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Probing the Oxidation of Functionalized (Hexahydro)xanthenols

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Dedicated to Hans Musso (1925–1988), a pioneer in biaryl syntheses

Keywords: Xanthones / Biomimetic synthesis / Natural products / Oxidation

The oxidation of (hexahydro)xanthenols was investigated in terms of substrate spectrum and reaction conditions: Depending on the structure, diaryl ethers, biaryls or quinone acetals were formed.

Introduction

Nature provides a considerable number of oxidized natural products with great structural divergence. For most of them, a biosynthetic origin of linkage by oxidative phenolic coupling is most probable or has even been proven.[1–4] Following this biosynthetic guide, a great number of naturally occurring and designed oxidized systems have been prepared biomimetically, utilizing a broad range of oxidizing agents,[2,3,5–7] which usually have to be investigated specifically for each particular case. As a necessary prerequisite for these coupling reactions, the aromatic portions have to be electron-rich (ideally phenolic). But even if this condition is fulfilled, additional problems can arise from the presence of more than one reactive site in the phenolic precursor, so that, depending on the steric and electronic situation, the formation of different regioisomers must be taken into account, besides polymers, overoxidized products, or diaryl ethers.[2,3,6] For this reason, it is not always predictable which of the possible products will be formed predominantly, so that the choice and thorough optimization of the oxidizing reagent becomes an important prerequisite for successful transformations. Numerous investigations on oxidative coupling reagents and their use in biomimetic oxidative natural product syntheses have been part of reviews.[2,3,5,7]

A great number of biaryl natural products belong to the class of tetrahydroxanthone dimers, with the secalonic acids being the most prominent examples (Figure 1).

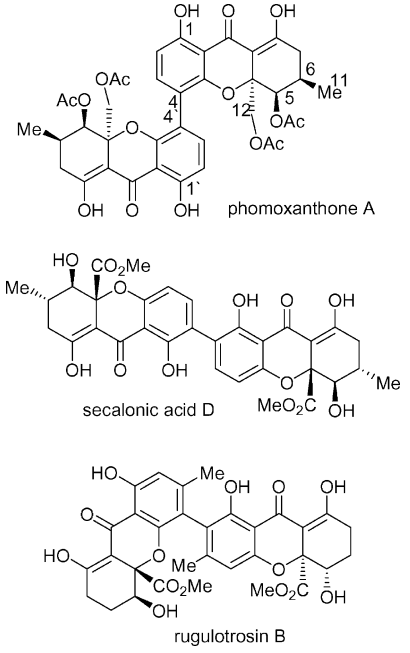

Figure 1. Natural products with tetrahydroxanthenone core.

The first elemental composition of a bisxanthone, ergoflavin, was disclosed about seventy years ago.[8] Its structure was published fifty years ago.[9] However, neither monomers nor the dimeric secalonic acids/ergoflavin have been prepared so far. In addition, to the best of our knowledge there is only one report on the dimerization of xanthone monomers.[10,11]

A large number of natural products having a dimeric (tetrahydro)xanthonyl unit have been isolated, most are symmetrical 2,2′-[12,13] and 4,4′-dimers.[14] A special case is the puupehenone family which dimerizes to symmetrical dimers.[15]

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Few unsymmetrical xanthone dimers such as 2,4-, like rugulotrosin[16] (Figure 1), and 1,4′-[17] are also known. In addition, some symmetrical 1,1′-,[18] 2,2′-,[19] 3,3′-,[20] 4,4′-dimers[18,21] have been prepared.

It is known that secalonic acids (2,2′-isomers) can isomerize to give 2,4′- or 4,4′-bond isomers by heating in a polar solvent. For example, they were heated in pyridine at 45 °C for 4 d to give a mixture of 2,4′- and 4,4′-isomers, which can be separated by chromatography. It is interesting to note that the 2,4′- and 4,4′-isomers showed a greater bactericidal activity than 2,2′-isomers.[22] Even if there are more than hundred xanthones known having a 3-hydroxy group, they are apparently not prone to oxidation in nature since 2,2′-dimers have not been isolated so far. In contrast, 2-xanthonyl-anthraquinones are known (euxanmodin B)[23] showing that nature uses this building block for biaryl linkage.

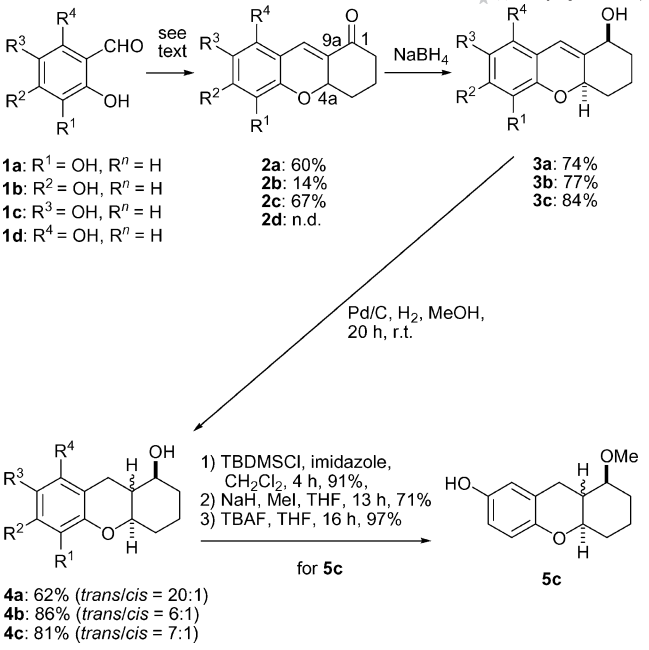
By evaluation of the literature, some remarks should be noted:

a) Specific requirements are necessary in general for oxidative biaryl coupling and many novel reagents have been developed to overcome these restrictions.

b) While naphthols can be dimerized under various conditions, chromanes (or even more xanthones) were reluctant to dimerization.[24,25] In fact, there are only three reports for the synthesis of bixanthonyls (according to CAS).[26]

c) Only few reagents gave high yield of desired biaryls[1]

In this manuscript we describe a systematic investigation on the oxidation of (hexahydro)xanthenols.



Scheme 1. Synthesis and modification of xanthenols.

Results and Discussion

First of all we studied the phenolic oxidation of the tetrahydroxanthenones **2**, which were synthesized according to a methodology developed in our group.[27] Thereby a mixture of a salicylic aldehyde **1** and cyclohexenone was sonicated in the presence of a base (methylimidazole or DABCO) for several days (Scheme 1).

The attempts to dimerize the tetrahydroxanthenones **2** with oxidizing agents like $[K_3Fe(CN)_6]$, $FeCl_3{\cdot}6H_2O$, Cu(OH)Cl·TMEDA and $(t\mathrm{Bu})_2O_2$ failed. Besides decomposition, we got isomerization of the double bond (Table 1, compound **6**). This might be caused by the conjugation of the ketone double bond and the acidic α-position of the carbonyl group.

Modification of the core was achieved by standard protocols: reduction of the carbonyl function proceeded stereoselectively[27] with sodium borohydride to give the novel alcohols **3a**–**c**. Hydrogenation to remove the double bond was performed with Pd/C under H_2 atmosphere to give xanthenols **4a**–**c**.[28] The stereochemistry of the mainly formed diastereoisomers (1,9a-*trans*) was established at a later stage (vide infra, compound **12**).

The *p*-(hydro)xanthenols **3c**, **4c** and **5c** proved to be suitable substrates for oxidation reactions while the other isomers **a**, **b** withstand all attempts to yield isolable dimeric products. We assume that the *meta*-phenoxy radicals products are not as stable as the *para*-phenoxy radicals derived from **3c** (see Scheme 3). The radicals generated form **3a** apparently react in an unselective manner yielding mixtures of isomers, oligomers and/or polymers.

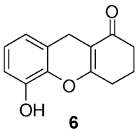
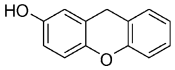
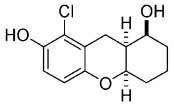
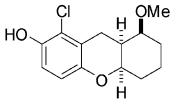
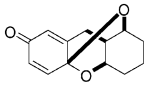
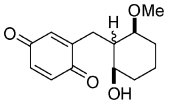
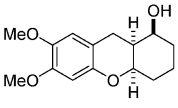
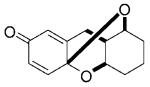
Dimerization of the (tetrahydro)xanthenol **3c** was achieved with $[K_3Fe(CN)_6]$ to give the 3,3′-dimer **7** in up to 45% yield as a mixture of *rac* and *meso* compounds (Table 1, entry 2). (Hexahydro)xanthenol **4c** lacking the double bond gave the diarylether **8** (Figure 2, Table 1, entry 3), again as a mixture of diastereoisomers. When the same reaction conditions were applied to (hydro)xanthenols **3a**,**b** and **4a**,**b**, no products could be isolated (data not shown).[29]

Interestingly, iron(III) chloride, a very common reagent for the dimerization of naphthols, gave different products depending on the reaction conditions. The reaction in solid state – e.g. using a conventional mortar or a ball-mill[30] – gave either chlorinated products **10**, **11** and/or aromatized product **9** (Table 1, entries 3–5).

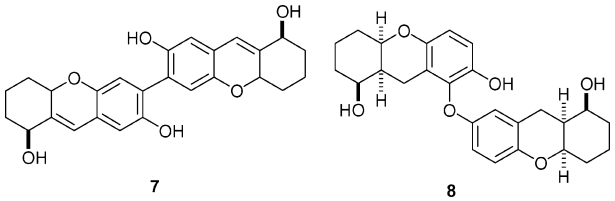
A novel heterocycle **12** was formed in excellent yield when water was used as solvent (Table 1, entry 7; see also Scheme 2). It is noteworthy that this product is generated from the 1,9a-*trans*-diastereoisomer of the starting material almost in a quantitative yield. The 1,9a-*cis*-diastereoisomer of **4c** was isolated unchanged.

The product **12** was also isolated by treatment of (hexahydro)xanthenol **4c** with lead tetraacetate (Table 1, entry 10). The methoxy-substituted isomer **5c** led to the quinone **13** as a single diastereoisomer (Table 1, entry 8). The formation of *p*-quinone acetals by lead(IV) reagents[31] or iron(III) chloride[32,33] has been reported. However, intramolecular formation of quinone acetals is less common.[34]

Table 1. Oxidation of xanthenols prepared.[29]

Entry	Xanthenol	Conditions	Product	Yield (%)[a]
1	**2a**	$FeCl_3$·6 H_2O, NaCl, 50 °C, 24 h	 **6**	16 (7% SM)
2	**3c**	$[K_3Fe(CN)_6]$, KOH, H_2O, MeOH, 4 d	dimer **7**	24–45[b]
3	**4c**	$[K_3Fe(CN)_6]$, KOH, H_2O, MeOH, 4 d	diaryl ether **8**	10 (13% SM)
4	**3c**	$FeCl_3$·6 H_2O, NaCl, ball milling, 2 h, 300 rpm	 **9**	15
5	**4c**	$FeCl_3$·6 H_2O, NaCl, ball milling, 1 h, 350 rpm	 **10**	43 (32% SM)
6	**5c**	$FeCl_3$·6 H_2O, NaCl, mortar	 **11**	34 (11% SM)
7	**4c**	$FeCl_3$·6 H_2O, H_2O, r.t., 24 h	 **12**	77 (14% *cis*-**4c**)
8	**5c**	$FeCl_3$·6 H_2O, H_2O, r.t., 7 h	 **13**	50
9	**4c**	$FeCl_3$·6 H_2O, MeOH, reflux, 17 h	 **14**	8 (9% **10**, 14% SM)
10	**4c**	$Pb(OAc)_4$, BF_3·OEt_2, CH_2Cl_2, 0 °C, 30 min	 **12**	45 (14% *cis*-**4c**)

[a] Isolated yields. SM: reisolated starting material. [b] The very poor solubility of the product led to various yields depending on scale and reaction vessel. The protocol in the experimental part furnished the optimized yield (45% plus 15% starting material) and is fully reproducible.



