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ELECTROREDUCTIVE CYCLIZATION REACTIONS: ATTEMPTS TO USE 2(5H)FURANONES (α,β-UNSATURATED BUTENOLIDES). DOMINANCE OF ACID-BASE OVER CYCLIZATION CHEMISTRY

Mary A. Amputch[1] and R. Daniel Little*

Department of Chemistry
University of California, Santa Barbara
Santa Barbara, CA 93106

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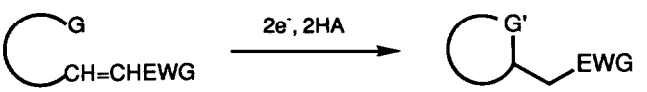
Abstract. The potential utility of butenolides as substrates in the electroreductive cyclization reaction has been investigated. A variety of butenolides bearing either an α,β-unsaturated ester, an α,β,γ,δ-unsaturated ester, allylic bromide, bromide, mesylate or aldehyde functionality on the appending side chain have been examined. The performance of each of these systems under electroreductive cyclization reaction conditions is severely limited by the presence of acidic protons at C5 of the butenolide ring and at C1 of the appending side chain

INTRODUCTION. The electroreductive cyclization (ERC) reaction, typified by equation 1, has proven to be a valuable tool in the construction of a variety of ring systems,[2] among them the five-membered ring subunit of sterpurene[3] and both the five and the six-membered rings found in the bicyclo[3.2.1] subunit of quadrone.[4] Recent unpublished results from these laboratories suggest its utility in the stereoselective synthesis of the Corey lactone[5] and its potential applicability to construction of the C-ring of the phorbol esters.[6]



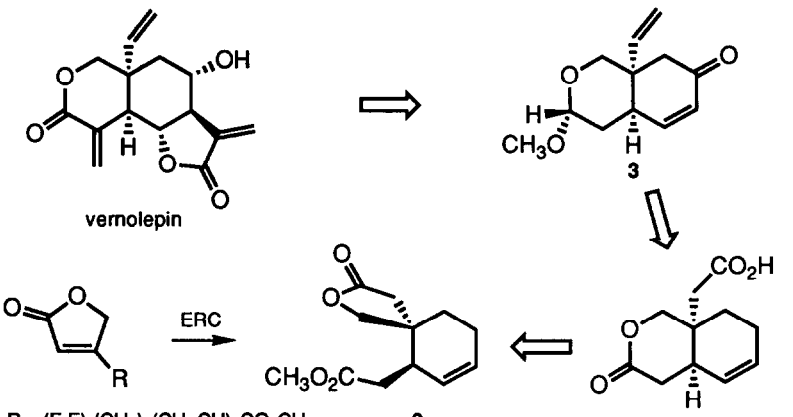
(1)

G = CH_2OMs,[7] CHO, COR, C(=NR)R', CH=CHEWG
EWG = electron withdrawing group
G' = CH_3, CH_2OH, CHOHR, CH(NHR)R', CH_2CH_2EWG

The reaction is believed to occur by a one-electron transfer to CH=CHEWG, closure of the resulting radical anion onto G, protonation of the intermediate, addition of a second electron and a second proton.[2] The initially formed radical anion can undergo the desired cyclization and/or participate in acid-base chemistry leading to saturation of the C=C bond of the CH=CHEWG unit Most often, cyclization occurs fast enough to preclude/minimize saturation.[8]

2(5H)FURANONES (BUTENOLIDES) AS SUBSTRATES IN THE ERC PROCESS; POTENTIAL APPLICATION TO THE SYNTHESIS OF VERNOLEPIN. When these studies were initiated, 2(5H)furanones (butenolides) had not been used in the electroreductive cyclization process and there did not appear to be any reason to believe that their use would prove problematic. The simple formal total synthesis of the cytotoxic sesquiterpene vernolepin[9] illustrated in Scheme 1 was designed with butenolide **1** promising to serve as an intermediate *en route* to enone **3**, a compound which has previously been used in the construction of vernolepin.[10] Before examining this route, we first elected to examine the simpler butenolide **4**.

Scheme 1. Potential synthetic route to vernolepin



1, R = (E,E)-$(CH_2)_2(CH{=}CH)_2CO_2CH_3$

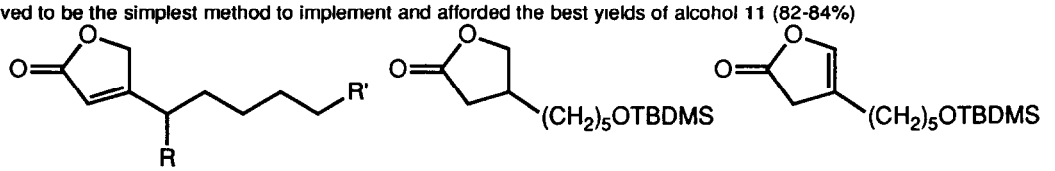
4, R = (E)-$(CH_2)_4CH{=}CHCO_2CH_3$

5, R = CH_2SO_2Ph

ERC = ElectroReductive Cyclization

PREPARATION OF BUTENOLIDE 4. Treatment of the anion of sulfone **5** (NaH, DMF, 0 °C, 30-45 min)[11,12] with 4-bromo-1-(dimethyl*t*-butylsilyloxy)butane (**6**) afforded the desired product **7** as a white crystalline solid in 75-88% yield. Initial efforts to achieve desulfonylation used sodium amalgam/methanol/Na_2HPO_4 buffer [13] All efforts to convert **7** to butenolide **8** in this manner resulted only in the isolation of lactone **9**, in which both desulfonylation and reduction of the butenolide carbon-carbon double had taken place. Use of aluminium amalgam[14] (0 °C, 9.1 THF/H_2O, 7-8 h) however, resulted in facile conversion of butenolide sulfone **7** to desulfonylated butenolide **8** in 88-91% yield.

Of the three methods attempted to remove the silyl ether, the use of a 1:1 HF/*n*-Bu_4NF solution in THF resulted predominantly in decomposition of the butenolide and production of 26% of the β,γ-unsaturated lactone **10**, with the protecting group still intact. Utilization of a 3:1:1 solution of CH_3COOH/THF/H_2O,[15] afforded the required alcohol **11** in 77% yield, but the acetic acid proved to be difficult to eliminate completely from the product The use of 1:5 HF/CH_3CN proved to be the simplest method to implement and afforded the best yields of alcohol **11** (82-84%)



7, R = SO_2Ph, R' = OTBDMS **9** **10**

8, R = H, R' = OTBDMS

11, R = H, R' = OH

12, R = H, R' = CHO

The butenolide alcohol **11** was converted to aldehyde **12** (PCC, CH_2Cl_2, 45 min-1 h) in 66-87% yield. Pyridinium dichromate may also be used; however, conversion of the alcohol to the aldehyde is much slower (*ca.* 8 h) and the reaction did not reach completion Exposure of alcohol **11** to Swern reaction conditions[16] resulted in deconjugation and isolation of the $\Delta^{\beta,\gamma}$ butenolide in 58% yield.[17]

Exposure of aldehyde **12** to Wittig reaction conditions, furnished butenolide **4** in 48% yield (*trans/cis* ratio, 8.1) The Horner-Emmons reaction [$(CH_3O)_2P(O)CHCO_2CH_3$, NaH, THF] was also explored, but without success Butenolide **4** was

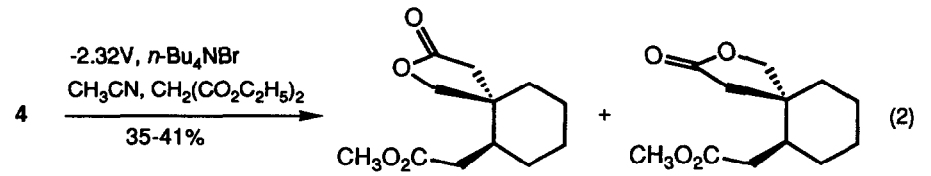
found to be unstable and was usually used within a day. Also, availability and purification of this butenolide was greatly hampered by it's instability on silica gel.

CYCLIC VOLTAMMETRY. Experiments were conducted in a 0.1 M solution of *n*-Bu_4NBr in dry CH_3CN, using a saturated calomel reference electrode (SCE) or a Ag/AgCl reference electrode (standardized to SCE), a platinum counter electrode, and a hanging mercury drop working electrode. All cathodic peak potentials (E_{pc}) are reported relative to SCE

It is important to note that the cyclic voltammograms were obtained over a limited range of scan rates (100-900 mV/sec) which were not sufficiently fast to determine redox potentials. Irreversibility, indicative of the existence of a follow-up reaction proceeding at a rate greater than the scan rate, was observed in every case. This leads to peak potentials which are shifted to more positive values than those obtained under reversible conditions Therefore, the assignment of an observed peak potential (E_{pc}) to a specific functionality, is done so with extreme caution; when assignments have been made, the purpose is simply to aid in the development of a qualitative discussion and rationalization of results obtained from the preparative electrochemical experiments.

The cyclic voltammogram of compound **4** exhibited two irreversible waves with cathodic peak potentials of -2.32 V and -2.52 V. That the wave at -2.52 V may be attributable to reduction of the α,β-unsaturated lactone rather than the α,β-unsaturated ester, was suggested by obtaining a cyclic voltammogram of compound **8**, which contains within the range scanned, only the α,β-unsaturated lactone as the electroreducible unit. In this case, only one wave with a E_{pc} at -2.52 V was observed. Since it was known from previous studies that the reduction potentials (E_{pc}) for monosubstituted α,β-unsaturated esters are usually in the range -2.20 to -2.35 V, the wave at -2 32 V was tentatively attributed to the reduction potential of the α,β-unsaturated methyl ester, and the wave at -2.52 V was assigned as the reduction potential due to the α,β-unsaturated lactone.

ELECTROREDUCTIVE CYCLIZATION OF BUTENOLIDE 4. The electrochemical reaction was carried out at a controlled potential of -2.32 V in a standard H-cell, using a mercury pool cathode, a platinum anode, a saturated calomel reference electrode, or a Ag/AgCl reference electrode (standardized to SCE), and a degassed solution of dry CH_3CN containing *n*-Bu_4NBr as the electrolyte (ca. 0.1 M solution). Initial experiments used d*imethyl* malonate as the proton source. It was subsequently found that d*iethyl* malonate was easier to separate from the products on chromatography and its use was adopted During the early stages of this work, the butenolide was introduced to the cathode chamber in one portion, always leading to a build-up of heat as the reaction progressed. This problem was alleviated however, by the dropwise addition (30 min to 1 h) of a solution of the butenolide and the proton donor in CH_3CN to the cathode chamber The progress of the reaction was monitored by coulometry. The results are illustrated in equation 2.[18]



13 **14**

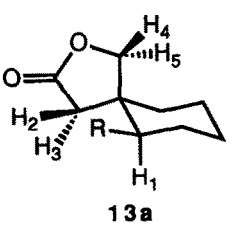
The spirocyclic lactones **13** and **14** were obtained in a ratio of 1 0:1.1, and a disappointing combined yield of 35-41%. Proton and carbon NMR, IR and mass spectral data did not allow them to be distinguished. The molecular ion (m/z 226) was observed in both the low and high resolution mass spectrum of each diastereomer The diastereomer with the lower retention time (by HPLC), which for the purposes of discussion is referred to as diastereomer 1, exhibited IR carbonyl

absorptions of 1778 cm^{-1} (lactone) and 1737 cm^{-1} (ester), while the other, referred to as diastereomer 2, showed absorptions at 1776 cm^{-1} and 1735 cm^{-1}.

