

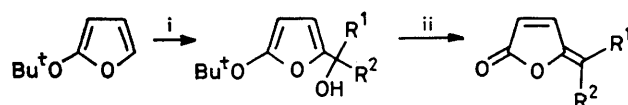
Facile Synthesis of 4-Alkylidenebut-2-enolides by Double Dehydrochlorination of 2,2-Dichloro-4-alkylbutanolides

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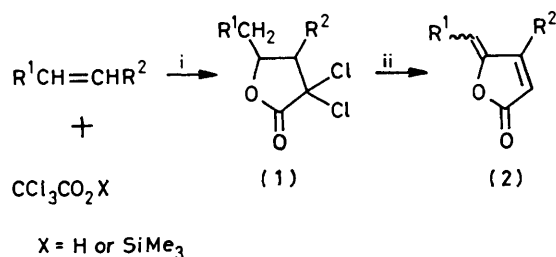
Summary Dehydrochlorination of 2,2-dichloro-4-alkylbutanolides with refluxing pyridine gave 4-alkylidenebut-2-enolides, analogues of protoanemonin.

4-ALKYLIDENE BUT-2-ENOLIDES such as protoanemonin¹ or patulin² are known to possess antibiotic activity. Although much work has been devoted to the synthesis of similar lactones, a general route to this class of compound is still lacking.³



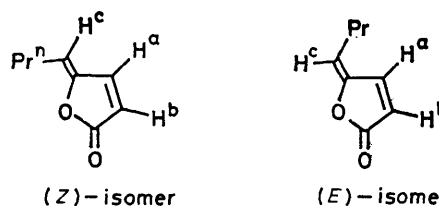
SCHEME 1. Reagents: i, BuⁿLi, then R¹R²CO; ii, *p*-MeC₆H₄SO₃H in tetrahydrofuran-water.

Recently, Kraus and Sugimoto⁴ developed a method of some general applicability illustrated in Scheme 1. We report herein an alternative method which provides a simple one-step synthesis starting from 2,2-dichloro-4-alkylbutanolides⁵ (1) that are readily accessible in quantities (Scheme 2).



SCHEME 2. Reagents: i, [RuCl₂(PPh₃)₃], heat; ii, pyridine, heat.

Typically, a mixture of 2,2-dichloro-4-butyl-4-butanolide (23.6 mmol) and pyridine (72.1 mmol) was heated under reflux for 1 h. G.l.c. of the resulting mixture showed that it consisted of (*Z*)- and (*E*)-4-butyldenebut-2-enolide in the ratio 82:18, formed in nearly quantitative yield. The usual work-up gave a 64% yield of a pure mixture of (*Z*)-



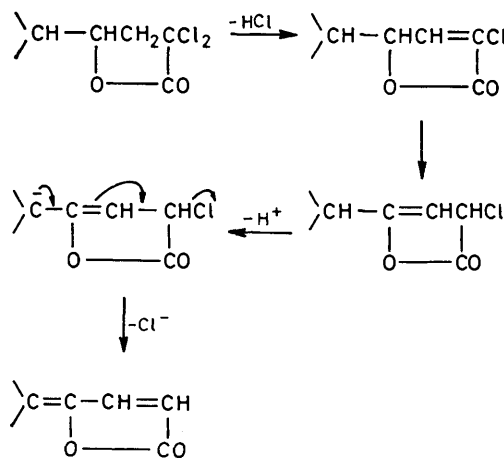
and (*E*)-isomers, b.p. 85 °C at 6 mmHg, which was separated by g.l.c. Structures were assigned on the basis of i.r., mass, and n.m.r. spectroscopy. The ¹H n.m.r. coupling constants

TABLE. Results for the double dehydrochlorination in Scheme 2

Reaction time/h	Butenolide (2)			
	R ¹	R ²	% Yield	Z/E
1	H	n-C ₃ H ₇	64 ^a	82/18
1.5	H	n-C ₄ H ₉	58 ^a	84/16
1	H	n-C ₆ H ₁₁	50 ^a	84/16
1	H	n-C ₈ H ₁₃	50 ^a	84/16
2.5		-[CH ₂] ₃ -	50 ^b	—

^a Isolated yield. ^b Determined by g.l.c.

for the vinylic protons of the (*Z*)- and (*E*)-products were especially useful for structural assignment,⁶ e.g. (*Z*)-4-butyldenebut-2-enolide, δ (CCl₄) (*inter alia*) 7.29 (1H, d, *J* 5.4 Hz,



SCHEME 3

H^a), 6.06 (1H, dd, *J* 5.4 and 0.6 Hz, H^b), and 5.22 (1H, dt, *J* 7.2 and 0.6 Hz, H^c); (*E*)-isomer, δ 7.73 (1H, d, *J* 5.6 Hz, H^a), 6.17 (1H, dd, *J* 5.6 and 1.8 Hz, H^b), and 5.70 (1H, dt, *J* 8.6 and 1.8 Hz, H^c). Other results are summarised in the

Table, which clearly shows the synthetic utility of this reaction. We propose the mechanism in Scheme 3.

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