7 **8**

Figure 2. Biaryl **7** and diaryl ether **8**.

On the other hand, when the regioisomers **4a** and **4b** were treated with $FeCl_3$·$6H_2O$ in H_2O, no reaction took place (data not shown). In a further reaction, methanol was chosen as solvent instead of water. In that case, (hexahydro)xanthenol **4c** was oxidized yielding the catechol **14** and the chlorinated product **10** in albeit lower yields (Table 1, entry 9).

As shown in Table 1, a number of products were formed during oxidation of the xanthenols. The formation of these products origins from the generation of phenoxy radicals which react either via the oxygen atom or the ring carbon atoms (Scheme 3). Beside the desired dimers, the formation of *p*-quinones **13** as well as substitution of the aromatic ring are favored.

The stereochemistry of the heterocycle **12** was unequivocally proved by X-ray crystallography (see Exp. Sect.). It is interesting to note that this compound is a *meso* compound, prepared from a racemic structure having three stereogenic centers (Figure 3). Thus it is ideal for asymmetric synthesis.[35] A similar core was discovered before.[36]

Reaction of **12** with hydrogen peroxide under basic conditions led to the formation of the highly functionalized double oxirane **15** in 46% yield (Scheme 2). The stereo-

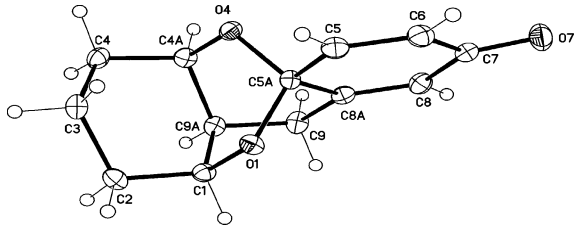
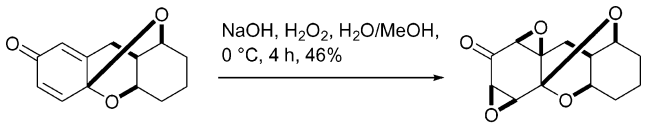


Figure 3. Molecular structure of **12**. Thermal ellipsoids are drawn at 50% probability level.



12 *rac*-**15**

Scheme 2. Synthesis of highly oxygenated xanthone **15**.

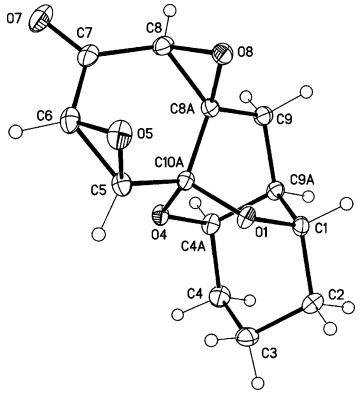
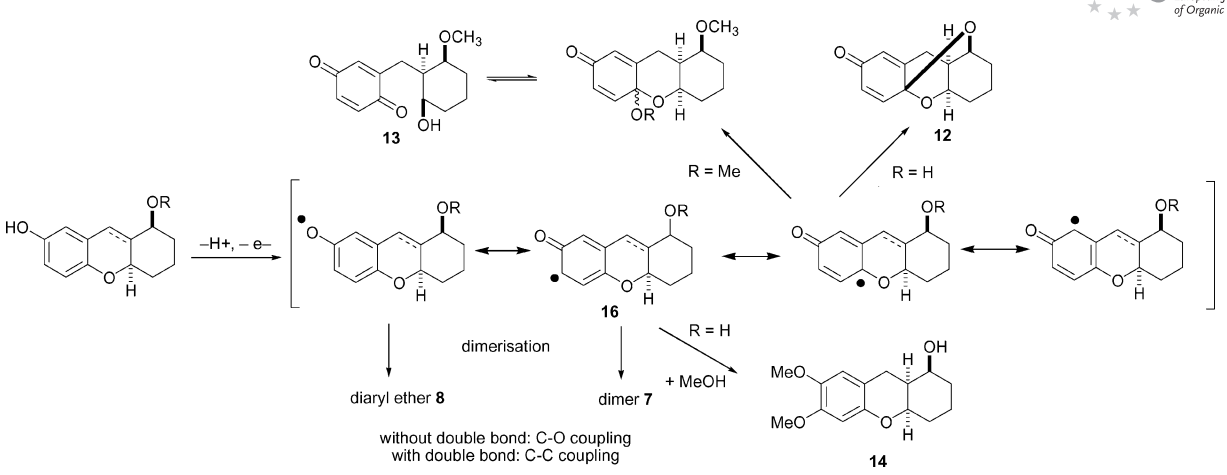


Figure 4. Molecular structure of **15**. Thermal ellipsoids are drawn at 50% probability level.



Scheme 3. Mechanism of the oxidation of xanthenols.

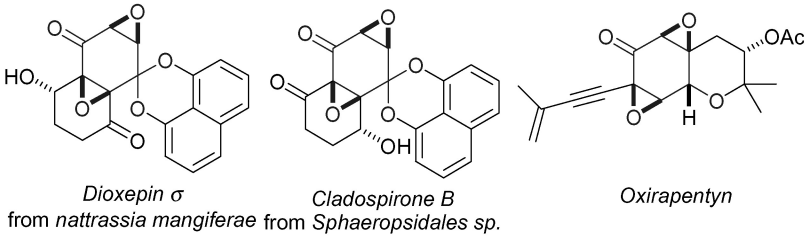


Figure 5. Oxygenated natural occurring cyclohexanes.

chemistry of the four new stereogenic centers[33,37] was determined by X-ray crystallography (see Exp. Sect. and Figure 4).

This heterocycle is a part of some natural products, namely oxirapentyn,[38] dioxepin σ[33] or the cladospirones (Figure 5).[39]

Discussions and Conclusions

Substituted xanthones proved to be challenging substrates for oxidation reactions. While *m*-substituted xanthones are reluctant to oxidation reactions, the *p*-substituted xanthenols **4c**, **5c** gave mesomeric stabilized radicals **16** which react depending on their substitution pattern. The more-stabilized radical **16** originated from the cinnamyl-like phenol **3c** smoothly gave the dimer **7** by C–C coupling. The analogue lacking the double bond (**4c**) gave no dimer under the same conditions, but in this case the carbon-centered radical reacts with a phenoxy-radical to give diaryl ether **8**. This tendency for C–O is also prone for the intramolecular acetalization to form the tricycle **12**.

In summary, we have investigated the oxidation of (hexahydro)xanthenols, depending on their substitution pattern, using phenolic oxidation. Despite difficulties of the reactions like polymerization, decomposition and the low solubility of the products formed, we were able to find the suitable reaction conditions for dimerization and/or quinone trapping. Besides looking for the suitable oxidizing agents, functionalization of the (hexahydro)xanthenols was undertaken. In addition, an unusual dienone **12** was detected.

Experimental Section

General: ^{1}H NMR spectra were recorded on a Bruker AM 400 (400 MHz), a Bruker DRX 500 (500 MHz) or on a Bruker Avance 600 (600 MHz) spectrometer. Chemical shifts are expressed in parts per million (ppm, δ) downfield from tetramethylsilane (TMS) and are referenced to $CHCl_3$ (δ =7.26 ppm), [D_5]acetone (δ =2.05 ppm) or [D_5]DMSO (δ = 2.50 ppm) as internal standard. All couplings constants are absolute values and *J* values are expressed in Hertz (Hz). The description of signals include: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, ddd = doublet of dd, dt = doublet of triplets, td = triplet of doublets. The spectra were analyzed according to first order. ^{13}C NMR spectra were recorded on a Bruker AM 400 (100 MHz), a Bruker DRX 500 (125 MHz) or on a Bruker Avance 600 (125 MHz) spectrometer. Chemical shifts are expressed in parts per million (ppm, δ) downfield from tetramethylsilane (TMS) and are referenced to $CDCl_3$ (δ = 77.4 ppm), to [D_6]acetone (δ = 29.8 ppm, 206.3 ppm) or to [D_6]DMSO (δ = 39.5 ppm) as internal standard. MS (EI) (electron-impact mass spectrometry): Finnigan MAT 90 (70 eV). The molecular fragments are quoted as the relation between mass and charge (*m*/*z*), the intensities as a percentaged value relative to the intensity of the base signal (100%). The abbreviation [M^+] re-

fers to the molecular ion. IR (infrared spectroscopy): FT-IR Bruker IFS 88. IR spectra of solids were recorded in KBr, and as thin films on KBr for oils and liquids. The deposit of the absorption band was given in wave numbers $\tilde{\nu}$ in cm^{-1}. – Elemental analysis: Elementar Vario Microcube. Descriptions without nominated temperature were done at room temperature (r.t.), and the following abbreviations were used: calcd. (theoretical value), found (measured value). Information is given in mass percent. – Routine monitoring of reactions were performed using silica gel coated aluminium plates (Merck, silica gel 60, F_{254}), which were analyzed under UV-light at 254 nm and/or dipped into a solution of molybdatophosphate (5% phosphormolybdic acid in ethanol, dipping solution) and heated with a heat gun. Solvent mixtures are understood as volume/volume. Solid materials were powdered. Solvents, reagents and chemicals were purchased from Aldrich, Fluka and Acros. Tetrahydrofuran was distilled from sodium/benzophenone under argon prior use. Dichloromethane, ethyl acetate and diethyl ether were distilled from calcium hydride. All reactions involving moisture-sensitive reactants were executed under an argon atmosphere using oven dried and/or flame dried glassware. All other solvents, reagents and chemicals were used as purchased unless stated otherwise. Ball milling reactions were performed in a Ball Mill PM 100 Retsch.

Crystal Structure Studies: The single-crystal X-ray diffraction studies were carried out on a Bruker-Nonius Kappa-CCD diffractometer at 123(2) K using Mo-K_α radiation (λ = 0.71073 Å). Direct Methods (SHELXS-97)[40] were used for structure solution, and full-matrix least-squares refinement on F^2 (SHELXL-97[40]). H atoms were localized by difference Fourier synthesis and refined using a riding model.

12: Colorless crystals, $C_{13}H_{14}O_3$, M = 218.24, crystal size 0.40 × 0.32 × 0.16 mm, monoclinic, space group $P2_1/c$ (No. 14): a = 9.520(1) Å, b = 6.255(1) Å, c = 17.611(3) Å, β = 104.48(1)°, V = 1015.4(3) Å^3, Z = 4, ρ(calcd.) = 1.428 Mg m^{-3}, F(000) = 464, μ = 0.101 mm^{-1}, 10236 reflections ($2\theta_{max}$ = 55°), 2304 unique (R_{int} = 0.023), 145 parameters, R_1 [$I > 2\sigma(I)$] = 0.037, wR_2 (all data) = 0.093, GooF = 1.04, largest diff. peak and hole 0.355 and –0.206 e Å^{-3}.