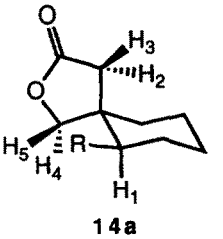
The regions between 2.0-2.5 ppm and 4.0-4.2 ppm of the proton NMR spectrum of each diastereomer are of interest, as they display differences between them. In diastereomer 1, the lactone methylene protons adjacent to the oxygen (CH_2O) appear as a pair of doublets centered at 4.16 ppm and 4.05 ppm ($J = 9.5$ Hz, $\Delta\nu = 55.0$ Hz), whereas those for diastereomer 2 appear as a pair of doublets centered at 4.20 ppm and 4.00 ppm ($J = 9.5$ Hz, $\Delta\nu = 97.4$ Hz). The lactone methylene protons adjacent to the carbonyl carbon (CH_2CO) however, appear as a pair of doublets centered at 2.46 ppm and 2.25 ppm ($J = 17.9$ Hz, $\Delta\nu = 106.5$ Hz) in diastereomer 1, and as a doublet at 2.44 ppm ($J = 3.0$ Hz) in diastereomer 2 The methylene protons next to the methyl ester carbonyl carbon ($CH_2CO_2CH_3$) appear as a pair of doublet of doublets for both diastereomers; for diastereomer 1, the two doublets are centered at 2.40 ppm and 2.13 ppm ($J = 15.1, 3.5$ Hz and $J = 15.1, 10.3$ Hz, $\Delta\nu = 139.3$ Hz), while these appear at 2.34 ppm and 2.21 ppm ($J = 15.1, 3.8$ Hz and $J = 15.1, 10.0$ Hz, $\Delta\nu = 62.3$ Hz) in diastereomer 2. For both diastereomers, the cyclohexyl ring methine proton appears as an apparent triplet of triplets at 2.0 ppm ($J = 10.3, 3.5$ Hz) for diastereomer 1 and at 2.04 ppm ($J = 10.0, 3.8$ Hz) for diastereomer 2.

The only significant differences observed in the fully decoupled and APT ^{13}C NMR (125 MHz) spectrum of each diastereomer were due to both sets of lactone methylene carbons. In diastereomer 1, the methylene carbon adjacent to the oxygen (CH_2O) appears as a singlet at 77.85 ppm, while the methylene carbon next to the lactone carbonyl carbon (CH_2CO) appears as a singlet at 42.97 ppm. In diastereomer 2, these carbon chemical shifts occur at 74.16 ppm and 40.66 ppm respectively.

Proton nOe experiments were conducted on each spirocyclic lactone diastereomer. MM2 calculations indicate that both diastereomers adopt a chair conformation in which the ester side chain ($CH_2CO_2CH_3$) is equatorial If it is assumed that each diastereomer preferentially adopts the conformations **13a** and **14a**, then H_1 in **13a** is closest to H_2 on the methylene carbon vicinal to the lactone carbonyl (2.46 Å by MM2), whereas in **14a**, H_1 is closest to H_5 (also 2.46 Å by MM2) which is attached to the methylene carbon adjacent to the lactone oxygen, and further away from H_2 and H_3 (3.77 and 4.31 Å, respectively). Therefore, saturation of the proton signal due to H_1 could result in an nOe at the signal corresponding to H_2 in **13a** and H_5 in **14a**. Also, since the signals for H_2 and H_3 for one of the diastereomers (diastereomer 1) appear as two separated doublets (in diastereomer 2, they appear as one doublet), saturation of each of them in turn, should show an nOe at the signal for H_1.



13a

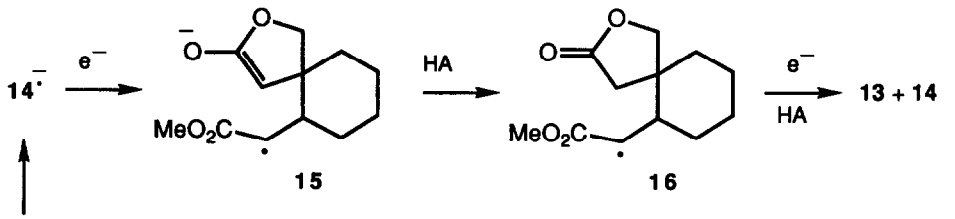


14a

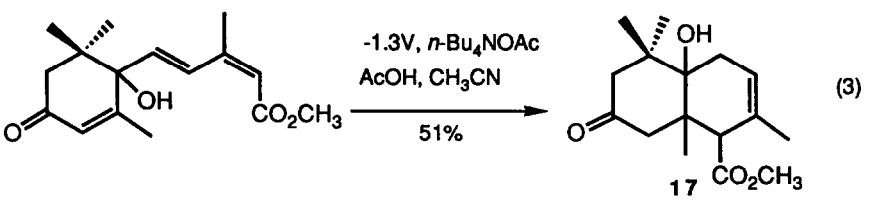
In practice however, the anticipated nOe's were not observed and differentiation between the diasteriomers was not possible, saturation of the signal corresponding to H_1, resulted in small nOe's (-0 6 to 1 8%) at H_2, H_3, H_4 and H_5. The only significant effects observed were between H_2 and H_3, and H_4 and H_5, and this was to be expected, since the protons in each set are attached to the same carbon

PROPOSED PATHWAY FOR THE FORMATION OF SPIROCYCLIC LACTONE 13 AND 14. The mechanism for the conversion of butenolide **4** to the spirocyclic lactones **13** and **14** presumably involves electron transfer to the α,β-unsaturated methyl ester electrophore to generate anion radical **14**$^{-\bullet}$, which cyclizes onto the β-carbon of the

butenolide. The resulting radical anion **15** acquires a proton, giving rise to the neutral radical **16**, which undergoes successive electron transfer and protonation, affording lactones **13** and **14**. The initially generated radical anion **14**$^{-\bullet}$ may also participate in other reactions (*i.e.*, acid-base chemistry, *vide infra*) which would account for the side products observed.[8]



Despite the disappointing results obtained thus far, plans for the preparation and ERC reaction of the α,β,γ,δ-unsaturated ester-butenolide **1**, the material originally earmarked for use in the proposed construction of vernolepin, were implemented. That α,β,γ,δ-unsaturated esters can successfully be employed as electrophores in the ERC reaction, was previously demonstrated by Terem and Utley, who found that exposure of the methyl ester of abscisic acid to reductive electrochemical conditions resulted in the formation of bicyclic ester **17** [19] Since the double bonds

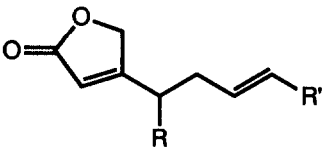


(3)

in the acyclic chain have the E,E-geometry, isomerization subsequent to the formation of the initial radical anion must have taken place prior to cyclization. That closure occurred between the β-carbon of the enone and the α-carbon of the dienoate unit is also germane. In the case of butenolide **1**, cyclization between the two relevant β-carbon atoms resulting in the formation of a six-membered ring, is expected to be favored over closure between the α-carbon of the dienoate and the β-carbon of the butenolide, which would give rise to a seven-membered ring.

SYNTHESIS OF ERC SUBSTRATE 1. Treatment of methyl 4-bromo-2-butenoate with diisobutylaluminium hydride (2.2 equiv., THF, -78 °C, 4 h), resulted in facile conversion to the corresponding bromo alcohol in 79-97% yield Protection was achieved by treatment with TBDMSiCl and imidazole in DMF at 0 °C (91-92%). Butenolide sulfone **18** was prepared in 45-68% yield as a white crystalline solid, by treatment of the anion of sulfone **5**[12] (NaH, DMF, 0 °C, 30-45 min) with the silyl ether described above. Desulfonylation [Al(Hg), 9:1 THF/H_2O, 0 °C, 6-8 h] was easily effected, affording silyl ether **19** in 82-99% yield. Alcohol **20** was obtained in 66-94% yield by deprotection of **19** with HF/CH_3CN (v/v 1.5, 0.5-1 h). Aldehyde **21** resulted from oxidation of **20** with either PCC (CH_2Cl_2, 2-3 h) or Dess-Martin periodinane[20] ($CHCl_3$, 3-4 h). Oxidation with PCC was adopted however, due to shorter reaction times, and the availability and lower cost of this oxidant. Since this aldehyde proved to be unstable, it was not purified, but rather used in crude form. Oxidation with barium manganate[21] and manganese dioxide[22] was also attempted, without success Wittig reaction of aldehyde **21** ($Ph_3P{=}CHCO_2CH_3$, $CHCl_3$, room temp), afforded butenolide **1** as an unstable pale yellow liquid, which decomposed significantly on exposure to silica gel column chromatography. The highest isolated yield of this butenolide was 10%. Therefore, the conversion of alcohol to aldehyde to butenolide **1** had to be repeated many times, usually in rapid

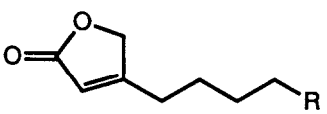
succession, to collect enough material to carry out the ERC reaction. Exposure of aldehyde **21** to Horner-Emmons reaction conditions [NaH, THF, $(CH_3O)_2P(O)CH_2CO_2CH_3$ or $(EtO)_2P(O)CH_2CN$) produced only unidentified material. Several attempts were made to develop a more efficient synthesis, but to no avail.



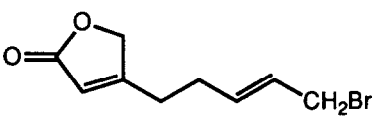
18, R = SO_2Ph, R' = $CH_2OTBDMS$
19, R = H, R' = $CH_2OTBDMS$
20, R = H, R' = CH_2OH
21, R = H, R' = CHO
1, R = H, R' = (E)-CH=$CHCO_2CH_3$

CYCLIC VOLTAMMETRY AND ELECTROREDUCTIVE CYCLIZATION OF BUTENOLIDE 1. The cyclic voltammogram of butenolide **1** displayed two irreversible waves with cathodic peak potentials of -2.00 V and -2.48 V

The ERC reaction was conducted at a controlled potential of -2.00 V, employing the conditions specified previously for butenolide **4**. Unfortunately no identifiable products were obtained; repeated attempts to improve the results met with failure. This result has reinforced the idea that there are significant problems associated with the use of $\Delta^{\alpha,\beta}$ butenolides as substrates in the ERC reaction. Insight into the factors which govern the outcome of the ERC reaction of butenolides, was gained through an examination of substrates **12**, **22**, **23** and **24**



12, R = CHO
22, R = CH_2OMs
23, R = CH_2Br



24

PREPARATION OF ERC SUBSTRATES 12, 22, 23 AND 24. Aldehyde **12** was prepared as previously indicated (*vide supra*). Initial attempts to synthesize bromide **23** from alcohol **11**, employed PBr_3/pyridine[23] and Ph_3P/CBr_4[24] as reagents, with CH_2Cl_2 as solvent Both methods resulted in extensive decomposition of the substrate[21] and none of the required bromide. However, treatment of alcohol **11** with S-collidine and mesyl chloride in DMF (0 °C to ambient), afforded mesylate **22** in 59-63% yield. Conversion to bromide **23** in 75-92% yield, was then accomplished by treatment of mesylate **22** with LiBr in DMF (oil-bath temp, 50-60 °C). The allylic bromide **24** was prepared in 63% yield by exposure of the allylic alcohol to S-collidine, mesyl chloride and LiBr in DMF at 0 °C.

