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The synthesis of fused and spiro annulated carbohydrate structures using copper(I) catalysed intramolecular photoannulation of glucose derivatives †

David J. Holt, William D. Barker, Subrata Ghosh ‡ and Paul R. Jenkins *
Department of Chemistry, The University of Leicester, Leicester, UK LE1 7RH

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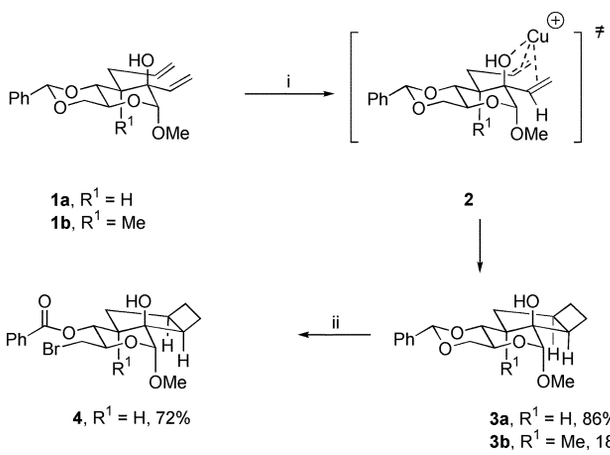
Intramolecular [2 + 2] photoannulation catalysed by copper(I)triflate has been applied to a series of carbohydrate derivatives obtained from glucose. Dienes **1a** and **1b** lead to cyclobutanes **3a** and **3b** whereas the diastereoisomeric dienes **5a** and **5b** gave diastereoisomeric products **7a** and **7b**. These results demonstrate that the reaction is stereospecific. Products **3a** and **7a** were converted into bromoesters **4** and **9** respectively. The Vasella elimination of **8** lead to the expected bicyclic aldehyde **10** and the ring expanded hydroxy ketone **12**. The stereospecific formation of enantiomerically pure spiro annulated carbohydrates **18a** and **18b** was demonstrated whereas in example **19** no selectivity in the formation of **20** and **21** was observed.

Intra and intermolecular [2 + 2] photocycloaddition reactions have been used to synthesise a wide variety of cyclobutane containing natural products and to generate cyclobutane intermediates, which subsequently undergo ring expansion in routes to other important target molecules.[1] Light absorbtion at a practical wavelength is usually achieved in the [2 + 2] photocyclisation by using an enone chromophore in reaction with an alkene. The stereochemistry of this process has been studied extensively with varying degrees of success.[2] The [2 + 2] photocyclisation of two non-conjugated alkenes is also possible using a metal catalyst;[3] the most successful catalyst for this reaction is bis(copper(I)trifluoromethanesulfonate)-benzene complex $[(CuSO_3CF_3)_2.C_6H_6](CuOTf)$ first reported by Salomon and Kochi.[4]

Attempts to achieve asymmetric induction of the copper(I) catalysed [2 + 2] reaction with a chiral auxilliary have met with some success, with ee's up to 60%, however reactions in the presence of a chiral ligand gave very poor results, with ee's < 5%.[5] As part of our interest in new methods of carbohydrate annulation.[6,7] we were attracted to the idea of using carbohydrate substrates[8] as a means of synthesising chiral cyclobutanes. We report here in full the first successful synthesis of chiral cyclobutane derivatives in enantiomerically pure form using carbohydrate substrates in the copper(I) catalysed [2 + 2] photcycloaddition reaction.[9] Recently a related study using furanose sugars has appeared.[10]

Results and discussion

When the two *trans*-alcohol **1a** was irradiated in the presence of bis(copper(I)trifluoromethane sulfonate) $[(CuSO_3CF_3)_2.C_6H_6]$ = CuOTf according to the method introduced by Salomon and Kochi[4] a single diastereoisomer of the product **3a** was obtained in 86% yield, Scheme 1. We account for this result by applying the explanation given for simpler cases put forward by Salomon *et al.*[11] The Cu(I) from the copper triflate coordinates both double bonds and the OH before the photoannulation takes place, as shown in the proposed transition state **2**. This causes the cyclobutane ring to form on the same side as the OH leading to product **3a**. The structure of product **3a** was confirmed by an X-ray crystallography[12] crystal structure



Scheme 1 *Reagents and conditions*: i) *hν*, CuOTf, benzene; ii) NBS, $BaCO_3$, $CHCl_3$, reflux.

determination. A similar result was obtained with alcohol **1b**, which was converted into product **3b** in 18% yield, the structure **3b** follows by comparison with the NMR spectra of **3a**. The low yield of **3b** may be due to the extra steric hinderance of the quaternary centre in **1b** making cyclisation to **3b** more difficult. Finally, tetracyclic-alcohol **3a** was reacted with NBS according to the procedure by Hannessian and Plessas[13] to produce the tricyclic-bromoester **4** in 72% yield.

The stereospecific nature of the photoannulation process became clear when the *cis*- isomer **5a** was subjected to irradiation in the presence of copper(I) triflate (Scheme 2) to give a single isomer of tetracyclic alcohol **7a** in 86% yield. In this example the same explanation applies as in Scheme 1. Both double bonds and the OH coordinate to the copper (I) as shown in transition state **6**. The cyclobutane ring forms on the same side as the OH group leading to structure **7a**. The structure of this compound was determined by spectroscopic comparison with compound **3a** on which an X-ray crystal structure had been determined. A similar result was obtained using the alcohol **5b** leading to the product **7b** in 89% yield.

