# Preparation of Acyltetronic Acids using t-Butyl Acetothioacetate: Total Synthesis of the Fungal Metabolites Carolic, Carlosic, and Carlic Acids

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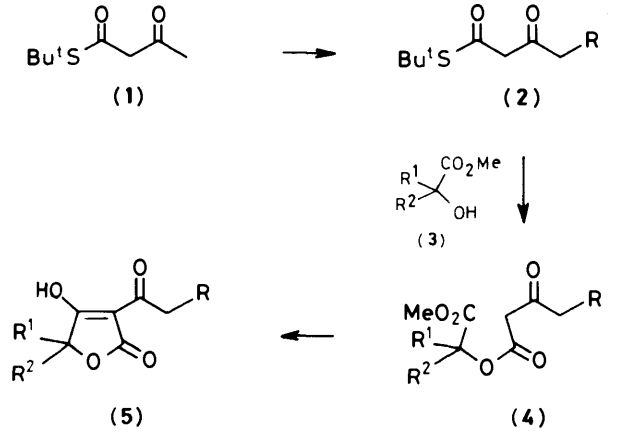
Dianions generated from *S*-t-butyl acetothioacetate (**1**) were alkylated with a variety of electrophiles at the γ-carbon centre. Treatment of the alkylated products with 2-hydroxy esters in the presence of silver(I) salts gave transesterified acetoacetate derivatives in good yields. These acetoacetates were cyclised efficiently to acyltetronic acid derivatives using tetrabutyl ammonium fluoride in THF solution at room temperature. By an appropriate choice of substituents the total syntheses of the fungal metabolite natural products carlosic, carolic, and carlic acids have been achieved.

Tetronomycin,[1] ICI 139603,[2] tetrocarcin,[3] and kijanimicin[4] are all recently isolated examples of biologically active natural products containing the 3-acyltetronic acid unit. Although there are now a number of procedures for the preparation of simple acyltetronic acids[5–7] there is a need to develop improved methodology which may eventually be applicable to more complex systems. Here we describe the use of *S*-t-butyl acetothioacetate (**1**) for the preparation of a number of tetronic acids some of which are natural products.

The choice of *S*-t-butyl acetothioacetate (**1**) was deliberate in that we hoped that this could be selectively deprotonated to either mono- or di-anions and that after alkylation the resulting t-butyl thio ester may be readily transesterified. In this way compound (**1**) would behave as a synthetic equivalent to diketene, but with the advantage that more highly substituted derivatives could also be obtained. Conceptually the route to acyltetronic acids (**5**) using (**1**) would require only three operations: alkylation of the dianion to give (**2**), transesterification with a 2-hydroxy ester (**3**), followed by Dieckmann cyclisation of the resulting product (**4**) (Scheme 1). The




**Scheme 1.**

advantage of this sequence over the original Lacey procedure,[5] upon which it is based, is that a much wider range of 3-acyl substituents would be more readily available. Also we recognised that there would be a need to improve the cyclisation reaction so that 5-mono- and 5-unsubstituted tetronic acids could be prepared in good yield which was not possible using the original Lacey protocol. Furthermore, it would be desirable to preserve any inherent stereochemistry of the 2-hydroxy ester during cyclisation to 5-monosubstituted derivatives.

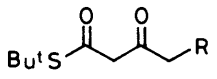
**Table 1.** Alkylation reactions of the dianion from compound (**5**)

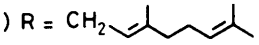
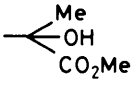
| Alkylating agent | Product | Yield (%) |
|---|---|---|
| MeI | (**6**) | 78 |
| EtI | (**7**) | 69 |
| $CH_2$=$CHCH_2Br$ | (**8**) | 70 |
| $Me_2C$=$CHCH_2CH_2CH(Me)CH$=$CHCH_2Cl$ | (**9**) | 60 |
| Furan-2-yl-$CH_2CH_2CH_2CH_2I$ | (**10**) | 63 |
| Bu$^t$Me$_2$SiO$CH_2CH_2I$ | (**11**) | 63 |
| THPO$CH_2CH_2I$ | (**12**) | 75 |
| $MeC(CO_2Me)(OLi)(CH_2)_8I$ | (**13**) | 56 |
| Cyclohexanone | (**14**) | 80 |
| PhCHO | (**15**) | 64 |

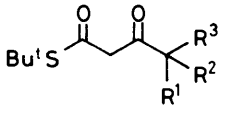
Preparation of the *S*-t-butyl acetothioacetate (**1**)[8] was achieved in 69% yield by reaction of sodium 1,1-dimethylethanethiolate with diketene at −10 °C. The use of the thiolate anion in this manner circumvents addition of thiol to the double bond of diketene noted by others.[9] Employing similar methodology to that developed by Weiler[10] for methyl acetoacetate, the dianion of (**1**) was generated by sequential treatment with sodium hydride (1 equiv.) at 0 °C, and butyllithium (1 equiv.) at −30 °C in dimethoxyethane (DME) solution. Alkylation of the dianion from (**1**)† in DME with a number of electrophiles gave products in moderate to good yields (Table 1). The use of other solvents such as ether or tetrahydrofuran in these reactions led to much lower yields and many unwanted side products, as did addition of cosolvents such as HMPA. Further alkylation of the dianion from (**6**) with methyl iodide gave compound (**16**) in 69% yield while methylation of the dianion from (**16**) gave compound (**17**) in only 34% yield. The lower yields in these examples clearly reflect the increased steric bulk at the alkylating centre. Reaction of the dianion from (**6**) with cyclohexanone as the electrophile gave compound (**18**) (73%). Similar reaction with benzaldehyde gave (**19**) (64%) as a mixture of diastereoisomers.

We next turned our attention to the transesterification of these alkylated β-keto thio ester derivatives with 2-hydroxy esters. Masamune[12] had previously established the principle of transesterification of t-butyl thioesters with alcohols utilising appropriate heavy metal salts as catalysts, and we were hopeful

† Attempts to generate anions or dianions from the corresponding *S*-phenyl acetothioacetate were generally unsuccessful owing to their rapid decomposition by loss of benzenethiolate.

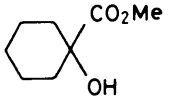


(1) R = H
(6) R = Me
(7) R = Et
(8) R = $CH_2CH{=}CH_2$
(9) R = 
(10) R = $(CH_2)_4$ 
(11) R = $CH_2CH_2OSiBu^tMe_2$
(12) R = $CH_2CH_2OTHP$
(13) R = $(CH_2)_7$ 
(14) R = 
(15) R = 

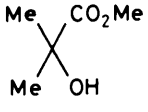


(16) $R^1 = R^2 = Me$, $R^3 = H$
(17) $R^1 = R^2 = R^3 = Me$
(18) $R^1 = Me$, $R^2 = H$, $R^3$ = 
(19) $R^1 = Me$, $R^2 = H$, $R^3$ = 

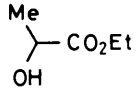
this method could be extended to our systems. Indeed we found that the β-keto thio ester derivatives underwent rapid transesterification with a number of 2-hydroxy esters (**20**)—(**23**) to give acetoacetate products (**24**—(**34**) in the presence of silver(I) trifluoroacetate in THF (Table 2). Additionally intramolecular transesterification was also possible since compound (**13**) could be smoothly converted into the lactone (**35**) using copper(I) trifluoroacetate. Reaction of (**14**) with silver(I) trifluoroacetate gave the spirocyclic β-keto lactone (**36**) in 70% yield.



(**20**)



(**21**)



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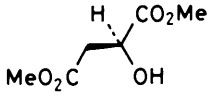


(**23**)

The Dieckmann cyclisation of the acetoacetates (**24**)—(**35**) to the corresponding acyltetronic acids (Table 3) requires more detailed discussion. In the early work by Lacey, alkali metal alkoxides were used as the bases for cyclisation, although it was

**Table 2.** Transesterification reactions

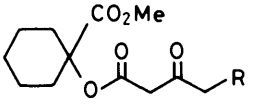
| β-Keto thio ester | 2-Hydroxy ester | Acetoacetate product | Yield (%) |
|---|---|---|---|
| (**8**) | (**20**) | (**25**) | 83 |
| (**9**) | (**20**) | (**26**) | 73 |
| (**5**) | (**21**) | (**27**) | 73 |
| (**10**) | (**22**) | (**29**) | 64 |
| (**11**) | (**22**) | (**30**) | 72 |
| (**12**) | (**22**) | (**31**) | 74 |
| (**7**) | (**23**) | (**33**) | 71 |
| (**12**) | (**23**) | (**34**) | 73 |
| (**13**) | | (**34**) | 40 |
| (**14**) | | (**35**) | 79 |

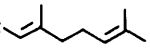
**Table 3.** Formation of tetronic acids

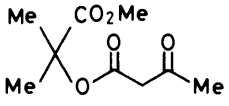
| Starting acetoacetate | Cyclisation method[b] | Tetronic acid | Yield (%) |
|---|---|---|---|
| (**25**) | A | (**38**) | 95 |
| (**26**) | A | (**39**) | 65 |
| (**27**) | B | (**40**) | 55 |
| (**28**) | B | (**41**) | 85 |
| (**29**) | B | (**42**) | 47 |
| (**31**) | B | (**43**) | 76 |
| (**32**)[a] | B | (**44**) | 44 |
| (**33**) | B | (**45**) | 74 |
| (**34**) | B | (**46**) | 45 |
| (**35**) | A or B | (**50**) | 0 |

[a] Prepared by reaction of (*S*)-dimethyl malate with diketene. [b] A $MeO^-$; B $Bu_4N^+F^-$ in THF at room temperature.

noted that with secondary 2-hydroxy ester derivatives lower yields were obtained owing to competitive alcoholysis of the acetoacetate moiety. For example, in the cyclisation of

