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SYNTHESIS OF CYCLIC AND ACYCLIC β,γ-UNSATURATED CARBOXYLIC ACIDS VIA AN E_1-TYPE IONIZATION/ELIMINATION OF β-LACTONES

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Abstract

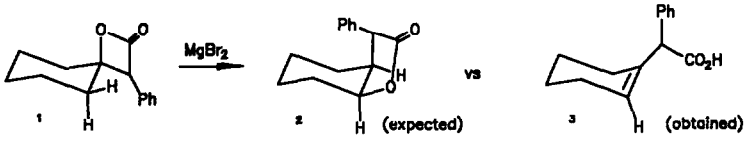
Cyclic and acyclic ketones were converted in three steps into 3-alkenoic acids, bearing a variety of substituents in the α-position. The sequence, involving ionization/elimination of a β-lactone, affords high yields of pure products uncontaminated with conjugated isomers. Support for an E1-type mechanism is also provided.

Introduction

Unsaturated carboxylic acids occupy a position of considerable importance in synthetic and natural products chemistry.[1] Although conjugated species are most common, 3-alkenoic acids are also encountered in natural sources. In addition, they comprise valuable synthetic intermediates to other functionalities. Specifically, cyclic cases (i.e., 1-cycloalkenyl acetic acid derivatives)[2] have served as substrates for halo- and selenolactonizations,[3] vinylogous Wolff rearrangements,[4] cycloadditions,[5] and as precursors to naturally-occurring[6] and other[7] butyrolactones. They also have been employed commercially as precursors to insecticides and herbicides[8] and as antirust/antiwear compounds.[9]

Acyclic 3-alkenoic acids are useful in pheromone chemistry,[1] especially when the olefin is trisubstituted. Many methods are available for the synthesis of trisubstituted alkenes,[10] but most are incapable of affording carboxylic acids directly.[11] Also, the synthesis of non-conjugated acids is considerably more difficult[12] than that of their conjugated counterparts.[13]

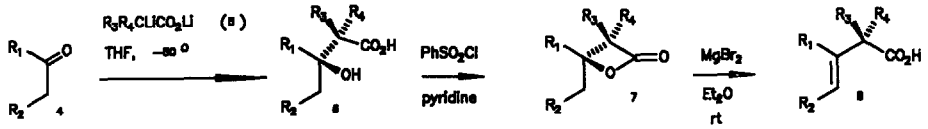
As part of our investigation[14] of β-lactone rearrangements as applied to organic synthesis, we prepared the spiro lactone 1, anticipating that, by analogy to non-spiro cases, the adjacent axial protons would be ideally situated for magnesium-catalyzed rearrangement to the corresponding cis-fused butyrolactone 2. We were most surprised, then, to discover that the sole product of the reaction was the β,γ-unsaturated acid 3. Further examination of this result has revealed the reaction to be quite general - it is applicable to both spiro and acyclic cases, compatible with a wide variety of substituents, and completely stereoselective with regard to position of the alkene bond. We report herein the full details of this method,[15] including a rationale for the reaction course.



Results and Discussion

Our primary goals in this investigation were to define the scope and limitations of the method and to determine the structural features responsible for the reaction pathway. The synthetic sequence is outlined in Scheme A, and yield data for intermediates and final products are arranged

SCHEME A



in the Table. We first prepared a large number of cyclohexanone-derived ß-lactones[16] bearing a variety of alpha substituents (7c-i); we were

