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Palladium-Catalyzed Intramolecular C–O Bond Formation: An Approach to the Synthesis of Chiral Benzodioxocines

Arpita Neogi,[a] Tirtha P. Majhi,[a] Basudeb Achari,[a] and Partha Chattopadhyay*[a]

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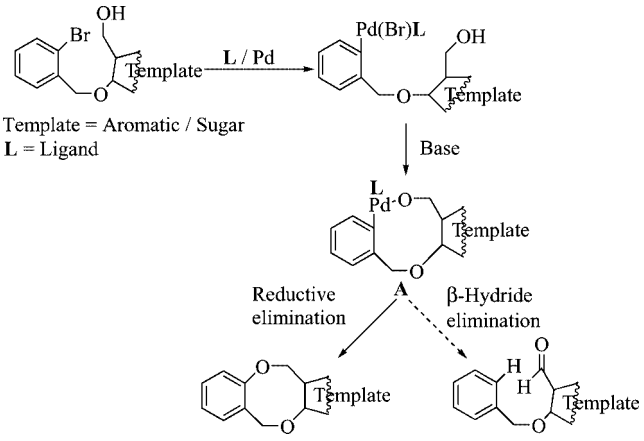
Palladium-catalyzed intramolecular aryl etherification using bulky binaphthylphosphane or bis(diphenylphosphanyl)ferrocene ligands is shown to be a convenient method for the synthesis of eight-membered oxygen heterocycles. Application of this methodology to a sugar derivative led to the synthesis of chiral benzodioxocine.

Introduction

Palladium-mediated amination of aryl halides has emerged as a versatile and efficient method for the synthesis[1] of nitrogen heterocycles. The analogous process for the addition of alcohols to produce aromatic ethers has also been successfully established.[2] The initial work in this field by Buchwald and co-workers focused on the intramolecular etherification of *o*-haloaryl-substituted alcohols to give benzo-fused cyclic ethers having five- to seven-membered rings.[3] However, to the best of our knowledge, eight-membered rings have not been generated using this method.

Reported approaches to the construction of eight-membered rings by intramolecular etherification include nucleophilic aromatic substitution of fluorine by the OH group of substituted phenols,[4a] cyclization of bromoallenes bearing nucleophilic oxygen functionalities in the presence of a palladium catalyst,[4b] and palladium-induced cyclization of phenols substituted with a tethered alkyne functionality.[4c]

The above methodologies either require a lengthy sequence of reactions or furnish low yields of the reaction products. As a part of our research exploring the synthesis of medium-sized ring compounds,[5] we have now applied the process of intramolecular palladium-induced aryl etherification using various aliphatic alcohols to the synthesis of benzo-fused dioxocine derivatives (Scheme 1), the structural unit found in some natural products,[6a,6b] some analogues of which have a high affinity for the M_3 muscarinic receptor.[6c] These reactions appear to be the first examples of the application of this useful reaction in the synthesis of eight-membered rings. Herein we report the results of this investigation and demonstrate the applicability of this methodology to the synthesis of enantiopure benzannulated dioxocine derivatives.



Scheme 1. Mechanism of intramolecular aryl etherification in the synthesis of medium-sized rings.

Results and Discussion

Our initial studies concerned the reaction of [2-(2-bromo/iodobenzyloxy)phenyl]methanols **1a**,**b** and their analogue **1c**, prepared from salicylaldehyde/*o*-hydroxyacetophenone by thioacetalization using propanedithiol,[7] arylation with 2-bromo/iodobenzyl bromides,[8] and dethioacetalization in the presence of MeI/aqu. MeCN.[9] Compounds **1a**,**b** were readily converted (Scheme 2, Table 1) into dibenzodioxocine **2** by Pd-catalyzed intramolecular etherification in the presence of base and ligands (**L1** and **L2**) (Figure 1).

[a] Department of Chemistry, Indian Institute of Chemical Biology,
4 Raja S. C. Mullick Road, Kolkata 700032, India
Fax: +91-33-24735197
E-mail: partha@iicb.res.in
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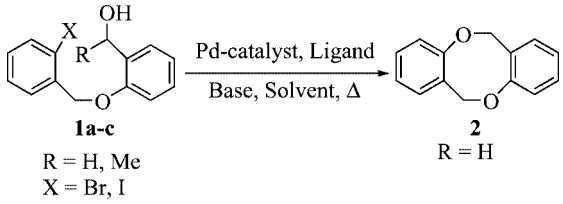
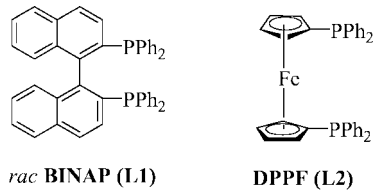


Scheme 2. Synthesis of dibenzodioxocines.

Table 1. Palladium-catalyzed synthesis of dibenzodioxocines.

Entry	Substrate	R	X	Product[a]	% Yield
1	**1a**	H	Br	**2**	62[b]
2	**1b**	H	I	**2**	62[b]
3	**1a**	H	Br	**2**	61[c]
4	**1a**	H	Br	**2**	44[d]
5	**1b**	H	I	**2**	45[e]
6	**1c**	Me	Br	–	–[b,f]

[a] β-Eliminated products (8–10%) were detected in all cases. [b] Reaction conditions: 5 mol-% $Pd_2(dba)_3$, 7 mol-% **L1**, 2.0 equiv. K_3PO_4, toluene (10 mL/mmol substrate), 90 °C, 16 h. [c] Reaction conditions: 5 mol-% $Pd_2(dba)_3$, 7 mol-% **L2**, 2.0 equiv. K_3PO_4, toluene (10 mL/mmol substrate), 90 °C, 16 h. [d] Reaction conditions: 4 mol-% $Pd_2(dba)_3$, 5 mol-% **L1**, 2.0 equiv. Cs_2CO_3, toluene (10 mL/mmol substrate), 90 °C, 10 h. [e] Reaction conditions: 4 mol-% $Pd_2(dba)_3$, 5 mol-% **L1**, 2.0 equiv. NaO*t*Bu, toluene (10 mL/mmol substrate), 90 °C, 10 h. [f] No cyclized product detected.



rac **BINAP (L1)** **DPPF (L2)**

Figure 1. Ligands used in Pd-catalyzed C–O bond formation.

