Stereocontrolled synthesis of highly functionalised spirocyclic pyrans†

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Highly functionalised spirocyclic pyrans can be obtained through the Achmatowicz rearrangement of furyl carbinols by taking advantage of the different rates of reaction for epoxidation and nucleophilic addition. Through this methodology, spirocyclic units of various ring sizes can be selectively generated with complete stereocontrol.

Introduction

Spirocyclic pyrans and piperidines have been reported in a number of highly active natural products and both synthetic and semi-synthetic derivatives, such as polymaxenolide, pinnaic acid, and a number of spirocyclic saccharides and nucleosides.[1–4] As such, a number of synthetic approaches have been developed for the generation of spirocyclic pyrans and piperidines as building blocks for natural product libraries and combinatorial chemistry approaches.[5,6]

Unfortunately, most of the methods currently available for the synthesis of spirocyclic pyrans tend to be substrate specific and afford a limited number of functional handles from which synthetic diversification can take place.[2–6] We would now like to report our efforts into the synthesis of highly functionalised spirocyclic pyran units starting from α-hydroxy furan building blocks taking advantage of a selective Achmatowicz rearrangement, followed by a stereoselective allylation and ring-closing metathesis (RCM) sequence (Fig. 1).

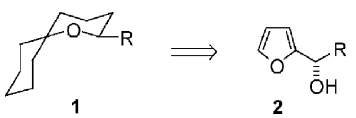


Fig. 1 Proposed approach to the synthesis of spirocyclic pyrans.

The Achmatowicz rearrangement has been used for the synthesis of poly-oxygenated units, particularly carbohydrate derivatives; however, its full potential is yet to be realised.[7,8] We have previously reported the use of the Achmatowicz rearrangement to generate biologically relevant polyfunctionalised lactol and pyran rings from simple α-hydroxy furan units (Fig. 2).[9]

Significantly during this process, the Achmatowicz rearrangement was selectively performed in the presence of highly substituted electron-rich olefins (Fig. 2).[9]

The observed selectivity of the rearrangement provided the possibility of generating a potentially labile lactol reactive intermediate **4** from a C_5-alkenyl substituted α-hydroxy furan **3**. The C_5-alkenyl chain would become the pseudo-equatorial lactol C_6 arm which could provide a handle for generation of the spirocyclic pyran **5** (Scheme 1).

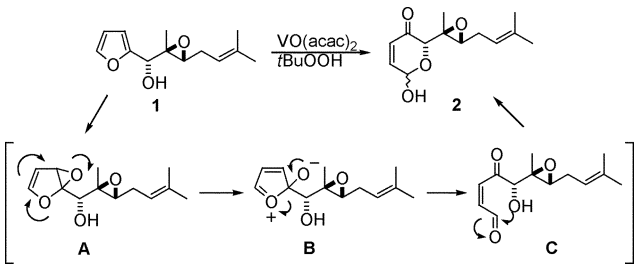
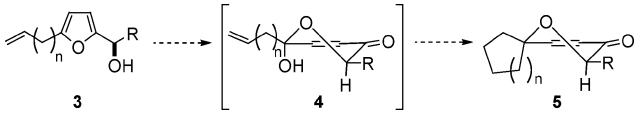


Fig. 2 Selective Achmatowicz rearrangement in the presence of substituted olefins.



Scheme 1 Use of alkenyl substituents for spirocycle generation.

Results and discussion

Our synthesis of the C_5-alkenyl precursor began with furan which was deprotonated and alkylated with 5-bromo-1-pentene to generate the desired alkenyl furan **6** in high yield. A second regioselective metallation of the furan ring followed by trapping of the 2-lithiofuran intermediate with isobutyraldehyde proceeded to afford the α-hydroxy furan unit **7**.

Oxidative rearrangement of furyl carbinol **7** using *m*CPBA generated successfully the crucial lactol intermediate as a mixture of α : β (8 : 1) anomers **8a** and **8b** in excellent yield. Satisfyingly, the hydroxy-directed nature of the oxidative rearrangement was completely selective as no side chain epoxidation was detected based on NMR analysis (Scheme 2).

At this point, we decided to take advantage of the previously reported allylation of lactols using allyltrimethylsilane to introduce the spirocyclisation coupling partner, which if successful would provide us with two handles which could then be used to generate the spirocyclic unit.[10]

Although we were confident that the stabilising nature of the trimethylsilyl group would promote the desired intermolecular allylation, there was concern that the addition would not be able

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† Dedicated to Professor Michael E. Jung.

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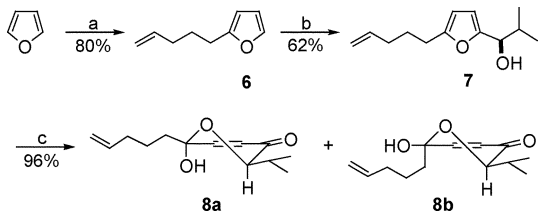
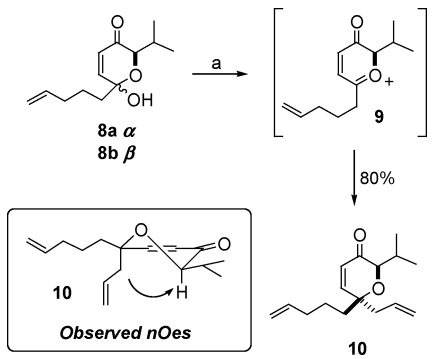


Scheme 2 *Reagents and conditions*: (a) *n*BuLi, 5-bromo-1-pentene, THF, 0 °C to rt; (b) *n*BuLi, TMEDA, Et_2O, 0 °C to rt; isobutyraldehyde, −78 to 0 °C; (c) *m*CPBA, CH_2Cl_2, 0 °C to rt.

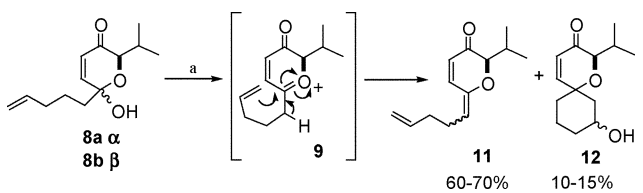
to compete with a potential intramolecular Prins-like cyclisation of the alkenyl side chain onto the oxonium intermediate.[11]

Gratifyingly, treatment of the α/β-mixture of lactol anomers **8a** and **8b** with allyltrimethylsilane in dichloromethane at 0 °C generated the desired 6,6-disubstituted pyran core **10** in excellent yield and as single diastereomer. NMR studies of the newly generated compound were consistent with that of pseudo-axial allylation of the oxonium intermediate **9**. Thus, we have effectively taken advantage of the furfuryl alcohol stereochemistry at the C_2 position to dictate the relative stereochemistry of the newly-formed C_6 quaternary stereocentre and, as a consequence, that of the spirocyclic ring as well. The observed allylation stereoselectivity is consistent with Woerpel's model for the nucleophilic substitution of pyran-derived oxocarbenium ions (Scheme 3).[12]



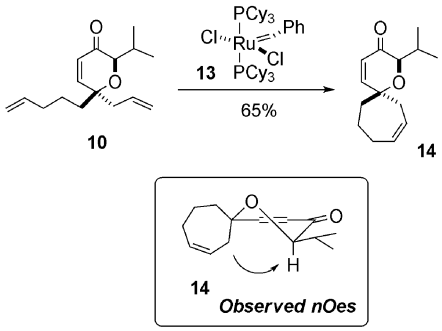
Scheme 3 *Reagents and conditions*: (a) allyltrimethylsilane, $BF_3{\cdot}OEt_2$, CH_2Cl_2, −78 to rt.

