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Intramolecular acylative ring-switching reactions of 3-(tetrahydro-2′-furyl)propanoic acid derivatives to give butanolides: mechanism and scope

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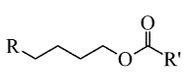
Received 3rd February 2003, Accepted 10th April 2003
First published as an Advance Article on the web 6th May 2003

The mechanism by which dihydro-5-(3′-trifluoroacetoxypropyl)-2(3*H*)-furanone is formed when 3-(tetrahydro-2′-furyl)propanoic-trifluoroacetic mixed anhydride is treated with an acidic catalyst is defined, and routes to some potentially useful butanolide synthons are described.

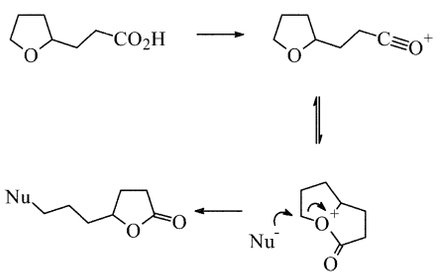
Introduction

An important property of tetrahydrofuran is the ability of its Lewis-basic oxygen atom to coordinate to electron-deficient species. This has been exploited when acid-catalysed cleavage reactions of the tetrahydrofuran ring have been carried out. For example, reactions of tetrahydrofuran with the acylating species derived from acyl chlorides have been used[1–3] for the preparation of 4-chlorobutyl alkanoates **1**. Similarly, reactions of tetrahydrofuran with acylium ions generated from carboxylic anhydrides[4–6] have been employed in the synthesis of diesters **2** of butane-1,4-diol.



1 R = Cl
2 R = OCOR'

In a preliminary communication[7] we have reported that the tethered acylium ions derivable from 3-(tetrahydro-2′-furyl)-propanoic acids can be efficiently trapped in an *intramolecular* manner *via* electron-donation from the ethereal oxygen atom of the tetrahydrofuryl ring. The bicyclic acyloxonium species that are formed then react with nucleophiles which are present in the reaction mixture to yield 5-substituted dihydro-2(3*H*)-furanones (Scheme 1).

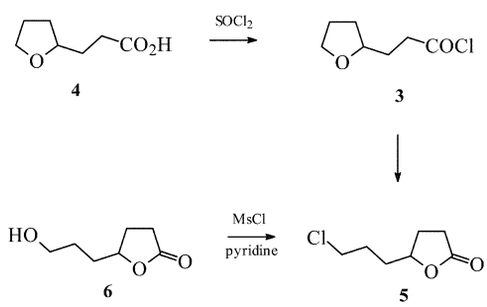


Scheme 1

The present paper provides full details of this work, including determination of the reaction mechanism, and describes how some additional nucleophiles may be utilised to capture the acyloxonium ions that are reaction intermediates.

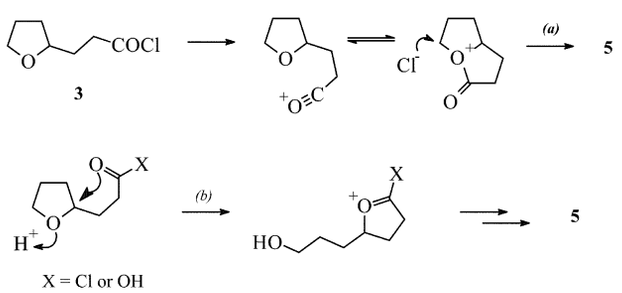
Results and discussion

We initially studied the behaviour of 3-(tetrahydro-2′-furyl)-propanoyl chloride **3**. Reaction of 3-(tetrahydro-2′-furyl)propanoic acid **4** with thionyl chloride did not lead to isolable quantities of the expected acyl chloride **3**. Instead, dihydro-5-(3′-chloropropyl)furan-2(3*H*)-one **5** was formed in 83% yield. The structure of the chloropropyl derivative **5** was readily deduced from its spectroscopic data, and was confirmed by its unambiguous synthesis from the known[8] 5-(3′-hydroxypropyl)furan-3(2*H*)-one **6** (Scheme 2).



Scheme 2

We consider that this overall conversion may take place because the hydrogen chloride liberated during the reaction promotes formation of an acylium ion from the acyl chloride **3** which then reacts further *via* pathway (*a*) outlined in Scheme 3.



Scheme 3

Alternatively, protonation of the tetrahydrofuryl oxygen atom of either the acyl chloride **3** or of its precursor acid **4** might trigger the different reaction sequence (*b*) shown in Scheme 3.

Attempts to synthesise the acyl chloride **3** under much milder conditions by reaction[9] of the acid **4** with CCl_4–PPh_3 were more successful, and even better yields of **3** were obtained when the lithium salt of **4** (the sodium salt proved to be rather hygroscopic) was treated with 0.33 equivalents of PCl_3 in dry chloroform.[10] When the pure acid chloride **3** which had been prepared by either of the above methods was subjected to conditions that

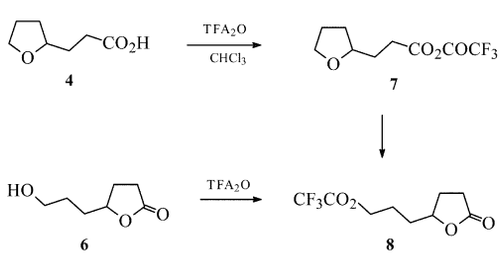
DOI: 10.1039/b301329b

have been described[3] for the intermolecular reaction between tetrahydrofuran and an acyl chloride (catalytic $ZnCl_2$ in refluxing anhydrous dichloromethane) good yields of the chlorobutanolide **5** were obtained. Since, with careful attention to the exclusion of moisture, hydrogen chloride may be absent it seems possible that the molecular rearrangement of **3** to **5** occurs *via* pathway (*a*) of Scheme 3 under these conditions.

However, both of the procedures that were used for the successful synthesis of the acyl chloride **3** possessed practical disadvantages. Thus, it proved difficult to separate the by-product triphenylphosphine oxide from the acyl chloride **3** when the PPh_3–CCl_4 method was employed, and removal of the finely-divided lithium salts produced as by-products in the PCl_3–RCO_2Li process required tedious filtrations under anhydrous conditions. Furthermore, the acid chloride **3** could not be stored for any length of time as the presence of even minor amounts of hydrogen chloride led to its rapid decomposition. It was clear that an alternative acylium ion precursor was needed that was easily prepared and relatively stable, and that would afford acylium species under mild conditions.

Mixed anhydrides of trifluoroacetic acid with alkanoic and benzoic acids have been usefully employed as acylium ion precursors in Friedel–Crafts reactions.[11] In the present work, we have found that the use of mixed anhydrides with trifluoroacetic acid avoids all of the difficulties associated with labile acyl chlorides that are mentioned above. Additionally, because of the poor nucleophilicity of the trifluoroacetate ion, use of these mixed anhydrides permits the introduction of a wider variety of functionality into the product butanolides whenever better nucleophiles are added to the reaction mixture.

When 3-(tetrahydro-2′-furyl)propanoic acid **4** was reacted with one equivalent of trifluoroacetic anhydride at 0 °C in anhydrous chloroform the mixed anhydride **7** was formed in virtually quantitative yield. This could be isolated by careful evaporation of the solvent and the by-product trifluoroacetic acid provided that the temperature was not allowed to exceed *ca.* 10 °C. The mixed anhydride **7** that was obtained in this way proved to be rather stable in dry, boiling chloroform, and it could be recovered unchanged even after prolonged periods of heating. However, if a catalytic amount of trifluoroacetic acid was added to the reaction mixture then the dihydrofuranone **8** (86%) was rapidly formed as the sole product of the reaction. The structure of **8** was confirmed by its synthesis from 5-(3′-hydroxypropyl)butanolide **6** (Scheme 4).