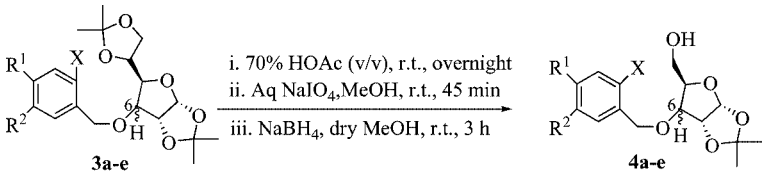
By screening a variety of bases, we found K_3PO_4 to be the most effective for the intramolecular etherification reaction. With respect to the product yield, K_3PO_4 is clearly superior[10] to other bases, including Cs_2CO_3, K_2CO_3, and NaO*t*Bu, which are less effective for this reaction (Table 1). The most versatile ligand was found to be (±)-BINAP (**L1**). This could be employed in several instances, for example, in the cyclization of the model substrates **1a**,**b** at ≥90 °C in toluene with $Pd_2(dba)_3$ as the palladium source in the presence of K_3PO_4. The yield of dibenzodioxocine **2** was about 62%. Use of 1,1′-bis(diphenylphosphanyl)ferrocene (DPPF) (**L2**) as the ligand to cyclize **1a** furnished a similar yield of **2** (Entry 3, Table 1). This method works satisfactorily with primary alcohols, but fails to produce any reductive elimination product when a secondary alcohol is used (Entry 6, Table 1).

We then explored the reaction of various aryl halides tethered to a sugar nucleus to obtain ethereal products. In this cyclization, sugar plays a double role (a) as a chiral source involving a strategy that is based on the concept of "chiral template" and generates "chirons" which are enantiomerically pure synthons and (b) by bringing rigidity to the substrate. The rigidity imposed on the precursor by the aromatic and tetrahydrofuran rings may assist the cyclization.[11] The starting material, *O*-2-bromobenzylated 1,2:5,6-di-*O*-isopropylideneglucofuranoside **3a**, its analogues **3b**–**d**,[8] and the epimeric allofuranoside **3e**[8] were converted into the nor-aldehydes by selective deketalization and $NaIO_4$ oxidation. Subsequent reduction of the crude aldehydes with $NaBH_4$ furnished the sugar alcohols **4a**–**e**[12] in good yields (Scheme 3, Table 2). The spectroscopic data of the product alcohols are in excellent agreement with the assigned structures.

Table 2. Preparation of furano sugar alcohols.

Entry	Substrate	C-6config.	R^1	R^2	X	Product	% Yield
1	**3a**	*S*	H	H	Br	**4a**	80
2	**3b**	*S*	H	H	I	**4b**	75
3	**3c**	*S*	H	OMe	Br	**4c**	85
4	**3d**	*S*	–OCH_2O–		Br	**4d**	82
5	**3e**	*R*	H	H	Br	**4e**	77

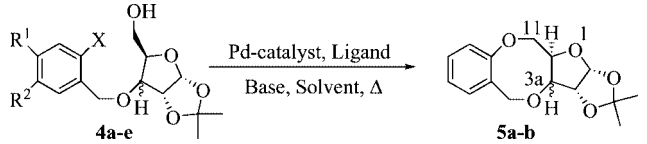
Pd-catalyzed intramolecular aryl etherification of **4a**–**e** in the presence of base and ligands afforded furobenzodioxocine derivatives **5a**,**b** (Scheme 4; no cyclization products were detected with **4c**,**d**). The reactions carried out in the presence of K_3PO_4 and ligands afforded the desired benzodioxocine-annulated furanose derivatives **5a**,**b** in around 65% yield. (Entries 1–3 and 8, Table 3). As in the previous case,



a $R^1 = R^2$ = H, X = Br, *6S*
b $R^1 = R^2$ = H, X = I, *6S*
c R^1 = H, R^2 = OMe, X = Br, *6S*
d $R^1 + R^2$ = O-CH_2-O, X = Br, *6S*
e $R^1 = R^2$ = H, X = Br, *6R*

Scheme 3. Construction of *O*-bromo/iodobenzylated sugar alcohols.

use of the ferrocene ligand (**L2**) gave a similar yield of the reductive elimination product to that obtained with ligand **L1** (Entry 3, Table 3). The structures of the products **5a**,**b** were ascertained by ^{1}H NMR spectroscopy as well as by ^{13}C NMR, ^{1}H–^{1}H COSY and mass spectral analyses. As expected from the studies of Buchwald and co-workers,[3c,13] compounds bearing an electron-donating group (methoxy or methylenedioxy) *para* to the halogen (Entries 6 and 7, Table 3) proved difficult substrates for this type of cyclization reaction.



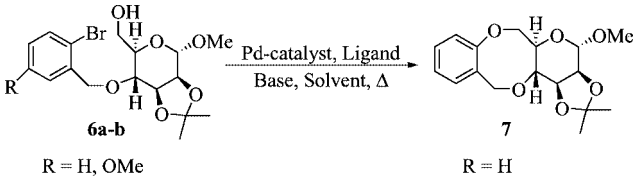
Scheme 4. Intramolecular aryl etherification of furanose derivatives.

Table 3. Optimization of the intramolecular aryl etherification of furanose derivatives.

Entry	Substrate	C-6 config.	Product[a]	% Yield
1	**4a**	*S*	**5a**	65[b]
2	**4b**	*S*	**5a**	65[b]
3	**4a**	*S*	**5a**	64[c]
4	**4a**	*S*	**5a**	45[d]
5	**4a**	*S*	**5a**	46[e]
6	**4c**	*S*	–	–[b,f]
7	**4d**	*S*	–	–[b,f]
8	**4e**	*R*	**5b**	65[b]
9	**4e**	*R*	**5b**	45[e]

[a] β-Eliminated products (5–10%) were detected in all cases. [b] Reaction conditions: 5 mol-% $Pd_2(dba)_3$, 7 mol-% **L1**, 2.0 equiv. K_3PO_4, toluene (10 mL/mmol substrate), 90 °C, 18 h. [c] Reaction conditions: 5 mol-% $Pd_2(dba)_3$, 7 mol-% **L2**, 2.0 equiv. K_3PO_4, toluene (10 mL/mmol substrate), 90 °C, 18 h. [d] Reaction conditions: 3 mol-% $Pd(OAc)_2$, 4 mol-% **L1**, 2.0 equiv. NaO*t*Bu, toluene (10 mL/mmol substrate), 90 °C, 16 h. [e] Reaction conditions: 4 mol-% $Pd_2(dba)_3$, 5 mol-% **L1**, 2.0 equiv. Cs_2CO_3, toluene (10 mL/mmol substrate), 90 °C, 10 h. [f] No cyclized product detected.

