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A HIGHLY EFFICIENT SYNTHESIS OF γ- AND δ-LACTONES BY OXIDATIVE CYCLIZATION[1)]

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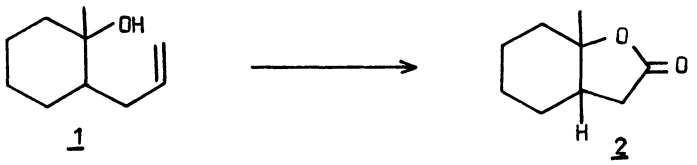
Treatment of tertiary γ- and δ-hydroxyolefins with pentavalent chromium reagent, $(BipyH_2)CrOCl_5$, give good yields of γ- and δ-lactones by oxidative cyclization, with loss of one carbon. Pyridinium chlorochromate (PCC) also effects tnis transformation to γ-lactones in reasonable yields.

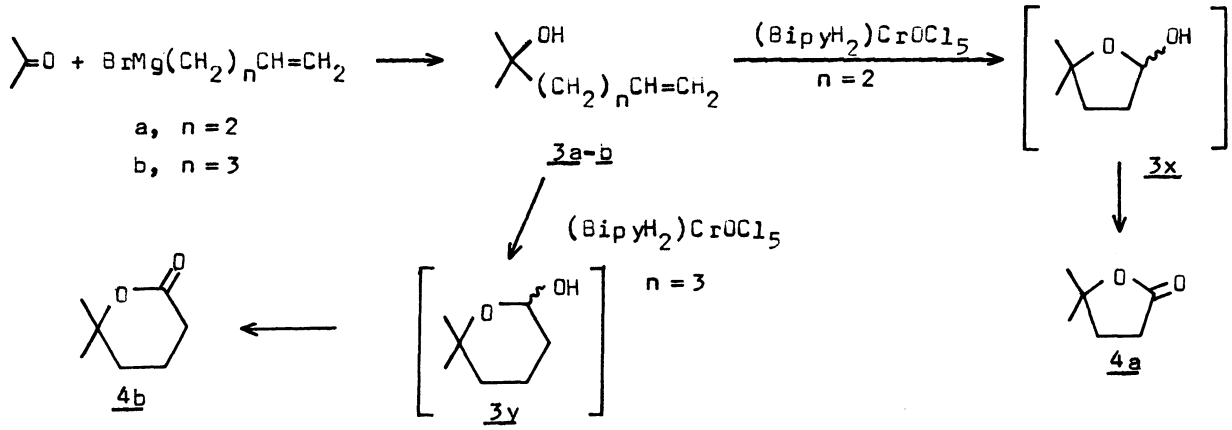
In the course of our studies on oxidation of organic substrates with chromium(V) reagents, we have recently shown that tertiary hydroxy olefins (1) are smoothly converted to bicyclic γ-lactones (2) in good yields.[2)] In this communication we wish to report a highly efficient synthesis of γ- and δ-lactones in



1 2

general and spirolactones in particular from suitably substituted hydroxyolefins with pentavalent chromium reagents. We also wish to disclose similar oxidative cyclization with pyridinium chlorochromate, hitherto unobserved.[3)]

Treatment of 3a and 3b with five molar equivalents of $(BipyH_2)CrOCl_5$ in



dichloromethane under reflux undergo a net oxidative cleavage to give γ-lactone 4a and δ-lactone 4b, respectively in very good yields. A few otner examples are shown in Table 1.

Table 1.

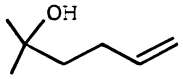
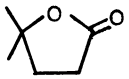
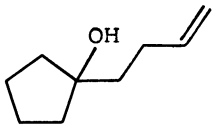
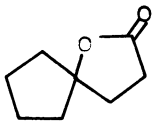
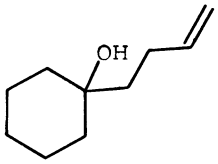
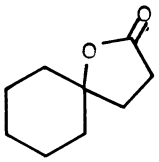
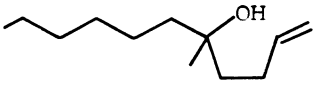
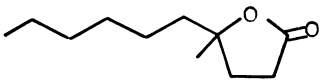
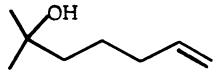
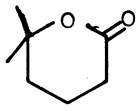
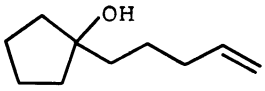
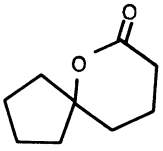
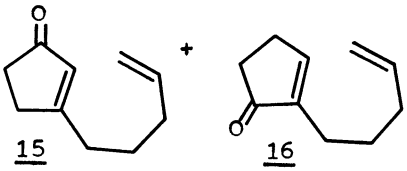
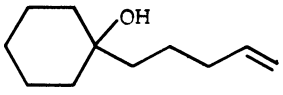
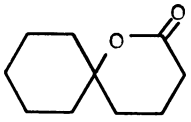
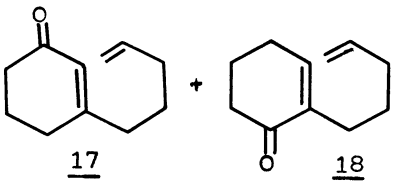
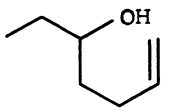
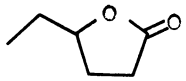
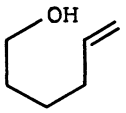
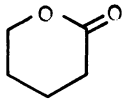
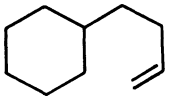
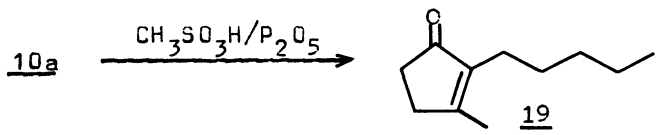
Entry	Substrate		Oxidant	Product[9]		Yield/%
1		3a	Cr(V)		4a	80
2	,,	,,	PCC	,,	,,	53
3		5a	Cr(V)		6a	72
4	,,	,,	PCC	,,	,,	52
5		7a	Cr(V)		8a	71
6	,,	,,	PCC	,,	,,	55
7		9a	Cr(V)		10a	75
8	,,	,,	PCC	,,	,,	54
9		3b	Cr(V)		4b	72
10		5b	Cr(V)		6b	75
11	,,	,,	PCC	 15 + 16		30
12		7b	Cr(V)		8b	75
13	,,	,,	PCC	 17 + 18		35