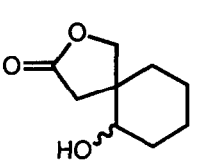
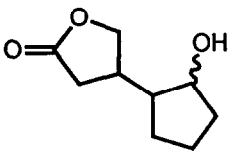
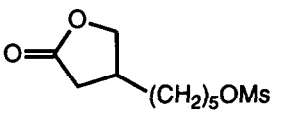
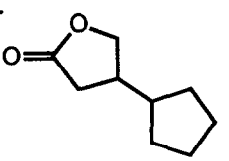
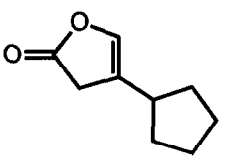
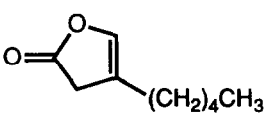
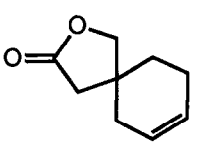
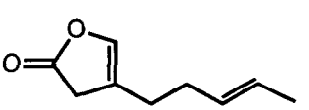
CYCLIC VOLTAMMETRY. The cyclic voltammogram of aldehyde **12** displayed one irreversible wave at -2.35 V, as did mesylate **22**. The observation of two closely spaced irreversible waves, with cathodic peak potentials of -2 25 V and -2.35 V, complicated distinction between the reduction potentials of each of the electroreducible functional groups in substrate **23**. Two waves with cathodic peak potentials of -2.15 V and -2 50 V, were observed for allylic bromide **24**

ELECTROREDUCTIVE CYCLIZATION REACTION OF SUBSTRATES 12, 22, 23 AND 24 The ERC reactions were carried out at a controlled potential, employing the same conditions as described previously. In all cases, a solution of the substrate and diethyl malonate in CH_3CN was added dropwise, during one hour, to the cathode chamber The progress of each reaction was monitored by TLC and coulometry.

The results from the ERC reactions are indicated in Table 1 In addition to the products shown, other material was also isolated, though not in sufficient quantity to allow structural assignments to be made

In substrate **12**, the initially formed radical anion of this α,β-unsaturated lactone would be expected to initiate cyclization by formation of a new C-C bond between it's β-carbon and the carbon of the aldehyde unit, leading primarily to a

Table 1. Results from the electro-reduction of substrates **12**, **22**, **23**, and **24**

Substrate	Potential used in reduction	Product(s)
12	-2.35 V	 **25** (*ca* 1%, 4:1 ratio)  **26** (60%, 1:3:4:2.5)
22	-2.35 V	 **27** (75%)
23	-2 25 V	 **28** (10%)  **29** (59%)  **30** (trace amounts)
24	-2.15 V	 **31** (6%, 4:1 ratio)  **32** (77%)

mixture of diastereomeric spirocyclic lactone alcohols **25**. This however, was not borne out in practice. Instead, a diastereomeric mixture of lactone cyclopentanols **26** (ratio 1 3·4:2 5), was obtained in 60% yield, while the expected diastereomeric cyclohexanols **25** were obtained in approximately 1% yield (ratio 4:1) The lactone cyclopentanols can be distinguished from the lactone cyclohexanols, primarily on the basis of ^{1}H NMR (500 MHz) spectral data. The methylene protons adjacent to the lactone oxygen (CH_2O) in the cyclohexanols **25** appear as a pair of doublets in the region 3.94-4 44 ppm, with coupling constants of approximately 9 0 Hz, whereas these same protons in the lactone cyclopentanols **26** appear as two doublet of doublets in the region 3 99-4 45 ppm, with coupling constants in the range 7 1-9.1 Hz. Also, the other set

of lactone methylene protons (CH_2CO_2) appear as a pair of doublets in the lactone cyclohexanols, and as two doublet of doublets for at least three of the four diastereomeric lactone cyclopentanols. Although there are differences, especially in the ^1H and ^{13}C NMR spectra of each diastereomeric lactone cyclopentanols, they do not permit a distinction to be made between each of the diastereomers. Proton nOe experiments also have not allowed definitive distinction between each of the four diastereomers, since overlap in chemical shifts of several protons have prevented saturation of a number of signals for protons that may have provided crucial information.

Lactone **27** was the only product (75% yield) isolated from the ERC reaction of butenolide mesylate **22**. In this case, proton transfer to the initially formed radical anion was faster than cyclization, leading exclusively to saturation of the butenolide carbon-carbon double bond

The reduction potentials (-2.25 V and -2.35 V) of the two functional groups in substrate **23** are very similar (the foot potential of the second wave overlaps with the first wave), and therefore reduction of the bromide unit (E_{pc} -2.25 V) as well as partial reduction of the α,β-unsaturated lactone was to be expected, and has been observed in product **28**. The major product, $\Delta^{\beta,\gamma}$ butenolide **29** was obtained in 59% yield, while lactone **28** was obtained in a yield of 10%. Trace amounts of butenolide **30** also appear to to be present by ^1H NMR, but large enough quantities for complete spectral analysis were not obtained. As observed with aldehyde **12**, cyclization has taken place, but not in the desired manner. Instead, a new sigma bond formed between the bromine-bearing carbon and the carbon located gamma to the butenolide. In product **29**, cyclization was accompanied by C-C double bond migration from the α,β to the β,γ position in the butenolide ring

The results obtained from the use of substrate **24** in the ERC reaction indicate that proton transfer to the radical anion generated from the allylic bromide unit was faster than cyclization, resulting predominantly in the formation of $\Delta^{\beta,\gamma}$ butenolide **32** in 77% yield and only a small amount of cyclized product **31** (6% yield, ratio 4:1).

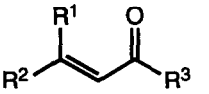
RATIONALE. The formation of products **26**, **28**, **29** and **32** provide unequivocal evidence that the methylene protons of the butenolide ring, and those at C1 of the appending side chain have sufficient acidic character to render them prone to removal under the ERC reaction conditions. The species responsible for proton abstraction is thought to be the initially generated radical anion. In every case, proton abstraction is a highly competitive reaction, leading to a significant decrease in yield of the anticipated spirocyclic lactone products, or eliminating their formation entirely

Involvement of the proton abstraction step, enables further reaction via a variety of pathways. These include: (1) exclusive saturation of the butenolide carbon-carbon double bond as in product **27**, (2) saturation of the butenolide carbon-carbon double bond with cyclization as in products **26** and **28**, and (3) bond migration from the α,β to the β,γ position of the butenolide ring with cyclization as in product **29**, or with saturation as in products **30** and **32**.

In products **26**, **28**, and **29**, cyclization, though initiated by proton abstraction from C1 of the appending side chain, is facilitated by: (1) the faster rate of ring closure to five- rather than six-membered rings and, (2) the possible lower strain associated with the resulting five-membered rings compared to the corresponding spirocyclic lactone products. Also, with regard to the observation of bond migration and attendant cyclization as in product **29**, if bond migration from the α,β to the β,γ position did take place first, then the butenolide β-carbon can no longer act as an acceptor in the same way as the β-carbon of an activated olefin such as an α,β-unsaturated lactone, thereby further promoting cyclization at C1 of the appending side chain

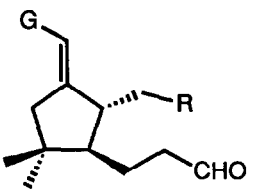
House and coworkers have previously encountered complications arising from undesirable acid-base chemistry in both cyclic voltammetry and preparative electrochemical experiments involving alkyl-substituted α,β-unsaturated ketones.[25] They proposed, and were able to establish, that the initially formed radical anions abstract a proton from the starting ketone

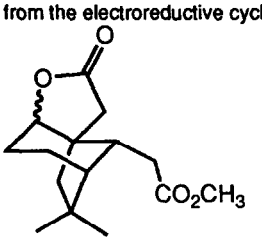
or, in the absence of proton donor, from the solvent. Also, the observed longer half-lives ($t_{1/2}$ > 10 sec) of the radical anions derived from the E- and Z-di-*t*-butyl enones **33** and **34**, compared to other aliphatic enones such as **35** ($t_{1/2}$ = 3 x 10^{-3} sec) was attributed to the absence of acidic hydrogen atoms in enones **33** and **34**.

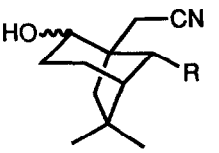


33, $R^1 = R^3 = C(CH_3)_3$, $R^2 = H$
34, $R^2 = R^3 = C(CH_3)_3$, $R^1 = H$
35, $R^2 = R^3 = CH_3$, R' = H

Other examples of the deleterious effect acid-base chemistry can have upon the ERC reaction are available from our work. For instance, the low yield (30%) of **38** obtained from the electroreductive cyclization of







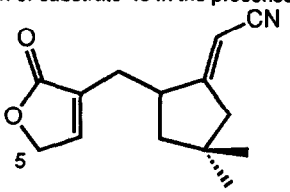
36, G = R = CO_2CH_3
37, G = CN, R = CH_2OSiPh_2t-Bu

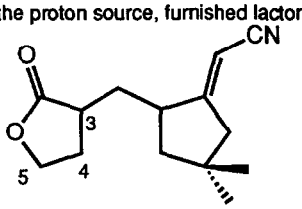
38

39, R = $CH_2CH_2OPh_2t$-Bu

36 may be accounted for by suggesting that the methylene protons α to the methyl ester in **36** act as a proton source, leading to undesirable side reactions.[26] In accord with this suggestion is the finding that the yield of cyclic product was improved to 90% by replacing the methyl ester in **36** with a CH_2OSiPh_2t-Bu group (**37** → **39**).[4]

Another illustration stems from a recently completed effort to form the tricyclo[6 3.0 $0^{3,7}$]undecane ring system. The ERC reaction of substrate **40** in the presence of dimethyl malonate as the proton source, furnished lactone **41** as the





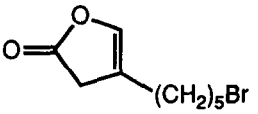
40

41

exclusive product in >95% yield.[8] When the ERC reaction was conducted in the presence of deuterated dimethyl malonate, deuterium incorporation was observed at C3, C4, and C5 in lactone **41**. This result clearly attests to the acidity of the C5 methylene protons under the electrochemical reaction conditions used.[27] To account for exclusive saturation of the butenolide carbon-carbon double bond rather than cyclization, it was proposed that the C5 methylene protons in **40** served as a source of protons for the initially formed butenolide radical anion, facilitating complete saturation and eliminating the cyclization pathway.

ATTEMPTED CYCLIZATION VIA A COBALT(I) REAGENT. The Co(I) species derived from vitamin B_{12} and several bis(dimethylglyoximato)cobalt(III) complexes have been employed in catalytic amounts to generate radicals from alkyl halides. When the alkyl halide is tethered to a suitable acceptor group, cyclization can be achieved.[28-34]

Electrochemical methods for achieving formation of Co(I) from chlorocobalt(III) complexes have been devised.[32,33] Since the butenolide **23** contains a C-Br bond for radical generation and an α,β-unsaturated lactone which could serve as an acceptor unit for reaction with Co(I), it was treated with a catalytic quantity of the Co(I) species generated electrochemically (-1.8 V, $LiClO_4$, MeOH) from chloro(pyridino)bis(di-methylglyoximato)cobalt(III) [32,33] Once again, cyclization was thwarted by C=C pi bond migration leading to the $\Delta^{\beta,\gamma}$ unsaturated butenolide **42** in 70% yield Attempts to effect free radical cyclization using *n*-Bu_3SnH/AIBN in benzene at reflux also met with failure.



42

CONCLUDING COMMENTS. $\Delta^{\alpha,\beta}$ Butenolides, specifically substituted at the β-carbon atom of the butenolide ring, were employed in the ERC reaction with a view to synthesizing spirocyclic lactones. However, the performance of each of the butenolides was severely limited by the presence of acidic protons at carbon-5 of the butenolide ring and at carbon-1 of the appending side chain. These acidic sites were seen to serve as an internal source of protons for the initially formed radical anion, and have permitted several competing reaction pathways to operate Due to the variety of products formed, the ERC reactions of the $\Delta^{\alpha,\beta}$ butenolides used in this study are not considered to be useful for further synthetic application.

