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ScienceDirect
Tetrahedron
Tetrahedron 62 (2006) 12003–12010

Sequential Baylis–Hillman reaction and radical cyclization of furanose derivatives: expeditious approach to enantiopure benzo-fused nine-membered oxacycles

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Received 29 June 2006; revised 4 September 2006; accepted 21 September 2006
Available online 27 October 2006

Abstract—A regioselective 9-*endo-trig* aryl radical cyclization of D-glucose derived diastereomeric Baylis–Hillman reaction products with Bu_3SnH led to highly functionalized tricyclic benzannulated ethers incorporating *cis*- and *trans*-9,5 bicyclic systems in good yields. Degradation of one of the products afforded an enantiopure multifunctionalized benzoxonine derivative.

1. Introduction

Benzo-fused cyclic molecules are often referred to as 'privileged structures' owing to their ubiquitous appearance in natural products as well as modern pharmaceuticals.[1] Recently, benzannulated medium-ring heterocycles and related bicyclic analogues have been reported[2] to be useful as CCR-5 antagonists and as anti-HIV agents. The abundance of annulated oxonine rings in biologically important compounds[3] continues to ensure that they are important synthetic targets. This has prompted the use of a large number of methods for their synthesis.[4] Compared to benzoxepines or benzoxocines, synthetic routes to benzoxonine rings are not reported. We had earlier reported successful preparation of the benzannulated seven- and eight-membered oxacycles through radical cyclization on unsubstituted olefins (Fig. 1).[5,6] Unfortunately, this method could not be extended to the synthesis of nine-membered ring system despite repeated attempts with variations in reagents or conditions.

We envisaged that the presence of an electron withdrawing group conjugated to the olefinic bond might help the ring closure by 1,4 addition, leading to the formation of the desired ring system.[7] Starting from our carbohydrate derived chirons **1a–c** and **1d**, suitably designed substrates **2a–e**, **3a–e**, **2f**, and **3f** for the cyclization could be accessible by application of the Baylis–Hillman reaction.

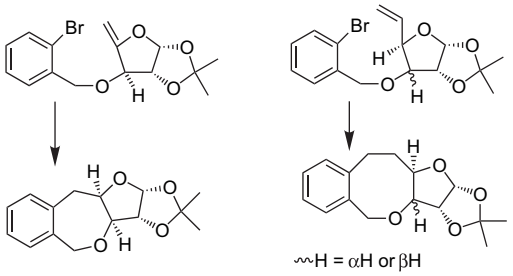

Figure 1. Syntheses of seven- and eight-membered ring ethers.

In this paper we report a sequential Baylis–Hillman reaction and intramolecular radical cyclization[8] to the synthesis of sugar annulated benzoxonine derivatives. Cleavage of the sugar ring of one of these tricyclic derivatives provides multifunctionalized enantiopure benzoxonine.

2. Results and discussion

Initially, *O*-2-bromobenzylated-1,2:5,6-di-*O*-isopropylidene glucofuranoside **1a**,[5] its analogues **1b–c**,[5] and the 3-*O*-epimeric sugar derivative **1d**[5,9] were converted to the noraldehydes through selective deketalization and sodium periodate oxidation. Subsequent Baylis–Hillman reactions of the crude aldehydes were carried out with suitable acrylates

Keywords: Benzoxonine; Free radical reaction; Baylis–Hillman reaction; Carbohydrate.
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0040–4020/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2006.09.080

and acrylonitriles (3 equiv) in the presence of 100 mol % of DABCO in dioxane–water (7:3).[10] The reactions afforded mixtures of the adducts **2a–f** and **3a–f** in approximately 70–80% yield (Table 1) along with small amounts of the unreacted aldehydes (Scheme 1). Subsequently, the isomeric mixtures of **2a–d** and **2f** with **3a–d** and **3f** were separated by flash chromatography. The relative stereochemistries of **2a–d**, **2f**, **3a–d**, and **3f** are based upon comparison of the observed chemical shifts and *J* values with those reported for the corresponding *O*-methyl analogues by Krishna et al.[11]

Radical cyclization of each of the diastereoisomeric alkenes **2a–d** and **3a–d** in refluxing benzene with Bu_3SnH (1.5 equiv) and AIBN (5 mol %) followed by separation of the tin compounds,[12] acetylation, and chromatography furnished (Scheme 2) the respective tricyclic ethers **4a–d** and **5a–d** as the only isolable products (Table 2). Similar treatment of the diastereomeric mixture of **2e+3e** furnished **4e** and **5e**, which could be resolved chromatographically.

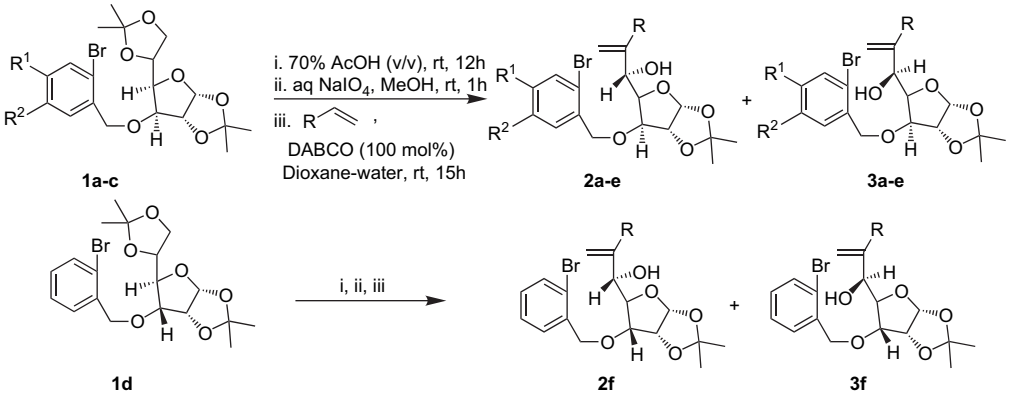
Table 1. Preparation of diastereomeric alkenes **2a–f** and **3a–f**

Entry	Substrate	R	R^1	R^2	Products (yield %)
1	**1a**	$-CO_2Me$	H	H	**2a** (31), **3a** (46)
2	**1b**	$-CO_2Me$	–OMe	–OMe	**2b** (34), **3b** (46)
3	**1c**	$-CO_2Me$	$-OCH_2O-$	—	**2c** (31), **3c** (45)
4	**1a**	$-CO_2Et$	H	H	**2d** (32), **3d** (43)
5	**1a**	–CN	H	H	**2e+3e** (76)[a]
6	**1d**	$-CO_2Me$	H	H	**2f** (18), **3f** (60)

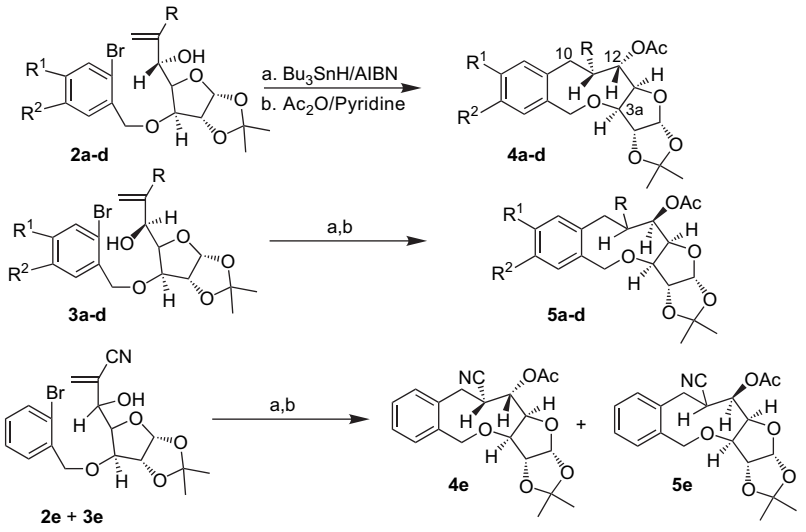
[a] Attempts to separate the diastereomeric mixture of **2e** and **3e** were unsuccessful. We therefore used the mixture for the next step.

