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Radical Cascade Processes Leading to Fused- and Spiro-Bicyclic Ring Systems

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Abstract—The course of the reaction of 2-propargyl-2-(2-carboethoxyvinyl)cyclohexanone with tributyltin hydride and AIBN either neat or in benzene solution is discussed. The structure of the spirocyclic major product is shown to differ from that previously suggested and plausible reaction pathways are presented to account for the outcome.

Introduction

Recently we had occasion to repeat the reaction of enyne **1** with tributyltin hydride under homolytic conditions, a process that has been reported[1] to generate spirocycle **3** after treatment of the proposed intermediate **2** with PPTS (Scheme 1).

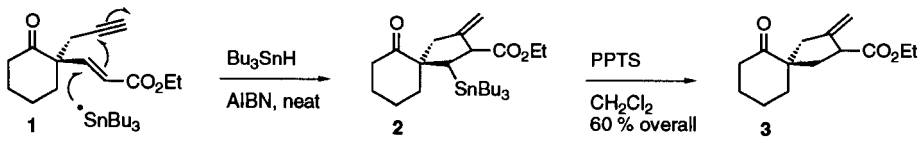
This process intrigued us in view of the likely steric impediment towards attack at the β-position of the enoate alkene, which bears an adjacent quaternary centre, particularly because an unhindered terminal alkyne is present in the same molecule. Although radical additions to alkynes are generally slower[2] than those to comparable alkenes, we envisaged that the steric bias in this example was such that a more likely reaction pathway would initiate with attack of stannyl radical at the exposed sp-centre.[3] However, in order to form the reported product (**3**), a stereoelectronically unfavourable 5-*endo*-trig[4] cyclisation is required (Scheme 2); alternatively 4-*exo*-trig cyclisation and ring-expansion[5] would generate the same product although this would have to involve a bicyclo[2.1.0]pentane intermediate that is expected to be inaccessible under these conditions. This scheme has the advantage that a *vinyl* stannane (**4**) would be generated which should be much more readily protiodestannylated[6] than the proposed intermediate **2**.

We set out to investigate this reaction further in order to find support for some of these interesting mechanistic possibilities and in this report we show that, in fact, a different sequence of events takes place and that none of the compounds **2**, **3**, or **4** are produced.

Results and Discussion

The required precursor **1** was prepared by a slight modification of the literature procedure, the Wadsworth–Emmons olefination being run directly on the crude product obtained by propargylation of 2-formylcyclohexanone to minimise deformylation processes. Subjecting this material to the conditions reported for the radical reaction [tributyltin hydride (ca. 1.2 equiv.), AIBN (0.48 equiv.), neat, 80°C, 15 min] followed by treatment with PPTS in dichloromethane (RT, 48 h) produced hydrostannylated compound **5** as a mixture of *E*- and *Z*- isomers (21%), known allylcyclohexanone derivative **6**[7] (24%), and a third component, assigned as structure **7**[8] (35%) (Scheme 3). This result supported the view that stannyl radical attack at the alkyne occurs in preference to attack at the (relatively hindered) alkene.

Next, in an effort to promote a radical cascade sequence, the tin hydride was added over 6 h (syringe pump) to a 10 mM



Scheme 1.

Keywords: cyclopropanes; radicals and radical reactions; rearrangements; spiro compounds.

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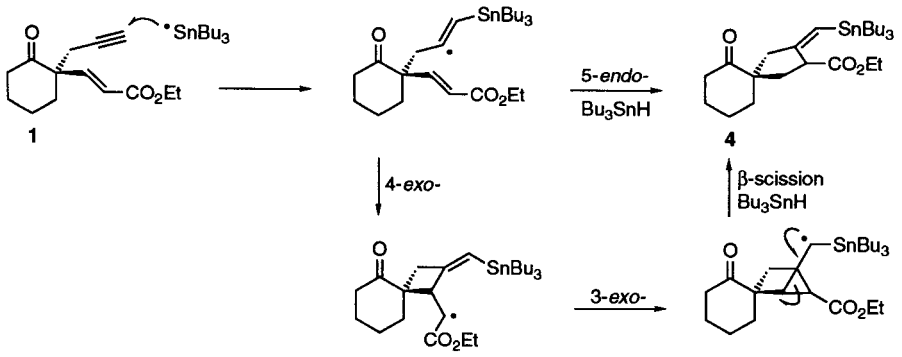
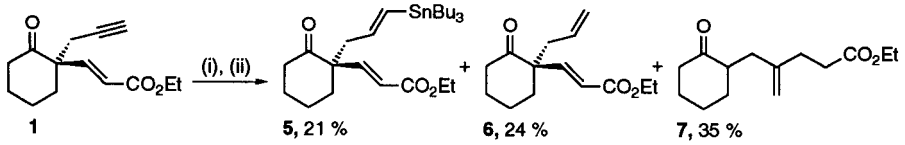
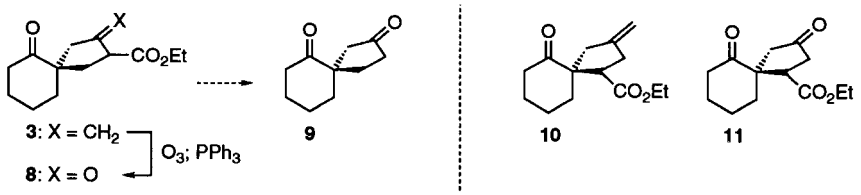


Scheme 2.



