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Note

Trifluoroacetic acid-mediated facile transformation of 2-*C*-hydroxymethyl-D-glycals to chiral pyrano[2,3-*b*]benzopyrans

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ABSTRACT

Treatment of 2-*C*-hydroxymethyl-D-glycals with phenols in trifluoroacetic acid at ambient temperature leads to an extremely facile transformation affording chiral pyrano[2,3-*b*]benzopyrans in high yields.
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Benzopyrans, an important class of oxygenated heterocycles, constitute the core skeleton of many complex natural products.[1,2] In general, most of the benzopyran derivatives are synthesized by condensation of salicylaldehyde or its derivatives with various conjugated olefins.[3–8] Booma and Balasubramanian reported the synthesis of fused chiral pyrano[2,3-*b*]benzopyrans from the reaction of 3,4,6-tri-*O*-protected 2-*C*-acetoxymethyl-D-glycals with phenols in the presence of $BF_3{\cdot}Et_2O$.[9] Yadav et al. described the synthesis of 3,4-dihydro-2*H*-1-benzopyrans from the reaction of 3,4-dihydro-2*H*-pyrans and salicylaldehydes.[10] Since then, only a few reports have appeared in the literature on the use of other catalysts for effecting this transformation.[11,12] A survey of the literature indicated that the Ferrier rearrangement has been carried out mostly on protected glycals, such as allylic acetates of glycals, and not directly on glycals with free allylic-OH groups, indicating that prior activation of the allylic hydroxyl group is necessary for realizing the Ferrier rearrangement.[13,14] However, there are a few examples of trifluoroacetic acid (TFA) and trifluoromethanesulfonic acid-catalyzed Ferrier rearrangements involving the unactivated allylic hydroxyl group of exocyclic and endocyclic glycals.[15,16] TFA is known to mediate various types of glycosidation, addition and cyclization reactions,[17–21] and to our knowledge, the transformation of 2-*C*-hydroxymethyl or 2-*C*-acetoxymethylglycals to pyranobenzopyrans with phenols using TFA has not yet been investigated.

Herein, we report on an extremely facile transformation of 2-*C*-hydroxymethyl-D-glycals **1**–**4** to chiral pyrano[2,3-*b*]benzopyrans catalyzed by TFA at ambient temperature in good-to-excellent yields without prior activation of the allylic hydroxyl group.

The key glycals **1**–**4** were synthesized as reported in the literature starting from tri-*O*-acetyl-D-glycals.[22–25] Exposure of **1** and *p*-cresol **5a** with TFA at ambient temperature led to an instantaneous reaction that resulted in the formation of the α-pyrano[2,3-*b*]benzopyran **6a** as the major product and β-pyrano[2,3-*b*]benzopyran **10a** as the minor product (Scheme 1), in 94% yield (Table 1, entry 1). The reaction was also equally facile in the case of the reaction of other 2-*C*-hydroxymethylglycals **2**–**4** with *p*-cresol. The generality of this transformation has been successfully tested on glycals **1**–**4** using *p*-cresol **5a**, *p*-methoxyphenol **5b** (Scheme 1) and β-naphthol **5c** (Scheme 2). We observe that in the case of glucals **1** and **3**, the α anomer was found to be the major product and the β anomer the minor product (Table 1, entries 1–3 and 7–9). In the case of galactals **2** and **4**, the α anomer is almost the exclusive product (Table 1, entries 4–6 and 10–12). All the pyrano [2,3-*b*]benzopyrans listed in Table 1 were characterized by NMR spectroscopy, and all are in accord with those reported in the literature.[9,11,12] The assignments of α and β configurations were based on NOE experiments and also on the comparison of the NMR spectral data with those reported in the literature.[9,12] The regioselectivity of phenol addition was based on earlier literature reports of these products and also on the NMR chemical shifts of the anomeric protons.[9] The exact mechanism of this transformation is unknown.

