**Electrocyclic Ring-opening of 6,6-Dichlorobicyclo[3.1.0]hexanes and
Trapping of the Resulting π -Allyl Cations by C-1 Tethered Hydroxyamine
Derivatives: Formation of 2-Oxa-1-azaspiro[4.5]decan-3-ones**

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ABSTRACT: The C-1 substituted 6,6-dichlorobicyclo[3.1.0]hexanes **1a**, **1b** and **1c** have been prepared and shown to undergo electrocyclic ring-opening to give the corresponding π -allyl cations **2** that cyclise to afford the spirocyclic products **3b-d**, each of which has been subject to single-crystal X-ray analysis.

INTRODUCTION

We have previously shown that certain substituted 6,6-dihalobicyclo[3.1.0]hexanes undergo silver ion-promoted electrocyclic ring-opening reactions¹ with the resulting six-membered π -allyl cations being trapped by tethered nucleophiles and thus affording a range of cyclohexannulated heterocycles.² Various of these products can be manipulated to afford a range of structurally diverse natural products or natural product frameworks including those of the anatoxin-a,^{2a} γ -lycorane,^{2b} maritamine,^{2c} histrionicotoxin,^{2d} erythramine,^{2e} crinine^{2f} and haemanthamine^{2f} alkaloid classes. In considering possible extensions of such protocols we were attracted to the ring-expansion/spirocyclisation sequence shown in Scheme 1. Thus, it was envisaged that 6,6-

dichlorobicyclo[3.1.0]hexanes tethered through C-1 and an *O*-acetyl-linkage to various *N*-functionalised hydroxyamines, as shown in structure **1**, would engage in a ring-expansion process and that the product π -allyl cation **2** would then be captured, in a favoured 5-exo-trig cyclisation process,³ by the pendant nucleophile to give novel spirocyclic products of the general form **3**.⁴ Such products are of interest because of their necessarily three-dimensional nature and their capacity, therefore, to serve as scaffolds for drug design and development.^{5,6} Furthermore, N-O bond cleavage within such spirocyclic systems would provide novel β -amino acids that could be deployed in a variety of settings, including in the synthesis of the hasubanan alkaloids⁷ and perhaps other ones as well. The outcomes of an exploratory study concerned with such possibilities are detailed below.

Scheme 1. The proposed electrocyclic ring-opening/spirocyclisation reaction of C-1 functionalised 6,6-dichlorobicyclo[3.1.0]hexanes leading, via the corresponding π -allyl cation **2**, to 2-oxa-1-azaspiro[4.5]decan-3-ones

RESULTS AND DISCUSSION

The reaction sequence shown in Scheme 2 was used to prepare the substrates needed to test the proposal outlined above. This started from the commercially available, unsaturated nitrile **4** and the first five steps traversed involved those used in our earlier studies^{2d} but which are detailed again here for the sake of completeness. Thus, treatment of the starting material with sodium hydroxide in an ethylene glycol/water mixture gave, after acidic workup, the acid **5** in quantitative yield. All attempts to add dichlorocarbene to this unsaturated acid and thus form the desired dichlorocyclopropanated carboxylic acid directly were unsuccessful. As a result, compound **5** was treated with lithium aluminium hydride in diethyl ether and so affording the previously reported primary alcohol **6** (88%) but this too was not a suitable substrate for the dichlorocarbene addition

