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# Nucleophilic vinylic substitution in bicyclic methyleneaziridines: $S_NV_\pi$ or $S_NV_\sigma$ ?†

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A stereodefined monodeuterated methyleneaziridine is shown to be prepared *via* coordinated reductive ring-opening of an alkynyl epoxide and diastereoselective tethered allene aziridination. Ring-opening of this aziridine with copper-based organometallics follows a pathway that results in stereoretentive substitution, replacing the *exo*-C–N bond with a corresponding C–C bond; this stereochemical outcome supports either an overall  $S_NV_\pi$  mechanism or a C–N insertion/reductive coupling process.

## Introduction

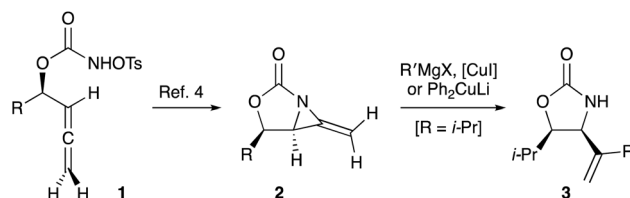
In 2010 both we<sup>1</sup> and Blakey<sup>2</sup> reported the first examples of intramolecular allene aziridination with sulfamate substrates, with the major products being derived in most cases *via* 2-amidoallylcation intermediates.<sup>3</sup> Our group followed this up with the first report<sup>4</sup> of analogous reactions of carbamate substrates **1** (Scheme 1) and, in that work, somewhat unstable bicyclic 1,3-oxazolidin-2-one methyleneaziridines **2** were obtained following Lebel's modification<sup>5</sup> of the Du Bois protocol<sup>6</sup> for Rh(II)-nitrenoid generation. Soon afterwards, Schomaker's group took on the area and developed it extensively, engineering the substrates for synthetic tractability (non-terminal allenes, formation of 1,3-oxazin-2-ones), and elaborating the products into a variety of hydroxy/amino stereotriads and -tetrads and rearranged heterocycles.<sup>7</sup>

In our original publication we noted that the methyleneaziridines were constrained by the ring-fusion such that only the exocyclic aziridine C–N bond is electronically activated in the ground state through hyperconjugation with the carbamate carbonyl  $\pi$ -system. This suggested the possibility of effecting direct substitution/ring-opening at the  $sp^2$ -carbon, in contrast to the prevailing reactivity of unconstrained methyleneaziridines in which ring-opening occurs preferentially at the  $sp^3$ -carbon.<sup>8</sup> At the time, the only  $sp^2$ -C–N bond-cleaving processes involved either transition metal-mediated processes<sup>9</sup> or stepwise radical addition/ $\beta$ -scission.<sup>10</sup> In the event,

treatment of methyleneaziridine **2** (R = *i*-Pr) with lithium diphenylcuprate, or various Grignard reagents in the presence of CuI, led to moderate to good yields of the products **3** of nucleophilic vinylic substitution ( $S_NV$ ).<sup>11</sup> That publication concluded with an intention to clarify the stereochemical details of the  $S_NV$  reaction; the current paper describes studies to that end.

## Results and discussion

A stereochemically defined monodeuterated analogue **4** (Scheme 2) of methyleneaziridine **2** (R = *i*-Pr) was targeted that would allow the stereochemistry of the  $S_NV$  process to be probed without presenting any steric or electronic bias compared with the original methyleneaziridine. At the outset of this study, a dissociative mechanism for the substitution reaction was ruled out on the basis of the aprotic, low-temperature conditions for the process and the relative instability of a vinylic cation. An out-of-plane (relative to the cleaving C–N bond) stepwise  $\pi$ -addition/elimination process, proceeding *via* a short-lived formal carbanion located on the terminal methylene carbon, or an equivalent concerted mechanism, would proceed with retention of configuration ( $S_NV_\pi$  pathway,  $\rightarrow$  **5**). An in-plane concerted process, akin to an  $S_N2$  reaction in aliphatic



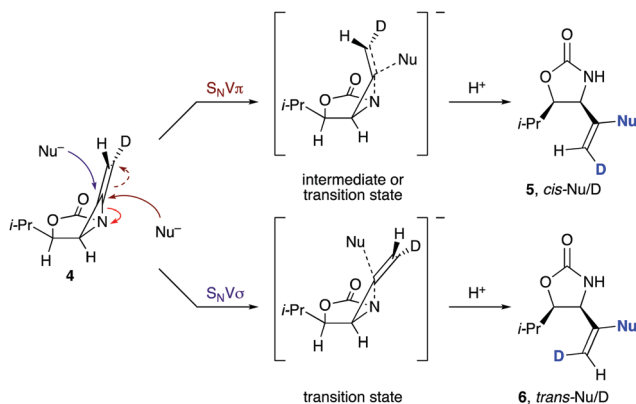
**Scheme 1** The formation and  $S_NV$  ring-opening of fused 1,3-oxazolidin-2-one methyleneaziridines.

