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A New Method for the Synthesis of 3,5-Disubstituted 2(5*H*)-Furanones. Synthesis of (±)-Acarenoic Acid

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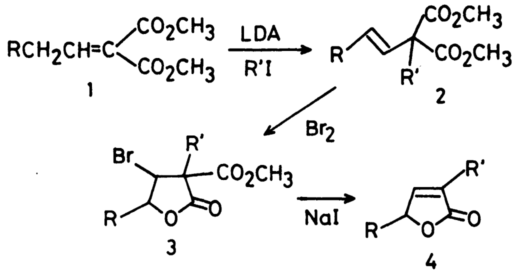
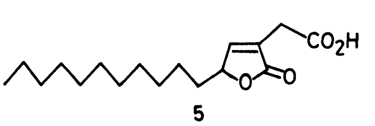
Heating of 3,5-disubstituted 4-bromo-3-methoxycarbonyldihydro-2(3*H*)-furanones with NaI in 3-pentanone gave 3,5-disubstituted 2(5*H*)-furanones in 55.8—93.3% isolated yields. A total synthesis of (±)-acarenoic acid was established in 33% overall yield via 4 steps.

The γ-lactone ring system is a common feature in a wide variety of natural products, and a number of methods are available for its construction.[1] Especially, the synthesis of unsaturated γ-lactones has attracted the attention of organic chemists because of their biological activities and versatile utilization in organic synthesis.[2] In connection with our continuous interest in the chemistry of γ-lactones,[3] we reported a convenient synthesis of enolic δ-lactones with a Wittig reaction.[4]

In a previous paper we reported highly stereo- and regioselective alkylation of alkylidenemalonates **1** giving (3*E*)-2-methoxycarbonyl-2-alkyl-3-alkenoate **2**.[5] Recently, we found that the heating of bromolactonization products **3** with sodium iodide in an appropriate solvent affords 3,5-disubstituted 2(5*H*)-furanones **4** in good yields. This paper describes a new synthesis of **4** and its application for the synthesis of acarenoic acid **5**.[6]





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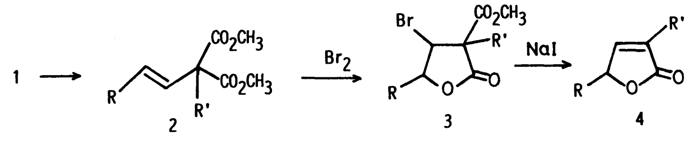
Compound **2** was prepared by the reaction of **1** with alkyl iodide in the presence of lithium diisopropylamide (LDA) as reported previously.[5] Bromolactonization of **2**[5] was carried out in chloroform for 2—3 h at 0 °C and the various alkyl-substituted bromolactones **3** were obtained in 42.3—86.6% yields as shown in Table 1. The stereochemistry of **3** was determined by NOE techniques[7] of ^{1}H NMR. For example, when the 3-methyl protons of **3a** were irradiated, a peak enhancement (5%) was observed for the 4-methine proton, while the irradiation on 5-methine proton did not show any effect for signals due to 3-methyl and 4-methine protons.

Conversion of **3** to 2(5*H*)-furanone **4** was extremely facilitated by heating the 3-pentanone solution of **3** with an excess amount of NaI. Various 3,5-disubstituted 2(5*H*)-furanons **4** were prepared from **3** and the results are tabulated in Table 1. The reaction was completed within 3 days and product **4** was obtained in good isolated yields (55.8—93.3%). Furthermore, the effectiveness of other reagents and solvents for the present reaction was investigated. The conversion of (3*R**, 4*R**, 5*S**)-4-bromo-5-butyl-3-ethoxycarbonylmethyl-3-methoxycarbonyldihydro-2(3*H*)-furanone (**3c**) to **4c** was attempted under various con-

Table 1. Syntheses of Malonates **2**, Bromolactones **3**, and 2(5*H*)-Furanones **4**



No.	R	R′	Yield[a)]/%			Reaction time (d) for **4**
			2	**3**	**4**	
a	C_2H_5	CH_3	63.4	73.7	71.7(89.2)[c)]	2
b	C_2H_5	CH_2CO_2Et	98.4	63.6	71.9	2.5
c	$CH_3(CH_2)_3$	CH_2CO_2Et	88.8	53.0	88.5	2
d	$CH_3(CH_2)_5$	CH_3	95[b)]	42.3	82.4	3
e	$CH_3(CH_2)_5$	$CH_3(CH_2)_3$	61.1	86.6	55.8(92.6)[c)]	2
f	$CH_3(CH_2)_5$	CH_2CO_2Et	86.4	65.1	82.7	2.5
g	$CH_3(CH_2)_{10}$	CH_2CO_2Et	68.8	71.0	93.3	3

a) Isolated yield. b) Previously reported (Ref. 5). c) Yield based on the consumed **3**.

ditions and the results are tabulated in Table 2. Sodium chloride, silica-alumina, silica gel, and alumina were not effective, although KI showed a slight effectiveness. Ethanol, as well as 3-pentanone, was a good solvent for this reaction. Although the reaction in benzene resulted in a recovery of the starting material, that in the presence of 15-crown-5[8] gave **4c** in 50% yield.