EXPERIMENTAL SECTION

Melting points are uncorrected. Thin-layer chromatography (TLC) used silica gel precoated glass plates (E Merck 60 F254, 0 25 mm thick). Visualization was achieved with an ultraviolet hand-lamp or *p*-anisaldehyde (with heat) and $KMnO_4$ stain. Column chromatography was carried out on E. Merck 60 (230-400 mesh, ASTM), Fisher (230-425 mesh), Fluka 60 (230-400 mesh, ASTM) or ICN (32-63, 60 A) silica gel Solvent mixtures were prepared, and are reported by volume (v/v) High performance liquid chromatography (HPLC) was accomplished with an Altex 110A pump, a Hewlett-Packard 1037A refractive index detector, a Linear Model 1200 recorder and an Altex UltrasilTm-Si (10 mm ID x 25 mm) column

Acetonitrile, methylene chloride and dimethylformamide were distilled from CaH_2, and tetrahydrofuran and diethyl ether from sodium/benzophenone, immediately prior to use. HPLC grade or distilled reagent grade solvents were used for high performance liquid chromatography. Reagent grade solvents were used for all other purposes without further purification. The petroleum ether used (PE or SSF) was the fraction boiling at 30-60 °C. Hydrobromic acid (48% aqueous) and hydrofluoric acid (48% aqueous) were purchased from Mallinckrodt, *t*-butyldimethylsilyl chloride from Petrarch and all Wittig and Horner-Emmons reagents from Lancaster. All other chemicals were purchased from Aldrich The commercially available NaH (60% dispersion in mineral oil) was washed with petroleum ether prior to use. Glassware was oven-dried or flame-dried before use Standard syringe techniques for handling moisture-sensitive materials were used to add reagents and solvents (for electrochemistry, CH_3CN was degassed with Argon before use) to reaction vessels All reactions were conducted under a nitrogen atmosphere.

Electrochemistry was performed using a Electrosynthesis Company model 410 potentiostat controler, a model 8460 potentiostat power supply and a model 640 digital coulometer. A Fluke 8022B multimeter was used to measure current

Compound purity was assessed chromatographically and spectroscopically Unless indicated otherwise, all data refer to pure materials

4-[1-Phenylsulfonyl-5[[(1,1-dimethylethyl)dimethylsilyl]oxy]-pentyl]-2(5H)-furanone (7). A solution of 4-(phenylsulfonylmethyl)-2(5H)-furanone[12] (5.2 g, 21.7 mmol, 1 equiv) in dry freshly distilled DMF (15 mL) was

added dropwise over 5-10 min to a slurry of NaH (60% dispersion in mineral oil, 1.1 g, 26.1 mmol, 1.2 equiv) in dry DMF (200 mL) at approximately 0 °C (ice-bath) The solution turned a deep yellow immediately. After 30-45 min (or when H_2 evolution had ceased), a solution of 4-bromo-1-[[(1,1-dimethylethyl)-dimethylsilyl]oxy]butane (5.8 g, 21.7 mmol, 1 equiv) in dry DMF (15 mL) was introduced dropwise over 5-10 min, and the reaction mixture stirred for 18 h at ambient temperature. The mixture was poured into cold saturated NaCl solution (250 mL) and extracted with ether (5 x 50 mL). The combined ether extracts were washed once with half-saturated NaCl solution (75 mL), dried over anhydrous $MgSO_4$ and concentrated *in vacuo*, to yield a semi-solid still contaminated with DMF. Chromatography of the crude product on 300 g of silica gel (Fisher) in a 4.5 cm x 60 cm column, using 3:7 ethyl acetate/SSF as the eluting solvent [TLC: R_f = 0.5; UV, $KMnO_4$, and *p*-anisaldehyde (stains green) active], yielded 7.0 g (76%) of the required product as a white solid, mp 69-74 °C; ^{1}H NMR(300 MHz) δ 7.70 (m, 5 H, phenyl), 5.81 (m, 1 H, butenolide vinyl), 4.88 (m, 2 H, *J* = 18.9, 1.8 Hz, C*H*$_2$O butenolide), 4.00 (dd, 1 H, *J* = 11.5, 3.3 Hz, C*H*SO$_2$), 3.57 (t, 2 H, *J* = 5.9 Hz, C*H*$_2$OSi), 2.26 and 1 87 (2 m, 1 H and 1 H, SCHC*H*$_2$), 1.46 (m, 4 H, C*H*$_2$C*H*$_2$CH$_2$OSi), 0.86 (s, 9 H, *t*-butyl), 0.01 (s, 6 H, (C*H*$_3$)$_2$Si); IR (KBr) 2953, 2919, 2893, 1776, 1750, 1636, 1447, 1340, 1301, 1257, 1168, 1132, 1097, 1083, 1037, 1011, 922, 836 cm^{-1}; LRMS (EI), m/z 425 (M), 368, 367 (M - *t*-butyl), 283, 225, 201, 200, 199 (base), 151, 136, 135, 125, 110, 105, 101, 89, 79, 78, 77, 75, 74, 73, 59, 51; HRMS (CI), m/z 425.1809 (calcd for $C_{21}H_{33}O_5SiS$, M + 1, 425 1819).

4-[5-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]pentyl]-2(5H)-furanone (8). Aluminium amalgam[14] was prepared as follows: aluminium foil (8.6 g, 317 mmol, 14 equiv) was cut into strips (*ca* 10 cm x 1 cm) and immersed in a 2% aqueous solution of mercuric chloride for 15 sec. The strips were rinsed in absolute ethanol and then ether, and cut into pieces (*ca.* 1 cm x 1 cm) directly into the reaction vessel.

A solution of sulfone **7** (9 6 g, 22 6 mmol) in aqueous THF (9:1 THF/H_2O, 400 mL) was cooled in an ice-bath. Aluminium amalgam (8.6 g, 317 mmol, 14 equiv) was then added and the mixture stirred for 7.5 h The reaction mixture was filtered and the filtrate concentrated *in vacuo* to remove most of the THF The remaining aqueous layer was extracted with ether (4 x 75 mL). The ether extracts were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. Chromatography on 300 g of silica gel in a 4.5 cm x 60 cm column, using 3:7 ethyl acetate/SSF as the eluting solvent [TLC· R_f = 0.51; $KMnO_4$ and *p*-anisaldehyde (stains blue) active], afforded 5.9 g (91%) of compound **8** as a clear colorless liquid, ^{1}H NMR (300 MHz) δ 5.45 (m, 1 H, butenolide vinyl), 4.84 (m, 2 H, C*H*$_2$O butenolide), 3 61 (t, 2 H, *J* = 6.0 Hz, C*H*$_2$OSi), 3.16 (m, 2 H, CH=CC*H*$_2$CH$_2$), 2.03 (m, 2 H, CH=CCH$_2$C*H*$_2$), 1 47 (m, 4 H, C*H*$_2$C*H*$_2$CH$_2$OSi), 0 89 (s, 9 H, *t*-butyl), 0 05 (s, 6 H, (C*H*$_3$)$_2$Si), IR (neat) 2955, 2933, 2893, 2858, 1785, 1483, 1416, 1397, 1263, 1157, 1127, 1004, 837, 776 cm^{-1}; HRMS (CI), m/z 285 (M + 1), 269, 227 (M - *t*-butyl), 209, 183, 153, 141, 135, 109, 107, 93 (base), 89, 79, 75, 73; HRMS (CI), m/z 285 1873 (calcd for $C_{15}H_{29}O_3Si$, M + 1, 285 1887).

4-[5-Hydroxypentyl]-2(5H)-furanone (11). Method A: A 1·5 mixture of hydrofluoric acid (48% aqueous, 0 26 mL, 7.0 mmol) and CH_3CN (1.3 mL) was added dropwise to a solution of silyl ether **8** (2 0 g, 7.0 mmol) in CH_3CN (70 mL, *ca.* 0.1 M solution) at 22-25 °C The mixture was stirred for 2 5 h, poured into saturated NaCl solution (50 mL) and extracted with ethyl acetate (5 x 30 mL). The ethyl acetate extracts were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. Chromatography of the crude product on 90 g of silica gel in a 2 5 cm x 55 cm column, using ethyl acetate (or 7:3 CH_2Cl_2/ ether, R_f = 0.2) as the eluting solvent [TLC R_f = 0 4; $KMnO_4$ and *p*-anisaldehyde active (stains dark blue), yielded 1.0 g (84%) of alcohol **11** as a clear colorless liquid. Method B: A solution of the silyl ether **8** (100 mg, 0.35 mmol) in aqueous THF (1.1 THF/H_2O, 5 4 mL) was treated with glacial acetic acid (8.1 mL) and stirred at ambient temperature for 3 h. The reaction mixture was then diluted with water (15 mL) and extracted with ethyl acetate (5 x 10 mL) The combined organic layers were washed with cold 5% aqueous $NaHCO_3$ solution (3 x 10 mL), dried over anhydrous MgSO4 and concentrated *in*

vacuo. The crude product was chromatographed on 9 g of silica gel in a 1 cm x 32 cm column, using 3:7 ethyl acetate/SSF as the eluting solvent [TLC: R_f = 0.26), to afford 46 mg (77%) of alcohol **11**; ^{1}H NMR (300 MHz) δ 5.48 (m, 1 H, butenolide vinyl), 4.85 (m, 2 H, C*H*$_2$O butenolide), 3.66 (t, 2 H, *J* = 6.2 Hz, C*H*$_2$OH), 3.18 (m, 2 H, CH=CC*H*$_2$), 2.05 (m, 2 H, C*H*$_2$CH$_2$OH), 1.57 (m, 5 H, C*H*$_2$C*H*$_2$(CH$_2$)$_2$OH); IR (neat) 3557-3224, 2936, 2864, 1773, 1648, 1481, 1458, 1399, 1388, 1168, 1018, 862 cm^{-1}; LRMS (EI), m/z 170 (M), 140, 124, 111, 98, 97, 96, 95, 93, 91, 82, 81, 80, 79, 78, 77, 71, 69; HRMS (CI), m/z 171.1029 (calcd for $C_9H_{15}O_3$, M + 1, 171.1022).

4-[5-Oxopentyl]-2(5H)-furanone (12). A solution of the alcohol **11** (100 mg, 0.59 mmol, 1 equiv), PCC (191 mg, 0.89 mmol, 1.5 equiv), Celite (200 mg) and dry CH_2Cl_2 (6 ml) was stirred at 22-25 °C for 45 min. The reaction mixture was then diluted with ether (6 mL) and filtered through florisil. The florisil was washed several times with ether. The filtrate was concentrated *in vacuo* to give a slightly crude product which was ***used directly*** in the next reaction. In cases where the crude aldehyde was chromatographed [silica gel (Fisher, E. Merck or ICN); 7:3 CH_2Cl_2/ether; R_f = 0.57; UV, $KMnO_4$ and *p*-anisaldehyde (stains blue-black) active], the yield of aldehyde **12** (clear colorless liquid) isolated was in the range 66-87%; ^{1}H NMR (300 MHz) δ 9.78 (t, 1 H, *J* = 1.2 Hz, C*H*O aldehyde), 5.45 (m, 1 H, butenolide vinyl), 4.85 (m, 2 H, C*H*$_2$O butenolide), 3.18 (m, 2 H, CH=CC*H*$_2$CH$_2$), 2.47 (dt, 2 H, *J* = 7.0. 1.2 Hz, C*H*$_2$CHO), 2.07 (m, 2 H, C*H*$_2$CH$_2$CHO), 1.75 (m, 2 H, CH=CCH$_2$C*H*$_2$); IR (neat) 2936, 2889, 2856, 2738, 1777, 1720, 1465, 1399, 1367, 1347, 1168, 1020, 843 cm^{-1}