It is of interest to note that, unlike the electron-donating phenols, the reaction of glycals **1**–**4** with *p*-nitrophenol as the nucleophile did not afford any clean product. As acetic acid is relatively weaker as an acid and is cheaper than TFA, we explored the Ferrier

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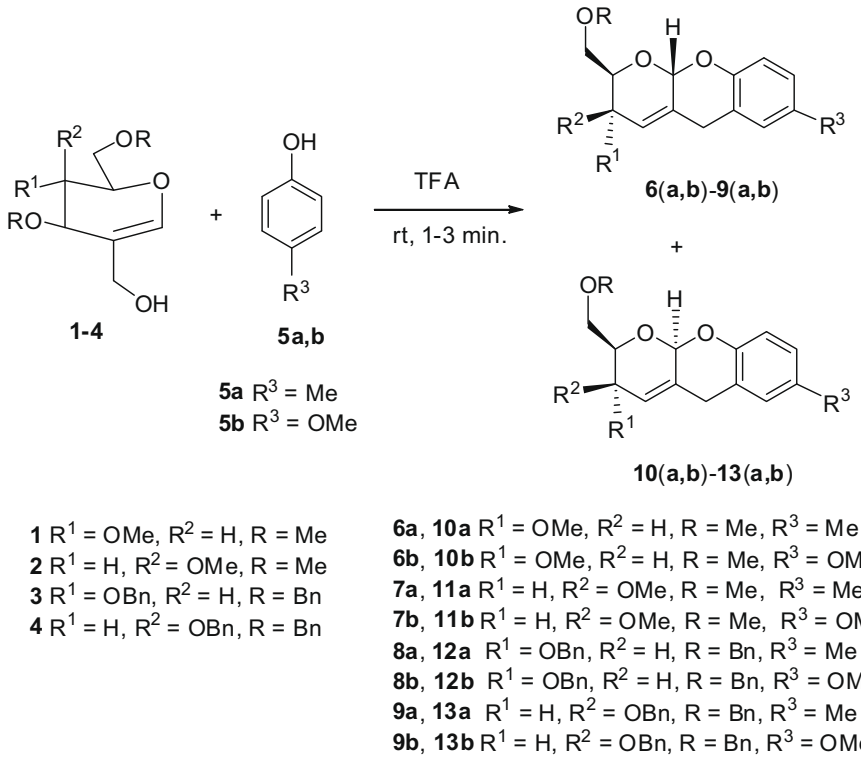


Scheme 1. Synthesis of chiral pyranobenzopyrans.

rearrangement of glycals **1**–**4** with *p*-cresol **5a** using acetic acid solvent. Surprisingly, it did not lead to any product formation, even after a 48-h reaction time.

In conclusion, TFA is found to be a versatile reagent for the facile conversion of 2-*C*-hydroxylmethylglycals with phenols to chiral pyrano[2,3-*b*]benzopyrans without the need for prior activation of the allylic hydroxyl group of glycals as acetates.

1. Experimental

1.1. General

Trifluoroacetic acid purchased from Sigma–Aldrich was used directly without further purification. All solvents used for workup were purchased from commercial sources. All TFA reactions were carried out in open glass flasks. NMR spectra were recorded on Bruker DPX-300 (300 MHz) in $CDCl_3$ containing trimethylsilane. Specific optical rotations were recorded on Autopol-V80000 instrument. IR spectra were recorded on a Perkin–Elmer instrument. High-resolution mass spectra (HRESIMS) were recorded on a QSTAR instrument. Melting points were determined on a Veego (VMP-PM) apparatus and are uncorrected. In the case of glucals, α and β anomers could not be separated by column chromatography. However, the α anomer could be obtained by repeated crystallization of the mixture. In the case of galactals, the α anomer was the major product, and it was isolated by column chromatography. All the new compounds were thoroughly characterized by NMR, HSQC and NOE experiments. For TLC analysis, the solvent system used was 7:3 hexane–EtOAc.