The same reaction was then studied with the *O*-(2-bromoaryl)mannopyranose derivatives **6a**,**b**[14] (Scheme 5). Evaluation of reagents and conditions showed that the optimum conditions for this reaction were with $Pd(OAc)_2$ as the palladium source, (±)-BINAP (**L1**) as the ligand, K_3PO_4 as the base, and toluene as the solvent. The yield of purified pyranobenzodioxocine **7** was 67% (Entry 2, Table 4). The structure of the product **7** was ascertained by ^{1}H NMR spectroscopy as well as by ^{13}C NMR and mass spectral analyses. As in the furanose system (Entries 6 and 7, Table 3), an aryl bromide tethered substrate containing a strongly electron-donating group *para* to the bromide was not amenable to cyclization (Entry 4, Table 4).



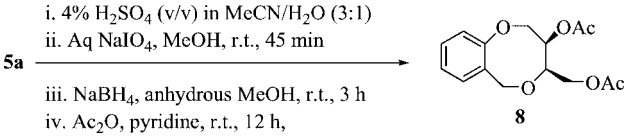
Scheme 5. Intramolecular aryl etherification of pyranose derivatives.

Table 4. Optimization of the intramolecular aryl etherification of pyranose derivatives.

Entry	Substrate	R	Product[a]	% Yield
1	**6a**	H	**7**	50[b]
2	**6a**	H	**7**	67[c]
3	**6a**	H	**7**	65[d]
4	**6b**	OMe	–	–[e]

[a] Small amounts of β-eliminated products (nearly 4%) were detected. [b] Reaction conditions: 3 mol-% $Pd(OAc)_2$, 4 mol-% **L1**, 2.0 equiv. Cs_2CO_3, toluene (10 mL/mmol substrate), 90 °C, 10 h. [c] Reaction conditions: 5 mol-% $Pd(OAc)_2$, 7 mol-% **L1**, 2.0 equiv. K_3PO_4, toluene (10 mL/mmol substrate), 90 °C, 18 h. [d] Reaction conditions: 5 mol-% $Pd_2(dba)_3$, 7 mol-% **L2**, 2.0 equiv. K_3PO_4, toluene (10 mL/mmol substrate), 90 °C, 18 h. [e] No cyclized product detected.

The feasibility of synthesizing chiral benzodioxocines from the annulated sugar derivatives could then be realized by using **5a** (Scheme 6). Thus, **5a** was converted into the functionalized benzodioxocine **8** in 60% overall yield by a sequence of reactions involving the removal of the 1,2-*O*-isopropylidene group, oxidative cleavage of the diol, reduction of the carbonyl group, and acetylation. The formation of **8** was deduced from the appearance of three methylene carbon signals at δ = 64.4, 72.7, and 75.5 in its ^{13}C NMR spectrum besides other corroborative evidence.



Scheme 6. Conversion of **5a** to a benzodioxocine derivative.

Conclusions

In conclusion, we have developed a strategy for palladium-catalyzed intramolecular C–O bond formation which can be applied to the synthesis of benzodioxocines fused to an aromatic or sugar template. The reaction is applicable to a variety of aromatic- or hexose-tethered primary alcohols, as shown in Tables 1, 2, 3, and 4, and can be used in the synthesis of enantiopure functionalized benzodioxocines.

Experimental Section

General: Melting points are uncorrected. ^{1}H (300 MHz, 600 MHz) and ^{13}C (75 MHz, 150 MHz) NMR spectra were recorded with

Bruker DPX-300 and AVANCE-600 spectrometers using $CDCl_3$ as solvent and TMS as the internal standard. Mass spectra were recorded with a JEOL AX-500/Micromass Q-Tof micro™ instrument. Elemental analyses were carried out with a C,H,N analyzer. Specific rotations were measured at 589 nm with a JASCO P-10 polarimeter. TLC was performed on precoated plates (0.25 nm, silica gel 60 F_{254}). Organic extracts were dried with anhydrous sodium sulfate. Solvents were distilled and dried immediately prior to use. Column chromatography and flash chromatography were carried out by using commercial grade silica gel (60–120 or 230–400 mesh). PS and EA stand for petroleum spirit (boiling range 60–80 °C) and ethyl acetate.

General Procedure for Dethioacetalization: A solution of the thioacetal/ketal (1 mmol) and CH_3I (710 mg, 5.0 mmol) in 84% aqueous CH_3CN (20 mL) was stirred at 25 °C for 12 h. After completion of the reaction, as revealed by TLC, the reaction mixture was evaporated under reduced pressure. The residue obtained was extracted with CH_2Cl_2 (3 × 20 mL), the combined organic layer was washed successively with a saturated aqueous solution of $Na_2S_2O_3$ and water, and then dried (Na_2SO_4). Without further purification, the crude mass was dissolved in absolute ethanol (30 mL) at 0 °C and treated with $NaBH_4$ (113 mg, 3 mmol) in small portions over a period of 1 h; the stirring was continued for another 2 h at room temperature to complete the reaction. The solvent was evaporated under reduced pressure and the residue was extracted with CH_2Cl_2 (4 × 25 mL). The combined organic layers were washed with water and dried (Na_2SO_4). Evaporation of solvent afforded the alcohol as a crude oil, which, on column chromatography over silica gel, furnished the pure alcohol derivatives **1a**–**c**.

[2-(2-Bromobenzyloxy)phenyl]methanol (1a): White crystalline solid, m.p. 77 °C. Yield 234 mg (80%) (eluent: PS/EA, 9:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.88 (br. s, 1 H), 4.77 (s, 2 H), 5.18 (s, 2 H), 6.97 (dd-like, 2 H), 7.19–7.37 (m, 4 H), 7.51 (d, J = 7.3 Hz, 1 H), 7.61 (d, J = 7.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 62.1, 69.5, 111.5, 121.2, 122.6, 127.7, 128.9, 129.0, 129.4, 129.6, 133.0, 136.0, 156.2 ppm. MS (ESI): m/z = 315, 317 $[MNa]^+$ (for Br^{79}, Br^{81}). $C_{14}H_{13}BrO_2$ (293.16): calcd. C 57.36, H 4.47; found C 57.10, H 4.62.

[2-(2-Iodobenzyloxy)phenyl]methanol (1b): White crystalline solid, m.p. 79 °C. Yield 245 mg (72%) (eluent: PS/EA, 9:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.25 (br. s, 1 H), 4.77 (s, 2 H), 5.09 (s, 2 H), 6.93–7.08 (m, 3 H), 7.22–7.62 (m, 4 H), 7.89 (d, J = 7.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 61.7, 73.7, 97.4, 111.4, 121.1, 127.6, 128.4, 128.5, 128.8, 129.0, 129.6, 138.7, 139.3, 156.0 ppm. IR (film): $\tilde{\nu}_{max}$ = 3296, 2912, 2860, 1604, 1488, 1369, 1237, 1044 cm^{-1}. MS (ESI): m/z = 363 $[MNa]^+$. $C_{14}H_{13}IO_2$ (340.16): calcd. C 49.43, H 3.85; found C 49.16, H 3.70.