reaction (because of the potential for competing insertion of this species into the associated O–H bond). Accordingly, the readily derived acetate, **7** (82%), of the last compound was subjected to reaction with dichlorocarbene generated under Makosza's conditions⁸ using triethylbenzylammonium chloride (TEBAC) as the phase-transfer catalyst and the cyclopropane **8** thus obtained in 78% yield. Cleavage of the acetate residue within compound **8** was achieved using potassium carbonate in methanol and the resulting alcohol **9** oxidized to the corresponding and previously unreported acid **10** (60%) using Jones' reagent.⁹ The spectral data derived from product **10** were in complete accord with the assigned structure. In particular, the derived ¹³C NMR spectrum displayed the expected eight resonances including one at δ 177.6 that is attributed to the carbon of the acid residue while an absorption observed at ν_{max} 1706 cm⁻¹ in the infra-red spectrum is assigned to stretching of the associated carbonyl unit. Dicyclohexylcarbodiimide (DCC)-promoted coupling of acid **9** with freshly prepared *tert*-butylhydroxycarbamate,¹⁰ *N*-hydroxy-4-methylbenzenesulfonamide,¹¹ or commercially available *N*-hydroxyacetamide, then gave the anticipated *O*-acylhydroxyamine derivatives **1a** (P=Boc) (81%), **1b** (P=Ts) (68%) or **1c** (P=Ac) (60%), respectively. Once again, all the spectral data acquired on these compounds were in complete accord the illustrated structures, with the signature features being carbonyl carbon resonances appearing in the range δ 170.9-169.8 and carbonyl stretching bands observed between 1790 and 1731 cm⁻¹ in the corresponding infra-red spectrum. In the case of compounds **1a** and **1b** appropriate molecular ion-associated clusters were observed in a 100:60:10 (relative) ratio in the electrospray ionisation mass spectra as a result of the presence of two chlorines in each compound. In the case of congener **1c** the equivalent M⁺⁺ ions were not observed in the electron-impact mass spectrum. Rather, only fragment ions were observed in this instance.

Scheme 2. The reaction sequence used to prepare substrates **1a-c**

The pivotal, silver tetrafluoroborate-promoted electrocyclic ring-opening/spirocyclisation reactions of the dichlorocyclopropanes **1a-c** were carried out, as shown in Scheme 3, in refluxing THF and each proceeded smoothly to give the hoped for spirocyclic product although in the case of the Boc-protected substrate (**1a**) this group was lost, presumably as a result of the co-production of HBF_4 . Products **3b** (41%), **3c** (88%) and **3d** (53%) were each obtained as a crystalline solid after chromatographic purification and could thus be subject to single-crystal X-ray analysis and so serving to confirm their structures. The precise ordering of events associated with the conversion **1a** $\rightarrow$ **3b** remains unclear, at least in terms of whether loss of the Boc group takes place before or after the spirocyclization event.

Scheme 3. The pivotal electrocyclic ring-opening/spirocyclisation reactions leading to products **3b-d**

CONCLUSIONS

The silver(I)-promoted electrocyclic ring-opening/spirocyclization of the compounds **1a-c** can be used to prepare 2-oxa-1-azaspiro[4.5]decan-3-ones **3b-d** in a relatively efficient manner. This process, which complements the more commonly used dipolar cycloaddition reactions used to assemble such systems,^{6a-e,j,k,l} allows for the incorporation of functionality (most notably a chlorinated olefin) in the six-membered, carbocyclic ring that might otherwise be difficult to introduce. The utility of such chloro-olefin residues in intramolecular radical addition/elimination reactions has been highlighted in earlier work^{2e} and could prove useful in the present setting as well. There is also the potential for the construction of enantiomerically enriched or pure variants of the title compounds through desymmetrizing processes involving homochiral forms of the group P attached at nitrogen in substrates such as **1a-c**.

EXPERIMENTAL SECTION

General Experimental Procedures.

Unless otherwise specified, proton (¹H) and carbon (¹³C) NMR spectra were recorded at room temperature in base-filtered CDCl₃ on a spectrometer operating at 400 MHz for proton and 101 MHz for carbon nuclei. The signal due to residual CHCl₃ appearing at δ_{H} 7.26 and the central resonance of the CDCl₃ “triplet” appearing at δ_{C} 77.16 were used to reference ¹H and ¹³C NMR spectra, respectively. ¹H NMR data are recorded as follows: chemical shift (δ) [multiplicity, coupling constant(s) *J* (Hz), relative integral] where multiplicity is defined as: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet or combinations of the above. Infrared spectra (ν_{max}) were recorded on a FTIR spectrometer. Samples were analyzed as thin films. Low-resolution ESI mass spectra were recorded on a single quadrupole liquid chromatograph-mass spectrometer, while high-resolution measurements were conducted on a time-of-flight instrument. Low- and high-resolution EI mass spectra were recorded on a magnetic-sector machine. Analytical thin layer chromatography (TLC) was performed on aluminum-backed 0.2 mm thick silica gel 60 F₂₅₄ plates. Eluted plates were visualized using a 254 nm UV lamp and/or by treatment with a suitable dip followed by heating. These dips included phosphomolybdic acid : ceric sulfate : sulfuric acid (conc.) : water (37.5 g : 7.5 g : 37.5 g : 720 mL) or potassium permanganate : potassium carbonate : 5% sodium hydroxide aqueous solution : water (3 g

