Application of the semi-pinacol rearrangement towards the generation of alkenyl-substituted quaternary carbon centres

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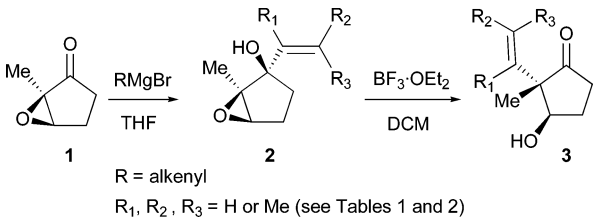
The semi-pinacol rearrangement has been carried out on 2-methyl-2,3-epoxy-cyclopentanone† derivatives, generating alkenyl-substituted quaternary carbon centred aldols with a defined relative stereochemistry.

Introduction

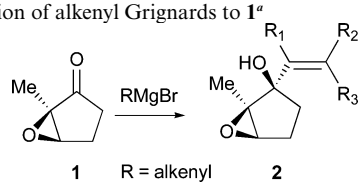
α-Vinylation of ketones has been studied in great detail over the past couple of decades, with initial forays studying the nucleophilic attack of enolates onto a vinyl cation synthon,[1] and more recent advances utilising the methodology developed by Piers, which incorporates intramolecular palladium-mediated direct α-vinylation of enolates.[2] The importance of such α-vinylated products is demonstrated with the synthesis of numerous natural products based on these methodologies,[3] and the synthesis of important structural building blocks.[1,4]

Similarly, the rearrangement of epoxy alcohols has also seen widespread use over the past few decades.[5,6] This class of rearrangement has been extensively studied, with a great deal of effort spent elucidating the mechanism and product distribution of these Lewis acid promoted rearrangements.[7,8,9] Of particular interest to us is the semi-pinacol rearrangement of epoxy alcohols resulting in α-substituted *anti*-aldols.[6,7,8] To date, the reaction has primarily been studied on acyclic substrates[6] or cyclic substrates where the migrating group lies outside the ring.[7]‡ The rearrangement has also been sucessfully applied to the synthesis of quaternary carbon centres.[6,7] Until recently, to our knowledge, no examples were known of such a reaction applied to ring systems with the migrating groups attached directly to the ring itself. Such a reaction has recently been described by Walsh and co-workers with simple methyl and ethyl substituents as the migrating groups.[10] Based on the need for alternative synthetic routes to α-vinylated carbonyl compounds, and such a dearth of alkenyl migrating groups in ring-based semi-pinacol rearrangements, we set out to determine if the two shortfalls could be met by applying the semi-pinacol rearrangement to 2,3-epoxycyclopentanone derivatives incorporating alkenyl substituents as the migrating groups (Scheme 1).



Scheme 1 Proposed synthetic scheme; all compounds are racemic.

Table 1 Addition of alkenyl Grignards to **1**[a]

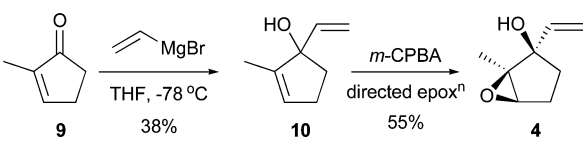


Entry	R_1	R_2	R_3	Product	Yield (%)[b]
1	H	H	H	**4**	73
2	Me	H	H	**5**	32
3	H	Me	Me	**6**	58[c]
4	H	Me	H	(*E*)-**7**	43[d]
5	H	H	Me	(*Z*)-**8**	32[d]

[a] *Reagents and conditions*: **1**, THF, −78 °C, then RMgBr (1.5 eq.). [b] Isolated yield. [c] The product began to rearrange in $CDCl_3$. [d] The product was isolated from an *E*/*Z* mixture.

Results and discussion

The synthesis began with the preparation of racemic epoxyketone **1** following a literature procedure (34%).[11] Subsequent addition of alkenyl Grignard reagents to **1** (see Table 1) proceeded as expected, to generate **2** as a single diastereomer.[12] The relative stereochemistry of **2** was initially assigned on the basis of a successful rearrangement (*vide infra*) and later confirmed with an alternative synthesis to **4** *via* a directed epoxidation (Scheme 2).[13] It is interesting to note that, upon addition of the alkenyl Grignard reagents to **1**, only a single diastereomer was observed in the ^{1}H NMR of the crude products.