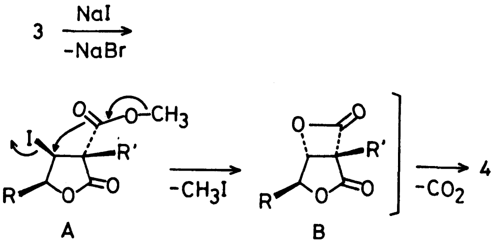
The structure of **4** was elucidated by IR and NMR data and elemental analysis. IR, ^{1}H NMR, and analytical data are given in Table 3. IR absorptions of **4** near 1760 and 1660 cm^{-1} are consistent with the structure of α,β-unsaturated γ-lactone.[3b,9] Signals of olefinic protons appeared at δ 6.8—7.4 as a result of a deshielding effect of the α,β-unsaturated carbonyl system. The ^{13}C NMR spectra of the lactone **4** prepared in this work were measured and tentatively assigned as shown in Table 4. These data afford additional support for assigning the structure of 3,5-disubstituted 2(5*H*)-furanone.

Table 2. Attempts in the Synthesis of **4c** with Various Reagents

Reagent[a)]	Reaction condition		Yield/%[b)]
	Solvent	Time/d	**4**
NaI	3-Pentanone	2	89
NaI	Ethanol	2	80
NaI	Water	2	0[d)]
NaI	Benzene	2	0[d)]
NaI	Benzene—15-crown-5[c)]	2	50
NaI	Xylene	2	0[d)]
KI	3-Pentanone	2	21
NaCl	3-Pentanone	4	0[d)]
SiO_2-Al_2O_3	3-Pentanone	4	0[d)]
SiO_2	3-Pentanone	2	0[d)]
Al_2O_3	3-Pentanone	2	0[d)]

a) A solution of **3c** in a solvent was heated at the reflux temperature in the presence of an excess amount (5—10 equiv) of the reagent. b) Estimated by ^{1}H NMR analysis. c) An equimolar amount of 15-crown-5 to NaI was used. d) The starting material **3c** was recovered.

This novel reaction of the 2(5*H*)-furanone formation can be explained by the following mechanism. Initially, the reaction would start to give iodo lactone **A** by the substitution of the bromine with NaI.[10] The elimination of methyl iodide from **A** would yield unstable β-lactone **B**, which would release carbon dioxide to afford the 2(5*H*)-furanone **4**.

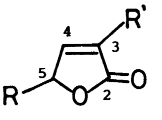


The present reaction was applied for the synthesis of (±)-acarenoic acid **5**, a component of *Acarospora chlorophana*,[6] whose total synthesis has never been reported. Our reaction sequence is shown in Scheme 1. A deconjugative alkylation of dimethyl tridecanylidenemalonate (**1g**) with ethyl iodoacetate afforded, exclusively, ethyl (*E*)-3,3-bis(methoxycarbonyl)-4-

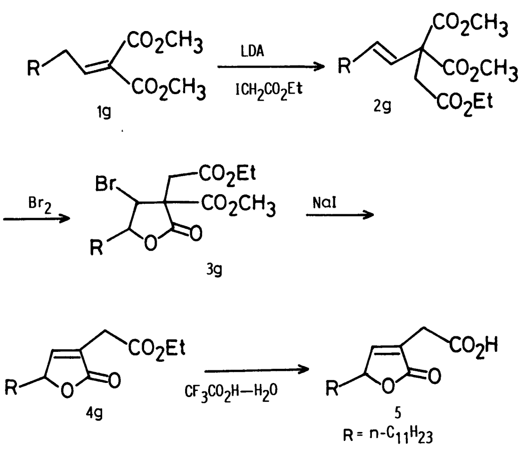
Table 3. Physical and Analytical Data of 2(5*H*)-Furanones **4**

