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Regioselective synthesis of amino- and nitroarenes based on [3+3] cyclocondensations of 1,3-bis(silyloxy)-1,3-butadienes

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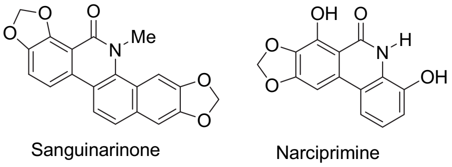
ABSTRACT

Functionalized amino- and nitro-substituted biaryls and dibenzo[*b*,*d*]pyrid-6-ones (6(5*H*)-phenanthridinones) were prepared by [3+3]cyclocondensation of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with nitro-substituted 1-aryl-1-silyloxy-1-en-3-ones and subsequent hydrogenation. 4-Nitro- and 4-aminophenols were prepared based on formal [3+3] cyclizations of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 3-ethoxy-2-nitro-2-en-1-ones.

1. Introduction

Functionalized 4-nitro- and 4-aminophenols are of considerable pharmacological relevance and occur in several natural products.[1] 4-Nitrophenols show antiandrogenetic,[2a] vasodilative,[2b] and estrogenic activity.[2c] A wide range of pharmacological activities has been reported for functionalized 4-aminophenols and related molecules.[3–8] Amino- and nitro-substituted biaryl derivatives are also of considerable current interest, due to their anti-hepatitis and antimalarial activity, binding affinity to C5a receptor (human monocyte cell line U937), inhibition of cyclic nucleotide phosphorodiesterases (PDEs), and activity for topoisomerases I and II-mediated DNA cleavage.[8] Dibenzo[*b*,*d*]pyrid-6-ones (6(5*H*)-phenanthridinones) can be regarded as lactams derived from amino-substituted biaryls. Similar to amino-substituted biaryls, they are of considerable pharmacological relevance and occur in a variety of natural products. For example, sanguinarinone shows anti-proliferative activity against leukemia HL-60 cells, antiparasitic activity, and anticoagulant activity.[9] Anti-proliferative activity against P-388 and human colon carcinoma HT-29 cells have been reported for oxotoddaline.[10] Oxynitidine possesses cytotoxic activity.[11] Several other biologically active natural products, such as narciprimine, chelirubinone, oxychelirubine, arolycoricidine, pratosine, turraeanthin B, or kalbretorine, are known.[12]



The synthesis of nitro- and amino-substituted arenes and biaryls by nitration[13] of arenes and biphenyls suffers from the low regioselectivity. The classical synthesis of parent *p*-nitrophenol relies on the nitration of phenol with nitric acid and subsequent steam distillation (15% yield). The competing formation of *o*-nitrophenol is a severe problem.[14] Various studies to increase the yield of pure 4-nitrophenol and related derivatives have been carried out.[15] Recently, *p*-nitrophenol has been prepared in 80% yield by nitration of phenol with $Fe(NO_3)_3 \cdot 9H_2O$ in the ionic liquid [bbim][BF_4].[16] An additional problem arises from the fact that, due to the harsh reaction conditions, several side-reactions are possible for more complex substrates. Nitro-substituted biaryls are available by Ullmann-type reactions and by nucleophilic aromatic substitutions.[17] However, the scope of these reactions is limited by steric and electronic effects (low conversion, formation of regioisomeric mixtures). The synthesis of amino-substituted biaryls by

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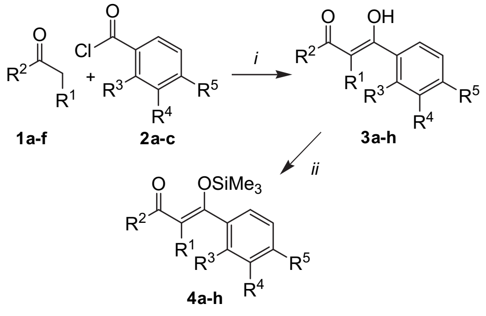
palladium(0)-catalyzed coupling reactions[18] suffers from the fact that electron-rich arenes, in particular sterically encumbered substrates, often react sluggishly or not at all. Last but not the least, the synthesis of the required starting materials, highly functionalized or sterically encumbered aryl halides or triflates (the latter derived from the corresponding phenols), can be a difficult and tedious task. 6(5*H*)-Phenanthridinones have been prepared from 2-alkoxycarbonyl-2-nitrobiaryls by reduction of the nitro into an amino group (using Fe/AcOH, Fe/THF, Zn/HOAc, Raney-Ni, or H_2-Pd/C) and subsequent cyclization.[19] Whereas this process is straightforward, problems are, as described above, associated to the synthesis of functionalized biaryl systems.

All syntheses of nitro- and amino-substituted arenes and biaryls, which were outlined above, rely on the functionalization of a suitable arene. An interesting alternative is based on the use of synthetic building blocks in cyclocondensation reactions. Davies et al. reported the regioselective synthesis of anilines by addition of ketones to vinamidinium salts.[20] Carter and co-workers reported the synthesis of nitro-substituted biaryls based on Diels–Alder reactions.[21] Chan and co-workers were the first to report[22] a convenient synthesis of functionalized phenols by $TiCl_4$-mediated [3+3] cyclization[23] of 1,3-bis(trimethylsilyloxy)-1,3-butadienes[24] with 3-silyloxy-2-en-1-ones. Recently, we have reported[25] the application of this reaction to the synthesis of nitro- and amino-substituted biaryls and of 6(5*H*)-phenanthridinones. We have also reported the synthesis of 4-nitro- and 4-aminophenols based on formal [3+3] cyclizations of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 3-ethoxy-2-nitro-2-en-1-ones.[26] Herein, we report full details of both studies. All products reported herein are not readily available by other methods.

2. Results and discussion

The novel nitro-substituted benzoylacetones **3a**–**e**,**g**,**h** were prepared in 34–85% yields by LDA-mediated reaction of ketones **1a**–**e** with benzoyl chlorides **2a**–**c** (Scheme 1, Table 1). The reaction of **3c** with *N*-chlorosuccinimide (NCS) gave the chlorinated benzoylacetone **3f**. The silylation of **3a**–**h** afforded the 1-aryl-1-silyloxy-1-en-3-ones **4a**–**h** in high yields.



Scheme 1. Synthesis of **3a**–**h** and **4a**–**h**; *i*: LDA (1.5 equiv), THF; ii: 1) NEt_3 (1.6 equiv), Me_3SiCl (1.8 equiv), C_6H_6, 20 °C, 3 d. Products **4** exist as mixtures of *E*/*Z* isomers.

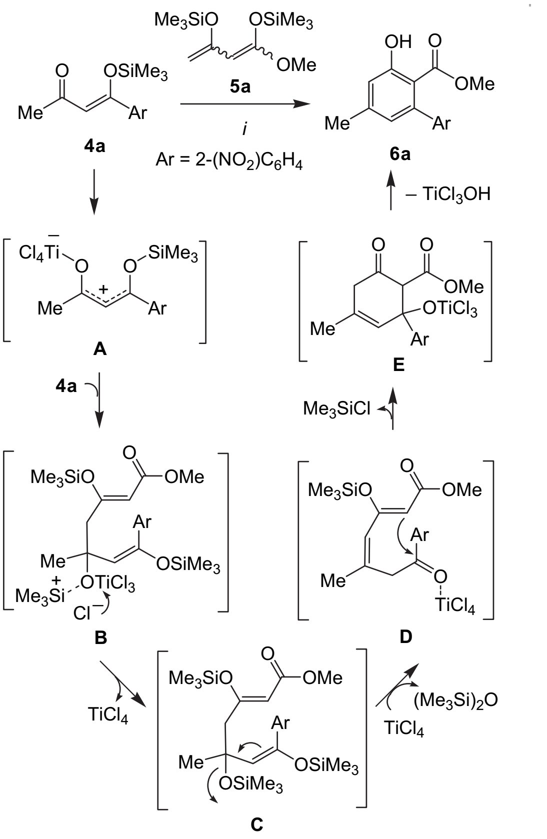
Table 1
Synthesis of **3a**–**h** and **4a**–**h**

3,4	R^1	R^2	R^3	R^4	R^5	% (**3**)[a]	% (**4**)[a]
a	H	Me	NO_2	H	H	54	91
b	H	Et	NO_2	H	H	45	95
c	H	*n*Pr	NO_2	H	H	45	88
d	H	*n*Bu	NO_2	H	H	40	93
e	Me	Et	NO_2	H	H	48	94
f	Cl	*n*Pr	NO_2	H	H	85[b]	92
g	H	Me	H	NO_2	H	34	90
h	H	Me	H	H	NO_2	43	92

[a] Yields of isolated products.

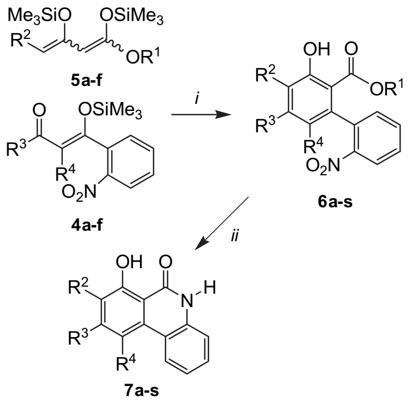
[b] **3f** was prepared by chlorination of **3c**, conditions: NCS (1.0 equiv), CCl_4, 8 h, 75–80 °C.

The $TiCl_4$-mediated cyclization of **4a** with 1,3-bis(trimethylsilyloxy)-1,3-butadiene **5a**, prepared in two steps from methyl 3-oxopentanoate,[22] afforded the nitro-substituted biaryl **6a**. The formation of the product can be explained by the mechanism depicted in Scheme 2. During optimization, it proved to be important to carry out the reactions in a highly concentrated solution. We have observed earlier that employment of other Lewis acids results in a decrease of the yield of [3+3] cyclocondensation reactions. It is important to be noted that the cyclization proceeded with very good regioselectivity.



Scheme 2. Possible mechanism of the formation of **6a**; i: $TiCl_4$, CH_2Cl_2, −78→20 °C, 18 h.

The $TiCl_4$-mediated cyclization of **4a**–**f** with 1,3-bis(trimethylsilyloxy)-1,3-butadienes **5a**–**f**, readily available in two steps from the corresponding β-ketoesters,[22] afforded the nitro-substituted biaryls **6a**–**s** (Scheme 3, Table 2). All cyclizations proceeded with very good regioselectivity. The moderate yields can be explained by competing, $TiCl_4$-mediated oxidative dimerization of the 1,3-bis(silyloxy)-1,3-



Scheme 3. Synthesis of **6a**–**s** and **7a**–**s**; i: $TiCl_4$, CH_2Cl_2, −78→20 °C, 18 h ii: H_2, Pd/C (10 mol %), 20 °C, 48 h.

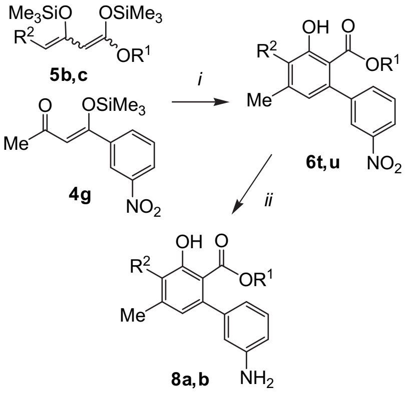
Table 2
Synthesis of **6a**–**s** and **7a**–**s**

4	5	6,7	R^1	R^2	R^3	R^4	% (**6**)[a]	% (**7**)[a]
a	**a**	**a**	Me	H	Me	H	36	64
a	**b**	**b**	Me	Me	Me	H	41	52
a	**c**	**c**	Et	Et	Me	H	35	70
a	**f**	**d**	Me	*n*Oct	Me	H	40	69
b	**a**	**e**	Me	H	Et	H	43	75
b	**b**	**f**	Me	Me	Et	H	42	53
b	**c**	**g**	Et	Et	Et	H	38	52
b	**d**	**h**	Me	*n*Hex	Et	H	41	51
b	**e**	**i**	Me	*n*Hept	Et	H	39	49
b	**f**	**j**	Me	*n*Oct	Et	H	38	50
c	**a**	**k**	Me	H	*n*Pr	H	48	56
c	**b**	**l**	Me	Me	*n*Pr	H	38	50
c	**c**	**m**	Et	Et	*n*Pr	H	37	63
c	**d**	**n**	Me	*n*Hex	*n*Pr	H	25	74
d	**a**	**o**	Me	H	*n*Bu	H	42	70
d	**b**	**p**	Me	Me	*n*Bu	H	39	54
d	**d**	**q**	Me	*n*Hex	*n*Bu	H	38	50
e	**d**	**r**	Me	*n*Hex	Et	Me	38	50
f	**a**	**s**	Me	H	*n*Pr	Cl	55	49

[a] Yields of isolated products.

butadiene and by partial hydrolysis of the starting materials during the reaction. No clear trend is observed for the yield with respect to the influence of the substitution pattern. The Pd/C-catalyzed hydrogenation of **6a**–**s** directly afforded the 6(5*H*)-phenanthridinones **7a**–**s** in good yields (Scheme 3, Table 2). The configuration of all products was established by spectroscopic methods.

The $TiCl_4$-mediated cyclization of **4g** with 1,3-bis(trimethylsilyloxy)-1,3-butadienes **5b**,**c** afforded the 3-nitro-3′-hydroxybiaryls **6t**,**u** (Scheme 4, Table 3). The hydrogenation of **6t** and **6u** afforded the 3-amino-3′-hydroxy-biphenyls **8a** and **8b**.



Scheme 4. Synthesis of **6t**,**u** and **8a**,**b**; *i*: $TiCl_4$, CH_2Cl_2, −78→20 °C, 18 h ii: H_2, Pd/C (10 mol %), 20 °C, 48 h.

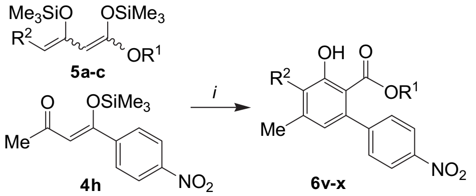
Table 3
Synthesis of **6t**,**u** and **8a**,**b**

5	6	8	R^1	R^2	% (**6**)[a]	% (**8**)[a]
b	**t**	**a**	Me	Me	50	81
c	**u**	**b**	Et	Et	37	78

[a] Yields of isolated products.

The $TiCl_4$-mediated cyclization of **4h** with 1,3-bis(trimethylsilyloxy)-1,3-butadienes **5a**–**c** afforded the 4-nitro-3′-hydroxy-biaryls **6v**–**x** (Scheme 5, Table 4).

Aryl phenolates **12a**–**c** were prepared from aroyl chlorides **9a**–**c** according to the literature.[27] The reaction of **10a**–**c** with nitromethane, following a known procedure,[28] gave the α-nitroacetophenones **11a**–**c** (Scheme 6). The reaction of the latter with triethyl orthoformate and acetic anhydride afforded the 3-ethoxy-2-nitro-2-en-1-ones **12a**–**c**.

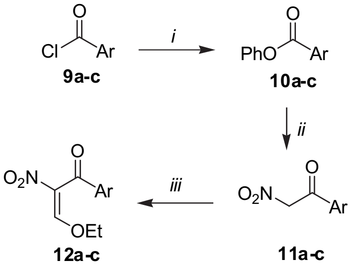


Scheme 5. Synthesis of **6v**–**x**; i: $TiCl_4$, CH_2Cl_2, −78→20 °C, 18 h ii: H_2, Pd/C (10 mol %), 20 °C, 48 h.

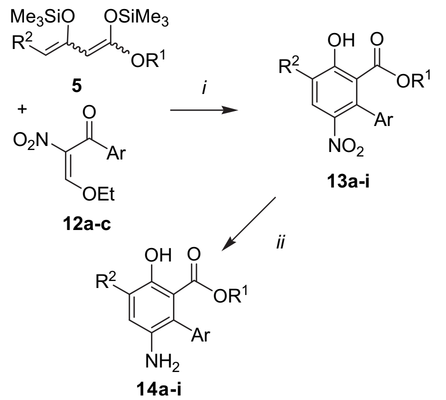
Table 4
Synthesis of **6v**–**x**

5	6	R^1	R^2	% (**6**)[a]
a	**v**	Me	H	36
b	**w**	Me	Me	46
c	**x**	Et	Et	33

[a] Yields of isolated products.



Scheme 6. Synthesis of **12a**–**c**; i: PhOH (1.0 equiv), **9a**–**c** (1.03 equiv), 60 °C; ii: CH_3NO_2 (1.0 equiv), **10a**–**c** (0.33 equiv), *t*-BuOK (1.0 equiv), urea (equiv) DMSO, 12 h, 0–10 °C; iii: **11a**–**c** (1.0 equiv), Ac_2O (1.0 equiv), $HC(OEt)_3$ (1.2 equiv), 120 °C, 6 h.



Scheme 7. Synthesis of **14a**–**i**; i: $TiCl_4$, CH_2Cl_2, −78→20 °C, 18 h, *ii*: H_2, Pd/C (10 mol %), 20 °C, 48 h.

Table 5
Synthesis of **14a**–**i**

12	5	13,14	Ar	R^1	R^2	% (**13**)[a]	% (**14**)[a]
a	**a**	**a**	Ph	Me	H	56	86
a	**b**	**b**	Ph	Me	Me	57	85
a	**c**	**c**	Ph	Et	Et	65	95
a	**k**	**d**	Ph	Me	*n*Bu	58	92
a	**f**	**e**	Ph	Me	*n*Oct	62	90
b	**a**	**f**	$2\text{-}MeC_6H_4$	Me	H	68	91
b	**b**	**g**	$2\text{-}MeC_6H_4$	Me	Me	72	89
c	**a**	**h**	$2\text{-}ClC_6H_4$	Me	H	56	88
c	**b**	**i**	$2\text{-}ClC_6H_4$	Me	Me	70	90

[a] Yields of isolated products.

The $TiCl_4$-mediated cyclization of 3-ethoxy-2-nitro-2-en-1-ones **12a**–**c** with 1,3-bis(trimethylsilyloxy)-1,3-butadienes **5a**–**c**,**k**,**f** afforded the 4-nitrophenols **13a**–**i** in 56–72% yield (Scheme 7, Table 5). The yields of the products derived from dienes **5b**,**c**,**k**,**f**, containing a substituent located at carbon atom C-4 of the diene, were higher than those derived from **5a**. The hydrogenation of 4-nitrophenols **13a**–**i**, in the presence of catalytic amounts of Pd/C (10 mol %), afforded the 4-aminophenols **14a**–**i** in excellent yields.

3. Conclusions

In conclusion, we have reported a regioselective approach to functionalized nitro- and amino-substituted biaryls and of 6(5*H*)-phenanthridinones by [3+3]cyclocondensation of 1,3-bis-(trimethylsilyloxy)-1,3-butadienes with nitro-substituted 1-aryl-1-silyloxy-1-en-3-ones and subsequent hydrogenation. We have also reported the synthesis of 4-nitro- and 4-aminophenols based on formal [3+3] cyclizations of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 3-ethoxy-2-nitro-2-en-1-ones. The products are not readily available by other methods.

4. Experimental section

4.1. General comments

All solvents were dried by standard methods and all reactions were carried out under an Argon atmosphere. For ^1H and ^{13}C NMR spectra the deuterated solvents indicated were used. Mass spectrometric data (MS) were obtained by electron ionization (EI, 70 eV), chemical ionization (CI, isobutane) or electrospray ionization (ESI). For preparative scale chromatography silica gel 60 (0.063–0.200 mm, 70–230 mesh) was used.

4.2. General procedure for the synthesis of 1,3-dicarbonyl compounds 3a–h

To a stirred solution of LDA (75.0 mmol) in THF (1.2 mL/1.0 mmol of LDA) was added ketone **1a**–**e** (50.0 mmol) at −78 °C. After stirring of the solution for 1 h, **2a**–**c** (60.0 mmol) was added. The temperature of the solution was allowed to rise to 20 °C during 12 h. A saturated aqueous solution of NH_4Cl was added, the layers were separated, and the aqueous layer was extracted with EtOAc (3×50 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was removed in vacuo. The residue was purified by chromatography (silica gel, *n*-heptane/EtOAc = 30:1 →20:1) to give **3**. Compounds **1a**–**e** and **2a**–**c** are commercially available.

*4.2.1. 4-Hydroxy-4-(2-nitrophenyl)but-3-en-2-one (**3a**).* Starting with LDA (1.5 equiv) in THF (62 mL), **1a** (2.9 mL, 50.0 mmol), and **2a** (7.9 mL, 60.0 mmol), **3a** was isolated as a red to yellow oil (5.405 g, 54%). ^1H NMR (250 MHz, $CDCl_3$): δ=2.19 (s, 3H, CH_3), 6.16 (s, 1H, CH), 7.45–7.60 (m, 3H, CH_{Ar}), 7.82 (m, 1H, CH_{Ar}), 15.12 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=24.2 (CH_3), 99.9 (CH), 124.3, 129.3, 130.0, 133.0 (CH_{Ar}), 134.7, 147.8, (C_{Ar}), 187.1 (COH), 190.2 (C=O). MS (EI 70 eV): *m*/*z* (%)=207 ($[M]^+$, 38), 192 (100), 160 (19), 150 (36), 120 (8), 89 (9), 85 (27), 76 (18), 43 (45). HRMS (EI): Calcd for $C_{10}H_9O_4N$: 207.05261; found: 207.05232.

*4.2.2. 1-Hydroxy-1-(2-nitrophenyl)pent-1-en-3-one (**3b**).* Starting with LDA (1.5 equiv) in THF (62 mL), **1b** (4.5 mL, 50.0 mmol), and **2a** (7.9 mL, 60.0 mmol), **3b** was isolated as a yellowish solid (11.93 g, 45%), mp=58–60 °C. ^1H NMR (250 MHz, $CDCl_3$): δ=1.10 (t, ^3J=7.7 Hz, 3H, $CH_2\mathit{CH_3}$), 2.58 (q, ^3J=7.1 Hz, 2H, $\mathit{CH_2}CH_3$), 5.73 (s, 1H, CH), 7.45–7.55 (m, 3H, CH_{Ar}), 7.80–7.83 (m, 1H, CH_{Ar}), 15.10 (br s, 1H, OH).^{13}C NMR (75 MHz, $CDCl_3$): δ=9.6 (CH_3), 31.5 (CH_2), 98.5 (CH), 124.4, 129.1, 130.8, 132.8 (CH_{Ar}), 134.2, 148.1 (C_{Ar}), 186.6 (COH), 194.5 (CO). MS (EI 70 eV): *m*/*z* (%)=221 ($[M]^+$, 2), 151 (11), 150 (100), 136 (24), 135 (24), 134 (11), 104 (16), 92 (17), 79 (10), 77 (14), 76 (18), 57 (43), 51 (16), 43 (300). HRMS (EI): Calcd for $C_{11}H_{11}O_4N$: 221.06826; found: 221.068437.