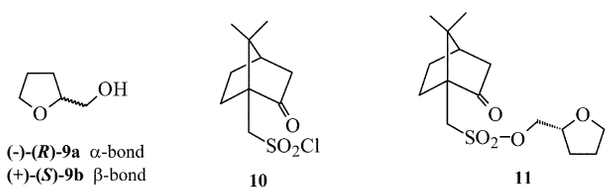


Scheme 4

The same overall conversion of the tetrahydrofurylpropanoic acid derivative **4** into the dihydrofuranone **8** could be achieved on a "one-pot" basis by simply allowing the mixed anhydride **7** to form in chloroform solution and then refluxing this in the presence of the liberated equivalent of trifluoroacetic acid.

It was clear that the mechanism of this ring-switching reaction involving the mixed anhydride **7** could be probed if optically active 3-(tetrahydro-2′-furyl)propanoic acid **4** of known absolute configuration was used as starting material. Thus, if the acylium–acyloxonium ion reaction mechanism (*a*) that is outlined in Scheme 3 applies, the dihydrofuranone **8** produced should exhibit retention of the configuration at C-2′ of the starting acid **4**. On the other hand, if the reaction proceeds *via* mechanism (*b*) of Scheme 3, *i.e.*, through direct protonation of the tetrahydrofuryl ether oxygen atom followed by neighbouring group participation by a carbonyl group located on the side-chain, then the product **8** should be formed *via* inversion of configuration at C-2′ of the starting acid **4**.

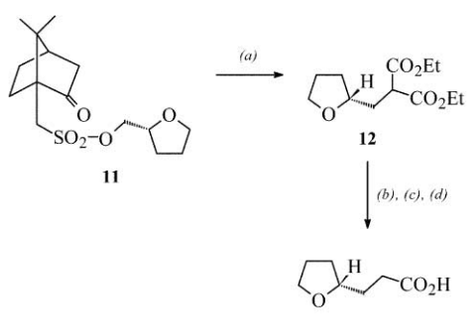
Potential starting materials for the synthesis of the acid **4** in its optically active forms are the enantiomeric tetrahydrofurfuryl alcohols **9**. Tetrahydrofurfuryl alcohol was first resolved by Balfe *et al.*[12] through fractional crystallisation of the diastereoisomeric brucine salts of the derived hydrogen phthalate. The (−)-form **9a** was later assigned the (*R*)-configuration following its synthesis from D-ribose,[13,14] and the (+)-form **9b** was shown to possess the (*S*)-configuration when it was synthesised from L-glutamic acid.[15] Further confirmation of the correctness of these assignments is available from the work of Gagnaire and Butt,[16] who converted both enantiomers **9a** and **9b** of tetrahydrofurfuryl alcohol into acyclic products of known absolute configurations, and from the work of Descours *et al.*,[17] who indirectly validated the absolute configuration of the (*R*)-alcohol **9a** when they determined the X-ray crystal structure of the (+)-tartaric acid salt of one diastereoisomer of the vasodilator naftidrofuryl.



Merz *et al.*[18] described the formation of a diastereoisomerically pure crystalline sulfonate by reaction of (±)-tetrahydrofurfuryl alcohol with (+)-(1*S*)-camphor-10-sulfonyl chloride **10**, and assigned the (*S*)-configuration to C-2′ of the tetrahydrofuryl ring of the product. However, after further experimental work, Merz and Stockhaus later[19] reversed this assignment, showing that this solid diastereoisomer **11** actually possessed the (*R*)-configuration at C-2′. In the present work, we opted to utilise the diastereoisomeric camphorsulfonates described by these authors as precursors to optically active forms of 3-(tetrahydro-2′-furyl)propanoic acid **4** since their conversion into these target molecules had already been described.

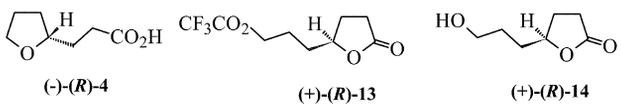
Thus, (Scheme 5), enantiomerically enriched, crystalline (+)-(1*S*)-[(2′*R*)-tetrahydro-2′-furyl]camphor-10-sulfonate **11** was reacted with diethyl sodiomalonate to give diethyl (2′*R*)-tetrahydro-2′-furfurylmalonate **12** which was then hydrolysed and decarboxylated to give scalemic (−)-(2′*R*)-3-(tetrahydro-2′-furyl)propanoic acid (*R*)-**4**.[19] A similar sequence carried out using material enriched in the (1*S*,2′*R*)-diastereoisomer of the camphorsulfonate **11** afforded scalemic (+)-(2′*S*)-3-(tetrahydro-2′-furyl)propanoic acid (*S*)-**4**.

(−)-(2′*R*)-**4** was converted into its mixed anhydride using trifluoroacetic anhydride in dry chloroform and the solution was refluxed in the presence of trifluoroacetic acid in the usual way



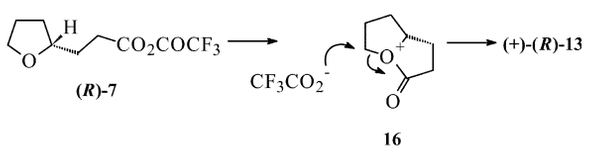
Scheme 5 *Reagents and conditions*: (*a*) diethyl malonate, NaOEt; (*b*) KOH; (*c*) HCl; (*d*) heat.

to give (+)-(5*R*)-dihydro-5-(3′-trifluoroacetoxypropyl)-2(3*H*)-furanone (*R*)-**13**. The furanone **13** could be assigned the absolute configuration shown by virtue of its hydrolysis using sodium hydrogen carbonate to give the (+)-(*R*)-enantiomer **14** of the known[20] compound (−)-(*S*)-dihydro-5-(3′-hydroxypropyl)-2(3*H*)-furanone, the absolute configuration of which has been established by Fuji *et al*.[21]



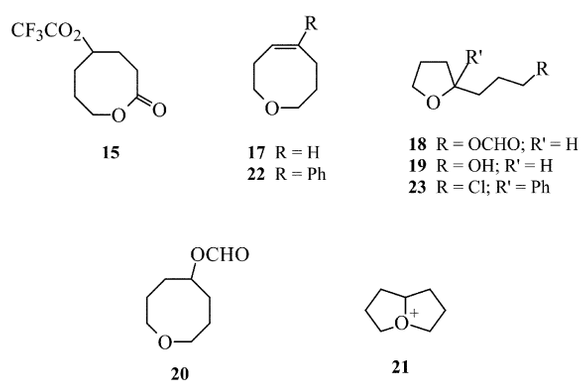
A parallel series of reactions carried out using (+)-(*S*)-acid **4** (of somewhat lower enantiomeric purity) gave, as expected, (−)-(*S*)-dihydro-5-(3′-hydroxypropyl)-2(3*H*)-furanone **14**.

These overall stereochemical results, *e.g.*, the conversion of (−)-(2′*R*)-3-(tetrahydro-2′-furyl)propanoic acid **4** into the (+)-(*R*) butanolide **13**, are consistent only with a reaction pathway (Scheme 6) that involves retention of the original configuration at C-2′ of the acid **4**, and do not agree with the alternative pathway *(b)* that appears in Scheme 3 which requires inversion at that asymmetric centre.



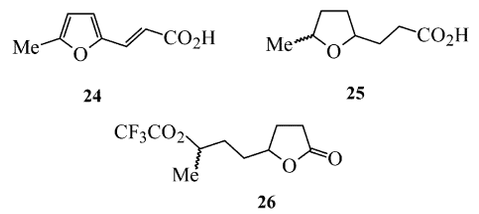
Scheme 6

Careful scrutiny of the product obtained when the mixed anhydride **7** was rearranged to the butanolide **8** in the presence of trifluoroacetic acid failed to reveal any traces of the heptanolide **15**, indicating that the reaction was completely regioselective. Formation of the lactone **15** would necessitate nucleophilic attack by trifluoroacetate at the bridgehead carbon atom of the bicyclic acyloxonium intermediate **16**, and the stereoelectronic requirements for this process are incompatible with the rigid butterfly conformation of **16**.