4	IR (neat)	^{1}H NMR	Elemental analysis/% (Calcd)	
	cm^{-1}	(CCl_4, δ/ppm)	C	H
4a	1755, 1659, 1458	0.98 (3H, t, *J*=6Hz, CH_3), 1.26—2.49 (2H, m, $C\underline{H}_2CH_3$), 1.85 (3H, s, =C-CH_3), 4.60—4.96 (1H, m, CHO-), 6.98—7.14 (1H, m, CH=)	66.42 (66.65)	8.19 (7.99)
4b	1763, 1742, 1663	0.99 (3H, t, *J*=7Hz, CH_3), 1.25 (3H, t, *J*=7Hz, $CO_2CH_2C\underline{H}_3$), 1.45—2.03 (2H, m, $C\underline{H}_2CH_3$), 3.21 (2H, s, CH_2CO_2Et), 4.13 (2H, q, *J*=7Hz, CH_2CO_2Et) 4.71—5.05 (1H, m, CHO-), 7.28—7.42 (1H, m, =CH)	60.87 (60.59)	7.27 (7.12)
4c	1761, 1745, 1665	0.93 (3H, t, *J*=6Hz, CH_3), 1.08—2.01 (6H, m, $3CH_2$), 1.26 (3H, t, *J*=7Hz $CO_2CH_2C\underline{H}_3$), 3.11—3.33 (2H, m, CH_2CO_2Et), 4.12 (2H, q, *J*=7Hz, $CO_2C\underline{H}_2CH_3$), 4.71—5.04 (1H, m, CHO-), 7.24—7.40 (1H, m, =CH)	63.81 (63.70)	8.25 (8.02)
4d	1753, 1659, 1465	0.89 (3H, t, *J*=6Hz, CH_3), 1.10—1.77 (10H, m, $5CH_2$), 1.86 (3H, s, =$CHCH_3$), 4.59—4.93 (1H, m, CHO-), 6.89—7.04 (1H, m, =CH)	72.29 (72.49)	9.76 (9.95)
4e	1755, 1650, 1464	0.66—1.12 (6H, m, $2CH_3$), 1.12—1.94 (14H, m, $7CH_2$), 2.02—2.42 (2H, m, =$CHC\underline{H}_2$), 4.54—4.92 (1H, m, CHO-), 6.83—7.00 (1H, m, =CH)	75.06 (74.95)	10.66 (10.78)
4f	1760, 1740, 1660	0.89 (3H, t, *J*=5Hz, CH_3), 1.29 (3H, t, *J*=7Hz, $CO_2CH_2C\underline{H}_3$), 1.10—1.96 (10H, m, $5CH_2$), 3.21 (2H, s, CH_2CO_2Et), 4.14 (2H, q, *J*=7Hz, $CO_2C\underline{H}_2CH_3$), 4.63—5.08 (1H, m, CHO-), 7.32—7.45 (1H, m, =CH)	66.07 (66.12)	8.73 (8.72)
4g	1760, 1742, 1660	0.88 (3H, t, *J*=5Hz, CH_3), 1.06—1.81 (20H, m, $10CH_2$), 3.15—3.29 (2H, m, $C\underline{H}_2CO_2Et$), 4.13 (2H, q, *J*=7Hz, $CO_2C\underline{H}_2CH_3$), 4.70—5.04 (1H, m, CHO-), 7.17—7.39 (1H, m, =CH)	70.42 (70.33)	9.85 (9.94)

Table 4. ^{13}C NMR Data of 2(5*H*)-Furanones **4**



4	C2(s)	C3(s)	C4(d)	C5(d)	R	R′ (CH_3 or CH_2CO_2Et)
4a	174.4	130.1	148.5	82.1	9.1(q), 26.6(t)	10.6(q)
4b	173.0	127.2	151.3	82.7	8.9(q), 26.1(t)	14.1(q), 33.5(t), 61.2(t), 169.4(s)
4d	174.3	129.7	148.9	81.2	14.0(q), 22.5(t), 25.0(t), 29.0(t), 31.6(t), 30.5(t)	10.5(q)
4f	173.0	126.9	151.6	81.8	14.0(q), 22.5(t), 24.9(t), 29.0(t), 31.6(t), 30.5(t)	14.0(q), 33.3(t), 61.2(t), 169.4(s)
4g	173.0	126.9	151.5	81.8	14.1(q), 22.7(t), 25.0(t), 29.3(t), 29.6(t), 30.5(t), 31.9(t)	14.1(q), 33.3(t), 61.2(t), 169.4(s)



Scheme 1.

hexadecenoate (**2g**) in 68.8% yield; this was subsequently brominated to give (3*R**, 4*R**, 5*S**)-4-bromo-3-ethoxycarbonylmethyl-3-methoxycarbonyl-5-undecyl-dihydro-2(3*H*)-furanone (**3g**) in 71.0% yield. A treatment of **3g** with 6 equiv of NaI gave (±)-ethyl acarenoate (**4g**) in 93.3% yield and the hydrolysis of **4g** with trifluoroacetic acid-water afforded acarenoic acid **5**[6] in 73% yield.