1-[2-(2-Bromobenzyloxy)phenyl]ethanol (1c): White crystalline solid, m.p. 82 °C. Yield 215 mg (70%) (eluent: PS/EA, 9:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.54 (d, J = 6.5 Hz, 3 H), 2.51 (br. s, 1 H), 5.16–5.25 (m, 3 H), 6.93 (d, J = 8.2 Hz, 1 H), 7.00 (t-like, 1 H), 7.23 (dd-like, 2 H), 7.34–7.42 (m, 2 H), 7.51 (d, J = 7.5 Hz, 1 H), 7.60 (d, J = 7.9 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 23.0, 65.6, 69.3, 111.4, 121.2, 122.3, 126.0, 127.5, 128.1, 128.7, 129.3, 132.6, 134.0, 136.0, 155.0 ppm. MS (ESI): m/z = 329, 331 $[MNa]^+$ (for Br^{79}, Br^{81}). $C_{15}H_{15}BrO_2$ (307.18): calcd. C 58.65, H 4.92; found C 58.57, H 4.74.

General Procedure for the Synthesis of Bromo/iodobenzylfurano Sugar Derivatives: Bu_4NBr (50 mg) followed by aqueous NaOH (50%, 20 mL) were added to a magnetically stirred solution of 1,2:5,6-di-*O*-isopropylidenegluco/allofuranoside (260 mg, 1 mmol) and the appropriate 2-bromobenzyl bromide (1.2 mmol) in CH_2Cl_2 (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 bromo/iodobenzyl derivatives **3a**–**e**.

(3a*R*,5*R*,6*S*,6a*R*)-6-(2-Bromobenzyloxy)-5-(2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydro-2*H*-furo[2,3-*d*][1,3]dioxole (3a): Thick oil. Yield 300 mg (70%) (eluent: PS/EA, 13:1). $[\alpha]_D^{25}$ = –21.6 (c = 0.25, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.32 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3), 1.50 (s, 3 H, CH_3), 4.00 (dd, J = 5.8, 8.4 Hz, 1 H, 5-H), 4.07–4.18 (m, 3 H), 4.39 (dd, J = 13.6, 6.0 Hz, 1 H, 6-H), 4.65–4.69 (d-like, 2 H, 6a-H signal overlapped by H^a of $ArCH_2O$), 4.76 (d, J = 12.8 Hz, 1 H, H^b of $ArCH_2O$), 5.92 (d, J = 3.6 Hz, 1 H, 3a-H), 7.15–7.54 (m, 4 H, ArH) ppm. ^{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 ppm. IR (film): $\tilde{\nu}_{max}$ = 2985, 1450, 1376, 1215, 1078, 1024 cm^{-1}. MS (ESI): m/z = 451, 453 $[MNa]^+$ (for Br^{79}, Br^{81}). $C_{19}H_{25}BrO_6$ (429.30): calcd. C 53.16, H 5.87; found C 53.00, H 5.75.

(3a*R*,5*R*,6*S*,6a*R*)-6-(2-Iodobenzyloxy)-5-(2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydro-2*H*-furo[2,3-*d*][1,3]dioxole (3b): Thick pale-yellow oil. Yield 333 mg (70%) (eluent: PS/EA, 13:1). $[\alpha]_D^{25}$ = –21.2 (c = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.33 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.43 (s, 3 H, CH_3), 1.51 (s, 3 H, CH_3), 4.01 (dd-like, 1 H, 5-H), 4.09–4.18 (m, 3 H), 4.39 (dd, J = 12.8, 6.9 Hz, 1 H, 6-H), 4.58–4.74 (m, 3 H, 6a-H and $ArCH_2$ protons), 5.92 (d, J = 3.2 Hz, 1 H, 3a-H), 6.97–7.83 (m, 4 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 25.4, 26.2, 26.7, 26.8, 67.3, 71.5, 72.4, 81.2, 82.0, 82.4, 97.5, 105.2, 108.9, 111.8, 128.1, 128.7, 129.1, 129.3, 139.8 ppm. MS (ESI): m/z = 499 $[MNa]^+$. $C_{19}H_{25}IO_6$ (476.30): calcd. C 47.91, H 5.29; found C 47.67, H 5.30.

(3a*R*,5*R*,6*S*,6a*R*)-6-(2-Bromo-5-methoxybenzyloxy)-5-(2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydro-2*H*-furo[2,3-*d*][1,3]dioxole (3c): Thick oil. Yield 330 mg (72%) (eluent: PS/EA, 10:1). $[\alpha]_D^{25}$ = –24.5 (c = 0.22, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.32 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3), 1.50 (s, 3 H, CH_3), 3.79 (s, 3 H, OCH_3), 4.00 (dd, J = 8.4, 5.8 Hz, 1 H, 5-H), 4.08–4.18 (m, 3 H), 4.41 (dd, J = 12.1, 5.9 Hz, 1 H, 6-H), 4.61–4.66 (d-like, 2 H, 6a-H signal overlapped by H^a of $ArCH_2O$), 4.72 (d, J = 13.1 Hz, 1 H, H^b of $ArCH_2O$), 5.92 (d, J = 3.6 Hz, 1 H, 3a-H), 6.71 (dd, J = 8.6, 2.9 Hz, 1 H, ArH), 7.07 (d, J = 2.8 Hz, 1 H, ArH), 7.41 (d, J = 8.7 Hz, 1 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 25.3, 26.2, 26.7, 26.8, 55.4, 67.3, 71.4, 72.4, 81.2, 82.1, 82.4, 105.2, 109.0, 111.8, 112.5, 114.4, 114.9, 133.0, 137.9, 159.1 ppm. IR (film): $\tilde{\nu}_{max}$ = 2986, 1577, 1473, 1375, 1215, 1079, 1021 cm^{-1}. MS (ESI): m/z = 481, 483 $[MNa]^+$ (for Br^{79}, Br^{81}). $C_{20}H_{27}BrO_7$ (459.33): calcd. C 52.30, H 5.92; found: C 52.17, H 5.88.