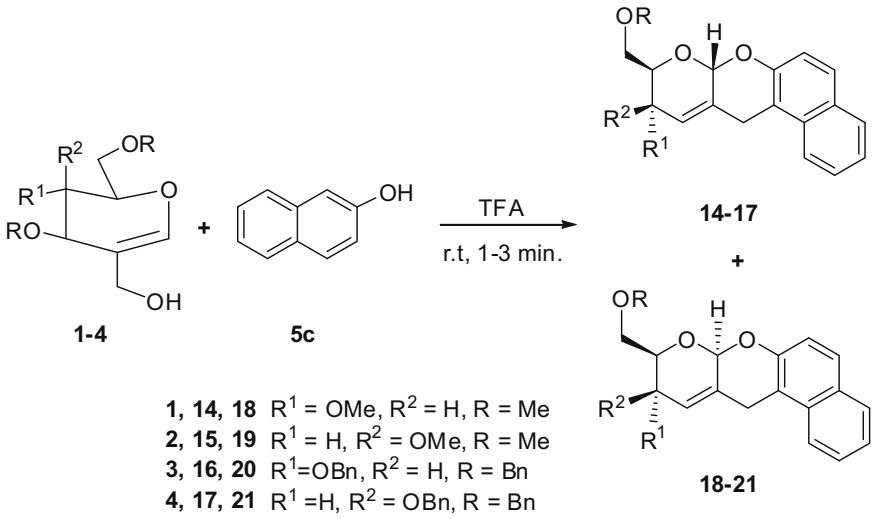
1.2. General experimental procedure

To a solution of 2-*C*-hydroxymethyl-D-glucal **1**–**4** (0.4 mmol) and phenol **5a**–**c** (0.8 mmol) was added TFA (2 mL), and the mix-

Table 1
TFA mediated synthesis of pyrano[2,3-*b*]pyrans

Entry	Glycal	Phenol	Product (s) (α and β)	Yield[a] (%)	Ratio[b] (α:β)
1	**1**	*p*-Cresol	**6a** and **10a**	94	2.5:1
2	**1**	*p*-Methoxyphenol	**6b** and **10b**	81	3.5:1
3	**1**	β-Naphthol	**14** and **18**	96	3.5:1
4	**2**	*p*-Cresol	**7a** and **11a**	94	~95% α
5	**2**	*p*-Methoxyphenol	**7b** and **11b**	88	~98% α
6	**2**	β-Naphthol	**15** and **19**	94	~98% α
7	**3**	*p*-Cresol	**8a** and **12a**	94	2.1: 0.9
8	**3**	*p*-Methoxyphenol	**8b** and **12b**	96	3: 2
9	**3**	β-Naphthol	**16** and **20**	97	3:1.5
10	**4**	*p*-Cresol	**9a** and **13a**	93	~95% α
11	**4**	*p*-Methoxyphenol	**9b** and **13b**	94	~98% α
12	**4**	β-Naphthol	**17** and **21**	92	~98% α

[a] Isolated yields after column chromatography.
[b] Determined by relative integration of proton H-10a/H-12a in glucal series and H-4 proton in galactal series in the ^{1}H NMR spectrum of the crude product.



Scheme 2. Synthesis of pyranonaphthopyrans.

ture was stirred at rt for 1–3 min. The reaction was monitored by TLC (and can also be monitored by ^{1}H NMR spectrum with TFA-*d*). The reaction mixture was diluted with H_2O (10 mL) and extracted with EtOAc (3 × 10 mL). The organic layer was washed with 10% NaOH (2 × 5 mL), followed by brine (5 mL), dried over anhyd Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash column chromatography on silica gel (230–400 mesh) using hexane–EtOAc as the eluant.

1.2.1. (2*R*,3*S*,10a*R*)-3,10a-Dihydro-2-methoxymethyl-3-methoxy-7-methy1-2*H*,5*H*-pyrano[2,3-*b*][1]benzopyran (6a)[11]

Mp 107–108 °C (lit.[11] 107 °C); R_f: 0.38; ^{1}H NMR (δ): 2.24 (s, 3H, CH_3), 3.35 (br d, *J* = 18 Hz, 1H, H-5A), 3.42 (s, 3H, OCH_3), 3.46 (s, 3H, OCH_3), 3.66–3.76 (m, 3H, H-5B, H-2′), 3.85 (dt, *J* = 3.0, 9.0 Hz, 1H, H-2), 4.01 (dd, *J* = 3.0, 9.0 Hz, 1H, H-3), 5.5 (s, 1H, H-10a), 6.00 (s, 1H, H-4), 6.78–6.92 (m, 3H, arom.H); ^{13}C NMR (δ): 20.46 (q, CH_3), 32.97 (t, C-5), 56.68, 59.47 (2q, OCH_3), 71.12 (t, C-2′), 71.57, 72.12 (2d, C-2, C-3), 93.61 (d, C-10a), 117.02 (d, C-4), 120.61 (s, C-4a), 123.09, 128.23, 128.91 (3d, arom.CH), 130.38, 130.66, 151.40 (3*s*, arom.C).