The present method provides a convenient route to 3,5-disubstituted 2(5*H*)-furanones because of the availability of the starting material, the simplicity of the experiment, and no use of a heavy metal.

Experimental

The melting and boiling points are uncorrected. Infrared (IR) spectra were obtained with a JASCO Model A-102 infrared spectrophotometer. ^{1}H NMR spectra (60 MHz) were recorded with a JEOL JNM-PMX 60SI apparatus. ^{13}C NMR spectra (25 MHz) were obtained with a JEOL JNM-FX100 apparatus, using $CDCl_3$ as a solvent. NOE experiments were conducted on a deoxygenated sample with a Varian VXR 300 spectrometer. Column chromatography was accomplished with a 100—200 mesh Wakogel C-200. 3-Pentanone was dried over $CaCl_2$ and distilled prior to use. Commercial first-grade aldehydes were distilled prior to use. Ethyl iodoacetate was obtained by a reaction of ethyl bromoacetate with NaI.[10]

Alkylidenemalonates **1** were prepared according to procedures reported in the literature.[11] Compounds, boiling points, and yields are as follows: **1a** ($R=C_2H_5$), bp 77.5—80 °C/3 Torr (1 Torr=133.322 Pa), **1c** ($R=n\text{-}C_4H_9$),[5,11] bp 102 °C/2 Torr, 76%; **1d** ($R=n\text{-}C_6H_{13}$), bp 118—120 °C/2 Torr, 80%; **1g** ($R=n\text{-}C_{11}H_{23}$),[12] 42%.

Compound **2** was prepared according to procedures reported previously.[5] The following exemplifies the synthesis of **2**.

Methyl (*E*)-2-Methoxycarbonyl-2-methyl-3-hexenoate (2a). To a stirred solution of 0.90 ml (6.40 mmol) of diisopropylamine in 6 ml of dry THF was added dropwise 4.1 ml (6.51 mmol) of 1.6 M (1M=1 mol dm^{-3}) butyllithium in hexane at 0 °C. After 20 min, 2.8 ml of HMPA was added, and then the mixture was cooled to −78 °C. Dimethyl butylidenemalonate (1.0 g, 5.38 mmol) was added dropwise and the mixture was stirred for 30 min. After the dropwise addition of methyl iodide (1.43 g, 10.1 mmol), the mixture was allowed to warm up to room temperature for 1 h and was then heated under reflux for 30 min. It was cooled to room temperature, and poured into ice water. The organic material was extracted with ethyl acetate and the combined extracts were washed with dilute HCl and water, and dried over $MgSO_4$. Removal of the solvent gave 0.987 mg of an oil, which was purified by bulb-to-bulb distillation to give 0.682 mg (63.4%) of **2a**: bp 130 °C/7 Torr; IR (neat) 2970 and 1740 cm^{-1}; ^{1}H NMR (CCl_4) δ=1.02 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.45 (3H, s, CCH_3), 1.87—2.44 (2H, m, $C\underline{H}_2CH_3$), 3.65 (6H, s, $2CO_2CH_3$), 5.40 (1H, dt, J=15.5 Hz, $CH_2C\underline{H}{=}CH$), and 5.81 (1H, d, J=16 Hz, $CH_2CH{=}CH$). Found: C, 59.92; H, 7.88%. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05%.

Ethyl (*E*)-3,3-Bis(methoxycarbonyl)-4-undecenoate (2f). Dimethyl octylidenemalonate (1.0 g, 4.13 mmol) was treated with LDA and allowed to react with ethyl iodoacetate (1.65 g, 7.77 mmol) as described above. The standard work-up gave 1.57 g of the crude product, which was purified by column chromatography (SiO_2, hexane–ethyl acetate, 30 : 1—5 : 1) to afford 1.17 g (86.4%) of **2f**: TLC (SiO_2; hexane-ethyl acetate, 4 : 1), R_f 0.33; IR (neat) 2950 and 1740 cm^{-1}; ^{1}H NMR (CCl_4) δ=0.89 (3H, t, J=5 Hz), 1.10—1.58 (11H, m, $4CH_2$, $CO_2CH_2C\underline{H}_3$), 1.96—2.36 (2H, m, $C\underline{H}_2CH{=}$), 3.01 (2H, s, $C\underline{H}_2CO_2Et$), 3.69 (6H, s, $2CO_2CH_3$), 4.04 (2H, q, J=8 Hz, $CO_2C\underline{H}_2CH_3$), 5.42 (1H, dt, J=15 and 5.5 Hz, $CH_2C\underline{H}{=}$

and 5.95 (1H, d, J=15 Hz, $\mathrm{CH_2CH{=}C\underline{H}}$).