Table

Yield Data for α-Substituted ß,γ-Unsaturated Acid Synthesis

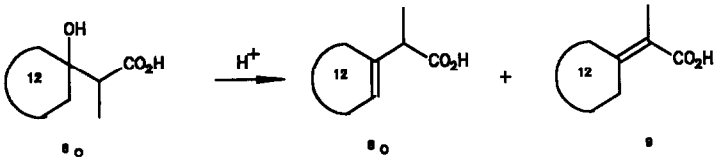
	R_1	R_2	R_3	R_4	Yield (%) 6	7	8		R_1	R_2	R_3	R_4	Yield (%) 6	7	8
a	$-(CH_2)_3-$		Me	H	42	51	75	n	$-(CH_2)_6-$		Et	H	86	95	99
b	$-(CH_2)_3-$		Me	Me	73	74	75	o	$-(CH_2)_{10}-$		Et	H	81	98	71
c	$-(CH_2)_4-$		Me	H	63	96	99	p	$-(CH_2)_{10}-$		Me	Me	62	98	71
d	$-(CH_2)_4-$		Et	H	66	89	80	q	Me	Me	Me	H	85	100	94
e	$-(CH_2)_4-$		Ph	H	95	80	74	r	Me	Et	Me	H	62	51	64
f	$-(CH_2)_4-$		PhS	H	84	74	80	s	Me	Pr	Me	H	93	85	74
g	$-(CH_2)_4-$		*	H	60	40	93	t	Me	n-Bu	Me	H	84	94	100
h	$-(CH_2)_4-$		**	H	92	84	92	u	Me	C_5H_{11}	Me	H	100	80	56
i	$-(CH_2)_4-$		Me	Me	67	94	74	v	Et	Me	Me	H	93	99	60
j	$-(CH_2)_5-$		Me	H	71	92	70	w	Et	Me	Ph	H	88	95	83
k	$-(CH_2)_5-$		Et	H	55	91	85	x	Pr	Et	Me	H	98	63	100
l	$-(CH_2)_5-$		Me	Me	70	65	93	y	n-Bu	Pr	Me	H	50	67	100
m	$-(CH_2)_6-$		Me	H	80	93	84	z	Et	Pr	Me	H	100	79	77
								aa	Et	n-Bu	Me	H	96	70	90

(*=1-naphthyl; **=p-methoxyphenyl)

particularly interested in aromatic groups, which might favor the formation of conjugated alkene isomers. Various ring sizes, from five-membered (7a,b) to twelve-membered (7o,p) were also examined in order to detect any conformational factors which might have been operative in the cyclohexanone cases. Finally, a series of acyclic ketones (4q-aa) was employed as precursors to further test the reaction generality and to probe the regio- and stereoselectivity of the alkene formation step.

The reaction sequence is operationally very straightforward and rapid. The ketone 4 was added at -50 °C to a solution of the dianion 5 (derived from a substituted acetic acid), affording the corresponding ß-hydroxy acid 6. This was dehydrated to the ß-lactone 7, whereupon exposure to anhydrous magnesium bromide in ether for six hours effected the rearrangement to the unsaturated acid 8. The ß-lactones must be promptly carried on to the last step, since their tendency towards thermally-induced decarboxylation precludes a lengthy storage time.

In no case was any isomeric (conjugated) alkene product detected. This is significant, since earlier synthetic approaches often have necessitated difficult purifications and/or a separate deconjugation step.[17] As a point of comparison, ß-hydroxy acid 6o was treated with a catalytic amount of p-toluenesulfonic acid in refluxing toluene for 48 hours, generating a 47:53 mixture of alkene isomers 8o and its conjugated isomer 9 (determined by



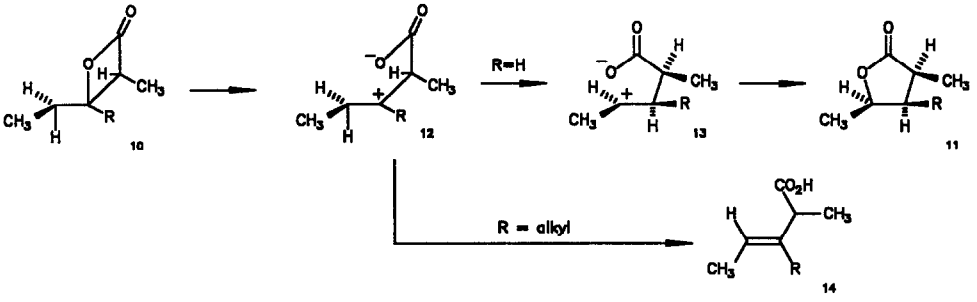
8o 8o 9

proton NMR).

A principal motivation behind the study of acyclic ketones 4q-aa was to assess the regiospecificity of the alkene-forming reaction. In all cases derived from methyl ketones (4q-u), elimination occurred exclusively toward the more highly substituted carbon atom.

