# Catalytic tin radical mediated tricyclisations. Part 2†‡

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Propenyl 4-*O*-propargyl-, propargyl 4-*O*-propenyl-, and propargyl 4-*O*-propargyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosides undergo catalytic, tin radical initiated, cascade reactions, in which three rings are constructed in a single reaction. In each case, a lack of stereoselectivity in the second cyclisation results in an additional product which is produced non-catalytically. The dienes which result from catalytic cyclisation of propargyl 4-*O*-propargyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosides, undergo *in situ* hydrostannylation to give unusual allylstannanes.

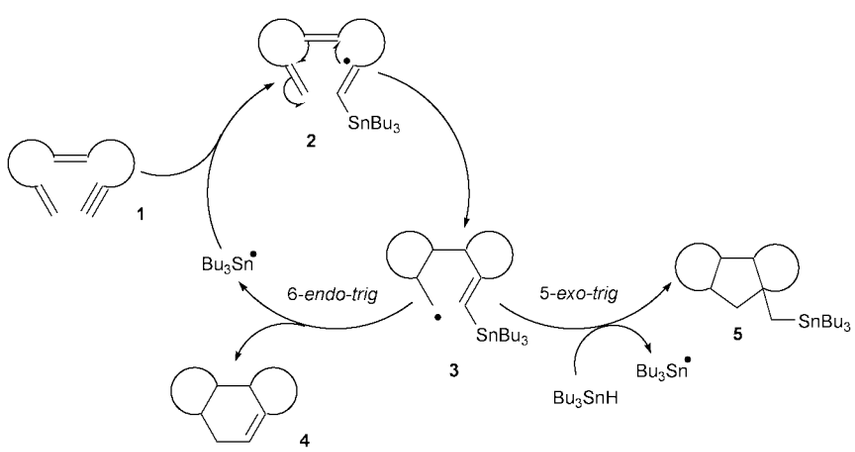
Cascade reactions[1] enable the creation of complex molecular architecture, quickly and efficiently. In their most useful form, a minimum number of pre-existing chiral centres are exploited to control a sequence of diastereoselective bond formation reactions.[2,3]

The development of catalytic free radical cascade reactions has lagged behind that of similar transition metal (*e.g.* palladium) mediated processes, because of a dearth of processes for elimination of the initiating radical.[4] In the preceding paper[5] we outlined a strategy for constructing polycyclic molecules using catalytic amounts of organotin radicals. This involves the addition of an organotin radical to an array of unsaturated bonds such that a cascade of addition reactions delivers the radical centre to a position at which the moiety which has initiated the process can be eliminated. Similar strategies have been reported by Marco-Contelles,[6] Spino[7] and Pancrazi[8] subsequent to our preliminary report.[9] Successful implementation of this strategy would enable the inherent chemoselectivity of organotin radicals,[10] to be utilised with catalytic amounts of reagents in a cost efficient manner, with minimal workup and/or isolation problems.[11] In this paper we report successful alkyne–alkene–alkene and alkyne–alkene–alkyne tricyclisations. The strategy for the former is shown in Scheme 1. Thus preferential addition to the alkyne side chain **1** initiates a series of addition reactions, which delivers the radical centre to a position **3** such that the tri-*n*-butyltin moiety can be displaced by an 6-*endo-trig*-addition–elimination reaction.[12] Although 5-*exo-trig* radical cyclisations are most commonly observed, recent studies have shown that the *6-endo-trig* manifold can be accessed by alkyl,[13] acyl[14] and vinyl[15] radicals.

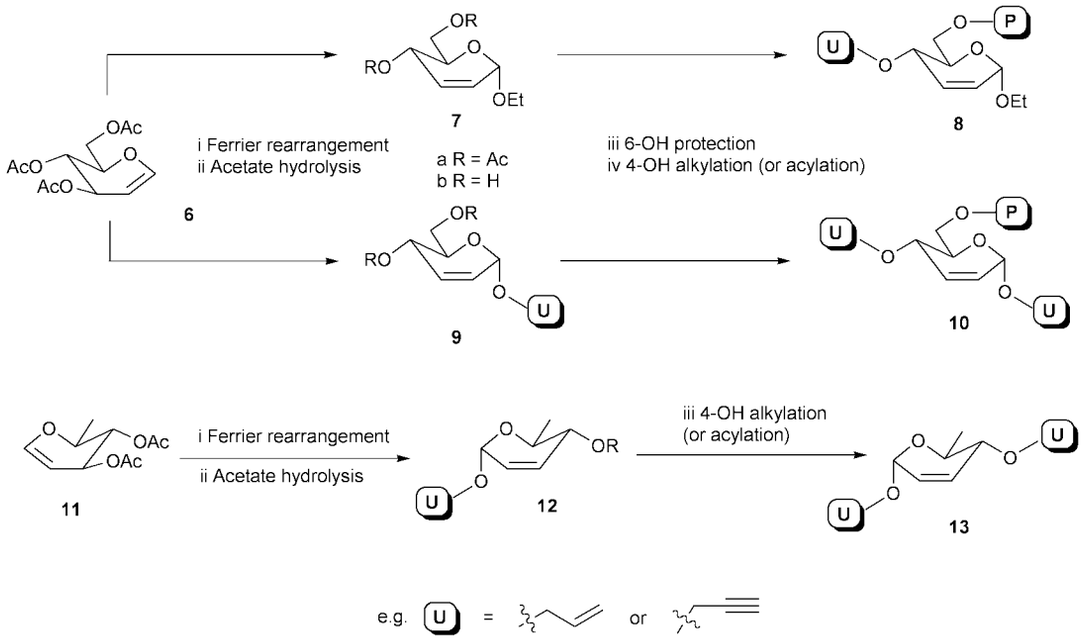
## Results and discussion

Substrates for mono-cyclisation **8**, **9a** were prepared previously by Ferrier rearrangement[16] of tri-*O*-acetyl-D-glucal **6**, deacetylation, protection of the 6-hydroxy group **7b** and functionalisation of the 4-hydroxy group **8** (Scheme 2).[5] This seemingly straightforward sequence was stymied by poor yields in the selective protection of the 6-hydroxy group **7b** and more importantly, complex mixtures of products were produced during allylation or propargylation of the 4-hydroxy group **8** (propargyl = prop-2-ynyl). These precedents did not augur well for extension to the tricyclisation substrates **10**. Consequently, we elected to use the more expensive di-*O*-acetyl-6-deoxy-L-glucal **11** for much of the current work. This has the added bonus that in the $^1$H-NMR spectrum of the intermediates and cyclisation products, the doublet for the 6-methyl group appears at a chemical shift which is well removed from other diagnostic signals, and hence acts as an unambiguous origin for assignment of $^1$H–$^1$H-*J* COSY NMR data. Conversely, the absence of the 6-methylene group protons from the downfield region abolishes the possibility of overlap with other signals. Large amounts of intermediates from the prior work with

† For Part 1, see ref. 5.
‡ The full experimental and spectroscopic data for D-series compounds are available as supplementary data. For direct electronic access see http://www.rsc.org/suppdata/p1/b0/b000662i/ (this includes the following compounds in order of appearance: **15a**, **15b**, **16**, **17a**, **18a**, **17b**, **18b**, **24b**, **24c**, **24d**, **24e**, **25**, **26**, **27a**, **28a**, **46a**, **46b**, **48**, **49a**, **49b** and tabular data for **43**, **53a**, **53b**).

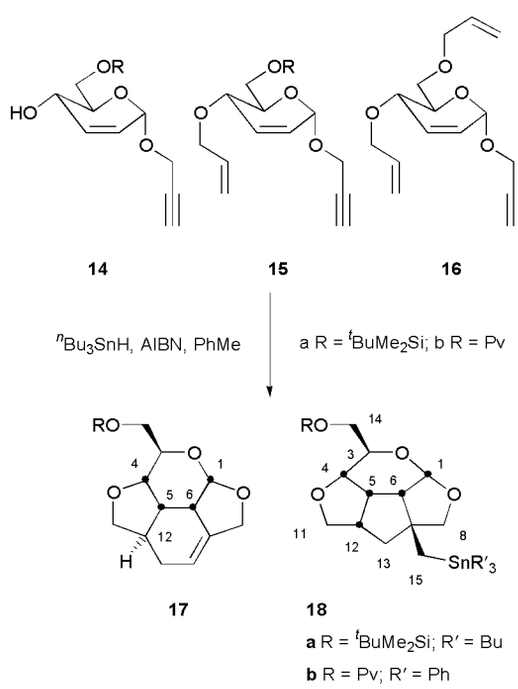



**Scheme 1**




**Scheme 2**

6-substituted D-sugars had accumulated and hence reactions were run using this material (referred to as the D-series) as well as the new intermediates (referred to as the L-series). The experimental conditions and spectroscopic data for the D-series compounds can be found in the electronic supplementary data for this paper.




### 4-*O*-Allyl-1-*O*-propargyl cyclisations

Allylation of the 6-*O*-TBDMS **14a** and 6-*O*-pivaloyl **14b** derivatives with sodium hydride and allyl iodide gave a mixture of starting material (**14a**, 33%; **14b** 14%), the desired 4-*O*-allyl ethers (**15a** 41%; **15b** 28%) and the 4,6-di-*O*-allyl ether **16** (3% yield in both cases).

Treatment of the 6-*O*-TBDMS derivative **15a** with TBTH in refluxing toluene (syringe pump addition over 3.5 hours) gave a crude reaction mixture containing two major products **17a**, **18a** (ratio 66 : 33), which were separated by column chromatography (23%, 15% yields respectively of analytically pure material). The faster running component **18a** contained a tri-*n*-butylstannyl group and no alkenic signals. The lowest field signal ($\delta$ 5.37, d, $J$ 7.5 Hz) was assigned to 1-H and a coupling pathway was observed from this to 6-H and on to 5-H, however further extension of the pathway was hindered by signal overlap. The slower running component **17a** contained no tri-*n*-butylstannyl group, but a single alkene signal ($\delta$ 6.02, br d, $J$ 6.7 Hz). The next lowest field signal was assigned to 1-H ($\delta$ 5.47, d, $J$ 5.5 Hz), which was coupled to a broad hump (6-H). Signal overlap (11a-H/15a-H, 3-H/15b-H, 5-H/13a-H) precluded rigorous assignment of the key coupling constants ($^{3}J_{4,5}$, $^{3}J_{5,6}$, $^{3}J_{5,12}$) which were required to define the stereochemistry of the ring fusion. Signals at $\delta$ 1.92 (1H, app qdd = ddddd, $J$ 11.8, 11.8, 11.8, 6.4, 2.6 Hz) and $\delta$ 1.81 (1H, br tm, $J$ *ca.* 13 Hz) were provisionally assigned to 12-H and *exo*-13-H respectively. The large coupling vicinal couplings indicate that 12-H is located on the *endo*-face *anti*-periplanar to *exo*-11-H and *exo*-13-H. In summary, the NMR data of the two products **17a**, **18a** were clearly in accord with the gross structures, but were insufficient to unambiguously assign the complete stereochemistry. With this in mind the 6-*O*-pivalate **15b** was treated with triphenyltin hydride with the expectation that the products **17b**, **18b** would be easier to purify and the phenyl groups might selectively deshield the protons on the *exo*-face of the tetracycle **18b** which would facilitate interpretation of $^{1}$H-NMR spectra. Unfortunately, the isolated yields of the products **17b** (9.6%), **18b** (4% yield) were extremely low and they were only characterised by $^{1}$H-NMR. The $^{1}$H-NMR spectrum of the stannane **18b** in $CDCl_3$ had too many overlapped signals to be useful, however the spectrum in $C_6D_6$ gave distinct signals for virtually all protons. This data is discussed later and compared with that of the L-series.

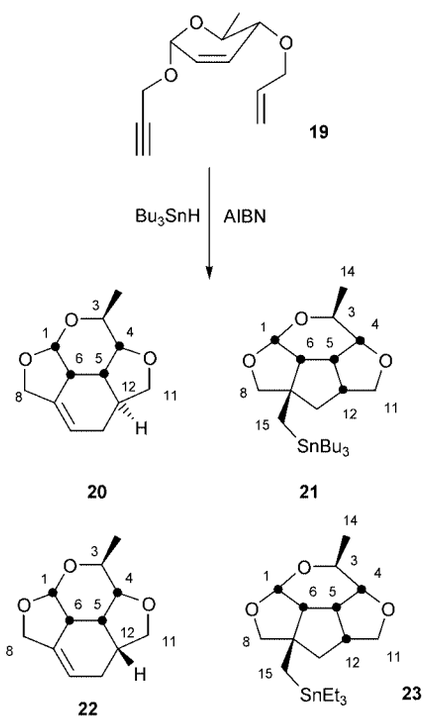
The L-series 4-*O*-allyl-1-*O*-propargyl sugar **19** was prepared by the standard sequence of Ferrier rearrangement (68%), alkaline deacetylation (63%) and allylation (21% yield). Treatment with TBTH under the standard slow addition conditions gave a remarkably clean crude reaction mixture consisting of two products **20**, **21**; in the ratio 56 : 44 by $^{1}$H-NMR measurement of the integration of the anomeric proton signals. Column chromatography afforded analytically pure samples of the fast running stannane **21** (17% yield) and the slower alkene **20** (43% yield).

The $^{1}$H-NMR spectrum of the alkene **20** in either $CDCl_3$ or $C_6D_6$ was mostly well dispersed, except for the high field region

**Table 1** Comparison of averaged measured $^1$H-NMR coupling constants for **20** ($CDCl_3$) and calculated coupling constants for **22**

| | | Calculated values for **20**[a] | | Calculated values for **22**[b] | |
|---|---|---|---|---|---|
| *x*,*y* | Actual $^3J_{x,y}$/Hz | $^3J_{x,y}$/Hz | ∠*l*/° | $^3J_{x,y}$/Hz | ∠*l*/° |
| 1,6 | 6.3 | 7.4 | 2 | 6.2 | 25 |
| 5,6 | — | 11.3 | 5 | 4.9 | 48 |
| 4,5 | 7.5 | 7.1 | 35 | 7.8 | 18 |
| 3,4 | 6.1 | 9.0 | 179 | 7.6 | 155 |
| 5,12 | — | 12.7 | 177 | 10.7 | 6 |
| *endo*-11,12 | 6.2 | 5.8 | 49 | 1.4 | 93 |
| *exo*-11,12 | 11.1 | 11.7 | 173 | 6.2 | 30 |
| 12,*endo*-13 | — | 2.5 | 65 | 1.2 | 77 |
| 12,*exo*-13 | — | 12.1 | 172 | 6.3 | 39 |
| *endo*-13,14 | 6.9 | 6.2 | 19 | 6.2 | 17 |
| *exo*-13,14 | <1.5 | 3.1 | 103 | 2.8 | 97 |

[a] **20** MMX energy 200.3 kJ mol$^{-1}$. Average absolute coupling constant error 1.1 Hz. Above average errors $\Delta^3J_{3,4}$ −2.9, $\Delta^3J_{exo\text{-}13,14}$ −1.6 Hz. [b] **22** MMX energy 159.6 kJ mol$^{-1}$. Average absolute coupling constant error 1.9 Hz. Above average errors $\Delta^3J_{endo\text{-}11,12}$ −4.8, $\Delta^3J_{exo\text{-}11,12}$ −4.9 Hz.




containing protons (5-H, 12-H) attached to the newly formed stereocentres. 6-H was a broad featureless hump. Overlapping signals for 3-H in deuteriochloroform and 4-H in benzene-$d_6$ both with 11a-H rendered coupling constant calculations less accurate than usual. However it was possible to estimate that in both solvents $^3J_{4,5}$ was *ca.* 7.2 Hz and $^3J_{1,6}$ was *ca.* 6.5 Hz. These values are consistent with *cis*-ring fusions and small dihedral angles between the bridgehead protons. The only evidence that could be gleaned about 12-H was deduced from the two 11-H protons which were separated by 0.5 ppm ($\delta$ 3.87 dd, *J* 6.8, 6.2 Hz; $\delta$ 3.37, dd, *J* 11.1, 7.2 Hz). The geminal coupling constant (7.0 Hz) is less than is seen with the geminal H-8 pair (10.6 Hz), whereas the larger vicinal coupling constant (11.1 Hz) indicates an antiperiplanar relationship between H-11b and H-12. This information is insufficient to determine the stereochemistry of the 5,12 ring fusion without an unambiguous assignment of the two H-11 protons. However, molecular modelling of the C-12 epimers **20**, **22** with coupling constant calculations (Table 1) yielded $^3J_{11,12}$ values of 1.4 and 6.2 Hz for the *exo*-12-H epimer **22** and 5.8, 11.7 Hz for the *endo*-12-H epimer **20**. The latter calculations are in excellent agreement with the observed values

**Table 2** Comparison of consensus $^1$H-NMR coupling constants for **18a**,**b**, **21** and calculated coupling constants for **23**

| | | Calculated | |
|---|---|---|---|
| *x*,*y* | Actual $J_{x,y}$/Hz | $J_{x,y}$/Hz | ∠*l*/° |
| 1,6 | 7.9 | 6.8 | 16 |
| 5,6 | 9.6 | 11.3 | 2 |
| 4,5 | 9.4 | 9.4 | 6 |
| 3,4 | 9.3 | 7.7 | 155 |
| 3,14 **21** only | 6.4 | — | — |
| 5,12 | 9.5 | 8.2 | 29 |
| *endo*-11,12 | 1.8 | 0.90 | 82 |
| *exo*-11,12 | 5.7 | 4.6 | 40 |

[a] MMX energy 191.1 kJ mol$^{-1}$. Average absolute coupling constant error 1.1 Hz. Coupling constants with above average errors $^3J_{5,6}$ −1.7 Hz, $^3J_{3,4}$ −1.6 Hz and $^3J_{5,12}$ 1.3 Hz.

