Sesquiterpenes from the New Zealand Liverwort *Lepidolaena hodgsoniae*

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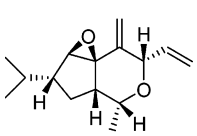
Received February 21, 2005

NMR studies have shown that seven new sesquiterpenoids, **3**, **4**, **5a**, and **7**−**10**, isolated from dried samples of the New Zealand liverwort *Lepidolaena hodgsoniae* have the same substituted cyclopentapyran ring system as the previously described insecticidal sesquiterpene diene hodgsonox (**1**), which has been reported only from this plant. In all but one compound, **10**, the 1,1-disubstituted double bond of hodgsonox has migrated into an endocyclic position, but only two, **5a** and **9**, have the double bonds in conjugation. These seven new compounds represent a variety of different oxidation levels. Two of the new derivatives, **9** and **10**, were isolated only from an aged sample and are presumably artifacts. The only other terpenoid isolated in significant quantity was (7*R*,10*R*)-calamenene (**2**).

As part of our continuing studies into the discovery of new biologically active compounds from New Zealand's native flora, we recently reported the isolation of a new insecticidal sesquiterpene, hodgsonox (**1**), from the New Zealand endemic liverwort *Lepidolaena hodgsoniae* Grolle.[1] New Zealand liverworts have proved to be a particularly rich source of new natural products, and we have reported results from studies on three additional members of the genus *Lepidolaena* (family Lepidolaenaceae).[2−4] Hodgsonox (**1**) contains a novel sesquiterpene ring system and includes a unique doubly allylic ether function. Our studies on the biosynthesis of **1** have revealed that it is formed exclusively by the methylerythritol biosynthetic pathway.[5] This is the only liverwort sesquiterpenoid known to be formed in this way. On TLC, visualizing with anisaldehyde, hodgsonox is revealed as a characteristic purple spot. During our biosynthetic studies on cultures of *L. hodgsoniae*, it became apparent that there were other minor components that showed a similar response with this TLC system, and we undertook the present study to determine if any of these were related to **1**. We now report the reinvestigation of *L. hodgsoniae*, resulting in the isolation of the known sesquiterpene (7*R*,10*R*)-calamenene (**2**) and seven new hodgsonox-type sesquiterpenes (**3**, **4**, **5a**, **7**−**10**).

Results and Discussion

Samples of *L. hodgsoniae* were collected from a mixed podocarp forest at Makarora in the South Island of New Zealand. A dichloromethane extract was chromatographed over silica using a cyclohexane−dichloromethane gradient (column 1). Early fractions yielded a sesquiterpene containing a benzene ring that was determined by NMR studies to be a calamenene. Comparison of the ^{1}H NMR spectrum with those published for the *cis* and *trans* isomers[6] showed that it had a *cis* relationship between the isopropyl and methyl groupings. Optical rotation studies showed that this compound was the (7*R*,10*R*)-isomer (**2**).[7]



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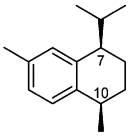

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Hodgsonox (**1**) was isolated in high levels (1% dry plant w/w), as described previously, and was identified by TLC and by comparison of ^{1}H NMR data.[1] The ^{1}H NMR spectra of a slightly more polar component contained distinct vinyl proton signals similar to those of **1**. This compound (**3**) was named hodgsonox B.

The molecular formula of hodgsonox B was determined to be $C_{15}H_{24}O$ by HREIMS. ^{1}H and ^{13}C NMR spectroscopic observations confirmed the proton and carbon counts. The absence of hydroxyl or carbonyl bands in the IR spectrum suggested that the compound is an ether, and this was supported by the presence of two oxygenated methine carbon signals at δ 70.1 and 77.7 in the ^{13}C NMR spectrum. These peaks were associated (HSQC) with two one-proton multiplets (δ_H = 4.24, dq, J = 6.5, 6.5 Hz; δ_H = 4.32, br dd, J = 3, 9 Hz) in the ^{1}H NMR spectrum. The compound contained two double bonds, one of which was monosubstituted, as evidenced by a characteristic vinyl pattern (δ_H = 5.86, ddd, J = 9, 10, 17 Hz; δ_H = 5.18, ddd J = 0.5, 2, 10 Hz; δ_H = 5.27, ddd, J = 1, 2, 17 Hz) in the ^{1}H NMR spectrum. The ^{13}C NMR spectrum revealed that the remaining double bond was tetrasubstituted, with two signals corresponding to unprotonated carbons at δ 122.3 and 134.5. Also featured in the ^{1}H NMR spectrum were signals for an isopropyl group (δ_H = 0.94, 0.95, both d, J = 6.5 Hz, δ_H = 1.43 ddq, J = 8.5, 6.5, 6.5 Hz), an olefinic methyl (δ_H = 1.52, dddd, J = 1.5, 1.5, 1.5, 2.5 Hz), and a tertiary methyl group (δ_H 1.16, d, J = 6.5 Hz).

Correlations from a COSY experiment established the connectivity between most of the protonated carbons. Incorporation of the results of a series of single-frequency, homonuclear decoupling experiments completed the connectivity and established a substructure, based around the previously determined ether linkage. This accounted for all but three of the carbon atoms, those of the tetrasubstituted double bond and an attached methyl group.

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10.1021/np050058x CCC: $30.25
Published on Web 05/13/2005

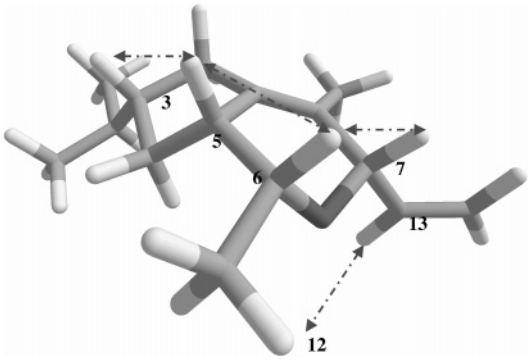
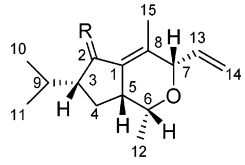


Figure 1. Calculated lowest energy conformer (MM3[8–10]) of **3** showing key NOESY correlations.

A CIGAR-HMBC experiment provided further verification of these structural features. In addition, correlations from the methine proton signal at δ 4.24 (H-6) and from a methylene proton signal at δ 1.86 (H-4) to the carbon signal at δ 134.5 (C-1) identified the olefinic carbon attached to C-5. A correlation from the vinyl proton signal at δ 5.86 (H-13) to the signal of the remaining carbon of the tetrasubstituted double bond (δ_C 122.3, C-8) enabled the incorporation of this ring into a dihydropyran ring system. The remaining bonding connections could now be made to give structure **3** for hodgsonox B. The alternative anti-Bredt structure could be discounted on the basis of ring strain.