15: Colorless crystals, $C_{13}H_{14}O_5$, M = 250.24, crystal size 0.20 × 0.15 × 0.10 mm, orthorhombic, space group $Pbca$ (No. 61): a = 10.946(1) Å, b = 10.842(1) Å, c = 18.321(2) Å, V = 2174.3(4) Å^3, Z = 8, ρ(calcd.) = 1.529 Mg m^{-3}, F(000) = 1056, μ = 0.118 mm^{-1}, 29541 reflections ($2\theta_{max}$ = 55°), 2486 unique (R_{int} = 0.053), 163 parameters, R_1 [$I > 2\sigma(I)$] = 0.043, wR_2 (all data) = 0.100, GooF = 1.08, largest diff. peak and hole 0.372 and –0.245 e Å^{-3}.

CCDC-699460 (for **12**) and -716929 (for **15**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

General Procedure for the Domino Oxa-Michael Addition Aldol-Reaction (GP 1): Salicylic aldehyde (1.00 equiv.), cyclohexenone (2.00 equiv.) and base (0.50 equiv.) were added to a previously degassed solvent. The resulting mixture was sonicated for the indicated time and extracted with ethyl acetate. The organic phase was dried with sodium sulfate, evaporate, and purified by flash column chromatography.

5-Hydroxy-2,3,4,4a-tetrahydro-1*H*-xanthen-1-one (2a): According to GP1, 2,3-dihydroxybenzaldehyde (8.00 g, 58.0 mmol), 2-cyclohexen-1-one (11.7 mL, 116 mmol) and methylimidazole (2.32 mL, 29.0 mmol) were added to a degassed mixture of dioxane and water (120 mL, 1:2 v/v). The resulting mixture was sonicated 3 d and extracted with ethyl acetate (4 × 200 mL). The organic phase was dried with sodium sulfate, evaporated, and the residue was purified by flash column chromatography (cyclohexane/ethyl acetate, 3:1) yielding **2a** (7.49 g, 60%) as a yellow solid. R_f = 0.31 (CH/EtOAc, 3:1); m.p. 146–147 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.54–1.75 (m, 1 H, cyclohexyl-CH_2), 1.93–2.10 (m, 2 H, cyclohexyl-CH_2), 2.31–2.57 (m, 3 H, cyclohexyl-CH_2), 4.95 (ddd, ^3J = 10.6, 6.0, ^4J = 2.3 Hz, 1 H, 4a-H), 5.44 (s, 1 H, OH_{Ar}), 6.74 (dd, ^3J = 7.6, ^4J = 1.7 Hz, 1 H, H_{Ar}), 6.79 (t, ^3J = 7.6 Hz, 1 H, H_{Ar}), 6.86 (dd, ^3J = 7.6, ^4J = 1.7 Hz, 1 H, H_{Ar}), 7.38 (d, ^4J = 2.3 Hz, 1 H, 9-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.8, 29.6, 38.7 (cyclohexyl-CH_2), 75.3 (C-4a), 118.1 (C_{Ar}), 121.1 (C_{Ar}), 122.3 (C_{Ar}), 122.3 (C_{quat}), 130.5 (C_{quat}), 131.6 (C-9), 142.3 (C_{quat}), 144.0 (C_{quat}), 197.3 (C=O) ppm. FTIR (film on KBr): $\tilde{\nu}$ = 1570, 1595, 1657 (C=O), 3182 cm^{-1} (OH). EI-MS m/z (%) = 216 (93) [M^+], 160 (100) [M^+ – C_3H_4O]. HR-EIMS: calcd: 216.0786; found 216.0784. $C_{13}H_{12}O_3$ (216.24): calcd. C 72.21, H 5.59; found C 71.99, H 5.68.

6-Hydroxy-2,3,4,4a-tetrahydro-1*H*-xanthen-1-one (2b): According to GP1, 2,4-dihydroxybenzaldehyde (8.00 g, 58.0 mmol), 2-cyclohexen-1-one (11.7 mL, 116 mmol) and methylimidazole (2.32 mL, 29.0 mmol) were added to degassed mixture of dioxane and water (120 mL, 1:2 v/v). The resulting mixture was sonicated for 4 d and extracted with ethyl acetate (4 × 200 mL). The organic phase was dried with sodium sulfate, evaporated, and the residue was purified by flash column chromatography (cyclohexane/ethyl acetate, 3:1) yielding **2b** (1.77 g, 14%) as a yellow solid. R_f = 0.19 (CH/EtOAc, 3:1); m.p. 200–205 °C. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 1.68–1.83 (m, 1 H, cyclohexyl-CH_2), 1.81–1.99 (m, 2 H, cyclohexyl-CH_2), 2.29–2.41 (m, 3 H, cyclohexyl-CH_2), 4.94 (ddd, ^3J = 10.6, 6.0, ^4J = 2.1 Hz, 1 H, 4a-H), 6.30 (d, ^4J = 2.2 Hz, 1 H, H_{Ar}), 6.43 (dd, ^3J = 8.3, ^4J = 2.2 Hz, 1 H, H_{Ar}), 7.23 (d, ^3J = 8.3 Hz, 1 H, H_{Ar}), 7.33 (d, ^4J = 2.1 Hz, 1 H, 9-H), 10.2 (s, 1 H, OH_{Ar}) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 17.4, 29.0, 38.2, (cyclohexyl-CH_2), 74.4 (C-4a), 102.4 (C_{Ar}), 109.9 (C_{Ar}), 113.9 (C_{quat}), 126.6 (C_{quat}), 130.8 (C_{Ar}), 131.5 (C-9), 157.2 (C_{quat}), 161.4 (C_{quat}) 196.0 (C=O) ppm. FTIR (film on KBr): $\tilde{\nu}$ = 1544, 1651 (C=O), 3151 cm^{-1} (OH). EI-MS m/z (%) = 216 (20) [M^+], 160 (100) [M^+ – C_3H_4O]. HR-EIMS: calcd: 216.0786; found 216.0784. $C_{13}H_{12}O_3$ (216.24): calcd. C 72.21, H 5.59; found C 71.95, H 5.65.

7-Hydroxy-2,3,4,4a-tetrahydro-1*H*-xanthen-1-one (2c): According to GP1, 2,5-dihydroxybenzaldehyde (3.00 g, 21.7 mmol), 2-cyclohexen-1-one (4.22 mL, 43.4 mmol) and DABCO (1.22 g, 10.9 mmol) were added to degassed water (87 mL). The resulting mixture was treated with ultrasound for 2 d and extracted with ethyl acetate (4 × 100 mL). The organic phase was dried with sodium sulfate, evaporated, and the residue was purified by flash column chromatography (cyclohexane/ethyl acetate, 2:1) yielding **2c** (1.76 g, 67%) as a yellow solid. R_f = 0.29 (CH/EtOAc, 2:1). ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 1.55–1.71 (m, 1 H, cyclohexyl-CH_2), 1.91–2.12 (m, 2 H, cyclohexyl-CH_2), 2.31–2.52 (m, 3 H, cyclohexyl-CH_2), 4.92 (ddd, ^3J = 10.5, 6.1, ^4J = 2.4 Hz, 1 H, 4a-H), 6.73–6.88 (m 3 H, H_{Ar}), 7.28 (d, ^4J = 2.4 Hz, 1 H, 9-H), 8.18 (s, 1 H, OH_{Ar}) ppm. ^{13}C NMR (100 MHz, [D$_6$]acetone): δ = 18.5, 30.4, 39.4 (cyclohexyl-CH_2), 75.5 (C-4a), 115.9 (C_{Ar}), 117.3 (C_{Ar}), 119.5 (C_{Ar}), 123.8 (C_{quat}), 131.0 (C-9), 132.6 (C_{quat}), 149.9 (C_{quat}), 152.9 (C_{quat}), 196.9 (C=O) ppm. FTIR (film on KBr): $\tilde{\nu}$ = 1557, 1652 (C=O), 3200 cm^{-1} (OH). EI-MS m/z (%) = 216 (1) [M^+], 192 (100). HR-EIMS: calcd: 216.0786; found 216.0790. $C_{13}H_{12}O_3$ (216.24): calcd. C 72.21, H 5.59; found C 72.02, H 5.68.

General Procedure for the Reduction of Tetrahydro-1*H*-xanthen-1-ones (GP 2): To a solution of the relevant tetrahydro-1*H*-xanthen-

1-one (1.70 g, 7.86 mmol, 1.00 equiv.) in methanol (50 mL) sodium borohydride (297 mg, 7.86 mmol, 1.00 equiv.) was added at 0 °C. The reaction mixture was warmed to room temperature and stirred for 2 h. After this time, water (20 mL) was added and the mixture was extracted with dichloromethane (4 × 30 mL). The organic phase was dried with sodium sulfate, evaporated and purified by flash column chromatography (cyclohexane/ethyl acetate, 2:1).

2,3,4,4a-Tetrahydro-1*H*-xanthene-1,5-diol (3a): The product was synthesized according to GP 2: 1.27 g (74%) of light yellow solid. R_f = 0.26 (CH/EtOAc, 2:1); m.p. 162–164 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.16–1.29 (m, 1 H, cyclohexyl-CH$_2$), 1.36–1.47 (m, 1 H, cyclohexyl-CH$_2$), 1.53–1.64 (m, 1 H, cyclohexyl-CH$_2$), 1.73–1.78 (m, 1 H, cyclohexyl-CH$_2$), 1.94–1.97 (m, 1 H, cyclohexyl-CH$_2$), 2.07–2.11 (m, 1 H, cyclohexyl-CH$_2$), 3.89–3.97 (m, 1 H, 1-H), 4.90 (dd, ^3J = 11.2, 5.4 Hz, 1 H, 4a-H), 5.21 (d, ^3J = 5.5 Hz, 1 H, OH$_{aliphat}$), 6.24 (s, 1 H, 9-H), 6.41–6.45 (m, 1 H, H$_{Ar}$), 6.57–6.59 (m, 2 H, H$_{Ar}$), 8.75 (s, 1 H, OH$_{Ar}$) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 19.5, 34.4, 35.9 (cyclohexyl-CH$_2$), 68.7 (C-1) 75.6 (C-4a), 112.8 (C$_{Ar}$), 115.7 (C$_{Ar}$), 116.8 (C$_{Ar}$), 120.3 (C-9), 121.5 (C$_{quat}$), 136.9 (C$_{quat}$), 141.3 (C$_{quat}$), 144.1 (C$_{quat}$) ppm. FTIR (film on KBr): $\tilde{\nu}$ = 1477, 3376 cm^{-1} (OH). EI-MS *m*/*z* (%) = 218 (100) [M^+], 173 (52) [M^+ – C$_2$H$_5$O], 147 (68). HR-EIMS: calcd: 218.0943; found 218.0938. C$_{13}$H$_{14}$O$_3$ (218.25): calcd. C 71.54, H 6.47; found C 70.71, H 6.42.

