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TETRAHEDRON

Biaryl Hydroxy Aldehydes as Intermediates in the Metal-Assisted Atropo-Enantioselective Reduction of Biaryl Lactones: Structures and Aldehyde-Lactol Equilibria[1]

Gerhard Bringmann*, Matthias Breuning, Heike Endress and Daniel Vitt
Institut für Organische Chemie, Universität Würzburg, Am Hubland, D-97074 Würzburg, Germany

Karl Peters and Eva-Maria Peters
Max-Planck-Institut für Festkörperforschung, Heisenbergstraße 1, D-70506 Stuttgart, Germany

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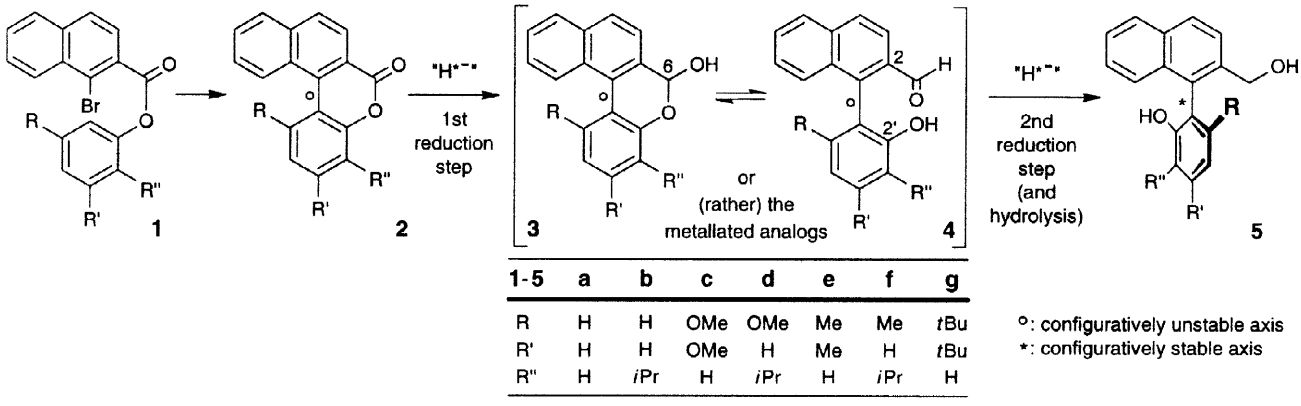
Abstract: The synthesis of substituted 1-(2'-hydroxyphenyl)naphthalene-2-carbaldehydes **4** and 6-alkoxy -6H-pyrans **7** and **8**, analogs of the postulated metallated intermediates in the atropo-enantioselective ring cleavage of configuratively unstable biaryl lactones **2**, is described. While the equilibria between the open hydroxy aldehydes **4** and the cyclic lactol structures **3** are completely shifted towards **4** for the derivatives **4c-g** with substituents *ortho* to the biaryl axis, the lactol forms are the dominating structures (*ca.* 50-100%) for the *ortho*-unsubstituted compounds. For the lactols **3** and their acetalic analogs **6**, **7**, and **8**, those diastereomeric conformations are preferred (77-100%) that have the *exo*-oxygen function axial.

INTRODUCTION

The atropo-enantioselective ring cleavage of biaryl lactones of type **2** (Scheme 1) to configuratively stable biaryls, *e.g.* to **5**, is a most efficient and mechanistically intriguing approach to the preparation of enantiomerically pure biaryls.[2,3] This useful strategy has been successfully applied to the preparation of axially chiral model biaryls,[4,5] naturally occurring naphthylisoquinoline alkaloids,[6] mastigophorene analogs,[7] and efficient catalysts for asymmetric synthesis.[8] The lactones **2** can easily be prepared by intramolecular aryl coupling of the corresponding substituted bromo esters **1**.[9] Depending on the degree of steric hindrance, they are more or



1-5	a	b	c	d	e	f	g
R	H	H	OMe	OMe	Me	Me	*t*Bu
R'	H	H	OMe	H	Me	H	*t*Bu
R''	H	*i*Pr	H	*i*Pr	H	*i*Pr	H

Scheme 1. Synthesis and atropo-enantioselective reduction of configuratively unstable biaryl lactones **2**.[9]

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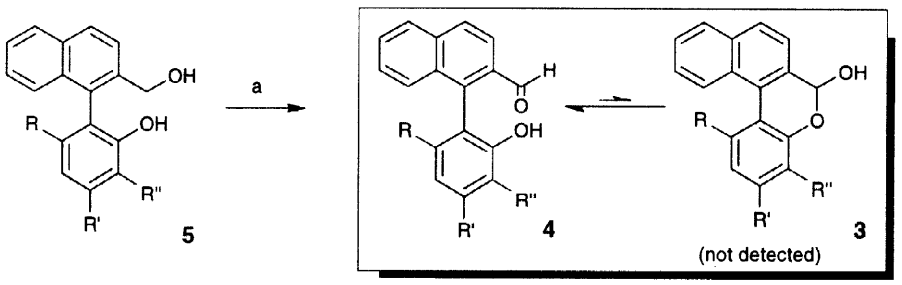
less helically distorted[9,10] and thus chiral, but, due to the lactone bridge, they are configuratively unstable and thus rapidly helimerize.[3,11,12] Out of this enantiomeric equilibrium mixture, they can be ring opened atropisomer-selectively, *e.g.* with oxazaborolidine-activated borane or metal-activated hydride transfer reagents, to give excellent enantiomeric ratios of up to 98.5:1.5.[4] The process requires two reduction steps, involving the lactols **3** as initial products, in an equilibrium with the corresponding aldehydes **4** (or their metallated analogs).[4,13,14] Hydroxy aldehydes of type **4** are configuratively unstable, probably not through a merely *physical* rotation, but rather by a *chemical* cyclization to the corresponding lactols **3**, which, as bridged biaryls, should have a low atropisomerization barrier, like the lactones **2**.[13] Such a 'stereochemical leakage'[4,14,15] on the level of these primary reduction products **3** and **4** might lead to the loss of an asymmetric induction possibly attained in the first reduction step. This assumption was supported by semiempirical AM1 calculations of the entire mechanistic course of the reaction,[12] which indeed confirmed the existence of such a stereochemical leakage and indicated that the eventually attained high asymmetric inductions should be generated during the *second* reduction step, which would thus constitute an atropo-enantioselective reduction of configuratively unstable hydroxy aldehydes **4**, by dynamic kinetic resolution. These predictions make the directed synthesis of hydroxy aldehydes **4** (or their lactol analogs **3**) highly rewarding, including the spectroscopic and computational investigation of their chemical and stereochemical equilibria and their possible use as novel starting materials for atropo-enantioselective reductions to **5**. In this paper, we describe the synthesis of a broad series of such aldehydes **4** with different steric hindrance at the biaryl axis, and of related acetals **7**, as chemically stable '*O*-alkyl protected' analogs of the corresponding (metallated) lactols **3**, and the experimental investigation of their structures and ring-chain equilibria. In the following paper,[15] the computational investigation of these species will be described.

RESULTS AND DISCUSSION

Preparation of the hydroxy aldehydes 4 / lactols 3

In a previous study, a first such hydroxy biaryl aldehyde, **4e**, had been prepared in an enantiomerically enriched form, which required a protection-deprotection strategy.[13] Its configurative lability hinted at the existence of the corresponding lactol **3e**, which, however, could not be detected spectroscopically.[13] For this reason, we embarked on the systematic preparation of such hydroxy aldehydes **4** (see Scheme 2) with a large variety of *ortho*-substituents and thus different steric hindrance at the axis, ranging from R = H up to R = *t*Bu.

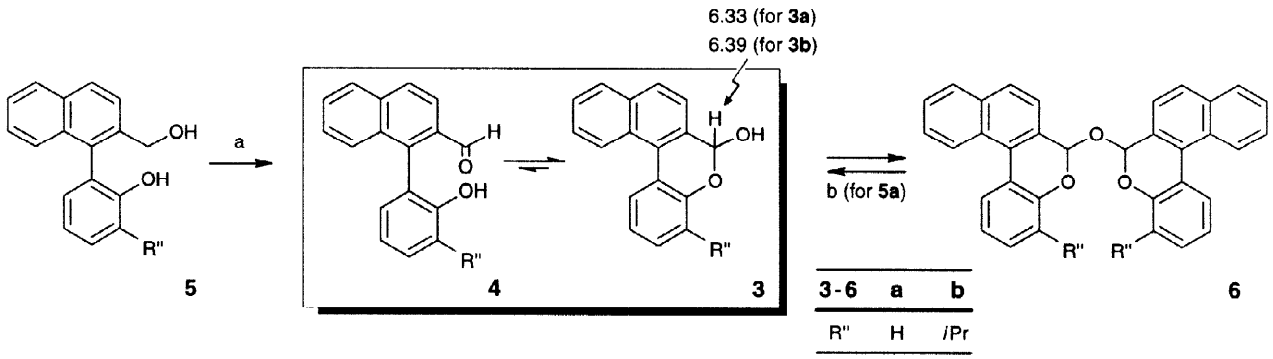


3-5	c	d	e	f	g
R	OMe	OMe	Me	Me	*t*Bu
R'	OMe	H	Me	H	*t*Bu
R''	H	*i*Pr	H	*i*Pr	H

Scheme 2. Synthesis of the sterically hindered hydroxy aldehyde biaryls **4c-g**. Reaction conditions: a) PCC, THF, 0 °C → rt, 73-90%.