Scheme 3. *Reagents*: (i) Bu_3SnH, AIBN, neat; (ii) PPTS, CH_2Cl_2.



Scheme 4.

solution of substrate **1** in benzene at reflux. Once more, the intermediate stannylated compounds were not isolated at this point but directly subjected to PPTS treatment. Under these conditions the major isolated product (42% in the first run) exhibited ^1H and ^{13}C NMR data that appeared consistent with the proposed structure (**3**) for the spirocyclic ketoester. In an effort to simplify the spectra and allow correlation with known diketone **9**[9] the alkene was cleaved ozonolytically giving, we presumed, diketoester **8** but ester hydrolysis and decarboxylation of this material failed. Whilst hydrolysis could be effected there was no sign of loss of carbon dioxide, even under forcing conditions, and it appeared likely that the structure of ketoester **8** and, by implication, that of its precursor (**3**) were incorrect. On the basis of extensive NMR investigations the regioisomeric structures **10** and **11** were proposed for **3** and **8** respectively (Scheme 4).

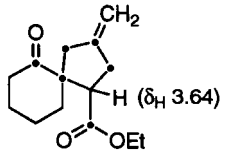
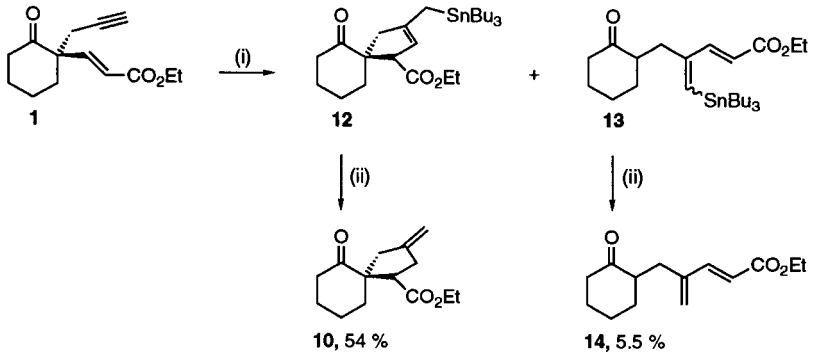
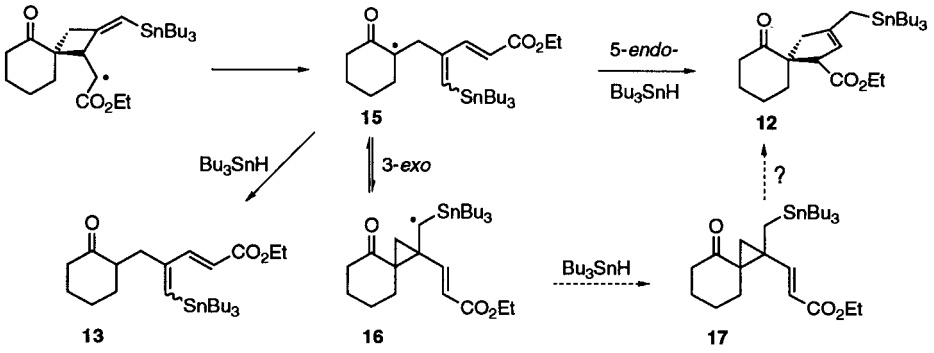


Figure 1. Carbons marked (·) show a strong cross-peak to the ester α-proton in the HMBC spectrum.

Crucially, in the HMBC spectrum of alkene **10**, the resonance corresponding to C*H*CO_2Et showed two- and three-bond couplings to the highlighted carbons (·) shown



Scheme 5. *Reagents*: (i) Bu_3SnH, AIBN, 7.6 mM in PhH; (ii) PPTS, CH_2Cl_2.



Scheme 6.

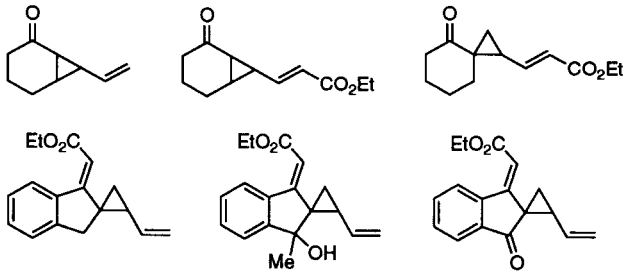


Figure 2.