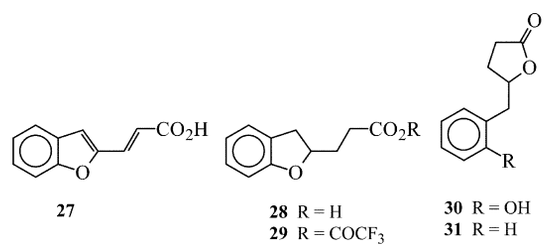
These findings are in broad agreement with results obtained by Paquette who showed[22] that the ether **17** yielded a mixture of the formate **18** and the alcohol **19** when it was treated with formic acid. None of the eight-membered formate **20** was produced in this reaction, which likely proceeds *via* the bicyclic oxonium ion **21**. Similarly, the related substituted ether **22** gives[23] only the tetrahydrofuran **23** when it is treated with hydrogen chloride, despite the electronic bias provided by the phenyl group.

Hydrogenation of (*E*)-3-(5′-methyl-2′-furyl)prop-2-enoic acid **24** gave the derived 3-(tetrahydro-2′-furyl)propanoic acid **25** which was obtained as an 80 : 20 mixture of *cis*- and *trans*-diastereoisomers as judged by ^{13}C NMR. This reacted smoothly with trifluoroacetic anhydride in refluxing chloroform to yield



the expected butanolide **26**. ^{13}C NMR spectroscopy of this product revealed an almost identical diastereoisomeric ratio to that of the starting material, a result which confirms that the formation of **26** must involve S_N2 attack by trifluoroacetate at C-5′ of the acyloxonium species which is a reaction intermediate.

It follows from the reaction mechanism that we have determined for the ring-switching of the mixed anhydride **7** into the dihydrofuranone **8** that a 3-(tetrahydro-2′-furyl)propanoic acid derivative which cannot suffer nucleophilic attack at C-5′ of its tetrahydrofuran ring should fail to react under our conditions, or should engage in some other reaction pathway.



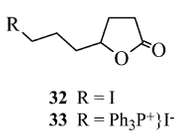
Hydrogenation of (*E*)-3-(2′-benzofuryl)propenoic acid **27**, obtained *via* Heck reaction of benzofuran with ethyl propenoate,[24] afforded the 2,3-dihydrobenzofuran **28**. This reacted smoothly with trifluoroacetic anhydride to give the mixed anhydride **29** which stubbornly resisted all attempts to rearrange it to a butanolide in the presence of trifluoroacetic acid.

The anhydride **29** was also indifferent to $BF_3{\cdot}Et_2O$, but it underwent slow conversion into the phenolic lactone **30** when it was heated in chloroform solution in the presence of the stronger Lewis acid $TiCl_4$. This compound exhibited IR maxima at 3350 and 1760 cm^{-1}, and had a ^{1}H NMR spectrum that was consistent with its structure and which was closely similar to that of the known compound **31**.[25]

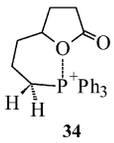
It seems reasonable to suggest that the phenolic lactone **30** is formed when the alternative reaction mechanism *(b)* outlined in Scheme 3 is imposed on the anhydride **29** as a consequence of the inability of the derived acyloxonium ion to undergo nucleophilic attack at its sp^2-hybridised C-7′. However, the poorer basicity and nucleophilicity of the 2,3-dihydrobenzofuryl ether oxygen by comparison with that of the tetrahydrofuran derivative **7** may also be relevant to the outcome.

We anticipated that the relatively poor nucleophilicity of trifluoroacetate ion would provide an opportunity to assemble a range of functionalised butanolides when reactions of the mixed anhydride **7** were being carried out. Thus, we expected that the incorporation of a better nucleophile in the reaction mixture would lead to its preferential introduction into the propyl side-chain of the product.

When the mixed anhydride **7** was reacted in acetone solution in the presence of catalytic amounts of trifluoroacetic acid together with a small excess of sodium iodide the iodopropyl[26] derivative **32** was formed in 70% yield. Formation of the iodide **32** may well occur as a result of reaction of iodide ion with the bicyclo[3.3.0] acyloxonium intermediate formed from the mixed anhydride **7**, but we cannot rule out the possibility that the acyl iodide derived from the acid **4** is formed under these conditions and that this is involved in the reaction.



32 R = I
33 R = Ph_3P^+}I^-



34

Treatment of the iodide **32** with triphenylphosphine yielded the phosphonium salt **33**. In the ^{1}H NMR spectrum of **33**, obtained in $CDCl_3$ solution, the methylene protons adjacent to the triphenylphosphonium group resonated as a well-separated AB system at δ 3.67 ppm and at δ 4.12 ppm. Spin-decoupling experiments revealed values for J_{gem} and for $^2J_{H,P}$ of, respectively, 15 and 13 Hz. H–H COSY experiments showed that, whereas both protons of the middle methylene group of the propyl chain of **33** appeared at much the same chemical shifts, the protons of the methylene group adjacent to the furanone ring also formed an AB system, resonating at δ 1.85 ppm and at δ 2.46 ppm.

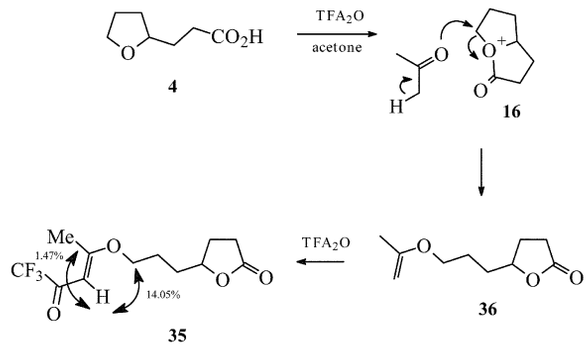
The diastereotopicity shown by the protons of the C-3 methylene group, which is immediately adjacent to the asymmetric centre of **33**, is not unexpected, but the observed $\Delta\delta$ value of *ca*. 0.6 ppm is surprisingly large. The existence of significant diastereotopicity at the distal end of the propyl side-chain ($\Delta\delta$ 0.45 ppm) also seems unusual. It may be that this effect reflects the presence of the quasi-cyclic species **34** which could arise *via* electrostatic interaction between the positively charged phosphonium centre and the oxygen atoms of the lactone function.

The remainder of the various NMR spectra of the phosphonium salt **33** were unexceptional, and the three ^{13}C–^{31}P coupling constants for the methylene carbon atoms of its propyl side-chain are in good agreement with typical literature[27] values for *n*-alkyl(triphenyl)phosphonium systems.

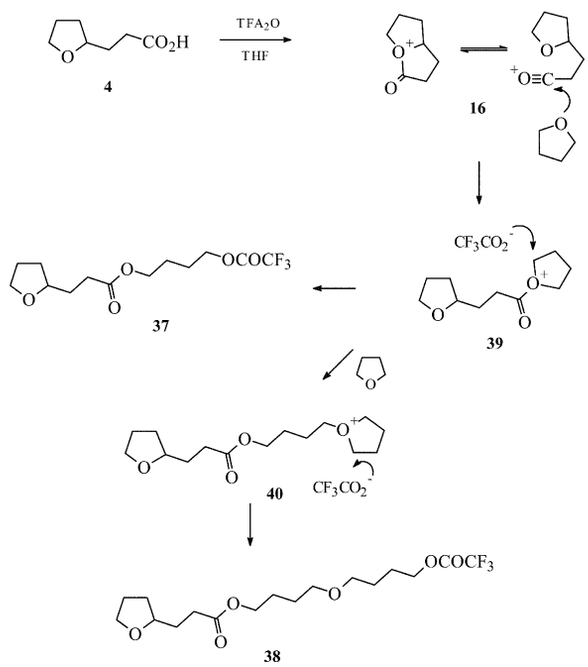
We were unable to satisfactorily generate a phosphonium ylid from the salt **33**. Treatment with LDA followed by introduction of an aldehyde routinely led to recovery of **33** from the aqueous phase following work-up of the reaction. Minor amounts of Wittig products were occasionally encountered, but competitive deprotonation α to the lactonic carbonyl function or the intervention of intramolecular condensation reactions[28] are likely hazards here.