3 R = H,H
4 R = O

It seemed probable that the relative stereochemistry would be the same as that of the co-occurring hodgsonox (**1**),[1] and key correlations from a 2D NOESY experiment, summarized in Figure 1, confirmed this. Correlations between H-3 (δ_H = 1.64) and H-5 (δ_H = 2.59), H-5 and H-6 (δ_H = 4.24), and H-6 and H-7 (δ_H = 4.32) revealed that these four protons projected in the same direction. In addition, a correlation between H-13 (δ_H = 5.86) and H-12 (δ_H = 1.16) showed that the C-7 vinyl and C-6 methyl groups pointed to the same side. Thus, the structure of hodgsonox B is **3**.

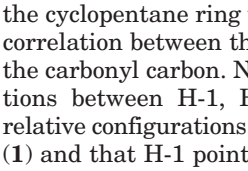
A further compound, hodgsonox E, eluting from column 1 soon after **3**, showed very similar NMR spectroscopic data and gave a HRMS consistent with an elemental formula of $C_{15}H_{22}O_2$. The ^{13}C NMR spectrum showed that this compound had one less methylene group than **3** and revealed a carbonyl carbon signal at δ 207.2. This was assigned to a ketone function at C-2, as the allylic methyl protons (H-15) resonated at δ 2.07 rather than δ 1.52 as in **3**. In addition, the H-3 signal was significantly deshielded relative to its position in **3** (δ 2.20 compared to δ 1.43), and the UV spectrum showed a λ_{max} at 249 nm (log ϵ 3.85). Thus, hodgsonox E is the 2-keto derivative (**4**) of **3**. COSY and CIGAR correlations supported this structure, and NOESY correlations, similar to those observed for **3**, confirmed the stereochemistry.

The ^1H NMR spectrum of the methanol eluent from column 1 also contained some hodgsonox-like signals. Further chromatography of this fraction on silica (column 2) yielded two components with ^1H NMR spectra resembling that of hodgsonox. The less polar of these was named hodgsonox C and the other hodgsonox D.

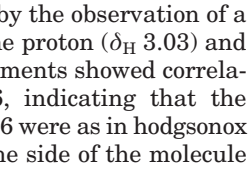
Hodgsonox C (**5a**) was determined by HREIMS, supported by a ^{13}C NMR spectrum showing 15 distinct signals, to have the molecular formula $C_{15}H_{22}O_3$. The IR spectrum showed bands typical of hydroxyl (3400 cm^{-1}) and ketone functions (1700 cm^{-1}). Further support for a ketone came from a peak at δ 215.8 in the ^{13}C NMR spectrum. As in compounds **1**, **3**, and **4**, signals indicative of a monosubstituted double bond were present in the ^1H NMR spectrum. However, the pattern for hodgsonox C was simpler (δ_H = 5.11, br dd, J = 1.5, 11 Hz; δ_H = 5.59, br ddd, J = 0.5, 2, 17 Hz; δ_H = 6.44, dd, J = 11, 17 Hz), an indication that this grouping was attached to an unprotonated carbon. A tetrasubstituted double bond was also present, with peaks in the ^{13}C NMR spectrum at δ_C 101.2 and 147.9. The chemical shift of the former suggested an enol ether unit. As in **3**, there was a methyl group attached to the tetrasubstituted double bond (δ_H 1.71, d, J = 1.2 Hz).

The COSY spectrum revealed a subunit involving carbons 1, 4, 5, 6 (oxygenated), and 12, and this was substantiated by a complete analysis of the ^1H NMR coupling pattern for this portion of the molecule. CIGAR correlations from the olefinic proton signals at δ 5.11 and 5.59 (H-14) to the more deshielded double-bond carbon (δ_C 147.9, C-7) established that the two double bonds were conjugated and that the vinyl and oxygen linkages were to the same end of the enol ether C=C linkage. Substitution at the other end of this bond was established by CIGAR correlations from the methyl signal at δ 1.71 (H-15) and the methine proton signal at δ 3.03 (H-1) to both of the tetrasubstituted alkene carbons. This linked the diene system to the previously determined subunit.

An isopropyl group with methyl signals at δ 0.63 (d, J = 6.5 Hz) and 0.96 (d, J = 6.6 Hz) was connected to a quaternary center, as the associated methine proton resonance (δ_H 1.85) appeared as a less complex pattern (qq, J = 6.5, 6.5 Hz) than the corresponding signal of compounds **1**, **3**, and **4**. A CIGAR correlation from the isopropyl methine proton signal to the methylene carbon signal at δ 26.8 (C-4) enabled the positioning of the only unassigned quaternary carbon between C-4 and C-9. Its chemical shift established that it was oxygenated (δ_C 82.2, C-3). A further correlation from H-9 to the carbonyl carbon (δ_C 215.8, C-2) enabled the inclusion of all the carbon atoms. Closure of the cyclopentane ring was enabled by the observation of a correlation between the C-1 methine proton (δ_H 3.03) and the carbonyl carbon. NOESY experiments showed correlations between H-1, H-5, and H-6, indicating that the relative configurations at C-5 and C-6 were as in hodgsonox (**1**) and that H-1 pointed to the same side of the molecule as H-5 and H-6. The only remaining feature to establish was the stereochemistry at C-3. Thus, hodgsonox C is either **5a** or **5b**.



5a R = 3β-OH
5b R = 3α-OH
9 R = 3β-H



6a R = 3β-OH
6b R = 3α-OH

The COSY experiment identified some interesting long-range couplings involving H-1. These comprised a four-bond coupling ($^4J_{HH}$ = 1 Hz) between H-1 and the allylic methyl

Table 1. Selected ^{1}H/^{1}H NMR Coupling Constants (Hz) for Hodgsonox C Compared to Values Calculated for Structures **5a**, **5b**, **6a**, and **6b** Derived from Conformational Searches (MM3)

		J_{calc}			
	J_{obs}	**5a**	**5b**	**6a**	**6b**
n_{conf}[a]		3	5	3	4
$J_{1,4}$ (*cis*)	1.5	1.5	1.5	0.5	0.5
$J_{1,4}$ (*trans*)	< 0.5	0.5	0.5	0.5	0.5
$J_{1,5}$	7	7	7	13	13
$J_{4,5}$ (*trans*)	11.5	11.5	11.5	12	12
$J_{4,5}$ (*cis*)	7.5	6	6	5	5
$J_{5,6}$	2	2	2	3	3

[a] Number of unique conformations generated within a 3.5 kcal mol^{-1} energy window.