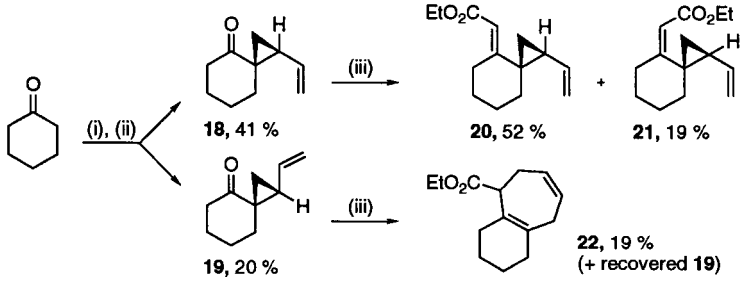
in Fig. 1, there being no cross-peak to the alkene CH_2 which discounts structure **3** as a possibility.

Further investigation revealed that a second component **14** (5.5%, radical reaction run at a final substrate concentration of 7.6 mM) was formed in addition to the spirocycle **10** (54%), and this became the major product when the concentration of the radical reaction was increased to ca. 40 mM. Full characterisation of the stannanes leading to these two products was hampered by their instability but, on the basis of their spectroscopic data and their products of protiodestannylation, the structures **12** and **13** (Scheme 5) are proposed (see Experimental for details).

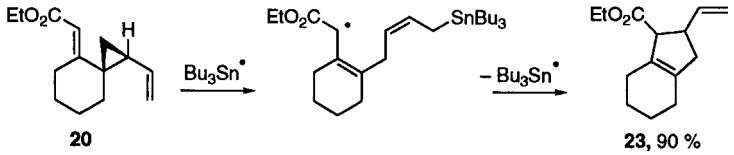
The mechanism of this transformation remains obscure but, taking all the results together, the early part of the sequence is most readily explained by a 4-*exo*-trig cyclisation as originally suggested (Scheme 2) but the reaction pathway diverges at this point (Scheme 6). Fragmentation would lead to α-carbonyl radical **15** which, in a concentration-dependent process, could be either reduced directly to give diene **13** or could cyclise to give spirocycle **12**. The mode of cyclisation is far from obvious; 5-*endo*-trig cyclisation would give the spirocycle directly (after reduction) but this is likely to be slow.[10] In principle, a reversible but kinetically preferred 3-*exo*-trig process could generate vinyl cyclopropane intermediate **16** whose evolution to the product is conceivable by a vinyl cyclopropane–cyclopentene rearrangement[11] although further work is needed before firm conclusions can be drawn.

Although spirocycle **17** may well not be an intermediate in this reaction, the possibility that a stannyl radical-catalysed rearrangement of this compound operates to give **12** led us to prepare a series of structurally related vinyl cyclopropane substrates (Fig. 2) whose reactivity might shed light on the mechanism.[12] In fact, these studies[13] revealed complex behaviour in which a fascinating interplay of electronic and steric effects operates to dictate the course of the rearrangements and a substantial discussion of the results will be presented in a separate report.

However, the preparation and reaction of cyclopropane **20** (Scheme 7) are worth noting in this context as this substrate proved to possess the correct combination of structural features for a vinyl cyclopropane–cyclopentene rearrangement catalysed by stannyl radical. Thus, enolate alkylation of cyclohexanone with 4-chloro-1-iodobut-2-ene and treatment of the crude product with potassium *t*-butoxide under equilibrating conditions afforded separable vinyl cyclopropanes[14] **18** and **19** (2:1 ratio). These were olefinated separately under Wadsworth–Emmons conditions, the *trans*-isomer (**18**) being converted in high yield into a 3:1 ratio of alkene diastereomers **20** and **21**. Interestingly, under the same conditions, the more crowded *cis*-cyclopropane isomer (**19**) reacted only very slowly with the olefination reagent and the so-formed enoate underwent



Scheme 7. *Reagents*: (i) LDA, 4-chloro-1-iodobut-2-ene, THF; (ii) KO*t*-Bu, THF; (iii) NaH, $(EtO)_2P(O)CH_2CO_2Et$, DME.



Scheme 8. *Reagents*: Bu_3SnH (0.25 equiv.), AIBN, PhH.

divinylcyclopropane rearrangement[15] under the reaction conditions to give bicyclic ester **22**.

Treatment of a 5 mM benzene solution of diastereomer **20** with 0.25 molar equivalents of tributyltin hydride in the presence of AIBN resulted in a smooth transformation (90%) to give the hexahydroindene derivative **23** (Scheme 8). We suggest a catalytic cascade sequence consisting of (i) addition of stannyl radical to the unconjugated alkene; (ii) cyclopropyl carbinyl fragmentation; (iii) 5-*exo*-trig cyclisation of the so-formed allylic radical; (iv) re-ejection of stannyl radical to continue the chain.

Conclusion

Further studies are required in order to be confident of the mechanism for the transformation of cyclohexanone **1** into spirocycle **12**, in particular whether or not a direct 5-*endo*-trig pathway from intermediate **15** can be ruled out as a possibility. Whichever mechanism proves to be supported in future work, our studies have already led to the identification of novel rearrangement processes and we hope that, ultimately, the results will prove to be of synthetic value as well as mechanistic interest.