(*J* 6.2, 11.1 Hz) and corroborate the assignments of 12-H and *exo*-13-H made for the 14-*O*-silyl derivative **17a**.

Prolonged randomisation of **20** gave a slightly more stable conformer (198.7 kJ mol$^{-1}$) with the pyran ring in a boat conformation with 15-C axial. The coupling constants of protons attached to the pyran ring were $^3J_{3,4}$ 4.3 (129°), $^3J_{4,5}$ 6.4 (40°), $^3J_{5,6}$ 10.3 (18°), $^3J_{1,6}$ 4.9 (37°), but those away from the pyran ring were barely changed. Partial population of this conformer acts to reduce $^3J_{3,4}$ which may explain the low value of the observed coupling constant relative to the calculated value.

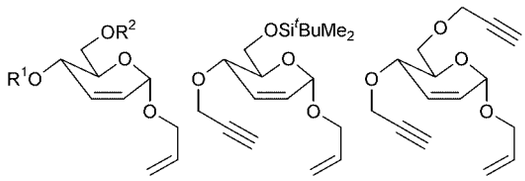
The stereochemistry of the stannanes **18a**,**b**, **21** was anticipated to be easier to assign because the smaller rings ensure that *cis*-ring fusions are much more favourable than *trans*. $^1$H-NMR spectra run in both $CDCl_3$ and $C_6D_6$ enabled deduction of the majority of the coupling constants. 1-H and 6-H appeared as distinct signals in all six spectra and 5-H in five spectra. Hence $^3J_{1,6}$ and $^3J_{5,6}$ can be reliably estimated, whereas other signals such as 3-H, 4-H and 11-$H_2$ only appeared as distinct signals in a few spectra. The span of "equivalent" coupling constants of the three stannanes **18a**,**b**, **21** was typically <1.2 Hz. Consequently, Table 2 reports consensus values taken from the whole data set of six spectra. The structure of the stannane **21** was modelled by molecular mechanics using the triethylstannyl analogue **23**.

The comparatively large vicinal couplings indicate that (with the exception of 3-H, 4-H) the vicinal protons are close to eclipsed with each other as found in the modelling study. 12-H appeared as a very broad signal from which no coupling constant data could be obtained. However the signal for 5-H appeared as an apparent quartet (ddd, *J* 9.4–9.6 Hz) and hence $^3J_{5,12}$ is *ca.* 9.5 Hz. Again this is consistent with an eclipsed conformation for 5-H and 6-H. The small coupling constants for $^3J_{endo\text{-}11,12}$ and $^3J_{exo\text{-}11,12}$ indicate an *exo*-envelope conformer for tetrahydrofuran ring D. The molecular mechanics model indicated that the pyran ring was a flattened half boat (sofa) with 3-C to 6-C in a plane (dihedral angle, 3-C–4-C–5-C–6-C 1°) and 1-H in a pseudo-axial position.

### 1-*O*-Allyl-4-*O*-propargyl cyclisation

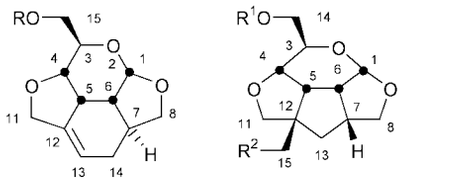
The cyclisation of the 1-*O*-allyl-4-*O*-propargyl substrates is subtly different to that of the 4-*O*-allyl-1-*O*-propargyl cyclisations. The initial vinyl radical cyclisation occurs from a substituent in the equatorial position and the second cyclisation occurs on to an axial allyl ether. The converse is true for the 4-*O*-allyl-1-*O*-propargyl cyclisations.

The requisite D-series allyl propargyl cyclisation precursor **25** was prepared by a sequence parallel to those reported previously. Deacetylation under basic conditions gave an excellent yield of the diol **24b** (93%), but silylation gave a poor yield of the 6-*O*-silyl ether **24c** (25%) accompanied by the 4,6-di-*O*-silyl ether **24d** (0.4% yield) and on one occasion the 6-*O*-acetyl-4-*O*-



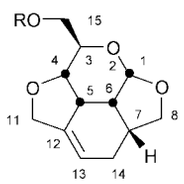
**24** **25** **26**

**a** $R^1 = R^2 = Ac$
**b** $R^1 = R^2 = H$
**c** $R^1 = H$, $R^2 = Si^tBuMe_2$
**d** $R^1 = R^2 = Si^tBuMe_2$
**e** $R^1 = Si^tBuMe_2$ $R^2 = Ac$



**27**
**a** $R = {}^tBuMe_2Si$
**b** R = Me

**28**
**a** $R^1 = {}^tBuMe_2Si$, $R^2 = Bu_3Sn$
**b** $R^1$ = Me, $R^2 = Me_3Sn$



**29**
**a** $R = {}^tBuMe_2Si$
**b** R = Me

silyl ether **24e** (2.7% yield), presumably due to incomplete deacetylation in the previous step. Curiously, the 4,6-di-*O*-silyl ether **24d** was isolated as a 50 : 50 mixture of anomers, although all of the other products were single anomers. Propargylation with sodium hydride and propargyl iodide gave the desired 4-*O*-propargyl ether **25** (44%) accompanied as before, by the 4,6-di-*O*-propargyl ether **26** (9%) and starting material **24c** (19% yield).

Treatment of the 4-*O*-propargyl ether **25** with TBTH under the standard cyclisation conditions gave as before a mixture of the fast running stannane **28a** and the slower running alkene **27a**. The latter overlapped with the starting material **25** by TLC and so extra portions of TBTH and AIBN were added to ensure maximum conversion and aid purification. The ratio of products **27a** : **28a** was 50 : 50 from the integration of the anomeric protons in the $^1$H-NMR spectrum ($\delta$ 5.40, d, $J$ 6.0 Hz; $\delta$ 5.37, d, $J$ 7.0 Hz). The removal of the extra tin residues prolonged purification by column chromatography and this is reflected in the low yields of isolated compounds (**27a**, 18%; **28a**, 8% yield).

In the $^1$H-NMR spectrum of the alkene **27a** all protons gave discrete signals except for the key bridgehead proton 7-H, and *exo*-14-H. The key coupling constants were $^3J_{1,6}$ 6.2, $^3J_{3,4}$ 9.9, $^3J_{4,5}$ 9.8, $^3J_{5,6}$ 9.8, $^3J_{6,7}$ 12.6, $^3J_{7,endo\text{-}8}$ 6.0 and $^3J_{7,exo\text{-}8}$ 10.7 Hz. As noted previously, the large coupling constants indicate that with the exception of 3-H and 4-H all the protons on the pyran ring are virtually eclipsed with their vicinal neighbours. The key unexpected observation was the huge coupling constant for $^3J_{6,7}$ which could not be observed in the tetracycles **17a**, **b**, **20** derived from the 4-*O*-allyl-1-*O*-propargyl substrates **15a**, **b**, **19**. The values for $^3J_{7,endo\text{-}8}$ and $^3J_{7,exo\text{-}8}$ are similar to those observed for $^3J_{endo\text{-}11,12}$ and $^3J_{exo\text{-}11,12}$ which are comparable protons in the regioisomeric tetracyclic alkene **20** ($J$ 6.2 and 11.1 Hz).

Firstly, we attempted to identify the 7-H signal which overlaps with that of *exo*-14-H by using $^1$H–$^1$H decoupling experiments. Irradiation of the alkenic proton (13-H, $\delta$ 5.93) removed the fine couplings in 5-H to give a clean apparent triplet (dd, $J$ 9.7, 9.7 Hz) due to $^3J_{4,5}$ and $^3J_{5,6}$. The signal for *endo*-14-H became a doublet (12.3 Hz) due to geminal coupling alone. There was no apparent change in the 7-H, *exo*-14-H multiplet which reflects the low value for $^3J_{13,exo\text{-}14}$. Irradiation of *exo*-8-H ($\delta$ 3.279) reduced *endo*-8-H to an apparent triplet, due to insufficient coupling power to completely remove the large geminal coupling. There was a small change in the 7-H, *exo*-14-H multiplet, but this was insufficient to deduce a coupling pattern. Similarly irradiation of the signal for *endo*-14-H ($\delta$ 2.357) strongly changed the shape of the multiplet, but no coupling features could be seen. In summary these results confirmed the couplings seen previously, but did not reveal any new coupling constant data from the 7-H, *exo*-14-H multiplet. In a further attempt to unravel the multiplet, a *pseudo*-INDOR (internuclear double organic resonance), spin tickling experiment was performed. In this experiment individual lines of a signal are irradiated and only those transitions connected to the irradiated transition are observed as "tickling doublets". Irradiation of the four lines of *exo*-8-H ($\delta$ 3.24) enabled the coupling to *endo*-8-H to be clearly seen and the values averaged across the four spectra were 7.6 Hz, which is the same as that measured in the non-irradiated spectra. The signals for 7-H were very broad and noisy, but enabled $^3J_{7,exo\text{-}8}$ to be estimated as *ca.* 10 Hz. This is in broad agreement with the value measured from the signal for *exo*-8-H (10.7 Hz). *endo*-14-H has a small or zero coupling with 7-H hence irradiation should give signals exclusively for *exo*-14-H. Irradiation of the four lines of the signal for *endo*-14-H ($\delta$ 2.38) gave a series of noisy doublets with an average separation of 12.2 Hz, which again is in agreement with the value measured (12.3 Hz) from the non-irradiated spectra.

It was clear at this stage that coupling constant information alone would be insufficient to unambiguously assign the stereochemistry of the 6,7-fusion. The two structures **27a**, **29a** considered, place 7-H either on the *endo*-face of the ring system or the *exo*-face respectively. Thus NOE experiments should be capable of defining its position. A comprehensive series of irradiations was made, but two key observations were that irradiation of 3-H caused a 21% enhancement of the 7-H, *exo*-14-H multiplet and irradiation of *exo*-8-H caused no enhancement of this multiplet. This is only possible if 7-H is on the *endo*-face and hence establishes the structure is assigned as **27a**. This was confirmed by a molecular mechanics study of models of the two epimers **27b**, **29b** and calculation of the coupling constants (Table 3).

The $^1$H-NMR spectra of the stannane **28a** in $CDCl_3$ was severely congested in the region $\delta$ 3.5 to 4.0 with 3-H, 4-H, 8-$H_2$ and 14-$H_2$ forming a complex multiplet; however in $C_6D_6$ most of the signals were discrete. The key coupling constants: $^3J_{1,6}$ 7.2, $^3J_{3,4}$ 8.6, $^3J_{4,5}$ 9.8, $^3J_{5,6}$ 9.9, $^3J_{6,7}$ 10.1 Hz (consensus values), were all large as seen previously and the connectivity was fully established by $^1$H–$^1$H $J$-COSY and $^{13}$C–$^1$H COSY spectra. These data are interpreted in greater detail in the discussion of the corresponding L-series compounds **32**.

The 1-*O*-allyl-4-*O*-propargyl sugar **30** was prepared by the usual sequence of Ferrier rearrangement (68%), alkaline deacetylation (92%) and propargylation (52% yield) and treated with TBTH. The $^1$H-NMR spectrum of the crude reaction mixture showed two compounds **31**, **32** in the ratio 58 : 42. Column chromatography afford three components (in order of elution) the bicycle **33** (6%), the tetracyclic stannane **32** (17%) and the tetracyclic alkene **31** (49% yield). The bicycle **33** was only characterised by $^1$H-NMR, however the key signals were identical to those of the D-series bicycle **34** and hence there is little doubt over the structure assigned. The bicycle **33** is the only partially cyclised product seen throughout the five propargyl allyl cyclis-

**Table 3** Comparison of averaged measured ($CDCl_3$) coupling constants for **27a** and calculated $^1$H-NMR coupling constants for **27b** and **29b**

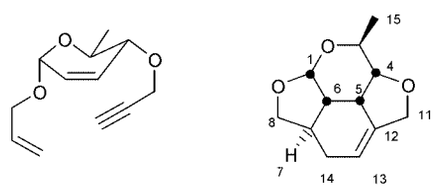
| | | **27b** (*trans*-6,7-)[a] | | **29b** (*cis*-6,7-)[b] | |
|---|---|---|---|---|---|
| *x*,*y* | Actual $^3J_{x,y}$/Hz | $^3J_{x,y}$/Hz | ∠/° | $^3J_{x,y}$/Hz | ∠/° |
| 1,6 | 6.2 | 6.2 | 24 | 7.2 | 9 |
| 6,7 | 12.6 | 12.9 | 176 | 9.6 | 22 |
| 5,6 | 9.8 | 9.9 | 21 | 9.9 | 21 |
| 4,5 | 9.8 | 8.7 | 21 | 5.8 | 44 |
| 7,*endo*-14 | <1 | 2.8 | 63 | 7.4 | 137 |
| 7,*exo*-14 | — | 12.3 | 175 | 9.3 | 20 |
| 7,*endo*-8 | 6.0 | 6.0 | 48 | 1 | 85 |
| 7,*exo*-8 | 10.7 | 11.7 | 172 | 5.1 | 37 |
| 13,*endo*-14 | 8.3 | 6.0 | 24 | 3.5 | 61 |
| 13,*exo*-14 | 1.4 | 2.7 | 98 | 4.1 | 52 |
| 3,4 | 10 | 9.4 | 175 | 9.4 | 175 |

[a] **27b** MMX energy 198.7 kJ mol$^{-1}$. Average absolute coupling constant error 0.8 Hz. Errors >2 × average $\Delta^3J_{7,endo\text{-}14}$ −1.8, $\Delta^3J_{13,endo\text{-}14}$ +2.3 Hz. [b] **29b** MMX energy 195.8 kJ mol$^{-1}$. Average absolute coupling constant error 3.3 Hz. Maximum error $\Delta^3J_{7,endo\text{-}14}$ −6.3 Hz.

**Table 4** Comparison of averaged measured coupling constants for **28a** in $CDCl_3$ and calculated $^1$H-NMR coupling constants for **28b** (coupling constants shown in brackets were measured in $C_6D_6$)

| | | $^4C_1$ chair conformer[a] | | Boat conformer[a] | |
|---|---|---|---|---|---|
| *x*,*y* | Actual $^3J_{x,y}$/Hz | $^3J_{x,y}$/Hz | ∠/° | $^3J_{x,y}$/Hz | ∠/° |
| 1,6 | 7.0 (7.3) | 7.2 | 10 | 7.1 | 12 |
| 3,4 | (8.6) | 7.9 | 154 | 1.2 | 74 |
| 4,5 | 9.8 (9.8) | 9.1 | 0 | 8.7 | 10 |
| 5,6 | 10 (9.8) | 10.8 | 12 | 11.3 | 6 |
| 6,7 | 10.1 | 10.4 | 15 | 8.1 | 31 |
| 7,*exo*-13 | — | 6.5 | 39 | 5.9 | 43 |
| 7,*endo*-13 | — | 10.8 | 157 | 11.6 | 164 |
| 7,*endo*-8 | (1.9) | 1.1 | 89 | 0.96 | 85 |
| 7,*exo*-8 | (6.4) | 5.6 | 33 | 5.1 | 37 |
| 3,14a | (1.9) | 0.7 | 63 | 1.7 | 74 |
| 3,14b | (4.7) | 3.3 | 55 | 2.5 | 44 |

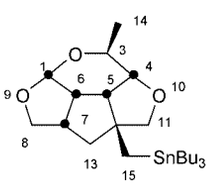
[a] $^4C_1$ chair MMX energy 186.6 kJ mol$^{-1}$; boat MMX energy 188.2 kJ mol$^{-1}$. Average absolute coupling constant error for $^4C_1$ chair conformer 0.7 Hz. Maximum error $\Delta^3J_{3\text{-}H,14b\text{-}H}$ 1.5 Hz.



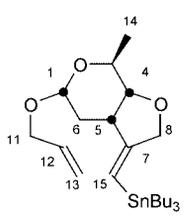
**30**



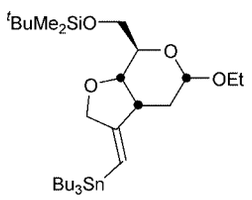
**31**



**32**



**33**



**34**

ations in the current work, however an analogous product was isolated by Marco-Contelles in a 1-*O*-allyl-4-*O*-propargyl cyclisation in the D-series.[6]

The spectroscopic data for the alkene **31** were, as expected, similar to those of the D-series silyl derivative **27a**. However in the $^1$H-NMR spectrum in $C_6D_6$, *exo*-14-H was identified as a discrete signal for the first time. The apparent broadened triplet could not be analysed accurately, however the couplings $^2J_{14,14}$ 12.1 Hz and $^3J_{13,exo\text{-}14}$ 1.4 Hz observed in other signals enable the residual bandwidth to be assigned to $^3J_{7,exo\text{-}14}$ *ca.* 10 Hz. This is further evidence for 7-H being located on the *endo*-face.