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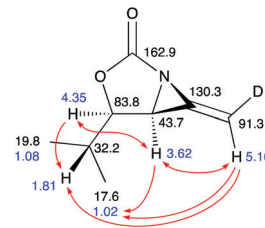




**Scheme 2** Simplified  $S_NV$  reaction modes of methyleneaziridine **4** with a generic nucleophile  $Nu^-$ .

substrates, would lead to inversion of configuration ( $S_NV_\sigma$  pathway,  $\rightarrow$  **6**). The operation of either of these reaction modes would then be revealed in the relative disposition of the newly-formed C–C bond and the adjacent H/D atoms, as shown.

In the absence of any literature precedent for the synthesis of a stereodefined terminally monodeuterated buta-2,3-dienol,<sup>12</sup> a synthesis of methyleneaziridine **4** was proposed based upon diastereoselective coordinated delivery of hydride<sup>13</sup> to deuterated alkyne epoxide **7** (Scheme 3) and the known stereochemical course of the intramolecular aziridination. Following this proposal, *trans*-2-ethynyl-3-isopropoxyirane<sup>14</sup> was stirred with an excess of  $D_2O$  under basic conditions<sup>15</sup> to yield the deuterated alkyne **7** (94% deuterium incorporation). Alkyne **7** was treated with DIBAL in dichloromethane as a non-coordinating solvent that would support epoxide chelation with the aluminium centre, and allene **8** was isolated apparently as one predominant stereoisomer,<sup>16</sup> depicted as that expected, and confirmed retrospectively from the NMR data for methyleneaziridine **4**. A slightly modified variant of Lebel's protocol for nitrenoid formation afforded consistent yields ( $\sim 25\%$ ) of methyleneaziridine **4** from *N*-tosyloxy carbamate **9**; lower yields were obtained from carbamate **10** with a range of Rh(II) catalysts including  $Rh_2(OAc)_4$ ,  $Rh_2(esp)_2$ ,<sup>17</sup> and  $Rh_2(TPA)_4$ .<sup>18</sup> The stereochemistry in methyleneaziridine **4** was confirmed by comparisons with the NMR data for non-deuterated methyleneaziridine **2**,<sup>4</sup> and the NOE correlations shown in Fig. 1. In the  $^1H$  NMR spectrum of methyleneaziridine **4**, the adjacent methine protons at  $\delta$  1.81 and 4.35 show  $^3J_{HH} = 9.5$  Hz, indicating a dominating *trans*-antiperiplanar disposition that places one of the diastereotopic methyls more regularly in



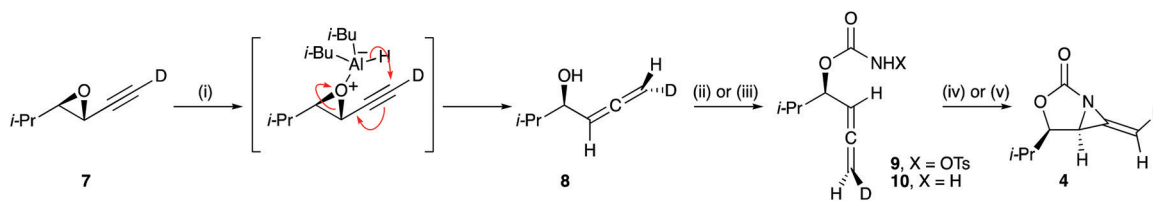
**Fig. 1** NMR chemical shifts and diagnostic NOE correlations to support the assigned stereochemistry in methyleneaziridine **4**.

close proximity to the CHN and =CHD protons, as seen in the NOE spectra. A simple dihedral drive calculation supports this view (ESI<sup>†</sup>).<sup>19</sup>