Experimental

General

^1H and ^{13}C NMR spectra were recorded on Varian Gemini 200, Bruker AC 200, Bruker DPX 400, or Bruker AM 500 spectrometers with ^1H assignments being made on the basis of a combination of chemical shift, coupling constant, COSY, and NOE data as appropriate; ^{13}C assignments were supported by DEPT and HMQC experiments. Coupling constants (*J*) are quoted to the nearest 0.5 Hz. Infrared spectra were recorded on either Perkin–Elmer 1750 or Perkin–Elmer Paragon 1000 FT spectrometers as thin films. Mass spectra were recorded on VG Micromass ZAB 1F, Masslab 20-250, VG Platform, or VG TRIO-1 spectrometers. Accurate mass data were obtained by the EPSRC Mass Spectrometry Service Centre at Swansea. All solvents and commercially available reagents were dried and purified according to standard procedures. 'Petrol' refers to the fraction of light petroleum ether boiling in the range 30–40°C; 'ether' refers to diethyl ether. All experiments involving air-sensitive reagents were performed under an argon atmosphere.

Treatment of enyne 1 with tributyltin hydride without solvent. A mixture of enyne **1**[1] (490 mg, 2.1 mmol), AIBN (170 mg, 1 mmol) and tributyltin hydride (ca. 70% hydride content by NMR, 970 μl, 2.5 mmol) was stirred at 80°C for 15 min then, after cooling, dichloromethane (20 mL) and PPTS (2.15 g, 8.4 mmol) were added and the mixture was stirred at RT for 48 h. The solvent was removed in vacuo and the residue was triturated repeatedly with a 2:3 mixture of petrol and ethyl acetate (10×10 mL). The combined extracts were concentrated in vacuo to give a viscous yellow oil. Purification by chromatography (12:1 petrol:ether) gave *2-(2-carboethoxyvinyl)-2-[3-(tributylstannyl)prop-2-enyl]-cyclohexanone* (**5**) in which the (*E*)-isomer predominated (230 mg, 21%), 2-allyl-2-(2-carboethoxyvinyl)cyclohexanone[7] (**6**) (420 mg, 24%) and *2-(4-carboethoxy-2-methyl-enebutyl)cyclohexanone* (**7**) (170 mg, 35%) as colourless oils. Data for **5** [(*E*)-isomer]: Found: C, 59.41; H, 9.01. $C_{26}H_{46}O_3Sn$ requires: C, 59.44; H, 8.83%; R_f 0.66 (1:1 petrol:ether); ν_{max}/cm^{-1} 2929s, 2871m, 1715s, 1644m, 1597m, 1464s, 1312s, 1271s, 1180s, 1039s, 989m, 864m; δ_H (500 MHz, $CDCl_3$) 0.87–0.92 (15H, m), 1.27–1.34 (9H, m), 1.45–1.50 (6H, m), 1.75–1.82 (4H, m), 1.89–2.03 (2H, m), 2.41–2.45 (2H, m), 2.51–2.53 (2H, m), 4.20 (2H, q, *J*=7.0 Hz), 5.75 (1H, d, *J*=16.5 Hz) overlays 5.74 (1H, dt, *J*=18.5, 7.0 Hz), 5.96 (1H, d, *J*=18.5 Hz), 7.06 (1H, d, *J*=16.5 Hz); δ_C (50.3 MHz, $CDCl_3$) 9.3, 13.5, 14.1, 21.2, 26.8, 27.1, 29.0, 35.4, 39.7, 45.1, 54.6, 60.5, 122.1, 133.7, 143.1, 150.9, 166.4, 211.2; *m/z* (CI) 527 ($M(^{120}Sn)H^+$, 29%), 526 ($M(^{119}Sn)H^+$, 15), 525 ($M(^{118}Sn)H^+$, 28), 524 ($M(^{117}Sn)H^+$, 12), 523 ($M(^{116}Sn)H^+$, 16), 469 (100), 291 (45), 235 (43), 177 (44), 121 (14), 83 (13). Data for **6**:[7] R_f 0.57 (1:1 petrol:ether); ν_{max}/cm^{-1} 2938m, 2866m, 1713s, 1643m, 1448m, 1368m, 1314s, 1272m, 1188s, 1036m, 986m, 919w; δ_H (500 MHz, $CDCl_3$) 1.29 (3H, t, *J*=7.0 Hz), 1.72–1.81 (4H, m), 1.89–1.94 (1H, m), 1.98–2.04 (1H, m), 2.36–2.49 (4H, m), 4.20 (2H, q, *J*=7.0 Hz), 5.04 (1H, dd, *J*=10.0, 1.5 Hz), 5.06 (1H, dd, *J*=17.0, 1.5 Hz), 5.64 (1H, ddt, *J*=17.0, 10.0, 7.5 Hz), 5.76 (1H, d *J*=16.5 Hz), 7.03 (1H, d, *J*=16.5 Hz); δ_C (50.3 MHz, $CDCl_3$) 14.0, 21.2, 26.8, 35.6, 39.6, 41.1, 54.4, 60.5, 118.8, 122.4, 133.1, 150.6, 166.3, 211.0; *m/z* (CI) 254 (MNH_4^+, 100%), 237 (MH^+, 64), 191 (22), 61 (15). Data for **7**: R_f 0.51 (1:1 petrol:ether); Accurate mass: Found 239.1647, $C_{14}H_{23}O_3$ (MH^+) requires 239.1647; ν_{max}/cm^{-1} 2999m, 2942s, 1736s, 1711s, 1462s, 1440m, 1369s, 1230s, 1184s, 1039w, 707w; δ_H (400 MHz, $CDCl_3$) 1.23 (3H, t, *J*=7.0 Hz), 1.25–1.33 (1H, m), 1.61–1.69 (2H, m), 1.87 (1H, dd, *J*=14.5, 9.0 Hz), 1.79–1.87 (1H, m), 2.02–2.13 (2H, m), 2.22–2.35 (3H, m), 2.38 (1H, t, *J*=4.0 Hz), 2.41–2.50 (3H, m), 2.59 (1H, dd, *J*=14.5, 5.0 Hz), 4.11 (2H, q, *J*=7.0 Hz), 4.71 (1H, br s), 4.76 (1H, br s); δ_C (100.6 MHz, $CDCl_3$) 14.2, 24.9, 28.0, 30.6, 32.5, 33.4, 35.8, 42.0, 48.4, 60.3, 111.0, 145.5, 173.2, 212.6; *m/z* (CI) 256 (MNH_4^+, 5%), 240 (14), 239 (MH^+, 100), 238 (14), 193 (100).

