Synthesis of chiral *cis*- and *trans*-furo[3,2-*c*][2]benzoxocines from D-glucose by regioselective 8-*endo* aryl radical cyclisation

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A simple chiral synthesis of *cis*- and *trans*-furo[3,2-*c*][2]benzoxocines **8a–d** and **9a–d** through a regioselective 8-*endo*-*trig* aryl radical cyclisation of the respective 5,6-dideoxy-D-*xylo*-hex-5-enofuranosides **6a–d** and 5,6-dideoxy-D-*ribo*-hex-5-enofuranosides **7a–d** with tributyltin hydride is described.

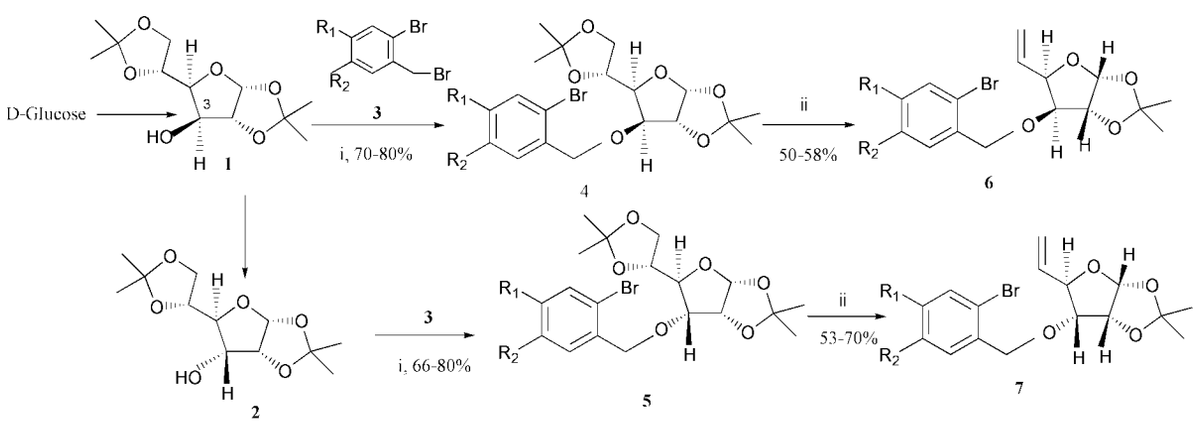
Introduction

The synthesis of conformationally flexible medium-ring ethers, featuring the unique structural core of a large number of linearly condensed cyclic polyether marine neurotoxins,[1] speculated to be responsible for alteration of the gating mechanism or inactivation mechanism of the voltage-sensitive sodium channel,[1c,2] has received considerable attention. In this area, the development of new and general methodology for this class of compounds,[1,3,4] especially in chiral form, continues to dominate. The potential of carbohydrates as a chiral pool for the synthesis of medium-ring ethers was first reported[5] in the preparation of 9-membered chiral ethers from D-glucose through oxy-Cope rearrangement. Soon thereafter, we disclosed[6] a simple and convenient conversion of D-glucose to highly functionalised chiral condensed tricyclic benzoethers incorporating a *cis*-8,5-oxabicyclic system by regioselective 8-*endo*-*trig* aryl radical cyclisation. In 1998, Nicolaou and his group completed a total synthesis of brevetoxin-A,[7] which includes condensed 8- and 9-membered cyclic ethers, from D-glucose and D-mannose using Yamaguchi lactonisation and enol phosphate cross-coupling.[8] Very recently, ring-closing metathesis reaction has been successfully applied to a series of glucose derivatives leading to a variety of 8- and 9-membered condensed cyclic ethers,[9] including a number of intermediates and models towards ciguatoxin.[10] A few other reactions have also been extended for the construction of medium-ring ethers from sugar derivatives.[11] Herein we report details of the synthesis of chiral *cis*- and *trans*-furo[3,2-*c*][2]benzoxocines from D-glucose by aryl radical cyclisation.

Results and discussion

The key olefinic substrates **6a–d** and **7a–d** for the radical cyclisation were prepared from D-glucose through 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranoside **1** and the α-D-allofuranoside **2** (Scheme 1). *O*-Alkylation of **1** and **2** with each of the bromides **3a–d** in the presence of aqueous sodium hydroxide in biphasic medium, using tetrabutylammonium bromide as the phase-transfer catalyst, afforded the respective *O*-2-bromobenzylated glucofuranosides **4a–d** and allofuranosides **5a–d**. Treatment of each of the benzylated products **4a–d** and **5a–d** with 75% aq. acetic acid at 25 °C selectively removed the 5,6-*O*-isopropylidene group, and the resulting diols on didehydroxylation with iodine–triphenylphosphine–imidazole in boiling toluene[12] furnished the desired olefins **6a–d** and **7a–d** in good yields. The spectral data of **6a–d** and **7a–d** are in close agreement with the assigned structures. As expected, the ^{1}H NMR spectra of the C-3 epimeric olefins were very similar except that the H-3 signal of **6a–d** appeared as doublet at around δ 3.96 (J 3 Hz), whereas that of **7a–d** exhibited a double doublet at about δ 3.55 (J 4.2, 9 Hz), in addition to slight differences in the chemical shifts and the coupling pattern of other signals in the two series (Scheme 1).

Radical cyclisation of each of the gluco-series alkenes **6a–d** with Bu_3SnH and a catalytic amount of azoisobutyronitrile (AIBN) in refluxing benzene furnished the respective crystalline tricyclic ethers **8a–d** (Scheme 2) in 50–58% yield as the only isolable products after separation of the tin compounds[13] followed by chromatography. The assigned structures of the products **8a–d**, resulting from 8-*endo*-*trig* aryl radical



a: R_1–R_2–H; **b**: R_1–H, R_2–OMe; **c**: R_1–R_2–OMe; **d**: R_1+R_2–O-CH_2-O

Scheme 1 *Reagents and conditions*: i Bu_4NBr, 50% NaOH, CH_2Cl_2; 25 °C, 12 h. ii 75% AcOH, 25 °C, 12 h; then Ph_3P, I_2, imidazole, PhMe, reflux, 4 h.

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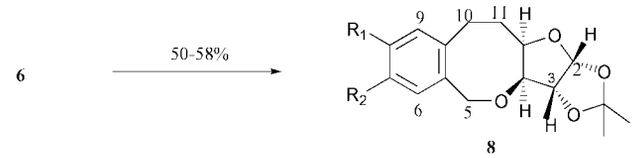
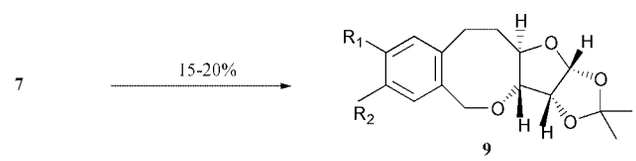


a: R_1–R_2–H; **b**: R_1–H, R_2–OMe; **c**: R_1–R_2–OMe; **d**: $R_1 \cdot R_2$–O-CH_2-O

Scheme 2 *Reagents and conditions*: Bu_3SnH (1.5 equiv.), AIBN, benzene, 300 W lamp, reflux, 4 h.

cyclisation,[14–16]† were based upon spectroscopic data. Unequivocal confirmation of the structure of **8a** was obtained from X-ray crystal-structure determination.[6]

With the successful 8-*endo*-*trig* aryl radical cyclisation in the D-glucose-derived series of the olefins having *cis*-disposition of the bonds forming the ring in the oct-7-enyl radicals, we next focused upon the corresponding D-allose-derived olefins **7a**–**d** where the ring-forming bonds are *trans*-oriented. The radical cyclisation of **7a**–**d**, unlike that of the epimeric olefins, could only be effected under relatively high-dilution conditions by very slow addition of Bu_3SnH in benzene containing a catalytic amount of AIBN to a gently refluxing solution of each of the substrates. Usual work-up and chromatographic purification gave the respective tricyclic ethers **9a**–**d** in only 15–20% yield, along with predominantly the uncyclised debrominated compound (Scheme 3). Repeating the cyclisation in toluene or *ortho*-xylene gave a complex mixture of debrominated products.



a: R_1=R_2=H; **b**: R_1=H, R_2=OMe; **c**: R_1=R_2=OMe; **d**: R_1+R_2=O-CH_2-O

Scheme 3 *Reagents and conditions*: Bu_3SnH (1.1 equiv.) AIBN, benzene, 300 W lamp, reflux, 12 h.