(3a*R*,5*R*,6*S*,6a*R*)-5-Bromo-6-{5-[2,2-dimethyl-1,3-dioxolan-4-yl]-2,2-dimethyltetrahydro-2*H*-furo[2,3-*d*][1,3]dioxol-6-yloxymethyl}-benzo[1,3]dioxole (3d): Thick oil. Yield 331 mg (70%). $[\alpha]_D^{27}$ = –29.3 (c = 0.71, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3), 1.43 (s, 3 H, CH_3), 1.50 (s, 3 H, CH_3), 3.99 (dd, J = 5.8, 8.5 Hz, 1 H, 5-H), 4.03 (d, J = 2.9 Hz, 1 H, 6-H), 4.09–4.15 (m, 2 H), 4.37 (dd, J = 6.0, 13.9 Hz, 1 H), 4.58 (d, J = 12.6 Hz, 1 H, H^a of $ArCH_2O$), 4.64 (d, J = 3.7 Hz, 1 H, 6a-H), 4.67 (d, J = 12.6 Hz, 1 H, H^b of $ArCH_2O$), 5.91 (d, J = 3.6 Hz, 1 H, 3a-H), 5.96 (s, 2 H, O-CH_2-O), 6.99 (s, 1 H, ArH), 7.03 (s, 1 H, ArH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.7, 26.7, 27.1, 27.2, 68.0, 71.8, 72.8, 81.7, 82.3, 82.9, 102.1, 105.7, 109.5, 109.8, 112.2,

113.0, 113.5, 130.6, 148.0, 148.2 ppm. MS (ESI): *m*/*z* (%) = 472, 474 (40) $[M]^+$ (for Br^{79}, Br^{81}]. $C_{20}H_{25}BrO_8$ (473.31): calcd. C 50.75, H 5.32; found C 50.42, H 5.29.

(3a*R*,5*R*,6*R*,6a*R*)-6-(2-Bromobenzyloxy)-5-(2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydro-2*H*-furo[2,3-*d*][1,3]dioxole (3e): White solid. Yield 317 mg (74%) (eluent: PS/EA, 6:1). $[\alpha]_D^{25}$ = +99.1 (*c* = 1.07, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.36 (s, 9 H, 3 × CH_3), 1.59 (s, 3 H, CH_3), 3.93 (dd, *J* = 8.5, 4.6 Hz, 1 H, 5-H), 4.00 (d, *J* = 7.0 Hz, 2 H), 4.16 (dd, *J* = 8.5, 3.4 Hz, 1 H, 6-H), 4.33–4.39 (m, 1 H), 4.68 (d, *J* = 12.8 Hz, 1 H, H^a of $ArCH_2O$), 4.72 (d, *J* = 4.2 Hz, 1 H, 6a-H), 4.85 (d, *J* = 12.8 Hz, 1 H, H^b of $ArCH_2O$), 5.80 (d, *J* = 3.7 Hz, 1 H, 3a-H), 7.16 (dt-like, 1 H, ArH), 7.32 (dt-like, 1 H, ArH), 7.55 (dd-like, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 25.2, 26.2, 26.7, 26.8, 65.2, 71.3, 74.9, 77.8, 78.2, 78.3, 104.0, 109.6, 113.0, 122.7, 127.4, 129.2, 129.6, 132.5, 137.0 ppm. IR (film): $\tilde{\nu}_{max}$ = 2985, 1450, 1376, 1215, 1078, 1024 cm^{-1}. MS (ESI): *m*/*z*: 451, 453 $[MNa]^+$ (for Br^{79}, Br^{81}]. $C_{19}H_{25}BrO_6$ (429.30): calcd. C 53.16, H 5.87; found C 52.97, H 5.71.

General Procedure for the Synthesis of Sugar Alcohols 4a–e: The appropriate bromo/iodobenzyl derivative **3a**–**e** (2 mmol) was stirred overnight with 70% aqueous HOAc (25 mL, v/v) at room temperature (monitored by TLC until disappearance of the starting material). Removal of HOAc on a rotary evaporator under reduced pressure (temp. 40 °C) by codistillation with dry toluene (4 × 25 mL) afforded the intermediate diol as a viscous syrup. A solution of the diol in a minimum volume of methanol was cooled to 0 °C and treated with aqueous $NaIO_4$ (513 mg, 2.4 mmol, dissolved in 20 mL of water) dropwise with stirring (45 min). The reaction mixture was evaporated under reduced pressure and the residual mass was extracted with $CHCl_3$ (4 × 25 mL). The combined organic layer was washed with water (3 × 25 mL) and dried (Na_2SO_4). The solvent was evaporated to furnish the crude aldehyde. Without further purification, this was dissolved in absolute ethanol (30 mL) at 0 °C and treated with $NaBH_4$ (113 mg, 3 mmol) in small portions over a period of 1 h. Stirring was continued for another 2 h at room temperature. The solvent was evaporated under reduced pressure and the residue was extracted with CH_2Cl_2 (4 × 25 mL). The combined organic layer was washed with water and dried (Na_2SO_4). Evaporation of the solvent afforded the alcohol as a crude oil, which, on column chromatography over silica gel, furnished the pure alcohol derivatives **4a**–**e**.

(3a*R*,5*R*,6*S*,6a*R*)-[6-(2-Bromobenzyloxy)-2,2-dimethyltetrahydro-2*H*-furo[2,3-*d*][1,3]dioxol-5-yl]methanol (4a): Thick oil. Yield 574 mg (80%) (eluent: PS/EA, 17:3). $[\alpha]_D^{25}$ = –34.2 (*c* = 1.2, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.35 (s, 3 H), 1.51 (s, 3 H), 2.12 (br. s, 1 H), 3.90–3.97 (m, 2 H), 4.10 (d, *J* = 3.1 Hz, 1 H), 4.34 (d, *J* = 4.0 Hz, 1 H), 4.58 (d, *J* = 12.3 Hz, 1 H), 4.72 (d, *J* = 3.6 Hz, 1 H), 4.76 (d, *J* = 12.4 Hz, 1 H), 6.01 (d, *J* = 3.5 Hz, 1 H), 7.17–7.41 (m, 3 H), 7.57 (d, *J* = 7.9 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 26.3, 26.8, 60.8, 71.4, 80.2, 82.2, 83.3, 105.1, 112.0, 123.0, 127.6, 129.5, 129.6, 133.0, 136.4 ppm. IR (film): $\tilde{\nu}_{max}$ = 3476, 2986, 2935, 1441, 1375, 1214, 1081 cm^{-1}. MS (ESI): *m*/*z* = 381, 383 $[MNa]^+$ (for Br^{79}, Br^{81}). $C_{15}H_{19}BrO_5$ (359.21): calcd. C 50.15, H 5.33; found C 49.90, H 5.21.

