Tetrahedron 67 (2011) 3546–3552

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Cyclopropanespiro-β-lactones derived from 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one: diastereoselective formation and rearrangement reactions

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ARTICLE INFO

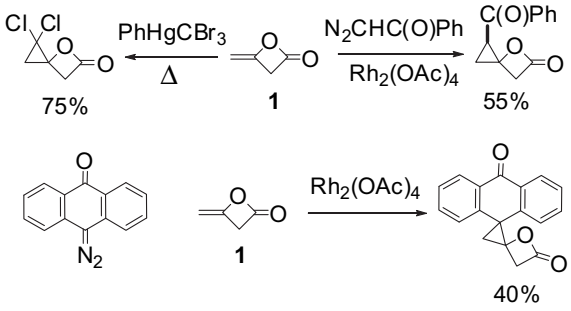
Article history:
Received 5 August 2010
Received in revised form 24 February 2011
Accepted 7 March 2011
Available online 15 March 2011

ABSTRACT

The metal catalysed reaction of monosubstituted diazo esters and ketones with 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one results in the formation of cyclopropanespiro-β-lactones. In contrast to most alkene cyclopropanations, including those involving diketene, the reaction occurs diastereoselectively. A computational model of the reaction has been developed that accounts for the observed stereochemistry. The metal promoted thermal rearrangement of these spiro compounds is also unusual in that it affords pyranones, rather than the decarboxylation products characteristic of β-lactones in general, or the furanones formed from diketene derived cyclopropanespiro-β-lactones.

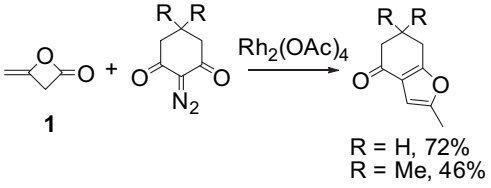
1. Introduction

The cyclopropanation of diketene **1** using α-diazo esters or ketones,[1] diazoalkanes,[1c] (α-diazoalkyl)phosphonates[2] or phenyl-(tribromomethyl)mercury[3] leads to the formation of cyclopropanespiro-β-lactones (Scheme 1). These methods afford access to a wide range of structurally diverse cyclopropanespiro-β-lactones, with, for example, diazocycloalkanes producing doubly spiro systems (Scheme 1).



Scheme 1. Synthesis of cyclopropanespiro-β-lactones from diketene **1**.

Only 2-diazo-1,3-dicarbonyl compounds fail to produce cyclopropanespiro-β-lactones, affording instead benzofurans through a formal 1,3-dipolar cycloaddition of a carbenoid to the exocyclic double bond of diketene[4] (Scheme 2).



Scheme 2. Reaction of 2-diazo-1.3-dicarbonyl compounds with diketene **1**.

As cyclopropanespiro-β-lactones are highly strained and, although relatively small, contain a significant amount of functionality, these compounds are potentially valuable synthetic intermediates. As would be expected from their structure, they react readily with a variety of nucleophiles, including amines,[1b,2] giving acyclic products and with carbanions[2] from acetoacetate giving cyclopentenones. BF_3 promoted ring opening also results in the formation of acyclic products. Surprisingly however, unlike larger cycloalkanespiro-β-lactones, they do not undergo thermal decarboxylation, the classic reaction of β-lactones. Instead they undergo a metal-promoted rearrangement to furanones (Scheme 3).[1c,5]

Although all cyclopropanespiro-β-lactones reported to date have been derived from diketene, the related 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one **2** is also readily available[6] through the diastereoselective base promoted dimerization of methylketene generated from propionyl chloride. If the base used in the dimerization reaction is chiral, the β-lactone is formed enantioselectively.[7] The range of reactivity previously observed for **1** and the fact that **2** is readily available in both racemic and enantioenriched forms, provided the justification for a consideration of the synthesis and reactions of cyclopropanespiro-β-lactones based on the latter. The successful synthesis of a number of these compounds is reported

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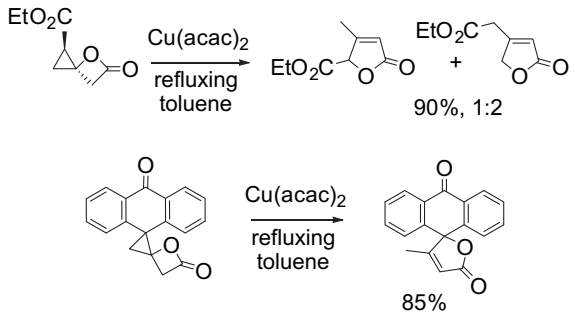
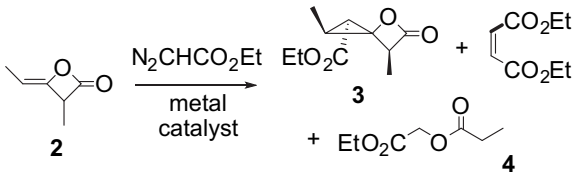
doi:10.1016/j.tet.2011.03.013



Scheme 3. Metal promoted rearrangement of cyclopropanespiro-β-lactones.

here. Surprisingly, unlike most cyclopropanation reactions with diazo compounds, including those involving diketene **1**, the reaction of **2** with a range of monosubstituted diazo compounds resulted in the diastereoselective formation of a cyclopropanespiro-β-lactone, albeit in at best modest yield (Scheme 4). The chemistry of these molecules was also surprising in that metal promoted thermal rearrangement led to the formation of a pyranone ring system, rather than the furanones obtained from the diketene derived analogues.



Scheme 4. Reaction 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one **2** with ethyl diazoacetate.

2. Results and discussion

2.1. Reaction of diazo compounds with 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one 2

The β-lactone **2** was prepared by the reaction of triethylamine with propionyl chloride[6] and was obtained as a mixture with propionic anhydride. The removal of the last traces of the latter proved difficult and so the 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one **2** used in the experiments described here contained ~20% of the anhydride. The reaction between **2** and ethyl diazoacetate was carried using a fivefold excess of the lactone and a variety of standard cyclopropanation catalysts (Table 1). Although copper(I) triflate proved to be the most efficient catalyst, the outcome of the reaction was in all cases the same: the diastereoselective formation of ethyl (1*R**,2*R**,3*S**,6*R**)-2,6-dimethyl-5-oxo-4-oxaspiro[2,3]hexane-1-carboxylate **3** (Scheme 4) in, at best, modest yield. ^{1}H NMR and GC analysis confirmed the diastereoselectivity of the process, indicating that the only low molecular mass compounds present in the crude product were **3**, diethyl maleate and fumarate and 2-ethoxy-2-oxoethyl propionate **4**,[8] which resulted from the reaction of the diazo compound with the propionic anhydride present as an impurity in the lactone **2**.