2,3,4,4a-Tetrahydro-1*H*-xanthene-1,6-diol (3b): The product was synthesized according to GP 2: 1.33 g (77%) of light yellow solid. R_f = 0.24 (CH/EtOAc, 2:1); m.p. 174–175 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.16–1.25 (m, 1 H, cyclohexyl-CH$_2$), 1.33–1.44 (m, 1 H, cyclohexyl-CH$_2$), 1.49–1.59 (m, 1 H, cyclohexyl-CH$_2$), 1.67–1.78 (m, 1 H, cyclohexyl-CH$_2$), 1.91–1.95 (m, 1 H, cyclohexyl-CH$_2$), 1.97–2.07 (m, 1 H, cyclohexyl-CH$_2$), 3.82–3.94 (m, 1 H, 1-H), 4.85 (dd, ^3J = 11.1, 5.3 Hz, 1 H, 4a-H), 5.14 (d, ^3J = 5.5 Hz, 1 H, OH$_{aliphat}$), 6.07 (d, ^4J = 2.2 Hz, 1 H, 9-H), 6.14–6.23 (m, 1 H, H$_{Ar}$), 6.75 (d, ^3J = 8.1 Hz, 2 H, H$_{Ar}$), 9.32 (s, 1 H, OH$_{Ar}$) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 19.5, 34.4, 36.0 (cyclohexyl-CH$_2$), 68.7 (C-1) 75.7 (C-4a), 101.8 (C$_{Ar}$), 107.4 (C$_{Ar}$), 112.3 (C$_{Ar}$), 112.5 (C$_{quat}$), 126.6 (C-9), 137.2 (C$_{quat}$), 153.2 (C$_{quat}$), 157.7 (C$_{quat}$) ppm. FTIR (film on KBr): $\tilde{\nu}$ = 1150, 3416 cm^{-1} (OH). EI-MS *m*/*z* (%) = 218 (100) [M^+], 173 (88) [M^+ – C$_2$H$_5$O], 147 (81). HR-EIMS: calcd: 218.0943; found 218.0941. C$_{13}$H$_{14}$O$_3$ (218.25): calcd. C 71.54, H 6.47; found C 71.42, H 6.52.

2,3,4,4a-Tetrahydro-1*H*-xanthene-1,7-diol (3c): The product was synthesized according to GP 2: 1.44 g (84%) of light yellow solid. R_f = 0.31 (CH/EtOAc, 1:1); m.p.196–197 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.15–1.30 (m, 1 H, cyclohexyl-CH$_2$), 1.31–1.47 (m, 1 H, cyclohexyl-CH$_2$), 1.47–1.63 (m, 1 H, cyclohexyl-CH$_2$), 1.66–1.78 (m, 1 H, cyclohexyl-CH$_2$), 1.90–1.99 (m, 1 H, cyclohexyl-CH$_2$), 1.98–2.07 (m, 1 H, cyclohexyl-CH$_2$), 3.86–3.96 (m, 1 H, 1-H), 4.81 (dd, ^3J = 11.1, 5.4 Hz, 1 H, 4a-H), 5.20 (d, ^3J = 5.5 Hz, 1 H, OH$_{aliphat}$), 6.21 (s, 1 H, 9-H), 6.35–6.49 (m, 3 H, H$_{Ar}$), 8.78 (s, 1 H, OH$_{Ar}$) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 19.4, 34.2, 35.8 (cyclohexyl-CH$_2$), 68.7 (C-1) 75.3 (C-4a), 112.4 (C$_{Ar}$), 112.7 (C$_{Ar}$), 114.0 (C$_{Ar}$), 114.7 (C-9), 121.5 (C$_{quat}$), 142.1 (C$_{quat}$), 144.7 (C$_{quat}$), 151.1 (C$_{quat}$) ppm. FTIR (film on KBr): $\tilde{\nu}$ = 1221, 1490, 3226, 3367 cm^{-1} (OH). EI-MS *m*/*z* (%) = 218 (4) [M^+], 176 (100) 148 (53). HR-EIMS: calcd: 218.0943; found 218.0941. C$_{13}$H$_{14}$O$_3$ (218.25): calcd. C 71.54, H 6.47; found C 71.00, H 6.21.

General Procedure for the Hydrogenation of Tetrahydro-1*H*-xanthene-diols (GP 3): A mixture of the relevant tetrahydro-1*H*-xanthene-diol (1.50 g, 6.88 mmol, 1.00 equiv.) and 5% Pd/C (7 mg, 69 μmol, 1 mol-%) in methanol (50 mL) was evacuated and backfilled with hydrogen. After stirring for 18 h under ambient pressure of hydrogen (balloon) the reaction mixture was filtered through a filter paper. The filtrate was evaporated, and purified by flash column chromatography (cyclohexane/ethyl acetate, 1:1).

4a,1-*trans*-2,3,4,4a,9,9a-Hexahydro-1*H*-xanthene-1,5-diol (4a): The product was synthesized according to GP 3: 938 mg (62%) of light yellow solid (2 diastereoisomers: *cis*-1,9a/*trans*-1,9a 1:20). R_f = 0.12 (CH/EtOAc, 2:1); m.p. 164–168 °C. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 1.17–1.32 (m, 2 H, *cis*/*trans*-cyclohexyl-CH$_2$), 1.32–1.48 [m, 5 H: *cis*/*trans*-cyclohexyl-CH$_2$ (4 H) and *cis*-9a-H], 1.50–1.62 (m, 2 H, *trans*-cyclohexyl-CH$_2$), 1.61–1.70 (m, 1 H, *trans*-cyclohexyl-CH$_2$), 1.70–1.79 (m, 1 H, *cis*-cyclohexyl-CH$_2$), 1.81–1.89 (m, 1 H, *cis*-cyclohexyl-CH$_2$), 2.03–2.12 (m, 1 H, *cis*-cyclohexyl-CH$_2$), 2.37 (dt, ^3J = 10.4, 4.8 Hz, 1 H, *trans*-9a-H), 2.42–2.49 (m, 1 H, *cis*-9-H), 2.54–2.74 (m, 2 H, *trans*-9-H), 2.98 (dd, ^3J = 16.6, 5.0 Hz 1 H, *cis*-9-H), 3.12–3.22 (m, 1 H, *cis*-1-H), 3.61 (dt, ^3J = 10.5, 4.3 Hz, 1 H, *cis*-4a-H), 3.76 (dt, ^3J = 8.5, 4.3 Hz, 1 H, *trans*-1-H), 4.24 (td, ^3J = 11.5, 4.4 Hz, 1 H, *trans*-4a-H), 4.75 (d, ^3J = 3.8 Hz, 1 H, *trans*-OH$_{aliphat}$), 4.79 (d, ^3J = 5.8 Hz, 1 H, *cis*-OH$_{aliphat}$), 6.38–6.65 (m, 6 H, *cis*/*trans*-H$_{Ar}$), 8.62 (s, 1 H, *trans*-OH$_{Ar}$), 8.66 (s, 1 H, *cis*-OH$_{Ar}$) ppm. ^{13}C NMR (100 MHz, [D$_6$]-DMSO): δ = 19.6 (*trans*-CH$_2$), 19.8 (*cis*-CH$_2$), 20.0, 25.7, 27.8 (*trans*-CH$_2$), 28.9, 31.4, 34.7 (*cis*-CH$_2$), 37.7 (*trans*-C-9a), 44.4 (*cis*-C-9a), 68.9 (*trans*-C-1), 72.2 (*cis*-C-1), 73.8 (*trans*-C-4a), 76.5 (*cis*-C-4a), 113.7 (*trans*-C$_{Ar}$), 114.0 (*cis*-C$_{Ar}$), 119.1 (*trans*-C$_{Ar}$), 19.5, 119.7 (*cis*-C$_{Ar}$), 120.0 (*trans*-C$_{Ar}$), 120. (*cis*-C$_{quat}$), 121.2, 141.2 (*trans*-C$_{quat}$), 142.5, 145.2 (*cis*-C$_{quat}$), 145.6 (*trans*-C$_{quat}$) ppm. FTIR (film on KBr): $\tilde{\nu}$ = 1475, 3270 cm^{-1} (OH). EI-MS *m*/*z* (%) = 220 (100) [M^+], 202 (27) [M^+ – H$_2$O], 173 (27), 123 (65). HR-EIMS: calcd: 220.1099; found 220.1102. C$_{13}$H$_{16}$O$_3$ (220.27): calcd. C 70.89, H 7.32; found C 70.84, H 7.25.

4a,1-*trans*-2,3,4,4a,9,9a-Hexahydro-1*H*-xanthene-1,6-diol (4b): The product was synthesized according to GP 3: 1.30 g (86%) of light yellow solid (2 diastereoisomers: *cis*-1,9a/*trans*-1,9a 1:6). R_f = 0.14 (CH/EtOAc, 2:1); m.p. 172–174 °C. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 1.16–1.26 (m, 2 H, *cis*/*trans*-cyclohexyl-CH$_2$), 1.30–1.45 [m, 5 H: *cis*/*trans*-cyclohexyl-CH$_2$ (4 H) and *cis*-9a-H], 1.50–1.57 (m, 2 H, *trans*-cyclohexyl-CH$_2$), 1.62–1.66 (m, 1 H, *trans*-cyclohexyl-CH$_2$), 1.69–1.76 (m, 1 H, *cis*-cyclohexyl-CH$_2$), 1.79–1.84 (m, 1 H, *cis*-cyclohexyl-CH$_2$), 1.99–2.01 (m, 1 H, *cis*-cyclohexyl-CH$_2$), 2.25–2.36 (m, 1 H, *trans*-9a-H), 2.54–2.74 [m, 3 H, *trans*-9-H (2 H), *cis*-9-H (1 H)], 2.91 (dd, ^3J = 16.0, 4.8 Hz 1 H, *cis*-1-H), 3.11–3.18 (m, 1 H, *cis*-4a-H), 3.70–3.76 (m, 1 H, *trans*-1-H), 4.12 (td, ^3J = 8.8, 4.1 Hz, 1 H, *trans*-4a-H), 4.71 (d, ^3J = 3.6 Hz, 1 H, *trans*-OH$_{aliphat}$), 4.76 (d, ^3J = 4.7 Hz, 1 H, *cis*-OH$_{aliphat}$), 6.06–6.15 (m, 2 H, *cis*/*trans*-H$_{Ar}$), 6.21–6.28 (m, 2 H, *cis*/*trans*-H$_{Ar}$), 6.83 (d, ^3J = 8.2 Hz, 2 H, *cis*/*trans*-H$_{Ar}$); 9.06 (s, 1 H, *trans*-OH$_{Ar}$), 9.09 (s, 1 H, *cis*-OH$_{Ar}$) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 19.2, 19.6 (*trans*-CH$_2$), 19.9 (*cis*-CH$_2$), 25.7, 27.9 (*trans*-CH$_2$), 28.3, 31.3, 34.7 (*cis*-CH$_2$), 37.9 (*trans*-C-9a), 44.6 (*cis*-C-9a), 68.9 (*trans*-C-1), 72.1 (*cis*-C-1), 73.8 (*trans*-C-4a), 76.4 (*cis*-C-4a), 102.3 (*cis*-C$_{Ar}$), 102.5 (*trans*-C$_{Ar}$), 107.5 (*trans*-C$_{Ar}$), 107.8 (*cis*-C$_{Ar}$), 110.9 (*trans*-C$_{quat}$), 112.5 (*cis*-C$_{quat}$), 129.9 (*cis*-C$_{Ar}$), 130.2 (*trans*-C$_{Ar}$), 153.5 (*trans*-C$_{quat}$), 154.6 (*cis*-C$_{quat}$), 156.3 (*cis*-C$_{quat}$), 156.4 (*trans*-C$_{quat}$) ppm. FTIR (film on KBr): $\tilde{\nu}$ = 1151, 1509, 3340 cm^{-1} (OH). EI-MS *m*/*z* (%) = 220 (71) [M^+], 201 (24), 173 (100), 123 (76), 43 (76). HR-EIMS: calcd. for C$_{13}$H$_{14}$O$_3$: 220.1099; found 220.1101.

