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Syntheses of Sterically Hindered Pyridinium Phenoxides as Model Compounds in Nonlinear Optics

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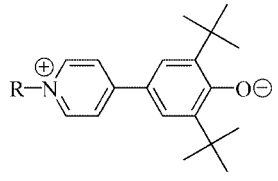
Noncentrosymmetric molecules with a π-conjugated system and, among them, push–pull molecules such as pyridinium phenoxide, are a promising new class of materials for applications in optoelectronics due to their nonlinear optical (NLO) properties. Modelling studies have indicated that an increase in the twist angle between the two aromatic rings leads to an enhancement of the NLO properties. In order to confirm this feature experimentally, it was necessary to prepare a series of new hindered pyridinium phenoxides. Their efficient syntheses by Suzuki cross-coupling reactions are described herein.

Introduction

Nonlinear optical (NLO) materials have been largely developed in the last few decades because of their promising applications in photoelectronics and photonics.[1] Such materials have often been developed by using π-conjugated organic compounds and especially push–pull molecules as a framework.[2] These molecules, consisting of a donor and acceptor end-group connected via a π-conjugated system, possess a large dissymmetric delocalized π-electron system which provides a large quadratic nonlinearity. In this field, biphenyl chromophores **1** bearing *tert*-butyl substituents anchored at the two *ortho* positions of the phenoxide function have been studied in detail (Scheme 1). Semi-empirical calculations point to a crucial influence of the dihedral angle on charge transfer but experimental results have not yet conclusively supported these calculations.[3] Therefore, it has become necessary to develop a series of biaryls with different twist angles between the two aromatic rings. Such molecules may be obtained by introducing alkyl groups of increasing size at the α positions of the intercyclic bond. The ultimate goal would be to compare the results of semi-empirical calculations, which predict a huge hyperpolarizability, with the increase in the twist angle[4] and the experimental NLO results in order to understand clearly the interplay between structure and NLO properties of these molecules. With this intention, we describe herein the synthesis of a series of substituted or unsubstituted pyridinium phenoxides.



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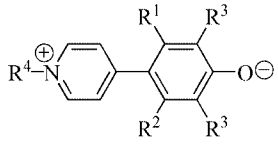

2a–g, R^4 = Me
3c $R^4 = C_4H_9$
4a, **4c**, **4d**, $R^4 = C_8H_{17}$

a $R^1 = R^2 = H$, $R^3 = H$
b $R^1 = H$, $R^2 = Me$, $R^3 = H$
c $R^1 = R^2 = Me$, $R^3 = H$
d $R^1 = R^2 = Et$, $R^3 = H$
e $R^1 = R^2 = i$Pr, $R^3 = H$
f $R^1 = R^2 = Me$, $R^3 = Me$
g $R^1 = R^2 = H$, $R^3 = Me$

Scheme 1.

Results and Discussion

Therefore, starting from the unsubstituted pyridinium phenoxide **2a**, alkyl groups of increasing size (methyl, ethyl, isopropyl) were introduced at the *meta* positions of the

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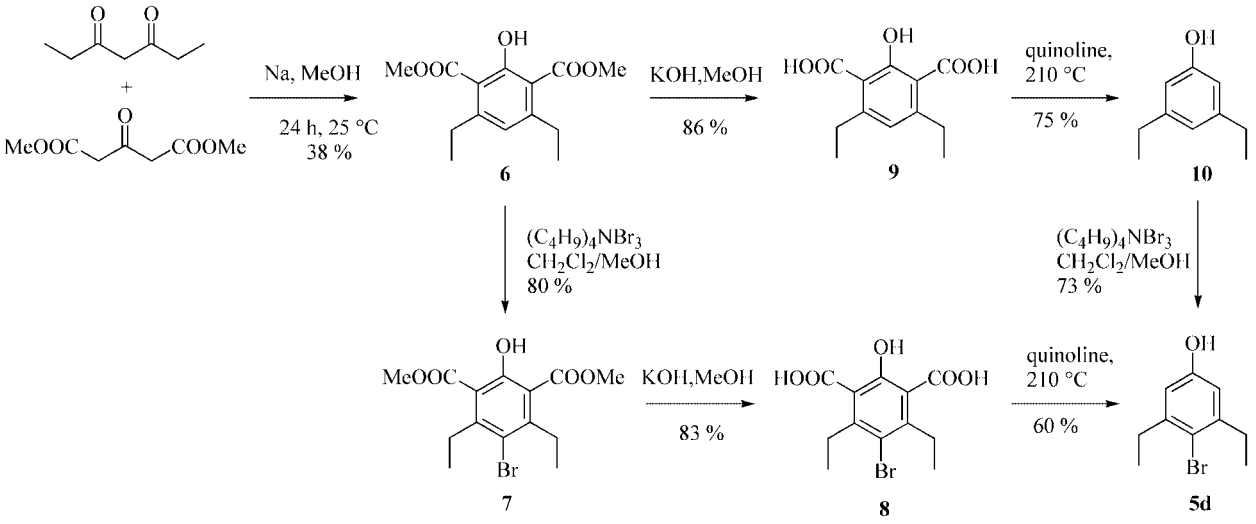
phenoxide to prepare compounds **2b**–**e**. Pyridinium phenoxides **2f**,**g** possessing an intermediate structure between our zwitterions and those of Combellas and co-workers[3] were synthesized by the introduction of methyl groups at the *ortho* positions of the phenoxide. Lastly, with the aim of increasing the solubility of pyridinium phenoxide in organic solvents, compounds **3c** and **4a**,**c**,**d** were prepared by lengthening the *N*-alkyl chains R^4 on the pyridinium ring (Scheme 1).

The palladium(0)-catalysed Suzuki cross-coupling reaction of arylboronic acids or arylboronates with aryl halides (iodides, bromides), aryl triflates or diazonium salts is a well established and powerful tool for the construction of biaryl bonds due to its efficiency and versatility.[5] Such a reaction may be favourably used for the syntheses of zwitterionic pyridinium phenoxides. To this end, 4-pyridinylboronic species were allowed to react with a series of halophenols. However, note that Suzuki coupling reactions between the halo derivatives of anilines or phenols and aryl- or heteroarylboronic acids are not straightforward. Even though some examples have been published[6] in which a bulky and expensive palladium(II) catalyst was used, the obvious solution would be to mask the electron-donating function (i.e. the hydroxy group in our case). Moreover, this protection of the hydroxy group becomes a necessity as the Suzuki cross-coupling reaction proceeds only in the presence of bases.[7] Indeed, in our hands, no reaction occurred when 4-bromophenol was allowed to react with 4-pyridinylboronic ester in the presence of Ag_2CO_3 and $[Pd(PPh_3)_4]$ in anhydrous THF. Another important feature of the Suzuki cross-coupling reaction of arylboronic acid is that, with sterically hindered coupling partners, the coupling generally gives low yields and hydrolytic deboronation of the C–B bond predominates.[8] In these cases, the replacement of classical catalysts by expensive and bulky monodentate catalysts has been recommended. But the best alternative would be to proceed under anhydrous conditions using boronates instead of boronic acids. In addition, preliminary experimental trials have shown that it is difficult to obtain properly purified 4-pyridinylboronic acid. As a result, we intended to couple a 4-pyridinylboronic ester with bromophenols protected as MOM derivatives in the presence of a base and $[Pd(PPh_3)_4]$ as catalyst.

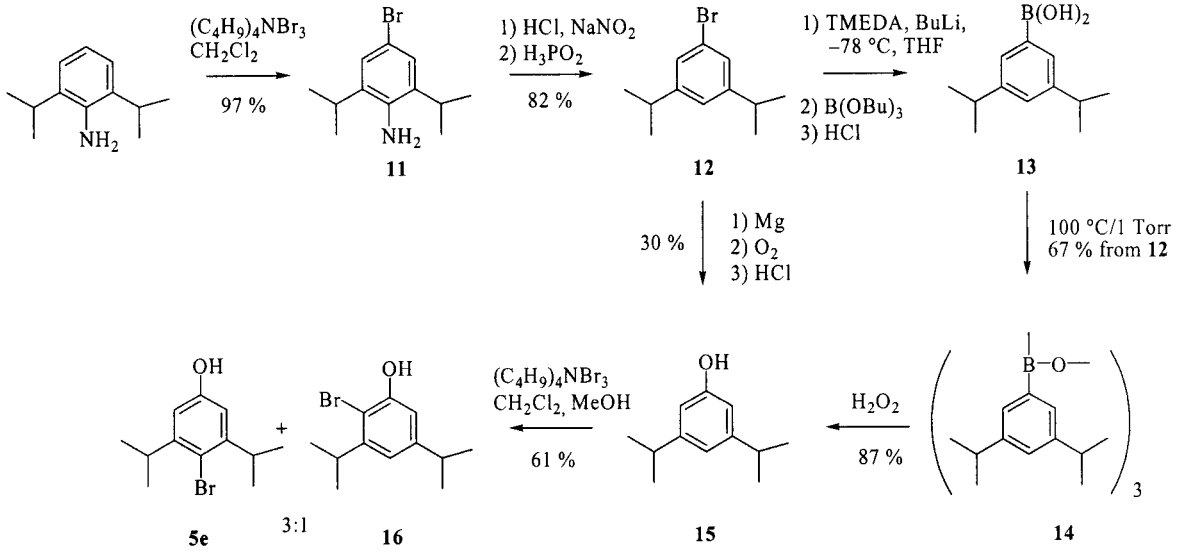
4-Bromophenol (**5a**), 4-bromo-3-methylphenol (**5b**), 4-bromo-3,5-dimethylphenol (**5c**) and 4-bromo-2,6-dimethylphenol (**5g**) are commercially available, but all the other substituted bromophenols had to be synthesized.

Preparation of Bromophenols 5d–f

The 3,5-diethyl-4-bromophenol (**5d**) was prepared in four steps from the commercially available heptane-3,5-dione and dimethyl 1,3-acetonedicarboxylate (Scheme 2). In the first step, applying the reported procedure,[9] under anhydrous and strongly basic conditions the condensation of these two derivatives led to the phenol derivative **6** in a modest yield. According to the literature,[10] no reaction has been detected by using NaOH as the base. At this stage, two possible synthetic pathways were tested that differ only in the order of the reactions: saponification, decarboxylation and bromination (Scheme 2). In both cases, saponification and decarboxylation readily occurred in high yields. The phenols **6** and **10** were readily brominated by reaction of an equivalent amount of tetrabutylammonium tribromide (*n*-Bu_4NBr_3) in CH_2Cl_2/MeOH.[11] Note that no *ortho*-bromination of **10** was detected in spite of the steric hindrance of the ethyl groups. This bromination reaction is strikingly selective. However, phenol **6** was not completely brominated and **7** was obtained with small amounts of unreacted **6**. Unfortunately, the separation of bromophenol **7** from **6** by classical methods of purification was not easily achieved. Furthermore, during the decarboxylation of **8**, a



Scheme 2. Preparation of **5d**.