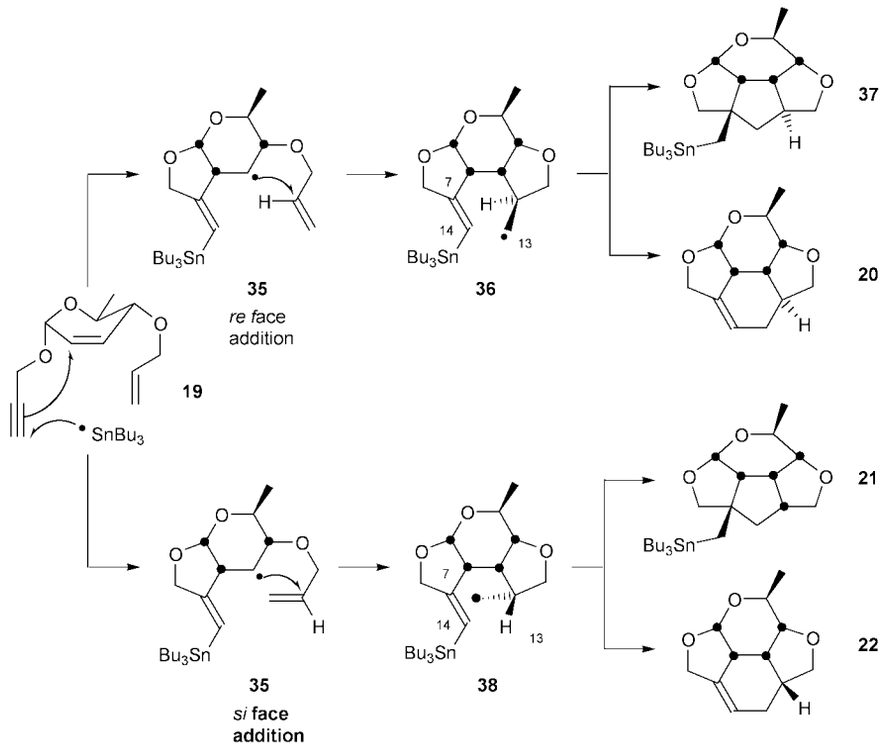
The $^1$H-NMR data of the stannane **32** were also very similar ($^3J_{1,6}$ 7.7, $^3J_{3,4}$ 9.0, $^3J_{4,5}$ 9.5, $^3J_{5,6}$ 9.6, $^3J_{6,7}$ 10.2 Hz, $C_6D_6$) to that of the D-series analogue **28a**. This gave some assurance that the measured values were correct, given that the key coupling constant values were mostly only measurable in one of the signals in each spectrum. Molecular modelling using the 15-*O*-methyl analogue **28b** yielded two distinct conformers (Table 4). A conformer with an equatorial methoxymethyl group was the most stable (186.6 kJ mol$^{-1}$), but surprisingly a conformer with an axial methoxymethyl group had a similar energy (188.3 kJ mol$^{-1}$). This was discarded as a viable possibility because the predicted value for $^3J_{3\text{-}H,4\text{-}H}$ was grossly in error. The calculated vicinal coupling constants for the conformer with an equatorial methoxymethyl group were in excellent agreement, with a maximum error of 1.5 Hz ($^3J_{3\text{-}H,14b\text{-}H}$) and an average absolute error of 0.7 Hz.

### Conformational analysis of alkyne–alkene–alkene cyclisations

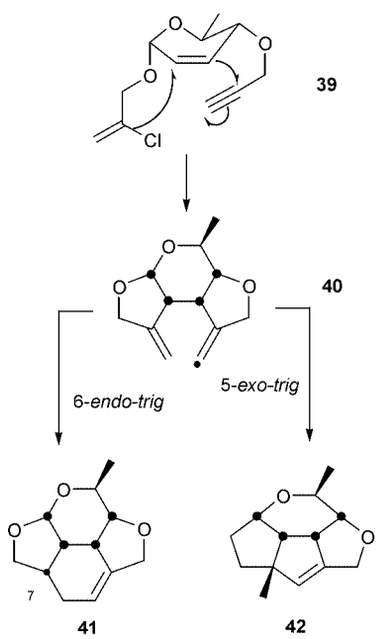
Concomitant formation of the alkenes **17a**,**b**, **20**, **27a**, **31** and the stannanes **18a**,**b**, **21, 28a**, **32** is a consequence of a lack of diastereofacial selectivity in the second cyclisation. This is illustrated by the 1-*O*-propargyl-4-*O*-allyl L-series substrate **19**. Addition of tri-*n*-butyltin radical to the alkyne gives exclusively the (*Z*)-alkene **35** (Scheme 3). Addition of the pyranyl radical to the *re*-face of the alkene rotomer **35** gives an *exo*-alkyl radical **36** which attacks the vinylstannane moiety on the *si*-face of 14-C to give the addition-elimination product **20** *via* a 6-*endo*-*trig* cyclisation. The 5-*exo*-*trig* cyclisation which results in a strained *trans*-bicyclo[3.3.0]octane moiety **37** is disfavoured because the radical centre 13-C is located directly above 14-C in a position perpendicular to a plane containing the alkene bond. Appreciable distortion is required to place it in a comparable position relative to 7-C. Conversely, attack of the *si*-face of the alkene rotamer **35** gives the *endo*-alkyl radical **38** which undergoes addition to the *si*-face of 7-C (5-*exo*-*trig* cyclisation) to give an α-stannyl radical. This abstracts hydrogen from TBTH to give the stannane **21**. The *endo*-alkyl radical **38** is ideally placed to attack 7-C, but not 14-C.

The *si*-face addition could probably be made less favourable by substitution at the terminus of the alkene, but this would also probably slow the rate of the final cyclisation. We reasoned that the if the radical cascade could be initiated by cleavage of the chloro substituent **39**, the vinyl radical **40** formed in the second cyclisation should preferentially undergo 6-*endo*-*trig* cyclisation to give a radical which would be captured by tin hydride on the outer face to give the tetracycle **42** (Scheme 4). This compound is epimeric at 7-C to the products isolated previously **31** (*cf.* **27a**,**b**). A previous successful monocyclisation of a chloropropenyl substituent (50% yield), augured well for this proposal, albeit that the cyclisation requires stoichiometric amounts of the tin hydride reagent.[5]

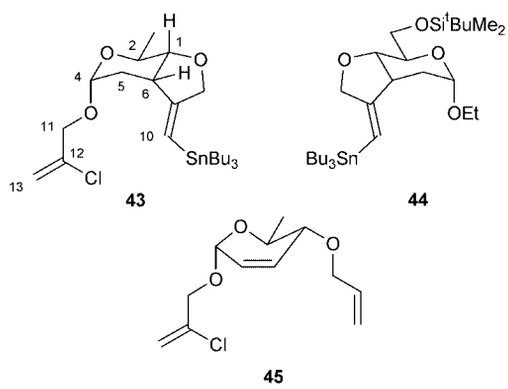
Treatment with TBTH yielded a single major product **43** which was isolated by column chromatography (42% yield). The $^1$H-NMR spectrum of the product contained the signals for an intact chloropropenyl group (δ 5.37, d, *J* 1.2 Hz; 5.25, s) and an




**Scheme 3**




**Scheme 4**



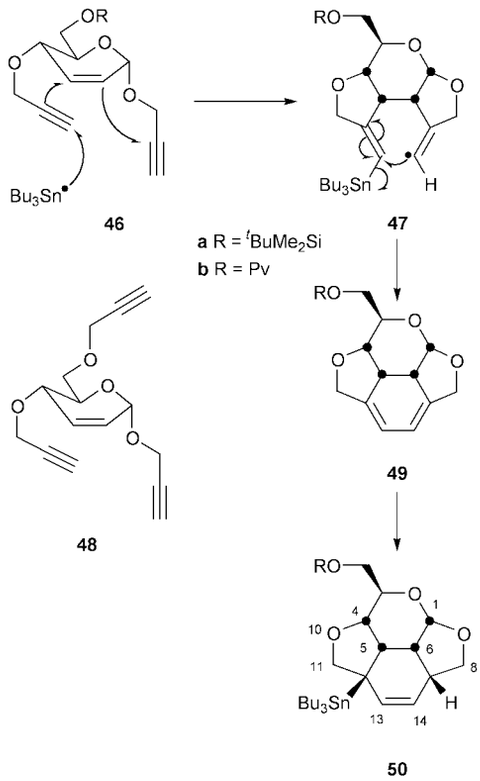

acetylenic proton was absent. The lowest field signal ($\delta$ 5.78, dm, $J$ 2.0, <1 Hz) showed a large coupling to tin ($^2J_{Sn,H}$ 56.3 Hz) indicating a vinylstannane. This signal and much of the remainder of the spectrum was very similar to that of the product **44** formed by cyclisation of a 1-*O*-ethyl-4-*O*-propargyl D-series sugar. In particular the coupling constants of the signals due to 1-H, 6-H, 5-$H_2$ and 4-H were virtually identical. Clearly, this product is formed by hydrostannylation and reduction of the pyranyl radical before the second cyclisation. The presence of the chloro substituent renders this cyclisation less favourable than the corresponding alkene due to both steric and electronic factors; moreover it is notable that the two cases in which the second cyclisation failed both involve additions from the pyranyl ring to axial 1-*O*-allyl substituents (*cf.* **39**). The chloropropenyl compounds **39**, **43** and their precursors are unstable materials which polymerise upon standing at room temperature. The 1-*O*-chloropropenyl-4-*O*-propenyl derivative **45** was prepared, but decomposed before cyclisation could be attempted.

### 1,4-Di-*O*-propargyl cyclisations

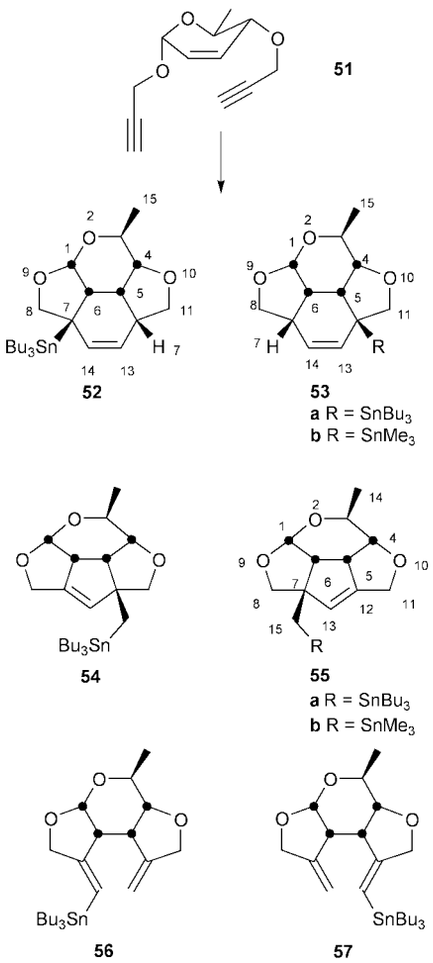
The 1,4-di-*O*-propargyl substrates **46a**,**b** were conceived as a means to avoid the stereochemical ambiguities of the second cyclisation (*cf.* **35**→**36**) and to probe the feasibility of a 6-(π-*endo*)-*endo*-*trig* cyclisation. One disadvantage of these substrates is that addition of the tin radical will be regiorandom. In principle, both radical adducts can give the same product **50**, but the two tricyclisation pathways have different stereochemical constraints dictated by the conformation of the pyran ring.

The 4-*O*-propargyl-6-*O*-silyl substrate **46a** was prepared by treatment with of the alcohol **14a** with sodium hydride and propargyl bromide (Scheme 5). As in previous cases, the product **46a** was isolated in low yield (12%), together with starting material **14a** (16%) and a mixture of both (21% yield). The 4-*O*-propargyl-6-*O*-pivalate **46b** was prepared by identical means in fair yield (41%), but was accompanied by starting material **14a** (10%) and the trialkyne **48** (19% yield).

The 6-*O*-silyl **46a** and 6-*O*-pivaloyl **46b** dialkynes were treated with TBTH under the standard slow addition condi-




**Scheme 5**




tions. In each case a complex mixture of products was formed, but only one component **50a**,**b** was isolated in each case, in very low yield (6%) and characterised by $^1$H-NMR. Other products were clearly present, but could not be purified sufficiently to assign structures. The poor yields did not encourage pursuit of these compounds and as previously we turned to the corresponding L-series analogues, which were easier to prepare and had inherently less complex NMR spectra.

The dialkyne **51** was treated with TBTH using the standard slow addition conditions. The $^1$H-NMR spectrum of the crude reaction mixture indicated the absence of starting material and a complex mixture of products. Approximately 50% of the mixture consisted of a 60 : 40 mixture of the cyclohexenylstannane **53a** and the cyclopentenylmethylstannane **57**. Amongst the remainder of the material was a third component (approx 20%) which is probably a mixture of partially cyclised isomers **56**, **57** and the cyclopentenylmethylstannane isomer **54**. Column chromatography yielded the cyclohexenylstannane **53a** (12%), the cyclopentenylmethyl stannane **55a** (7%) and a trace of partially cyclised material **56/57** (3%). The NMR spectra of the cyclohexenylstannane **53a** had obvious similarities to those of the D-series compounds **50b**,**c**. The assignment of the latter was made on the basis of the rigorous assignment of the former.

The connectivity of the carbon framework of the cyclohexenylstannane **53a** was inferred from $^1$H–$^1$H-*J* COSY NMR experiments and vicinal pairs of protons were assigned from $^1$H–$^{13}$C-COSY experiments. Both of the alkenic protons ($\delta$ 5.82, 5.43) appeared as doublets of doublets (*ca.* 10.1 and 2.5 Hz). A $^1$H–$^1$H NOESY ($C_6D_6$) experiment indicated that the lower field signal was close to *exo*-11-H and the higher field signal to to *exo*-8-H, hence these are assigned to 13-H and 14-H respectively. 13-H is apparently deshielded by the vicinal tri-*n*-butylstannyl group. 1-H was assigned to a low field doublet ($\delta$ 5.50, d, *J* 7.1 Hz) which acts as the origin for $^1$H–$^1$H-*J* COSY assignments. This signal is coupled to a high field doublet of doublets of doublets ($\delta$ 3.01, *J* 11.2, 10.6, 6.9 Hz) which is assigned to 6-H. Clearly, this signal has three vicinal neighbours, which excludes the 7-tri-*n*-butylstannyl derivative **52**. 5-H only has two vicinal neighbours which suggests the tri-*n*-butylstannyl group is attached to 12-H. The presence of an "isolating group" at this position is also supported by the signals for 11-$H_2$ which only have a geminal coupling (*J* 8.4 Hz). 7-H was overlapped with other signals in both sets of spectra. The couplings deduced from other signals suggest that it should be a ddddd (32 lines), which with normal line broadening should reduce to an apparent dtt (18 lines, *J* 11.2, 8.5, 2.5 Hz). In benzene-$d_6$ the bandwidth was estimated to be 31 Hz (calculated 33 Hz) and five non-overlapped lines were reported in the peak list. These had separations of 11.1, 8.1 and 2.9 Hz (2, 3, 2 occurrences respectively), which is in good agreement with the proposed couplings. The structure was modelled using the trimethylstannyl analogue of **53a**. The annulated rings distort the pyran ring from the commonly observed $^4C_1$ conformation towards a flattened half boat (sofa) with 3-C to 6-C in an approximate plane (dihedral angle, 3-C–4-C–5-C–6-C 13°) and 1-H in a pseudo-axial position (dihedral angle, 1-H–1-C–6-C–7-C 138°). Only protons with internuclear distances of 2.46 Å or less gave cross peaks in the $^1$H–$^1$H NOESY spectrum, although the 3-H *endo*-8-H correlation could not be established unambiguously because of overlap of the signals for 3-H and *exo*-8-H.

The calculated coupling constants are in satisfactory agreement with those observed (Table 5, average absolute error 0.9 Hz). The larger than average error for $^3J_{5,6}$ (2.2 Hz) reflects the larger range of values observed for vicinal protons which are not adjacent to electronegative groups and hence the greater sensitivity to errors in estimating the dihedral angle and/or modelling the angular dependence.