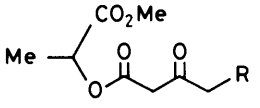


(**24**) R = H
(**25**) R = $CH_2CH{=}CH_2$
(**26**) R = 

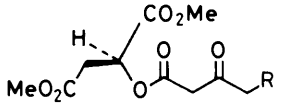


(**27**)

compound (**28**) to the furanone (**41**) Lacey reported yields of between 30 and 50% depending upon the method used. More



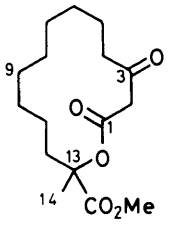
(**28**) R = H
(**29**) R = $(CH_2)_4$ 
(**30**) R = $CH_2CH_2OSiBu^tMe_2$
(**31**) R = $CH_2CH_2OTHP$



(**32**) R = H
(**33**) R = Et
(**34**) R = $CH_2CH_2OTHP$

recent work by Bloomer and Kappler[13] suggested improvements involving the use of a t-butoxide in t-butyl alcohol under reflux, where it was shown that up to 95% yield of compound

(41) could be realised. However during their synthesis of the mould metabolite (*S*)-carlosic acid (48) by using Bu$^t$O$^-$–Bu$^t$OH at 0 °C only a poor 39% yield of the furanone (45) from (33) could be obtained. Use of a t-butoxide at higher temperatures was unsuccessful in this example owing to elimination of the acetoacetic acid moiety to give dimethyl fumarate.



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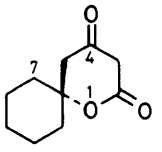
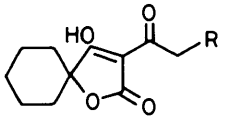


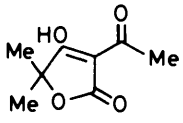
(36)

From these observations it was clear that improved methods for effecting the cyclisation were essential. We therefore undertook a brief study of alternative bases, including sodium hydride, potassium t-butoxide, and potassium carbonate in a variety of solvents, but all were equally ineffective. However, when we turned our attention to the use of tetrabutylammonium fluoride[14] in tetrahydrofuran at room temperature, excellent yields of the acyltetronic acids were obtained (Table 3). This mild and rapid fluoride-induced cyclisation method constitutes a considerable improvement over the traditional methods of cyclisation and is highly recommended for all future applications. This method should also be ideal for more complex situations where base epimerisation of chiral centres could be a problem.

Of the examples of acyltetronic acids reported in Table 3 three constitute routes to natural product fungal metabolites and should be highlighted further. Firstly conversion of compound (31) to (43) represents a synthesis of the natural product carolic acid.[13,15] The use of $Bu_4NF$ was necessary to effect the cyclisation and acidic work-up led directly to the acid (43) by deprotection of the tetrahydropyranyl group and spontaneous loss of water from a presumed intermediate hydroxyacyltetronic acid.



(37) R = H
(38) R = $CH_2CH{=}CH_2$
(39) R = $CH_2$



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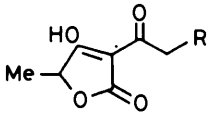
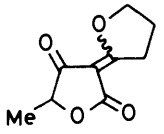


(41) R = H
(42) R = $(CH_2)_4$

The hydrofuran structure of carolic acid has recently been established by n.m.r. spectroscopic and *X*-ray crystallographic methods.[16] While the present synthesis was effected on racemic material it is not unreasonable to expect that the use of (*R*)-ethyl lactate in the transesterification process would afford the natural material in its optically pure form.*

In the second synthesis it was shown that (33) was smoothly converted to the acyltetronic acid (45) in an excellent 74% yield using the fluoride-induced cyclisation method and that the configuration of the initial (*S*)-malic ester was preserved in the product. Hydrolysis of compound (45) using 5M-sodium hydroxide as described by Bloomer and Kappler[13] did not afford (*S*)-carlosic acid as reported; racemic material only was obtained. In order to overcome these epimerisation problems



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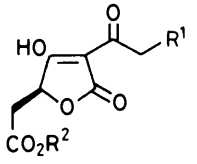
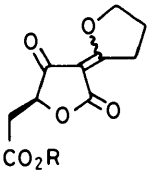
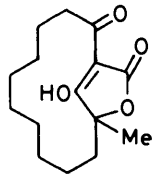


(44) $R^1$=H, $R^2$=Me
(45) $R^1$=Et, $R^2$=Me
(46) $R^1$=$R^2$=H
(48) $R^1$=Et, $R^2$=H



(46) R = Me
(49) R = H



(50)

we embarked on a brief model study using the chiral acyltetronic acid ester (44). Treatment of the ester (44) with milder basic hydrolysis conditions, 1M-lithium hydroxide, on work-up by acidification and extraction again gave racemic material (47). However when (44) was hydrolysed under acidic conditions of 1M-hydrochloric acid at 90 °C for 45 min, the crude tetronic acid product (61%) showed an optical rotation {$[\alpha]_D$ 102.9° (*c* 1.12, $CHCl_3$)}. No effort was made to purify this material to constant rotation. Application of these reaction conditions to the hydrolysis of the methyl ester (45) gave a low yield of (*S*)-carlosic acid (48). However by carrying out the reaction at ambient temperature for 10 days a 71% yield of optically pure (*S*)-carlosic acid (48) was obtained.[13,15b,18] This route to (*S*)-carlosic acid using the new chemistry is markedly superior to the previously reported route.[13]

Finally the synthesis of the natural tetronic acid carlic acid (49)[15,18,19] has also been achieved for the first time in its optically pure form, using a combination of strategies discussed for compounds (43) and (48) above. The required tetrahydropyranyl protected acetoacetate derivative (34) (Table 2) was prepared from compound (12) by treatment with (*S*)-dimethyl malate and silver(I) trifluoroacetate using modified conditions (ether–sodium hydrogen phosphate buffer) in 73% yield. The buffer was necessary in this reaction to avoid premature removal of the THP protecting group. Treatment of compound (34) with two equivalents of tetrabutylammonium fluoride

* Owing to the unavailability of (*R*)-ethyl lactate at the time of our studies, racemic material was used. However, the synthesis was repeated using the antipodal (*S*)-ethyl lactate (but not reported here) and does lead to (*S*)-carolic acid, as expected.[17]

followed by acidification and extraction with ether gave the methyl ester (**46**). Recrystallisation of the ester (**46**) from $CH_2Cl_2$ afforded pale orange crystals which was shown by $^1H$ n.m.r. spectroscopy to be a 1:1 mixture of *Z*- and *E*-isomers about the double bond.* Treatment of (**46**) with 1M-HCl as before afforded the natural product carlic acid (**49**) identical in all respects to the authentic compound.[15]

We believe the routes to acyltetronic acids using the novel diketene synthetic equivalent, t-butyl acetothioacetate (**1**) described above are short, highly efficient, and afford enantiomerically pure materials and should find application in more complex situations.

## Experimental

Melting points were determined using a Kofler hot-stage apparatus and are uncorrected. Optical rotations were measured using an Optical Activity AA-1000 or Perkin-Elmer 151 polarimeter. I.r. spectra were recorded on a Perkin-Elmer 983 grating i.r. spectrophotometer using a thin film or KBr disc. $^1H$ N.m.r. spectra were recorded at 60 MHz on a Varian EM-360A, at 90 MHz on a Jeol FX 90Q or at 250 MHz on a Bruker WM-250 machine and are quoted for $CDCl_3$ solutions with tetramethyl silane as the internal standard. Mass spectra were determined with a VG micromass 7070B instrument. Microanalyses were performed in the Imperial College Chemistry Department microanalytical laboratory.

Analytical t.l.c. was performed on Merck precoated silica gel $F_{254}$ plates and preparative chromatography was conducted under low pressure using Merck Kieselgel 60 (230—400 mesh). Petroleum refers to the fraction with b.p. 40—60 °C and was redistilled before use. All solvents were purified by standard techniques. Solutions were dried over sodium sulphate.

*Preparation of* S-*t-Butyl* 3-*Oxobutanethioate* (**1**).—To a suspension of sodium hydride (1.76 g of a 50% dispersion in oil, 36.7 mmol), previously washed with dry petroleum (2 × 25 ml), in THF (50 ml), cooled to 0 °C, was added slowly a solution of 1,1-dimethylethanethiol (3.0 g, 33.3 mmol) in THF (5 ml). Upon completion, a white precipitate was observed. After the reaction had been stirred for 10 min a solution of diketene (2.8 g, 33.3 mmol) in THF (5 ml) was added slowly. The solution was stirred for 15 min and quenched with saturated aqueous $NH_4Cl$ (20 ml). The mixture was extracted into ether (250 ml) and the ethereal extracts were dried, evaporated, and chromatographed (5% ether–petroleum) to yield *S*-t-butyl 3-oxobutanethioate (**1**) (3.62 g, 63%) as a pale red oil, δ(60 MHz; $CDCl_3$) (23% enol form) 1.5 (9 H, s, SBu$^t$), 1.9 and 2.2 (3 H, 2 s, Me enol and keto), 3.5 (1.6 H, s, 4-H keto), and 5.3 (0.2 H, s, 2-H enol); $\nu_{max.}$(film) 2 965, 1 721, 1 676, 1 621, 1 364, and 1 082 cm$^{-1}$.