1.2.2. (2*R*,3*S*,10a*R*)-3,10a-Dihydro-2-methoxymethyl-3-methoxy-7-methoxy-2*H*,5*H*-pyrano[2,3-*b*][1]benzopyran (6b)

Mp 94–95 °C; R_f: 0.28; $[\alpha]_D^{28}$ −140.39° (*c* 0.84, CH_2Cl_2); ^{1}H NMR: δ 3.37 (d, *J* = 18.0 Hz, 1H, H-5A), 3.43, 3.46 (2s, 6H, 2 × OCH_3), 3.67–3.76 (m, 6H, H-5B, H-2′, OCH_3), 3.85 (td, *J* = 3.0, 9.0 Hz, 1H, H-2), 4.01 (dd, *J* = 6.0, 9.0 Hz, 1H, H-3), 5.48 (s, 1H, H-10a), 6.01 (br s, 1H, H-4), 6.56 (d, *J* = 3.0 Hz, 1H, H-6), 6.69 (dd, *J* = 3.0, 9.0 Hz, 1H, H-8), 6.82 (d, *J* = 9.0 Hz, 1H, H-9); ^{13}C NMR: δ 33.19 (t, C-5), 55.73, 56.72, 59.47 (3q, 3 × OCH_3), 71.13 (t, C-2′), 71.61 (d, C-2), 72.14 (d, C-3), 93.57 (d, C-10a), 113.12, 113.66, 117.93 (3d, arom.CH), 121.54 (s, C-4a), 123.24 (d, C-4), 130.57, 147.61, 154.00 (3s, arom.C); IR (KBr, cm^{-1}): 2994, 2921, 2833, 1592, 1500, 1435, 1393, 1268, 1108, 956, 923; ESIMS (*m*/*z*): 315.12 [M+Na], 261.11 [M−OCH_3]; HRESIMS: Calcd for [$C_{16}H_{20}O_5$+Na]: 315.1208, found: 315.1213.

1.2.3. (2*R*,3*S*,12a*R*)-2,3,5,12a-Tetrahydro-2-methoxymethyl-3-methoxy-[2,3-*b*]naphtho[1,2-*e*]pyran (14)[12]

Mp 199–200 °C (lit.[12] 201 °C); R_f: 0.41; ^{1}H NMR: δ 3.45, 3.49 (2s, 6H, 2 × OCH_3), 3.73–3.77 (m, 2H, H-2′), 3.78–3.81 (m, 1H, H-5A), 3.91–3.97 (m, 2H, H-5B, H-2), 4.07 (dd, *J* = 3.3, 9.2 Hz, 1H, H-3), 5.62 (s, 1H, H-12a), 6.13 (s, 1H, H-4), 7.12, 7.64 (2d, *J* = 8.9 Hz, 2H, H-10, H-11), 7.36, 7.50 (2t, *J* = 7.5 Hz, 2H, H-7, H-8), 7.72–7.78 (m, 2H, H-6, H-9); ^{13}C NMR: δ 30.38 (t, C-5), 56.71, 59.49 (2*q*, 2×OCH_3), 71.14 (t, C-2′), 71.80 (d, C-2), 72.19 (d, C-3), 93.65 (d, C-12a), 112.75 (s, C-4a), 119.03, 121.83, 123.63 (d, arom.CH), 123.69 (d, C-4), 126.63, 128.34, 128.50 (3d, arom.CH), 129.20, 130.50, 132.18, 151.20 (4s, arom.C).

1.2.4. (2*R*,3*R*,10a*R*)-3,10a-Dihydro-2-methoxymethyl-3-methoxy-7-methy1-2*H*,5*H*-pyrano[2,3-*b*][1]benzopyran (7a)