Table 1
The reaction of **2** with ethyl diazoacetate

Metal catalyst	Solvent/ temperatute	Time[a] h	Fumarate/ maleate[b]	**3**[b]	**4**[b]
Cu powder	Neat **2**, 80°	2/1	13	10	11
$Rh_2(OAc)_4$	Neat **2**, rt	2/17	11	3	1
CuOTf	**2**/DCM, reflux	2/1	20	20	6
CuOTf (syringe pump)	**2**/DCM, reflux	12/1	6	29	4
$Cu(acac)_2$	Neat **2**, rt	2/1	8	1	Trace

[a] Diazoacetate addition time/additional stirring time needed for complete reaction of diazoacetate (IR).
[b] Isolated yield based on diazoacetate (%)

The gross structure of **3** was assigned on the basis of its IR, ^{1}H and ^{13}C NMR spectra. A coupling constant of 6.0 Hz is indicative of a trans relationship between the cyclopropyl protons.[9] The only significant correlation in the NOE difference spectrum of **3** involved 2-H and 6-CH_3. This established the stereochemical relationship of these protons as a Hartree–Fock (3-21G) generated structure[10] for **3** indicated a separation of only 3.00 Å between 2-H and the carbon atom of 6-CH_3, whereas the other three diastereomeric possibilities for a cyclopropanespiro-β-lactone with *trans* cyclopropyl protons involved significantly larger separations: 3.98, 4.09 and 4.69 Å.

The reaction of **2** with a range of other monosubstituted diazo compounds was carried out using CuOTf, in general, as catalyst (Table 2). The reactions of diazoacetophenone and diazoheptanone also proceeded diastereoselectively to give a single cyclopropanespiro-β-lactone, in low to modest isolated yield, accompanied by small amounts of a product derived from the propionic anhydride present as an impurity in **2**. The stereochemistry of the cyclopropanation product was assigned on the basis of ^{1}H NMR coupling constant and NOE data, and in the case of the cyclopropanespiro-β-lactone **5** derived from diazoacetophenone, it was confirmed by X-ray crystallography[11] (Fig. 1).

Table 2
The reaction of **2**[a,b,c] with diazo compounds

Diazo compound / Reaction conditions	Products (isolated yield)	
H, CO_2Et, N_2 CuOTf, Δ, CH_2Cl_2, 12 h (syringe pump)/1 h[b]	**3** 29%	**4** 4%
H, C(O)Ph, N_2 CuOTf, Δ, ether 3 h/1 h[b]	**5** 24%	**6** 13%
H, C(O)nC_5H_{11}, N_2 CuOTf, Δ, ether 9½ h/1 h[b]	**7** 17%	**8** 18%
MeO_2C, CO_2Me, N_2 Ph_2CO, MeCN, hν 3 h[c]	**9**	**11**
	10	**12**
	1:1.5, 23%	1:1.1, 13%

[a] Containing ~20% propionic anhydride.
[b] Addition time/stirring to complete reaction of diazo compound (IR).
[c] Time for complete reaction (IR) with diazo compound added in a single amount.

The outcome of the reaction of **2** with a disubstituted diazo compound depended on the nature of the latter. The photochemical[12] reaction of diethyl diazomalonate with **2** was not stereoselective and resulted in the formation of a partially separable mixture of diastereomeric cyclopropanespiro-β-lactones (**9**–**12**, Table 2). The relative stereochemistry at C-2 and C-3 is assigned on the basis that the system is electronically similar to a vinyl acetate.[13] The cis relationship between 2-H and the oxetanone ring *O*-atom in **9** and **10** is reflected in the downfield shift observed for 2-H with these compounds, δ 2.75 and 2.54, respectively, relative to those observed for **11** (δ 2.23) and **12** (δ 2.00) in which the relationship is trans. The relative stereochemistry at 6-C in **9** and **10** can be assigned on the basis of the chemical shift of 6-H: the downfield shift of this proton in **9** (δ 4.42), compared to that of the corresponding proton in **10** (δ 3.88), is accounted for by

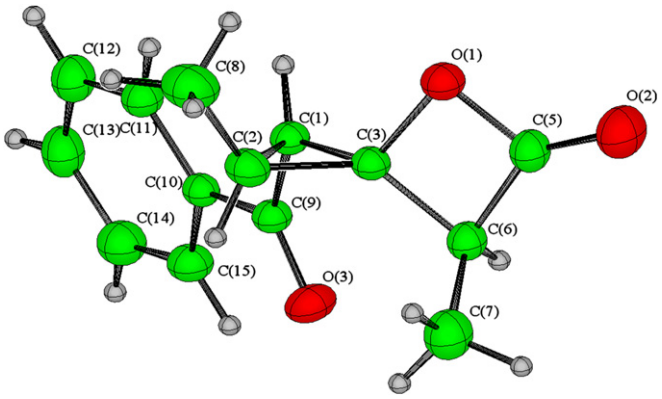
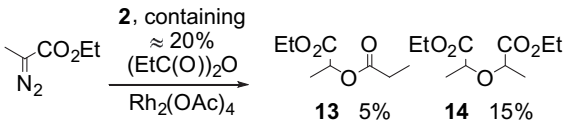


Fig. 1. (1*R**,2*R**,3*R**,6*R**)-1-Benzoyl-2,6-dimethyl-4-oxaspiro[2.3]-hexan-5-one **5**.

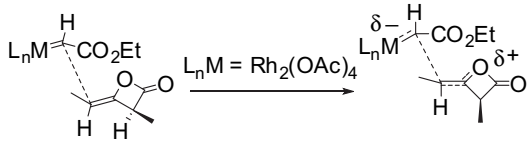
the close spatial relationship between 6-H and one of the ester groups in the 1-position in the former. The difference between the chemical shift of H-6 in **11** and **12** is only 0.03 ppm, and so the stereochemical assignment at 6-C is more tentative in this case. However the relative chemical shifts of 6-CH_3 in **11** (δ 1.27) and **12** (δ 1.35) are also in keeping with the proposed assignment.

Although the reaction of diazofluorene with diketene **1** results in the formation of a cyclopropanespiro-β-lactone,[1c] this is not the case for its CuOTf catalysed reaction with **2**. Instead other carbenoid derived products, such as 9,9′-bifluorenylidene are formed, suggesting that cyclopropanation of **2** is not competitive with processes such as dimerization, presumably for steric reasons. Reaction in the presence of $Rh_2(OAc)_4$ also gave 9,9′-bifluorenylidene and in addition another dimerization product, difluoren-9-ylidene hydrazine. Photochemical reaction, which would involve free carbenes, also failed to produce any cyclopropanation products, giving 9,9′-bifluorenylidene and 9*H*-fluoren-9-yl propionate, a propionic anhydride derived product. In a similar fashion, the disubstituted ethyl 2-diazopropionate gave only propionic anhydride derived products (Scheme 5).



Scheme 5. The metal catalysed reaction of ethyl 2-diazopropionate in the presence of **2** containing approx. 20% propionic anhydride.

A computational approach was used to obtain an understanding of the stereoselectivity observed in the cyclopropanation of the alkene bond in **2** with monosubstituted diazo compounds. The generally accepted mechanism for such reactions is based on a transition state involving the metal carbenoid and the alkene, in which the metal atom has a partial negative charge and one of the alkene carbons a partial positive charge.[14] The computational approach adopted considered the reaction as a two-step process involving a dipolar intermediate corresponding to this transition state. A starting geometry for a $Rh_2(OAc_4)$ derived intermediate of this type was generated on the basis that the formation of the first C–C bond involved an approach of the alkene to the carbenoid, which avoided steric interactions between the ester group and the olefinic and oxetanone methyl groups, and between the oxetanone and the catalyst ligands (Scheme 6).



Scheme 6. Transition state for cyclopropanation of **2**.