protons (H-15), weak $^6J_{HH}$ vinylogous allylic couplings between H-1 and both H-14 protons, and a significant long-range coupling (J = 1.5 Hz) to one of the C-4 methylene proton signals (δ_H 1.77). As a consequence, the H-1 signal appeared as a broadened doublet. The latter coupling suggested a *cis* ring junction as in **5a** and **5b**. Conformational searches (MM3 force field[8−10]) were conducted on four possible diastereoisomers, **5a**, **5b**, **6a**, and **6b**, to explore this point in more detail. Small numbers (3−5) of low-energy conformations were generated in each case with only minor variations predicted in the ring conformations. In all modeled conformations the geometry of the H-1/C-1/C-5/C-4/H-4α and H-1/C-1/C-5/C-4/H-4β systems deviated appreciably from the classical planar *W* arrangement. In cases that approximated this geometry, C-4 was skewed appreciably out of plane (Figure 2). Torsion angles (φ_1 = H-1/C-1/C-5/C-4 and φ_2 = C-1/C-5/C-4/H-4) measured for individual structures derived from the conformational search were used to calculate predicted four-bond couplings, $J_{1,4}$, by way of an empirical relationship:

$$J_{1,4} = 0.82\cos^2\varphi_1\cos^2\varphi_2 - 0.62\cos\varphi_1\cos\varphi_2(\cos\varphi_{1+}\cos\varphi_2) + 0.21\cos\varphi_1\cos\varphi_2 - 0.32 \text{ Hz}$$

derived from an ab initio analysis of propanic systems.[11] These results were used to calculate Boltzmann weighted averaged values for the H-1/H-4 couplings for each isomer (Table 1). Results for structures with a *cis* ring junction agreed well with the observed value for $J_{1,4}$. A modified Karplus equation[12] was used to calculate averaged three-bond coupling constants for H-5 in the generated structures (Table 1). Those calculated for isomers **5a** and **5b** are in good agreement with the observed values.

In structures **5a** and **5b** it is predicted that the 4β-proton would be that coupling strongly to H-1. In agreement with this was the fact that the coupled H-4 signal showed a NOESY correlation to H-5, whereas its geminal partner did not (Figure 2). H-4β showed NOESY correlation to only one of the isopropyl methyls, whereas H-4α correlated to both. On this basis, the isopropyl group was deemed to lie on the α-face of the molecule as in **5a**.

Another fraction from column 2 was subjected to preparative TLC, which yielded hodgsonox D (**7**), which gave a characteristic blue/purple TLC spot (vanillin). The ^{1}H NMR spectrum clearly showed the presence of an acetate signal at δ 2.04 and a CH−O signal at δ 4.42.

HREIMS suggested that the molecular formula of hogsonox D is $C_{17}H_{24}O_3$. The ^{13}C NMR spectrum confirmed the carbon count, but analysis of the carbon types revealed that there were 25 hydrogens bonded to carbons. The presence of a hydroxyl stretch in the IR spectrum raised the hydrogen count to at least 26. ^{1}H and ^{13}C NMR spectroscopic observations showed that the two additional carbons came from an acetate group (δ_H 2.04, s; δ_C 21.2, 171.6), while the ^{13}C NMR spectrum revealed signals for three oxygenated methine carbons (δ 70.2, 73.7, and 76.4) and one oxygenated methylene carbon (δ 61.5). Two of these carbons could be accounted for by the ether linkage of the hodgsonox skeleton. The remaining two would accommodate the acetate and the hydroxyl groups. Thus, the molecular formula is $C_{17}H_{26}O_4$ and the peak observed in the HREIMS was due to loss of water.

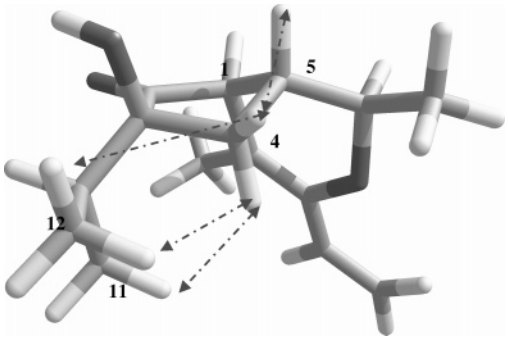
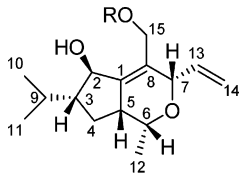


Figure 2. Calculated lowest energy conformer (MM3[8−10]) of **5a** showing key NOESY correlations.

The gross features of the ^{1}H and ^{13}C NMR spectra bore considerable similarity to those of **3** and **4**. A notable difference was the lack of a methyl group attached to a double bond. It appeared that this group (C-15) had been oxygenated. CIGAR correlations from the oxygenated methylene protons (δ_H = 4.40, br d, J = 12 Hz; δ_H = 5.09, d, J = 12 Hz) to the ester carbonyl carbon (δ_C = 171.6) and to two unprotonated alkene carbons, C-1 (δ_C = 145.5) and C-8 (δ_C = 126.8), confirmed that the acetate group was at C-15. A doublet at δ 4.42 (J = 4.5 Hz, H-2) in the ^{1}H NMR spectrum showed CIGAR correlations to both the C-1 and C-8 signals, and the hydroxyl group could therefore be placed at C-2. Further CIGAR correlations confirmed the structure as **7**.



7 R = Ac
8 R = H

An unusual feature of the ^{1}H NMR spectra of **3**, **4**, and **7** was the large homoallylic coupling observed between the doubly allylic proton, H-7, and the ring junction proton, H-5 (3 Hz for **3**, 2.3 Hz for **4**, and 2.9 Hz for **7**). This requires that the C−H bonds associated with each proton are essentially parallel and at right angles to the intervening carbon−carbon double bond. The similarities in NMR spectra suggest that **3**, **4**, and **7** have the same stereochemistry at C-3, C-5, C-6, and C-7. This was confirmed by the observation of NOESY correlations between H-3/H-5, H-5/H-6, and H-6/H-7 as observed for hodgsonox B (**3**). Correlations between H-2 (δ_H = 4.42) and the isopropyl methyl proton signals (δ_H = 0.89, 1.03) showed that the hydroxy group at C-2 and the isopropyl group at C-3 are in a *trans* relationship.

The methanol eluent from column 2 was further chromatographed on silica with $CHCl_3/Et_2O$ (column 3) to yield a further derivative, hodgsonox F. This compound had HREIMS data consistent with a molecular formula of

Table 2. Comparison of NMR Chemical Shifts for Compounds **7** and **8**[a]

	δ_C		δ_H			δ_C		δ_H	
position	**8**	**7**	**8**	**7**	position	**8**	**7**	**8**	**7**
1	141.8	146.1	–	–	9	32.3	32.3	1.46	1.46
2	75.5	74.1	4.37	4.47	10	21.0	20.9	0.84	0.85
3	54.4	53.8	1.52	1.70	11	21.9	21.7	1.08	1.14
4	30.4	29.8	0.74	0.80	12	18.4	18.5	1.04	1.06
			1.53	1.55	13	138.4	137.4	5.75	5.90
5	42.1	41.8	2.62	2.60	14	118.0	117.9	5.01	5.14
6	69.9	70.3	4.01	3.92				5.18	5.40
7	76.4	76.4	4.54	4.58	15	60.3	61.6	3.84	4.27
8	132.8	127.0	–	–				4.11	5.09

[a] C_6D_6; 125 MHz (^{13}C); 500 MHz (^1H).

