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LACTONIZATION OF γ-HALO ESTERS WITH SILICA GEL CATALYST

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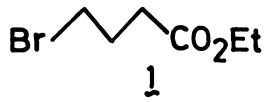
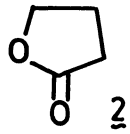
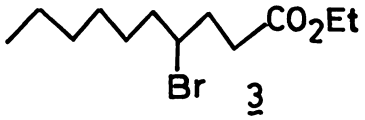
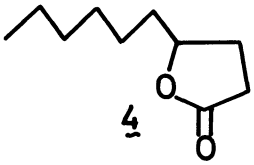
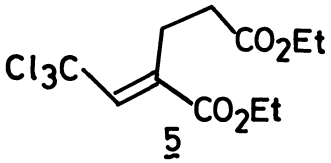
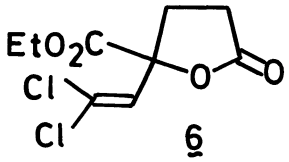
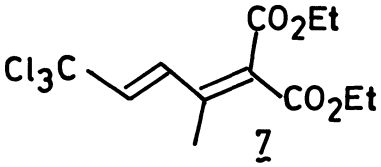
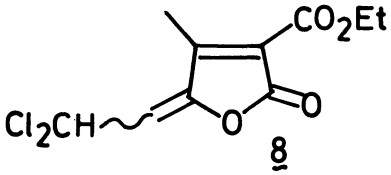
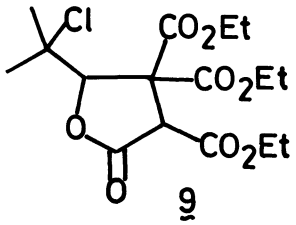
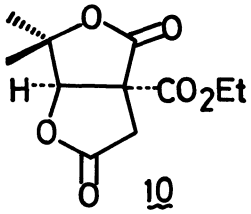
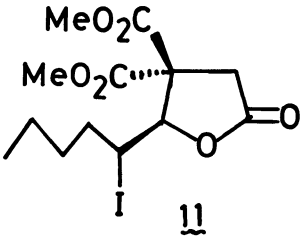
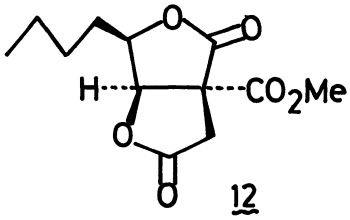
A facile synthesis of γ-butyrolactones by the lactonization of γ-halo esters with silica gel catalyst and its application to the stereoselective synthesis of (±)-canadensolide are described.

The acid-catalyzed lactonization of γ-halo acids is one of representative synthetic methods of γ-butyrolactones, but is not suitable for compounds containing functional groups lable to the hydrolytic conditions since they are usually derived from the corresponding esters.[1] In the course of our studies on the allylic rearrangement of vinylogs of α-halo ketones,[2,3] we found silica gel promotes the lactonization of γ-halo esters under neutral conditions. The present communication describes this simple and convenient method for the preparation of γ-butyrolactones with silica gel catalyst and its application to the synthesis of bis-γ-butyrolactones.

Table I shows several examples of the lactonizations of γ-halo esters with silica gel catalyst. The reaction was carried out by the following procedures. The stirred mixture of γ-halo esters, silica gel[4] (2-6 equiv.), and xylene was heated at the reflux temperature for 3-15 h. After the mixture was filtered, concentration of the filtrate gave a crude product, which was purified by chromatography or distillation. The effectiveness of silica gel catalyst for the lactonization was investigated representatively on the conversion of ethyl 4-bromobutanoate (1) to γ-butyrolactone (2). When the solution of 1 in xylene was heated at the reflux temperature in the presence of silica gel (3.4 equiv.), lactone 2 was obtained in 66% yield. On the other hand, the thermal treatment of 1 in xylene in the absence of silica gel resulted in the recovery of the starting material 1. Although it was reported that the thermal treatment of γ-halo esters without solvents afforded the corresponding γ-butyrolactones in moderate yields, it required more drastic condition (170-180°C) than the present method.[7]