Interestingly, treatment of the lactol mixture **8a**/**8b** with boron trifluoride diethyl etherate on its own under identical reaction conditions produced significant amounts of the exocyclic triene **11**, together with minor amounts of the spirocyclic alcohols **12**. The generation of the triene unit **11** is consistent with a very slow nucleophilic addition, which allows deprotonation α to the oxonium intermediate to become the preferred reaction pathway (Scheme 4).[13]



Scheme 4 *Reagents and conditions*: (a) $BF_3{\cdot}OEt_2$, CH_2Cl_2, −20 °C to rt.

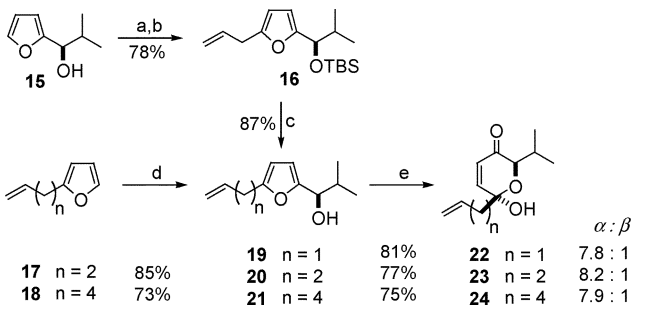
Once the two alkenyl-bearing substituents were firmly in place, we turned our attention to the spiro-annulation step. Thus, treatment of the bis-alkenyl pyran unit **10** with a first generation Grubbs catalyst **13** proceeded cleanly to afford a single diastereomer of the desired [5.6]spirododecadienone unit **14** in good yield (Scheme 5).[14] Two-dimensional NMR data of the final product corroborated once again the relative stereochemistry of the spirocyclic pyran in which the relative stereochemistry of the spirocyclic unit **14** has been dictated by that of the original furfuryl alcohol **7**.



Scheme 5 *Reagents and conditions*: **13** (5 mol%), CH_2Cl_2, reflux.

Having successfully achieved the stereoselectively controlled synthesis of the [5.6]spirododecadienone ring system, the flexibility of the methodology for the generation of other spirocyclic pyrans of various ring sizes was assessed. As such, the synthesis of the [4.5]decadiene, the [5.5]undecadiene, and the [5.7]tridecadiene systems were attempted.

The synthesis of the [4.5]decadiene cyclisation precursor began with 2-lithiofuran which was trapped with isobutyraldehyde to generate furfuryl alcohol **15**.[15] Protection of the resulting hydroxy group as the corresponding TBS ether followed by C_5 allylation then generated alkene **16**, which upon deprotection afforded the desired precursor **19** (Scheme 6).

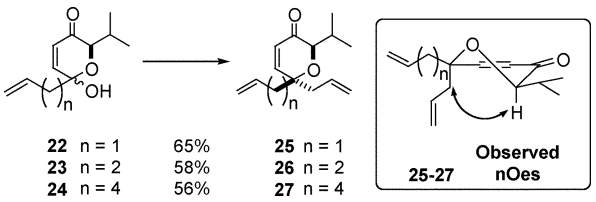


Scheme 6 *Reagents and conditions*: (a) TBSCl, Et_3N, CH_2Cl_2, rt; (b) *n*BuLi, TMEDA, Et_2O, 0 °C to rt; allylbromide, −78 to 0 °C; (c) TBAF, THF, 0 °C to rt; (d) *n*BuLi, TMEDA, Et_2O, 0 °C to rt; isobutyraldehyde, −78 to 0 °C; (e) *m*CPBA, CH_2Cl_2, 0 °C to rt.

For the synthesis of the [5.5]undecadiene and the [5.7]tridecadiene precursors, however, 2-lithiofuran was alkylated with 4-bromo-1-butene and 6-bromo-1-hexene respectively to generate the 2-alkenyl units **17** and **18**.[16] Regioselective metallation of the furan ring followed by trapping with isobutyraldehyde proceeded in good overall yield to generate the Achmatowicz precursors **20** and **21**. Hydroxy-directed rearrangement of all three furfuryl

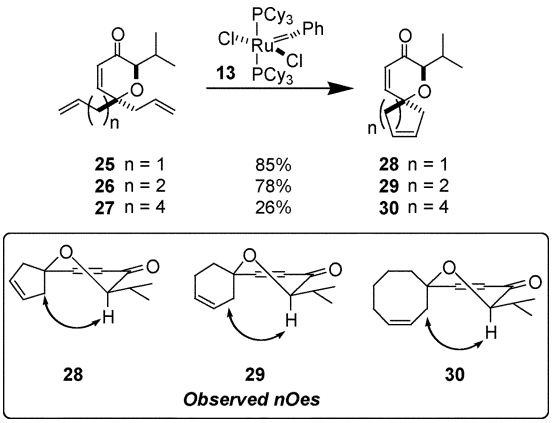
alcohols then generated the desired lactol units **22**–**24** as mixtures of C_6 anomers in a highly conserved ratio (*ca.* 8 : 1 α : β), with the α anomer being the major one in each case (Scheme 6).

Treatment of the newly generated 6-alkenyl lactols **22**–**24** under the same allylation conditions as before generated the bis-alkenyl cyclisation precursors **25**–**27** as single diastereomers cleanly and in acceptable yields. In each case, NMR analysis clearly showed that the allylation had proceeded stereoselectively to generate the 6,6-dialkenyl pyran with the allyl group at the pseudo-axial position (Scheme 7).



Scheme 7 *Reagents and conditions*: allyltrimethylsilane, $BF_3{\cdot}OEt_2$, CH_2Cl_2, −78 to rt.

Ring-closing metathesis of the spirocyclic precursors using a first generation Grubbs catalyst proceeded in acceptable yields to generate a single product in each case. As expected, the efficiency of cyclisation appears to be dependent on the ring size being formed. The yields steadily increased as the ring size of the spirocycle decreased; thus, while the [5.7]tridecadiene system **30** was formed in 26%, the [4.5]decadiene **28** system formed in 85% (Scheme 8).