Further transformations of tetracyclic alcohol **7a** were carried out to remove the sugar ring from the molecule. Reaction with NBS[13] gave the bromoester **8** in 73% yield followed by a Vasella elimination[14] with zinc in aqueous isopropanol to give a 29% yield of the expected aldehyde **10**. A second product was also obtained *via* a ring expansion reaction of α-hydroxy aldehyde **10**. We reasoned that Zn^{2+} was

† Electronic supplementary information (ESI) available: NMR data and ORTEP diagrams. See http://www.rsc.org/suppdata/ob/b3/b315623k/

‡ *On leave from*: Organic Chemistry Department, Indian Association for the Cultivation of Science, Jadavpur, Calcutta 700 032, India.

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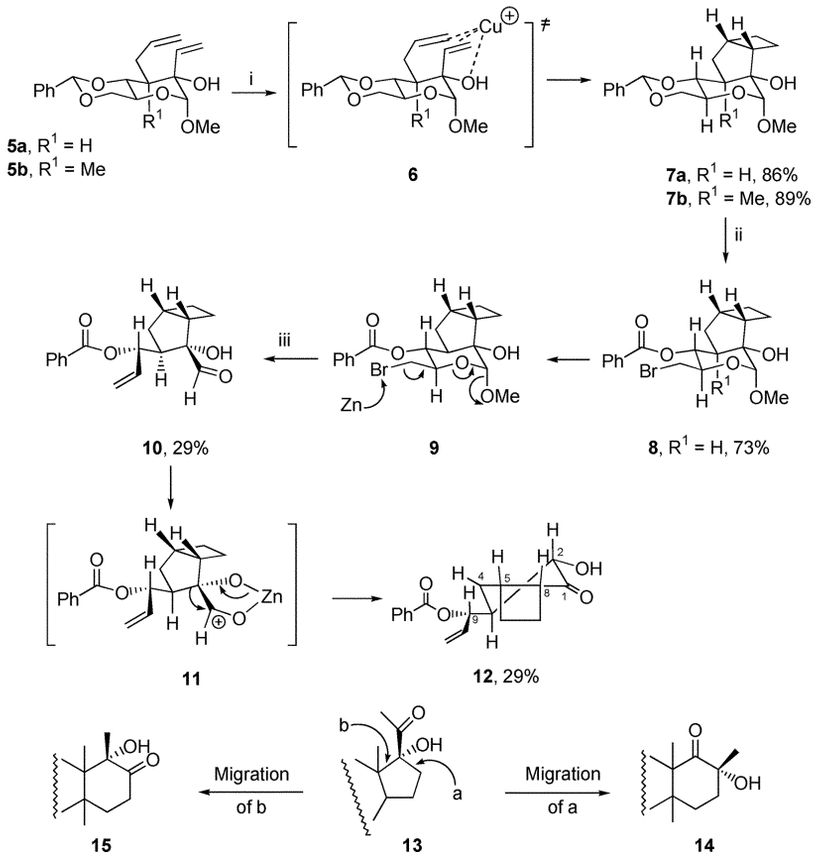


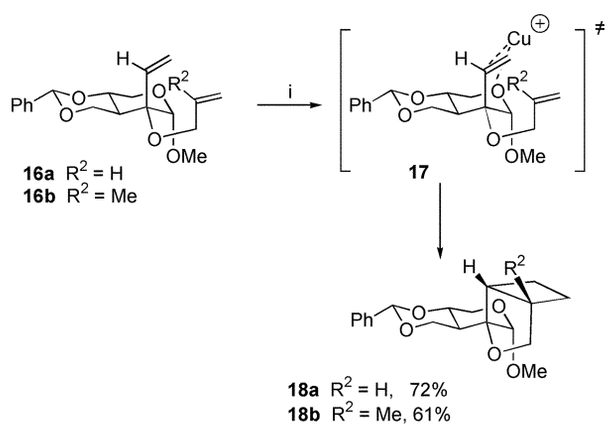
Scheme 2 *Reagents and conditions*: i) *hv*, CuOTf, benzene; ii) NBS, $BaCO_3$, $CHCl_3$, reflux; iii) activated Zn, 2-propanol : H_2O (10 : 1), reflux.

present in the Vasella reaction and that it is likely to coordinate the OH and carbonyl oxygen to give intermediate **11**, migration of the carbon–carbon bond will then take place leading to the hydroxyketone **12**. The configurational assignment for compound **12** was based on the NOESY spectrum in which protons 2, 4-axial, 5, 8, 9 show strong NOE effects.

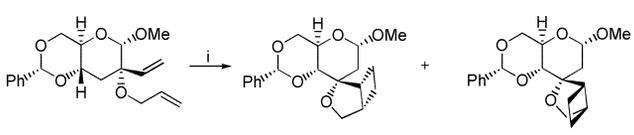
We observed a related reaction to this in our work on the transformation of annulated carbohydrates obtained by ring closing metathesis.[7] To the best of our knowledge the closest analogy to this reaction in the literature is the rearrangement of 17α-hydroxy-2*O*-oxopregnanes **13**, into 17α-hydroxy-17β-methyl-17a-ketones **14**.[15] This reaction occurs in Lewis acid conditions using BF_3, alumina or $Al(^tBuO)_3$ and involves the migration of the less substituted carbon, a in structure **13** leading to **14**. Subsequent work by Gros, Seldes and co-workers[16] has demonstrated that with ZnI_2 a stereospecific rearrangement takes place with exclusive migration of the more substituted carbon, b in structure **13**, leading to the 17aα-hydroxy-17aβ-methyl-17-oxo derivative **15**. In our case the selective migration of the carbon not bearing the cyclobutane in the proposed chelated intermediate **11** occurs.