*4.2.3. 1-Hydroxy-1-(2-nitrophenyl)hex-1-en-3-one (**3c**).* Starting with LDA (1.5 equiv) in THF (62 mL), **1c** (5.3 mL, 50.0 mmol), and **2a** (7.9 mL, 60.0 mmol), **3c** was isolated as a yellowish oil (5.98 g, 46%). ^1H NMR (250 MHz, $CDCl_3$): δ=1.12 (t, ^3J=7.6 Hz, 3H, $CH_2CH_2\mathit{CH_3}$), 1.40–1.45 (m, 2H, $CH_2\mathit{CH_2}CH_3$), 2.40 (t, ^3J=7.4 Hz, 2H, $\mathit{CH_2}CH_2CH_3$), 5.70 (s, 1H, CH), 7.46–7.56 (m, 3H, CH_{Ar}), 7.83–7.86 (m, 1H, CH_{Ar}), 15.12 (br s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=13.5 (CH_3), 18.5, 32.5 (CH_2), 98.4 (CH), 124.4, 129.2, 130.9, 132.9 (CH_{Ar}), 134.1, 148.1 (C_{Ar}), 186.5 (COH), 194.6 (CO).

*4.2.4. 1-Hydroxy-1-(2-nitrophenyl)hept-1-en-3-one (**3d**).* Starting with LDA (1.5 equiv) in THF (62 mL), **1d** (6.2 mL, 50.0 mmol), and **2a** (7.9 mL, 60.0 mmol), **3d** was isolated as a red to yellow oil (5.98 g, 40%). ^1H NMR (250 MHz, $CDCl_3$): δ=0.95 (t, ^3J=7.4 Hz, 3H, $CH_2CH_2CH_2\mathit{CH_3}$), 1.35–1.44 (m, 2H, CH_2), 1.59–1.70 (m, 2H, CH_2), 2.38 (t, ^3J=7.8 Hz, 2H, $\mathit{CH_2}CH_2CH_2CH_3$), 5.79 (s, 1H, CH), 7.54–7.64 (m, 3H, CH_{Ar}), 7.90–7.93 (m, 1H, CH_{Ar}), 15.24 (br s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=13.7 (CH_3), 22.2, 27.8, 37.5 (CH_2), 99.1 (CH), 124.4, 129.1, 131.0, 132.8 (CH_{Ar}), 134.6, 147.8 (C_{Ar}), 186.9 (COH), 193.2 (CO).

*4.2.5. 2-Methyl-1-(2-nitrophenyl)pentane-1,3-dione (**3e**).* Starting with LDA (1.5 equiv) in THF (24 mL), **1e** (2.1 mL, 20.0 mmol), and **2a** (3.2 mL, 24.0 mmol), **3e** was isolated as a red to yellow oil (2.70 g, 48%). ^1H NMR (250 MHz, $CDCl_3$): δ=1.12 (t, ^3J=7.0 Hz, 3H, $CH_2\mathit{CH_3}$), 1.41 (d, ^3J=6.7 Hz, 3H, $\mathit{CH_3}CHCOC_2H_5$), 2.46 (q, ^3J=7.3 Hz, 2H, $\mathit{CH_2}CH_3$), 4.04 (q, ^3J=7.1 Hz, 1H, $\mathit{CH}CH_3$), 7.34–7.67 (m, 3H, CH_{Ar}), 8.05–8.08 (m, 1H, CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ=7.5, 13.6 (CH_3), 34.9 (CH_2), 60.0 (CH), 124.3, 128.4, 130.6, 134.6 (CH_{Ar}), 137.0, 145.4 (C_{Ar}), 196.3, 207.6 (CO). MS (EI 70 eV): *m*/*z* (%)=235 ($[M]^+$, 2), 151 (10), 150 (78), 136 (15), 135 (13), 104 (13), 92 (12), 79 (13), 77 (16), 76 (31), 57 (100), 51 (22), 50 (14), 43 (9), 29 (25). HRMS (EI): Calcd for $C_{12}H_{13}NO_4$: 235.08391; found: 235.083664.

*4.2.6. 2-Chloro-1-(2-nitrophenyl)hexane-1,3-dione (**3f**).* A mixture of **3c** (2.00 g, 8.5 mmol) and of NCS (1.04 g, 7.8 mmol) in CCl_4 (18 mL) was heated under reflux for 8 h. After cooling, the precipitate of succinimide was filtered off and water was added, the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3×150 mL). The combined organic layers were dried (Na_2SO_4) and filtered, and the solvent was removed in vacuo. The residue was purified by chromatography (silica gel, *n*-heptane/EtOAc, 30:1→20:1) to give **3f** as a yellowish oil (1.95 g, 85%). ^1H NMR ($CDCl_3$, 250 MHz): δ=0.96 (t, ^3J=7.1 Hz, 3H, $CH_2CH_2\mathit{CH_3}$), 1.61–1.73 (m, 2H, $CH_2\mathit{CH_2}CH_3$), 2.55 (t, ^3J=7.4 Hz, 2H, $\mathit{CH_2}CH_2CH_3$), 5.23 (s, 1H, CH), 7.53–7.78 (m, 3H, CH_{Ar}), 8.23–8.27 (m, 1H, CH_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=13.7 (CH_3), 18.6, 37.3 (CH_2), 69.6 (CH), 124.4, 130.0, 131.7, 134.9 (CH_{Ar}), 139.5, 145.4 (C_{Ar}), 189.5, 199.8 (CO).

*4.2.7. 4-Hydroxy-4-(4-nitrophenyl)but-3-en-2-one (**3h**).* Starting with LDA (1.5 equiv) in THF (62 mL), **1a** (2.9 mL, 50.0 mmol), and **2c** (11.130 g, 60.0 mmol), **3h** was isolated as a yellow solid (4.405 g, 43%), mp=54–56 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=2.11 (s, 3H, CH_3), 5.74 (s, 1H, CH), 7.95 (d, ^3J=8.7 Hz, 2H, CH_{Ar}), 8.21 (d, ^3J=9.0 Hz, 2H, CH_{Ar}), 15.80 (s, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ=27.0 (CH_3), 98.5 (CH), 124.3 ($2CH_{Ar}$), 128.6 ($2CH_{Ar}$), 140.9, 149.9 (C_{Ar}), 179.8 (COH), 196.6 (C=O). GC–MS (EI 70 eV): *m*/*z* (%)=207 ($[M]^+$, 38), 192 (100), 165 (8), 160 (19), 150 (36), 120 (8), 104 (18), 89 (9), 85 (27), 76 (18), 63 (7), 50

(12), 43 (45). HRMS (EI): Calcd for $C_{10}H_9NO_4$: 207.05261; found: 207.05232.

4.3. General procedure for the synthesis of silyl enol ethers 4a–h and 10

To a stirred benzene solution (2.5 mL/1.0 mmol of **3** or **9**) of **3** or **9** (10.0 mmol) was added triethylamine (16.0 mmol). After stirring of the solution for 2 h, trimethylchlorosilane (18.0 mmol) was added. After stirring of the solution for 72 h, the solvent was removed in vacuo and hexane (25 mL) was added to the residue to give a suspension. The latter was filtered under argon atmosphere. The filtrate was concentrated in vacuo to give silyl enol ethers **4a–h** or **10**. Due to the unstable nature of the silyl enol ethers, they were characterized only by NMR spectroscopy. All products exist as mixtures of *E*/*Z* isomers.

*4.3.1. 4-(2-Nitrophenyl)-4-(trimethylsilyloxy)but-3-en-2-one (**4a**).* Starting with benzene (90.0 mL), **3a** (6.121 g, 29.5 mmol), triethylamine (6.6 mL, 47.2 mmol) and trimethylchlorosilane (6.7 mL, 53.2 mmol), **4a** was isolated as a reddish oil (7.30 g, 91%). ^1H NMR (300 MHz, $CDCl_3$): δ=0.05–0.30 (m, 9H, $Si(CH_3)_3$), 2.15 (s, 3H, CH_3), 6.06 (s, 1H, CH), 7.45–7.60 (m, 3H, CH_{Ar}), 7.82 (m, 1H, CH_{Ar}), ^{13}C NMR (75 MHz, $CDCl_3$): δ=0.2 ($Si(CH_3)_3$), 24.5 (CH_3), 98.9 (CH), 124.9, 129.6, 130.5, 133.5 (CH_{Ar}), 134.9, 148.8, (C_{Ar}), 180.1 (C–$OSiMe_3$), 191.2 (C═O).

*4.3.2. 1-(2-Nitrophenyl)-1-(trimethylsilyloxy)pent-1-en-3-one (**4b**).* Starting with benzene (52.0 mL), **3b** (4.62 g, 20.9 mmol), triethylamine (4.6 mL, 33.4 mmol) and trimethylchlorosilane (4.7 mL, 37.6 mmol), **4b** was isolated as a reddish oil (5.80 g, 95%). ^1H NMR (250 MHz, $CDCl_3$): δ=0.21–0.31 (m, 9H, $Si(CH_3)_3$), 0.98 (t, ^3J=7.6 Hz, 3H, CH_2CH_3), 2.58 (q, ^3J=7.1 Hz, 2H, CH_2CH_3), 5.81 (s, 1H, CH), 7.44–7.53 (m, 3H, CH_{Ar}), 7.80–7.83 (m, 1H, CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ=0.3 ($Si(CH_3)_3$), 7.8 (CH_3), 36.8 (CH_2), 98.4 (CH), 123.6, 127.9, 129.4, 131.9 (CH_{Ar}), 134.6, 145.0 (C_{Ar}), 177.4 (C–$OSiMe_3$), 198.5 (CO).

*4.3.3. 1-(2-Nitrophenyl)-1-(trimethylsilyloxy)hex-1-en-3-one (**4c**).* Starting with benzene (63.0 mL), **3c** (4.83 g, 20.2 mmol), triethylamine (4.5 mL, 43.0 mmol) and trimethylchlorosilane (4.6 mL, 33.1 mmol), **4c** was isolated as a reddish oil (5.60 g, 88%). ^1H NMR (250 MHz, $CDCl_3$): δ=0.21–0.43 (m, 9H, $Si(CH_3)_3$), 1.06–1.14 (m, 3H, CH_3), 1.69–1.85 (m, 2H, CH_2), 2.43–2.53 (m, 2H, CH_2), 5.85 (s, 1H, CH), 7.50–8.00 (m, 3H, CH_{Ar}), 8.07–8.19 (m, 1H, CH_{Ar}), ^{13}C NMR (75 MHz, $CDCl_3$): δ=0.2 ($Si(CH_3)_3$), 13.8 (CH_3), 36.4, 39.5 (CH_2), 98.9 (CH), 124.1, 128.1, 129.3, 131.6 (CH_{Ar}), 139.4, 148.3, (C_{Ar}), 178.0 (C–$OSiMe_3$), 193.2 (C═O).

*4.3.4. 1-(2-Nitrophenyl)-1-(trimethylsilyloxy)hept-1-en-3-one (**4d**).* Starting with benzene (22.5 mL), **3d** (2.20 g, 8.9 mmol), triethylamine (2.0 mL, 14.2 mmol) and trimethylchlorosilane (2.0 mL, 16.0 mmol), **4d** was isolated as a reddish oil (2.66 g, 93%). ^1H NMR (250 MHz, $CDCl_3$): δ=0.24–0.27 (m, 9H, $Si(CH_3)_3$), 0.89 (t, ^3J=7.6 Hz, 3H, $CH_2CH_2CH_2CH_3$), 1.31–1.38 (m, 2H, CH_2), 1.51–1.60 (m, 2H, CH_2), 2.34 (t, ^3J=6.8 Hz, 2H, $CH_2CH_2CH_2CH_3$), 5.79 (s, 1H, CH), 7.53–7.65 (m, 3H, CH_{Ar}), 7.91–7.94 (m, 1H, CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ=0.3 ($Si(CH_3)_3$), 13.6 (CH_3), 22.1, 27.7, 37.4 (CH_2), 99.0 (CH), 124.1, 129.0, 131.1, 132.8 (CH_{Ar}), 133.4, 139.1 (C_{Ar}), 176.5 (C–$OSiMe_3$), 193.3 (CO).

*4.3.5. 2-Methyl-1-(2-nitrophenyl)-1-(trimethylsilyloxy)pent-1-en-3-one (**4e**).* Starting with benzene (29.0 mL), **3e** (2.70 g, 11.5 mmol), triethylamine (2.6 mL, 18.4 mmol) and trimethylchlorosilane (2.6 mL, 20.7 mmol), **4e** was isolated as a yellowish oil (3.31 g, 94%). ^1H NMR (250 MHz, $CDCl_3$): δ=0.1–0.29 (m, 9H, $Si(CH_3)_3$), 0.88 (t, ^3J=6.8 Hz, 3H, CH_2CH_3), 2.02 (s, 3H, CH_3), 2.36 (q, ^3J=8.7 Hz, 2H, CH_2CH_3), 7.28–7.54 (m, 3H, CH_{Ar}), 8.00–8.03 (m, 1H, CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ=0.2 ($Si(CH_3)_3$), 7.1, 12.5 (CH_3), 34.0 (CH_2), 118.2 (C), 123.6, 128.9, 130.5, 132.6 (CH_{Ar}), 145.6, 152.9 (C_{Ar}), 168.5 (C–$OSiMe_3$), 202.8 (CO).

*4.3.6. 2-Chloro-1-(2-nitrophenyl)-1-(trimethylsilyloxy)hex-1-en-3-one (**4f**).* Starting with benzene (52.0 mL), **3f** (1.95 g, 7.22 mmol), triethylamine (1.6 mL, 11.6 mmol) and trimethylchlorosilane (1.6 mL, 13.0 mmol), **4f** was isolated as a yellowish oil (2.27 g, 92%). ^1H NMR (250 MHz, $CDCl_3$): δ=0.10–0.23 (m, 9H, $Si(CH_3)_3$), 0.93 (t, ^3J=7.4 Hz, 3H, $CH_2CH_2CH_3$), 1.58–1.69 (m, 2H, CH_2), 2.53 (t, ^3J=7.6 Hz, 2H, $CH_2CH_2CH_3$), 7.42–7.63 (m, 3H, CH_{Ar}), 8.13–8.23 (m, 1H, CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ=0.1 ($Si(CH_3)_3$), 13.4 (CH_3), 18.2, 37.0 (CH_2), 108.9 (CCl), 124.2, 129.9, 131.2, 132.8 (CH_{Ar}), 143.2, 147.6 (C_{Ar}), 165.1 (C–$OSiMe_3$), 189.1 (CO).

*4.3.7. 4-(4-Nitrophenyl)-4-(trimethylsilyloxy)but-3-en-2-one (**4h**).* Starting with benzene (52.0 mL), **3h** (4.405 g, 21.3 mmol), triethylamine (4.7 mL, 33.0 mmol) and trimethylchlorosilane (5.1 mL, 37.8 mmol), **4h** was isolated as a yellow solid (5.350 g, 92%), mp=55–57 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=0.02–0.22 (m, 9H, $Si(CH_3)_3$), 2.10 (s, 3H, CH_3), 6.08 (s, 1H, CH), 7.80–7.89 (m, 2H, CH_{Ar}), 8.09–8.17 (m, 2H, CH_{Ar}). ^{13}C NMR (75 MHz, $CDCl_3$): δ=0.6 ($Si(CH_3)_3$), 24.6 (CH_3), 96.8 (CH), 121.5 ($2CH_{Ar}$), 125.9 ($2CH_{Ar}$), 138.4, 147.0 (C_{Ar}), 177.2 (C–$OSiMe_3$), 194.1 (C═O).

4.4. General procedure for the synthesis of salicylates 6a–x

To a CH_2Cl_2 solution of silyl enol ether **4** (1.0 equiv) and 1,3-bis(silyl enol ether) **5** (1.1 equiv) was dropwise added $TiCl_4$ (1.1 equiv) at −78 °C under argon atmosphere. The solution was stirred at −78 °C for 30 min and then allowed to warm to 20 °C during 18 h. To the solution was added an aqueous solution of HCl (10%). The organic layer was separated and the aqueous layer was repeatedly extracted with CH_2Cl_2. The combined organic extracts were dried (Na_2SO_4) and filtered. The filtrate was concentrated in vacuo and the residue was purified by chromatography (silica gel, *n*-hexane/EtOAc) to give salicylates **6**.

*4.4.1. Methyl 3-hydroxy-5-methyl-2′-nitro[1,1′-biphenyl]-2-carboxylate (**6a**).* Starting with **5a** (1.145 g, 4.4 mmol), $TiCl_4$ (0.835 g, 4.4 mmol), CH_2Cl_2 (6 mL) and **4a** (1.117 g, 4.0 mmol), **6a** was isolated (0.420 g, 36%) as a yellowish oil. ^1H NMR ($CDCl_3$, 250 MHz): δ=2.21 (s, 3H, CH_3), 3.33 (s, 3H, OCH_3), 6.35 (d, ^4J=1.9 Hz, 1H, CH_{Ar}), 6.74 (d, ^4J=1.4 Hz, 1H, CH_{Ar}), 7.10–7.13 (m, 1H, CH_{Ar}), 7.36 (ddd, ^3J=7.4 Hz, ^3J=7.2 Hz, ^4J=1.4 Hz, 1H, CH_{Ar}), 7.47 (ddd, ^3J=7.5 Hz, ^3J=7.4 Hz, ^4J=1.5 Hz, 1H, CH_{Ar}), 7.92 (dd, ^3J=8.0 Hz, ^4J=1.5 Hz, 1H, Ar), 11.10 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=21.6 (CH_3), 51.9 (OCH_3), 108.4 (C_{Ar}), 118.0, 122.5, 123.6, 127.8, 131.1. 132.4 (CH_{Ar}), 138.2, 140.2, 145.6, 147.8, 162.4 (C_{Ar}), 170.4 (C═O). GC–MS (EI, 70 eV): *m*/*z* (%)=287 ([M]$^+$, 26), 255 (100), 227 (27), 197 (5), 181 (11), 152 (30), 115 (5), 76 (7). HRMS (EI): Calcd for $C_{15}H_{13}NO_5$: 287.07882; found: 287.07873.

*4.4.2. Methyl 3-hydroxy-4,5-dimethyl-2′-nitrobiphenyl-2-carboxylate (**6b**).* Starting with **5b** (1.207 g, 4.4 mmol), $TiCl_4$ (0.834 g, 4.4 mmol), CH_2Cl_2 (8 mL), and **4a** (1.117 g, 4.0 mmol), **6b** was isolated (0.500 g, 41%) as a yellow oil. ^1H NMR ($CDCl_3$, 250 MHz): δ=2.10 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 3.32 (s, 3H, OCH_3), 6.35 (s, 1H, CH_{Ar}), 7.11 (dd, ^3J=7.5 Hz, ^4J=1.6 Hz, 1H, CH_{Ar}), 7.33 (ddd, ^3J=7.7 Hz, ^3J=7.6 Hz, ^4J=1.5 Hz, 1H, CH_{Ar}), 7.46 (ddd, ^3J=7.6 Hz, ^3J=7.5 Hz, ^4J=1.3 Hz, 1H, CH_{Ar}), 7.88 (dd, ^3J=8.3 Hz, ^4J=1.4 Hz, 1H, CH_{Ar}), 11.47 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C=11.5, 20.5 (CH_3), 51.9 (OCH_3), 108.0 (C_{Ar}), 122.6, 123.5, (CH_{Ar}), 125.0 (C_{Ar}), 127.6, 131.2, 132.3 (CH_{Ar}), 136.9, 138.5, 143.6, 148.0, 160.5 (C_{Ar}), 171.4 (C═O). GC–MS (EI, 70 eV): *m*/*z* (%)=301 ([M]$^+$, 64), 269 (100), 255 (24), 224 (27), 208 (48), 195 (13), 180 (49), 165 (29), 152 (28), 128 (11), 115

(16), 77 (7). HRMS (EI): Calcd for $C_{16}H_{15}NO_5$: 301.09447; found: 301.09434.

*4.4.3. Ethyl 4-ethyl-3-hydroxy-5-methyl-2′-nitrobiphenyl-2-carboxylate (**6c**).* Starting with **5c** (0.998 g, 3.3 mmol), $TiCl_4$ (0.625 g, 3.3 mmol), CH_2Cl_2 (6 mL), and **4a** (0.789 g, 3.0 mmol), **6c** was isolated (0.350 g, 35%) as a yellow solid, mp=80–82 °C. ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta=0.59$ (t, $^{3}J=7.4$ Hz, 3H, CH_3), 1.04 (t, $^{3}J=7.5$ Hz, 3H, CH_3), 2.19 (s, 3H, CH_3), 2.61 (m, 2H, CH_2), 3.82 (q, $^{3}J=7.5$ Hz, 2H, OCH_2), 6.32 (s, 1H, CH_{Ar}), 7.12 (dd, $^{3}J=7.5$ Hz, $^{4}J=1.5$ Hz, 1H, CH_{Ar}), 7.34 (ddd, $^{3}J=8.0$ Hz, $^{3}J=7.5$ Hz, $^{4}J=1.5$ Hz, 1H, CH_{Ar}), 7.45 (ddd, $^{3}J=7.5$ Hz, $^{3}J=7.5$ Hz, $^{4}J=1.5$ Hz, 1H, CH_{Ar}), 7.88 (dd, $^{3}J=7.6$ Hz, $^{4}J=1.6$ Hz, 1H, CH_{Ar}), 11.58 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): $\delta_C=4.8$, 14.8, 21.3 (CH_3), 21.5 (CH_2), 62.8 (OCH_2), 110.0 (C_{Ar}), 124.6, 125.5, 129.4 (CH_{Ar}), 132.8 (C_{Ar}), 133.1, 134.1 (CH_{Ar}), 138.8, 140.8, 144.5, 149.9, 162.5 (C_{Ar}), 172.5 (C=O). GC–MS (EI, 70 eV): *m*/*z* (%)=329 ($[M]^+$, 100), 283 (80), 255 (24), 238 (32), 222 (78), 207 (40), 194 (99), 165 (64), 152 (29), 139 (13), 115 (18), 77 (13). HRMS (EI): Calcd for $C_{18}H_{19}NO_5$: 329.12577; found: 329.12546.

*4.4.4. Methyl 3-hydroxy-5-methyl-2′-nitro-4-octylbiphenyl-2-carboxylate (**6d**).* Starting with **5f** (1.100 g, 3.3 mmol), $TiCl_4$ (0.625 g, 3.3 mmol), CH_2Cl_2 (6 mL) and **4a** (0.789 g, 3.0 mmol), **6d** was isolated (0.476 g, 40%) as a yellow viscous oil. ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta=0.73$–0.79 (m, 3H, CH_3), 1.13–1.30 (m, 12H, CH_2), 2.18 (s, 3H, CH_3), 2.52–2.60 (m, 2H, CH_2), 3.31 (s, 3H, OCH_3), 6.32 (s, 1H, CH_{Ar}), 7.11 (dd, $^{3}J=7.5$ Hz, $^{4}J=1.2$ Hz, 1H, CH_{Ar}), 7.33 (ddd, $^{3}J=8.0$ Hz, $^{3}J=7.7$ Hz, $^{4}J=1.3$ Hz, 1H, CH_{Ar}), 7.45 (ddd, $^{3}J=7.4$ Hz, $^{3}J=7.1$ Hz, $^{4}J=1.6$ Hz, 1H, CH_{Ar}), 7.88 (dd, $^{3}J=7.5$ Hz, $^{4}J=1.5$ Hz, 1H, CH_{Ar}), 11.43 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): $\delta_C=16.0$, 21.8 (CH_3), 24.6, 28.3, 30.6, 31.2, 31.4, 32.0, 33.8 (CH_2), 53.8 (OCH_3), 110.0 (C_{Ar}), 124.8, 125.4, 129.5 (CH_{Ar}), 131.8 (C_{Ar}), 133.2, 134.1 (CH_{Ar}), 138.9, 140.5, 144.5, 150.0, 162.5 (C_{Ar}), 172.9 (C=O). GC–MS (EI, 70 eV): *m*/*z* (%)=399 ($[M]^+$, 100), 353 (49), 340 (13), 306 (17), 268 (69), 225 (84), 208 (80), 194 (58), 180 (27), 165 (65), 152 (21), 115 (10), 77 (5), 43 (18). HRMS (EI): Calcd for $C_{23}H_{29}NO_5$: 399.20402; found: 399.20336.