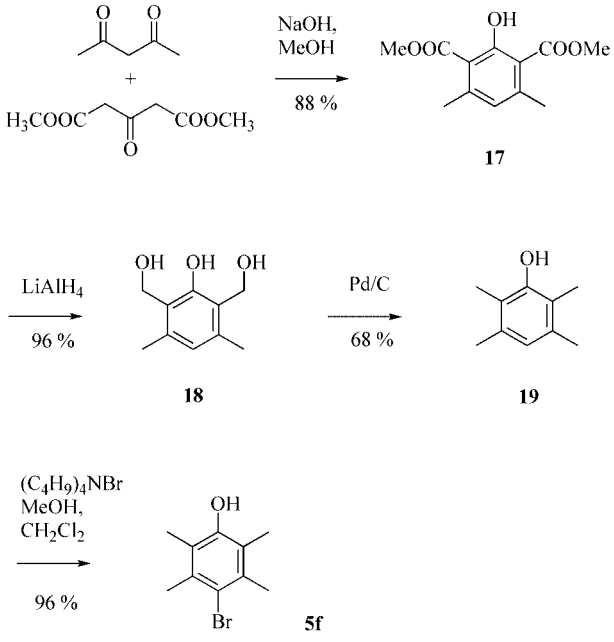
Scheme 3. Preparation of **5e**.

noticeable amount of debrominated products were detected. As a consequence, we had to favour the pathway starting from **6** via **7** and **8**.

The synthesis of bromophenol **5e** started with the bromination of 2,6-diisopropylaniline with *n*-Bu_4NBr_3 as above (Scheme 3). Diazotization of the resulting bromoaniline **11** with sodium nitrite in an acidic solution followed by reduction with hypophosphorous acid led to 1-bromo-3,5-diisopropylbenzene (**12**).[12] In a first approach and according to the literature,[13] the Grignard reagent of **12** was directly oxidized to give the phenol **15** in a low yield of 30%. A better method was to convert the bromo derivative **12**, first, by lithiation with *n*-BuLi followed by borylation with $B(OBu)_3$, to boroxine **14**.[14] Then, oxidation with hydrogen peroxide according to the Hawthorne method[15] led to phenol **15** in a 57% overall yield from **12**. Phenol **15** was subsequently brominated with *n*-Bu_4NBr_3 to give a mixture of *ortho* and *para* isomers **16** and **5e** in a 1:3 ratio. This lower regioselectivity ensues from the steric hindrance of the two isopropyl groups.

The first step in the synthesis of bromophenol **5f** (Scheme 4) was the condensation of pentane-2,4-dione and dimethyl 1,3-acetonedicarboxylate. Contrary to the synthesis of **6**, use of sodium hydroxide as the base in aqueous methanol was sufficient to provide the phenol dimethyl ester **17** in an 88% yield, in accord with the literature.[10] Phenol **17** was then reduced to **18** with $LiAlH_4$[16] and thoroughly hydrogenated on Pd/C. In the final step, the resulting tetramethylphenol **19** was readily brominated to **5f**.

Attempts to prepare 4-bromo-3,5-di-*tert*-butylphenol starting from commercially available 3,5-di-*tert*-butylphenol failed. The bulky *tert*-butyl groups certainly prevented substitution of the *para* position of the phenol and only the *ortho*-substituted product was isolated. This result illustrates the limitation of the bromination of sterically hindered phenols with *n*-Bu_4NBr_3.



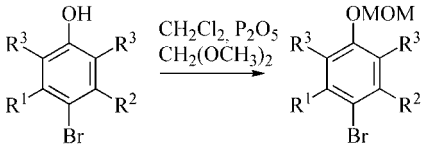
Scheme 4. Preparation of **5f**.

Preparation of Pyridinium Phenoxides

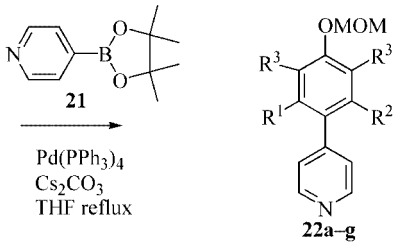
Protection of the Bromophenols

The Suzuki cross-coupling reaction demanded protection of the bromophenols (vide supra). Therefore, each of the bromophenols (**5a**–**g**) was protected using formaldehyde dimethyl acetal in the presence of phosphorus pentoxide in CH_2Cl_2.[17] All the expected protected compounds **20a**–**g** were isolated in good-to-excellent yields after chromatography (Table 1).

Table 1. Protection of the bromophenols **1a**–**g** and Suzuki cross-coupling reaction.



5a–g **20a–g**



22a–g

Entry	Yield **20a**–**g** [%]	Yield **22a**–**g** [%]
a	90	82
b	76	65
c	77	56
d	70	79
e	77	73
f	89	79
g	78	95

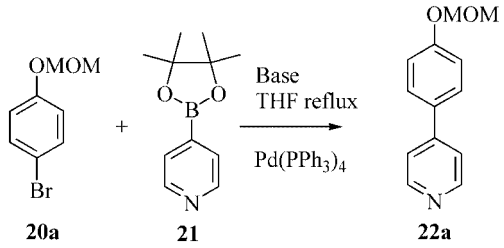
Synthesis of the Boronic Ester 21

The preparation of the boronic ester **21** from bromopyridine gave poor and nonreproducible results due to the instability of this free base, obtained by base extraction of its hydrochloride. A much more convenient alternative was the preparation of **21** from the more stable iodopyridine, synthesized from 4-aminopyridine,[18] in spite of an additional step. Then, in accord with the literature,[18] in a one-pot procedure, iodopyridine was lithiated in a metal/halide exchange, treated with tributylborate and finally with pinacol to obtain **21**. Overall, this procedure yielded 47% of the desired boronic ester from 4-aminopyridine.

Suzuki Cross-Coupling Reaction

In order to optimize the Suzuki cross-coupling reaction, the reaction between **21** and the unsubstituted protected bromophenol **20a** was performed in THF using seven bases (Table 2). The reaction proceeded in very low yields using K_3PO_4 and $Ba(OH)_2$ as base, in accord with our previous results.[19] On the other hand, the reaction of **21** with **20a** afforded a disappointing 8% yield of biaryl **22** with sodium phenolate as the base contradicting those same published results which indicate the promotion of sterically demanding coupling reactions. Coupling reactions of boronic esters have often been promoted by thallium(I) salts.[7e,19,20] Here, by using Tl_2CO_3, a yield of 23% was obtained. This poor result is nevertheless consistent with the work of Sniekus and co-workers who claimed that Tl_2CO_3 was inefficient for the coupling of arylboronate esters with an aryl iodide in THF.[21]

Table 2. Effect of base on the yields of the Suzuki cross-coupling reaction.



20a **21** **22a**

	Yield[a] [%]		Yield[a] [%]
Cs_2CO_3	100	NaOPh	8
Ag_2CO_3	77	$Ba(OH)_2$	2
Ag_2O	34	K_3PO_4	0
Tl_2CO_3	23	–	–

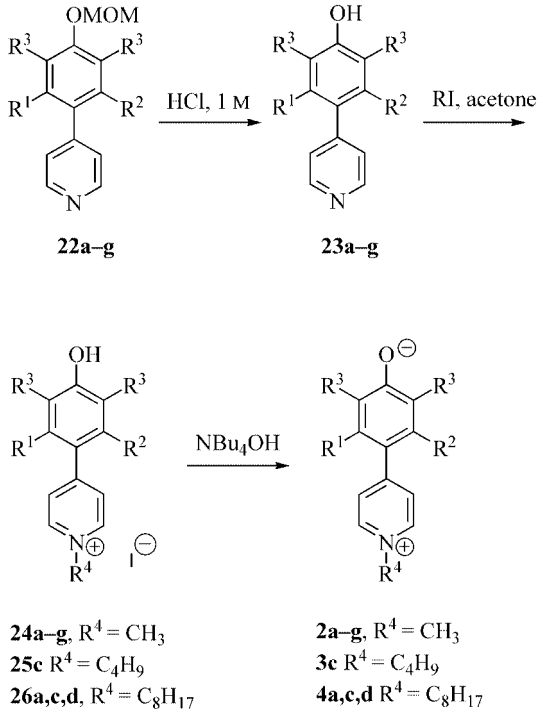
[a] Yields were determined by NMR analysis.

The best yields were achieved by using Ag_2CO_3 and especially Cs_2CO_3. Therefore, the following cross-coupling reactions were performed in THF by using Cs_2CO_3 as the base and $[Pd(PPh_3)_4]$ as the catalyst. In this way, all the expected phenylpyridines were readily obtained (Table 1). Slightly lower yields were obtained with **20d**–**f**, as expected because of the increase in steric hindrance. Curiously, the yield of the coupling reaction lowered to 65% with **20b** and to 56% with **20c**; no satisfactory explanation can be put forward for these results.

Deprotection, Quaternization and Deprotonation

The next stage of the venture involved the preparation of the final zwitterions by *O*-deprotection, *N*-alkylation and deprotonation (Scheme 5). In order to prepare these zwitterions free from traces of inorganic salts, the order of reactions took on a crucial importance. The best alternative was to first remove the MOM protecting group on the phenylpyridines **22a**–**g** by treatment with 1 M HCl overnight. After neutralization, the pyridinylphenols **23a**–**g** precipitated from solution and were recovered by filtration. A final sublimation gave pure deprotected compounds **23a**–**g** totally free of inorganic salts in moderate-to-good yields. The next step was the alkylation of the pyridine moiety to give *p*-(4-pyridinio)phenol iodides **24a**–**g**, **25c** and **26a**,**c**,**d**. This quaternization was obtained classically by nucleophilic substitution with alkyl iodides rather than with alkyl bromides in a polar solvent such as DMSO, acetonitrile or acetone.[22] Thus, the alkylation reactions of **23a**–**g** were performed in acetone with methyl iodide to give **24a**–**g**. To enhance the solubilities of the final zwitterions in organic solvents in order to make the physical measurements easier (vide supra), some alkylation reactions were carried out with *n*-iodobutane and -octane to give **25c** and **26a**,**c**,**d**, respectively.

In the final step, the biaryl iodide salts **24a**–**g**, **25c** and **26a**,**c**,**d** had to be deprotonated and then carefully purified. Because of comparable solubilities, the use of classical bases such as KOH or NaOH did not allow an easy separation of the zwitterions from the inorganic salts produced during



Scheme 5. Deprotection, quaternization and deprotonation of **22a**–**g** to give **2a**–**g**, **3c**, and **4a**,**c**,**d**.

the acid–base reaction. The best alternative was to treat the biaryl salts with a small excess of *n*-Bu_4NOH. The organic solvents were first evaporated until the residue crystallized. This residue was then treated with CH_2Cl_2 or with a mixture of CH_2Cl_2 and Et_2O in which tetrabutylammonium iodide was totally soluble, but in which the zwitterionic compounds were totally insoluble. The zwitterions free from traces of tetrabutylammonium iodide were then easily recovered from solution after centrifugation or filtration. The purity of the zwitterions was estimated by NMR spectroscopy using duroquinone in CD_3OD as an internal reference.