Starting from the lactones **2**, the target molecules **4** were now obtained in only two steps and good yields (73-90%), *via* the alcohols **5**.[16] The subsequent oxidation was best done with pyridinium chlorochromate (PCC) in anhydrous THF, as shown for the sterically more hindered hydroxy aldehydes **4c-g**, *i.e.* with R ≠ H.

For **4a** and **4b**, which have no substituents R next to the biaryl axis (see Scheme 3), problems arose from the higher portion of the lactol form **3** (cf. also next section), resulting in an over-oxidation back to the lactones **2**, and, even more severely, leading to the formation of bisacetals **6**. In particular for **4a/3a**, which are devoid of an isopropyl group next to phenolic oxygen function, the tendency to condense to **6a** was so strong[17] that even TLC-pure samples, as obtained by column chromatography, resulted in mixtures of **4a/3a** and **6a** upon removal of the solvent, even at -10 °C *in vacuo*. Crystallization of **4a/3a** from diethyl ether / petroleum ether gave the bisacetal **6a**, exclusively. On an analytical scale, a pure solution of **4a/3a** could be obtained, by treatment of **6a** with traces of DCl in D_8-THF / D_6-DMSO / D_2O (10:10:1) in an NMR tube for several days.[18]



Scheme 3. Synthesis of the sterically less hindered biaryls **4/3** and formation of the bisacetals **6**. Reaction conditions: a) PCC, THF, 0 °C → rt, yield **4b/3b**: 64%. b) D_8-THF / D_6-DMSO / D_2O / DCl, 7 d, quantitative (according to ^{1}H NMR).

The hydroxy aldehyde / lactol equilibrium 4 ⇌ 3

In solution, no ^{1}H NMR evidence on the existence of lactols **3** was found for **4c-g**. For the sterically less hindered biaryls **3a/4a** and **3b/4b**, however, the lactol form **3**, with its characteristic semiacetalic proton around δ = 6.5 ppm (cf. Scheme 3), was the dominating structure. The hydroxy aldehyde / lactol ratio varied in the margins of 48 : 52 to 0 : 100 in favor of the lactol structure (Table 1).[19] In contrast to **4a/3a** (see obove), **4b/3b** crystallized as the lactol **3b** from diethyl ether / petroleum ether (see Fig. 2, below).

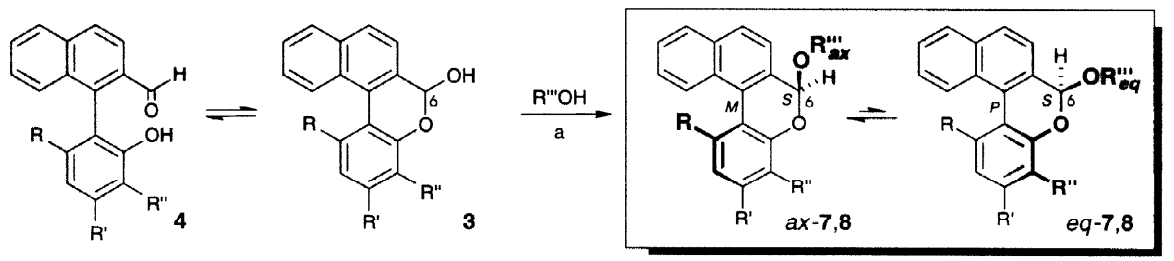
Table 1. The ratio **4a** : **3a** and **4b** : **3b** in different solvent systems (determined by ^{1}H NMR)

equilibrium **4/3**	deuterated solvent	ratio **3** : **4**
4a/3a	D_8-THF / D_2O / D_6-DMSO (10:10:1)[a]	52 : 48
4b/3b	D_8-THF / D_2O / D_6-DMSO (10:10:1)[a]	92 : 8
4b/3b	$CDCl_3$	83 : 17
4b/3b	D_6-DMSO	100 : 0

[a]Acidified with traces of DCl (relative ratios **a/b** for **3** and **4** confirmed by joint measurement in the same solvent).

Synthesis of the 'O-alkyl protected' lactol analogs 7 and 8

Due to the fact that the equilibrium **4** ⇌ **3** is entirely on the side of the ring-open hydroxy aldehydes **4** for the sterically more hindered compounds **c-g**, an investigation of these lactol intermediates **3** in the atrop-isomerization of configuratively unstable hydroxy aldehydes **4** and in the atropisomer-selective cleavage of the lactones **2** was not possible. For this reason, we have synthesized the *O*-alkyl protected analogs **7** and **8** as model compounds for the lactols **3** (and their metallated analogs).[4] In an earlier paper, we described the preparation of a first such acetal by addition of methanol to the corresponding pyrylium salt.[14] This method, however, was practicable only for sterically non-hindered biaryls, *viz.* with R = H, not for the needed sterically more hindered compounds (*e.g.* with R = Me). We have now found a simpler and more straightforward general procedure for the preparation of even sterically congesting cyclic acetals **7** (see Scheme 4), by refluxing the hydroxy aldehydes **4** in the alcohol as the solvent with a catalytic amount of *p*TosOH and removal of water by molecular sieve (4 Å).[18]



	3b,4b	3e,4e
R	H	Me
R'	H	Me
R''	*i*Pr	H

	7a	7b	7c	7d	8a	8b
R	Me	Me	Me	Me	H	H
R'	Me	Me	Me	Me	H	H
R''	H	H	H	H	*i*Pr	*i*Pr
OR'''	OMe	OEt	O*i*Pr	OCH_2tBu	OMe	OEt

Scheme 4. Synthesis and diastereomeric structures of the (racemic) 6-alkoxy-6H-pyrans **7** and **8**. Reaction conditions: a) *p*TosOH, reflux, 62-91%.

Structures of the sterically more hindered acetal-bridged biaryls 7

The good availability of these lactol-related, but chemically stable bridged biaryls **7** and **8** allowed a thorough structural characterization, without the complication of ring cleavage with aldehyde formation. Due to the presence of the stereogenic biaryl axis and the (now configuratively stable) stereocenter at C-6, the dimethyl substituted (racemic) compounds **7** gave two sets of ^{1}H NMR data for the two atropo-diastereomeric compounds on the NMR time scale (Fig. 1). NOE experiments clearly allowed to distinguish these diastereo-

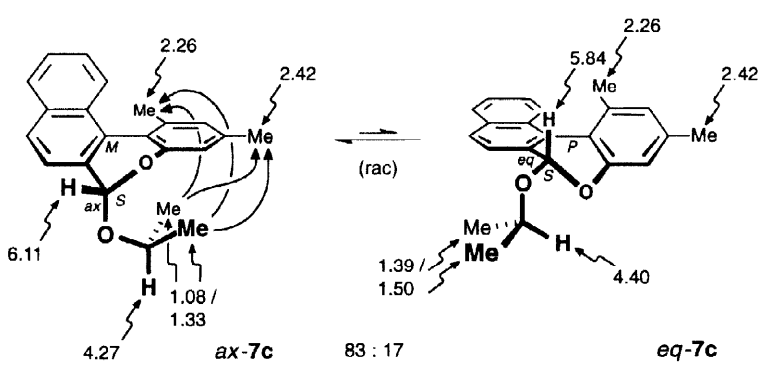


Fig. 1. Selected NOE interactions (in $CDCl_3$) and significant chemical shifts (δ-values in ppm) decisive of the relative configurations of the two diastereomeric forms of (racemic) **7c**.

mers, showing the main atropisomer (Fig. 1, left) to have the 6-alkoxy substituent in an axial position, in agreement with the expected stereoelectronically stabilizing[20] *exo*-anomeric[21] effect.