: 20 g: 5 mL : 300 mL). Flash chromatographic separations were carried out following protocols defined by Still *et al.*¹² with silica gel 60 (40–63 μ m) as the stationary phase and using the AR- or HPLC-grade solvents indicated. Starting materials, reagents, drying agents, and other inorganic salts were generally commercially available and used as supplied. Tetrahydrofuran (THF), methanol and dichloromethane were dried using a solvent purification system that is based upon a technology originally described by Grubbs *et al.*¹³ Where necessary, reactions were performed under an atmosphere of nitrogen.

Specific Chemical Transformations

2-(Cyclopent-1-en-1-yl)acetic acid (5)

A magnetically stirred mixture of commercially available 2-(cyclopent-1-en-1-yl)acetonitrile (**4**) (5.90 g, 55.1 mmol, containing *ca.* 15% of the isomeric 2-cyclopentylideneacetonitrile), ethylene glycol (150 mL) and NaOH (35 g in 150 mL of water) was heated under reflux for 18 h. The cooled reaction mixture was diluted with water (100 mL) and the resulting mixture acidified to pH 2 with HCl (37% aqueous solution) then extracted with dichloromethane (3 $\times$ 150 mL). The combined organic extracts were dried (Na₂SO₄), filtered and then concentrated under reduced pressure to give an 85:15 mixture of acid **5**^{2d} and its conjugated isomer (7.02 g, quantitative yield) as a brown oil. δ_{H} (major isomer) δ 5.59 (s, 1H), 3.17 (s, 2H), 2.36–(m, 4H), 1.91 (m, 2H) (resonance due due carboxylic acid group proton not observed).

The material was used without purification in the next step of the reaction sequence as detailed immediately below.

2-(Cyclopent-1-en-1-yl)ethan-1-ol (6)

A magnetically stirred suspension of LiAlH₄ (2.50 g, 65.9 mmol) in anhydrous diethyl ether (50 mL) was cooled to 0 °C then treated, dropwise, with a solution of an 85:15 mixture of acid **5** and its conjugated isomer (6.94 g, 55.0 mmol) in anhydrous diethyl ether (50 mL). After the addition was complete, the reaction mixture was warmed to 22 °C, stirred for a further 1.5 h before being cautiously acidified to pH 2 using HCl (2 M aqueous solution), diluted with diethyl ether (200 mL) and the layers were separated. The aqueous layer was extracted with diethyl ether (3 $\times$ 200 mL) then then combined organic extracts were dried (Na₂SO₄), filtered and concentrated under reduced pressure to give a

ca. 85:15 mixture of compound **6**^{2d} and 2-cyclopentylideneethan-1-ol (5.42 g, 88%) as a clear, light-yellow oil. δ_{H} (major isomer) δ 5.48 (m, 1H), 3.72 (t, J = 6.2 Hz, 2H), 2.39–2.21 (complex m, 6H), 1.89 (m, 2H) (resonance due to hydroxyl group proton not observed)

The material was used without purification in the next step of the reaction sequence as detailed immediately below.