*4.4.5. Methyl 5-ethyl-3-hydroxy-2′-nitrobiphenyl-2-carboxylate (**6e**).* Starting with **5a** (1.720 g, 6.6 mmol), $TiCl_4$ (1.251 g, 6.6 mmol), CH_2Cl_2 (12 mL) and **4b** (1.760 g, 6.0 mmol), **6e** was isolated (0.780 g, 43%) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta=1.05$ (t, $^{3}J=7.5$ Hz, 3H, $CH_2\mathit{CH_3}$), 2.45 (q, $^{3}J=7.5$ Hz, 2H, $\mathit{CH_2}CH_3$), 3.27 (s, 3H, OCH_3), 6.31 (d, $^{4}J=2.0$ Hz, 1H, CH_{Ar}), 6.70 (d, $^{4}J=1.7$ Hz, 1H, CH_{Ar}), 7.07 (dd, $^{3}J=7.7$ Hz, $^{4}J=1.3$ Hz, 1H, CH_{Ar}), 7.31 (ddd, $^{3}J=7.0$ Hz, $^{3}J=7.0$ Hz, $^{4}J=1.5$ Hz, 1H, CH_{Ar}), 7.43 (ddd, $^{3}J=7.5$ Hz, $^{3}J=7.5$ Hz, $^{4}J=1.5$ Hz, 1H, CH_{Ar}), 7.87 (dd, $^{3}J=8.4$ Hz, $^{4}J=1.3$ Hz, 1H, CH_{Ar}), 11.05 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=14.6$ (CH_3), 28.9 (CH_2), 52.4 (OCH_3), 108.8 ($\mathit{C}COOCH_3$), 117.2, 121.5, 123.8, 127.8, 131.3, 132.5 (CH_{Ar}), 138.5, 140.4, 148.1, 151.8, 162.8 (C_{Ar}), 170.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}=3022$ (w), 2949 (w), 2872 (w), 1659 (s), 1607 (m), 1571 (m), 1522 (s), 1436 (m), 1417 (w), 1386 (w), 1344 (s), 1272 (m), 1211 (s), 1160 (m), 1145 (m), 1102 (m), 1039 (w), 947 (w), 870 (w), 804 (m), 743 (s), 688 (s), 635 (m), 544 (w). GC–MS (EI, 70 eV): *m*/*z* (%)=301 ($[M]^+$, 45), 270 (15), 269 (86), 256 (17), 255 (100), 242 (14), 241 (16), 240 (18), 213 (18), 198 (10), 197 (17), 196 (14), 195 (21), 181 (14), 180 (12), 170 (16), 168 (16), 167 (16), 166 (10), 165 (26), 153 (12), 152 (36), 151 (14), 139 (15), 128 (12), 127 (11), 115 (24), 77 (11), 76 (10). HRMS (EI): Calcd for $C_{16}H_{15}NO_5$: 301.09447; found: 301.094496.

*4.4.6. Methyl 5-ethyl-3-hydroxy-4-methyl-2′-nitrobiphenyl-2-carboxylate (**6f**).* Starting with **5b** (1.207 g, 4.4 mmol), $TiCl_4$ (0.834 g, 4.4 mmol), CH_2Cl_2 (8 mL) and **4b** (1.170 g, 4.0 mmol), **6f** was isolated (0.530 g, 42%) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta=1.05$ (t, $^{3}J=7.4$ Hz, 3H, $CH_2\mathit{CH_3}$), 2.12 (s, 3H, CH_3), 2.52 (q, $^{3}J=7.5$ Hz, 2H, $\mathit{CH_2}CH_3$), 3.32 (s, 3H, OCH_3), 6.35 (s, 1H, CH_{Ar}), 7.12 (dd, $^{3}J=7.3$ Hz, $^{4}J=1.4$ Hz, 1H, CH_{Ar}), 7.34 (ddd, $^{3}J=7.6$ Hz, $^{3}J=7.6$ Hz, $^{4}J=1.8$ Hz, 1H, CH_{Ar}), 7.46 (ddd, $^{3}J=7.3$ Hz, $^{3}J=7.3$ Hz, $^{4}J=1.6$ Hz, 1H, CH_{Ar}), 7.90 (dd, $^{3}J=8.3$ Hz, $^{4}J=1.4$ Hz, 1H, CH_{Ar}), 11.48 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=11.0$, 14.1 (CH_3), 27.0 (CH_2), 51.9 (OCH_3), 108.0 ($\mathit{C}COOCH_3$), 121.0, 123.5, 124.4, 127.6, 131.3, 132.6 (CH_{Ar}), 137.1, 138.7, 143.3, 149.2, 160.8 (C_{Ar}), 170.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}=3065$ (w), 2967 (w), 2874 (w), 1659 (s), 1606 (m), 1567 (m), 1522 (s), 1437 (m), 1397 (m), 1345 (s), 1269 (s), 1214 (m), 1173 (m), 1144 (m), 1108 (w), 1044 (w), 927 (w), 867 (w), 809 (m), 730 (s), 683 (m), 632 (w), 605 (w). GC–MS (EI, 70 eV): *m*/*z* (%)=315 ($[M]^+$, 59), 284 (19), 283 (100), 269 (21), 254 (12), 238 (28), 224 (22), 222 (20), 195 (10), 194 (38), 193 (10), 181 (10), 178 (10), 168 (10), 167 (16), 166 (12), 165 (32), 153 (10), 152 (20), 151 (9), 139 (10), 128 (9), 127 (8), 115 (12), 77 (8), 76 (7). HRMS (EI): Calcd for $C_{17}H_{17}NO_5$: 315.11012; found: 315.110575.

*4.4.7. Ethyl 4,5-diethyl-3-hydroxy-2′-nitrobiphenyl-2-carboxylate (**6g**).* Starting with **5c** (1.996 g, 6.6 mmol), $TiCl_4$ (1.251 g, 6.6 mmol), CH_2Cl_2 (12 mL) and **4b** (1.760 g, 6.0 mmol), **6g** was isolated (0.782 g, 38%) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta=0.54$–0.62 (m, 6H, $2\times CH_2\mathit{CH_3}$), 1.10 (t, $^{3}J=6.9$ Hz, 3H, $OCH_2\mathit{CH_3}$), 2.52 (q, $^{3}J=7.7$ Hz, 2H, $\mathit{CH_2}CH_3$), 2.65 (q, $^{3}J=7.7$ Hz, 2H, $\mathit{CH_2}CH_3$), 3.76 (q, $^{3}J=7.5$ Hz, 2H, $O\mathit{CH_2}CH_3$), 6.34 (s, 1H, CH_{Ar}), 6.99 (dd, $^{3}J=7.4$ Hz, $^{4}J=1.3$ Hz, 1H, CH_{Ar}), 7.34 (ddd, $^{3}J=7.3$ Hz, $^{3}J=7.2$ Hz, $^{4}J=1.4$ Hz, 1H, CH_{Ar}), 7.42 (ddd, $^{3}J=7.5$ Hz, $^{3}J=7.5$ Hz, $^{4}J=1.5$ Hz, 1H, CH_{Ar}), 7.94 (dd, $^{3}J=7.9$ Hz, $^{4}J=1.4$ Hz, 1H, CH_{Ar}), 11.43 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): $\delta=13.3$, 13.8, 17.2 (CH_3), 19.0, 19.8 (CH_2), 60.9 (OCH_2), 108.0 ($\mathit{C}COOC_2H_5$), 124.1, 123.8, 127.4, 131.2, 132.6 (CH_{Ar}), 125.8, 135.4, 137.1, 142.6, 148.5, 158.4 (C_{Ar}), 170.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}=3066$ (w), 2965 (w), 2873 (w), 1656 (m), 1606 (m), 1563 (w), 1525 (s), 1463 (w), 1396 (m), 1347 (m), 1276 (s), 1212 (m), 1177 (m), 1111 (w), 1056 (w), 906 (w), 838 (s), 784 (m), 680 (m), 649 (w), 632 (w). GC–MS (EI, 70 eV): *m*/*z* (%)=344 ($[M]^+ +1$, 25), 343 ($[M]^+$, 100), 298 (11), 297 (52), 280 (10), 270 (11), 269 (20), 253 (16), 252 (35), 250 (11), 238 (16), 237 (16), 235 (16), 234 (18), 224 (17), 222 (11), 221 (24), 220 (49), 218 (11), 210 (11), 208 (56), 207 (63), 206 (26), 196 (11), 194 (18), 193 (25), 192 (15), 181 (21), 180 (29), 178 (25), 168 (12), 167 (20), 166 (14), 165 (47), 153 (12), 152 (25), 151 (10), 139 (11), 128 (12), 115 (14), 77 (11), 29 (20). HRMS (EI): Calcd for $C_{19}H_{21}NO_5$: 343.14142; found: 343.141422.

*4.4.8. Methyl 5-ethyl-4-hexyl-3-hydroxy-2′-nitrobiphenyl-2-carboxylate (**6h**).* Starting with **5d** (1.516 g, 4.4 mmol), $TiCl_4$ (0.834 g, 4.4 mmol), CH_2Cl_2 (8 mL) and **4b** (1.170 g, 4.0 mmol), **6h** was isolated (0.631 g, 41%) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 250 MHz): $\delta=0.78$ (t, $^{3}J=7.3$ Hz, 3H, $(CH_2)_5\mathit{CH_3}$), 1.06 (t, $^{3}J=7.6$ Hz, 3H, $CH_2\mathit{CH_3}$), 1.08–1.14 (m, 8H, $4\times CH_2$), 2.46 (q, $^{3}J=7.2$ Hz, 2H, $\mathit{CH_2}CH_3$), 2.48–2.52 (m, 2H, CH_2), 3.32 (s, 3H, OCH_3), 6.35 (s, 1H, CH_{Ar}), 6.99 (dd, $^{3}J=7.6$ Hz, $^{4}J=1.3$ Hz, 1H, CH_{Ar}), 7.35 (ddd, $^{3}J=7.0$ Hz, $^{3}J=7.0$ Hz, $^{4}J=1.5$ Hz, 1H, CH_{Ar}), 7.45 (ddd, $^{3}J=7.5$ Hz, $^{3}J=7.5$ Hz, $^{4}J=1.5$ Hz, 1H, CH_{Ar}), 7.88 (dd, $^{3}J=8.5$ Hz, $^{4}J=1.3$ Hz, 1H, CH_{Ar}), 11.43 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): $\delta=14.9$, 17.3 (CH_3), 22.6, 25.9, 26.1, 29.4, 29.8, 31.7 (CH_2), 51.8 (OCH_3), 108.1 ($\mathit{C}COOCH_3$), 121.2, 123.5, 127.5, 131.2, 132.1 (CH_{Ar}), 129.3, 137.0, 138.7, 142.9, 148.9, 160.7 (C_{Ar}), 170.0 (CO). IR (neat, cm^{-1}): $\tilde{\nu}=3066$ (w), 2954 (w), 2856 (w), 1661 (s), 1606 (w), 1564 (w), 1526 (s), 1439 (m), 1399 (m), 1349 (m), 1273 (m), 1213 (m), 1175 (m), 1118 (w), 1035 (w), 908 (m), 854 (w), 786 (w), 732 (s), 708 (w), 633 (w). GC–MS (EI, 70 eV): *m*/*z* (%)=386 ($[M]^+ +1$, 25), 385 ($[M]^+$, 100), 339 (21), 338 (64), 336 (23), 292 (29), 290 (10), 282 (47), 268 (20), 253 (10), 252 (10), 250 (15), 249 (36), 248 (27), 240 (11), 239 (50), 238 (21), 237 (30), 235 (18), 234 (12), 224 (14), 223 (19), 222 (53), 221 (13), 210 (20), 208 (39), 207 (38), 195 (13), 194 (42), 193 (22), 181 (10), 180 (12), 179 (19), 178 (37), 167 (14), 166 (13), 153 (11), 152 (20), 115 (12), 43 (20), 41 (15), 29 (12). HRMS (EI): Calcd for $C_{22}H_{27}NO_5$: 385.18837; found: 385.187845.

*4.4.9. Methyl 5-ethyl-4-heptyl-3-hydroxy-2′-nitrobiphenyl-2-carboxylate (**6i**).* Starting with **5e** (2.367 g, 6.6 mmol), $TiCl_4$ (1.251 g, 6.6 mmol), CH_2Cl_2 (12 mL) and **4b** (1.760 g, 6.0 mmol), **6i** was isolated

(0.934 g, 39%) as a yellowish oil. ^{1}H NMR (CDCl$_3$, 250 MHz): δ=0.79–0.80 (m, 3H, (CH$_2$)$_6$*CH*$_3$), 1.12 (t, ^{3}J=7.6 Hz, 3H, CH$_2$*CH*$_3$), 1.21–1.26 (m, 10H, 5×CH$_2$), 2.57 (q, ^{3}J=7.3 Hz, 2H, *CH*$_2$CH$_3$), 2.61–2.66 (m, 2H, CH$_2$), 3.37 (s, 3H, OCH$_3$), 6.40 (s, 1H, CH$_{Ar}$), 7.17 (dd, ^{3}J=7.4 Hz, ^{4}J=1.4 Hz, 1H, CH$_{Ar}$), 7.38 (ddd, ^{3}J=7.1 Hz, ^{3}J=7.2 Hz, ^{4}J=1.5 Hz, 1H, CH$_{Ar}$), 7.51 (ddd, ^{3}J=7.6 Hz, ^{3}J=7.5 Hz, ^{4}J=1.5 Hz, 1H, CH$_{Ar}$), 7.92 (dd, ^{3}J=7.9 Hz, ^{4}J=1.3 Hz, 1H, CH$_{Ar}$), 11.48 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 62 MHz): δ=13.1, 16.3 (CH$_3$), 21.7, 24.9, 25.1, 28.2, 28.5, 29.1, 30.9 (CH$_2$), 50.8 (OCH$_3$), 107.1 (*C*COOCH$_3$), 120.2, 122.5, 126.5, 130.3, 131.1 (CH$_{Ar}$), 124.9, 136.1, 137.6, 141.9, 147.8, 159.7 (C$_{Ar}$), 170.0 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3066 (w), 2953 (w), 2853 (w), 1660 (m), 1606 (w), 1564 (w), 1525 (s), 1438 (m), 1399 (m), 1347 (m), 1281 (m), 1212 (m), 1174 (m), 1118 (w), 1055 (w), 907 (m), 854 (w), 782 (w), 730 (s), 708 (m), 633 (w). GC–MS (EI, 70 eV): *m/z* (%)=400 ([M]$^{+}$+1, 28), 399 ([M]$^{+}$, 100), 353 (20), 350 (22), 322 (10), 306 (27), 282 (48), 268 (20), 264 (10), 263 (10), 253 (15), 252 (12), 250 (15), 249 (33), 248 (27), 240 (11), 239 (51), 238 (25), 237 (32), 236 (17), 235 (18), 234 (12), 224 (20), 223 (20), 222 (53), 221 (13), 210 (17), 209 (17), 208 (45), 207 (36), 195 (13), 194 (38), 193 (20), 181 (10), 180 (12), 179 (17), 178 (33), 167 (14), 166 (50), 165 (15), 153 (9), 152 (17), 115 (11), 43 (26), 41 (17), 29 (13). HRMS (EI): Calcd for C$_{23}$H$_{29}$NO$_5$: 399.20402; found: 399.202985.

*4.4.10. Methyl 5-ethyl-3-hydroxy-2′-nitro-4-octylbiphenyl-2-carboxylate (**6j**).* Starting with **5f** (1.639 g, 4.4 mmol), TiCl$_4$ (0.834 g, 4.4 mmol), CH$_2$Cl$_2$ (8 mL) and **4b** (1.173 g, 4.0 mmol), **6j** was isolated (0.627 g, 38%) as a yellowish oil. ^{1}H NMR (CDCl$_3$, 250 MHz): δ=0.71 (t, ^{3}J=7.3 Hz, 3H, (CH$_2$)$_7$*CH*$_3$), 1.02 (t, ^{3}J=7.5 Hz, 3H, CH$_2$*CH*$_3$), 1.04–1.12 (m, 12H, 6×CH$_2$), 2.47 (q, ^{3}J=7.3 Hz, 2H, *CH*$_2$CH$_3$), 2.52–2.55 (m, 2H, CH$_2$), 3.27 (s, 3H, OCH$_3$), 6.30 (s, 1H, CH$_{Ar}$), 7.08 (dd, ^{3}J=7.3 Hz, ^{4}J=1.1 Hz, 1H, CH$_{Ar}$), 7.28 (ddd, ^{3}J=7.7 Hz, ^{3}J=7.7 Hz, ^{4}J=1.3 Hz, 1H, CH$_{Ar}$), 7.40 (ddd, ^{3}J=7.3 Hz, ^{3}J=7.3 Hz, ^{4}J=1.3 Hz, 1H, CH$_{Ar}$), 7.84 (dd, ^{3}J=8.5 Hz, ^{4}J=1.5 Hz, 1H, CH$_{Ar}$), 11.38 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 62 MHz): δ=15.2, 16.1 (CH$_3$), 23.8, 27.1, 27.3, 30.3, 30.4, 30.5, 30.7, 33.1 (CH$_2$), 50.0 (OCH$_3$), 109.4 (*C*COOCH$_3$), 122.3, 124.7, 128.7, 132.4, 133.3 (CH$_{Ar}$), 130.4, 138.2, 139.9, 149.3, 150.0, 162.2 (C$_{Ar}$), 172.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=2953 (w), 2853 (w), 1753 (w), 1661 (m), 1606 (m), 1563 (w), 1526 (s), 1437 (m), 1398 (m), 1348 (m), 1275 (m), 1213 (m), 1174 (m), 1120 (w), 1053 (w), 904 (m), 841 (w), 753 (m), 706 (m), 630 (w). GC–MS (EI, 70 eV): *m/z* (%)=414 ([M]$^{+}$+1, 28), 413 ([M]$^{+}$, 100), 368 (11), 367 (42), 354 (13), 353 (22), 352 (91), 336 (19), 320 (14), 306 (20), 283 (14), 282 (82), 266 (20), 253 (21), 252 (16), 250 (15), 249 (15), 248 (20), 240 (12), 239 (46), 238 (25), 237 (27), 236 (24), 235 (23), 234 (12), 224 (34), 223 (16), 222 (49), 221 (20), 210 (14), 209 (14), 208 (35), 207 (23), 206 (11), 205 (10), 196 (12), 194 (30), 193 (29), 192 (14), 181 (12), 180 (12), 179 (14), 178 (26), 167 (14), 166 (12), 165 (54), 153 (9), 152 (20), 55 (12), 43 (26), 41 (25), 29 (16). HRMS (EI): Calcd for C$_{24}$H$_{31}$NO$_5$: 413.21967; found: 413.220441.

*4.4.11. Methyl 3-hydroxy-2′-nitro-5-propylbiphenyl-2-carboxylate (**6k**).* Starting with **5a** (1.145 g, 4.4 mmol), TiCl$_4$ (0.835 g, 4.4 mmol), CH$_2$Cl$_2$ (8 mL) and **4c** (1.229 g, 4.0 mmol), **6k** was isolated (0.607 g, 48%) as a yellow gummy solid. ^{1}H NMR (CDCl$_3$, 250 MHz): δ=0.80 (t, ^{3}J=7.5 Hz, 3H, CH$_3$), 1.47–1.56 (m, 2H, CH$_2$), 2.44 (t, ^{3}J=7.0 Hz, 2H, CH$_2$), 3.27 (s, 3H, OCH$_3$), 6.36 (d, ^{4}J=1.8 Hz, 1H, CH$_{Ar}$), 6.74 (d, ^{4}J=1.8 Hz, 1H, CH$_{Ar}$), 7.12 (dd, ^{3}J=7.5 Hz, ^{4}J=1.8 Hz, 1H, CH$_{Ar}$), 7.36 (ddd, ^{3}J=7.3 Hz, ^{3}J=7.0 Hz, ^{4}J=1.4 Hz, 1H, CH$_{Ar}$), 7.47 (ddd, ^{3}J=7.6 Hz, ^{3}J=7.3 Hz, ^{4}J=1.5 Hz, 1H, CH$_{Ar}$), 7.91 (dd, ^{3}J=7.2 Hz, ^{4}J=1.2 Hz, 1H, CH$_{Ar}$), 11.10 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 62 MHz): δ_C=13.8 (CH$_3$), 23.4, 37.7 (CH$_2$), 51.8 (OCH$_3$), 108.6 (C$_{Ar}$), 117.3, 122.0, 123.7, 127.8, 131.1, 132.5 (CH$_{Ar}$), 138.4, 140.3, 147.8, 150.2, 162.4 (C$_{Ar}$), 170.3 (C=O). GC–MS (EI, 70 eV): *m/z* (%)=315 ([M]$^{+}$, 47), 269 (100), 255 (17), 240 (11), 227 (14), 197 (10), 181 (18), 165 (16), 152 (31), 115 (19), 77 (8). HRMS (EI): Calcd for C$_{17}$H$_{17}$NO$_5$: 315.11062; found: 315.11032.

*4.4.12. Methyl 3-hydroxy-4-methyl-2′-nitro-5-propylbiphenyl-2-carboxylate (**6l**).* Starting with **5b** (1.207 g, 4.4 mmol), TiCl$_4$ (0.835 g, 4.4 mmol), CH$_2$Cl$_2$ (8 mL) and **4c** (1.229 g, 4.0 mmol), **6l** was isolated (0.500 g, 38%) as a yellowish oil. ^{1}H NMR (CDCl$_3$, 250 MHz): δ=0.82 (t, ^{3}J=7.6 Hz, 3H, CH$_3$), 1.41–1.50 (m, 2H, CH$_2$), 2.12(s, 3H, CH$_3$), 2.47 (t, ^{3}J=7.5 Hz, 2H, CH$_2$), 3.32 (s, 3H, OCH$_3$), 6.34 (s, 1H, CH$_{Ar}$), 7.11 (dd, ^{3}J=8.7 Hz, ^{4}J=1.5 Hz, 1H, CH$_{Ar}$), 7.34 (ddd, ^{3}J=8.0 Hz, ^{3}J=7.9 Hz, ^{4}J=1.4 Hz, 1H, CH$_{Ar}$), 7.45 (ddd, ^{3}J=7.5 Hz, ^{3}J=7.5 Hz, ^{4}J=1.5 Hz, 1H, CH$_{Ar}$), 7.88 (dd, ^{3}J=7.5 Hz, ^{4}J=1.6 Hz, 1H, CH$_{Ar}$), 11.49 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 62 MHz): δ_C=10.3, 12.9 (CH$_3$), 22.1, 35.0 (CH$_2$), 50.8 (OCH$_3$), 107.0 (C$_{Ar}$), 121.0, 122.6 (CH$_{Ar}$), 127.7 (CH$_{Ar}$), 126.5, 130.3, 131.2 (CH$_{Ar}$), 135.8, 137.6, 146.8, 147.0, 159.8 (CH$_{Ar}$), 170.1 (C=O). GC–MS (EI, 70 eV): *m/z* (%)=329 ([M]$^{+}$, 55), 297 (100), 283 (20), 238 (18), 224 (30), 208 (14), 194 (12), 165 (25), 139 (7), 115 (9), 77 (5). HRMS (EI): Calcd for C$_{18}$H$_{19}$NO$_5$: 329.12577; found: 329.12597.