The stereochemistry of the oxonine derivatives **4a–e** could not be established by ^1H NMR spectroscopy due to their poorly resolved spectra. However, the structure of **4a**[13] was determined by X-ray diffraction study (Fig. 2), which clearly established a cis-orientation of the acetoxy and carbomethoxy groups at the C_{11}–C_{12} bond. The gross structures of **5a–e** were ascertained by ^1H NMR spectroscopy as well as by adequate ^{13}C NMR, ^1H–^1H COSY, and mass spectral analyses.

We next focused our attention on the corresponding D-allose derived olefins **2f** and **3f** where the ring forming bonds are trans-oriented. The radical cyclization of **2f** and **3f** could indeed be effected under similar condition as described above. Usual work up and chromatographic purification gave the respective tricyclic ethers **6** and **7** in 47% and 52% yields (Scheme 3).



Scheme 1. Baylis–Hillman reaction of sugar derived aldehydes with activated olefins.



Scheme 2. Radical cyclization of alkenes.

Table 2. Syntheses of tricyclic benzannulated ethers **4a–e** and **5a–e**

Entry	Substrate	Product	Yield (%)
1	**2a**	**4a**	64
2	**2b**	**4b**	57
3	**2c**	**4c**	58
4	**2d**	**4d**	53
5	**3a**	**5a**	71
6	**3b**	**5b**	67
7	**3c**	**5c**	63
8	**3d**	**5d**	67
9	**2e+3e**	**4e**,[a] **5e**[a]	42, 37

[a] The isomeric mixture of **4e** and **5e** was separated by flash chromatography.

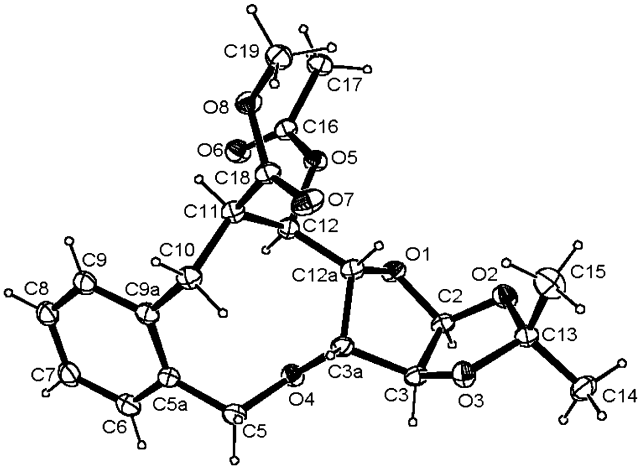
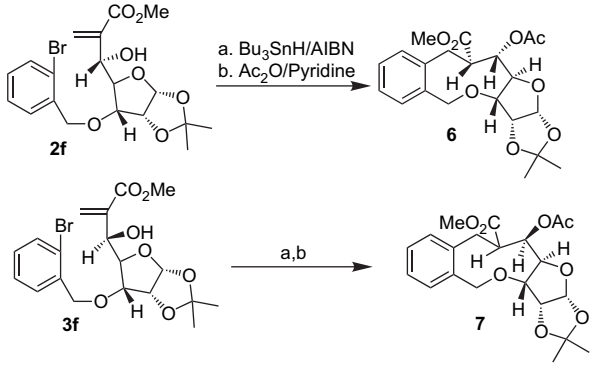
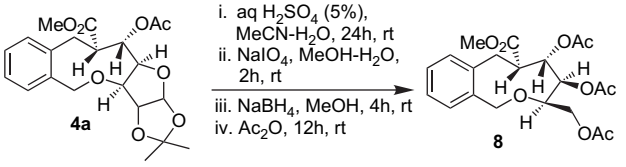


Figure 2. ORTEP diagram of **4a**.



Scheme 3. Radical cyclization of alkenes **2f** and **3f**.

The assigned structures of **6** and **7** were based upon spectroscopic data. These studies showed that the cyclization preferred the 9-*endo-trig* pathway in agreement with the general trend observed in the radical cyclization of medium and large rings, where *endo* cyclization modes are favored,[14] and with other experimental results on ring closures.[6] The feasibility of synthesizing benzoxonine derivatives from the annulated sugar derivatives could also be realized. Thus, **4a** was converted (Scheme 4) into the multifunctionalized benzoxonine **8** (overall yield 22%) through a sequence of reactions involving removal of the 1,2-*O*-isopropylidene group with 5% H_2SO_4 (v/v) in CH_3CN–H_2O (3:1), $NaIO_4$ cleavage of the resulting diol, $NaBH_4$ reduction of the generated carbonyl group and acetylation.



Scheme 4. Conversion of **4a** to the benzoxonine derivative **8**.

3. Conclusion

In summary, we have developed a straightforward and an efficient synthetic route to benzannulate nine-membered oxacycles using sequential Baylis–Hillman reaction and radical cyclization on appropriate furanose derivatives. The reaction worked on a variety of D-glucose derived substrates and could be extended to other sugar derived products. The findings open up the possibility of obtaining enantiopure multifunctionalized benzoxonine derivatives starting from an appropriate sugar derivatives.

4. Experimental

4.1. General

^1H and ^{13}C NMR spectra were recorded in a Bruker AM 300L or ADVANCE 600 MHz spectrometer using $CDCl_3$ as solvent and TMS as an internal standard. Mass spectra were obtained using either JEOL AX-500 or Micromass Q-Tofmicro™ spectrometers. IR spectra were obtained from JASCO FT/IR Model 410. Elemental analyses were carried out with a C,H,N analyzer. Specific rotations were measured at 589 nm on a JASCO P-1020 polarimeter. TLC was performed on pre-coated plates (0.25 mm, silica gel 60 F_{254}). Column chromatography and flash chromatography were carried out using commercial-grade silica gel (60–120 mesh or 230–400 mesh). PS and EA are abbreviated for petroleum spirit (60–80 °C) and ethyl acetate, respectively.