Treatment of enyne 1 with tributyltin hydride in benzene. To a solution of the enyne **1** (110 mg, 0.47 mmol) and AIBN (10 mg) in degassed benzene (52 mL) at reflux was

added a solution of tributyltin hydride (ca. 70% hydride content by NMR, 219 μl, 0.57 mmol) in degassed benzene (10 mL) over 3 h (syringe pump). The mixture was left at reflux for 1 h and then the solvent was removed in vacuo to afford a yellow oil. In a separate experiment (for characterisation purposes) purification of a small portion of this oil by chromatography (15:1 petrol:ether) yielded *1-carboethoxy-3-(tributylstannyl)methylspiro[4.5]dec-2-en-6-one* (**12**) as a labile, colourless oil. R_f 0.48 (2:1 petrol:ether); ν_{max}/cm^{-1} 2926s, 2870s, 2880s, 1732s, 1712s, 1645w, 1464s, 1178s, 1038m, 669m; δ_H (500 MHz, $CDCl_3$) 0.85–0.98 (15H, m), 1.25 (3H, t, J=7.0 Hz) overlays 1.23–1.35 (6H, m), 1.35–1.56 (6H, m), 1.62–1.80 (4H, m), 1.86–1.90 (1H, m), 1.92–2.00 (1H, m), 2.36–2.56 (6H, m), 4.12 (2H, q, J=7.0 Hz), 4.33 (1H, d, J=1.5 Hz), 5.03 (1H, d, J=1.5 Hz); δ_C (125 MHz, $CDCl_3$) 9.5, 12.5, 13.7, 14.3, 22.3, 26.7, 27.5, 29.1, 34.4, 39.2, 47.3, 54.3, 59.3, 60.2, 116.8, 143.4, 173.7, 210.6. Also obtained was *ethyl 4-[(2-oxocyclohexyl)-methyl]-5-tributylstannylpenta-2,4-dienoate* (**13**) as a labile, colourless oil. ν_{max}/cm^{-1} 2929s, 2855s, 1714s, 1619s, 1555w, 1464m, 1280s, 1176s, 1043m, 866m; δ_H (400 MHz, $CDCl_3$) 0.82–0.94 (9H, m), 0.99 (6H, app. t, J=8.0 Hz), 1.20–1.33 (9H, m), 1.40–1.51 (6H, m), 1.52–1.62 (3H, m), 1.75–1.86 (1H, m), 1.96–2.14 (3H, m), 2.23–2.35 (1H, m), 2.36–2.47 (2H, m), 3.03 (1H, dd, J=14.5, 4.0 Hz), 4.18 (2H, q, J=7.0 Hz), 5.80 (1H, d, J=16.0 Hz), 6.40 (1H, s), 7.22 (1H, d, J=16.0 Hz); δ_C (100 MHz, $CDCl_3$) 10.6, 13.6, 14.2, 25.0, 27.2, 27.9, 28.9, 33.4, 35.4, 42.1, 49.0, 60.2, 118.3, 146.9, 147.6, 150.5, 167.0, 211.9. The crude product from the radical reaction was dissolved in dichloromethane (15 mL), PPTS (472 mg, 1.88 mmol) was added and the mixture was stirred at RT for 48 h. The solvent was removed in vacuo and the residue triturated with a 2:3 mixture of petrol and ethyl acetate (10×5 mL). The combined extracts were concentrated in vacuo to afford a viscous yellow oil that was purified by chromatography (12:1 petrol:ether) to yield *1-carboethoxy-3-methylene-spiro[4.5]decan-6-one* (**10**) (60 mg, 54%). R_f 0.38 (2:1 petrol:ether); Accurate mass: Found 237.1491, $C_{14}H_{21}O_3$ (MH^+) requires 237.1491; ν_{max}/cm^{-1} 2935m, 2866m, 1729s, 1710s, 1448w, 1371m, 1264w, 1181m, 1041m, 879w; δ_H (500 MHz, $CDCl_3$) 1.24 (3H, t, J=7.0 Hz), 1.62–1.74 (3H, m), 1.75–1.83 (2H, m), 1.95–2.01 (1H, m), 2.36–2.50 (3H, m), 2.62–2.66 (3H, m), 3.64 (1H, t, J=8.5 Hz), 4.06–4.21 (2H, m), 4.88–4.89 (2H, m); δ_C (125 MHz, $CDCl_3$) 14.2, 21.9, 26.1, 32.4, 33.2, 39.2, 43.3, 47.9, 58.4, 60.3, 107.5, 147.0, 173.5, 211.3; *m/z* (CI) 254 (MNH_4^+, 10%), 238 (14), 237 (MH^+, 100), 191 (39), 190 (28), 163 (28), 162 (18), 146 (21). Also obtained was *ethyl 4-[(2-oxocyclohexyl)methyl]penta-2,4-dienoate* (**14**) (6 mg, 5.5%). Accurate mass: Found 237.1486, $C_{14}H_{21}O_3$ (MH^+) requires 237.1491; ν_{max}/cm^{-1} 2937s, 2863m, 1711br s, 1631s, 1603m, 1448m, 1367m, 1308s, 1274s, 1177s, 1038s, 986m, 866m; δ_H (400 MHz, $CDCl_3$) 1.30 (3H, t, J=7.0 Hz), 1.56–1.71 (3H, m), 1.82–1.89 (1H, m), 2.02 (1H, dd, J=14.5, 9.0 Hz) overlaying 2.02–2.14 (2H, m), 2.26–2.37 (1H, m), 2.40–2.49 (2H, m), 2.91 (1H, ddd, J=14.5, 4.0, 0.5 Hz), 4.21 (2H, q, J=7.0 Hz), 5.30 (1H, s), 5.43 (1H, s), 5.85 (1H, d, J=16.0 Hz), 7.28 (1H, d, J=16.0 Hz); δ_C (100 MHz, $CDCl_3$) 14.3, 25.1, 27.9, 31.4, 33.8, 42.1, 48.6, 60.4, 118.4, 125.0, 142.4, 146.2, 167.0, 211.9; *m/z* (CI) 237 (MH^+, 11%), 191 (100), 163 (9).