4a,1-*trans*-2,3,4,4a,9,9a-Hexahydro-1*H*-xanthene-1,7-diol (4c): The product was synthesized according to GP 3: 1.32 (87%) of white solid (2 diastereoisomers: *cis*-1,9a/*trans*-1,9a 1:7). R_f = 0.24 (CH/EtOAc, 1:1); m.p. 199–201 °C. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 1.15–1.28 (m, 2 H, *cis*/*trans*-cyclohexyl-CH$_2$), 1.29–1.46 [m, 5

H: *cis*/*trans*-cyclohexyl-CH_2 (4 H) and *cis*-9a-H], 1.47–1.57 (m, 2 H, *trans*-cyclohexyl-CH_2), 1.58–1.68 (m, 1 H, *trans*-cyclohexyl-CH_2), 1.68–1.75 (m, 1 H, *cis*-cyclohexyl-CH_2), 1.80–1.86 (m, 1 H, *cis*-cyclohexyl-CH_2), 1.95–2.01 (m, 1 H, *cis*-cyclohexyl-CH_2), 2.33 (dt, ^3J = 10.1, 4.6 Hz, 1 H, *trans*-9a-H), 2.42 Hz (dd, ^2J = 16.5, ^3J = 11.6 Hz, 1 H, *cis*-9-H), 2.51–2.69 (m, 2 H, *trans*-9-H), 2.92 (dd, ^2J = 16.7, ^3J = 5.0 Hz, 1 H, *cis*-9-H), 3.11–3.18 (m, 1 H, *cis*-1-H), 3.55 (dt, ^3J = 10.1, 4.6 Hz, 1 H, *cis*-4a-H), 3.73 (dt, ^3J = 8.7, 4.2 Hz, 1 H, *trans*-1-H), 4.09 (td, ^3J = 11.2, 4.2 Hz, 1 H, *trans*-4a-H), 4.69 (d, ^3J = 3.8 Hz, 1 H, *trans*-$OH_{aliphat}$), 4.76 (d, ^3J = 5.7 Hz, 1 H, *cis*-$OH_{aliphat}$), 6.41–6.55 (m, 6 H, *cis*/*trans*-H_{Ar}), 8.68 (s, 1 H, *trans*-OH_{Ar}), 8.73 (s, 1 H, *cis*-OH_{Ar}) ppm. ^{13}C NMR (125 MHz, [D_6]-DMSO): δ = 20.1 (*trans*-CH_2), 20.5 (*cis*-CH_2), 20.9, 26.1, 28.4 (*trans*-CH_2), 29.6, 31.9, 35.2 (*cis*-CH_2), 38.1 (*trans*-C-9a), 44.9 (*cis*-C-9a), 69.8 (*trans*-C-1), 72.9 (*cis*-C-1), 74.0 (*trans*-C-4a), 76.1 (*cis*-C-4a), 114.4 (*cis*-C_{Ar}), 114.5 (*trans*-C_{Ar}), 115.8 (*cis*-C_{Ar}), 116.1 (*trans*-C_{Ar}), 116.3 (*cis*-C_{Ar}), 117.0 (*trans*-C_{Ar}), 121.6 (*trans*-C_{quat}), 123.0 (*cis*-C_{quat}), 146.0 (*trans*-C_{quat}), 147.3 (*cis*-C_{quat}), 150.5 (*trans*-C_{quat}), 150.9 (*cis*-C_{quat}) ppm. FTIR (film on KBr): $\tilde{\nu}$ = 1493, 3228 cm^{-1} (OH). FAB-MS (matrix: 3-NBA): *m*/*z* (%) = 220 (100) [M^+], 136 (44). HR-EIMS: calcd: 220.1099; found 220.1119. $C_{13}H_{16}O_3$ (220.27): calcd. C 70.89, H 7.32; found C 70.36, H 7.39.

4a,1-*trans*-7-(*tert*-Butyldimethysilyloxy)2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-1-ol: To an ice-cooled suspension of **4c** (3.60 g, 16.4 mmol, 1.00 equiv.) in dichloromethane (100 mL) imidazole (1.39 g, 19.7 mmol, 1.20 equiv.) and TBDMSCl (2.96 g, 16.7 mmol, 1.20 equiv.) were added under argon atmosphere. The reaction mixture was then warmed to room temperature and stirred for 4 h. After this time, saturated $NaHCO_3$ solution was added and the mixture was extracted with dichloromethane (3 × 100 mL). The organic phase was dried with sodium sulfate, evaporated and purified by flash column chromatography (cyclohexane/ethyl acetate, 3:1), yielding 4a,1-*trans*-7-(*tert*-butyldimethysilyloxy)2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-1-ol (5.22 g, 91%) as a white solid (2 diastereoisomers: *cis*-1,9a/*trans*-1,9a 1:8). R_f = 0.31 (CH/EtOAc, 3:1); m.p. 87 °C. ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 0.00 (s, 12 H, *cis*/*trans*-CH_3), 0.80 (s, 18 H, *cis*/*trans*-*tert*-butyl), 0.98–1.15 (m, 2 H, *cis*/*trans*-cyclohexyl-CH_2), 1.17–1.33 [m, 5 H: *cis*/*trans*-cyclohexyl-CH_2 (4 H) and *cis*-9a-H], 1.34–1.45 (m, 2 H, *trans*-cyclohexyl-CH_2), 1.46–1.54 (m, 1 H, *trans*-cyclohexyl-CH_2), 1.55–1.63 (m, 1 H, *cis*-cyclohexyl-CH_2), 1.65–1.75 (m, 1 H, *cis*-cyclohexyl-CH_2), 1.81–1.91 (m, 1 H, *cis*-cyclohexyl-CH_2), 2.09–2.25 (m, 1 H, *trans*-9a-H), 2.30 (dd, ^2J = 16.8, ^3J = 11.6 Hz, 1 H, *cis*-9-H), 2.39–2.59 (m, 2 H, *trans*-9-H), 2.83 (dd, ^2J = 16.9, ^3J = 5.0 Hz, 1 H, *cis*-9-H), 2.96–3.06 (m, 1 H, *cis*-1-H), 3.44 (dt, ^3J = 10.2, 4.64 Hz, 1 H, *cis*-4a-H), 3.60 (dt, ^3J = 8.8, 4.4 Hz, 1 H, *trans*-1-H), 3.99 (td, ^3J = 11.4, 4.32 Hz, 1 H, *trans*-4a-H), 4.58 (d, ^3J = 3.8 Hz, 1 H, *trans*-$OH_{aliphat}$), 4.64 (d, ^3J = 5.8 Hz, 1 H, *cis*-$OH_{aliphat}$), 6.30–6.49 (m, 6 H, *cis*/*trans*-H_{Ar}) ppm. ^{13}C NMR (100 MHz, [D_6]DMSO): δ = –4.6 (*cis*/*trans*-CH_3), 19.5, 20.3 (*trans*-CH_2), 25.6 (*cis*/*trans*-*tert*-butyl), 25.7 (*trans*-CH_2), 26.3 (*cis*-CH_2), 27.9 (*trans*-CH_2), 29.0, 31.3, 34.7 (*cis*-CH_2), 37.5 (*trans*-C-9a), 44.2 (*cis*-C-9a), 68.8 (*trans*-C-1), 72.1 (*cis*-C-1), 73.7 (*trans*-C-4a), 76.3 (*cis*-C-4a), 116.2 (*cis*-C_{Ar}), 116.6 (*trans*-C_{Ar}), 118.2 (*cis*-C_{Ar}), 118.3 (*trans*-C_{Ar}), 120.0 (*cis*-C_{Ar}), 120.2 (*trans*-C_{Ar}), 121.3 (*trans*-C_{quat}), 122.8 (*cis*-C_{quat}), 147.3 (*trans*-C_{quat}), 147.6 (*trans*-C_{quat}), 147.9 (*cis*-C_{quat}), 148.6 (*cis*-C_{quat}) ppm. FTIR (film on KBr): $\tilde{\nu}$ = 1494, 3259 cm^{-1} (OH). EI-MS *m*/*z* (%) = 334 (86) [M^+], 84 (100), 56 (70). HR-EIMS: calcd: 334.1964; found 334.1960. $C_{19}H_{30}O_3Si$ (334.53): calcd. C 68.22, H 9.04; found C 68.14, H 9.25.

4a,1-*trans*-*tert*-Butyl(1-methoxy-2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-7-yloxy)dimethylsilane: To an ice-cooled solution of 4a,1-*trans*-7-(*tert*-butyldimethysilyloxy)2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-1-ol (194 mg, 581 μmol, 1.00 equiv.) in THF (15 mL), sodium hydride (17 mg, 697 μmmol, 1.20 equiv.) and methyl iodide (36 μL, 581 μmol, 1.00 equiv.) were added under argon atmosphere. The reaction mixture was then warmed to room temperature and stirred for 7 h. After this time water was added and the mixture was extracted with EtOAc (3 × 15 mL). The organic phase was dried with sodium sulfate, evaporate, and purified by flash column chromatography (cyclohexane/ethyl acetate, 20:1) yielding 4a,1-*trans*-*tert*-butyl(1-methoxy-2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-7-yloxy)dimethylsilane (138 mg, 68%) as a colorless oil. (2 diastereoisomers: *cis*-1,9a/*trans*-1,9a 1:8). R_f = 0.27 (CH/EtOAc, 20:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.19 (s, 12 H, *cis*/*trans*-CH_3), 1.00 (s, 18 H, *cis*/*trans*-*tert*-butyl), 1.22–1.37 (m, 2 H, *cis*/*trans*-cyclohexyl-CH_2), 1.40–1.61 (m, 4 H, *cis*/*trans*-cyclohexyl-CH_2), 1.64–1.77 (m, 2 H, *cis*/*trans*-cyclohexyl-CH_2), 1.77–1.88 (m, 4 H, *cis*/*trans*-cyclohexyl-CH_2), 1.88–1.98 (m, 1 H, *cis*-9a-H), 2.10–2.25 (m, 2 H, *cis*-9-H), 2.52–2.67 (m, 1 H, *trans*-9a-H), 2.69–2.82 (m, 2 H, *trans*-9-H), 2.93 (dt, ^3J = 10.4, 4.2 Hz, 1 H, *cis*-1-H), 3.41 (s, 6 H, *cis*/*trans*-OCH_3), 3.41–3.46 (m, 1 H, *trans*-1-H), 3.64 (dt, ^3J = 10.6, 4.5 Hz, 1 H, *cis*-4a-H), 4.15 (td, ^3J = 11.8, 4.0 Hz, 1 H, *trans*-4a-H), 6.54–6.76 (m, 6 H, *cis*/*trans*-H_{Ar}) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = –4.5 (*cis*/*trans*-CH_3), 19.9 (*trans*-CH_2), 20.2 (*cis*-CH_2), 20.7, 25.3 (*trans*-CH_2), 25.8 (*cis*/*trans*-*tert*-butyltyl), 26.1 (*trans*-CH_2), 29.5, 29.7, 31.6 (*cis*-CH_2), 34.5 (*trans*-C-9a), 43.0 (*cis*-C-9a), 56.0 (*trans*-OCH_3), 56.7 (*cis*-OCH_3), 74.3 (*trans*-C-1), 77.3 (*cis*-C-1), 80.0 (*trans*-C-4a), 83.0 (*cis*-C-4a), 116.5 (*cis*-C_{Ar}), 117.0 (*trans*-C_{Ar}), 118.8 (*cis*-C_{Ar}), 118.9 (*trans*-C_{Ar}), 120.4 (*cis*-C_{Ar}), 120.5 (*trans*-C_{Ar}), 120.8 (*trans*-C_{quat}), 122.5 (*cis*-C_{quat}), 147.4 (*cis*/*trans*-C_{quat}), 148.6 (*cis*/*trans*--C_{quat}) ppm. FTIR (film on KBr): $\tilde{\nu}$ = 1493, 2937 cm^{-1}. EI-MS *m*/*z* (%) = 348 (100) [M^+], 259 (23). HR-EIMS: calcd. for $C_{20}H_{32}SiO_3$: 348.2121; found 348.2119.