Mp 84–86 °C; R_f: 0.55; $[\alpha]_D^{25}$ −175.2° (*c* 0.4, $CHCl_3$); ^{1}H NMR: δ 2.24 (s, 3H, CH_3), 3.43, 3.45 (2s, 6H, 2 × OCH_3), 3.37 (d, *J* = 18 Hz, 1H, H-5A), 3.63 (dd, *J* = 2.0, 5.6 Hz, 1H, H-3), 3.70 (br d, *J* ∼ 6.0 Hz, 2H, H-2′), 3.75 (d, *J* = 18 Hz, 1H, H-5B), 4.17 (td, *J* = 2.4, 6.0 Hz, 1H, H-2), 5.57 (s, 1H, H-10a), 6.18 (dd, *J* = 2.4, 6.0 Hz, 1H, H-4), 6.80 (d, *J* = 8.4 Hz, 1H, H-9), 6.84 (br s, 1H, H-6), 6.90 (d, *J* = 8.0 Hz, 1H, H-8); ^{13}C NMR: δ 20.47 (q, CH_3), 33.56 (t, C-5), 56.85, 59.33 (2q, 2 × OCH_3), 69.66, 71.52 (2d, C-2, C-3), 71.48 (t, C-2′), 93.39 (d, C-10a), 120.58 (s, C-4a), 117.11, 119.21, 128.33, 128.94 (4d, C-4, 3 × arom.CH), 120.58, 130.50, 135.16, 151.32 (4s, C-4a, arom.C); IR (neat, cm^{-1}): 2912, 2886, 1577, 1491, 1450, 1380, 1210, 1190, 1050, 980; HRESIMS: Calcd for [$C_{16}H_{20}O_4$+Na]: 299.1259, found:299.1259.

1.2.5. (2*R*,3*R*,10a*R*)-3,10a-Dihydro-2-methoxymethyl-3-methoxy-7-methoxy-2*H*,5*H*-pyrano[2,3-*b*][1]benzopyran (7b)

Mp 67–68 °C; R_f: 0.32; $[\alpha]_D^{25}$ −380.5° (*c* 0.55, CH_2Cl_2); ^{1}H NMR: δ 3.39 (d, *J* = 18 Hz, 1H, H-5A), 3.43, 3.45 (2s, 6H, 2 × OCH_3), 3.63 (dd, *J* = 2.3, 5.7 Hz, 1H, H-3), 3.70 (br d, *J* = 6.3 Hz, 2H, H-2′), 3.74 (s, 3H, OCH_3), 3.81 (d, *J* = 18 Hz, 1H, H-5B), 4.18 (td, *J* = 2.3, 6.6 Hz, 1H, H-2), 5.56 (s, 1H, H-10a), 6.19 (dd, *J* = 1.8, 5.7 Hz, 1H, H-4), 6.58 (d, *J* = 1.8 Hz, 1H, H-6), 6.69 (dd, *J* = 2.7, 9.0 Hz, 1H, H-8), 6.84 (d, *J* = 9.0 Hz, 1H, H-9); ^{13}C NMR: δ 33.79 (t, C-5), 55.75, 56.88, 59.32 (3q, OCH_3), 69.68 (d, C-3), 71.53 (t, C-2′), 71.55 (d, C-2), 93.40 (d, C-10a), 113.16, 113.79, 118.05 (3d, arom.CH), 119.38 (d, C-4), 121.52, 135.08, 147.57, 154.08 (4s, C-4a, arom.C); IR (neat, cm^{-1}): 3054, 2985, 2832, 1494, 1429, 1212, 1094, 1039, 959; HRESIMS: Calcd for [$C_{16}H_{20}O_5$+Na]: 315.1208, found: 315.1203.

1.2.6. (2*R*,3*R*,12a*R*)-2,3,5,12a-Tetrahydro-2-methoxymethyl-3-methoxy-[2,3-*b*]naphtho[1,2-*e*]pyran (15)[12]

Mp 93–94 °C (lit.[12] 91 °C); R_f: 0.47; ^{1}H NMR: δ 3.46, 3.47 (2s, 6H, 2 × OCH_3), 3.66 (dd, *J* = 2.1, 5.8 Hz, H-3), 3.71–3.80 (m, 3H, H-5A, H-5B, H-2′A), 3.97 (d, *J* = 18.0 Hz, 1H, H-2′B), 4.24 (dt, *J* = 2.1, 6.0 Hz, 1H, H-2), 5.70 (s, 1H, H-12a), 6.30 (dd, *J* = 2.1, 5.7 Hz, 1H, H-4), 7.13, 7.63 (2d, *J* = 9.0 Hz, 2H, H-10, H-11), 7.36, 7.51 (2dd,

J = 2.1, 8.3 Hz, 2H, H-6, H-9), 7.70–7.77 (m, 2H, H-7, H-8); ^{13}C NMR: δ 3.96 (t, C-5), 56.90, 59.35 (2q, 2 × OCH_3), 69.70, 71.70 (2d, C-2, C-3), 71.59 (t, C-2′), 93.50 (d, C-12a), 112.72 (s, C-4a), 119.05, 119.74, 121.80, 123.76, 126.70, 128.42, 128.53 (7d, arom.CH), 129.23, 132.18, 135.05, 151.20 (4s, arom.C).