A molecular mechanics search procedure[15] was used to explore the conformational space of this intermediate. A five-membered ring, involving stabilization of the developing electrophilic carbon by the ester carbonyl, was a feature of all the low energy conformers located. Such an arrangement is compatible with the stereoselectivities observed with other systems[14] and is a feature of most of the mechanisms suggested for these cyclopropanation reactions;[16] the fact that it arises naturally from the conformational search provides validation for the appropriateness of this computational approach. The low energy conformers divided into two groups on the basis of the stereochemical relationship between the ring oxygen of the oxetanone and the methyl substituent of what was the alkene. The lowest energy conformer in each set was refined using a DFT calculation (B3LYP 6-31G*):[10] the structure in which the oxygen and the methyl have a cis relationship (Fig. 2), as they have in the product **3**, was found to be 2.04 kJ mol^{-1} lower in energy than that in which the relationship is trans (Fig. 3).

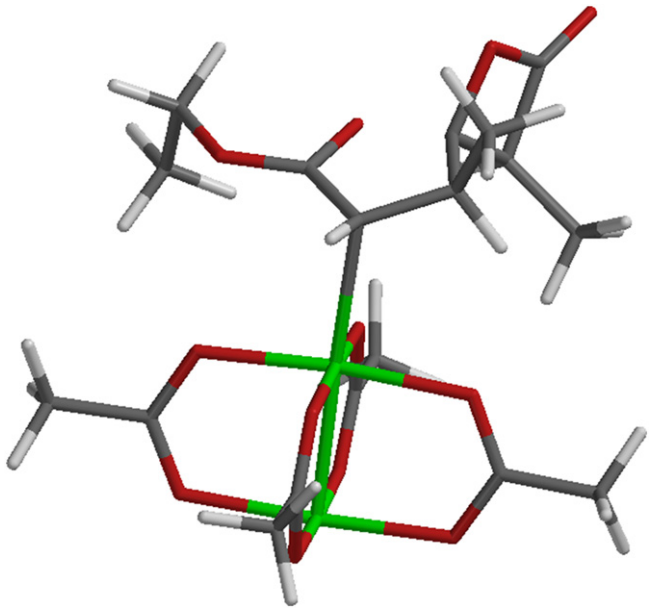


Fig. 2. B3LYP 6-31G* optimized geometry of the product forming intermediate.

The C–C bond formation, which completes the cyclopropane is accompanied by a lengthening of the metal–C bond, a process, which reduces the steric influence of the catalyst framework. It also involves the rotation of the ester group into its final position: in the case of diketene **1** there is no difference between the two possible rotation directions and a mixture of diastereomers results. In the case of **2** rotation of the ester group occurs under the influence of what was the ethylidene methyl group, resulting in the stereoselectivity observed for the reaction of this molecule with diazo esters and ketones. The success of the molecular modelling approach used here in providing an insight into the factors determining the stereochemical outcome of the cyclopropanation reaction under consideration, suggests that it could be used to explore the behaviour of other related reaction systems as well.

2.2. Rearrangement reactions of cyclopropanespiro-β-lactones derived from 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one 2

As their strained nature might lead one to expect, the cyclopropanespiro-β-lactones derived from diketene **1** undergo a range of rearrangement reactions, the most unexpected of which is their metal-catalysed conversion to furanones (Scheme 3).[1c,5] Interestingly, and in contrast to the behaviour of cyclobutanespiro-β-lactones[17] and

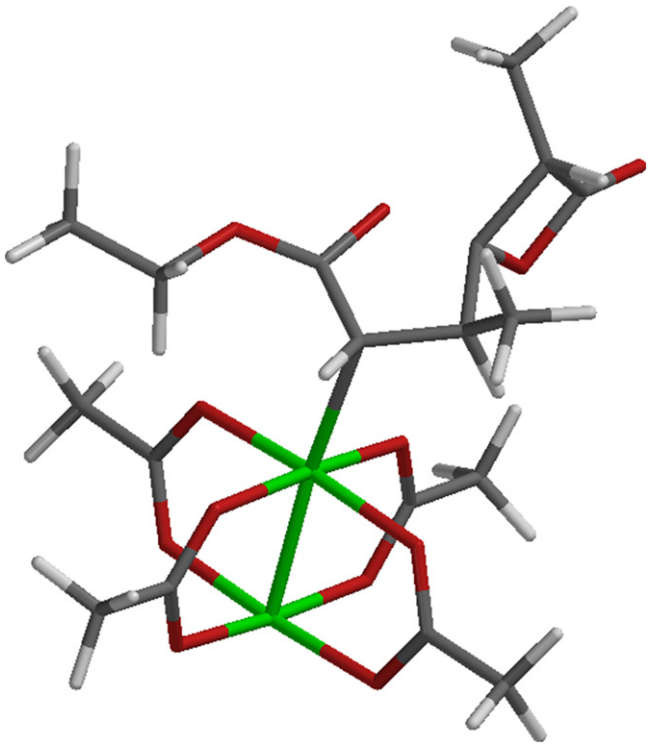
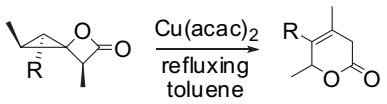


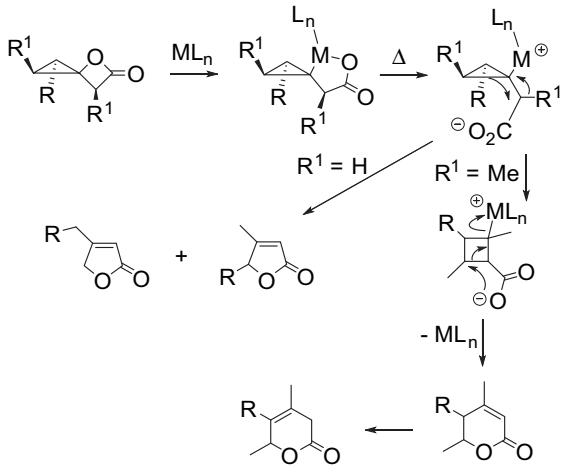
Fig. 3. B3LYP 6-31G* optimized geometry of the non-product forming intermediate.

larger ring analogues,[18] simple thermal reaction does not result in the elimination of carbon dioxide. Instead, a range of different products results depending on the structure of the spiro-β-lactone involved, with the formation of a dimeric pyranone from the spiro-β-lactone produced by the reaction of ethyl diazoacetate with diketene being the most remarkable.[1c] The boron trifluoride catalysed rearrangement of diketene derived cyclopropanespiro-β-lactones leads to the formation of β-keto acids. The availability of methyl substituted cyclopropanespiro-β-lactones through the cyclopropanation of 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one **2** facilitated an exploration of the effect of substitution on these rearrangement pathways.



Scheme 7. Rearrangement of cyclopropanespiro-β-lactones derived from **2**.