Scheme 2 Alternative synthesis of racemic **4**, confirming the relative stereochemistry.

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† IUPAC nomenclature is 1-methyl-6-oxabicyclo[3.1.0]hexan-2-one.

‡ The semi-pinacol rearrangement has been applied to the preparation of ring-contracted products, whereby the nature of the reaction has the migrating group within the ring.[5]

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A possible mechanistic explanation for such selectivity could be that the very rigid and flat nature of the 2,3-epoxycyclopentanone ring causes there to be no hindrance of any kind to a nucleophile approaching from the face of the carbonyl opposite to the epoxide; this rigidity places substituents at C-2 and C-3 in the plane of the ring (Fig. 1).[12]

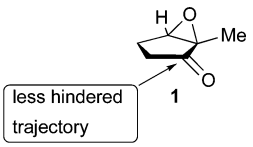
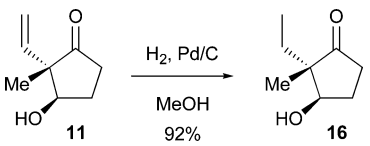


Fig. 1

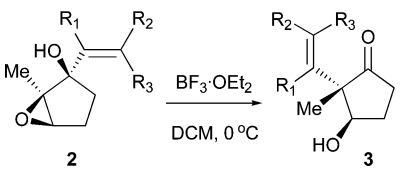
With the synthesis of the desired tertiary alcohols in hand, we attempted the rearrangement of **2** using $BF_3{\cdot}OEt_2$ (2.0 eq.). As expected, we obtained the rearranged aldols in moderate to good yields (Table 2). The rearrangement was also shown to proceed cleanly with various other Lewis acids, and even catalytically (Table 3).

Although the relative stereochemistry of the rearranged products can be inferred from the stereochemical course of the reaction, the stereochemistry was confirmed by the conversion of **11** into the known product **16** (Scheme 3).[10]



Scheme 3

Table 2 Rearrangement of alcohols **4** to **8**[a]



Entry	R_1	R_2	R_3	Product	Yield (%)[b]
1	H	H	H	**11**	78
2	Me	H	H	**12**	70
3	H	Me	Me	**13**	56
4	H	Me	H	(*E*)-**14**	83
5	H	H	Me	(*Z*)-**15**	90

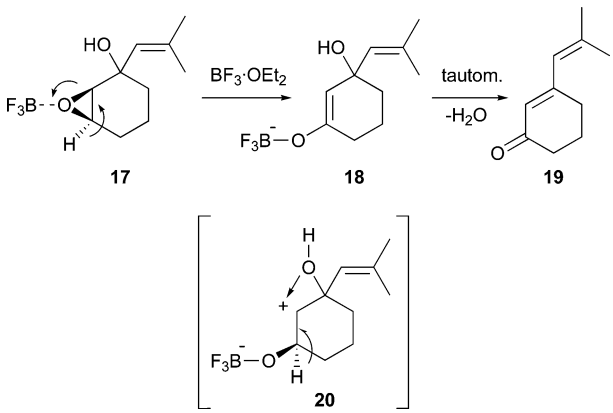
[a] *Reagents and conditions*: $BF_3{\cdot}OEt_2$ (2.0 eq.), DCM, 0 °C. [b] Isolated yield.

Table 3 The semi-pinacol rearrangement of **4** promoted by various Lewis acids

Entry	Catalyst	Catalyst (eq.)	Time	Yield (%)[a]
1	$BF_3{\cdot}OEt_2$	2.0	10 min	78
2	$BF_3{\cdot}OEt_2$	1.0	20 min	89
3	$SnCl_4$	1.0	20 min	79
4	$FeCl_3$	1.0	15 min	86
5	TMSOTf	1.0	20 min	79
6	$Yb(OTf)_3$	0.1	44 h	53[b]

[a] Isolated yield. [b] Incomplete reaction, yield determined by integration of ^1H NMR signals.