*General Procedure for the Formation and Alkylation of Dianions from* S-*t-Butyl* 3-*Oxobutanethioate* (**1**).—The compound (**1**) (10 mmol) in dimethoxyethane (DME) (5 ml) was added dropwise to a suspension of sodium hydride (11 mmol; 50% dispersion previously washed with dry petroleum) in DME (40 ml) at 0 °C under argon. After 5 min the mixture was cooled to −30 °C and butyl-lithium (11 mmol in hexane) was added to generate an orange solution of the dianion. After 10 min the appropriate alkylating agent (11 mmol) was added to the mixture and allowed to warm to room temperature. After 1 h the reaction mixture was poured into saturated aqueous $NH_4Cl$ (20 ml) and extracted with ether (2 × 50 ml). The ether extracts were washed with brine, dried, and the solvent was removed under reduced pressure to give the crude product which was purified by chromatography.

*Compound* (**6**). The dianion from (**1**) (11.5 mmol) with methyl iodide gave S-*t-butyl* 3-*oxopentanethioate* (**6**) (1.51 g, 70%) as a colourless oil, δ (60 MHz, $CDCl_3$) (30% enol form) 1.1 (3 H, t, *J* 7 Hz, $CH_2$*Me*), 1.5 (9 H, s, SBu$^t$), 2.2 and 2.6 (2 H, 2 q, *J* 7 Hz, 4-H enol and keto), 3.6 (1.4 H, s, 2-H keto), and 5.3 (0.3 H, s, 2-H enol); $\nu_{max.}$(film) 2 970, 1 725, 1 680, 1 610, 1 365, 1 085, and 958 cm$^{-1}$; *m/z* 188 ($M^+$), 131, 99, 69, 57, and 28 (Found: C, 57.45; H, 8.7. $C_9H_{16}O_2S$ requires C, 57.41; H, 8.56%).

*Compound* (**7**). The dianion from (**1**) (10.3 mmol) with ethyl iodide gave S-*t-butyl* 3-*oxohexanethioate* (**7**) (1.45 g, 69%) as a red oil, δ (250 MHz; $CDCl_3$) (15% enol form) 0.92 (3 H, t, *J* 6.7 Hz, $CH_2CH_2$*Me*), 1.49 and 1.52 (9 H, 2 s, Bu$^t$S keto and enol), 1.63 (2 H, sextet, *J* 6.7 Hz, $CH_2CH_2$Me), 2.11 and 2.53 (2 H, 2 t, *J* 6.7 Hz, 4-H enol and keto), 3.55 (1.7 H, s, 2-H keto), and 5.33 (0.15 H, s, 2-H enol); $\nu_{max.}$(film) 2 965, 1 724, 1 676, 1 615, 1 455, 1 364, and 1 093 cm$^{-1}$; *m/z* 202 ($M^+$), 146, 113, 86, 58, and 43 (Found: $M^+$, 202.1024. $C_{10}H_{18}O_2S$ requires 202.1028).

*Compound* (**8**). The dianion from (**1**) (1 mmol) with allyl bromide gave S-*t-butyl* 3-*oxohept*-6-*enethioate* (**8**) as a pink oil (150 mg, 70%) in a 2:1 keto:enol ratio, δ (250 MHz) 1.47 (9 H, s, keto Bu$^t$), 1.51 (9 H, s, Bu$^t$ enol), 2.24 (2 H, t, *J* 8 Hz, 4-H enol), 2.23 (2 H, m, 5-H), 2.64 (2 H, t, *J* 8 Hz, 4-H keto), 3.57 (2 H, s, 2-H keto), 4.95—5.10 (2 H, m, methylene), 5.32 (1 H, s, 2-H enol), 5.79 (1 H, m, vinylic), and 12.83 (1 H, s, OH enol); $\nu_{max.}$ 2 950, 1 720, 1 660, and 1 610 cm$^{-1}$; *m/z* 214 ($M^+$), 157 ($M^+$ − Bu$^t$), 124 ($M^+$ − Bu$^t$SH), and 83 (Found: C, 61.75; H, 8.6; S, 14.7. $C_{11}H_{18}O_2S$ requires C, 61.64; H, 8.46; S, 14.96%).

*Compound* (**9**). The dianion from (**1**) (4.1 mmol) with geranyl chloride gave (E)-S-*t-butyl* 7,11-*dimethyl*-3-*oxododeca*-6,10-*dienethioate* (**9**) (760 mg, 60%) as a 3.5:1 keto:enol ratio, δ (250 MHz) keto: 1.47 (9 H, s, Bu$^t$), 1.60 (6 H, br s, 2 × Me), 1.68 (3 H, br s, Me), 1.97 (4 H, m, 8- and 9-$H_2$), 2.28 (2 H, m, 5-$H_2$), 2.57 (2 H, t, *J* 8 Hz, 4-$H_2$), 3.56 (2 H, s, 2-H), and 5.07 (2 H, m, vinylic); enol: 1.51 (9 H, s, Bu$^t$), 1.60 (6 H, br s, 2 × Me), 1.68 (3 H, br s, Me), 1.97 (4 H, m, 8- and 9-$H_2$), 2.04 (2 H, m, 4-$H_2$), 2.28 (2 H, m, 5-$H_2$), 5.07 (2 H, m, 6-and 10-H), and 5.33 (1 H, s, 2-H); $\nu_{max.}$(neat) 2 966, 2 923, 1 722, 1 675, and 1 616 cm$^{-1}$; *m/z* 310 ($M^+$), 253 ($M^+$ − Bu$^t$) and 221 ($M^+$ − Bu$^t$S) (Found: C, 69.9; H, 9.95; S, 10.05. $C_{18}H_{30}O_2S$ requires C, 69.63; H, 9.74; S, 10.33%).

*Compound* (**10**). The dianion from (**1**) (11 mmol) with 1-iodo-4-furan-2-ylbutane gave S-*t-butyl* 8-*furan*-2-*yl*-3-*oxo-octanethioate* (**10**) (1.7 g, 50%) as a pale red oil, δ (90 MHz; $CDCl_3$) (48% enol) 1.11—1.80 (15 H, m, including δ 1.47 and 1.51, 2 s, SBu$^t$ keto and enol, 5-, 6-, and 7-$H_2$), 2.11 and 2.45 (2 H, 2 t, *J* 7.0 Hz, 4-H enol and keto), 2.60 (2 H, t, *J* 7.0 Hz, 8-$H_2$), 3.53 (1 H, s, 2-H keto), 5.31 (0.5 H, s, 2-H enol), 5.49 (1 H, d, *J* 3.1 Hz, 3-H furan), 6.24 (1 H, dd, *J* 3.1, 1.9 Hz, 4-H furan), and 7.26 (1 H, br s, 5-H furan); $\nu_{max.}$(film) 2 910, 1 725, 1 680, 1 625, 1 590, 1 075, and 730 cm$^{-1}$ (Found: C, 65.05; H, 8.25; S, 10.75. $C_{16}H_{24}O_3S$ requires C, 64.83; H, 8.16; S, 10.82%).

*Compound* (**11**). The dianion from (**1**) (1.03 mmol) with 2-iodoethyl dimethyl-t-butylsilyl ether gave S-*t-butyl* 6-(*dimethyl-t-butylsilyloxy*)-3-*oxohexanethioate* (**11**) (215 mg, 63%) in 2:1 keto:enol ratio, δ (250 MHz) keto: 0.20 (6 H, s, $SiMe_2$), 0.87 (9 H, s, Bu$^t$Si), 1.46 (9 H, s, Bu$^t$S), 1.80 (2 H, m, 5-$H_2$), 2.62 (2 H, t, *J* 7 Hz, 4-$H_2$), 3.67 (2 H, s, 2-$H_2$), and 3.50 (2 H, m, 6-$H_2$); enol: 0.21 (6 H, s, $SiMe_2$), 0.88 (9 H, s, Bu$^t$Si), 1.50 (9 H, s, Bu$^t$S), 1.80 (2 H, m, 5-$H_2$), 2.21 (2 H, t, *J* 7 Hz, 4-$H_2$), 3.60 (2 H, m, 6-$H_2$), 5.34 (1 H, s, 2-H), and 9.88 (1 H, br s, OH); $\nu_{max.}$(neat) 2 950, 2 910, 1 720, 1 675, and 1 610 cm$^{-1}$; *m/z* 332 ($M^+$), 275 ($M^+$ − Bu$^t$), and 242 ($M^+$ − Bu$^t$SH) (Found: C, 57.9; H, 10.0; S, 9.75%; $M^+$ − Bu$^t$, 275.1137. $C_{16}H_{32}O_3SSi$ requires C, 57.78; H, 9.70; S, 9.64; $C_{12}H_{23}O_3SSi$ requires *M* − Bu$^t$, 275.1137).

*Compound* (**12**). The dianion from (**1**) (17.2 mmol) with 1-iodo-2-tetrahydropyran-2-yloxyethane gave S-*t-butyl* 3-*oxo-*

* Structure (**46**) was also confirmed by *X*-ray crystallography; we thank Dr. D. J. Williams, Imperial College, for this result.

6-*tetrahydropyran*-2-*yloxyhexanethioate* (**12**) (3.92 g, 75%) as a pale red oil, δ (250 MHz; $CDCl_3$) (26% enol form) 1.42—1.93 (17 H, m, including δ 1.44 and 1.47, 2 s, Bu$^t$ keto and enol, and δ 1.86, quintet, *J* 7.1 Hz, 5-H$_2$; 3′-, 4′-, and 5-H$_2$, THP), 2.21 (0.5 H, t, *J* 7.1 Hz, 4-H enol), 2.61 and 2.62 (1.5 H, 2 t, *J* 7.1 Hz, 4-H keto), 3.33—3.52 and 3.69—3.85 (4 H, 2 m, 6- H$_2$ and 6′-H$_2$, THP), 3.55 (1.5 H, s, 2-H keto), 4.51 (1 H, m, 2-H, THP), 5.32 (0.25 H, s, 2-H enol), and 12.85 (0.25 H, s, OH enol); $\nu_{max.}$(film), 2 947, 1 721, 1 676, 1 613, 1 364, 1 034, and 989 cm$^{-1}$; *m*/*z* 245 ($M^+$ − Bu$^t$), 213, 201, 145, 129, 85, 57, and 41 (Found: C, 59.75; H, 8.95; S, 10.85. $C_{15}H_{26}O_4S$ requires C, 59.57; H, 8.67; S, 10.60%).