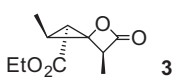
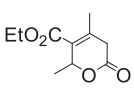
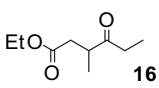
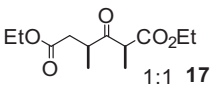
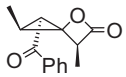
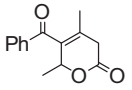
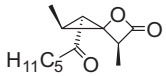
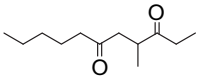
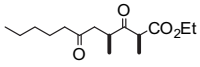
Surprisingly, although the cyclopropanespiro-β-lactones derived from **2** do undergo a metal-catalysed rearrangement, the product is, in general, a pyranone (Scheme 7, Table 3). The rearrangement of the diketene derived cyclopropanespiro-β-lactones has been rationalized in terms of a mechanism involving the formation of a metallocycle (Scheme 8, R^1=H).[1c,5] Cleavage of the metallocycle generates a carboxylate anion, nucleophilic attack of which on the now electron-deficient cyclopropane generates the furanones. The rearrangement reactions of the cyclopropanespiro-β-lactones derived from **2** (Scheme 8, R^1=Me) involves a new reaction pathway: a methyl migration accompanied by a cyclopropane to cyclobutane ring expansion, which occurs to the exclusion of the pathway observed when R^1=H. The addition of a small amount of ethyl diazoacetate did not have the same accelerating effect on these reactions as had been observed for the diketene derived cyclopropanespiro-β-lactones.[5b] The formation of the 1,4-diketone **19** from cyclopropanespiro-β-lactone **7** under these conditions is atypical. The structure of **19** is analogous to that of the minor product **16** obtained in the boron trifluoride catalysed reaction of **3** and in both cases the products may be the result of a reaction between the cyclopropanespiro-β-lactone and adventitious water.



Scheme 8. Rearrangement of cyclopropanespiro-β-lactones derived from **4**.

The major, or sole, reaction pathway in the boron trifluoride promoted rearrangement of the cyclopropanespiro-β-lactones derived from **2**, parallels that observed for their diketene derived analogues.[1c] Although the products formed (Table 3) are formally the result of a reaction between the cyclopropanespiro-β-lactone

Table 3
The rearrangement of cyclopropanespiro-β-lactones derived from **2**

Cyclopropanespiro-β-lactone	Product of metal-catalysed rearrangement	Isolated Yield (%)	Product of BF_3 catalysed rearrangement	Isolated Yield (%)
 **3**	 **15**	68	 **16**  1:1 **17**	**16**, 5 **17**, 33
 **5**	 **18**	52	Complex mixture of products	—
 **7**	 **19**	30	 **20**	19%

and ethanol, the source of the latter or its synthetic equivalent remains unclear.[1c]

3. Conclusion

Parallelling the behaviour of diketene **1**, the reaction of the unsaturated β-lactone **2** with monosubstituted diazo compounds leads to the formation of cyclopropanespiro-β-lactones in poor to modest yield. These reactions, unusually and in contrast to those of diketene and most alkenes, are diastereoselective. A computational model has been developed to account for the observed stereochemistry and may be of value in exploring the mechanisms of related cyclopropanations. Surprisingly the metal-catalysed rearrangement of the cyclopropanespiro-β-lactones derived from **2** produces pyranones, rather than the furanones formed from the cyclopropanespiro-β-lactones derived from diketene **1**. Overall these cyclopropanespiro-β-lactones continue to surprise in terms of their formation and their reactions; their chemistry warrants further study.

4. Experimental

4.1. General

^{1}H NMR and ^{13}C NMR spectra were measured in $CDCl_3$ using a Joel JNM-LA400 or ECX400 spectrometer. All GC analyses were carried out on a Varian 3900 chromatograph, using an Agilent HP-5 (95% dimethylpolysiloxane-5% diphenylpolysiloxane) column (30 m×0.32 mm×0.25 μm). IR spectra were measured on a Perkin–Elmer Spectrum 1 FT-IR equipped with a diamond ATR attachment. The photochemical reactions were carried out in cylindrical quartz tubes in a Rayonet reactor, RPR-100, fitted with sixteen 254 nm mercury lamps. Flash column chromatography was carried out using Merck silica gel 60, 234–400 mesh, with gradient elution using ether/petroleum ether (40–60 °C) or DCM. Melting points were determined using a Stuart Scientific SMP3 apparatus and are uncorrected. A Waters GCT spectrometer was used for GC–MS. Elemental analyses were carried out using a Perkin–Elmer 2400 analyser. All solvents were dried and distilled according to literature procedures.

4.2. Reaction of 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one 2 with diazo compounds

4.2.1. Reaction with ethyl diazoacetate. A solution of ethyl diazoacetate (2.70 g, 24.0 mmol) in DCM (20 mL) was added dropwise via a syringe pump over 12 h to a refluxing solution of copper(I) triflate benzene complex (0.10 g, 0.198 mmol) and 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one **2** (containing ~15% propionic anhydride) (13.27 g, 0.118 mol) in DCM (20 mL). The solution was refluxed until complete reaction of the diazo compound had occurred (IR, 1 h). Removal of solvent and excess lactone, and chromatography (SiO_2, ether (2–8%)/pet. ether), gave diethyl fumarate (0.16 g, 4%), (1*R**,2*R**,3*S**,6*R**)-2,6-dimethyl-5-oxo-4-oxaspiro[2,3]hexane-1-carboxylate **3** (1.36 g, 29%), a colourless liquid, 2-ethoxy-2-oxoethyl propionate **4**[8] (0.17 g, 4%) and diethyl maleate (0.08 g, 2%).

Compound **3**: IR: 1841, 1732 cm^{-1}. ^{1}H NMR (400 MHz): δ 4.15–4.09 (2H, m), 3.79 (1H, q, *J*=7.6 Hz), 1.95 (1H, d, *J*=6.0 Hz), 1.73–1.67 (1H, m), 1.37 (3H, d, *J*=7.6 Hz), 1.27 (3H, d, *J*=6.2 Hz), 1.25 (3H, t, *J*=7.1 Hz). ^{13}C NMR (100 MHz): δ 171.0, 170.8, 74.2, 61.2, 48.6, 28.7, 20.7, 14.3, 11.7, 11.4. (*m*/*z*) (CI, CH_4) 199 (100), 171 (80), 153 (86), 125 (6), 69 (3). HRMS (CI, CH_4) (*m*/*z*): $[M+H]^+$ calcd for $C_{10}H_{15}O_4$ 199.0970; found: 199.0966.

Compound **4**:[8] IR: 1744, 1167 cm^{-1}. ^{1}H NMR (400 MHz): δ 4.60 (2H, s), 4.21 (2H, q, *J*=7.1 Hz), 2.44 (2H, q, *J*=7.6 Hz), 1.28 (3H, t, *J*=7.1 Hz), 1.18 (3H, t, *J*=7.6 Hz). ^{13}C NMR (100 MHz): δ 173.9, 168.0, 61.4, 60.7, 27.2, 14.2, 11.4.

4.2.2. Reaction with diazoacetophenone. A solution of diazoacetophenone (1.73 g, 12.0 mmol) in ether (20 mL) was added dropwise over 3 h at 40 °C to a solution of copper(I) triflate benzene complex (0.05 g, 0.099 mmol) and 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one **2** (containing ~19% propionic anhydride) (6.64 g, 0.059 mol) in ether (20 mL). After the addition was completed, the mixture was stirred for a further hour to ensure complete reaction of the diazo compound (IR) and was then eluted through a short column of silica with ether. Following removal of solvent and excess lactone, chromatography (silica; ether (2–20%)/pet. ether) gave (1*R**,2*R**,3*R**,6*R**)-1-benzoyl-2,6-dimethyl-4-oxaspiro[2.3]hexan-5-one **5** (0.65 g, 24%), a yellow solid, 2-oxo-2-phenylethyl propionate **6**[19] (0.30 g, 13%) and propionic acid (0.25 g) (^{1}H NMR).