4.2. General procedure for the syntheses of compounds 1a–d[5]

To a magnetically stirred solution of 1,2:5,6-di-*O*-isopropylidene glucofuranoside (1 mmol) and the appropriate 2-bromobenzyl bromide (1.2 mmol) in CH_2Cl_2 (20 mL) was added Bu_4NBr (50 mg) followed by aqueous NaOH (50%, 20 mL) at 0 °C. The reaction mixture was stirred at room temperature for 12 h and extracted with CH_2Cl_2 (4×25 mL). The combined organic layers were washed with H_2O (3×25 mL), dried (Na_2SO_4), and evaporated to afford a syrup, which on column chromatography over silica gel yielded the corresponding bromobenzyl derivatives.

4.2.1. (3a*R*,5*R*,6*S*,6a*R*)-6-(2-Bromo-benzyloxy)-5-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-tetrahydro-furo[2,3-*d*][1,3]dioxole (1a). Thick oil (300 mg, 70%); $[\alpha]_D^{27}$ −21.6 (*c* 0.25, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.32 (s, 3H), 1.35 (s, 3H), 1.42 (s, 3H), 1.50 (s, 3H), 4.00 (dd, *J* 5.8, 8.4 Hz, 1H), 4.07–4.18 (m, 3H), 4.39 (dd, *J* 13.6, 6.0 Hz, 1H), 4.65–4.69 (d-like, 2H), 4.76 (d, *J* 12.8 Hz, 1H), 5.92 (d, *J* 3.6 Hz, 1H), 7.15–7.54 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.7, 26.6, 27.1, 27.2, 67.8, 70.0, 72.8,

81.7, 82.6, 82.9, 105.7, 109.4, 112.2, 123.0, 127.7, 129.5, 129.6, 132.9, 137.4; IR (Neat) ν_{max} 2985, 1450, 1376 cm^{-1}; Anal. Calcd for $C_{19}H_{25}BrO_6$: C, 53.16; H, 5.87. Found: C, 53.00; H, 5.75; ESIMS: *m/z* 451, 453 (MNa^+ for Br^{79}, Br^{81}).

4.2.2. (3a*R*,5*R*,6*S*,6a*R*)-6-(2-Bromo-4,5-dimethoxy-benzyloxy)-5-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-tetrahydro-furo[2,3-*d*][1,3]dioxole (1b). Thick oil (366 mg, 75%); $[\alpha]_D^{27}$ −30.5 (*c* 0.65, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.32 (s, 3H), 1.34 (s, 3H), 1.42 (s, 3H), 1.50 (s, 3H), 3.86 (s, 3H), 3.87 (s, 3H), 4.03–4.18 (m, 4H), 4.39 (dd, *J* 13.6, 5.9 Hz, 1H), 4.60 (d, *J* 12.1 Hz, 1H), 4.65 (d, *J* 3.7 Hz, 1H), 4.71 (d, *J* 12.1 Hz, 1H), 5.90 (d, *J* 3.7 Hz, 1H), 6.98 (s, 1H), 7.01 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.8, 26.6, 2×27.2, 56.5, 56.6, 67.7, 71.9, 73.0, 81.6, 82.3, 82.9, 105.6, 109.4, 112.2, 112.9, 113.4, 115.9, 129.4, 148.9, 149.6; IR (Neat) ν_{max} 2946, 1509, 1269 cm^{-1}; Anal. Calcd for $C_{21}H_{29}BrO_8$: C, 51.54; H, 5.97. Found: C, 51.40; H, 5.85; ESIMS: *m/z* 511, 513 (MNa^+ for Br^{79}, Br^{81}).

4.2.3. (3a*R*,5*R*,6*S*,6a*R*)-5-Bromo-6-[5-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-tetrahydro-furo[2,3-*d*][1,3]dioxole-6-yloxymethyl]-benzo[1,3]dioxole (1c). Thick oil (330 mg, 70%); $[\alpha]_D^{27}$ −29.3 (*c* 0.71, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.33 (s, 3H), 1.37 (s, 3H), 1.43 (s, 3H), 1.50 (s, 3H), 3.99 (dd, *J* 6, 8 Hz, 1H), 4.03–4.15 (m, 3H), 4.37 (dd, *J* 6, 13.8 Hz), 4.56 (d, *J* 12.6 Hz, 1H), 4.64 (d, *J* 3.7 Hz, 1H), 4.67 (d, *J* 12.6 Hz, 1H), 5.91 (d, *J* 3.6 Hz, 1H), 5.96 (s, 2H), 6.99 (s, 1H), 7.03 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.8, 26.7, 27.2, 68.0, 71.8, 72.8, 81.8, 82.3, 82.9, 102.1, 105.7, 109.5, 109.8, 112.3, 113.0, 113.5, 130.6, 147.9, 148.3; IR (Neat) ν_{max} 2983, 2925, 1728 cm^{-1}; Anal. Calcd for $C_{20}H_{25}BrO_8$: C, 50.75; H, 5.32. Found: C, 50.42; H, 5.29; MS (EI): *m/z* 472, 474 (40%, M^+ for Br^{79}, Br^{81}).

4.2.4. (3a*R*,5*R*,6*R*,6a*R*)-6-(2-Bromo-benzyloxy)-5-(2,2-dimethyl-[1,3]dioxolan-4-yl)-2,2-dimethyl-tetrahydro-furo[2,3-*d*][1,3]dioxole (1d). White solid (317 mg, 74%); mp 54 °C; $[\alpha]_D^{27}$ +99.1 (*c* 1.07, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 3H), 1.37 (s, 3H), 1.59 (s, 6H), 3.93 (dd, *J* 4.5, 8.5 Hz, 1H), 4.03 (d, *J* 7.0 Hz, 2H), 4.16 (dd, *J* 3.4, 8.5 Hz, 1H), 4.36 (dt, *J* 3.4, 6.9 Hz, 1H), 4.68 (d, *J* 12.8 Hz, 1H), 4.71 (t-like, 1H) 4.85 (d, *J* 12.8 Hz, 1H), 5.79 (d, *J* 3.8 Hz, 1H), 7.16–7.57 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.2, 26.2, 26.7, 26.8, 65.2, 71.3, 74.9, 75.0, 77.9, 78.3, 104.0, 109.6, 113.0, 122.7, 127.5, 129.2, 129.7, 132.5, 137.0; IR (Neat) ν_{max} 2979, 1439, 1374 cm^{-1}; Anal. Calcd for $C_{19}H_{25}BrO_6$: C, 53.15; H, 5.87. Found: C, 52.96; H, 5.84; MS (EI): *m/z* 413, 415 (45%, M^+-15 for Br^{79}, Br^{81}).

4.3. General procedure for the syntheses of olefins 2a–f and 3a–f

The appropriate bromobenzyl derivative **1a–d** (1 mmol) was stirred overnight with 70% aqueous HOAc (v/v, 50 mL) at room temperature (monitored by TLC till disappearance of starting material). Removal of HOAc on a rotary evaporator under reduced pressure (temp 40 °C) using dry toluene (4×25 mL) afforded the intermediate diol as viscous syrup. A solution of the intermediate diol in the minimum volume of methanol was cooled to 0 °C and treated with aqueous $NaIO_4$ (1.2 mmol, dissolved in 20 mL of water) dropwise with stirring (45 min). The reaction mixture was evaporated under reduced pressure and the residual syrup was extracted with $CHCl_3$ (4×25 mL). The combined organic layers were washed with water (3×25 mL), dried (Na_2SO_4), and evaporated to furnish the crude aldehyde.[5] To a solution of this crude aldehyde in dioxane–water [(7:3), 10 mL], DABCO (100 mol %) and methylacrylate (3 mmol) [or ethylacrylate (3 mmol) or acrylonitrile (3 mmol)] were added and stirred for 15 h at room temperature. After the completion of reaction (TLC), the mixture was extracted with ethyl acetate (3×15 mL). The extract was washed with brine (25 mL), dried (Na_2SO_4), and concentrated under reduced pressure to afford a residue, which was purified by flash chromatography on silica gel (230–400 mesh) using 30–40% ethyl acetate in petroleum ether (60°–80 °C) to furnish corresponding Baylis–Hillman adducts **2a–f** and **3a–f**.