When structure **16a** was irradiated in the presence of copper(I) triflate another stereospecific cyclobutanation took place *via* the proposed transition state **17**, Scheme 3. In this case the coordination of the copper(I) is with the oxygen of the sugar ring and the 'outside edge' of the vinyl group which prevents its free rotation, suprafacial approach of the second double bond then takes place as shown in **17** to produce a *cis*-fused 5–6 ring system of the spiro-tetracyclic structure **18a** in 72% yield. A similar result was obtained starting from diene **16b** leading to **18b** in 61% yield. Structures **18a** and **18b** were proved by X-ray crystallography.[12] This method provides a useful route to spiro-annulated sugar derivatives in enantiomerically pure form.

Stereoselectivity is lost in Scheme 4 where simultaneous coordination of the Cu(I) and the two double bonds is not possible. Structure **19** gave spiro product **20** in 33% yield and a 30% yield of its isomer **21**.



Scheme 3 *Reagents and conditions*: i) *hv*, CuOTf, benzene.



Scheme 4 *Reagents and conditions*: i) *hv*, CuOTf, benzene.

In conclusion we report full details of our study of carbohydrate annulation of glucose derivatives using copper(I)triflate catalysed photoannulation. The results demonstrate the synthesis of fused and spiro-tetracyclic carbohydrate derivatives in enantiomerically pure form. We have further demonstrated that a combination of Hanessian bromination[13] and Vasella elimination[14] removes the sugar ring from the tetracyclic structure and produces functionalised enantiomerically pure bicyclic structures that could be readily transformed further.

Experimental

All reactions were performed under an atmosphere of nitrogen (unless otherwise stated in the text) and solvent extractions dried with anhydrous magnesium sulfate. Tetrahydrofuran and diethyl ether were freshly distilled from sodium benzophenone ketyl. Benzene was distilled form sodium under nitrogen. Chloroform was distilled from phosphorous pentoxide and stored under nitrogen. Dichloromethane was distilled from calcium hydride. Petroleum ether refers to the 40–60 °C boiling fraction. Flash chromatography was performed on Sorbsil C-60 silica gel (Crosfield Chemicals), 40–60 μM. Melting points are uncorrected. All chemical shifts were taken directly from the spectra, and *J* values are given in hertz. Specific optical rotations are measured in units of 10^{-1} deg cm^2 g^{-1}.

General procedure for the copper(I) triflate catalysed photoannulation reaction

(2*R*,4a*R*,6*S*,6a*S*,6b*S*,8a*S*,9a*S*,9b*S*)-6-Methoxy-2-phenyl-octahydro-1,3,5-trioxacyclobuta-[3,4]cyclo-penta[1,2-*a*]naphthalen-6a-ol (**3a**) $(CF_3SO_3Cu)_2.C_6H_6$ (10 mg, 0.020 mmol, 5 mol%) was added to a solution of methyl (*R*)-4,6-*O*-benzylidene-2-*C*-ethenyl-3-deoxy-3-*C*-propenyl-α-D-glucopyranoside[7] **1a** (140 mg, 0.42 mmol) in dry benzene (10 mL), in a quartz photolysis tube, water-cooled by a cold finger extending into the solution. Irradiation was carried out at 254 nm, using a Rayonet™ photochemical reactor, for 6 h. The reaction mixture was diluted with diethyl ether (40 mL) and washed with aqueous ammonia solution (35%, 2 × 20 mL). The organic layer was washed with water (20 mL), dried and concentrated under reduced pressure to leave a yellow oil. Chromatography on silica gel with petroleum ether–diethyl ether (3 : 1) as the eluent yielded **3a** as a white solid (121 mg, 86%): mp 101–103 °C (ethanol); R_f 0.36, petroleum ether–diethyl ether (1 : 1); $[\alpha]_D^{20}$ + 34.2 (*c* 4.1, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3580w, 3010w, 1090s, 1060s, 1030s; δ_H (400 MHz, $CDCl_3$) 1.58 (1H, dt, *J* 5.7, 12.3), 1.81 (1H, m), 1.97–2.08 (3H, m), 2.15 (1H, br s), 2.15–2.29 (2H, overlapping m), 2.73–2.84 (2H, m), 3.42 (3H, s), 3.70 (1H, ddd, *J* 4.7, 9.2, 10.2), 3.87 (1H, t, *J* 10.2), 3.88 (1H, dd, overlapping, *J* 9.2, 11.0), 4.31 (1H, dd, *J* 4.7, 10.2), 4.60 (1H, s), 5.59 (1H, s), 7.33–7.55 (5H, m); δ_C (100.6 MHz, $CDCl_3$) 17.2 (CH_2), 29.4 (CH_2), 33.6 (CH_2), 37.1 (CH), 42.7 (CH), 48.0 (CH), 55.6 (CH_3), 65.1 (CH), 69.6 (CH_2), 81.4 (CH), 81.9 (C), 102.3 (CH), 102.9 (CH), 126.6 (CH), 128.7 (CH), 129.3 (CH), 138.2 (C); *m*/*z* (FAB) 333 (MH^+, 15%) (found MH^+, 333.1703; $C_{19}H_{25}O_5$ requires 333.1702). Anal. found: C, 68.75; H, 7.32. $C_{19}H_{24}O_5$ requires C, 68.66; H, 7.28%.