In an attempt to expand the scope of the reaction, we sought to apply the methodology to six-membered rings. In contrast to published work,[14] the addition of 2-methyl-1-propenylmagnesium bromide to 2,3-epoxycyclohexanone§ (THF, −78 °C) gave only a (separable) 0.6 : 1 mixture of diastereomeric alcohols **17**, and none of the other expected by-products;[14] the stereochemistry of the quaternary centre is unknown. Unfortunately, when the alcohols were separately subjected to the rearrangement conditions ($BF_3{\cdot}OEt_2$ (1.0 or 2.0 eq.), DCM, 0 °C) both alcohols gave the *same* rearranged product **19** (Scheme 4), suggesting that the mechanism progresses through a common intermediate. A possible explanation is shown below: boron trifluoride assists the epoxide opening, generating a potentially stabilised carbocation **20**, which is subsequently captured by loss of a proton, generating an enolate (**17** → **18**).[15] Tautomerisation and loss of water, or E1cb elimination, would then generate the known 3-substituted cyclohexen-1-one.[16]



Scheme 4 Possible mechanism for the formation of **19**.

Conclusions

In conclusion, we have demonstrated the semi-pinacol rearrangement utilising alkenyl migrating groups on cyclopentanone epoxy alcohols, and the developed methodology provides an alternative to the synthesis of α-alkenylated carbonyl compounds. Work continues to expand the scope of the reaction.

Experimental

General

All reactions were performed in oven-dried glassware under an atmosphere of nitrogen. Commercially available anhydrous solvents were used as supplied. All other commercially available reagents were used as received without purification. Analytical thin layer chromatography was performed with Keiselgel 60 F_{254}, in a variety of solvents on aluminium-backed plates. The plates were visualised by UV light (254 nm) and potassium permanganate. Flash column chromatography was conducted with Merck silica gel 60H (40–60 μm, 230–400 mesh) under bellows pressure. Nominal mass spectra were recorded on an Agilent 1100 series

§ IUPAC nomenclature is 7-oxabicyclo[4.1.0]heptan-2-one.

spectrometer using electrospray (ES), and high resolution mass spectra were recorded using a Thermo Finnigan MAT 95 XP spectrometer. Infrared spectra were recorded on a Nicolet Nexus FTIR spectrometer, over the range 4000–400 cm^{-1}; all samples were run as evaporated films on a sodium chloride plate. ^1H and ^{13}C NMR spectra were recorded on either a Bruker Avance 300 (300 MHz) or Bruker DPX 400 (400 MHz) spectrometer. All chemical shifts are quoted in ppm relative to a calibration reference of the residual solvent. The following abbreviations are used to define the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. The coupling constants (*J*) are measured in hertz (Hz). Petroleum ether refers to the fraction of petroleum ether that boils between 40 and 60 °C.

Typical experimental procedures

Grignard addition to 1. Alkenylmagnesium bromide (1.5 mol eq.) was slowly added to a solution of 1-methyl-6-oxabicyclo[3.1.0]hexan-2-one **1** (1 mol eq.) in tetrahydrofuran (5 mL $mmol^{-1}$) at −78 °C under an atmosphere of nitrogen. The reaction was stirred at −78 °C, until deemed complete by TLC, before being quenched with saturated aqueous ammonium chloride. The mixture was warmed to room temperature, the layers separated, and the aqueous layer extracted with ethyl acetate. The combined extracts were washed with brine, dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified by column chromatography on silica.

Rearrangement of tertiary alcohols. Boron trifluoride diethyl etherate (2 mol eq.) was added to a solution of the tertiary alcohol (1 mol eq.) in dichloromethane (10 mL $mmol^{-1}$) at 0 °C under an atmosphere of nitrogen. The reaction was stirred at 0 °C, until deemed complete by TLC, before being quenched with water. The mixture was warmed to room temperature, the layers separated, and the aqueous layer extracted with dichloromethane. The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified by column chromatography on silica.