The tricyclic products **9a**–**d** were characterised from spectral and analytical data. The ^{1}H NMR spectral comparisons of each pair of *cis* and *trans* products **8a**–**d** and **9a**–**d** revealed the expected difference between the corresponding ring-junction proton signals. Thus, in the *cis*-fused products **8a**–**d**, H-3a is *trans* to H-3 and *cis* to H-11a, while H-3 is *cis* to H-2. In the ^{1}H NMR spectrum‡ H-2, H-3 and H-3a signals appeared as doublets (in **8a** and **8b**, the H-3 signal was overlapped by one of the benzylic methylene protons), while H-11a exhibited a double triplet. There is no coupling between H-3 and H-3a, indicating that the dihedral angle is ≈90°; $J_{2,3}$ and $J_{3a,11a}$ are around 3.8 Hz (**8b**–**d**) and 2.8 Hz (**8a**–**d**), corresponding to a dihedral angle of ≈60°. In the *trans*-fused products **9a**–**d**,‡ H-3a is *trans* to H-11a but *cis* to H-3. The coupling constants are around 7.9 Hz ($J_{3a,11a}$) and 5.1 Hz ($J_{3,3a}$), corresponding to dihedral angles of ≈160° and ≈40° respectively, suggesting that H-3 is not orthogonal to either of the neighbouring protons. The significantly higher yield of the *cis* products **8a**–**d**§ compared with that of *trans* products **9a**–**d** clearly reflects that the bond-forming carbon atoms in the oct-7-enyl aryl radicals generated from the corresponding olefins **6a**–**d** are in relatively favourable dispositions compared with those in the olefins **7a**–**d**.

† As predicted by MO calculations and experimentally corroborated by Beckwith (ref. 14) and others (refs. 15, 16) 8-*endo* cyclisation is preferred over the 7-*exo* process.

‡ The ^{1}H NMR assignments are based on ^{1}H–^{1}H COSY results.

§ The minimum-energy calculation (using MM^+ force field, Hyperchem Software-Release 6.02 Professional) indicates that **9a** is less stable than the corresponding *cis* product **8a** by 4.58 kcal mol^{-1} (1 cal = 4.184 J).

In conclusion, we have demonstrated the potential of regioselective aryl radical cyclisation from carbohydrate-derived substrates[16] in the synthesis of functionalised chiral benz-annulated cyclic ethers incorporating *cis*- and *trans*-8,5-oxabicyclic systems. Studies are in progress to extend this simple protocol[15,17] to other carbohydrate-derived intermediates, and to analyse the synthetic scope for similar condensed benz-annulated medium-ring chiral ethers or related compounds.

Experimental

Mps were taken on a Thomas–Hoover capillary melting-point apparatus and are uncorrected. NMR spectra of $CDCl_3$ solutions were recorded with JEOL FX-100 or Bruker DPX-300 spectrometers. In all cases, chemical shifts are in δ(ppm) relative to TMS as internal standard, *J*-values are given in Hz, and multiplicity is quoted as follows: s, singlet; d, doublet; t, triplet; q, quartet; dd, double doublet; dt, double triplet; br, broad; m, multiplet, *etc*. Optical rotations are measured at 25 °C with a JASCO P-1020 polarimeter, and $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. A Perkin-Elmer 240C elemental analyser was used to perform C, H analyses. EI-MS was conducted using a JEOL AX-500 mass spectrometer. All reagents were of commercial quality from freshly opened containers and were used without further purification. Organic solvents were dried by standard method and distilled before use. Reaction progress was monitored by thin-layer chromatography (TLC) on pre-coated aluminium-backed plates (Merck Kieselgel $60F_{254}$) and products were visualised by UV light or Liebermann reagent. Column chromatography was carried out using commercial-grade silica gel (60–120 mesh) with petroleum spirit (PS; boiling range 60–80 °C)–ethyl acetate as eluent. Bu_3SnH was purchased from Aldrich. All the solid products were crystallised from ether and petroleum spirit (boiling range 40–60 °C). Ether refers to diethyl ether.

General procedure for the synthesis of 3-*O*-(2-bromobenzyl) compounds 4a–d and 5a–d

1,2:5,6-Diisopropylidene-α-D-glucofuranose **1** was prepared in a single step by an acid-catalysed reaction of D-glucose in anhydrous acetone in 50–55% yield according to the reported procedure.[18] To a magnetically stirred solution of **1** or 1,2:5,6-diisopropylidene-α-D-allofuranose **2**[19] (10 mmol) and the appropriate 2-bromobenzyl bromide **3a**–**d** (12 mmol) in CH_2Cl_2 (10 mL) was added Bu_4NBr (100 mg) followed by aq. NaOH (50%; 10 mL) at 0 °C. Stirring was continued at room temperature until the starting material disappeared (monitored by TLC). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (20 mL × 3). The combined organic layer was washed with water, dried (Na_2SO_4) and evaporated on a rotary evaporator; the residual oil on column chromatography (PS–ethyl acetate) yielded the corresponding 3-*O*-(2-bromobenzyl) derivative.

3-*O*-(2-Bromobenzyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranoside 4a. *Thick oil*; 70.5% yield (eluent PS–ethyl acetate 9 : 1); $[\alpha]_D$ −21.6 (*c* 0.25, $CHCl_3$); δ_H (300 MHz) 1.33 (3H, s, CH_3), 1.35 (3H, s, CH_3), 1.43 (3H, s, CH_3), 1.51 (3H, s, CH_3), 3.99 (1H, dd, *J* 5.9, 8.5, H-3), 4.07–4.18 (3H, m), 4.40 (1H, dd, *J* 6, 13.8, H-4), 4.66 (1H, d, *J* 3.6, H-2), 4.69 (1H, overlapped by H-2 signal, H^a of $ArCH_2$), 4.74–4.78 (1H, d, *J* 12.8, H^b of $ArCH_2$), 5.92 (1H, d, *J* 3.6, H-1), 7.15–7.54 (4H, m, ArH); δ_C (75 MHz) 25.79 (CH_3), 26.67 (CH_3), 27.16 (CH_3), 27.25 (CH_3), 67.86 (CH_2), 72.06 (CH_2), 72.87 (CH), 81.75 (CH), 82.60 (CH), 82.95 (CH), 105.73 (CH), 109.43 (C), 112.27 (C), 123.02 (C), 127.78 (CH), 129.53 (CH), 129.61 (CH), 132.94 (CH), 137.44 (C); MS (EI) *m*/*z* 413, 415 (40%, M^+ − 15 for Br^{79}, Br^{81}) (Found: C, 53.36, H, 5.90. Calc. for $C_{19}H_{25}BrO_6$: C, 53.15; H, 5.87%).