*Compound* (**13**). To di-isopropylamine (37 mg, 0.37 mmol) stirred at 0 °C under argon was added dropwise BuLi (0.20 ml, 0.30 mmol). On completion of the addition, the mixture was diluted with DME (0.5 ml) and cooled to −20 °C and methyl 2-acetoxy-10-iodo-2-methyldecanoate (96 mg, 0.28 mmol) was added slowly as a solution in DME (1.5 ml).

To a suspension of sodium hydride (16 mg of a 50% dispersion in oil; 0.33 mmol) previously washed with dry petroleum (2 × 1 ml), in DME (0.5 ml), cooled to 0 °C was added the thioester (**1**) (54 mg, 0.31 mmol) as a solution in DME (0.5 ml). After the reaction had been stirred for 5 min the solution was cooled to −25 °C and BuLi (0.22 ml of a 1.52M solution in hexane; 0.33 mmol) was added. The deep orange dianion solution was warmed to −20 °C and the lithio iodide (prepared as described above) was added. The reaction mixture was warmed to room temperature and stirred for 90 min. The reaction was quenched with saturated aqueous $NH_4Cl$ (2 ml), and extracted with ether (2 × 25 ml). The combined ethereal extracts were washed with brine (5 ml), dried ($Na_2SO_4$), evaporated and chromatographed (25% ether–petroleum) to yield *S*-t-butyl 13-methoxycarbonyl-13-hydroxy-3-oxotetradecanethioate (**13**) (61 mg, 56%) as a pale yellow oil in a 3:1 keto:enol ratio, δ (250 MHz) keto: 1.40 (3 H, s, Me), 1.48 (9 H, s, Bu$^t$), 1.21—1.76 [16 H, m, $(CH_2)_8$], 2.52 (2 H, t, *J* 7 Hz, 4-H$_2$), 3.12 (1 H, br, s, OH), 3.55 (2 H, s, 2-H$_2$), and 3.78 (3 H, s, OMe); enol: 1.40 (3 H, s, Me), 1.51 (9 H, s, Bu$^t$), 1.21—1.76 [16 H, m, $(CH_2)_8$], 2.12 (2 H, t, *J* 7 Hz, 7-H$_2$), 3.12 (1 H, br, s, OH), 3.78 (3 H, s, OMe), and 5.23 (1 H, s, 2-H); $\nu_{max.}$(neat) 3 529, 2 928, 2 856, 1 728, 1 674, and 1 614 cm$^{-1}$; *m*/*z* 282 ($M^+$ − OMe − Bu$^t$ − $H_2O$), 240 ($M^+$ − Bu$^t$S − $CO_2$Me), and 198 ($M^+$ − Bu$^t$S − $CO_2$Me − $C_2H_3OH$).

*Compound* (**14**). The dianion from (**1**) (0.57 mmol) with cyclohexanone gave S-*t-butyl* 4-(1-*hydroxycyclohexyl*)-3-*oxobutanethioate* (**14**) (152 mg, 94%) as a pale red oil, δ (90 MHz; $CDCl_3$) (25% enol form) 1.14—1.78 (19 H, m, including δ 1.46 and 1.49, 2 s, SBu$^t$ keto and enol, cyclohexyl-H), 2.26 and 2.29 (2 H, 2 s, 4-H$_2$ enol and keto), 3.23 (1 H, br s, OH), 3.57 (1.5 H, s, 2-H keto), and 5.34 (0.25 H, s, 2-H enol); $\nu_{max.}$(film) 3 511, 2 930, 1 707, 1 673, 1 615, 1 363, and 1 078 cm$^{-1}$; *m*/*z* 272 ($M^+$), 216, 183, 140, 99, 57, 41, and 29 (Found: C, 61.65; H, 9.15. $C_{13}H_{24}O_3S$ requires C, 61.73; H, 8.88%).

*Compound* (**15**). The dianion from (**1**) (1.1 mmol) with benzaldehyde gave *S*-t-butyl 5-hydroxy-3-oxo-5-phenylpentanethioate (**15**) (250 mg, 74%) as a pale red oil; δ (250 MHz; $CDCl_3$) (20% enol form) 1.46 and 1.52 (9 H, 2 s, SBu$^t$ keto and enol), 2.51 (0.4 H, m, 4-H enol), 2.88 (0.8 H, dd, *J* 17.5, 5.0 Hz, 4-H keto), 3.00 (0.8 H, dd, *J* 17.5, 8.5 Hz, 4-H keto), 3.60 (1.6 H, s, 2-H keto), 5.16 (1 H, dd, *J* 8.5, 5.0 Hz, 5-H), 5.39 (0.2 H, s, 2-H enol), 7.20—7.60 (5 H, m, Ph), and 8.08 (1 H, d, *J* 7.5 Hz, OH); $\nu_{max.}$(film) 3 446, 2 963, 1 716, 1 671, 1 617, 1 360, 1 175, and 700 cm$^{-1}$; *m*/*z* 280 ($M^+$), 262, 223 ($M^+$ − Bu$^t$), 190, 146, 122, 105, 77, and 57 (Found: $M^+$ − Bu$^t$, 223.0423. $C_{11}H_{11}O_3S$ requires *M* − Bu$^t$ 223.0429).

*Compound* (**16**). The dianion from (**6**) (2.1 mmol) with methyl iodide gave S-*t-butyl* 4-*methyl*-3-*oxopentanethioate* (**16**) (230 mg, 69%) as a colourless oil; δ (60 MHz; $CDCl_3$) (10% enol form) 1.1 (6 H, d, *J* 7 Hz, CH*Me*$_2$), 1.5 (9 H, s, SBu$^t$), 2.3 and 2.7 (1 H, 2 × septet, *J* 7 Hz, 4-H enol and keto), 3.6 (1.8 H, s, 2-H keto), and 5.2 (0.1 H, s, 2-H enol); $\nu_{max.}$(film) 2 980, 1 720, 1 670, 1 610, 1 370, 1 075, and 780 cm$^{-1}$; *m*/*z* 202 ($M^+$), 113, 71, 57, and 29 (Found: C, 59.2; H, 9.05. $C_{10}H_{18}O_2S$ requires C, 59.37; H, 8.97%).

*Compound* (**17**). The dianion from (**16**) (0.49 mmol) with methyl iodide gave S-*t-butyl* 4,4-*dimethyl*-3-*oxopentanethioate* (**17**) (36 mg, 34%), as a white waxy solid, δ (90 MHz; $CDCl_3$) (62% enol form) 1.14 and 1.16 (9 H, s, Bu$^t$ enol and keto), 1.46 and 1.50 (9 H, 2 s, SBu$^t$ keto and enol), 3.69 (0.8 H, s, 2-H keto), and 5.40 (0.6 H, s, 2-H enol); $\nu_{max.}$(film) 2 995, 1 715, 1 665, 1 600, 1 380, 1 050, and 865 cm$^{-1}$; *m*/*z* 216 ($M^+$, 160, 127, 103, 100, 90, and 57 (Found: $M^+$, 216.1184. $C_{11}H_{20}O_2S$ requires *M*, 216.1177).

*Compound* (**18**). The dianion from (**6**) (2.66 mmol) with cyclohexanone gave S-*t-butyl* 4-(1-*hydroxycyclohexyl*)-3-*oxopentanethioate* (**18**) (555 mg, 73%) as a pale red oil, δ (250 MHz; $CDCl_3$) (29% enol form) 1.15 (3 H, d, *J* 7.4 Hz, 4-*Me*), 1.32—1.76 (19 H, m, including δ 1.48 and 1.52, 2 s, SBu$^t$, keto and enol, cyclohexyl-H), 2.12 and 2.82 (1 H, 2 q, *J* 7.4 Hz, 4-H, enol and keto), 2.96 (1 H, br s, OH), 3.66 (1.4 H, s, 2-H keto), and 5.35 (0.3 H, s, 2-H enol); $\nu_{max.}$(film), 3 520, 2 970, 1 710, 1 680, 1 620, 1 450, 1 370, and 1 080 cm$^{-1}$; *m*/*z* 286 ($M^+$), 269, 197, 188, 132, 99, and 57 (Found: $M^+$, 286.1595. $C_{15}H_{26}O_3S$ requires *M*, 286.1603).

*Compound* (**19**). The dianion from (**6**) (3.6 mmol) with benzaldehyde gave S-*t-butyl* 5-*hydroxy*-4-*methyl*-3-*oxo*-5-*phenylpentanethioate* (**19**) (680 mg, 64%) as a pale red oil, δ (250 MHz; $CDCl_3$) (1:1 mixture of diastereoisomers, 20% enol form) diastereoisomer 1: 0.88 (3 H, d, *J* 6.8 Hz, 4-Me), 1.47 and 1.51 (9 H, 2 s, SBu$^t$ keto and enol), 2.26 and 3.08 (1 H, 2 dq, *J* 9.1, 6.8 Hz, 4-H enol and keto), 3.68 and 3.72 (1.6 H, 2 d, *J* 14.8 Hz, 2-H keto), 4.67 and 4.72 (1 H, 2 d, *J* 9.1 Hz, 5-H keto and enol), 5.45 (0.2 H, s, 2-H enol), and 7.32 (5 H, m, Ph); diastereoisomer 2: 1.07 (3 H, d, *J* 6.8 Hz, 4-*Me*), 1.47 and 1.50 (9 H, 2 s, SBu$^t$ keto and enol), 2.47 and 2.99 (1 H, 2 dq, *J* 3.9, 6.8 Hz, 4-H enol and keto), 3.52 and 3.57 (1.6 H, 2 d, *J* 14.8 Hz, 2-H keto), 5.03 and 5.10 (1 H, 2 d, *J* 3.9 Hz, 5-H enol and keto), 5.33 (0.2 H, s, 2-H enol), and 7.32 (5 H, m, Ph); $\nu_{max.}$(film), 3 422, 2 970, 1 716, 1 673, 1 612, 1 364, 1 082, and 761 cm$^{-1}$ (Found: $M^+$ − Bu$^t$, 237.0585. $C_{12}H_{13}O_3S$ requires $M^+$ − Bu$^t$ 237.0585).