Other compounds **2** were also prepared by the same procedures as described above.

2b: TLC ($\mathrm{SiO_2}$; hexane-ethyl acetate, 4 : 1), R_f 0.29; IR (neat) 1740 cm^{-1}. ^{1}H NMR ($\mathrm{CCl_4}$) δ=1.01 (3H, t, J=7 Hz, $\mathrm{C\underline{H}_3CH_2}$), 1.22 (3H, t, J=7 Hz, $\mathrm{CO_2CH_2C\underline{H}_3}$), 1.86—2.37 (2H, m, $\mathrm{CH_3C\underline{H}_2}$), 3.00 (2H, s, $\mathrm{C\underline{H}_2CO_2Et}$), 3.70 (6H, s, $\mathrm{2CO_2CH_3}$), 4.05 (2H, q, J=7 Hz, $\mathrm{CO_2C\underline{H}_2CH_3}$), 5.47 (1H, dt, J=16 and 6 Hz, $\mathrm{CH_2C\underline{H}{=}CH}$), and 5.95 (1H, d, J=16 Hz, $\mathrm{CH_2CH{=}C\underline{H}}$). Found: C, 57.51; H, 7.40%. Calcd for $\mathrm{C_{13}H_{20}O_6}$: C, 57.34; H, 7.40%.

2c: Bp 170 °C/4 Torr (bulb-to-bulb distillation); IR (neat) 2990, 1748, 1735, 1650, and 1438 cm^{-1}; ^{1}H NMR ($\mathrm{CCl_4}$) δ=0.88 (3H, t, J=6 Hz, $\mathrm{(CH_2)_3C\underline{H}_3}$), 1.05—1.53 (4H, m, $\mathrm{2CH_2}$), 1.20 (3H, t, J=7 Hz, $\mathrm{CO_2CH_2C\underline{H}_3}$), 1.85—2.66 (2H, m, $\mathrm{C\underline{H}_2CH{=}}$), 2.98 (2H, s, $\mathrm{C\underline{H}_2CO_2Et}$), 3.66 (6H, s, $\mathrm{2CO_2CH_3}$), 4.01 (2H, q, J=7 Hz, $\mathrm{CO_2C\underline{H}_2CH_3}$), 5.40 (1H, dt, J=16 and 5.5 Hz, $\mathrm{CH_2C\underline{H}{=}CH}$), and 5.92 (1H, d, J=16 Hz, $\mathrm{CH_2CH{=}C\underline{H}}$).

2e: TLC ($\mathrm{SiO_2}$; hexane-ethyl acetate, 4 : 1), R_f 0.53; IR (neat) 1742, 1460, 1436, and 1380 cm^{-1}; ^{1}H NMR ($\mathrm{CCl_4}$) δ=0.89 (3H, t, J=5 Hz, $\mathrm{C\underline{H}_3CH_2}$), 1.08—1.70 (12H, m, $\mathrm{6CH_2}$), 1.70—2.42 (4H, m, $\mathrm{2CH_2}$), 3.65 (6H, s, $\mathrm{2CO_2CH_3}$), 5.38 (1H, dt, J=15 and 5.5 Hz, $\mathrm{CH_2C\underline{H}{=}CH}$), and 5.86 (1H, d, J=15 Hz, $\mathrm{CH_2CH{=}C\underline{H}}$). Found: C, 68.14; H, 10.09%. Calcd for $\mathrm{C_{17}H_{30}O_4}$: C, 68.42; H, 10.13%.