(±)-1-Methyl-2-vinyl-6-oxabicyclo[3.1.0]hexan-2-ol (4)

Flash chromatography using 20% diethyl ether in petroleum ether as eluent gave the tertiary alcohol **4** (491 mg, 73%) as a colourless oil, R_f 0.17 (10% ethyl acetate in petroleum ether). ν_{max}/cm^{-1} 3450 br (OH), 2933 (C–H), 1441 (C=C); δ_H (400 MHz; $CDCl_3$) 5.81 (1H, dd, J = 11.0 and 17.4 Hz, C*H*=CH_2), 5.35 (1H, d, J = 17.4 Hz, CH=C*H*H), 5.13 (1H, d, J = 11.0 Hz, CH=CH*H*), 3.36 (1H, s, C(5)H), 2.50 (1H, br s, OH), 2.02 (1H, dd, J = 5.6 and 10.8 Hz, CH), 1.75–1.56 (3H, m, 3 × CH), 1.33 (3H, s, CH_3); δ_C (100 MHz; $CDCl_3$) 138.8 (CH), 113.2 (CH_2), 80.9, 67.2 (C), 63.0 (CH), 34.4, 25.1 (CH_2), 12.2 (CH_3); *m/z* (ES+) 123 ([M − OH]$^+$, 100%).

(±)-(2*S*,3*R*)-3-Hydroxy-2-methyl-2-vinylcyclopentanone (11)

Flash chromatography using 20% ethyl acetate in petroleum ether as eluent gave the title compound **11** (42 mg, 78%) as a colourless oil, R_f 0.08 (10% ethyl acetate in petroleum ether). ν_{max}/cm^{-1} 3458 br (OH), 2931 (C–H), 1737 (C=O); δ_H (300 MHz; $CDCl_3$) 5.71 (1H, dd, J = 10.7 and 17.6 Hz, C*H*=CH_2), 5.15 (1H, d, J = 10.7 Hz, CH=C*H*H), 5.08 (1H, d, J = 17.6 Hz, CH=CH*H*), 4.26 (1H, s, C(3)H), 2.49–2.38 (1H, m, CH), 2.31–2.17 (2H, m, 2 × CH), 2.14 (1H, br s, OH), 1.97–1.89 (1H, m, CH), 1.13 (3H, s, CH_3); δ_C (100 MHz; $CDCl_3$) 218.0 (C), 138.3 (CH), 116.2 (CH_2), 76.6 (CH), 57.4 (C), 34.2, 27.6 (CH_2), 15.2 (CH_3); *m/z* (ES+) 141 ([M + H]$^+$, 100%); found 158.1178, $C_8H_{16}NO_2$ (M + NH_4^+) requires 158.1176.

(±)-1-Methyl-2-(prop-1-en-2-yl)-6-oxabicyclo[3.1.0]hexan-2-ol (5)

Flash chromatography using 20% diethyl ether in petroleum ether as eluent gave the tertiary alcohol **5** (111 mg, 32%) as a colourless solid, R_f 0.26 (10% ethyl acetate in petroleum ether). Mp (Et_2O; petroleum ether) 41–42 °C; ν_{max}/cm^{-1} 3396 br (OH), 2927 (C–H), 1437 (C=C); δ_H (300 MHz; $CDCl_3$) 5.06 (1H, s, =C*H*H), 4.84 (1H, s, =CH*H*), 3.46 (1H, s, C(5)H), 2.29 (1H, br s, OH), 2.11–2.02 (1H, m, CH), 1.89–1.68 (5H, m, 2 × CH and CH_3), 1.61–1.51 (1H, m, CH), 1.31 (3H, s, CH_3); δ_C (75 MHz; $CDCl_3$) 145.8 (C), 110.3 (CH_2), 82.8, 68.2 (C), 64.8 (CH), 35.9, 26.6 (CH_2), 19.0, 12.2 (CH_3); *m/z* (ES+) 178 ([M + H + ^{23}Na]$^+$, 55%), 155 ([M + H]$^+$, 100); found 177.0883, $C_9H_{14}O_2Na$ requires 177.0886.