*General Procedure for Transesterification of t-Butylthio Esters.*—The substituted β-keto thio ester and the requisite hydroxy ester were dissolved in ether (or THF) at room temperature and a solution of silver(I) trifluoroacetate in ether added to give a dark solution. The mixture was worked up and chromatographed to give the required product.

*Compound* (**25**). To the thio ester (**8**) (162 mg, 0.66 mmol) and hydroxy ester (**20**) (115 mg, 0.73 mmol, 1.1 equiv.) in ether (10 ml) was added $CF_3CO_2Ag$ (176 mg, 0.8 mmol, 1.2 equiv.) in ether (5 ml). After the reaction had been stirred at room temperature for 10 min, the mixture was filtered through silica, evaporated under reduced pressure, and chromatographed to give 1′-*methoxycarbonylcyclohexyl* 3-*oxohept*-6-*enoate* (**25**) as a clear oil (150 mg, 83%), δ (250 MHz) 1.14—1.88 [10 H, m,, $(CH_2)_5$], 2.36 (2 H, m, 5-H), 2.68 (2 H, t, *J* 7.8 Hz, 4-H$_2$), 3.47 (2 H, s, 2-H$_2$), 3.72 -3 H, s, OMe), 5.02 (2 H, m, =$CH_2$), and 5.80 (1 H, m, vinyl); $\nu_{max.}$(film) 2 920, 2 850, 1 735, 1 715, 1 630, and 1 130 cm$^{-1}$; *m*/*z* 282 ($M^+$), 250 ($M^+$ − MeOH), 223 ($M$ − $CO_2$Me), and 141 (Found: C, 64.05; H, 7.95. $C_{15}H_{22}O_5$ requires C, 63.81; H, 7.85%).

*Compound* (**26**). The β-keto thio ester (**9**) (146 mg, 0.47 mmol) and the hydroxy ester (**20**) (86 mg, 0.54 mg, 1.16 equiv.) in ether (10 ml) were treated with $CF_3CO_2Ag$ (129 mg, 0.58 mmol, 1.24 equiv.) in ether (5 ml). After stirring for 1 h, the reaction mixture was diluted with ether (50 ml), washed with water (10 ml), dried,

evaporated and chromatographed (25% ether–petroleum) to give (6E)-1′-*methoxycarbonylcyclohexyl* 7,11-*dimethyl*-3-*oxododeca*-6,10-*dienoate* (**26**) as a clear oil (130 mg, 73%), δ (250 MHz) 1.58 (3 H, br s, Me), 1.60 (3 H, br s, Me), 1.68 (3 H, br s, Me), 1.20—2.35 [16 H, m, $(CH_2)_5$ + 5-, 8-, and 9-$H_2$], 2.62 (2 H, t, *J* 8 Hz, 4-$H_2$), 3.48 (2 H, s, 2-$H_2$), 3.71 (3 H, s, OMe), and 5.10 (2 H, m, 6- and 10-H); $\nu_{max.}$(neat) 2 910, 1 740, 1 710, and 1 650 $cm^{-1}$; *m/z* 378 ($M^+$), 360 ($M^+ - H_2O$), 346 ($M^+$ − MeOH), and 220 (Found: C, 69.5; H, 9.25. $C_{22}H_{34}O_5$ requires C, 69.81; H, 9.05%).

*Compound* (**27**). Silver trifluoroacetate (1.4 g, 6.4 mmol) was added to the thio ester (**1**) (885 mg, 5.1 mmol) and compound (**21**) (500 mg, 4.3 mmol) in THF (20 ml). The solution was stirred for 1 h, concentrated (10 ml), and diluted with petroleum (30 ml). The resulting orange-brown precipitate was filtered off, washed with petroleum (2 × 10 ml) and the combined filtrate and washings were dried. Removal of the solvent and chromatography (50% ether–petroleum) gave 1′-*methoxycarbonyl*-1′-*methylethyl* 3-*oxobutanoate* (**27**) (621 mg, 73%) as a pale yellow oil, δ (90 MHz; $CDCl_3$) (15% enol form) 1.45 (6 H, s, $CMe_2$), 1.83 and 2.16 (3 H, 2 s, 4-$H_3$ enol and keto), 3.32 (1.7 H, s, 2-H keto), 3.60 (3 H, s, $CO_2Me$), and 5.21 (0.15 H, s, 2-H enol); $\nu_{max.}$(film) 2 996, 2 954, 1 754, 1 720, 1 295, and 1 131 $cm^{-1}$; *m/z* 202, 143 ($M^+ - CO_2Me$), 101, 85, 59, and 43 (Found: $M^+$, 202. 0855. $C_9H_{14}O_5$ requires *M*, 202, 0841).

*Compound* (**29**). Silver trifluoroacetate (0.82 g, 4 mmol) was added to the thio ester (**10**) (1 g, 3.4 mmol) and (*S*)-ethyl lactate (**22**) (0.44 g, 4 mmol) in THF (20 ml). After 12 h the solvent was removed to give an oily residue which was taken up in ether and filtered through a short column of silica gel. Removal of the solvent under reduced pressure and chromatography (30% ether–petroleum) gave (1′S)-1′-*ethoxycarbonylethyl* 8-*furan*-2-*yl*)-3-*oxo*-*octanoate* (**29**) (700 mg, 64%), as a colourless oil; $[\alpha]_D$ −21.9° (*c* 1.43, $CHCl_3$); δ (250 MHz; $CDCl_3$) 1.22—1.41 (5 H, m, including δ 1.28, t, *J* 7.2 Hz, $CO_2CH_2Me$, 6-$H_2$), 1.50 (3 H, d, *J* 7.5 Hz, 2′-$H_3$), 1.58—1.71 (4 H, m, 5-, 7-$H_2$), 2.59 (2 H, t, *J* 7.0 Hz, 4-$H_2$), 2.62 (2 H, t, *J* 7.0 Hz, 8-$H_2$), 3.50 (2 H, s, 2-$H_2$), 4.22 (2 H, q, *J* 7.2 Hz, $CO_2CH_2Me$), 5.12 (1 H, q, *J* 7.5 Hz, 1′-H), 5.97 (1 H, dd, *J* 3.1, 0.8 Hz, 3-H furan), 6.27 (1 H, dd, *J* 3.1, 1.8 Hz, 4-H furan), and 7.29 (1 H, dd, *J* 1.8, 0.8 Hz, 5-H furan); $\nu_{max.}$(film) 2.862, 1 747, 1 720, 1 625, 1 208, and 733 $cm^{-1}$; *m/z* 324 ($M^+$), 306 ($M^+ - H_2O$), 279, 207, 165, and 160 (Found: C, 62.95; H, 7.65. $C_{17}H_{24}O_6$ requires C, 62.95; H, 7.46%).

*Compound* (**30**). To a mixture of compounds (**11**) (77 mg, 0.23 mmol) and (**22**) (74 mg, 0.63 mmol, 2.7 equiv.) in ether (4 ml) containing $Na_2HPO_4$ buffer (150 mg) was added $CF_3CO_2Ag$ (0.46 mmol, 2 equiv.). The resulting black solution was stirred for 1 h then was poured into dilute HCl (3 ml) and extracted with ether (25 ml). The ethereal solution was dried, filtered through a short pad of silica, and evaporated under reduced pressure. Chromatography (25% ether–petroleum) gave 1′-*ethoxycarbonylethyl* 6-(*dimethyl*-*t*-*butylsilyloxy*)-3-*oxohexanoate* (**30**) (60 mg, 72%) as a colourless oil in a 7:1 keto:enol ratio, δ (250 MHz) keto: 0.03 (6 H, s, $SiMe_2$), 0.87 (9 H, s, Bu$^t$Si), 1.27 (3 H, t, *J* 9 Hz, ester Me), 1.50 (3 H, d, *J* 8 Hz, Me), 1.82 (2 H, m, 5-$H_2$), 2.66 (2 H, t, *J* 8 Hz, 4-$H_2$), 3.53 (2 H, s, 2-$H_2$), 3.62 (2 H, t, *J* 6 Hz, 6-$H_2$), 4.20 (2 H, q, *J* 8 Hz, ester $CH_2$), and 5.12 (1 H, q, *J* 8 Hz, 1′-H); enol: as above except 2.30 (2 H, t, *J* 8 Hz, 4-$H_2$) and 10.95 (1 H, br s, enol OH); $\nu_{max.}$(neat) 3 426, 2 931, 1 750, and 1 719 $cm^{-1}$; *m/z* 314 ($M^+$ − EtOH) 303 (*M* − Bu$^t$), and 243 (Found: C, 56.8; H, 9.2%; $M^+$ − Bu$^t$, 303.126 73. $C_{17}H_{32}O_6Si$ requires C, 56.64; H, 8.95%); $C_{13}H_{23}O_6Si$ requires *M* − Bu$^t$, 303.126 4).