2g: TLC ($\mathrm{SiO_2}$; hexane-ethyl acetate, 4 : 1), R_f 0.41; IR (neat) 2950, 1745, 1460, and 1435 cm^{-1}; ^{1}H NMR ($\mathrm{CCl_4}$) δ=0.88 (3H, t, J=4 Hz, $\mathrm{(CH)_{10}C\underline{H}_3}$), 1.03—1.53 (18H, m, $\mathrm{9CH_2}$), 1.80—2.25 (2H, m, $\mathrm{CH_2}$), 2.99 (2H, s, $\mathrm{C\underline{H}_2CO_2Et}$), 3.68 (6H, s, $\mathrm{2CO_2CH_3}$), 4.02 (2H, q, J=7 Hz, $\mathrm{CO_2C\underline{H}_2CH_3}$), 5.40 (1H, dt, J=15 and 6 Hz, $\mathrm{CH_2C\underline{H}{=}}$), and 5.92 (1H, d, J=15 Hz, $\mathrm{CH_2CH{=}C\underline{H}}$). Found: C, 66.36; H, 9.57%. Calcd for $\mathrm{C_{22}H_{38}O_6}$: C, 66.30; H, 9.61%.

(3*R, 4*R**, 5*S**)-4-Bromo-3-methoxycarbonyl-5-ethyl-3-methyldihydro-2(3*H*)-furanone (3a).** To a solution of **2a** (0.3 g, 1.5 mmol) in chloroform (2.6 ml) was added dropwise bromine (0.264 g, 1.65 mmol) at 0 °C. After the mixture had been stirred for 2.5 h, the solvent was evaporated to give 435 mg of the crude product which crystallized on standing for 1 d. Recrystallization from hexane afforded 0.293 g (73.7%) of **3a**: mp 86.3—87.2 °C; IR (KBr) 2970, 1790, 1742, 1443, and 1428 cm^{-1}; ^{1}H NMR ($\mathrm{CDCl_3}$) δ=1.11 (3H, t, J=7 Hz, $\mathrm{CH_2C\underline{H}_3}$), 1.50 (3H, s, $\mathrm{CH_3}$), 1.39—2.30 (2H, m, $\mathrm{C\underline{H}_2CH_3}$), 3.78 (3H, s, $\mathrm{CO_2CH_3}$), 3.83 (1H, d, J=8 Hz, CHBr), and 4.46—4.88 (1H, m, CH-O); ^{13}C NMR ($\mathrm{CDCl_3}$) δ=9.7 (q, $\mathrm{CH_2\underline{C}H_3}$), 18.1 (q, $\mathrm{C_3{-}\underline{C}H_3}$), 25.1 (t, $\mathrm{\underline{C}H_2CH_3}$), 51.7 (d, CHBr), 53.1 (q, $\mathrm{CO_2\underline{C}H_3}$), 57.0 (s, $\mathrm{C_3}$), 84.7 (d, $\mathrm{C_5}$), 167.2 (s, $\mathrm{\underline{C}O_2CH_3}$), and 172.0 (s, $\mathrm{C_2}$). Found: C, 40.75; H, 4.99%. Calcd for $\mathrm{C_9H_{13}BrO_4}$: C, 40.78; H, 4.94%.

(3*R, 4*R**, 5*S**)-4-Bromo-3-ethoxycarbonylmethyl-5-ethyl-3-methoxycarbonyldihydro-2(3*H*)-furanone (3b).** To a solution of **2b** (0.509 g, 1.87 mmol) in chloroform (3 ml) was added dropwise bromine (0.33 g, 2.06 mmol) at 0 °C. The mixture was stirred for 3 h and the solvent was removed in vacuo. The crude product (0.688 g) was chromatographed on $\mathrm{SiO_2}$ (hexane-ethyl acetate, 10 : 1—5 : 1) to give 0.401 g (63.6%) of **3b**: TLC ($\mathrm{SiO_2}$; hexane-ethyl acetate, 4 : 1), R_f 0.31; IR (neat) 3000, 1790, 1750, 1730, 1460, and 1435 cm^{-1}; ^{1}H NMR ($\mathrm{CCl_4}$) δ=1.24 (3H, t, J=6 Hz, $\mathrm{CH_2C\underline{H}_3}$), 1.27 (3H, t, J=7 Hz, $\mathrm{CO_2CH_2C\underline{H}_3}$), 1.56—2.19 (2H, m, $\mathrm{C\underline{H}_2CH_3}$), 2.79 (1H, d, J=18 Hz, $\mathrm{CH_2}$), 3.81 (3H, s, $\mathrm{CO_2CH_3}$), 4.14 (2H, q, J=7 Hz, $\mathrm{CO_2C\underline{H}_2CH_3}$), and 4.46—4.80 (2H, m, BrCHCHO-). Found: C, 42.65; H, 5.04%. Calcd for $\mathrm{C_{12}H_{17}BrO_6}$: C, 42.75; H, 5.08%.