Table 3. Comparison of NMR Chemical Shifts for Compounds **5a** and **9**[a]

	δ_C		δ_H			δ_C		δ_H	
position	**9**[b]	**5a**[c]	**9**[d]	**5a**[e]	position	**9**[b]	**5a**[c]	**9**[d]	**5a**[e]
1	53.1	52.4	2.85	3.03	9	27.9	33.3	2.14	1.85
2	217.0	215.8	–	–	10	18.1	17.4	0.69	0.63
3	54.9	82.2	2.21	–	11	21.1	16.1	0.94	0.96
4	20.7	26.8	1.73	1.77	12	18.2	17.9	1.35	1.32
			1.95	1.89	13	128.5	128.1	6.47	6.44
5	39.7	37.5	2.39	2.66	14	114.0	114.4	5.10	5.11
6	69.9	69.8	3.97	3.97				5.58	5.59
7	147.5	147.9	–	–	15	14.3	14.0	1.75	1.71
8	102.5	101.2	–	–					

[a] $CDCl_3$. [b] 75 MHz. [c] 125 MHz. [d] 300 MHz. [e] 500 MHz.

$C_{15}H_{22}O_2$. However, the presence of four oxygenated carbon signals in the ^{13}C NMR spectrum (CH_2 signal at δ 60.3 and CH peaks at δ 69.9, 75.5, and 76.4), coupled with a very close similarity of the ^1H and ^{13}C NMR spectra with that of hodgsonox D (Table 2), suggested that this compound is the diol **8**. Hence, the observed MS peak resulted from a loss of water. 2D NMR experiments (GHMBC, COSY, and NOESY) confirmed this analysis by showing correlations similar to those observed for **7**.

Chromatography of a sample of dried *L. hodgsoniae* that had been stored at room temperature for 15 months yielded (7*R*,10*R*)-calamenene (**2**), hodgsonox (**1**), and hodgsonox B, C, D, E, and F (**3**, **4**, **5a**, **6**, and **7**) as before. However, it was noteworthy that the levels of hodgsonox were dramatically lower than had been found with fresh plant material. Significant amounts of two new ketones were obtained; one, hodgsonox G, that was less polar than hodgsonox, and another, hodgsonox H, that was more polar than hodgsonox E. Both gave HREIMS data consistent with a molecular formula of $C_{15}H_{22}O_2$ and proved to be double-bond positional isomers of hodgsonox E. The ^{13}C NMR data for hodgsonox G (**9**) and C (**5a**) showed a close correspondence (Table 3). Like **5a**, hodgsonox G contains a CH_3 attached to a double bond (δ_H 1.75), and the two double bonds are conjugated, as was evident from the H-13 coupling pattern. A broad doublet was observed for H-1 at δ 2.85 (J = 8.5 Hz) similar to that observed for **5a**.

Hodgsonox H (**10**) clearly has retained the 1,1-disubstituted double bond of hodgsonox (**1**) (δ_H 5.23, 5.26). Like **1**, the ^1H NMR coupling pattern of H-13 (δ_H = 5.78, ddd, J = 7, 10.5, 17 Hz) showed that hodgsonox H has a vinyl group attached to a methine center. This methine was oxygenated as expected for a hodgsonox derivative (δ_C = 77.9). COSY and HMBC spectra established the remainder of the hodgsonox skeleton, and a ketone function (δ_C = 215.0, IR ν_{max} = 1730 cm^{-1}) was identified at C-2 by HMBC correlations to the methine protons assigned to H-1 (δ 2.60) and H-3/H-9 (δ 2.18, 2.20). NOESY correlations supported a *cis* arrangement of hydrogens at the methane carbons C-3, C-5, C-6, and C-7, as has been noted in the other hodgsonox derivatives. Like hodgsonox G (**9**) it also exhibited a broad doublet for H-1 in the ^1H NMR spectrum, but with a much larger coupling constant (J = 14.5 Hz compared to 8.5 Hz for **9**). This suggested the possibility of a *trans* ring junction. Confirmation was achieved by NOESY experiments that revealed exchange between H-1 and the methyl proton systems, H-11 and H-12. H-1 also interacted with one of the C-4 protons, which in turn correlated with H-11. These results from the NOESY experiment fit well with the lowest energy structure generated from an MM3 conformation search (Figure 3) for the *trans*-fused structure **10**.

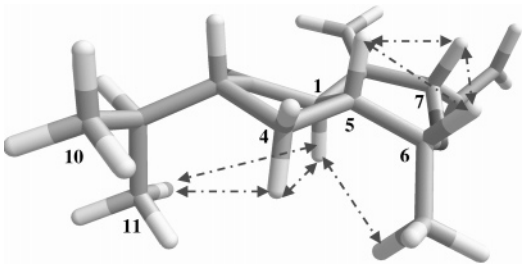
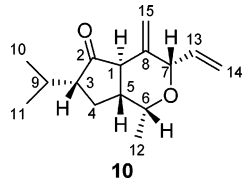


Figure 3. Calculated lowest energy conformer (MM3[8–10]) of **10** showing key NOESY correlations.



10

The seven sesquiterpenes (**3**, **4**, **5a**, **6**–**10**) isolated from dichloromethane extracts of the liverwort, *L. hodgsoniae*, are all new compounds with the same substituted cyclopentapyran skeleton as hodgsonox (**1**). Five of the compounds were clearly identifiable by the R_f and color of their spots (visualized with vanillin) in the TLC of the crude extract and are unlikely to have resulted from the extraction and separation processes. However, compounds **9** and **10** were isolated only from a stored sample of the dried plant and are presumably artifacts. The fact that the level of **1** had fallen considerably during the interval between analyses of the same bulk sample suggests that these compounds arise from modification of the structure of **1**. This is chemically feasible, as an acid-induced hydride shift from C-2 to C-1 with concomitant ketone formation at C-2 would lead from **1** to the *trans*-fused **10**, although we were unable to reproduce this process by treating **1** with boron trifluoride etherate, which generated a complex mixture. Hodgsonox G (**9**), and also hodgsonox E (**4**), could follow from **10** by double-bond migration.

The compounds isolated represent various oxidation levels, with hodgsonox B (**4**) being less oxidized than **1** and hodgsonox C (**5a**) being more so. Hodgsonox D (**7**) and hodgsonox F (**8**) might be formed from **1** by acid-induced epoxide opening, accompanied by migration of the exocyclic double bond into the ring and nucleophilic attack at C-15.