*Compound* (**31**). To a mixture of compounds (**12**) (298 mg, 0.99 mmol) and (**22**) (233 mg, 1.97 mmol) in ether (10 ml) was added $CF_3CO_2Ag$ (450 mg, 2.04 mmol). The black solution was stirred for 2 h, poured into water, filtered, and the organic layer dried, evaporated, and chromatographed (50% ether–petroleum) to yield 1′-ethoxycarbonylethyl 3-oxo-6-tetrahydropyran-2-yloxyhexanoate (**31**) as a clear oil (241 mg, 74%); δ (250 MHz) (major diastereoisomer): 1.29 (3 H, t, *J* 7 Hz, ester Me), 1.51 (3 H, d, *J* 7 Hz, Me), 1.45—2.00 (6 H, m,), 1.91 (2 H, m, 5-$H_2$), 2.50 (2 H, m, 4-$H_2$), 3.35—3.55 (2 H, m, 6-, 11 H, 6-H THP), 3.56 (2 H, s, 2-$H_2$), 3.70—3.90 (2 H, m, 6- and 6-H, THP), 4.23 (2 H, q, *J* 7 Hz, ester $CH_2$), 4.55 (1 H, m, 2-H THP), and 5.13 (1 H, q, *J* 7 Hz, 1′-H); $\nu_{max.}$(neat) 2 920, 1 740, 1 715, and 1 630 $cm^{-1}$; *m/z* 330 ($M^+$), 245 ($M^+$ − THP), and 229 ($M^+$ − OTHP).

*Compound* (**32**). Diketene (1.4 ml, 18 mmol) was added dropwise to (2*S*)-dimethyl 2-hydroxybutanedioate (**23**) (2.5 g, 15 mmol) and 4-(*N*,*N*-dimethylamino)pyridine (10 mg) in ether (40 ml) at −40 °C. The solution was allowed to warm to 0 °C over 45 min, poured into saturated aqueous $NH_4Cl$ (40 ml) and extracted with ether (100 ml). The organic phase was washed with water (20 ml), 1M-HCl (20 ml), and brine (20 ml), and then dried and the solvent removed under reduced pressure. Chromatography (80% ether–petroleum) gave (1′*S*)-1′,2′-bis(methoxycarbonyl)ethyl 3-oxobutanoate (**32**) (3.0 g, 79%) as a colourless oil; $[\alpha]_D^{26}$ −20.9° (*c* 1.16, $CHCl_3$) {lit.,[13] $[\alpha]_D^{21}$ −21.6° (*c* 1.45)}, δ (250 MHz; $CDCl_3$) (15% enol form) 1.98 and 2.30 (3 H, 2 s, COMe enol and keto), 2.92 (2 H, d, *J* 5.5 Hz, 2′-$H_2$), 3.52 (1.7 H, s, 2-H keto), 3.71 and 3.78 (6 H, 2 s, 2 × $CO_2Me$), 5.09 (0.15 H, s, 2-H enol), 5.53 (1 H, t, *J* 5.5 Hz, 1′-H), and 11.50 (0.15 H, s, OH enol); $\nu_{max.}$(film) 2 958, 1 744, 1 438, 1 174, and 1 059 $cm^{-1}$; *m/z* 246 ($M^+$), 204 ($M^+ - COCH_2$), 172, 145, 113, 85, and 43 (Found: $M^+$, 246.0745. $C_{10}H_{14}O_7$ requires *M*, 246.0740).

*Compound* (**33**). Silver trifluoroacetate (480 mg, 2.16 mmol) was added to the thio ester (**7**) (400 mg, 1.98 mmol) and (*S*)-dimethyl-2-hydroxybutanedioate (**23**) (352 mg, 2.16 mmol) in THF (50 ml). After 30 min, the solvent was removed under reduced pressure and the residue was taken up in ether (10 ml) and filtered through a pad of silica gel. Removal of the solvent under reduced pressure followed by chromatography (50% ether–petroleum) gave (1′S)-1′,2′-*bis*(*methoxycarbonyl*)*ethyl* 3-*oxohexanoate* (**33**) (385 mg, 71%) as a pale yellow oil; $[\alpha]_D^{28}$ −9.83° (*c* 10.71, $CHCl_3$), δ (250 MHz; $CDCl_3$) (12% enol form) 0.92 (3 H, t, *J* 6.7 Hz, $CH_2CH_2Me$), 1.62 (2 H, sextet, *J* 6.7 Hz, $CH_2CH_2Me$), 2.20 and 2.54 (2 H, 2 t, *J* 6.7 Hz, $CH_2CH_2Me$ enol and keto), 2.90 (2 H, d, *J* 5.5 Hz, 2′-$H_2$), 3.51 (1.8 H, s, 2-H keto), 3.73 and 3.78 (6 H, 2 s, 2 × $CO_2Me$), 5.10 (0.1 H, s, 2-H enol), and 5.54 (1 H, t, *J* 5.5 Hz, 1′-H); $\nu_{max.}$(film) 2 960, 1 720, 1 435, 1 165, and 755 $cm^{-1}$; *m/z* 274, ($M^+$), 214, 113, 71, and 43 (Found: C, 52.45; H, 6.8. $C_{12}H_{18}O_7$ requires C, 52.55; H, 6.62%).

*Compound* (**34**). Silver trifluoroacetate (6.8 g, 31.8 mmol) was added to the thio ester (**12**) (3.2 g, 10.6 mmol), (*S*)-dimethyl-2-hydroxybutanedioate (**23**) (1.6 g, 9.6 mmol) and $Na_2HPO_4$ buffer (4 g) in ether (70 ml). After 45 min, the brown solution was filtered to remove $Na_2HPO_4$ and precipitated salts and then the filtrate was washed with saturated aqueous $NaHCO_3$ and brine (20 ml of each). The aqueous washings were extracted with ether (20 ml) and the combined organic extracts dried. Removal of the solvent followed by chromatography (60% ether–petroleum) gave (1′S)-1′,2′-*bis*(*methoxycarbonyl*)*ethyl* 3-*oxo*-6-*tetrahydropyran*-2-*yloxyhexanoate* (**34**) (2.89 g, 73%) as a pale yellow oil; $[\alpha]_D$ −11.3° (*c* 1.15, $CHCl_3$), δ (250 MHz; $CDCl_3$) 1.44—1.85 (6 H, m, 3-, 4-, and 5-$H_2$ THP), 1.92 (2 H, quintet, *J* 6.7 Hz, 5-$H_2$), 2.70 (2 H, t, *J* 6.7 Hz, 4-$H_2$), 2.94 (2 H, d, *J* 6.7 Hz, 2′-$H_2$), 3.38—3.56 and 3.71—3.90 (4 H, 2 m, 6- Hz, 6-$H_2$ THP), 3.57 (2 H, s, 2-H), 3.74 and 3.80 (6 H, 2 s, 2 × $CO_2Me$), 4.57 (1 H, m, 2-H, THP), and 5.57 (1 H, t, *J* 6.7 Hz, 1′-H); $\nu_{max.}$(film) 2 952, 1 746, 1 710, 1 438, 1 200, and 1 173 $cm^{-1}$; *m/z* 289 ($M^+$ − THP), 273, 259, 246, 185, 111, and 85 (Found: C, 54.35; H, 7.25. $C_{17}H_{26}O_9$ requires C, 54.54; H, 7.00%).

*Compound* (**35**). To a stirred solution of $CF_3CO_2Cu$ (200 mg,

1.13 mmol) in $CH_2Cl_2$ (2 ml) at room temperature was added a solution of (**13**) (68 mg, 0.17 mmol) in $CH_2Cl_2$ (3 ml). The mixture was stirred for 30 min and poured into saturated aqueous $NH_4Cl$ (3 ml). Extraction with $CH_2Cl_2$ (20 ml), drying of the organic layer, and evaporation afforded a brown oil. Chromatography (25% ether–petroleum) gave 13-*methoxycarbonyl*-3-*oxotetradecan*-13-*olide* (**35**) as a clear oil (21 mg, 40%), δ (250 MHz) 1.20—2.05 (16 H, m), 1.60 (3 H, s, Me), 2.49 (1 H, ddd, *J* 17, 7.5, 7 Hz, 4-H), 2.79 (1 H, ddd, *J* 17, 8.5, 7.5 Hz, 4-H), 3.46 (2 H, m, 2-$H_2$), and 3.73 (3 H, s, OMe); $\nu_{max.}$(neat) 2 929, 2 857, 1 740, and 1 717 $cm^{-1}$; *m/z* 298 ($M^+$), 283 ($M^+$ − Me), 267 ($M^+$ − OMe), 239 ($M^+$ − $CO_2Me$), and 197 ($M^+$ − COMe − $C_2H_2O$) (Found: $M^+$, 298.1790. $C_{16}H_{26}O_5$ requires *M*, 298.1750).

*Compound* (**36**). Silver trifluoroacetate (45 mg, 0.20 mmol) was added to thio ester (**14**) (50 mg, 0.18 mmol) in THF (10 ml). Removal of the solvent after 15 min followed by chromatography (ether) gave 1-oxaspiro[5.5]undeca-2,4-dione (**36**) (24 mg, 79%) as a colourless oil which crystallised when allowed to stand, m.p. 110—111 °C, δ (60 MHz; $CDCl_3$) 1.1—1.9 (10 H, m, cyclohexyl-H), 2.7 (2 H, s, 3-$H_2$), and 3.4 (2 H, s, 5-$H_2$); $\nu_{max.}$ (KBr disc) 2 934, 1 647, 1 577, 1 324, 1 221, and 1 013 $cm^{-1}$; *m/z* 182 ($M^+$), 139, 126, 99, 83, and 55 (Found: $M^+$, 182.0937. $C_{10}H_{14}O_3$ requires *M*, 182.0943).

*Preparation of Acyltetronic Acids.* All reactions were performed at room temperature unless otherwise noted.