Two variants of the  $S_NV$  reaction were carried out, both of which converted methyleneaziridine **4** into products with reasonable overall efficiency (Scheme 4). In the first, addition of lithium dimethylcuprate gave a 77% isolated yield of 4-isopropenyl oxazolidinone **11**, in which the methyl group was found (see below) to be *cis*- to the deuterium atom. In the second, a copper-catalysed Grignard reaction with vinylmagnesium bromide gave 4-(buta-1,3-dien-2-yl) oxazolidinone **12** as the major product, again with the new C–C bond formed *cis*- to the deuterium atom. The azirine **13** was also isolated in this work; its formation may be explained by competing addition at the carbonyl followed by 1,4-vinylation of the so-formed  $\alpha,\beta$ -unsaturated ester.<sup>20</sup>

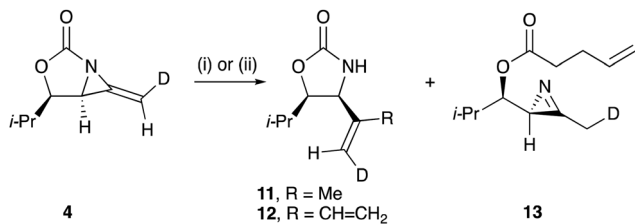
A combination of NMR experiments, including NOE (Fig. 2) provided support for the stereochemical assignments in  $S_NV$  products **11** and **12**. Notably, in **11** no NOE correlation was observed between the vinyl methyl protons and =CHD; similarly, in compound **12**, there were no significant correlations between the vinyl protons and =CHD.

An invertive  $S_NV_\sigma$  reaction appears to be stereoelectronically accessible in methyleneaziridines **2** and **4**, and the microscopic reverse of such a process is supported in the  $NaNH_2$ -mediated formation of simple methyleneaziridines from 2-bromoallylic amines.<sup>21</sup> Despite this, our results clearly rule out the  $S_NV_\sigma$  mode of ring-opening, the stereochemical outcome being consistent with a (retentive)  $S_NV_\pi$  mode of reaction. Setting aside the extent of the involvement of the metal counterions in this process, at one simplistic mechanistic extreme, as the delivery of the methyl or vinyl ligand to the methylene group initiates and charge begins to build on the terminal carbon, the  $sp^2$ -C–N bond weakens, with progression along this pathway

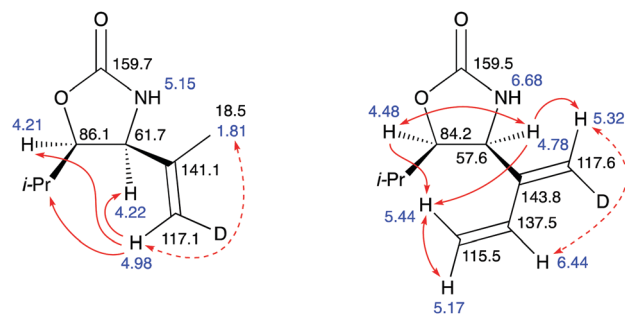


**Scheme 3** Reagents and conditions: (i) DIBAL,  $CH_2Cl_2$ ,  $0^\circ C$ , 1 h (53%); (ii) (a) CDI,  $CH_3CN$ , RT, 24 h then add  $NH_2OH \cdot HCl$ , RT, 24 h; (b)  $TsCl$ ,  $Et_3N$ ,  $Et_2O$ ,  $0^\circ C \rightarrow RT$ , 18 h (**9**, 62%); (iii)  $Cl_3CCO \cdot NCO$ ,  $CH_2Cl_2$ ,  $0^\circ C$ , 4 h then  $K_2CO_3$ , MeOH, RT, 4 h (**10**, 97%); (iv) [from **9**]  $K_2CO_3$ ,  $Rh_2(OAc)_4$  (5 mol%),  $CH_3CN$ , RT, 1.5 h (25%); (v) [from **10**] Rh(II) catalyst (5 mol%; see text),  $PhI(OAc)_2$ ,  $MgO$ ,  $CH_2Cl_2$ , reflux, 48 h (4–17%).