2-(Cyclopent-1-en-1-yl)ethyl acetate (7)

A magnetically stirred solution of a 85:15 mixture of alcohol **6** and 2-cyclopentylideneethan-1-ol (5.30 g, 47.2 mmol), pyridine (11.4 mL, 142 mmol) and DMAP (106 mg, 0.95 mmol) in dichloromethane (250 mL) was cooled to 0 °C then treated, dropwise, with acetic anhydride (13.4 mL, 142 mmol). After the addition was complete, the reaction mixture was warmed to 22 °C and stirred for further 1 h before being quenched with HCl (250 mL of a 1 M aqueous solution). The separated aqueous layer was extracted with dichloromethane (3 $\times$ 250 mL) then the combined organic extracts were dried (Na₂SO₄), filtered and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 99:1→95:5 v/v hexanes/ethyl acetate gradient elution) to afford, after concentration of the appropriate fractions (R_f = 0.9 in 1:1 v/v hexanes/ethyl acetate), ester **7**^{2d} (6.00 g, 95% from **6**) as a clear, colourless oil. δ_{H} 5.40 (m, 1H), 4.17 (t, J = 7.0 Hz, 2H), 2.40 (m, 2H), 2.34–2.19 (complex m, 4H), 2.04 (s, 3H), 1.85 (m, 2H).

2-(6,6-Dichlorobicyclo[3.1.0]hexan-1-yl)ethyl acetate (8)

A magnetically stirred solution of ester **7** (3.00 g, 19.5 mmol) and TEBAC (150 mg, 0.66 mmol) in chloroform (60 mL) was treated, dropwise, with NaOH (30 mL of a 50% w/v aqueous solution). The reaction mixture thus formed was stirred at 22 °C for 20 h then diluted with dichloromethane (100 mL) and water (100 mL). The separated aqueous layer was extracted with dichloromethane (3 $\times$ 100 mL) and the combined organic extracts then dried (Na₂SO₄), filtered and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 98:2→95:5 v/v hexanes/ethyl acetate gradient elution) to afford, after concentration of the appropriate fractions (R_f = 0.9 in 4:1 v/v hexanes/ethyl acetate), compound **8**^{2d} (4.06 g, 88%) as a clear, light-yellow oil. δ_{H} 4.30–4.17 (complex m, 2H), 2.17–1.99 (complex m, 6H), 2.09 (s, 3H), 1.83–1.66 (complex m, 3H).

2-(6,6-Dichlorobicyclo[3.1.0]hexan-1-yl)ethan-1-ol (**9**)

A magnetically stirred solution of compound **8** (4.04 g, 17.0 mmol) in methanol (225 mL) was treated with K_2CO_3 (7.07 g, 51.1 mmol). The ensuing mixture was stirred at 22 °C for 1.5 h then diluted with water (250 mL) and extracted with dichloromethane (3×200 mL). The combined organic extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure to give alcohol **9**^{2d} (3.13 g, 94%) as a clear, colourless oil. δ_H 3.82 (m, 2H), 2.17–1.96 (complex m, 6H), 1.85–1.64 (complex m, 3H), 1.40 (broad s, 1H).

The material was used without purification in the next step of the reaction sequence as detailed immediately below.

2-(6,6-Dichlorobicyclo[3.1.0]hexan-1-yl)acetic acid (**10**)

A magnetically stirred suspension of alcohol **9** (3.10 g, 15.9 mmol) and diatomaceous earth (3.0 g) in acetone (70 mL) was cooled to 0 °C then treated, dropwise, with Jones' reagent (11 mL of a *ca.* 3M solution)⁸ until the dark-red colour persisted and the formation of a dark-green precipitate was observed. The reaction mixture was stirred for a further 0.5 h before being filtered through a sintered-glass funnel containing a 2 cm deep pad of diatomaceous earth. The residues thus retained were washed with ethyl acetate (100 mL) then water (100 mL). The separated aqueous layer associated with the filtrate was extracted with ethyl acetate (2×100 mL) and then combined organic extracts then dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 8:2→2:8 v/v hexanes/ethyl acetate gradient elution) to afford, after concentration of the appropriate fractions (R_f = 0.4 in 1:1 v/v hexanes/ethyl acetate), carboxylic acid **10** (2.54 g, 71%) as a clear, light-yellow oil. δ_H 2.90 (ABq, J = 17.3 Hz, 2H), 2.29–2.14 (complex m, 2H), 2.13–1.99 (complex m, 2H), 1.89 (d, J = 5.9 Hz, 1H), 1.87–1.78 (complex m, 1H), 1.77–1.65 (complex m, 1H) (resonance due to carboxylic acid group proton not observed). δ_C 177.6, 71.8, 42.0, 40.9, 37.8, 33.9, 28.6, 25.6. ν_{max}/cm^{-1} 2932, 2866, 1707, 1409, 1245, 830. m/z (ESI, –ve) 209 and 207 $[M-H]^-$ (66 and 100%), 95 and 93 (18 and 28). HRMS 206.9976; calcd for $C_8H_9O_2^{35}Cl_2$, $[M-H]^-$ 206.9980.