$^1$H-NMR spectra of the cyclopentenylstannane **55a** in deuteriochloroform gave few useful coupling constant data, due to signal overlap, whereas spectra obtained in benzene-$d_6$ enabled measurement of virtually all the coupling constants. The two most downfield signals were a doublet due to 1-H

**Table 5** Comparison of averaged measured $^1$H-NMR coupling constants **53a** and calculated coupling constants for **53b**

| | | Calculated[a] | |
|---|---|---|---|
| *x*,*y* | Actual $^3J_{x,y}$/Hz | $^3J_{x,y}$/Hz | ∠/° |
| 1,6 | 6.9 | 6.1 | 26 |
| 5,6 | 10.6 | 8.4 | 30 |
| 4,5 | 9.7 | 9.2 | 9 |
| 3,4 | 9.7 | 8.9 | 175 |
| 6,7 | 11.2 | 11.1 | 4 |
| 7,*exo*-8 | 8.4 | 9.0 | 24 |
| 7,*endo*-8 | 8.5 | 9.7 | 146 |
| 7,14 | 2.0 | 2.8 | 77 |

[a] MMX energy 161.5 kJ mol$^{-1}$. Average absolute coupling constant error 0.9 Hz. Larger than average errors $\Delta^3J_{5,6}$ −2.2 Hz, $^3J_{7,endo\text{-}8}$ −1.2 Hz.

**Table 6** Comparison of averaged measured $^1$H-NMR coupling constants for **55a** and calculated coupling constants for **55b**

| | | Calculated[a] | |
|---|---|---|---|
| *x*,*y* | Actual $J_{x,y}$/Hz | $J_{x,y}$/Hz | ∠/° |
| 1,6 | 7.3 | 6.7 | 18 |
| 5,6 | 8.4 | 8.5 | 29 |
| 4,5 | 7.8 | 5.8 | 44 |
| 3,4 | 9.4 | 8.7 | 169 |
| 3,14 | 6.3 | — | — |
| 8,8 | 9.2 | — | 109 |
| 11,11 | 13.4 | — | 111 |

[a] MMX energy 185.5 kJ mol$^{-1}$. Average absolute coupling constant error 0.9 Hz. Larger than average error $\Delta^3J_{4,5}$ 2.0 Hz.

($\delta$ 5.47, *J* 7.3 Hz) and a broadened singlet due to 13-H ($\delta$ 5.11). The connectivity of the pyran ring was inferred from $^1$H–$^1$H-*J* COSY experiments using 1-H as the origin. The couplings are reported in Table 5. There are clearly no substantial couplings between the protons on the pyran ring and 8-$H_2$, 11-$H_2$ and 13-$H_2$; however the $^1$H–$^1$H-*J* COSY experiment showed weak couplings between 13-H and 11-$H_2$ and 5-H. These correlations enable 8-$H_2$ to be distinguished from 11-$H_2$ and the structure to be assigned as **55a**. To confirm this result, the signal for 2-H was carefully examined, it showed no line broadening beyond that normally observed.

The cyclopentenyl tri-*n*-butylstannane **55a** was modelled as the trimethylstannyl analogue **55b** (final MMX energy 185.5 kJ mol$^{-1}$) and the calculated coupling constants are shown in Table 6. The calculated coupling constants are in good agreement with those observed (average absolute error 0.9 Hz). Only $^3J_{4,5}$ has a larger than average error (2.0 Hz).

A third fraction gave $^1$H-NMR spectra which indicated a mixture of components. The key observation was the presence of two high field doublets ($\delta$ 1.15, *J ca.* 6 Hz, 15-$H_3$?), which were both coupled with a multiplet at $\delta$ 3.2 (3-H?), which in turn was correlated with two similar doublets of doublets ($\delta$ 3.59, 3.69, dd *J* 9.5, 7.1, 4-H?). No further correlations were observed from these signals. A broad singlet ($\delta$ 6.0, br s, $^2J_{Sn,H}$) appeared at the correct shift for a proton attached to a 2,2-dialkylvinylstannane suggesting that partially cyclised products (*cf.* **44**) had been formed. There were no signals for alkynic protons ($\delta$ 2.0–2.5) suggesting that the tricyclic adducts **56**, **57** had been formed, however signals at the shift expected for the protons attached to a 1,1-dialkylalkene ($\delta$ 4.8–4.9) were absent. Other aspects of the data did not inspire facile interpretations and these assignments must be considered as highly tentative.

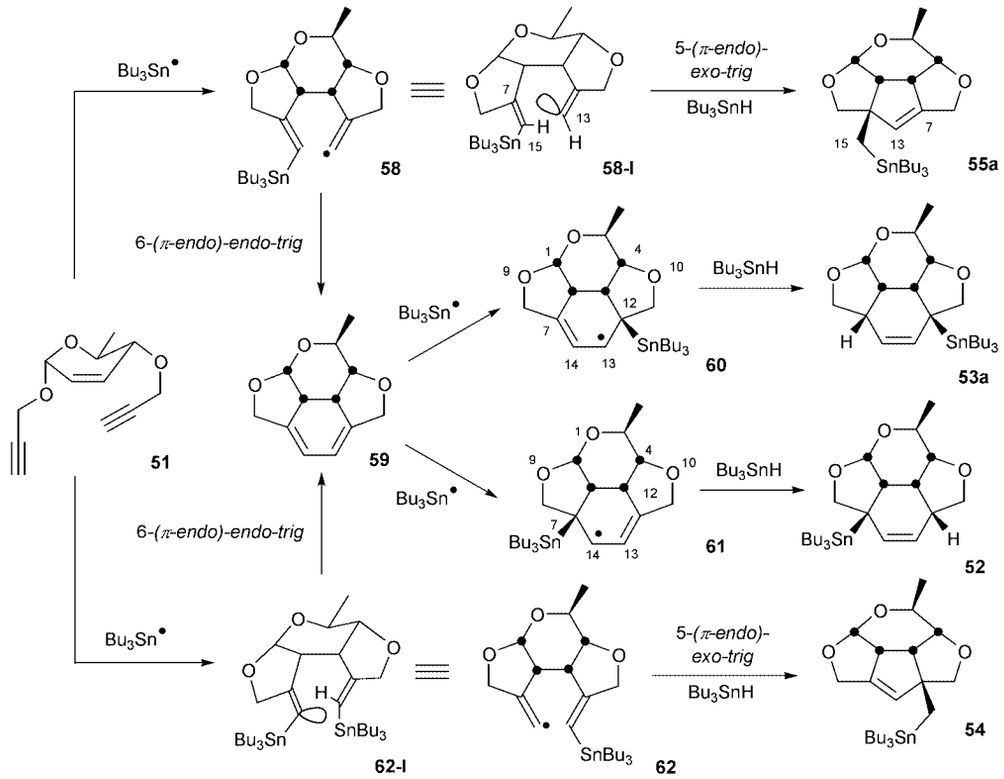
### Conformational analysis of alkyne–alkene–alkyne cyclisations

Although only low yields were achieved in the 1,4-di-*O*-propargyl cyclisations, analysis of the crude reaction mixture provides assurance that no major components have been overlooked. Prior experience with monocyclisations of 1-*O*-propargyl and 4-*O*-propargyl substituents had shown that both undergo cyclisation with comparable ease. We therefore anticipated that addition to either substituent of the dialkynes **46a**,**b**, **51** would yield at least bicyclic products. The structure of the cyclopentenylstannane **55a** provides unimpeachable evidence of its origins. Tri-*n*-butyltin radical addition to the 1-*O*-propargyl group, yields a vinyl radical which undergoes addition to the dihydropyran ring, the radical so formed then undergoes addition to the 4-*O*-propargyl substituent to give a vinyl radical **58**, which in turn undergoes 5-(π-*endo*)-*exo*-*trig* to the vinylstannane group to give an α-stannyl radical which reacts with TBTH (Scheme 6). The mode of cyclisation is explicable by postulating a flattened $^4C_1$ conformation for the pyran ring. Attack of the vinyl radical occurs perpendicular to 7-C of the 7,15-alkene bond **58-I**, whereas attack at C-15 requires an oblique trajectory. Conversely, addition of tri-*n*-butyltin radical to the 4-*O*-propargyl substituent and the subsequent annulation steps gives the vinyl radical **62**, which is ideally placed for 6-(π-*endo*)-*endo*-*trig* cyclisation to give the diene **59**. The cyclohexenylstannane **53a** presumably arises by 1,4-hydrostannylation of the diene **59**. This is by no means surprising, however the regioselectivity is extraordinary. This arises from differences in the stability of the allylic radicals **60**, **61**. If the 1-C–9-O bond is pseudo-axial and the 4-C–10-O bond is pseudo-equatorial, the allylic radical **60** can easily attain planarity. The alternative allylic radical **61** can attain planarity of 13-C and 14-C or 12-C and 13-C, but not both without severe distortion. Allylstannanes are stable to thermolysis (<100 °C) in non-polar solvents,[17] but undergo 1,3-allylic rearrangement in polar solvents[18] and in the presence of radical initiators and/or organotin radicals[19] to give the more stable isomer, in which the organotin moiety is attached to the less substituted terminus. Although, an example has been reported, in which tri-*n*-butyltin radical catalysed allylic rearrangement between two secondary centres was not observed.[20] Given the conditions of the tricyclisation reaction, it might be anticipated that the initially formed tertiary stannane **53a** would undergo 1,3-allylic rearrangement by an $S_H2'$ mechanism to give the secondary stannane **59**.

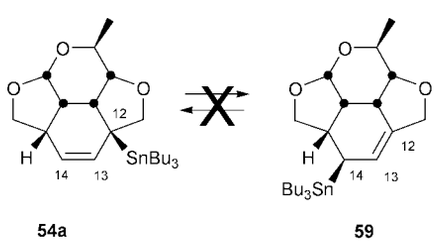
Rearrangement would likely proceed with retention of configuration, because the *endo*-face of the molecule is too hindered to accept an tri-*n*-butyltin radical. The absence of this process can be attributed to two factors. Addition of tri-*n*-butyltin radicals to internal alkenes is a comparatively slow process and the reaction is thermodynamically disfavoured because coplanarity of the alkenic carbons 12-C and 13-C **59** forces the cyclohexene ring to adopt a boat conformation, with the tri-*n*-butylstannyl group in an axial (flagstaff) position.

## Conclusions

Catalytic free radical tricyclisation reactions have been achieved, but stoichiometric consumption of the radical species is a competing process. 5-*exo*-*trig* Cyclisation of pendant alkyl or vinyl radicals attached to either equatorial or axial positions invariably gives adducts with a *cis*-ring fusion. Whereas addition of 2- or 3-pyranyl radicals to pendant *O*-allyl substituents gives both *trans*- and *cis*-adducts which undergo a further cyclisation, by catalytic and stoichiometric pathways respectively. Nevertheless the catalytic pathway provides a rare example of a 6-*endo*-*trig* cyclisation, which is enforced wholly by geometric constraints. Radical addition to the 1,4-di-*O*-propargyl substrates **46a**, **46b**, **51** is non-regioselective as anticipated, but unexpectedly the two families of adducts evolve to different products as a consequence of the conformation of the pyran ring. Similarly, the tetracyclic dienes **49a**, **49b**, **59** undergo an unprecedented, regioselective hydrostannylation, which can be rationalised as a consequence of the conformation of




**Scheme 6**




the pyran ring. Further developments of catalytic free radical reactions, will require careful engineering of each step to prevent the intervention of stoichiometric processes and may be restricted to sequences which leave minimal residual unsaturation in the product.

We gratefully acknowledge sponsorship of this work by Warner-Lambert, Parke-Davis and the provision of spectrometer time by the EPSRC at the National Mass Spectrometry Service at the University of Swansea.

## Experimental

Purified or dried solvents were freshly distilled under an argon or nitrogen atmosphere from a suitable drying agent. Reagents were purchased from commercial sources and used without purification. All the compounds reported here, originate from either tri-*O*-acetyl-D-glucal **6** or di-*O*-acetyl-L-glucal **11**. The previous paper in the series should be consulted for the preparation of some starting materials.[5]

All reactions were monitored by thin layer chromatography (TLC) using Merck aluminium backed precoated silica gel plates (0.2 mm, 60, $F_{254}$) with UV light or ethanolic phosphomolybdic acid (3%) and heat for visualisation. Virtually all products were purified by flash column chromatography using Merck silica gel 60 (70–230 mesh). Columns were eluted with a gradient starting with a low polarity solvent and then increasing amounts of a more polar solvent. All products were homogenous as judged by TLC unless stated otherwise.

Infra red (IR) spectra were recorded on a Perkin-Elmer 1600 Series FTIR spectrophotometer, using sodium chloride cells. Elemental analyses were performed on a Perkin-Elmer 240c.

Low resolution mass spectra were recorded on VG Trio 1 and VG platform II spectrometers using electron impact (EI) or chemical ionisation (CI–$CH_4$). Some low resolution spectra, CI–$NH_3$ spectra and all accurate mass measurements were recorded at the EPSRC Mass Spectrometry Centre at Swansea. Mass spectra data for large compounds (particularly those containing tin and halogens) were simulated using the computer program HiMass.[21] This calculates the abundance of the ions in an ion cluster for a given elemental formula (cluster analysis).

NMR spectra were recorded on Perkin-Elmer R12B, Varian T60, Bruker AMX-360, and Bruker Advance DPX-400 spectrometers. $CDCl_3$ was used as solvent unless indicated. Tetramethylsilane or residual solvent peaks (*e.g.* $CHCl_3$) were used as frequency standards. $^{13}$C-NMR spectra were recorded with full and partial proton decoupling and using the DEPT technique. The numbering used in the spectroscopic data is as shown in the diagrams throughout the Experimental section, and does not necessarily correspond to IUPAC nomenclature.

Coupling constants were determined using the computer program Multiplet[22] and are quoted in hertz (Hz). Multiplet uses peak positions from peak listings to calculate line spacings which are averaged to give putative couplings. These in turn are permutated to give possible coupling patterns. Thus the calculated coupling constants have an accuracy which is only limited by the digital resolution of the NMR machine and line broadening effects. Values are reported to 0.1 Hz, but have an uncertainty of ±*ca.* 0.3 Hz (at 360 MHz), due to the digital resolution of the FID accumulation and Fourier transformation. $^1$H-NMR spectra were simulated using RACCOON.[23] Vinylic $^1$H and $^{13}$C-NMR chemical shifts were predicted using Shoolery's rules.[24]

Molecular modelling was performed initially with PC-Model[25] on Compusys, 33 MHz (Intel 80486) and PCS Aurora 330 MHz (AMD K5) machines. The program implements Allinger's MM2 force field, version MM88 with several enhancements. Structures were optimised using the Randomise

option (global energy minimum search), with all defaults except as follows. The program file format can only store 70 conformers from randomisation trials. In the early work with the Intel equipped machine, 200–300 trials were typically made with conformers up to 5 kcal $mol^{-1}$ (21 kJ $mol^{-1}$) above the initial structure stored as candidate structures. A selection of the lower energy structure conformers were then randomised again. In the later work with the K5 equiped machine, 2000–5000 trials were typically made, but only structures of lower energy than the initial structure were stored, because of the structure storage constraint. In several cases, the structures of acyclic portions of the structures were simplified (*e.g.* $Bu_3Sn$ to $Et_3Sn$ or $Me_3Sn$). This was done partially to reduce structure refinement time, but more importantly to avoid saving conformers derived from the acyclic portions of the structures with trivial differences.

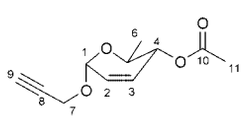
Standard molecular mechanics models (such as MM2) are not sensitive to the anomeric effect. In order to implicitly include this feature, all structures reported here were constructed by annulating rings on to a pre-minimised $^4C_1$ conformer with the 1-C–1-O bond axial. Modelling commencing with $^1C_4$ conformers gave less satisfactory results, in terms of final energies and coupling constant fits.

Most structures were also optimised using Cerius 2[26] on SGI machines, running UNIX, using 3D-Sketch, the Clean option and the Conformer package. All results showed negligible differences to the PC-Model structures. We are indebted to David Willock for providing these facilities.

The PMR option in PC-Model was used to calculate vicinal coupling constants. This implements modified versions of the Karplus equation[27] parameterised to take account of the effect of substituents on coupling constants. An average absolute error of 1 Hz for all the vicinal coupling constants of a given molecule, with no single value with an error of >±2 Hz constitutes a satisfactory fit between experimental data and calculated values.

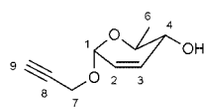
The full experimental and spectroscopic data for all L-series compounds prepared are described in the Experimental section which follows. Data for D-series compounds are provided in the electronic supplementary data for this paper. This includes the following compounds in order of appearance: **15a**, **15b**, **16**, **17a**, **18a**, **17b**, **18b**, **24b**, **24c**, **24d**, **24e**, **25**, **26**, **27a**, **28a**, **46a**, **46b**, **48**, **49a**, **49b** and tabular data for **43**, **53a**, **53b**.