As a typical additional criterion and in agreement with the observed NOE effects, the chemical shifts for the *O*-alkyl part of the axially substituted isomer *ax*-**7c** are distinctly high-field shifted as compared to the values for *eq*-**7c** with the *O*-alkyl group in an equatorial position, where it is not influenced by the anisotropic effect of the aromatic system. *Vice versa*, the acetalic proton at C-6 shows a significant low-field shift for *ax*-**7c** *vs.* *eq*-**7c**. Due to the similar NMR behavior of the diastereomeric pairs of the other cyclic acetals **7**, their relative configurations were deduced accordingly. In all cases, the axial isomer prevailed over the equatorial one, depending on the steric demand of the 6-alkoxy substituent. In agreement with parallel quantumchemical calculations,[22] the *ax*-**7** : *eq*-**7** ratio decreased with increasing size of the 6-alkoxy substituent (see Table 2).

Table 2. Influence of the steric demand of the 6-alkoxy group on the *ax*-**7** : *eq*-**7** ratio (in $CDCl_3$)

6-alkoxy-6H-pyran	OR‴	ratio[a] *ax*-**7** : *eq*-**7**
7a	OMe	91 : 9
7b	OEt	88 : 12
7c	O*i*Pr	83 : 17
7d	OCH_2tBu	77 : 23

[a]Analyzed by the ^1H NMR ratio of signals of the acetalic proton at C-6 and of the 6-alkoxy groups.

Stereostructures of the less hindered acetals ***8****, of the free lactol* ***3b****, and of the bisacetals* ***6***

By contrast, due to the absence of a sterically demanding *ortho* substituent R next to the axis, the acetals **8** show but a single set of ^1H NMR spectroscopic data. In agreement with the low isomerization barrier for the related lactone **2b**,[3] this reveals a rapid atropisomerization at room temperature, rather than hinting at the existence of only one stable atropo-diastereomer. In the crystal (see Fig. 2),[23] the *unlike* diastereomer, *i.e.* with the alkoxy substituent in an axial position, was found both for **8a** and also for the corresponding free lactol, **3b**,[15] likewise in agreement with quantumchemical calculations parallelly performed (see subsequent paper).

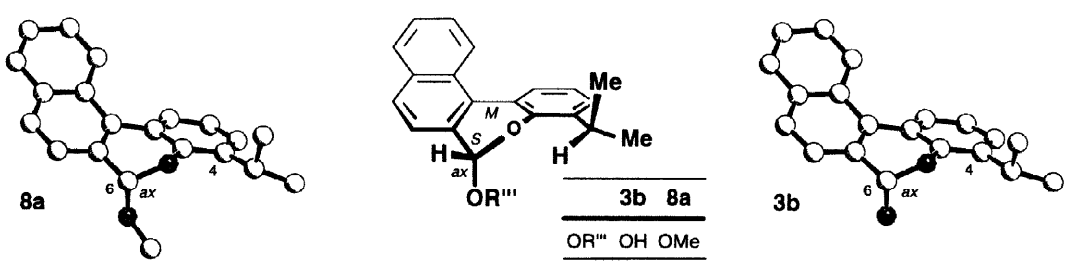


Fig. 2. Crystal structures of the acetal **8a** and its parent lactol **3b**.[23]

Likewise stereochemically homogeneous, although disposing of no less than four stereogenic elements, were the bisacetals **6a** and **6b**, as obtained above (cf. Scheme 3), their ^1H NMR spectra displaying only a single set of data. In the crystal,[23] **6b** was found to adopt a C_2-symmetric structure (see Fig. 3, right), with the *exo*-oxygen occupying axial positions for both molecular halves, again underlining the general predominance of axial over equatorial substituents for all these cyclic acetals and half acetals, apparently for stereoelectronic reasons.[20]

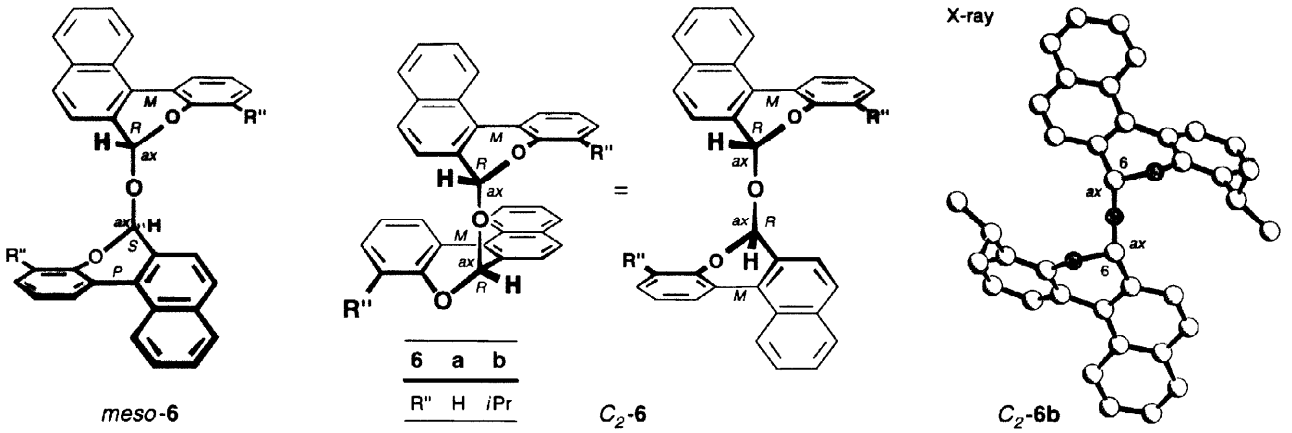


Fig. 3. The two possible diastereomeric forms of the bisacetals **6a,b** that have only axial *exo*-oxygen substituents, and the C_2-symmetrical structure of C_2-**6b** found in the crystal.[23]

In conclusion, the biaryl hydroxy aldehydes **4** presented in this paper were found to be in equilibrium with the corresponding lactols **3**. While for the *ortho*-substituted compounds **4c-g**, the equilibrium is entirely on the side of the ring-open aldehydes, the lactol form **3** is the dominating structure (*ca.* 50-100%) for the *ortho*-unsubstituted representatives **4a/3a** and **4b/3b** (R = H), the latter easily giving the bisacetals **6a** and **6b**, respectively. From NMR and X-ray crystallographic data, a clear preference of those diastereomers can be deduced in with the *exo*-hydroxy or -alkoxy substituent occupies an axial position. The synthetic availability of these compounds and their structural properties make them promising substrates for atropo-enantioselective reductions as a novel method in stereoselective biaryl synthesis.[24] Quantumchemical calculations on structures and dynamics of these compounds are described in the following paper.[15]

EXPERIMENTAL

Melting points were determined with an Kofler hot plate apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1420 infrared spectrophotometer and are reported in wave numbers (cm^{-1}). ^1H NMR and ^{13}C NMR spectra were taken on a Bruker AC 200 (200 MHz), AC 250 (250 MHz) or DMX 600 (600 MHz). Chemical shifts are given in parts per million (ppm) with the deuterated solvent as internal reference. Coupling constants, *J*, are given in Hertz. In ^{13}C NMR spectra, sometimes not all quaternary Ar-C signals were detected due to their similary shifts and to their long T_1 relaxation times. Mass spectra were recorded on a Finnigan MTA 8200 spectrometer at 70 eV in the EI mode.

The alcohols **5a**, **5c**, **5e**, and **5g** were prepared according to the general procedure A as described previously.[16] All reactions were carried out in absolute solvents with dry glassware under an argon atmosphere.

General procedure A for the reduction of the lactones 2b, 2d, and 2f to the alcohols 5b, 5d, and 5f. According to a previously described procedure,[16] 2.00 equivalents of $LiAlH_4$ were added to a solution of the lactone **2** in THF (5 ml/mmol **2**). After 1 h of stirring at room temperature, the reaction mixture was quenched carefully with water (5 ml/mmol **2**), slightly acidified with 2N HCl, extracted with diethyl ether (3 x 5ml/mmol **2**), and dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue was chromatographed on silica

gel (petroleum ether / diethyl ether 3:1 → 1:1) to give the alcohol **5**.