(2*R*,4a*R*,6*S*,6a*S*,6b*S*,8a*S*,9a*S*,9b*S*)-6-Methoxy-9a-methyl-2-phenyl-octahydro-1,3,5-trioxacyclobuta-[3,4]cyclopenta[1,2-*a*]-naphthalen-6a-ol (3b). In the same was as for the preparation of **3a** $(CF_3SO_3Cu)_2.C_6H_6$ (22 mg, 0.044 mmol, 13mol%) methyl (*R*)-4,6-*O*-benzylidene-2-*C*-ethenyl-3-deoxy-3-*C*-methyl-3-*C*-propenyl-α-D-mannopyranoside[7] **1b** (118 mg, 0.34 mmol) in dry benzene (10 mL) was irradiated for 22 h. The reaction mixture was worked up as described in the preparation of **3a** above to produce a yellow oil. Chromatography on silica gel with petroleum ether–diethyl ether (3 : 1) as the eluent yielded **3b** as a colourless oil (21 mg, 18%): R_f 0.50, petroleum ether–diethyl ether (1 : 1); $[\alpha]_D^{20}$ −59.2 (*c* 2.1, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3580w, 3010w, 1090s, 1060s, 1030s; δ_H (250 MHz, $CDCl_3$) 0.93 (3H, s), 1.72–1.94 (4H, m), 2.00–2.26 (2H, m), 2.57 (1H, s), 2.57–2.69 (1H, m), 2.80–3.00 (1H, m), 3.50 (3H, s), 3.79 (1H, ddd, *J* 4.1, 9.1, 9.8), 3.87 (1H, t, *J* 9.8), 4.23 (1H, d, *J* 9.1), 4.33 (1H, dd, *J* 4.1, 9.8), 4.71 (1H, s), 5.58 (1H, s), 7.29–7.54 (5H, m); δ_C (100.6 MHz, $CDCl_3$) 15.8 (CH_3), 17.4 (CH_2), 28.4 (CH_2), 37.2 (CH), 42.5 (CH_2), 42.9 (CH), 51.6 (C), 57.2 (CH_3), 66.9 (CH), 70.1 (CH_2), 82.2 (C), 82.7 (CH), 102.1 (CH), 103.3 (CH), 126.7 (CH), 128.6 (CH), 129.3 (CH), 138.4 (C); *m*/*z* (FAB) 347 (MH^+, 12%) (found MH^+, 347.1859; $C_{20}H_{27}O_5$ requires 347.1859).

(2*R*,4a*R*,6*S*,6a*R*,6b*R*,8a*R*,9a*S*,9b*S*)-6-Methoxy-2-phenyl-octahydro-1,3,5-trioxacyclobuta[3,4]-cyclopenta[1,2-*a*]naphthalen-6a-ol (7a). In the same way as for the preparation of **3a** above $(CF_3SO_3Cu)_2.C_6H_6$ (23 mg, 0.046 mmol, 13 mol%), methyl (*R*)-4,6-*O*-benzylidene-2-*C*-ethenyl-3-deoxy-3-*C*-propenyl-α-D-glucopyranoside[7] **5a** (118 mg, 0.36 mmol) in dry benzene (10 mL) was irradiated for 5.5 h. The reaction mixture was worked up as described for **3a** above to leave a yellow oil. Chromatography on silica gel with petroleum ether–diethyl ether (4 : 1) as the eluent yielded **7a** as a colourless oil (101 mg, 86%): R_f 0.52, petroleum ether–diethyl ether (1 : 1); $[\alpha]_D^{20}$ + 4.3 (*c* 1.0, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3580w, 3010w, 1090s, 1060s, 1030s; δ_H (400 MHz, $CDCl_3$) 1.74–1.90 (2H, m), 1.94–2.07 (1H, m), 2.13–2.34 (4H, m), 2.71 (1H, s), 2.75–2.83 (1H, m), 2.83–2.95 (1H, m), 2.96 (1H, dd, overlapping, *J* 9.7, 10.5), 3.48 (3H, s), 3.65 (1H, t, *J* 10.3), 3.80 (1H, ddd, *J* 4.8, 9.7, 10.3), 4.28 (1H, dd, *J* 4.8, 10.3), 4.46 (1H, s), 5.45 (1H, s), 7.32–7.54 (5H); δ_C (62.9 MHz, $CDCl_3$) 16.6 (CH_2), 28.6 (CH_2), 34.1 (CH_2), 36.3 (CH), 44.0 (CH), 52.7 (CH), 55.8 (CH_3), 62.8 (CH), 69.8 (CH_2), 78.9 (CH), 80.9 (C), 100.5 (CH), 102.2 (CH), 126.6 (CH), 128.7 (CH), 129.4 (CH), 138.1 (C); *m*/*z* (FAB) 333 (MH^+, 18%) (found MH^+, 333.1703; $C_{19}H_{25}O_5$ requires 333.1702).