(*E*)-4-(7-Carbomethoxy-5-heptenyl)-2(5H)-furanone (4) Methyl(triphenylphosphoranyli-dene)acetate (256 mg, 0.8 mmol, 1.3 equiv) was added to a solution of the aldehyde **12** (99 mg, 0.6 mmol, 1 equiv) in $CHCl_3$ (10 mL) at 22-25 °C. TLC analysis (silica gel, 7:3 CH_2Cl_2/ether, R_f = 0.63) of the reaction mixture indicated immediate conversion of the aldehyde to product. The reaction mixture was concentrated *in vacuo* and cold ether added to the remaining semi-solid. The solid triphenylphosphine oxide was removed by filtration and washed several times with cold ether. The filtrate was concentrated *in vacuo*. Chromatography of the crude product on 9 g of silica gel (E. Merck) in a 1 cm x 32 cm column, using ether as the eluting solvent [TLC: R_f (*cis*) = 0.58, R_f (*trans*) = 0.54; UV and *p*-anisaldehyde (stains blue) active], yielded 63 mg (48%) of the *cis* and *trans* isomers of compound **4** as an unstable clear pale yellow liquid (*trans*/*cis* ratio determined by ^{1}H NMR, 8:1). This mixture of isomers was later separated by column chromatography, employing the same conditions as descnbed above, so that complete spectral data could be obtained. Due to *significant decomposition during column chromatography*, the crude product was in some instances, filtered through a short pad of silica gel and *used directly* in the next reaction; *trans* isomer: ^{1}H NMR (300 MHz) δ 6.94 (td, 1 H, *J* = 15.7, 7.3 Hz, fine coupling 1.2 Hz, vinyl β to ester), 5.83 (td, 1 H, *J* = 15.7, 1 2 Hz, vinyl α to ester), 5.45 (m, 1 H, butenolide vinyl), 4.83 (m, 2 H, C*H*$_2$O butenolide), 3.73 (s, 3 H, OC*H*$_3$), 3.17 (m, 2 H, CH=CC*H*$_2$), 2.22 (q, 2 H, *J* = 7.3 Hz, methylene γ to ester), 2.02 (m, 2 H, CH=CCH$_2$C*H*$_2$), 1.57 (m, 2 H, methylene δ to ester); IR (neat) 2952, 2932, 1780, 1719, 1654, 1437, 1319, 1275, 1204, 1165, 1021 cm^{-1}; LRMS (EI), m/z 223 (M - 1), 193, 192, 164, 150, 149 (base), 68, 67, 59, 57, 56, 55, 53, 43, HRMS (EI), m/z 223.0975 (calcd for $C_{12}H_{15}O_4$, M - 1, 223.0971), *cis* isomer: ^{1}H NMR (300 MHz) δ 6.21 (td, 1 H, *J* = 11.5, 7.5 Hz, fine coupling 1 1 Hz, vinyl β to ester), 5.82 (td, 1 H, *J* = 11 5, 1.5 Hz, vinyl α to ester), 5.47 (m, 1 H, butenolide vinyl), 4 85 (m, 2 H, C*H*$_2$O butenolide), 3.71 (s, 3 H, OC*H*$_3$), 3.18 (m, 2 H, CH=CC*H*$_2$), 2 68 (m, 2 H, *J* = 7.5, 1 5 Hz, methylene γ to ester), 2 05 (m, 2 H, CH=CH$_2$C*H*$_2$), 1.57 (m, 2 H, methylene δ to ester); IR (neat) 2951, 2938, 1781, 1722, 1641, 1440, 1411, 1200, 1167, 1024, 822 cm^{-1}; LRMS (EI), m/z 224 (M), 223 (M - 1), 192, 156, 150, 149 (base), 119, 111, 107, 105, 100, 98, 83, 82, 81 79, 77, 69, 68, 67, 59, 57,56, 55, 53, 43; HRMS (EI), m/z 223 0961 (calcd for $C_{12}H_{15}O_4$, M - 1, 223.0971).

6-(Carbomethoxymethyl)-2-oxaspiro[4.5]decan-3-one (13) and (14) This reaction was conducted under a nitrogen atmosphere in a standard H-cell with a medium porosity sintered-glass frit The anode chamber was fitted with a platinum electrode (surface area 1 cm^2), and a degassed solution of *n*-Bu_4NBr in CH_3CN (0.1 M solution, 25 mL) and

cyclohexene were introduced. The cathode chamber contained the mercury pool, a Ag/AgCl reference electrode (standardized to SCE) and a degassed solution of *n*-Bu_4NBr in CH_3CN (0.1 M solution, 25 mL). After obtaining a background current reading at a potential of -2.32 V, a solution of the butenolide **4** (80 mg, 0.36 mmol), diethyl malonate (0.22 mL, 1.42 mmol, 4 equiv) and CH_3CN (5 mL) was introduced dropwise by syringe pump, over a 1 h period, to the cathode chamber. The reduction was carried out at a controlled potential of -2.32 V. After a further 30 min, the reaction mixture from the cathode chamber was poured into saturated NaCl solution and extracted with a 7:3 CH_2Cl_2/ether solution (3 x 100 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*

Chromatography of the crude product mixture on silica gel in a 1 cm x 35 cm column, using ether/PE as the eluting solvent [TLC: R_f (mixture of spirocyclic lactones **13** and **14**) 0.35, not UV active, *p*-anisaldehyde (stains blue) active] yielded two liquid fractions, of which the first fraction (R_f = 0.35), containing a mixture of the diastereomeric spirocyclic lactones, was found to be separable by HPLC. HPLC conditions: flow rate 5 mL/min; refractive index detector temp 30 °C; solvent 9:0.9:0.1, hexanes/ethyl acetate/methanol. Retention times (min); yield (%) for diastereomer 1. 10.8; 21. For diastereomer 2: 11.4; 20.

Spirocyclic lactone, diastereomer 1: ^{1}H NMR (500 MHz) δ 4 16 and 4 05 (2 d, 1 H and 1 H, *J* = 9 5 Hz, C*H*$_2$O lactone), 3.68 (s, 3 H, OC*H*$_3$), 2.46 and 2.25 (2 d, 1 H and 1 H, *J* = 17.9 Hz, C*H*$_2$CO$_2$ lactone), 2.40 and 2 13 (2 d, 1 H and 1 H, *J* = 15.1, 3.5 Hz and *J* = 15.1, 10.3 Hz, C*H*$_2$CO$_2$CH$_3$), 2.00 (apparent tt, 1 H, *J* = 10 3, 3.5 Hz, cyclohexyl methine), 1 65 - 1 33 (several m, 8 H, cyclohexyl methylenes); ^{13} C NMR (125 MHz, fully decoupled and APT) δ 176.45 (lactone carbonyl), 172.85 (ester carbonyl), 77.85 (*C*H$_2$O lactone), 51.81 (O*C*H$_3$), 42.97 (*C*H$_2$CO$_2$ lactone), 40.27 (cyclohexyl methine carbon), 36.07 (quaternary spiro carbon), 35.97, 35.42, 28.32, 24.01, 22 77; IR (neat) 2928, 2867, 1778, 1737, 1437, 1383, 1299, 1176, 1021, 846 cm^{-1}; LRMS (EI), m/z 226 (M), 195, 180, 166, 153, 152, 124, 111, 109, 108, 107, 106, 95, 94, 93 (base), 91, 81, 80, 79, 77, 74, 67, 59, 55, 53, 43, HRMS (EI), m/z 226.1119 (calcd for $C_{12}H_{18}O_4$, M, 226.1205); Diastereomer 2. ^{1}H NMR (500 MHz) δ 4.19 and 4.00 (2 d, 1 H and 1 H, *J* = 9.5 Hz, C*H*$_2$O lactone), 3 68 (s, 3 H, OC*H*$_3$), 2.44 (d, 2 H, *J* = 3 0 Hz, C*H*$_2$CO$_2$ lactone), 2.34 and 2.21 (2 dd, 1 H and 1 H, *J* = 15.0, 3.8 Hz and *J* = 15 0, 10 0 Hz, C*H*$_2$CO$_2$CH$_3$), 2.04 (apparent tt, 1 H, *J* = 10.0, 3.8 Hz, cyclohexyl methine), 1.63 - 1.33 (several m, 8 H, cyclohexyl methylenes); ^{13}C NMR (125 MHz, fully decoupled) δ 176.52 (lactone carbonyl), 172.83 (ester carbonyl), 74.16 (*C*H$_2$O lactone), 51.85 (O*C*H$_3$), 40.66 (*C*H$_2$CO$_2$ lactone), 40.24 (cyclohexyl methine carbon), 35.77 (quaternary spiro carbon), 35.72, 34.91, 28.29. 23.62, 22.42, IR (neat) 2934, 2871, 1776, 1735, 1450, 1437, 1419, 1314, 1286, 1180, 1025, 1011, 849 cm^{-1}, LRMS (EI), m/z 226 (M), 195, 167, 166, 153, 152, 124, 111, 109, 108, 107, 106, 95, 94, 93 (base), 91, 81, 80, 79, 75, 74, 67, 59, 55, 53, 43; HRMS (EI), m/z 226.1189 (calcd for $C_{12}H_{18}O_4$, M, 226.1205).

(*E*)-4-[1-Phenylsulfonyl-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3-pentenyl]-2(5H)-furanone (18). A solution of sulfone **5**[12] (5.0 g, 20.9 mmol) in dry DMF (15 mL) was added dropwise over 5-10 min to an ice-bath-cooled slurry of NaH (60% dispersion in mineral oil, 921 mg, 23 mmol, 1 1 equiv) in DMF (80 mL). The resulting yellow solution was stirred at approximately 0 °C for 45 min. A solution of the silyl ether, (E)-4-bromo-1-[[(1.1-dimethylethyl)dimethylsilyl]oxy]but-2-ene (5.55 g, 20.9 mmol) in DMF (15 mL) was introduced dropwise over 5-10 min and the mixture stirred at 21-24 °C for 5 h The reaction mixture was poured into cold saturated NaCl solution (100 mL) and extracted with ether (4 x 75 mL). The combined ether extracts were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*, to yield a semi-solid still contaminated with DMF. Chromatography of the crude product on silica gel (Fisher, ICN) in a 4 cm x 50 cm column, using ether as the eluting solvent [TLC: R_f = 0 58, UV, KMnO4 and *p*-anisaldehyde (stains green) active], yielded 6.0 g (68%) of the required product as a white solid, mp 121-122 °C; ^{1}H NMR (300 MHz) δ 7.73 (m, 5 H, phenyl), 5 81 (m, 1 H, butenolide vinyl), 5 65 (ttd, 1 H, *J* = 15.2, 4.2, 1.1 Hz, CH=C*H*CH$_2$O), 5.45 (m, 1 H, C*H*=CHCH$_2$O),

4.85 (m. 2 H, J = 18.0, 1.7 Hz, CH_2O butenolide), 4.07 (m, 2 H, CH_2OSi), 4.03 (d, 1 H, J = 3.7 Hz, CHSO$_2$), 3.02 and 2.55 (2 m, 1 H and 1 H, SCHCH_2), 0.86 (s, 9 H, t-butyl), 0.02 (s, 6 H, (CH_3)$_2$Si), IR (KBr) 2950, 2929, 2890, 2860, 1779, 1752, 1629, 1473, 1450, 1344, 1306, 1145, 1124, 1023, 986, 885, 836, 774, 735 cm^{-1}; LRMS (CI), m/z 407 [(M + 1) - CH$_3$], 225, 223, 199, 151, 150, 149, 143, 135, 133, 125, 121, 117, 115, 111, 110, 109, 107, 105, 93, 91,89, 79, 78, 77, 75 (base), 73, 65; HRMS (CI), m/z 407.1357 (calcd for $C_{20}H_{27}O_5SiS$, (M + 1) - CH$_3$, 407.1349).