4.3.1. 2-{(*R*)-[(3a*R*,5*R*,6*S*,6a*R*)-6-(2-Bromo-benzyloxy)-2,2-dimethyl-tetrahydro-furo[2,3-*d*][1,3]dioxol-5-yl]-hydroxy-methyl}-acrylic acid methyl ester (2a). Colorless liquid (137 mg, 31%); $[\alpha]_D^{27}$ −10.8 (*c* 3.70 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.33 (s, 3H), 1.48 (s, 3H), 3.52 (d, *J* 3.1 Hz, 1H), 3.73 (s, 3H), 4.14 (d, *J* 3.6 Hz, 1H), 4.50 (t, *J* 3.5 Hz, 1H), 4.57 (d, *J* 12.0 Hz, 1H), 4.71 (d, *J* 3.7 Hz, 1H), 4.78 (d, *J* 12.0 Hz, 1H), 4.92 (s, 1H), 6.02 (d, *J* 3.7 Hz, 1H), 6.06 (s, 1H), 6.38 (s, 1H), 7.19 (t-like, 1H), 7.32 (t-like, 1H), 7.41 (d-like, 1H), 7.58 (d-like, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.3, 26.8, 51.8, 68.7, 71.5, 80.1, 82.0, 84.2, 104.9, 112.0, 123.0, 127.6, 127.8, 129.5, 129.7, 132.7, 135.8, 138.3, 166.4; IR (Neat) ν_{max} 3497, 2985, 2936, 1713, 1631 cm^{-1}; Anal. Calcd for $C_{19}H_{23}BrO_7$: C, 51.48; H, 5.23. Found: C, 51.43; H, 5.19; ESIMS: *m/z* 465, 467 (MNa^+).

4.3.2. 2-{(*R*)-[(3a*R*,5*R*,6*S*,6a*R*)-6-(2-Bromo-4,5-dimethoxy-benzyloxy)-2,2-dimethyl-tetrahydro-furo[2,3-*d*][1,3]dioxol-5-yl]-hydroxy-methyl}-acrylic acid methyl ester (2b). Colorless liquid (170 mg, 34%); $[\alpha]_D^{27}$ −31.8 (*c* 0.53 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.33 (s, 3H), 1.47 (s, 3H), 3.56 (s, 1H), 3.73 (s, 3H), 3.87 (s, 3H), 3.88 (s, 3H), 4.13 (d, *J* 3.5 Hz, 1H), 4.48 (m, 1H), 4.51 (d, *J* 11.7 Hz, 1H), 4.70 (s, 1H), 4.72 (d, *J* 11.7 Hz, 1H), 4.91 (s, 1H), 6.02 (d, *J* 3.6 Hz, 1H), 6.08 (s, 1H), 6.39 (s, 1H), 6.91 (s, 1H), 7.02 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.3, 26.7, 51.7, 56.0, 56.1, 68.4, 71.4, 79.9, 82.0, 84.0, 104.8, 111.9, 112.5, 113.5, 115.4, 127.6, 127.7, 138.3, 148.4, 149.4, 166.3; IR (Neat) ν_{max} 3502, 2988, 2944, 2887, 1725, 1607 cm^{-1}; Anal. Calcd for $C_{21}H_{27}BrO_9$: C, 50.11; H, 5.41. Found: C, 49.89; H, 5.39; ESIMS: *m/z* 525, 527 (MNa^+).

4.3.3. 2-{(*R*)-[(3a*R*,5*R*,6*S*,6a*R*)-6-(6-Bromo-benzo[1,3]-dioxol-5-ylmethoxy)-2,2-dimethyl-tetrahydro-furo[2,3-*d*][1,3]dioxol-5-yl]-hydroxy-methyl}-acrylic acid methyl ester (2c). Colorless liquid (150 mg, 31%); $[\alpha]_D^{27}$ −17.7 (*c* 0.92 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 1.34 (s, 3H), 1.48 (s, 3H), 3.75 (s, 3H), 4.10 (d, *J* 3.3 Hz, 1H), 4.13 (m, 2H), 4.49 (m, 2H), 4.67 (m, 2H), 5.99 (m, 3H), 6.07 (s, 1H), 6.39 (s, 1H), 6.88 (s, 1H), 7.02 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 26.3, 26.7, 51.7, 68.6, 71.4, 80.0,

81.7, 83.8, 101.9, 105.1, 109.6, 111.8, 112.7, 113.9, 127.8, 128.9, 138.3, 147.4, 148.3,166.3; IR (Neat) ν_{max} 3501, 2987, 2934, 1722, 1628 cm^{-1}; Anal. Calcd for $C_{20}H_{23}BrO_9$: C, 49.30; H, 4.76. Found: C, 49.41; H, 4.73; ESIMS: *m/z* 509, 511 (MNa^+).

4.3.4. 2-{(*R*)-[(3a*R*,5*R*,6*S*,6a*R*)-6-(2-Bromo-benzyloxy)-2,2-dimethyl-tetrahydro-furo[2,3-*d*][1,3]dioxol-5-yl]-hydroxy-methyl}-acrylic acid ethyl ester (2d). Colorless liquid (145.9 mg, 32%); $[\alpha]_D^{27}$ −16.2 (*c* 5.35 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.34 (m, 6H), 1.48 (s, 3H), 4.13 (d, *J* 3.6 Hz, 1H), 4.19 (q, *J* 7.1 Hz, 2H), 4.51–4.80 (m, 5H), 4.91 (s, 1H), 6.02 (m, 2H), 6.38 (s, 1H), 7.12–7.58 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.5, 26.8, 27.3, 61.2, 69.2, 71.9, 80.7, 82.5, 84.6, 105.4, 112.4, 123.4, 127.9, 128.0, 130.0, 130.1, 133.2, 136.4, 139.1, 166.4; IR (Neat) ν_{max} 3507, 2985, 2935, 1713, 1631 cm^{-1}; Anal. Calcd for $C_{20}H_{25}BrO_7$: C, 52.53; H, 5.51. Found: C, 52.59; H, 5.43; ESIMS: *m/z* 479, 481 (MNa^+).