tert-Butyl *N*-(2-(6,6-dichlorobicyclo[3.1.0]hexan-1-yl)acetoxy)carbamate (**1a**)

A magnetically stirred solution of carboxylic acid **10** (570 mg, 2.73 mmol) and *tert*-butylhydroxycarbamate (364 mg, 2.73 mmol)¹⁰ in dry dichloromethane (15 mL) was cooled to 0 °C then treated with a solution of DCC (598 mg, 2.90 mmol) in dry

dichloromethane (5 mL). The ensuing mixture was warmed to 22 °C and stirred for further 3 h during which time a white precipitate was observed. The reaction mixture was then filtered through a thin pad of diatomaceous earth and the filtrate concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 95:5→9:1 v/v hexanes/ethyl acetate gradient elution) to afford, after concentration of the appropriate fractions (R_f = 0.95 in 1:1 v/v hexanes/ethyl acetate), carbamate **1a** (715 mg, 81%) as a clear, light-yellow oil. δ_H 7.93 (broad s, 1H), 2.96 (ABq, J = 17.1 Hz, 2H), 2.30–1.97 (complex m, 4H), 1.94 (m, 1H), 1.83 (m, 1H), 1.70 (m, 1H), 1.48 (s, 9H). δ_C 170.9, 155.5, 83.5, 71.5, 42.0, 40.8, 35.6, 33.7, 28.6, 28.2, 25.5. $\nu_{\max}/\text{cm}^{-1}$ 3287, 2978, 2934, 1784, 1733, 1369, 1250, 1158, 1106, 831. m/z (ESI, +ve) 348 and 346 [(M+Na)⁺, 61 and 100%], 292 and 290 (22 and 35), 256 and 254 (22 and 15), 212 and 210 (19 and 44), 156 (22), 107 (10). HRMS 346.0582; calcd for C₁₃H₁₉NO₄³⁵Cl₂Na, [M+Na]⁺ 346.0589.

***N*-(2-(6,6-Dichlorobicyclo[3.1.0]hexan-1-yl)acetoxy)-4-methylbenzenesulfonamide (1b).**

A magnetically stirred solution of carboxylic acid **10** (1.48 g, 7.08 mmol) and *N*-hydroxy-4-methylbenzenesulfonamide (1.33 g, 7.08 mmol)¹¹ in dry dichloromethane (40 mL) was cooled to 0 °C and treated with a solution of DCC (1.61 g, 7.79 mmol) in dry dichloromethane (10 mL). The ensuing mixture was warmed to 22 °C and stirred for a further 3 h during which time formation of a white precipitate was observed. The reaction mixture was then filtered through a thin pad of diatomaceous earth and the filtrate concentrated under reduced pressure. The residue thus formed was subjected to flash chromatography (silica, 95:5→9:1→8:2 v/v hexanes/ethyl acetate gradient elution) to afford, after concentration of the appropriate fractions (R_f = 0.6 in 7:3 v/v hexanes/ethyl acetate), a clear, colourless oil that solidified on standing. Recrystallisation (hexanes/dichloromethane) of this material afforded sulfonamide **1b** (1.51 g, 56%) as a white crystals, m.p. = 83–89 °C. δ_H 8.98 (s, 1H), 7.84 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 2.82 (ABq, J = 17.0 Hz, 2H), 2.45 (s, 3H), 2.19–1.93 (complex m, 3H), 1.86–1.53 (complex m, 4H). δ_C 169.9, 146.0, 132.4, 130.2, 129.1, 71.1, 41.9, 40.3, 35.5, 33.5, 28.5, 25.4, 21. $\nu_{\max}/\text{cm}^{-1}$ 3183, 2934, 1772, 1387, 1352, 1172, 1087, 815, 708. m/z (ESI, +ve) 402 and 400 [(M+Na)⁺, 72 and 100%], 366 and 364 (30 and 71), 193 (18), 120 (26), 102 (14). HRMS 400.0135; calcd for C₁₅H₁₇NO₄S³⁵Cl₂Na, [M+Na]⁺ 400.0148.