2-Hydroxymethyl-1-(2'-hydroxy-3'-isopropylphenyl)naphthalene (5b). According to the general procedure A, reduction of **2b** (1.35 g, 4.68 mmol) gave **5b** (1.34 g, 4.58 mmol, 98%) as a colorless oil. From petroleum ether / diethyl ether, **5b** (1.20 g, 4.10 mmol, 88%) was obtained as white crystals: mp 117 °C; IR (KBr): $\tilde{\nu}$ 3320, 3040, 2950, 2850, 1425, 1240, 1050, 810, 745; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.30, 1.31 [d, J = 7.0 Hz each, 3H each, $CH(CH_3)_2$], 3.35 [sept, J = 7.0 Hz, 1H, $CH(CH_3)_2$], 4.58 (d, J = 5.5 Hz, 2H, CH_2OH), 4.84 (s, 1H, 2'-OH), 6.96 (dd, J = 7.6 Hz, J = 1.8 Hz, 1H, 4'-H or 6'-H), 7.05 (t, J = 7.5 Hz, 1H, 5'-H), 7.34 (dd, J = 7.2 Hz, J = 1.8 Hz, 1H, 4'-H or 6'-H), 7.36-7.55 (m, 3H, Ar-H), 7.72 (d, J = 8.3 Hz, 1H, 3-H or 4-H), 7.90 (d, J = 7.9 Hz, 1H, 8-H), 7.97 (d, J = 8.5 Hz, 1H, 3-H or 4-H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 22.59, 22.65 [$CH(CH_3)_2$], 27.13 [$CH(CH_3)_2$], 63.65 (CH_2OH), 120.6, 123.9, 126.1, 126.2, 126.3, 126.7, 128.0, 128.3, 129.0, 132.2, 132.8, 133.3, 135.8, 137.5, 150.5 (Ar-C); MS: *m/z* (%) = 292 (7) [M^+], 274 (100) [M^+ - H_2O], 273 (56) [M^+ - H_3O], 259 (32) [M^+ - CH_5O], 232 (21), 231 (31); Anal. calcd. for $C_{20}H_{20}O_2$ (292.4): C, 82.16; H, 6.89. Found: C, 81.88; H, 6.97.

2-Hydroxymethyl-1-(2'-hydroxy-3'-isopropyl-6'-methoxyphenyl)naphthalene (5d). According to the general procedure A, **2d** (350 mg, 1.10 mmol) was reduced to yield in **5d** (344 mg, 1.07 mmol, 97%) as a colorless oil, which gave white crystals of **5d** from petroleum ether / diethyl ether: mp 158 °C; IR (KBr): $\tilde{\nu}$ 3515, 3280, 3040, 2940, 1590, 1480, 1280, 1205, 1090, 955, 820, 790, 755; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.28, 1.29 [d, J = 7.0 Hz each, 3H each, $CH(CH_3)_2$], 2.31 (br. s, 1H, CH_2OH), 3.26 [sept, J = 7.0 Hz, 1H, $CH(CH_3)_2$], 3.60 (s, 3H, OCH_3), 4.49 (m_c, 2H, CH_2OH), 4.69 (s, 1H, 2'-OH), 6.65 (d, J = 8.5 Hz, 1H, 5'-H), 7.30 (d, J = 8.5 Hz, 1H, 4'-H), 7.38-7.46 (m, 2H, Ar-H), 7.47-7.56 (m, 1H, Ar-H), 7.71 (d, J = 8.5 Hz, 1H, 3-H or 4-H), 7.90 (d, J = 7.8 Hz, 1H, 8-H), 7.95 (d, J = 8.5 Hz, 1H, 3-H or 4-H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 22.73 [$CH(CH_3)_2$], 26.82 [$CH(CH_3)_2$], 55.83 (OCH_3), 64.17 (CH_2OH), 103.2, 112.5, 125.5, 126.2, 126.3, 126.8, 127.0, 128.2, 128.4, 129.3, 132.5, 133.5, 138.7, 151.2, 155.5 (Ar-C); MS: *m/z* (%) = 322 (16) [M^+], 304 (67) [M^+ - H_2O], 289 (100) [M^+ - CH_5O], 202 (12); Anal. calcd. for $C_{21}H_{22}O_3$ (322.4): C, 78.23; H, 6.88. Found: C, 78.06; H, 7.05.

2-Hydroxymethyl-1-(2'-hydroxy-3'-isopropyl-6'-methylphenyl)naphthalene (5f). According to the general procedure A, **2f** (1.40 g, 4.63 mmol) was converted into **5f** (1.41 g, 4.60 mmol, 99%) as a gummy oil: IR (film): $\tilde{\nu}$ 3470, 3370, 3040, 2940, 2910, 2860, 1410, 1255, 1195, 1145, 815, 750; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.26 [d, J = 7.0 Hz, 6H, $CH(CH_3)_2$], 1.78 (s, 3H, 6'-CH_3), 3.27 [sept, J = 7.0 Hz, 1H, $CH(CH_3)_2$], 4.48 (s, 2H, CH_2OH), 4.72 (s, 1H, 2'-OH), 6.93 (d, J = 7.9 Hz, 1H, 5'-H), 7.24 (d, J = 7.9 Hz, 1H, 4'-H), 7.33-7.44 (m, 2H, Ar-H), 7.47-7.55 (m, 1H, Ar-H), 7.71 (d, J = 8.5 Hz, 1H, 3-H or 4-H), 7.90 (d, J = 7.9 Hz, 1H, 8-H), 7.93 (d, J = 8.5 Hz, 1H, 3-H or 4-H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.03, 23.09, 23.21 [CH_3 and $CH(CH_3)_2$], 27.55 [$CH(CH_3)_2$], 64.05 (CH_2OH), 122.6, 124.1, 125.9, 126.3, 126.8, 127.4, 128.7, 129.6, 131.5, 132.9, 133.2, 134.0, 135.6, 138.2, 150.8 (Ar-C); MS: *m/z* (%) = 306 (7) [M^+], 288 (100) [M^+ - H_2O], 273 (69) [M^+ - CH_5O], 245 (19), 215 (14); Anal. calcd. for $C_{21}H_{22}O_2$ (306.4): C, 82.32; H, 7.24. Found: C, 81.74; H, 7.38.

General procedure B for the oxidation of the alcohols 5a-g to the hydroxy aldehydes 4a-g. 2.50 equivalents of pyridinium chlorochromate (PCC, for **5a** and **5b** only 1.25 equivalents of PCC) were added in portions at -10 °C to a solution of the alcohol **5** in THF (5 ml/mmol **5**). After stirring at room temperature for 0.5 - 2.0 h, the reaction mixture was quenched with water (5 ml/mmol **5**), extracted with diethyl ether (3 x 5 ml/mmol **5**), and dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue chromatographed on silica gel (petroleum ether / diethyl ether 10:1 → 3:1) to yield the pure hydroxy aldehyde **4** as a slightly yellow oil.

6H-Benzo[b]naphtho[1,2-d]pyran-6-ol (3a) ⇌ 1-(2'-hydroxyphenyl)naphthalene-2-carbaldehyde (4a) and 6,6'-oxybis-(6H-benzo[b]naphtho[1,2-d]pyran) (6a). According to the general procedure B, **5a** (450 mg, 1.80 mmol) was oxidized. After chromatographic removal of the more rapidly eluting side products, bisacetal **6a** (40.1 mg, 83.8 μmol, 5%) and lactone **2a** (70.8 mg, 287 μmol, 16%), a pure solution of **3a/4a** was obtained (no formation of **6a** detected by TLC.). If this solution was left standing overnight or if the solvent was removed at room temperature or at -10 °C, condensation of **3a/4a** to **6a** occurred partially. **3a/4a** was further characterized by its conversion into pure **6a** (301 mg, 629 μmol, 70%), by crystallization from petroleum ether / diethyl ether.