1.2.7. (2*R*,3*S*,10a*R*)-3,10a-Dihydro-2-benzyloxymethyl-3-benzyloxy-7-methy1-2*H*,5*H*-pyrano[2,3-*b*][1]benzopyran (8a)[9]

Mp 84–85 °C; R_f: 0.58; $[\alpha]_D^{25}$ −81° (*c* 0.6, CH_2Cl_2); ^{1}H NMR: δ 2.24 (s, 3H, CH_3), 3.34 (d, J = 18.0 Hz, 1H, H-5A), 3.68 (br d, J = 18.0 Hz, 1H, H-5B), 3.81 (d, J = 2.1 Hz, 1H, H-2′), 3.94 (br d, J = 8.0 Hz, 1H, H-2), 4.34 (dd, J = 3.0, 6.0 Hz, 1H, H-3), 4.46–4.70 (m, 4H, 2 × CH_2), 5.52 (s, 1H, H-10a), 5.99 (br s, 1H, H-4), 6.77–6.92 (m, 3H, arom.H), 7.23–7.36 (m, 10H, arom.H); ^{13}C NMR: δ 20.46 (q, CH_3), 32.97 (t, C-5), 68.22 (d, C-2′), 70.37 (d, C-3), 71.38 (t, CH_2), 71.89 (d, C-2), 73.55 (t, CH_2), 93.67 (d, C-10a), 116.96, 120.60, 127.66, 127.80, 127.97, 128.23, 128.39 (8d, arom.CH), 123.75 (d, C-4),128.91, 130.36, 130.52, 137.91, 138.09, 151.39 (6s, C-4a, 5×arom.C); IR ($CHCl_3$, cm^{-1}): 3040, 2864, 1605, 1590, 1495, 1390, 1310, 1200, 1170, 1120, 1075, 960, 930.; HRESIMS: Calcd for [$C_{28}H_{28}O_4$+Na]: 451.1885, found: 451.1887.

1.2.8. (2*R*,3*S*,10a*R*)-3,10a-Dihydro-2-benzyloxymethyl-3-benzyloxy-7-methoxy-2*H*,5*H*-pyrano[2,3-*b*][1]benzopyran (8b)[9]

Mp 102–103 °C; R_f: 0.50; $[\alpha]_D^{25}$ −83° (*c* 1.1, CH_2Cl_2); ^{1}H NMR: δ 3.36 (d, J = 18.0 Hz, 1H, H-5A), 3.71 (d, J = 18.0 Hz, 1H, H-5B), 3.73 (s, 3H, OCH_3), 3.80 (br d, J = 3.0 Hz, 2H, H-2′), 3.94 (dt, J = 2.1, 9.0 Hz, 1H, H-2), 4.34 (dd, J = 3.0, 9.0 Hz, 1H, H-3), 4.46–4.70 (m, 4H, 2 × CH_2), 5.50 (s, 1H, H-10a), 5.99 (s, 1H, H-4), 6.55 (d, J = 3.0 Hz, 1H, H-6), 6.69 (dd, J = 2.1, 9.3 Hz, 1H, H-8), 6.80 (d, J = 9.3 Hz, H-9); ^{13}C NMR: δ 33.19 (t, C-5), 55.70 (q, OCH_3), 68.21 (t, C-2′), 70.37 (d, C-3), 71.42 (t, CH_2), 71.91 (d, C-2), 73.55 (t, CH_2), 93.61 (d, H-10a), 113.11, 113.63, 117.87, (3d, arom.CH), 121.53 (s, C-4a), 123.89 (d, C-4), 127.67, 127.82, 127.88, 127.97, 128.39 (5d, arom.C); IR ($CHCl_3$, cm^{-1}): 3040, 2860, 1605, 1590, 1495, 1390, 1365, 1310, 1200, 1170, 1075, 960; HRESIMS: Calcd for [$C_{28}H_{28}O_5$+Na]: 467.1834, found: 467.1836.