4.3.5. 2-{(*R*)-[(3a*R*,5*R*,6*R*,6a*R*)-6-(2-Bromo-benzyloxy)-2,2-dimethyl-tetrahydro-furo[2,3-*d*][1,3]dioxol-5-yl]-hydroxy-methyl}-acrylic acid methyl ester (2f). Colorless liquid (79.6 mg, 18%); $[\alpha]_D^{27}$ +64.5 (*c* 1.63 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 3H), 1.56 (s, 3H), 2.80 (d, *J* 7.2 Hz, 1H), 3.65 (s, 3H), 3.99 (dd, *J* 4.2, 8.7 Hz, 1H), 4.20 (dd, *J* 3.2, 8.7 Hz, 1H), 4.58–4.81 (m, 4H), 5.80 (d, *J* 3.4 Hz, 1H), 5.99 (s, 1H), 6.36 (s, 1H), 7.12–7.53 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 26.6, 26.9, 51.8, 69.4, 71.2, 76.9, 78.7, 80.7, 104.4, 113.3, 122.2, 126.9, 127.4, 129.0, 132.3, 136.9, 139.1, 166.6; IR (Neat) ν_{max} 3452, 2985, 2936, 1720, 1631 cm^{-1}; Anal. Calcd for $C_{19}H_{23}BrO_7$: C, 51.48; H, 5.23. Found: C, 51.37; H, 5.26; ESIMS: *m/z* 465, 467 (MNa^+).

4.3.6. 2-{(*S*)-[(3a*R*,5*R*,6*S*,6a*R*)-6-(2-Bromo-benzyloxy)-2,2-dimethyl-tetrahydro-furo[2,3-*d*][1,3]dioxol-5-yl]-hydroxy-methyl}-acrylic acid methyl ester (3a). Colorless liquid (203 mg, 46%); $[\alpha]_D^{27}$ −28.2 (*c* 2.25 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 3H), 1.49 (s, 3H), 3.79 (s, 3H), 4.17 (d, *J* 2.7 Hz, 1H), 4.42 (m, 1H), 4.56–4.80 (m, 5H), 5.92 (s, 1H), 5.96 (d, *J* 3.6 Hz, 1H), 6.34 (s, 1H), 7.18 (d-like, 1H), 7.32 (m, 1H), 7.47 (d-like, 1H), 7.56 (d-like, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.3, 26.8, 51.9, 69.5, 71.7, 80.2, 81.9, 82.5, 105.1, 111.9, 122.9, 127.6, 128.0, 129.5, 129.6, 132.6, 136.5, 139.0, 166.8; IR (Neat) ν_{max} 3489, 2987, 2941, 1724, 1630 cm^{-1}; Anal. Calcd for $C_{19}H_{23}BrO_7$: C, 51.48; H, 5.23. Found: C, 51.40; H, 5.16; ESIMS: *m/z* 465, 467 (MNa^+).

4.3.7. 2-{(*S*)-[(3a*R*,5*R*,6*S*,6a*R*)-6-(2-Bromo-4,5-dimethoxy-benzyloxy)-2,2-dimethyltetrahydro-furo[2,3-*d*][1,3]dioxol-5-yl]-hydroxy-methyl}-acrylic acid methyl ester (3b). Colorless liquid (230 mg, 46%); $[\alpha]_D^{27}$ −26.5 (*c* 1.1 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.33 (s, 3H), 1.48 (s, 3H), 3.51 (d, *J* 8.7 Hz, 1H), 3.78 (s, 3H), 3.87 (s, 3H), 3.88 (s, 3H), 4.15 (d, *J* 2.8 Hz, 1H), 4.41 (dd, *J* 2.8, 7.8 Hz, 1H), 4.57 (d, *J* 12.0 Hz, 1H), 4.69 (d, *J* 3.6 Hz, 1H), 4.74 (d, *J* 12.0 Hz, 1H), 4.80 (d, *J* 7.8 Hz, 1H), 5.92 (s, 1H), 5.95 (d, *J* 3.6 Hz, 1H), 6.35 (s, 1H), 7.00 (s, 1H), 7.02 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.2, 26.7, 51.8, 56.0, 56.1, 69.5, 71.5, 80.2, 81.8, 82.3, 105.1, 111.8, 112.6, 113.2, 115.3, 127.8, 128.3, 138.9, 148.4, 149.2, 166.8; IR (Neat) ν_{max} 3502, 2987, 2944, 2889, 1725, 1608 cm^{-1}; Anal. Calcd for $C_{21}H_{27}BrO_9$: C, 50.11; H, 5.41. Found: C, 50.19; H, 5.46; ESIMS: *m/z* 525, 527 (MNa^+).

4.3.8. 2-{(*S*)-[(3a*R*,5*R*,6*S*,6a*R*)-6-(6-Bromo-benzo[1,3]-dioxol-5-ylmethoxy)-2,2-dimethyl-tetrahydro-furo[2,3-*d*][1,3]dioxol-5-yl]-hydroxy-methyl}-acrylic acid methyl ester (3c). Colorless liquid (218 mg, 45%); $[\alpha]_D^{27}$ −30.4 (*c* 0.81 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 3H), 1.48 (s, 3H), 3.79 (s, 3H), 4.13 (d, *J* 3.0 Hz, 1H), 4.40 (dd, *J* 3.0, 7.8 Hz, 1H), 4.54 (d, *J* 12.0 Hz, 1H), 4.67 (m, 2H), 4.76 (d, *J* 7.8 Hz, 1H), 4.94 (m, 2H), 5.99 (s, 2H), 6.36 (s, 1H), 6.97 (s, 1H), 7.01 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 26.4, 26.9, 52.0, 69.7, 71.7, 80.2, 82.0, 82.3, 101.9, 105.2, 109.8, 111.9, 112.8, 113.8, 128.2, 129.6, 138.8, 147.5, 148.2, 166.9; IR (Neat) ν_{max} 3495, 2987, 2934, 1716, 1630 cm^{-1}; Anal. Calcd for $C_{20}H_{23}BrO_9$: C, 49.30; H, 4.76. Found: C, 49.32; H, 4.71; ESIMS: *m/z* 509, 511 (MNa^+).

4.3.9. 2-{(*S*)-[(3a*R*,5*R*,6*S*,6a*R*)-6-(2-Bromo-benzyloxy)-2,2-dimethyl-tetrahydro-furo[2,3-*d*][1,3]dioxol-5-yl]-hydroxy-methyl}-acrylic acid ethyl ester (3d). Colorless liquid (196 mg, 43%); $[\alpha]_D^{27}$ −45.8 (*c* 0.65 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.32 (m, 6H), 1.48 (s, 3H), 3.55 (d, *J* 7.8 Hz, 1H), 4.17 (d, *J* 2.9 Hz, 1H), 4.24 (q, *J* 7.1 Hz, 2H), 4.42 (dd, *J* 3.0, 7.7 Hz, 1H), 4.67 (m, 2H), 4.78 (d, *J* 12.1 Hz, 1H), 5.91 (s, 1H), 5.95 (d, *J* 3.6 Hz, 1H), 6.34 (s, 1H), 7.18 (t-like, 1H), 7.33 (d, *J* 7.3 Hz, 1H), 7.47 (d, *J* 7.3 Hz, 1H), 7.56 (d, *J* 7.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.0, 26.3, 26.8, 60.9, 69.5, 71.6, 80.2, 81.9, 82.4, 105.1, 111.8, 122.9, 127.5, 127.6, 129.4, 129.5, 132.6, 136.4, 139.1, 166.4; IR (Neat) ν_{max} 3494, 2986, 2936, 1714, 1629 cm^{-1}; Anal. Calcd for $C_{20}H_{25}BrO_7$: C, 52.53; H, 5.51. Found: C, 52.42; H, 5.48; ESIMS: *m/z* 479, 481 (MNa^+).