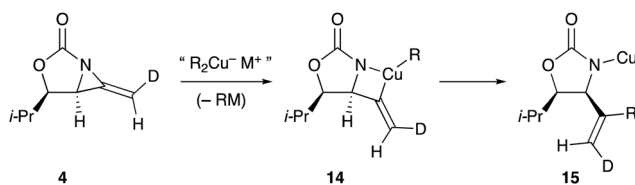




**Scheme 4** Reagents and conditions: (i) Me<sub>2</sub>CuLi (1.0 eq.), THF, -20 °C → RT, 30 min (**11**, 77%); (ii) vinyl-MgBr (2.0 eq), CuI (5 mol%), THF, -50 °C → 0 °C, 1 h (**12**, 31%; **13**, 23%).



**Fig. 2** Diagnostic NOE correlations to support the assigned stereochemistry in S<sub>N</sub>V products **11** (left, in CDCl<sub>3</sub>) and **12** (right, in acetone-*d*<sub>6</sub>). Dashed lines indicate important weak/absent correlations.



**Scheme 5** Retentive ring-opening via formal C–N insertion then ligand coupling from Cu(III) intermediate **14**.

constituting an overall concerted process (*cf.* Scheme 2). At the other end of the spectrum, an initial carbocupration reaction from the exposed face of the methylene group would generate a short-lived organocopper intermediate that rapidly fragments following rotation *via* the lower energy pathway<sup>11c</sup> to place the C–Cu and C–N bonds antiperiplanar to one another. Alternatively, a cross-coupling mechanism may be considered<sup>22</sup> in which formal-Cu(I) insertion into the activated sp<sup>2</sup>-C–N bond ( $\rightarrow$  **14**, Scheme 5) and reductive elimination/ligand coupling ( $\rightarrow$  **15**) would deliver the same stereochemical outcome; further research would be necessary to evaluate the viability and implications of such a mechanistic pathway.

## Conclusions

To the best of our knowledge, the direct nucleophilic sp<sup>2</sup> C–N bond cleavage reactions that we reported in 2010 remain the only examples in methyleneaziridine chemistry. In this work,

we have demonstrated that the substitution is stereoretentive, ruling out an S<sub>N</sub>V<sub>σ</sub> pathway, but the detailed mechanism of these reactions remains open to speculation and further work is intended to close this particular chapter of methyleneaziridine reactivity.<sup>23</sup>

## Experimental

### General information

All solvents for anhydrous reactions were obtained dry from Grubbs solvent dispenser units after being passed through an activated alumina column under argon. THF was additionally distilled from sodium/benzophenone ketyl under argon. Commercially available reagents were used as supplied unless otherwise specified. Triethylamine was distilled from CaH<sub>2</sub> and stored over KOH pellets under argon. ‘Petrol’ refers to the fraction of light petroleum ether boiling between 30 and 40 °C; ‘ether’ refers to diethyl ether. All reactions were carried out in oven-dried glassware and under an atmosphere of argon unless otherwise specified. Thin layer chromatography (TLC) was carried out using Merck aluminium backed DC60 F254 0.2 mm pre-coated plates. Spots were then visualised by the quenching of ultraviolet light fluorescence ( $\lambda_{\text{max}}$  254 nm) and then stained and heated with either anisaldehyde or KMnO<sub>4</sub> solutions as appropriate. Retention factors (*R<sub>f</sub>*) are reported along with the solvent system used in parentheses. Flash column chromatography was performed using Merck 60 silica gel (particle size 40–63 μm) and the solvent system used is reported in parentheses. Infrared spectra were recorded using a Bruker Tensor 27 FT-IR fitted with a diamond ATR module. Absorption maxima ( $\nu_{\text{max}}$ ) are reported in wavenumbers (cm<sup>-1</sup>) and are described as strong (s), medium (m), weak (w) or broad (br). Proton (<sup>1</sup>H) and carbon-13 (<sup>13</sup>C) spectra were recorded on Bruker AVIII HD 500, AVII 500, or AVIII HD 400 spectrometers. Chemical shifts ( $\delta_{\text{H}}$  or  $\delta_{\text{C}}$ ) are reported in parts per million (p.p.m.) downfield of tetramethylsilane, internally referenced (in MestReNova) to the appropriate solvent peak: CDCl<sub>3</sub>, 7.26/77.16; acetone-*d*<sub>6</sub>, 2.05/29.84. Peak multiplicities are described as singlet (s), doublet (d), triplet (t), quartet (q), septet (sept), octet (oct), multiplet (m), and broad (br) or a combination thereof. Coupling constants (*J*) are rounded to the nearest 0.5 Hz. Assignments are made on the basis of chemical shifts, integrations, and coupling constants, using COSY, HSQC and nOe experiments where appropriate. High Resolution Mass Spectra (HRMS) were recorded by the staff at the Chemistry Research Laboratory (University of Oxford) using a Waters GC-TOF spectrometer (EI/FI). Melting points were recorded on a Griffin melting point apparatus and are uncorrected.