1.2.9. (2*R*,3*S*,12a*R*)-2,3,5,12a-Tetrahydro-2-benzyloxymethyl-3-benzyloxy-[2,3-*b*]naphtho[1,2-*e*]pyran (16)

Mp 164–165 °C; R_f: 0.61; $[\alpha]_D^{25}$ −206.6° (*c* 0.79, CH_2Cl_2); ^{1}H NMR: δ 3.74 (d, J = 18.0 Hz, 1H, H-5A), 3.85 (d, J = 1.8 Hz, 2H, H-2′), 3.92 (d, J = 18.0 Hz, 1H, H-5B), 4.03 (dt, J = 3.0, 9.0 Hz, 1H, H-2), 4.40 (dd, J = 3.0, 9.0 Hz, 1H, H-3), 4.49–4.72 (m, 4H, 2 × CH_2), 5.64 (s, 1H, H-10a), 6.12 (br s, 1H, H-4), 7.12, 7.64 (2d, J = 9.0 Hz, 2H, H-10, H-11), 7.27–7.37 (m, 11H, arom.H), 7.50 (br t, J = 6.0 Hz, 1H, arom.H), 7.71–7.78 (m, 2H, 2 × arom.H); ^{13}C NMR: δ 30.38 (t, C-5), 68.27 (t, C-2′), 70.47 (d, C-3), 71.43 (t, CH_2), 72.15 (d, C-2), 73.58 (t, CH_2), 93.71 (d, C-12a), 112.76 (s, C-4a), 119.00, 121.84, 123.68 (3d, arom.CH), 124.31 (*d*, C-4), 126.62, 127.68, 127.83, 127.89, 127.97, 128.40, 128.49 (7d, arom.CH), 129.21, 130.38, 132.20, 137.89, 138.10, 151.21 (6s, arom.C); IR (KBr, cm^{-1}): 3030, 2902, 1596, 1465, 1391, 1363, 1230, 1176, 1073, 971; HRESIMS: Calcd for [$C_{31}H_{28}O_4$+Na]: 487.1885, found: 487.1884.

1.2.10. (2*R*,3*R*,10a*R*)-3,10a-Dihydro-2-benzyloxymethyl-3-benzyloxy-7-methy1-2*H*,5*H*-pyrano[2,3-*b*][1]benzopyran (9a)[9]

Mp 99–100 °C; R_f: 0.64; $[\alpha]_D^{25}$ −268° (*c* 1.1, CH_2Cl_2); ^{1}H NMR: δ 2.24 (s, 3H, CH_3), 3.34 (d, 1H, J = 18.0 Hz, H-5A), 3.73 (br d, J = 18.0 Hz, 1H, H-5B), 3.76–3.89 (m, 3H, H-2′, H-3), 4.24 (td, J = 2.3, 7.3 Hz, H-2), 4.56–4.68 (AB quartet, J = 12.0 Hz, 2 × $PhCH_2$), 5.59 (s, 1H, H-10a), 6.06 (dd, J = 2.5, 6.4 Hz, 1H, H-4), 6.72 (d, J = 8.0 Hz, 1H, H-9), 6.78 (s, 1H, H-6), 6.88 (d, J = 8.0 Hz, H-8), 7.24–7.35 (m, 10H, arom.H); ^{13}C NMR: δ 20.46 (q, CH_3), 33.5 (t, C-5), 67.6 (d, C-3), 68.82 (t, C-2′), 71.22 (t, CH_2), 71.59 (d, C-2), 73.54 (t, CH_2), 93.48 (d, C-10a), 117.05 (d, arom.C), 119.80 (d, C-4), 120.64 (s, C-4a), 127.66, 127.33, 127.82, 127.86, 128.31, 128.38, 128.95, 129.98 (8d, arom.C), 130.47, 134.74, 138.08, 138.33, 151.32 (5s, arom.C); IR (KBr, cm^{-1}): 3040, 2886, 1600, 1588, 1485, 1390, 1360, 1335, 1180, 1085, 950, 825; ESIMS (*m*/*z*): 451.18 [M+Na], 429.5 [M+H], 321.15 [M−OBn]; HRESIMS: Calcd for $C_{28}H_{28}O_4$+Na: 451.1885, found: 451.1884.