1-Carboethoxyspiro[4.5]decan-3,6-dione (11). Ozone gas was bubbled through a solution of spirocyle **10** (150 mg, 0.64 mmol) in a solution of ethanol:dichloromethane (1:1, 12 mL) at −78°C, until the solution became pale blue (ca. 5 min). Oxygen gas was then bubbled through the solution to remove residual ozone then triphenylphosphine (167 mg, 0.63 mmol) was added and the mixture stirred for 2 h at RT. The solvent was removed in vacuo to give an oil which was purified by chromatography (2:1 petrol:ether) to yield the *title compound* (**11**) as a colourless oil (99 mg, 66%). R_f 0.32 (1:3 petrol:ether); Accurate mass: Found 239.1283, $C_{13}H_{19}O_4$ (MH^+) requires 239.1283; ν_{max}/cm^{-1} 2939m, 2867m, 1752s, 1727s, 1706s, 1373m, 1337m, 1262m, 1194m, 1161m, 1126m, 1033m; δ_H (500 MHz, $CDCl_3$) 1.28 (3H, t, J=7.0 Hz), 1.65–1.73 (1 H, m), 1.78–1.97 (5 H, m), 2.43–2.59 (6 H, m), 3.66 (1 H, dd, J=7.5, 5.0 Hz), 4.13–4.24 (2H, m); δ_C (125 MHz, $CDCl_3$) 14.2, 21.8, 26.4, 34.8, 38.4, 40.1, 45.7, 46.2, 55.8, 61.0, 172.9, 210.6, 213.2; *m/z* (CI) 256 (MNH_4^+, 60%), 239 (MH^+, 100), 193 (17), 138 (27).

(*Z*)-2-(4-Chlorobut-2-enyl)cyclohexanone. To a stirred solution of diisopropylamine (3.24 mL, 23 mmol) in THF (88 mL) at 0°C was added *n*-butyllithium (9.24 mL of a 2.5 M solution in hexanes, 23.1 mmol) followed, after 30 min, by the addition of cyclohexanone (0.95 mL, 22 mmol). After stirring for a further 30 min at 0°C *Z*-4-chloro-1-iodobut-2-ene (4.93 g, 23 mmol) was added and the mixture was allowed to warm slowly to RT. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution (150 mL), the separated aqueous layer was extracted with ether (3×100 mL) then the combined organic portions were dried (magnesium sulfate), filtered, and concentrated in vacuo to give an orange/brown oil (5.3 g) that was used directly in the next reaction. ν_{max}/cm^{-1} 2936m, 2862m, 1710s, 1448m, 1129m, 972m; δ_H (400 MHz, $CDCl_3$) 1.31–1.44 (1H, m), 1.53–1.72 (2H, m), 1.82–1.93 (1H, m), 1.97–2.18 (3H, m), 2.27–2.44 (3H, m), 2.53 (1H, dt, J=14.5, 6.0 Hz), 4.02 (2H, d, J=7.0 Hz), 5.59–5.68 (1H, m), 5.70–7.80 (1H, m); δ_C (125 MHz, $CDCl_3$) 25.0, 27.9, 32.0, 33.5, 42.1, 45.2, 50.2, 127.7, 133.5, 212.2; *m/z* (CI), 151 (100%).