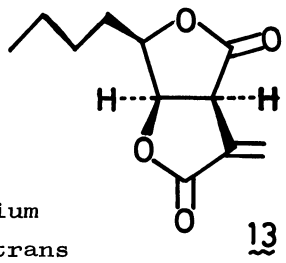
Vinylogs of γ-halo esters such as 5 and 7 were also converted to the corresponding γ-butyrolactones 6 and 8 in 63 and 46% yields, respectively. Furthermore, the present method was adapted to the cyclization of γ-halo esters possessing γ-butyrolactone skeleton. Treatment of the lactone triester 9 with

Table I. Lactonization of γ-Halo Esters and Its Vinylogs Using Silica Gel Catalyst

Halo Esters[a]	γ-Butyrolactones[b]	Yield[c] (%)	Reaction Time (h)
 1	 2	66[d]	15
 3	 4	79[d]	12
 5	 6	63	10
 7	 8	46	3
 9	 10	70	10
 11	 12	78	3

[a] Preparations are outlined in ref 5. [b] Physical data are described in ref 6. [c] Isolated yields unless otherwise noted. [d] Determined by GLC.

silica gel afforded bis-γ-butyrolactone 10 in good yield. The last example is the application of this procedure to the preparation of a key intermediate for the synthesis of (±)-canadensolide (13)[8] which is one of metabolites produced by Penicillium canadense. Lactone diester 11 was treated with silica gel to give exclusively the bis-γ-butyrolactone 12, of which the conversion to 13 has been established in our laboratory.[9]



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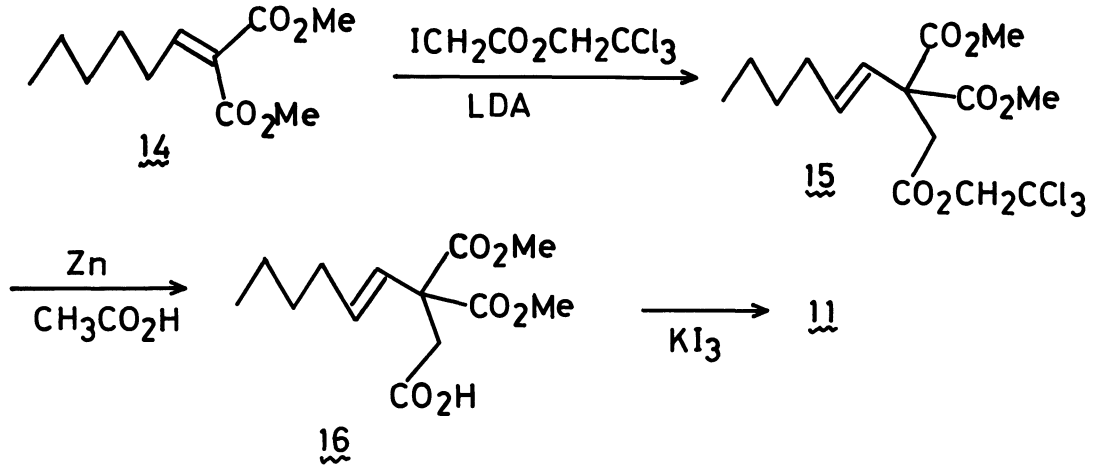
Lactone 11 was prepared according to the following scheme. Alkylation of dimethyl n-hexylidenemalonate 14 with trichloroethyl iodoacetate in the presence of lithium diisopropylamide (LDA) afforded stereospecifically the trans



olefin 15 in 58% yield. Chemoselective hydrolysis of 15 with zinc in acetic acid gave the acid 16 in 53% yield, which was subsequently converted to the lactone 11 as a sole product (63% yield) by the iodolactonization.

The present note provides a operationally convenient, and economical method for the syntheses of γ-butyrolactones with several ester groups.

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1) For example, see: (a) F. F. Blicke, W. B. Wright, Jr., M. F. Zienty, J. Am. Chem. Soc., 63, 2488 (1941). (b) B. M. Trost and M. J. Bogdanowicz, ibid., 95, 2038 (1973).
2) A. Takeda and S. Tsuboi, J. Org. Chem., 35, 2690 (1970).
3) A. Takeda and S. Tsuboi, ibid., 38, 1709 (1973).
4) Silica gel for column chromatography (Wakogel C-200) was used after drying at 200-250°C/20 mmHg for 3 h.