(2*R*,4a*R*,6*S*,6a*R*,6b*R*,8a*R*,9a*S*,9b*S*)-6-Methoxy-9a-methyl-2-phenyl-octahydro-1,3,5-trioxa-cyclobuta[3,4]cyclopenta-[1,2-*a*]naphthalen-6a-ol (7b). In the same way as for **3a** above $(CF_3SO_3Cu)_2.C_6H_6$ (20 mg, 0.040 mmol, 14 mol%) methyl (*R*)-4,6-*O*-benzylidene-2-*C*-ethenyl-3-deoxy-3-*C*-methyl-3-*C*-propenyl-α-D-glucopyranoside[7] **5b** (96 mg, 0.28 mmol) in dry benzene (10 mL), was irradiated for 6 h. The reaction was worked out as described for **3a** above to leave a yellow oil. Chromatography on silica gel with petroleum ether–diethyl ether (3 : 1) as the eluent yielded **7b** as a colourless oil (85 mg, 89%): R_f 0.69, petroleum ether–diethyl ether (1 : 1); $[\alpha]_D^{20}$ + 13.6 (*c* 7.0, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3580w, 3010w, 1090s, 1060s, 1030s; δ_H (250 MHz, $CDCl_3$) 1.20 (3H, s), 1.50 (1H, dd, *J* 6.3, 13.2), 1.60–1.82 (1H, m), 1.86–2.09 (1H, m), 2.12–2.31 (3H, m), 2.70–2.98 (2H, m), 2.75 (1H, broad s), 3.11 (1H, d, *J* 9.4), 3.42 (3H, s), 3.62 (1H, t, *J* 10.1), 3.86 (1H, ddd, *J* 5.0, 9.4, 10.1), 4.27 (1H, dd, *J* 5.0, 10.1), 4.37 (1H, s), 5.44 (1H, s), 7.28–7.55 (5H, m); δ_C (62.9 MHz, $CDCl_3$) 14.3 (CH_3), 16.9 (CH_2), 28.2 (CH_2), 35.5 (CH), 43.4 (CH_2), 45.7 (CH), 53.3 (C), 56.1 (CH_3), 59.3 (CH), 70.0 (CH_2), 80.1 (CH), 80.3 (C), 101.8 (CH), 102.1 (CH), 126.6 (CH), 128.6 (CH), 129.3 (CH), 138.3 (C); *m*/*z* (FAB) 347 (MH^+, 20%) (found MH^+, 347.1858; $C_{20}H_{27}O_5$ requires 347.1859).

General procedure for NBS bromination of benzylidene acetals

(2a*S*,2b*S*,3*S*,5*S*,6*S*,6a*S*,7a*S*)-Benzoic acid 5-bromomethyl-2b-hydroxy-3-methoxy-decahydro-4-oxa-cyclobuta[*a*]inden-6-yl ester (4). Barium carbonate (542 mg, 2.75 mmol) and *N*-bromosuccinimide (135 mg, 0.76 mmol) were added sequentially to a solution of (2*R*,4a*R*,6*S*,6a*S*,6b*S*,8a*S*,9a*S*,9b*S*)-6-methoxy-2-phenyl-octahydro-1,3,5-trioxa-cyclobuta[3,4]-cyclopenta[1,2-*a*]naphthalen-6a-ol, **3a** (228 mg, 0.69 mmol) in dry chloroform (30 mL). The mixture was heated under reflux for 23 h, allowed to cool to room temperature, barium carbonate removed by filtration and the residue washed with dichloromethane (2 × 20 mL). The filtrate was washed with water (2 × 50 mL), dried and concentrated under reduced pressure to leave a yellow oil. Chromatography on silica gel with petroleum ether–diethyl ether (3 : 1) as the eluent yielded **4** as a colourless oil (204 mg, 72%): R_f 0.60, petroleum ether–diethyl ether (1 : 1); ν_{max} ($CHCl_3$)/cm^{-1} 3580w, 1725s, 1275s, 1115s, 1030s; δ_H (300 MHz, $CDCl_3$) 1.63–2.27 (7H, 3-H, m), 2.33 (1H, broad s), 2.63–2.80 (2H, m), 3.41 (3H, s), 3.44 (1H, dd, overlapping, *J* 6.7, 11.0), 3.52 (1H, dd, *J* 2.5, 11.0), 3.83 (1H, ddd, *J* 2.5, 6.7, 10.2), 4.59 (1H, s), 5.29 (1H, t, *J* 10.2), 7.37 (2H, m), 7.49 (1H, m), 7.94 (2H, m); δ_C (75.8 MHz, $CDCl_3$) 17.3

(CH_2), 29.1 (CH_2), 33.1 (CH_2), 34.5 (CH_2), 36.9 (CH), 42.3 (CH), 48.8 (CH), 55.9 (CH_3), 70.6 (CH), 73.7 (CH), 81.0 (C), 102.1 (CH), 128.9 (CH), 130.0 (C), 130.1 (CH), 133.8 (CH), 165.9 (C).