Remarkably, when the tetrahydrofurylpropanoic acid **4** was heated in acetone solution in the presence of excess trifluoroacetic anhydride without any other nucleophile being present it was efficiently converted, not into the expected dihydrofuranone **8**, but into the novel vinylogous ester **35**. This compound exhibited a ^{1}H NMR spectrum that revealed the presence of a 5-substituted butanolide and of the conjugated enol ether system. The latter moiety showed signals for the vinylic methyl group at δ 2.43 ppm and for the vinylic proton at δ 5.68 ppm. We assign the stereochemistry of **35** on the basis of a set of NOE experiments that delivered the results indicated on the structural formula. The formation of **35** can be rationalised as shown in Scheme 7. Here, we suggest that trapping of the bicyclic acyloxonium ion **16** by acetone initially affords the enol ether **36**. This electron-rich alkene then undergoes Friedel–Crafts acylation by the trifluoroacetic anhydride present in the reaction mixture to give **35**.

When the acid **4** was dissolved in tetrahydrofuran and converted *in situ* into its carboxylic–trifluoroacetic mixed anhydride **7** by reaction with trifluoroacetic anhydride, and the mixture was then heated, the solvent competed successfully with trifluoroacetate ion in reaction with the generated acylium and oxonium ions. Thus, although the expected rearrangement of **7** to the dihydrofuranone **8** did occur, the yield was poor and the product was accompanied by small amounts of each of the diesters **37** and **38**. The formation of **37** can be rationalised (Scheme 8) by invoking intermolecular attack on the acylium species **16** derived from the mixed anhydride **7** by tetrahydrofuran to give **39**. Nucleophilic attack on **39** by trifluoroacetate



Scheme 7



Scheme 8

ion leads to ring-cleavage and production of **37**. Similarly (Scheme 8), the chain-extended ester **38** can be formed *via* the same oxonium intermediate **39**, which then reacts with a second molecule of tetrahydrofuran to give **40** before reaction with trifluoroacetate ion takes place.

Experimental

^{1}H NMR spectra were recorded for solutions in $CDCl_3$ using JEOL PMX-60, Bruker MSL-300 or Bruker AVANCE DPX-400 spectrometers, with Me_4Si as internal standard for 60 MHz spectra. *J* values are given in Hz. Assignments were verified by appropriate H–H COSY, C–H COSY and ^{13}C-DEPT experiments. IR spectra were recorded for Nujol mulls (N) or for liquid films (L) between sodium chloride plates using Perkin-Elmer 883 or Paragon-FT spectrometers. Some spectra were obtained using a Genesis FT-IR spectrometer and were processed using WinFirst software. High-resolution mass spectra were obtained using a VG Alto Spec instrument. Melting points (uncorrected) were measured in unsealed capillary tubes using a Stuart Scientific SMP2 digital apparatus. Optical rotations were measured for solutions in a 1 dm cell using a Perkin-Elmer 141 polarimeter and are given in 10^{-1} deg cm^2 g^{-1}. Thin layer chromatography was carried out using Merck Kieselgel 60 F_{254} 0.2 mm silica gel plates. Column chromatography was carried out using Merck Kieselgel 60 (70–230 mesh) silica gel. All solvents were distilled before use. Ethereal extracts of reaction products were dried over anhydrous magnesium sulfate.

Elemental analyses were performed by the Microanalytical Laboratory, University College Dublin.

3-(Tetrahydro-2′-furyl)propanoic acid 4

(*E*)-3-(2-Furyl)propenoic acid[29] (10 g) in ethyl acetate (100 cm^3) was hydrogenated at 1 atm over palladium/charcoal catalyst (10%; 0.4 g) to give the acid **4** (9.8 g; 95%) as an oil,[30] bp 110 °C/1 mmHg; ν_{max} (L) 2966, 2877, 1710, 1444, 1353, 1261, 1180, 1070, 1024, 908 and 788 cm^{-1}; δ_H (400 MHz) 1.52 (1H, m, including J_{gem} 12.0, 3′-H_a), 1.79–2.08 (4H, m, 3-CH_2 and 4′-CH_2), 2.03 (1H, m, 3′-H_b), 2.48 (2H, m, AB system including J_{gem} 16.5, 2-CH_aH_b), 3.76 (1H, m, 5′-CH_a), 3.87 (2H, m, 2′-*H* and 5′-CH_b) and 10.3 (1H, br s, exch. D_2O, –CO_2H) ppm; δ_C (100.6 MHz) 25.7 (4′-*C*H_2), 30.3 (3-*C*H_2), 31.0 (2-*C*H_2), 31.1 (3′-*C*H_2), 67.8 (5′-*C*H_2), 78.3 (2′-*C*H) and 178.2 (*C*=O) ppm.

Dihydro-5-(3′-chloropropyl)-2(3*H*)-furanone 5 by reaction of the acid 4 with thionyl chloride

The acid **4** (2.24 g) was dissolved in freshly distilled thionyl chloride (2.8 g). After 12 h at room temperature, excess reagent was removed under reduced pressure to give a dark-coloured oil. This was taken up in ether and the extract was washed with sodium hydrogen carbonate solution, dried, and evaporated to give crude lactone **5** as an *oil* (2.1 g) that was chromatographed over silica gel using 50 : 50 ethyl acetate : hexane as eluant to give pure material (1.45 g); ν_{max} (L) 1775 and 1178 cm^{-1}; δ_H (60 MHz) 1.7–1.95 (6H, m, 4-, 1′- and 2′-CH_2 groups), 2.4 (2H, m, 3-CH_2), 3.5 (2H, t, *J* 6.7 Hz, –CH_2Cl) and 4.4 (1H, m, H-5) ppm. [*Calculated* for $C_7H_{11}ClO_2$: C 51.69, H 6.77; *found* C 51.92, H 6.83%].

3-(Tetrahydro-2′-furyl)propanoyl chloride 3

(a)[8] The acid **4** (5 g) was dissolved in chloroform (50 cm^3) containing tetrachloromethane (5.4 g) and triphenylphosphine (9.1 g). This mixture was refluxed during 0.5 h and solvent was then evaporated at reduced pressure. The acid chloride **3** was separated from by-product triphenylphosphine oxide by extraction into hexane. Evaporation of solvent gave an unstable oil (3.8 g), containing a little unreacted acid **4**, which could not be distilled without decomposition; ν_{max} (L) 2954, 2872, 1772, 1438, 1184, 1120 and 1070 cm^{-1}; δ_H (400 MHz) 1.48 (1H, m, 3-H_a), 1.8–2.1 (4H, m, 3-CH_2 and 4′-CH_2), 2.05 (1H, m, 3′-H_b), 2.54 (2H, m, 2-CH_2), 3.74 (1H, m, 5′-CH_a) and 3.85 (2H, m, 2′-*H* and 5′-CH_b) ppm.

(b)[9] The acid **4** (4.5 g) was treated with lithium hydroxide monohydrate (1.3 g) in water (30 cm^3). Solvent was removed under reduced pressure and the lithium salt was dried at 110 °C, ground into a fine powder, and suspended in anhydrous chloroform (50 cm^3). Phosphorus trichloride (1.1 g; 0.33 mol) was added and the mixture was stirred during 12 h. It was then diluted with ether, filtered through a pad of Celite, and evaporated to yield the acid chloride **3** (3.6 g; 70%), identical with that described under *(a)* above, which was used without further purification.