We were also intrigued by the possible reasons for this unexpected reaction, especially in view of the profound contrast with earlier reactions involving structurally similar molecules (see Scheme B). Earlier work from our laboratory has established that ß-lactones derived from aldehydes, e.g., 10 (R=H), rearrange to butyrolactones 11 (R=H) under the influence of magnesium bromide; the ring expansion is accompanied by a highly stereoselective migration of an attached hydride or alkyl group into the lactone ring.[14] A truly concerted mechanism for the reaction is untenable

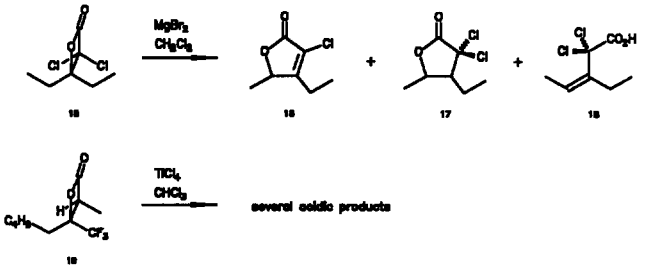
SCHEME B



on theoretical grounds; the pathway likely involves a rate-determining ionization of the ß-lactone to produce a carbocation/carboxylate species such as 12, with subsequent and rapid cation rearrangement to 13 followed by capture by the carboxylate anion. The primary difference between the aldehyde-derived (R=H) and ketone-derived (R=alkyl) cases is the incipient tertiary carbocation contained in the latter. Rearrangement of 12 (R=H) to 13 involves a hydride transfer between two secondary carbocations, presumably of similar energy. Hydride migration toward cation 12 (R=alkyl), however, would necessitate a tertiary-to-secondary carbocation rearrangement; the unfavorable energetics of such an event evidently suffice to induce the loss (as opposed to migration) of an adjacent proton instead to form the alkene 14.

In order to assess the possibility that an initial ß-lactone ionization is the rate-determining step of these reactions, two ß-lactones bearing electron-withdrawing groups were prepared and subjected to the rearrangement conditions (Scheme C). Dichloro ß-lactone 15, prepared via the reaction of

SCHEME C



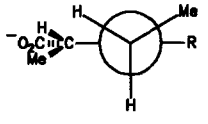
dichloroketene[18] with 3-pentanone, was treated with magnesium bromide in ether for 60 hours, whereupon starting material was recovered quantitatively. However, employing dichloromethane as the solvent effected a reaction which produced chloro butenolide 16, dichloro butyrolactone 17,

and dichloro acid 18 in 55%, 17%, and 6% yields, respectively.[19] We also examined 19, the trifluoro analog of 7t (prepared from 1,1,1-trifluoro-2-heptanone[20]), which proved even more unreactive than 15, being recovered unchanged from prolonged exposure to magnesium bromide in a variety of solvents. Extended reflux time with titanium tetrachloride[21] in chloroform was necessary to effect a reaction, which produced an inseparable mixture of at least four acidic products.

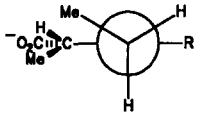
Thus, increasing the electronegativity of the carbon adjacent to the potential carbocation evidently impedes the reaction to the point where forcing conditions must be employed, supporting the hypothesis that accrual of positive charge on C-3 of the ß-lactone is the requisite, rate-determining event in the reaction mechanism. Additional support for an E1-type process was provided by a series of experiments wherein ß-lactone 7e was treated with several bases of varying strength in an attempt to initiate an E2 elimination. Exposure of 7b to excess triethylamine, potassium tert-butoxide, or DBN resulted in the quantitative recovery of starting material in all cases. The dependence of the reaction course (rearrangement to a butyrolactone versus elimination to an unsaturated acid) on the proposed carbocation rearrangements is being examined in detail and will be reported at the appropriate time.

Several representative 3-alkenoic acids were examined with an eye toward identifying any E/Z stereoselectivity, but only a modest (ca. 2:1) preference for E over Z alkene isomers was noted. These ratios were calculated from both proton NMR, via comparison of the vinyl proton integrals, and carbon NMR, by contrasting the peak heights corresponding to the allylic carbon atoms. These two methods provided similar ratios, and the correlation of chemical shifts to specific alkene isomers was based on published observations involving trisubstituted alkenes.[22]

The preference for E isomers is probably due to energetic differences inherent in the two conformations of the cation (e.g., 12) from which proton loss is most likely. Rotomer 12E would appear less congested than is 12Z, in which the methyl group is in close proximity to the carboxylate-bearing



12E



12Z

carbon atom. However, the energetic difference between the conformations is obviously dependent on the size of the R substituent, and the low

selectivity of the reaction would indicate that either this difference may not be great (even when R is not large) or that the proton loss is so rapid as not to allow conformationally-based energetics to manifest themselves.