4a,1-*trans*-1-Methoxy-2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-7-ol (5c): TBAF (9.38 mL, 9.38 mmol, 2.00 equiv., 1 M THF) was added to a solution of 4a,1-*trans*-*tert*-butyl(1-methoxy-2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-7-yloxy)dimethylsilane (1.63 g, 4.69 mmol, 1.00 equiv.) in THF (80 mL) and the mixture was stirred for 13 h. After this time water was added and the mixture was extracted with Et_2O (3 × 50 mL). The organic phase was dried with sodium sulfate, evaporated, and purified by flash column chromatography (cyclohexane/ethyl acetate, 3:1), yielding **5c** (5.22 g, 91%) as a white solid (2 diastereoisomers: *cis*-1,9a/*trans*-1,9a 1:8). R_f = 0.27 (CH/EtOAc, 3:1); m.p. 191–193 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.02–1.17 (m, 1 H, *cis*-cyclohexyl-CH_2), 1.21–1.45 (m, 6 H, *cis*/*trans*-cyclohexyl-CH_2), 1.46–1.61 (m, 2 H, *cis*/*trans*-cyclohexyl-CH_2), 1.60–172 (m, 2 H, *trans*-cyclohexyl-CH_2), 1.73–1.83 (m, 1 H, *cis*-9a-H), 1.95–2.03 (m, 1 H, *cis*-cyclohexyl-CH_2), 2.06–2.18 (m, 1 H, *cis*-cyclohexyl-CH_2), 2.37–2.54 (m, 1 H, *cis*-9-H), 2.55–2.72 (m, 2 H, *trans*-9-H), 2.79–2.99 (m, 3 H, *trans*-9a-H, *cis*-9-H, *cis*-1-H), 3.26 (s, 3 H, *trans*-OCH_3), 3.30 (s, 3 H, *cis*-OCH_3), 3.37–3.42 (m, 1 H, *trans*-1-H), 3.56 (dt, ^3J = 10.4, 4.4 Hz, 1 H, *cis*-4a-H), 4.08 (td, ^3J = 11.4, 4.0 Hz, *trans*-4a-H), 6.43–6.56 (m, 6 H, *cis*/*trans*-H_{Ar}), 8.71 (s, 1 H, *trans*-OH_{Ar}); 8.76 (s, 1 H, *cis*-OH_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.4 (*trans*-CH_2), 19.6 (*cis*-CH_2), 20.2, 24.7, 25.7 (*trans*-CH_2), 28.8, 29.2, 31.2 (*cis*-CH_2), 34.1 (*trans*-C-9a), 42.6 (*cis*-C-9a), 55.2 (*trans*-OCH_3), 55.9 (*cis*-OCH_3), 73.2 (*trans*-C-1), 75.9 (*cis*-C-1), 78.7 (*trans*-C-4a), 81.7 (*cis*-C-4a), 113.9 (*cis*-C_{Ar}), 114.1 (*trans*-C_{Ar}), 115.3 (*cis*-C_{Ar}), 115.6 (*trans*-C_{Ar}), 116.2 (*cis*-C_{Ar}), 116.5 (*trans*-C_{Ar}), 120.7 (*trans*-C_{quat}), 122.3 (*cis*-C_{quat}), 145.4 (*trans*-C_{quat}), 146.7 (*cis*-C_{quat}), 150.2 (*trans*-C_{quat}), 150.5 (*cis*-C_{quat}) ppm. FTIR (film on KBr): $\tilde{\nu}$ = 1222, 1495, 2943, 3235 (OH) cm^{-1}. EI-MS *m*/*z* (%) = 234 (100) [M^+], 202 (19), 173 (35). HR-EIMS: calcd: 234.1260; found 234.1258. $C_{14}H_{18}O_3$ (234.29): calcd. C 71.77, H 7.74; found C 71.75, H 7.83.

7-Hydroxy-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (6): A mixture of **2a** (546 mg, 2.50 mmol, 1.00 equiv.), $FeCl_3 \cdot 6H_2O$ (1.35 g, 5.00 mmol, 2.00 equiv.), and NaCl (1.25 g) was ground by mortar and pestle. The mixture was then put in a tube and kept at 50 °C overnight. After this time water (50 mL) was added and the mixture was extracted with EtOAc (3 × 40 mL). The organic phase was dried with sodium sulfate, evaporated and purified by flash column chromatography (cyclohexane/ethyl acetate, 2:1) yielding **6** (89 mg, 16% and 7% of starting material) as a yellow solid. R_f = 0.17 (CH/EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.93–2.07 (m, 2 H, cyclohexyl-CH_2), 2.38–2.44 (m, 2 H, cyclohexyl-CH_2), 2.51–2.58 (m, 2 H, cyclohexyl-CH_2), 3.43 (s, 1 H, 9-H), 5.40 (s, 1 H, OH_{Ar}), 6.62 (dd, ^3J = 7.6, ^4J = 1.4 Hz, 1 H, H_{Ar}), 6.62 (dd, ^3J = 8.1, ^4J = 1.4 Hz, 1 H, H_{Ar}), 6.88 (t, ^3J = 7.9 Hz, 1 H, H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.5 (cyclohexyl-CH_2), 20.0 (C-9), 26.6, 36.6 (cyclohexyl-CH_2), 109.7 (C_{quat}), 113.0, 119.6 (C_{Ar}), 120.3 (C_{quat}), 123.8 (C_{Ar}), 136.6, 142.9, 164.7 (C_{quat}), 197.0 (C=O) ppm. EI-MS *m*/*z* (%) = 216 (57) [M^+], 215 (67), 160 (58), 43 (100). HR-EIMS: calcd. for $C_{13}H_{12}O_3$: 216.0786; found 216.0783.

6,6′,7,7′,8,8′,10a,10a′-Octahydro-5*H*,5′*H*-3,3′-bixanthene-2,2′,8,8′-tetraol (7): A solution of potassium ferricyanide (0.825 g, 2.50 mmol, 1.00 equiv.) and potassium hydroxide (0.211 g, 3.75 mmol, 1.50 equiv.) in water (20 mL) was added dropwise to a solution of **3c** (0.550 g, 2.50 mmol, 1.00 equiv.) in methanol (20 mL). After stirring for 4 d 1 M HCl (20 mL) was added and the mixture was extracted with EtOAc (3 × 40 mL). The organic phase was dried with sodium sulfate, evaporated and purified by flash column chromatography (cyclohexane/ethyl acetate, 1:2), yielding **7** (250 mg, 45%, 14% starting material) as a yellow solid. R_f = 0.14 (CH/EtOAc, 1:1). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.15–1.30 (m, 1 H, cyclohexyl-CH_2), 131–1.47 (m, 1 H, cyclohexyl-CH_2), 1.48–1.64 (m, 1 H, cyclohexyl-CH_2), 1.68–1.79 (m, 1 H, cyclohexyl-CH_2), 1.91–2.00 (m, 1 H, cyclohexyl-CH_2), 2.01–2.10 (m, 1 H, cyclohexyl-CH_2), 3.90–3.99 (m, 1 H, 1-H), 4.85 (dd, ^3J = 11.1, 5.4 Hz, 1 H, 4a-H), 5.24 (d, ^3J = 5.5 Hz, 1 H, $OH_{aliphat}$), 6.21 (s, 1 H, 9-H), 6.45 (s, 1 H, H_{Ar}), 6.51 (s, 1 H, H_{Ar}), 8.76 (s, 1 H, OH_{Ar}) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 19.5, 34.4, 35.9 (cyclohexyl-CH_2), 68.8 (C-1) 75.4 (C-4a), 112.5 (C-9), 113.3 (C_{Ar}), 116.5 (C_{Ar}), 120.6, 124.6, 142.2 144.6, 147.7 (C_{quat}) ppm. EI-MS *m*/*z* (%) = 434 (67) [M^+], 416 (100), 218 (45), 147 (51). HR-EIMS: calcd. for $C_{26}H_{26}O_6$: 434.1729; found 434.1733.

8-(1-Hydroxy-2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-7-yloxy)-2,3,4,4a,9,9a-hexahydro-1*H*-xanthene-1,7-diol (8): A solution of potassium ferricyanide (0.660 g, 2.00 mmol, 1.00 equiv.) and potassium hydroxide (0.157 g, 2.80 mmol, 1.50 equiv.) in water (16 mL) was added dropwise to a solution of **3c** (0.440 g, 2.00 mmol, 1.00 equiv.) in methanol (16 mL). After stirring for 2 d 1 M HCl (15 mL) was added and the mixture was extracted with EtOAc (3 × 30 mL). The organic phase was dried with sodium sulfate, evaporated and purified by flash column chromatography (cyclohexane/ethyl acetate, 1:2) yielding **8** (45 mg, 10% and 13% of starting material) as a yellow solid. R_f = 0.29 (CH/EtOAc, 1:2). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.15–1.30 (m, 1 H, cyclohexyl-CH_2), 131–1.47 (m, 1 H, cyclohexyl-CH_2), 1.48–1.64 (m, 1 H, cyclohexyl-CH_2), 1.68–1.79 (m, 1 H, cyclohexyl-CH_2), 1.91–2.00 (m, 1 H, cyclohexyl-CH_2), 2.01–2.10 (m, 1 H, cyclohexyl-CH_2), 3.90–3.99 (m, 1 H, 1-H), 4.85 (dd, ^3J = 11.1, 5.4 Hz, 1 H, 4a-H), 5.24 (d, ^3J = 5.5 Hz, 1 H, $OH_{aliphat}$), 6.21 (s, 1 H, 9-H), 6.45 (s, 1 H, H_{Ar}), 6.51 (s, 1 H, H_{Ar}), 8.76 (s, 1 H, OH_{Ar}) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 19.5, 34.4, 35.9 (cyclohexyl-CH_2), 68.8 (C-1) 75.4 (C-4a), 112.5 (C-9), 113.3 (C_{Ar}), 116.5 (C_{Ar}), 120.6, 124.6, 142.2 144.6, 147.7 (C_{quat}) ppm. EI-MS *m*/*z* (%) = 434 (67) [M^+], 416 (100), 218 (45), 147 (51). HR-EIMS: calcd. for $C_{26}H_{26}O_6$: 434.1729; found 434.1733.