Table 1. (contd.)

Entry	Substrate		Oxidant	Product		Yield/%
14		11	Cr(V)		12	40
15		13	Cr(V)		14	32
16		20	PCC	No reaction	-	-

In the reaction of 3a and 3b with $(BipyH_2)CrOCl_5$ it is easy to visualise oxidative cleavage of the carbon-carbon double bond[4] followed by cyclization to form the cyclic hemiacetals (3x and 3y) respectively, which undergo further oxidation to the corresponding lactones. It is surprising to note that pyridinium chlorochromate (PCC),[3,5] supposedly inert towards carbon-carbon double bonds, also effects this oxidative cyclization of γ-hydroxy olefin (3a) to γ-lactone(4a) in dichloromethane under reflux for 48 h in moderate yields.[6] This reaction is also general for the synthesis of γ-lactones as shown in Table 1. However, δ-hydroxyolefins (5b and 7b) on treatment with PCC under similar conditions do not undergo oxidative cyclization to form the corresponding δ-lactones. 5b gives rise to a mixture of α,β-unsaturated ketones (15 and 16) (1:1.2) in 30% yield. Similarly 7b yields a mixture of 17 and 18 (1:1.3) in 35% yield. In the case of δ-hydroxy olefins, presumably, PCC effects dehydration followed by allylic oxidation to give rise to the observed products. Because of the presence of a readily oxidizable hydoxyl group, oxidation of sec-hydroxy olefin (11) (entry 14) with $(BipyH_2)CrOCl_5$ proceeded to yield only 40% of the γ-lactone (12), and primary hydroxy olefin (13) (entry 15) under the same conditions affords δ-valarolactone (14) in only 32% yield. 11 and 13 on treatment with PCC give mainly the corresponding carbonyl compounds.

This simple two step methodology using oxidative cyclization was applied to establish an alternate route to dihydrojasmone 19[7] via the lactone 10a (entry 7). Lactone 10a on treatment with methane sulfonic acid containing 10% by weight



of phosphorous pentoxide[8] under N_2, yields dihydrojasmone (19) in 89% yield.

The oxidative cyclization of γ-hydroxyolefins with PCC seems to be the hydroxyl group directed oxidative cleavage, since compound 20 (entry 16) does not react under the reaction conditions. The mechanism of this substituent directed

oxidation with PCC and optimization of the method are currently under progress and will be published in detail elsewhere. Typical procedures for oxidative cyclization with $(BipyH_2)CrOCl_5$ and PCC are given below.

A mixture of 3a (0.228 g, 2 mmol) and $(BipyH_2)CrOCl_5$ (4.0 g, 10 mmol) in dichloromethane (15 ml) was gently refluxed with stirring under nitrogen atmosphere for 7 h. It was then cooled to room temperature, diluted with ether and filtered through a short pad of celite. The filter cake was washed thoroughly with ether. The filtrate and washings were combined and solvent evaporated. The residue was purified by flash chromatography on silica gel (20% ether-petroleum ether) to get 4a as a colorless oil (0.182 g, 80%). IR ($CHCl_3$): 1775 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.4 (s, 6 H), 1.8-2.27 (m, 2 H), 2.4-2.85 (m, 2 H); MS m/e: 114 (M^+), 99, 70, 55, and 39.

A mixture of 3a (0.228 g,2 mmol), PCC (2.155 g, 10 mmol), and celite (2.0 g) in dichloromethane (15 ml) was refluxed gently with stirring for 48 h. It was then cooled to room temperature, diluted with ether and filtered through a short pad of silica gel and the filter cake was washed thoroughly with ether. The residue obtained after evaporation of solvent was purified by flash chromatography on silica gel (20% ether-petroleum ether) to yield 4a as a colorless oil (0.12 g, 53%).

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References

1) This work was presented at the 5th IUPAC Intl. Conf. on Org. Synth. (abstract No. M13), Friedurg, August (1984).
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5) E-J. Corey and J.W. Suggs, Tetranedron Lett., 1975, 2647.
6) Similar results of oxidative cleavage of γ-hydroxyolefins with modified Fieser's reagent (CrO_3/acetic acid/acetic anhydride) to form γ-lactones have been observed. M.F. Schlecht and H.J. Kim, 5th IUPAC Intl. Conf. on Org. Synth. (abstract No. T22) and submitted to Tetrahedron Lett.
7) T.L. Ho, Synth. Commun., 4, 265 (1974).
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9) All yields refer to isolated products and all new compounds gave satisfactory spectral data.

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