3-*O*-(2-Bromo-5-methoxybenzyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranoside 4b. *Thick oil*; 73% yield (eluent PS–ethyl acetate 19 : 1); $[\alpha]_D$ −24.5 (*c* 0.22, $CHCl_3$); δ_H (100 MHz) 1.33 (3H, s, CH_3) 1.35 (3H, s, CH_3), 1.43 (3H, s, CH_3), 1.51 (3H, s, CH_3), 3.80 (3H, s, OCH_3), 3.88–3.92 (1H, s, H-3), 4.04–4.20 (3H, m), 4.30–4.48 (1H, t, *J* 6, H-4), 4.68 (1H, overlapped by $ArCH_2$ proton signal, H-2), 4.38–4.70 (2H, br s, $ArCH_2$), 5.94 (1H, d, *J* 4, H-1), 6.64–6.84 (1H, dd, *J* 8, 2.5, ArH), 7.10 (1H, d, *J* 2.5, ArH), 7.36–7.52 (1H, d, *J* 4, ArH); δ_C (75 MHz) 25.32 (CH_3), 26.25 (CH_3), 26.78 (CH_3), 26.83 (CH_3), 55.44 (OCH_3), 67.39 (CH_2), 71.42 (CH_2), 72.44 (CH), 81.27 (CH), 82.14 (CH), 82.42 (CH), 105.26 (CH), 109.07 (C), 111.85 (C), 112.54 (C), 114.39 (CH), 114.95 (CH), 133.02 (CH), 137.97 (C), 159.12 (C) (Found: C, 52.52; H, 5.98. Calc. for $C_{20}H_{27}BrO_7$: C, 52.30; H, 5.92%).

3-*O*-(2-Bromo-4,5-dimethoxybenzyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranoside 4c. Thick oil; 80% yield (eluent PS–ethyl acetate 9 : 1); $[\alpha]_D$ −30.5 (*c* 0.65, $CHCl_3$); δ_H (300 MHz) 1.33 (3H, s, CH_3), 1.34 (3H, s, CH_3), 1.42 (3H, s, CH_3), 1.50 (3H, s, CH_3), 3.86 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 4.03–4.18 (4H, m), 4.39 (1H, dd, *J* 6, 13.8, H-4), 4.56–4.62 (1H, d, *J* 12, H^a of $ArCH_2$), 4.63 (1H, d, *J* 3.9, H-2), 4.69–4.73 (1H, d, *J* 12, H^b of $ArCH_2$), 5.91 (1H, d, *J* 3.9, H-1), 6.98 (1H, s, ArH), 7.01 (1H, s, ArH); δ_C (75 MHz) 25.82 (CH_3), 26.68 (CH_3), 27.21 (CH_3), 27.27 (CH_3), 56.54 (OCH_3), 56.63 (OCH_3), 67.74 (CH_2), 71.89 (CH_2), 72.99 (CH), 81.67 (CH), 82.36 (CH), 82.91 (CH), 105.67 (CH), 109.43 (C), 112.25 (C), 112.98 (CH), 113.46 (C), 115.93 (CH), 129.40 (C), 148.98 (C), 149.85 (C); MS (EI) *m*/*z* 488, 490 (50%, M^+ for Br^{79}, Br^{81}) (Found: C, 51.19; H, 5.86. Calc. for $C_{21}H_{29}BrO_8$: C, 51.54; H, 5.97%).

3-*O*-(2-Bromo-4,5-methylenedioxybenzyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranoside 4d. *Thick oil*; 70% yield (eluent PS–ethyl acetate 9 : 1); $[\alpha]_D$ −29.3 (*c* 0.71, $CHCl_3$); δ_H (300 MHz) 1.33 (3H, s, CH_3), 1.37 (3H, s, CH_3), 1.43 (3H, s, CH_3), 1.50 (3H, s, CH_3), 3.99 (1H, dd, *J* 6, 8, H-3), 4.03–4.15 (3H, m), 4.37 (1H, dd, *J* 6, 13.8, H-4), 4.56 (1H, d, *J* 12.6, H^a of $ArCH_2$), 4.64 (1H, d, *J* 3.7, H-2), 4.67 (1H, d, *J* 12.6, H^b of $ArCH_2$), 5.91 (1H, d, *J* 3.6, H-1), 5.96 (2H, s, OCH_2O), 7.03 (1H, s, ArH), 6.99 (1H, s, ArH); δ_C (75 MHz) 25.76 (CH_3), 26.67 (CH_3), 27.16 (CH_3), 27.24 (CH_3), 67.96 (CH_2), 71.83 (CH_2), 72.77 (CH), 81.75 (CH), 82.25 (CH), 82.94 (CH), 102.14 (CH), 105.72 (CH), 109.50 (C), 109.80 (CH), 112.26 (C), 112.97 (CH), 113.51 (C), 130.61 (C), 147.90 (C), 148.26 (C); MS (EI) *m*/*z* 472, 474 (40%, M^+ for Br^{79}, Br^{81}) (Found: C, 50.42; H, 5.29. Calc. for $C_{20}H_{25}BrO_8$: C, 50.75; H, 5.32%).

3-*O*-(2-Bromobenzyl)-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranoside 5a. *White solid*; mp 54 °C; 74% yield (eluent PS–ethyl acetate 6 : 1); $[\alpha]_D$ +99.1 (*c* 1.07, $CHCl_3$); δ_H (300 MHz) 1.36 (3H, s, CH_3), 1.37 (3H, s, CH_3), 1.59 (6H, s, CH_3), 3.93 (1H, dd, *J* 4.5, 8.5, H-3), 4.03 (2H, d, *J* 7.0), 4.16 (1H, dd, *J* 3.4, 8.5, H-4), 4.36 (1H, dt, *J* 3.4, 6.9, H-5), 4.68 (1H, d, *J* 12.8, H^a of $ArCH_2$), 4.71 (1H, t-like, *J* 4.2, overlapped by $ArCH_2$ signal), 4.85 (1H, d, *J* 12.8, H^b of $ArCH_2$), 5.79 (1H, d, *J* 3.8, H-1), 7.16–7.57 (4H, m, ArH); δ_C (75 MHz) 25.18 (CH_3), 26.18 (CH_3), 26.69 (CH_3), 26.80 (CH_3), 65.23 (CH_2), 71.28 (CH_2), 74.87 (CH), 74.97 (CH), 77.85 (CH), 78.26 (CH), 104.03 (CH), 109.64 (C), 113.00 (C), 122.75 (C), 127.45 (CH), 129.17 (CH), 129.65 (CH), 132.49 (CH), 136.99 (C); MS (EI), *m*/*z* 413, 415 (45%, M^+ − 15 for Br^{79}, Br^{81}) (Found: C, 52.96; H, 5.84. Calc. for $C_{19}H_{25}BrO_6$: C, 53.15; H, 5.87%).