### Trans-2-(deuterioethynyl)-3-isopropylloxirane (**7**)

*Trans*-2-ethynyl-3-isopropylloxirane (2.03 g, 18.4 mmol) was added to a stirring solution of K<sub>2</sub>CO<sub>3</sub> (3.76 g, 27.2 mmol) in acetonitrile (42 mL). After 30 min, D<sub>2</sub>O (20 mL) was added and stirring was continued for 5 h. The product was extracted from the reaction mixture into petrol (5 × 100 mL). The combined



extracts were dried ( $\text{MgSO}_4$ ) and the solvent was removed *in vacuo* [CARE: the product is volatile] to afford the title compound as a pale yellow oil (1.50 g, 73%, 94% deuterium incorporation).  $R_f$  0.58 (petrol/ether, 3:1);  $\nu_{\text{max}}/\text{cm}^{-1}$  (thin film): 2966m, 2589m, 1980w, 1469m;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 0.97 (3H, d,  $J = 7.0$  Hz), 0.99 (3H, d,  $J = 7.0$  Hz), 1.52 (1H, oct,  $J = 7.0$  Hz), 2.29 (0.1H, d,  $J = 1.5$  Hz, residual  $\equiv\text{CH}$ ), 2.89 (1H, dd,  $J = 7.0, 2.0$  Hz), 3.11 (1H, d,  $J = 2.0$  Hz);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 18.1, 18.7, 30.4, 43.9, 65.4, 71.5 (t,  $J = 38.5$  Hz), 80.3 (t,  $J = 7.5$  Hz).

#### (3R\*,5R\*)-6-Deuterio-2-methylhexa-4,5-dien-3-ol (8)

A solution of epoxyalkyne **7** (1.50 g, 13.5 mmol) in dichloromethane (100 mL) was added dropwise to a stirred solution of DIBAL (33.7 mL, 1.0 M in hexane, 33.7 mmol) in dichloromethane (100 mL) at 0 °C. The reaction mixture was stirred for 1 h then quenched by careful addition of water. A satd. aq. solution of Rochelle's salt (200 mL) was added dropwise and the mixture was stirred overnight to allow the solvent layers to separate completely. The mixture was extracted with dichloromethane (5 × 50 mL), the organic layers were combined and washed with brine (50 mL), then dried ( $\text{MgSO}_4$ ) and the solvent removed *in vacuo*. Purification by flash chromatography (petrol/ether, 8:1) afforded the title compound as a pale yellow oil (810 mg, 53%).  $R_f$  0.23 (petrol/ether 3:1);  $\nu_{\text{max}}/\text{cm}^{-1}$  (thin film) 3409br, 2957m, 2924s, 2854m, 1953w, 1464w, 1379w, 1261w, 1024w;  $\delta_{\text{H}}$  (500 MHz,  $\text{CDCl}_3$ ) 0.93 (3H, d,  $J = 7.0$  Hz), 0.95 (3H, d,  $J = 7.0$  Hz), 1.67 (1H, d,  $J = 4.5$  Hz), 1.77 (1H, oct,  $J = 7.0$  Hz), 3.92–3.97 (1H, m), 4.83–4.87 (1H, m), 5.23 (1H, t,  $J = 6.5$  Hz);  $\delta_{\text{C}}$  (125 MHz,  $\text{CDCl}_3$ ) 17.9, 18.2, 34.4, 74.7, 77.3 (t,  $J = 25.5$  Hz), 93.2, 207.5; HRMS ( $\text{FI}^+$ )  $m/z$ : [ $\text{M}^+$ ] calcd for  $\text{C}_7\text{H}_{11}\text{DO}$ , 113.0945; found, 113.0951.

