h) time to form the γ -lactones 4a-d and the products are formed in moderate yields (52-58%) (entries 1-4 in Table). On the otherhand compounds 3f-i having tertiary hydroxyl group reacted faster (3 to 3.5 h) with PCC to give the γ -butyrolactones 4b, 4g, 4h and 4i respectively in excellent yields (73-95%) (entries 6-9). Tetrahydrofuran methanol derivative 3e having a secondary

hydroxyl group gave the γ -butyrolactone 4b (57%) along with a small amount of ketone 5 (5%) in 5 h.

It appears that in the case of substrates 3a-d the γ -lactones are formed via the intermediacy of aldehyde 6 which undergoes oxidative cleavage with excess oxidant to form the γ -butyrolactone (Scheme-2). Oxidative cleavage of enol of aldehyde with pyridinium dichromate (PDC) is preceded in the literature⁵.



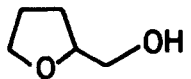
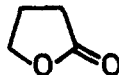
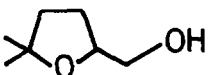
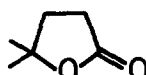
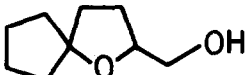
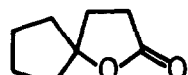
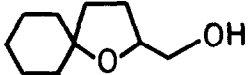
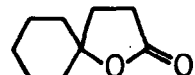
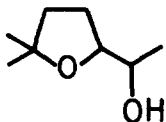
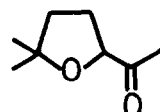
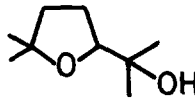
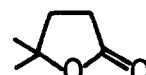
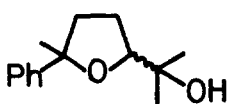
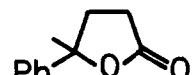
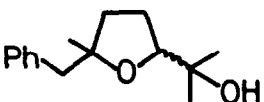

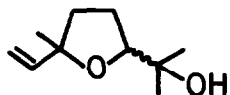
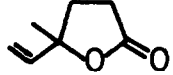
That this is one of the possible modes of formation of the γ -butyrolactone 4a-d from 3a-d is borne out by the observation that under controlled conditions (4 mole eq of PCC, 5 h, 28°C) 3a gave rise to the aldehyde 6a⁶ (10%) and γ -lactone 4a (10%). Aldehyde 6a independently when treated with PCC [4 eq, (40°C, 6 h)] gave 4a (55%).

In the oxidative transformation of substrates 3f-i with PCC it is believed that these tertiary alcohols undergo dehydration to form enol ether intermediates 7f-i under the reaction condition which subsequently undergo oxidative cleavage with PCC to form the γ -butyrolactone (Scheme-3). We have earlier reported facile and selective oxidative cleavage of ketone derived enol ethers with PCC at room temperature⁷. However, in the reaction of substrates 3f-i under controlled condition (PCC 2 mole eq, 28°C, 1 h) the enol ether intermediates 7f-i could not be detected or isolated.

Oxidation of tetrahydrofurfuryl alcohol with other oxidants like molecular oxygen⁸, silver carbonate-Celite⁹ and chromic acid¹⁰ to γ -butyrolactone has been reported to proceed in low yield and has never been utilised as a general synthetic method for the synthesis of substituted butanolides.

The present methodology appears to be very general and can be used for

Table

Entry	Substrate	Time (h)	Product ^a	Yield % ^b
1	 <u>3a</u>	8	 <u>4a</u>	52
2	 <u>3b</u>	8	 <u>4b</u>	53
3	 <u>3c</u>	7	 <u>4c</u>	58
4	 <u>3d</u>	8	 <u>4d</u>	54
5	 <u>3e</u>	5	<u>4b</u> +  <u>5</u>	57
6	 <u>3f</u>	3.5	 <u>4b</u>	73
7	 <u>3g</u>	3.5	 <u>4g</u>	82
8	 <u>3h</u>	3.0	 <u>4h</u>	95
9	 <u>3i</u>	3.0	 <u>4i</u>	73

^aAll the products gave satisfactory spectroscopic values and elemental analyses.

^bIsolated yields.

the synthesis of a wide variety of α -substituted γ -butyrolactones from tetrahydrofuran methanol derivatives using a readily available reagent and under mild reaction conditions.

General Procedure for the oxidation of tetrahydrofuran methanol derivatives 3 with PCC: Powdered molecular sieves ($3A^0$) (1.7 g) was heated under N_2 at $320^\circ C$ with a Bunsen burner for 1h. It was allowed to come to room temperature and pyridinium chlorochromate (1.7 g, 8mmol) and dry dichloromethane (10 ml) were added. To this mixture was added a solution of 3 (2 mmol) in dichloromethane (5 ml) and stirred under reflux (3-8 h). Diethyl ether (50 ml) was added and the reaction mixture was filtered through a short pad of Celite and silica gel. The filter cake was washed thoroughly with ether (2 x 30 ml) and the filtrate was concentrated. The residue after flash chromatography (1:2 ether-petroleum ether) afforded the butanolide 4 (52-93%).

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