Dihydro-5-(3′-chloropropyl)-2(3*H*)-furanone 5 from the acid chloride 3

The acid chloride **3** (1.15 g) was dissolved in dry chloroform (15 cm^3) with freshly fused zinc chloride (10 mg), and the mixture was refluxed under dry nitrogen during 2 h. It was then washed sequentially with water, aqueous sodium hydrogen carbonate solution and brine, and then dried and evaporated to give the lactone **5** (0.89 g; 77%).

Dihydro-5-(3′-hydroxypropyl)-2(3*H*)-furanone 6[8]

4-Oxoheptane-1,7-dioic acid (2.2 g) was dissolved with sodium hydroxide (1.1 g) in water (20 cm^3). Sodium borohydride (0.32 g) was added and the mixture was stirred during 12 h. It was then acidified using dilute sulfuric acid and continuously extracted with ether during 6 h. Evaporation of the dried extract yielded dihydro-5-(2′-carboxyethyl)-2(3*H*)-furanone (1.9 g; 96%); δ_H (60 MHz) 1.7–2.3 (6H, m, –CH_2 groups), 2.65 (2H, t, *J* 7.0, 2′-CH_2), 4.5 (1H, m, 5-*H*) and 10.0 (1H, s, exch. D_2O, –CO_2H) ppm. To the above acid (2.0 g; 12.5 mmol) in ether (20 cm^3) was added borane–methylsulfide complex (1.4 cm^3; 14.2 mmol) and the mixture was stirred during 2 h. It was then evaporated to yield dihydro-5-(3′-hydroxypropyl)-2(3*H*)-furanone **6** (1.7 g; 92%) as an oil that had ν_{max} (L) 3427, 1765 and 1186 cm^{-1}; δ_H (60 MHz) 1.6–2.7 (6H, m, CH_2 groups), 2.31 (1H, br s, exch. D_2O, –O*H*), 2.54 (2H, m, 3-CH_2), 3.65 (2H, t, *J* 7.0, 3′-CH_2) and 4.55 (1H, m, 5-*H*) ppm.

Dihydro-5-(3′-chloropropyl)-2(3*H*)-furanone 5 from dihydro-5-(3′-hydroxypropyl)-2(3*H*)-furanone 6

Methanesulfonyl chloride (0.2 g) was added to the furanone **6** (0.1 g) in pyridine (3 cm^3) at 0 °C. The ice-bath was then removed and, after a further 3 h, the usual work-up afforded the dihydrofuranone **5** (0.1 g), identical with material prepared as described above.

3-(Tetrahydro-2′-furyl)propanoic-trifluoroacetic anhydride 7

The acid **4** (2 g) was dissolved in dry chloroform (20 ml) and the solution was cooled to 0 °C. Trifluoroacetic anhydride (3 g; 1 equiv.) was added with stirring at such a rate that the temperature did not rise above 0 °C. After a further 2 h at this temperature, solvent and trifluoroacetic acid were evaporated at reduced pressure (0.1 mmHg) at temperatures that were not allowed to exceed 10 °C to give the *anhydride* **7** (3 g; 90%) as an *oil* which had ν_{max} (L) 2925, 1789, 1735, 1450, 1361, 1219, 1163, 1043, 970, 914, 779 and 732 cm^{-1}; δ_H (400 MHz) 1.61–2.05 (6H, overlapping ms, 3-CH_2, 3′-CH_2 and 4′-CH_2), 2.47 (2H, m, 2-CH_2), 3.95 (1H, m, 5′-CH_a) and 4.18 (2H, m, 2′-*H* and 5′-CH_b) ppm. This material did not give $[M]^+$ under any conditions that were tried and, due to its labile nature, did not give satisfactory combustion analysis results.

Dihydro-5-(3′-trifluoroacetoxypropyl)-2(3*H*)-furanone 8

The anhydride **7** (2 g) was dissolved in chloroform (20 cm^3) with trifluoroacetic acid (0.1 g) and the solution was refluxed during 1 h. The reaction mixture was then washed with sodium hydrogen carbonate solution, dried, and evaporated to yield the *dihydrofuranone* **8** as an *oil*, (1.7 g), bp 115–117 °C/0.5 mmHg; ν_{max} (L) 2954, 1779 (overlapping C=O absorptions), 1463, 1406, 1354, 1221, 1165, 1022, 968, 910, 777 and 731 cm^{-1}; δ_H (400 MHz) 1.78–2.07 (5H, m, 4-CH_a, 1′-CH_2 and 2′-CH_2), 2.39 (1H, m, 4-CH_b), 2.56 (1H, ddd, *J* 9.0, 6.5 and 1.0, 3-CH_a), 2.58 (1H, ddd, *J* 9.0, 7.0 and 1.0, 3-CH_b), 4.41 (1H, m, 3′-CH_a), 4.45 (1H, m, 3′-CH_b) and 4.53 (1H, m, 5-C*H*) ppm; δ_C (100.6 MHz) 24.5 (2′-*C*H_2), 27.9 (4-*C*H_2), 28.6 (3-*C*H_2), 31.8 (1′-*C*H_2), 67.3 (3′-*C*H_2), 79.7 (5-*C*H), 114.02 (quaternary, q, $J_{C,F}$ 286, –*C*F_3), 159.05 (quaternary, q, $J_{C,F}$ 42, –*C*OCF_3) and 176.1 (lactone *C*=O) ppm; δ_F (376.3 MHz) −75.6 (CF_3) ppm. [*Calculated* for $C_9H_{11}F_3O_4$: C 45.00, H 4.58; *found* C 44.86, H 4.66%].

"One-pot" conversion of the acid 4 into dihydro-5-(3-trifluoroacetoxypropyl)-2(3*H*)-furanone 8

The acid **4** (2 g) was dissolved in dry chloroform (20 cm^3) with trifluoroacetic anhydride (3 g) and the mixture was refluxed during 1 h. Work-up as described for the previous experiment afforded the dihydrofuranone **8** (2.9 g; 86.5%).

Dihydro-5-(3′-trifluoroacetoxypropyl)-2(3*H*)-furanone 8 from dihydro-5-(3′-hydroxypropyl)-2(3*H*)-furanone 6

Dihydro-5-(3′-hydroxypropyl)-2(3*H*)-furanone **6** (0.11 g) was refluxed with trifluoroacetic anhydride (0.19 g) in chloroform (5 cm^3) during 1 h. Work up afforded the dihydrofuranone **8**

(0.12 g; 66%), identical in every respect with material prepared as described above.

(−)-(2′*R*)-3-(Tetrahydro-2′-furyl)propanoic acid (*R*)-4

rac-Tetrahydrofurfuryl alcohol (5 g) was reacted with (+)-(1*S*)-camphor-10-sulfonyl chloride **10** (12.7 g) in dry pyridine (15 cm^3) according to a described [19] procedure to give a mixture of diastereoisomeric camphorsulfonate esters. Fractional crystallisation of this mixture from tetrachloromethane–hexane followed by several recrystallisations from the same solvent afforded enantiomerically enriched (+)-(2*R*)-tetrahydrofurfuryl (*S*)-camphorsulfonate **11** (4 g; 29%), mp 67 °C (*lit.* [19] 67 °C for its solvate with 0.25 mole of CCl_4) and $[\alpha]_D$ +11 (*c.* 1.0 in EtOH) (lit.[18] $[\alpha]_D$ +12.3).