*Compound* (**38**). To a solution of NaOMe (20 mg, 0.37 mmol, 1.2 equiv.) in methanol (3 ml) was added a solution of compound (**25**) (90 mg, 0.32 mmol) in benzene (6 ml). The mixture was heated under reflux for 4 h and allowed to stand overnight. The solution was diluted with water (1 ml) followed by concentrated (36%) HCl (10 drops), and extracted with ether (25 ml). The aqueous layer was further extracted with chloroform (20 ml). The combined organic extracts were dried and evaporated under reduced pressure to afford *compound* (**38**) as an oil which crystallised when cooled (82 mg, 95%), m.p. 42—44 °C, (250 MHz) 1.75 [10 H, m, $(CH_2)_5$], 2.46 (2 H, t, *J* 8 Hz, 2'-$H_2$), 3.02 (2 H, m, 3'-$H_2$), 4.97—5.16 (2 H, m, 5'-$H_2$), 5.82 (1 H, m, 4'-H), and 11.34 (1 H, br s, OH); $\nu_{max.}$($CHCl_3$) 3 536, 3 078, 1 751, 1 683, 1 645, and 1 602 $cm^{-1}$; *m/z* 250 ($M^+$), 232 ($M^+$ − $H_2O$), and 177 (Found: $M^+$, 250.1208. $C_{14}H_{18}O_4$ requires *M*, 250.1205).

*Compound* (**39**). To a solution of NaOMe (15 mg, 0.29 mmol) in methanol (1 ml) was added a solution of compound (**26**) (98 mg, 0.26 mmol) in benzene (6 ml). The mixture was heated under reflux for 4 h and allowed to stand overnight. The solution was diluted with water (1 ml) and concentrated HCl (10 drops), and the product was extracted into ether (50 ml). The ether layer was dried and evaporated to yield *compound* (**39**) as thick syrup (58 mg, 65%), δ (250 MHz) 1.55—2.12 (10 H, m), 1.60 (3 H, br s), 1.62 (3 H, br s), 1.66 (3 H, br s), 2.40 (2 H, m, 3'-H), 2.95 (2 H, m, 2'-$H_2$), 5.10—5.20 (2 H, m, 4'- and 8'-H), and 11.12 (1 H, br s, OH); $\nu_{max.}$($CHCl_3$) 3 422, 2 937, 1 740, 1 716, and 1 632 $cm^{-1}$; *m/z* 346 ($M^+$), 328 ($M^+$ − $H_2O$), 251, and 220 (Found: $M^+$, 346.2142. $C_{21}H_{30}O_4$ requires *M*, 346.2144).

*Compound* (**40**). Tetrabutylammonium fluoride (37 ml; 1M solution in THF; 37 mmol) was added dropwise over 5 min to the β-keto ester (**27**) (5 g, 25 mmol) in THF (5 ml), and the solution was stirred for 3 h. The reaction mixture was acidified (6M-HCl) and poured into ether (50 ml) and water (50 ml). The aqueous phase was extracted with ether (4 × 20 ml), each extract being washed with brine (5 ml). The combined organics were dried and the solvent removed to give the crude tetronic acid as a yellow solid (4.3 g). Recrystallisation (× 2) from ether–petroleum gave 3-*acetyl*-4-*hydroxy*-5,5-*dimethylfuran*-2(5H)-*one* (**40**) (2.3 g, 55%) as pale yellow needles, m.p. 55—57 °C, δ (60 MHz; $CDCl_3$) 1.45 and 1.5 (6 H, 2 s, *gem Me*), 2.5 (3 H, s, COMe), and 9.4 (1 H, br s, OH); $\nu_{max.}$(film) 2 989, 1 758, 1 685, 1 610, 1 382, and 1 135 $cm^{-1}$; *m/z* 170 ($M^+$), 142, 84, 59, and 43 (Found: C, 56.25; H, 5.9. $C_8H_{10}O_4$ requires C, 56.47; H, 5.92%).

*Compound* (**41**). To the neat ester (**28**) (1.20 g, 6 mmol), rapidly stirred under argon was added $Bu_4NF$ (12 ml of a 1M solution in THF; 12 mmol, 2 equiv.), and the solution was stirred overnight. Volatiles were removed under reduced pressure and 10% HCl (15 ml) was added. The resulting clear solution was extracted with ether (5 × 50 ml) and the combined organic extracts were dried and evaporated to yield the crude compound (**41**) as a white solid. Recrystallisation from ether afforded the pure *furan*-2(5H)-*one* (**41**) as white crystals (789 mg, 85%), m.p. 70—72 °C; $[\alpha]_D$ −70.1° (*c* 0.74, water); δ (250 MHz) 1.53 (3 H, d, *J* 8 Hz, Me), 2.56 (3 H, s, COMe), 4.80 (1 H, q, *J* 8 Hz, 5-H), and 11.41 (1 H, br s, OH); $\nu_{max.}$($CHCl_3$) 3 682, 3 619, 3 078, 1 761, 1 689, and 1 619 $cm^{-1}$; *m/z* 156 ($M^+$), 138 ($M^+$ − $H_2O$), and 84 (Found: C, 53.6; H, 5.0. $C_7H_8O_4$ requires C, 53.85; H, 5.16%).

*Compound* (**42**). Tetrabutylammonium fluoride (6.1 ml; 1M solution in THF; 6.1 mmol) was added dropwise to the β-keto ester (**29**) (495 mg, 1.5 mmol) in THF (5 ml). The solution was stirred for 24 h, then the mixture was dissolved in water (10 ml). The aqueous solution was washed with ether (5 ml), and then acidified (3M-HCl). This acidic solution was extracted with ether (4 × 10 ml), the combined organic extracts were dried ($Na_2SO_4$), and the solvent removed to give the crude product as a yellow oil. The crude product was taken up in chloroform and filtered through a short column of Florisil (chloroform). Removal of the solvent under reduced pressure gave a colourless oil which on trituration with ether afforded (5*S*)-4-hydroxy-5-methyl-3-(6-furan-2-yl-1-oxohexyl)furan-2(5*H*)-one (**42**) (200 mg, 47%) as a white powder, m.p. 136—138 °C, δ {90 MHz; $CDCl_3$–$^2H_6Me_2SO$ (4:1)} 1.34 (3 H, d, *J* 6.9 Hz, Me), 1.25—1.70 (6 H, m, 3'-, 4'-, and 5'-H), 2.57 (2 H, t, *J* 7.5 Hz, 2'-H), 2.83 (2 H, t, *J* 7.5 Hz, 6'-$H_2$), 4.46 (1 H, q, *J* 6.9 Hz, 5-H), 5.97 (1 H, d, *J* 3.1 Hz, 3-H furan), 6.23 (1 H, dd, *J* 3.1, 1.5 Hz, 5-H furan); $\nu_{max.}$ (KBr disc) 3 060br, 2 937, 1 762, 1 688, 1 653, 1 602, 1 055, and 732 $cm^{-1}$.

*Compound* (**43**). To the neat compound (**31**) (148 mg, 0.45 mmol) was added $Bu_4NF$ (1 ml of a 1M-solution in THF, 1 mmol). The mixture was stirred overnight and poured into 10% HCl (2 ml). Extraction with ether (4 × 20 ml), drying of the combined organic extracts, and evaporation gave a buff solid. Recrystallisation from ethyl acetate–petroleum afforded carolic acid (**43**) (62 mg, 76%), m.p. 112 °C (lit.,[15] m.p. 112 °C); $^1H$ n.m.r. identical to that described.[20]

*Compound* (**44**). Tetrabutylammonium fluoride (10 ml; 1M solution in THF; 10 mmol) was added dropwise to the β-keto ester (**32**) (2.5 g, 10 mmol) in THF (10 ml). The solution was stirred for 2 h when no starting material remained (t.l.c.). The reaction mixture was acidified (6M-HCl), poured into water (30 ml) and extracted with ether (4 × 20 ml), each extract being washed with brine (5 ml). The combined organics were dried and the solvent removed under reduced pressure to give a viscous orange oil. This oil was taken up in ether (10 ml) and cooled to give (2S)-*methyl* 4-*acetyl*-2,5-*dihydro*-3-*hydroxy*-5-*oxofuran*-2-*ylacetate* (**44**) (0.92 g, 44%) as a yellow solid, m.p. 83—85 °C; $[\alpha]_D$ −102.9° (*c* 1.12, $CHCl_3$) {lit.,[13] m.p. 86—87 °C, $[\alpha]_D^{21}$ −55.5° (*c* 1.21)}, δ (250 MHz; $CDCl_3$) (α:β 1:1)* 2.57 (3 H, s, COMe), 2.88 and 3.04 (1 H, 6 dd, *J* 17.1, 6.8 Hz and *J* 17.1, 3.4 Hz, $CHCH_2CO_2Me$, α), 2.92 and 3.04 (1 H, 2 dd, *J* 17.1, 6.8 Hz and *J* 17.1, 3.4 Hz, $CHCH_2CO_2Me$, β), 3.72 (3 H, s, $CO_2Me$), 4.89 (0.5 H, t, *J* 6.8 Hz, $CHCH_2CO_2Me$, β), and 5.00 (0.5 H, t, *J* 6.8 Hz, $CHCH_2CO_2Me$, α); $\nu_{max.}$ (KBr disc) 1 766, 1 742, 1 696, 1 608, 1 376, and 1 190 $cm^{-1}$; *m/z* 214 ($M^+$), 182, 154, 113, 85, and 43 (Found: C, 50.38; H, 4.63. $C_9H_{10}O_6$ requires C, 50.47; H, 4.71%).