9*H*-Xanthen-2-ol (9): A ball-mill vessel was charged with **3c** (218 mg, 1.00 mmol, 1.00 equiv.), $FeCl_3 \cdot 6H_2O$ (270 mg, 1 mmol, 2.00 equiv.), NaCl (500 mg) and ZrO_2 balls (100 g, *d* = 3 mm) and rotated at 300 rpm for 2 h. After this time 1 M HCl (30 mL) was added and the mixture was extracted with EtOAc (3 × 30 mL). The organic phase was dried with sodium sulfate, evaporated and purified by flash column chromatography (cyclohexane/ethyl acetate, 5:1) yielding **9** (30 mg, 15%) as a white solid. R_f = 0.41 (CH/EtOAc, 3:1). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 3.97 (s, 2 H, CH_2), 6.59–6.65 (m, 2 H, H_{Ar}), 6.78–6.94 (m, 2 H, H_{Ar}), 6.99–7.06 (m, 2 H, H_{Ar}), 7.17–7.25 (m, 2 H, H_{Ar}), 9.20 (s, 1 H, OH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 27.2 (CH_2), 114.4, 114.6, 115.9, 116.6 (C_{Ar}), 120.2, 121.1 (C_{quat}), 122.7, 127.6, 129.1 (C_{Ar}), 144.0, 151.7, 153.0 (C_{quat}) ppm. HR-EIMS: calcd. for $C_{13}H_9O_2$: 197.0603; found 197.0606.

4a,1-*trans*-8-Chloro-2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-1,7-diol (10): A ball-mill vessel was charged with **4c** (660 mg, 3.00 mmol, 1.00 equiv.), $FeCl_3 \cdot 6H_2O$ (2.43 g, 9 mmol, 3.00 equiv.), NaCl (2.00 g) and ZrO_2 balls (100 g, *d* = 3 mm) and rotated at 350 rpm for 1 h. After this time 1 M HCl (30 mL) was added and the mixture was extracted with EtOAc (3 × 30 mL). The organic phase was dried with sodium sulfate, evaporated and purified by flash column chromatography (cyclohexane/ethyl acetate, 1:1) yielding **10** (331 mg, 43% and 32% of starting material) as a white solid (2 diastereoisomers: *cis*-1,9a/*trans*-1,9a 1:14). R_f = 0.58 (CH/EtOAc, 1:1); m.p. 165–168 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.11–1.60 (m, 4 H, *trans*-cyclohexyl-CH_2), 1.59–1.70 (m, 2 H, *cis*/*trans*-cyclohexyl-CH_2), 1.46–1.61 (m, 2 H, *cis*/*trans*-cyclohexyl-CH_2), 1.70–2.05 (m, 5 H, *cis*-cyclohexyl-CH_2), 2.25–2.38 (m, 2 H, *trans*-9a-H and *cis*-9-H), 2.42–2.50 (m, 1 H, *trans*-9-H), 2.62–2.82 (m, 2 H, *cis*-9a-H, *trans*-9-H), 3.09 (dd, ^3J = 17.5, 5.4 Hz, 1 H, *cis*-9-H), 3.15–3.25 (m, 1 H, *cis*-1-H), 3.53 (dt, ^3J = 10.2, 4.4 Hz, 1 H, *cis*-4a-H), 3.77 (dt, ^3J = 8.8, 4.4 Hz, 1 H, *trans*-1-H), 4.11 (td, ^3J = 11.1, 4.2 Hz, 1 H, *trans*-4a-H), 4.78 (d, ^3J = 3.8 Hz, *trans*-$OH_{aliphat}$), 4.87 (d, ^3J = 5.9 Hz, *cis*-$OH_{aliphat}$), 6.57 (d, ^3J = 8.8 Hz, 2 H, *cis*/*trans*-H_{Ar}), 6.72 (d, ^3J = 8.8 Hz 2 H, *cis*/*trans*-H_{Ar}), 9.37 (s, 1 H, *trans*-OH_{Ar}), 9.43 (s, 1 H, *cis*-OH_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.3, 19.8 (*trans*-CH_2), 19.9 (*cis*-CH_2), 25.4, 27.9 (*trans*-CH_2), 29.7, 31.0, 34.7 (*cis*-CH_2), 37.1 (*trans*-C-9a), 44.0 (*cis*-C-9a), 68.8 (*trans*-C-1), 71.9 (*cis*-C-1), 73.1 (*trans*-C-4a), 75.7 (*cis*-C-4a), 114.3 (*cis*-C_{Ar}), 114.5 (*trans*-C_{Ar}), 114.6 (*cis*-C_{Ar}), 114.9 (*trans*-C_{Ar}), 119.5 (*cis*-C_{quat}), 119.8 (*trans*-C_{quat}), 121.3 (*cis*-C_{quat}), 146. (*trans*-C_{quat}), 146.3 (*trans*-C_{quat}), 146.6 (*cis*-C_{quat}), 147.5 (*cis*-C_{quat}) ppm. FTIR (film on KBr): $\tilde{\nu}$ = 1489, 3218 (OH) cm^{-1}. EI-MS *m*/*z* (%) = 256/254 (33/100) [M^+], 209/207 (20/54), 159/157 (14/36). HR-EIMS: calcd: 254.0710; found 254.07.12. $C_{13}H_{15}ClO_3$ (254.71): calcd. C 61.30, H 5.94; found C 61.19, H 5.96.

4a,1-*trans*-8-Chloro-1-methoxy-2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-7-ol (11): A mixture of **5c** (115 mg, 0.50 mmol, 1.00 equiv.), $FeCl_3 \cdot 6H_2O$ (270 mg, 1 mmol, 2.00 equiv.), and NaCl (250 mg) was ground by mortar and pestle. The mixture was then put in a tube and kept at 50 °C for 2 h. After this time, 1 M HCl (20 mL) was added and the mixture was extracted with EtOAc (3 × 20 mL). The organic phase was dried with sodium sulfate, evaporated and purified by flash column chromatography (cyclohexane/ethyl acetate, 5:1) yielding **11** (46 mg, 34% and 14% of starting material) as a white solid (2 diastereoisomers: cis-1,4a/*trans*-1,4a 1:8). R_f = 0.45 (CH/EtOAc, 3:1); m.p. 150–154 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12–1.29 (m, 2 H, *cis*/*trans*-cyclo-

hexyl-CH_2), 1.33–1.52 (m, 4 H, *cis*/*trans*-cyclohexyl-CH_2), 1.55–1.64 (m, 2 H, *cis*/*trans*-cyclohexyl-CH_2), 1.69–1.80 (m, 2 H, *trans*-cyclohexyl-CH_2), 1.80–1.90 (m, 1 H, *cis*-9a-H), 2.28 (dd, ^2J = 17.5, ^3J 1 = 1.3 Hz, 1 H, *cis*-9-H), 2.44–2.59 (m, 1 H, *trans*-9a-H), 2.59–2.79 (m, 2 H, *trans*-9-H), 2.87 (dt, ^3J = 10.4, 4.3 Hz, 1 H, *cis*-1-H), 3.17 (dd, ^2J = 17.1, ^3J 5 = .1 Hz, 1 H, *cis*-1-H), 3.32 (s, 3 H, *trans*-OCH_3), 3.34–3.41 (m, 4 H, *trans*-1-H and *cis*-OCH_3), 3.47 (dt, ^3J = 10.8, 4.5 Hz, 1 H, *cis*-4a-H), 5.12 (s, 1 H, *trans*-OH_{Ar}), 6.58–6.64 (m, 2 H, *cis*/*trans*-H_{Ar}), 6.70–6.77 (m, 2 H, *cis*/*trans*-H_{Ar}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.7, 19.8 (*trans*-CH_2), 20.1 (*cis*-CH_2), 25.2, 25.8 (*trans*-CH_2), 28.1, 29.6, 31.3 (*cis*-CH_2), 34.1 (*trans*-C-9a), 42.6 (*cis*-C-9a), 56.2 (*trans*-OCH_3), 56.8 (*cis*-OCH_3), 73.9 (*trans*-C-1), 76.3 (*cis*-C-1), 79.6 (*trans*-C-4a), 82.9 (*cis*-C-4a), 113.9 (*cis*-C_{Ar}), 114.1 (*trans*-C_{Ar}), 115.6 (*cis*-C_{Ar}), 116.0 (*trans*-C_{Ar}), 119.0 (*trans*-C_{quat}), 119.6 (*cis*-C_{quat}), 119.9 (*trans*-C_{quat}), 120.7 (*cis*-C_{quat}), 145.0 (*trans*-C_{quat}), 145.2 (*cis*-C_{quat}), 147.3 (*trans*-C_{quat}), 148.7 (*cis*-C_{quat}) ppm. FTIR (film on KBr): $\tilde{\nu}$ = 1242, 1480, 2926, 3259 (OH) cm^{-1}. EI-MS *m*/*z* = 268/269/270 (47/100/43) [M^+], 207/208/209 (24/28/26). HR-EIMS: calcd: 268.0867; found 268.0869. $C_{14}H_{17}ClO_3$ (268.74): calcd. C 62.57, H 6.38; found C 62.33, H 6.31.

(1*S,4a*R**,9a*S**,10a*R**)-1,10a-Epoxy-2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-7(10aH)-one (12). Method A:** To a suspension of **4c** (144 mg, 0.63 mmol, 1.00 equiv.) in water (20 mL), $FeCl_3 \cdot 6H_2O$ (338 mg, 1.26 mmol, 2.00 equiv.) was added. After stirring for 24 h at room temperature 1 M HCl (10 mL) was added and the mixture was extracted with EtOAc (3 × 15 mL). The organic phase was dried with sodium sulfate, evaporated and purified by flash column chromatography (cyclohexane/ethyl acetate, 2:1) yielding **12** (105 mg, 77%) as a white solid (+ 14% of *cis*-starting material was isolated).

Method B: To a suspension of **4c** (220 mg, 1.00 mmol, 1.00 equiv.) in CH_2Cl_2 (50 mL) at 0 °C, $BF_3 \cdot OEt_2$ (1.90 mL, 15.0 mmol, 15.0 equiv.) was added under argon atmosphere. After stirring for 1 min a solution of $Pb(OAc)_4$ (554 mg, 1.25 mmol, 1.25 equiv.) in CH_2Cl_2 (25 mL) was added dropwise and the mixture was stirred for 30 min. After this time water was added and the mixture was extracted with EtOAc (3 × 30 mL). The organic phase was dried with sodium sulfate, evaporated and purified by flash column chromatography (cyclohexane/ethyl acetate, 1:1) yielding **12** (99 mg, 45%) as a white solid. R_f = 0.22 (CH/EtOAc, 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29–1.52 (m, 3 H, cyclohexyl-CH_2), 1.72–1.78 (m, 1 H, cyclohexyl-CH_2), 1.87–1.99 (m, 2 H, cyclohexyl-CH_2), 2.00–2.17 (m, 1 H, 9a-H), 2.68–2.74 (m, 2 H, 1-H), 4.13 (s, 2 H, 1-H and 4a-H), 5.89 (d, ^4J = 1.9 Hz, 1 H, 8-H), 6.11 (dd, ^3J = 10.1, ^4J = 1.8 Hz, 1 H, 6-H), 6.57 (d, ^3J = 10.1 Hz, 1 H, 5-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.2, 30.5, (CH_2), 31.6 (C-9), 32.3 (C-9a), 72.6 (C-1 and C-4a), 86.1 (C_{quat}), 120.9 (C-8), 130.4 (C-6), 141.6 (C-5), 154.1 (C_{quat}), 185.7 (C=O) ppm. FTIR (film on KBr): $\tilde{\nu}$ = 977, 1673 (C=O), 2922 cm^{-1}. EI-MS *m*/*z* (%) = 218 (100) [M^+], 174 (23), 161 (26), 147 (26). HR-EIMS: calcd: 218.0943; found 218.0946. $C_{134}H_{14}O_3$ (1671.58): calcd. C 71.54, H 6.47; found C 71.59, H 6.37.