Acknowledgement

We wish to thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, along with the Research Corporation, for support of this research.

Experimental Section

All reactions were carried out under an atmosphere of nitrogen, unless otherwise specified. Glassware was routinely oven-dried at 120 °C for a minimum of 4 hrs, then was assembled under a nitrogen stream. Anhydrous solvents were obtained by distillation, immediately prior to use, from sodium benzophenone ketyl (diethyl ether, tetrahydrofuran), or barium oxide (diisopropylamine). Infrared spectra were obtained using a Nicolet Model 20-DXB Fourier Transform spectrophotometer. Proton nuclear magnetic resonance spectra were recorded either on a Varian T-60 or General Electric GN-500 instrument; carbon-13 spectra were obtained on the latter. Peak multiplicities are abbreviated as follows: singlet, s; doublet, d; triplet, t; quartet, q; multiplet, m; envelope, e. Coupling constants (J) are reported in hertz (Hz). Thin-layer chromatographic analyses were carried out on Analtech silica gel "G" (250 micron) plates using ethyl acetate as eluent; visualization was effected by either ultraviolet light or by charring with phosphomolybdic acid. Preparative column chromatography employed Merck silica gel 60 (230-400 ASTM mesh). High Resolution Mass Spectral (HRMS) analyses were performed by the Mass Spectrometry Laboratory of the University of Illinois at Urbana-Champaign.

General Procedure for the Preparation of Unsaturated Acids.

An oven-dried 25 mL three-necked flask was equipped with a nitrogen inlet and stirring bar and was charged with a 1.0 M solution (10 mL, 10 mmol) of ß-lactone 7[16] in anhydrous ether. Stirring was begun, and magnesium bromide etherate (2.58 g, 10 mmol) was added in one portion. The light yellow mixture was stirred under nitrogen for 6 hours, whereupon the reaction was terminated by the cautious addition of 10 mL of water. The layers are separated, the ether layer was dried over anhydrous magnesium sulfate and filtered, and the solvent was removed under reduced pressure to afford the product. Attempted combustion analyses routinely indicated decarboxylation, thus, formula confirmation was acquired via high-resolution mass spectrometry (HRMS). The above protocol was utilized in the synthesis of all unsaturated acids, which displayed the following anayltical data.

2-(1-Cyclopentenyl)-2-methylacetic acid (8a): IR (neat): λ = 3049, 2955, 2877, 1707, 1238, 1176 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 1.09-1.54 (d, 3H, J=8.0Hz, CH_3); 1.54-2.20 (m, 2H, CH_2); 2.22-2.60 (m, 4H, allylic H); 3.11-3.31 (m, 1H, CHCOOH); 5.57-5.71 ppm (t, 1H, CH=). HRMS: calc. for $C_8H_{12}O_2$ 140.08367; found 140.0836051.

2-(1-Cyclopentenyl)-2,2-dimethylacetic acid (8b): IR (neat): λ = 3041, 2957, 2915, 2871, 1704, 1172 cm^{-1}. NMR ($CDCl_3$/TMS): δ = 1.23-1.50 (s, 6H, CH_3);

1.57-2.47 (m, 6H, CH_2), 5.48-5.61 ppm (t, 1H, CH=). HRMS: calc. for $C_9H_{14}O_2$ 154.09937; found 154.0993654.

2-(1-Cyclohexenyl)-2-methylacetic acid (8c): IR (neat): λ = 2970, 2933, 2862, 1708, 1458, 1159 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.95-2.29 (m, 11H, CH_2), 1.33-2.29 (e, 8H, CH_2), 2.87-3.30 (q, 1H, J=7.2Hz, $CHCH_3$), 5.41-5.78 (br s, 1H, =CH), 11.92 ppm (s, 1H, COOH). HRMS: calc. for $C_9H_{14}O_2$ 154.09937; found 154.0993728.