### Prop-2-ynyl 4-*O*-acetyl-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside[28]



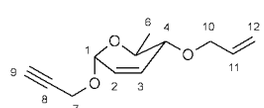
Di-*O*-acetyl-L-glucal **11** (1.0 g, 4.7 mmol) was dissolved in dry benzene (25 ml) containing propargyl alcohol (prop-2-ynol) (0.39 g, 6.9 mmol, 1.5 equiv.) under nitrogen. Anhydrous zinc chloride (0.9 g, 6.6 mmol, 1.4 equiv.) was added in one portion to the mechanically stirred solution. A pink colour developed over 15 min, the supernatant was decanted from the gelatinous solid, neutralised with solid sodium bicarbonate, filtered and concentrated to give a mixture of α- and β-anomers ($\delta$ 5.17, s, β-1-H) as a clear oil, ratio α : β, 87 : 13. The crude mixture was purified by column chromatography, eluent hexane to 15% ethyl acetate, to yield the title product as a waxy solid (0.86 g, 68%). Combustion analysis; $C_{11}H_{14}O_4$ requires C 62.85, H 6.71; found C 62.47, H 6.89%; $\delta_H$ 5.88 (1H, d, *J* 10.2, 3-H), 5.80 (1H, ddd, *J* 10.2, 2.6, 2.0, 2-H), 5.17 (1H, dq, *J* 9.2, 1.6, 4-H), 5.07 (1H, dq, *J* 9.2, 1.6, 1-H), 4.30 (2H, app d, *J* 2.42, 7-$H_2$), 3.91 (1H, dq, *J* 9.2, *J* 6.27, 5-H), 2.47 (1H, t, *J* 2.4, 9-H), 2.09 (3H, s, $CH_3CO$), 1.23 (2H, d, *J* 6.3, $CH_3$); $\delta_H$ ($C_6D_6$) 5.72 (1H, d, *J* 10.2, 3-H), 5.52 (1H, dt, *J* 10.3, 2.4, 2-H), 5.20 (1H, dd, *J* 9.0, 1.5, 4-H), 5.02 (1H, s, 1-H), 4.04 (3H, m, 5-H, 7-$H_2$), 1.95 (1H, t, *J* 2.3, 9-H), 1.56 (3H, s, $CH_3CO$), 1.12 (3H, d, *J* 6.4, 6-$H_3$); $\delta_C$ 170.2 (C, 10-C, CO), 130.5, 127.8 (2CH, 2-C, 3-C), 92.9 (CH, 1-C), 79.6 (C, 8-C), 77.1, 74.1, 65.4, (3CH, 4-C, 5-C, 9-C), 54.8 ($CH_2$, 7-C), 21.2 ($CH_3CO$), 18.0 (CH, 6-C); *m*/*z* ($EI^+$) 210 (M, $C_{11}H_{14}O_4$, absent), 166 (14%, M − $CH_3CHO$, diene from retro Diels–Alder), 155 (17%, M − $HC{\equiv}CCH_2O$), 124 (100%, diene from retro Diels–Alder − $H_2C{=}C{=}O$), 95 (98%, M − $HC{\equiv}CCH_2O$ − AcOH), 85 (85%), 84 (65%), 57 (57%); $\nu_{max}$ (neat)/$cm^{-1}$ 3320, 3005, 2925, 2105 (weak, C≡C), 1735, 1470, 1380, 1235, 1065; $R_f$ 0.6 (hexane–EtOAc, 50 : 50).

### Prop-2-ynyl 2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside



Prop-2-ynyl 4-*O*-acetyl-2,3-dideoxy-α-L-*erythro*-hex-2-enopyranoside (1.2 g, 4.5 mmol) was dissolved in dry methanol (200 ml). Sodium methoxide was added portionwise until the reaction solution recorded basic to universal indicator paper. The solution was stirred under nitrogen for 24 hours. TLC analysis indicated two products and the complete absence of starting material. The solution was neutralised with solid $CO_2$, filtered and concentrated to a yellow syrup. The syrup was twice redissolved in dry chloroform (20 ml), evaporated and concentrated to a clear oil. Purification by flash column chromatography, eluent hexane to 20% EtOAc in hexane, gave the title compound (605 mg, 63%) as a white waxy solid, and a mixture of the title compound and a trace of the β-anomer (90 : 10, 173 mg, 18%). Combustion analysis; $C_9H_{12}O_3$ requires C 64.27, H 7.19; found C 64.11, H 7.39%; $\delta_H$ 5.96 (1H, d, *J* 10.1, 3-H), 5.74 (1H, dt, *J* 10.1, 2.4, 2-H), 5.13 (1H, s, 1-H), 4.29 (2H, app d, *J* 2.5, 7-$H_2$), 3.85 (1H, td, *J* 9.2, 1.7, 4-H), 3.71 (1H, dq, *J* 8.9, 6.2, 5-H), 2.45 (1H, t, *J* 2.4, 9-H), 1.32 (3H, d, *J* 6.2, 6-$H_3$); $\delta_C$ 133.8 (CH, 3-C), 126.3 (CH, 2-C), 92.7 (CH, 1-C), 79.5 (C, 8-C), 74.5 (CH, 9-C), 69.6 (CH, 4-C), 68.3 (CH, 5-C), 54.8 ($CH_2$, 7-C), 17.9 (CH, 6-C); *m*/*z* ($EI^+$) 168 (M, $C_9H_{12}O_3$, absent), 113 (42%, M − $HC{\equiv}CCH_2O$), 112 (32%, M − $HC{\equiv}CCH_2OH$), 95 (34%), 80 (41%), 71 (66%), 69 (49%, M − $CH_3CHO$ [retro Diels–Alder] − $HC{\equiv}CCH_2O^+$), 57 (50%, $C_3H_5O^+$), 55 (100%, $C_3H_3O^+$); $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 3480, (br, OH), 3280, 2960, 2920, 1380, 1250, 1065; $R_f$ 0.35 (hexane–EtOAc, 75 : 25).

### Prop-2-ynyl 4-*O*-(prop-2-enyl)-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside 19

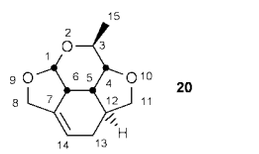


**19**

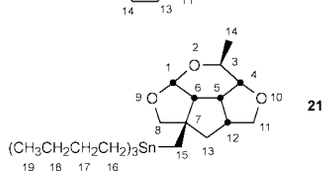
Prop-2-ynyl 2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside (200 mg, 1.2 mmol) was dissolved in dry DMF (5 ml) under nitrogen. Sodium hydride (60% in mineral oil, 57 mg + 35 mg, 1.44 mmol, 1.2 equiv.) was added portionwise and the reaction solution cooled to 0 °C. Allyl iodide (280 mg, 1.68 mmol, 1.4 equiv.) was added dropwise to maintain the above temperature. The solution was stirred for 2 hours, the solvent removed, the residue redissolved in chloroform (10 ml), and washed with water (4 × 15 ml) until no DMF was detected by TLC in the aqueous layer. The organic layer was dried over sodium sulfate, filtered, and concentrated to afford a mixture of products as a yellow oil. Purification of the oil by column chromatography, eluent hexane to 20% ethyl acetate in hexane, afforded the title compound **19** (52 mg, 21%) as a clear liquid and recovered starting material (28 mg, 14%) as a yellow oil. $\delta_H$ 6.06 (1H, d,

*J* 10.3, 3-H), 5.91 (1H, ddt, *J* 17.0, 10.7, 5.4, 11-H), 5.75 (1H, dt, *J* 10.4, 2.2, 2-H), 5.27 (1H, dq, *J* 17.1, 1.5, 12a-H), 5.18 (1H, dq, *J* 10.3, 1.3, 12b-H), 5.13 (1H, br s, 1-H), 4.28 (2H, d, *J* 2.5, 7-$H_2$), 4.13 (1H, ddt, *J* 12.7, 5.5, 1.3, 10a-H), 4.24 (1H, ddt, *J* 12.7, 5.8, 1.3, 10b-H), 3.85 (1H, dq, *J* 9.0, 6.2, 5-H), 3.64 (1H, dq, *J* 9.0, 1.5, 4-H), 2.43 (1H, t, *J* 2.3, 9-H), 1.30 (3H, d, *J* 6.2, 6-$H_3$); $\delta_C$ 134.7 (CH, 2-C), 131.5 (CH, 11-C), 126.1 (CH, 3-C), 117.2 ($CH_2$, 12-C), 92.9 (CH, 1-C), 79.3 (CH, 8-C), 76.1 (CH, 9-C), 74.3 (CH, 10-C), 69.9 (CH, 4-C), 66.1 (CH, 5-C), 54.7 ($CH_2$, 7-C), 18.1 ($CH_3$, 6-C); *m*/*z* ($EI^+$) 208 (M, absent), 207 (3%, M − H; $C_{12}H_{15}O_3$ requires 207.1021; found 207.1021), 164 (85%, M − $CH_3CHO$, retro Diels–Alder), 153 (66%, M − $HC{\equiv}CH_2O^+$), 125 (42%, M − retro Diels–Alder − $HC{\equiv}CH_2^+$), 123 (64%, M − retro Diels–Alder − $H_2C{=}CHCH_2^+$), 97 (15%, M − $HC{\equiv}CH_2O^+$ − $H_2C{=}CHCH_2O^+$), 95 (51%, M − $HC{\equiv}CH_2OH$ − $H_2C{=}CHCH_2OH$), 83 (42%), 81 (54%), 67 (83%), 55 (100%, $C_3H_3O^+$); $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 3308, 3023, 2160 (weak), 1218, 1094; $R_f$ 0.70 (hexane–EtOAc, 75 : 25).

### Preparation of the tetracycles 20, 21




**20**



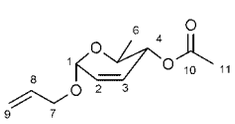

**21**

Prop-2-ynyl 4-*O*-(prop-2-enyl)-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside **19** (50 mg, 0.25 mmol) was dissolved in dry toluene (2 ml) and warmed to reflux. AIBN (1 mg, 0.003 mmol, 0.04 equiv.) was added and the reaction solution refluxed for a further 15 mins. A solution of tri-*n*-butyltin hydride (110 mg, 0.38 mmol, 1.5 equiv.) in dry toluene (3 ml) was added dropwise over 3 hours by a syringe pump. The reaction solution was then refluxed for 16 hours. TLC analysis indicated a complex mixture including two major products. Purification by column chromatography, eluent hexane to 10% ethyl acetate, afforded (in order of elution) the stannane **21** (18 mg, 17%) as a clear oil and the dioxahydrindacene **20** (22 mg, 43%) as a white, waxy solid.

Spectroscopic data for **20**: combustion analysis; $C_{12}H_{26}O_3$ requires C 69.21, H 7.74; found C 68.94, H 7.92%; $\delta_H$ 6.07 (1H, br d, *J* 6.9, 14-H), 5.27 (1H, d, *J* 6.3, 1-H), 4.35 (1H, d, *J* 10.6, 8a-H), 4.27 (1H, d, *J* 10.7, 8b-H), 3.87 (1H, dd, *J* 6.8, 6.2, 11a-H), 3.84 (1H, dq, *J* 6.3, 6.3; 3-H, coupling constants inaccurate due to overlap with signal at $\delta$ 3.87), 3.74 (1H, dd, *J* 7.5, 5.8, 4-H), 3.37 (1H, dd, *J* 11.1, 7.2, 11b-H), 2.79 (1H, br m, 6-H), 2.25 (2H, m, 5-H, 13a-H), 1.89 (2H, m, 12-H, 13b-H), 1.31 (3H, d, *J* 6.7, 15-$H_3$); $\delta_H$ ($C_6D_6$) 5.46 (1H, br m, 14-H), 5.03 (1H, d, *J* 6.7, 1-H), 3.98 (1H, dd, *J* 10.5, 0.9, 8a-H), 3.82 (1H, app d quintet, *J* 10.6, 1.6, 8b-H), 3.73 (1H, dq, *J* 6.6, 6.6, 3-H), 3.46 (1H, dd, *J* 6.8, 6.0, 11a-H), 3.43 (1H, dd, *J* 6.9, 6.9, 4-H), 2.97 (1H, dd, *J* 11.0, 7.1, 11b-H), 2.07 (1H, br m, H-6), 1.55 (3H, br m, 5-H, 13-$H_2$), 1.18 (1H, br m, 12-H), 1.03 (3H, d, *J* 6.4, 15-$H_3$); $^1H$–$^1H$ *J*-COSY NMR 1-H to 6-H to 5-H (weak) to 4-H, 3-H to 15-$H_3$, 8a-H to 8b-H, 5-H to 12-H or 13a-H to 13b-H, 11a-H to 11b-H, $^1H$–$^1H$ *J*-COSY NMR ($C_6D_6$) 1-H to 6-H to 5-H to 4-H, 3-H to 15-$H_3$, 5-H to 12-H or 12-H to 13-$H_2$ to 14-H, 8a-H to 8b-H, 11a to 11b; $\delta_C$ 138.8 (C, 7-C), 124.0 (CH, 14-C), 98.2 (CH, 1-C), 76.4 (CH, 4-C), 73.8 (CH, 3-C), 69.6, 69.2 ($CH_2$, $CH_2$, 8-C, 11-C), 43.8 (CH, 6-C), 42.1 (CH, 5-C), 37.8 (CH, 12-C), 25.1 ($CH_2$, 13-C), 18.5 ($CH_3$, 15-C); *m*/*z* ($EI^+$) 209 (1%, M + 1), 208 (3%, M, $C_{12}H_{16}O_3$), 180 (4%, M − $(CH_2)_2$), 151 (5%, M − $(CH_2)_2$-$CH_3$), 119 (12%), 105 (62%), 91 (100%), 79 (82%), 69 (59%), 55 (35%); $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 2955, 2855, 2858, 1737, 1410; $R_f$ 0.15 (hexane–$Et_2O$, 50 : 50)

Spectroscopic data for **21**: $\delta_H$ ($CDCl_3$)/$cm^{-1}$ 5.38 (1H, d, *J* 7.8, 1-H), 3.75 (4H, m, 3-H, 8a-H, 11-$H_2$), 3.58 (1H, t, *J* 9.2, 4-H), 3.25 (1H, d, *J* 8.9, 8b-H), 3.06 (1H, br m, 12-H), 2.87 (1H, app q = ddd, *J* 9.5, 9.5, 9.5, 5-H), 2.38 (1H, dd, *J* 9.9, 8.0, 6-H), 1.67 (2H, m, 13-$H_2$), 1.56 (6H, m, 18-$H_6$, $Sn(CH_2)_2CH_2$-), 1.26 (10H, m, 15a-H, 14-$H_3$, 17-$H_6$, $SnCH_2$-$CH_2$), 1.09 (1H, d, *J* 10.4, 15b-H), 0.89 (15H, m, 16-$H_6$, 19-$H_9$, $SnCH_2$, $Sn(CH_2)_3$-$CH_3$); $^1H$–$^1H$ *J*-COSY NMR 1-H to 6-H to 5-H to 4-H, 3-H to 15-$H_3$, 8a-H to 8b-H, 12-H to 13-$H_2$, 14a-H to 14b-H, 16-$H_6$ to 17-$H_6$ to 18-$H_6$ to 19-$H_9$; $\delta_H$ ($C_6D_6$) 5.57 (1H, d, *J* 7.9, 1-H), 4.15 (1H, dq, *J* 9.3, 6.1, 3-H), 3.86 (1H, d, *J* 8.8, 8a-H), 3.69 (1H, dd, *J* 9.3, 9.3, 4-H), 3.67 (1H, dd, *J* 8.7, 5.8, 11a-H), 3.61 (1H, dd, *J* 8.7, 1.9, 11b-H), 3.28 (1H, d, *J* 8.8, 8b-H), 2.75 (1H, m, 12-H), 2.64 (1H, ddd, *J* 9.6, 9.6, 9.6, 5-H), 2.18 (1H, dd, *J* 9.0, 9.0, 6-H), 1.65 (3H, d, *J* 6.4, 14-$H_3$), 1.60 (8H, m, 13-$H_2$, 18-$H_6$, $Sn(CH_2)_2CH_2$), 1.45 (6H m, 17-$H_6$, $SnCH_2CH_2$), 1.25 (1H, d, *J* 13.1, 15a-H), 1.05 (9H, t, *J* 7.3, 19-$H_9$, $Sn(CH_2)_3CH_3$), 0.95 (7H, m, 15b-H, 16-$H_6$, $SnCH_2$); $^1H$–$^1H$ *J*-COSY NMR ($C_6D_6$) 1-H to 6-H to 5-H, 3-H to 14-$H_3$, 8a-H to 8b-H, 11a-H to 11b-H, 12-H to 13-$H_2$, 15a-H to 15b-H, 16-$H_6$ to 17-$H_6$ to 18-$H_6$ to 19-$H_9$; note: weak spectrum, several expected correlations missing; $\delta_C$ 100.3 (CH, 1-C), 78.0 (CH, 4-C), 76.2, 75.7 ($CH_2$, $CH_2$, 8-C, 11-C), 66.8 (CH, 3-C), 59.8 (C, 7-C), 54.2 (CH, 12-C), 48.5 (CH, 6-C), 45.9 ($CH_2$, 13-C), 44.0 (CH, 5-C), 28.9 ($CH_2$, 18-C, $Sn(CH_2)_2CH_2$), 27.2 ($CH_2$, 17-C, $SnCH_2$-$CH_2$), 19.4 ($CH_3$, 15-C), 18.2 ($CH_2$, 14-C), 13.4 ($CH_3$, 19-C, $Sn(CH_2)_3CH_3$), 9.7 ($CH_2$, 16-C, $SnCH_2$); *m*/*z* (EI) $M^+$ 500 (0%, $C_{24}H_{44}O_3{}^{120}Sn$), 443, 442, 441, 440, 439 (% abundances, predicted values in square brackets: 100% [100], 45% [40], 84% [74], 33% [31], 55% [40], M − Bu, Sn cluster), 291 (4%, $Bu_3{}^{120}Sn$, cluster), 179 (21%, $Bu^{120}SnH_2$), 177 (25%, $Bu^{120}Sn$); *m*/*z* ($CI^+$, $NH_3$) 518, 516, 514 (22%, 16%, 10%, M + $NH_4^+$), 501, 499, 497 (14%, 10%, 7%, M + H, $C_{24}H_{45}O_3{}^{120}Sn$ requires 501.2390, found 501.2390), 443, 441, 439 (15%, 11%, 7%, M − Bu), 308, 306, 304 (100%, 76%, 44%), 228 (22%); $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 2929 (br), 1464, 1257, 1036; $R_f$ 0.6 (hexane–$Et_2O$, 50 : 50).