Lepidolaena hodgsoniae has proved to be a rich source of unusual hodgsonox-type terpenes, which predominate over terpenoids from more conventional biosynthetic pathways. As yet, none of these compounds has been studied for insecticidal activity.

Experimental Section

General Experimental Procedures. Optical rotations were performed in $CHCl_3$ solution on a JASCO DIP 1000

polarimeter using deuterium (Na, 589 nm) and mercury (Hg 577, 546, 435, 405 nm) lamps with specified filters. The instrument was first calibrated using cholesterol (20 mg/mL). UV spectra were recorded on a Varian Cary 500 scan spectrophotometer as EtOH solutions. IR spectra were recorded on a Perkin-Elmer 1600 FT-IR instrument as neat films on NaCl plates. ^{1}H and ^{13}C NMR spectra were recorded at 298 K in $CDCl_3$ or C_6D_6 on Varian Inova 500 or Varian Inova 300 FT/NMR spectrometers operating at 500 MHz (^{1}H)/125 MHz (^{13}C) or 300 MHz (^{1}H)/75 MHz (^{13}C), respectively. Chemical shifts are referenced to solvent peaks ($CDCl_3$ spectra: ^{1}H at 7.25 ppm, ^{13}C at 77.0 ppm; C_6D_6 spectra: ^{1}H at 7.16 ppm, ^{13}C at 128.4 ppm). Spectra were assigned with the aid of double-quantum filtered COSY (^{1}H−^{1}H correlations), HSQC (one-bond ^{1}H−^{13}C correlations), and HMBC-CIGAR experiments (two- and three-bond ^{1}H−^{13}C correlations).[11] Mass spectra were recorded on an EI/CI/FAB Kratos MS80RFA spectrometer operating at 4 kV and 70 eV or on a VG70-250S double-focusing magnetic sector mass spectrometer (EI, 70 eV). Normal-phase column flash chromatography was performed using silica gel 60 (200−400 mesh, 40−63 μm, Merck) as adsorbent. Columns were pre-equilibrated with the initial solvent before use. Analytical TLC was performed with Macherey-Nagel silica gel F254, 0.2 mm coated on aluminum. Plates were visualized under UV, then with vanillin. Preparative TLC was performed using PSC-Platten, 20 × 20 cm, Kieselgel 60 F_{254} of 0.5 mm thickness (Merck). Compounds were eluted using diethyl ether. Solvents were removed from chromatographic fractions by rotary evaporation at temperatures of <40 °C. Solvents were distilled before use, and spectral grade solvents were used for spectroscopic measurements.

Molecular Mechanics Calculations. These were performed with the aid of PCModel version 7.[13] Conformational searches used MM3[8−10] force fields, with the mixed Monte Carlo coordinate movements/bond rotations strategy[14] for the generation of initial structures. The default cutoff criteria were employed. Coupling constants were derived for each of the structures generated within a 3.5 kcal mol^{-1} energy window, using the in-built modified Karplus calculation,[12] and Boltzmann averaged values were determined.

Plant Material. Entire aerial parts of *Lepidolaena hodgsoniae* were collected at Makarora, Mt. Aspiring National Park, South Island, New Zealand, in November 2000 and June 2003 (Department of Conservation Collection Permits #03, 2000, OT-13587-FLO). Voucher specimens (001127-01, 031005-01) have been deposited with the Plant Extract Research Unit, University of Otago, Dunedin, New Zealand.

Extraction. Frozen plant material (−20 °C) was dried for 96 h at room temperature away from direct sunlight. Dry plant material (35 g) was ground in liquid N_2 and extracted by first shaking in dry CH_2Cl_2 (250 mL) for 36 h followed by filtration and ultrasonication of the solids in CH_2Cl_2 (150 mL) for 20 min. After filtration, the solvent was removed from combined extracts to give a green material (1.17 g).

Column 1. The crude extract (1.17 g) was adsorbed onto silica gel (2 g) and chromatographed on silica gel (60 g) with an elution gradient of pentane/CH_2Cl_2. Fractions were collected as 10 mL volumes and were combined on the basis of visually similar TLC results (UV_{254}, vanillin) to give nine fractions (label, solvent ratio, number of fractions, mass): *A*, 1:0, 10, 0.032 g; *B*, 9:1, 7 then 8:2, 6, 0.049 g; *C*, 4:1, 2 then 7:3, 4, 0.173 g; *D*, 7:3, 3 then 3:2, 9, 0.056 g; *E*, 1:1, 2, 0.032 g; *F*, 1:1, 5 then 2:3, 8 then 3:7, 4, 0.072 g; *G*, 3:7, 3 then 1:4, 2, 0.027 g; *H*, 1:4, 6 then 1:9, 8 then 0:1, 8 then 1:1 CH_2Cl_2/MeOH, 14, 0.110 g; *I*, MeOH, 20, 0.621 g.

Fraction *A* was purified by preparative silica gel TLC (pentane, −18 °C) to yield (7*R*,10*R*)-calamenene (**2**) (0.016 g). Fraction *C* (0.173 g) was hodgsonox (**1**). Fraction *E* was further separated by preparative TLC (CH_2Cl_2) to yield hodgsonox B (**3**) (0.020 g). Fraction *G* (0.027 g) was hodgsonox E (**4**).

Column 2. Fraction *I* was adsorbed onto silica gel (1 g) and chromatographed on silica gel (25 g) with an elution gradient of pentane/Et_2O. Fractions were collected as 10 mL volumes and were combined on the basis of visually similar TLC results (UV_{254}, vanillin) to give six fractions (label, solvent ratio, number of fractions, mass): *I1*, 1:0, 12 then 9:1, 7 then 4:1, 6 then 7:3, 7 then 3:2, 9 then 1:1, 1, 0.049 g; *I2*, 1:1, 4, 0.056 g; *I3*, 1:1, 3 then 2:3, 7, 0.099 g; *I4*, 2:3, 2 then 3:7, 6, 0.054 g; *I5*, 3:7, 1 then 1:4, 8 then 1:9, 6 then 0:1, 0.53 g; *I6*, MeOH, 24, 0.224 g.

Fraction *I2* was purified by preparative TLC (pentane/Et_2O, 7:3) to give hodgsonox C (**5a**) (0.040 g). Fraction *I4* was purified by preparative TLC (pentane/Et_2O, 7:3) to give hodgsonox D (**7**) (0.038 g).

Column 3. Fraction *I6* was adsorbed onto silica gel (0.5 g) and chromatographed on silica gel (5 g) with an elution gradient of $CHCl_3$/Et_2O. Fractions were collected as 4 mL volumes and were combined on the basis of visually similar TLC results (UV_{254}, vanillin) to give two fractions (label, solvent ratio, number of fractions, mass): *I6A*, 2:3, 6 then 3:7, 5 then 1:4, 1, 0.015 g; *I6B*, 1:4, 9 then 1:9, 7 then 0:1, 1, 0.032 g. Fractions *I6B* was purified by preparative TLC to yield hodgsonox F (**8**) (0.010 g).