3-*O*-(2-Bromo-5-methoxybenzyl)-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranoside 5b. *White solid*; mp 122–123 °C; 80% yield (eluent PS–ethyl acetate 6 : 1); $[\alpha]_D$ +92.1 (*c* 0.38, $CHCl_3$); δ_H (300 MHz) 1.36 (3H, s, CH_3), 1.37 (3H, s, CH_3), 1.38 (3H, s, CH_3), 1.59 (3H, s, CH_3), 3.80 (3H, s, OCH_3), 3.93 (1H, dd, *J* 4.6, 8.6, H-3), 4.01 (2H, d, *J* 6.7), 4.16 (1H, dd, *J* 3.5, 8.5, H-4), 4.36 (1H, dt, *J* 3.4, 6.9, H-5), 4.63–4.67 (1H, d, *J* 13.1, H^a of $ArCH_2$), 4.71 (1H, t, *J* 4.2), 4.78–4.83 (1H, d, *J* 13.1, H^b of $ArCH_2$), 5.80 (1H, d, *J* 3.8, H-1), 6.72 (1H, dd, *J* 3.0, 8.7, ArH), 7.16 (1H, d, *J* 3.0, ArH), 7.41 (1H, d, *J* 8.7, ArH); δ_C (75 MHz) 25.55 (CH_3), 26.61 (CH_3), 27.09 (CH_3), 27.23 (CH_3), 55.82 (OCH_3), 65.70 (CH_2), 71.76 (CH_2), 75.36 (CH), 78.28 (CH), 78.64 (CH), 78.96 (CH), 104.38 (CH), 110.11 (C), 113.06 (C), 113.38 (C), 115.28 (CH), 115.46 (CH), 133.36 (CH), 138.42 (C), 159.57 (C); MS (EI) *m*/*z* 458, 460 (60%, M^+ for Br^{79}, Br^{81}) (Found: C, 52.64; H, 5.91. Calc. for $C_{20}H_{27}BrO_7$: C, 52.30; H, 5.92%).

3-*O*-(2-Bromo-4,5-dimethoxybenzyl)-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranoside 5c. *White solid*; mp 97 °C; 70% yield (eluent PS–ethyl acetate 6 : 1); $[\alpha]_D$ +89.8 (*c* 0.38, $CHCl_3$); δ_H (300 MHz) 1.36 (3H, s, CH_3), 1.38 (3H, s, CH_3), 1.42 (3H, s, CH_3), 1.59 (3H, s, CH_3), 3.86 (3H, s, OCH_3), 3.88 (3H, s, OCH_3), 3.90 (1H, m, overlapped by OCH_3 signal), 4.01–4.03 (2H, m), 4.15 (1H, dd, *J* 3.3, 8.7, H-4), 4.36 (1H, dt, *J* 3.6, 6.9, H-5), 4.64–4.67 (1H, d, *J* 12.3, H^a of $ArCH_2$), 4.65 (1H, t, *J* 4.2), 4.76–4.81 (1H, d, *J* 12.3, H^b of $ArCH_2$), 5.77 (1H, d, *J* 3.6, H-1), 6.99 (1H, s, ArH), 7.10 (1H, s, ArH); δ_C (75 MHz) 25.49 (CH_3), 26.59 (CH_3), 27.07 (CH_3), 27.26 (CH_3), 56.42 (OCH_3), 56.62 (OCH_3), 65.58 (CH_2), 71.68 (CH_2), 75.26 (CH), 78.39 (CH), 78.57 (CH), 78.60 (CH), 104.35 (CH), 110.12 (C), 113.12 (CH), 113.19 (C), 113.32 (C), 115.68 (CH), 129.49 (C), 149.12 (C), 149.68 (C); MS (EI) *m*/*z* 488, 490 (54%, M^+ for Br^{79}, Br^{81}) (Found: C, 51.86; H, 6.01. Calc. for $C_{21}H_{29}BrO_8$: C, 51.54; H, 5.97%).

3-*O*-(2-Bromo-4,5-methylenedioxybenzyl)-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranoside 5d. *Thick oil*; 66% yield (eluent PS–ethyl acetate 9 : 1); $[\alpha]_D$ +123.9 (*c* 0.47, $CHCl_3$); δ_H (300 MHz) 1.37 (3H, s, CH_3), 1.38 (3H, s, CH_3), 1.39 (3H, s, CH_3), 1.59 (3H, s, CH_3), 3.90 (1H, dd, *J* 4.5, 8.4, H-3), 3.99 (2H, d, *J* 6.9), 4.13 (1H, dd, *J* 3.6, 8.4, H-4), 4.34 (1H, dt, *J* 3.6, 6.9, H-5), 4.59 (1H, d, *J* 12.5, H^a of $ArCH_2$), 4.71 (1H, t-like, *J* 4.2, overlapped by $ArCH_2$ signal), 4.73 (1H, d, *J* 12.5, H^b of $ArCH_2$), 5.79 (1H, d, *J* 3.8, H-1), 5.97 (2H, s, OCH_2O), 6.98 (1H, s, ArH), 7.08 (1H, s, ArH); δ_C (75 MHz) 25.57 (CH_3), 26.60 (CH_3), 27.10 (CH_3), 27.22 (CH_3), 65.81 (CH_2), 71.57 (CH_2), 75.47 (CH), 78.26 (CH), 78.66 (CH), 78.75 (CH), 102.11 (CH_2), 104.47 (CH), 110.12 (CH), 110.20 (C), 112.84 (CH), 113.43 (C), 113.63 (C), 130.67 (C), 147.97 (C), 148.33 (C); MS (EI) *m*/*z* 472, 474 (54%, M^+ for Br^{79}, Br^{81}) (Found: C, 50.42; H, 5.29. Calc. for $C_{20}H_{25}BrO_8$: C, 50.75; H, 5.32%).

General procedure for the synthesis of the olefins 6a–d and 7a–d

The appropriate 3-*O*-(2-bromobenzyl)-1,2:5,6-di-*O*-isopropylidene-[α-D-glucofuranoside (**4a**–**d**) and α-D-allofuranoside (**5a**–**d**)] (5 mmol) was stirred overnight with 70% aq. HOAc (v/v) at 25 °C (monitored by TLC till the disappearance of starting material). Removal of HOAc on a rotary evaporator (temp. 40 °C) using dry toluene (50 mL × 3) afforded the intermediate diol as a highly viscous syrup. A solution of the crude diol, imidazole (15 mmol) and Ph_3P (15 mmol) in dry toluene (100 mL) was heated under reflux, while I_2 (13 mmol) was added to the boiling mixture in small portions over a period of 1 h; refluxing was continued for an additional 3 h, until the reaction was completed. The organic layer was decanted off and residue was extracted with toluene (20 mL × 6). The combined organic layer was washed with water, dried (Na_2SO_4) and evaporated under reduced pressure to afford oily material. To remove the unchanged Ph_3P, this was dissolved in dry ether (50 mL) and the mixture was stirred with CH_3I (5 mL) at room temperature for 6 h. Removal of the solvent under vacuum afforded an oily residue. The crude product thus obtained yielded the olefins on column chromatography (PS–ethyl acetate).

5,6-Dideoxy-1,2-*O*-isopropylidene-3-*O*-(2-bromobenzyl)-α-D-*xylo*-hex-5-enofuranoside 6a. *Thick oil*; 55% yield (eluent PS–ethyl acetate 19 : 1); $[a]_D$ −57.9 (*c* 0.39, $CHCl_3$); δ_H (100 MHz) 1.34 (3H, s, CH_3), 1.50 (3H, s, CH_3), 3.96 (1H, d, *J* 3, H-3), 4.80 (4H, m), 5.32 (1H, d, J_{cis} 8, H^a of $=CH_2$), 5.46 (1H, d, J_{trans} 16, H^b of $=CH_2$), 5.86–6.26 (2H, m, overlapped by C*H*=CH_2 signal, H-1), 7.04–7.6 (4H, m, ArH); δ_C (75 MHz) 26.16 (CH_3), 26.71 (CH_3), 71.36 (CH_2), 81.49 (CH), 82.64 (CH), 84.18 (CH), 104.77 (CH), 111.50 (C), 119.15 (CH_2), 122.31 (C), 127.33 (CH), 128.90 (CH), 129.01 (CH), 132.08 (CH), 132.38 (CH), 136.85 (C); MS (EI) *m*/*z* 354, 356 (10%, M^+ for Br^{79}, Br^{81}) (Found: C, 53.77; H, 5.29. Calc. for $C_{16}H_{19}BrO_4$: C, 54.09; H, 5.39%).