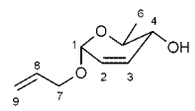
### Prop-2-enyl 4-*O*-acetyl-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside




Di-*O*-acetyl-L-glucal **11** (5.0 g, 23.6 mmol) was dissolved in dry toluene (100 ml) containing allyl alcohol (1.5 g, 31.0 mmol, 1.1 equiv.). Anhydrous zinc chloride (4.2 g, 30.7 mmol, 1.3 equiv.) was added portionwise and the solution stirred under nitrogen. On development of a purple colouration after 35 min, the supernatant was decanted, neutralised with solid sodium bicarbonate, filtered and concentrated to a light yellow oil. TLC analysis indicated a major product and a faint impurity. Purification by column chromatography, eluent hexane to 20% EtAOc in hexane, afforded the title compound (3.4 g, 68%) as a clear oil. $\delta_H$ 5.89 (1H, 8-H), 5.80 (1H, d, *J* 10.4, 3-H), 5.74 (1H, ddd, *J* 10.2, 2.0, 2.0, 2-H), 5.31 (1H, dd, *J* 17.1, 1.5, *cis*-9-H), 5.20 (1H, dd, *J* 10.3, 1.3, *trans*-9-H), 5.06 (1H, dd, *J* 9.3, 1.4, 4-H), 5.01 (1H, br s, 1-H), 4.26 (1H, dddd, *J* 12.8, 5.2, 1.3, 1.3, 7a-H), 4.07 (1H, br dd, *J* 12.8, 6.4, 7b-H), 3.98 (1H, dq, *J* 9.2, 6.3, 5-H), 2.08 (3H, s, 11-$H_3$), 1.22 (3H, d, *J* 6.2, 6-$H_3$); $^1H$–$^1H$ *J*-COSY NMR, 2-H to 3-H to 4-H (weak) to 5-H to 6-$H_3$, 7a-H to 7b-H to 8-H (weak), 7a-H to 8-H (weak) to 9a-H, 8-H to 9b-H; $\delta_C$ 171.0 (10-C, CO), 134.8 (8-C), 130.2 (2-C), 128.1 (3-C), 117.7 (9-C), 94.0 (1-C), 71.3 (4-C), 69.5 (5-C), 65.2 (7-C), 21.5 (11-C), 18.3 (6-C); *m*/*z* ($EI^+$, probe temperature 30–200 °C) 212 ($M^+$, $C_{11}H_{16}O_4$, absent), 168 (45%, M − $CH_3CHO$, diene from

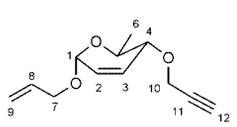
retro Diels–Alder), 155 (47%, M − $H_2C$=CH-$CH_2O^+$), 126 (100%, M − $CH_3CHO$ − $H_2C$=C=O), 95 (74%, M − $H_2C$=CH-$CH_2O^+$ − AcOH), 85 (94%), 55 (60%); *m*/*z* ($CI^+$, $NH_3$) 230 (5%, M + $NH_4$), 213 (3%, M + H, $C_{11}H_{17}O_4$ requires 213.1127, found 213.1127), 190 (3%), 188 (6%, M + $NH_4$ − $H_2C$=C=O), 172 (18%, M + $NH_4$ − $H_2C$=CH-$CH_2OH$), 155 (100%, M − $H_2C$=CH-$CH_2O^+$ or M + $NH_4$ − $H_2C$=CH-$CH_2^+$), 114 (18%), 97 (17%), 95 (30%); $\nu_{max}$ (neat)/$cm^{-1}$ 2981, 2933, 1744 (str, C=O), 1402, 1375, 1237, 1154, 1104, 1038 (str), 919; $R_f$ 0.65 (hexane–EtOAc, 15 : 85).

**Prop-2-enyl 2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside**



To a solution of prop-2-enyl 4-*O*-acetyl-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside (1.0 g, 4.76 mmol) dissolved in dry methanol (20 ml) was added solid sodium methoxide until the solution was basic to universal indicator paper. The yellow solution was stirred under nitrogen for 18 hours. TLC analysis indicated a single product. The reaction solution was neutralised with solid $CO_2$ as judged by universal indicator paper, concentrated, dissolved in ether (20 ml), filtered and reconcentrated to give the title compound (0.78 g, 92%) as a tan solid. $\delta_H$ 5.94 (2H, m, 2-H, 8-H), 5.74 (1H, dt, *J* 10.1, 3.0, 3-H), 5.29 (1H, dt, *J* 17.2, 1.5, *cis*-9-H), 5.19 (1H, dq, *J* 10.4, 1.3, *trans*-9-H), 4.97 (1H, d, *J* 1.1, 1-H), 4.24 (1H, ddt, *J* 12.8, 5.2, 1.4, 7a-H), 4.05 (1H, ddt, *J* 12.8, 6.4, 1.8, 7b-H), 3.81 (1H, br m, 4-H), 3.72 (1H, m, 5-H), 2.30 (1H, br m, OH), 1.32 (3H, dd, *J* 6.1, 0.8, 6-$H_3$); $\delta_H$ ($C_6D_6$) 5.94 (1H, m, 8-H), 5.88 (1H, d, *J* 10.4, 3-H), 5.71 (1H, dt, *J* 10.2, 2.4, 2-H), 5.37 (2H, m, 9-$H_2$), 5.12 (1H, dd, *J* 10.5, 1.5, 4-H), 4.95 (1H, s, 1-H), 4.24 (2H, m, 5-H, 7a-H), 3.97 (1H, ddt, *J* 13.2, 5.9, 1.4, 7b-H), 1.71 (3H, s, $CH_3CO$), 1.29 (3H, d, *J* 6.3, 6-$H_3$); $\delta_C$ 134.7 (CH, 8-C), 134.2 (CH, 2-C), 126.6 (CH, 3-C), 117.8 (CH, 9-C), 93.8 (CH, 1-C), 69.8 (CH, 4-C), 69.3 (CH, 5-C), 68.3 ($CH_2$, 7-C), 18.3 ($CH_3$, 6-C); *m*/*z* ($EI^+$) 170 (M, absent), 169 (3%, M − 1), 124 (72%), 113 (72%, M − $OCH_2$-CH=$CH_2$), 98 (22%, M − retro Diels–Alder − $H_2C$=$CH_2$), 95 (47%), 85 (94%, M − retro Diels–Alder − $C_3H_5$), 69 (46%, M − retro Diels–Alder − $OCH_2CH$=$CH_2$), 57 (100%); *m*/*z* ($CI^+$, $NH_3$) 188 (3%, M + $NH_4^+$, $C_9H_{18}NO_3$ requires 188.1287, found 188.1287), 172 (9%), 155 (12%), 130 (13%), 114 (32%), 97 (36%), 74 (58%), 46 (100%); $\nu_{max}$ (Nujol)/$cm^{-1}$ 3400 (v br), 2900 (str), 1590 (br); $R_f$ 0.80 (hexane–EtOAc, 50 : 50).

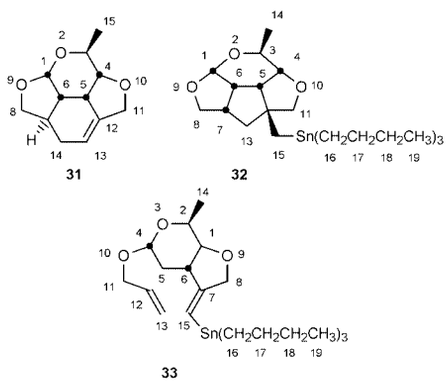
**Prop-2-enyl 4-*O*-prop-2-ynyl-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside 30**



**30**

Prop-2-enyl 2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside (200 mg, 1.12 mmol) was dissolved in dry DMF (5 ml) and treated with sodium hydride (60% suspension in mineral oil, 54 mg + 32 mg, 1.34 mmol, 1.2 equiv.) and cooled to 0 °C. Propargyl bromide (80% in toluene, 200 mg + 160 mg, 1.34 mmol, 1.2 equiv.) dissolved in dry DMF (2 ml) was added dropwise. The dark brown solution was allowed to attain ambient temperature and stirred for 18 hours. TLC analysis indicated a single product plus minor impurities. Purification by flash column chromatography afforded the title compound **30** (120 mg, 52%) as an amber oil. $\delta_H$ 6.07 (1H, d, *J* 10.3, 3-H), 5.92 (1H, dddd, *J* 17.0, 10.4, 6.3, 5.2, 8-H), 5.77 (1H, ddd, *J* 10.3, 2.5, 1.9, 2-H), 5.29 (1H, ddd, *J* 17.0, 3.1, 1.5, *cis*-9-H), 5.18 (1H, dt, *J* 10.4, 1.3, *trans*-9-H), 4.97 (1H, d, *J* 2.3, 1-H), 4.24 (3H, m, 4-H, 10-$H_2$), 4.03 (1H, ddd, *J* 12.9, 6.3, 1.2, 7a-H), 3.83 (2H, m, 5-H, 7b-H), 2.46 (1H, t, *J* 2.4, 12-H), 1.31 (3H, d, *J* 5.8, 6-$H_3$); $\delta_C$ 135.0 (CH, 8-C), 130.8 (CH, 3-C), 127.5 (CH, 2-C), 117.7 ($CH_2$, 9-C), 94.1 (CH, 1-C), 76.4 (CH, 4-C), 75.0 (C, 11-C), 69.4 ($CH_2$, 7-C), 66.1 (CH, 5-C), 56.8 ($CH_2$, 10-C), 18.6 ($CH_3$, 6-C), 12-C absent due to $^1J_{H\text{-}C}$; *m*/*z* ($EI^+$) 208 (3%, $C_{12}H_{16}O_3$, M), 207 (5%, $C_{12}H_{15}O_3$ requires 207.1027, found 207.1027), 166 (65%, M − $CH_3CHO$, retro Diels–Alder), 151 (100%, M − $H_2C$=$CHCH_2O^+$), 125 (32%, M − $CH_3CHO$ − HC≡C-$CH_2^+$), 123 (48%, M − $CH_3CHO$ − $H_2C$=$CHCH_2^+$), 95 (62%), 83 (56%), 67 (30%); $\nu_{max}$ (neat)/$cm^{-1}$ 3271 (C≡*C*-*H*), 2977, 2901, 2869, 2105 (weak, C≡C), 1402, 1125, 1040, 1017; $R_f$ 0.75 (hexane–EtOAc, 75 : 25).

**Preparation of the tetracycles 31, 32 and the bicycle 33**



**31** **32** **33**

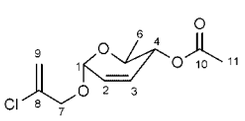
Prop-2-enyl 4-*O*-prop-2-ynyl-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside **30** (100 mg, 0.48 mmol), was dissolved in dry toluene (3 ml) and warmed to reflux. AIBN (2 mg, 0.005 mmol, 0.04 equiv.) was added and the reaction solution refluxed for a further 15 min. A solution of tri-*n*-butyltin hydride (210 mg, 0.72 mmol, 1.5 equiv.) in dry toluene (3 ml) was added dropwise over 3 hours *via* a syringe pump. The reaction solution was then refluxed for 18 hours. TLC analysis indicated a complex mixture of products. Purification by column chromatography afforded in order of elution a non-polar fraction containing the bicycle **33** (8 mg, 6%), the stannane **32** (23 mg, 17%) and the dioxahydrindacene **31** (48 mg, 49%).

Spectroscopic data for **31**: combustion analysis; $C_{12}H_{16}O_3$ requires C 69.21, H 7.74; found C 69.52, H 7.53%; $\delta_H$ 5.93 (1H, dd, *J* 7.8, 1.3, 13-H), 5.38 (1H, d, *J* 6.2, 1-H), 4.16 (1H, d, *J* 10.0, 11a-H), 4.08 (1H, d, *J* 10.0, 11b-H), 3.93 (1H, dd, *J* 7.6, 5.9, 8a-H), 3.60 (2H, m, 4-H, 3-H), 3.25 (1H, dd, *J* 10.9, 7.8, 8b-H), 2.87 (1H, br m, 5-H), 2.33 (1H, dd, *J* 12.1, 7.9, *endo*-14-H), 2.12 (1H, ddd, *J* 13.0, 9.7, 6.4, 6-H), 1.83 (2H, m, *exo*-14-H, 7-H), 1.18 (3H, d, *J* 5.4, 15-$H_3$); $^1H$–$^1H$ *J*-COSY NMR 1-H to 6-H to 5-H to 4-H to 3-H (obscured) to 15-$H_3$, 6-H to 7-H to *exo*-8-H to *endo*-8-H to 7-H, 11a-H to 11b-H, 13-H to *endo*-14-H to *exo*-14-H to 13-H (weak); $\delta_H$ ($C_6D_6$) 5.45 (1H, br d, *J* 6.6, 13-H), 5.37 (1H, d, *J* 5.8, 1-H), 3.96 (1H, dt, *J* 9.9, 1.4, 11a-H), 3.87 (1H, d, *J* 9.8, 11b-H), 3.65 (2H, m, 3-H, 8a-H), 3.51 (1H, t, *J* 9.6, 4-H), 2.87 (1H, dd, *J* 10.6, 7.5, 8b-H), 2.31 (1H, m, br t, *J* 9.2, 5-H), 1.72 (1H, ddd, *J* 12.1, 7.8, 2.6, *endo*-14-H), 1.49 (2H, m, 6-H, 7-H), 1.38 (3H, d, *J* 5.9, 15-$H_3$), 1.34 (1H, m, *exo*-14-H); $^1H$–$^1H$ *J*-COSY NMR ($C_6D_6$) 1-H to 6-H to 5-H to 4-H to 3-H (obscured) to 15-$H_3$, 7-H to *exo*-8-H to *endo*-8-H to 7-H, 11a-H to 11b-H, 13-H to *endo*-14-H to *exo*-14-H to 13-H; $\delta_C$ 139.4 (C, 12-C), 121.7 (CH, 13-C), 96.1 (CH, 1-C), 76.5 (CH, 4-C), 68.5 ($CH_2$, 11-C), 67.8 (CH, 3-C), 67.6 ($CH_2$, 8-C), 42.4, 42.3 (CH, CH, 5-H, 6-H), 34.1 (CH, 7-C), 24.8 ($CH_2$, 14-C), 13.2 ($CH_3$, 15-C); *m*/*z* ($EI^+$) 208 (1%, M, $C_{12}H_{16}O_3$), 105 (33%), 95 (100%), 91 (89%), 77 (58%), 67 (43%); $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 2960, 2874, 1463, 1380; $R_f$ 0.15 (hexane–$Et_2O$).