As the NLO properties will be studied in anhydrous solvents, it was crucial to determine the behaviour of pyridinium phenoxides with water. There is every indication that the high polarity of pyridinium phenoxides leads to a strong interaction between these charged molecules and water. For example, the compound E_T(**30**), the well-known empirical parameter of polarity, crystallizes with 0.5 molecules of water.[23] In the particular case of the simpler molecule **2a**, after drying at 50 °C in vacuo, yellow-orange crystals were obtained. Microanalysis of these crystals indicated that each zwitterion crystallizes with two molecules of water. After 12 hours in a higher vacuum (10^{-2} Torr), the compound turned orange and about one molecule of crystallization had been eliminated. On the other hand, at atmospheric pressure, **2a** turned yellow and was in equilibrium with around 2.2 molecules of water. The same behaviour was observed with the zwitterions **2b** and **2c**. Thus, it can be concluded that each zwitterion crystallizes with two molecules of water.

In a basic methanolic solution, the ^1H NMR spectrum of **2a** exhibited only the zwiterionic structure whilst in an acidic solution the spectrum was that of the protonated form. In neutral conditions, the spectrum of **2a** shows that the zwiterionic and the protonated forms coexist and are in equilibrium.

Conclusion

In summary, 11 new zwitterionic pyridinium phenoxides have been readily synthesized in yields ranging from 14 to 47.5% starting from the corresponding phenols. Some of them have already been the subject of theoretical studies but none of them have until now been synthesized. The NLO properties of each derivative will soon be studied in detail to confirm experimentally the semi-empirical predictions which anticipate the enhancement of NLO properties with increasing twist angle between the two aromatic rings. In addition, we have already published the first results of a solvatochromic study of the POMP derivative **2a**[24] and we also intend to study the solvatochromism of the substituted zwitterions in detail.

Experimental Section

General: Reagents were purchased from commercial suppliers and used without further purification. THF and Et_2O were freshly distilled from sodium/benzophenone, MeOH from Mg/I_2 and CH_2Cl_2 from P_2O_5. All melting points were determined with a Kofler hotplate apparatus. IR spectra were recorded with a Nicolet 205 FTIR spectrometer. ^1H (400 MHz) and ^{13}C NMR (100.6 MHz) spectra were measured with a Bruker Avance series 400 spectrometer. Chemical shifts are reported in ppm relative to $SiMe_4$. Microanalyses were performed by the analytical service of the Service de Microanalyse du CNRS in Vernaison. High-resolution MS were measured with a Waters Micromass Q-Tof Ultima API spectrometer at Basilea Pharmaceuticals in Basel (Swiss).

Previously reported procedures were used to prepare dimethyl 2-hydroxy-4,6-dimethylisophthalate (**17**),[10] 4-iodopyridine[18] and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (**21**).[18] [Pd-$(PPh_3)_4$] was prepared according to ref.[25] and used directly or within 3 months at the longest while being stored under N_2 at –30 °C.

General Procedures

Procedure A. Bromination: The phenol (1 equiv.) was dissolved in CH_2Cl_2/MeOH (3:2, 60 mL per 10 mmol) in a flask. nBu_4NBr_3 (1 equiv.) in CH_2Cl_2/MeOH (3:2, 50 mL per 10 mmol) was added dropwise with stirring. The reaction mixture was allowed to react at room temp. and monitored by TLC. The solvents were evaporated and the residue dissolved in Et_2O. The organic layer was extracted three times with H_2O, dried with $MgSO_4$ and concentrated in vacuo.

Procedure B. Hydrolysis of the Diesters: Methanolic KOH (3.5 mL, 4 g of KOH in 20 mL of MeOH) was added to the diester (1 mmol) under Ar. The reaction mixture was stirred for 16 h at reflux. The precipitate formed was filtered and dissolved in H_2O (2 mL). Concentred HCl was added dropwise until complete precipitation of the diacid. The desired product was recovered by filtration and then washed with cold H_2O and dried.

Procedure C. Decarboxylation: A mixture of quinoline (6 mL, 51 mmol) and diacid (2.5 mmol) was progressively heated to 210 °C under Ar. The temperature was maintained at 210 °C for 20 min after the emission of CO_2 had ceased. The mixture was allowed to cool to room temp. and then Et_2O (70 mL) was added. This organic layer was washed three times with 1 M HCl (50 mL) in order to discard the excess of quinoline, dried with $MgSO_4$ and concentrated in vacuo.

Procedure D. Protection of the Bromophenols:[17] Formaldehyde dimethyl acetal (10 equiv.) was added to a solution of bromophenol **5a**–**g** in anhydrous CH_2Cl_2 (20 mL per 1 mmol of bromophenol) under argon followed by P_2O_5 (ca. 500 mg per 1 mmol of bromophenol). The reaction mixture was stirred at room temp. and monitored by TLC. After decanting the solution, solid Na_2CO_3 was added. The insoluble salts were removed by filtration and the solvent was evaporated in vacuo. The crude protected bromophenols were purified by chromatography or by distillation.

Procedure E. Coupling Reaction: In a flask equipped with a Dean–Stark apparatus the protected bromophenol **20a**–**g** (0.5 mmol) was dissolved in anhydrous THF (25 mL) under Ar. Cs_2CO_3 (193 mg, 0.6 mmol), boronic ester **21** (123 mg, 0.6 mmol) and $[Pd(PPh_3)_4]$ (46 mg, 0.04 mmol) were successively introduced. The reaction mixture was stirred at reflux (overnight for **20a**, **20b** and **20g**, 72 h for **20c** and **20f**, 144 h for **20d** and **20e**). On completion of the reaction, the suspension was filtered through Celite with AcOEt used as eluent. After removing the solvents, the desired biaryl was purified by chromatography.

Procedure F. Deprotection of Biaryls: Under Ar, a solution of a protected biaryl **22a**–**g** (1 equiv.) in HCl 1 M (2.5 equiv.) was stirred for 16 h at room temp. A solution of 1 M $NaHCO_3$ was then slowly added until a pH of 7–8 was obtained. The crude precipitate **23a**–**g** was filtered, thoroughly washed with H_2O, Et_2O and then dried in vacuo.

Procedure G. Alkylation Reactions: Under Ar, iodoalkane (4 equiv.) was added to a suspension of the deprotected biaryl **23a**–**g** (1 equiv.) in acetone (16 mL per 1 mmol of biaryl). The reaction mixture was then refluxed (4 h for MeI, 48 h for *n*-BuI, 96 h for *n*-octyl iodide). On completion of the reaction, acetone was removed in vacuo. In the case of the alkylation with MeI, the residue of **24a**–**g** was washed with Et_2O and then with AcOEt. In the case of the alkylation with *n*-BuI or *n*-octyl iodide, the residues of **25c** and **26a**,**c**,**d** were dissolved in MeOH and this layer was washed three times with heptane. MeOH was removed in vacuo. The iodide salts were not further purified and only characterized by NMR spectroscopy.

Procedure H. Deprotonation: A 0.1 M solution of NBu_4OH in *i*PrOH/MeOH (9:1) was added to a stirred solution of **24a**–**g**, **25c** and **26a**,**c**,**d** (1 equiv.) in MeOH (6.7 mL per 1 mmol). After 2 min of reaction, the solvents were removed in vacuo. CH_2Cl_2/Et_2O (1:1, 10.3 mL per 1 mmol) was added to the crushed crystalline residue. The precipitate was filtered, washed with CH_2Cl_2/Et_2O (1:1) and dried.

Dimethyl 4,6-Diethyl-2-hydroxyisophthalate (6): 3,5-Heptanedione (13 mL, 96.2 mmol) was added dropwise at room temp. to a solution of NaOMe [prepared by addition of Na (2.28 g, 96.2 mmol) to anhydrous MeOH (56 mL) under Ar at 0 °C]. The solution turned yellow and dimethyl 1,3-acetonedicarboxylate (13.9 mL, 96.2 mmol) was added dropwise. The reaction mixture was stirred for 24 h. The mixture was then neutralized with 1 M HCl (150 mL). This solution was extracted three times with Et_2O. The combined extracts were dried with $MgSO_4$ and concentrated in vacuo. The crude product was purified by chromatography (cyclohexane/AcOEt, 9:1) to yield **6** as a colourless solid (9.58 g, 38%). Diester **6** was then crystallized from pentane: M.p. 39 °C. ^{1}H NMR ($CDCl_3$): δ = 1.20 (t, J = 7.5 Hz, 6 H), 2.75 (q, J = 7.5 Hz, 4 H), 3.95 (s, 6 H), 6.64 (s, 1 H), 11.66 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.6, 28.5, 52.4, 115.4, 122.1, 148.1, 159.9, 170.0 ppm. IR (KBr): $\tilde{\nu}$ = 569, 785, 816, 846, 876, 942, 987, 1018, 1043, 1071, 1124, 1180, 1205, 1240, 1264, 1294, 1327, 1366, 1403, 1438, 1452, 1467, 1564, 1620, 1650, 1737, 2877, 2973 cm^{-1}. $C_{14}H_{18}O_5$ (266.28): C 63.15, H 6.81; found C, 62.99, H, 6.90.

Dimethyl 5-Bromo-4,6-diethyl-2-hydroxyisophthalate (7): Following procedure A, from **6** (5 g, 18.8 mmol) was obtained crude **7**. After crystallization from cyclohexane with traces of pentane [crystallization from ethanol or sublimation was also possible (130 °C, 1 Torr)], **7** was obtained as colourless crystals (5.47 g, 80%). M.p. 89 °C. ^{1}H NMR ($CDCl_3$): δ = 1.21 (t, J = 7.4 Hz, 6 H), 2.95 (q, J = 7.4 Hz, 4 H), 3.96 (s, 6 H), 11.15 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.8, 29.6, 52.8, 117.9, 118.9, 147.32, 157.6, 169.2 ppm. IR (KBr): $\tilde{\nu}$ = 778, 794, 812, 942, 956, 984, 1033, 1057, 1071, 1125, 1196, 1221, 1231, 1286, 1306, 1356, 1396, 1441, 1550, 1605, 1656, 1736, 2871, 2930, 2963, 2981 cm^{-1}. $C_{14}H_{17}BrO_5$ (345.19) C 48.71, H 4.96, Br 23.15; found C 48.92, H 5.12, Br 22.95.