5,6-Dideoxy-1,2-*O*-isopropylidene-3-*O*-(2-bromo-5-methoxybenzyl)-α-D-*xylo*-hex-5-enofuranoside 6b. *Thick oil*; 50% yield (eluent PS–ethyl acetate 19 : 1); $[a]_D$ −50.7 (*c* 0.54, $CHCl_3$); δ_H (300 MHz) 1.34 (3H, s, CH_3), 1.53 (3H, s, CH_3), 3.79 (3H, s, OCH_3), 3.96 (1H, d, *J* 2.7, H-3), 4.52–4.57 (1H, d, *J* 13.2, H^a of $ArCH_2$), 4.65–4.70 (3H, m), 5.35 (1H, d, J_{cis} 10.2, H^a of CH_2=), 5.44–5.50 (1H, d, J_{trans} 17.2, H^b of CH_2=), 5.98–6.08 (2H, m, CH_2=C*H* and H-1), 6.72 (1H, dd, *J* 2.7, 8.7, ArH), 7.02 (1H, d, *J* 2.1, ArH), 7.38 (1H, d, *J* 8.7, ArH); δ_C (75 MHz) 26.06 (CH_3), 26.60 (CH_3), 55.25 (OCH_3), 71.06 (CH_2), 81.34 (CH), 82.47 (CH), 84.09 (CH), 104.67 (CH), 111.39 (C), 112.11 (C), 114.11 (CH), 114.61 (CH), 118.96 (CH_2), 132.06 (CH), 132.81 (CH), 137.76 (C), 158.93 (C); MS (EI) *m*/*z* 384, 386 (8%, M^+ for Br^{79}, Br^{81}) (Found: C, 53.35; H, 5.61. Calc. for $C_{17}H_{21}BrO_5$: C, 52.99; H, 5.49%).

5,6-Dideoxy-1,2-*O*-isopropylidene-3-*O*-(2-bromo-4,5-dimethoxybenzyl)-α-D-*xylo*-hex-5-enofuranoside 6c. *Thick oil*; 58% yield (eluent PS–ethyl acetate 9 : 1); $[a]_D$ −47.2 (*c* 0.33, $CHCl_3$); δ_H (300 MHz) 1.34 (3H, s, CH_3), 1.52 (3H, s, CH_3), 3.85 (3H, s, OCH_3), 3.86 (3H, s, OCH_3), 3.92 (1H, d, *J* 3.1, H-3), 4.51–4.55 (1H, d, *J* 12.7, H^a of $ArCH_2$), 4.64–4.68 (3H, m), 5.29–5.33 (1H, dd, *J* 10.6, 1, H^a of $=CH_2$), 5.42–5.48 (1H, dd, *J* 17.2, 1.2, H^b of $=CH_2$), 5.97 (1H, d, *J* 3.6, H-1), 5.97–6.09 (1H, m, CH_2=C*H*), 6.95 (1H, s, ArH), 6.99 (1H, s, ArH); δ_C (75 MHz) 26.27 (CH_3), 26.80 (CH_3), 56.10 (OCH_3), 56.25 (OCH_3), 71.17 (CH_2), 81.52 (CH), 82.79 (CH), 84.02 (CH), 104.89 (CH), 111.64 (C), 112.15 (CH), 112.67 (C), 115.48 (CH), 118.95 (CH_2), 129.03 (C), 132.35 (CH), 148.66 (C), 149.19 (C); MS (EI) *m*/*z* 414, 416 (90%, M^+ for Br^{79}, Br^{81}) (Found: C, 52.42; H, 5.69. Calc. for $C_{18}H_{23}BrO_6$: C, 52.06; H, 5.58%).

5,6-Dideoxy-1,2-*O*-isopropylidene-3-*O*-(2-bromo-4,5-methylenedioxybenzyl)-α-D-*xylo*-hex-5-enofuranoside 6d. *Thick oil*; 50% yield (eluent PS–ethyl acetate 19 : 1); $[a]_D$ −53.3 (*c* 0.49, $CHCl_3$); δ_H (300 MHz) 1.33 (3H, s, CH_3), 1.52 (3H, s, CH_3), 3.91 (1H, d, *J* 3, H-3), 4.47–4.67 (4H, m), 5.31–5.35 (1H, d, J_{cis} 10.6, H^a of CH_2=), 5.42–5.48 (1H, d, J_{trans} 17.32, H^b of CH_2=), 5.97 (2H, s, OCH_2O), 5.98–6.07 (2H, m, CH_2=C*H* and H-1), 6.93 (1H, s, ArH), 6.98 (1H, s, ArH); δ_C (75 MHz) 26.64 (CH_3), 27.18 (CH_3), 71.77 (CH_2), 81.94 (CH), 83.18 (CH), 84.38 (CH), 102.14 (CH_2), 105.25 (CH), 109.58 (CH), 112.01 (C), 112.95 (CH), 113.39 (C), 119.59 (CH_2), 130.57 (C), 132.55 (CH), 147.88 (C), 148.27 (C), MS (EI) *m*/*z* 398, 400 (12.5%, M^+ for Br^{79}, Br^{81}) (Found: C, 50.89; H, 4.62. Calc. for $C_{17}H_{19}BrO_6$: C, 51.14; H, 4.79%).

5,6-Dideoxy-1,2-*O*-isopropylidene-3-*O*-(2-bromobenzyl)-α-D-*ribo*-hex-5-enofuranoside 7a. *Thick oil*; 70% yield (eluent PS–ethyl acetate 9 : 1); $[a]_D$ +62.9 (*c* 0.82, $CHCl_3$); δ_H (300 MHz) 1.37 (3H, s, CH_3), 1.61 (3H, s, CH_3), 3.56 (1H, dd, *J* 4.2, 8.8, H-3), 4.5 (1H, t, *J* 7.7, H-4), 4.68 (1H, t-like, *J* 4.1, overlapped by $ArCH_2$ signal), 4.69 (1H, d, *J* 13.1, H^a of $ArCH_2$), 4.81 (1H, d, *J* 13.0, H^b of $ArCH_2$), 5.25–5.29 (1H, dd, *J* 10.4, 1, H^a of $=CH_2$), 5.42–5.49 (1H, dd, *J* 17.2, 1.2, H^b of $=CH_2$), 5.79 (1H, d, *J* 3.6, H-1), 5.79–5.90 (1H, m, CH_2=C*H*), 7.15–7.54 (4H, m, ArH); δ_C (300 MHz) 26.95 (CH_3), 27.12 (CH_3), 71.87 (CH_2), 77.92 (CH), 79.43 (CH), 83.23 (CH), 104.27 (CH), 113.37 (C), 119.06 (CH_2), 123.02 (CH), 127.81 (CH), 129.53 (CH), 129.75 (CH), 132.88 (CH), 135.19 (CH), 137.43 (C); MS (EI) *m*/*z* 354, 356 (5%, M^+ for Br^{79}, Br^{81}), 339, 341 (100%, M^+ − 15 for Br^{79}, Br^{81}) (Found: C, 53.78; H, 5.19. Calc. for $C_{16}H_{19}BrO_4$: C, 54.09; H, 5.39%).