2-(1-Cyclohexenyl)-2-ethylacetic acid (8d): IR (neat): 3043, 2967, 2932, 2850, 1704, 910 cm^{-1}. NMR ($CDCl_3$/TMS): δ = 0.80-1.80 (t, 3H, CH_3); 1.31-1.94 (m, 6H, CH_2, $CHCH_3$); 1.94-2.38 (m, 4H, allylic H); 2.68-3.03 (t, 1H, CHCOOH); 5.34-5.81 ppm (m, 1H, CH=). HRMS: calc. for $C_{10}H_{16}O_2$ 168.11502; found 168.1148670.

2-(1-Cyclohexenyl)-2-phenylacetic acid (8e): mp 80-82 °C (hexane); IR (KBr): λ = 3088, 3083, 2988, 1697, 1220, 700 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 1.51-2.30 (e, 8H, CH_2); 4.27 (s, 1H, PhCH); 5.65 (s, 1H, =CH); 7.00-7.60 ppm (m, 5H, ArH). HRMS: calc. for $C_{14}H_{16}O_2$ 216.11502; found 216.1150555.

2-(1-Cyclohexenyl)-2-thiophenylacetic acid (8f): IR (neat): λ = 3074, 3060, 2927, 1708, 1439, 1293 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.39-2.41 (e, 8H, CH_2); 4.20 (s, 1H, SPhCH); 5.40-5.80 (br s, 1H, =CH); 7.00-7.59 (m, 5H, ArH); 12.38 ppm (s, 1H, COOH). HRMS: calc. for $C_{14}H_{16}O_2S$ 248.08709; found 248.0868613.

2-(1-Cyclohexenyl)-2-(1-naphthyl)acetic acid (8g): IR (neat): λ = 3048, 2929, 2856, 1707, 1215, 1167 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.48-2.18 (e, 8H, CH_2); 4.79-5.06 (s, 1H, $C_{10}H_7CH$); 5.41-5.75 (br s, 1H, =CH); 6.95-8.04 ppm (m, 7H, ArH). HRMS: calc. for $C_{18}H_{18}O_2$ 266.13067; found 266.1306851.

2-(1-Cyclohexenyl)-2-(p-methoxyphenyl)acetic acid (8h): IR (neat): λ = 2932, 2836, 1705, 1512, 1214, 1179 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.65-2.19 (e, 8H, CH_2); 3.88 (s, 3H, OCH_3); 4.09-4.27 (br s, 1H, ArCH); 5.48-5.78 (br s, 1H, =CH); 6.68-7.30 ppm (m, 4H, C_6H_4). HRMS: calc. for $C_{15}H_{18}O_3$ 246.12558; found 246.1255950.

2-(1-Cyclohexenyl)-2,2-dimethylacetic acid (8i): mp 68-70 °C (hexane); IR (KBr): λ = 2985, 2983, 2921, 1698, 1282, 800 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 1.26-1.48 (s, 6H, CH_3); 1.48-1.91 (m, 4H, CH_2); 1.91-2.30 (m, 4H, allylic H); 5.60-5.80 ppm (m, 1H, CH=). HRMS: calc. for $C_{10}H_{16}O_2$ 168.11502; found 168.1150300.

2-(1-Cycloheptenyl)-2-methylacetic acid (8j): IR (neat): λ = 2966, 2939, 2883, 1709, 1449, 1214 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 1.26-1.41 (d, 3H, J=10Hz, CH_3); 1.41-2.00 (m, 6H, CH_2), 2.00-2.41 (m, 4H, allylic H); 3.00-3.41 (m, 1H, CHCOOH); 5.62-5.90 (t, 1H, CH=); 12.10-12.20 ppm (s, 1H, COOH). HRMS: calc. for $C_{10}H_{16}O_2$ 168.11502; found 168.1150290.

2-(1-Cycloheptenyl)-2-ethylacetic acid (8k): IR (neat): λ = 2966, 2925, 2877, 2851, 1703 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.86-1.07 (t, 6H, CH_3); 1.37-1.94 (m, 8H, CH_2 + CH_2CH_3); 1.94-2.36 (m, 4H, allylic H); 2.71-3.09 (t, 1H, CHCOOH); 5.61-5.91 ppm (t, 1H, CH=). HRMS: calc. for $C_{11}H_{18}O_2$ 182.13067; found 182.1308932.