*4.4.13. Ethyl 4-ethyl-3-hydroxy-2′-nitro-5-propylbiphenyl-2-carboxylate (**6m**).* Starting with **5c** (0.998 g, 3.3 mmol), TiCl$_4$ (0.625 g, 3.3 mmol), CH$_2$Cl$_2$ (7 mL) and **4c** (0.876 g, 3.0 mmol), **6m** was isolated (0.400 g, 37%) as a yellowish oil. ^{1}H NMR (CDCl$_3$, 250 MHz): δ=0.59 (t, ^{3}J=7.3 Hz, 3H, CH$_3$), 0.83 (t, ^{3}J=6.5 Hz, 3H, CH$_3$), 1.07 (t, ^{3}J=7.4 Hz, 3H, CH$_3$), 1.39–1.48 (m, 2H, CH$_2$), 2.43–2.50 (m, 2H, CH$_2$), 2.57–2.66 (m, 2H, CH$_2$), 3.82 (q, ^{3}J=6.5 Hz, 2H, OCH$_2$), 6.32 (s, 1H, CH$_{Ar}$), 7.12 (dd, ^{3}J=7.5 Hz, ^{4}J=1.5 Hz, 1H, CH$_{Ar}$), 7.34 (ddd, ^{3}J=8.0 Hz, ^{3}J=7.5 Hz, ^{4}J=1.5 Hz, 1H, CH$_{Ar}$), 7.44 (ddd, ^{3}J=7.5 Hz, ^{3}J=7.4 Hz, ^{4}J=1.5 Hz, 1H, CH$_{Ar}$), 7.88 (dd, ^{3}J=7.6 Hz, ^{4}J=1.3 Hz, 1H, CH$_{Ar}$), 11.58 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 62 MHz): δ_C=8.9, 14.4, 15.2 (CH$_3$), 20.3, 25.1, 36.3 (CH$_2$), 62.0 (OCH$_2$), 109.4 (C$_{Ar}$), 123.1, 124.7, 128.6 (CH$_{Ar}$), 131.7 (C$_{Ar}$), 132.4, 133.2 (CH$_{Ar}$), 137.9, 140.1, 148.1, 149.1, 162.0 (C$_{Ar}$), 171.8 (C=O). GC–MS (EI, 70 eV): *m/z* (%)=357 ([M]$^{+}$, 100), 311 (54), 283 (21), 266 (38), 250 (43), 235 (20), 220 (58), 194 (20), 180 (39), 165 (39), 152 (27), 115 (15), 77 (11). HRMS (EI): Calcd for C$_{20}$H$_{23}$NO$_5$: 357.15707; found: 329.15710.

*4.4.14. Methyl 4-hexyl-3-hydroxy-2′-nitro-5-propylbiphenyl-2-carboxylate (**6n**).* Starting with **5d** (1.1366 g, 3.3 mmol), TiCl$_4$ (0.625 g, 3.3 mmol), CH$_2$Cl$_2$ (6 mL) and **4c** (0.876 g, 3.0 mmol), **6n** was isolated (0.315 g, 26%) as a yellow oil. ^{1}H NMR (CDCl$_3$, 250 MHz): δ=0.70–0.81 (m, 6H, 2×CH$_3$), 1.34–1.43 (m, 4H, 2×CH$_2$), 2.38–2.44 (m, 2H, CH$_2$), 2.47–2.55 (m, 2H, CH$_2$), 3.26 (s, 3H, OCH$_3$), 6.28 (s, 1H, CH$_{Ar}$), 7.06 (dd, ^{3}J=7.5 Hz, ^{4}J=1.3 Hz, 1H, CH$_{Ar}$), 7.28 (ddd, ^{3}J=7.5 Hz, ^{3}J=7.5 Hz, ^{4}J=1.5 Hz, 1H, CH$_{Ar}$), 7.40 (ddd, ^{3}J=7.5 Hz, ^{3}J=7.5 Hz, ^{4}J=1.5 Hz, 1H, CH$_{Ar}$), 7.82 (dd, ^{3}J=7.6 Hz, ^{4}J=1.3 Hz, 1H, CH$_{Ar}$), 11.39 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 62 MHz): δ_C=15.2, 15.3 (CH$_3$), 22.8, 25.1, 27.2, 30.7, 31.0, 32.9, 36.4 (CH$_2$), 53.0 (OCH$_3$), 109.4 (C$_{Ar}$), 123.4, 124.7, 128.8 (CH$_{Ar}$), 130.8 (C$_{Ar}$), 132.4, 133.4 (CH$_{Ar}$), 138.0, 139.9, 148.6, 149.3, 162.0 (C$_{Ar}$), 171.2 (C=O). GC–MS (EI, 70 eV): *m/z* (%)=399 ([M]$^{+}$, 100), 353 (18), 350 (11), 340 (13), 325 (15), 324 (89), 322 (14), 306 (17), 296 (41), 278 (14), 253 (16), 238 (13), 236 (17), 235 (13), 224 (14), 222 (13), 220 (10), 208 (11), 207 (11), 193 (10), 177 (18), 165 (14), 164 (10), 161 (12), 149 (10), 111 (11), 109 (12), 97 (16), 85 (14), 83 (17), 81 (15), 71 (22), 57 (37), 55 (26), 43 (27), 41 (21). HRMS (EI): Calcd for C$_{23}$H$_{29}$NO$_5$: 399.20402; found: 399.203444.

*4.4.15. Methyl 5-butyl-3-hydroxy-2′-nitrobiphenyl-2-carboxylate (**6o**).* Starting with **5a** (1.289 g, 4.9 mmol), TiCl$_4$ (0.938 g, 4.9 mmol), CH$_2$Cl$_2$ (9 mL) and **4d** (1.446 g, 4.5 mmol), **6o** was isolated (0.621 g, 42%) as a yellowish oil. ^{1}H NMR (CDCl$_3$, 250 MHz): δ=0.78 (t, ^{3}J=7.3 Hz, 3H, (CH$_2$)$_3$*CH*$_3$), 1.17–1.26 (m, 2H, CH$_2$), 1.41–1.53 (m, 2H, CH$_2$), 2.46 (t, ^{3}J=7.9 Hz, 2H, *CH*$_2$(CH$_2$)$_2$CH$_3$), 3.32 (s, 3H, OCH$_3$), 6.35 (d, ^{4}J=1.7 Hz, 1H, CH$_{Ar}$), 6.74 (d, ^{4}J=1.7 Hz, 1H, CH$_{Ar}$), 7.12 (dd, ^{3}J=7.5 Hz, ^{4}J=1.6 Hz, 1H, CH$_{Ar}$), 7.36 (ddd, ^{3}J=7.7 Hz, ^{3}J=8.1 Hz, ^{4}J=1.6 Hz, 1H, CH$_{Ar}$), 7.47 (ddd, ^{3}J=7.5 Hz, ^{3}J=7.7 Hz, ^{4}J=1.5 Hz, 1H, CH$_{Ar}$), 7.92 (dd, ^{3}J=7.7 Hz, ^{4}J=1.2 Hz, 1H, CH$_{Ar}$), 11.10 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=12.9 (CH$_3$), 21.3, 31.6, 34.6 (CH$_2$), 50.9 (OCH$_3$), 107.6 (*C*COOCH$_3$), 116.4, 120.9, 122.7, 126.9, 130.1, 131.3 (CH$_{Ar}$), 137.3, 139.2, 146.9, 149.5, 161.5 (C$_{Ar}$), 169.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3066 (w), 2954 (w), 2859 (w), 1662 (s), 1608 (m), 1570 (m), 1522 (s), 1438 (m), 1417 (m), 1346 (s), 1266 (s), 1216 (s), 1161 (m), 1146 (m), 1103 (m), 1008 (w), 950 (w), 856 (w), 808 (m), 753 (m), 702 (s), 632 (w), 545 (w). GC–MS (EI, 70 eV): *m*/*z* (%)=329 ([M]$^+$, 43), 297 (32), 284 (20), 283 (100), 270 (14), 256 (10), 255 (56), 226 (12), 182 (12), 181 (15), 180 (15), 166 (10), 165 (13), 154 (26), 153 (12), 152 (27), 151 (10), 139 (10), 115 (15), 97 (12). HRMS (EI): Calcd for C$_{18}$H$_{19}$NO$_5$: 329.12577; found: 329.125715.

*4.4.16. Methyl 5-butyl-3-hydroxy-4-methyl-2′-nitrobiphenyl-2-carboxylate (**6p**).* Starting with **5b** (1.509 g, 5.5 mmol), TiCl$_4$ (1.043 g, 5.5 mmol), CH$_2$Cl$_2$ (10 mL) and **4d** (1.607 g, 5.0 mmol), **6p** was isolated (0.670 g, 39%) as a yellowish oil. ^{1}H NMR (CDCl$_3$, 250 MHz): δ=0.79 (t, ^3J=7.1 Hz, 3H, (CH$_2$)$_3$*CH*$_3$), 1.19–1.28 (m, 2H, CH$_2$), 1.30–1.44 (m, 2H, CH$_2$), 2.12 (s, 3H, CH$_3$), 2.49 (t, ^3J=7.1 Hz, 2H, *CH*$_2$(CH$_2$)$_2$CH$_3$), 3.32 (s, 3H, OCH$_3$), 6.34 (s, 1H, CH$_{\mathrm{Ar}}$), 7.11 (dd, ^3J=7.4 Hz, ^4J=1.3 Hz, 1H, CH$_{\mathrm{Ar}}$), 7.34 (ddd, ^3J=8.0 Hz, ^3J=8.1 Hz, ^4J=1.6 Hz, 1H, CH$_{\mathrm{Ar}}$), 7.45 (ddd, ^3J=8.0 Hz, ^3J=7.7 Hz, ^4J=1.6 Hz, 1H, CH$_{\mathrm{Ar}}$), 7.88 (dd, ^3J=8.2 Hz, ^4J=1.6 Hz, 1H, CH$_{\mathrm{Ar}}$), 11.48 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=13.3, 16.0 (CH$_3$), 24.7, 34.1, 35.8 (CH$_2$), 53.9 (OCH$_3$), 110.0 (*C*COOCH$_3$), 124.0, 125.6, 129.7, 133.4, 134.3 (CH$_{\mathrm{Ar}}$), 126.7, 136.5, 138.9, 140.7, 150.2, 163.0 (C$_{\mathrm{Ar}}$), 173.0 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=2953 (w), 2870 (w), 1659 (s), 1606 (m), 1566 (m), 1522 (s), 1437 (m), 1397 (m), 1345 (s), 1267 (s), 1196 (m), 1173 (m), 1144 (m), 1112 (m), 1010 (m), 962 (w), 852 (m), 809 (m), 752 (m), 705 (m), 633 (w), 546 (w). GC–MS (EI, 70 eV): *m*/*z* (%)=344 ([M]$^+$+1, 11), 343 ([M]$^+$, 53), 312 (20), 311 (100), 297 (22), 225 (19), 224 (18), 208 (24), 207 (10), 195 (11), 194 (14), 181 (10), 180 (15), 167 (11), 166 (10), 165 (26), 152 (18), 115 (10). HRMS (EI): Calcd for C$_{19}$H$_{21}$NO$_5$: 343.14142; found: 343.141424.

*4.4.17. Methyl 5-butyl-4-hexyl-3-hydroxy-2′-nitrobiphenyl-2-carboxylate (**6q**).* Starting with **5d** (2.274 g, 6.6 mmol), TiCl$_4$ (1.251 g, 6.6 mmol), CH$_2$Cl$_2$ (12 mL) and **4d** (1.928 g, 6.0 mmol), **6q** was isolated (0.941 g, 38%) as a yellowish oil. ^{1}H NMR (CDCl$_3$, 250 MHz): δ=0.74 (m, 6H, 2×CH$_3$), 1.08–1.25 (m, 12H, 6×CH$_2$), 2.42 (t, ^3J=7.4 Hz, 2H, *CH*$_2$(CH$_2$)$_2$*CH*$_3$), 2.48–2.55 (m, 2H, CH$_2$), 3.26 (s, 3H, OCH$_3$), 6.28 (s, 1H, CH$_{\mathrm{Ar}}$), 7.07 (dd, ^3J=8.1 Hz, ^4J=1.6 Hz, 1H, CH$_{\mathrm{Ar}}$), 7.28 (ddd, ^3J=7.4 Hz, ^3J=7.4 Hz, ^4J=1.6 Hz, 1H, CH$_{\mathrm{Ar}}$), 7.42 (ddd, ^3J=7.1 Hz, ^3J=7.7 Hz, ^4J=1.6 Hz, 1H, CH$_{\mathrm{Ar}}$), 7.83 (dd, ^3J=8.1 Hz, ^4J=1.6 Hz, 1H, CH$_{\mathrm{Ar}}$), 11.38 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=15.1, 15.2 (CH$_3$), 23.8, 23.9, 27.2, 30.6, 31.0, 32.9, 34.2, 34.3 (CH$_2$), 52.9 (OCH$_3$), 109.3 (*C*COOCH$_3$), 123.2, 124.7, 128.7, 132.5, 133.4 (CH$_{\mathrm{Ar}}$), 130.7, 138.0, 139.9, 148.9, 149.3, 162.1 (C$_{\mathrm{Ar}}$), 172.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=2954 (m), 2856 (m), 1933 (w), 1702 (w), 1661 (m), 1606 (m), 1562 (w), 1525 (s), 1437 (m), 1397 (m), 1347 (s), 1271 (m), 1228 (m), 1174 (m), 1145 (m), 1121 (m), 1009 (w), 954 (w), 842 (m), 813 (m), 754 (m), 706 (m), 632 (w), 562 (w). GC–MS (EI 70 eV): *m*/*z* (%)=414 ([M]$^+$+1, 27), 413 ([M]$^+$, 98), 368 (11), 367 (38), 364 (11), 336 (19), 325 (22), 324 (100), 320 (20), 310 (26), 300 (10), 280 (11), 278 (25), 276 (16), 264 (14), 252 (13), 250 (22), 249 (17), 248 (11), 239 (13), 238 (13), 236 (20), 235 (26), 234 (19), 233 (10), 226 (11), 225 (54), 224 (15), 223 (15), 222 (16), 221 (15), 220 (20), 210 (13), 209 (12), 208 (26), 207 (15), 206 (10), 196 (12), 195 (14), 194 (33), 193 (14), 181 (13), 180 (22), 179 (12), 178 (20), 167 (14), 166 (14), 165 (36), 152 (21), 43 (23), 41 (20), 29 (13). HRMS (EI): Calcd for C$_{24}$H$_{31}$NO$_5$: 413.21967; found: 413.219007.

*4.4.18. Methyl 5-ethyl-4-hexyl-3-hydroxy-6-methyl-2′-nitrobiphenyl-2-carboxylate (**6r**).* Starting with **5d** (2.274 g, 6.6 mmol), TiCl$_4$ (1.251 g, 6.6 mmol), CH$_2$Cl$_2$ (12 mL) and **4e** (1.844 g, 6.0 mmol), **6r** was isolated (0.577 g, 38%) as a yellowish oil. ^{1}H NMR (CDCl$_3$, 250 MHz): δ=0.78–0.81 (m, 3H, (CH$_2$)$_5$*CH*$_3$), 1.07 (t, ^3J=7.6 Hz, 3H, CH$_2$*CH*$_3$), 1.29–1.33 (m, 8H, 4×CH$_2$), 2.49 (s, 3H, CH$_3$), 2.56–2.68 (m, 4H, 2×CH$_2$), 3.28 (s, 3H, OCH$_3$), 7.04 (dd, ^3J=7.8 Hz, ^4J=1.5 Hz, 1H, CH$_{\mathrm{Ar}}$), 7.40 (ddd, ^3J=7.8 Hz, ^3J=7.8 Hz, ^4J=1.5 Hz, 1H, CH$_{\mathrm{Ar}}$), 7.51 (ddd, ^3J=7.5 Hz, ^3J=7.2 Hz, ^4J=1.5 Hz, 1H, CH$_{\mathrm{Ar}}$), 8.0 (dd, ^3J=8.1 Hz, ^4J=1.5 Hz, 1H, CH$_{\mathrm{Ar}}$), 11.19 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 62 MHz): δ=13.9, 14.1, 16.4 (CH$_3$), 22.4, 25.8, 28.5, 29.9, 31.4, 31.8 (CH$_2$), 51.8 (OCH$_3$), 108.5 (*C*COOCH$_3$), 123.7, 127.5, 131.1, 132.6 (CH$_{\mathrm{Ar}}$), 125.1, 129.3, 136.1, 138.5, 148.3, 148.4, 158.6 (C$_{\mathrm{Ar}}$), 171.6 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=2954 (w), 2926 (m), 2856 (w), 1753 (m), 1659 (s), 1594 (w), 1525 (s), 1438 (m), 1411 (m), 1348 (s), 1263 (m), 1211 (s), 1175 (m), 1119 (w), 1016 (w), 919 (w), 853 (w), 788 (w), 752 (m), 707 (w), 627 (w). GC–MS (EI, 70 eV): *m*/*z* (%)=400 ([M]$^+$+1, 15), 399 ([M]$^+$, 59), 339 (23), 338 (100), 296 (27), 292 (23), 263 (11), 253 (10), 252 (10), 250 (10), 249 (21), 238 (17), 236 (13), 234 (10), 222 (14), 221 (10), 208 (14), 207 (21), 179 (13), 178 (21), 165 (14), 152 (9), 43 (13), 41 (10). HRMS (EI): Calcd for C$_{23}$H$_{29}$NO$_5$: 399.20402; found: 399.203491.

*4.4.19. Methyl 6-chloro-3-hydroxy-2′-nitro-5-propylbiphenyl-2-carboxylate (**6s**).* Starting with **5a** (1.260 g, 4.8 mmol), TiCl$_4$ (0.920 g, 4.8 mmol), CH$_2$Cl$_2$ (9 mL) and **4f** (1.50 g, 4.4 mmol), **6s** was isolated (0.841 g, 55%) as a yellowish oil. ^{1}H NMR (CDCl$_3$, 250 MHz): δ=0.87 (t, ^3J=7.5 Hz, 3H, (CH$_2$)$_2$*CH*$_3$), 1.51–1.59 (m, 2H, CH$_2$), 2.58 (t, ^3J=7.5 Hz, 2H, *CH*$_2$CH$_2$CH$_3$), 3.28 (s, 3H, OCH$_3$), 6.84 (s, 1H, CH$_{\mathrm{Ar}}$), 7.03 (dd, ^3J=7.5 Hz, ^4J=1.8 Hz, 1H, CH$_{\mathrm{Ar}}$), 7.42 (ddd, ^3J=8.1 Hz, ^3J=8.1 Hz, ^4J=1.8 Hz, 1H, CH$_{\mathrm{Ar}}$), 7.55 (ddd, ^3J=8.1 Hz, ^3J=8.1 Hz, ^4J=1.7 Hz, 1H, CH$_{\mathrm{Ar}}$), 8.08 (dd, ^3J=7.8 Hz, ^4J=1.8 Hz, 1H, CH$_{\mathrm{Ar}}$), 10.94 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=13.8 (CH$_3$), 22.2, 36.4 (CH$_2$), 52.3 (OCH$_3$), 69.68 (CH$_{\mathrm{Ar}}$), 110.3 (*C*COOCH$_3$), 124.4, 130.0, 131.7, 134.9 (CH$_{\mathrm{Ar}}$), 128.3, 136.3, 138.9, 145.3, 148.2, 160.7 (C$_{\mathrm{Ar}}$), 169.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3102 (w), 3017 (w), 2959 (w), 2862 (w), 1723 (m). 1668 (w), 1601 (w), 1569 (w), 1524 (s), 1440 (m), 1340 (s), 1297 (m), 1266 (m), 1196 (m), 1164 (w), 1144 (m), 1113 (w), 1040 (w), 997 (m), 857 (m), 787 (s), 762 (m), 717 (m), 698 (s), 650 (m), 634 (s), 555 (w). GC–MS (EI 70 eV): *m*/*z* (%)=351 ([M$^+$], ^{37}Cl, 25), 349 ([M$^+$], ^{35}Cl, 71), 317 (20), 314 (44), 313 (11), 305 (12), 303 (35), 290 (10), 283 (18), 282 (100), 274 (18), 272 (24), 257 (16), 255 (13), 254 (70), 246 (11), 244 (20), 231 (14), 230 (13), 227 (17), 226 (33), 225 (38), 218 (15), 216 (13), 215 (14), 214 (15), 209 (18), 208 (11), 198 (21), 195 (13), 193 (24), 186 (11), 182 (13), 181 (17), 180 (22), 178 (23), 177 (34), 170 (10), 168 (21), 167 (19), 166 (10), 165 (26), 163 (13), 158 (10), 155 (16), 153 (24), 152 (49), 151 (33), 149 (17), 139 (40), 131 (13), 128 (15), 126 (16), 124 (21), 115 (12), 114 (10), 77 (11), 76 (12), 75 (11), 67 (14), 29 (10). HRMS (EI): Calcd for C$_{17}$H$_{16}$NO$_5$Cl: 349.07115; found: 349.070500.

*4.4.20. Methyl 3-hydroxy-4,5-dimethyl-3′-nitrobiphenyl-2-carboxylate (**6t**).* Starting with **5b** (0.598 g, 2.2 mmol), TiCl$_4$ (0.413 g, 2.2 mmol), CH$_2$Cl$_2$ (4 mL) and **4g** (0.548 g, 2.0 mmol), **6t** was isolated (0.305 g, 50%) as a yellowish oil. ^{1}H NMR (CDCl$_3$, 250 MHz): δ=2.09 (s, 3H, CH$_3$), 2.21 (s, 3H, CH$_3$), 3.36 (s, 3H, OCH$_3$), 6.46 (s, 1H, CH$_{\mathrm{Ar}}$), 7.30–7.40 (m, 2H, CH$_{\mathrm{Ar}}$), 7.97 (m, 1H, CH$_{\mathrm{Ar}}$), 8.03–8.07 (m, 1H, CH$_{\mathrm{Ar}}$), 11.19 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ_{C}=12.0, 21.3 (CH$_3$), 52.1 (OCH$_3$), 108.7 (C$_{\mathrm{Ar}}$), 121.9, 123.5, 124.3 (CH$_{\mathrm{Ar}}$), 125.7 (C$_{\mathrm{Ar}}$), 128.6, 134.9 (CH$_{\mathrm{Ar}}$), 139.0, 144.0, 145.4, 148.1, 160.7, (C$_{\mathrm{Ar}}$), 171.6 (C═O). GC–MS (EI 70 eV): *m*/*z* (%)=301 ([M]$^+$, 46), 269 (100), 252 (66), 222 (40), 195 (17), 165 (33), 152 (28), 139 (7), 82 (5). HRMS (EI): Calcd for C$_{16}$H$_{15}$NO$_5$: 301.09444; found: 301.09431.