The acid catalyzed cleavage of **6a** with traces of DCl in D_8-THF / D_6-DMSO / D_2O (10:10:1), performed in an NMR tube in an analytical scale, yielded a pure mixture of **4a/3a**: ratio of isomers **4a** : **3a** = 52 : 48. The assignment of the NMR signals was done by 2D correlation spectra (TOCSY, HH-COSY and HMQC). ^{1}H NMR (600 MHz, D_8-THF / D_2O / D_6-DMSO / DCl 10:10:1:trace): **4a**: δ = 5.61 (s, 0.2H, 2'-OH), 6.97 (td, *J* = 7.5 Hz, *J* = 1.1 Hz, 1H, 5'-H), 7.14 (m_c, 2H, 3'-H and 6'-H), 7.35 (tm, *J* = 7.5 Hz, 1H, 4'-H), 7.46 (tm, *J* = 7.6 Hz, 1H, 6-H), 7.63 (m_c, 2H, 5-H and 7-H), 7.94, 7.98 (d, d, *J* = 8.6 Hz each, 1H each, 3-H and 4-H), 7.98 (m_c, 1H, 8-H), 9.84 (d, *J* = 0.9 Hz, 1H, CHO). **3a**: δ = 6.33 (s, 1H, 6-H), 7.17 (m_c, 2H, 2-H and 5-H), 7.33 (tm, *J* = 8.7 Hz, 1H, 3-H), 7.54 (d, *J* = 8.4 Hz, 1H, 7-H or 8-H), 7.58 (tm, *J* = 7.6 H, 1H, 11-H), 7.90 (d, *J* = 8.2 Hz, 7-H or 8-H), 7.96 (m_c, 1H, 9-H), 8.12 (dd, *J* = 7.7 Hz, *J* = 1.5 Hz, 1H, 1-H), 8.65 (d, *J* = 8.5 Hz, 1H, 12-H). ^{13}C NMR (150 MHz, D_8-THF / D_2O / D_6-DMSO/DCl 10:10:1:trace): **4a**: δ = 116.7 (C-3'), 119.7 (C-5'), 122.4 (C-3 or C-4), 127.6 (C-6), 128.3 (C-5 or C-7), 128.9, 129.2 (C-3 or C-4 and C-8), 129.6 (C-5 or C-7), 130.9 (C-4'), 133.1 (C-6'), 193.1 (CHO). **3a**: δ = 94.48 (C-6), 119.9, 122.4 (C-2 and C-4), 124.5 (C-7 or C-8), 126.2 (C-12), 126.8 (C-10), 127.7 (C-11), 128.6 (C-1), 129.1 (C-7 or C-8), 129.6 (C-3), 130.0 (C-9). Signals for quaternary C-atoms not assigned: 122.5, 123.6, 126.4, 132.1, 133.5, 134.3, 135.6, 137.3, 144.9, 153.9, 157.0 (Ar-C); MS: *m/z* (%) = 248 (97) [M^+], 247 (42) [M^+ - H], 231 (100) [M^+ - OH], 203 (35), 202 (37); **6a**: mp 200 °C; IR (KBr): $\tilde{\nu}$ 3040, 1575, 1465, 1220, 1030, 950, 905, 795, 730; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.76 (s, 2H, 6-H and 6'-H), 7.02 (d, *J* = 8.5 Hz, 2H, Ar-H), 7.20-7.30 (m, 2H, Ar-H), 7.42-7.57 (m, 8H, Ar-H), 7.66 (d, *J* = 8.2 Hz, 2H, Ar-H), 7.80 (dm, *J* = 7.6 Hz, 2H, Ar-H), 8.11 (d, *J* = 7.6 Hz, 2H, Ar-H), 8.63 (d, *J* = 7.6 Hz, 2H, Ar-H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 93.64 (6-C and 6'-C), 118.6, 122.5, 122.8, 123.2, 125.6, 126.2, 126.4, 126.7, 128.4, 128.5, 128.8, 129.5, 134.8, 151.4 (ArC); MS: *m/z* (%) = 478 (0.2) [M^+], 476 (0.3) [M^+ - H_2], 246 (16) [$C_{17}H_{10}O_2^+$], 231 (100) [$C_{17}H_{11}O^+$], 218 (14), 202 (30); Anal. calcd. for $C_{34}H_{22}O_3$ (478.6): C, 85.34; H, 4.63. Found: C, 85.87; H, 4.52.

4-Isopropyl-6H-benzo[b]naphtho[1,2-d]pyran-6-ol (3b) ⇌ 1-(2'-hydroxy-3'-isopropylphenyl)-naphthalene-2-carbaldehyde (4b) and 6,6'-oxybis-(4-isopropyl-6H-benzo[b]naphtho[1,2-d]pyran (6b). According to the general procedure B, **5b** (5.00 g, 17.1 mmol) was oxidized with PCC. Chromatographic separation gave the bisacetal **6b** (192 mg, 342 μmol, 2%), the lactone **2b** (520 mg, 1.80 mmol, 11%), the lactol **3b** / hydroxy aldehyde **4b** (3.18 g, 11.0 mmol, 64%) and the alcohol **5b** (260 mg, 889 μmol, 5%) as slightly yellow oils in the oder of elution. From dichloromethane / diethyl ether / petroleum ether, **6b** was obtained as colorless crystals in nearly quantitative yield, while **3b** afforded colorless crystals from diethyl ether / petroleum ether (2.15 g, 7.42 mmol, 60%), mp 90 °C; IR (KBr): $\tilde{\nu}$ 3270, 3030, 2950, 2860, 1455, 1185, 1050, 1000, 980, 825, 810, 745; in $CDCl_3$, ratio of isomers **4b** : **3b** = 17 : 83; ^{1}H NMR (250 MHz, $CDCl_3$): **4b**: δ = 1.32, 1.35 (d, d, J = 6.9 Hz each, 3H each, $CH(CH_3)_2$), 3.34 (sept, J = 6.9 Hz, 1H, $CH(CH_3)_2$), 4.60 (s, 1H, 2'-OH), 7.08 (m_c, 2H, Ar-H), 7.41 (m_c, 1H, Ar-H), 7.51 (m_c, 1H, Ar-H), 7.62 (m_c, 1H, Ar-H), 7.65 (m_c, 1H, Ar-H), 7.68 (m_c, 1H, Ar-H), 7.91 (m_c, 1H, Ar-H), 8.10 (d, J = 8.5 Hz, 1H, 12-H), 9.89 (d, J = 0.9 Hz, 1H, CHO); **3b**: δ = 1.33, 1.34 [d, d, J = 6.9 Hz each, 3H each, $CH(CH_3)_2$], 3.26 (d, J = 8.5 Hz, 1H, 6-OH), 3.56 [sept, J = 6.9 Hz, 1H, $CH(CH_3)_2$], 6.39 (d, J = 8.2 Hz, 1H, 6-H), 7.19 (t, J = 7.7 Hz, 1H, 2-H), 7.33 (dd, J = 7.7 Hz, J = 1.2 Hz, 1H, 3-H), 7.46 (d, J = 8.2 Hz, 1H, 7-H or 8-H), 7.57 (m_c, 2H, Ar-H), 7.83 (d, J = 8.2 Hz, 1H, 7-H or 8-H), 7.91 (m_c, 1H, Ar-H), 7.98 (dd, J = 7.7 Hz, J = 1.2 Hz, 1H, 1-H), 8.69 (m_c, 1H, 12-H); ^{13}C NMR (63 MHz, $CDCl_3$): **4b**: δ = 22.58, 22.61 [$CH(CH_3)_2$], 27.10 [$CH(CH_3)_2$], 120.5, 122.4, 126.1, 127.0, 127.1, 127.5, 128.5, 132.3, 135.3, 136.4, 141.0, 150.7 (Ar-C), 192.5 (CHO); **3b**: δ = 22.68, 22.87 [$CH(CH_3)_2$], 27.10 [$CH(CH_3)_2$], 93.60 (C-6), 121.7, 121.8, 122.9, 125.6, 125.9, 126.2, 126.7, 128.4, 128.9, 129.0, 129.3, 131.5, 134.8, 139.0, 148.5 (Ar-C); MS: *m/z* (%) = 290 (100) [M^+], 273 (70) [M^+ - OH], 257 (23) [M^+ - CH_5O], 247 (47) [M^+ - C_3H_7], 202 (31), 101 (30); Anal. calcd. for $C_{20}H_{18}O_2$ (290.4): C, 82.73; H, 6.25. Found: C, 82.05; H, 6.27. **6b**: mp 248 °C; IR (KBr): $\tilde{\nu}$ 3050, 3030, 2950, 2910, 2850, 1580, 1560, 1505, 1455, 1380, 1180, 1050, 990, 935, 805, 785, 735; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.42, 1.55 [d, d, J = 7.0 Hz each, 6H each, 2 $CH(CH_3)_2$], 3.88 [sept, J = 7.0 Hz, 1H, 2 $CH(CH_3)_2$], 6.81 (d, J = 8.2 Hz, 1H, 6-H and 6'-H), 6.92 (d, J = 7.9 Hz, 2H, 1-H and 1'-H or 3-H and 3'-H), 7.24 (t, J = 7.9 Hz, 1H, 2-H and 2'-H), 7.38-7.58 (m, 6H, Ar-H), 7.64 (d, J = 8.5 Hz, 2H, Ar-H), 7.80 (dm, J = 7.9 Hz, 2H, 7-H and 7'-H or 8-H and 8'-H), 7.95 (d, J = 6.7 Hz, 2H, 12-H and 12'-H), 8.64 (d, J = 7.9 Hz, 2H, 7-H and 7'-H or 8-H and 8'-H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 22.27, 24.55 [$CH(CH_3)_2$], 26.85 [$CH(CH_3)_2$], 94.08 (C-6 and C-6'), 122.0, 122.3, 122.7, 125.6, 125.8, 126.1, 126.6, 127.0, 128.3, 128.8, 129.0, 129.5, 134.8, 137.9, 148.2 (Ar-C); MS: *m/z* (%) = 562 (0.1) [M^+], 289 (4) [M^+ - $C_{20}H_{17}O$], 288 (17) [M^+ - $C_{20}H_{18}O$], 274 (39) [$C_{20}H_{18}O^+$], 273 (100) [$C_{20}H_{17}O^+$]; Anal. calcd. for $C_{40}H_{34}O_3$ (562.7): C, 85.38; H, 6.09. Found: C, 85.07; H, 6.18.