Spectroscopic data for **32**: $\delta_H$ ($CDCl_3$)/$cm^{-1}$ 5.32 (1H, d, *J* 7.4, 1-H), 3.76 (2H, m, 8-$H_2$), 3.64 (3H, m, 3-H, 4-H, 11a-H), 3.27 (1H, d, *J* 8.5, 11b-H), 3.01 (1H, m, 7-H), 2.95 (1H, ddd,

*J* 10.0, 10.0, 7.7, 6-H), 2.18 (1H, ddd, *J* 8.9, 8.9, 0.9, 5-H), 1.60 (2H, m, 13-$H_2$), 1.38 (6H, m, 18-$H_6$, $Sn(CH_2)_2CH_2$), 1.21 (9H, m, 14-$H_3$, 17-$H_6$, $SnCH_2CH_2$), 0.94 (1H, dd, *J* 13.2, 1.2, 15a-H), 0.80 (16H, m, 15b-H, 16-$H_6$, 19-$H_9$, $SnCH_2(CH_2)_2CH_3$); $^1$H–$^1$H *J*-COSY NMR 1-H to 6-H to 5-H to 4-H, 3-H to 14-$H_3$, 7-H to 8-$H_2$, 7-H to 13-$H_2$, 11a-H to 11b-H, 16-$H_6$ to 17-$H_6$ to 18-$H_6$ to 19-$H_9$; $\delta_H$ ($C_6D_6$) 5.52 (1H, d, *J* 7.5, 1-H), 4.13 (1H, dq, *J* 8.6, 6.2, 3-H), 3.86 (1H, dd, *J* 9.5, 9.5, 4-H), 3.83 (1H, d, *J* 8.4, 11a-H), 3.75 (1H, br d, *J* 9.0, *endo*-8-H), 3.59 (1H, dd, *J* 8.8, 6.5, *exo*-8-H), 3.43 (1H, d, *J* 8.4, 11b-H), 2.73 (1H, m, 7-H), 2.65 (1H, ddd, *J* 10.2, 9.5, 8.0, values estimated from broad lines, not accurate, 6-H), 2.13 (1H, t, *J* 9.8, 5-H), 1.62 (11H, m, 13-$H_2$, 14-$H_3$, 18-$H_6$, $Sn(CH_2)_2CH_2$-), 1.47 (6H, m, 17-$H_6$, $SnCH_2CH_2$), 1.25 (1H, d, *J* 13.2, 15a-H), 1.08 (16H, m, 15b-H, 16-$H_6$, 19-$H_9$, $SnCH_2(CH_2)_2CH_3$); $^1$H–$^1$H *J*-COSY NMR ($C_6D_6$) 1-H to 6-H to 5-H to 4-H to 3-H to 14-$H_3$, 7-H to 13-$H_2$, 8a-H to 8b-H, 11a-H to 11b-H, 16-$H_6$ to 17-$H_6$ to 18-$H_6$ to 19-$H_9$; $\delta_C$ 99.7 (CH, 1-C), 78.2 (CH, 4-C), 76.2 ($CH_2$, 11-C), 69.9 ($CH_2$, 8-C), 66.8 (CH, 3-C), 60.8 (CH, 5-C), 52.0 (C, 12-C), 45.8 (CH, 7-C), 43.9 ($CH_2$, 13-C), 43.3 (CH, 6-C), 28.9 ($CH_2$, 18-C, $Sn(CH_2)_2CH_2$), 27.2 ($CH_2$, 17-C, $SnCH_2CH_2$), 19.4 ($CH_3$, 14-C), 18.2 ($CH_2$, 15-C), 13.4 ($CH_3$, 19-C, $Sn(CH_2)_3CH_3$), 9.7 ($CH_2$, 16-C, $SnCH_2$,); *m*/*z* ($EI^+$) 499 (M, $C_{24}H_{44}O_3Sn$, absent), 443, 441, 439 (100%, 80%, 48%, tin cluster, M − Bu), 385, 383, 381 (5%, 4%, 3%, tin cluster, M − Bu − BuH), 329 (2%, tin cluster, M − Bu); *m*/*z* ($CI^+$, $NH_3$) 518, 516, 514 (100%, 74%, 38%, M + $NH_4$; $C_{24}H_{48}O_3{}^{120}Sn_1N$ requires 518.2656, found 518.2656), 501, 499, 497 (27%, 22%, 12%, M + H), 443, 441, 439 (78%, 60%, 35%, M − Bu), 308, 306, 304 (28%, 22%, 13%), 228 (52%); $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 3019, 1224, 1154; $R_f$ 0.60 (hexane–$Et_2O$).

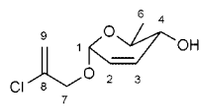
Spectroscopic data for **33**: $\delta_H$ ($CDCl_3$)/$cm^{-1}$ 5.84 (2H, m, 12-H, 15-H), 5.20 (1H, d, *J* 17.2, 1.2, *cis*-13-H), 5.08 (1H, d, *J* 10.5, 1.5, *trans*-13-H), 4.76 (1H, dd, *J* 6.0, 6.0, 4-H), 4.18 (3H, m, 1-H, 8-$H_2$), 3.90 (1H, dddd, *J* 13.2, 5.9, <1, <1, 11a-H), 3.70 (2H, m, 3-H, 11b-H), 2.67 (1H, br m, 6-H), 1.98 (1H, ddd, *J* 14.3, 5.7, 5.7, 5a-H), 1.74 (1H, ddd, *J* 14.3, 10.5, 6.6, 5b-H), 1.41 (6H, m, 18-$H_6$, $Sn(CH_2)_2CH_2$-), 1.24 (9H, m, 14-$H_3$, 17-$H_6$, $SnCH_2CH_2$), 0.84 (15H, m, 16-$H_6$, 19-$H_9$, $SnCH_2(CH_2)_2CH_3$); $R_f$ 0.85 (hexane–$Et_2O$).



### 2′-Chloroprop-2-enyl 4-*O*-acetyl-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside

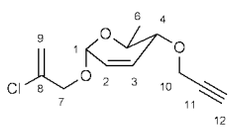
Di-*O*-acetyl-L-glucal **11** (2.5 g, 11.8 mmol) was dissolved in dry toluene (40 ml) containing 2-chloroprop-2-enol (1.2 g, 13.0 mmol, 1.1 equiv.) under nitrogen. Anhydrous zinc chloride (2.1 g, 15.3 mmol, 1.3 equiv.) was added portionwise to the mechanically stirred solution. The reaction solution developed a pink coloration over 15 min. The supernatant was decanted, neutralised with solid sodium bicarbonate, filtered and concentrated to afford a dark yellow oil. TLC analysis indicated a two component mixture, which was purifed by flash column chromatography, eluent hexane to 10% EtOAc in hexane, to afford the title compound (140 mg, 4.6%) as an amber light oil and unseparated mixture (68%). A second column, eluent hexane to 5% EtOAc in hexane, afforded a further 110 mg, 3.5% of the title compound. $\delta_H$ 5.90 (1H, d, *J* 10.3, H-3), 5.83 (1H, ddd, *J* 10.2, 2.2, 2.2, H-2), 5.48 (1H, q, *J* 1.2, 9-H, *cis* to Cl, Shoolery's rules predict $\delta$ 5.41), 5.37 (1H, d, *J* 0.6, 9-H, *trans* to Cl, Shoolery's rules predict $\delta$ 5.37), 5.07 (1H, dq, *J* 9.2, 1.5, 4-H), 5.03 (1H, br s, 1-H), 4.22 (2H, m, 7-$H_2$), 4.01 (1H, dq, *J* 9.2, 6.3, 5-H), 2.09 (3H, s, $CH_3CO$), 1.23 (3H, d, *J* 6.2, 6-$H_3$); $\delta_C$ 172.3 (C-10), 138.5 (8-C), 130.6 (3-C), 128.0 (2-C), 114.4 (9-C), 94.0 (1-C), 71.7 (7-C), 71.1 (4-C), 65.6 (5-C), 21.5 (11-C), 18.3 (6-C); *m*/*z* ($EI^+$) 248, 246 (M, $C_{11}H_{15}O_4Cl$, absent), 204, 202 (24%, 52%, M − $CH_3CHO$, retro Diels–Alder), 189, 187 (22%, 37%, M − AcO), 160 (100%), 155 (42%, M − $^+OCH_2C$-(Cl)=$CH_2$), 111 (71%), 94 (70%), 81 (81%), 57 (73%), 55 (86%); *m*/*z* ($CI^+$, $NH_3$) 266, 264 (32%, 87%, M + $NH_4^+$), 249, 247 (12%, 39%, M + $H^+$, $C_{11}H_{16}O_4{}^{35}Cl$ requires 247.0737, found 247.0737), 172 (48%, M + $NH_4^+$ − $HOCH_2C(Cl)=CH_2$), 155 (100%, M − $OCH_2C(Cl)=CH_2$), 95 (43%); $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 2933, 1744 (C=O), 1238, 1107; $R_f$ 0.70 (hexane–EtOAc, 75 : 25).

### 2-Chloroprop-2-enyl 2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside



Prop-2-ynyl 4-*O*-acetyl-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside (140 mg, 0.57 mmol) was dissolved in dry methanol (50 ml) and sodium methoxide added until the solution was basic to universal indicator paper. The solution was stirred under nitrogen for 28 hours. The reaction mixture was neutralised with solid $CO_2$ as judged by universal indicator paper. Purification by flash column chromatography, eluent hexane to 10% EtAOc in hexane, afforded the title compound (70 mg, 60%) as a clear oil. Combustion analysis; $C_9H_{13}O_3Cl$ requires C 52.82, H 6.40; found C 52.91, H 6.35%; $\delta_H$ 5.95 (1H, d, *J* 10.1, 3-H), 5.75 (1H, ddd, *J* 10.3, 2.4, 2.4, 2-H), 5.49 (1H, dd, *J* 2.5, 1.3, *cis*-9-H), 5.37 (1H, t, *J* 0.7, *trans*-9-H), 4.99 (1H, d, *J* 1.1, H-1), 4.26 (1H, dm, *J* 13, 7a-H), 4.18 (1H, dm, *J* 13, 7b-H), 3.84 (1H, m, 4-H), 3.75 (1H, m, 5-H), 2.3 (1H, br m, OH), 1.26 (3H, d, *J* 6.1, 6-$H_3$); $\delta_C$ 134.3 (8-C), 126.6 (3-C), 126.3 (2-C), 114.3 (9-C), 94.0 (1-C), 70.7 (4-C), 70.0 (5-C), 68.7 (7-C), 18.3 (6-C); *m*/*z* ($EI^+$) 206, 204 (0%, M, $C_9H_{13}O_3Cl$), 189, 187 (5%, 14%, M − OH), 162, 160 (35%, 63%, M − $CH_3CHO$, retro Diels–Alder), 113 (100%, M − $OCH_2C(Cl)=CH_2$), 85 (54%, M − $CH_3CHO$ − $CH_2C(Cl)=CH_2$), 57 (38%); $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 3430 (br, OH), 2902, 2253, 1638, 1381, 1051; $R_f$ 0.40 (hexane–EtOAc, 75 : 25).

### 2-Chloroprop-2-enyl 4-*O*-(prop-2-ynyl)-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside **39**

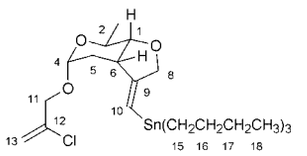


**39**

2-Chloroprop-2-enyl 2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside (100 mg, 0.49 mmol) was dissolved in dry DMF (2 ml) and treated with sodium hydride (60% suspension in mineral oil, 26 mg + 16 mg, 0.66 mmol, 1.4 equiv.) under nitrogen and cooled to 0 °C. Propargyl bromide (80% solution in toluene, 88 mg + 74 mg, 0.58 mmol, 1.2 equiv.) in dry DMF (1 ml) was added dropwise, the solution was allowed to attain ambient temperature and stirred under nitrogen for 14 hours. TLC analysis indicated a two component mixture of products. The crude reaction solution was concentrated and purified by flash column chromatography, eluent hexane to EtOAc 10% in hexane, to afford the title compound **39** (40 mg, 33%) as a clear oil, plus recovered starting material (28 mg, 28%). $\delta_H$ 6.10 (1H, dt, *J* 10.3, 1.1, 3-H), 5.78 (1H, ddd, *J* 10.2, 2.7, 1.9, 2-H), 5.47 (1H, q, *J* 1.3, *cis*-9-H), 5.35 (1H, d, *J* 0.7, *trans*-9-H), 4.98 (1H, d, *J* 1.3, 1-H), 4.19 (4H, m, 7-$H_2$, 10-$H_2$), 3.85 (2H, m, 4-H, 5-H), 2.44 (1H, dd, *J* 2.4, 2.4, 12-H), 1.30 (3H, d, *J* 5.9, 6-$H_3$); $\delta_C$ 138.6 (8-C), 131.1 (3-C), 126.8 (2-C), 114.1 (9-C), 94.0 (1-C), 80.1 (11-C), 76.2 (10-C), 75.0 (12-C), 70.1 (7-C), 66.3 (4-C), 56.8 (5-C), 18.4 (6-C); *m*/*z* ($EI^+$) 244, 242 (0%, M, $C_{12}H_{15}O_3Cl$), 200, 198 (10%, 24%, M − $CH_3CHO$, retro Diels–Alder), 151 (18%,

M − $OCH_2C(Cl)=CH_2$), 123 (43%, M − $CH_3CHO$ − $^+CH_2C(Cl)=CH_2$), 95 (67%), 85, 83 (37%, 100%), 75 (79%), 67 (63%), 55 (55%); *m/z* ($CI^+$, $NH_3$) 262, 260 (8%, 16%, M + $NH_4^+$, $C_{12}H_{19}NO_3Cl^{35}$ requires 260.1053 found 260.1053), 186, 184 (12%, 48%), 170, 168 (22%, 78%), 153 (18%), 152 (23%), 151 (100%, M − $OCH_2C(Cl)=CH_2$); $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 3304 (C≡*C*-*H*), 2958, 2118 (weak, *C*≡*C*-H), 1782, 1636, 1587, 1362, 1092, 1045; $R_f$ 0.70 (hexane–EtOAc, 75 : 25).

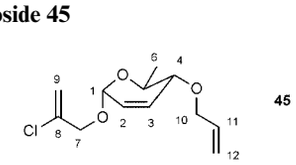
**(1*R*,3*S*,4*S*,5*R*,9*Z*)-4-(2-chloroprop-2-enyloxy)-2-methyl-7-tri-*n*-butylstannylmethylene)-2,9-dioxabicyclo[4.3.0]nonane 43**



**43**

2-Chloroprop-2-enyl 4-*O*-(prop-2-enyl)-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside **39** (50 mg, 0.2 mmol) was dissolved in dry toluene (2 ml) and warmed to reflux under nitrogen. AIBN (2 mg, 0.0013 mmol, 0.04 equiv.) was added portionwise and the solution refluxed for 20 min. A solution of tri-*n*-butyltin hydride (91 mg, 0.31 mmol, 1.5 equiv.) in dry toluene (3 ml) was added dropwise from a syringe pump over 3 hours and the solution refluxed for 16 hours. TLC analysis indicated a complex mixture of products containing one major product and many minor impurities. The reaction solution was concentrated to approximately 1 ml and purified by column chromatography, eluent hexane to 10% diethyl ether in hexane, to afford the title compound **43** (46 mg, 42%). Combustion analysis; $C_{24}H_{43}OSnCl$ requires C 54.01, H 8.12; found C 54.34, H 8.08%; $\delta_H$ 5.78 (1H, dm, *J* 2.0, multiplet coupling <1 Hz, not resolved, $^2J_{Sn,H}$ 56.3, 10-H), 5.37 (1H, d, *J* 1.2, 13a-H), 5.25 (1H, s, 13b-H), 4.78 (1H, t, *J* 6.0, 4-H), 4.26 (1H, ddd, *J* 13.0, 1.5, 1.5, 8a-H), 4.17 (1H, dm *J* 13.0, multiplet coupling <1 Hz, not resolved, 8b-H), 4.12 (1H, d, *J* 14.0, 11a-H), 4.01 (1H, d, *J* 14.0, 11b-H), 3.73 (1H, dd, *J* 8.3, 7.1, 1-H), 3.67 (1H, dq, *J* 8.2, 6.2 2-H), 2.68 (1H, m, calculated bandwidth = 10.3 + 7.1 + 5.7 = 23.1 Hz; measured 22.1 Hz; 6-H), 2.01 (1H, ddd, *J* 14.3, 5.7, 5.7, 5a-$H_{eq}$), 1.77 (1H, ddd, *J* 14.3, 10.3, 6.4, 5b-$H_{ax}$), 1.39 (6H, m, 17-$H_6$, $Sn(CH_2)_2CH_2$), 1.23 (9H, m and d, *J* 6.0, 16-$H_6$ and 14-$H_3$, $SnCH_2CH_2$ and pyran methyl group), 0.82 (15H, m, 15-$H_6$, 18-$H_9$, $SnCH_2(CH_2)_2CH_3$). Coupling constant correlations are shown in Table 5 of the electronic supplementary data for this paper; $^1H$–$^1H$ *J*-COSY NMR 1-H to 2-H to 14-$H_3$, 1-H to 6-H (weak) to 5a-H, 6-H to 5b-H, 5a-H to 4-H, 5b-H to 4-H, 5a to 5b, 8a-H to 8b-H, 8a-H and/or 8b-H to 10-H (unresolved), 11a-H to 11b-H, 11a to 13a-H (very weak); $\delta_C$ 159.2 (9-C), 138.1 (12-C), 118.2 (10-C), 113.4 (13-C), 97.2 (4-C), 83.1 (1-C), 73.2 (8-C), 69.7 (11-C), 66.2 (2-C), 41.8 (6-C), 31.3 (5-C), 29.5 (17-C, $Sn(CH_2)_2CH_2$), 27.7 (16-C, Sn-$CH_2$-$CH_2$), 18.8 (14-C), 14.1 (18-C, $Sn(CH_2)_3CH_3$), 10.1 (15-C, $SnCH_2$); *m/z* ($EI^+$) 479, 477, 475, 473 (6%, 13%, 10%, 8%, M − Bu, $C_{20}H_{34}O_3SnCl$), 385, 383, 381 (100%, 90%, 71%, M − Bu − $HOCH_2C(Cl)=CH$); $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 2960, 2928, 1762, 1637, 1587, 1378, 1057; $R_f$ 0.80 (hexane–$Et_2O$).