*4.4.21. Ethyl 4-ethyl-3-hydroxy-5-methyl-3′-nitrobiphenyl-2-carboxylate (**6u**).* Starting with **5c** (0.659 g, 2.2 mmol), TiCl$_4$ (0.41 g, 2.2 mmol), CH$_2$Cl$_2$ (4 mL) and **4g** (0.548 g, 2.0 mmol), **6u** was isolated (0.250 g, 37%) as a yellow gummy solid, mp=90–92 °C. ^{1}H NMR (CDCl$_3$, 300 MHz): δ=0.63 (t, ^3J=7.7 Hz, 3H, CH$_3$), 1.04 (t, ^3J=7.7 Hz, 3H, CH$_3$), 2.23 (s, 3H, CH$_3$), 2.62 (q, ^3J=7.0 Hz, 2H, CH$_2$), 3.87 (q, ^3J=6.0 Hz, 2H, OCH$_2$), 6.46 (s, 1H, CH$_{\mathrm{Ar}}$), 7.37–7.45 (m, 2H, CH$_{\mathrm{Ar}}$), 7.99 (m, 1H, CH$_{\mathrm{Ar}}$), 8.03–8.07 (m, 1H, CH$_{\mathrm{Ar}}$), 11.32 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ_{C}=11.9, 12.0, 18.4 (CH$_3$), 18.6 (CH$_2$), 60.0 (OCH$_2$), 107.6 (C$_{\mathrm{Ar}}$), 120.3, 122.2, 123.1, 127.2, 130.3 (CH$_{\mathrm{Ar}}$), 133.5, 137.8, 141.6, 144.1, 146.6, 159.3 (C$_{\mathrm{Ar}}$), 169.7 (C═O). GC–MS (EI, 70 eV): m/z (%)=329 ([M]$^+$, 58), 283 (92), 266 (100), 236 (23), 209 (30), 194 (8), 178 (11), 165 (41), 152 (16), 139 (7), 115 (6). HRMS (EI): Calcd for $C_{18}H_{19}NO_5$: 329.12577; found: 329.12659.

*4.4.22. Methyl 3-hydroxy-5-methyl-4′-nitrobiphenyl-2-carboxylate (**6v**).* Starting with **5a** (0.568 g, 2.2 mmol), $TiCl_4$ (0.413 g, 2.2 mmol), CH_2Cl_2 (4 mL) and **4h** (0.558 g, 4.0 mmol), **6v** was isolated (0.206 g, 36%) as a colourless solid, mp=85–87 °C. ^{1}H NMR ($CDCl_3$, 250 MHz): δ=2.23 (s, 3H, CH_3), 3.36 (s, 3H, OCH_3), 6.44 (d, ^4J=1.6 Hz, 1H, CH_{Ar}), 6.77 (d, ^4J=1.3 Hz, 1H, CH_{Ar}), 7.25 (d, ^3J=8.8 Hz, 2H, CH_{Ar}), 8.10 (d, ^3J=8.8 Hz, 2H, CH_{Ar}), 10.81 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C=21.6 (CH_3), 51.7 (OCH_3), 108.6 (C_{Ar}), 118.2 (CH_{Ar}), 122.8 ($2CH_{Ar}$), 123.5 (CH_{Ar}), 129.0 ($2CH_{Ar}$), 142.1, 145.4, 146.9, 149.9, 162.2 (C_{Ar}), 170.0 (C=O). GC–MS (EI 70 eV): m/z (%)=287 ([M]$^+$, 27), 255 (100), 197 (9), 181 (30), 152 (20), 115 (5), 76 (7). HRMS (EI): Calcd for $C_{15}H_{13}NO_5$: 287.07882; found: 287.07879.

*4.4.23. Methyl 3-hydroxy-4,5-dimethyl-4′-nitrobiphenyl-2-carboxylate (**6w**).* Starting with **5b** (0.598 g, 2.2 mmol), $TiCl_4$ (0.413 g, 2.2 mmol), CH_2Cl_2 (4 mL) and **4h** (0.558 g, 2.0 mmol), **6w** was isolated (0.276 g, 46%) as a colourless solid, mp=87–89 °C. ^{1}H NMR ($CDCl_3$, 250 MHz): δ=2.16 (s, 3H, CH_3), 2.25 (s, 3H, CH_3) 3.40 (s, 3H, OCH_3), 6.49 (s, 1H, CH_{Ar}), 7.29 (d, ^3J=8.8 Hz, 2H, CH_{Ar}), 8.14 (d, ^3J=8.8 Hz, 2H, CH_{Ar}), 11.18 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C=11.5, 20.4 (CH_3), 51.7 (OCH_3), 108.2 (C_{Ar}), 122.7 ($2CH_{Ar}$), 123.6 (CH_{Ar}), 125.4 (CH_{Ar}), 129.0 ($2CH_{Ar}$), 138.9, 143.5, 146.6, 150.2, 160.2 (C_{Ar}), 171.1 (C=O). GC–MS (EI 70 eV): m/z (%)=301 ([M]$^+$, 40), 269 (100), 254 (19), 223 (42), 195 (17), 180 (6), 165 (32), 152 (29), 139 (7), 115 (7), 76 (5). HRMS (EI): Calcd for $C_{16}H_{15}NO_5$: 301.09447; found: 301.09477.

*4.4.24. Ethyl 4-ethyl-3-hydroxy-5-methyl-4′-nitrobiphenyl-2-carboxylate (**6x**).* Starting with **5c** (0.659 g, 2.2 mmol), $TiCl_4$ (0.413 g, 2.2 mmol), CH_2Cl_2 (4 mL) and **4h** (0.558 g, 2.0 mmol), **6x** was isolated (0.217 g, 33%) as a colourless solid, mp=80–82 °C. ^{1}H NMR ($CDCl_3$, 250 MHz): δ=0.65 (t, ^3J=7.4 Hz, 3H, CH_3), 1.09 (t, ^3J=7.5 Hz, 3H, CH_3), 2.27 (s, 3H, CH_3), 2.67 (q, ^3J=7.5 Hz, 2H, CH_2), 3.92 (q, ^3J=7.4 Hz, 2H, OCH_2), 6.46 (s, 1H, CH_{Ar}), 7.30 (d, ^3J=8.8 Hz, 2H, CH_{Ar}), 8.14 (d, ^3J=8.8 Hz, 2H, CH_{Ar}), 11.27 (s, 1H, OH). ^{13}C NMR ($CDCl_3$, 62 MHz): δ_C=12.9, 13.1, 19.4 (CH_3), 19.6 (CH_2), 61.1 (OCH_2), 108.5 (C_{Ar}), 122.7 ($2CH_{Ar}$), 123.7 (CH_{Ar}), 129.1 ($2CH_{Ar}$), 131.3, 139.1, 142.5, 146.5, 150.5, 160.2 (C_{Ar}), 170.7 (C=O). GC–MS (EI 70 eV): m/z (%)=329 ([M]$^+$, 58), 283 (100), 266 (50), 240 (46), 222 (9), 209 (13), 178 (10), 165 (56), 152 (19), 139 (8), 115 (7), 77 (4). HRMS (EI): Calcd for $C_{18}H_{19}NO_5$: 329.12577; found: 329.12590.

4.5. General procedure for the synthesis of phenanthridinones 7a–s

To a stirred methanol suspension (25 mL) of Pd/C (10 mol %) was added **6a–s** (1.0 equiv). The mixture was set under a hydrogen atmosphere. After stirring for 48 h at 20 °C, the reaction mixture was filtered (Celite) and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/EtOAc=2:1).

*4.5.1. 7-Hydroxy-9-methyl-6(5H)-phenanthridinone (**7a**).* Starting with **6a** (0.429 g, 1.6 mmol), **7a** was isolated (0.215 g, 64%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=245–247 °C. ^{1}H NMR (DMSO-d_6, 250 MHz): δ=2.45 (s, 3H, CH_3), 6.82 (s, 1H, CH_{Ar}), 7.27–7.30 (m, 1H, CH_{Ar}), 7.33–7.41 (m, 1H, CH_{Ar}), 7.49–7.55 (m, 1H, CH_{Ar}), 7.76 (m, 1H, CH_{Ar}), 8.34 (d, ^3J=7.9 Hz, 1H, CH_{Ar}), 12.02 (br s, 1H, NH), 13.25 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 62 MHz): δ_C=21.8 (CH_3), 107.9 (C_{Ar}), 113.1 115.0, 116.6 (CH_{Ar}), 118.0 (C_{Ar}), 123.2, 123.6, 128.4 (CH_{Ar}), 129.8, 135.6, 146.0, 159.4 (C_{Ar}), 165.7 (C=O). MS (EI, 70 eV): m/z (%)=225 ([M]$^+$, 100), 206 (10), 196 (16), 99 (14), 73 (16), 57 (27), 43 (52). HRMS (EI): Calcd for $C_{14}H_{11}NO_2$: 225.07853; found: 225.07843.

*4.5.2. 7-Hydroxy-8,9-dimethylphenanthridin-6(5H)-one (**7b**).* Starting with **6b** (0.504 g, 1.7 mmol), **7b** was isolated (0.200 g, 52%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=260–261 °C. ^{1}H NMR (DMSO-d_6, 250 MHz): δ=2.08 (s, 3H, CH_3), 2.21 (s, 3H, CH_3), 7.27–7.52 (m, 3H, CH_{Ar}), 7.74 (s, 1H, CH_{Ar}), 8.34 (d, ^3J=7.5 Hz, 1H, CH_{Ar}), 11.97 (br s, 1H, NH), 13.60 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 62 MHz): δ_C=10.6, 13.9 (CH_3), 107.3 (C_{Ar}), 112.4, 116.4, 121.3, (CH_{Ar}), 123.0 (C_{Ar}), 123.2, 123.6, 129.2 (CH_{Ar}), 135.1, 148.3, 159.2, (C_{Ar}), 165.6 (C=O). MS (EI, 70 eV): m/z (%)=239 ([M]$^+$, 89), 224 (34), 191 (10), 97 (26), 84 (100), 66 (98), 57 (95). Anal. Calcd for $C_{15}H_{13}NO_2$: C 75.30, H 5.48, N 5.85; found: C 75.40, H 5.42, N 5.70.

*4.5.3. 8-Ethyl-7-hydroxy-9-methylphenanthridin-6(5H)-one (**7c**).* Starting with **6c** (0.137 g, 0.4 mmol), **7c** was isolated (0.070 g, 70%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=257–259 °C. ^{1}H NMR (DMSO-d_6, 250 MHz): δ=1.10 (t, ^3J=8.0 Hz, 3H, CH_3), 2.47 (s, 3H, CH_3), 2.68 (q, ^3J=7.5 Hz, 2H, CH_2), 7.26–7.32 (m, 1H, CH_{Ar}), 7.36–7.39 (m, 1H, CH_{Ar}), 7.46–7.52 (m, 1H, CH_{Ar}), 7.75 (s, 1H, CH_{Ar}), 8.31 (d, ^3J=8.4 Hz, 1H, CH_{Ar}), 11.99 (br s, 1H, NH), 13.59 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 62 MHz): δ_C=13.0, 18.5 (CH_3), 19.8 (CH_2), 107.6 (C_{Ar}), 113.5, 116.5 (CH_{Ar}), 118.3 (C_{Ar}), 123.0, 123.3, (CH_{Ar}), 127.8 (CH_{Ar}), 129.3 (CH_{Ar}), 132.2, 135.2, 143.6, 158.9 (C_{Ar}), 165.8 (C=O). MS (EI, 70 eV): m/z (%)=253 ([M]$^+$, 39), 238 (100), 220 (2), 190 (5), 165 (6), 104 (4), 95 (3), 63 (3). HRMS (EI): Calcd for $C_{16}H_{15}NO_2$: 253.10973; found: 253.10991.

*4.5.4. 7-Hydroxy-9-methyl-8-octylphenanthridin-6(5H)-one (**7d**).* Starting with **6d** (0.275 g, 0.7 mmol), **7d** was isolated (0.200 g, 69%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=268–269 °C. ^{1}H NMR (DMSO-d_6/$CDCl_3$, 250 MHz): δ=0.77–0.85 (m, 3H, CH_3), 1.85–1.24 (m, 8H, CH_2), 1.41–1.49 (m, 4H, CH_2), 2.41 (s, 3H, Ch_3), 2.60–2.66 (m, 2H, CH_2), 7.16–7.32 (m, 3H, CH_{Ar}), 7.53 (s, 1H, CH_{Ar}), 8.12 (d, ^3J=7.8 Hz, 1H, CH_{Ar}), 11.70 (br s, 1H, NH), 13.44 (s, 1H, OH). ^{13}C NMR (DMSO-d_6/$CDCl_3$, 62 MHz): δ_C=13.8, 20.1 (CH_3), 22.1, 25.3, 28.4, 28.6, 29.0, 29.3, 31.5 (CH_2), 107.6 (C_{Ar}), 112.8, 112.9, 116.3 (CH_{Ar}), 118.2 (C_{Ar}), 122.6 (CH_{Ar}), 126.6, 126.7 (C_{Ar}), 128.6 (CH_{Ar}), 132.0, 143.2, 159.2 (C_{Ar}), 165.6 (C=O). MS (EI, 70 eV): m/z (%)=337 ([M]$^+$, 28), 308 (4), 276 (3), 252 (7), 238 (100), 224 (5), 192 (3), 160 (4) 128 (25), 97 (14), 69 (15). HRMS (EI): Calcd for $C_{22}H_{27}NO_2$: 337.20363; found: 337.20310.

*4.5.5. 9-Ethyl-7-hydroxyphenanthridin-6(5H)-one (**7e**).* Starting with **6e** (0.190 g, 0.6 mmol), **7e** was isolated (0.113 g, 75%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=260–261 °C. ^{1}H NMR (DMSO-d_6, 250 MHz): δ=1.27 (t, ^3J=7.7 Hz, 3H, CH_2CH_3), 2.75 (q, ^3J=7.2 Hz, 2H, CH_2CH_3), 6.85 (br s, 1H, CH_{Ar}), 7.28–7.34 (m, 1H, CH_{Ar}), 7.38–7.41 (m, 1H, CH_{Ar}), 7.49–7.55 (m, 1H, CH_{Ar}), 7.76 (br s, 1H, CH_{Ar}), 8.36 (d, ^3J=8.3 Hz, 1H, CH_{Ar}), 12.02 (br s, 1H, NH), 13.25 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 62 MHz): δ=15.0 (CH_3), 28.8 (CH_2), 107.9 (C_{Ar}), 111.7 113.7, 116.5 (CH_{Ar}), 118.1 (C_{Ar}), 123.0, 123.7, 129.6 (CH_{Ar}), 135.2, 135.5, 151.8, 161.5 (C_{Ar}), 165.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3172 (w), 3042 (w), 2956 (m), 2928 (m), 2867 (m), 1650 (s), 1620 (m), 1594 (w), 1556 (m), 1462 (w), 1453 (m), 1430 (m), 1371 (w), 1347 (m), 1299 (m), 1224 (m), 1174 (m), 1128 (w), 1100 (w), 1058 (w), 1014 (m), 948 (w), 909 (w), 846 (m), 770 (w), 747 (s), 720 (m), 680 (m), 633 (m), 553 (m). MS (EI, 70 eV): m/z (%)=240 ([M]$^+$+1, 17), 239 ([M]$^+$, 100), 238 (32), 207 (13), 196 (11). HRMS (EI): Calcd for $C_{15}H_{13}NO_2$: 239.09408; found: 239.094189.

*4.5.6. 9-Ethyl-7-hydroxy-8-methylphenanthridin-6(5H)-one (**7f**).* Starting with **6f** (0.228 g, 0.7 mmol), **7f** was isolated (0.097 g, 53%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=265–267 °C. ^{1}H NMR (DMSO-d_6, 250 MHz): δ=1.14 (t, ^{3}J=7.0 Hz, 3H, CH$_2$CH$_3$), 2.18 (s, 3H, CH$_3$), 2.77 (q, ^{3}J=7.1 Hz, 2H, CH$_2$CH$_3$), 7.26–7.32 (m, 1H, CH$_{Ar}$), 7.36–7.39 (m, 1H, CH$_{Ar}$), 7.45–7.51 (m, 1H, CH$_{Ar}$), 7.70 (s, 1H, CH$_{Ar}$), 8.34 (d, ^{3}J=7.8 Hz, 1H, CH$_{Ar}$), 11.95 (br s, 1H, NH), 13.62 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 62 MHz): δ=13.8, 15.4 (CH$_3$), 28.8 (CH$_2$), 107.4 (C$_{Ar}$), 111.8, 116.4 (CH$_{Ar}$), 118.1 (C$_{Ar}$), 123.0, 123.3 (CH$_{Ar}$), 126.0 (C$_{Ar}$), 129.2 (CH$_{Ar}$), 132.4, 135.1, 149.5, 159.3, (C$_{Ar}$), 165.0 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3172 (w), 3041 (w), 2955 (m), 2930 (m), 2866 (m), 1651 (s), 1622 (m), 1590 (w), 1550 (m), 1457 (w), 1435 (m), 1369 (w), 1345 (m), 1300 (m), 1220 (m), 1170 (m), 1128 (w), 1098 (w), 1060 (w), 1012 (m), 945 (w), 908 (w), 845 (m), 770 (w), 746 (s), 719 (m), 682 (m), 633 (m), 552 (m). MS (EI, 70 eV): m/z (%)=255 ([M]$^{+}$+2, 11), 254 ([M]$^{+}$+1, 26), 253 ([M]$^{+}$, 100), 252 (45), 239 (10), 238 (13), 226 (10), 225 (18), 224 (24), 84 (10), 66 (18), 44 (35), 43 (12). Anal. Calcd for C$_{16}$H$_{15}$NO$_2$: C 75.30, H 5.48, N 5.85; found.: C 75.38, H 5.43, N 5.75.

*4.5.7. 8,9-Diethyl-7-hydroxyphenanthridin-6(5H)-one (**7g**).* Starting with **6g** (0.171 g, 0.5 mmol), **7g** was isolated (0.069 g, 52%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=242–244 °C. ^{1}H NMR (DMSO-d_6, 250 MHz): δ=1.13 (t, ^{3}J=7.0 Hz, 3H, CH$_2$CH$_3$), 1.27 (t, ^{3}J=7.0 Hz, 3H, CH$_2$CH$_3$), 2.66–2.74 (m, 2H, CH$_2$CH$_3$), 2.76–2.83 (m, 2H, CH$_2$CH$_3$), 7.26–7.29 (m, 1H, CH$_{Ar}$), 7.36–7.40 (m, 1H, CH$_{Ar}$), 7.44–7.49 (m, 1H, CH$_{Ar}$), 7.74 (s, 1H, CH$_{Ar}$), 8.34 (d, ^{3}J=7.8 Hz, 1H, CH$_{Ar}$), 11.96 (br s, 1H, NH), 13.62 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 62 MHz): δ=15.4, 16.8 (CH$_3$), 18.1, 26.0 (CH$_2$), 107.4 (C$_{Ar}$), 111.9, 116.4 (CH$_{Ar}$), 118.3 (C$_{Ar}$), 123.0, 123.3 (CH$_{Ar}$), 128.2 (C$_{Ar}$), 129.2 (CH$_{Ar}$), 132.4, 135.1, 149.5, 159.2, (C$_{Ar}$), 165.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3173 (w), 3035 (w), 2953 (m), 2927 (m), 2865 (m), 1651 (s), 1628 (m), 1592 (w), 1562 (m), 1460 (w), 1455 (m), 1433 (m), 1370 (w), 1347 (m), 1297 (m), 1222 (m), 1170 (m), 1123 (w), 1115 (w), 1058 (w), 1012 (m), 945 (w), 909 (w), 845 (m), 768 (w), 745 (s), 723 (m), 678 (m), 630 (m), 552 (m). MS (EI, 70 eV): m/z (%)=267 ([M]$^{+}$, 41), 253 (17), 252 (100). HRMS (EI): Calcd for C$_{17}$H$_{17}$NO$_2$: 267.12538; found: 267.125175.

*4.5.8. 9-Ethyl-8-hexyl-7-hydroxyphenanthridin-6(5H)-one (**7h**).* Starting with **6h** (0.255 g, 0.7 mmol), **7h** was isolated (0.109 g, 51%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=230–232 °C. ^{1}H NMR (CD$_3$OD, 250 MHz): δ=0.96–0.99 (m, 3H, (CH$_2$)$_5$CH$_3$), 1.03–1.08 (m, 3H, CH$_2$CH$_3$), 1.34–1.41 (m, 8H, 4×CH$_2$), 2.87–2.95 (m, 4H, 2×CH$_2$), 7.24–7.30 (m, 1H, CH$_{Ar}$), 7.44–7.45 (m, 1H, CH$_{Ar}$), 7.48–7.51 (m, 1H, CH$_{Ar}$), 7.74 (s, 1H, CH$_{Ar}$), 8.29 (d, ^{3}J=7.8 Hz, 1H, CH$_{Ar}$). ^{13}C NMR (CD$_3$OD, 62 MHz): δ=14.5, 15.4 (CH$_3$), 23.5, 26.4, 27.1, 27.6, 29.8, 32.8 (CH$_2$), 108.8 (C$_{Ar}$), 124.4, 117.0 (CH$_{Ar}$), 120.0 (C$_{Ar}$), 122.7, 124.1 (CH$_{Ar}$), 129.1 (C$_{Ar}$), 130.0 (CH$_{Ar}$), 134.0, 136.9, 151.0, 161.1, (C$_{Ar}$), 167.5 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=2971 (m), 2910 (w), 2831 (m), 2758 (m), 2719 (m), 2487 (m), 2096 (w), 1586 (w), 1467 (m), 1397 (w), 1330 (w), 1202 (w), 1151 (m), 1103 (m), 978 (m), 957 (m), 840 (w), 805 (w), 612 (m). MS (EI, 70 eV): m/z (%)=324 ([M]$^{+}$+1, 11), 323 ([M]$^{+}$, 31), 266 (11), 254 (19), 253 (78), 252 (100), 237 (10). HRMS (EI): Calcd for C$_{21}$H$_{25}$NO$_2$: 323.18798; found: 323.18.7220.

*4.5.9. 9-Ethyl-8-heptyl-7-hydroxyphenanthridin-6(5H)-one (**7i**).* Starting with **6i** (0.265 g, 0.7 mmol), **7i** was isolated (0.109 g, 49%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=232–234 °C. ^{1}H NMR (DMSO-d_6, 250 MHz): δ=0.85–0.86 (m, 3H, (CH$_2$)$_6$CH$_3$), 1.10 (t, ^{3}J=7.1 Hz, 3H, CH$_2$CH$_3$), 1.26–1.29 (m, 10H, 5×CH$_2$), 2.63–2.72 (m, 2H, CH$_2$), 2.78 (q, ^{3}J=7.7 Hz, 2H, CH$_2$CH$_3$), 7.23–7.29 (m, 1H, CH$_{Ar}$), 7.36–7.41 (m, 1H, CH$_{Ar}$), 7.46–7.52 (m, 1H, CH$_{Ar}$), 7.74 (s, 1H, CH$_{Ar}$), 8.34 (d, ^{3}J=7.7 Hz, 1H, CH$_{Ar}$), 11.94 (br s, 1H, NH), 13.63 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 62 MHz): δ=13.9, 15.4 (CH$_3$), 22.0, 26.0, 28.5, 28.6, 29.1, 29.3, 31.3 (CH$_2$), 107.4 (C$_{Ar}$), 111.8, 116.4 (CH$_{Ar}$), 118.3 (C$_{Ar}$), 123.1, 123.3 (CH$_{Ar}$), 126.1 (C$_{Ar}$), 129.3 (CH$_{Ar}$), 132.4, 135.2, 149.5, 159.3 (C$_{Ar}$), 165.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3172 (w), 3062 (w), 3022 (w), 2956 (m), 2926 (m), 2867 (m), 1717 (w), 1651 (s), 1623 (m), 1595 (m), 1554 (m), 1460 (w), 1455 (m), 1437 (m), 1370 (m), 1347 (m), 1300 (m), 1225 (m), 1180 (m), 1126 (w), 1098 (w), 1056 (w), 1015 (m), 948 (w), 908 (w), 845 (m), 770 (w), 747 (s), 720 (m), 682 (m), 635 (m), 552 (m). MS (EI, 70 eV): m/z (%)=338 ([M]$^{+}$+1, 8), 337 ([M]$^{+}$, 34), 308 (12), 266 (13), 254 (15), 253 (72), 252 (100), 237 (10), 209 (9), 208 (12), 207 (39), 191 (9), 44 (11). HRMS (EI): Calcd for C$_{22}$H$_{27}$NO$_2$: 337.20363; found: 337.203119.