(±)-(2*S*,3*R*)-3-Hydroxy-2-methyl-2-(prop-1-en-2-yl)cyclopentanone (12)

Flash chromatography using 30% diethyl ether in petroleum ether as eluent gave the title compound **12** (51 mg, 70%) as a colourless oil, R_f 0.13 (20% ethyl acetate in petroleum ether). ν_{max}/cm^{-1} 3445 br (OH), 2974 (C–H), 1732 (C=O), 1635, 1451 (C=C); δ_H (300 MHz; $CDCl_3$) 4.93 (1H, s, =C*H*H), 4.74 (1H, s, =CH*H*), 4.41 (1H, t, J = 5.0 Hz, C(3)H), 2.50–2.38 (1H, m, CH), 2.31–2.15 (2H, m, 2 × CH), 1.95–1.83 (2H, m, OH and CH), 1.72 (3H, s, CH_3), 1.14 (3H, s, CH_3); δ_C (75 MHz; $CDCl_3$) 218.7, 144.3 (C), 113.5 (CH_2), 74.9 (CH), 60.0 (C), 34.8, 27.5 (CH_2), 19.8, 14.6 (CH_3); *m/z* (ES+) 155 ([M + H]$^+$, 100%); found 155.1066, $C_9H_{15}O_2$ requires 155.1067.

(±)-(2*S*,3*R*)-3-Hydroxy-2-methyl-2-(2-methylprop-1-enyl)cyclopentanone (13)

Flash chromatography using 20% diethyl ether in petroleum ether as eluent gave the tertiary alcohol **6** (90 mg, 58%) as a colourless oil, R_f 0.22 (10% ethyl acetate in petroleum ether). ν_{max}/cm^{-1} 3473 br (OH), 2930 (C–H), 1440, 1374. The compound rearranged partially (~20%) in $CDCl_3$ – the diagnostic ^1H NMR signals follow: δ_H (400 MHz; $CDCl_3$) 5.15 (1H, s, C*H*=C(CH_3)$_2$), 3.35 (1H, s, C(5)H), 1.88 (3H, s, CH_3), 1.72 (3H, s, CH_3), 1.40 (3H, s, CH_3); *m/z* (ES+) 359 ([2M + ^{23}Na]$^+$, 70%), 223 ([M + ^{23}Na + MeOH]$^+$, 100), 191 ([M + ^{23}Na]$^+$, 30), 186 ([M + NH_4]$^+$, 20); found 186.1484, $C_{10}H_{20}NO_2$ (M + NH_4^+) requires 186.1489. The neat, unrearranged material was taken on to the rearrangement. Flash chromatography using 20% ethyl acetate in petroleum ether as eluent gave the title compound **13** (22 mg, 56%) as a colourless oil, R_f 0.27 (20% ethyl acetate in petroleum ether). ν_{max}/cm^{-1} 3446 br (OH), 2972 (C–H), 1733 (C=O); δ_H (400 MHz; $CDCl_3$) 4.93 (1H, s, C*H*=C(CH_3)$_2$), 4.19 (1H, t, J = 4.4 Hz, C(3)H), 2.41–2.31 (2H, m, 2 × CH), 2.27–2.19 (1H, m, CH), 2.04 (1H, br s, OH), 1.91–1.82 (1H, m, CH), 1.68 (3H, s, CH_3), 1.59 (3H, s, CH_3), 1.17 (3H, s, CH_3); δ_C (100 MHz; $CDCl_3$) 218.1, 137.3 (C), 124.3, 78.5 (CH), 55.4 (C), 33.7 (CH_2), 27.2 (CH_3), 27.1 (CH_2), 19.2,

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15.8 (CH_3); *m/z* (ES+) 169 ([M + H]$^+$, 100%); found 186.1485, $C_{10}H_{20}NO_2$ (M + NH_4^+) requires 186.1489.