1-Vinylspiro[2.5]octan-4-one[14] (18) and (19). To a stirred solution of the crude chloride from the previous reaction (<23 mmol) in THF (50 mL) at RT was added potassium *t*-butoxide (2.6 g, 23 mmol) and stirring continued for 6 h. Saturated aqueous ammonium chloride solution (100 mL) was added, the separated aqueous layer was extracted with ether (3×100 mL) and the combined extracts were dried (magnesium sulfate), filtered, and concentrated in vacuo. The obtained yellow/brown oil was purified by chromatography (40:1 petrol:ether) to give the two diastereomers **18** (1.35 g, 41% from cyclohexanone) and **19** (645 mg, 20% from cyclohexanone) as colourless oils. Data for **18**: R_f 0.28 (9:1 petrol:ether); ν_{max}/cm^{-1} 2933m, 1697s, 1634w, 1448m, 1362m, 1118m, 996m, 901m; δ_H (400 MHz, $CDCl_3$) 0.75–0.85 (1H, m), 1.35 (1H, dd, J=14.0, 2.5 Hz), 1.64–1.88 (5H, m), 1.98–2.13 (3H, m), 2.46 (1H, br dd, J=13.5, 3.0 Hz), 4.95 (1H, dt, J=10.0, 1.5 Hz), 5.15 (1H, dt, J=17.0, 1.5 Hz), 5.31 (1H, dddt, J=17.0, 10.0, 8.5, 1.5 Hz); δ_C (100 MHz, $CDCl_3$) 17.9, 23.9, 25.4, 35.0, 35.8, 37.4, 41.7, 115.6, 135.6, 208.4; *m/z* (CI) 168 (MNH_4^+, 10%), 151 (MH^+, 100). Data

for **19**: R_f 0.21 (9:1 petrol:ether); ν_{max}/cm^{-1} 3082w, 2940s, 2863m, 1692s, 1635m, 1449m, 1360m, 1136m, 987m, 904m; δ_H (400 MHz, $CDCl_3$) 0.68 (1H, dd, J=6.5, 4.0 Hz), 1.65 (1H, dd, J=9.0, 4.0 Hz) overlaying 1.60–1.82 (4H, m), 1.84–1.95 (2H, m), 2.01 (1H, app. q, J=8.0 Hz), 2.33–2.46 (2H, m), 5.14 (1H, ddd, J=10.5, 1.5, 0.5 Hz), 5.19 (1H, ddd, J=17.0, 1.5, 0.5 Hz), 5.59 (1H, ddd, J=17.0, 10.5, 8.0 Hz); *m/z* (CI) 168 (MNH_4^+, 10%), 151 (MH^+, 100).

4-Carboethoxymethylene-1-vinylspiro[2.5]octane (20) and (21). To a suspension of sodium hydride (88 mg of a 60% dispersion in mineral oil, 2.2 mmol) in anhydrous DME (3 mL) at RT was added triethylphosphonoacetate (0.46 mL, 2.2 mmol). The mixture was stirred for 1 h then a solution of ketone **18** (220 mg, 1.46 mmol) in DME (1 mL) was added at such a rate that the temperature of the mixture remained below 30°C. After a further 14 h, the reaction mixture was diluted with saturated aqueous ammonium chloride solution (15 mL), extracted with ether (3×10 mL), dried (magnesium sulfate), filtered, and concentrated in vacuo. Purification by chromatography (40:1 petrol:ether) afforded the diastereomeric *alkenes* **20** (168 mg, 52%) and **21** (59 mg, 19%) as colourless oils. Data for **20**: R_f 0.41 (9:1 petrol:ether); Accurate mass: Found 221.1542, $C_{14}H_{21}O_2$ (MH^+) requires 221.1541; ν_{max}/cm^{-1} 2981m, 2932s, 2857m, 1716s, 1642s, 1447m, 1372m, 1305m, 1178s, 1038s, 901m; δ_H (400 MHz, $CDCl_3$) 0.60 (1H, app. t, J=5.5 Hz), 1.22 (1H, dd, J=8.5, 5.5 Hz), 1.28 (3H, t, J=7.0 Hz), 1.43–1.71 (6H, m), 1.76–1.83 (1H, m), 2.36–2.43 (1H, m), 3.42 (1H, app. dt, J=13.5, 4.0 Hz), 4.14 (2H, q, J=7.0 Hz), 5.08 (1H, ddd, J=10.0, 2.0, 0.5 Hz), 5.16 (1H, ddd, J=17.0, 2.0, 0.5 Hz), 5.52 (1H, s), 5.62 (1H, ddd, J=17.0, 10.0, 8.5 Hz); δ_C (100 MHz, $CDCl_3$) 14.3, 18.5, 24.7, 27.1, 29.2, 29.5, 32.3, 33.3, 59.6, 110.9, 115.7, 136.5, 165.7, 167.3; *m/z* (CI) 238 (MNH_4^+, 19%), 221 (MH^+, 100), 147 (33). Data for **21**: R_f 0.36 (9:1 petrol:ether); ν_{max}/cm^{-1} 2981m, 2934s, 2857m, 1720s, 1644s, 1445m, 1228m, 1179s, 1116m, 1037m, 901m; δ_H (400 MHz, $CDCl_3$) 0.78 (1H, app. t, J=5.5 Hz), 1.09 (1H, dd, J=8.5, 5.5 Hz), 1.29 (3H, t, J=7.0 Hz), 1.42–1.85 (7H, m), 2.25–2.29 (2H, m), 4.08–4.22 (2H, m), 5.06 (1H, dd, J=10.5, 2.0 Hz), 5.14 (1H, ddd, J=17.0, 2.0, 0.5 Hz), 5.57 (1H, s), 5.74 (1H, ddd, J=17.0, 10.5, 8.5 Hz); δ_C (100 MHz, $CDCl_3$) 14.2, 21.1, 24.8, 29.2, 29.5, 30.9, 32.7, 37.9, 60.0, 112.9, 115.0, 137.1, 162.2, 166.5; *m/z* (CI) 238 (MNH_4^+, 4%), 221 (MH^+, 100), 175 (7), 147 (15).