(*E*)-4-[5-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-3-pentenyl]-2(5H)-furanone (19) A solution of the butenolide sulfone **18** (4.4 g, 10.4 mmol) in aqueous THF (9:1 THF/H$_2$O, 100 mL) was cooled in an ice-bath. Aluminium amalgam[14] (3.9 g, 145.7 mmol, 14 equiv) was added and the reaction mixture stirred at approximately 0 °C for 6 h. The reaction mixture was then filtered and the filtrate concentrated *in vacuo* to remove most of the THF. The remaining aqueous layer was extracted with ether (3 x 50 mL). The combined ether extracts were dried over anhydrous MgSO$_4$ and concentrated *in vacuo*. Chromatography of the crude product on silica gel (Fisher, ICN) in a 3 cm x 50 cm column, using 7:3 ether/SSF as the eluting solvent [TLC: R_f = 0.66, not UV active, KMnO$_4$ and *p*-anisaldehyde (stains blue) active], yielded 2 5 g (85%) of the product as a viscous clear colorless liquid; ^{1}H NMR (300 MHz) δ 5.55 (m, 3 H, butenolide vinyl and CH=CH), 4 82 (m, 2 H, CH_2O butenolide), 4.12 (d, 2 H, J = 1.6 Hz, CH_2OSi), 3.19 (m, 2 H, CH_2CH$_2$CH=CH), 2.70 (m, 2 H, CH$_2$CH_2CH=CH), 0.91 (s, 9 H, t-butyl), 0.07 (s, 6 H, (CH_3)$_2$Si); IR (neat) 2934, 2889, 2859, 1789, 1472, 1387, 1254, 1171, 1144, 1115, 1060, 1034, 1019, 976, 836, 776 cm^{-1}; LRMS (CI), m/z 283 (M + 1), 225, 223, 181, 151 (base), 133, 123, 115, 107, 105, 97, 91, 79, 75, 73; HRMS (CI), m/z 283.1742 (calcd for $C_{15}H_{27}O_3Si$, M + 1, 283 1730).

(*E*)-4-[5-Hydroxy-3-pentenyl]-2(5H)-furanone (20). A 1:5 mixture of hydrofluoric acid (48% aqueous, 0.06 mL, 1 8 mmol), in CH$_3$CN (0.32 mL) was added dropwise to a solution of the silyl ether **19** (500 mg, 1 77 mmol) in CH$_3$CN (17 mL, *ca.* 0.1 M solution) at 22-24 °C. The mixture was stirred for 0.5 h and concentrated *in vacuo*. Chromatography of the crude product on silica gel (ICN) in a 3 cm x 34 cm column, using 7 3 CH$_2$Cl$_2$/ether as the eluting solvent [TLC· R_f = 0.24; not UV active, *p*-anisaldehyde (stains green) active], yielded 280 mg (94%) of the alcohol as a viscous clear colorless liquid; ^{1}H NMR (300 MHz) δ 5.69 (m, 2 H, CH=CH), 5.52 (m, 1 H, butenolide vinyl), 4 88 (m, 2 H, CH_2O butenolide), 4.12 (s, 2 H, CH_2OH), 3.21 (m, 2 H, CH_2CH$_2$CH=CH), 2 75 (m, 2 H, CH$_2$CH_2CH=CH), 1 58 (s, 1 H, CH$_2$OH); IR (neat) 3520-3187, 2929, 2892, 2868, 1774, 1399, 1382, 1177, 1148, 1094, 1012, 975, 848 cm^{-1}; LRMS (EI), m/z 168 (M), 137, 122, 121, 98, 95, 93, 91, 83, 81, 80, 79 (base), 78, 77, 67, 57, 55, 54, 53, 51, 43, HRMS (CI), m/z 169.0853 (calcd for $C_9H_{13}O_3$, M + 1, 169.0864).

(*E*)-4-[5-Oxo-3-pentenyl]-2(5H)-furanone (21) Method A A solution of alcohol **20** (500 mg, 3 0 mmol), PCC (961 mg, 4 5 mmol, 1.5 equiv) and dry CH$_2$Cl$_2$ (12 mL) was stirred at 22-24 °C for 2.5 h [TLC: R_f = 0.49; 7·3 CH$_2$Cl$_2$/ether, *p*-anisaldehyde (stains green-blue) active] The reaction mixture was then diluted with ether (12 mL) and filtered through florisil. The florisil was washed several times with ether. The product-containing filtrate was concentrated *in vacuo* to a volume of 12 mL and used directly in the next reaction; *attempts to isolate the aldehyde resulted in decomposition* Method B: A solution of alcohol **20** (100 mg, 0.59 mmol), Dess-Martin periodinane (265 mg, 0 62 mmol, 1.05 equiv) and CHCl$_3$ was stirred for 3-4 h [20] The mixture was then diluted with ether (4 mL) and poured into a 5% aqueous NaHCO$_3$ solution containing a seven-fold excess of Na$_2$S$_2$O$_3$ solution (10 mL) The solution was shaken until all the solid had dissolved, and then extracted with ether (4 x 10 mL). The combined ether extracts were dried over anhydrous MgSO$_4$, concentrated to a volume of 10 mL and *used directly* in the next reaction. A satisfactory ^{1}H NMR of the aldehyde **21** was obtained by addition of Dess-Martin periodinane to alcohol **20** and CDCl$_3$ in an NMR tube; ^{1}H NMR (500 MHz) δ 9 53 (d, 1 H, J = 13.0 Hz, CHO aldehyde), 6 81 (dtd, 1 H, J = 15.7, 6 1, 4 5 Hz, CH=CHCHO), 6.15 (tdd, 1 H, J = 15 7, 7 2, 1 5 Hz, CH=CHCHO), 5 55 (m, 1 H, butenolide vinyl), 3 24 (m, 2 H, CH_2CH$_2$CH=CH), 3 05 (m, 2 H, CH$_2$CH_2CH=CH)

(*E,E*)-4-[7-Carbomethoxy-3,5-heptadienyl]-2(5H)-furanone (1). Methyl(triphenylphosphoranylidene)acetate (1.19 g, 3.56 mmol, 1.2 equiv) was added to a solution of the crude aldehyde **21** (493 mg, 2.97 mmol) in $CHCl_3$ (35 mL). TLC analysis of the reaction mixture [R_f = 0.62; 7:3 CH_2Cl_2/ether; UV and *p*- anisaldehyde (stains blue) active] indicated immediate conversion of the aldehyde to product. The chloroform was removed *in vacuo*, and ether (100 mL) added to the remaining semi-solid. The solid triphenylphosphine oxide was removed by filtration and the filtrate concentrated *in vacuo*. TLC analysis of the reaction mixture at this stage, indicated that a spot with R_f = 0.5 (not the compound required) had intensified greatly. Chromatography of the crude reaction mixture on silica gel (Fisher) in a 3 cm x 34 cm column, using 7:3 CH_2Cl_2/ether as the eluting solvent [TLC: R_f (product **1**) = 0.62; UV and *p*-anisaldehyde (stains blue) active and R_f (unidentified compound) = 0.5; UV and *p*-anisaldehyde (stains yellow) active], afforded 66 mg (10%) yield of product **1** (*cis* and *trans* isomers) as a clear colorless liquid which *began to decompose on standing*. This decomposition was evidenced by an intensifying yellow color. Because of overlap of the vinyl protons in the ^1H NMR spectrum, a ratio of isomers (*cis, trans*) could not be determined. Due to *significant decomposition during column chromatography*, the crude product was filtered through a short pad of silica gel and *used directly* in the next reaction; ^1H NMR 500 MHz) δ 7 41 (dd, 1 H, *J* = 15 4, 11.5 Hz, vinyl β to ester), 6.19 (dd, 1 H, *J* = 15 1, 11.5 Hz, vinyl γ to ester), 5 99 (td, 1 H, *J* = 15 1, 6 6 Hz, vinyl δ to ester), 5.85 (d, 1 H, *J* = 15.4 Hz, vinyl α to ester), 5.53 (m, 1 H, butenolide vinyl), 4.87 (m, 2 H, C*H*$_2$O butenolide), 3.74 (s, 3 H, OC*H*$_3$), 3.22 (m, 2 H, CH=CC*H*$_2$), 2.90 (m, 2 H, CH=CCH$_2$C*H*$_2$); IR (neat) 3041, 2995, 2951, 2925, 2853, 1781, 1749, 1715, 1641, 1606, 1439, 1249, 1166, 1033, 929, 846, 743 cm^{-1}; HRMS (EI), m/z 222 (M), 191 (M - CH_3), 117, 111 (base), 105, 98, 91, 79, 77, 65, 59, 53, 51; HRMS (EI), m/z 191.0730 (calcd for $C_{11}H_{11}O_3$, M - CH3, 191.0708).

4-(5-Methylsulfonyloxypentyl)-2(5H)-furanone (22). A solution of alcohol alcohol **11** (400 mg, 2.4 mmol) and dry DMF (9 mL) was cooled to approximately 0 °C in an ice-bath. *s*-Collidine (0.4 mL, 3.1 mmol, 1.3 equiv, freshly distilled from KOH pellets) was added, followed by dropwise addition of distilled mesyl chloride (0.25 mL, 3.1 mmol, 1.3 equiv). The reaction mixture was stirred in an ice-bath for 2 h and allowed to gradually warm to room temperature. The mixture was then poured onto ice and extracted with ether (5 x 50 mL) The combined ether extracts were washed with saturated $Cu(NO_3)_2$ solution (3 x 40 mL), dried over anhydrous $MgSO_4$ and concentrated *in vacuo* The crude product was immediately chromatographed on 90 g of silica gel (ICN) in a 3 cm x 34 cm column, using 7 3 CH_2Cl_2/ether as the eluting solvent [TLC· R_f = 0.56; not UV active, *p*-anisaldehyde (stains dark blue) active], to yield 367 mg (63%) of the product as a clear colorless liquid; ^1H NMR (500 MHz) δ 5.46 (m, 1 H, butenolide vinyl), 4.85 (m, 2 H, C*H*$_2$O butenolide), 4.24 (t, 2 H, *J* = 6.4 Hz, C*H*$_2$OSO$_2$), 3.18 (m, 2 H, CH=CC*H*$_2$), 3 02 (s, 2 H, OSO$_2$C*H*$_3$), 2.07 (m, 2 H, C*H*$_2$CH$_2$OSO$_2$), 1.76 (m, 2 H, CH=CCH$_2$C*H*$_2$), 1 53 (m, 2 H, C*H*$_2$(CH$_2$)$_2$OSO$_2$); IR (neat) 3028, 2941, 2874, 1777, 1471, 1346, 1249, 1168, 1151, 1111, 1017, 977, 939, 838 cm^{-1}, LRMS (CI), m/z 249 (M + 1), 231, 153, 135(base), 111, 109, 107, 97, 95, 94, 93, 79, 68, 66; HRMS (CI), m/z 249 0799 (calcd for $C_{10}H_{17}O_5S$, M + 1, 249 0797)

4-(5-Bromopentyl)-2(5H)-furanone (23). Lithium bromide (anhydrous, 184 mg, 2 12 mmol, 1 5 equiv) was added to a solution of the mesylate **22** (350 mg, 1 41 mmol) in dry DMF (6 mL) and the resulting solution was heated in an oil-bath (50-60 °C) for 2 h. The reaction mixture was then poured into cold water (75 mL) and extracted with ether (3 x 50 mL). The combined ether extracts were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. Chromatography of the crude product on 90 g of silica gel (ICN) in a 3 cm x 34 cm column, using 1 1 ether/PE as the eluting solvent [TLC · R_f = 0.31; not UV active, *p*-anisaldehyde (stains dark blue) active] yielded 245 mg (75%) of the required product as a clear colorless liquid; ^1H NMR (500 MHz) δ 5.46 (m, 1 H, butenolide vinyl), 4.86 (m, 2 H, C*H*$_2$O butenolide), 3.42 (t, 2 H, *J* = 6.6 Hz, C*H*$_2$Br), 3 18 (m, 2 H, C*H*$_2$(CH$_2$)$_4$Br, 2.07 (m, 2 H, C*H*$_2$CH$_2$Br), 1.87 (m, 2 H, C*H*$_2$(CH$_2$)$_3$Br, 1.56 (m, 2 H, C*H*$_2$(CH$_2$)$_2$Br); IR (neat) 3024, 2939, 2866, 1781, 1454, 1398, 1343, 1249, 1160, 1145, 1020, 939, 847 cm^{-1}, HRMS (EI), m/z 234, 232 (M), 176, 174, 111,

109, 98, 97, 95, 93, 83, 82, 81 (base), 79, 69, 68, 67, 55, 54, 53; HRMS (EI), m/z 232.0070 (calcd for $C_9H_{13}O_2Br$, M, 232.0158).