4.3.10. 2-{(*S*)-[(3a*R*,5*R*,6*R*,6a*R*)-6-(2-Bromo-benzyloxy)-2,2-dimethyl-tetrahydro-furo[2,3-*d*][1,3]dioxol-5-yl]-hydroxy-methyl}-acrylic acid methyl ester (3f). Colorless liquid (265 mg, 60%); $[\alpha]_D^{27}$ +81.2 (*c* 1.07 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 3H), 1.58 (s, 3H), 2.94 (br s, 1H), 3.68 (s, 3H), 3.83 (dd, *J* 4.5, 8.4 Hz, 1H), 4.46 (m, 2H), 4.66 (m, 2H), 4.84 (s, 1H), 5.80 (d, *J* 3.4 Hz, 1H), 5.96 (s, 1H), 6.26 (s, 1H), 7.13 (t-like, 1H), 7.30 (t-like, 1H), 7.43 (d-like, 1H), 7.50 (d-like, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.7, 26.9, 51.6, 68.8, 70.6, 76.9, 77.8, 80.3, 104.4, 113.2, 122.0, 125.7, 127.1, 128.8, 129.2, 132.1, 136.9, 137.5, 165.9; IR (Neat) ν_{max} 3440, 2991, 2950, 1727, 1631 cm^{-1}; Anal. Calcd for $C_{19}H_{23}BrO_7$: C, 51.48; H, 5.23. Found: C, 51.32; H, 5.22; ESIMS: *m/z* 465, 467 (MNa^+).

4.4. General procedure for radical cyclization of the olefins 2a–d, 2f, 3a–d, 3f, and 2e+3e

To a gently refluxing (400 W lamp) solution of the olefins **2a–d**, **2f**, **3a–d**, **3f** or **2e+3e** (1 mmol) and AIBN (2.5 mol %) in dry benzene (120 mL) under N_2 atmosphere was added a solution of Bu_3SnH (1.5 mmol) and AIBN (2.5 mol %) in dry benzene (150 mL) slowly over a period of 3 h. After complete addition the mixture was heated at reflux for another 3 h. The solvent was removed under

vacuum and the residue was dissolved in diethyl ether (100 mL) and stirred vigorously for 10 h with a saturated solution of aqueous KF (75 mL). The white precipitate was filtered off and washed with diethyl ether. After separation of ether layer, the aqueous layer was extracted with diethyl ether (6×25 mL), the combined organic layers were washed with water (3×30 mL), dried (Na_2SO_4), and evaporated under reduced pressure to give a thick oil. This was purified by flash chromatography on silica gel using 30–40% ethyl acetate in petroleum ether (60°–80 °C) to furnish **4a–e**, **5a–e**, **6**, and **7**.

4.4.1. Compound 4a. White crystalline solid (260 mg, 64%); mp 191 °C; $[\alpha]_D^{27}$ +28.4 (*c* 0.62 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 3H), 1.50 (s, 3H), 2.04 (s, 3H), 2.92 (br s, 1H), 3.06 (br s, 1H), 3.25 (br s, 1H), 3.74 (s, 3H), 4.30 (br s, 1H), 4.45 (br s, 1H), 4.62 (m, 2H), 4.88 (d, *J* 12.6 Hz, 1H), 5.12 (br s, 1H), 5.85 (s, 1H), 7.14–7.27 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0, 26.3, 26.7, 31.6, 48.4, 51.9, 78.9, 84.6, 104.0, 111.7, 126.9, 128.9, 129.4, 130.6, 136.8, 137.5, 169.7, 173.7; IR (KBr) ν_{max} 2987, 2932, 1739 cm^{-1}; Anal. Calcd for $C_{21}H_{26}O_8$: C, 62.06; H, 6.45. Found: C, 62.13; H, 6.43; ESIMS: *m*/*z* 429 (MNa^+).

4.4.2. Compound 4b. White crystalline solid (266 mg, 57%); mp 154 °C; $[\alpha]_D^{27}$ +21.9 (*c* 2.19 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 3H), 1.51 (s, 3H), 2.04 (s, 3H), 2.91 (br s, 1H), 2.98 (br s, 1H), 2.26 (br s, 1H), 3.75 (s, 3H), 3.85 (s, 3H), 3.87 (s, 3H), 4.30 (br s, 1H), 4.52 (m, 2H), 4.62 (d, *J* 3.6 Hz, 1H), 4.81 (d, *J* 12.6 Hz, 1H), 5.08 (br s, 1H), 5.85 (d, *J* 3.6 Hz, 1H), 6.60 (s, 1H), 6.76 (s, 1H); ^{13}C NMR (75 MHz) δ 21.0, 26.7, 27.2, 32.0, 49.0, 52.3, 56.3, 56.4, 70.3, 71.7, 79.3, 85.3, 104.4, 112.1, 113.2, 113.9, 129.7, 147.8, 149.5, 170.1, 173.4; IR (KBr) ν_{max} 2937, 1742, 1720 cm^{-1}; Anal. Calcd for $C_{23}H_{30}O_{10}$: C, 59.22; H, 6.48. Found: C, 58.98; H, 6.41; ESIMS: *m*/*z* 489 (MNa^+).

4.4.3. Compound 4c. Foamy solid (261 mg, 58%); $[\alpha]_D^{27}$ +16.9 (*c* 1.25 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 3H), 1.50 (s, 3H), 2.04 (s, 3H), 2.89 (br s, 2H), 3.19 (br s, 1H), 3.75 (s, 3H), 4.28 (br s, 1H), 4.37 (d, *J* 12.6 Hz, 2H), 4.61 (d, *J* 3.3 Hz, 1H), 4.76 (d, *J* 12.1 Hz, 1H), 5.11 (br s, 1H), 5.85 (s, 1H), 5.94 (d, *J* 1.9 Hz, 2H), 6.64 (s, 1H), 6.75 (s, 1H); ^{13}C NMR (150 MHz) δ 21.1, 26.3, 26.8, 31.5, 48.4, 51.9, 71.5, 73.1, 83.5, 101.2, 109.7, 111.8, 128.0, 146.2, 148.0, 169.8, 173.2; IR (Neat) ν_{max} 2987, 2937, 2924, 1742 cm^{-1}; Anal. Calcd for $C_{22}H_{26}O_{10}$: C, 58.66; H, 5.82. Found: C, 58.61; H, 5.87; ESIMS: *m*/*z* 473 (MNa^+).