(3a*R*,5*R*,6*S*,6a*R*)-[6-(2-Iodobenzyloxy)-2,2-dimethyltetrahydro-2*H*-furo[2,3-*d*][1,3]dioxol-5-yl]methanol (4b): Thick oil. Yield 608 mg (75%) (eluent: PS/EA, 17:3). $[\alpha]_D^{25}$ = –15.4 (*c* = 2.4, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.35 (s, 3 H), 1.51 (s, 3 H), 1.85 (br. s, 1 H), 3.89–4.02 (m, 2 H), 4.10 (d, *J* = 3.4 Hz, 1 H), 4.34 (d-like, 1 H), 4.51 (d, *J* = 12.2 Hz, 1 H), 4.70 (d-like, 2 H), 6.00 (d, *J* = 3.7 Hz, 1 H), 7.00–7.04 (m, 1 H), 7.32–7.36 (m, 2 H), 7.84 (d, *J* = 8.0 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 26.2, 26.7, 60.7, 75.5, 80.3, 82.0, 83.0, 98.0, 105.0, 112.0, 128.3, 129.0, 129.3, 129.6, 139.2 ppm. IR (film) $\tilde{\nu}_{max}$ = 3443, 2981, 2933, 1438, 1375, 1252, 1014 cm^{-1}. MS (ESI): *m*/*z* = 429 $[MNa]^+$. $C_{15}H_{19}IO_5$ (406.21): calcd. C 44.35, H 4.71; found C 44.62, H 4.49.

(3a*R*,5*R*,6*S*,6a*R*)-[6-(2-Bromo-5-methoxybenzyloxy)-2,2-dimethyltetrahydro-2*H*-furo[2,3-*d*][1,3]dioxol-5-yl]methanol (4c): Thick oil. Yield 660 mg (85%) (eluent: PS/EA, 4:1). $[\alpha]_D^{25}$ = –36.3 (*c* = 2.23, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.35 (s, 3 H), 1.51 (s, 3 H), 2.14 (br. s, 1 H), 3.79 (s, 3 H), 3.90–4.02 (m, 2 H), 4.10 (d, *J* = 3.4 Hz, 1 H), 4.35 (d-like, 1 H), 4.53 (d, *J* = 12.6 Hz, 1 H), 4.71 (d-like, 2 H), 6.00 (d, *J* = 3.8 Hz, 1 H), 6.74 (dd, *J* = 8.7, 3.0 Hz, 1 H), 6.96 (d, *J* = 3.0 Hz, 1 H), 7.43 (d, *J* = 8.7 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 26.3, 26.8, 55.5, 61.0, 71.3, 80.1, 82.2, 83.3, 105.1, 112.0, 113.0, 115.0, 115.1, 133.3, 137.4, 159.1 ppm. IR (film): $\tilde{\nu}_{max}$ = 3493, 2985, 2936, 1475, 1454, 1375, 1240 cm^{-1}. MS (ESI): *m*/*z* = 411, 413 $[MNa]^+$ (for Br^{79}, Br^{81}). $C_{16}H_{21}BrO_6$ (389.24): calcd. C 49.37, H 5.44; found C 49.10, H 5.17.

(3a*R*,5*R*,6*S*,6a*R*)-{6-[6-Bromobenzo[1,3]dioxol-5-ylmethoxy]-2,2-dimethyltetrahydro-2*H*-furo[2,3-*d*][1,3]dioxol-5-yl}methanol (4d): Thick oil. Yield 660 mg (82%) (eluent: PS/EA, 4:1). $[\alpha]_D^{25}$ = –26.7 (*c* = 1.8, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.35 (s, 3 H), 1.51 (s, 3 H), 2.09–2.10 (br. s, 1 H), 3.84–4.00 (m, 2 H), 4.06 (d, *J* = 3.2 Hz, 1 H), 4.32 (d-like, 1 H), 4.49 (d, *J* = 12.0 Hz, 1 H), 4.67 (d-like, 2 H), 5.99 (s, 3 H), 6.88 (s, 1 H), 7.02 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 26.3, 26.7, 61.0, 71.2, 80.2, 82.2, 83.0, 102.0, 105.0, 109.5, 112.0, 113.0, 114.0, 129.4, 147.4, 148.1 ppm. IR (film): $\tilde{\nu}_{max}$ = 3478, 2984, 2934, 1503, 1481, 1454, 1375, 1238 cm^{-1}. MS (ESI): *m*/*z* = 425, 427 $[MNa]^+$ (for Br^{79}, Br^{81}). $C_{16}H_{19}BrO_7$ (403.22): calcd. C 47.66, H 4.75; found C 47.41, H 4.92.

(3a*R*,5*R*,6*R*,6a*R*)-[6-(2-Bromobenzyloxy)-2,2-dimethyltetrahydro-2*H*-furo[2,3-*d*][1,3]dioxol-5-yl]methanol (4e): Thick oil. Yield 552 mg (77%) (eluent: PS/EA, 4:1). $[\alpha]_D^{25}$ = +84.6 (*c* = 1.5, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.38 (s, 3 H), 1.60 (s, 3 H), 3.70 (d, *J* = 11.0 Hz, 1 H), 3.89–3.97 (m, 2 H), 4.16 (d, *J* = 8.9 Hz, 1 H), 4.68 (d-like, 2 H), 4.83 (d, *J* = 12.7 Hz, 1 H), 5.79 (d, *J* = 3.4 Hz, 1 H), 7.17 (t-like, 1 H), 7.33 (t-like, 1 H), 7.53 (t-like, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 26.5, 27.0, 61.0, 71.5, 77.3, 77.5, 79.0, 104.2, 113.2, 123.0, 127.5, 129.3, 129.5, 132.6, 137.0 ppm. IR (film): $\tilde{\nu}_{max}$ = 3538, 2966, 2935, 1408, 1375, 1210, 1023, 1009 cm^{-1}. MS (ESI): *m*/*z* = 381, 383 $[MNa]^+$ (for Br^{79}, Br^{81}). $C_{15}H_{19}BrO_5$ (359.21): calcd. C 50.15, H 5.33; found C 50.21, H 5.11.

General Procedure for the Deprotection of Silyl Ethers: A mixture of the silyl ether[14] (1 mol-equiv.) and TBAF (tetrabutylammonium fluoride) (1.2 mol equiv.) in dry THF was refluxed under nitrogen for 4 h. Excess THF was then removed from the reaction mixture under reduced pressure. The residue was diluted with water and extracted with CH_2Cl_2 (4 × 25 mL). The combined organic extracts were washed with water and dried (Na_2SO_4). The solvent was evaporated to furnish the crude product, which, on column chromatography over silica gel, furnished the pure alcohol derivatives **6a**,**b**.