***N*-(2-(6,6-Dichlorobicyclo[3.1.0]hexan-1-yl)acetoxy)acetamide (**1c**)**

A magnetically stirred solution of carboxylic acid **10** (1.65 g, 7.89 mmol) and acetohydroxamic acid (1.18 g, 15.8 mmol) in dry acetonitrile (50 mL) was cooled to 0 °C then treated with a solution of DCC (1.95 g, 9.47 mmol) in dry acetonitrile (10 mL). The ensuing mixture was warmed to 22 °C and stirred for further 1 h during which time the formation of a white precipitate was observed. The reaction mixture was filtered through a thin pad of diatomaceous earth and the filtrate concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 8:2 v/v hexanes/EtOAc elution) to afford, after concentration of the appropriate fractions (R_f = 0.4 in 8:2 v/v hexanes/ethyl acetate) a solid that upon recrystallization (hexanes/dichloromethane) afforded acetamide **1c** (1.26 g, 60%) as a white, crystalline solid, m.p. = 93–113 °C. δ_H 9.03 (broad s, 1H), 3.00 (ABq, J = 16.8 Hz, 2H), 2.30–1.97 (complex m, 7H), 1.95 (d, J = 6.0 Hz, 1H), 1.92–1.64 (complex m, 2H). δ_C 169.9, 71.4, 42.1, 40.8, 35.6, 33.7, 28.6, 25.5, 19.9 (one signal obscured or overlapping). ν_{max}/cm^{-1} 3175, 2936, 1791, 1677, 1369, 1108, 996, 831. m/z (EI, +ve) 191 (8), 165 and 163 (11 and 18), 128 (100), 113 (76), 91 (29). HRMS (ESI, –ve) 264.0198; calcd for $C_{10}H_{12}^{35}Cl_2NO_3$, $[M-H]^-$ 264.0194.

6-Chloro-1-tosyl-2-oxa-1-azaspiro[4.5]dec-6-en-3-one (3b**)**

An oven-dried, round-bottom flask fitted with a magnetic stirring bar was charged, under a nitrogen atmosphere, with $AgBF_4$ (576 mg, 2.96 mmol) that was then dissolved in dry THF (30 mL) and the resulting solution treated with a solution of sulfonamide **1b** (930 mg, 2.47 mmol) in dry THF (10 mL). The ensuing mixture was heated under reflux for 15.5 h before being cooled to 22 °C, treated with $NaHCO_3$ (10 mL of a saturated aqueous solution) then filtered through a thick pad of diatomaceous earth. The filtrate was dried (Na_2SO_4), filtered and concentrated under reduced pressure and the residue thus obtained subjected to flash chromatography (silica, 8:2 v/v hexanes/ethyl acetate elution). Concentration of the appropriate fractions (R_f = 0.8 in 6:4 v/v hexanes/ethyl acetate) and recrystallisation of the resulting solid (hexanes/dichloromethane) afforded the spirocycle **3b** (745 mg, 88%) as a white, crystalline solid, m.p. = 120–125 °C. δ_H 7.87 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 6.23 (t, J = 4.1 Hz, 1H), 3.35 (d, J = 17.2 Hz, 1H), 2.86–2.72 (m, 2H), 2.45 (s, 3H), 2.37 (m, 1H), 2.25–2.03 (complex m, 3H), 1.70 (m, 1H). δ_C 171.4, 145.9, 134.2, 133.3, 129.9, 129.4, 129.3, 72.4, 40.8, 33.2, 26.4, 21.9, 19.3; ν_{max}/cm^{-1}