4.4.4. Compound 4d. Colorless liquid (223 mg, 53%); $[\alpha]_D^{27}$ +18.1 (*c* 1.00 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (m, 6H), 1.50 (s, 3H), 2.03 (s, 3H), 2.95 (m, 1H), 3.05 (m, 1H), 3.24 (m, 1H), 4.12–4.32 (m, 3H), 4.46 (m, 1H), 4.62 (m, 2H), 4.87 (d, *J* 12.5 Hz, 1H), 5.09 (br s, 1H), 5.86 (d, *J* 3.3 Hz, 1H), 7.14–7.29 (m, 4H); ^{13}C NMR (150 MHz) δ 14.2, 21.1, 26.3, 26.8, 31.7, 48.7, 61.0, 77.1, 103.8, 111.8, 127.0, 129.0, 129.5, 137.6, 169.9; IR (Neat) ν_{max} 2984, 2947, 1728 cm^{-1}; Anal. Calcd for $C_{22}H_{28}O_8$: C, 62.85; H, 6.71. Found: C, 62.77; H, 6.74; ESIMS: *m*/*z* 443 (MNa^+).

4.4.5. Compound 4e. Foamy solid (157 mg, 42%); $[\alpha]_D^{27}$ −2.5 (*c* 0.31 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 3H), 1.48 (s, 3H), 2.11 (s, 3H), 3.02 (t, *J* 12.7, 1H), 3.29 (dd, *J* 2.3, 14.1 Hz, 1H), 3.44 (d, *J* 11.4 Hz, 1H), 4.09 (s, 1H), 4.46 (dd, *J* 3.1, 8.9 Hz, 1H), 4.54 (d, *J* 13.2 Hz, 1H), 4.62 (d, *J* 3.5 Hz, 1H), 4.98 (d, *J* 13.2 Hz, 1H), 5.09 (d, *J* 7.2 Hz, 1H), 5.90 (d, *J* 3.5 Hz, 1H), 7.17–7.41 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.1, 26.3, 26.8, 32.6, 35.5, 80.0, 84.0, 104.5, 112.3, 128.1, 129.2, 129.9, 134.8, 170.1; IR (Neat) ν_{max} 2987, 2933, 2245, 1736 cm^{-1}; Anal. Calcd for $C_{20}H_{23}NO_6$: C, 64.33; H, 6.21; N, 3.75. Found: C, 64.47; H, 6.24; N, 3.76; ESIMS: *m*/*z* 396 (MNa^+).

4.4.6. Compound 5a. Colorless liquid (288 mg, 71%); $[\alpha]_D^{27}$ +16.2 (*c* 1.92 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (s, 3H), 1.42 (s, 3H), 1.85 (s, 3H), 2.89 (dd, *J* 4.2, 14.0 Hz, 1H), 3.51 (dd, *J* 7.0, 14.0 Hz, 1H), 3.63 (m, 1H), 3.69 (s, 3H), 4.07 (s, 1H), 4.16 (s, 1H), 4.59 (m, 2H), 4.98 (d, *J* 13.2 Hz, 1H), 5.17 (d, *J* 8.0 Hz, 1H), 5.92 (d, *J* 3.5 Hz, 1H), 7.09–7.26 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.8, 26.3, 26.8, 32.8, 44.9, 51.8, 71.2, 74.7, 79.8, 83.0, 84.2, 104.4, 112.0, 126.8, 126.9, 128.6, 128.7, 131.7, 136.2, 170.0, 173.9; IR (Neat) ν_{max} 2987, 2938, 1738 cm^{-1}; Anal. Calcd for $C_{21}H_{26}O_8$: C, 62.06; H, 6.45. Found: C, 62.17; H, 6.34; ESIMS: *m*/*z* 429 (MNa^+).

4.4.7. Compound 5b. Colorless liquid (319 mg, 67%); $[\alpha]_D^{27}$ +19.9 (*c* 1.46 in $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.31 (s, 3H), 1.42 (s, 3H), 1.90 (s, 3H), 2.85 (d, *J* 14.4 Hz, 1H), 3.45 (m, 1H), 3.65 (br s, 1H), 3.68 (s, 3H), 3.89 (s, 3H), 3.90 (s, 3H), 4.00 (s, 1H), 4.12 (s, 1H), 4.50 (d, *J* 13.2 Hz, 1H), 4.56 (s, 1H), 4.93 (d, *J* 13.2 Hz, 1H), 5.13 (br s, 1H), 5.93 (s, 1H), 6.61 (s, 1H), 6.80 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.8, 26.2, 26.7, 32.1, 51.7, 55.8, 56.0, 71.1, 74.0, 76.7, 80.0, 82.2, 84.1, 104.3, 111.7, 111.9, 112.3, 115.0, 128.0, 147.2, 148.6, 169.8, 174.2; IR (Neat) ν_{max} 2941, 1738 cm^{-1}; Anal. Calcd for $C_{23}H_{30}O_{10}$: C, 59.22; H, 6.48. Found: C, 59.13; H, 6.39; ESIMS: *m*/*z* 489 (MNa^+).

4.4.8. Compound 5c. Colorless liquid (284 mg, 63%); $[\alpha]_D^{27}$ +21.1 (*c* 0.85 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (s, 3H), 1.41 (s, 3H), 1.93 (s, 3H), 2.77 (dd, *J* 3.2, 14.2 Hz, 1H), 3.39 (dd, *J* 7.7, 14.2 Hz, 1H), 3.59 (m, 1H), 3.72 (s, 3H), 3.98 (s, 1H), 4.15 (s, 1H), 4.41 (d, *J* 12.9 Hz, 1H), 4.55 (d, *J* 3.5 Hz, 1H), 4.85 (d, *J* 13.0 Hz, 1H), 5.11 (d, *J* 7.8 Hz, 1H), 5.94 (br s, 3H), 6.60 (s, 1H), 6.76 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.8, 26.2, 26.7, 32.6, 44.3, 51.7, 71.4, 73.9, 79.5, 82.1, 84.0, 101.1, 104.3, 108.8, 111.7, 111.9, 129.3, 131.4, 146.3, 147.7, 169.7, 174.1; IR (Neat) ν_{max} 2989, 2941, 2881, 1731, 1726 cm^{-1}; Anal. Calcd for $C_{22}H_{26}O_{10}$: C, 58.66; H, 5.82. Found: C, 58.78; H, 5.74; ESIMS: *m*/*z* 473 (MNa^+).

4.4.9. Compound 5d. Colorless liquid (281 mg, 67%); $[\alpha]_D^{27}$ +11.4 (*c* 1.16 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (t, *J* 7.1 Hz, 3H), 1.31 (s, 3H), 1.42 (s, 3H), 1.84 (s, 3H), 2.88 (dd, *J* 3.7, 13.2 Hz, 1H), 3.56 (m, 2H), 4.08–4.18 (m, 4H), 4.51 (m, 2H), 4.99 (d, *J* 13.3 Hz, 1H), 5.20 (d, *J* 7.5 Hz, 1H), 5.92 (d, *J* 3.6 Hz, 1H), 7.10 (d, *J* 7.1 Hz, 1H), 7.16–7.32 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.2, 20.8, 26.3, 26.8, 32.7, 45.2, 60.7, 71.2, 74.8, 76.9, 84.2, 104.3, 111.9, 126.8, 128.5, 128.6, 136.2, 170.0, 173.3; IR (Neat) ν_{max} 2985, 2936, 1733 cm^{-1}; Anal. Calcd for $C_{22}H_{28}O_8$: C, 62.85; H, 6.71. Found: C, 62.89; H, 6.69; ESIMS: *m*/*z* 443 (MNa^+).

