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# An Efficient γ-Lactone Formation Relating To Prostaglandin Synthesis

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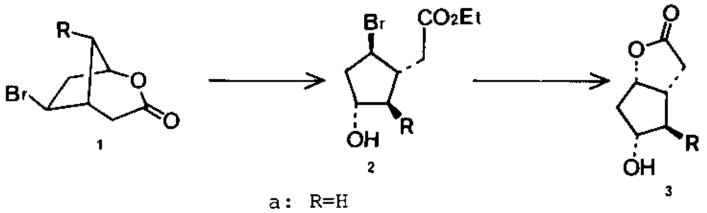
A simple and efficient γ-lactone formation relating to prostaglandin synthesis is described.

In the recent synthetic studies on the prostaglandin series by this group,[1∿4] a γ-lactone formation through an intramolecular substitution has been employed in a key stage and we have developed a new method using silver perchlorate or mercuric acetate as a catalyst. Although the method led to excellent formation of the γ-lactones(3, a and b) from the corresponding bromo precursors(1, a and b),[1,2,4] it gave only 10 % yield of the γ-lactone(3c) from the precursor(1c) containing an acetylenic group using silver perchlorate as catalyst,[2] and some improvement could be realized by using sodium hydroxide as catalyst[2], however, the yield obtained was 18 % at best.

We now report here a simple method which allows an excellent formation of the γ-lactone(3c) possessed an acetylenic group as well as its congener(3a) without using the expensive silver salt or the poisonous mercuric salt as a catalyst. The present method involved none of difficult conditions and it gave the γ-lactone[2](3c) in 79 % yield by simply refluxing the bromo precursor(1c) in 95 % ethanol in the presence of a catalytic amout of *p*-toluenesulfonic acid. Similarly 3a was obtained in 85 % yield from 1a. Interestingly this could not be effectively applied to 1b with a ketene dichlordie group yielding the γ-lactone[1] (3b) in 34 % yield. In the conversion, a formation of the ethyl esters(2, a∿c) could be recognized by tlc and a separate experiment using the ethyl ester(2, a∿c) also yielded the corresponding lactones[5](3, a∿c) in a comparable yield, respectively. A representative experimental procedure for the conversion of 1a to 3a as follows.

## 2α, 4α-Dihydroxycyclopentane-1α-acetic Acid γ-Lactone(3a)

A solution of 1a(410 mg, 2.0 m mol) in 95 % EtOH(40 ml) containing a catalytic amount of *p*-toluenesulfonic acid monohydrate was refluxed for 30 h. Removal of the solvent under the reduced pressure left an yellow oil which was crystallized from benzene to afford 3a(241 mg, 85 %) as colorless leaflets: mp 76-77°; IR $\nu_{max}^{Nujol}$(cm$^{-1}$) 3445, 1745; NMR(CDCl$_3$)(δ) 1.79-3.15(7H, m), 3.63(1H, s, disappeared with D$_2$O, -O$\underline{H}$), 4.46(1H, br.s,$>$C$\underline{H}$-OH), 5.10(1H, m,$>$C$\underline{H}$-OCO); *Anal*. Calcd. for $C_7H_{10}O_3$: C, 59.14; H, 7.09. Found: C, 59.30; H, 6.97.



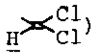
a: R=H

b: R=CH=CCl$_2$

c: R=C≡CH

| lactone / catalyst | 3a | 3b | 3c |
|---|---|---|---|
| Hg(OAc)$_2$ |  | 79 % | 0 % |
| AgClO$_4$ | 91 % | 83 % | 10 % |
| *p*-TsOH | 85 % | 34 % | 79 % |

## References and Notes

1. S. Takano, N. Kubodera, and K. Ogasawara, J. Org. Chem., 42, 786 (1977).
2. S. Takano, N. Kubodera, H. Iwata, and K. Ogasawara, Heterocycles, 8, 325 (1977).
3. S. Takano, H. Iwata, and K. Ogasawara, Heterocycles, 9, 845 (1978).
4. S. Takano, H. Iwata, and K. Ogasawara, Heterocycles, 9, 1249 (1978).
5. The esters (2 a$\sim$c) were obtained as unstable oil: 2a; IR $\nu_{max}^{neat}$(cm$^{-1}$) 3420, 1720; NMR(CDCl$_3$) (δ) 1.26(3H, t, J=7 Hz, -CH$_2$C$\underline{H}_3$), 2.10-3.10(8H, m, disappeared 1H, with D$_2$O), 4.20(2H, q, J=7 Hz, -C$\underline{H}_2$CH$_3$), 3.90-4.60(2H, m). 2b; IR $\nu_{max}^{CHCl_3}$(cm$^{-1}$) 3400, 1720, 1608; NMR(CDCl$_3$)(δ) 1.31(3H, t, J=7.5 Hz, -CH$_2$C$\underline{H}_3$), 2.56(6H, m), 3.14(1H, br.s, disappeared with D$_2$O, -O$\underline{H}$), 4.18(2H, q, -C$\underline{H}_2$CH$_3$), 4.32(2H, m), 5.79(1H, d, J=9.0 Hz,  $\underline{H}{>}{=}{<}^{Cl}_{Cl}$). 2c; IR $\nu_{max}^{neat}$(cm$^{-1}$) 3420, 1720; NMR(CDCl$_3$)(δ) 1.26(3H, t, J= 7 Hz, -CH$_2$C$\underline{H}_3$), 2.10-3.10(8H, m, disappeared 1H,with D$_2$O), 4.20(2H, q, J= 7 Hz, -C$\underline{H}_2$CH$_3$), 3.90-4.60(2H, m).

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