2-(1-Cycloheptenyl)-2,2-dimethylacetic acid (8l): mp 74-75 °C (hexane); IR (KBr): λ = 2845, 1704, 1463, 1446, 1285, 1276 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 1.23-1.50 (s, 6H, CH_3); 1.58-2.20 (m, 6H, CH_2), 2.20-2.79 (m, 4H, allylic H); 5.57-5.71 ppm (t, 1H, CH=). HRMS: calc. for $C_{11}H_{18}O_2$ 182.13067; found

182.1305052.

2-(1-Cyclooctenyl)-2-methylacetic acid (8m): IR (neat): λ = 3070, 3029, 2929, 1707, 1451, 1219 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 1.23-1.41 (d, 3H, J=8.5Hz, CH_3); 1.41-1.79 (s, 8H, CH_2); 1.90-2.46 (m, 4H, allylic H); 2.99-3.41 (m, 1H, CHCOOH); 5.43-5.79 (t, 1H, CH=); 11.60-11.80 ppm (s, 1H, COOH). HRMS: calc. for $C_{11}H_{18}O_2$ 182.13067; found 182.1305052.

2-(1-Cyclooctenyl)-2-ethylacetic acid (8n): IR (neat): λ = 3016, 2876, 2852, 1704, 1468, 1215 cm^{-1}; NMR (DMSO-d_6): δ = 0.80-1.00 (t, 3H, CH_3); 1.20-1.80 (m, 8H, CH_2); 1,80-1.90 (m, 2H, CH_2CH_3); 1.90-2.50 (m, 4H, allylic H); 2.48-3.00 (t, 1H, CHCOOH); 5.40-5.73 ppm (t, 1H, CH=). HRMS: calc. for $C_{12}H_{20}O_2$ 196.14632; found 196.1463253.

2-(1-Cyclododecenyl)-2-ethylacetic acid (8o): IR (neat): λ = 3030, 2862, 1704, 1446, 1265, 1120 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.80-1.27 (t, 3H, CH_3); 1.27-1.90 (m, 18H, CH_2 + CH_2CH_3); 1.90-2.50 (m, 4H, allylic H); 2.70-3.19 (t, 1H, CHCOOH); 5.37-5.63 ppm (t, 1H, CH=). HRMS: calc. for $C_{16}H_{28}O_2$ 252.20892; found 252.2089184.

2-(1-Cyclododecenyl)-2,2-dimethylacetic acid (8p): IR (neat): λ = 2926, 2860, 1704, 1466 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 1.00-1.13 (s, 6H, CH_3); 2.15-2.30 (m, 16H, CH_2); 2.97-3.15 (m, 4H, allylic H); 5.60-5.80 ppm (m, 1H, CH=). HRMS: calc. for $C_{16}H_{28}O_2$ 252.20892; found 252.2096321.

2,3-Dimethyl-3-pentenoic acid (8q): IR (neat): λ = 2980, 2940, 2888, 1708, 1413, 1235 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.44-2.40 (m, 9H, CH_2 + CH_3); 2.81-3.41 (q, 1H, J=7.0Hz, $CHCH_3$, (Z)); 3.41-3.89 (q, 1H, J=7.2Hz, $CHCH_3$, (E)); 5.10-5.70 (m, 1H, =CH); 13.00 ppm (s, 1H, COOH). HRMS: calc. for $C_7H_{12}O_2$ 128.08372; found 128.0837297.

2,3-Dimethyl-3-hexenoic acid (8r): IR (neat): λ = 2965, 2937, 2876, 1708, 1480, 1233 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.49-2.20 (m, 11H, CH_2 + CH_3); 2.85-3.35 (q, 1H, J=7.0Hz, $CHCH_3$, (Z)); 3.35-3.87 (q, 1H, J=7.2Hz, $CHCH_3$, (E)); 4.80-5.52 (m, 1H, =CH); 12.85 ppm (s, 1H, COOH). HRMS: calc. for $C_8H_{14}O_2$ 142.09937; found 142.0993759.

2,3-Dimethyl-3-heptenoic acid (8s): IR (neat): λ = 2962, 2935, 2874, 1708, 1459, 1228 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.50-2.44 (m, 13H, CH_2 + CH_3); 2.89-3.32 (q, 1H, J=7.0Hz, $CHCH_3$, (Z)); 3.40-3.89 (q, 1H, J=7.2Hz, $CHCH_3$, (E)); 5.04-5.57 (t, 1H, =CH); 12.91 ppm (s, 1H, COOH). HRMS: calc. for $C_9H_{16}O_2$ 156.11502; found 156.1147342.