#### (3R\*,5R\*)-6-Deuterio-2-methylhexa-4,5-dien-3-yl *p*-toluenesulfonyloxycarbamate (9)

*N,N*-Carbonyldiimidazole (1.43 g, 8.82 mmol) was added to a solution of alcohol **8** (500 mg, 4.42 mmol) in acetonitrile (25 mL) and the mixture was stirred at RT until the reaction was complete by TLC (~24 h). Imidazole (1.20 g, 17.6 mmol) and  $\text{NH}_2\text{OH}\cdot\text{HCl}$  (1.54 g, 22.2 mmol) were added, and stirring was continued until the reaction was complete by TLC (~24 h). The mixture was filtered and the solvent was removed *in vacuo*. The residue was then partitioned between hydrochloric acid (12 mL, 1.0 M) and ether (10 mL), and the aqueous phase was extracted with ether (3 × 50 mL). The combined organic layers were washed with brine (25 mL), then dried ( $\text{Na}_2\text{SO}_4$ ) and the solvent was removed *in vacuo*. Purification of the crude product by flash chromatography (petrol/ether, 3:1 → 1:1) afforded (3R\*,5R\*)-6-deuterio-2-methylhexa-4,5-dien-3-yl hydroxycarbamate as a pale yellow oil [454 mg, 60%; 73% based on recovered **8** (90 mg, 18%)].  $R_f$  0.26 (petrol/ether, 1:1);  $\nu_{\text{max}}/\text{cm}^{-1}$  (thin film) 3301br, 2965m, 1956m, 1717s, 1469m, 1387w, 1261s, 1112m, 1024m, 759m;  $\delta_{\text{H}}$  (500 MHz,  $\text{CDCl}_3$ ) 0.94 (6H, d,  $J = 7.0$  Hz), 1.93 (1H, oct,  $J = 7.0$  Hz), 4.84 (1H, dd,  $J = 7.0, 1.5$  Hz), 5.03 (1H, td,  $J = 7.0, 1.5$  Hz), 5.14 (1H, t,  $J = 7.0$  Hz), 6.77 (1H, br s), 7.21 (1H, s);  $\delta_{\text{C}}$  (125 MHz,  $\text{CDCl}_3$ ) 18.1 (two peaks), 32.5, 77.1 (t,  $J = 30.0$  Hz),

79.0, 88.9, 159.1, 209.1; HRMS ( $\text{ESI}^+$ )  $m/z$ : [ $\text{M} + \text{Na}$ ] $^+$  calcd for  $\text{C}_8\text{H}_{12}\text{DNNaO}_3$ , 195.0850; found, 195.0846. Recrystallised *p*-TsCl (619 mg, 3.25 mmol) was added to a stirred solution of the hydroxycarbamate (554 mg, 3.22 mmol) in dry ether (30 mL) at 0 °C. Triethylamine (0.45 mL, 3.23 mmol) was then added dropwise and stirring was continued for 18 h. The mixture was then diluted with ether (30 mL), washed with brine (2 × 20 mL), dried ( $\text{Na}_2\text{SO}_4$ ), and the solvent removed *in vacuo*. The crude product was purified by flash chromatography (petrol/ether, 5:1 → pure ether) to afford the title compound as a pale yellow oil (893 mg, 85%).  $R_f$  0.50 (petrol/ether, 1:1);  $\nu_{\text{max}}/\text{cm}^{-1}$  (thin film) 3284br, 2967m, 1770s, 1737s, 1598m, 1467m, 1379s, 1192s, 1179s, 1019m, 742m;  $\delta_{\text{H}}$  (400 MHz,  $\text{CDCl}_3$ ) 0.82 (3H, d,  $J = 7.0$  Hz), 0.84 (3H, d,  $J = 7.0$  Hz), 1.80 (1H, oct,  $J = 7.0$  Hz), 2.46 (3H, s), 4.77 (1H, d,  $J = 6.0$  Hz), 4.85–4.95 (2H, m), 7.35 (2H, d,  $J = 8.0$  Hz), 7.76 (1H, s), 7.88 (2H, d,  $J = 8.0$  Hz);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 17.8, 18.0, 21.9, 32.4, ~76.6 (from HSQC; obscured by solvent peak in 1D spectrum), 80.3, 88.2, 129.8, 129.9, 130.5, 146.2, 155.0, 209.1; HRMS ( $\text{ESI}^+$ )  $m/z$ : [ $\text{M} + \text{Na}$ ] $^+$  calcd for  $\text{C}_{15}\text{H}_{18}\text{DNNaO}_5\text{S}$ , 349.0939; found, 349.0932.