1-(4',6'-Dimethoxy-2'-hydroxyphenyl)naphthalene-2-carbaldehyde (4c). According to the general procedure B, oxidation of **5c** (200 mg, 644 μmol) gave **4c** (145 mg, 470 μmol, 73%). From diethyl ether / petroleum ether, **4c** was obtained as a yellow-green powder: mp 177-178 °C; IR (KBr): $\tilde{\nu}$ 3220, 2960, 2920, 1645, 1605, 1580, 1415, 1235, 1205, 1155, 1095, 815; ^{1}H NMR (200 MHz, CD_3OD): δ = 3.37 (s, 3H, 6'-OCH_3), 3.65 (s, 3H, 4'-OCH_3), 6.04, 6.08 (d, J = 2.1 Hz each, 1H each, 3'-H and 5'-H), 7.20 (m_c, 1H, Ar-H), 7.31-7.45 (m, 2H, Ar-H), 7.62-7.77 (m, 3H, Ar-H), 9.63 (s, 1H, CHO), [In $CDCl_3$ **4b** decomposed.]; ^{13}C NMR (63 MHz, CD_3OD): δ = 55.84, 56.05 (OCH_3 at C-4' and OCH_3 at C-6'), 91.21, 94.56, 104.2, 122.6, 127.5, 128.3, 128.9, 129.2, 129.7, 133.2, 134.5, 138.0, 142.6, 158.2, 160.9, 163.6 (Ar-C), 195.1 (CHO); MS: *m/z* (%) = 308 (100) [M^+], 307 (11) [M^+ - H], 291 (10) [M^+ - OH], 280 (26) [M^+ - CO], 249 (13) [M^+ - $C_2H_3O_2$], 248

(13) [M^+ - $C_2H_4O_2$]; HR-MS *m/z* calcd. for $C_{19}H_{16}O_2$: 308.105. Found: 308.105.

1-(2'-Hydroxy-3'-isopropyl-6'-methoxyphenyl)naphthalene-2-carbaldehyde (4d). According to the general procedure B, **5d** (100 mg, 310 μmol) was converted into **4d** (73.9 mg, 231 μmol, 75%), which gave colorless crystals of **4d** from petroleum ether / diethyl ether: mp 190 °C; IR (KBr): $\tilde{\nu}$ 3350, 3040, 2940, 2860, 1665, 1585, 1475, 1420, 1275, 1085, 815, 785; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.27, 1.30 [d, d, *J* = 6.9 Hz each, 3H each, $CH(CH_3)_2$], 3.23 [sept, *J* = 6.9 Hz, 1H, $CH(CH_3)_2$], 3.61 (s, 3H, OCH_3), 4.46 (s, 0.7H, 2'-OH), 6.64 (d, *J* = 8.7 Hz, 1H, 5'-H), 7.33 (d, *J* = 8.7 Hz, 1H, 4'-H), 7.52 (m_c, 1H, Ar-H), 7.62 (m_c, 2H, Ar-H), 7.95 (m, 1H, Ar-H), 8.00, 8.12 (d, d, *J* = 8.7 Hz each, 1H each, 3-H and 4-H), 9.88 (s, 1H, CHO); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 23.44 [$CH(CH_3)_2$], 27.73 [$CH(CH_3)_2$], 56.04 (OCH_3), 103.6, 112.2, 122.8, 127.8, 128.0, 128.1, 129.3, 129.5, 129.8, 130.0, 133.4, 134.2, 138.1, 142.1, 154.0, 157.8 (Ar-C), 194.7 (CHO); MS: *m/z* (%) = 320 (61) [M^+], 305 (100) [M^+ - CH_3], 277 (39) [M^+ - C_3H_7], 202 (11); Anal. calcd. for $C_{21}H_{20}O_3$ (320.4): C, 78.73; H, 6.29. Found: C, 77.97; H, 6.45.

1-(4',6'-Dimethyl-2'-hydroxyphenyl)naphthalene-2-carbaldehyde (4e). According to the general procedure B, **5e** (896 mg, 3.22 mmol) was converted into **4e** (787 mg, 2.85 mmol, 88%), which gave colorless crystals of **4e** from petroleum ether / diethyl ether: mp 151-152 °C (lit.[13]: 143-145 °C); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 20.06, 21.32 (CH_3 at C-4' and CH_3 at C-6'), 113.8, 118.0, 122.4, 123.3, 126.5, 127.5, 128.5, 129.1, 129.3, 132.1, 132.2, 136.6, 138.5, 140.0, 140.8, 153.6 (Ar-C), 192.7 (CHO). The further spectroscopic data were identical to those of material previously obtained.[13]

1-(2'-Hydroxy-3'-isopropyl-6'-methylphenyl)naphthalene-2-carbaldehyde (4f). According to the general procedure B, oxidation of **5f** (378 mg, 1.23 mmol) yielded **4f** (342 mg, 1.12 mmol, 90%). From diethyl ether / petroleum ether, **4f** was obtained as colorless crystals: mp 183 °C; IR (KBr): $\tilde{\nu}$ 3400, 3040, 2940, 2860, 1665, 1445, 1420, 1230, 820, 800; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.27, 1.30 [d, d, *J* = 6.9 Hz each, 3H each, $CH(CH_3)_2$], 1.82 (s, 3H, 6'-CH_3), 3.24 [sept, *J* = 6.9 Hz, 1H, $CH(CH_3)_2$], 4.33 (s, 1H, 2'-OH), 6.95 (d, *J* = 7.8 Hz, 1H, 5'-H), 7.28 (d, *J* = 7.8 Hz, 1H, 4'-H), 7.42-7.61 (m, 2H, Ar-H), 7.62-7.73 (m, 1H, Ar-H), 7.97 (d, *J* = 8.5 Hz, 1H, 3-H or 4-H), 8.01 (d, *J* = 9.0 Hz, 1H, 12-H), 8.13 (d, *J* = 8.5 Hz, 1H, 3-H or 4-H), 9.84 (d, *J* = 0.7 Hz, 1H, CHO); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.88, 22.61, 22.68 [CH_3 and $CH(CH_3)_2$], 27.02 [$CH(CH_3)_2$], 120.5, 122.0, 122.5, 126.4, 126,6, 127.7, 128.6, 129.4, 129.5, 132.1, 132.3, 132.4, 135.6, 136.7, 140.5, 150.7 (Ar-C), 192.4 (CHO); MS: *m/z* (%) = 304 (100) [M^+], 289 (89) [M^+ - CH_3], 261 (56) [M^+ - C_3H_7], 228 (18), 202 (14); Anal. calcd. for $C_{21}H_{20}O_2$ (304.4): C, 82.86; H, 6.62. Found: C, 82.89; H; 6.66.

1-(4',6'-Di-*tert*-butyl-2'-hydroxyphenyl)naphthalene-2-carbaldehyde (4g). According to the general procedure B, **5g** (384 mg, 106 mmol) was oxidized to yield **4g** (318 mg, 882 μmol, 83%). Crystallization from petroleum ether / diethyl ether afforded **4g** as colorless crystals: mp 175 °C; IR (KBr): $\tilde{\nu}$ 3340, 2940, 2850, 1645, 1600, 1445, 1400, 1295, 1235, 970, 855, 810, 760; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.96 [s, 9H, 6'-$C(CH_3)_3$], 1.40 [s, 9H, 4'-$C(CH_3)_3$], 4.18 (s, 1H, 2'-OH), 6.92, 7.32 (d, *J* = 1.8 Hz each, 1H each, 3'-H and 5'-H), 7.48 (tm, *J* = 7.5 Hz, 1H, Ar-H), 7.57-7.69 (m, 2H, Ar-H), 7.95 (m_c, 1H, Ar-H), 7.99, 8.09 (d, d, *J* = 8.6 Hz each, 1H each, 3-H and 4-H), 9.88 (d, *J* = 0.6 Hz, 1H, CHO); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 31.35, 32.54 [$C(CH_3)_3$ at C-4' and $C(CH_3)_3$ at C-6'], 34.97, 37.24 [$C(CH_3)_3$ at C-4' and $C(CH_3)_3$ at C-6'], 110.3, 112.9,

117.5, 122.3, 127.3, 127.4, 128.4, 129.3, 133.1, 133.6, 136.3, 149.9, 153.0 (Ar-C), 192.8 (CHO); MS: *m/z* (%) = 360 (18) [M^+], 303 (100) [M^+ - C_4H_9], 247 (19) [M^+ - C_8H_{17}], 57 (38) [$C_4H_9^+$]; Anal. calcd. for $C_{25}H_{28}O_2$ (360.5): C, 83.30; H, 7.83. Found: C, 83.02; H, 7.73.