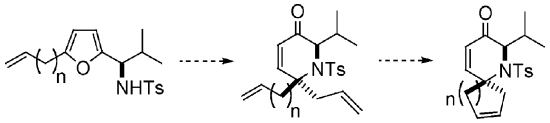
Scheme 8 *Reagents and conditions*: **13** (5 mol%), CH_2Cl_2, reflux.

In all cases, however, the NMR data obtained clearly corroborated our first set of results in which the stereochemistry of the furfuryl position C_2 position dictates the stereochemistry of the newly-formed spirocyclic unit.

Conclusions

In conclusion, we have demonstrated a rapid, flexible and highly efficient synthetic approach for the synthesis of highly functionalised spirocyclic pyrans. Our approach is based on the very efficient Achmatowicz rearrangement and takes advantage of the different rates of reaction for epoxidation and nucleophilic addition, and both expands and complements the synthetic methods currently available for the synthesis of spirocyclic units. Furthermore, the products obtained are highly yet differentially functionalised which should allow for their selective manipulation.

Efforts in our laboratories are currently on their way to optimise the spirocyclisation yields, and to explore intramolecular variations. We are also exploring the application of this methodology to the synthesis of both natural and unnatural spirocyclic piperidines starting from the corresponding furfuryl amines[17] (Scheme 9).



Scheme 9 Work currently underway for the synthesis of spirocyclic piperidines.

Experimental

General methods

All reactions were performed in oven-dried glassware under an inert argon atmosphere. Tetrahydrofuran (THF), diethyl ether, and dichloromethane (CH_2Cl_2) were distilled before use. Anhydrous dichloromethane was obtained by refluxing over calcium hydride for one hour, followed by distillation under argon. Anhydrous THF and diethyl ether were obtained by refluxing over sodium-benzophenone for one hour, followed by distillation under argon. All reagents were used as received, unless otherwise stated. Solvents were evaporated under reduced pressure at 30–40 °C using a Buchi Rotavapor.

IR spectra were recorded as thin films on NaCl plates using a Perkin-Elmer Spectrum BX Fourier Transform spectrometer. Only significant absorptions (ν_{max}) are reported in wavenumbers (cm^{-1}) with the following abbreviations used to describe absorption intensity: w, weak; m, medium; s, strong and br, broad.

Proton magnetic resonance spectra (^{1}H-NMR) were recorded at 500 MHz using a Bruker Avance500 instrument. Chemical shifts (δ_H) are reported in parts per million (ppm), and are referenced to the residual solvent peak. The order of citation in parentheses is (1) number of equivalent nuclei (by integration), (2) multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet, br = broad), (3) coupling constant (J) quoted in Hertz to the nearest 0.5 Hz, and (4) assignment. Carbon magnetic resonance spectra (^{13}C) were recorded at 75.1 or 125.7 MHz using Bruker DPX300, or Bruker Avance500 instruments. Chemical shifts (δ_C) are quoted in parts per million (ppm) and are referenced to the appropriate solvent peak. The assignment is quoted in parentheses.

High resolution mass spectra were recorded on a Bruker MicroTOF spectrometer by electrospray ionisation mass spectrometry operating at a resolution of 15 000 full widths at half height.

Flash chromatography was performed using silica gel (Apollo Scientific Silica Gel 60, 40–63 micron) as the stationary phase. TLC was performed on aluminium sheets pre-coated with silica (Merck Silica Gel 60 F_{254}). The plates were visualised by the quenching of UV fluorescence (λ_{max}254 nm) and/or by staining with either anisaldehyde, molybdic acid, or potassium permanganate followed by heating.

Representative procedures

(A) Synthesis of alkenyl furans 6, 17, 18. A solution of furan (1 equiv.) in anhydrous THF at 0 °C was treated with *n*BuLi (1 equiv.), and the resulting mixture allowed to warm up to room temperature. The solution was stirred for 24 h, at which point the alkenyl bromide (1.05 equiv.) was added slowly. The resulting reaction mixture was then stirred at room temperature for a further 24 h.

The reaction was then poured onto ice and the resulting mixture diluted with diethyl ether. The resulting brown liquid was then stirred for 20 min after which it was extracted with diethyl ether. The combined organic extracts were washed with water (2×), brine (1×) and then dried over sodium sulfate. Following concentration under vacuum, the residue was purified by short path distillation.

(B) Synthesis of furfuryl alcohols 7, 19, 20 and 21. To a solution of alkenyl furan (1 equiv.) and TMEDA (1 equiv.) in anhydrous diethyl ether at 0 °C was added slowly *n*BuLi (1 equiv.). The resulting solution was allowed to warm to room temperature over a period of 3 h; at this point it was cooled to −78 °C and treated with isobutyraldehyde (1.1 equiv.). The reaction was then stirred for 30 min at −78 °C, after which it was allowed to warm up to 0 °C and stirred for 2 h.

Upon completion as determined by TLC analysis, the reaction was quenched by slow addition of saturated aqueous ammonium chloride before being extracted with cold diethyl ether. The combined organic phases were washed with water (2×), brine (1×), dried over sodium sulfate and concentrated under vacuum. The crude residue obtained was then purified by flash column chromatography (silica gel, 5% Et_2O in 40–60 petroleum spirit).

2-Methyl-1-(5-pent-4-enylfuran-2-yl)-propan-1-ol, ***7***. ν_{max}(film)/cm^{-1}: 3438 (bs), 2960 (s), 2932 (s), 2871 (s), 1640 (s), 1384 (s), 907 (s). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.06 (1H, d, J = 3.0 Hz, ArH), 5.87 (1H, d, J = 3.0 Hz, ArH), 5.77 (1H, m, CH_2CHCH_2), 4.99 (1H, dq, J = 17.1, 1.6 Hz, CH_2CHCH_2), 4.94 (1H, dm, J = 10.2 Hz, CH_2CHCH_2), 4.24 (1H, d, J = 7.2 Hz, ArC*H*(OH)iPr), 2.57 (2H, t, J = 7.5 Hz, CH_2Ar), 2.15 (1H, bs, OH), 2.09–2.00 (3H, m, CH_2CHCH_2 and $CH(CH_3)_2$), 1.69 (2H, q, J = 7.5 Hz, $CH_2CH_2CH_2$), 0.98 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$), 0.81 (3H, d, J = 6.7 Hz, $CH(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.3 (Ar*C*), 154.3 (Ar*C*), 138.2 (CH_2CH), 114.9 (CH_2CH), 107.0 (Ar*C*H), 105.2 (Ar*C*H), 73.5 (Ar*C*H(OH)iPr), 33.2 (CH_2Ar), 33.1 (CH_2CHCH_2), 27.3 ($CH_2CH_2CH_2$), 27.2 ($CH(CH_3)_2$), 18.8 ($CH(CH_3)_2$), 18.4 ($CH(CH_3)_2$). *m/z* (EI) 191.12 (M^+ − OH, 100%). HRMS calcd for $C_{13}H_{20}NaO_2$ (M^+ + Na): 231.1360. Found 231.1312.