Compound **5**: mp 76–78 °C; IR: 1838, 1663 cm^{-1}. ^{1}H NMR (400 MHz): δ 8.09–7.42 (5H, m), 3.77 (1H, q, *J*=7.8 Hz), 3.05 (1H, d, *J*=6.0 Hz,), 2.09–2.02 (1H, m), 1.48 (3H, d, *J*=7.8 Hz), 1.40 (3H, d, *J*=6.4 Hz). ^{13}C NMR (100 MHz): δ 197.1, 170.8, 137.2, 133.0, 128.9, 128.3, 76.9, 48.4, 33.0, 23.5, 11.9, 11.5. Found: C, 72.82; H, 6.50; $C_{14}H_{14}O_3$ requires: C, 73.03; H, 6.13. A crystal suitable for X-ray diffraction was obtained by crystallisation from deuterochloroform/cyclohexane.[11]

Compound **6**:[19] IR: 1744, 1702 cm^{-1}. ^{1}H NMR (400 MHz): δ 7.93–7.46 (5H, m), 5.35 (2H, s), 2.53 (2H, q, *J*=7.4 Hz), 1.22 (3H, t, *J*=7.4 Hz). ^{13}C NMR (100 MHz): δ 192.3, 173.9, 134.2, 133.8, 128.8, 127.7, 65.8, 27.2, 9.0.

4.2.3. Reaction with 1-diazo-2-heptanone. 1-Diazo-2-heptanone (1.66 g, 0.012 mol) was dissolved in ether (30 mL) and was added via syringe pump over 9½ h to a refluxing solution of copper(I) triflate benzene complex (0.05 g, 0.099 mmol) and 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one **2** (which contained ~19% propionic anhydride) (6.64 g, 0.059 mol) in ether (20 mL). The solution was refluxed for a further hour to ensure complete reaction of the diazo compound (IR). Removal of solvent and excess lactone, and chromatography (SiO_2, ether (2–15%)/pet. ether), gave (1*R**,2*R**,3*R**,6*R**)-1-hexanoyl-2,6-dimethyl-4-oxaspiro[2.3]hexan-5-one (0.44 g, 17%) **7** and some analytically impure 2-oxoheptyl propionate **8** (0.40 g, 18%), both as pale yellow liquids.

Compound **7**: IR: 1840, 1693 cm^{-1}. ^{1}H NMR (400 MHz): δ 3.67 (1H, q, *J*=7.4 Hz), 2.59 (2H, t, *J*=7.6 Hz), 2.31 (1H, d, *J*=6.0 Hz), 1.83–1.76 (1H, m), 1.63–1.55 (2H, m), 1.41 (3H, d, *J*=7.4 Hz), 1.37–1.24 (4H, m), 1.30 (3H, d, *J*=6.4 Hz), 0.90 (3H, t, *J*=6.9 Hz). ^{13}C NMR (100 MHz): δ 207.8, 170.8, 76.5, 48.3, 44.8, 35.8, 31.3, 23.3, 23.0, 22.4, 13.8, 11.7, 11.3. (*m*/*z*) (CI, CH_4) 225 (100), 169 (42), 99 (50). HRMS (CI, CH_4) (*m*/*z*): $[M+H]^+$ calcd for $C_{13}H_{20}O_3$ 225.1491; found 225.1487.

Compound **8**: IR: 1747, 1731 cm^{-1}. ^{1}H NMR (400 MHz): δ 4.44 (2H, s), 2.46 (2H, q, *J*=7.3 Hz), 2.41 (2H, t, *J*=7.3 Hz), 1.64–1.59 (2H, m), 1.35–1.25 (4H, m), 1.19 (3H, t, *J*=7.3 Hz), 0.89 (3H, t, *J*=7.1 Hz). ^{13}C NMR (100 MHz): δ 204.3, 173.8, 67.8, 38.7, 31.3, 27.1, 23.0, 22.4, 13.8, 9.0.

4.2.4. Reaction with dimethyl diazomalonate. A solution of dimethyl diazomalonate (1.26 g, 8.07 mmol), 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one **2** (containing ~24% propionic anhydride) (6.72 g, 0.060 mol) and benzophenone (1.46 g, 8.01 mmol) in acetonitrile (60 mL) in a quartz tube was degassed for 15 min using N_2, and was irradiated at 254 nm until the diazo compound had completely reacted (IR, 3 h). Removal of solvent and excess lactone gave a yellow oil containing four products (1:1.4:1:1, GC), chromatography (silica, ether (2–24%)/pet. ether) of which gave two fractions. The first fraction was an inseparable mixture of dimethyl (2*R**,3*S**,6*R**)-2,6-dimethyl-5-oxo-4-oxaspiro[2.3]hexane-1,1-dicarboxylate **9** and dimethyl (2*R**,3*S**,6*S**)-2,6-dimethyl-5-oxo-4-oxaspiro[2.3]-hexane-1,1-dicarboxylate (1:1.5, 0.45 g, 23%) **10**. The second fraction was an inseparable mixture of dimethyl (2*R**,3*R**,6*S**)-2,6-dimethyl-5-oxo-4-oxaspiro[2.3]hexane-1,1-dicarboxylate **11** and dimethyl (2*R**,3*R**,6*R**)-2,6-dimethyl-5-

oxo-4-oxaspiro[2.3]hexane-1,1-di-carboxylate **12** (1.1:1, 0.24 g, 13%). Both fractions were obtained as pale yellow liquids.

Compounds **9**/**10**: IR: 1845, 1728 cm^{-1}. ^1H NMR (400 MHz) (from the mixture): **9**: δ 4.42 (1H, q, J=7.6 Hz), 3.74 (3H, s), 3.73 (3H, s), 2.75 (1H, q, J=6.9 Hz), 1.46 (3H, d, J=7.6 Hz), 1.19 (3H, d, J=6.9 Hz); **10**: δ 3.88 (1H, q, J=7.8 Hz), 3.74 (3H, s), 3.71 (3H, s), 2.54 (1H, q, J=6.9 Hz), 1.51 (3H, d, J=7.8 Hz), 1.21 (3H, d, J=6.9 Hz). ^{13}C NMR (100 MHz) (mixture of **9** and **10**): δ 169.9, 169.8, 166.4, 165.7, 165.6, 165.5, 74.3, 73.1, 53.4, 53.3, 52.8, 52.6, 49.2, 47.9, 39.44, 39.4, 26.4, 25.7, 12.9, 11.2, 8.3, 8.1. Found: C, 54.32; H, 6.10; $C_{11}H_{14}O_6$ requires: C, 54.54; H, 5.83.

Compounds **11**/**12**: IR: 1849, 1730 cm^{-1}. ^1H NMR (400 MHz) (from the mixture): **11**: δ 3.86 (1H, q, J=7.8 Hz), 3.78 (3H, s), 3.75 (3H, s), 2.23 (1H, q, J=6.6 Hz), 1.27 (3H, d, J=7.8 Hz), 1.22 (3H, d, J=6.6 Hz); **12**: δ 3.83 (1H, q, J=7.6 Hz), 3.78 (3H, s), 3.75 (3H, s), 2.00 (1H, q, J=6.6 Hz), 1.35 (3H, d, J=7.6 Hz), 1.26 (3H, d, J=6.6 Hz). ^{13}C NMR (100 MHz) (mixture of **11** and **12**): δ 169.7, 169.6, 168.6, 167.7, 164.2, 164.1, 74.0, 73.9, 53.1, 53.06, 52.8, 52.77, 49.8, 49.3, 37.6, 36.6, 26.0, 24.5, 11.2, 11.1, 8.8, 8.6. Found: C, 54.61; H, 6.05; $C_{11}H_{14}O_6$ requires: C, 54.54; H, 5.83.