#### (4R\*,5S\*,Z)-4-Isopropyl-6-(methylene-*d*)-3-oxa-1-azabicyclo[3.1.0]hexane-2-one (4)

$\text{Rh}_2(\text{OAc})_4$  (6.8 mg, 15.4  $\mu\text{mol}$ ) and  $\text{K}_2\text{CO}_3$  (127 mg, 0.919 mmol) were added to a stirred solution of carbamate **9** (100 mg, 0.306 mmol) in dry acetonitrile (3 mL) at 25 °C. The reaction mixture was stirred vigorously for 90 min then diluted with acetonitrile, filtered, and concentrated *in vacuo* at RT to give the crude product. Purification by flash chromatography (petrol/ether, 7:1) afforded the title compound as a pale yellow oil (12 mg, 25%).  $R_f$  0.49 (petrol/ether 1:1);  $\nu_{\text{max}}/\text{cm}^{-1}$  (thin film) 2966w, 1793s, 1761w, 1176m, 1116w, 1072m, 1031s;  $\delta_{\text{H}}$  (500 MHz,  $\text{CDCl}_3$ ) 1.02 (3H, d,  $J = 7.0$  Hz), 1.08 (3H, d,  $J = 7.0$  Hz), 1.81 (1H, dsept,  $J = 9.5, 7.0$  Hz), 3.62 (1H, d,  $J = 5.5$  Hz), 4.35 (1H, dd,  $J = 9.5, 5.5$  Hz), 5.16 (1H, s);  $\delta_{\text{C}}$  (100 MHz,  $\text{CDCl}_3$ ) 17.6, 19.8, 32.2, 43.7, 83.8, 91.3 (t,  $J = 25.5$  Hz), 130.3, 162.9; HRMS ( $\text{FI}^+$ )  $m/z$ : [ $\text{M}^+$ ] calcd for  $\text{C}_8\text{H}_{10}\text{DNO}_2$ , 154.0847; found, 154.0847.

#### (4S\*,5R\*)-5-Isopropyl-4-[(*E*)-propen-2-yl-1-*d*]oxazolidin-2-one (11)

Methylolithium (0.16 mL, 1.6 M solution in ether, 0.256 mmol) was added dropwise to a stirred suspension of  $\text{CuI}$  (25 mg, 0.131 mmol) in THF (1 mL) in a pear-shaped flask at –20 °C. After 15 min, a solution of methyleneaziridine **4** (20 mg, 0.130 mmol) in THF (1 mL) was added. The mixture was stirred for 30 min, quenched with satd. aq.  $\text{NH}_4\text{Cl}$  solution (3 mL), and then allowed to warm to RT. The organic components were extracted into ether (3 × 20 mL), then the combined organic extracts were washed with brine (5 mL), dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated *in vacuo*. The residue was purified by recrystallisation from ether to afford the title compound (17 mg, 77%) as an off-white solid.  $R_f$  0.20 (ether); m.p. 105–106 °C;  $\nu_{\text{max}}/\text{cm}^{-1}$  (thin film) 3244br, 2985m, 1745s, 1722s, 1468w, 1386s, 1375s, 1220m, 1075m, 993m, 860m;  $\delta_{\text{H}}$  (500 MHz,  $\text{CDCl}_3$ ) 0.90 and 1.08 (2 × 3H, 2 × d,  $J = 6.5$  Hz), 1.81 (3H, s), 1.87 (1H, oct,  $J = 6.5$  Hz), 4.18–4.24 (2H, m), 4.98 (1H, s), 5.15 (1H, br s);  $\delta_{\text{C}}$



(125 MHz, CDCl<sub>3</sub>) 18.5, 19.1, 19.6, 28.2, 61.7, 86.1, 117.1 (t,  $J = 24.0$  Hz), 141.1, 159.7; HRMS (ESI<sup>+</sup>)  $m/z$ : [M + Na]<sup>+</sup> calcd for C<sub>9</sub>H<sub>14</sub>DNNaO<sub>2</sub>, 193.1058; found, 193.1049.