*Compound* (**45**). Tetrabutylammonium fluoride (4 ml; 1M

solution in THF; 4 mmol) was added dropwise to β-keto ester (**33**) (1 g, 3.6 mmol) in THF (5 ml). The reaction mixture was stirred for 1.5 h, when no starting material remained (t.l.c.). The solution was acidified (6M-HCl), poured into water (10 ml) and extracted with ether (4 × 10 ml), each extract being washed with brine (5 ml). The combined organic extracts were dried, and the solvent removed under reduced pressure to give (2S)-*methyl* 2,5-*dihydro*-3-*hydroxy*-5-*oxo*-4-*butanoylfuran*-2-*ylacetate* (**45**) (658 mg, 74%) as an off-white solid, m.p. 58—60 °C, $[\alpha]_D$ −100.9° (*c* 0.96, $CHCl_3$); $\delta_H$ (250 MHz; $CDCl_3$) (α:β 1:1)* 1.03 (3 H, t, *J* 7.4 Hz, 4′-*H*), 1.76 and 1.77 (2 H, 2 × sextet, *J* 7.4 Hz, 3′-$H_2$, α and β), 2.87 and 3.03 (1 H, 2 dd, *J* 17.3, 6.3 Hz and *J* 17.3, 4.3 Hz, $CHCH_2CO_2Me$, α), 2.90 and 3.04 (1 H, 2 dd, *J* 17.3, 6.3 Hz and *J* 17.3, 4.3 Hz, $CHCH_2CO_2Me$, β), 2.92 (2 H, t, *J* 7.4 Hz, 2′-$H_2$), 3.71 and 3.72 (3 H, 2 s, $CO_2Me$, α and β), 4.88 (0.5 H, dd, *J* 6.3, 4.3 Hz, $CHCH_2CO_2Me$, β), and 5.01 (0.5 H, dd, *J* 6.3, 4.3 Hz, $CHCH_2CO_2Me$, α), $\delta_C$ (22.5 MHz; $CDCl_3$), 13.5 (C-4′, α and β), 18.8 and 19.4 (C-3′, α and β), 34.5, 35.3, 35.4, and 36.0 (C-2′, $CHCH_2CO_2Me$, α and β), 52.1 (OMe), 75.9 (C-2, α), 80.5 (C-2, β), 97.3 (C-4, β), 100.0 (C-4, α), 167.1 (C-5, α), 168.7 and 169.0 ($CO_2Me$, α and β), 175.7 (C-5, β), 191.6 (C-1′, β), 193.0 (C-1′, α), 196.0 (C-3, β), and 199.7 (C-3, α); $\nu_{max.}$ (KBr disc) 2 962, 1 765, 1 741, 1 695, 1 603, 1 174, and 1 020 $cm^{-1}$; *m/z* 242 ($M^+$) 224 ($M^+ - H_2O$), 192, 167, 84, and 71 (Found: $M^+$, 242.0795. $C_{11}H_{14}O_6$ requires *M*, 242.0790).

*Compound* (**46**). Tetrabutylammonium fluoride (10.7 ml; 1M solution in THF; 10.7 mmol) was added dropwise to the β-keto ester (**34**) (2 g, 5.3 mmol) in THF (5 ml) to give a yellow solution. The reaction mixture was stirred for 40 min after which time no starting material remained (t.l.c.). The solution was acidified to pH 3 (1M-HCl) and poured into ether (20 ml) and 1M-HCl (10 ml). The organic phase was washed with water and brine (10 ml of each) and the aqueous washings re-extracted with ether (2 × 10 ml). The combined organics were dried and the solvent removed under reduced pressure. Recrystallisation from $CH_2Cl_2$–ether gave (2S)-*methyl* 3,5-*dioxo*-4-*tetrahydrofuran*-2-*ylidenetetrahydrofuran*-2-*ylacetate* (**46**) (577 mg, 45%) as colourless needles, m.p. 135—137 °C, $[\alpha]_D$ −104° (*c* 0.87, $CHCl_3$), δ (250 MHz; $CDCl_3$) 2.29 (2 H, quintet, *J* 7.5 Hz, 4′-$H_2$), 2.85 and 3.01 (2 H, 2 dd, *J* 17.2, 6.3 Hz and *J* 17.2, 4.1 Hz, $CH_2CO_2Me$), 3.45 and 3.46 (2 H, 2 t, *J* 7.5 Hz, 3′-H *cis* and *trans*), 3.69 (3 H, s, $CO_2Me$), 4.79 (2 H, t, *J* 7.5 Hz, 5′-$H_2$), and 4.81 (1 H, dd, *J* 6.3, 4.1 Hz, 2-H); $\nu_{max.}$ (KBr disc) 2 951, 1 749, 1 740, 1 706, 1 609, 1 262, and 1 037 $cm^{-1}$; *m/z* 240 ($M^+$), 209, 181, 167, 149, and 110 (Found: $M^+$, 240.0626. $C_{11}H_{12}O_6$ requires *M*, 240.0634).

*Compound* (**47**). The ester (**44**) (100 mg, 0.47 mmol) was dissolved in 1M-HCl (5 ml) and the solution brought to reflux over 45 min. The solution was cooled, poured into water (20 ml), and extracted with ether (4 × 10 ml). The combined organic extracts were dried and the solvent removed under reduced pressure to give (2*S*)-4-acetyl-2,5-dihydro-3-hydroxy-5-oxofuran-2-ylacetic acid (**47**) (57 mg, 61%) as a pale yellow semi-solid, $[\alpha]_D$ −36.4° (*c* 3.58, acetone) {lit.,[13] $[\alpha]_D^{21}$ −10.3° (*c* 1.93)}, δ [60 MHz $(CD_3)_2CO$] 2.49 (3 H, s, MeCO), 3.0—3.2 (2 H, m, $CH_2$), 5.05 (1 H, t, *J* 5 Hz, $CH_2CHO$), 8.05 (1 H, br s, $CO_2H$), and 10.5 (1 H, br s, OH).

*Compound* (**48**). The ester (**45**) (245 mg, 1.0 mmol) was dissolved in 1M-hydrochloric acid (20 ml) and the reaction mixture was stirred at room temperature for 10 days. The solution was poured into water (10 ml) and extracted with chloroform (3 × 20 ml). The combined organic extracts were dried and the solvent removed under reduced pressure to give carlosic acid (**48**) (164 mg, 71%) as a pale yellow solid. Recrystallisation from benzene gave off-white crystals, m.p. 165—166 °C, $[\alpha]_D$ −138° (*c* 0.28, water), $[\alpha]_{5461}$ −158° (*c* 0.28, water) {lit.,[15b] m.p. 181° $[\alpha]_{5461}$ −160° (*c* 0.21 water); lit.,[13] m.p. 174—176 °C, $[\alpha]_D$ −137° (*c* 1.21)}, $\delta_H$ {250 MHz; $CDCl_3$–$[^2H_6]Me_2SO$ (4:1)} 1.01 (3 H, t, *J* 7.4 Hz, 4′-*H*), 1.73 (2 H, sextet, *J* 7.4 Hz, 3′-$H_2$), 2.78 and 2.98 (2 H, 2 dd, *J* 17.1, 6.6 Hz and J 17.1, 4.1 Hz, $CHCH_2CO_2H$), 2.88 (2 H, t, *J* 7.4 Hz, 2′-H), 4.96 (1 H, dd, *J* 6.6, 4.1 Hz, $CHCH_2CO_2H$), and 6.93 (2 H, br s, $CO_2H$ and OH), $\delta_C$ {62.5 MHz; $CDCl_3$–$[^2H_6]Me_2SO$ (4:1)} 12.7 (C-4′), 17.9 (C-3′), 34.9 and 35.2 (C-2′, $CHCH_2CO_2H$), 98.2 (C-4), 169.3 ($CO_2H$), 170.1 (C-5), 192.5 (C-1′), and 194.9 (C-3); $\nu_{max.}$ (KBr disc) 3 060, 2 962, 1 748, 1 663, 1 609, 1 239, and 1 020 $cm^{-1}$; *m/z* 228, 210, 167, 151, 97, and 84 (Found: $M^+$, 228.0625. $C_{10}H_{12}O_6$ requires *M*, 228.0634).

*Compound* (**49**). The ester (**46**) (100 mg, 0.42 mmol) was dissolved in 1M-hydrochloric acid (15 ml) and the reaction mixture was stirred at room temperature for 7 days. The solution was poured into water (10 ml) and extracted with chloroform (3 × 15 ml). The combined organics were dried and the solvent removed under reduced pressure to give the crude product as a yellow solid. Recrystallisation from ethanol gave carlic acid (**49**) (33 mg, 35%) as pale yellow crystals, m.p. 172—173 °C, $[\alpha]_D$ −145° (*c* 0.22, water), $[\alpha]_{5461}$ −161° (*c* 0.22, water) {lit.,[15b] m.p. 176 °C, $[\alpha]_{5461}$ −160° (*c* 0.28 water)}; δ (250 MHz; $[^2H_6]Me_2SO$) 2.16 (2 H, quintet, *J* 7.5 Hz, 4′-$H_2$), 2.68 and 2.69 (1 H, 2 dd, *J* 16.6, 6.3 Hz, $CHCHHCO_2H$ *cis* and *trans*), 2.82 and 2.83 (1 H, 2 dd, *J* 16.6, 4.1 Hz, $CHCHHCO_2H$ *cis* and *trans*), 3.29 and 3.31 (2 H, 2 t, *J* 7.5 Hz, 3′-$H_2$ *cis* and *trans*), 4.73 (2 H, t, *J* 7.5 Hz, 5′-$H_2$), 4.78 and 4.53 (1 H, 2 dd, *J* 6.3, 4.1 Hz, 2-H *cis* and *trans*), and 12.54 (1 H, br s, $CO_2H$); $\nu_{max.}$ (KBr disc) 3 060, 2 900, 1 750, 1 740, 1 706, 1 262, and 1 037 $cm^{-1}$.

* The $^1H$ n.m.r. spectrum indicated two forms to be present: α is equivalent to a 3-hydroxy-5-oxo structure whereas β represents a 5-hydroxy-3-oxo arrangement.[21]

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