2,3-Dimethyl-3-octenoic acid (8t): IR (neat): λ = 2960, 2929, 2860, 1708, 1460, 1233 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.49-2.39 (m, 15H, CH_2 + CH_3); 2.93-3.44 (q, 1H, J=7.0Hz, $CHCH_3$, (Z)); 3.44-3.88 (q, 1H, J=7.2Hz, $CHCH_3$, (E)); 4.90-5.66 (m, 1H, =CH); 12.83 ppm (s, 1H, COOH). HRMS: calc. for $C_{10}H_{18}O_2$ 170.13067; found 170.1306759.

2,3-Dimethyl-3-nonenoic acid (8u): IR (neat): λ = 2959, 2931, 2859, 1708, 1460, 1234 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.40-2.68 (m, 17H, CH_2 + CH_3); 2.82-3.41 (q, 1H, J=7.0Hz, $CHCH_3$ (Z)); 3.41-3.88 (q, 1H, J=7.2Hz, $CHCH_3$ (E)); 4.75-5.52 (m, 1H, =CH); 13.20 ppm (s, 1H, COOH). HRMS: calc. for $C_{11}H_{20}O_2$ 184.14632; found 184.1463300.

3-Ethyl-2-methyl-3-pentenoic acid (8v): IR (neat): λ = 3047, 3006, 2962, 1706, 1216, 756 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.66-2.38 (m, 11H, CH_2 + CH_3); 2.80-3.30 (q, 1H, J=7.0Hz, $CHCH_3$, (Z)); 3.30-3.88 (q, 1H, J=7.2Hz, $CHCH_3$, (E)); 5.10-5.68 (m, 1H, =CH); 12.71 ppm (s, 1H, COOH). HRMS: calc. for

$C_8H_{14}O_2$ 142.09937; found 141.0008636.

3-Ethyl-2-phenyl-3-pentenoic acid (8w): IR (neat): λ = 2968, 2935, 1708, 1454, 1214, 699 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.74-2.19 (m, 8H, CH_2 + CH_3); 4.90 (s, 1H, PhCH), 5.23-5.79 (m, 1H, =CH), 6.98-7.68 ppm (m, 5H, ArH). HRMS: calc. for $C_{13}H_{16}O_2$ 204.11502; found 204.1154133.

2-Methyl-3-propyl-3-hexenoic acid (8x): IR (neat): λ = 2962, 2936, 2875, 1708, 1459, 1230 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.50-2.72 (m, 15H, CH_2 + CH_3); 2.80-3.49 (q, 1H, J=7.0Hz, $CHCH_3$, (Z)); 2.49-3.77 (q, 1H, J=7.2Hz, $CHCH_3$, (E)); 4.98-5.50 (m, 1H, =CH); 12.80 ppm (s, 1H, COOH). HRMS: calc. for $C_{10}H_{18}O_2$ 170.13067; found 170.1304491.

3-Butyl-2-methyl-3-heptenoic acid (8y): IR (neat): λ = 2960, 2932, 2874, 1707, 1459, 1231 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.40-2.60 (m, 19H, CH_2 + CH_3); 2.70-3.26 (q, 1H, J=7.0Hz, $CHCH_3$, (Z)); 3.26-3.74 (q, 1H, J=7.2Hz, $CHCH_3$, (E)); 4.84-5.48 (m, 1H, =CH); 12.43 ppm (s, 1H, COOH). HRMS: calc. for $C_{12}H_{22}O_2$ 198.16197; found 198.1619800.

3-Ethyl-2-methyl-heptenoic acid (8z): IR (neat): λ = 2962, 2935, 2875, 1707, 1413, 1234 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.44-2.40 (m, 15H, CH_2 + CH_3); 2.80-3.30 (q, 1H, J=7.0Hz, $CHCH_3$ (Z)); 3.30-3.60 (qd, 1H, J=7.2Hz, $CHCH_3$ (E)); 5.03-5.64 (m, 1H, =CH); 12.70 ppm (s, 1H, COOH). HRMS: calc. for $C_{10}H_{18}O_2$ 170.13067; found 170.1305139.