4.4.10. Compound 5e. Colorless liquid (138 mg, 37%); $[\alpha]_D^{27}$ +19.9 (*c* 1.46 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 3H), 1.43 (s, 3H), 2.11 (s, 3H), 3.04 (dd, *J* 2.6, 14.0 Hz, 1H), 3.66 (dd, *J* 7.7, 14.0 Hz, 1H), 3.97 (s, 2H), 4.11 (s, 1H), 4.48 (d, *J* 13.5 Hz, 1H), 4.56 (d, *J* 3.3 Hz, 1H), 4.75 (d, *J* 8.2 Hz, 1H), 5.02 (d, *J* 13.5 Hz, 1H), 5.95 (d, *J* 3.2 Hz, 1H), 7.13 (d-like, 1H), 7.27 (t-like, 1H), 7.37 (t-like, 1H), 7.48 (d-like, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.9, 26.2, 26.7, 31.1, 33.4, 69.5, 74.0, 79.7, 82.0, 83.6, 104.7, 112.3, 120.4, 127.8, 128.5, 129.2, 132.2, 135.5, 135.7, 170.0; IR (Neat) ν_{max} 2987, 2933, 2243, 1747 cm^{-1}; Anal. Calcd for $C_{20}H_{23}NO_6$: C, 64.33; H, 6.21; N, 3.75. Found: C, 64.35; H, 6.34; N, 3.68; ESIMS: *m*/*z* 396 (MNa^+).

4.4.11. Compound 6. Foamy solid (191 mg, 47%); $[\alpha]_D^{27}$ +69.8 (*c* 0.81 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 3H), 1.70 (s, 3H), 2.03 (s, 3H), 2.99 (dd, *J* 6.1, 13.6 Hz, 1H), 3.28 (m, 1H), 3.59 (m, 2H), 3.74 (s, 3H), 4.64 (m, 2H), 4.82 (m, 2H), 5.24 (d, *J* 13.4 Hz, 1H), 5.61 (d, *J* 3.5 Hz, 1H), 7.12–7.31 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.0, 26.4, 26.7, 29.2, 49.2, 52.1, 72.5, 73.2, 74.2, 78.6, 79.0, 103.1, 113.1, 127.0, 129.2, 129.9, 130.6, 135.6, 137.8, 169.9, 172.5; IR (Neat) ν_{max} 2982, 2928, 1741 cm^{-1}; Anal. Calcd for $C_{21}H_{26}O_8$: C, 62.06; H, 6.45. Found: C, 62.01; H, 6.39; ESIMS: *m*/*z* 429 (MNa^+).

4.4.12. Compound 7. Colorless liquid (251.7 mg, 62%); $[\alpha]_D^{27}$ +85.9 (*c* 1.38 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 3H), 1.40 (s, 3H), 1.62 (s, 3H), 3.05 (dd, *J* 4.9, 13.6 Hz, 1H), 3.50 (m, 1H), 3.77 (m, 4H), 3.99 (dd, *J* 4.3, 8.8 Hz, 1H), 4.45 (d, *J* 8.8 Hz, 1H), 4.66 (m, 2H), 5.28 (d, *J* 13.6 Hz, 1H), 5.51 (d, *J* 2.5 Hz, 1H), 5.58 (d, *J* 3.3 Hz, 1H), 7.10–7.37 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.6, 26.3, 26.8, 30.1, 46.6, 52.5, 70.6, 72.4, 73.6, 77.9, 78.1, 103.4, 113.4, 126.3, 128.8, 129.4, 130.7, 136.3, 141.1, 170.0, 173.9; IR (Neat) ν_{max} 2989, 2935, 1734 cm^{-1}; Anal. Calcd for $C_{21}H_{26}O_8$: C, 62.06; H, 6.45. Found: C, 62.21; H, 6.42; ESIMS: *m*/*z* 429 (MNa^+).

4.5. Synthesis of benzoxonine derivative 8

Compound **4a** (1 mmol) was dissolved in CH_3CN–H_2O (1:1) containing 5% H_2SO_4 and kept at room temperature for 24 h. The acidic solution was neutralized with solid $NaHCO_3$, filtered, and the filtrate was evaporated in vacuum. The residue was dissolved in MeOH (20 mL) and treated dropwise at 0 °C with an aqueous solution (25 mL) of $NaIO_4$ (1.2 mmol) with stirring for 1 h. Usual work up followed by $NaBH_4$ reduction in MeOH afforded the diol. This was acetylated with Ac_2O (0.5 mL) and pyridine (2 mL) at room temperature for 12 h to furnish a crude product, which was purified by silica gel flash chromatography using 10% ethyl acetate in petroleum ether (60–80 °C) to afford **8**.

4.5.1. Benzoxonine 8. Colorless liquid (93 mg, 22%); $[\alpha]_D^{27}$ +6.20 (*c* 0.61 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 2.07 (s, 3H), 2.08 (s, 3H), 2.14 (s, 3H), 2.81 (d, *J* 13.4 Hz, 1H), 3.17 (dd, *J* 7.1, 14.2 Hz, 1H), 3.36 (m, 1H), 3.74 (s, 3H), 4.22 (m, 3H), 4.71 (d, *J* 11.7 Hz, 1H), 4.89 (d, *J* 11.7 Hz, 1H), 5.22 (br s, 1H), 5.30 (s, 1H), 7.18–7.42 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.06, 20.07, 20.08, 20.09, 27.8, 46.6, 51.9, 52.4, 64.2, 69.9, 71.9, 75.8, 126.5, 128.8, 129.0, 130.6, 136.4, 169.4, 169.9, 170.7, 174.0; IR (Neat) ν_{max} 2953, 1743 cm^{-1}; Anal. Calcd for $C_{21}H_{26}O_9$: C, 59.71; H, 6.20. Found: C, 59.67; H, 6.26; MS (ESI^+): *m*/*z* 445 (MNa^+).

Acknowledgements

We are grateful to Dr. B. Achari and Dr. Anup Bhattacharjya of our department for helpful suggestion and CSIR for the award of Senior Research Fellowships (to A.N. and T.P.M.).

Supplementary data

^1H NMR and ^{13}C NMR spectra for all new compounds are provided in the supplementary data files. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2006.09.080.

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13. Crystal data of **4a**: $C_{21}H_{26}O_8$, M=406.4, orthorhombic, space group $P2_12_12_1$, a=8.659 (1), b=11.419 (1), c=20.395 (3) Å, V=2016.6 (4) Å^3, Z=4, F(000)=864, T=293 (2)K, μ (μ_0 K_α)=0.103 mm^{-1}. A total of 2692 unique reflection were measured (θ_{max}=25.0°) on a MacScience DIP Labo 32001 diffractometer using graphite monochromatised Mo Kα radiation (λ=0.71073 Å). The structure was determined by direct methods with SHELXS 97[15]and refined by full-matrix least-squares method on F^2 using SHELXL 97.[15] Non-hydrogen atoms were refined anisotropically and the hydrogen atoms located from the difference Fourier maps were treated as riding on their parent atoms. Final R_1=0.0704, ωR_2=0.1932, a goodness of fit=0.862 for all 2692 reflections; for the 2087 observed data [$I>2\sigma(I)$] only, R_1=0.0601. CCDC 295094.
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