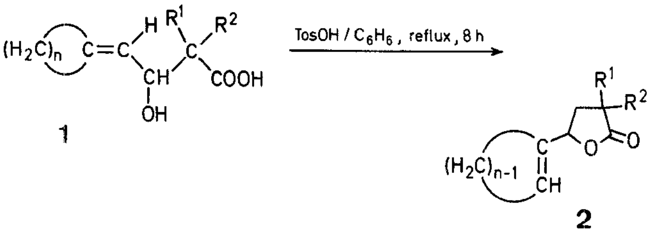
A Convenient Preparation of 4-(1-Cycloalkenyl)-4-butanolides from 4-Cycloalkylidene-3-hydroxyalkanoic Acids

Tsutomu Fujita*, Shoji Watanabe, Yoshiki Higuchi, Kyoichi Suga

Department of Applied Chemistry, Faculty of Engineering, Chiba University, Yayoicho, Chiba, 260 Japan

Various methods for the preparation of lactones are known[1]; for example, the reactions of 3-hydroxy acids[2] or esters of 3-hydroxy acids[3] with sulfuric acid give saturated γ-lactones.

Recently, we reported a preparation of 2,3-dialkylparasorbic acids from the reaction of 2-alkyl-3-allyl-3-hydroxyalkanoic acids with sulfuric acid[4]. We now report a new synthesis of 4-(1-cycloalkenyl)-4-butanolides **2** from the reaction of the 4-cycloalkylidene-3-hydroxyalkanoic acids **1** with *p*-toluenesulfonic acid.



When a mixture of 4-cyclohexylidene-3-hydroxy-4-butanoic acid (**1 b**) and *p*-toluenesulfonic acid in benzene was refluxed for 8 h, 4-(1′-cyclohexenyl)-4-butanolide (**2b**) was obtained in 88 % yield. The structure of compound **2b** was confirmed by spectral data and microanalyses. The reaction has also

Table. Preparation of 4-(1-Cycloalkenyl)-4-butanolides **2a–i**

Product	n	R^1	R^2	Yield[a] [%]	b.p. [°C]/ torr	Molecular Formula[b]	I.R. (film) $\nu_{C=O}$ [cm^{-1}]	^{1}H-N.M.R. (CCl_4/TMS) δ [ppm]
2a	4	H	H	73	78–82°/3	$C_9H_{12}O_2$ (152.2)	1770	1.3–2.1 (m, 4H, CH_2CH_2); 2.1–2.9 (m, 6H, $CH_2C{=}C \times 2$, CH_2CO); 5.01 (t, $J = 7.4$ Hz, 1H, $CH_2C\underline{H}O$—); 5.92 (br. s, 1H, $CH{=}C$)
2b	5	H	H	88	86–89°/6	$C_{10}H_{14}O_2$ (166.2)	1770	1.3–1.8 (m, 6H, $CH_2 \times 3$); 1.8–2.7 (m, 6H, $CH_2C{=}C \times 2$, CH_2CO); 4.78 (t, $J = 7.1$ Hz, 1H, $CH_2C\underline{H}O$—); 5.75 (br. s, 1H, $CH{=}C$)
2c	5	CH_3	H	78	93–95°/4	$C_{11}H_{16}O_2$ (180.2)	1770	1.24 (d, $J = 6.8$ Hz, 3H, $C\underline{H}_3CH$); 1.4–1.8 (m, 6H, $CH_2 \times 3$); 1.8–2.4 (m, 5H, $CH_2C{=}C \times 2$, $CH_3C\underline{H}$); 4.71 (t, $J = 6.8$ Hz, 1H, $CH_2C\underline{H}O$—); 5.80 (br. s, 1H, $CH{=}C$)
2d	5	CH_3	CH_3	89	116–119°/3	$C_{12}H_{18}O_2$ (194.3)	1760	1.26 [s, 6H, $(CH_3)_2C$]; 1.5–1.9 (m, 6H, $CH_2 \times 3$); 1.9–2.2 (m, 4H, $CH_2C{=}C \times 2$); 4.75 (t, $J = 7.6$ Hz, 1H, $CH_2C\underline{H}O$—); 5.78 (br. s, 1H, $CH{=}C$)
2e	5	C_2H_5	H	79	109–112°/4	$C_{12}H_{18}O_2$ (194.3)	1760	0.99 (t, $J = 6.4$ Hz, 3H, $C\underline{H}_3CH_2$); 1.2–1.9 (m, 8H, $CH_2 \times 4$); 1.9–2.5 (m, 5H, $CH_2C{=}C \times 2$, CHCO); 4.71 (t, $J = 6.6$ Hz, 1H, $CH_2C\underline{H}O$—); 5.72 (br. s, 1H, $CH{=}C$)
2f	5	n-C_3H_7	H	81	112–115°/3	$C_{13}H_{20}O_2$ (208.3)	1765	0.97 (t, $J = 6.4$ Hz, 3H, $C\underline{H}_3CH_2$); 1.1–1.9 (m, 10H, $CH_2 \times 5$); 1.9–2.7 (m, 5H, $CH_2C{=}C \times 2$, CHCO); 4.82 (t, $J = 6.9$ Hz, 1H, $CH_2C\underline{H}O$—); 5.80 (br. s, 1H, $CH{=}C$)
2g	5	i-C_3H_7	H	86	110–113°/4	$C_{13}H_{20}O_2$ (208.3)	1765	0.97 [d, $J = 6.6$ Hz, 6H, $(C\underline{H}_3)_2CH$]; 1.4–1.8 [m, 7H, $CH_2 \times 3$, $(CH_3)_2C\underline{H}$]; 1.8–2.4 (m, 5H, $CH_2C{=}C \times 2$, CHCO); 4.62 (t, $J = 6.7$ Hz, 1H, $CH_2C\underline{H}O$—); 5.79 (br. s, 1H, $CH{=}C$)
2h	6	H	H	78	108–112°/3	$C_{11}H_{16}O_2$ (180.2)	1775	1.2–1.9 (m, 8H, $CH_2 \times 4$); 1.9–2.7 (m, 6H, $CH_2C{=}C \times 2$, CH_2CO); 4.70 (t, $J = 7.1$ Hz, 1H, $CH_2C\underline{H}O$—); 5.92 (t, $J = 7.4$ Hz, 1H, $CH{=}C$)
2i	7	H	H	84	111–113°/2	$C_{12}H_{18}O_2$ (194.3)	1775	1.2–1.9 (m, 10H, $CH_2 \times 5$); 1.9–2.6 (m, 6H, $CH_2C{=}C \times 2$, CH_2CO); 4.79 (t, $J = 7.1$ Hz, 1H, $CH_2C\underline{H}O$—); 5.71 (t, $J = 7.6$ Hz, 1H, $CH{=}C$)