(2a*R*,2b*R*,3*S*,5*S*,6*S*,6a*S*,7a*R*)-Benzoic acid 5-bromomethyl-2b-hydroxy-3-methoxy-decahydro-4-oxa-cyclobuta[*a*]inden-6-yl ester (8). In the same way as for **4** above barium carbonate (552 mg, 2.80 mmol) and *N*-bromosuccinimide (137 mg, 0.77 mmol), (2*R*,4a*R*,6*S*,6a*R*,6b*R*,8a*R*,9a*S*,9b*S*)-6-methoxy-2-phenyl-octahydro-1,3,5-trioxa-cyclobuta[3,4]cyclopenta[1,2-*a*]naphthalen-6a-ol **7a** (232 mg, 0.70 mmol) in dry chloroform (30 ml) were reacted together for 23 h. The reaction was worked up as described for **4** above to leave a yellow oil. Chromatography on silica gel with petroleum ether–diethyl ether (3 : 1) as the eluent yielded **8** as a colourless oil (211 mg, 73%): R_f 0.62, petroleum ether–diethyl ether (1 : 1); $[\alpha]_D^{20}$ + 54.3 (*c* 1.1, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3580w, 1725s, 1275s, 1115s, 1030s; δ_H (250 MHz, $CDCl_3$) 1.61–2.47 (7H, 3-H, m), 2.65 (1H, broad s), 2.76–2.98 (2H, m), 3.35 (1H, dd, *J* 8.2, 11.0), 3.47 (1H, dd, *J* 2.5, 11.0), 3.57 (3H, s), 4.10 (1H, ddd, *J* 2.5, 8.2, 9.8), 4.53 (1H, s), 4.64 (1H, dd, *J* 9.1, 9.8), 7.47 (2H, m), 7.59 (1H, m), 8.04 (2H, m); δ_C (62.9 MHz, $CDCl_3$) 16.6 (CH_2), 27.5 (CH_2), 32.9 (CH_2), 35.3 (CH_2), 35.9 (CH), 43.7 (CH), 52.4 (CH), 56.0 (CH_3), 69.7 (CH), 71.7 (CH), 80.5 (C), 100.2 (CH), 128.9 (CH), 129.8 (C), 130.2 (CH), 133.9 (CH), 166.4 (C); *m*/*z* (EI) 410/412 (M^+, 1%), 105 ($PhCO^+$, 84) (found M^+, 410.0728; $C_{19}H_{23}O_5Br$ requires 410.0729).

(1*S*,1′*R*,3′*S*,4′*R*,5′*R*)-Benzoic acid 1-(4′-formyl-4′-hydroxy-bicyclo[3.2.0]hept-3′-yl)-allyl ester (10) and (1*S*,1′*R*,3′*R*,4′*S*,-6′*R*)-benzoic acid 1-(4′-hydroxy-5′-oxo-bicyclo[4.2.0]oct-3′-yl)-allyl ester (12). Zinc powder (60 g) was activated by washing sequentially with 2 M hydrochloric acid (6 × 30 mL), water (5 × 35 mL), 10% w/v aqueous potassium carbonate solution (30 mL), water (4 × 40 mL), isopropanol (2 × 35 mL) and diethyl ether (3 × 35 mL). The bromo compound (2a*R*,2b*R*,3*S*,-5*S*,6*S*,6a*S*,7a*R*)-benzoic acid 5-bromomethyl-2b-hydroxy-3-methoxy-decahydro-4-oxa-cyclobuta[*a*]inden-6-yl ester **8** (200 mg, 0.49 mmol) was heated under reflux with the activated zinc (4.14 g, 0.063 mol) in isopropanol : water (20:2 mL) for 2.5 h. The zinc was removed by filtration, washed with diethyl ether (3 × 25 mL), the combined organic layers washed with water (2 × 50 mL), saturated sodium chloride solution (50 mL), dried, and evaporated to leave a colourless oil. Chromatography on kieselgel silica with petroleum ether–diethyl ether (4 : 1 to 3 : 1) as the eluent yielded **10** as a colourless oil (42 mg, 29%) and **12** as a colourless oil (43 mg, 29%): **10** R_f 0.49, petroleum ether–diethyl ether (1 : 1); $[\alpha]_D^{20}$ −38.9 (*c* 1.6, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3510w, 1715s, 1610w, 1275s; δ_H (250 MHz, $CDCl_3$) 1.69–1.93 (2H, m), 2.08–2.37 (3H, m), 2.38–2.58 (1H, m), 2.64–2.77 (1H, m), 2.90–3.05 (1H, m), 3.12 (1H, ddd, *J* 3.6, 6.9, 13.4), 3.41 (1H, s), 5.19–5.38 (2H, m), 5.67–5.75 (1H, m), 5.83–6.01 (1H, m), 7.44 (2H, m), 7.58 (1H, m), 7.99 (2H, m), 9.52 (1H, s); δ_C (100.6 MHz, $CDCl_3$) 18.5 (CH_2), 26.2 (CH_2), 31.2 (CH_2), 34.8 (CH), 42.0 (CH), 51.6 (CH), 72.5 (CH), 86.5 (C), 117.5 (CH_2), 128.9 (CH), 129.9 (CH), 130.3 (C), 133.6 (CH), 135.5 (CH), 165.2 (C), 200.3 (CH); *m*/*z* (FAB) 301 (MH^+, 5%), 323 (MNa^+, 7) (found MH^+, 301.1440; $C_{18}H_{21}O_4$ requires 301.1440).