(3a*S*,4*S*,6*R*,7*R*,7a*S*)-[7-(2-Bromobenzyloxy)-4-methoxy-2,2-dimethyltetrahydro-2*H*,4*H*-[1,3]dioxolo[4,5-*c*]pyran-6-yl]methanol (6a): Thick oil. Yield 282 mg (70%) (eluent: PS/EA, 5:1). $[\alpha]_D^{25}$ = +43.5 (*c* = 0.5, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.38 (s, 3 H), 1.55 (s, 3 H), 1.95 (br. s, 1 H), 3.39 (s, 3 H), 3.56–3.68 (m, 2 H), 3.80 (dd-like, 1 H), 3.89 (dd, *J* = 11.7, 2.6 Hz, 1 H), 4.15 (d, *J* = 5.7 Hz, 1 H), 4.33 (t, *J* = 6.1 Hz, 1 H), 4.68 (d, *J* = 12.2 Hz, 1 H), 4.95 (d-like, 2 H), 7.15 (t-like, 1 H), 7.28 (t-like, 1 H), 7.46 (dd-like, 1 H), 7.56 (d, *J* = 7.9 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz):

δ = 26.2, 28.0, 55.0, 62.3, 68.4, 72.1, 75.6, 76.3, 78.4, 98.0, 109.3, 123.0, 127.2, 129.0, 130.0, 132.5, 137.3 ppm. IR (film): $\tilde{\nu}_{max}$ = 3267, 2921, 1460, 1370, 1246, 1022 cm^{-1}. MS (ESI): *m*/*z* = 425, 427 [MNa]$^+$ (for Br^{79}, Br^{81}). $C_{17}H_{23}BrO_6$ (403.26): calcd. C 50.63, H 5.75; found C 50.34, H 5.51.

(3a*S*,4*S*,6*R*,7*R*,7a*S*)-[7-(2-Bromo-5-methoxybenzyloxy)-4-methoxy-2,2-dimethyltetrahydro-2*H*,4*H*-[1,3]dioxolo[4,5-*c*]pyran-6-yl]methanol (6b): White crystalline solid, m.p. 83 °C. Yield 294 mg (68%) (eluent: PS/EA, 5:1). $[\alpha]_D^{25}$ = +23.1 (*c* = 0.3, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.37 (s, 3 H), 1.54 (s, 3 H), 3.39 (s, 3 H), 3.56–3.65 (m, 2 H), 3.79 (s-like, 4 H), 3.80–3.87 (m, 1 H), 4.15 (d, *J* = 6.3 Hz, 1 H), 4.33 (t, *J* = 6.1 Hz, 1 H), 4.65 (d, *J* = 12.5 Hz, 1 H), 4.90 (d-like, 2 H), 6.71 (dd, *J* = 8.7, 3.1 Hz, 1 H), 7.04 (d, *J* = 3.1 Hz, 1 H), 7.41 (d, *J* = 8.7 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 26.3, 28.0, 55.0, 55.5, 62.5, 68.4, 72.2, 76.0, 76.6, 78.5, 98.3, 109.4, 113.2, 115.0, 115.4, 133.1, 138.4, 159.0 ppm. IR (film): $\tilde{\nu}_{max}$ = 3283, 2910, 1573, 1472, 1370, 1297, 1096 cm^{-1}. MS (ESI): *m*/*z* = 455, 457 [MNa]$^+$ (for Br^{79}, Br^{81}). $C_{18}H_{25}BrO_7$ (433.29): calcd. C 49.90, H 5.82; found C 49.63, H 5.54.

General Procedure for the Synthesis of Dioxocine Derivatives: $Pd_2(dba)_3$ or $Pd(OAc)_2$ (5 mol-%), (±)-BINAP or DPPF (7 mol-%) and K_3PO_4 (2.0 equiv.) were added to a solution of the alcohol (1 mmol) in dry toluene (10 mL/mmol substrate) and the reaction mixture was heated at 90 °C for 16–18 h under argon. After completion of the reaction, the crude mixture was passed through a bed of silica gel. The solvent was evaporated and the residue was extracted with CH_2Cl_2 (4 × 25 mL). The organic layer was washed with water (4 × 25 mL) and dried. The solvent was evaporated under reduced pressure to give the crude product which was purified by column chromatography over silica gel to furnish the pure cyclized product.

6*H*,12*H*-Dibenzo[*b*,*f*][1,5]dioxocine (2): White crystalline solid, m.p. 77 °C. Yield 131 mg (62%) (eluent: PS/EA, 19:1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.12 (s, 4 H), 7.03–7.11 (m, 4 H), 7.23–7.42 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 75.4, 122.0, 124.0, 130.0, 130.1, 131.0, 160.3 ppm. IR (film): $\tilde{\nu}_{max}$ = 2950, 1600, 1488, 1305, 1273, 1186 cm^{-1}. MS (ESI): *m*/*z* = 235 [MNa]$^+$. $C_{14}H_{12}O_2$ (212.24): calcd. C 79.22, H 5.70; found C 79.46, H 5.56.

(2*R*,3*R*,3a*S*,11a*R*)-2,3-Isopropylidenedioxy-3,3a,11,11a-tetrahydro-2*H*,5*H*-1,4,10-trioxabenzo[*a*]cyclopenta[*e*]cyclooctene (5a): Pale yellow solid, m.p. 102 °C. Yield 181 mg (65%) (eluent: PS/EA, 9:1). $[\alpha]_D^{25}$ = +24.0 (*c* = 2.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.34 (s, 3 H), 1.52 (s, 3 H), 3.78 (t, *J* = 10.5 Hz, 1 H), 4.45 (d, *J* = 3.3 Hz, 1 H), 4.55 (dd, *J* = 10.7, 5.5 Hz, 1 H), 4.63 (d, *J* = 14.2 Hz, 1 H), 4.66 (d, *J* = 5.4 Hz, 1 H), 4.71–4.75 (m, 1 H), 4.89 (d, *J* = 13.6 Hz, 1 H), 5.91 (d, *J* = 3.4 Hz, 1 H), 7.24–7.77 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 26.4, 27.1, 74.3, 76.2, 79.5, 85.4, 89.0, 105.2, 112.0, 122.3, 124.2, 129.8, 130.0, 131.5 161.0 ppm. IR (film): $\tilde{\nu}_{max}$ = 2989, 2934, 1492, 1253, 1084 cm^{-1}. MS (ESI): *m*/*z* = 301 [MNa]$^+$. $C_{15}H_{18}O_5$ (278.30): calcd. C 64.74, H 6.52; found C 64.49, H 6.35.