1-(5-Allylfuran-2-yl)-2-methylpropan-1-ol, ***19***. ν_{max}(film)/cm^{-1}: 3540 (bs), 2970 (s), 2932 (s), 1470 (s). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.02 (1H, d, J = 3.0 Hz, ArH), 5.84 (2H, m, ArH and CH_2CHCH_2), 5.04 (1H, m, CH_2CHCH_2), 5.01 (1H, m, CH_2CHCH_2), 4.20 (1H, d, J = 7.2 Hz, ArC*H*(OH)iPr), 3.27 (2H, dm, J = 6.5 Hz, ArCH_2CHCH_2), 1.98 (1H, app. sept, J = 7.0 Hz, $CH(CH_3)_2$), 0.93 (3H, d, J = 6.7 Hz, $CH(CH_3)_2$), 0.76 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$). *m/z* (EI) 163.10 (M^+ – OH, 85%). HRMS calcd for $C_{11}H_{17}O_2$ (M^+ + H): 181.1229. Found 181.0281.

1-(5-But-3-enylfuran-2-yl)-2-methylpropan-1-ol, ***20***. ν_{max}(film)/cm^{-1}: 3601 (s), 2960 (s), 2926 (s), 1468 (s), 1014 (s). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.02 (1H, d, J = 3.0 Hz, ArH), 5.85 (1H, dm, J = 2.2 Hz, ArH), 5.79 (1H, m, CH_2CHCH_2), 4.97 (1H, dq, J = 15.4, 1.7 Hz, CH_2CHCH_2), 4.91 (1H, dm, J = 10.2 Hz, CH_2CHCH_2), 4.21 (1H, dd, J = 7.0, 3.3 Hz, ArC*H*(OH)iPr), 2.62 (2H, appt, J = 7.6 Hz, ArCH_2CH_2), 2.34–2.28 (2H, m, CH_2CHCH_2), 2.01 (1H, app. sext, J = 6.9 Hz, $CH(CH_3)_2$), 1.83 (1H, d, J = 2.8 Hz, OH), 0.94 (3H, d, J = 6.7 Hz, $CH(CH_3)_2$), 0.77 (3H, d, J = 6.7 Hz, $CH(CH_3)_2$). *m/z* (EI) 177.11 (M^+ − OH, 50%).

1-(5-Hex-5-enylfuran-2-yl)-2-methylpropan-1-ol, ***21***. ν_{max}(film)/cm^{-1}: 3437 (bs), 2959 (s), 2931 (s), 1462 (s), 1011 (s), 910 (s). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.06 (1H, d, J = 3.1 Hz, ArH), 5.87 (1H, d, J = 3.0 Hz, ArH), 5.77 (1H, m, CH_2CHCH_2), 4.97 (1H, dq, J = 17.1, 1.9 Hz, CH_2CHCH_2), 4.92 (1H, dq, J = 10.1, 0.9 Hz, CH_2CHCH_2), 4.25 (1H, dm, J = 6.8 Hz, ArC*H*(OH)iPr), 2.57 (2H, app. t, J = 7.5 Hz, ArCH_2CH_2), 2.09–1.96 (4H, m, CH_2CHCH_2, $CH(CH_3)_2$, OH), 1.61 (2H, app. q, J = 7.6 Hz, CH_2CH_2), 1.41 (2H, app. qn, J = 7.8 Hz, CH_2CH_2), 0.99 (3H, d, J = 6.7 Hz, $CH(CH_3)_2$), 0.82 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.9 (Ar*C*), 154.5 (Ar*C*), 138.9 (CH_2CH), 114.7 (CH_2CH), 107.3 (Ar*C*H), 105.4 (Ar*C*H), 77.8 (Ar*C*H(OH)iPr), 33.7 (CH_2Ar), 33.5 (CH_2CHCH_2), 28.6 ($CH(CH_3)_2$), 28.1 (CH_2CH_2), 27.7 (CH_2CH_2), 19.1 ($CH(CH_3)_2$), 18.7 ($CH(CH_3)_2$). *m/z* (EI) 205.12 (M^+ − OH, 95%). HRMS calcd for $C_{14}H_{22}NaO_2$ (M^+ + Na): 245.1517. Found 245.1489.

(C) Procedure for the synthesis of lactols 8a/8b, 22, 23 and 24. A 0 °C solution of furfuryl alcohol (1 equiv.) in dichloromethane was treated with *meta*-chloroperoxybenzoic acid (*m*CPBA) (1.1 equiv.) and the resulting opaque solution was stirred at 0 °C for 1 h. The mixture was allowed to warm to room temperature and the reaction stirred for a further 2 h. Once the reaction was complete, as determined by TLC analysis, the reaction was cooled to 0 °C and quenched by slow addition of saturated aqueous sodium bicarbonate. The resulting emulsion was allowed to separate and was then extracted with dichloromethane. The combined organic extracts were washed with water (1×), brine (1×) and dried over sodium sulfate. The solution was concentrated *in vacuuo*, and the residue obtained purified by flash column chromatography (silica gel, 10% diethyl ether in 40–60 petroleum spirits).

*6-Hydroxy-2-isopropyl-6-pent-4-enyl-6*H*-pyran-3-one,* ***8***. ν_{max}(film)/cm^{-1}: 3400 (bs), 2966 (s), 2930 (s), 1676 (s), 1382 (s), 908 (s). *m/z* (EI) 207.12 (M^+ − OH, 100%). HRMS calcd for $C_{13}H_{20}NaO_3$ (M^+ + Na): 247.1310. Found 247.1305.

Major anomer (α) **8a**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.76 (1H, d, J = 10.2 Hz, $CHCHCO$), 6.02 (1H, d, J = 10.2 Hz, $CHCHCO$), 5.75 (1H, m, CH_2CHCH_2), 5.03–4.93 (2H, m, CH_2CHCH_2), 4.32 (1H, d, J = 2.7 Hz, $COCH(O)CH$), 2.89 (1H, bs, OH), 2.42 (1H, m, CH_2CHCH_2), 2.05 (2H, m, CH_2CHCH_2 and $CH(CH_3)_2$), 1.84–1.79 (2H, m, $CH_2C(O)OH$), 1.56 (1H, m, $CH_2CH_2CH_2$), 1.47 (1H, m, $CH_2CH_2CH_2$), 1.00 (3H, d, J = 6.9 Hz, $CH(CH_3)_2$), 0.82 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.0 ($CHCHCO$), 147.5 ($CHCHCO$), 138.1 ($CHCHCH_2$), 127.9 ($CHCHCO$), 119.5 (CH_2CHCH_2), 93.9 ($C(O)OH$), 78.2 ($COCH(O)CH$), 41.1 (CH_2CHCH_2), 33.0 ($CH_2C(O)OH$), 28.7 ($CH(CH_3)_2$), 22.8 ($CH_2CH_2CH_2$), 19.0 ($CH(CH_3)_2$), 16.9 ($CH(CH_3)_2$).