This camphorsulfonate (3 g) was added to a solution of diethyl malonate (2 g) in ethanol (15 cm^3) containing sodium ethoxide (0.68 g) and the resulting mixture was refluxed during 18 h. The usual work up afforded an oil which was fractionally distilled to give ethyl (2′*R*)-2-carboethoxy-3-(tetrahydro-2′-furyl)propanoate **12** (0.9 g; 39%). This ester (0.83 g) was dissolved in a solution of potassium hydroxide (0.6 g) in water (10 cm^3) and ethanol (10 cm^3) and the mixture was refluxed for 6 h. Ethanol was removed at reduced pressure and the aqueous residue was extracted with ether. It was then acidified with concentrated hydrochloric acid, extracted several times with ether, and the combined extract was dried and evaporated to give (2′*R*)-2-carboxy-3-(tetrahydro-2′-furyl)propanoic acid (0.42 g) as an oil.

The above acid (0.39 g) was heated at 150–160 °C during 2 h after which time evolution of carbon dioxide had ceased. The residual (−)-(2′*R*)-3-(tetrahydro-2′-furyl)propanoic acid (*R*)-**4** (0.25 g) had $[\alpha]_D$ −14 (*c.* 1.0 in EtOH) (lit.[19] $[\alpha]_D$ −10.2), and was spectroscopically identical with racemic **4** synthesised as described above.

(+)-(2′*S*)-3-(Tetrahydro-2′-furyl)propanoic acid (*S*)-4

The mother liquor remaining after crystallisation of (+)-(2*R*)-tetrahydrofurfuryl (*S*)-camphorsulfonate **11** (described above) was evaporated at reduced pressure. The oily residue was dissolved in carbon tetrachloride (8 cm^3) and the solution was diluted with hexane (10 cm^3) and refrigerated for 24 h. The crystals that formed were removed and the filtrate was evaporated to give a viscous oil enriched in (+)-(2*S*)-tetrahydrofurfuryl (*S*)-camphorsulfonate (3.8 g; 30%) that had $[\alpha]_D$ +37 (*c.* 1.0 in EtOH) (lit.[18] $[\alpha]_D$ +46.6).

This (*S,S*)-camphorsulfonate (3.0 g) was converted into (+)-(2′*S*)-3-(tetrahydro-2′-furyl)propanoic acid (*S*)-**4** exactly as described above for the (*R*)-isomer. The product, spectroscopically identical with racemic **4**, had bp 110 °C/1 mmHg and $[\alpha]_D$ +5.3 (*c.* 4.7 in EtOH) (lit.[19] $[\alpha]_D$ +8.8, *c.* 1.0 in EtOH).

(+)-(5*R*)-Dihydro-5-(3′-trifluoroacetoxypropyl)-2(3*H*)-furanone (+)-13

The acid (−)-(*R*)-**4** (0.17 g) was dissolved in chloroform (5 cm^3) with trifluoroacetic anhydride (0.37 g) and the mixture was refluxed during 1 h. The usual work-up afforded *(+)-(5R)-dihydro-5-(3′-trifluoroacetoxypropyl)-2(3H)-furanone* (+)-**13** (0.2 g; 70%), bp 115–117 °C/0.5 mmHg, IR and NMR spectra identical to those detailed for the racemate **8** above, $[\alpha]_D$ +21 (*c.* 0.9 in EtOH).

(+)-(5*R*)-Dihydro-5-(3′-hydroxypropyl)-2(3*H*)-furanone (+)-14

The trifluoroacetate (+)-**13** (0.12 g) was stirred during 6 h with methanol (10 cm^3) and aqueous sodium hydrogen carbonate (10 cm^3). Methanol was removed under reduced pressure and the aqueous residue was continuously extracted into ether during 6 h. The ethereal extract was dried and evaporated to give *(+)-(5R)-dihydro-5-(3′-hydroxypropyl)-2(3H)-furanone* (+)-**14** (0.07 g; 90%); ν_{max} (L) 3427 and 1765 cm^{-1}; δ_H (60 MHz) as for the racemate **6** described above, $[\alpha]_D$ +22 (*c.* 0.7 in EtOH) (lit.[20] $[\alpha]_D$ −24.2 (*c.* 0.33 in EtOH) for the (−)-(*S*)-enantiomer of **14** that was determined to be of 47% ee).

(−)-(5*S*)-Dihydro-5-(3′-trifluoroacetoxypropyl)-2(3*H*)-furanone (−)-13

The acid (+)-(*S*)-**4** (1.0 g) was dissolved in chloroform (10 cm^3) with trifluoroacetic anhydride (1.5 g) and the mixture was refluxed during 1 h. The usual work-up followed by distillation afforded *(−)-(5S)-dihydro-5-(3′-trifluoroacetoxypropyl)-2(3H)-furanone* (−)-**13** (0.93 g; 56%), bp 115–117 °C/0.5 mmHg, IR and NMR spectra identical to those detailed for the racemate **8** above, $[\alpha]_D$ −12 (*c.* 3.6 in EtOH).

(−)-(5*S*)-Dihydro-5-(3′-hydroxypropyl)-2(3*H*)-furanone (−)-14

The trifluoroacetate (−)-**13** (0.12 g) was stirred during 6 h with methanol (10 cm^3) and aqueous sodium hydrogen carbonate (10 cm^3). Methanol was removed under reduced pressure and the aqueous residue was continuously extracted into ether during 6 h. The ethereal extract was dried and evaporated to give *(−)-(5S)-dihydro-5-(3′-hydroxypropyl)-2(3H)-furanone* (−)-**14** (0.07 g; 90%); ν_{max} (L) 3427 and 1765 cm^{-1}; δ_H (60 MHz) as for the racemate **6** described above, $[\alpha]_D$ −12 (*c.* 3.6 in EtOH).

3-(5′-Methyltetrahydro-2′-furyl)propanoic acid 25

(*E*)-3-(5′-Methyl-2′-furyl)prop-2-enoic acid **24** [31] (1.8 g) in ethyl acetate (20 cm^3) was hydrogenated at 1 atm over palladium/charcoal catalyst (5%; 0.2 g) to give an 80 : 20 mixture of the *cis*- and *trans*-diastereoisomers of the acid **25** (1.7 g; 86%) as an oil,[32] ν_{max} (L) 2964, 2875, 1708, 1445, 1354, 1265, 1182, 1073, 1027, 912 and 790 cm^{-1}; δ_H (300 MHz; major diastereoisomer) 1.16 (3H, d, *J* 6.1, Me), 1.40 (2H, m), 1.78 (2H, m), 1.93 (2H, m), 2.37 (2H, distorted t, 2-CH_2), 3.78 (2H, m, 2′-*H* and 5′-*H*) and 8.60 (1H, br s, exch. D_2O, –CO_2H) ppm; δ_C (75.5 MHz) 21.2 (5′-*C*H_3), 29.2 (*C*H_2), 30.8 (*C*H_2), 30.94 (*C*H_2), 32.72 (*C*H_2), 75.63 (5′-*C*H), 78.21 (2′-*C*H) and 178.74 (*C*=O) ppm.

Dihydro-5-(3′-trifluoroacetoxybutyl)-2(3*H*)-furanone 26

The acid **25** (0.95 g) was dissolved with trifluoroacetic anhydride (0.9 cm^3; 1.1 equiv.) in dry chloroform (10 cm^3) and the mixture was refluxed during 1 h. It was then cooled, diluted with additional chloroform, washed with aqueous sodium hydrogen carbonate solution, dried and evaporated to give an 80 : 20 (NMR) mixture of diastereoisomers of dihydro-5-(3′-trifluoroacetoxybutyl)-2(3*H*)-furanone **26** (1.0 g; 67%) as an *oil* that had ν_{max} (L) 2954, 1780 (overlapping C=O absorptions), 1461, 1406, 1354, 1226, 1163, 1019, 971, 910, 779 and 730 cm^{-1}; δ_H (300 MHz; major diastereoisomer) 1.39 (3H, d, *J* 6.3, –CH_3), 1.80 (4H, m, 4-CH_2 and 1′-CH_2), 2.45 (4H, m, 2′-CH_2 and 3-CH_2), 4.50 (1H, m, 5-*H*) and 5.19 (1H, m, 4′-*H*) ppm; δ_C (75.5 MHz; major diastereoisomer) 19.10 (–*C*H_3), 27.69 (–*C*H_2), 28.47 (–*C*H_2), 30.71 (–*C*H_2), 31.01 (–*C*H_2), 75.48 (–*C*H), 79.67 (–*C*H), 114.33 (quaternary, q, $J_{F,C}$ 285.8, –*C*F_3), 156.81 (quaternary, q, $J_{F,C}$ 42.21, –*C*OCF_3) and 176.66 (quaternary, lactone –*C*=O) ppm. [*Calculated* for $C_{10}H_{13}F_3O_4$: C 47.24, H 5.12; *found* C 47.51, H 5.27%].