Extraction of Aged Sample. A sample of dry *L. hodgsoniae* plant material that had been stored at room temperature for 5 months (61.2 g) was ground in liquid N_2 and extracted by first shaking in dry CH_2Cl_2 (350 mL) for 36 h followed by filtration and ultrasonication of the solids in CH_2Cl_2 (150 mL) for 20 min. After filtration, the solvent was removed from the combined extracts to give a green oil (3.27 g). The crude extract was adsorbed onto silica gel (4 g) and chromatographed under pressure on silica gel (80 g) with an elution gradient of pentane/CH_2Cl_2. Fractions were collected as 10 mL volumes and were combined on the basis of visually similar TLC results (UV_{254}, vanillin) to give six fractions (label, solvent ratio, number of fractions, mass): *J* 1:0, 7 then 9:1, 8 then 4:1, 8 then 7:3, 8 then 3:2, 8 then 1:1, 8 then 2:3, 8 then 3:7, 2, 0.207 g; *K*, 3:7, 6 then 1:4, 3, 0.174 g; *L*, 1:4, 4 then 1:9, 4, 0.049 g; *M*, 1:9, 5 then 0:1, 4, 0.038 g; *N* 0:1, 5, 0.083 g; *O*, MeOH, 30, 1.54 g.

Analysis of the ^{1}H NMR spectra revealed that fraction *J* was predominantly (+)-calamenene (**2**), fraction *K* contained a new compound, hodgsonox G (**9**), fraction *L* was hodgsonox (**1**), fraction *M* was mainly hodgsonox B (**3**), and fraction *N* was hodgsonox E (**4**). Purification of a subsample (0.040 g) of fraction *K* by preparative TLC (CH_2Cl_2) gave hodgsonox G (**9**) (0.010 g).

Fraction *O* was adsorbed onto silica gel (3 g) and chromatographed under pressure on silica gel (60 g) with an elution gradient of pentane/Et_2O/MeOH. Fractions were collected as 10 mL volumes and were combined on the basis of visually similar TLC results (UV_{254}, vanillin) to give 10 fractions: *O1*, 1:0:0, 8 then 9:1:0, 8 then 4:1:0, 7, 0.036 g; *O2*, 7:3:0, 4, 0.100 g; *O3*, 7:3:0, 3, 0.050 g; *O4*, 3:2:0, 3, 0.041 g; *O5*, 3:2:0, 1 then 1:1:0, 2, 0.022 g; *O6*, 1:1:0, 2, 0.039 g; *O7*, 2:3:0, 4, 0.130 g; *O8*, 3:7:0, 7 then 1;4:0, 8 then 1:9:0, 7 then 0:1:0, 5, 0.254 g; *O9*, 0:1:0, 2 then 0:3:7, 3, 0.050 g; *O10*, 0:3:7, 7, then 0:6:4, 9 then 0:0:1, 30, 0.510 g.

^{1}H NMR showed that fraction *O2* contained a new compound, hogsonox H (**10**), fraction *O3* was largely hodgsonox E (**4**), fraction *O5* was predominantly hodgsonox C (**5a**), fraction *O7* was mainly hodgsonox D (**7**), and fraction *O9* was mainly hodgsonox F (**8**). Purification of fraction *O2* by preparative TLC (CH_2Cl_2) gave hodgsonox H (0.036 g) (**10**).

Hodgsonox {(1a*R*,2*R*,3a*S*,4*R*,6*S*,7a*R*)-*rel*-(+)-6-ethenylhexahydro-4-methyl-7-methylene-2-(1-methylethyl)-3*H*-oxireno[2,3]cyclopenta[1,2-*c*]pyran} (1): CAS No. 340986-15-4; $[\alpha]_D$, IR, ^{1}H and ^{13}C NMR as in ref 1.

(7*R*,10*R*)-Calamenene {(1*R*,4*R*)-1,2,3,4-tetrahydro-1,6-dimethyl-4-(1-methylethyl)naphthalene} (2): CAS No. 22339-23-7; colorless oil; TLC R_f = 0.73 (pentane, −18 °C); $[\alpha]^{21}_{589}$ 27.6° (*c* 0.2, $CHCl_3$), lit[7] +33.4°; IR (film) ν_{max} 3006, 2957, 2925, 2869, 1731, 1614, 1499, 1463, 1383, 1373, 1261, 1038, 814 cm^{-1}; ^{1}H and ^{13}C NMR as in refs 5, 6.

Hodgsonox B {(1*R*,3*S*,6*S*,7a*R*)-(−)-3-ethenyl-1,4-dimethyl-6-(1-methylethyl)hexahydrocyclopenta[*c*]pyran} (3): colorless oil; TLC R_f = 0.5 (CH_2Cl_2), dark blue with vanillin; $[\alpha]^{21}_D$ −1.4°, $[\alpha]^{21}_{405}$ −79.9°, $[\alpha]^{21}_{435}$ −64.5°, $[\alpha]^{21}_{546}$ −14.2°, $[\alpha]^{21}_{577}$ −7.1° (*c* 0.5, $CHCl_3$); IR (film) ν_{max} 2900, 1440, 1370, 1260, 1110, 1050 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.91 (1H,

ddd, J = 11.5, 12, 12 Hz, H-4), 0.94 (3H, d, J = 6.5 Hz, H-10), 0.95 (3H, d, J = 6.5 Hz, H-11), 1.16 (3H, d, J = 6.5 Hz, H-12), 1.43 (1H, dqq, J = 8.5, 6.5, 6.5 Hz, H-9), 1.52 (3H, dddd, J = 1.5, 1.5, 1.5, 2.5 Hz, H-15), 1.64 (1H, ddddd, J = 6, 8.5, 9, 10, 12 Hz, H-3), 1.86 (1H, br.ddd, J = 5.5, 6, 11.5 Hz, H-4), 1.91 (1H, ddm, J = 10, 17 Hz, H-2), 2.52 (1H, ddddq, J = 1, 3, 9, 17, 1 Hz, H-2), 2.59 (1H, m, H-5), 4.24 (1H, dq, J = 6.5, 6.5 Hz, H-6), 4.32 (1H, br dd, J = 3, 9 Hz, H-7), 5.18 (1H, ddd, J = 0.5, 2, 10 Hz, H-14), 5.27 (1H, ddd, J = 1, 2, 17 Hz, H-14), 5.86 (1H, ddd, J = 9, 10, 17 Hz, H-13); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.7 (CH_3, C-15), 18.3 (CH_3, C-12), 21.6 (CH_3, C-10), 21.8 (CH_3, C-11), 34.0 CH, C-9), 34.2 (CH_2, C-4), 34.5 (CH_2, C-2), 44.2 (CH, C-5), 45.9 (CH, C-3), 70.1 (CH, C-6), 77.7 (CH, C-7), 117.8 (CH_2, C-14), 122.3 (C, C-8), 134.5 (C, C-1), 139.6 (CH, C-13); HREIMS *m/z* 220.1826 $[M]^+$ (calcd for $C_{15}H_{24}O$, 220.1827).