1.2.11. (2*R*,3*R*,10a*R*)-3,10a-Dihydro-2-benzyloxymethyl-3-benzyloxy-7-methy1-2*H*,5*H*-pyrano[2,3-*b*][1]benzopyran (9b)[9]

Mp 89–90 °C; R_f: 0.52; $[\alpha]_D^{25}$ −281° (*c* 1.1, CH_2Cl_2); ^{1}H NMR: δ 3.36 (d, J = 18.0 Hz, 1H, H-5A), 3.74 (s, 3H, OCH_3), 3.79–3.89 (m, 4H, H-2′, H-5B, H-3), 4.24 (td, J = 2.4, 6.0 Hz, 1H, H-2), 4.65–4.69 (AB quartet, 4H, J = 12.0 Hz, 2 × CH_2), 5.57 (s, 1H, H-10a), 6.08 (dd, J = 2.9 Hz, 1H, H-4), 6.55 (d, J = 2.9 Hz, 1H, H-6), 6.69 (dd, J = 2.9, 8.1 Hz, 1H, H-8), 6.83 (d, J = 8.1 Hz, 1H, H-9), 7.25–7.39 (m, 10H, arom.H); ^{13}C NMR: δ 33.70 (t, C-5), 55.71 (q, OCH_3), 67.55 (d, C-3), 68.80 (t, C-2′), 71.26 (t, CH_2), 71.60 (d, C-2), 73.53 (t, CH_2), 93.43 (d, C-10a), 113.12, 113.72, 117.97 (3d, arom.CH), 119.94 (d, C-4), 121.56 (s, C-4a), 127.66, 127.74, 127.79, 127.82, 127.83, 128.37, 128.38 (7d, arom.CH), 134.61, 138.09, 138.32, 147.50, 154.02 (5s, arom.C); IR (KBr, cm^{-1}): 3040, 2885, 1600, 1588, 1485, 1390, 1365, 1330, 1180, 1080, 960, 830; HRESIMS: Calcd for [$C_{28}H_{28}O_5$+Na]: 467.1834, found: 467.1839.

1.2,12. (2*R*,3*R*,12a*R*)-2,3,5,12a-Tetrahydro-2-benzyloxymethyl-3-benzyloxy-[2,3-*b*]naphtho[1,2-*e*]pyran (17)

R_f: 0.61; $[\alpha]_D^{25}$ −254.89° (*c* 0.45, CH_2Cl_2); ^{1}H NMR: δ 3.73 (d, 1H, J = 18.0 Hz, H-5A), 3.87–3.97 (m, 4H, H-5B, H-2′, H-3), 4.31 (td, 1H, J = 3.2, 6.0 Hz, 1H, H-2), 4.61 (dd, J = 3.2, 12.0 Hz, 2H, CH_2), 4.70 (AB quartet, J = 12 Hz, 2H, CH_2), 5.70 (s, 1H, H-12a), 6.18 (dd, J = 1.5, 6.0 Hz, 1H, H-4), 7.06–7.13 (m, 2H, arom.H), 7.23–7.42 (m, 7H, arom.H), 7.49 (td, J = 1.2, 9.0 Hz, 1H, arom.H) 7.63 (dd, J = 3.0, 9.0 Hz, 2H, arom.H), 7.70–7.77 (m, 4H, arom.H); ^{13}C NMR: δ 30.89 (t, C-5), 67.61 (d, C-3), 68.88 (t, C-2′), 71.31 (t, CH_2), 71.86 (d, C-2), 73.59 (t, CH_2), 93.55 (d, C-12a), 112.77 (s, C-4a), 117.83, 119.00 (2d), 120.29 (d, C-4), 121.82, 123.48, 123.76 (3d, arom.CH), 126.33, 126.43, 126.70, 127.72, 127.82, 127.88, 128.42, 128.53, 128.82, 129.74 (11d, arom.CH), 132.18, 134.62, 138.00, 138.24, 151.13 (5s, arom.C); IR (KBr, cm^{-1}): 3067, 3018, 2855, 1598, 1466, 1397, 1215, 1115, 959, 927; ESIMS (*m*/*z*): 487.18 [M+Na], 471.35 [M−O+Na], 457.33 [M−O−CH_2+Na]; HRESIMS: Calcd for [$C_{31}H_{28}O_4$+Na]: 487.1885, found: 487.1864.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2008.12.020.

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