3-(2′-[2′,3′-Dihydrobenzofuryl])propanoic acid 28

Ethyl 3-(2′-benzofuryl)propenoate (0.6 g; 58%) was prepared according to a literature method [24] from ethyl propenoate (0.5 g), benzofuran (0.7 g), and palladium acetate (1.12 g) in acetic acid (50 cm^3). This ester (0.21 g) was hydrolysed using sodium hydroxide (0.4 g) in 50% aqueous ethanol (5 cm^3) to give the derived unsaturated acid **27** as an oil (0.16 g) which was hydrogenated at 1 atm over palladium/charcoal (5%; 10 mg) in ethyl acetate (10 cm^3) to give the title compound **28** (0.12 g) as

an oily solid (lit.[33] mp 66 °C); δ_H (60 MHz) 1.8–2.2 (2H, m, –C*H*$_2$CH$_2$CO$_2$H), 2.3–2.7 (2H, m, 3-C*H*$_2$), 2.7–3.3 (2H, m, –C*H*$_2$CO$_2$H), 4.6 (1H, m, *H*-2), 6.4–7.1 (4H, ms, Ar*H*) and 10.5 (1H, s, exch. D_2O, –CO$_2$*H*) ppm.

3-(2′-[2′,3′-Dihydrobenzofuryl])propanoic-trifluoroacetic anhydride 29

The acid **28** (0.12 g) was refluxed with trifluoroacetic anhydride (0.1 cm^3) in chloroform (3 cm^3) during 3 h. Solvent, excess trifluoroacetic anhydride, and trifluoroacetic acid were evaporated at reduced pressure to give the oily *anhydride* **29** (0.13 g); ν_{max} (L) 1785 and 1739 cm^{-1}; δ_H (60 MHz) 2.0 (2H, m, 3-C*H*$_2$), 2.54 (2H, m, 3′-C*H*$_2$), 2.95 (2H, m, –C*H*$_2$CO$_3$CF$_3$), 4.7 (1H, m, *H*-2) and 6.4–7.1 (4H, ms, Ar*H*) ppm.

Attempted reaction of 3-(2′-[2′,3′-dihydrobenzofuryl])-propanoic-trifluoroacetic anhydride 29 with BF_3·Et_2O

The anhydride **29** (0.1 g) was dissolved in chloroform (5 cm^3) with boron trifluoride etherate (0.1 cm^3) and the mixture was refluxed during 2 h. It was then diluted with chloroform (20 cm^3) and washed sequentially with water and with sodium hydrogen carbonate solution. After drying and evaporation the anhydride **29** (0.07 g) was (IR, NMR) recovered.

Reaction of 3-(2′-[2′,3′-dihydrobenzofuryl])propanoic-trifluoroacetic anhydride 29 with $TiCl_4$

The anhydride **29** (0.07 g) was dissolved in ice-cold chloroform (3 cm^3) to which was added titanium tetrachloride (0.09 g; excess). The mixture immediately turned green and, after standing at rt during 12 h, it was diluted with chloroform (20 cm^3) and washed successively with water, sodium hydrogen carbonate solution, and brine. After drying and evaporation *dihydro-5-([2′-hydroxyphenyl]methyl)-2(3H)-furanone* **30** (0.03 g; 64%) was obtained as an *oil* which had ν_{max} (L) 3350 and 1760 cm^{-1}; δ_H (60 MHz) 1.9 (2H, m, 4-C*H*$_2$), 2.4 (2H, m, 3-C*H*$_2$), 2.95 (2H, d, *J* 5.5 Hz, ArC*H*$_2$–), 3.6 (1H, s, exch. D_2O, –O*H*), 4.7 (1H, m, 5-*H*) and 6.5–7.2 (4H, overlapping m, Ar*H*) ppm. [*Calculated* for $C_{11}H_{12}O_3$: C 68.75, H 6.25; *found* C 68.54, H 6.33%).

Dihydro-5-(3′-iodopropyl)-2(3*H*)-furanone 32

The acid **4** (1.5 g) and dry sodium iodide (4.68 g) were dissolved in acetone (50 cm^3) and the stirred solution was cooled to 0 °C. Trifluoroacetic anhydride (2.4 g) was added at such a rate that the temperature did not rise above 0 °C. After a further 0.5 h at this temperature, the mixture was refluxed during 4 h. Much of the acetone was removed by evaporation at reduced pressure and the residue was then diluted with ether and washed sequentially with water, 5% aqueous sodium hydrogen carbonate, 10% aqueous sodium thiosulfate and brine, dried and evaporated to give the lactone **32** as an oil[26] (1.85 g; 70%); ν_{max} (L) 2935, 1774 and 1176 cm^{-1}; δ_H (400 MHz) 1.78–2.12 (5H, m, C-4 C*H*$_a$, C-1′ C*H*$_2$, C-2′ C*H*$_2$), 2.33–2.41 (1H, m, C*H*$_b$), 2.54–2.58 (2H, m, C-3 C*H*$_2$), 3.20–3.27 (2H, m, C-3′ C*H*$_2$) and 4.49–4.55 (1H, m, C-5 C*H*) ppm; δ_C (100.6 MHz) 5.6 (C-3′ *C*H$_2$), 27.9 (C-4 *C*H$_2$), 28.6 (C-3 *C*H$_2$), 29.2 (C-2′ *C*H$_2$), 36.4 (C-1′ *C*H$_2$), 79.6 (C-5 *C*H) and 176.3 (lactone *C*=O) ppm.

[3-(5′-Oxotetrahydro-2′-furyl)propyl]triphenylphosphonium iodide 33

The iodolactone **32** (0.92 g) was refluxed in toluene (30 cm^3) with triphenylphosphine (1.05 g) during 5 h. Solvent was decanted from the solid product which was then extracted twice with warm toluene. The solid was dried to give the crude phosphonium salt **33** as a *solid* (1.92 g; 72%). A sample recrystallised from ethyl acetate had mp 148–150 °C; ν_{max} (N) 2952, 2923, 2853, 1761, 1610, 1586, 1483, 1462, 1437, 1406, 1377, 1365, 1316, 1275, 1229, 1188, 1160, 1110, 1045, 1026, 996, 969, 944, 892, 848, 808, 787, 755, 739, 723 and 690 cm^{-1}; δ_H (400 MHz) 1.76–1.94 (4H, m, 3-*H*$_a$, 2-C*H*$_2$ and 3′-*H*$_a$), 2.39–2.54 (4H, m, 3-*H*$_b$, 4′-C*H*$_2$ and 3′-*H*$_b$), 3.67 (1H, m, 1-*H*$_a$), 4.12 (1H, m, 1-*H*$_b$), 4.76 (1H, m, 2′-*H*), 7.71–7.75 (6H, m, Ar*H*) and 7.82 (9H, m, Ar*H*) ppm; δ_C (100.6 MHz) 19.4 (d, $J_{P,C}$ 3.8, 2-*C*H$_2$), 22.5 (d, $J_{P,C}$ 51.5, 1-*C*H$_2$), 28.0 (3′-*C*H$_2$), 28.7 (4′-*C*H$_2$), 35.5 (d, $J_{P,C}$ 16.5, 3-*C*H$_2$), 80.1 (2′-*C*H), 117.5 (quaternary, d, $J_{P,C}$ 85.5, Ar–*C*), 130.1 (d, $J_{P,C}$ 11.6, Ar–*C*H), 133.3 (d, $J_{P,C}$ 9.7, Ar–*C*H), 134.7 (d, $J_{P,C}$ 2.9, Ar–*C*H) and 176.8 (*C*=O) ppm; δ_P (162 MHz) 25.5 (*P*$^+$–Ar$_3$) ppm.