(2*R*,3*R*,3a*R*,11a*R*)-2,3-Isopropylidenedioxy-3,3a,11,11a-tetrahydro-2*H*,5*H*-1,4,10-trioxabenzo[*a*]cyclopenta[*e*]cyclooctene (5b): Pale-yellow sticky liquid. Yield 180 mg (65%) (eluent: PS/EA, 17:3). $[\alpha]_D^{25}$ = –28.3 (*c* = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.33 (s, 3 H), 1.49 (s, 3 H), 3.78 (t, *J* = 11.3 Hz, 1 H), 4.06 (dd, *J* = 8.0, 4.8 Hz, 1 H), 4.19–4.24 (m, 1 H), 4.50 (dd, *J* = 11.4, 5.4 Hz, 1 H), 4.69 (t, *J* = 3.7 Hz, 1 H), 4.74 (d, *J* = 12.1 Hz, 1 H), 4.85 (d, *J* = 12.1 Hz, 1 H), 5.72 (d, *J* = 3.2 Hz, 1 H), 7.12–7.38 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 26.5, 27.0, 69.1, 75.1, 77.3, 80.8, 82.7, 103.6, 113.4, 121.5, 125.1, 130.8, 131.1, 131.7, 158.0 ppm. IR (film): $\tilde{\nu}_{max}$ = 2930, 1453, 1372, 1252, 1029 cm^{-1}. MS (ESI): *m*/*z* = 301 [MNa]$^+$. $C_{15}H_{18}O_5$ (278.30): calcd. C 64.74, H 6.52; found C 64.61, H 6.59.

(2*S*,3*S*,4*S*,4a*R*,12a*R*)-3,4-Isopropylidenedioxy-2-methoxy-2,3,4,4a,12,12a-hexahydro-6*H*-1,5,11-trioxadibenzo[*a*,*e*]cyclooctene (7): White crystalline solid, m.p. 124 °C. Yield 216 mg (67%) (eluent: PS/EA, 9:1). $[\alpha]_D^{25}$ = +62.9 (*c* = 0.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 1.48 (s, 3 H), 1.59 (s, 3 H), 3.39 (s, 3 H), 3.68–3.72 (m, 1 H), 3.77–3.83 (m, 3 H), 3.89–3.96 (m, 2 H), 4.73 (d, *J* = 13.2 Hz, 1 H), 4.79 (d, *J* = 13.2 Hz, 1 H), 4.88 (d, *J* = 4.2 Hz, 1 H), 7.01–7.04 (m, 1 H), 7.13–7.17 (m, 2 H), 7.22–7.26 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 19.1, 29.2, 55.2, 62.5, 63.3, 71.7, 72.9, 81.0, 83.0, 99.3, 99.8, 121.4, 123.8, 129.3, 129.5, 132.3, 158.2 ppm. IR (film): $\tilde{\nu}_{max}$ = 2993, 2918, 1487, 1372, 1264 cm^{-1}. MS (ESI): *m*/*z* = 345 [MNa]$^+$. $C_{17}H_{22}O_6$ (322.35): calcd. C 63.34, H 6.88; found C 63.06, H 6.64.

(3*R*,4*R*)-4-Acetoxymethyl-3,4-dihydro-2*H*,6*H*-benzo[1,5]dioxocin-3-yl Acetate (8): Compound **5a** (1 mmol) was dissolved in CH_3CN/H_2O (3:1) containing 4% H_2SO_4. The mixture was stirred at 0 °C for 3 h and then at room temperature for 5 h. The acidic solution was neutralized with solid $NaHCO_3$ at 0 °C and filtered. The filtrate was evaporated in vacuo. The residue was extracted with ethyl acetate (6 × 25 mL) and the combined organic layers were dried and concentrated under vacuum. The colorless residue was dissolved in a minimum volume of methanol and treated with aqueous $NaIO_4$ (256 mg, 1.2 mmol, dissolved in 3 mL of water) at 0 °C, then stirred for 45 min at room temperature. Usual work up followed by $NaBH_4$ (1.5 mmol, 57 mg) reduction of the crude in dry methanol (20 mL) afforded the diol. This was dissolved in dry pyridine (5 mL), treated with Ac_2O (0.5 mL), and stirred at room temperature for 12 h. Pyridine was evaporated from the reaction mixture under reduced pressure and the product was extracted with $CHCl_3$ (6 × 25 mL). The combined organic layers were washed successively with cold aqueous HCl (1% v/v, 2 × 30 mL) and water (3 × 50 mL) and then dried. The solvent was evaporated under vacuum. The crude mass was purified by silica gel flash chromatography to afford the diacetate **8** as a colorless oil.

Overall yield 176 mg (60%) (eluent: PS/EA, 17:3). $[\alpha]_D^{25}$ = –42.0 (*c* = 1.1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 1.93 (s, 3 H), 2.08 (s, 3 H), 4.03 (dd, *J* = 12.3, 5.4 Hz, 1 H), 4.09 (dd, *J* = 10.8, 5.4 Hz, 1 H), 4.22 (dd, *J* = 10.8, 7.2 Hz, 1 H), 4.26 (dt, *J* = 7.2, 1.8 Hz, 1 H), 4.38 (dd, *J* = 12.6, 4.8 Hz, 1 H), 4.73 (d, *J* = 13.2 Hz, 1 H), 4.90 (d, *J* = 13.2 Hz, 1 H), 5.15 (dt, *J* = 4.8, 1.8 Hz, 1 H), 7.09–7.31 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 20.6, 20.8, 64.4, 71.8, 72.7, 75.5, 78.1, 122.0, 124.7, 130.0, 130.1, 132.0, 159.6, 170.3, 170.7 ppm. IR (film): $\tilde{\nu}_{max}$ = 2935, 1744, 1491, 1454, 1371, 1232 cm^{-1}. MS (ESI): *m*/*z* = 317 [MNa]$^+$. $C_{15}H_{18}O_6$ (294.30): calcd. C 61.22, H 6.16; found C 61.03, H 6.24.

Supporting Information (see also the footnote of the first page of this article): Experimental details and ^{1}H and ^{13}C NMR spectra for compounds **1a**–**c**, **2**, **4a**–**e**, **5a**,**b**, **6a**,**b**, **7**, **8**.

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