*4.5.10. 9-Ethyl-7-hydroxy-8-octylphenanthridin-6(5H)-one (**7j**).* Starting with **6j** (0.347 g, 0.8 mmol), **7j** was isolated (0.147 g, 50%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=241–243 °C. ^{1}H NMR (DMSO-d_6, 250 MHz): δ=0.85–0.87 (m, 3H, (CH$_2$)$_7$CH$_3$), 1.08 (t, ^{3}J=7.1 Hz, 3H, CH$_2$CH$_3$), 1.24–1.27 (m, 12H, 6×CH$_2$), 2.60–2.67 (m, 2H, CH$_2$), 2.78 (q, ^{3}J=7.4 Hz, 2H, CH$_2$CH$_3$), 7.26–7.32 (m, 1H, CH$_{Ar}$), 7.36–7.42 (m, 1H, CH$_{Ar}$), 7.46–7.49 (m, 1H, CH$_{Ar}$), 7.74 (s, 1H, CH$_{Ar}$), 8.33 (d, ^{3}J=7.7 Hz, 1H, CH$_{Ar}$), 11.96 (br s, 1H, NH), 13.62 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 62 MHz): δ=13.8, 15.3 (CH$_3$), 22.0, 26.0, 26.8, 28.5, 28.6, 29.1, 29.3, 31.3 (CH$_2$), 107.3 (C$_{Ar}$), 111.6, 116.4 (CH$_{Ar}$), 118.3 (C$_{Ar}$), 123.0, 123.3 (CH$_{Ar}$), 128.3 (C$_{Ar}$), 129.3 (CH$_{Ar}$), 132.3, 135.2, 150.0, 159.2 (C$_{Ar}$), 165.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3169 (w), 3082 (w), 3020 (w), 2963 (m), 2921 (m), 2875 (m), 1716 (w), 1650 (s), 1594 (m), 1500 (m), 1430 (m), 1408 (s), 1372 (m), 1330 (m), 1319 (m), 1295 (m), 1235 (m), 1194 (m), 1112 (w), 1091 (m), 1047 (w), 1008 (w), 940 (w), 912 (w), 853 (m), 810 (s), 798 (m), 750 (s), 698 (m), 687 (m), 639 (m), 592 (m), 529 (m). MS (EI, 70 eV): m/z (%)=352 ([M]$^{+}$+1, 11), 351 ([M]$^{+}$, 49), 253 (88), 252 (100), 237 (8). HRMS (EI): Calcd for C$_{23}$H$_{29}$NO$_2$: 351.22063; found: 351.220119.

*4.5.11. 7-Hydroxy-9-propylphenanthridin-6(5H)-one (**7k**).* Starting with **6k** (0.563 g, 1.8 mmol), **7k** was isolated (0.240 g, 56%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=240–241 °C. ^{1}H NMR (DMSO-d_6, 250 MHz): δ=0.92 (t, ^{3}J=7.1 Hz, 3H, CH$_3$), 1.63–1.72 (m, 2H, CH$_2$), 2.68 (t, ^{3}J=7.1 Hz, 2H, CH$_2$), 6.81 (br s, 1H, CH$_{Ar}$), 7.25–7.29 (m, 1H, CH$_{Ar}$), 7.32–7.39 (m, 1H, CH$_{Ar}$), 7.47–7.53 (m, 1H, CH$_{Ar}$), 7.74 (br s, 1H, CH$_{Ar}$), 8.35 (d, ^{3}J=7.7 Hz, 1H, CH$_{Ar}$), 12.01 (br s, 1H, NH), 13.25 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 62 MHz): δ_C=13.6 (CH$_3$), 23.6, 38.6 (CH$_2$), 107.9 (C$_{Ar}$), 112.3, 114.3, 116.5 (CH$_{Ar}$), 118.2 (C$_{Ar}$), 123.1, 123.7, 129.7 (CH$_{Ar}$), 135.2, 135.5, 150.2, 161.4 (C$_{Ar}$), 165.7 (C=O). MS (EI, 70 eV): m/z (%)=253 ([M]$^{+}$, 40), 225 (100), 196 (20), 177 (30), 149 (60), 115 (15), 89 (12), 69 (20), 44 (70), 43 (9). HRMS (EI): Calcd for C$_{16}$H$_{15}$NO$_2$: 253.10973; found: 253.10991.

*4.5.12. 7-Hydroxy-8-methyl-9-propylphenanthridin-6(5H)-one (**7l**).* Starting with **6l** (0.480 g, 1.45 mmol), **7l** was isolated (0.190 g, 50%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=245–247 °C. ^{1}H NMR (DMSO-d_6, 250 MHz): δ=0.90 (t, ^{3}J=7.4 Hz, 3H, CH$_3$), 1.50–1.59 (m, 2H, CH$_2$), 2.12 (s, 3H, CH$_3$), 2.65 (t, ^{3}J=7.5 Hz, 2H, CH$_2$), 7.18–7.24 (m, 1H, CH$_{Ar}$), 7.28–7.32 (m, 1H, CH$_{Ar}$), 7.32–7.43 (m, 1H, CH$_{Ar}$), 7.64 (s, 1H, CH$_{Ar}$), 8.25 (d, ^{3}J=8.2 Hz, 1H, CH$_{Ar}$), 11.89 (br s, 1H, NH), 13.55 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 62 MHz): δ_C=10.5, 13.8 (CH$_3$), 23.0, 35.9 (CH$_2$), 107.4 (C$_{Ar}$), 112.3, 116.6 (CH$_{Ar}$), 118.5, 121.5 (C$_{Ar}$), 123.0, 123.3, 129.3 (CH$_{Ar}$), 131.9, 135.2, 148.6, 159.4 (C$_{Ar}$), 165.7 (C=O). MS (EI, 70 eV): m/z (%)=267 ([M]$^{+}$, 100), 252 (76), 239 (75), 224 (34), 210 (5), 190 (7), 165 (7), 78 (34), 63 (43), 43 (9). HRMS (EI): Calcd for C$_{17}$H$_{17}$NO$_2$: 267.12535; found: 267.12538.

*4.5.13. 8-Ethyl-7-hydroxy-9-propylphenanthridin-6(5H)-one (**7m**).* Starting with **6m** (0.202 g, 0.6 mmol), **7m** was isolated (0.100 g, 63%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=232–234 °C. ^{1}H NMR

(DMSO-d_6, 250 MHz): δ=1.00 (t, ^3J=8.1 Hz, 3H, CH$_3$), 1.13 (t, ^3J=7.2 Hz, 3H, CH$_3$), 1.66 (q, ^3J=7.3 Hz, 2H, CH$_2$), 2.66–2.77 (m, 4H, CH$_2$), 7.26–7.36 (m, 2H, CH$_{Ar}$), 7.49–7.58 (m, 2H, CH$_{Ar}$), 8.34 (d, ^3J=8.0 Hz, 1H, CH$_{Ar}$), 11.90 (br s, 1H, NH), 13.62 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 62 MHz): δ_C=13.9, 14.0 (CH$_3$), 18.3, 24.0, 35.0 (CH$_2$), 107.5 (C$_{Ar}$), 112.6, 116.6 (CH$_{Ar}$), 118.4, 121.6 (C$_{Ar}$), 123.0, 123.8, 131.3 (CH$_{Ar}$), 132.3, 135.2, 147.8, 159.2 (C$_{Ar}$), 165.7 (C=O). MS (EI, 70 eV): *m*/*z* (%)=281 ([M]$^+$, 100), 238 (76), 207 (12), 224 (30), 190 (7), 165 (5), 78 (40), 63 (23), 43 (8). HRMS (EI): Calcd for $C_{17}H_{17}NO_2$: 267.12535; found: 267.12538. Anal. Calcd for $C_{18}H_{19}NO_2$: C 76.84, H 6.81, N 4.98; found.: C 76.90, H 6.60, N 4.90.

*4.5.14. 8-Hexyl-7-hydroxy-9-propylphenanthridin-6(5H)-one (**7n**).* Starting with **6n** (0.250 g, 0.62 mmol), **7n** was isolated (0.150 g, 74%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=237–239 °C. ^{1}H NMR (CDCl$_3$, 250 MHz): δ=0.83 (t, ^3J=7.8 Hz, 3H, CH$_3$), 0.99 (t, ^3J=7.5 Hz, 3H, CH$_3$), 1.26–1.48 (m, 8H, CH$_2$), 1.60–1.69 (m, 2H, CH$_2$), 2.66–2.72 (m, 4H, CH$_2$), 7.11–7.15 (m, 1H, CH$_{Ar}$), 7.21–7.25 (m, 1H, CH$_{Ar}$), 7.37–7.40 (m, 1H, CH$_{Ar}$), 7.48 (s, 1H, CH$_{Ar}$), 8.10 (d, ^3J=8.5 Hz, 1H, CH$_{Ar}$), 9.49 (br s, 1H, NH), 13.92 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ_C=14.1, 14.2 (CH$_3$), 22.6, 24.4, 25.8, 29.5, 29.8, 31.7, 36.0 (CH$_2$), 107.5 (C$_{Ar}$), 112.0, 112.6, 116.2 (CH$_{Ar}$), 119.4 (C$_{Ar}$), 123.2 (CH$_{Ar}$), 123.5 (C$_{Ar}$), 127.9 (CH$_{Ar}$), 129.1, 131.4, 133.5, 148.7 (C$_{Ar}$), 160.0 (C=O). MS (EI 70 eV): *m*/*z* (%)=337 ([M]$^+$, 42), 280 (9), 266 (100), 225 (19), 161 (9), 128 (40), 83 (24), 69 (43) 43 (9). HRMS (EI): Calcd for $C_{22}H_{27}NO_2$: 337.20363; found: 337.20310.

*4.5.15. 9-Butyl-7-hydroxyphenanthridin-6(5H)-one (**7o**).* Starting with **6o** (0.164 g, 0.5 mmol), **7o** was isolated (0.931 g, 70%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=234–235 °C. ^{1}H NMR (DMSO-d_6, 250 MHz): δ=0.92 (t, ^3J=7.1 Hz, 3H, (CH$_2$)$_3$*CH$_3$*), 1.27–1.41 (m, 2H, CH$_2$), 1.59–1.71 (m, 2H, CH$_2$), 2.71 (t, ^3J=7.6 Hz, 2H, *CH$_2$*(CH$_2$)$_2$CH$_3$), 6.83 (s, 1H, CH$_{Ar}$), 7.28–7.33 (m, 1H, CH$_{Ar}$), 7.38–7.41 (m, 1H, CH$_{Ar}$), 7.49–7.55 (m, 1H, CH$_{Ar}$), 7.75 (s, 1H, CH$_{Ar}$), 8.35 (d, ^3J=8.8 Hz, 1H, CH$_{Ar}$), 12.02 (br s, 1H, NH), 13.26 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 62 MHz): δ=13.7 (CH$_3$), 21.7, 32.6, 35.5 (CH$_2$), 107.9 (C$_{Ar}$), 112.2, 114.2, 116.5 (CH$_{Ar}$), 118.2 (C$_{Ar}$), 123.0, 123.7, 129.7 (CH$_{Ar}$), 135.1, 135.5, 150.5, 161.5 (C$_{Ar}$) 165.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3170 (w), 3075 (w), 3012 (w), 2953 (m), 2923 (m), 2856 (m), 1659 (s), 1626 (m), 1595 (m), 1552 (m), 1503 (m), 1455 (w), 1426 (m), 1406 (m), 1378 (m), 1349 (m), 1296 (m), 1229 (m), 1163 (m), 1126 (w), 1078 (w), 1037 (w), 1006 (m), 938 (w), 916 (w), 862 (m), 805 (m), 774 (m), 747 (s), 680 (m), 639 (m), 617 (m), 553 (m). MS (EI, 70 eV): *m*/*z* (%)=268 ([M]$^+$+1, 8), 267 ([M]$^+$, 53), 226 (24), 225 (100), 224 (23), 196 (10), 178 (8), 78 (24), 63 (26), 44 (10). HRMS (EI): Calcd for $C_{17}H_{17}NO_2$: 267.12538; found: 267.125349.

*4.5.16. 9-Butyl-7-hydroxy-8-methylphenanthridin-6(5H)-one (**7p**).* Starting with **6p** (0.171 g, 0.5 mmol), **7p** was isolated (0.076 g, 54%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=257–259 °C. ^{1}H NMR (DMSO-d_6, 250 MHz): δ=0.94 (t, ^3J=7.1 Hz, 3H, (CH$_2$)$_3$*CH$_3$*), 1.36–1.44 (m, 2H, CH$_2$), 1.52–1.61 (m, 2H, CH$_2$), 2.20 (s, 3H, CH$_3$), 2.76 (t, ^3J=7.4 Hz, 2H, *CH$_2$*(CH$_2$)$_2$CH$_3$), 7.26–7.32 (m, 1H, CH$_{Ar}$), 7.36–7.39 (m, 1H, CH$_{Ar}$), 7.46–7.52 (m, 1H, CH$_{Ar}$), 7.73 (s, 1H, CH$_{Ar}$), 8.34 (d, ^3J=8.1 Hz, 1H, CH$_{Ar}$), 11.96 (br s, 1H, NH), 13.62 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 62 MHz): δ=10.6, 13.7 (CH$_3$), 22.1, 31.9, 33.5 (CH$_2$), 107.3 (C$_{Ar}$), 112.4, 116.4 (CH$_{Ar}$), 118.3, 121.3 (C$_{Ar}$), 123.0, 123.3, 129.2 (CH$_{Ar}$), 132.1, 135.1, 148.6, 159.2 (C$_{Ar}$) 165.6 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3305 (w), 3169 (w), 3017 (w), 2953 (m), 2932 (m), 2860 (m), 1731 (w), 1657 (s), 1651 (s), 1632 (m), 1595 (m), 1553 (m), 1503 (m), 1449 (w), 1409 (m), 1372 (m), 1348 (m), 1304 (m), 1268 (m), 1236 (m), 1195 (m), 1113 (m), 1098 (m), 1057 (m), 935 (m), 857 (m), 843 (m), 805 (s), 789 (s), 743 (s), 713 (m), 668 (m), 629 (m), 620 (m), 560 (s), 539 (s). MS (EI, 70 eV): *m*/*z* (%)=282 ([M]$^+$+1, 12), 281 ([M]$^+$, 57), 252 (15), 240 (16), 239 (100), 238 (15), 224 (31). HRMS (EI): Calcd for $C_{18}H_{19}NO_2$: 281.14103; found: 281.141039.

*4.5.17. 9-Butyl-8-hexyl-7-hydroxyphenantridin-6(5H)-one (**7q**).* Starting with **6q** (0.098 g, 0.6 mmol), **7q** was isolated (0.097 g, 50%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=220–222 °C. ^{1}H NMR (DMSO-d_6, 250 MHz): δ=0.84–0.90 (m, 3H, (CH$_2$)$_5$CH$_3$),0.95 (t, ^3J=7.3 Hz, 3H, (CH$_2$)$_3$*CH$_3$*), 1.22–1.31 (m, 6H, 3×CH$_2$), 1.37–1.43 (m, 4H, 2×CH$_2$), 1.57–1.64 (m, 2H, CH$_2$), 2.63–2.77 (m, 4H, 2×CH$_2$), 7.26–7.32 (m, 1H, CH$_{Ar}$), 7.36–7.39 (m, 1H, CH$_{Ar}$), 7.46–7.51 (m, 1H, CH$_{Ar}$), 7.73 (s, 1H, CH$_{Ar}$), 8.33 (d, ^3J=8.7 Hz, 1H, CH$_{Ar}$), 11.95 (br s, 1H, NH), 13.63 (s, 1H, OH).^{13}C NMR (DMSO-d_6, 62 MHz): δ=13.7, 13.9 (CH$_3$), 21.9, 22.2, 24.9, 28.9, 30.6, 31.0, 32.7, 33.0 (CH$_2$), 107.4 (C$_{Ar}$), 112.5, 116.4 (CH$_{Ar}$), 118.3 (C$_{Ar}$), 121.3, 123.3 (CH$_{Ar}$), 126.2 (C$_{Ar}$), 129.2 (CH$_{Ar}$), 132.3, 135.1, 148.2, 159.3 (C$_{Ar}$) 165.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3166 (w), 2951 (m), 2923 (m), 2867 (m), 1714 (w), 1650 (s), 1626 (m), 1597 (m), 1551 (w), 1502 (m), 1454 (w), 1409 (m), 1376 (w), 1349 (m), 1309 (m), 1267 (m), 1233 (m), 1195 (m), 1101 (w), 1041 (w), 1014 (w), 937 (w), 872 (m), 845 (m), 809 (m), 786 (s), 747 (s), 729 (m), 672 (m), 659 (m), 621 (w), 559 (m), 535 (w). MS (EI, 70 eV): *m*/*z* (%)=352 ([M]$^+$+1, 27), 351 ([M]$^+$, 90), 322 (17), 294 (29), 281 (42), 280 (86), 266 (13), 252 (18), 250 (18), 240 (18), 239 (87), 238 (100), 226 (11), 225 (13), 224 (12), 210 (15), 63 (13). HRMS (EI): Calcd for $C_{23}H_{29}NO_2$: 351.21958; found: 351.219174.

*4.5.18. 9-Ethyl-8-hexyl-7-hydroxy-10-methylphenanthridin-6(5H)-one (**7r**).* Starting with **6r** (0.199 g, 0.5 mmol), **7r** was isolated (0.084 g, 50%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=193–194 °C. ^{1}H NMR (DMSO-d_6, 250 MHz): δ=0.87 (t, ^3J=6.5 Hz, 3H, CH$_2$*CH$_3$*), 1.16 (t, ^3J=7.1 Hz, 3H, (CH$_2$)$_5$*CH$_3$*), 1.25–1.36 (m, 6H, 3×CH$_2$), 2.50 (s, 3H, CH$_3$), 2.67–2.73 (m, 4H, 2×CH$_2$), 2.82 (q, ^3J=7.7 Hz, 2H, *CH$_2$*CH$_3$), 7.23–7.29 (m, 1H, CH$_{Ar}$), 7.38–7.41 (m, 1H, CH$_{Ar}$), 7.43–7.49 (m, 1H, CH$_{Ar}$), 8.23 (d, ^3J=8.0 Hz, 1H, CH$_{Ar}$), 11.93 (br s, 1H, NH), 13.95 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 62 MHz): δ=13.8, 14.1, 19.5 (CH$_3$), 22.0, 23.2, 25.5, 29.0, 29.3, 31.1 (CH$_2$), 108.1 (C$_{Ar}$), 116.1 (CH$_{Ar}$) 119.3 (C$_{Ar}$), 121.8 (CH$_{Ar}$), 122.1, 126.6 (C$_{Ar}$), 128.3, 128.4 (CH$_{Ar}$), 132.1, 135.8, 149.0, 157.7 (C$_{Ar}$), 166.1 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3305 (w), 3169 (w), 3033 (w), 2955 (m), 2921 (m), 2856 (m), 1722 (w), 1656 (m), 1586 (m), 1549 (m), 1503 (m), 1465 (m), 1408 (s), 1376 (m), 1344 (m), 1291 (m), 1275 (m), 1261 (m), 1180 (m), 1164 (m), 1128 (m), 1113 (m), 1011 (m), 981 (w), 945 (w), 911 (m), 857 (m), 810 (s), 751 (m), 720 (m), 692 (m), 665 (m), 634 (w), 591 (m), 556 (m), 538 (m). MS (EI, 70 eV): *m*/*z* (%)=338 ([M]$^+$+1, 25), 337 ([M]$^+$, 84), 308 (10), 280 (15), 267 (86), 266 (100), 250 (14), 238 (12), 237 (12). HRMS (EI): Calcd for $C_{22}H_{27}NO_2$: 337.20363; found: 337.203114.

*4.5.19. 10-Chloro-7-hydroxy-9-propylphenanthridin-6(5H)-one (**7s**).* Starting with **6s** (0.174 g, 0.5 mmol), **7s** was isolated (0.070 g, 49%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=258–260 °C. ^{1}H NMR (DMSO-d_6, 250 MHz): δ=0.99 (t, ^3J=8.1 Hz, 3H, CH$_3$), 1.62–1.71 (m, 2H, CH$_2$*CH$_2$*CH$_3$), 2.82 (t, ^3J=7.4 Hz, 2H, *CH$_2$*CH$_2$CH$_3$), 7.02 (s, 1H, CH$_{Ar}$), 7.28–7.34 (m, 1H, CH$_{Ar}$), 7.42–7.46 (m, 1H, CH$_{Ar}$), 7.54–7.60 (m, 1H, CH$_{Ar}$), 9.35 (d, ^3J=8.7 Hz, 1H, CH$_{Ar}$), 12.27 (br s, 1H, NH), 14.00 (s, 1H, OH). ^{13}C NMR (DMSO-d_6, 62 MHz): δ=13.7 (CH$_3$), 22.1, 36.7 (CH$_2$), 110.1 (C$_{Ar}$), 116.7, 117.0 (CH$_{Ar}$) 117.5, 118.6 (C$_{Ar}$), 122.3, 127.3, 130.0 (CH$_{Ar}$), 131.9, 136.2, 149.1, 160.4 (C$_{Ar}$), 165.0 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3116 (w), 3129 (w), 3078 (w), 3014 (w), 2957 (m), 2933 (m), 2868 (m), 2743 (m), 1656 (s), 1610 (m), 1580 (m), 1552 (m), 1503 (m), 1465 (m), 1408 (s), 1338 (m), 1290 (m), 1275 (m), 1242 (m), 1190 (m), 1174 (m), 1134 (m), 1090 (m), 1040 (w), 1018 (w), 944 (w), 923 (w), 872 (m), 850 (m), 808 (s), 784 (m), 772 (m), 755 (s), 711 (s), 661 (m), 627 (m), 610 (w), 598 (m), 548 (m). MS (EI, 70 eV): m/z (%)=289 ([M$^+$] ^{37}Cl, 27), 287 ([M$^+$] ^{35}Cl, 88), 261 (30), 260 (15), 259 (100), 253 (12), 252 (31), 225 (40), 224 (40), 211 (10), 196 (20), 178 (10), 177 (11), 84 (12), 78 (70), 66 (11), 63 (78), 61 (13), 45 (10), 44 (12). HRMS (EI): Calcd for $C_{16}H_{14}NO_2Cl$: 287.07076; found: 287.070305.

4.6. General procedure for the synthesis of aminobiaryls 8a,b

To a stirred methanol suspension (25 mL) of Pd/C (10 mol %) was added **6t**,**u** (1.0 equiv). The mixture was set under a hydrogen atmosphere. After stirring for 48 h at 20 °C, the reaction mixture was filtered (Celite) and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/EtOAc=2:1).