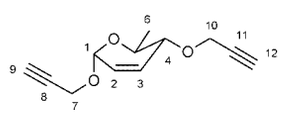
**2-Chloropropenyl 4-*O*-prop-2-enyl-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside 45**



**45**

2-Chloroprop-2-enyl 2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside (100 mg, 0.49 mmol) was dissolved in dry DMF (2 ml) and treated with sodium hydride (60% suspension in mineral oil, 27 mg + 16 mg, 0.66 mmol, 1.4 equiv.) under nitrogen and cooled to 0 °C. Allyl iodide (100 mg, 0.59 mmol, 1.2 equiv.) in dry DMF (1 ml) was added dropwise, the solution was allowed to attain ambient temperature and stirred under nitrogen for 16 hours. TLC analysis indicated an intense product spot with a minor impurity of similar $R_f$. The crude reaction solution was concentrated and purified by flash column chromatography, eluent hexane to 10% EtOAc in hexane, to yield the title compound **45** (67 mg, 56%) as a clear oil, which decomposed upon standing. $\delta_H$ 6.04 (1H, dd, *J* 10.2, 0.9, 2-H), 5.88 (1H, m, 11-H), 5.75 (1H, dq, *J* 10.3, 2.0, 3-H), 5.46 (1H, dd, *J* 2.8, 1.0, 9-H *cis* to Cl), 5.33 (1H, dd, *J* 2.0, 0.6, *trans* to 9-H), 5.26 (1H, dt, *J* 17.2, 1.5, *cis*-12-H), 5.17 (1H, dt, *J* 10.3, 1.3, *trans*-12-H), 4.97 (1H, s, 1-H), 4.16 (3H, m, 10-$H_2$, 7a-H), 4.07 (1H, m, 7b-H), 3.85 (1H, m, 5H), 3.62 (1H, dt, *J* 9.0, 1.5, 4-H), 1.28 (3H, d, *J* 5.9, 6-$H_3$); $\delta_H$ ($C_6D_6$) 5.72 (1H, d, *J* 10.2, 2-H), 5.62 (1H, ddd, *J* 22.5, 10.5, 5.3, 11-H), 5.48 (1H, dt, *J* 10.2, 2.3, 3-H), 5.13 (1H, d, *J* 1.3, *cis*-9-H), 5.05 (1H, dd, *J* 10.5 (estimated due to overlap), 1.2, 12a-H, 5.03 (1H, s, *trans*-9-H), 4.88 (1H, dd, *J* 10.5, 1.5, 12b-H), 4.71 (1H, br s, 1-H), 4.03 (1H, d, *J* 14.0, 10-H), 3.96 (1H, m, 5-H), 3.83 (1H, d, *J* 14.0, 10-H), 3.72 (1H, dd, *J* 9.0, 1.6, 4-H), 1.15 (3H, d, *J* 6.2, 6-$H_3$); $\delta_C$ 138.5 (8-C), 135.0 (11-C), 131.8 (3-C), 126.4 (2-C), 117.7 (12-C), 114.0 (9-C), 94.1 (1-C), 76.5 (4-C), 70.5, 70.3 (7-C and 10-C), 66.5 (5-C), 18.5 (6-C); $R_f$ 0.80 (hexane–EtOAc, 75 : 25).

**Prop-2-ynyl 4-*O*-prop-2-ynyl-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside 51**

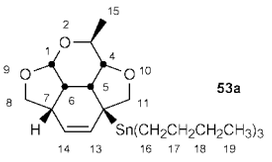


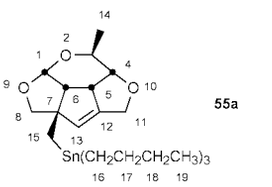
**51**

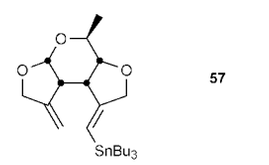
Prop-2-ynyl 2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside (200 mg, 1.2 mmol) was dissolved in dry DMF (5 ml) under nitrogen. Sodium hydride (60% suspension in mineral oil, 117 mg + 70 mg, 3.0 mmol, 1.5 equiv.) was added portionwise and the reaction solution cooled to 0 °C. Propargyl bromide (80% solution in toluene, 360 mg + 290 mg, 2.4 mmol, 2.0 equiv.) in DMF (1 ml) was added dropwise to maintain the above temperature. The solution was stirred for 2 hours, and then left to stand for a further 3 days. The solvent was removed, and the residue redissolved in chloroform (5 ml), and washed with water (4 × 5 ml), until no DMF was detected by TLC in the aqueous layer. The organic layer was dried over magnesium sulfate, filtered, and concentrated to afford a mixture of product and starting material as a yellow oil. Purification of the oil by column chromatography, eluent hexane to 25% ethyl acetate in hexane, afforded starting material as a white waxy solid (40 mg, 20%) and title compound **51** as an amber oil (120 mg, 48%). $\delta_H$ 6.09 (1H, d, *J* 10.3, 3-H), 5.77 (1H, d, *J* 10.6, 2-H), 5.14 (1H, d, *J* 2.5, 1-H), 4.29 (2H, d, *J* 2.5, 7-$H_2$), 4.24 (2H, d, *J* 2.4, 10-$H_2$), 3.83 (2H, m, H-4, H-5), 2.44 (1H, t, *J* 2.3, 9-H or 12-H), 2.42 (1H, t, *J* 2.3, 9-H or 12-H), 1.32 (3H, 6-$H_3$); $\delta_C$ 130.8 (CH, 3-C), 126.5 (CH, 2-C), 92.8 (CH, 1-C), 79.7, 79.6 (2CH, 11-C or 8-C), 75.8, 74.6 (2CH, 12-C or 9-C), 74.4 (CH, 4-C), 65.9 (CH, 5-C), 56.4, 54.7 ($2CH_2$, 7-C or 10-C), 18.0 ($CH_3$, 6-C); *m/z* ($EI^+$) 206 (M, absent), 162 (45%, M − $CH_3CHO$, retro Diels–Alder, $C_{10}H_{10}O_2$ requires 162.0681, found 162.0681), 151 (55%, M − $HC\equiv CH_2O^+$), 136 (46%, M − 70, M − retro Diels–Alder − HC≡CH ?), 123 (100%, M − retro Diels–Alder − $HC\equiv CCH_2^+$), 95 (55%), 93 (48%), 67 (100%); *m/z* ($CI^+$, $NH_3$) failed to give usable spectrum; $\nu_{max}$ ($CDCl_3$)/$cm^{-1}$ 3307 (C≡*C*-*H*), 2929, 2362, 2110 (*C*≡CH), 1451, 1382, 1262, 1090; $R_f$ 0.65 (hexane–EtOAc, 75 : 25).

**Cyclisation of prop-2-ynyl 4-*O*-prop-2-ynyl-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside 51**

Prop-2-ynyl 4-*O*-prop-2-ynyl-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside **51** (80 mg, 0.40 mmol) was dissolved in dry




toluene (2 ml) and warmed to reflux. AIBN (2 mg, 0.005 mmol, 0.04 equiv.) was added and the reaction solution refluxed for a further 15 min. A solution of tri-*n*-butyltin hydride (180 mg, 0.60 mmol, 1.5 equiv.) in dry toluene (2 ml) was added dropwise over 4 hours *via* a syringe pump. The reaction solution was then refluxed for 16 hours. TLC analysis indicated a complex mixture from which repeated flash column chromatography, eluent hexane to 10% ether in hexane, afforded in order of elution a mixture **54**, **56**, **57** (6 mg, 3% yield), the cyclopentylmethylstannane **55a** (13 mg, 7% yield), and the cyclohexenylstannane **53a** (23 mg, 12% yield).

Spectroscopic data for **53a**: $\delta_H$ 5.82 (1H, dd, *J* 10.0, 2.9, 13-H), 5.50 (1H, d, *J* 7.1, 1-H), 5.43 (1H, dd, *J* 10.2, 2.0, 14-H), 4.12 (1H, dd, *J* 8.6, 8.6, 8a-H), 3.96 (1H, d, *J* 8.4, 11a-H), 3.67 (1H, dd, *J* 8.4, 8.4, 8b-H), 3.58 (1H, d, *J* 8.6, 11b-H), 3.36 (2H, m, 3-H, 4-H), 3.01 (1H, ddd, *J* 11.5, 10.6, 7.1, 6-H), 2.69 (2H, m, 5-H, 7-H), 1.44 (6H, m, 17-$H_6$, $SnCH_2CH_2$), 1.31 (6H, m, 18-$H_6$, $Sn(CH_2)_2CH_2$), 1.12 (3H, d, overlap *J ca.* 6, 15-$H_3$), 0.90 (15H, m, 19-$H_9$, 16$H_6$, $SnCH_2(CH_2)_2CH_3$); $^1$H–$^1$H *J*-COSY NMR 1-H to 6-H to 5-H/7-H to 3-H/4-H to 15-$H_3$, 5-H/7-H to 8a-H to 8b-H to 5-H/7-H, 11a-H to 11b-H, 13-H to 14-H, 16-$H_6$ to 17-$H_6$ to 18-$H_6$ to 19-$H_9$; $\delta_C$ + $^{13}$C–$^1$H COSY 136.5 (13-C), 122.7 (14-C), 101.34 (1-C), 78.8 (3-C or 4-C), 76.3 (11-C), 72.9 (3-C or 4-C), 72.3 (8-C), 41.0, 37.7, 36.2, 35.4 (5-C, 6-C, 7-C, 12-C), 29.7 (18-$C_3$), 27.9 (17-$C_3$), 19.9 (15-C), 14.1 (16-$C_3$), 9.5 (19-$C_3$); $\delta_H$ ($C_6D_6$) 5.80 (1H, dd, *J* 9.9, 2.9, 13-H), 5.63 (1H, d, *J* 6.7, 1-H), 5.28 (1H, dd, *J* 10.2, 2.0, 14-H), 4.05 (1H, d *J* 8.4, 11a-H), 3.95 (1H, dd, *J* 8.5, 8.5, 8a-H), 3.70 (2H, m, 3-H, 8b-H), 3.66 (1H, d, *J* 8.4, 11b-H), 3.56 (1H, dd, *J* 9.7, 9.7, 4-H), 2.73 (1H, ddd, *J* 10.9, 10.9, 6.8, 6-H), 2.64 (1H, dd, *J* 10.4, 9.7, 5-H), 2.62 (1H, m, 7-H), 1.60 (3H, d *J* 6.0, 15-$H_3$), 1.55 (6H, m, 17-$H_6$, $SnCH_2CH_2$), 1.40 (6H, m, 18-$H_6$, $Sn(CH_2)_2CH_2$), 1.05 (9H, m, 19-$H_9$, $Sn(CH_2)_3CH_3$), 1.0 (6H, m, 16$H_6$, $SnCH_2$); $^1$H–$^1$H *J*-COSY NMR $\delta_H$ ($C_6D_6$) 1-H to 6-H to 7-H to 8a-H to 8b-H to 7-H, 3-H to 15-$H_3$, 4-H to 5-H, 11a-H to 11b-H, 13-H to 14-H, 16-$H_6$ to 17-$H_6$ to 18-$H_6$ to 19-$H_9$, collected coupling constant data are reported in Table 6 of the electronic supplementary data for this paper; $^1$H–$^1$H-NOESY ($C_6D_6$) data and internuclear distances for **53b** are reported in Table 7 of the electronic supplementary data for this paper; $\delta_C$ + $^{13}$C–$^1$H COSY ($C_6D_6$) 137.0 (CH, 13-C), 123.5 (CH, 14-C), 101.6 (CH, 1-C), 79.4 (CH, 4-H), 76.2 ($CH_2$, 11-C), 73.0 (CH, 3-C), 72.1 ($CH_2$, 8-C), 41.5 (C, 12-C), 38.3 (CH, 5-C), 36.6 (CH, 6-H), 36.0 (CH, 7-H), 30.1 ($CH_2$, 17-C), 28.3 ($CH_2$, 18-C), 20.4 ($CH_3$, 15-C), 14.3 ($CH_3$, 19-$C_3$), 9.6 ($CH_2$, 16-$C_3$).

Spectroscopic data for **55a**: $\delta_H$ 5.23 (1H, d *J* 7.5, 1-H), 5.22 (1H, overlaps with signal at $\delta$ 5.23 br d or t?, *J* 1.8, 13-H), 4.09 (2H, s, 11-$H_2$), 3.81 (1H, d *J* 9.4, 8a-H), 3.55 (2H, m, 3-H, 4-H), 3.45 (1H, m, 5-H), 3.24 (1H, d, *J* 9.4, 8b-H), 2.28 (1H, dd, *J* 8.0, 8.0, 6-H), 1.37 (6H, m, 17-$H_6$, $SnCH_2CH_2$), 1.23 (10H, m, 14-$H_3$, 15a-H, 18-$H_6$, $Sn(CH_2)_2CH_2$), 1.07 (1H, d, *J* 13.0, 15b-H), 0.82 (9H, t, *J* 7.2, 19-$H_9$, $Sn(CH_2)_3CH_3$), 0.77 (6H, m, 16$H_6$, $SnCH_2(CH_2)_2CH_3$); $^1$H–$^1$H *J*-COSY NMR, 1-H/13-H to 6-H to 5-H to 3-H/4-H to 14-H, 8a-H to 8b-H, 1-H/13-H to 11-$H_2$; $\delta_H$ ($C_6D_6$) 5.47 (1H, d, *J* 7.3, 1-H), 5.11 (1H, br s, 13-H), 4.15 (1H, br d, *J* 13.6, 11a-H), 4.07 (1H, br d, *J* 13.3, 11b-H), 4.05 (1H, dq, *J* 9.4, 6.3, 3-H), 3.94 (1H, d, *J* 9.2, 8a-H), 3.79 (1H, dd, *J* 9.5, 7.9, 4-H), 3.45 (1H, ddd, *J* 8.5, 7.7, <1, 5-H), 3.27 (1H, d, *J* 9.3, 8b-H), 2.16 (1H, dd, *J* 8.3, 7.6, 6-H), 1.63 (6H, m, 17-$H_6$, $SnCH_2CH_2$), 1.56 (3H, d, *J* 6.4, 14-$H_3$), 1.46 (6H, m, 18-$H_6$, $Sn(CH_2)_2CH_2$), 1.16 (1H, d, *J* 13.0, 15a-H), 1.05 (9H, t, *J* 7.3, 19-$H_9$, $Sn(CH_2)_3CH_3$), 1.03 (1H, d, *J* 13.0 ? overlap, 15b-H), 0.96 (6H, m, 16$H_6$, $SnCH_2$); $^1$H–$^1$H *J*-COSY NMR $\delta_H$ ($C_6D_6$) 1-H to 6-H to 5-H to 4-H to 3-H to 14-$H_3$, 5-H to 13-H weak to 11a-H to 11b-H, 8a-H to 8b-H, 15a-H to 15b-H ?, 16-$H_6$ to 17-$H_6$ to 18-$H_6$ to 19-$H_9$; $\delta_C$ 146.7 (C, 12-C), 129.7 (CH, 13-C), 101.0 (CH, 1-C), 76.1 ($CH_2$, 8-C), 75.6 (CH, 4-C), 69.6 (7-C), 63.2 (CH, 3-C), 63.1 ($CH_2$, 11-C), 50.2 (CH, 5-C), 49.7 (CH, 6-C), 29.6 ($CH_2$, 18-$C_3$), 27.9 ($CH_2$, 17-$C_3$), 18.2 ($CH_2$, 15-C), 18.0 ($CH_3$, 14-C), 14.1 ($CH_2$, 19-$C_3$), 10.3 ($CH_2$, 16-$C_3$); assignments confirmed by $^{13}$C–$^1$H *J*-COSY NMR spectrum.

Spectroscopic data for the mixture **54, 56, 57**: $\delta_H$ (integrations assigned relative to $Bu_3Sn$ + 15-$H_3$, all assignments tentative) 6.0 (0.45H, br s, $^2J_{Sn,H}$ 55, **56** 15-H), 5.26 (0.35H, d, *J* 3.6, 1-H), 5.09 (1.8H, br m, 1-H and/or **54** 13-H), 4.50 (2.2H, m), 4.45 (0.45H, dd, *J* 13.4, 1.9), 4.28 (0.45H, dd, *J ca.* 13, 2), 3.79 (0.25H, dd, *J* 9.6, 7.1, 4-H), 3.69 (0.45H, dd, *J ca.* 9.5, 7, 4-H), 3.29 (1H, m, 3-H+?), 3.11 (0.4H, br s, 6-H), 3.05 (0.4H, br s, 6-H), 1.48 (6H, m, 17-$H_6$, $SnCH_2CH_2$), 1.34 (6H, m, 18-$H_6$, $Sn(CH_2)_2CH_2$), 1.28, 1.25 (3H, d and d, *J* 6.0 and 6.0, 14-$H_3$), 0.96 (15H, m, 16$H_6$, 19-$H_9$, $SnCH_2$, $Sn(CH_2)_3CH_3$); $^1$H–$^1$H *J*-COSY NMR $\delta$ 6.0 to 3.05 and 4.50, 5.26 to 3.05, 5.09 to 3.29 and 3.11, 4.50 to 4.28 and 3.05, 3.79 to 3.29, 3.69 to 3.29, 3.29 to 1.25, 16-$H_6$ to 17-$H_6$ to 18-$H_6$ to 19-$H_9$.

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