4.2.5. Reaction with diazofluorene. (i) Using $Rh_2(OAc)_4$ as catalyst. A solution of diazofluorene (2.00 g, 0.010 mol) in ether (60 mL) was added dropwise (2 h) to a stirred solution of $Rh_2(OAc)_4$ (3.0 mg, 7.0 μmol) in 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one **2** (which contained ~21% propionic anhydride) (5.60 g, 0.050 mol). On complete reaction of the diazo compound (IR, 3 h), the reaction mixture was cooled in ice for 1 h and filtered. The red solid obtained was washed with pet. ether (50 mL) and was shown spectroscopically to be 9,9′-bifluorenylidene (0.62 g, 38%). The mother liquor and washings were combined and concentrated. The solid, which precipitated was filtered and washed with pet. ether (50 mL) to give difluoren-9-ylidene hydrazine as a bright red solid (0.42 g, 24%).

9,9′-Bifluorenylidene: mp 184–186 °C (lit. 186–188 °C).[20] IR: 1598 cm^{-1}. ^1H NMR (400 MHz): δ 8.38 (4H, d, J=7.6 Hz), 7.70 (4H, d, J=7.6 Hz), 7.32 (4H, dt, J=7.6, 0.7 Hz), 7.20 (4H, dt, J=7.6, 0.7 Hz). ^{13}C NMR (100 MHz): δ 141.4, 141.1, 138.3, 129.3, 127.0, 126.8, 120.0.

Difluoren-9-ylidene hydrazine: mp 267–268 °C (lit. 269 °C).[21] IR: 1624, 1600 cm^{-1}. ^1H NMR (400 MHz): δ 8.13 (2H, d, J=7.6 Hz), 8.05 (2H, d, J=7.4 Hz), 7.65 (2H, d, J=7.3 Hz), 7.64 (2H, d, J=7.6 Hz), 7.49–7.45 (2H, m), 7.43–7.37 (4H, m), 7.26–7.24 (2H, m). ^{13}C NMR (100 MHz): δ 154.9, 142.4, 141.4, 136.6, 131.5, 131.4, 131.1, 129.9, 128.3, 129.4, 123.0, 120.2, 120.1.

(ii) Using copper(I) triflate benzene complex as catalyst. Repeating the reaction between **2** (containing ~25% propionic anhydride) (6.64 g, 0.059 mol) and diazofluorene (4.30 g, 0.022 mol) using copper(I) triflate benzene complex (0.10 g, 0.198 mmol) as catalyst gave, after chromatography (silica; ether (2–3%)/pet.[22] ether), 9,9′-bifluorenylidene[20] (0.37 g, 10%) and fluorenone[21] (1.21 g, 31%).

Fluorenone: IR: 1713 cm^{-1}. ^1H NMR (400 MHz): δ 7.49 (2H, d, J=7.3 Hz), 7.30–7.26 (4H, m), 7.14 (2H, d, J=7.1 Hz). ^{13}C NMR (100 MHz): δ 194.0, 144.5, 134.8, 134.2, 129.2, 124.4, 120.4.

(iii) Photochemical reaction. A solution of diazofluorene (0.50 g, 2.60 mmol) in 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one **2** (containing ~21% propionic anhydride) (1.40 g, 0.013 mol), in a quartz tube, was degassed (15 min) using N_2 and was irradiated at 254 nm. When no diazo compound remained (5 h, IR), solvent and excess lactone were removed to give an orange liquid. Chromatography (silica, ether (2–3%)/pet. ether) gave 9,9′-bifluorenylidene (0.15 g, 35%) and, as a colourless liquid, some analytically impure 9*H*-fluoren-9-yl propionate (0.13 g, 21%).

9*H*-Fluoren-9-yl propionate: IR: 1730 cm^{-1}. ^1H NMR (400 MHz): δ 7.66 (2H, d, J=7.6 Hz), 7.54 (2H, d, J=7.6 Hz), 7.40 (2H, t, J=7.6 Hz), 7.32–7.28 (2H, m), 6.81 (1H, s), 2.45 (2H, q, J=7.6 Hz), 1.22 (3H, t, J=7.6 Hz). ^{13}C NMR (100 MHz): δ 175.6, 142.2, 141.1, 129.5, 127.9, 125.9, 120.1, 74.8, 27.9, 9.4.

4.2.6. Reaction with ethyl 2-diazopropionate. Ethyl 2-diazopropionate (1.37 g, 0.011 mol) (containing some residual *p*-tosyl azide) was dissolved in dichloromethane (20 mL) and was added by syringe pump over 13 h to a refluxing solution of $Rh_2(OAc)_4$ (4.1 mg, 10.0 μmol) and 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one **2** (containing ~20% propionic anhydride) (5.99 g, 0.053 mol) in ether (20 mL). The solution was refluxed for a further hour to ensure complete reaction of the ethyl 2-diazopropionate (IR). Following removal of solvent and excess lactone, chromatography (silica, ether (10%)/pet. ether) gave *p*-tosyl azide (0.3 g), ethyl 2-(propionyloxy) propanoate[23] **13** (0.09 g, 5%) and diethyl 2,2′-oxydipropanoate[24] **14** (0.18 g, 15%).

Ethyl 2-(propionyloxy)propanoate **13**:[23] IR: 1745 cm^{-1}. ^1H NMR (400 MHz): δ 5.05 (1H, q, J=7.1 Hz), 4.18 (2H, q, J=7.1 Hz), 2.41–2.36 (2H, m), 1.46 (3H, d, J=7.1 Hz), 1.26 (3H, t, J=7.1 Hz), 1.15 (3H, t, J=7.4 Hz). ^{13}C NMR (100 MHz): δ 171.5, 168.5, 66.0, 58.9, 24.8, 14.4, 11.6, 6.4.

Diethyl 2,2′-oxydipropanoate **14**:[24] IR: 1747, 1735 cm^{-1}. ^1H NMR (400 MHz): δ 4.14 (4H, q, J=7.3 Hz), 4.07 (2H, q, J=6.7 Hz), 1.38 (6H, d, J=6.7 Hz), 1.23 (6H, t, J=7.3 Hz). ^{13}C NMR (100 MHz): δ 172.6, 74.3, 61.0, 18.4, 14.2.

4.3. Rearrangement reactions of cyclopropanespiro-β-lactones derived from 4-[(*Z*)-ethylidene]-3-methyloxetan-2-one 2

4.3.1. (1R,2R*,3S*,6R*)-2,6-Dimethyl-5-oxo-4-oxaspiro[2,3]hexane-1-carboxylate* ***3****.* (i) $Cu(acac)_2$ catalysed. A solution of the spiro-β-lactone **3** (0.22 g, 1.11 mmol) and $Cu(acac)_2$ (0.025 g, 0.096 mmol) in toluene (5 mL) was refluxed until none of the spiro-β-lactone remained (45 h, GC). Removal of the solvent and chromatography (silica, ether (1–35%)/pet. ether) gave ethyl 2,4-dimethyl-6-oxo-5,6-dihydro-2*H*-pyran-3-carboxylate **15** (0.15 g, 68%) as a white solid.