5,6-Dideoxy-1,2-*O*-isopropylidene-3-*O*-(2-bromo-5-methoxybenzyl)-α-D-*ribo*-hex-5-enofuranoside 7b. *Thick oil*; 69% yield (eluent PS–ethyl acetate 19 : 1); $[a]_D$ +55.2 (*c* 0.25, $CHCl_3$); δ_H (300 MHz) 1.25 (3H, s, CH_3), 1.62 (3H, s, CH_3), 3.57 (1H, dd, *J* 4.3, 8.9, H-3), 3.79 (3H, s, OCH_3), 4.50 (1H, t, *J* 7.7, H-4), 4.63–4.66 (1H, d, *J* 13.8, H^a of $ArCH_2$), 4.68 (1H, t-like, overlapped by $ArCH_2$ signal), 4.74–4.79 (1H, d, *J* 13.8, H^b of $ArCH_2$), 5.26–5.30 (1H, dd, *J* 2.4, 10.4, H^a of $=CH_2$), 5.42–5.50 (1H, dd, *J* 2.5, 17.2, H^b of $=CH_2$), 5.79 (1H, d, *J* 3.8, H-1), 5.83–5.91 (1H, m, CH_2=C*H*), 6.71 (1H, dd, *J* 3.1, 8.7, ArH), 7.11 (1H, d, *J* 3.1, ArH), 7.41 (1H, d, *J* 8.7, ArH); δ_C (75 MHz) 27.22 (CH_3), 27.41 (CH_3), 56.14 (OCH_3), 72.15 (CH_2), 78.15 (CH), 79.74 (CH), 83.54 (CH), 104.54 (CH), 113.25 (C), 113.67 (C), 115.09 (CH), 115.83 (CH), 119.86 (CH_2), 133.71 (CH), 135.47 (CH), 138.68 (C), 159.83 (C); MS (EI) *m*/*z* 384, 386 (27%, M^+ for Br^{79}, Br^{81}) (Found: C, 52.61; H, 5.32. Calc. for $C_{17}H_{21}BrO_5$: C, 52.99; H, 5.49%).

5,6-Dideoxy-1,2-*O*-isopropylidene-3-*O*-(2-bromo-4,5-dimethoxybenzyl)-α-D-*ribo*-hex-5-enofuranoside 7c. *White crystalline solid*; mp 50 °C; 53% yield (eluent PS–ethyl acetate 19 : 1); $[a]_D$ +55.8 (*c* 0.84, $CHCl_3$); δ_H (300 MHz) 1.37 (3H, s, CH_3), 1.62 (3H, s, CH_3), 3.52 (1H, dd, *J* 4.2, 9.0, H-3), 3.87 (6H, s, OCH_3), 4.47 (1H, t, *J* 7.8, H-4), 4.63 (1H, dd, *J* 3.9, 7.8), 4.65–4.69 (1H, d, *J* 12.9, H^a of $ArCH_2$), 4.72–4.76 (1H, d, *J* 12.9, H^b of $ArCH_2$), 5.24–5.28 (1H, d, J_{cis} 10.5, H^a of $=CH_2$), 5.42–5.48 (1H, d, J_{trans} 17.1, H^b of $=CH_2$), 5.77 (1H, d, *J* 3.3, overlapped by C*H*=CH_2 signal), 5.76–5.88 (1H, m, C*H*=CH_2), 6.99 (1H, s, ArH), 7.05 (1H, s, ArH); δ_C (75 MHz) 26.92 (CH_3), 27.14 (CH_3), 56.42 (OCH_3), 56.62 (OCH_3), 71.74 (CH_2), 77.92 (CH), 79.42 (CH), 82.92 (CH), 104.26 (CH), 112.74 (CH), 113.22 (C), 113.33 (C), 115.68 (CH), 119.09 (CH_2), 129.44 (C), 135.27 (CH), 149.07 (C), 149.61 (C); MS (EI) *m*/*z* 414, 416 (50%, M^+ for Br^{79}, Br^{81}) (Found: C, 51.84; H, 5.42. Calc. for $C_{18}H_{23}BrO_6$: C, 52.06; H, 5.58%).

5,6-Dideoxy-1,2-*O*-isopropylidene-3-*O*-(2-bromo-4,5-methylenedioxybenzyl)-α-D-*ribo*-hex-5-enofuranoside 7d. *Thick oil*; 54% yield (eluent PS–ethyl acetate 19 : 1); $[a]_D$ +75.1 (*c* 0.33, $CHCl_3$); δ_H (300 MHz) 1.37 (3H, s, CH_3), 1.61 (3H, s, CH_3), 3.53 (1H, dd, *J* 4.3, 8.8, H-3), 4.47 (1H, t, *J* 8, H-4), 4.60 (1H, d, *J* 12.8, H^a of $ArCH_2$), 4.66 (1H, t-like, overlapped by $ArCH_2$ proton), 4.69 (1H, d, *J* 12.8, H^b of $ArCH_2$), 5.26 (1H, d, J_{cis} 10.4, H^a of $=CH_2$), 5.46 (1H, d, J_{trans} 17.2, H^b of $=CH_2$), 5.77–5.89 (1H, m, overlapped by H-1 signal, C*H*=CH_2), 5.79 (1H, d, *J* 3.6, H-1), 5.97 (2H, s, OCH_2O), 6.98 (1H, s, ArH), 7.01 (1H, s, ArH); δ_C (75 MHz) 26.93 (CH_3), 27.10 (CH_3), 71.72 (CH_2), 77.89 (CH), 79.42 (CH), 82.88 (CH), 102.13 (CH_2), 104.25 (CH), 109.82 (CH), 112.88 (CH), 113.37 (C), 113.57 (C), 119.13 (CH_2), 130.65 (C), 135.17 (CH), 147.93 (C), 148.31 (C); MS (EI) *m*/*z* 398, 400 (25%, M^+ for Br^{79}, Br^{81}) (Found: C, 50.76; H, 4.70. Calc. for $C_{17}H_{19}BrO_6$: C, 51.14; H, 4.79%).

General procedure for the radical cyclisation of the olefins 6a–d

To a gently refluxing solution (300 W sunlamp) of the appropriate olefin **6a**–**d** (1 mmol) and AIBN (10 mg) in dry benzene (100 mL) under nitrogen atmosphere was added a solution of Bu_3SnH (1.5 equiv.) and AIBN (10 mg) in dry benzene (50 mL) slowly over a period of *ca.* 3 h. After complete addition, the mixture was refluxed for an additional 1 h, the solvent was removed under vacuum, and the residue was

taken up in ether (120 mL) and stirred vigorously for 10 h with saturated aq. KF (75 mL). The white precipitate was filtered off, and washed with ether. After separation of the ether layer, the aqueous layer was extracted with ether, and the combined organic layer was dried (Na_2SO_4), and evaporated under vacuum to give a thick oil which on chromatography (PS–ethyl acetate) yielded pure cyclised ethers.