5) Compd 3 was prepared by the known method.[7] Compd 5 was prepared by the reaction of chloral with diethyl α-acetylglutarate in 47% yield (K_2CO_3, THF, 45°C, 12 h): bp 125-130°C/0.1 mmHg. Compd 7 was obtained in 68% yield by the reaction of chloral with $(EtO)_2P(O)CH_2C(CH_3)=C(CO_2Et)_2$ in the presence of NaH: mp 20°C. Compd 9 was prepared by the reaction of 2-chloro-2-methylpropanal with diethyl 2.3-diethoxycarbonylbutanedioate (NaOEt, ethanol, 20 h at 25°C, 1 h at reflux temp). These compds except 1 and 3 are new and show satisfactory spectral (IR and NMR) and analytical properties.

6) Spectral data of γ-butyrolactones.

6: IR (neat) 1790, 1740, 1620 cm^{-1}; ^1H NMR (CCl_4) δ 1.32 (t, 3, J = 7 Hz, $CO_2CH_2C\underline{H}_3$), 2.55 (m, 4, CH_2CH_2), 4.25 (q, 2, J = 7 Hz, $CO_2C\underline{H}_2CH_3$), 6.32 ppm (s, 1, =CH).

8: mp 69-71°C; IR (neat) 1800, 1720, 1620 cm^{-1}; ^1H NMR (CCl_4) δ 1.33 (t, 3, J = 7 Hz, $CO_2CH_2C\underline{H}_3$), 2.45 (s, 3, $=C-CH_3$), 4.30 (q, 2, J = 7 Hz, $CO_2C\underline{H}_2CH_3$), 5.81 (d, 1, J = 10 Hz, $>CHCl_2$), 6.71 ppm (d, 1, J = 10 Hz, =CH).

10: IR (neat) 1800, 1780, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (t, 3, $CO_2CH_2C\underline{H}_3$), 1.50 (s, 3, $(CH_3)_2C<$), 1.55 (s, 3, $(CH_3)_2C<$), 3.02 (d, 1, J = 19 Hz, CH_2CO_2), 3.45 (d, 1, J = 19 Hz, CH_2CO_2), 4.30 (q, 2, J = 7 Hz, $CO_2C\underline{H}_2CH_3$), 4.85 ppm (s, 1, OCH<); ^{13}C NMR ($CDCl_3$) δ 14.0 (q), 22.8 (q), 26.5 (q), 36.3 (t), 58.9 (s), 63.9 (t), 86.3 (d), 86.9 (s), 166.6 (s), 171.6 ppm (s).

12: IR (neat) 1795, 1780, 1740 cm^{-1}; ^1H NMR (CCl_4) δ 0.95 (br t, 3, $C\underline{H}_3CH_2$), 1.5 (m, 4, $CH_3(C\underline{H}_2)_2$), 1.8 (m, 2, $CH_3(CH_2)_2C\underline{H}_2$), 2.85 (d, 1, J = 18 Hz, CH_2CO_2), 3.35 (d, 1, J = 18 Hz, CH_2CO_2), 3.8 (s, 3, CO_2CH_3), 4.75 (m, 1, OC<u>H</u>Bu), 5.05 ppm (d, 1, J = 4 Hz, $>C\underline{H}OCOCH_2$); ^{13}C NMR ($CDCl_3$) δ 13.8 (q), 82.6 (d), 165.6 (s), 171.5 ppm (s).

7) M. S. Kharach, P. S. Skell, and P. Fisher, J. Am. Chem. Soc., 70, 1055 (1948).

8) For the synthesis, see: (a) M. Kato, M. Kageyama, R. Tanaka, K. Kuwahara, and A. Yoshikoshi, J. Org. Chem., 40, 1932 (1975). (b) H. Kosugi, S. Sekiguchi, R. Sekita, and H. Uda, Bull. Chem. Soc. Jpn., 49, 520 (1976). (c) M. Utaka, H. Fujii, M. Iwamoto, M. Meguro, S. Tsuboi, and A. Takeda, the 37th Annual Meeting of the Chemical Society of Japan, Yokohama, April, 1978; Abstr. 2, 853. (d) R. C. Anderson and B. Fraser-Reid, Tetrahedron Lett., 1978, 3233. (e) H. Ohrui, N. Sueda, and H. Kuzuhara, Nippon Kagaku Kaishi, 1981, 769.

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