General procedure C for preparation of the 6-alkoxy-6H-pyrans 7 and 8. The hydroxy aldehyde **4**, molecular sieve (4 Å, 5 g/100 mg **4**), and a catalytic amount of *p*TosOH were dissolved in the alcohol (5 ml/100 mg **4**), and refluxed for 24 h. K_2CO_3 (100 mg/100 mg **4**) was added and the solvent removed *in vacuo*. Chromatography on deactivated silica gel (7.5% NH_3, petroleum ether / diethyl ether 20:1) afforded the 6-alkoxy-6H-pyrans **7** or **8** as slightly yellow oils.

For complete conversions to the 6-alkoxy-6H-pyrans **7a** and **7b**, toluene (3.5 ml/mmol **4e**) was added to the reaction mixture after refluxing. The residual alcohol was distilled off and the remaining solution refluxed again for 3 h, before workup was done as described above.

1,3-Dimethyl-6-methoxy-6H-benzo[b]naphtho[1,2-d]pyran (7a). According to the general procedure C, **4e** (300 mg, 1.09 mmol) was converted with methanol into **7a** (286 mg, 985 µmol, 90%), which gave colorless crystals (253 mg, 871 µmol, 80%) from petroleum ether / diethyl ether: mp 142 °C; IR (KBr): $\tilde{\nu}$ 3010, 2900, 2810, 1595, 1425, 1075, 1040, 935, 810; in $CDCl_3$, ratio of diastereomers *ax*-**7a** : *eq*-**7a** = 91:9; ^{1}H NMR (250 MHz, $CDCl_3$): *ax*-**7a**: δ = 2.26 (s, 3H, 1-CH_3), 2.42 (s, 3H, 3-CH_3), 3.55 (s, 3H, OCH_3), 5.91 (s, 1H, 6-H), 6.93, 6.95 (s, s, 1H each, 2-H and 4-H), 7.43-7.55 (m, 3H, Ar-H), 7.82-7.99 (m, 3H, Ar-H); *eq*-**7a**: δ = 2.26 (s, 3H, 1-CH_3), 2.42 (s, 3H, 3-CH_3), 3.88 (s, 1H, OCH_3), 5.67 (s, 1H, 6-H), 6.93, 6.95 (s, s, 1H each, 2-H und 4-H), 7.43-7.55 (m, 3H, Ar-H), 7.67-7.99 (m, 3H, Ar-H); ^{13}C NMR (63 MHz, $CDCl_3$): *ax*-**7a**: δ = 21.32, 22.94 (CH_3 at C-1 and CH_3 at C-3), 56.10 (OCH_3), 100.1 (C-6), 116.1, 120.4, 123.2, 125.4, 125.9, 126.8, 127.5, 127.7, 128.2, 129.0, 131.7, 134.3, 135.8, 138.6, 152.2 (Ar-C); *eq*-**7a**: δ = 22.46, 22.94 (CH_3 at C-1 and CH_3 at C-3), 57.50 (OCH_3), 102.6 (C-6), 115.1, 125.7, 126.4, 127.0, 127.1, 128.3, 139.1, 153.3 (Ar-C); MS: *m/z* (%) = 290 (25) [M^+], 259 (100) [M^+ - OCH_3], 216 (10), 215 (20), 101 (8); Anal. calcd. for $C_{20}H_{18}O_2$ (290.4): C, 82.73; H, 6.26. Found: C, 82.97; H, 6.37.

1,3-Dimethyl-6-ethoxy-6H-benzo[b]naphtho[1,2-d]pyran (7b). According to the general procedure C, **4e** (300 mg, 1.09 mmol) was cyclized with ethanol to **7b** (283 mg, 930 µmol, 85%). From diethyl ether / petroleum ether, **7b** (253 mg, 831 µmol, 76%) was obtained as colorless crystals: mp 124 °C; IR (KBr): $\tilde{\nu}$ 3020, 2950, 2880, 1600, 1435, 1315, 1080, 1030, 970, 810; in $CDCl_3$, ratio of diastereomers *ax*-**7b** : *eq*-**7b** = 88:12; ^{1}H NMR (250 MHz, $CDCl_3$): *ax*-**7b**: δ = 1.20 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 2.25 (s, 3H, 1-CH_3), 2.41 (s, 3H, 3-CH_3), 3.82, 3.88 (q, q, *J* = 7.0 Hz each, 2H each, OCH_2CH_3), 6.03 (s, 1H, 6-H), 6.91 (s, 2H, 2-H and 4-H), 7.42-7.54 (m, 3H, Ar-H), 7.82-7.90 (m, 3H, Ar-H); *eq*-**7b**: δ = 1.46 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 2.25 (s, 3H, 1-CH_3), 2.41 (s, 3H, 3-CH_3), 3.78, 3.92 (q, q, *J* = 7.0 Hz each, 2H each, OCH_2CH_3), 5.76 (s, 1H, 6-H), 6.91 (s, 2H, 2-H and 4-H), 7.42-7.54 (m, 3H, Ar-H), 7.73-7.90 (m, 3H, Ar-H); ^{13}C NMR (63 MHz, $CDCl_3$): *ax*-**7b**: δ = 15.04 (CH_2CH_3), 21.32, 22.96 (CH_3 at C-1 and CH_3 at C-3), 64.12 (OCH_2), 98.74 (C-6), 116.0, 120.4, 123.1, 125.3, 125.9, 126.6, 127.2, 127.5, 127.7, 128.1, 129.1, 131.9, 134.3, 135.8, 138.4, 152.4 (Ar-C); *eq*-**7b**: δ = 15.33 (CH_2CH_3), 22.44, 22.96 (CH_3 at C-1 and CH_3 at C-3), 65.90 (OCH_2), 101.5 (C-6), 115.1, 120.5, 121.4, 125.4, 125.6, 126.3, 127.0, 128.3, 128.7, 134.2, 134.7, 139.0 (Ar-C); MS: *m/z* (%) = 304 (24) [M^+], 259 (100) [M^+ - OC_2H_5], 216 (10), 215 (18); Anal. cacld. for $C_{21}H_{20}O_2$ (304.4): C, 82.86; H, 6.62. Found: C, 82.64; H, 6.76.

1,3-Dimethyl-6-isopropoxy-6H-benzo[b]naphtho[1,2-d]pyran (7c). According to the general procedure C, **4e** (300 mg, 1.09 mmol) was converted with isopropanol into **7c** (284 mg, 892 μmol, 82%), which gave colorless crystals (250 mg, 785 μmol, 72%) from petroleum ether / diethyl ether: mp 72 °C; IR (KBr): $\tilde{\nu}$ 3010, 2940, 2900, 1595, 1115, 1065, 1035, 970, 835, 805; in $CDCl_3$, ratio of diastereomers *ax*-**7c** : *eq*-**7c** = 83:17; ^{1}H NMR (250 MHz, $CDCl_3$): *ax*-**7c**: δ = 1.08, 1.33 [d, d, *J* = 6.4 Hz each, 3H each, $CH(CH_3)_2$], 2.26 (s, 3H, 1-CH_3), 2.42 (s, 3H, 3-CH_3), 4.27 [sept, *J* = 6.4 Hz, 1H, $OCH(CH_3)_2$], 6.11 (s, 1H, 6-H), 6.91 (s, 2H, 2-H and 4-H), 7.40-7.54 (m, 3H, Ar-H), 7.82-7.92 (m, 3H, Ar-H); *eq*-**7c**: δ = 1.39, 1.50 [d, d, *J* = 6.4 Hz each, 3H each, $CH(CH_3)_2$], 2.26 (s, 3H, 1-CH_3), 2.42 (s, 3H, 3-CH_3), 4.40 [sept, *J* = 6.4 Hz, 1H, $OCH(CH_3)_2$], 5.84 (s, 1H, 6-H), 6.91 (s, 2H, 2-H and 4-H), 7.40-7.54 (m, 3H, Ar-H), 7.74-7.92 (m, 3H, Ar-H); ^{13}C NMR (63 MHz, $CDCl_3$): *ax*-**7c**: δ = 21.30, 21.76, 22.96, 23.06 [CH_3 at C-1, CH_3 at C-3 and $CH(CH_3)_2$], 70.04 [$OCH(CH_3)_2$], 97.13 (C-6), 116.1, 122.9, 125.3, 125.8, 126.4, 127.2, 127.5, 127.7, 128.1, 129.1, 132.1, 134.2, 135.7, 138.3, 152.7 (Ar-C); *eq*-**7c**: δ = 21.36, 21.76, 22.08, 22.43 [CH_3 at C-1, CH_3 at C-3 and $CH(CH_3)_2$], 72.69 [$OCH(CH_3)_2$], 100.2 (C-6), 115.1, 120.3, 120.7, 125.3, 125.6, 126.2, 126.9, 127.9, 128.2, 128.7, 135.1, 135.7, 139.0, 153.6 (Ar-C); MS: *m/z* (%) = 318 (71) [M^+], 276 (100) [$M^+ - C_3H_6$], 261 (15) [$M^+ - OC_3H_5$], 260 (20) [$M^+ - OC_3H_6$], 259 (86) [$M^+ - OC_3H_7$], 248 (34), 233 (31), 215 (31); Anal. cacld. for $C_{22}H_{22}O_2$ (318.4): C, 82.99; H, 6.96. Found: C, 83.51; H, 7.05.