(*E*)-4-(5-Bromo-3-pentenyl)-2(5H)-furanone (24). A mixture of the alcohol **20** (280 mg, 1.66 mmol) and *s*-collidine (0.3 mL, 2.0 mmol, 1.2 equiv, freshly distilled from KOH pellets) was treated with a solution of LiBr (anhydrous, 173 mg, 2.0 mmol, 1.2 equiv) in dry DMF (8 mL) and cooled in an ice-bath. Mesyl chloride (0.20 mL, 2.0 mmol, 1.2 equiv, distilled immediately prior to use) was added dropwise and the resulting pale yellow cloudy solution stirred for 3 h at approximately 0 °C. The reaction mixture was then poured onto ice and extracted with ether (4 x 50 mL). The combined ether extracts were washed with saturated $Cu(NO_3)_2$ solution (2 x 35 mL), dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. Chromatography of the crude product on silica gel (ICN) in a 3 cm x 34 cm column, using 7:3 CH_2Cl_2/ether as the eluting solvent [TLC: R_f = 0.77; UV and *p*-anisaldehyde (stains blue) active], afforded 240 mg (63%) of the required product as a clear pale yellow liquid; ^{1}H NMR (500 MHz) δ 5.74 (m, 1 H, CH=C*H*CH_2Br), 5.66 (m, 1 H, C*H*=CHCH_2Br), 5.49 (m, 1 H, butenolide vinyl), 4.83 (m, 2 H, C*H*$_2$O butenolide), 4.03 (d, 2 H, *J* = 7.1 Hz, C*H*$_2$Br), 3.24 (m, 2 H, C*H*$_2$$CH_2$CH=CH), 2.76 (m, 2 H, CH_2C*H*$_2$CH=CH); IR (neat) 3040, 3020, 2980, 2915, 2900, 1780, 1665, 1400, 1370, 1255, 1175, 1020, 970, 845, 750 cm^{-1}, HRMS (CI), m/z 189, 187, 152, 151 [(M + 1) - Br, base], 133, 128, 123, 109, 107, 106, 105, 95, 93, 91, 79; HRMS (CI), m/z 151.0765 (calcd for $C_9H_{11}O_2$, (M + 1) - Br, 151.0759).

6-Hydroxy-2-oxaspiro[4.5]decan-3-one (25) and 4-(2-Hydroxycyclopentyl)oxacyclopentan-2-one (26). This reaction was conducted under a N_2 atmosphere in a standard electrochemical H-cell with a medium porosity sintered glass frit. The anode chamber was fitted with a platinum electrode (surface area 1 cm^2), and a degassed solution of *n*-Bu_4NBr in CH_3CN (0.1 M solution, 25 mL) and cyclohexene (2 mL) were introduced. The cathode chamber contained the mercury pool, a Ag/AgCl reference electrode (standardized to SCE) and a degassed solution of n-Bu_4NBr in CH_3CN (0.1 M solution, 25 mL). After obtaining a background current reading at a potential of -2.35 V, a solution of aldehyde **12** (140 mg, 0.83 mmol), diethyl malonate (0.51 mL, 3.33 mmol, 4 equiv) and CH_3CN (4 mL) was introduced dropwise by syringe pump, over a 1 h period, to the cathode chamber. The reduction was carried out at a controlled potential of -2.35 V. After a further 25 min, 145 coulombs of the theoretical 160 coulombs required had been consumed and the current dropped to the original background value The reaction mixture from the cathode chamber was poured into saturated NaCl solution (35 mL) and extracted with 7:3 CH_2Cl_2/ ether (7 x 75 mL). The combined organic extracts were dried over anhydrous MgSO4 and concentrated *in vacuo*. Chromatography of the crude product mixture on silica gel (ICN) in a 3 cm x 34 cm column, using 7.3 CH_2Cl_2 as the eluting solvent [TLC: R_f = 0.2; not UV active, *p*-anisaldehyde (stains dark blue) active], yielded 86 mg (61%) of a mixture of alcohols a a clear colorless liquid. This mixture of alcohols was separated by HPLC. HPLC conditions: pump flow rate 5 mL/min, refractive index detector temp 30 °C, solvent 1·1 ethyl acetate/ hexanes. Compound; retention times (min); yield (%): mixture of diastereomeric lactone cyclohexanols **25** diastereomeric lactone cyclopentanols **26**: 15 min; 1%. Diastereomer 1: 18.6 min; 5% Diastereomer 2: 21 min, 16%. Diastereomer 3: 22.2 min, 21%. Diastereomer 4: 28 2 min; 18%.

Compound **25** (diastereomeric mixture, ratio 4·1) Diastereomer 1 ^{1}H NMR (500 MHz) δ 4 44 and 4.05 (2 d, 1 H and 1 H, *J* = 9.2 Hz, C*H*$_2$O lactone), 3.64 (m, 1 H, *J* = 4.1 Hz, C*H*OH), 2.67 and 2.27 (2 d, 1 H and 1 H, *J* = 17.5 Hz, C*H*$_2$$CO_2$ lactone), 1.75-1.35 (several m, 9 H, CHO*H* and cyclohexyl methylenes); Diastereomer 2. ^{1}H NMR (500 MHz) δ 4.37 and 3.94 (2 d, 1 H and 1 H, *J* = 9 0 Hz, C*H*$_2$O lactone), 3 56 (m, 1 H, C*H*OH), 2.76 and 2.24 (2 d, 1 H and 1 H, *J* = 17.3 Hz, C*H*$_2$$CO_2$ lactone), 1.75-1.35 (several m, 9 H, CHO*H* and cyclohexyl methylenes); IR (neat, mixture of **25**) 3500-3200, 2930, 2860, 1760, 1255, 1420, 1380, 1265, 1200, 1070, 1025, 800 cm^{-1}, LRMS (CI, mixture of **25**), m/z 171 (M + 1), 154, 153 (base), 135, 125, 109, 107, 93, 81, 67; HRMS (CI, mixture of **25**), m/z 171.1002 (calcd for $C_9H_{15}O_3$, M + 1, 171 1022).

Compound **26**, diastereomer 1: ^{1}H NMR (500 MHz) δ 4.58 and 4.06 (2 dd, 1 H and 1 H, J = 8.9, 7.8 Hz, and J = 8.9, 7.7 Hz, CH_2O lactone), 4.19 (d, J = 3.3 Hz, C*H*OH), 2.76 (m, 6 lines, 1 H, J = 8.5, lactone methine), 2.62 and 2.26 (2 dd, 1 H and 1 H, J = 17 4, 8.5 Hz and J = 17.4, 8.9 Hz, CH_2CO_2 lactone), 1 88-1.66 (several m, 7 H, CHO*H* and cyclopentyl methylenes) 1.5 (m, 1 H, cyclopentyl methine); ^{13}C NMR (125 MHz, fully decoupled) δ 177.37 (lactone carbonyl), 73.32 (*C*HOH), 72.95 (*C*H_2O lactone), 48.73 (*C*H_2CO_2 lactone), 36 17, 36.00, 33 86, 27.90, 21.75; IR (neat) 3500-3200, 2950, 2929, 2901, 2874, 1765, 1449, 1418, 1332, 1178, 1145, 1017, 920, 861, 734 cm^{-1}; HRMS (CI), m/z 171 (M + 1, base), 169, 153, 141, 135, 123, 107, 95, 93, 67; HPMS (CI), m/z 171.1023 (calcd for $C_8H_{15}O_3$, M +1, 171.1022), Diastereomer 2· ^{1}H NMR (500 MHz) δ 4 43 and 4 02 (2 dd, 1 H and 1 H, J = 8.7, 7.4 Hz and J = 8 7, 7 8 Hz, CH_2O lactone), 4.20 (d, 1 H, J = 2.8 Hz, C*H*OH), 2 76 (m, 1 H, lactone methine), 2.72 and 2 31 (2 d, 1 H and 1 H, J = 8.2 Hz, CH_2CO_2 lactone), 1.89-1.68 (several m, 7 H, CHO*H* and cyclopentyl methylenes), 1.48 (m, 1 H, cyclopentyl methine); ^{13}C NMR (125 MHz, fully decoupled) δ 177.48 (lactone carbonyl), 74 03 (*C*HOH), 72 68 (*C*H_2O lactone), 48 80 (*C*H_2CO_2 lactone), 36.12, 35.59, 33.98, 26.65, 22.04; IR (neat) 3500-3200, 2961, 2948, 2933, 2906, 1767, 1452, 1424, 1174, 1112, 1019, 1001, 737 cm^{-1}; HRMS (CI), m/z 171 (M + 1), 169, 154, 153 (base), 151, 141, 135, 123, 107, 95, 93, 67; HRMS (CI), m/z 154.0975 (calcd for $C_9H_{14}O_2$, (M + 1) - OH, 154 0994), Diastereomer 3: ^{1}H NMR (500 MHz) δ 4 51 and 4 20 (2 dd, 1 H and 1 H, J = 9.1, 7 5 Hz and J = 9 1, 8.2 Hz, CH_2O lactone) 3.38 (d, 1 H, J = 6.7 Hz, C*H*OH), 2.57 and 2 26 (2 dd, 1 H and 1 H, J = 16.7, 8 3 Hz and J = 16 7, 8.7 Hz, CH_2CO_2 lactone), 2 51 (m, 6 lines, 1 H, J = 8 2 Hz, lactone methine), 1.94 (m, 16 lines, 2 H, cyclopentyl methylene), 1 78 (m, 10 lines, 2 H, cyclopentyl methylene), 1.62 (m, 3 H, CHO*H* and cyclopentyl methylene) 1.24 (m, 8 lines, 1 H, cyclopentyl methine); ^{13}C NMR (125 MHz, fully decoupled) δ 177.27 (lactone carbonyl), 77 57 (*C*HOH), 72.60 (*C*H_2O lactone), 50.39 (*C*H_2CO_2 lactone), 39 69, 35 22, 33.41, 28.37, 21 49; IR (neat) 3500-3200, 2956, 2936, 2874, 1767, 1172, 1074, 1000 cm^{-1}; HRMS (CI), m/z 171 (M + 1), 154, 153 (base), 135, 125, 109, 107, 95, 93, 85, 67; HRMS (CI), m/z 171 1008 (calcd for $C_9H_{15}O_3$, M + 1, 171.1022), Diastereomer 4· ^{1}H NMR (500 Mz) δ 4.39 and 3 99 (2 dd, 1 H and 1 H, J = 8 6, 7.1 Hz and J = 8.6, 8.4 Hz, CH_2O lactone), 3 91 (q, 1 H, J = 6 3 Hz, C*H*OH), 2 67 and 2.49 (2 dd, 1 H and 1 H, J = 20 5, 11.6 Hz and J = 20.5, 8.4 Hz, CH_2CO_2 lactone), 2 48 (m, 1 H, lactone methine), 1.92 (m, 16 lines, 2 H, cyclopentyl methylene), 1.76 (m, 2 H, cyclopentyl methylene), 1 62 (m, 3 H, CHO*H* and cyclopentyl methylene), 1 21 (m, 8 lines, 1 H, cyclopentyl methine), ^{13}C NMR (125 MHz, fully decoupled) δ 177 56 (lactone carbonyl), 77.55 (*C*HOH), 72 17 (*C*H_2O) lactone), 50 48 (*C*H_2CO_2 lactone), 39.48, 35.25, 33.28, 28.03, 21 74, IR (neat) 3500-3200, 2956, 2932, 2900, 2873, 1767, 1419, 1369, 1179, 1012, 916, 845 cm^{-1}, HRMS (CI), m/z 171 (M + 1), 169, 153 (base), 135, 125, 123, 109, 107, 95, 93, 79, 67; HRMS (CI), m/z 171.0997 (calcd for $C_9H_{15}O_3$, M + 1, 171 1022).