Minor anomer (β) **8b**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.86 (1H, d, J = 9.9 Hz, $CHCHCO$), 5.91 (1H, dd, J = 9.9, 0.4 Hz, $CHCHCO$), 5.77 (1H, m, CH_2CHCH_2), 5.05–4.93 (2H,

m, CH_2CHCH_2), 4.19 (1H, d, J = 4.8 Hz, $COCH(O)CH$), 2.35 (2H, app. q, J = 7.4 Hz, CH_2CHCH_2), 2.24–2.13 (3H, m, $CH(CH_3)_2$ and $CH_2C(O)OH$), 1.75 (1H, m, $CH_2CH_2CH_2$), 1.25 (1H, m, $CH_2CH_2CH_2$), 0.99 (3H, d, J = 7.0 Hz, $CH(CH_3)_2$), 0.91 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.2 ($CHCHCO$), 147.1 ($CHCHCO$), 141.9 (CH_2CHCH_2), 137.8 ($CHCHCO$), 121.9 (CH_2CHCH_2), 85.6 ($C(O)OH$), 78.2 ($COCH(O)CH$), 33.5 (CH_2CHCH_2), 32.8 ($CH_2C(O)OH$), 31.8 ($CH(CH_3)_2$), 24.8 ($CH_2CH_2CH_2$), 18.9 ($CH(CH_3)_2$), 16.1 ($CH(CH_3)_2$).

*6-Allyl-6-hydroxy-2-isopropyl-6*H*-pyran-3-one,* ***22***. ν_{max}(film)/cm^{-1}: 3403 (bs), 2965 (s), 2932 (s), 1691 (s), 1466 (s), 909 (s). m/z (EI) 179.09 (M^+ − OH, 100%). HRMS calcd for $C_{11}H_{16}NaO_3$ (M^+ + Na): 219.0997. Found 219.0992.

Major Anomer (α). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.69 (1H, d, J = 10.2 Hz, $CHCHCO$), 5.95 (1H, d, J = 10.1 Hz, $CHCHCO$), 5.81 (1H, m, CH_2CHCH_2), 5.18–5.12 (2H, m, CH_2CHCH_2), 4.26 (1H, d, J = 2.8 Hz, $COCH(O)CH$), 3.10 (1H, bs, OH), 2.58 (1H, dd, J = 13.6, 6.3 Hz, CH_2CHCH_2), 2.43 (1H, dd, J = 13.6, 8.3 Hz, CH_2CHCH_2), 2.35 (1H, qd, J = 6.9, 2.7 Hz, $CH(CH_3)_2$), 0.93 (3H, d, J = 7.4 Hz, $CH(CH_3)_2$), 0.76 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.1 ($CHCHCO$), 147.4 ($CHCHCO$), 131.2 (CH_2CHCH_2), 127.8 ($CHCHCO$), 120.7 (CH_2CHCH_2), 92.8 ($C(O)OH$), 78.2 ($COCH(O)CH$), 45.8 (CH_2CHCH_2), 28.7 ($CH(CH_3)_2$), 19.0 ($CH(CH_3)_2$), 16.0 ($CH(CH_3)_2$).

Minor anomer (β). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.75 (1H, d, J = 9.8 Hz, $CHCHCO$), 5.97 (1H, d, J = 9.8 Hz, $CHCHCO$), 5.81 (1H, m, CH_2CHCH_2), 5.18–5.12 (2H, m, CH_2CHCH_2), 3.89 (1H, d, J = 4.4 Hz, $COCH(O)CH$), 3.32 (1H, bs, OH), 2.61 (1H, m, CH_2CHCH_2), 2.42 (1H, m, CH_2CHCH_2), 2.34 (1H, m, $CH(CH_3)_2$), 0.92 (3H, d, J = 8.2 Hz, $CH(CH_3)_2$), 0.84 (3H, d, J = 6.0 Hz, $CH(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 186.4 ($CHCHCO$), 149.9 ($CHCHCO$), 130.8 (CH_2CHCH_2), 127.5 ($CHCHCO$), 120.6 (CH_2CHCH_2), 94.6 ($C(O)OH$), 82.1 ($COCH(O)C$), 41.7 (CH_2CHCH_2), 29.0 ($CH(CH_3)_2$), 18.9 ($CH(CH_3)_2$), 16.8 ($CH(CH_3)_2$).

*6-But-3-enyl-6-hydroxy-2-isopropyl-6*H*-pyran-3-one,* ***23***. ν_{max}(film)/cm^{-1}: 3432 (bs), 2967 (s), 2932 (s), 1686 (s), 1041 (s), 910 (s). m/z (EI) 193.10 (M^+ − OH, 85%). HRMS calcd for $C_{12}H_{18}NaO_3$ (M^+ + Na): 233.1153. Found 233.1148.

Major anomer (α). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.80 (1H, d, J = 10.2 Hz, $CHCHCO$), 6.05 (1H, d, J = 10.2 Hz, $CHCHCO$), 5.90 (1H, m, CH_2CHCH_2), 5.11 (1H, dm, J = 17.2 Hz, CH_2CHCH_2), 5.04 (1H, dm, J = 10.2 Hz, CH_2CHCH_2), 4.37 (1H, d, J = 2.7 Hz, $COCH(O)CH$), 3.05 (1H, bs, OH), 2.47 (1H, m, $CH(CH_3)_2$), 2.34 (1H, m, CH_2CHCH_2), 2.19 (1H, m, CH_2CHCH_2), 1.97 (2H, m, CH_2CH_2), 1.06 (3H, d, J = 7.0 Hz, $CH(CH_3)_2$), 0.87 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.2 ($CHCHCO$), 147.2 ($CHCHCO$), 135.4 (CH_2CHCH_2), 122.3 ($CHCHCO$), 116.9 (CH_2CHCH_2), 115.6 ($C(O)OH$), 85.4 ($COCH(O)CH$), 31.8 (CH_2CHCH_2), 30.9 ($CH(CH_3)_2$), 29.7 (CH_2CH_2), 18.9 ($CH(CH_3)_2$), 16.9 ($CH(CH_3)_2$).