2-Carboethoxybicyclo[5.4.0]undeca-1(7),4(5)-diene (22). Following a procedure analogous to that used for the preparation of **20** and **21** but starting with diastereomer **19** (150 mg, 1 mmol), the *title compound* (**22**) was obtained as a colourless oil (41 mg, 19%), the mass balance consisting of recovered starting ketone. Accurate mass: Found 221.1542, $C_{14}H_{21}O_2$ (MH^+) requires 221.1541; ν_{max}/cm^{-1} 2928s, 1735s, 1439m, 1370m, 1310m, 1195m, 1155s, 1096m, 1027m; δ_H (400 MHz, $CDCl_3$) 1.27 (3H, t, J=7.0 Hz), 1.49–1.68 (4H, m), 1.87–2.08 (4H, m), 2.32–2.49 (3H, m), 3.02 (1H, br. d, J=19.0 Hz), 3.60 (1H, dd, J=9.5, 3.0 Hz), 4.17 (2H, q, J=7.0 Hz), 5.54–5.64 (2H, m); δ_C (100 MHz, $CDCl_3$) 14.3, 22.8 (two peaks), 27.7, 28.4, 32.3, 33.5, 47.2, 60.3, 126.9, 128.1, 129.9, 134.7, 173.9; *m/z* (CI) 221 (MH^+, 100%), 147 (16).

1-Carboethoxy-2-vinyl-2,3,4,5,6,7-hexahydro-1H-indene (23). A degassed solution of vinylcyclopropane **20** (40 mg, 0.18 mmol), tributyltin hydride (12.5 μl, 0.045 mmol), and AIBN (6.0 mg, 0.036 mmol) in benzene (36 mL) was heated at reflux for 14 h. The cooled reaction mixture was concentrated in vacuo and the residue purified by chromatography (20:1 petrol:ether) to give the *title compound* (**23**) as a colourless oil (36 mg, 90%) and as an inseparable mixture of diastereomers. R_f 0.42 (9:1 petrol:ether); Accurate mass: Found 221.1537, $C_{14}H_{21}O_2$ (MH^+) requires 221.1541; ν_{max}/cm^{-1} 2929s, 1734s, 1641w, 1445m, 1368m, 1336m, 1162s, 1035m, 913m; δ_H (400 MHz, $CDCl_3$) 1.21–1.28 (3H, 2×overlapping t), 1.55–1.68 (4H, m), 1.86–2.05 (4H, m), 2.11–2.18 (0.5H, m), 2.37 (1H, app. br d, J=8.0 Hz), 2.52–2.58 (0.5H, m), 3.12–3.22 (1.5H, m), 3.41 (0.5H, app. d, J=8.5 Hz), 4.06–4.20 (2H, m), 4.94–5.10 (2H, m), 5.88 (1H, app. ddd, J=17.0, 10.0, 7.5 Hz); δ_C (100 MHz, $CDCl_3$) 14.4 (two peaks), 22.5, 22.7 (two peaks), 22.8, 24.2, 24.6, 25.7 (two peaks), 41.2, 41.6, 44.9, 45.4, 58.3, 59.6, 59.9, 60.3, 113.8, 115.3, 131.4, 132.1, 137.2, 138.3, 139.1, 141.5, 173.3, 174.6; *m/z* (CI) 238 (MNH_4^+, 17%), 221 (MH^+, 100), 147 (29).

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