5-Bromo-4,6-diethyl-2-hydroxyisophthalic Acid (8): From **7** (1.7 g, 4,9 mmol) was obtained **8**, following procedure B (1.3 g, 83%). ^{1}H NMR (CD_3OD): δ = 1.22 (t, J = 7.3 Hz, 6 H), 3.06 (q, J = 7.3 Hz, 4 H) ppm. ^{13}C NMR (CD_3OD): δ = 14.4, 29.8, 118.7, 120.4, 147.4, 158.9, 172.1 ppm. IR (KBr): $\tilde{\nu}$ = 628, 655, 673, 692, 754, 770, 803, 820, 847, 932, 1058, 1069, 1090, 1126, 1145, 1221, 1240, 1302, 1335, 1364, 1392, 1436, 1463, 1549, 1593, 1649, 1717, 1728, 2609, 2836, 2876, 2936, 2981, 3238, 3411 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{12}H_{13}BrO_5$ [M^{-+}] 315.9946; found 316.000.

4,6-Diethyl-2-hydroxyisophthalic Acid (9): From **6** (1 g, 3.7 mmol) was obtained **9**, following procedure B (770 mg, 86%). ^{1}H NMR (CD_3OD): δ = 1.20 (t, J = 7.5 Hz, 6 H), 2.93 (q, J = 7.5 Hz, 4 H), 6.55 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 16.2, 29.1, 116.8, 122.9, 149.8, 161.1, 173.0 ppm. IR (KBr): $\tilde{\nu}$ = 607, 717, 741, 760, 770, 790, 829, 841, 867, 935, 952, 1019, 1038, 1072, 1084, 1125, 1205, 1227, 1264, 1322, 1351, 1391, 1462, 1556, 1586, 1647, 1709, 1715, 2873, 2934, 2975 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{12}H_{14}O_5$ [M]$^{-+}$ 238.0841; found 238.0835.

3,5-Diethylphenol (10): From **9** (1 g, 4.2 mmol) was obtained crude **10**, following procedure C. After chromatography (CH_2Cl_2) **10** was obtained as colourless crystals (472 mg, 75%) which can be sublimated (70 °C, 1 Torr). M.p. 75 °C (ref.[26] 75 °C). ^{1}H NMR ($CDCl_3$): δ = 1.21 (t, J = 7.6 Hz, 6 H), 2.57 (q, J = 7.6 Hz, 4 H), 4.60 (s, 1 H), 6.50 (s, 2 H), 6.62 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.5, 28.9, 112.2, 120.3, 146.2, 155.6 ppm. IR (KBr): $\tilde{\nu}$ = 702, 855, 931, 992, 1063, 1070, 1154, 1223, 1270, 1290, 1335, 1372, 1455, 1509, 1594, 1619, 2868, 2929, 2964, 3025, 3233 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{10}H_{14}O$ [M]$^{-+}$ 150.1045; found 150.1062.

4-Bromo-3,5-diethylphenol (5d): From **8** (1.2 g, 3.8 mmol) was obtained crude **5d**, following procedure C. After purification by chromatography (cyclohexane/AcOEt, 8:2), **5d** was crystallized from cyclohexane to give a colourless solid (523 mg, 60%). From **10** (1.56 g, 10.4 mmol) was obtained crude **5d**, following procedure A. Crystallization from cyclohexane with traces of pentane gave a first batch of product. The mother liquor was then concentrated and the residue obtained was purified by chromatography (cyclohexane/AcOEt, 8:2). These two batches were combined. Phenol **5d** was obtained as colourless crystals (990 mg, 73%). M.p. 80 °C. ^{1}H NMR ($CDCl_3$): δ = 1.21 (t, J = 7.5 Hz, 6 H), 2.73 (q, J = 7.5 Hz, 4 H), 5.01 (s, 1 H), 6.59 (s, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.2,

30.2, 114.0, 117.1, 145.2, 154.7 ppm. IR (KBr): $\tilde{\nu}$ = 857, 944, 1011, 1156, 1250, 1275, 1327, 1436, 1459, 1583, 2879, 2908, 2936, 2967, 3301 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{10}H_{13}BrO$ $[M]^{+\cdot}$ 228.015; found 228.1.

4-Bromo-2,6-diisopropylaniline (11): nBu_4NBr_3 (12.8 g, 26.5 mmol) in CH_2Cl_2 (250 mL) was rapidly added to 2,6-diisopropylaniline (5 mL, 26.5 mmol) dissolved in CH_2Cl_2 (250 mL). The reaction was stirred at room temp. for 0.5 h. On completion of the reaction, the solvent was evaporated to dryness and Et_2O (250 mL) was added to the residue. The organic layer was extracted with 0.5 M NaOH and twice with H_2O (150 mL), then dried with $MgSO_4$ and concentrated in vacuo. Aniline **11** was obtained as a colourless oil (6.58 g, 97%) and was used without further purification. ^1H NMR ($CDCl_3$):[27] δ = 1.25 (d, J = 6.8 Hz, 12 H), 2.88 (sept, 6.8 Hz, 2 H), 7.11 (s, 2 H) ppm.

1-Bromo-3,5-diisopropylbenzene (12): Sodium nitrite (4.45 g, 64.5 mmol) was added portionwise to a suspension of **11** (6.6 g, 26 mmol) in 2 M HCl (70 mL) at –5 °C. The reaction was allowed to react for 10 min at –5 °C and then 50% H_3PO_2 (30 mL, 258 mmol) was introduced. The reaction mixture was left at 4 °C for 24 h and then at room temp. for 24 h. The aqueous layer was extracted with Et_2O (3×100 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. Purification by distillation (b.p. 80 °C, 1 Torr) gave **12** as a colourless oil (5.1 g, 82%). ^1H NMR ($CDCl_3$): δ = 1.23 (d, J = 6.8 Hz, 12 H), 2.84 (sept, 6.8 Hz, 2 H), 6.98 (t, J = 1.5 Hz, 1 H), 7.17 (d, J = 1.5 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 24.0, 34.2, 122.5, 132.9, 127.0, 151.2 ppm. IR (KBr): $\tilde{\nu}$ = 703, 778, 861, 892, 997, 1187, 1243, 1316, 1364, 1384, 1441, 1466, 1570, 1602, 2870, 2891, 2929, 2962 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{12}H_{17}Br$ $[M]^{+\cdot}$ 240.0514; found 240.0.

2,4,6-Tris(3,5-diisopropylphenyl)cyclotriboroxane (14): TMEDA (2.4 mL, 16 mmol) was added to a solution of **12** (3.85 g, 16 mmol) in anhydrous Et_2O (20 mL) under Ar and the reaction mixture was cooled to –78 °C. Then 1.6 M nBuLi (10 mL, 16 mmol) was added dropwise and 20 min later, $B(OBu)_3$ (5.16 mL, 19.2 mmol). The reaction mixture was allowed to warm to room temp. (ca. 1 h) and then 1 M HCl (30 mL) and then concd. aqueous HCl (3 mL) were added to the reaction mixture. The layers were separated. The aqueous layer was washed with Et_2O (2×30 mL) and the combined organic layers were extracted with 1 M NaOH (3×70 mL). The combined aqueous layers were acidified with concd. aqueous HCl. A white solid precipitated which was recovered by filtration and dried at 100 °C/1 Torr. A mixture (1.98 g, 66%) of **14** (92%) and 3,5-diisopropylphenylboronic acid (**13**) (8%) was obtained and used without further purification. **14**: ^1H NMR ($CDCl_3$): δ = 1.27 (d, J = 7.0 Hz, 36 H), 2.92 (sept, 7.0 Hz, 6 H), 7.21 (t, J = 1.5 Hz, 3 H), 7.42 (d, J = 1.5 Hz, 6 H) ppm. **13**: ^1H NMR ($CDCl_3$): δ = 1.34 (d, J = 7.0 Hz, 12 H), 3.03 (sept, 7.0 Hz, 2 H), 7.33 (t, J = 1.5 Hz, 1 H), 7.92 (d, J = 1.5 Hz, 2 H) ppm.

3,5-Diisopropylphenol (15): Cyclotriboroxane **14** (1 g, 1.77 mmol) was slowly added to 35% H_2O_2 (2 mL). After addition, the reaction mixture was heated at 70 °C for 20 min. Then 0.5 M HCl (30 mL) was added. The reaction mixture was extracted three times with Et_2O (30 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by chromatography (cyclohexane/AcOEt, 9:1) to give **15** as a colourless solid (822 mg, 87%). M.p. 46 °C (ref.[26] 52–53 °C). ^1H NMR ($CDCl_3$): δ = 1.23 (d, J = 6.8 Hz, 12 H), 2.83 (sept, 6.8 Hz, 2 H), 4.6 (br. s, 1 H), 6.53 (d, J = 1 Hz, 2 H), 6.67 (t, J = 1 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 24.1, 34.2, 110.7, 117.7, 150.9, 155.6 ppm. IR (KBr): $\tilde{\nu}$ = 707, 856, 966, 1175, 1278, 1363, 1384, 1449, 1450, 1597, 1617, 2869, 2928, 2961, 3313 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{12}H_{18}O$ $[M]^{+\cdot}$ 178.1358, found 178.1370.

4-Bromo-3,5-diisopropylphenol (5e) and 2-Bromo-3,5-diisopropylphenol (16): From **15** (356 mg, 2 mmol) a mixture of **5e** and **16** was obtained following procedure A. After purification by chromatography (cyclohexane/AcOEt, 9:1), **5e** was obtained as a colourless solid (315 mg, 61%). Further sublimation was also possible (90 °C, 1 Torr). M.p. 95 °C. ^1H NMR ($CDCl_3$): δ = 1.21 (d, J = 6.8 Hz, 12 H), 3.45 (sept, J = 6.8 Hz, 2 H), 4.62 (br. s, 1 H), 6.63 (s, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 23.1, 33.6, 111.6, 117.1, 149.4, 155.1 ppm. IR (KBr): $\tilde{\nu}$ = 616, 735, 858, 869, 963, 1021, 1073, 1104, 1133, 1180, 1218, 1252, 1279, 1327, 1362, 1385, 1425, 1464, 1584, 1604, 2870, 2928, 2966, 3317 cm^{-1}. $C_{12}H_{17}BrO$ (257.17): C 56.05, H 6.66, Br 6.22: found C 56.24, H, 6.74, Br 30.70.

Compound **16** was obtained as a colourless solid during the chromatography of **5e** (100 mg, 25%). ^1H NMR ($CDCl_3$): δ = 1.22 (d, J = 6.8 Hz, 6 H), 1.24 (d, J = 6.8 Hz, 6 H), 2.84 (sept, J = 6.8 Hz, 1 H), 3.27 (sept, J = 6.8 Hz, 1 H), 5.60 (br. s, 1 H), 6.70 (d, J = 2 Hz, 1 H), 6.78 (d, J = 2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 22.9, 24.0, 33.5, 34.1, 109.8, 111.3, 116.9, 147.7, 149.9, 152.0 ppm.