2-[(2-Hydroxy-6-methoxycyclohexyl)methyl]cyclohexa-2,5-diene-1,4-dione (13): To a suspension of **5c** (350 mg, 1.5 mmol, 1.00 equiv.) in water (50 mL) was added $FeCl_3 \cdot 6H_2O$ (810 mg, 3.00 mmol, 2.00 equiv.). After stirring for 7 h at room temperature, water (20 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 30 mL). The organic phase was dried with sodium sulfate, evaporated and purified by flash column chromatography (cyclohexane/ethyl acetate, 3:1), yielding **13** (250 mg, 50%) as a brown oil (2 diastereoisomers: *cis*-1,6/*trans*-1,6 1:5). R_f = 0.16 (CH/EtOAc, 3:1). ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 1.17–1.42 (m, 6 H, *cis*/*trans*-cyclohexyl-CH_2), 1.64–1.78 (m, 2 H, *cis*/*trans*-cyclohexyl-CH_2), 1.79–1.91 (m, 2 H, *cis*-cyclohexyl-CH_2), 1.92–2.05 (m, 2 H, *trans*-cyclohexyl-CH_2 and-CH_2), 2.39 (dd, ^2J = 12.9, ^3J = 7.5 Hz, 1 H, *cis*-CH_2), 2.53–2.61 (m, 1 H, *cis*-CH), 2.66 (dd, ^3J = 7.4, ^4J = 0.9 Hz, 2 H, *trans*-CH_2), 2.91 (dd, ^2J = 13.5, ^3J = 8.5 Hz, 1 H, *cis*-CH_2), 3.30 (s, 3 H, *trans*-OCH_3), 3.35 (s, 3 H, *cis*-OCH_3), 3.41–3.53 (m, 2 H, *cis*/ *trans*-CH), 3.61–3.74 (m, 2 H, *cis*/*trans*-CH), 6.49–6.67 (m, 2 H, *cis*/*trans*-H_{alkene}), 6.68–6.78 (m, 2 H, *cis*/*trans*-H_{alkene}), 6.79–6.92 (m, 2 H, *cis*/*trans*-H_{alkene}) ppm. ^{13}C NMR (100 MHz, [D$_6$]acetone): δ = 16.1 (*trans*-CH_2), 26.4 (*cis*-CH_2), 27.5 (*trans*-CH_2), 27.8, 28.4 (*cis*-CH_2), 33.3 (*trans*-CH_2), 44.1 (*trans*-CH), 45.9 (*cis*-CH), 56.8 (*trans*-OCH_3), 56.9 (*cis*-OCH_3), 70.0 (*cis*-CH), 70.2 (*trans*-CH), 80.4 (*trans*-CH), 81.0 (*cis*-CH), 114.5, 117.5, 118.4 (*cis*-C_{alkene}), 134.3, 137.1, 137.8 (*trans*-C_{alkene}), 149.3 (*trans*-C_{quat}), 151.2 (*cis*-C_{quat}), 188.3 (*trans*-C_{quat}), 188.4 (*trans*-C_{quat}), 196.7 (*cis*-C_{quat}), 196.9 (*cis*-C_{quat}) ppm. EI-MS *m*/*z* (%) = 250 (55) [M^+], 218 (100), 200 (86), 134 (83), 83 (82). HR-EIMS: calcd. for $C_{14}H_{18}O_4$: 250.1205; found 250.1202.

6,7-Dimethoxy-2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-1-ol (14): To a solution of **4c** (220 mg, 1.00 mmol, 1.00 equiv.) in methanol (20 mL) was added $FeCl_3 \cdot 6H_2O$ (841 mg, 3.00 mmol, 3.00 equiv.). After stirring at reflux for 24 h, the solvent was evaporated, and the crude product was purified by flash column chromatography (cyclohexane/ethyl acetate, 2:1) yielding **14** (22 mg, 8%) as a yellow solid (9% of **10** and 14% of starting material). R_f = 0.35 (CH/EtOAc, 1:1). ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.14–1.30 (m, 2 H, *cis*/*trans*-cyclohexyl-CH_2), 1.31–1.47 [m, 5 H: *cis*/*trans*-cyclohexyl-CH_2 (4 H) and *cis*-9a-H], 1.48–1.58 (m, 2 H, *trans*-cyclohexyl-CH_2), 1.59–1.74 (2 H, *cis*/*trans*-cyclohexyl-CH_2), 1.76–1.87 (m, 1 H, *cis*-cyclohexyl-CH_2), 1.93–2.04 (m, 1 H, *cis*-cyclohexyl-CH_2), 2.32 (dt, ^3J = 10.1, 4.6 Hz, 1 H, *trans*-9a-H), 2.38–2.46 (m, 1 H, *cis*-9-H), 2.53–2.65 (m, 2 H, *trans*-9-H), 2.91 (dd, ^2J = 16.9, ^3J = 5.1 Hz, 1 H, *cis*-9-H), 3.06–3.19 (m, 1 H, *cis*-1-H), 3.57–3.62 (m, 1 H, *cis*-4a-H), 3.66 (s, 6 H, *cis*/*trans*-OCH_3), 3.67 (s, 6 H, *cis*/*trans*-OCH_3), 3.69–3.79 (m, 1 H, *trans*-1-H), 4.12 (td, ^3J = 8.7, 4.1 Hz, 1 H, *trans*-4a-H), 4.76 (d, ^3J = 3.5 Hz, 1 H, *trans*-$OH_{aliphat}$), 4.77 (d, ^3J = 5.7 Hz, 1 H, *cis*-$OH_{aliphat}$), 6.34 (m, 2 H, *cis*/*trans*-H_{Ar}), 6.64 (m, 2 H, *cis*/*trans*-H_{Ar}) ppm. ^{13}C NMR (100 MHz, [D$_6$]-DMSO): δ = 19.5, 19.6 (*trans*-CH_2), 20.5 (*cis*-CH_2), 25.6, 27.9 (*trans*-CH_2), 29.6, 31.9, 35.2 (*cis*-CH_2), 37.8 (*trans*-C-9a), 44.9 (*cis*-C-9a), 55.4 (*cis*/*trans*-OCH_3), 56.1 (*cis*/*trans*-OCH_3), 68.8 (*trans*-C-1), 72.9 (*cis*-C-1), 73.6 (*trans*-C-4a), 76.1 (*cis*-C-4a), 100.8 (*cis*/*trans*-C_{Ar}), 113.6 (*cis*/*trans*-C_{Ar}), 116.6, 142.3, 146.6, 148.0 (*cis*/*trans*-C_{quat}) ppm. EI-MS *m*/*z* (%) = 264 (100) [M^+], 167 (47). HR-EIMS: calcd. for $C_{15}H_{20}O_4$: 264.1362; found 264.1364.

(1*S,4a*R**,5*S**,6*R**,8*S**,8a*R**,9a*S**,10a*R**)-5,6,8,8a,1,10a-Triepoxy-2,3,4,4a,5,6,9,9a-octahydro-1*H*-xanthen-7(10aH)-one (15):** To a solution of **12** (23 mg, 0.106 mmol, 1.00 equiv.) in methanol (1.2 mL) containing 30% H_2O_2 (120 μL, 1.16 mmol, 11 equiv.) was added 1 M NaOH (150 μL) at 0 °C. After stirring for 4 h at 0 °C the reaction mixture was diluted with brine (3 mL) and extracted with EtOAc (3 × 3 mL). The organic phase was dried with sodium sulfate, evaporated and purified by flash column chromatography (cyclohexane/ethyl acetate, 2:1) yielding **15** (12 mg, 46%) as a white solid. R_f = 0.19 (CH/EtOAc, 2:1). ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 1.14–1.30 (m, 2 H, *cis*/*trans*-cyclohexyl-CH_2), 1.31–1.47 [m, 5 H: *cis*/*trans*-cyclohexyl-CH_2 (4 H) and *cis*-9a-H], 1.48–1.58 (m, 2 H, *trans*-cyclohexyl-CH_2), 1.59–1.74 (2 H, *cis*/*trans*-cyclohexyl-CH_2), 1.76–1.87 (m, 1 H, *cis*-cyclohexyl-CH_2), 1.93–2.04 (m, 1 H, *cis*-cyclohexyl-CH_2), 2.32 (dt, ^3J = 10.1, 4.6 Hz, 1 H, *trans*-9a-H), 2.38–2.46 (m, 1 H, *cis*-9-H), 2.53–2.65 (m, 2 H, *trans*-9-H),

2.91 (dd, ^2J = 16.9, ^3J = 5.1 Hz, 1 H, *cis*-9-H), 3.06–3.19 (m, 1 H, *cis*-1-H), 3.57–3.62 (m, 1 H, *cis*-4a-H), 3.66 (s, 6 H, *cis*/*trans*-OCH_3), 3.67 (s, 6 H, *cis*/*trans*-OCH_3), 3.69–3.79 (m, 1 H, *trans*-1-H), 4.12 (td, ^3J = 8.7, 4.1 Hz, 1 H, *trans*-4a-H), 4.76 (d, ^3J = 3.5 Hz, 1 H, *trans*-$OH_{aliphat}$), 4.77 (d, ^3J = 5.7 Hz, 1 H, *cis*-$OH_{aliphat}$), 6.34 (m, 2 H, *cis*/*trans*-H_{Ar}), 6.64 (m, 2 H, *cis*/*trans*-H_{Ar}) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 19.5, 19.6 (*trans*-CH_2), 20.5 (*cis*-CH_2), 25.6, 27.9 (*trans*-CH_2), 29.6, 31.9, 35.2 (*cis*-CH_2), 37.8 (*trans*-C-9a), 44.9 (*cis*-C-9a), 55.4 (*cis*/*trans*-OCH_3), 56.1 (*cis*/*trans*-OCH_3), 68.8 (*trans*-C-1), 72.9 (*cis*-C-1), 73.6 (*trans*-C-4a), 76.1 (*cis*-C-4a), 100.8 (*cis*/*trans*-C_{Ar}), 113.6 (*cis*/*trans*-C_{Ar}), 116.6, 142.3, 146.6, 148.0 (*cis*/*trans*-C_{quat}) ppm. EI-MS: *m*/*z* (%) = 264 (100) [M^+], 167 (47). HR-EIMS: calcd. for $C_{15}H_{20}O_4$: 264.1362; found 264.1364.

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