[a] Yields based on **1**.

[b] The microanalyses were in satisfactory agreement with the calculated values (C ±0.36, H ±0.10).

been extended to other 4-cycloalkylidene-3-hydroxyalkanoic acids. As shown in the Table, a variety of 4-(1-cycloalkenyl)-4-butanolides **2** were obtained in good yields. However, when sulfuric acid was used instead of p-toluenesulfonic acid, the yields of products were poor and various unidentified products were obtained.

The reaction products were analyzed by G.L.C. on a Shimadzu Model GC-7A chromatograph using a 3 m × 3 mm glass column of 10% Silicone DC 200 on 60–80 mesh Celite 545. ^{1}H-N.M.R. spectra were obtained using carbon tetrachloride as a solvent on a Hitachi Model R-600 spectrometer. I.R. spectra were obtained on a Jasco Model IR-G infrared spectrophotometer. Mass spectra were obtained on a Hitachi Model RMU-7M mass spectrometer.

4-Cycloalkylidene-3-hydroxyalkanoic Acids 1:

These compounds were prepared from the corresponding aldehydes and carboxylic acids according to Ref.[4].

4-(1-Cycloalkenyl)-4-butanolides 2; General Procedure:

A mixture of the acid **1** (5.0 mmol) and p-toluenesulfonic acid monohydrate (0.19 g, 1.0 mmol) in benzene (50 ml) is refluxed for 8 h. The mixture is cooled to room temperature, washed with 5% sodium carbonate solution (2 × 50 ml) and water (5 × 100 ml), and dried with anhydrous sodium sulfate. The solvent is removed and the residue is chromatographed on a silica gel column [hexane/ethyl acetate, 4:1 (v/v) as an eluent] to afford the product **2**.

Received: April 3, 1984

---

[1] P.A. Grieco, *Synthesis* **1975**, 67.
Y.S. Rao, *Chem. Rev.* **76**, 625 (1976).
S. Masamune, G.S. Bates, J.W. Corcoran, Angew. Chem. **89**, 602 (1977); *Angew. Chem. Int. Ed. Engl.* **16**, 585 (1977).
K.C. Nicolaou, *Tetrahedron* **33**, 683 (1977).
T.G. Back, *Tetrahedron* **33**, 3041 (1977).
T. Mukaiyama, Angew. Chem. **91**, 798 (1979); *Angew. Chem. Int. Ed. Engl.* **18**, 707 (1979).

[2] T. Fujita, K. Suga, S. Watanabe, R. Yanagi, *J. Appl. Chem. Biotechnol.* **27**, 593 (1977).

[3] A. Dobrev, C. Ivanov, *Synthesis* **1977**, 562.

[4] T. Fujita, S. Watanabe, K. Suga, M. Saita, K. Sugahara, *J. Chem Technol. Biotechnol.* **32**, 421 (1982).