Minor anomer (β). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.87 (1H, d, J = 10.3 Hz, $CHCHCO$), 6.07 (1H, d, J = 10.2 Hz, $CHCHCO$), 5.89 (1H, m, CH_2CHCH_2), 5.09 (1H, dm, J = 16.9 Hz, CH_2CHCH_2), 5.02 (1H, dm, J = 10.1 Hz, CH_2CHCH_2), 3.95 (1H, d, J = 4.1 Hz, $COCH(O)CH$), 2.44 (1H, m, $CH(CH_3)_2$), 2.37 (1H, m, CH_2CHCH_2), 2.23 (1H, m, CH_2CHCH_2), 1.94 (2H, m, CH_2CH_2), 1.05 (3H, d, J = 6.9 Hz, $CH(CH_3)_2$), 0.95 (3H, d, J = 6.7 Hz, $CH(CH_3)_2$).

*6-Hex-5-enyl-6-hydroxy-2-isopropyl-6*H*-pyran-3-one,* ***24***. ν_{max}(film)/cm^{-1}: 3429 (bs), 2966 (s), 2931 (s), 1671 (s), 1382 (s), 908 (s). m/z (EI) 221.14 (M^+ − OH, 100%). HRMS calcd for $C_{14}H_{22}NaO_3$ (M^+ + Na): 261.1466. Found 261.1461.

Major anomer (α). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.76 (1H, d, J = 10.2 Hz, $CHCHCO$), 6.03 (1H, d, J = 10.2 Hz, $CHCHCO$), 5.77 (1H, m, CH_2CHCH_2), 4.98 (1H, dq, J = 17.1, 1.9 Hz, CH_2CHCH_2), 4.93 (1H, dm, J = 10.2 Hz, CH_2CHCH_2), 4.32 (1H, d, J = 2.7 Hz, $COCH(O)CH$), 2.42 (1H, m, $CH(CH_3)_2$), 2.05 (2H, m, CH_2CHCH_2), 1.82–1.81 (2H, m, $CH_2C(O)OH$), 1.54–1.35 (4H, m, CH_2CH_2), 1.00 (3H, d, J = 7.0 Hz, $CH(CH_3)_2$), 0.83 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$).

Minor anomer (β). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.82 (1H, d, J = 10.3 Hz, $CHCHCO$), 6.00 (1H, d, J = 10.3 Hz, $CHCHCO$), 5.77 (1H, m, CH_2CHCH_2), 5.00–4.91 (2H, m, CH_2CHCH_2), 3.90 (1H, d, J = 4.1 Hz, $COCH(O)CH$), 2.42 (1H, m, $CH(CH_3)_2$), 2.05 (2H, m, CH_2CHCH_2), 1.85–1.76 (2H, m, $CH_2C(O)OH$), 1.54–1.37 (4H, m, CH_2CH_2), 1.00 (3H, d, J = 6.9 Hz, $CH(CH_3)_2$), 0.90 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$).

(D) General procedure for the synthesis of bis-alkenyl units 10, 25, 26 and 27. A solution of the freshly obtained lactol (1 equiv.) in anhydrous dichloromethane was treated with allyltrimethylsilane (2.1 equiv.) and the resulting mixture was cooled to −78 °C. The reaction mixture was then treated through the slow addition of $BF_3{\cdot}OEt_2$ (3 equiv.) and the resulting solution stirred for 30 min at −78 °C. The reaction was then allowed to warm to room temperature and stirred for a further 2 h. Once the reaction was complete, as determined by TLC analysis, the reaction was quenched with saturated aqueous ammonium chloride and extracted with dichloromethane. The combined organic extracts were washed sequentially with sat. $NaHCO_3$ (1×), water (2×) and brine (1×). The combined organic extracts were dried over sodium sulfate and the solvent removed under vacuum. The crude residue was then purified by flash column chromatography (silica gel, 7% diethyl ether in 40–60 petroleum spirits) to afford the desired bis-alkenyl products.

*6-Allyl-6-hex-5-enyl-2-isopropyl-6*H*-pyran-3-one,* ***10***. ν_{max}(film)/cm^{-1}: 2924 (s), 1709 (s), 1381 (s), 911 (s). m/z (EI) 249.17 (M + H, 100%). HRMS calcd for $C_{16}H_{25}O_2$ (M^+ + H): 249.1855. Found 249.1849. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.75 (1H, d, J = 10.4 Hz, $CHCHCO$), 5.96 (1H, d, J = 10.4 Hz, $CHCHCO$), 5.78–5.65 (2H, m, CH_2CHCH_2), 5.07–4.85 (4H, m, CH_2CHCH_2), 4.02 (1H, d, J = 2.6 Hz, $COCH(O)CH$), 2.52–2.50 (1H, ddt, J = 8.0, 6.5, 1.0 Hz, $C(O)CH_2CHCH_2$), 2.34–2.40 (1H, m, $CH(CH_3)_2$), 2.32–2.30 (1H, m, $C(O)CH_2CHCH_2$), 2.00–2.01 (2H, m, CH_2CHCH_2), 1.70–1.64 (1H, m, CH_2CH_2), 1.53–1.44 (2H, m, CH_2CH_2), 1.30–1.22 (1H, m, CH_2CH_2), 0.95 (3H, d, J = 7.0 Hz, $CH(CH_3)_2$), 0.79 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.7 ($CHCHCO$), 154.6 ($CHCHCO$), 138.4 (CH_2CHCH_2), 132.6 (CH_2CHCH_2), 126.6 ($CHCHCO$), 118.6 (CH_2CHCH_2), 114.7 (CH_2CHCH_2), 78.5 ($COCH(O)CH$), 75.7 ($CHC(O)CH_2$), 39.7 (CH_2CHCH_2), 38.0 (CH_2CHCH_2), 33.8 ($CH_2C(O)$), 29.1 ($CH(CH_3)_2$), 22.7 ($CH_2CH_2CH_2$), 19.2 ($CH(CH_3)_2$), 16.9 ($CH(CH_3)_2$).

*6,6-Diallyl-2-isopropyl-6*H*-pyran-3-one,* ***25***. ν_{max}(film)/cm^{-1}: 2964 (s), 2930 (s), 1690 (s), 1366 (s), 1060 (s). m/z (EI) 221.15

(M + H, 95%). HRMS calcd for $C_{14}H_{21}O_2$ (M^+ + H): 221.1542. Found 221.1536. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.77 (1H, d, J = 10.4 Hz, C*H*CHCO), 5.95 (1H, d, J = 10.4 Hz, CHC*H*CO), 5.75 (2H, m, CH_2CHCH_2), 5.11–5.00 (4H, m, CH_2CHCH_2), 4.04 (1H, d, J = 2.6 Hz, COC*H*(O)CH), 2.51 (1H, ddt, J = 14.3, 6.3, 1.3 Hz, CH_2CHCH_2), 2.39 (2H, m, $CH(CH_3)_2$ and CH_2CHCH_2), 2.31–2.23 (2H, m, CH_2CHCH_2), 0.96 (3H, d, J = 7.0 Hz, $CH(CH_3)_2$), 0.80 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.6 (CHCH*C*O), 153.0 (*C*HCHCO), 131.9 (CH_2CHCH_2), 131.3 (CH_2CHCH_2), 125.3 (CH*C*HCO), 117.9 (CH_2CHCH_2), 117.3 (CH_2CHCH_2), 75.7 (CO*C*H(O)CH), 74.4 (CH*C*(O)CH_2), 42.0 (CH_2CHCH_2), 37.9 (CH_2CHCH_2), 28.1 (*C*H(CH_3)$_2$), 18.1 (CH(*C*H_3)$_2$), 14.9 (CH(*C*H_3)$_2$).