3-Ethyl-2-methyl-3-octenoic acid (8aa): IR (neat): λ = 2960, 2933, 2861, 1707, 1461, 1234 cm^{-1}; NMR ($CDCl_3$/TMS): δ = 0.35-2.32 (m, 17H, CH_2 + CH_3); 2.75-3.26 (q, 1H, J=7.0Hz, $CHCH_3$, (Z)); 3.26-3.75 (qd, 1H, J=7.2Hz, $CHCH_3$, (E)); 4.98-5.78 (m, 1H, =CH); 12.35 ppm (s, 1H, COOH). HRMS: calc. for $C_{11}H_{20}O_2$ 184.14632; found 184.1463300.

Rearrangement of 4,4-diethyl-3,3-dichlorooxetan-2-one (15).

An oven-dried, 100 mL flask was charged with a solution of 4,4-diethyl-3,3-dichlorooxetan-2-one (15, 500 mg, 2.68 mmol) in 30 mL of dichloromethane (30 ml), whereupon magnesium bromide etherate (3.45g, 13.4 mmol) was added in one portion. The mixture was stirred under nitrogen for 10 hours, water (50 ml) was added, and the layers are separated. The organic layer was dried by stirring with anhydrous magnesium sulfate, the drying agent was filtered, and the solvent was removed *in vacuo* to yield a dark brown oil. After standing at 0 °C overnight a very small amount of crystalline 18 separates, which was removed via filtration. The filtrate was purified by column chromatography on a 2.2 x 70 cm column, employing dichloromethane as eluent and collecting 300 drop fractions, providing 17 and then 16.

3-Chloro-4-ethyl-5-methyl-2(5H)-furanone (16): oil (55% yield); IR (neat): λ = 2982, 2941, 1767, 1383, 1172, 1026 cm^{-1}; ^{1}H-NMR ($CDCl_3$/TMS): δ = 4.97 (q, 1H, J=6.72Hz, OCH), 2.53 (sextet, 1H, J=7.38Hz, CH_2CH_3), 2.29 (sextet, 1H, J=7.39Hz, CH_2CH_3), 1.39 (d, 3H, J=6.71Hz, $CHCH_3$), 1.10 ppm (t, 3H, J=7.61Hz, CH_2CH_3). ^{13}C-NMR ($CDCl_3$/TMS): = 167.97 (C-2), 165.30 (C-4), 118.61 (C-3), 78.73 (CO), 20.08 (CH_2), 18.16 ($OCCH_3$), 11.14 ppm (CH_2CH_3).

3,3-Dichloro-4,5-dihydro-4-ethyl-5-methyl-2(3H)-furanone (17): oil (17% yield); IR (neat): λ = 2976, 1798, 1386, 1196, 1071, 1026 cm^{-1}; ^{1}H-NMR ($CDCl_3$/TMS): δ = 4.82 (quintuplet, 1H, J=7.28Hz, OCH), 2.97 (q, 1H, J=7.38Hz, Cl_2CCH), 1.96 (septet, 1H, J=6.33Hz, CH_2CH_3), 1.72 (septet, 1H, J=6.33Hz, CH_2CH_3), 1.43 (d, 3H, J=6.73Hz, $CHCH_3$), 1.11 ppm (t, 3H, J=7.45Hz, CH_2CH_3). ^{13}C-NMR ($CDCl_3$/TMS): = 168.59 (C-2), 80.76 (Cl_2C), 78.08 (CO), 54.76 (Cl_2CC), 18.99 (CH_2), 15.28 ($OCCH_3$), 11.37 ppm (CH_2CH_3).

2,2-Dichloro-3-ethyl-3-pentenoic acid (18): clear, needle-like crystals (6% yield), mp 72-73 °C; IR (KBr): λ = 2983, 2979, 2938, 1678, 1597, 1286 cm^{-1}; ^{1}H-NMR ($CDCl_3$/TMS): δ = 9.46 (br s, 1H, $CO_2\underline{H}$), 6.13 (q, 1H, $\underline{J}$=6.8Hz, C=C$\underline{H}$), 2.62 (q, 2H, $\underline{J}$=7.0Hz, $C\underline{H}_2CH_3$), 1.83 (d, 3H, $\underline{J}$=7.0Hz, $C=CC\underline{H}_3$), 1.27 ppm (t, 3H, $\underline{J}$=7.8Hz, $CH_2C\underline{H}_3$).

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