*4.6.1. Methyl 3′-amino-3-hydroxy-4,5-dimethylbiphenyl-2-carboxylate (**8a**).* Starting with **6t** (0.150 g, 0.5 mmol), **8a** was isolated (0.110 g, 81%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=140–141 °C. ^{1}H NMR (CDCl$_3$, 250 MHz): δ=2.13 (s, 3H, CH$_3$), 2.21 (s, 3H, CH$_3$), 3.41 (br m, 2H, NH$_2$), 3.44 (s, 3H, OCH$_3$), 6.40 (s, 1H, CH$_{Ar}$), 6.49–6.57 (m, 3H, CH$_{Ar}$), 7.00–7.06 (m, 1H, CH$_{Ar}$), 10.86 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 62 MHz): δ_C=11.4, 20.4 (CH$_3$), 51.6 (OCH$_3$), 109.1 (C$_{Ar}$), 113.3, 114.9, 119.0 (CH$_{Ar}$), 123.6 (C$_{Ar}$), 123.8, 128.3, (CH$_{Ar}$), 141.6, 142.8, 144.2, 145.7, 159.2 (C$_{Ar}$), 172.0 (C=O). GC–MS (EI, 70 eV): m/z (%)=271 ([M]$^+$, 72), 239 (100), 224 (87), 210 (13), 196 (21), 180 (6), 167 (13), 135 (5), 115 (5), 98 (6), 65 (4). HRMS (EI): Calcd for $C_{16}H_{17}NO_3$: 271.12029; found: 271.12050.

*4.6.2. Ethyl 3′-amino-4-ethyl-3-hydroxy-5-methylbiphenyl-2-carboxylate (**8b**).* Starting with **6u** (0.250 g, 0.8 mmol), **8b** was isolated (0.184 g, 78%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a colourless solid, mp=145–147 °C. ^{1}H NMR (CDCl$_3$, 300 MHz): δ=0.74 (t, ^3J=7.4 Hz, 3H, CH$_3$), 1.07 (t, ^3J=7.5 Hz, 3H, CH$_3$), 2.21 (s, 3H, CH$_3$), 2.63 (q, ^3J=7.4 Hz, 2H, CH$_2$), 3.42–3.60 (br m, 2H, NH$_2$), 3.93 (q, ^3J=7.5 Hz, 2H, OCH$_2$), 6.44–6.48 (m, 1H, CH$_{Ar}$), 6.49–6.54 (m, 3H, CH$_{Ar}$), 6.96–7.03 (m, 1H, CH$_{Ar}$), 10.95 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ_C=13.1, 13.2, 19.4 (CH$_3$), 19.6 (CH$_2$), 60.7 (OCH$_2$), 109.0 (C$_{Ar}$), 113.2, 115.1, 119.0, 123.9, 128.3 (CH$_{Ar}$), 129.6, 141.8, 141.9, 144.4, 145.7, 159.3 (C$_{Ar}$), 171.5 (C=O). GC–MS (EI, 70 eV): m/z (%)=299 ([M]$^+$, 96), 253 (64), 238 (100), 220 (34), 210 (16), 180 (15), 152 (7), 128 (5), 90 (7), 65 (3). HRMS (EI): Calcd for $C_{18}H_{21}NO_3$: 299.15160; found: 299.15146.

4.7. General procedure for the synthesis of 3-ethoxy-2-nitro-1-phenylprop-2-en-1-ones 12a–c

To a solution of **11a**–**c in** acetic anhydride (1.0 equiv/1.0 equiv of **11a**–**c**) was added triethyl orthoformate (1.2 equiv). The solution was stirred at 120 °C for 6 h. The solvent was concentrated in vacuo and the residue was purified by chromatography (silica gel, heptanes/EtOAc) to give **12a**–**c**.

*4.7.1. 3-Ethoxy-2-nitro-1-phenylprop-2-en-1-one (**12a**).* Starting with **11a** (3.50 g, 21.2 mmol), triethyl orthoformate (4.20 g, 26.5 mmol) and acetic anhydride (7.00 g, 44.3 mmol), **12a** was isolated as a reddish viscous oil (3.75 g, 80%). ^{1}H NMR (300 MHz, CDCl$_3$): δ=1.27 (t, ^3J=7.0 Hz, 3H, OCH$_2$*CH$_3$*), 4.20 (q, ^3J=6.9 Hz, 2H, O*CH$_2$*CH$_3$), 7.37–7.42 (m, 3H, CH$_{Ar}$), 7.76–7.79 (m, 2H, CH$_{Ar}$), 8.28 (s, 1H, CH$_{Olf}$). ^{13}C NMR (75 MHz, CDCl$_3$): δ=15.1 (CH$_3$), 74.2 (OCH$_2$), 128.1 (C), 128.8 (2×CH$_{Ar}$), 129.0 (2×CH$_{Ar}$), 134.1 (CH$_{Ar}$), 135.9 (C$_{Ar}$), 164.1 (CH$_{Olf}$), 185.3 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3063 (w), 2935 (w), 1778 (w), 1674 (m), 1597 (w), 1562 (w), 1535 (m), 1500 (m), 1449 (w), 1338 (w), 1300 (m), 1222 (m), 1153 (w), 1124 (w), 1001 (w), 908 (m), 873 (w), 728 (s), 689 (m), 648 (w). MS (EI 70 eV): m/z (%)=221 ([M]$^+$, 8), 128 (12), 105 (100), 100 (41), 94 (16), 7 (70), 72 (17), 51 (19), 29 (11). HRMS (EI): Calcd for $C_{11}H_{11}NO_4$: 221.06826; found: 221.068910.

*4.7.2. 3-Ethoxy-2-nitro-1-o-tolylprop-2-en-1-one (**12b**).* Starting with **11b** (2.5 g, 14.0 mmol), triethyl orthoformate (3.00 g, 18.9 mmol) and acetic anhydride (5.00 g., 31.65 mmol), **12b** was isolated as a red oil (2.69 g, 82%). ^{1}H NMR (300 MHz, CDCl$_3$): δ=1.29 (t, ^3J=7.1 Hz, 3H, OCH$_2$*CH$_3$*), 2.33 (s, 3H, CH$_3$), 4.20 (q, ^3J=7.0 Hz, 2H, O*CH$_2$*CH$_3$), 7.15–7.18 (m, 2H, CH$_{Ar}$), 7.31–7.39 (m, 2H, CH$_{Ar}$), 8.23 (s, 1H, CH$_{Olf}$). ^{13}C NMR (75 MHz, CDCl$_3$): δ=15.1, 20.8 (CH$_3$), 74.3 (OCH$_2$), 121.8 (C), 125.7, 127.0, 131.0, 133.0 (CH$_{Ar}$), 136.9, 139.6 (C$_{Ar}$), 161.6 (CH$_{Olf}$), 187.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3064 (w), 2927 (w), 1698 (m), 1634 (m), 1561 (m), 1532 (m), 1456 (m), 1367 (m), 1300 (m), 1219 (s), 1163 (m), 1094 (m), 1002 (m), 909 (m), 873 (m), 839 (w), 796 (w), 731 (s), 696 (w), 649 (m).

*4.7.3. 1-(2-Chlorophenyl)-3-ethoxy-2-nitroprop-2-en-1-one (**12c**).* Starting with **11c** (2.0 g, 10.0 mmol), triethyl orthoformate (2.4 g, 1.51 mmol) and acetic anhydride (4.0 g., 25.30 mmol), **12c** was isolated as a reddish viscous oil (2.0 g, 81%). ^{1}H NMR (300 MHz, CDCl$_3$): δ=1.30 (t, ^3J=7.0 Hz, 3H, OCH$_2$*CH$_3$*), 4.27 (q, ^3J=6.9 Hz, 2H, O*CH$_2$*CH$_3$), 7.29–7.30 (m, 1H, CH$_{Ar}$), 7.34–7.35 (m, 2H, CH$_{Ar}$), 7.49–7.51 (m, 1H, CH$_{Ar}$), 8.29 (s, 1H, CH$_{Olf}$). ^{13}C NMR (75 MHz, CDCl$_3$): δ=15.1 (CH$_3$), 75.1 (OCH$_2$), 126.6 (C), 128.9, 130.1, 131.9 (CH$_{Ar}$), 132.3 (C$_{Ar}$), 132.4 (CH$_{Ar}$), 136.4 (C$_{Ar}$), 160.0 (CH$_{Olf}$), 184.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3068 (w), 2930 (w), 1777 (w), 1683 (m), 1587 (m), 1560 (s), 1523 (m), 1470 (m), 1368 (m), 1319 (m), 1212 (m), 1163 (m), 1064 (m), 1037 (m), 917 (m), 816 (m), 739 (s), 684 (m), 606 (m), 583 (w), 549 (w).

4.8. General procedure for the synthesis of 4-nitrophenols 13a–i

To a CH$_2$Cl$_2$ solution (2 mL/1 mmol of **12a**–**c**) of **12a**–**c** was added **5** (1.65 mmol) and, subsequently, TiCl$_4$ (1.1 mmol) at −78 °C. The temperature of the solution was allowed to warm to 20 °C during 18 h with stirring. To the solution was added hydrochloric acid (10%, 20 mL) and the organic and the aqueous layer were separated. The latter was extracted with CH$_2$Cl$_2$ (3×20 mL). The combined organic layers were dried (Na$_2$SO$_4$), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, *n*-heptanes/EtOAc) to give **13a**–**i**.

*4.8.1. Methyl 3-hydroxy-6-nitrobiphenyl-2-carboxylate (**13a**).* Reaction starting with **12a** (0.331 g, 1.5 mmol) and **5a** (0.429 g, 1.7 mmol), **13a** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish solid (0.230 g, 56%), mp=137–138 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ=3.35 (s, 3H, OCH$_3$), 7.02 (d, ^3J=9.0 Hz, 1H, CH$_{Ar}$), 7.07–7.10 (m, 2H, CH$_{Ph}$), 7.27–7.31 (m, 3H, CH$_{Ph}$), 7.82 (d, ^3J=8.9 Hz, 1H, CH$_{Ar}$), 11.07 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=52.5 (OCH$_3$), 113.6 (*C*COOCH$_3$), 117.7, 127.7, 127.7, 127.7, 127.8, 127.8, 128.5 (CH$_{Ar}$), 133.7, 136.2, 139.0 (C$_{Ar}$), 163.8 (COH), 170.2 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3086 (w), 3062 (w), 2954 (w), 1735 (w), 1670 (m), 1599 (w), 1576 (w), 1525 (m), 1501 (w), 1442 (m), 1324 (m), 1220 (m), 1156 (w), 1132 (m), 1095 (w), 1074 (w), 1026 (w), 970 (w), 907 (m), 837 (w), 813 (w), 769 (w), 727 (s), 698 (m), 672 (m), 648 (w), 584 (w). GC–MS (EI, 70 eV): m/z (%)=273 ([M]$^+$, 80), 242 (17), 241 (100), 224 (15), 213 (25), 212 (13), 196 (14), 185 (18), 184 (11), 183 (13), 159 (16), 157 (11), 155 (20), 140 (15), 139 (66), 138 (10), 129 (25), 128 (14), 127 (19), 115 (10), 113 (10), 102 (10), 77 (12), 63 (11). HRMS (EI): Calcd for $C_{14}H_{11}O_5N$ ([M]$^+$): 273.06317; found: 273.063020.

*4.8.2. Methyl 3-hydroxy-4-methyl-6-nitrobiphenyl-2-carboxylate (**13b**).* Starting with **12a** (0.331 g, 1.5 mmol) and **5b** (0.457 g, 1.65 mmol), **13b** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish solid (0.245 g, 57%), mp=57–59 °C.

^{1}H NMR (300 MHz, CDCl$_3$): δ=2.28 (s, 3H, CH$_3$), 3.33 (s, 3H, OCH$_3$), 7.05–7.08 (m, 2H, CH$_{Ph}$), 7.26–7.29 (m, 3H, CH$_{Ph}$), 7.71 (s, 1H, CH$_{Ar}$), 11.33 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=15.9 (CH$_3$), 52.4 (OCH$_3$), 112.6 (*C*COOCH$_3$), 127.6 (CH$_{Ar}$), 127.7 (2$\times$CH$_{Ar}$), 127.9 (3$\times$CH$_{Ar}$), 133.2, 136.3, 136.6, 142.6 (C$_{Ar}$), 162.3 (*C*OH), 170.8 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3062 (w), 2958 (w), 1737 (w), 1665 (m), 1574 (w), 1526 (m), 1495 (w), 1441 (m), 1373 (m), 1302 (m), 1251 (m), 1200 (m), 1170 (m), 1129 (m), 1070 (m), 1031 (w), 1001 (w), 983 (w), 902 (w), 864 (w), 812 (w), 778 (m), 727 (m), 696 (m), 663 (m), 610 (m), 574 (m). GC–MS (EI, 70 eV): m/z (%)=287 ([M]$^+$, 80), 256 (17), 255 (100), 239 (15), 238 (75), 209 (15), 208 (76), 180 (10), 129 (14), 127 (10), 115 (14), 77 (10). HRMS (EI): Calcd for C$_{15}$H$_{13}$O$_5$N ([M]$^+$): 287.07882; found: 287.078935.

*4.8.3. Ethyl 4-ethyl-3-hydroxy-6-nitrobiphenyl-2-carboxylate (**13c**).* Starting with **12a** (0.331 g, 1.5 mmol) and **5c** (0.499 g, 1.65 mmol), **13c** was isolated after chromatography (silica gel, heptanes/EtOAc) as a viscous yellowish oil (0.306 g, 65%). ^{1}H NMR (300 MHz, CDCl$_3$): δ=0.52 (t, ^3J=7.6 Hz, 3H, CH$_2$*CH*$_3$), 1.12 (t, ^3J=7.5 Hz, 3H, OCH$_2$*CH*$_3$), 2.59 (q, ^3J=7.5 Hz, 2H, *CH*$_2$CH$_3$), 3.75 (q, ^3J=7.5 Hz, 2H, O*CH*$_2$CH$_3$), 6.96–7.0 (m, 2H, CH$_{Ph}$), 7.16–7.18 (m, 3H, CH$_{Ph}$), 7.61 (s, 1H, CH$_{Ar}$), 11.42 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=12.8, 13.0 (CH$_3$), 22.8, 61.8 (CH$_2$), 112.8 (*C*COOCH$_3$), 127.6 (CH$_{Ar}$), 127.7 (2$\times$CH$_{Ar}$), 128.1 (3$\times$CH$_{Ar}$), 133.3, 136.2, 136.8, 142.8 (C$_{Ar}$), 162.2 (*C*OH), 170.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3083 (w), 3002 (w), 2963 (w), 1737 (w), 1657 (m), 1600 (w), 1567 (w), 1512 (m), 1443 (m), 1329 (m), 1298 (m), 1241 (m), 1191 (s), 1149 (m), 1063 (m), 1018 (m), 968 (w), 900 (m), 822 (m), 803 (m), 733 (s), 695 (s), 668 (s), 621 (m), 581 (m), 524 (m). GC–MS (EI, 70 eV): m/z (%)=315 ([M]$^+$, 54), 270 (10), 269 (50), 253 (19), 252 (100), 223 (18), 222 (89), 165 (22), 152 (21), 129 (8). HRMS (EI): Calcd for C$_{17}$H$_{17}$O$_5$N ([M]$^+$): 315.11012; found: 315.110219.

*4.8.4. Methyl 4-butyl-3-hydroxy-6-nitrobiphenyl-2-carboxylate (**13d**).* Reaction starting with **12a** (0.331 g, 1.5 mmol) and **5k** (0.522 g, 1.7 mmol), **13d** was isolated after chromatography (silica gel, heptanes/EtOAc) as a viscous yellowish oil (0.285 g, 58%). ^{1}H NMR (300 MHz, CDCl$_3$): δ=0.88 (t, ^3J=7.2 Hz, 3H, (CH$_2$)$_3$*CH*$_3$), 1.28–1.40 (m, 2H, CH$_2$), 1.52–1.62 (m, 2H, CH$_2$), 2.64 (t, ^3J=7.2 Hz, 2H, CH$_3$(CH$_2$)$_2$*CH*$_2$Ph), 3.31 (s, 3H, OCH$_3$), 7.04–7.07 (m, 2H, CH$_{Ph}$), 7.23–7.27 (m, 3H, CH$_{Ph}$), 7.68 (s, 1H, CH$_{Ar}$), 11.27 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=13.9 (CH$_3$), 22.5, 29.4, 31.0 (CH$_2$), 52.4 (OCH$_3$), 112.9 (*C*COOCH$_3$), 127.6 (CH$_{Ar}$), 127.7 (2$\times$CH$_{Ar}$), 127.9 (2$\times$CH$_{Ar}$), 128.9 (CH$_{Ar}$), 132.1, 136.2, 136.6, 142.7 (C$_{Ar}$), 162.0 (*C*OH), 170.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3065 (w), 3006 (w), 2952 (w), 1674 (m), 1581 (w), 1531 (w), 1438 (m), 1380 (w), 1356 (m), 1311 (s), 1232 (m), 1140 (m), 1090 (m), 1030 (w), 940 (w), 914 (m), 850 (w), 808 (m), 771 (m), 732 (m), 698 (s), 671 (m), 628 (m), 608 (m). GC–MS (EI, 70 eV): m/z (%)=329 ([M]$^+$, 48), 281 (12), 280 (59), 255 (18), 239 (15), 238 (100), 209 (10), 208 (36), 180 (10), 152 (21). HRMS (EI): Calcd for C$_{18}$H$_{19}$O$_5$N ([M]$^+$): 329.12577; found: 329.125828.

*4.8.5. Methyl 3-hydroxy-6-nitro-4-octylbiphenyl-2-carboxylate (**13e**).* Starting with **12a** (0.331 g, 1.5 mmol) and **5f** (0.614 g, 1.7 mmol), **13e** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish oil (0.357 g, 62%). ^{1}H NMR (300 MHz, CDCl$_3$): δ=0.71 (t, ^3J=7.2 Hz, 3H, (CH$_2$)$_7$*CH*$_3$), 1.08–1.15 (m, 10H, 5$\times$CH$_2$), 1.43–1.55 (m, 2H, CH$_2$), 2.56 (t, ^3J=7.0 Hz, 2H, CH$_3$(CH$_2$)$_6$*CH*$_2$Ph), 3.23 (s, 3H, OCH$_3$), 6.96–6.99 (m, 2H, CH$_{Ph}$), 7.17–7.19 (m, 3H, CH$_{Ph}$), 7.60 (s, 1H, CH$_{Ar}$), 11.19 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=14.1 (CH$_3$), 22.6, 28.8, 29.2, 29.3, 29.4, 29.6, 31.8 (CH$_2$), 52.3 (OCH$_3$), 112.9 (*C*COOCH$_3$), 127.6 (CH$_{Ar}$), 127.4 (2$\times$CH$_{Ar}$), 127.9 (2$\times$CH$_{Ar}$), 128.9 (CH$_{Ar}$), 132.1, 136.2, 136.6, 142.7 (C$_{Ar}$), 162.0 (*C*OH), 170.8 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3060 (w), 2952 (w), 2923 (m), 1666 (m), 1570 (w), 1526 (m), 1437 (m), 1336 (s), 1250 (m), 1164 (m), 1126 (m), 1074 (w), 1029 (w), 964 (w), 914 (w), 843 (w), 814 (m), 754 (m), 733 (m), 697 (s), 669 (m), 612 (w). GC–MS (EI, 70 eV): m/z (%)=385 ([M]$^+$, 64), 337 (23), 336 (95), 255 (16), 254 (15), 239 (21), 238 (100), 209 (12), 208 (29), 180 (10), 152 (16). HRMS (EI): Calcd for C$_{12}$H$_{27}$O$_5$N ([M]$^+$): 385.18837; found: 385.188315.

*4.8.6. Methyl 3-hydroxy-2′-methyl-6-nitrobiphenyl-2-carboxylate (**13f**).* Starting with **12b** (0.352 g, 1.5 mmol) and **5a** (0.429 g, 1.7 mmol), **13f** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish solid (0.292 g, 68%), mp=74–76 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ=2.51 (s, 3H, CH$_3$), 3.28 (s, 3H, OCH$_3$), 6.96 (d, ^3J=8.4 Hz, 1H, CH$_{Ar}$), 7.11–7.15 (m, 3H, CH$_{Ar}$), 7.28–7.33 (m, 1H, CH$_{Ar}$), 7.93 (d, ^3J=8.4 Hz, 1H, CH$_{Ar}$), 11.33 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=19.8 (CH$_3$), 52.6 (OCH$_3$), 113.1 (*C*COOCH$_3$), 117.9, 125.2 (CH$_{Ar}$), 128.3 (2$\times$CH$_{Ar}$), 129.1, 130.0 (CH$_{Ar}$), 132.9, 135.9, 139.0, 141.3 (C$_{Ar}$), 164.4 (*C*OH), 170.2 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3063 (w), 2954 (w), 2649 (w), 1673 (m), 1598 (m), 1575 (m), 1518 (m), 1490 (m), 1441 (m), 1313 (s), 1313 (s), 1268 (m), 1232 (s), 1221 (s), 1173 (m), 1132 (m), 1086 (m), 1052 (m), 1034 (w), 964 (m), 912 (m), 832 (m), 814 (m), 763 (m), 733 (s), 689 (m), 658 (m), 593 (m), 531 (m). GC–MS (EI, 70 eV): m/z (%)=287 ([M]$^+$, 27), 270 (14), 269 (15), 256 (17), 239 (19), 238 (100), 237 (21), 228 (52), 226 (14), 181 (15), 153 (25), 127 (13), 115 (20), 63 (9). HRMS (EI): Calcd for C$_{15}$H$_{13}$O$_5$N ([M]$^+$): 287.07882; found: 287.078912.

*4.8.7. Methyl 3-hydroxy-2′,4-dimethyl-6-nitrobiphenyl-2-carboxylate (**13g**).* Starting with **12b** (0.352 g, 1.5 mmol) and **5b** (0.457 g, 1.7 mmol), **13g** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish solid (0.324 g, 72%), mp=70–72 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ=1.99 (s, 3H, CH$_3$), 2.29 (s, 3H, CH$_3$), 3.34 (s, 3H, OCH$_3$), 6.82–6.84 (m, 1H, CH$_{Ar}$), 7.03–7.16 (m, 3H, CH$_{Ar}$), 7.79 (s, 1H, CH$_{Ar}$), 11.63 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=15.9, 19.9 (CH$_3$), 52.6 (OCH$_3$), 112.2 (*C*COOCH$_3$), 125.2, 127.3 (CH$_{Ar}$), 127.7 (C$_{Ar}$), 128.8, 129.0, 130.1 (CH$_{Ar}$), 136.0, 136.2, 136.3, 142.3 (C$_{Ar}$), 163.0 (*C*OH), 170.8 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3061 (w), 2953 (w), 2854 (w), 1664 (m), 1573 (m), 1523 (m), 1494 (w), 1380 (m), 1334 (s), 1285 (m), 1254 (s), 1202 (s), 1166 (m), 1133 (m), 1133 (m), 1104 (m), 1041 (w), 1018 (m), 964 (m), 899 (m), 871 (w), 813 (m), 753 (m), 723 (s), 661 (m), 589 (m), 531 (m). GC–MS (EI, 70 eV): m/z (%)=301 ([M]$^+$, 29), 384 (12), 383 (10), 270 (17), 254 (15), 252 (100), 251 (21), 242 (41), 240 (12), 239 (31), 238 (54), 225 (13), 222 (63), 211 (11), 195 (10), 194 (16), 168 (12), 166 (23), 165 (62), 153 (14), 151 (11), 139 (14), 128 (12), 115 (23), 82 (12), 77 (10). HRMS (EI): Calcd for C$_{16}$H$_{15}$O$_5$N ([M]$^+$): 301.09447; found: 301.093882.