Other compounds **3** were prepared by the same procedures as those described for **3b**.

3c: IR (neat) 2975, 1792, 1755, 1731, 1435, and 1402 cm^{-1}; ^{1}H NMR ($\mathrm{CCl_4}$) δ=0.97 (3H, t, J=5 Hz, $\mathrm{CH_2C\underline{H}_3}$), 1.13—2.10 (8H, m, $\mathrm{CH_3(C\underline{H}_2)_3}$, $\mathrm{C\underline{H}_2CO_2}$), 1.27 (3H, t, J=7 Hz, $\mathrm{CO_2CH_2C\underline{H}_3}$), 2.77 (1H, d, J=18 Hz, $\mathrm{C\underline{H}_2CO_2Et}$), 3.15 (1H, d, J=18 Hz, $\mathrm{C\underline{H}_2CO_2Et}$), 3.76 (3H, s, $\mathrm{CO_2CH_3}$), 4.12 (2H, q, J=7 Hz, $\mathrm{CO_2C\underline{H}_2CH_3}$), and 4.40—4.84 (2H, m, CHBrCHO). Found: C, 46.17; H, 5.74%. Calcd for $\mathrm{C_{14}H_{21}BrO_6}$: C, 46.04; H, 5.80%.

3d: Mp 76.5—78.0 °C (hexane): IR (KBr) 2940, 1910, 1749, 1209, and 1108 cm^{-1}; ^{1}H NMR ($\mathrm{CDCl_3}$) δ=0.89 (3H, t, J=5 Hz, $\mathrm{(CH_2)_5C\underline{H}_3}$), 1.10—2.24 (10H, m, $\mathrm{5CH_2}$), 1.52 (3H, s, $\mathrm{CH_3}$), 3.69 (3H, s, $\mathrm{CO_2CH_3}$), 3.69 (1H, d, J=10 Hz, CHBr), and 4.42—4.93 (1H, m, CHO-). Found: C, 48.86; H, 6.60%. Calcd for $\mathrm{C_{13}H_{21}BrO_4}$: C, 48.61; H, 6.59%.

3e: TLC ($\mathrm{SiO_2}$; hexane-ethyl acetate, 4 : 1), R_f 0.54; IR (neat) 2950, 1789, 1755, 1460, and 1431 cm^{-1}; ^{1}H NMR ($\mathrm{CCl_4}$) δ=0.72—1.15 (6H, m, $\mathrm{2CH_3}$), 1.15—2.20 (16H, m, $\mathrm{8CH_2}$), 3.77 (3H, s, $\mathrm{CO_2CH_3}$), 3.90 (1H, d, J=8 Hz, CHBr), and 4.30—4.75 (1H, m, CHO-). Found: C, 52.89; H, 7.54%. Calcd for $\mathrm{C_{16}H_{27}BrO_4}$: C, 52.90; H, 7.49%.

3f: TLC ($\mathrm{SiO_2}$; hexane-ethyl acetate, 4 : 1), R_f 0.61; IR (neat) 2950, 1788, 1752, 1729, 1460, and 1375 cm^{-1}; ^{1}H NMR ($\mathrm{CCl_4}$) δ=0.91 (3H, t, J=5 Hz, $\mathrm{(CH_2)_5C\underline{H}_3}$), 1.10—2.06 (10H, m, $\mathrm{5CH_2}$), 1.27 (3H, t, J=6 Hz, $\mathrm{CO_2CH_2C\underline{H}_3}$), 2.79 (1H, d, J=18 Hz, $\mathrm{C\underline{H}_2CO_2Et}$), 3.16 (1H, d, J=18 Hz, $\mathrm{C\underline{H}_2CO_2Et}$), 3.70 (3H, s, $\mathrm{CO_2CH_3}$), 4.13 (2H, q, J=7 Hz, $\mathrm{CO_2C\underline{H}_2CH_3}$), and 4.48—4.70 (2H, m, BrCHCHO-). Found: C, 48.81; H, 6.39%. Calcd for $\mathrm{C_{16}H_{25}BrO_6}$: C, 48.87; H, 6.41%.