(±)-1-Methyl-2-((*E*)-prop-1-enyl)-6-oxabicyclo[3.1.0]hexan-2-ol (7) and (±)-1-methyl-2-((*Z*)-prop-1-enyl)-6-oxabicyclo[3.1.0]-hexan-2-ol (8)

The crude product (~0.8 : 1, *Z*/*E*) was purified by column chromatography on silica using 10% ethyl acetate in petroleum ether as eluent to give the (*E*)-tertiary alcohol **7** (134 mg, 43%) as a colourless oil, R_f 0.23 (10% ethyl acetate in petroleum ether), and the (*Z*)-tertiary alcohol **8** (100 mg, 32%) as a colourless oil, R_f 0.33 (10% ethyl acetate in petroleum ether). **7**: ν_{max}/cm^{-1} 3447 br (OH), 2935 (C–H); δ_H (300 MHz; $CDCl_3$) 5.84–5.73 (1H, dq, J = 6.5 and 15.3 Hz, CH=C*H*CH_3), 5.47 (1H, d, J = 15.3 Hz, C*H*=$CHCH_3$), 3.36 (1H, s, C(5)H), 2.06–2.00 (1H, m, CH), 1.91–1.88 (1H, m, CH), 1.81–1.52 (5H, m, 2 × CH and CH_3), 1.35 (3H, s, CH_3); δ_C (75 MHz; $CDCl_3$) 131.7, 124.3 (CH), 80.6, 67.3 (C), 63.1 (CH), 34.8, 25.3 (CH_2), 17.9, 12.3 (CH_3); *m/z* (ES+) 137 ([M − OH]$^+$, 100%); found 177.0889, $C_9H_{14}O_2Na$ requires 177.0886. **8**: ν_{max}/cm^{-1} 3465 br (OH), 2933 (C–H); δ_H (300 MHz; $CDCl_3$) 5.64–5.53 (1H, dq, J = 7.1 and 11.7 Hz, CH=C*H*CH_3), 5.30 (1H, d, J = 11.7 Hz, C*H*=$CHCH_3$), 3.37 (1H, s, C(5)H), 2.03–1.52 (7H, m, 4 × CH and CH_3), 1.42 (3H, s, CH_3); δ_C (75 MHz; $CDCl_3$) 130.2, 127.7 (CH), 82.0, 67.8 (C), 63.6 (CH), 36.7, 25.3 (CH_2), 14.8, 12.2 (CH_3); *m/z* (ES+) 137 ([M − OH]$^+$, 100%), 121 ([M − OH − O]$^+$, 75); found 177.0888, $C_9H_{14}O_2Na$ requires 177.0886.

(±)-(2*S*,3*R*)-3-Hydroxy-2-methyl-2-((*E*)-prop-1-enyl)cyclopentanone (14)

Flash chromatography using 20% ethyl acetate in petroleum ether as eluent gave the title compound **14** (95 mg, 83%) as a colourless oil. ν_{max}/cm^{-1} 3446 br (OH), 2933 (C–H), 1733 (C=O); δ_H (300 MHz; $CDCl_3$) 5.54–5.42 (1H, dq, J = 6.0 and 15.6 Hz, CH=C*H*CH_3), 5.29 (1H, dq, J = 1.5 and 15.6 Hz, C*H*=$CHCH_3$), 4.19 (1H, t, J = 4.5 Hz, C(3)H), 2.45–2.35 (1H, m, CH), 2.29–2.14 (3H, m, 2 × CH and OH), 1.96–1.84 (1H, m, CH), 1.65 (3H, dd, J = 1.5 and 6.0 Hz, CHC*H*$_3$), 1.09 (3H, s, CH_3); δ_C (75 MHz; $CDCl_3$) 219.0 (C), 131.2, 126.8, 77.0 (CH), 56.7 (C), 34.1, 27.4 (CH_2), 18.2, 15.7 (CH_3); *m/z* (ES+) 178 ([M + H + ^{23}Na]$^+$, 55%), 155 ([M + H]$^+$, 70), 137 ([M − OH]$^+$, 95); found 155.1068, $C_9H_{15}O_2$ requires 155.1067.