*6-Allyl-6-but-3-enyl-2-isopropyl-6*H*-pyran-3-one,* ***26***. ν_{max}(film)/cm^{-1}: 2964 (s), 2930 (s), 1686 (s), 1061 (s), 910 (s). *m/z* (EI) 325.16 (M + H, 90%). HRMS calcd for $C_{15}H_{23}O_2$ (M^+ + H): 235.1698. Found 235.1693. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.76 (1H, d, J = 10.4 Hz, C*H*CHCO), 5.98 (1H, d, J = 10.4 Hz, CHC*H*CO), 5.80–5.68 (2H, m, CH_2CHCH_2), 5.09–5.02 (2H, m, CH_2CHCH_2), 4.94 (1H, dq, J = 17.1, 1.7 Hz, CH_2CHCH_2), 4.88 (1H, dq, J = 10.2, 1.6 Hz, CH_2CHCH_2), 4.03 (1H, d, J = 2.5 Hz, COC*H*(O)CH), 2.51 (1H, ddm, J = 14.2, 6.4 Hz, CH_2CHCH_2), 2.39 (1H, qd, J = 6.9, 2.5 Hz, $CH(CH_3)_2$), 2.29 (1H, m, CH_2CHCH_2), 2.19 (1H, m, CH_2CHCH_2), 1.93 (1H, m, CH_2CHCH_2), 1.80 (1H, ddd, J = 13.6, 11.9, 4.7 Hz, CH_2CH_2), 1.54 (1H, ddd, J = 13.6, 11.6, 4.7 Hz, CH_2CH_2), 0.96 (3H, d, J = 7.0 Hz, $CH(CH_3)_2$), 0.80 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.7 (CHCH*C*O), 154.3 (*C*HCHCO), 138.4 (CH_2CHCH_2), 132.5 (CH_2CHCH_2), 126.7 (CH*C*HCO), 118.8 (CH_2CHCH_2), 114.6 (CH_2CHCH_2), 78.6 (CO*C*H(O)CH), 75.5 (CH*C*(O)CH_2), 39.8 (CH_2CHCH_2), 37.8 (CH_2CHCH_2), 29.1 (*C*H(CH_3)$_2$), 27.9 (CH_2CH_2), 19.2 (CH(*C*H_3)$_2$), 16.0 (CH(*C*H_3)$_2$).

*6-Allyl-6-hex-5-enyl-2-isopropyl-6*H*-pyran-3-one,* ***27***. ν_{max}(film)/cm^{-1}: 3075 (s), 2928 (s), 1686 (s), 1640 (s), 1388 (s), 911 (s). *m/z* (EI) 263.19 (M + H, 100%). HRMS calcd for $C_{17}H_{27}O_2$ (M^+ + H): 263.2012. Found 263.2006. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.80 (1H, d, J = 10.4 Hz, C*H*CHCO), 6.02 (1H, d, J = 10.4 Hz, CHC*H*CO), 5.75–5.73 (2H, m, CH_2CHCH_2), 5.13–5.07 (2H, m, CH_2CHCH_2), 4.97 (1H, dq, J = 17.1, 1.6 Hz, CH_2CHCH_2), 4.91 (1H, dm, J = 10.2 Hz, CH_2CHCH_2), 4.04 (1H, d, J = 2.6 Hz, COC*H*(O)CH), 2.54 (1H, ddm, J = 14.2, 6.3 Hz, CH_2CHCH_2), 2.43 (1H, qd, J = 6.9, 2.6 Hz, *C*H(CH_3)$_2$), 2.32 (1H, dd, J = 14.2, 8.2 Hz, CH_2CHCH_2), 2.02 (2H, qm, J = 6.9 Hz, CH_2CHCH_2), 1.71 (1H, m, $CH_2CH_2CH_2$), 1.54–1.43 (2H, m, $CH_2CH_2CH_2$), 1.41–1.33 (2H, m, $CH_2CH_2CH_2$), 1.23 (1H, m, $CH_2CH_2CH_2$), 1.00 (3H, d, J = 7.0 Hz, $CH(CH_3)_2$), 0.84 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.9 (CHCH*C*O), 154.7 (*C*HCHCO), 138.8 (CH_2CHCH_2), 132.7 (CH_2CHCH_2), 126.6 (CH*C*HCO), 118.6 (CH_2CHCH_2), 114.5 (CH_2CHCH_2), 78.6 (CO*C*H(O)CH), 75.8 (CH*C*(O)CH_2), 39.7 (CH_2CHCH_2), 38.5 (CH_2CHCH_2), 33.6 ($CH_2CH_2CH_2$), 29.2 (*C*H(CH_3)$_2$), 29.1 ($CH_2CH_2CH_2$), 22.9 ($CH_2CH_2CH_2$), 19.2 (CH(*C*H_3)$_2$), 16.0 (CH(*C*H_3)$_2$).

(E) General ring-closing metathesis procedure for the synthesis of spiropyrans 14, 28, 29, and 30. A solution of bis-alkenyl pyrone in dichloromethane in a darkened reaction vessel was treated with 5 mol% first generation Grubbs catalyst. The resulting mixture was then stirred and heated to reflux for 4 h (for the longer alkenyl chains, pentene and hexene, this time was increased to 6 and 7 h respectively).

Upon reaction completion, as determined by TLC analysis, the solvent was removed under vacuum and the crude residue obtained purified by flash column chromatography (silica gel, 7% diethyl ether in 40–60 petroleum spirits).