¹ 2927, 1812, 1596, 1351, 1162, 1088, 817, 680. *m/z* (ESI, +ve) 366 and 364 [M+Na]⁺ (39 and 100%). HRMS 342.0561; calcd for C₁₅H₁₇³⁵ClNO₄S, [M+H]⁺ 342.0559.

1-Acetyl-6-chloro-2-oxa-1-azaspiro[4.5]dec-6-en-3-one (3c)

An oven-dried, round-bottom flask fitted with a magnetic stirring bar was charged, under a nitrogen atmosphere, with AgBF₄ (320 mg, 1.65 mmol) that was then dissolved in dry THF (10 mL) before being treated with a solution of acetamide **1c** (200 mg, 0.75 mmol) in dry THF (5 mL). The ensuing mixture was heated under reflux for 3 h, cooled to room temperature, treated with NaHCO₃ (3 mL of a saturated aqueous solution) then filtered through a thick pad of diatomaceous earth. The filtrate was dried (Na₂SO₄), filtered and concentrated under reduced pressure with the residue thus obtained being subjected to flash chromatography (silica, 1:1 v/v hexanes/ethyl acetate elution). Concentration of the appropriate fractions (*R_f* = 0.8 in 1:1 v/v hexanes/ethyl acetate) and recrystallization (hexanes/dichloromethane) of the resulting solid gave spirocycle **3c** (91 mg, 53%) as a white, crystalline solid, m.p. = 113-122 °C. δ_H 6.05 (m, 1H), 3.23 (d, *J* = 18.1 Hz, 1H), 2.95 (d, *J* = 18.1 Hz, 1H), 2.70 (m, 1H), 2.34–2.23 (complex m, 1H), 2.21–2.10 (complex m, 4H), 2.05 (m, 1H), 1.94 (m, 1H), 1.54 (complex m, 1H). δ_C 169.7, 168.4, 130.4(0), 130.3(7), 69.1, 42.4, 35.1, 25.8, 22.6, 20.2. ν_{max}/cm⁻¹ 3174, 2935, 1788, 1676, 1369, 1101, 995, 830. *m/z* (EI, +ve) 231 and 229 (M⁺, 8 and 15%), 189 and 187 (46 and 92), 157 and 155 (61 and 100), 147 and 145 (47 and 90), 128 (42), 93 and 91 (42 and 69). HRMS 229.0506; calcd for C₁₀H₁₂³⁵ClNO₃, M⁺ 229.0506.

6-Chloro-2-oxa-1-azaspiro[4.5]dec-6-en-3-one (3d)

An oven-dried, round-bottomed flask fitted with a magnetic stirring bar was charged, under a nitrogen atmosphere, with AgBF₄ (562 mg, 2.89 mmol). This was dissolved in dry THF (30 mL) then a solution of carbamate **3a** (780 mg, 2.41 mmol) in dry THF (10 mL) was added to the flask. The reaction mixture thus formed was heated under reflux for 7 h before being cooled then treated with NaHCO₃ (10 mL of a saturated aqueous solution). The ensuing mixture was filtered through a thick pad of diatomaceous earth before being dried (Na₂SO₄), filtered then concentrated under reduced pressure. The residue thus obtained was subjected to flash chromatography (silica, 4:1 v/v hexanes/ethyl acetate elution) to afford, after concentration of the appropriate fractions (*R_f* = 0.3 in 4:1 v/v hexanes/ethyl acetate), a solid that upon recrystallization (hexanes/dichloromethane) gave compound **3d** (187 mg, 41%) as a white, crystalline solid, m.p. = 53-57 °C. δ_H 6.72 (broad