Hodgsonox E {**(1*R*,3*S*,6*R*,7a*R*)-(−)-3-ethenyl-1,4-dimethyl-6-(1-methylethyl)-7,7a-dihydrocyclopenta[*c*]pyran-5(1*H*,3*H*,6*H*)-one**} **(4):** colorless oil; TLC R_f = 0.37 (CH_2Cl_2), green with vanillin; $[\alpha]^{19}_D$ −82° (*c* 0.2, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 249 nm (3.85); IR (film) ν_{max} 2959, 2927, 2855, 2253, 1708, 1651, 1463, 1378, 1265, 1188, 1130, 1084, 986, 908, 734, 649 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.78 (3H, d, J = 6.5 Hz, H-10), 1.00 (3H, d, J = 6.5 Hz, H-11), 1.18 (3H, d, J = 6.5 Hz, H-12), 1.28 (1H, ddd, J = 11.5, 12, 12 Hz, H-4), 1.94 (1H, ddd, J = 7, 7.5, 11.5 Hz, H-4), 2.07 (3H, dd, J = 1, 3 Hz, H-15), 2.20 (1H, ddd, J = 4.5, 7.5, 12 Hz, H-3), 2.25 (1H, dqq, J = 4.5, 6.5, 6.5 Hz, H-9), 2.76 (1H, ddddq, J = 2.5, 6.5, 7, 12.0, 3 Hz, H-5), 4.27 (1H, dq, J = 6.5, 6.5 Hz, H-6), 4.40 (1H, br. ddd, J = 1, 2.5, 8.5 Hz, H-7), 5.29 (1H, ddd, J = 0.5, 1.5, 10 Hz, H-14), 5.35 (1H, ddd, J = 1, 1.5, 17 Hz, H-14), 5.83 (1H, ddd, J = 8.5, 10, 17 Hz, H-13); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.5 (CH_3, C-15), 17.5 (CH_3, C-12), 18.2 (CH_3, C-10), 21.1 (CH_3, C-11), 24.3 (CH_2, C-4), 27.0 (CH, C-9), 39.3 (CH, C-5), 55.2 (CH, C-3), 70.0 (CH, C-6), 78.2 (CH, C-7), 119.7 (CH_2, C-14), 130.3 (C, C-1), 136.5 (CH, C-13), 143.8 (C, C-8), 207.2 (C, C-2); HRFABMS *m/z* 235.1702 $[M + H]^+$ (calcd for $C_{15}H_{23}O_3$, 235.1698).

Hodgsonox C {**(1*R*,4a*S*,6*S*,7a*R*)-(+)-3-ethenyl-6-hydroxy-1,4-dimethyl-6-(1-methylethyl)-7,7a-dihydrocyclopenta-[*c*]pyran-5(1*H*,4a*H*,6*H*)-one**} **(5a):** colorless oil; TLC R_f = 0.56 (pentane/Et_2O, 3:2), pale pink-orange with vanillin; $[\alpha]^{20}_D$ 329° (*c* 0.2, $CHCl_3$); IR (film) ν_{max} 3400, 2900, 1700, 1650, 1450, 1370 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.63 (3H, d, J = 6.5 Hz, H-10), 0.96 (3H, d, J = 6.5 Hz, H-11), 1.32 (3H, d, J = 6.5 Hz, H-12), 1.71 (3H, br. d, J = 1 Hz, H-15), 1.77 (1H, ddd, J = 1.5, 7.5, 14 Hz, H-4), 1.85 (1H, qq, J = 6.5, 6.5 Hz, H-9), 1.89 (1H, dd, J = 11.5, 14 Hz, H-4), 2.66 (1H, dddd, J = 2, 7, 7.5, 11.5 Hz, H-5), 3.03 (1H, br. d, J = 7 Hz, H-1), 3.97 (1H, dq, J = 2, 6.5 Hz, H-6), 5.11 (1H, ddm, J = 2, 11 Hz, H-14), 5.59 (1H, ddm, J = 2.5, 17 Hz, H-14), 6.44 (1H, dd, J = 11, 17 Hz, H-13); ^{13}C NMR ($CDCl_3$, 75 MHz), see Table 3; HREIMS *m/z* 250.1563 $[M]^+$ (calcd for $C_{15}H_{22}O_3$, 250.1569).

Hodgsonox D {**((1*R*,3*S*,6*R*,7a*R*)-(+)-3-ethenyl-1-methyl-6-(1-methylethyl)-5-oxo-hexahydrocyclopenta[*c*]pyran-4-yl)methyl acetate**} **(7):** colorless oil; TLC R_f = 0.26 (pentane/Et_2O, 3:2), blue-purple with vanillin; $[\alpha]^{19}_D$ 25° (*c* 0.2, $CHCl_3$); IR (film) ν_{max} 3400, 2900, 1730, 1370, 1250, 1050 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.89 (3H, d, J = 6.5 Hz, H-10), 0.91 (1H, ddd, J = 11.5, 11.5, 13 Hz, H-4), 1.03 (3H, d, J = 6.5 Hz, H-11), 1.19 (3H, d, J = 6.5 Hz, H-12), 1.53 (1H, dqq, J = 8.5, 6.5, 6.5 Hz, H-9), 1.61 (1H, dddd, J = 4.5, 6.5, 8.5, 11.5 Hz, H-3), 1.83 (1H, ddd, J = 6.5, 6.5, 11.5 Hz, H-4), 2.04 (3H, s, OAc), 2.68 (1H, dddd, J = 3, 6.5, 6.5, 13 Hz, H-5), 3.30 (1H, br s, OH), 4.07 (1H, dq, J = 6.5, 6.5 Hz, H-6), 4.40 (1H, br d, J = 12 Hz, H-15), 4.42 (1H, d, J = 4.5 Hz, H-2), 4.45 (1H, dd, J = 3, 8.5 Hz, H-7), 5.09 (1H, d, J = 12 Hz, H-15), 5.30 (1H, ddd, J = 0.5, 1.5, 10.5 Hz, H-14), 5.39 (1H, ddd, J = 1, 1.5, 17 Hz, H-14), 5.83 (1H, ddd, J = 8.5, 10.5, 17 Hz, H-13); ^{13}C NMR ($CDCl_3$, 75 MHz), see Table 2; HREIMS *m/z* 276.1732 $[M^+ - H_2O]$ (calcd for $C_{17}H_{24}O_3$, 276.1725).