2-Isopropyl-1-oxaspiro[5.6]dodeca-4,8-dien-3-one, ***14***. ν_{max}(film)/cm^{-1}: 2923 (s), 1648, (s), 1368, 912 (s). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.98 (1H, d, J = 10.4 Hz, C*H*CHCO), 5.94 (1H, m, CHC*H*CO), 5.91 (1H, d, J = 10.3 Hz, C*H*CH), 5.50 (1H, m, CHC*H*), 3.94 (1H, d, J = 2.8 Hz, COC*H*(O)CH), 2.53 (1H, dd, J = 14.9, 5.9 Hz, $CHCHCH_2$), 2.46 (1H, dd, J = 14.9, 7.1 Hz, $CHCHCH_2$), 2.38 (1H, m, C*H*(CH_3)$_2$), 2.23 (1H, m, $CHCHCH_2$), 2.16 (1H, m, $CHCHCH_2$), 2.03 (1H, m, CH_2CH_2), 1.85 (1H, m, CH_2CH_2), 1.77 (1H, m, CH_2CH_2), 1.57 (1H, m, CH_2CH_2), 0.99 (3H, d, J = 6.9 Hz, $CH(CH_3)_2$), 0.83 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.4 (CHCH*C*O), 155.5 (*C*HCHCO), 134.4 (*C*HCH), 125.0 (CH*C*H), 124.9 (CH*C*HCO), 78.4 (CO*C*H(O)CH), 72.6 (CH*C*(O)CH_2), 43.2 ($CHCHCH_2$), 33.4 ($CHCHCH_2$), 28.8 (*C*H(CH_3)$_2$), 28.4 (CH_2CH_2), 21.3 (CH_2CH_2), 19.3 (CH(*C*H_3)$_2$), 16.0 (CH(*C*H_3)$_2$).

7-Isopropyl-6-oxaspiro[4.5]deca-2,9-dien-8-one, ***28***. ν_{max}(film)/cm^{-1}: 2928 (s), 1686 (s), 1476 (s), 1383 (s). *m/z* (EI) 193.12 (M + H, 90%). HRMS calcd for $C_{12}H_{17}O_2$ (M^+ + H): 193.1229. Found 193.1223. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.88 (1H, d, J = 10.2 Hz, C*H*CHCO), 5.89 (1H, d, J = 10.2 Hz, CHC*H*CO), 5.67 (1H, m, CHC*H*), 5.62 (1H, m, C*H*CH), 3.90 (1H, d, J = 2.9 Hz, COC*H*(O)CH), 2.78 (1H, dq, J = 16.9, 2.0 Hz, $CHCHCH_2$), 2.65 (1H, dm, J = 17.1, 1.9 Hz, $CHCHCH_2$), 2.58 (1H, dm, J = 17.1, 2.1 Hz, $CHCHCH_2$), 2.43 (1H, dm, J = 16.9 Hz, $CHCHCH_2$), 2.38 (1H, qd, J = 6.9, 2.9 Hz, C*H*(CH_3)$_2$), 0.93 (3H, d, J = 7.0 Hz, $CH(CH_3)_2$), 0.81 (3H, d, J = 6.9 Hz, $CH(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.9 (CHCH*C*O), 154.6 (*C*HCHCO), 128.4 (*C*HCH), 127.7 (CH*C*HCO), 124.5 (*C*HCH), 82.1 (CO*C*H(O)CH), 80.0 (CH*C*(O)CH_2), 46.8 ($CHCHCH_2$), 40.0 ($CHCHCH_2$), 28.4 (*C*H(CH_3)$_2$), 19.0 (CH(*C*H_3)$_2$), 16.1 (CH(*C*H_3)$_2$).

2-Isopropyl-1-oxaspiro[5.5]undeca-4,8-dien-3-one, ***29***. ν_{max}(film)/cm^{-1}: 2965 (s), 2926 (s), 1687 (s). *m/z* (EI) 207.13 (M + H, 100%). HRMS calcd for $C_{13}H_{19}O_2$ (M^+ + H): 207.1385. Found 207.1380. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.84 (1H, d, J = 10.3 Hz, C*H*CHCO), 5.91 (1H, d, J = 10.3 Hz, CHC*H*CO), 5.70 (1H, m, CHC*H*), 5.52 (1H, m, C*H*CH), 3.95 (1H, d, J = 2.9 Hz, COC*H*(O)CH), 2.37–2.24 (3H, m, $CHCHCH_2$, $CHCHCH_2$, and C*H*(CH_3)$_2$), 2.13 (1H, m, $CHCHCH_2$), 2.03 (1H, m, $CHCHCH_2$), 1.80 (1H, m, CH_2CH_2), 1.68 (1H, m, CH_2CH_2), 0.92 (3H, d, J = 6.9 Hz, $CH(CH_3)_2$), 0.80 (3H, d, J = 6.8 Hz, $CH(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.5 (CHCH*C*O), 154.2 (*C*HCHCO), 126.9 (*C*HCH), 125.6 (CH*C*HCO), 122.6 (CH*C*H), 78.4 (CO*C*H(O)CH), 71.3 (CH*C*(O)CH_2), 32.8 (CH_2CH_2), 30.4 ($CHCHCH_2$), 28.8 (*C*H(CH_3)$_2$), 21.9 ($CHCHCH_2$), 19.1 (CH(*C*H_3)$_2$), 16.1 (CH(*C*H_3)$_2$).

(Z)-2-Isopropyl-1-oxaspiro[5.7]trideca-4,8-dien-3-one, ***30***. ν_{max}(film)/cm^{-1}: 3154 (s), 2932 (s), 1685 (s), 1383 (s), 908 (s). HRMS calcd for $C_{15}H_{22}NaO_2$ (M^+ + Na): 257.1517. Found 257.1512. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.92 (1H, d, J = 10.4 Hz, C*H*CHCO), 5.94 (1H, d, J = 10.4 Hz, CHC*H*CO), 5.85 (1H, m, CHC*H*), 5.49 (1H, m, C*H*CH), 4.05 (1H, d, J = 2.9 Hz, COC*H*(O)CH), 2.52 (1H, dd, J = 13.5, 8.1 Hz, $CHCHCH_2$),

2.44–2.37 (2H, m, CHCHCH_2, CH(CH_3)$_2$), 2.19–2.14 (2H, m, CHCHCH_2), 1.88–1.76 (2H, m, CH_2CH_2CH_2), 1.66 (1H, m, CH_2CH_2CH_2), 1.61–1.42 (3H, m, CH_2CH_2CH_2, CH_2CH_2CH_2), 1.02 (3H, d, J = 6.9 Hz, CH(CH_3)$_2$), 0.83 (3H, d, J = 6.8 Hz, CH(CH_3)$_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.3 (CHCH*C*O), 155.4 (*C*HCHCO), 133.4 (*C*HCH), 125.9 (CH*C*HCO), 125.3 (CH*C*H), 78.8 (CO*C*H(O)CH), 65.9 (CH*C*(O)CH$_2$), 37.3 (CHCH*C*H$_2$), 29.8 (*C*H(CH$_3$)$_2$), 28.9 (CHCH*C*H$_2$), 26.8 (CH$_2$CH$_2$*C*H$_2$), 19.3 (*C*H$_2$CH$_2$CH$_2$), 15.9 (CH$_2$*C*H$_2$CH$_2$), 15.3 (2 × CH(*C*H$_3$)$_2$).

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