Irradiation of the 2-CH$_2$ protons simultaneously collapsed the multiplets at δ_H 3.67 ppm and at δ_H 4.00 ppm to a pair of double doublets exhibiting J_{gem} 15 Hz and $J_{H,P}$ 13 Hz. [*Calculated* for $C_{25}H_{26}IO_2P$: C 58.13, H 5.04; *found* C 57.94, H 4.97%].

(*E*)-5-[3′-(4″, 4″, 4″-Trifluoro-1″-methyl-3″-oxobut-1″-enyloxy)-propyl]dihydro-2(3*H*)-furanone 35

The acid **4** (0.15 g) was dissolved in acetone (9 cm^3) at 0 °C. Trifluoroacetic anhydride (0.48 g) was added with stirring at such a rate that the temperature did not rise above 0 °C. After a further 0.5 h at this temperature, the mixture was refluxed during 4 h. Acetone was removed by evaporation at reduced pressure and the residue was diluted with ether and the ethereal extract was washed sequentially with water, 5% aqueous sodium hydrogen carbonate and brine, dried and evaporated to give the lactone **35** (0.29 g; 64%) as an *oil* that could be chromatographed over silica gel using ethyl acetate–hexane as eluant and that had ν_{max} (L) 2954, 2927, 1774 (overlapping C=O absorptions), 1702 (C=C), 1577, 1465, 1421, 1322, 1259, 1184, 1141, 1103, 1043, 970, 914, 881, 804 and 727 cm^{-1}; δ_H (400 MHz) 1.75–2.05 (5H, m, 4-C*H*$_a$, 1′-C*H*$_2$ and 2′-C*H*$_2$), 2.35–2.44 (1H, m, 4-C*H*$_b$), 2.43 (3H, s, C*H*$_3$), 2.57–2.61 (2H, m, 3-C*H*$_2$), 3.93–4.05 (2H, m, 3′-C*H*$_2$), 4.52–4.59 (1H, apparent quintet, *J* 6.5, 5-C*H*) and 5.68 (1H, s, 2″-C*H*) ppm; δ_C (100.6 MHz) 21.0 (*C*H$_3$), 24.5 (2′-*C*H$_2$), 27.8 (4-*C*H$_2$), 28.5 (3-*C*H$_2$), 31.9 (1′-*C*H$_2$), 68.9 (3′-*C*H$_2$), 80.1 (5-*C*H), 91.9 (2″-*C*H), 116.5 (quartet, $J_{F,C}$ 291.5, *C*F$_3$), 176.4 (2-*C*=O), 178.5 (quartet, $J_{F,C}$ 33.0, *C*OCF$_3$) and 180.2 (1″-*C*) ppm; δ_F (376.3 MHz) −78.9 (C*F*$_3$) ppm. HRMS (+ve ion FAB): *found* 281.09970; *calculated* for $[C_{12}H_{15}F_3O_2 + H]^+$ 281.09838.

4″-Trifluoroacetoxybutyl 3-(tetrahydro-2′-furyl)propanoate 37 and 9″-trifluoroacetoxy-5″-oxanonyl 3-(tetrahydro-2′-furyl)-propanoate 38

The acid **4** (0.15 g) and trifluoroacetic anhydride (0.24 g) in tetrahydrofuran (10 cm^3) were refluxed together during 6 h. The usual work up gave an oily mixture of products that was chromatographed on silica gel using hexane : ethyl acetate 85 : 15 as eluant to give, sequentially, *4″-trifluoroacetoxybutyl 3-(tetrahydro-2′-furyl)propanoate* **37** (22 mg; 7%), *9″-trifluoroacetoxy-5″-oxanonyl 3-(tetrahydro-2′-furyl)propanoate* **38** (12 mg; 3%) and dihydro-5-(3′-trifluoroacetoxypropyl)-2(3*H*)-furanone **8** (62 mg; 25%).

4″-Trifluoroacetoxybutyl 3-(tetrahydro-2′-furyl)propanoate **37** was obtained as an *oil* that had ν_{max} (L) 2952, 2871, 1785, 1735, 1353, 1220, 1164, 1072, 1025 and 777 cm^{-1}; δ_H (400 MHz) 1.49 (1H, m, 3′-*H*$_a$), 1.73–1.94 (8H, m, 3-, 4′-, 2″- and 3″-C*H*$_2$ groups), 2.00 (1H, m, 3′-*H*$_b$), 2.43 (2H, m, 2-C*H*$_2$), 3.71 (1H, m, 5′-*H*$_a$), 3.85 (2H, m, 2′-*H* and 5′-*H*$_b$), 4.13 (2H, t, *J* 6.5, 1″- or 4″-C*H*$_2$) and 4.40 (2H, t, *J* 6.5, 4″- or 1″-C*H*$_2$) ppm; δ_C (100.6 MHz) 24.4 (*C*H$_2$), 24.5 (*C*H$_2$), 25.2 (*C*H$_2$), 30.2 (*C*H$_2$), 30.6 (*C*H$_2$), 30.7 (*C*H$_2$), 62.9 (1″- or 4″-*C*H$_2$), 67.2 (4″- or 1″-*C*H$_2$ and 5″-*C*H$_2$), 77.7 (2′-*C*H) and 173.0 (1-*C*=O) ppm; δ_F (376.3 MHz) −75.6 (C*F*$_3$) ppm. HRMS (+ve ion FAB): *found* 313.1267; *calculated* for $[C_{13}H_{19}F_3O_5 + H]^+$ 313.1280.

9″-Trifluoroacetoxy-5″-oxanonyl 3-(tetrahydro-2′-furyl)-propanoate **38** was obtained as an *oil* that had ν_{max} (L) 2952, 2871, 1785, 1735, 1457, 1353, 1220, 1164, 1072, 1025, 943, 777

and 730 cm^{-1}; δ_H (400 MHz) 1.49 (1H, m, 3′-H_a), 1.62–1.75 (6H, m, 2″- or 8″-, 4′-, 3″- and 7″-CH_2 groups), 1.81–1.95 (6H, m, 8″- or 2″-, 3- and 4′-CH_2 groups), 2.01 (1H, m, 3′-H_b), 2.42 (2H, m, 2-CH_2), 3.44 (4H, m, 4″-CH_2 and 6″-CH_2), 3.74 (1H, m, 5′-H_a), 3.85 (2H, m, 2′-H and 5′-H_b), 4.11 (2H, t, J 6.5, 1″- or 9″-CH_2) and 4.40 (2H, t, J 6.5, 9″- or 1″-CH_2) ppm; δ_C (100.6 MHz) 25.2 (CH_2), 25.5 (CH_2), 25.6 (CH_2), 25.7 (CH_2), 26.1 (CH_2), 30.6 (CH_2), 31.1 (2 × CH_2), 63.7 (1″- or 9″-CH_2), 67.2 (5′-CH_2), 67.6 (9″- or 1″-CH_2), 69.4 (4″- or 6″-CH_2), 69.9 (6″- or 4″-CH_2), 77.7 (2′-CH) and 173.1 (1-C=O) ppm; δ_F (376.3 MHz) −75.6 (CF_3) ppm. HRMS (+ve ion FAB): *found* 385.1842; *calculated* for $[C_{17}H_{28}F_3O_6 + H]^+$ 385.1852.

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