2,6-Dihydroxymethyl-3,5-dimethylphenol (18):[16] A solution of **17** (3 g, 12.6 mmol) in anhydrous Et_2O (120 mL) was added dropwise to a suspension of $LiAlH_4$ (1.19 g, 31.5 mmol) in anhydrous Et_2O (60 mL) at 0 °C under Ar. The reaction mixture was allowed to react at room temp. for 24 h. $LiAlH_4$ was neutralized with AcOEt. Then 1 M HCl (150 mL) was added. The organic layer was separated. The aqueous layer was extracted twice with Et_2O (150 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to give **18** as colourless crystals (2.22 g, 96%). Compound **18** was recrystallized from iPrOH. M.p. 152 °C. ^1H NMR (CD_3OD): δ = 2.24 (s, 6 H), 4.75 (s, 4 H), 6.51 (s, 1 H) ppm. ^{13}C NMR (CD_3OD): δ = 19.0, 58.6, 123.4, 124.4, 137.3, 156.7 ppm. IR (KBr): $\tilde{\nu}$ = 591, 840, 985, 1003, 1031, 1082, 1223, 1237, 1303, 1362, 1413, 1459, 1574, 1626, 2908, 2976, 3104, 3218, 3458 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{10}H_{14}O_3$ $[M]^{+\cdot}$ 182.0943; found 182.0930.

2,3,5,6-Tetramethylphenol (19): Compound **18** (2.15 g, 11.8 mmol) was hydrogenolysed over Pd/C (5%, 480 mg) in MeOH (40 mL) at room temp. for 8 h. The catalyst was removed by filtration through Celite using CH_2Cl_2 as eluent. After concentration in vacuo, the crude product was purified by chromatography (cyclohexane/CH_2Cl_2, 2:1). Phenol **19** was obtained as a colourless solid (1.14 g, 68%) and was sublimated for analytical purposes (90 °C, 1 Torr). M.p. 118 °C (ref.[28] 116–117 °C). ^1H NMR ($CDCl_3$): δ = 2.13 (s, 6 H), 2.22 (s, 6 H), 4.60 (br. s, 1 H), 6.59 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.8, 19.9, 119.1, 123.7, 134.4, 151.9 ppm. IR (KBr): $\tilde{\nu}$ = 581, 850, 996, 1006, 1018, 1031, 1089, 1230, 1262, 1303, 1333, 1382, 1403, 1441, 1466, 1496, 1567, 1622, 2865, 2921, 2946, 2962, 3460 cm^{-1}. $C_{10}H_{14}O$ (150.21): C 79.95, H 9.39; found C 79.91, H 9.41.

4-Bromo-2,3,5,6-tetramethylphenol (5f): From **19** (1.12 g, 7.46 mmol) **5f** was obtained following procedure A. Crude **5f** was recrystallized from cyclohexane and was obtained in its pure form as colourless needles (1.64 g, 96%); further sublimation was also possible (70 °C, 1 Torr). M.p. 118 °C (ref.[29] 118 °C). ^1H NMR ($CDCl_3$): δ = 2.22 (s, 6 H), 2.39 (s, 6 H), 4.60 (br. s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.4, 21.0, 120.2, 120.8, 134.1, 150.8 ppm. IR (KBr): $\tilde{\nu}$ = 732, 1012, 1082, 1213, 1301, 133, 1351, 1391, 3375 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{10}H_{13}BrO$ $[M]^{+\cdot}$ 228.015; found 228.

1-Bromo-4-(methoxymethoxy)benzene (20a): Crude **20a** was obtained from bromophenol **5a** (3.46 g, 20 mmol) following procedure D. Pure **20a** was obtained as a colourless liquid after distillation (3.90 g, 90%). The analytical data found are the same as reported in the literature.[30]

4-Bromo-1-(methoxymethoxy)-3-methylbenzene (20b): Crude **20b** was obtained from bromophenol **5b** (4.9 g, 26.2 mmol) following procedure D. Pure **20b** was obtained after chromatography (cyclohexane/AcOEt, 9:1) as a colourless oil (4.61 g, 76%). ^{1}H NMR ($CDCl_3$): δ = 2.36 (s, 3 H), 3.46 (s, 3 H), 5.13 (s, 2 H), 6.75 (dd, J = 2.8, 8.4 Hz, 1 H), 6.93 (d, J = 2.8 Hz, 1 H), 7.26 (d, J = 8.4 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 23.2, 56.1, 94.5, 115.4, 116.8, 118.8, 133.0, 139.0, 156.5 ppm. IR (KBr): $\tilde{\nu}$ = 810, 925, 991, 1022, 1037, 1082, 1154, 1209, 1239, 1276, 1294, 1310, 1442, 1478, 1579, 1596, 2901, 2955 cm^{-1}.

4-Bromo-1-(methoxymethoxy)-3,5-dimethylbenzene (20c): Crude **20c** was obtained from bromophenol **5c** (2.3 g, 11.4 mmol) following procedure D. Pure **20c** was obtained after chromatography (CH_2Cl_2/AcOEt, 9:1) as a colourless oil (2.16 g, 77%). ^{1}H NMR ($CDCl_3$): δ = 2.38 (s, 6 H), 3.46 (s, 3 H), 5.13 (s, 2 H), 6.79 (s, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 24.4, 53.0, 94.3, 116.2, 119.7, 139.3, 155.8 ppm. IR (KBr): $\tilde{\nu}$ = 857, 923, 933, 992, 1020, 1031, 1049, 1088, 1151, 1212, 1300, 1315, 1439, 1468, 1585, 1595, 2903, 2928 cm^{-1}.

4-Bromo-3,5-diethyl-1-(methoxymethoxy)benzene (20d): Crude **20d** was obtained from bromophenol **5d** (1 g, 4.3 mmol) following procedure D. Pure **20d** was obtained after chromatography (cyclohexane/AcOEt, 9:1) as a colourless oil (834 mg, 70%). ^{1}H NMR ($CDCl_3$): δ = 1.22 (t, J = 7.5 Hz, 6 H), 2.75 (q, J = 7.5 Hz, 4 H), 3.47 (s, 3 H), 5.14 (s, 2 H), 6.78 (s, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.2, 30.3, 56.0, 94.5, 114.8, 118.3, 144.9, 156.3 ppm. IR (KBr): $\tilde{\nu}$ = 864, 925, 978, 1009, 1036, 1069, 1094, 1151, 1210, 1251, 1284, 1311, 1334, 1373, 1393, 1404, 1437, 1450, 1584, 2826, 2847, 2875, 2900, 2934, 2968 cm^{-1}.

4-Bromo-3,5-diisopropyl-1-(methoxymethoxy)benzene (20e): Crude **20e** was obtained from bromophenol **5e** (247 mg, 0.96 mmol) following procedure D. Pure **20e** was obtained after chromatography (cyclohexane/AcOEt, 7:3) as a colourless oil (222 mg, 77%). ^{1}H NMR ($CDCl_3$): δ = 1.23 (d, J = 7.0 Hz, 12 H), 3.47 (sept, J = 7.0 Hz, 2 H), 3.49 (s, 3 H), 5.16 (s, 2 H), 6.83(s, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 23.1, 33.7, 56.2, 94.84, 112.4, 118.6, 149.1, 157.0 ppm. IR (KBr): $\tilde{\nu}$ = 865, 930, 1010, 1027, 1077, 1107, 1135, 1154, 1176, 1212, 1276, 1329, 1363, 1384, 1403, 1432, 1464, 1582, 1589, 2872, 2901 cm^{-1}.

1-Bromo-4-(methoxymethoxy)-2,3,5,6-tetramethylbenzene (20f): Crude **20f** was obtained from bromophenol **5f** (580 mg, 2.5 mmol) following procedure D. Pure **20f** was obtained after chromatography (cyclohexane/AcOEt, 9:1) as a colourless solid (615 mg, 89%). M.p. 37.8–38.5 °C. ^{1}H NMR ($CDCl_3$): δ = 2.27 (s, 6 H), 2.39 (s, 6 H), 3.61 (s, 3 H), 4.88 (s, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.7, 21.0, 57.9, 99.6, 124.5, 128.6, 135.0, 153.3 ppm. IR (KBr): $\tilde{\nu}$ = 723, 749, 908, 925, 975, 1055, 1104, 1158, 1204, 1222, 1297, 1368, 1382, 1386, 1453, 1477, 2827, 2867, 2918, 2955, 2989 cm^{-1}.

4-Bromo-1-(methoxymethoxy)-2,6-dimethylbenzene (20g): Crude **20g** was obtained from bromophenol **5g** (1.6 g, 7.9 mmol) following procedure D. Pure **20g** was obtained after chromatography (cyclohexane/AcOEt, 9:1) as a colourless oil (1.52 g, 78%). ^{1}H NMR ($CDCl_3$): δ = 2.26 (s, 6 H), 3.59 (s, 3 H), 4.93 (s, 2 H), 7.15 (s, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 16.6, 57.3, 99.0, 116.6, 131.3, 133.2, 154.0 ppm. IR (KBr): $\tilde{\nu}$ = 753, 851, 927, 974, 1074, 1159, 1181, 1223, 1398, 1475, 2929, 2954 cm^{-1}.

4-[4-(Methoxymethoxy)phenyl]pyridine (22a): Crude **22a** was obtained from protected bromophenol **20a** (2.9 g, 13.4 mmol) following procedure E. Pure **22a** was obtained after chromatography (cyclohexane/AcOEt, 5:5) as a colourless solid (2.36 g, 82%) which can be sublimated (120 °C, 1 Torr). M.p. 110 °C. ^{1}H NMR ($CDCl_3$): δ = 3.51 (s, 3 H), 5.24 (s, 2 H), 7.15 (d, J = 8.8 Hz, 2 H), 7.50 (d, J = 6.0 Hz, 2 H), 7.60 (d, J = 8.8 Hz, 2 H), 8.62 (d, J = 6 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 56.2, 94.5, 116.9, 121.3, 128.3, 131.7, 149.9, 150.3, 158.3 ppm. IR (KBr): $\tilde{\nu}$ = 811, 920, 974, 1031, 1081, 1154, 1184, 1209, 1226, 1252, 1279, 1405, 1488, 1522, 1597, 1606, 2850, 2930, 3000 cm^{-1}. $C_{13}H_{13}NO_2$ (215.09): C 72.54, H 6.09, N 6.51; found C 72.31, H 6.14, N 6.41.

4-[4-(Methoxymethoxy)-2-methylphenyl]pyridine (22b): Crude **22b** was obtained from protected bromophenol **20b** (150 mg, 0.6 mmol) following procedure E. Pure **22b** was obtained after chromatography (cyclohexane/AcOEt, 6:4) as a colourless oil (97 mg, 65%). ^{1}H NMR ($CDCl_3$): δ = 2.28 (s, 3 H), 3.35 (s, 3 H), 5.21 (s, 2 H), 6.94–6.98 (m, 2 H), 7.14 (d, J = 8.3 Hz, 1 H), 7.23–7.27 (m, 3 H), 8.62 (d, J = 4.5 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.1, 55.6, 93.8, 113.4, 117.8, 124.0, 130.1, 132.2, 136.2, 148.9, 149.1, 156.8 ppm. IR (KBr): $\tilde{\nu}$ = 816, 926, 992, 1013, 1032, 1082, 1125, 1153, 1167, 1207, 1237, 1278, 1486, 1509, 1606, 2976, 3349 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{14}H_{15}NO_2$ $[M]^{\cdot+}$ 229.1103; found 229.1072.