Ethyl 2,4-dimethyl-6-oxo-5,6-dihydro-2*H*-pyran-3-carboxylate **15**: mp 72–73 °C. IR: 1754, 1734, 1648 cm^{-1}. ^1H NMR (400 MHz): δ 5.06 (1H, br q, J=6.9 Hz), 4.17 (2H, q, J=7.1 Hz), 3.46 (1H, d, J=16.0 Hz), 3.27 (1H, d, J=16.0 Hz), 1.84 (3H, br s), 1.39 (3H, d, J=6.9 Hz), 1.27 (3H, t, J=7.1 Hz). ^{13}C NMR (100 MHz): δ 173.8, 168.2, 155.6, 126.2, 78.9, 61.8, 32.5, 18.1, 16.5, 8.9. (*m*/*z*) (CI, CH_4) 199 (55), 127 (25), 114 (100), 57 (22). HRMS (CI, CH_4) (*m*/*z*): $[M+H]^+$ calcd for $C_{10}H_{14}O_4$ 199.0970; found 199.0968.

(ii) BF_3 catalysed. The spiro-β-lactone **3** (0.13 g, 0.630 mmol) was dissolved in DCM (12.5 mL) and freshly distilled BF_3 etherate (1.25 mL) was added. The solution was refluxed for 13½ h at which point all of the spiro-β-lactone had reacted (GC). The reaction mixture was washed with 10% $NaHCO_3$ (2×20 mL) and water (2×20 mL) and the organic layer was dried over magnesium sulfate. Filtration, removal of the solvent and chromatography (silica, ether (2–6%)/pet. ether) gave ethyl 3-methyl-4-oxohexanoate **16**[25] (0.006 g, 5%) and, as an inseparable mixture of diastereomers (1:1, ^1H NMR), diethyl 2,4-dimethyl-3-oxohexanedioate **17** (0.05 g, 33%). Both materials were obtained as colourless liquids.

Ethyl 3-methyl-4-oxohexanoate **16**:[25] IR: 1735, 1712 cm^{-1}. ^1H NMR (400 MHz): δ 4.09 (2H, q, J=7.1 Hz), 3.04–2.96 (1H, m), 2.77 (1H, dd, J=7.8, 16.7 Hz), 2.57–2.52 (2H, m), 2.28 (1H, dd, J=5.2, 16.7 Hz), 1.23 (3H, t, J=7.1 Hz), 1.11 (3H, d, J=7.3 Hz), 1.06 (3H, t, J=7.1 Hz). ^{13}C NMR (100 MHz): δ 213.6, 172.5, 60.6, 41.8, 37.2, 34.4, 16.9, 14.2, 7.8.

Diethyl 2,4-dimethyl-3-oxohexanedioate **17**: IR: 1735, 1716 cm^{-1}. ^1H NMR (400 MHz) (from mixture containing predominantly one diastereomer): δ 4.21–4.14 (2H, m), 4.12–4.05 (2H, m), 3.79 (1H, q, J=7.1 Hz), 3.24–3.16 (1H, m), 2.77 (1H, dd, J=9.2, 16.9 Hz), 2.33 (1H, dd, J=5.1, 16.9 Hz), 1.35 (3H, d, J=7.1 Hz), 1.25 (3H, t, J=7.1 Hz), 1.22 (3H, t, J=7.1 Hz), 1.14 (3H, d, J=7.1 Hz). ^1H NMR (400 MHz) (from mixture containing predominantly other diastereomer): δ 3.74 (1H, q, J=7.1 Hz), 3.30–3.22 (1H, m), 2.75 (1H, dd, J=7.6, 16.6 Hz), 2.32 (1H, dd, J=6.6, 16.6 Hz), 1.33 (3H, d, J=7.1 Hz), 1.26 (3H, t, J=7.1 Hz), 1.24–1.20 (3H, m), 1.16 (3H, d,

J=7.1 Hz). ^{13}C NMR (100 MHz) (mixture): δ 208.7, 207.8, 172.1, 171.9, 170.5, 170.2, 61.5, 61.3, 60.8, 60.4, 52.0, 51.2, 41.6, 41.4, 37.8, 37.0, 16.9, 16.8, 14.2, 14.2, 14.1, 14.1, 13.1, 12.9. Found: C, 59.31; H, 8.19; $C_{12}H_{20}O_5$ requires: C, 59.00; H, 8.25.

4.3.2. (1R,2R*,3R*,6R*)-1-Benzoyl-2,6-dimethyl-4-oxaspiro[2.3]hexan-5-one* ***5***. (i) $Cu(acac)_2$ catalysed. A solution of the spiro-β-lactone **5** (0.09 g, 0.391 mmol) and $Cu(acac)_2$ (0.02 g, 0.076 mmol) in toluene (5 mL) was refluxed (69 h) until none of the spiro-β-lactone remained (IR, 69 h). Removal of the solvent and chromatography (silica, DCM) gave 5-benzoyl-4,6-dimethyl-3,6-dihydro-2*H*-pyran-2-one **18** (0.052 g, 52%) as an off-white solid.

5-Benzoyl-4,6-dimethyl-3,6-dihydro-2*H*-pyran-2-one **18**: mp 61–63 °C. IR: 1751, 1690, 1599 cm^{-1}. ^{1}H NMR (400 MHz): δ 7.99 (2H, d, J=7.3 Hz), 7.65 (1H, t, J=7.3 Hz), 7.53 (2H, t, J=7.3 Hz), 5.14 (1H, 6-H, J=6.4 Hz), 4.24 (1H, d, J=17.4 Hz), 3.88 (1H, d, J=17.4 Hz), 1.86 (3H, br s), 1.39 (3H, d, J=6.4 Hz). ^{13}C NMR (100 MHz): δ 193.9, 173.8, 156.7, 135.8, 134.0, 128.9, 128.2, 126.2, 78.9, 36.2, 18.0, 8.9. Found: C, 72.89; H, 6.01; $C_{14}H_{14}O_3$ requires: C, 73.03; H, 6.13.

(ii) BF_3 catalysed. Freshly distilled BF_3 etherate (0.63 mL) was added to a solution of the spiro-β-lactone **5** (0.073 g, 0.317 mmol) in DCM (6 mL). The solution was refluxed for 10 h and the reaction mixture was monitored by TLC. Spectroscopic analysis (^{1}H NMR) of the material resulting from the usual workup indicated it was a complex mixture. Chromatography failed to provide any identifiable products.

4.3.3. (1R,2R*,3R*,6R*)-1-Hexanoyl-2,6-dimethyl-4-oxaspiro[2.3]hexan-5-one* ***7***. (i) $Cu(acac)_2$ catalysed. The spiro-β-lactone **7** (0.098 g, 0.437 mmol) and $Cu(acac)_2$ (0.020 g, 0.076 mmol) were dissolved in toluene (5 mL) and the solution was then refluxed until all the spiro-β-lactone had reacted (7½ h, GC). Removal of the solvent and chromatography (silica, DCM) gave 4-methylundecane-3,6-dione **19** (0.03 g, 30%) as a colourless liquid.