Hodgsonox F {**(1*R*,3*S*,6*R*,7a*R*)-(−)-3-ethenyl-4-(hydroxymethyl)-1-methyl-6-(1-methylethyl)-7,7a-dihydrocyclopenta[*c*]pyran-5(1*H*,3*H*,6*H*)-one**} **(8):** colorless oil; TLC R_f = 0.71 (Et_2O), blue with vanillin; $[\alpha]^{28}_D$ −25.3° (*c* 0.25, $CHCl_3$); IR (film) ν_{max} 3361, 2955, 2929, 2871, 2360, 2341, 1717, 1457, 1380, 1239, 1132, 1081, 992, 925, 668, 440 cm^{-1}; ^{1}H NMR (C_6D_6, 500 MHz) δ_H 0.74 (1H, ddd, 13, 13, 13 Hz, H-4a), 0.84 (3H, d, J = 6.5 Hz, H-10), 1.04 (3H, d, J = 7 Hz, H-12), 1.08 (3H, d, J = 6.5 Hz, H-11), 1.46 (1H, dqq, J = 2, 6.5, 6.5 Hz, H-9), 1.52 (1H, m, H-3), 1.53 (1H, ddd, J = 10, 10, 10 Hz, H-4b), 2.62 (1H, m, H-5), 3.84 (1H, br d, J = 13 Hz, H-15a), 4.01 (1H, dq, J = 6.5, 7 Hz, H-6), 4.11 (1H, ddd, J = 1.5, 2, 13 Hz, H-15b), 4.37 (1H, ddd, J = 2, 2, 5.5 Hz, H-2), 4.54 (1H, br d, J = 8 Hz, H-7), 5.01 (1H, ddd, J = 0.5, 2, 10 Hz, *cis* H-14), 5.18 (1H, ddd, 1, 2, 17 Hz, *trans* H-14), 5.75 (1H, ddd, 8, 10, 17 Hz, H-13); ^{13}C NMR (C_6D_6, 75 MHz), see Table 2; HREIMS *m/z* 234.1611 $[M^+ - H_2O]$ (calcd for $C_{15}H_{22}O_2$, 234.1619).

Hodgsonox G {**(1*R*,4a*S*,6*R*,7a*R*)-(+)-3-ethenyl-1,4-dimethyl-6-(1-methylethyl)-7,7a-dihydrocyclopenta[*c*]pyran-5(1*H*,4a*H*,6*H*)-one**} **(9):** colorless oil; TLC R_f = 0.61 (CH_2Cl_2), blue-purple with vanillin; $[\alpha]^{19}_D$ 166° (*c* 0.5, $CHCl_3$); IR (film) ν_{max} 2958, 2916, 2872, 2848, 1730, 1592, 1462, 1385, 1249, 1154, 1058, 909, 751, 517 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.69 (3H, d, J = 6.5 Hz, H-10), 0.94 (3H, d, J = 6.5 Hz, H-11), 1.35 (3H, d, J = 6.5 Hz, H-12), 1.73 (1H, ddd, J = 11.5, 12.5, 12.5 Hz, H-4), 1.75 (3H, d, J = 1 Hz, H-15), 1.95 (1H, dddd, J = 1, 6.5, 8.5, 12.5 Hz, H-4), 2.14 (1H, dqq, J = 4.5, 6.5, 6.5 Hz, H-9), 2.21 (1H, dddd, J = 1, 4.5, 8.5, 12.5 Hz, H-3), 2.39 (1H, dddd, 2, 6.5, 8.5, 11.5 Hz, H-5), 2.85 (1H, br d, J = 8.5 Hz, H-1), 3.97 (1H, dq, J = 2, 6.5 Hz, H-6), 5.10 (1H, br. dd, J = 1.5, 11 Hz, H-14), 5.58 (1H, br. dd, J = 1.5, 17 Hz, H-14), 6.47 (1H, dd, J = 11, 17 Hz, H-13); ^{13}C NMR ($CDCl_3$, 75 MHz), see Table 3; HREIMS *m/z* 234.1621 $[M^+]$ (calcd for $C_{15}H_{22}O_2$, 234.1620).

Hodgsonox H {**(1*R*,3*S*,4a*R*,6*R*,7a*R*)-(−)-3-ethenyl-1-methyl-4-methylene-6-(1-methylethyl)- tetrahydrocyclopenta[*c*]pyran-5(1*H*,3*H*,6*H*)-one**} **(10):** colorless oil; TLC R_f = 0.45 (CH_2Cl_2), blue-purple with vanillin; $[\alpha]^{19}_D$ −164.63° (*c* 0.6, $CHCl_3$); IR (film) ν_{max} 2956, 1731, 1649, 1580, 1464, 1389, 1292, 1271, 1196, 1146, 1113, 1067, 988, 923, 708, 630 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.85 (3H, d, J = 6.5 Hz, H-10), 0.99 (3H, d, J = 6.5 Hz, H-11), 1.24 (3H, d, J = 6.5 Hz, H-12), 1.45 (1H, ddd, J = 11, 12, 12 Hz, H-4), 2.18 (1H, m, H-3), 2.20 (1H, m, H-9), 2.35 (1H, dddd, J = 5.5, 8, 12, 14.5 Hz, H-5), 2.60 (1H, dddd, J = 2, 2.5, 2.5, 14.5 Hz, H-1), 4.38 (1H, dq, J = 8, 6.5 Hz, H-6), 4.48 (1H, dm, J = 7 Hz, H-7), 4.92 (1H, ddd, J = 1, 2, 3 Hz, H-15), 5.23 (1H, ddd, J = 1, 1.5, 17 Hz, H-14), 5.26 (1H, ddd, J = 1, 1.5, 10.5 Hz, H-14), 5.72 (1H, ddd, J = 1, 2, 2.5 Hz, H-15), 5.78 (1H, ddd, J = 7, 10.5, 17 Hz, H-13); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 16.7 (CH_3, C-12), 18.4 (CH_3, C-10), 20.8 (CH_3, C-11), 24.2 (CH_2, C-4), 27.9 (CH, C-9), 39.8 (CH, C-5), 47.8 (CH, C-1), 56.8 (CH, C-3), 71.7 (CH, C-6), 77.9 (CH, C-7), 109.1 (CH_2, C-15), 118.1 (CH_2, C-14), 136.6 (CH, C-13), 143.6 (C, C-8), 215.0 (C, C-2); HREIMS *m/z* 234.1613 $[M^+]$ (calcd for $C_{15}H_{22}O_2$, 234.1620).

Acknowledgment. We thank the Department of Conservation for permission to collect from Mt. Aspiring National Park, J. Williams and E. Freeman for assistance with collection of plant material, and B. Clark and D. Rowan for mass spectra. This research was supported by the New Zealand Foundation for Research, Science and Technology and The University of Otago, Division of Sciences.

Supporting Information Available: Tables of 1D and 2D NMR data and ^{1}H and ^{13}C NMR spectra for compounds **3**, **4**, **5a**, and **7**−**10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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NP050058X