4-[4-(Methoxymethoxy)-2,6-dimethylphenyl]pyridine (22c): Crude **22c** was obtained from protected bromophenol **20c** (3.34 g, 13.6 mmol) following procedure E. Pure **22c** was obtained after chromatography (cyclohexane/AcOEt, 8:2) as a colourless oil which crystallized at 4 °C (1.86 g, 56%). M.p. 65 °C. ^{1}H NMR ($CDCl_3$): δ = 1.99 (s, 6 H), 3.51 (s, 3 H), 5.19 (s, 2 H), 6.81 (s, 2 H), 7.11 (d, J = 5.8 Hz, 2 H), 8.65 (d, J = 5.8 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.0, 56.2, 94.4, 115.3, 125.3, 132.9, 136.9, 149.78, 149.81, 156.7 ppm. IR (KBr): $\tilde{\nu}$ = 825, 857, 919, 933, 989, 1031, 1048, 1069, 1089, 1150, 1159, 1274, 1301, 1322, 1405, 1466, 1540, 1578, 1596, 1609, 2810 cm^{-1}. $C_{15}H_{17}NO_2$ (243.3): C 74.05, H 7.04, N 5.75; found C 74.16, H 7.19, N 5.62.

4-[2,6-Diethyl-4-(methoxymethoxy)phenyl]pyridine (22d): Crude **22d** was obtained from protected bromophenol **20d** (136 mg, 0.5 mmol) following procedure E. Pure **20d** was obtained after chromatography (cyclohexane/AcOEt, 8:2) as a colourless oil which crystallized at 4 °C (107 mg, 79%). M.p. 44 °C. ^{1}H NMR ($CDCl_3$): δ = 1.02 (t, J = 7.6 Hz, 6 H), 2.27 (q, J = 7.6 Hz, 4 H), 3.52 (s, 3 H), 5.22 (s, 2 H), 6.84 (s, 2 H), 7.14 (d, J = 5.6 Hz, 2 H), 8.66 (d, J = 5.6 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.5, 26.9, 56.2, 94.5, 113.6, 125.6, 131.9, 143.2, 149.1, 149.7, 157.3 ppm. IR (KBr): $\tilde{\nu}$ = 825, 859, 924, 973, 1005, 1031, 1065, 1094, 1147, 1213, 1275, 1287, 1330, 1405, 1463, 1575, 1603, 2894, 2966 cm^{-1}. $C_{17}H_{21}NO_2$ (271.16): C 75.24, H 7.80, N 5.16; found C 75.43, H 7.88, N 5.06.

4-[2,6-Diisopropyl-4-(methoxymethoxy)phenyl]pyridine (22e): Crude **22e** was obtained from protected bromophenol **20e** (151 mg, 0.5 mmol) following procedure E. Pure **20e** was obtained after chromatography (cyclohexane/AcOEt, 8:2) as a colourless oil which crystallized at 4 °C (110 mg, 73%). M.p. 97 °C. ^{1}H NMR ($CDCl_3$): δ = 1.07 (d, J = 6.8 Hz, 12 H), 2.49 (sept, 6.8 Hz, 2 H), 3.53 (s, 3 H), 5.22 (s, 2 H), 6.89 (s, 2 H), 7.14 (d, J = 5.8 Hz, 2 H), 8.65 (d, J = 5.8 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 24.1, 30.6, 56.3, 94.7, 110.8, 125.7, 130.7, 147.9, 149.5, 149.6, 157.8 ppm. IR (KBr): $\tilde{\nu}$ = 818, 834, 872, 918, 931, 1006, 1027, 1067, 1076, 1129, 1149, 1173, 1245, 1294, 1336, 1366, 1406, 1458, 1471, 1577, 2868, 2907, 2933, 2963 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{19}H_{25}NO_2$ $[M]^{\cdot+}$ 299.1885; found 299.1833.

4-[4-(Methoxymethoxy)-2,3,5,6-tetramethylphenyl]pyridine (22f): Crude **22f** was obtained from protected bromophenol **20f** (136 mg, 0.5 mmol) following procedure E. Pure **20f** was obtained after chromatography (cyclohexane/AcOEt, 6:4) as colourless crystals (107 mg, 79%). M.p. 74 °C. ^{1}H NMR ($CDCl_3$): δ = 1.88 (s, 6 H), 2.24 (s, 6 H), 3.66 (s, 3 H), 4.96 (s, 2 H), 7.14 (d, J = 5.5 Hz, 2 H), 8.67 (d, J = 5.5 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.0, 18.2, 58.1, 99.9, 125.5, 127.6, 132.8, 136.1, 150.3, 151.4, 154.3 ppm. IR (KBr): $\tilde{\nu}$ = 527, 641, 823, 925, 971, 989, 1050, 1078, 1101, 1156, 1216, 1267, 1384, 1402, 1415, 1465, 1541, 1596, 2875, 2924, 2942 cm^{-1}. $C_{17}H_{21}NO_2$ (271.35): C 75.25, H 7.80, N 5.16; found C 75.24, H 7.88, N 5.01.

4-[4-(Methoxymethoxy)-3,5-dimethylphenyl]pyridine (22g): Crude **22g** was obtained from protected bromophenol **20g** (470 mg, 1.9 mmol) following procedure E. The crude product was purified by chromatography (cyclohexane/AcOEt, 7:3) as colourless crystals (443 mg, 95%). M.p. 46 °C. ^{1}H NMR ($CDCl_3$): δ = 2.38 (s, 6 H), 3.64 (s, 3 H), 5.01 (s, 2 H), 7.31 (s, 2 H), 7.48 (d, J = 4.5 Hz, 2 H), 8.62 (d, J = 4.5 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 17.2, 57.6, 99.3, 121.6, 127.7, 132.0, 133.9, 148.3, 150.1, 156.1 ppm. IR (KBr): $\tilde{\nu}$ = 493, 570, 639, 718, 820, 920, 963, 1072, 1156, 1174, 1214, 1221, 1240, 1328, 1398, 1422, 1437, 1457, 1479, 1544, 1597, 2925, 2959 cm^{-1}. $C_{15}H_{17}NO_2$ (243.3): C74.05, H 7.04, N 5.76; found C 74.45, H 7.09, N 5.69.

4-(Pyridin-4′-yl)phenol (23a): The crude product, obtained from **22a** (890 mg, 4.13 mmol) following procedure F, was purified by recrystallization from EtOH (573 mg, 81%) and can be sublimated (180 °C, 1 Torr) to obtain a colourless solid. M.p. 256 °C. ^{1}H NMR (CD_3OD): δ = 6.91 (d, J = 8.5 Hz, 2 H), 7.62 (d, J = 8.5 Hz, 2 H), 7.63 (d, J = 5.6 Hz, 2 H), 8.49 (d, J = 5.6 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 117.1, 122.2, 129.3, 129.5, 150.3, 150.6, 160.4 ppm. IR (KBr): $\tilde{\nu}$ = 495, 502, 574, 726, 816, 1000, 1029, 1174, 1181, 1223, 1255, 1283, 1295,1398, 1414, 1450, 1490, 1520, 1583, 1600, 2581, 2904 cm^{-1}. $C_{11}H_9NO$ (171.07): C 77.17, H 5.3, N 8.18; found C 77.34, H 5.35, N 8.15.

3-Methyl-4-(pyridin-4′-yl)phenol (23b): The crude product, obtained from **22b** (72 mg, 0.31 mmol) following procedure F, was purified by sublimation (160 °C, 1 Torr) to give a colourless solid (35 mg, 60%). M.p. 206 °C. ^{1}H NMR (CD_3OD): δ = 2.23 (s, 3 H), 6.71 (dd, J = 8, 2.4 Hz, 1 H), 6.74 (d, J = 2.4 Hz, 1 H), 7.07 (d, J = 8 Hz, 1 H), 7.37 (dd, J = 4.8, 1.6 Hz, 2 H), 8.51 (dd, J = 4.8, 1.6 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 20.6, 114.3, 118.4, 126.2, 131.2, 131.7, 137.6, 149.6, 152.6, 159.0 ppm. IR (KBr): $\tilde{\nu}$ = 813, 1005, 1025, 1173, 1220, 1247, 1288, 1304, 1417, 1468, 1487, 1509, 1544, 1574, 1604, 2481, 2518, 2537, 2591, 2593, 2597, 2639, 2684, 2780, 2786, 2871, 2879, 2890, 2923, 2983 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{12}H_{11}NO$ $[M]^{\cdot+}$ 185.0841; found 185.0842.

3,5-Dimethyl-4-(pyridin-4′-yl)phenol (23c): Crude **23c**, obtained from **22c** (1.17 g, 4.81 mmol) following procedure F, was purified by sublimation (180 °C, 1 Torr) to give a colourless solid (767 mg, 80%). M.p. 270 °C. ^{1}H NMR (CD_3OD): δ = 1.95 (s, 6 H), 6.57 (s, 2 H), 7.21 (d, J = 5 Hz, 2 H), 8.65 (d, J = 5 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.8, 115.4, 127.3, 131.5, 137.4, 150.2, 152.5, 158.1 ppm. IR (KBr): $\tilde{\nu}$ = 607, 726, 833, 850, 858, 996, 1036, 1068, 1156, 1213, 1241, 1257, 1276, 1310, 1412, 1440, 1465, 1542, 1585, 1605, 1611, 3043 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{13}H_{13}NO$ $[M]^{\cdot+}$ 199.0997; found 199.0977.

3,5-Diethyl-4-(pyridin-4′-yl)phenol (23d): Crude **23d**, obtained from **22d** (271 mg, 1 mmol) following procedure F, was purified by sublimation (180 °C, 1 Torr) to give a colourless solid (199 mg, 87%). M.p. 230 °C. ^{1}H NMR (CD_3OD): δ = 0.99 (t, J = 7.6 Hz, 6 H), 2.24 (q, J = 7.6 Hz, 4 H), 6.60 (s, 2 H), 7.26 (d, J = 6 Hz, 2 H), 8.56 (d, J = 6 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 15.9, 27.7, 113.8, 127.8, 130.4, 144.0, 149.9, 152.1, 158.6 ppm. IR (KBr): $\tilde{\nu}$ = 834, 855, 866, 939, 997, 1065, 1157, 1205, 1216, 1244, 1259, 1284 1306, 1325, 1339, 1376, 1412, 1446, 1459, 1539, 1578, 1603, 2872, 2933, 2974, 3038, 3122, 3454 cm^{-1}. $C_{15}H_{17}NO$ (227.31): C 79.26, H 7.54, N 6.16; found C 79.23, H 7.54, N 6.05.