s, 1H), 6.25 (m, 1H), 3.41 (d, $J = 17.5$ Hz, 1H), 2.46 (d, $J = 17.5$ Hz, 1H), 2.35–2.08 (complex m, 3H), 1.86 (m, 1H), 1.68 (m, 2H). δ_{C} 177.2, 135.3, 128.3, 65.4, 39.9, 34.9, 26.8, 18.2. $\nu_{\text{max}}/\text{cm}^{-1}$ 2930, 1813, 1685, 1211, 1170, 884. m/z (EI, +ve) 189 and 187 (M^{+} , 9 and 21%) 157 and 155 (37 and 100), 147 and 145 (29 and 70), 130 and 128 (21 and 48). HRMS 187.0404; calcd for $\text{C}_8\text{H}_{10}^{35}\text{ClNO}_2$, M^{+} 187.0400.

Crystallographic Studies on Compounds 3b-d

Crystal data

Compound 3b: $\text{C}_{15}\text{H}_{16}\text{ClNO}_4\text{S}$, $M = 341.80$, $T = 150$ K, monoclinic, space group $\text{P2}_1/\text{c}$, $Z = 4$, $a = 14.6615(4)$, $b = 6.7850(1)$, $c = 15.3584(4)$ Å, $\beta = 90.457(2)^\circ$, $V = 1527.78(6)$ Å³, $D_x = 1.486$ g.cm⁻³, 3122 unique data ($2\theta_{\text{max}} = 52.8^\circ$), 2781 with $I > 2.0\sigma(I)$; $R = 0.029$, $R_w = 0.072$, $S = 1.05$.

Compound 3c: $\text{C}_{10}\text{H}_{12}\text{ClNO}_3$, $M = 229.66$, $T = 150$ K, orthorhombic, space group Pbca , $Z = 8$, $a = 7.8049(2)$, $b = 15.1100(4)$, $c = 17.9753(6)$ Å, $V = 2119.86(11)$ Å³, $D_x = 1.439$ g.cm⁻³, 2721 unique data ($2\theta_{\text{max}} = 58.6^\circ$), 2331 with $I > 2.0\sigma(I)$; $R = 0.037$, $R_w = 0.092$, $S = 1.03$.

Compound 3d: $\text{C}_8\text{H}_{10}\text{OCINO}_2$, $M = 187.62$, $T = 150$ K, monoclinic, space group $\text{P2}_1/\text{c}$, $Z = 4$, $a = 7.6625(4)$, $b = 7.6264(5)$, $c = 14.7384(4)$ Å, $\beta = 104.369(6)^\circ$, $V = 834.33(8)$ Å³, $D_x = 1.494$ g.cm⁻³, 1717 unique data ($2\theta_{\text{max}} = 52.8^\circ$), 1461 with $I > 2.0\sigma(I)$; $R = 0.031$, $R_w = 0.077$, $S = 1.04$.

Structure Determinations

Images were measured on an Agilent Xcalibur CCD diffractometer (MoK α , graphite monochromator, $\lambda = 0.71073$ Å) and data extracted using the CrysAlis PRO package.¹⁴ Structure solution was by ShelXT,¹⁵ and the structures of compounds **3b-d** were refined using ShelXL¹⁶ in the OLEX2 program package.¹⁷ Atomic coordinates, bond lengths and angles, and displacement parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC Deposition number 1885836, 1885837 and 1885838). These data can be obtained free-of-charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

ASSOCIATED CONTENT

Supporting Information

Anisotropic displacement ellipsoid plots from the single-crystal X-ray analysis of compound **3b-d**. ^1H and ^{13}C NMR spectra of compounds **1a-c**, **3b-d** and **10**. This material is available free-of-charge via the Internet at <http://ajc.....>

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Notes

The authors declare no competing financial interest

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Graphical Abstract Text:

The C-1 tethered 6,6-dichlorobicyclo[3.1.0]hexanes **1a-c** engage in a silver ion-promoted electrocyclic ring-opening/spirocyclization reaction sequence to give products **3b-d**

Graphical Abstract:

a: P = Boc; b: P = Ts; c: P = Ac; d: P = H