(2*R*,3*R*,3a*S*,11a*R*)-2,3-Isopropylidenedioxy-3,3a,5,10,11,11a-hexahydro-2*H*-furo[3,2-*c*][2]benzoxocine 8a. *White crystalline solid*; 58% yield (eluent PS–ethyl acetate 9 : 1); mp 151–152 °C; $[\alpha]_D$ −20.6 (*c* 0.34, $CHCl_3$); δ_H (100 MHz) 1.31 (3H, s, CH_3), 1.46 (3H, s, CH_3), 2.04–2.28 (2H, m, H_2-11), 2.44–2.68 (1H, m, H^a of H_2-10), 3.18–3.44 (1H, m, H^b of H_2-10), 4.04 (1H, d, *J* 2.8, H-3a), 4.28 (1H, dt, *J* 6.0, 2.8, H-11a), 4.58 (1H, d, *J* 14.0, H^a of $ArCH_2$ signal), 4.62 (1H, overlapped by $ArCH_2$ signal, H-3), 5.08 (1H, *J* 14.0, H^b of $ArCH_2$), 5.90 (1H, d, *J* 3.8, H-2), 7.02–7.34 (4H, m, ArH); δ_C (75 MHz) 26.24 (CH_3), 26.78 (CH_3), 28.64 (CH_2), 31.05 (CH_2), 75.07 (CH_2), 79.04 (CH), 84.46 (CH), 85.49 (CH), 104.01 (CH), 111.23 (C), 126.18 (C), 128.44 (C), 128.89 (C), 130.57 (C), 135.79 (C), 142.67 (C); MS (EI) *m*/*z* 276 (M^+, 27%) (Found: C, 69.89; H, 7.28. Calc. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.29%).

(2*R*,3*R*,3a*S*,11a*R*)-7-Methoxy-2,3-isopropylidenedioxy-3,3a,5,10,11,11a-hexahydro-2*H*-furo[3,2-*c*][2]benzoxocine 8b. *White crystalline solid*; 56% yield (eluent PS–ethyl acetate 9 : 1); mp 106–107 °C; $[\alpha]_D$ +2.6 (*c* 0.23, $CHCl_3$); δ_H (100 MHz) 1.31 (3H, s, CH_3), 1.46 (3H, s, CH_3), 2.09–2.21 (2H, m, H_2-11), 2.45 (1H, m, H^a of H_2-10), 3.17–3.33 (1H, m, H^b of H_2-10), 3.78 (3H, s, OCH_3), 4.02 (1H, d, *J* 2.6, H-3a), 4.22–4.29 (1H, dt, *J* 6.0, 2.8, H-11a), 4.56 (1H, d, *J* 14.0, H^a of $ArCH_2$), 4.62 (1H, d, *J* 3.8 overlapped by $ArCH_2$ signal, H-3), 5.05 (1H, d, *J* 14.0, H^b of $ArCH_2$), 5.89 (1H, d, *J* 3.8, H-2), 6.64 (1H, d, *J* 2.5, ArH), 6.76–6.80 (1H, dd, *J* 8.0, 2.5, ArH), 7.08 (1H, d, *J* 8.0, ArH); δ_C (75 MHz) 26.20 (CH_3), 26.73 (CH_3), 27.77 (CH_2), 31.27 (CH_2), 55.22 (OCH_3), 74.93 (CH_2), 78.87 (CH), 84.18 (CH), 85.41 (CH), 103.91 (CH), 111.21 (C), 113.29 (CH), 114.43 (CH), 131.63 (CH), 134.55 (C), 136.84 (C), 157.80 (C); MS (EI) *m*/*z* 306 (M^+, 30%) (Found: C, 66.91; H, 7.31. Calc. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24%).

(2*R*,3*R*,3a*S*,11a*R*)-7,8-Dimethoxy-2,3-isopropylidenedioxy-3,3a,5,10,11,11a-hexahydro-2*H*-furo[3,2-*c*][2]benzoxocine 8c. *White crystalline solid*; 50% yield (eluent PS–ethyl acetate 9 : 1); mp 85 °C; $[\alpha]_D$ +1.8 (*c* 1.7, $CHCl_3$); δ_H (300 MHz) 1.31 (3H, s, CH_3), 1.46 (3H, s, CH_3), 2.13–2.21 (2H, m, H_2-11), 2.46–2.53 (1H, m, H^a of H_2-10), 3.19–3.26 (1H, m, H^b of H_2-10), 3.84 (3H, s, OCH_3), 3.87 (3H, s, OCH_3), 3.99 (1H, d, *J* 2.7, H-3a), 4.22–4.27 (1H, dt, *J* 6.0, 2.7, H-11a), 4.52 (1H, d, *J* 13.3, H^a of $ArCH_2$), 4.60 (1H, d, *J* 3.8, H-3), 5.04 (1H, d, *J* 13.3, H^b of $ArCH_2$), 5.88 (1H, d, *J* 3.8, H-2), 6.59 (1H, s, ArH), 6.67 (1H, s, ArH); δ_C (75 MHz) 26.65 (CH_3), 27.21 (CH_3), 28.91 (CH_2), 31.65 (CH_2), 56.37 (OCH_3), 56.42 (OCH_3), 74.76 (CH_2), 79.63 (CH), 84.07 (CH), 85.98 (CH), 104.36 (CH), 111.04 (C), 113.12 (CH), 114.37 (CH), 127.89 (C), 135.48 (C), 147.43 (C), 149.07 (C); MS (FAB) *m*/*z* 336 (M^+, 100%), 337 ([M + H]$^+$, 35) (Found: C, 63.89; H, 7.01. Calc. for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19%).

(2*R*,3*R*,3a*S*,11a*R*)-7,8-Methylenedioxy-2,3-isopropylidenedioxy-3,3a,5,10,11,11a-hexahydro-2*H*-furo[3,2-*c*][2]benzoxocine 8d. *White crystalline solid*; 53% yield (eluent PS–ethyl acetate 9 : 1); mp 166 °C; $[\alpha]_D$ −19.5 (*c* 0.24, $CHCl_3$); δ_H (300 MHz) 1.30 (3H, s, CH_3), 1.46 (3H, s, CH_3), 2.15 (2H, m, H_2-11), 2.45 (1H, m, H^a of H_2-10), 3.23–3.14 (1H, m, H^b of H_2-10), 4.00 (1H, d, *J* 2.7, H-3a), 4.25 (1H, dt, *J* 6.2, 2.8, H-11a), 4.47 (1H, d, *J* 13.3, H^a of $ArCH_2$), 4.59 (1H, d, *J* 3.8, H-3), 4.98 (1H, d, *J* 13.3, H^b of $ArCH_2$), 5.58 (1H, d, *J* 3.8, H-2), 5.92 (2H, s, OCH_2O), 6.57 (1H, s, ArH), 6.65 (1H, s, ArH); δ_C (75 MHz) 26.67 (CH_3), 27.22 (CH_3), 29.06 (CH_2), 31.86 (CH_2), 74.82 (CH_2), 79.55 (CH), 84.21 (CH), 85.97 (CH), 101.43 (CH_2), 104.36 (CH), 109.80 (CH), 111.14 (CH), 111.66 (C), 129.18 (C), 137.00 (C), 146.18 (C), 147.89 (C); MS (EI) *m*/*z* 320 (M^+, 55%) (Found: C, 63.40; H, 6.16. Calc. for $C_{17}H_{20}O_6$: C, 63.74; H, 6.29%).

Radical cylisation of the olefins 7a–d

To a gently refluxing solution (300 W sunlamp) of an appropriate olefin **7a–d** (1 mmol) and AIBN (10 mg) in dry benzene (250 mL) under nitrogen atmosphere was added a solution of Bu_3SnH (1.1 mmol) and AIBN (10 mg) in dry benzene (150 mL) slowly over a period of 12 hours. The reaction mixture, on work-up as described for **8a–d**, gave a thick oily product which, on chromatography (PS–ethyl acetate), yielded the desired cyclised product.