(±)-(2*S*,3*R*)-3-Hydroxy-2-methyl-2-((*Z*)-prop-1-enyl)cyclopentanone (15)

Flash chromatography using 20% ethyl acetate in petroleum ether as eluent gave the title compound **15** (47 mg, 90%) as a colourless oil, R_f 0.26 (20% ethyl acetate in petroleum ether). ν_{max}/cm^{-1} 3445 br (OH), 3013 (C–H), 2934 (C–H), 1732 (C=O); δ_H (300 MHz; $CDCl_3$) 5.60–5.49 (1H, dq, J = 7.4 and 11.4 Hz, CH=C*H*CH_3), 5.14 (1H, dq, J = 1.5 and 11.4 Hz, C*H*=$CHCH_3$), 4.22 (1H, t, J = 4.2 Hz, C(3)H), 2.39–2.15 (4H, m, 3 × CH and OH), 1.94–1.83 (1H, m, CH), 1.60 (3H, dd, J = 1.5 and 7.4 Hz, CHC*H*$_3$), 1.19 (3H, s, CH_3); δ_C (75 MHz; $CDCl_3$) 218.2 (C), 129.9, 129.1, 78.1 (CH), 55.7 (C), 33.6, 27.3 (CH_2), 15.6, 14.4 (CH_3); *m/z* (ES+) 178 ([M + H + ^{23}Na]$^+$, 75%), 155 ([M + H]$^+$, 35), 137 ([M − OH]$^+$, 100); found 155.1076, $C_9H_{15}O_2$ requires 155.1067.

(±)-*syn*-2-(2-Methylprop-1-enyl)-7-oxabicyclo[4.1.0]heptan-2-ol and (±)-*anti*-2-(2-methylprop-1-enyl)-7-oxabicyclo[4.1.0]heptan-2-ol (17)

Flash chromatography using 10% ethyl acetate in petroleum ether as eluent gave the less polar product (112 mg, 15%) as a colourless oil, R_f 0.26 (10% ethyl acetate in petroleum ether), and the more polar product (164 mg, 22%) as a colourless oil, R_f 0.14 (10% ethyl acetate in petroleum ether). Less polar product: ν_{max}/cm^{-1} 3458 br (OH), 2937 (C–H), 1441; δ_H (300 MHz; $CDCl_3$) 5.37 (1H, s, C*H*=C(CH_3)$_2$), 3.40 (1H, m, CH_2C*H*O), 3.24 (1H, d, J = 3.6 Hz, C*H*OCHCH_2), 2.46 (1H, br s, OH), 2.05–1.97 (1H, m, CH), 1.85 (3H, s, CH_3), 1.75–1.61 (4H, m, CH_3 and CH), 1.48–1.33 (4H, m, 4 × CH); δ_C (75 MHz; $CDCl_3$) 136.2 (C), 128.4 (CH), 69.9 (C), 58.8, 56.1 (CH), 35.8 (CH_2), 26.8 (CH_3), 23.4 (CH_2), 19.6 (CH_3), 15.9 (CH_2); *m/z* (ES+) 169 ([M + H]$^+$, 55%), 151 ([M − OH]$^+$, 100); found 186.1498, $C_{10}H_{20}NO_2$ (M + NH_4^+) requires 186.1489. More polar product: ν_{max}/cm^{-1} 3437 br (OH), 2936 (C–H), 1446; δ_H (300 MHz; $CDCl_3$) 5.43 (1H, s, C*H*=C(CH_3)$_2$), 3.27 (1H, m, CH_2C*H*O), 3.12 (1H, d, J = 3.9 Hz, C*H*OCHCH_2), 1.93 (3H, s, CH_3), 1.88–1.84 (2H, m, CH and OH), 1.75 (3H, s, CH_3), 1.71–1.63 (2H, m, 2 × CH), 1.54–1.43 (2H, m, 2 × CH), 1.32–1.25 (1H, m, CH); δ_C (75 MHz; $CDCl_3$) 137.2 (C), 129.1 (CH), 70.2 (C), 58.2, 53.9 (CH), 34.5 (CH_2), 27.1 (CH_3), 23.1 (CH_2), 19.3 (CH_3), 15.5 (CH_2); *m/z* (ES+) 169 ([M + H]$^+$, 10%), 151 ([M − OH]$^+$, 100); found 186.1492, $C_{10}H_{20}NO_2$ requires 186.1489.