3,5-Diisopropyl-4-(pyridin-4′-yl)phenol (23e): Crude **23e**, obtained from **22e** (200 mg, 0.7 mmol) following procedure F, was purified by sublimation (170 °C, 1 Torr) to give a colourless solid (105 mg, 62%). M.p. 240 °C. ^{1}H NMR (CD_3OD): δ = 1.06 (d, J = 6.8 Hz, 12 H), 2.45 (sept, 6.8 Hz, 2 H), 6.66 (s, 2 H), 7.25 (d, J = 5.8 Hz, 2 H), 8.56 (d, J = 5.8 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 24.3, 31.6, 110.7, 127.7, 129.3, 148.7, 149.8, 152.5, 158.9 ppm. IR (KBr): $\tilde{\nu}$ = 569, 838, 1066, 1183, 1213, 1306, 1328, 1344, 1413, 1448, 1468, 1580, 1605, 2618, 2660, 2725, 2869, 2926 cm^{-1}. $C_{17}H_{21}NO$ (255.35): C 79.96, H 8.29, N 5.49; found C 79.68%, H 8.22, N 5.41.

2,3,5,6-Tetramethyl-4-(pyridin-4′-yl)phenol (23f): Crude **23f**, obtained from **22f** (271 mg, 1 mmol) following procedure F, was purified by sublimation (180 °C, 1 Torr) to give a colourless solid (156 mg, 68%). M.p. 270 °C. ^{1}H NMR (CD_3OD): δ = 1.86 (s, 6 H), 2.18 (s, 6 H), 7.17 (d, J = 4.3 Hz, 2 H), 8.55 (d, J = 4.3 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 12.8, 17.9, 122.4, 127.4, 132.1, 132.7, 149.9, 153.5, 154.3 ppm. IR (KBr): $\tilde{\nu}$ = 528, 647, 823, 1005, 1032, 1070, 1086, 1099, 1173, 1212, 1249, 1283, 1305, 1403, 1418, 1449, 1602, 2937, 2989, 3041, 3125. cm^{-1} $C_{15}H_{17}NO$ (227.29): C 79.26, H 7.54, N 6.16; found C 79.25, H 7.53, N 6.06.

2,6-Dimethyl-4-(pyridin-4′-yl)phenol (23g): Crude **23g**, obtained from **22g** (180 mg, 0.74 mmol) following procedure F, was purified by sublimation (150 °C, 1 Torr) to give a colourless solid (109 mg, 74%). M.p. 201 °C. ^{1}H NMR (CD_3OD): δ = 2.29 (s, 6 H), 7.36 (s, 2 H), 7.64 (d, J = 6 Hz, 2 H), 8.47 (d, J = 6 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 16.7, 122.3, 126.3, 128.0, 129.5, 150.2, 150.9, 156.3 ppm. IR (KBr): $\tilde{\nu}$ = 643, 819, 829, 1197, 1218, 1268, 1309, 1332, 1428, 1479, 1594, 2916 cm^{-1}. $C_{13}H_{13}NO$ (199.24): C 78.36, H 6.58, N 7.03; found C 78.69, H 6.73, N 6.94.

4-(4′-Hydroxyphenyl)-1-methylpyridinium Iodide (24a): Crude **24a** was synthesized from **23a** (100 mg, 0.58 mmol) following procedure G. After recrystallization from EtOH pure **24a** was obtained as a colourless solid (120 mg, 65%) and only characterized by NMR spectroscopy. ^{1}H NMR (CD_3OD): δ = 4.33 (s, 3 H), 7.00 (d, J = 8.8 Hz, 2 H), 7.92 (d, J = 8.8 Hz, 2 H), 8.27 (d, J = 6.5 Hz, 2 H), 8.73 (d, J = 6.5 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 47.8, 117.8, 124.0, 125.4, 131.1, 146.0, 156.9, 163.4 ppm.

4-(4′-Hydroxy-2′-methylphenyl)-1-methylpyridinium Iodide (24b): Compound **24b** was synthesized from **23b** (212 mg, 1.14 mmol) following procedure G and was obtained as a colourless solid (356 mg, 95%). Iodide **24b** was only characterized by NMR spectroscopy. ^{1}H NMR (CD_3OD): δ = 2.38 (s, 3 H), 4.24 (s, 3 H), 6.56–6.58 (m, 2 H), 7.26 (d, J = 9.3 Hz, 1 H), 7.88 (d, J = 6.8 Hz, 2 H), 8.52 (d, J = 6.8 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 21.8, 47.1, 119.6, 120.8, 123.8, 126.5, 133.8, 139.5, 144.3, 159.7, 173.9 ppm.

4-(4′-Hydroxy-2′,6′-dimethylphenyl)-1-methylpyridinium Iodide (24c): Compound **24c** was synthesized from **23c** (500 mg, 2.5 mmol) following procedure G and was obtained as a colourless solid (556 mg, 65%). Iodide **24c** was only characterized by NMR spectroscopy. ^{1}H NMR (CD_3OD): δ = 2.05 (s, 6 H), 4.45 (s, 3 H), 6.65 (s, 2 H), 7.94 (d, J = 6.5 Hz, 2 H), 8.91 (d, J = 6.5 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 20.9, 48.7, 116.1, 128.6, 131.0, 137.7, 146.4, 159.5, 160.9 ppm.

4-(2′,6′-Diethyl-4′-hydroxyphenyl)-1-methylpyridinium Iodide (24d): Compound **24d** was synthesized from **23d** (200 mg, 0.88 mmol) fol-

lowing procedure G and was obtained as a colourless solid (231 mg, 71%). Iodide **24d** was only characterized by NMR spectroscopy. ^{1}H NMR (CD_3OD): δ = 1.03 (t, J = 7.5 Hz, 6 H), 2.29 (q, J = 7.5 Hz, 4 H), 4.46 (s, 3 H), 6.67 (s, 2 H), 7.92 (d, J = 6.5 Hz, 2 H), 8.91 (d, J = 6.5 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 15.8, 27.6, 49.4, 114.2, 127.4, 131.1, 143.8, 146.2, 159.8, 160.9 ppm.

4-(4′-Hydroxy-2′,6′-diisopropylphenyl)-1-methylpyridinium Iodide (24e): Compound **24e** was synthesized from **23e** (80 mg, 0.31 mmol) following procedure G and was obtained as a colourless solid (75 mg, 60%). Iodide **24e** was only characterized by NMR spectroscopy. ^{1}H NMR (CD_3OD): δ = 1.12 (d, J = 6.8 Hz, 12 H), 2.41 (sept, 6.8 Hz, 2 H), 4.46 (s, 3 H), 6.74 (s, 2 H), 7.94 (d, J = 6.5 Hz, 2 H), 8.89 (d, J = 6.5 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 24.3, 31.7, 48.8, 111.3, 126.5, 131.6, 146.2, 148.6, 160.3, 161.5 ppm.

4-(4′-Hydroxy-2′,3′,5′,6′-tetramethylphenyl)-1-methylpyridinium Iodide (24f): Compound **24f** was synthesized from **23f** (200 mg, 0.88 mmol) following procedure G and was obtained as a colourless solid (195 mg, 60%). Iodide **24f** was only characterized by NMR spectroscopy. ^{1}H NMR (CD_3OD): δ = 1.94 (s, 6 H), 2.20 (s, 6 H), 4.44 (s, 3 H), 7.86 (d, J = 5.8 Hz, 2 H), 8.88 (d, J = 5.8 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD, DEPT): δ = 12.7, 18.0, 48.5, 123.0, 129.9, 131.2, 132.0, 146.3, 155.0, 162.9 ppm.

4-(4′-Hydroxy-3′,5′-dimethylphenyl)-1-methylpyridinium Iodide (24g): Compound **24g** was synthesized from **23g** (65 mg, 0.32 mmol) following procedure G and was obtained as a colourless solid (106 mg, 95%). Iodide **24g** was only characterized by NMR spectroscopy. ^{1}H NMR (CD_3OD): δ = 2.32 (s, 6 H), 4.30 (s, 3 H), 7.86 (s, 2 H), 8.26 (d, J = 7 Hz, 2 H), 8.67 (d, J = 6.8 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 20.9, 115.1, 119.3, 127.9, 128.7, 132.9, 139.2, 145.8, 159.7, 161.2 ppm.

1-Butyl-4-(4′-hydroxy-2′,6′-dimethylphenyl)pyridinium Iodide (25c): Crude **25c** was synthesized from **23c** (70 mg, 0.35 mmol) following procedure G and recrystallized from isopropanol to give a colourless solid (85 mg, 63%). Pure **25c** was only characterized by NMR spectroscopy. ^{1}H NMR (CD_3OD): δ = 1.04 (t, J = 7.3 Hz, 3 H), 1.48 (sext., 7.8 Hz, 2 H), 2.05 (s, 6 H), 2.06 (m, 2 H), 4.66 (t, J = 7.8 Hz, 2 H), 6.65 (s, 2 H), 7.94 (d, J = 6.3 Hz, 2 H), 8.98 (d, J = 6.3 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 13.8, 20.5, 20.9, 34.3, 62.3, 116.1, 128.4, 131.2, 137.6, 145.4, 159.5, 161.2 ppm.

4-(4′-Hydroxyphenyl)-1-octylpyridinium Iodide (26a): Crude **26a** was synthesized from **23a** (100 mg, 0.6 mmol) following procedure G and recrystallized from isopropanol to give a colourless solid (161 mg, 67%). Pure **26c** was only characterized by NMR spectroscopy. ^{1}H NMR (CD_3OD): δ = 0.89 (t, J = 5.8 Hz, 3 H), 1.22–1.45 (m, 10 H), 2.01 (m, 2 H), 4.52 (t, J = 7.5 Hz, 2 H), 6.99 (d, J = 8.8 Hz, 2 H), 7.93 (d, J = 8.8 Hz, 2 H), 8.28 (d, J = 6.7 Hz, 2 H), 8.80 (d, J = 6.7 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 14.4, 23.6, 27.2, 30.0, 30.1, 32.3, 32.8, 61.6, 117.8, 124.3, 125.5, 131.2, 145.2, 157.2, 163.6 ppm.

4-(4′-Hydroxy-2′,6′-dimethylphenyl)-1-octylpyridinium Iodide (26c): Crude **26c** was synthesized from **23c** (100 mg, 0.5 mmol) following procedure G and recrystallized from acetonitrile to give a colourless solid (167 mg, 76%). Pure **26c** was only characterized by NMR spectroscopy. ^{1}H NMR (CD_3OD): δ = 0.9 (t, J = 6.6 Hz, 3 H), 1.31–1.43 (m, 10 H), 2.05 (s, 6 H), 2.08 (m, 2 H), 4.65 (t, J = 7.6 Hz, 2 H), 6.65 (s, 2 H), 7.94 (d, J = 6.5 Hz, 2 H), 8.98 (d, J = 6.5 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 14.1, 20.9, 23.6, 27.2, 30.0, 30.1, 32.4, 32.8, 62.6, 116.1, 128.5, 131.3, 137.7, 145.5, 159.7, 161.3 ppm.