*4.8.8. Methyl 2′-chloro-3-hydroxy-6-nitrobiphenyl-2-carboxylate (**13h**).* Starting with **12c** (0.383 g, 1.5 mmol) and **5a** (0.429 g, 1.7 mmol), **13h** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish solid (0.258 g, 56%), mp=101–103 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ=3.41 (s, 3H, OCH$_3$), 6.92–7.02 (m, 1H, CH$_{Ar}$), 7.09 (d, ^3J=9.0 Hz, 1H, CH$_{Ar}$), 7.17–7.20 (m, 1H, CH$_{Ar}$), 7.22–7.25 (m, 1H, CH$_{Ar}$), 7.35–7.38 (m, 1H, CH$_{Ar}$), 8.01 (d, ^3J=9.0 Hz, 1H, CH$_{Ar}$), 11.52 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=52.8 (OCH$_3$), 113.0 (*C*COOCH$_3$), 118.6, 126.4, 128.7, 128.7, 129.2, 130.4 (CH$_{Ar}$), 132.9, 135.8, 136.5, 142.3 (C$_{Ar}$), 164.8 (*C*OH), 169.9 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3073 (w), 2952 (w), 1673 (m), 1599 (m), 1578 (m), 1519 (m), 1480 (w), 1440 (s), 1323 (s), 1230 (m), 1204 (s), 1127 (m), 1049 (m), 968 (m), 914 (m), 841 (m), 811 (m), 750 (s), 737 (s), 698 (s), 644 (m), 592 (w). GC–MS (EI, 70 eV): m/z (%)=307 ([M]$^+$, 10), 273 (15), 272 (100), 241 (10), 240 (66), 226 (12), 212 (18), 184 (15), 173 (10). HRMS (EI): Calcd for C$_{14}$H$_{10}$O$_5$NCl ([M]$^+$): 307.02420; found: 307.024320.

*4.8.9. Methyl 2′-chloro-3-hydroxy-4-methyl-6-nitrobiphenyl-2-carboxylate (**13i**).* Starting with **12c** (0.383 g, 1.5 mmol) and **5b** (0.457 g, 1.7 mmol), **13i** was isolated after chromatography (silica gel, heptanes/EtOAc) as a yellowish solid (0.337 g, 70%), mp=100–102 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ=2.31 (s, 3H, CH$_3$), 3.40 (s, 3H, OCH$_3$), 6.99

(dd, ^3J=6.9 Hz, ^4J=1.8 Hz, 1H, CH$_{\mathrm{Ar}}$), 7.15–7.26 (m, 2H, CH$_{\mathrm{Ar}}$), 7.35 (dd, ^3J=7.7 Hz, ^4J=1.5 Hz, 1H, CH$_{\mathrm{Ar}}$), 7.90 (s, 1H, CH$_{\mathrm{Ar}}$), 11.79 (s, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=16.0 (CH$_3$), 52.8 (OCH$_3$), 112.0 (*C*COOCH$_3$), 126.4 (CH$_{\mathrm{Ar}}$), 128.5 (C$_{\mathrm{Ar}}$), 128.6, 128.8, 129.0, 130.5 (CH$_{\mathrm{Ar}}$), 133.0, 133.8, 136.2, 141.6 (C$_{\mathrm{Ar}}$), 163.4 (*C*OH), 170.5 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=2955 (w), 2853 (w), 1731 (w), 1664 (s), 1574 (m), 1521 (m), 1429 (m), 1378 (m), 1341 (s), 1265 (s), 1200 (s), 1128 (m), 1057 (m), 98 (m), 946 (w), 899 (m), 859 (w), 810 (m), 754 (m), 739 (s), 698 (s), 657 (m), 630 (m), 534 (w). GC–MS (EI, 70 eV): *m*/*z* (%)=321 ([M]$^+$, 10), 287 (17), 286 (100), 255 (12), 254 (77), 226 (12), 198 (17), 152 (24), 139 (10). HRMS (EI): Calcd for C$_{15}$H$_{12}$O$_5$NCl ([M]$^+$): 321.03985; found: 321.039927.

4.9. General procedure for the synthesis of 4-aminophenols (14a–i)

To a methanol suspension (25 mL/1 mmol of **13a**–**i**) of **13a**–**i** (1.0 equiv) or an ethanol suspension of **13c** (1.0 equiv) was added Pd/C (10 mol %, 0.1 equiv). The mixture was set under a hydrogen atmosphere. After stirring for 48 h at 20 °C, the reaction mixture was filtered (Celite) and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, heptanes/EtOAc=2:1).

*4.9.1. Methyl 6-amino-3-hydroxybiphenyl-2-carboxylate (**14a**).* Starting with **13a** (0.130 g, 0.475 mmol), **14a** was isolated (0.099 g, 86%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a yellowish solid, mp=95–97 °C. ^{1}H NMR (300 MHz, CDCl$_3$): δ=3.02 (br, 2H, NH$_2$), 3.30 (s, 3H, OCH$_3$), 6.82–6.84 (m, 2H, CH$_{\mathrm{Ar}}$), 7.08–7.11 (m, 2H, CH$_{\mathrm{Ph}}$), 7.22–7.35 (m, 3H, CH$_{\mathrm{Ph}}$), 10.07 (br, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=51.6 (OCH$_3$), 112.5 (*C*COOCH$_3$), 117.7, 123.1, 127.0, (CH$_{\mathrm{Ar}}$), 127.5 (C$_{\mathrm{Ar}}$), 128.5 (2×CH$_{\mathrm{Ar}}$), 128.9 (2×CH$_{\mathrm{Ar}}$), 136.9, 139.1 (C$_{\mathrm{Ar}}$), 154.7 (*C*OH), 171.3 (CO). IR (KBr, cm^{-1}): $\tilde{\nu}$=3742 (w), 3060 (w), 2922 (w), 2788 (w), 2671 (w), 1721 (s), 1586 (m), 1488 (m), 1455 (m), 1433 (m), 1348 (m), 1302 (m), 1277 (s), 1239 (m), 1217 (s), 1158 (m), 1110 (m), 1087 (m), 1029 (w), 982 (m), 949 (m), 911 (m), 871 (m), 807 (m), 776 (m), 750 (m), 730 (m), 719 (s), 698 (s), 646 (m), 613 (m), 549 (m). GC–MS (EI, 70 eV): *m*/*z* (%)=243 ([M]$^+$, 32), 212 (16), 211 (100), 183 (24), 155 (15), 154 (67), 128 (16), 127 (10), 77 (10). HRMS (EI): Calcd for C$_{14}$H$_{13}$O$_3$N ([M]$^+$): 243.08899; found: 243.089209.

*4.9.2. Methyl 6-amino-3-hydroxy-4-methylbiphenyl-2-carboxylate (**14b**).* Starting with **13b** (0.140 g, 0.487 mmol), **14b** was isolated (0.107 g, 85%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a yellowish oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ=2.17 (s, 3H, CH$_3$), 3.09 (br, 2H, NH$_2$), 3.28 (s, 3H, OCH$_3$), 6.73 (s, 1H, CH$_{\mathrm{Ar}}$), 7.06–7.09 (m, 2H, CH$_{\mathrm{Ar}}$), 7.22–7.25 (m, 1H, CH$_{\mathrm{Ar}}$), 7.29–7.34 (m, 2H, CH$_{\mathrm{Ar}}$), 10.36 (br, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=16.3 (CH$_3$), 51.5 (OCH$_3$), 111.7 (*C*COOCH$_3$), 124.2 (CH$_{\mathrm{Ar}}$), 125.0 (C$_{\mathrm{Ar}}$), 126.8 (CH$_{\mathrm{Ar}}$), 128.4 (2×CH$_{\mathrm{Ar}}$), 129.3 (2×CH$_{\mathrm{Ar}}$), 132.5, 136.0, 139.4 (C$_{\mathrm{Ar}}$), 153.1 (*C*OH), 171.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3444 (w), 3057 (w), 2924 (w), 2851 (w), 1726 (w), 1658 (m), 1587 (m), 1499 (w), 1434 (m), 1347 (m), 1306 (m), 1280 (m), 1208 (s), 1149 (m), 1106 (m), 1072 (m), 1023 (m), 983 (m), 907 (m), 863 (m), 802 (m), 764 (m), 730 (s), 700 (s), 689 (s), 645 (m), 565 (m). GC–MS (EI, 70 eV): *m*/*z* (%)=257 ([M]$^+$, 33), 226 (17), 225 (100), 197 (24), 169 (11), 168 (53), 167 (14), 154 (12), 128 (9). HRMS (EI): Calcd for C$_{15}$H$_{15}$O$_3$N ([M]$^+$): 257.10464; found: 257.104582.

*4.9.3. Ethyl 6-amino-4-ethyl-3-hydroxybiphenyl-2-carboxylate (**14c**).* Starting with **13c** (0.130 g, 0.418 mmol), **14c** was isolated (0.111 g, 95%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a yellowish oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ=0.58 (t, ^3J=7.0 Hz, 3H, CH$_2$*CH*$_3$), δ=1.17 (t, ^3J=7.6 Hz, 3H, OCH$_2$*CH*$_3$), 2.60 (q, ^3J=7.6 Hz, 2H, *CH*$_2$CH$_3$), 3.09 (br, 2H, NH$_2$), 3.81 (q, ^3J=7.0 Hz, 2H, O*CH*$_2$CH$_3$), 6.76 (s, 1H, CH$_{\mathrm{Ar}}$), 7.08–7.11 (m, 2H, CH$_{\mathrm{Ar}}$), 7.21–7.34 (m, 3H, CH$_{\mathrm{Ar}}$), 10.58 (br, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=12.8, 13.7 (CH$_3$), 23.0 (CH$_2$), 60.6 (OCH$_2$), 111.8 (*C*COOCH$_3$), 122.5 (CH$_{\mathrm{Ar}}$), 125.1 (C$_{\mathrm{Ar}}$), 126.7 (CH$_{\mathrm{Ar}}$), 128.4 (2×CH$_{\mathrm{Ar}}$), 129.1 (2×CH$_{\mathrm{Ar}}$), 132.7, 136.0, 139.7 (C$_{\mathrm{Ar}}$), 153.0 (*C*OH), 171.4 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3447 (w), 3056 (w), 2964 (w), 2872 (w), 1654 (m), 1611 (m), 1585 (m), 1496 (w), 1429 (m), 1371 (m), 1326 (m), 1264 (m), 1205 (s), 1149 (m), 1106 (m), 1065 (m), 1014 (m), 968 (w), 909 (m), 853 (m), 803 (m), 762 (m), 731 (m), 699 (s), 681 (m), 645 (m), 569 (m). GC–MS (EI, 70 eV): *m*/*z* (%)=285 ([M]$^+$, 30), 240 (17), 239 (100), 221 (11), 211 (13), 196 (25), 167 (11). HRMS (EI): Calcd for C$_{17}$H$_{19}$O$_3$N ([M]$^+$): 285.13594; found: 285.135726.

*4.9.4. Methyl 6-amino-4-butyl-3-hydroxybiphenyl-2-carboxylate (**14d**).* Starting with **13d** (0.130 g, 0.394 mmol), **14d** was isolated (0.108 g, 92%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a yellowish oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ=0.82 (t, ^3J=6.7 Hz, 3H, (CH$_2$)$_3$*CH*$_3$), 1.15–1.18 (m, 2H, CH$_2$), 1.50–1.59 (m, 2H, CH$_2$), 2.56 (t, ^3J=7.6 Hz, 2H, CH$_3$(CH$_2$)$_2$*CH*$_2$Ph), 3.06 (br, 2H, NH$_2$), 3.29 (s, 3H, OCH$_3$), 6.75 (s, 1H, CH$_{\mathrm{Ar}}$), 7.07–7.12 (m, 2H, CH$_{\mathrm{Ar}}$), 7.21–7.25 (m, 1H, CH$_{\mathrm{Ar}}$), 7.32–7.36 (m, 2H, CH$_{\mathrm{Ar}}$), 10.35 (br, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=13.9 (CH$_3$), 22.5, 29.4, 31.0 (CH$_2$), 51.4 (OCH$_3$), 112.0 (*C*COOCH$_3$), 123.5 (CH$_{\mathrm{Ar}}$), 125.0 (C$_{\mathrm{Ar}}$), 126.7 (CH$_{\mathrm{Ar}}$), 128.5 (2×CH$_{\mathrm{Ar}}$), 129.1 (2×CH$_{\mathrm{Ar}}$), 131.4, 136.0, 139.5 (C$_{\mathrm{Ar}}$), 152.8 (*C*OH), 171.3 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3454 (w), 3055 (w), 2922 (m), 2851 (w), 1660 (m), 1598 (m), 1493 (w), 1433 (m), 1315 (m), 1263 (m), 1207 (s), 1152 (m), 1108 (m), 1071 (w), 998 (w), 920 (w), 871 (w), 809 (w), 764 (m), 721 (m), 700 (s), 683 (m), 647 (m), 569 (m). HRMS (EI): Calcd for C$_{18}$H$_{21}$O$_3$N ([M]$^+$): 299.15299; found: 299.152209.

*4.9.5. Methyl 6-amino-3-hydroxy-4-octylbiphenyl-2-carboxylate (**14e**).* Starting with **13e** (0.150 g, 0.389 mmol), **14e** was isolated (0.124 g, 90%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a yellowish oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ=0.81 (t, ^3J=6.5 Hz, 3H, (CH$_2$)$_7$*CH*$_3$), 1.17–1.25 (m, 10H, 5×CH$_2$), 1.51–1.61 (m, 2H, CH$_2$), 2.56 (t, ^3J=7.8 Hz, 2H, CH$_3$(CH$_2$)$_6$*CH*$_2$Ph), 3.08 (br, 2H, NH$_2$), 3.28 (s, 3H, OCH$_3$), 6.74 (s, 1H, CH$_{\mathrm{Ar}}$), 7.07–7.11 (m, 2H, CH$_{\mathrm{Ar}}$), 7.20–7.25 (m, 1H, CH$_{\mathrm{Ar}}$), 7.30–7.35 (m, 2H, CH$_{\mathrm{Ar}}$), 10.34 (br, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=14.1 (CH$_3$), 22.6, 29.3, 29.5, 29.5, 29.6, 30.3, 31.9 (CH$_2$), 51.5 (OCH$_3$), 111.9 (*C*COOCH$_3$), 123.4 (CH$_{\mathrm{Ar}}$), 125.1 (C$_{\mathrm{Ar}}$), 126.8 (CH$_{\mathrm{Ar}}$), 128.4 (2×CH$_{\mathrm{Ar}}$), 129.0 (2×CH$_{\mathrm{Ar}}$), 131.5, 135.9, 139.4 (C$_{\mathrm{Ar}}$), 152.9 (*C*OH), 171.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3455 (w), 3056 (w), 2922 (m), 2852 (w), 1659 (m), 1599 (m), 1497 (w), 1434 (m), 1317 (m), 1263 (m), 1208 (s), 1150 (m), 1108 (m), 1071 (w), 997 (w), 919 (w), 881 (w), 804 (w), 764 (m), 721 (m), 700 (s). GC–MS (EI, 70 eV): *m*/*z* (%)=355 ([M]$^+$, 65), 324 (27), 323 (100), 322 (11), 306 (12), 266 (25), 252 (18), 324 (27), 323 (100), 322 (11), 306 (12), 266 (25), 252 (18), 238 (27), 225 (41), 224 (47), 209 (10), 208 (10), 197 (10), 196 (30), 180 (11), 168 (23), 167 (21), 41 (10). HRMS (EI): Calcd for C$_{22}$H$_{29}$O$_3$N ([M]$^+$): 355.21420; found: 355.214070.

*4.9.6. Methyl 6-amino-3-hydroxy-2′-methylbiphenyl-2-carboxylate (**14f**).* Starting with **13f** (0.120 g, 0.417 mmol), **14f** was isolated (0.097 g, 91%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a yellowish viscous oil. ^{1}H NMR (300 MHz, CDCl$_3$): δ=1.98 (s, 3H, CH$_3$), 3.02 (br, 2H, NH$_2$), 3.31 (s, 3H, OCH$_3$), 6.68 (d, ^3J=8.0 Hz, 1H, CH$_{\mathrm{Ar}}$), 6.92–6.94 (m, 1H, CH$_{\mathrm{Ar}}$), 7.18–7.23 (m, 3H, CH$_{\mathrm{Ar}}$), 8.0 (d, ^3J=8.2 Hz, 1H, CH$_{\mathrm{Ar}}$), 9.98 (br, 1H, OH). ^{13}C NMR (CDCl$_3$, 75 MHz): δ=19.5 (CH$_3$), 51.7 (OCH$_3$), 112.1 (*C*COOCH$_3$), 117.6, 123.8, 126.1, 127.4 (CH$_{\mathrm{Ar}}$), 127.8 (C$_{\mathrm{Ar}}$), 128.9, 129.9 (CH$_{\mathrm{Ar}}$), 135.3, 136.2, 138.1 (C$_{\mathrm{Ar}}$), 153.5 (*C*OH), 171.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3451 (w), 3060 (w), 2921 (w), 2851 (w), 1664 (m), 1598 (m), 1489 (w), 1463 (m), 1436 (m), 1411 (w), 1335 (m), 1312 (m), 1287 (m), 1212 (s), 1119 (m), 1087 (m), 1037 (m), 982 (w), 913 (m), 806 (m), 757 (m), 734 (s), 689 (m), 624 (m), 565 (m). GC–MS (EI, 70 eV): *m*/*z* (%)=257 ([M]$^+$, 39), 226 (17), 225 (100), 169 (15), 168 (50), 167 (10), 154 (10), 115 (9). HRMS (EI): Calcd for C$_{15}$H$_{15}$O$_3$N ([M]$^+$): 257.10464; found: 257.104502.

*4.9.7. Methyl 6-amino-3-hydroxy-2′,4-dimethylbiphenyl-2-carboxylate (**14g**).* Starting with **13g** (0.140 g, 0.464 mmol), **14g** was isolated (0.112 g, 89%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.98 (s, 3H, CH_3), 2.19 (s, 3H, CH_3), 3.04 (br, 2H, NH_2), 3.30 (s, 3H, OCH_3), 6.77 (s, 1H, CH_{Ar}), 6.88–6.91 (m, 1H, CH_{Ar}), 7.12–7.18 (m, 3H, CH_{Ar}), 10.61 (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=16.0, 19.5 (CH_3), 51.6 (OCH_3), 111.3 ($CCOOCH_3$), 124.3 (CH_{Ar}), 124.5 (C_{Ar}), 126.0 (CH_{Ar}), 126.6 (C_{Ar}), 127.2, 128.8, 129.7 (CH_{Ar}), 135.5, 136.4, 138.6 (C_{Ar}), 153.5 (COH), 171.7 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3447 (w), 3057 (w), 2920 (w), 2850 (w), 1726 (w), 1658 (m), 1610 (m), 1456 (m), 1434 (s), 1377 (m), 1342 (m), 1284 (m), 1208 (s), 1150 (m), 1101 (m), 1023 (m), 983 (m), 909 (w), 869 (m), 804 (m), 758 (s), 728 (s), 678 (m), 645 (m), 578 (m). GC–MS (EI, 70 eV): m/z (%)=271 ([M]$^+$, 39), 240 (17), 239 (100), 183 (10), 182 (25), 168 (30), 167 (13). HRMS (EI): Calcd for $C_{16}H_{17}O_3N$ ([M]$^+$): 271.12029; found: 271.120370.

*4.9.8. Methyl 6-amino-2′-chloro-3-hydroxybiphenyl-2-carboxylate (**14h**).* Starting with **13h** (0.120 g, 0.390 mmol), **14h** was isolated (0.095 g, 88%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a brown oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.03 (br, 2H, NH_2), 3.30 (s, 3H, OCH_3), 6.85 (d, ^3J=8.0 Hz, 1H, CH_{Ar}), 7.09–7.11 (m, 2H, CH_{Ar}), 7.23–7.28 (m, 2H, CH_{Ar}), 7.32–7.37 (m, 2H, CH_{Ar}), 10.29 (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=51.6 (OCH_3), 112.4 ($CCOOCH_3$), 117.7, 123.3, 127.0 (CH_{Ar}), 127.8 (C_{Ar}), 128.5, 128.5, 128.8 (CH_{Ar}), 135.5, 136.4, 139.0 (C_{Ar}), 154.8 (COH), 171.2 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3445 (w), 3056 (w), 2950 (w), 2850 (w), 1728 (w), 1663 (m), 1594 (m), 1463 (m), 1435 (s), 1335 (m), 1285 (m), 1209 (s), 1092 (m), 1027 (m), 982 (m), 805 (m), 759 (m), 732 (m), 700 (s), 626 (m), 580 (m). GC–MS (EI, 70 eV): m/z (%)=277 ([M]$^+$, 42), 246 (14), 245 (100), 211 (19), 210 (59), 183 (10), 182 (52), 154 (62), 153 (13), 127 (14), 77 (11). HRMS (EI): Calcd for $C_{14}H_{12}O_3NCl$ ([M]$^+$): 277.05002; found: 277.050203.

*4.9.9. Methyl 6-amino-2′-chloro-3-hydroxy-4-methylbiphenyl-2-carboxylate (**14i**).* Starting with **13i** (0.120 g, 0.373 mmol), **14i** was isolated (0.097 g, 90%) by column chromatography (silica gel, heptanes/EtOAc=30:1→20:1) as a brown oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.19 (s, 3H, CH_3), 3.02 (br, 2H, NH_2), 3.29 (s, 3H, OCH_3), 6.78 (s, 1H, CH_{Ar}), 7.07–7.10 (m, 1H, CH_{Ar}), 7.23–7.26 (m, 1H, CH_{Ar}), 7.30–7.35 (m, 2H, CH_{Ar}), 10.42 (br, 1H, OH). ^{13}C NMR ($CDCl_3$, 75 MHz): δ=16.0 (CH_3), 51.5 (OCH_3), 111.7 ($CCOOCH_3$), 124.3 (CH_{Ar}), 125.3 (C_{Ar}), 126.8 (CH_{Ar}), 127.8 (C_{Ar}), 128.4 ($2\times CH_{Ar}$), 129.0 (CH_{Ar}), 132.5, 135.5, 139.2 (C_{Ar}), 153.4 (COH), 171.6 (CO). IR (neat, cm^{-1}): $\tilde{\nu}$=3447 (w), 3056 (w), 2949 (w), 2851 (w), 1731 (w), 1658 (m), 1612 (m), 1599 (m), 1498 (w), 1434 (s), 1377 (m), 1280 (m), 1206 (s), 1149 (m), 1105 (m), 1072 (m), 1005 (m), 983 (m), 919 (w), 803 (m), 763 (m), 700 (s), 644 (m), 588 (m). GC–MS (EI, 70 eV): m/z (%)=257 ([M]$^+$, 33), 226 (17), 225 (100), 197 (22), 168 (49), 167 (14), 154 (11). HRMS (EI): Calcd for $C_{15}H_{14}O_3NCl$ ([M]$^+$): 291.07029; found: 291.070370.

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