1,3-Dimethyl-6-neopentoxy-6H-benzo[b]naphtho[1,2-d]pyran (7d). According to the general procedure C, cyclization of **4e** (200 mg, 724 μmol) with neopentyl alcohol gave **7d** (155 mg, 447 μmol, 62%) as a slightly yellow gummy oil: IR (KBr): $\tilde{\nu}$ 3030, 2930, 2850, 1600, 1455, 1140, 1100, 1080, 1050, 1025, 810; in $CDCl_3$, ratio of diastereomers *ax*-**7d** : *eq*-**7d** = 77:23; ^{1}H NMR (250 MHz, $CDCl_3$): *ax*-**7d**: δ = 0.76 [s, 9H, $C(CH_3)_3$], 2.26 (s, 3H, 1-CH_3), 2.40 (s, 3H, 3-CH_3), 3.35, 3.52 (d, *J* = 9.0 Hz, 2H, OCH_2), 5.96 (s, 1H, 6-H), 6.90 (s, 2H, 2-H and 4-H), 7.41-7.53 (m, 3H, Ar-H), 7.79-7.90 (m, 3H, Ar-H); *eq*-**7d**: δ = 1.11 [s, 9H, $C(CH_3)_3$], 2.25 (s, 3H, 1-CH_3), 2.40 (s, 3H, 3-CH_3), 3.46, 4.02 (d, *J* = 8.9 Hz, 2H, OCH_2), 5.71 (s, 1H, 6-H), 6.90 (s, 2H, 2-H and 4-H), 7.41-7.53 (m, 3H, Ar-H), 7.75-7.90 (m, 3H, Ar-H); ^{13}C NMR (63 MHz, $CDCl_3$): *ax*-**7d**: δ = 21.27, 22.79 (CH_3 at C-1 and CH_3 at C-3), 26.44 [$C(CH_3)_3$], 31.77 [$C(CH_3)_3$], 78.09 (OCH_2), 99.24 (C-6), 116.2, 123.2, 125.3, 125.8, 126.3, 127.2, 127.4, 127.5, 128.1, 129.1, 132.4, 134.3, 135.6, 138.2, 152.5 (Ar-C); *eq*-**7d**: δ = 21.38, 22.44 (CH_3 at C-1 and CH_3 at C-3), 26.79 [$C(CH_3)_3$], 32.31 [$C(CH_3)_3$], 80.56 (OCH_2), 102.1 (C-6), 115.1, 120.6, 125.4, 125.6, 126.2, 127.0, 127.6, 128.3, 128.8, 134.2, 134.9, 135.7, 139.0, 153.5 (Ar-C); MS: *m/z* (%) = 346 (42) [M^+], 276 (48) [$M^+ - C_5H_{10}$], 259 (100) [$M^+ - OC_5H_{11}$], 248 (16), 215 (18), 71 (27) [$C_5H_{11}^+$]; Anal. cacld. for $C_{24}H_{26}O_2$ (346.5): C, 83.20; H, 7.56. Found: C, 83.98; H, 7.38.

4-Isopropyl-6-methoxy-6H-benzo[b]naphtho[1,2-d]pyran (8a). According to the general procedure C, **3b/4b** (100 mg, 344 μmol) was converted with methanol into **8a** (95.0 mg, 312 μmol, 91%), which gave colorless crystals (88.7 mg, 291 μmol, 85%) from petroleum ether / diethyl ether: mp 97-98 °C; IR (KBr): $\tilde{\nu}$ 3040, 2940, 1455, 1380, 1175, 1080, 980, 955, 805, 740; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.33, 1.39 [d, d, *J* = 7.0 Hz each, 3H each, $CH(CH_3)_2$], 3.61 (s, 3H, OCH_3), 3.68 [sept, *J* = 7.0 Hz, 1H, $CH(CH_3)_2$], 6.03 (s, 1H, 6-H), 7.21 (t, *J* = 7.6 Hz, 1H, 2-H), 7.35 (dd, *J* = 7.6 Hz, *J* = 1.5 Hz, 1H, 3-H), 7.46 (d, *J* = 8.5 Hz, 1H, 7-H or 8-H), 7.50-7.61 (m, 2H, Ar-H), 7.85 (d, *J* = 8.5 Hz, 1H, 7-H or 8-H), 7.88-7.95 (m, 1H, Ar-H), 8.01 (dd, *J* = 7.6 Hz, *J* = 1.5 Hz, 1H, 1-H), 8.71 (m_c, 1H, 12-H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 22.65, 24.02 [$CH(CH_3)_2$], 26.38 [$CH(CH_3)_2$], 56.37 (OCH_3), 100.3 (C-6), 121.7, 122.2, 123.2, 125.8, 126.0, 126.1, 126.6, 126.8, 128.2,

128.9, 129.1, 130.4, 134.9, 138.3, 148.5 (Ar-C); MS: *m/z* (%) = 304 (18) [M^+], 273 (100) [M^+ - OCH_3], 258(15), 257 (20), 202 (19), 101 (14); Anal. calcd. for $C_{21}H_{20}O_2$ (304.4): C, 82.87; H, 6.62. Found: C, 82.90; H, 6.54.

4-Isopropyl-6-ethoxy-6H-benzo[b]naphtho[1,2-d]pyran (8b). According to the general procedure C, **3b/4b** (100 mg, 344 µmol) was cyclized with ethanol to **8b** (99.1 mg, 311 µmol, 90%). From diethyl ether / petroleum ether, **8b** (89.3 mg, 280 µmol, 82%) was obtained as colorless crystals: mp 89-90 °C; IR (KBr): $\tilde{\nu}$ 3050, 2950, 2910, 2850, 1460, 1445, 1070, 985, 810, 740; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.23 [t, *J* = 7.0 Hz, 3H, CH_2CH_3], 1.32, 1.36 [d, d, *J* = 7.0 Hz each, 3H each, $CH(CH_3)_2$], 3.66 (sept, *J* = 7.0 Hz, 1H, $CH(CH_3)_2$), 3.90, 3.97 (dq, dq, *J* = 33.0 Hz each, *J* = 7.0 Hz each, 1H each, CH_2CH_3), 612 (s, 1H, 6-H), 7.19 (t, *J* = 7.6 Hz, 1H, 2-H), 7.33 (dd, *J* = 7.6 Hz, *J* = 1.5 Hz, 1H, 3-H), 7.46 (d, *J* = 8.2 Hz, 1H, 7-H or 8-H), 7.48-7.60 (m, 2H, Ar-H), 7.84 (d, *J* = 8.2 Hz, 1H, 7-H or 8-H), 7.88-7.93 (m, 1H, Ar-H), 8.00 (dd, *J* = 7.9 Hz, *J* = 1.5 Hz, 1H, 1-H), 8.70 (m_c, 1H, 12-H); ^{13}C NMR (63 MHz, $CDCl_3$): δ = 15.04 (OCH_2CH_3), 22.68, 23.88 [$CH(CH_3)_2$], 26.44 [$CH(CH_3)_2$], 64.30 (OCH_2CH_3), 98.82 (C-6), 121.5, 122.3, 123.1, 125.7, 125.8, 126.0, 126.5, 126.9, 128.2, 128.8, 129.2, 130.7, 134.9, 138.2, 148.7 (Ar-C); MS: *m/z* (%) = 318 (19) [M^+], 273 (100) [M^+ - OC_2H_5], 257 (13), 202 (13); Anal. calcd. for $C_{22}H_{22}O_2$ (318.4): C, 82.99; H, 6.96. Found: C, 82.62; H, 7.04.

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23. X-ray crystallographic data were deposited at the Cambridge Crystallographic Data Centre. Crystal data for **8a**: $C_{21}H_{20}O_2$, monoclinic, space group $P2_1/n$; unit cell parameters: a = 1053.4(2), b = 2916.6(4), c = 1167.0(2) pm; β = 111.88(1)°; V = 3327(1)·10^6 pm^3. Crystal data for **3b**: $C_{20}H_{18}O_2$, monoclinic, space group $P2_1/a$; unit cell parameters: a = 2697(1), b = 1118.6(3), c = 1065.9(3) pm; β = 92.65(3)°; V = 3212·10^6 pm^3. Crystal data for C_2-**6b**: $C_{40}H_{34}O_3$, monoclinic, space group $C2/c$; unit cell parameters: a = 2470.7(4), b = 836.8(2), c = 1598.9(3) pm; β = 113.37(1)°; V = 3035(1)·10^6 pm^3.
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