3-(2-Methylprop-1-enyl)cyclohex-2-enone (19)

From the more polar isomer: flash chromatography using 20% diethyl ether in petroleum ether as eluent gave the title compound (44 mg, 64%) as a colourless oil, R_f 0.26 (10% ethyl acetate in petroleum ether). ν_{max}/cm^{-1} 2930 (C–H), 1669 (C=O); δ_H (300 MHz; $CDCl_3$) 5.89 (1H, s, CH), 5.75 (1H, s, CH), 2.37–2.34 (4H, m, 2 × CH_2), 2.02–1.94 (2H, m, CH_2), 1.86 (6H, s, 2 × CH_3); δ_C (75 MHz; $CDCl_3$) 200.1, 159.3, 142.5 (C), 126.5, 125.7 (CH), 37.2, 30.4 (CH_2), 27.8 (CH_3), 22.8 (CH_2), 20.6 (CH_3); *m/z* (ES+) 151 ([M + H]$^+$, 100%); found 151.1111, $C_{10}H_{15}O$ requires 151.1117.

(±)-(2*S*,3*R*)-2-Ethyl-3-hydroxy-2-methylcyclopentanone (16)

(±)-(2*S*,3*R*)-3-Hydroxy-2-methyl-2-vinylcyclopentanone **11** (59 mg, 0.42 mmol) was dissolved in methanol (4.5 mL), 10% Pd/C (6 mg) added, and the reaction stirred under an atmosphere of hydrogen for 2 h. The reaction mixture was filtered through Celite® and evaporated under reduced pressure to give the title compound (55 mg, 92%) as a colourless oil, R_f 0.08 (10% ethyl acetate in petroleum ether). The compound displayed comparable data to the literature:[10] δ_H (300 MHz; C_6D_6) 3.69 (1H, t, J = 5.4 Hz, C(3)H), 2.20–2.07 (1H, m, CH), 1.82–1.62 (3H, m, 2 × CH and OH), 1.52–1.39 (1H, m, CH), 1.31–1.18 (2H, m, 2 × CH), 0.94 (3H, s, CH_3), 0.73 (3H, t, J = 7.5 Hz, CH_2C*H*$_3$); δ_C (75 MHz; $CDCl_3$) 221.4 (C), 75.2 (CH), 53.5 (C), 34.7, 27.7, 27.6 (CH_2), 14.4, 8.3 (CH_3).

(±)-1-Methyl-2-vinyl-6-oxabicyclo[3.1.0]hexan-2-ol (4)

Vinylmagnesium bromide (1.0 M, 5.6 mL, 5.6 mmol) was slowly added to a solution of 2-methylcyclopentanone (0.5 mL, 5.09 mmol) in tetrahydrofuran (25 mL) at −78 °C under an

atmosphere of nitrogen. The reaction was stirred at −78 °C for 1 h before warming to room temperature and being quenched with saturated aqueous ammonium chloride (10 mL). The layers were separated, the aqueous layer extracted with diethyl ether (3 × 10 mL), and the combined extracts washed with brine (10 mL), dried ($MgSO_4$) and evaporated under reduced pressure. The crude product was purified by column chromatography on silica using 5% ethyl acetate in petroleum ether as eluent to give the tertiary alcohol **10** (240 mg, 38%) as a colourless oil. The relatively unstable tertiary alcohol **10** (102 mg, 0.82 mmol) was dissolved in dichloromethane (8 mL) and cooled to 0 °C. *m*-CPBA (∼70%, 213 mg, 0.86 mmol) was added in one portion and the reaction stirred at 0 °C for 20 min. The reaction was quenched with saturated aqueous sodium thiosulfate (2 mL), warmed to room temperature, the layers separated, and the aqueous layer extracted with dichloromethane (2 × 5 mL). The combined extracts were washed with brine (5 mL), dried ($MgSO_4$), and evaporated under reduced pressure. The crude product (∼20 : 1 ratio of diastereomers) was purified by column chromatography on silica using 20% ethyl acetate in petroleum ether as eluent to give the title compound (63 mg, 55%) as a colourless oil. The compound displayed identical analytical data to that made by Grignard addition.

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