12 R_f 0.46, petroleum ether–diethyl ether (1 : 1); $[\alpha]_D^{20}$ + 5.5 (*c* 1.0, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3490w, 1725s, 1715s, 1610w, 1275s, 1115s; δ_H (400 MHz, $CDCl_3$) 1.72–2.30 (7H, 3-H, m), 2.87–2.97 (1H, m), 3.20–3.31 (1H, m), 3.87 (1H, broad s), 4.05 (1H, dd, *J* 1.3, 11.5), 5.23–5.38 (2H, m), 5.86–5.98 (1H, m), 6.04–6.10 (1H, m), 7.48 (2H, m), 7.60 (1H, m), 8.11 (2H, m); δ_C (100.6 MHz, $CDCl_3$) 23.0 (CH_2), 25.2 (CH_2), 25.6 (CH_2), 36.6 (CH), 45.4 (CH), 45.5 (CH), 73.8 (CH), 76.0 (CH), 117.2 (CH_2), 128.9 (CH), 130.1 (CH), 130.7 (C), 133.5 (CH), 135.1 (CH), 165.7 (C), 215.2 (C); *m*/*z* (FAB) 301 (MH^+, 15%), 323 (MNa^+, 13).

Methyl (*R*)-4,6-*O*-benzylidene-2,3-dideoxy-2(*S*)-spiro(2,7′-3′(*R*), 6′(*R*)-1′-oxa-bicyclo-[3.2.0]-heptane)-α-D-glucopyranoside (18a). In the same way as for **3a** above $(CF_3SO_3Cu)_2.C_6H_6$ (10 mg, 0.020 mmol, 6 mol%) methyl-(*R*)-4,6-*O*-benzylidene-2-*C*-ethenyl-2-*O*-propenyl-3-deoxy-α-D-glucopyranoside[7] **16a** (208 mg, 0.33 mmol) in dry benzene (10 mL) was irradiated for 8 h. The reaction mixture was worked up as described for **3a** to leave a yellow solid. Chromatography on silica gel with petroleum ether–diethyl ether (3 : 1) as the eluent yielded **18a** as a white solid (143 mg, 86%): mp 141.5–143 °C; R_f 0.26, petroleum ether–diethyl ether (1 : 1); $[\alpha]_D^{20}$ + 36.6 (*c* 3.3, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2900m br, 1410m, 1250s, 1080m br; δ_H (250MHz, $CDCl_3$) 1.67 (1H, m), 1.87 (2H, m), 2.01 (2H, m), 2.22 (1H, m), 2.93–3.16 (2H, m), 3.49 (1H, m), 3.49 (3H, s), 3.70 (1H, t, *J* 10.1), 3.80–3.98 (3H, m), 4.24 (1H, dd, *J* 4.4, 10.1), 4.67 (1H, s), 5.50 (1H, s), 7.30–7.55 (5H, m); δ_C (62.9 MHz, $CDCl_3$) 19.6 (CH_2), 24.1 (CH_2), 32.7 (CH_2), 39.1 (CH), 45.6 (CH), 55.4 (CH_3), 64.1 (CH), 69.9 (CH_2), 73.1 (CH_2), 77.4 (CH), 83.8 (C), 99.6 (CH), 102.3 (CH), 126.6 (CH), 128.7 (CH), 129.5 (CH), 137.8 (C); *m*/*z* (FAB) 333 (MH^+, 56), 301 (MH^+ − MeOH, 100); elemental analysis found C 68.46, H 7.22, $C_{19}H_{24}O_5$ requires C 68.66, H 7.30%.

Methyl (*R*)-4,6-*O*-benzylidene-2,3-dideoxy-2(*S*)-spiro(2,7′-3′(*R*), 6′(*R*)-3′-methyl-1′-oxa-bicyclo-[3.2.0]-heptane)-α-D-glucopyranoside (18b). In the same way as for **3a** above $(CF_3SO_3Cu)_2.C_6H_6$ (10 mg, 0.020 mmol, 4 mol%) was added to a solution of methyl(*R*)-4,6-*O*-benzylidene-2-*C*-ethenyl-2-*O*-(2-methylpropenyl)-3-deoxy-α-D-glucopyranoside[7] **16b** (165 mg, 0.47 mmol) in dry benzene (10 ml) was irradiated for 6 h. The reaction was worked up as described for **3a** above to leave a yellow solid. Chromatography on silica gel with petroleum ether–diethyl ether (3 : 1) as the eluent yielded starting material **16b** as a white solid (48 mg, 29%) and **18b** as a white solid (83 mg, 50%): mp 165.5–167 °C; R_f 0.29, petroleum ether–diethyl ether (1 : 1); $[\alpha]_D^{20}$ + 11.2 (*c* 4.9, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2940s br, 1450m, 1395m, 1100s; δ_H (250 MHz, $CDCl_3$) 1.25 (3H, s), 1.71–1.99 (6H, m), 2.54 (1H, m), 3.42 (3H, s), 3.46 (1H, m), 3.51 (1H, d, *J* 9.1), 3.63 (1H, t, *J* 10.2), 3.76 (1H, ddd, overlapping, *J* 4.4, 8.6), 3.79 (1H, d, *J* 9.1), 4.17 (1H, dd, *J*, 4.4, 10.2), 4.58 (1H, s), 5.45 (1H, s), 7.22–7.55 (5H, m); δ_C (62.9MHz, $CDCl_3$) 16.1 (CH_2), 24.9 (CH_3), 30.7 (CH_2), 31.3 (CH_2), 46.8 (C), 51.4 (CH), 55.4 (CH_3), 64.1 (CH), 69.8 (CH_2), 77.9 (CH), 78.7 (CH_2), 84.2 (C), 99.8 (CH), 102.4 (CH), 126.6 (CH), 128.8 (CH), 129.5 (CH), 137.8 (C); *m*/*z* (ES) 369 (MNa^+, 100); elemental analysis found C 69.34, H 7.56, $C_{20}H_{26}O_5$ requires C 69.35, H 7.35%.