(2*R*,3*R*,3a*R*,11a*R*)-2,3-Isopropylidenedioxy-3,3a,5,10,11,11a-hexahydro-2*H*-furo[3,2-*c*][2]benzoxocine 9a. *White crystalline solid*; 15% yield (eluent PS–ethyl acetate 7 : 1); mp 125 °C; $[\alpha]_D$ +1.8 (*c* 0.27, $CHCl_3$); δ_H (300 MHz) 1.34 (3H, s, CH_3), 1.39–1.53 (1H, m, H^a of H_2-11), 1.56 (3H, s, CH_3), 2.43–2.48 (1H, m, H^b of H_2-11), 2.84–3.01 (2H, m, H_2-10), 3.57 (1H, dd, *J* 5.2, 7.9, H-3a), 4.15–4.21 (1H, m, H-11a), 4.57 (1H, t, *J* 4.1, H-3), 4.74–4.78 (1H, d, *J* 12.4, H^a of $ArCH_2$), 4.87–4.92 (1H, d, *J* 12.4, H^b of $ArCH_2$), 5.65 (1H, d, *J* 3.2, H-2), 7.18–7.30 (4H, m, ArH); δ_C (75 MHz) 27.06 (CH_3), 27.45 (CH_3), 28.80 (CH_2), 35.27 (CH_2), 70.30 (CH_2), 79.49 (CH), 80.17 (CH), 81.53 (CH), 103.71 (CH), 113.30 (C), 127.0 (CH), 129.82 (CH), 130.13 (CH), 131.56 (CH), 134.61 (C), 142.16 (C); MS (FAB) *m*/*z* 277 ([M + H]$^+$, 22%) (Found: C, 69.25; H, 7.22. Calc. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.29%).

(2*R*,3*R*,3a*R*,11a*R*)-7-Methoxy-2,3-isopropylidenedioxy-3,3a,5,10,11,11a-hexahydro-2*H*-furo[3,2-*c*][2]benzoxocine 9b. *White crystalline solid*; 18% yield (eluent PS–ethyl acetate 7 : 1); mp 89 °C; $[\alpha]_D$ −29.2 (*c* 0.1, $CHCl_3$); δ_H (300 MHz) 1.34 (3H, s, CH_3), 1.34–1.44 (1H, m, H^a of H_2-11), 1.55 (3H, s, CH_3), 2.39–2.44 (1H, m, H^b of H_2-11), 2.82–2.90 (2H, m, H_2-10), 3.57 (1H, dd, *J* 5.1, 8.3, H-3a), 3.80 (3H, s, OCH_3), 4.14–4.22 (1H, m, H-11a), 4.57 (1H, dd, *J* 3.8, 4.8, H-3), 4.71 (1H, d, *J* 12.6, H^a of $ArCH_2$), 4.85 (1H, d, *J* 12.5, H^b of $ArCH_2$), 5.64 (1H, d, *J* 3.7, H-2), 6.82–7.12 (3H, m, ArH); δ_C (75 MHz) 26.69 (CH_3), 27.09 (CH_3), 27.60 (CH_2), 35.22 (CH_2), 55.32 (OCH_3), 70.13 (CH_2), 77.23 (CH), 79.12 (CH), 79.87 (CH), 81.15 (CH), 103.35 (CH), 112.94 (C), 115.01 (CH), 116.09 (CH), 130.50 (CH), 133.80 (C), 158.60 (C); MS (FAB) 306 (M^+, 90%) (Found: C, 66.44; H, 7.21. Calc. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24%).

(2*R*,3*R*,3a*R*,11a*R*)-7,8-Dimethoxy-2,3-isopropylidenedioxy-3,3a,5,10,11,11a-hexahydro-2*H*-furo[3,2-*c*][2]benzoxocine 9c. *White crystalline solid*; 20% yield (eluent PS–ethyl acetate 7 : 1); mp 143 °C; $[\alpha]_D$ −20.2 (*c* 0.21, $CHCl_3$); δ_H (300 MHz) 1.34 (3H, s, CH_3), 1.38–1.52 (1H, m, H^a of H_2-11), 1.57 (3H, s, CH_3), 2.41–2.43 (1H, m, H^b of H_2-11), 2.80–2.90 (2H, m, H_2-10), 3.55 (1H, dd, *J* 5.1, 8.1, H-3a), 3.87 (3H, s, OCH_3), 3.89 (3H, s, OCH_3), 4.15–4.18 (1H, m, H-11a), 4.57 (1H, t, *J* 4.3, H-3), 4.69 (1H, d, *J* 12.5, H^a of $ArCH_2$), 4.80 (1H, d, *J* 12.5, H^b of $ArCH_2$), 5.56 (1H, d, *J* 3.5, H-2), 6.68 (1H, s, ArH), 6.80 (1H, s, ArH); δ_C (75 MHz) 26.72 (CH_3), 27.11 (CH_3), 28.16 (CH_2), 35.18 (CH_2), 55.97 (OCH_3), 55.98 (OCH_3), 69.56 (CH_2), 79.10 (CH), 80.08 (CH), 81.39 (CH), 103.38 (CH), 112.35 (CH), 112.92 (C), 114.18 (CH), 126.24 (C), 134.29 (C), 148.00 (C), 149.00 (C); MS (FAB) *m*/*z* 337 ([M + H]$^+$, 35%), 336 (M^+, 100) (Found: C, 64.00; H, 6.96. Calc. for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19%).

(2*R*,3*R*,3a*R*,11a*R*)-7,8-Methylenedioxy-2,3-isopropylidenedioxy-3,3a,5,10,11,11a-hexahydro-2*H*-furo[3,2-*c*][2]benzoxocine 9d. *White crystalline solid*; 15% yield (eluent PS–ethyl acetate

7 : 1); mp 105 °C; $[a]_D$ −24.1 (*c* 0.14, $CHCl_3$); δ_H (300 MHz) 1.33 (3H, s, CH_3), 1.36–1.44 (1H, m, H^a of H_2-11), 1.56 (3H, s, CH_3), 2.37–2.45 (1H, m, H^b of H_2-10), 2.78–2.87 (2H, m, H_2-10), 3.55 (1H, dd, *J* 5.2, 8.2, H-3a), 4.13–4.21 (1H, m, H-11a), 4.56 (1H, t, *J* 4.3, H-3), 4.64 (1H, d, *J* 12.5, H^a of $ArCH_2$), 4.75 (1H, d, *J* 12.5, H^b of $ArCH_2$), 5.65 (1H, d, *J* 3.5, H-2), 5.94 (2H, s, OCH_2O), 6.67 (1H, s, ArH), 6.77 (1H, s, ArH); δ_C (75 MHz) 27.09 (CH_3), 27.48 (CH_3), 28.82 (CH_2), 35.52 (CH_2), 69.69 (CH_2), 79.38 (CH), 80.48 (CH), 81.78 (CH), 101.47 (CH_2), 103.68 (CH), 109.82 (CH), 111.41 (CH), 113.29 (C), 127.67 (C), 136.06 (C), 146.93 (C), 148.66 (C); MS (FAB) *m*/*z* 320 (M^+, 100%) (Found: C, 63.88; H, 6.10. Calc. for $C_{17}H_{20}O_6$: C 63.74; H, 6.29%).

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