**(4*S*\*,5*R*\*)-4-[(*E*)-buta-1,3-dien-2-yl-1-*d*]-5-isopropylloxazolidin-2-one (12) and (*R*\*)-2-methyl-1-[(*S*\*)-3-(methyl-*d*)-2*H*-azirin-2-yl]propyl pent-4-enoate (13)**

Vinylmagnesium bromide (0.25 mL, 1.0 M solution in THF, 0.25 mmol) was added dropwise to a stirred suspension of CuI (1.2 mg, 6.30 μmol) in THF (1 mL) in a pear-shaped flask at -50 °C. After 10 min, a solution of methyleneaziridine 4 (19 mg, 0.123 mmol) in THF (1 mL) was added *via* canula. The mixture was allowed to warm to -20 °C over 1 h and was then quenched with sat. aq. NH<sub>4</sub>Cl solution (1 mL). The mixture was stirred for 30 min, warmed to RT, and the organic components were extracted into ether (3 × 20 mL). The combined organic extracts were washed with brine (15 mL), dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated *in vacuo*. The residue was purified by flash chromatography (petrol/ether, 7:1 → 1:1) to afford diene 12 (7.0 mg, 31%) as a colourless oil.  $R_f$  0.12 (petrol/ether, 1:1);  $\nu_{\max}/\text{cm}^{-1}$  (thin film) 3276br, 2364m, 1753s, 1389m, 1235m, 1023m;  $\delta_{\text{H}}$  (400 MHz, CDCl<sub>3</sub>) 0.90 (3H, d,  $J = 6.5$  Hz), 1.01 (3H, d,  $J = 6.5$  Hz), 1.90 (1H, apparent oct,  $J = 6.5$  Hz), 4.44 (1H, dd,  $J = 8.0, 7.0$  Hz), 4.64 (1H, d,  $J = 8.0$  Hz), 4.97 (1H, br s), 5.19 (1H, d,  $J = 11.0$  Hz), 5.27 (1H, s), 5.31 (1H, d,  $J = 17.5$  Hz), 6.37 (1H, dd,  $J = 17.5, 11.0$  Hz);  $\delta_{\text{H}}$  (500 MHz, acetone-*d*<sub>6</sub>) 0.89 (3H, d,  $J = 6.5$  Hz), 0.95 (3H, d,  $J = 6.5$  Hz), 1.85 (1H, oct,  $J = 6.5$  Hz), 4.48 (1H, dd,  $J = 8.0, 6.5$  Hz), 4.78 (1H, d,  $J = 8.0$  Hz), 5.17 (1H, d,  $J = 11.0$  Hz), 5.32 (1H, s), 5.44 (1H, d,  $J = 17.5$  Hz), 6.44 (1H, dd,  $J = 17.5, 11.0$  Hz), 6.68 (1H, br s);  $\delta_{\text{C}}$  (125 MHz, acetone-*d*<sub>6</sub>) 18.0, 20.3, 29.3 (from HSQC; partially obscured by solvent peak), 57.6, 84.2, 115.5, 117.6 (t,  $J = 24.5$  Hz), 137.5, 143.8, 159.5; HRMS (ESI<sup>+</sup>)  $m/z$ : [M + Na]<sup>+</sup> calcd for C<sub>10</sub>H<sub>14</sub>DNNaO<sub>2</sub>, 205.1058; found, 205.1052. Also obtained was azirene 13, a colourless oil (6.0 mg, 23%).  $R_f$  0.74 (petrol/ether, 1:1);  $\nu_{\max}/\text{cm}^{-1}$  (thin film) 3080w, 2965m, 1772w, 1730s, 1469m, 1418w, 1370m, 1251m, 1175m, 1106m, 1002m, 915m;  $\delta_{\text{H}}$  (500 MHz, CDCl<sub>3</sub>) 1.02 (3H, d,  $J = 7.0$  Hz), 1.06 (3H, d,  $J = 7.0$  Hz), 1.81 (1H, d,  $J = 6.0$  Hz), 2.03 (1H, oct,  $J = 7.0$  Hz), 2.34–2.41 (4H, m), 2.41–2.45 (2H, m), 4.14 (1H, apparent t,  $J = 6.0$  Hz), 5.01 (1H, dq,  $J = 10.5, 1.5$  Hz), 5.07 (1H, dq,  $J = 17.0, 1.5$  Hz), 5.78–5.87 (1H, m);  $\delta_{\text{C}}$  (125 MHz, CDCl<sub>3</sub>) 14.2 (t,  $J = 20.0$  Hz), 17.8, 18.7, 29.1, 30.9, 31.3, 33.8, 81.2, 115.7, 136.8, 170.8, 172.6; HRMS (ESI<sup>+</sup>)  $m/z$ : [M + Na]<sup>+</sup> calcd for C<sub>12</sub>H<sub>18</sub>DNNaO<sub>2</sub>, 233.1371; found, 233.1361.

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

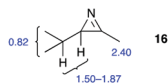
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