3g: 71.0% yield; TLC (hexane-ethyl acetate, 4 : 1), R_f 0.46; IR (neat) 2940, 1781, 1755, and 1735 cm^{-1}; ^{1}H NMR ($\mathrm{CCl_4}$) δ=0.89 (3H, t, J=5 Hz, $\mathrm{CH_3}$), 1.1—2.0 (25H, m, $\mathrm{(C\underline{H}_2)_{10}CH_3}$ and $\mathrm{C\underline{H}_2CO_2Et}$), 2.78 (1H, d, J=18 Hz, $\mathrm{C\underline{H}_2CO_2Et}$), 3.14 (1H, d, J=18 Hz, $\mathrm{C\underline{H}_2CO_2Et}$), 3.78 (3H, s, $\mathrm{CO_2CH_3}$), 4.12 (2H, q, J=7 Hz, $\mathrm{CO_2C\underline{H}_2CH_3}$), and 4.46—4.71 (2H, m, CHBrCHO-). Found C, 54.23; H, 7.51%. Calcd for $\mathrm{C_{21}H_{35}BrO_6}$: C, 54.43; H, 7.61%.

Some representative syntheses of 2(5*H*)-furanones **4** are shown below.

5-Ethyl-3-methyl-2(5*H*)-furanone (4a). Sodium iodide (275 mg, 1.83 mmol) was charged in a 10 ml two-necked flask and dried in vacuo. A solution of **3a** (81 mg, 0.31 mmol) in 3-pentanone (3 ml) was added and the mixture was heated at the reflux temperature under a nitrogen atmosphere. After 2 d it was poured into ice water and the organic material was extracted with ethyl acetate and the combined extracts were washed with 5% sodium thiosulfate and water, and dried over $\mathrm{MgSO_4}$. Removal of the solvent gave 63 mg of the crude product which was chromatographed on $\mathrm{SiO_2}$ (hexane-ethyl acetate, 30 : 1—5 : 1). The early fractions gave 15 mg of the starting material **3a**. The later fractions gave 28 mg (72%) (89% based on the consumed **3a**) of **4a**. Spectral and analytical data are shown in Table 3.

3-Ethoxycarbonylmethyl-5-butyl-2(5*H*)-furanone (4c). As shown in **4a**, a stirred mixture of **3c** (200 mg, 0.55 mmol), NaI (495 mg, 3.30 mmol), and 3-pentanone (3 ml) was heated at the reflux temperature under a nitrogen atmosphere for 2.5 d. Column chromatography ($\mathrm{SiO_2}$; hexane-ethyl acetate, 10 : 1) of the crude product gave 110 mg (88.5%) of **4c**: TLC ($\mathrm{SiO_2}$; hexane-ethyl acetate, 4 : 1), R_f 0.16. Spectral and analytical data are shown in Table 3.

3-Ethoxycarbonylmethyl-5-undecyl-2(5*H*)-furanone (4g). As shown in **4a**, a mixture of **3g** (200 mg, 0.43 mmol), NaI (387 mg, 2.58 mmol), and 3-pentanone (3 ml) was refluxed with stirring under a nitrogen atmosphere. Column chromatography (SiO_2; hexane-ethyl acetate, 15 : 1—10 : 1) gave 130 mg (93.3%) of **4g**: TLC (SiO_2; hexane-ethyl acetate, 4 : 1), R_f 0.23. Spectral and analytical data are shown in Table 3.

(±)-Acarenoic Acid (5). A mixture of **4g** (45 mg, 0.14 mmol), trifluoroacetic acid (1 ml), and water (2 ml) was stirred for 2 d and then poured into water. The organic material was extracted with dichloromethane, washed with water, and dried over $MgSO_4$. Evaporation of the solvent gave 50 mg of the crude product which was purified by preparative TLC (SiO_2; hexane-ethyl acetate, 4 : 1). The component of R_f 0.23 gave 12 mg of **4g**. The component of R_f 0—0.13 gave 22 mg (53%) (73% based on the consumed **4g**) of **5**: mp 83.8—84.2 °C (from benzene) (lit,[6] 144—146.5 °C for (−)-**5**); IR (KBr) 2925, 1738, 1708, 1655, 1390, 1298, and 1083 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta=0.88$ (3H, t, $J=5$ Hz, $(CH_2)_{10}C\underline{H}_3$), 1.04—1.95 (20H, m, $10CH_2$), 3.38 (2H, s, $C\underline{H}_2CO_2H$), 4.80—5.11 (1H, m, CHO-), 7.35 (1H, s, CH=C), and 8.94 (1H, br. s, CO_2H); ^{13}C NMR ($CDCl_3$) $\delta=14.0$ (q), 22.6 (t), 25.0 (t), 29.3 (t), 29.5 (t), 31.7 (t), 31.9 (t), 33.2 (t), 82.1 (d), 126.3 (s), 152.0 (d), 173.1 (s), and 184.2 (s).

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