4-Methylundecane-3,6-dione **19**: IR: 1711 cm^{-1}. ^{1}H NMR (400 MHz): δ 3.08–3.00 (1H, m), 2.94 (1H, dd, J=8.2, 17.6 Hz), 2.56 (2H, q, J=7.1 Hz), 2.41–2.33 (3H, m), 1.56–1.49 (2H, m), 1.30–1.21 (4H, m), 1.06 (3H, d, J=6.6 Hz), 1.03 (3H, t, J=7.1 Hz), 0.87 (3H, t, J=7.1 Hz). ^{13}C NMR (100 MHz): δ 214.4, 210.0, 45.8, 42.9, 40.7, 34.5, 32.0, 23.5, 22.5, 17.0, 14.0, 7.8. (m/z) (CI, CH_4) 199 (55), 181 (6), 127 (4). HRMS (CI, CH_4) (m/z): $[M+H]^+$ calcd for $C_{12}H_{22}O_2$ 199.1698; found 199.1705.

(ii) BF_3 catalysed. The spiro-β-lactone **7** (0.075 g, 0.334 mmol) was dissolved in DCM (6 mL) and freshly distilled BF_3 etherate (0.63 mL) was added. The usual workup and chromatography (silica, DCM) gave ethyl 2,4-dimethyl-3,6-dioxoundecanoate **20** (0.017 g, 19%), a light yellow solid, as an inseparable mixture of diastereomers (1:0.94, ^{1}H NMR).

Ethyl 2,4-dimethyl-3,6-dioxoundecanoate **20**: mp 90–92 °C. IR: 1742, 1712 cm^{-1}. ^{1}H NMR (400 MHz) (from mixture containing predominantly one diastereomer): δ 4.22–4.15 (2H, m), 3.87 (1H, q, J=6.9 Hz), 3.27–3.20 (1H, m), 2.98 (1H, dd, J=8.3, 15.1 Hz), 2.44 (1H, dd, J=6.8, 15.1 Hz), 2.39–2.35 (2H, m), 1.59–1.52 (2H, m), 1.37 (3H, d, J=6.8 Hz), 1.26 (3H, t, J=6.9), 1.29–1.20 (4H, m), 1.12 (3H, d, J=6.9 Hz), 0.88 (3H, t, J=6.9 Hz). ^{1}H NMR (400 MHz) (from mixture containing predominantly the other diastereomer): δ 4.23–4.16 (2H, m), 3.77 (1H, q, J=6.8 Hz), 3.36–3.28 (1H, m), 2.93 (1H, dd, J=8.2, 15.6 Hz), 2.44 (1H, dd, J=6.8, 15.6 Hz), 2.38–2.33 (2H, m), 1.58–1.51 (2H, m), 1.34 (3H, d, J=6.8 Hz), 1.26 (3H, t, J=6.9), 1.30–1.21 (4H, m), 1.13 (3H, d, J=6.9 Hz), 0.88 (3H, t, J=6.9 Hz). Found: C, 66.29; H, 9.45; $C_{15}H_{26}O_4$ requires: C, 66.64; H, 9.69.

Acknowledgements

The Embark Fellowship awarded to LMAM by the Irish Research Council for Science, Engineering and Technology (IRCSET) is gratefully acknowledged.

References and notes

1. (a) Kato, T.; Katagiri, N.; Sato, R. *Chem. Pharm. Bull.* **1979**, *27*, 1176–1180; (b) Kato, T.; Katagiri, N.; Sato, R. *J. Chem. Soc., Perkin Trans. 1* **1979**, 525–528; (c) Murphy, P. V.; O'Sullivan, T. J.; Geraghty, N. W. A. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2109–2119.
2. Kato, T.; Katagiri, N.; Sato, R. *J. Org. Chem.* **1980**, *45*, 2587–2592.
3. Kato, T.; Chiba, T.; Sato, R.; Yashima, T. *J. Org. Chem.* **1980**, *45*, 2020–2022.
4. (a) Cunningham, P. D.; Geraghty, N. W. A.; Kennedy, B. D.; McArdle, P. J.; Murphy, P. V.; O'Sullivan, T. J. *J. Chem. Soc., Perkin Trans. 1* **1997**, *1*, 1–4; (b) Murphy, P. V.; O'Sullivan, T. J.; Kennedy, B. D.; Geraghty, N. W. A. *J. Chem. Soc., Perkin Trans. 1* **2000**, *13*, 2121–2126.
5. (a) Kato, T.; Katagiri, N.; Sato, R. *Chem. Pharm. Bull.* **1981**, *29*, 2361–2366; (b) Geraghty, N. W. A.; Murphy, P. V. *Tetrahedron Lett.* **1994**, *35*, 6737–6740.
6. Hintermann, L.; Togni, A. *Helv. Chim. Acta* **2000**, *83*, 2425–2435.
7. Calter, M. A.; Liao, W. J. *J. Am. Chem. Soc.* **2002**, *124*, 13127–13129.
8. Burton, T. M.; Fife, W. B. *J. Am. Chem. Soc.* **1954**, *74*, 3935–3936.
9. Hoberg, J. O.; Claffey, D. J. *Tetrahedron Lett.* **1996**, *37*, 2533–2536.
10. *Spartan '06*; Wavefunction: Inc.: Irvine, 2006.
11. Crystallographic data (excluding structure factors) for **5** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 760958. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).
12. This reaction was carried out photochemically as the metal catalysed reaction of diethyl diazomalonate with diketene **2** led to the formation of a complex mixture of products: Geraghty, N. W. A.; Murphy, P. V., unpublished results.
13. House, H. O.; Kramar, V. *J. Org. Chem.* **1963**, *28*, 3362–3379.
14. (a) Doyle, M. P. *Acc. Chem. Res.* **1986**, *19*, 991–1001; (b) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; John Wiley: New York, NY, 1998, pp 178–183.
15. Monte Carlo; MMFF. *Spartan '06*; Wavefunction: Inc.: Irvine, 2006.
16. (a) Doyle, M. P.; Dorow, R. L.; Buhro, W. E.; Griffin, J. H.; Tamblyn, W. H. *Organometallics* **1984**, *3*, 44–52; (b) O'Bannon, P. E.; Dailey, W. P. *Tetrahedron* **1990**, *46*, 7341–7358; (c) Davies, H. M. L.; Clark, T. J.; Church, L. A. *Tetrahedron Lett.* **1989**, *30*, 5057–5060.
17. Domelsmith, L. N.; Houk, K. N.; Dagenhardt, C. R.; Paquette, L. A. *J. Am. Chem. Soc.* **1978**, *100*, 100–105.
18. Mulzer, J.; Speck, T.; Buschmann, J.; Luger, P. *Tetrahedron Lett.* **1995**, *36*, 7643–7646.
19. Manzocchi, A.; Fiecchi, A.; Santaniello, E. *J. Org. Chem.* **1988**, *53*, 4405–4407.
20. Nishida, S.; Komiya, Z.; Mizuno, T.; Mikuni, A.; Fukui, T.; Tsuji, T.; Murakami, M.; Shimizu, N. *J. Org. Chem.* **1984**, *49*, 495–502.
21. Pinck, L. A.; Hilbert, G. E. *J. Am. Chem. Soc.* **1946**, *68*, 867–868.
22. Jackman, L. M.; Trewella, J. C. *J. Am. Chem. Soc.* **1976**, *98*, 5712–5714.
23. Seebach, D.; Hungerbuehler, E.; Naef, R.; Schnurrenberger, P.; Weidmann, B.; Zueger, M. *Synthesis* **1982**, 138–141.
24. Parsons, D. G. *J. Chem. Soc., Perkin Trans. 1* **1975**, 245–250.
25. Ahlbrecht, H.; Kompter, H.-M. *Synthesis* **1983**, 645–647.