Methyl (*R*)-4,6-*O*-benzylidene-2,3-dideoxy-3(*R*)-spiro(3,7′-3′(*R*), 6′(*R*)-1′-oxa-bicyclo-[3.2.0]-heptane)-α-D-glucopyranoside (20) and methyl (*R*)-4,6-*O*-benzylidene-3(*R*)-2,3-dideoxy-spiro(3,7′-3′(*S*), 6′(*S*)-1′-oxa-bicyclo-[3.2.0]-heptane)-α-D-glucopyranoside (21). In the same way as for **3a** above $(CF_3SO_3Cu)_2.C_6H_6$ (10 mg, 0.020 mmol, 5 mol%) was added to a solution of methyl (*R*)-4,6-*O*-benzylidene-2-deoxy-3-*C*-ethenyl-3-*O*-propenyl-α-D-allopyrano-side[6] **19** (147 mg, 0.45 mmol) in dry benzene (10 mL) was irradiated for 6 h. The reaction mixture was worked up as described for **3a** above to leave a yellow solid. Chromatography by chromatatron with chloroform–ethyl acetate (4 : 1) as the eluent yielded **20** as a white solid (48 mg, 33%) and **21** as a white solid (40 mg, 30%): **20**: mp 141–143 °C; R_f 0.36, petroleum ether–diethyl ether (1 : 1); $[\alpha]_D^{20}$ + 87.9 (*c* 4.2, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2950m, 1390m, 1100s, 1050s; δ_H (400MHz, $CDCl_3$) 1.72 (1H, m), 1.85 (1H, dd, *J* 4.6, 14.6), 1.95 (1H, m), 2.03 (1H, m), 2.19 (1H, m), 2.21 (1H, dd, overlapping, *J* 0.6, 14.6), 2.93–2.98 (2H, m), 3.46 (3H, s), 3.47 (1H, m), 3.69 (1H, t, *J* 11.7), 3.97 (1H, d, *J* 8.0), 4.31 (1H, m), 4.31 (2H, d), 4.79 (1H, d, *J* 4.6), 5.45 (1H, s), 7.35–7.58 (5H, m); δ_C (100.6MHz, $CDCl_3$) 18.4 (CH_2), 24.8 (CH_2), 36.8 (CH_2), 40.2 (CH), 46.9 (CH), 56.0 (CH_3), 59.6 ($CH_,$), 69.7 (CH_2), 77.8

(CH_2), 81.3 (C), 86.3 (CH), 98.8 (CH), 102.4 (CH), 126.4 (CH), 128.6 (CH), 129.3 (CH), 138.3 (C); *m/z* (ES) 355 (MNa^+, 100); elemental analysis found C 68.58, H 6.88, $C_{19}H_{24}O_5$ requires C 68.66, H 7.30%.

21: mp 168–169 °C; R_f 0.25, petroleum ether–diethyl ether (1 : 1); $[\alpha]_D^{20}$ + 58.3 (*c* 4.6, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2960m br, 1390m, 1200m, 1100s; δ_H (400MHz, $CDCl_3$) 1.61 (1H, dd, *J* 4.6, 14.8), 1.79 (1H, m), 2.01 (1H, dd, *J* 0.8, 14.8), 1.98–2.12 (2H, m), 2.54–2.66 (2H, m), 2.95 (1H, m), 3.38 (3H, s), 3.71–3.79 (2H, m), 4.01 (1H, dd, *J* 3.4, 9.3), 4.07 (1H, dd, *J* 7.0, 9.3), 4.35 (2H, m), 4.66 (1H, d, *J* 4.6), 5.61 (1H, s), 7.38–7.57 (5H, m); δ_C (100.6MHz, $CDCl_3$) 20.6 (CH_2), 24.1 (CH_2), 38.6 (CH_2), 39.2 (CH), 48.7 (CH), 55.9 (CH_3), 60.6 (CH), 70.2 (CH_2), 73.8 (CH_2), 81.4 (C), 81.5 (CH), 98.8 (CH), 101.9 (CH), 126.5 (CH), 128.5 (CH), 129.1 (CH), 138.3 (C); *m/z* (ES) 355 (MNa^+, 100); elemental analysis found C 68.41, H 7.27, $C_{19}H_{24}O_5$ requires C 68.66, H 7.30%.

Configuration of diastereoisomers was confirmed by 2-D NOESY experiments. **20** showed a significant NOE signal between 7-H and 4-H, whereas **21** showed a significant NOE signal between 7-H and 2ax-H.

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