4-(5-Methylsulfonyloxypentyl)oxacyclopentan-2-one (27). This reaction was performed as indicated for compound **12** After obtaining a background current reading at a potential of -2 35 V, a solution of the mesylate **22** (100 mg, 0.04 mmol), diethyl malonate (0.25 mL, 1 62 mmol, 4 equiv) and CH_3CN (4 mL) was added by syringe pump, over a 1 h period, to the cathode chamber The reduction was carried out at a controlled potential of -2 35 V. After a further 15 min, the current had dropped to the onginal background value. The reaction mixture from the cathode chamber was poured into saturated NaCl solution (30 mL) and extracted with ether (5 x 50 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated *in vacuo* Chromatography of the crude product on silica gel (ICN) in a 3 cm x 34 cm column, using 7 3 CH_2Cl_2/ether as the eluting solvent [TLC R_f = 0 53, not UV active, *p*-anisaldehyde (stains blue) active], yielded 76 mg (75%) of the product **27** as a clear colorless liquid, ^{1}H NMR (500 MHz) δ 4 42 and 3 93 (2 dd, 1 H and 1 H, J = 8.9, 7 4 Hz and J = 8 9, 7.1 Hz, CH_2O lactone), 4 23 (t, 2 H, J = 6.4 Hz, CH_2SO_2), 3 01 (s, 3 H, SO_2CH_3), 2.63 and 2.18 (2 dd, 1 H and 1 H, J = 17 0, 8 4 Hz and J = 17 0, 7.8 Hz, CH_2CO_2 lactone), 2.55 (m, 7 lines, 1 H, J = 7.4 Hz, lactone methine), 1.77 (m, 2 H, CHCH_2CH_2), 1.53-1 33 (several m, 6 H, (CH_2)$_3$CH_2SO_2), IR (neat) 3019, 2944, 2903, 2861, 1771, 1465,

1420, 1345, 1340, 1183, 1067, 1020, 977, 936, 826, 724, 693 cm^{-1}, HRMS (CI), m/z 251 (M + 1), 155, 137, 109, 96, 95 (base), 93, 68, 67, 66, HRMS (CI), m/z 251.0930 (calcd for $C_{10}H_{19}O_5S$, M + 1, 251.0953).

4-(1-Cyclopentyl)oxacyclopentan-2-one (28) and 4-(1-Cyclopentyl)-2(3H)-furanone (29). This reaction was performed as indicated for compound **12** After obtaining a background current reading at a potential of -2 25 V, a solution of the bromide **23** (90 mg, 0.39 mmol), diethyl malonate (0.24 mL, 1 55 mmol, 4 equiv) and CH_3CN (4 mL) was introduced by syringe pump, over 1 h, to the cathode chamber. The reduction was carried out at a controlled potential of -2.25 V. After a further 1 h, the current reading had dropped to the onginal background value The reaction mixture from the cathode chamber was poured into saturated NaCl solution (30 mL) and extracted with ether (4 x 50 mL) and 7:3 CH_2Cl_2/ether (4 x 50 mL) The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated *in vacuo* Chromatography of the crude product on silica gel (ICN) in a 3 cm x 34 cm column, using 1:1 ether/PE as the eluting solvent [TLC: R_f (compound **28**) = 0 49; not UV active, *p*-anisaldehyde (stains blue) active, and R_f (compound **29**) = 0.25, not UV active, *p*-anisaldehyde (stains blue-green) active], yielded 6 mg (10%) of compound **28** and 34 mg (59%) of compound **29** as clear colorless liquids; Compound **28**: ^1H NMR (500 MHz) δ 4 40 and 4.00 (2 dd, 1 H and 1 H, J = 9.0, 8.0 Hz and J = 9.0, 7.8 Hz, CH_2O lactone) 2.59 and 2 25 (2 dd, 1 H and 1 H, J = 17.2, 8 6 Hz and J = 17.2, 8.6 Hz, CH_2CO_2 lactone), 2.39 (m, 1 H, lactone methine), 1.84-1.40 (several m, 9 H, cyclopentyl methine and methylenes); LRMS 154 (M), 96, 95, 86, 82, 81, 69, 68, 67 (base), 66, 55, 54, 53, Compound **29** ^1H NMR (500 MHz) δ 5.80 (t, 1 H, J = 1 6 Hz, butenolide vinyl), 4.76 (d, 2 H, J = 1 6 Hz, CH_2CO_2 butenolide), 2.79 (quintet, 1 H, J = 8.2 Hz, cyclopentyl methine), 2.00 (m, 2 H, cyclopentyl methylene), 1 76 (m, 2 H, cyclopentyl methylene), 1.65 (m, 2 H, cyclopentyl methylene), 1 54 (m, 2 H, cyclopentyl methylene); IR (neat) 2950, 2870, 1775, 1745, 1635, 1445, 1345, 1315, 1260, 1170, 1135, 1020, 970, 900 cm^{-1}; LRMS (EI), m/z 152 (M), 125, 123, 111, 108, 107, 95, 94, 93, 91, 85, 84, 83, 81, 80, 79, 77, 69, 68, 67, 66, 65, 57, 56, 55 (base), 54, 53, 52, 51; HRMS (CI), m/z 153.0901 (calcd for $C_9H_{13}O_2$, M + 1, 153.0915).

2-Oxaspiro[4.5]dec-7-en-3-one (31) and (*E*)-4-(3-Pentenyl)-2(3H)-furanone (32). This reaction was performed as indicated for compound **12**. After obtaining a background current reading at a potential of -2 15 V, a solution of the allylic bromide **24** (150 mg, 0.65 mmol), diethyl malonate (0 39 mL, 2 6 mmol, 4 equiv) and CH_3CN (4 mL) was added dropwise by syringe pump, over a 1 h period, to the cathode chamber. The reduction was carried out at a controlled potential of -2.15 V. After a further 45 min, the current had dropped to the original background value The reaction mixture from the cathode chamber was poured into saturated NaCl solution (35 mL) and extracted with ether (5 x 50 mL). The combined ether extracts were dried over anhydrous $MgSO_4$ and concentrated *in vacuo* Chromatography of the crude product mixture on silica gel (ICN) in a 3 cm x 34 cm column, using 1 1 ether /PE as the eluting solvent [TLC: R_f (compound **31**) = 0 36 and R_f (compound **32**) = 0.27; not UV active, *p*-anisaldehyde (stains blue) active], yielded 6 mg (6%) of compound **31** (mixture of diastereomers, ratio 4 1) and 76 mg (77%) of compound **32** as clear colorless liquids, Compound **31** (diastereomeric mixture, ratio 4:1), diastereomer 1 ^1H NMR δ 5 17 and 5 07 (2 m, 1 H and 1 H, cyclohexenyl vinyl), 4.41 and 4 10 (2 d, 1 H and 1 H, J = 9.5 Hz, CH_2O lactone), 2 56 (s, 2 H, CH_2CO_2 lactone), 2 07 (m, 2 H, cyclohexenyl methylene), 1.95 (m, 2 H, cyclohexenyl methylene), 1 88 (m, 2 H, cyclohexenyl methylene), Diastereomer 2 ^1H NMR (500 MHz) δ 5 18 and 5.06 (2 m, 1 H and 1 H, cyclohexenyl vinyls), 4 22 and 4 18 (2 d, 1 H and 1 H, J = 9 4 Hz CH_2O lactone), 2 68 and 2 36 (2 d, 1 H and 1 H, J = 17 5 Hz, CH_2CO_2 lactone), 2 07-1 88 (3 m, 6 H, cyclohexenyl methylenes);IR (neat, mixture of **31**) 3015, 2930, 2865, 1775, 1740, 1635, 1445, 1330, 1275, 1170, 1135, 1030, 970, 885, 855 cm^{-1}, LREI (EI, mixture of **31**), m/z 152 (M), 124, 123, 98, 97, 96, 95, 69, 68, 67, 55 (base), 54, 53, 42, HRMS (EI, mixture of **31**), m/z 152 0837 (calcd for $C_9H_{12}O_2$, M, 152.0837), Compound **32** ^1H NMR (500 MHz) δ 5 85 (t, 1 H, J = 1 2 Hz, butenolide vinyl), 5 52 and 5 40 (2 m, 1 H and 1 H, J = 14.8 Hz, CH=CH), 4 74 (d, 2 H, J = 1 2 Hz, CH_2CO_2 butenolide), 2 47 (t, 2 H, J =

7.3 Hz, methylene directly adjacent to butenolide ring), 2.27 (m, 2 H, $CH_2CH{=}CH$), 1.66 (d, 3 H, J = 7.6 Hz, $CH{=}CHCH_3$); IR (neat) 3015, 2915, 2880, 1775, 1740, 1635, 1440, 1335, 1275, 1135, 1030, 970, 885, 855 cm^{-1}; HRMS (CI), m/z 153 (M + 1), 151, 136, 135 (base), 124, 123, 109, 108, 107, 96, 95, 81; HRMS (CI), m/z 153.0935 (calcd for $C_9H_{13}O_2$, M + 1, 153 0915).

4-(Bromopentyl)-2(3H)-furanone (42). The chloro(pyridino)bis(di-methylglyoximato)cobalt(III) complex used for this procedure was prepared as follows: Pyridine (1 7 mL, 21 0 mmol) was added dropwise to a hot solution of cobalt(II) chloride 6-hydrate (2.5 g, 10.5 mmol) and dimethylglyoxime (2.44 g, 21 0 mmol) in 95% ethanol (100 mL). After cooling the mixture to approximately 20 °C, air was bubbled through it for 30 min The reaction mixture was then allowed to stand at approximately 20 °C for 1 h and the yellow-brown solid filtered. The filtered solid was washed with water (25 mL), ethanol (25 mL) and ether (25 mL), and dried under vacuum. The cobalt(III) complex was obtained in a yield of 2.0 g (47%).

A solution of the bromide **23** (50 mg, 0.22 mmol) in methanol (4 mL) was treated with a catalytic amount (0.1 equiv) of the Co(I) species generated electrochemically via Pattenden's method (-1 8 V, $LiClO_4$, MeOH) from the cobalt(III) complex [33,34] The reaction mixture was stirred for 15 min, at which time TLC analysis (7:3 CH_2Cl_2/ether) indicated the complete disappearance of bromide **23** and appearance of one new compound. The reaction mixture was concentrated *in vacuo*. Chromatography of the crude product on silica gel (ICN) in a 3 cm x 34 cm column, using 7:3 CH_2Cl_2/ether as the eluting solvent [TLC R_f =0.7; not UV active, *p*-anisaldehyde (stains yellow) active], afforded 35 mg (70%) of bromide **42** as a pale yellow liquid, ^1H NMR (500 MHz) δ 5.85 (t, 1 H, J = 1.4 Hz, butenolide vinyl), 4.74 (d, 1 H, J = 1.4 Hz, CH_2CO_2 butenolide), 3.42 (t, 2 H, J = 6.6 Hz, CH_2Br), 2.44 (t, 2 H, J = 7 6 Hz, $CH_2(CH_2)_4Br$), 1.90 (quintet, 2 H, J = 7.0 Hz, CH_2CH_2Br), 1.64 (quintet, 2 H, J = 7.6 Hz, $CH_2(CH_2)_3Br$), 1.55 (m, 2 H, $CH_2(CH_2)_2Br$); IR (neat) 2950, 1779, 1750, 1639, 1447, 1170, 1144, 1025, 887 cm-1, LRMS (EI), m/z 234, 232 (M), 205, 203, 153, 126, 98, 97, 95, 93, 81, 69, 67, 55 (base), 53; HRMS (CI), m/z 233.0202, (calcd for $C_9H_{14}O_2Br$, M + 1, 233.0173).

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