4-(2′,6′-Diethyl-4′-hydroxyphenyl)-1-octylpyridinium Iodide (26d): Crude **26d** was synthesized from **23d** (50 mg, 0.22 mmol) following procedure G and was recrystallized from AcOEt to give a colourless solid (65 mg, 63%). Pure **26d** was only characterized by NMR spectroscopy. ^{1}H NMR (CD_3OD): δ = 0.9 (t, J = 7.0 Hz, 3 H), 1.03 (t, J = 7.5 Hz, 6 H), 1.32–1.42 (m, 10 H), 2.09 (m, 2 H), 2.29 (q, J = 7.5 Hz, 4 H), 4.67 (t, J = 7.5 Hz, 2 H), 6.68 (s, 2 H), 7.96 (d, J = 6.5 Hz, 2 H), 8.99 (d, J = 6.5 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 14.4, 15.7, 23.6, 27.2, 27.6, 30.0, 30.1, 32.3, 32.8, 62.6, 114.3, 127.4, 131.5, 143.8, 145.3, 160.0, 161.3 ppm.

4-(1′-Methylpyridinio)phenolate (2a): Compound **2a** was obtained from **24a** (183 mg, 0.58 mmol) following procedure H and was recrystallized from *i*PrOH to give a yellow solid (93 mg, 72%). M.p. 120 °C (decomp.). ^{1}H NMR (CD_3OD): δ = 4.16 (s, 3 H), 6.70 (d, J = 8.8 Hz, 2 H), 7.80 (d, J = 8.8 Hz, 2 H), 8.05 (d, J = 7.0 Hz, 2 H), 8.40 (d, J = 7.0 Hz, 2 H) ppm. ^{1}H NMR (CD_3OD, NaOH): δ = 4.14 (s, 3 H), 6.67 (d, J = 8.8 Hz, 2 H), 7.77 (d, J = 8.8 Hz, 2 H), 8.01 (d, J = 7.0 Hz, 2 H), 8.35 (d, J = 7.0 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 46.3, 117.3, 120.7, 121.7, 131.1, 144.2, 156.4, 177.1 ppm. IR (KBr): $\tilde{\nu}$ = 492, 683, 829, 1180, 1233, 1314, 1355, 1496, 1554, 1579, 1652, 3230, 3385 cm^{-1}. $C_{12}H_{11}NO{\cdot}2H_2O$ (221.25): C 65.14, H 6.83, N 6.33; found C 65.5, H 6.7, N 6.6.

2-Methyl-4-(1′-methylpyridinio)phenolate (2b): Compound **2b** was obtained from **24b** (351 mg, 1.07 mmol) following procedure H as an orange solid (245 mg, 97%). M.p. 142 °C (decomp.). ^{1}H NMR (CD_3OD): δ = 2.37 (s, 3 H), 4.23 (s, 3 H), 6.57 (d, J = 6.8 Hz, 2 H), 7.26 (d, J = 8.8 Hz, 1 H), 7.87 (d, J = 6.8 Hz, 2 H), 8.51 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 21.8, 47.1, 119.6, 120.8, 123.8, 126.5, 133.8, 139.5, 144.3, 159.7, 173.9 ppm. IR (KBr): $\tilde{\nu}$ = 542, 823, 1105, 1198, 1242, 1303, 1338, 1357, 1478, 1492, 1522, 1558, 1580, 1639, 3024, 3140 cm^{-1}. $C_{13}H_{13}NO{\cdot}2H_2O$ (235.28): C 66.36,H 7.28, N 5.95; found C 65.67, H 6.66, N 5.66. HRMS (ESI-Q-Tof): calcd. for $C_{13}H_{13}NO$ $[M]^{+\cdot}$ 199.0997; found 199.0992.

2,6-Dimethyl-4-(1′-methylpyridinio)phenolate (2c): Compound **2c** was obtained from **24c** (790 mg, 2.3 mmol) following procedure H as a dark orange solid (381 mg, 66%). M.p. 128 °C (decomp.). ^{1}H NMR (CD_3OD): δ = 2.03 (s, 6 H), 4.36 (s, 3 H), 6.47 (s, 2 H), 7.76 (d, J = 6.5 Hz, 2 H), 8.71 (d, J = 6.5 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 21.1, 47.9, 120.1, 123.1, 130.9, 137.1, 145.2, 162.1, 169.6 ppm. IR (KBr): $\tilde{\nu}$ = 512, 593, 853, 863, 1166, 1336, 1455, 1464, 1470, 1579, 1634, 2917, 3030, 3110, 3390 cm^{-1}. $C_{14}H_{15}NO{\cdot}2H_2O$ (249.30): C 67.40, H 7.68, N 5.61; found C 67.28, H 7.13, N 5.37. HRMS (ESI-Q-Tof): calcd. for $C_{14}H_{15}NO$ $[M]^{+\cdot}$ 213.1154; found 213.1147.

2,6-Diethyl-4-(1′-methylpyridinio)phenolate (2d): Compound **2d** was obtained from **24d** (150 mg, 0.13 mmol) following procedure H (washing was performed with CH_2Cl_2/Et_2O 1:2) as a dark orange solid (36 mg, 96%). M.p. 130 °C (decomp.). ^{1}H NMR (CD_3OD): δ = 0.99 (t, J = 7.6 Hz, 6 H), 2.27 (q, J = 7.6 Hz, 4 H), 4.39 (s, 3 H), 6.51 (s, 2 H), 7.81 (d, J = 6.5 Hz, 2 H), 8.75 (d, J = 6.5 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 16.0, 27.6, 48.1, 118.1, 122.3, 131.4, 143.2, 145.4, 162.4, 169.6 ppm. IR (KBr): $\tilde{\nu}$ = 681, 854, 864, 1160, 1217, 1278, 1312, 1342, 1458, 1577, 1637, 2875, 2966, 3088, 3044, 3116, 3410 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{16}H_{19}NO$ $[M]^{+\cdot}$ 241.1467; found 241.1441.

2,6-Diisopropyl-4-(1′-methylpyridinio)phenolate (2e): Compound **2e** was obtained from **24e** (73 mg, 0.18 mmol) following procedure H (washing was performed with CH_2Cl_2/Et_2O 1:2) as a yellow solid (37 mg, 67%). M.p. 210 °C (decomp.). ^{1}H NMR (CD_3OD): δ = 1.08 (d, J = 6.8 Hz, 12 H), 2.39 (sept, 6.8 Hz, 2 H), 4.40 (s, 3 H), 6.59 (s, 2 H), 7.84 (d, J = 6.5 Hz, 2 H), 8.77 (d, J = 6.5 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 24.5, 31.5, 48.1, 114.8, 121.3, 131.5, 145.3, 147.5, 163.4, 169.6 ppm. IR (KBr): $\tilde{\nu}$ = 865, 971, 1184,

1254, 1312, 1349, 1365, 1384, 1465, 1583, 1636, 2869, 2929, 3041, 3112, 3390 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{18}H_{23}NO$ $[M]^{+}$ 269.178; found 269.1802.

2,3,5,6-Tetramethyl-4-(1′-methylpyridinio)phenolate (2f): Compound **2f** was obtained from **24f** (70 mg, 0.2 mmol) following procedure H (washing was performed with CH_2Cl_2/Et_2O 1:2) as a red solid (39 mg, 74%). M.p. 150 °C (decomp.). ^1H NMR (CD_3OD): δ = 1.95 (s, 6 H), 2.18 (s, 6 H), 4.37 (s, 3 H), 7.76 (d, J = 6.5 Hz, 2 H), 8.72 (d, J = 6.5 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 13.5, 18.4, 47.8, 124.1, 124.5, 131.2, 131.4, 145.0, 164.1, 164.9 ppm. IR (KBr): $\tilde{\nu}$ = 524, 607, 630, 670, 755, 766, 879, 1166, 1222, 1281, 1338, 1411, 1446, 1564, 1641, 2918, 2964, 3023, 3372 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{16}H_{19}NO$ $[M]^{+}$ 241.1467; found 241.1454.

3′,5′-Dimethyl-4-(1′-methylpyridinio)phenolate (2g): Compound **2g** was obtained from **24g** (485 mg, 1.42 mmol) following procedure H as an orange solid (322 mg, 91%). M.p. >260 °C. ^1H NMR (CD_3OD): δ = 2.18 (s, 6 H), 4.03 (s, 3 H), 7.57 (s, 2 H), 7.87 (d, J = 6.8 Hz, 2 H), 8.16 (d, J = 6.8 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 18.1, 45.9, 115.7, 119.9, 129.4, 143.5, 155.9, 176.1 ppm. IR (KBr): $\tilde{\nu}$ = 490, 764, 836, 1036, 1076, 1191, 1214, 1306, 1343, 1432, 1473, 1583, 1643, 3280, 3393 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{14}H_{15}NO$ $[M]^{+}$ 213.1154; found 213.112.

4-(1′-Butylpyridinio)-2,6-dimethylphenolate (3c): Compound **3c** was obtained from **25c** (70 mg, 0.18 mmol) following procedure H as a yellow solid (38 mg, 72%). M.p. 160–180 °C (decomp.). ^1H NMR (CD_3OD): δ = 1.04 (t, J = 7.3 Hz, 3 H), 1.45 (sext., 7.5 Hz, 2 H), 2.04 (m, 8 H), 4.57 (t, J = 7.5 Hz, 2 H), 6.47 (s, 2 H), 7.84 (d, J = 6.5 Hz, 2 H), 8.80 (d, J = 6.5 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 13.8, 20.5, 21.1, 34.2, 61.8, 120.0, 123.3, 131.2, 137.2, 144.3, 162.3, 169.2 ppm. IR (KBr): $\tilde{\nu}$ = 599, 740, 862, 1164, 1337, 1467, 1579, 1634, 1658, 2873, 2933, 2948, 3038, 3112, 3201, 3399 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{17}H_{21}NO$ $[M]^{+}$ 255.1623; found 255.1599.

4-(1′-Octylpyridinio)phenolate (4a): Compound **4a** was obtained from **26a** (106 mg, 0.26 mmol) following procedure H as a yellow solid (29 mg, 35%). M.p. 70 °C. ^1H NMR (CD_3OD): δ = 0.91 (t, J = 6.8 Hz, 3 H), 1.20–1.35 (m, 10 H), 1.74–2.05 (m, 2 H), 4.35 (t, J = 7.5 Hz, 2 H), 6.67 (d, J = 8.6 Hz, 2 H), 7.79 (d, J = 8.6 Hz, 2 H), 8.03 (d, J = 6.5 Hz, 2 H), 8.43 (d, J = 8.6 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 14.8, 24.0, 27.6, 30.5, 30.6, 32.5, 33.3, 60.9, 118.1, 121.5, 122.3, 131.7, 144.0, 157.5, 177.5 ppm. IR (KBr): $\tilde{\nu}$ = 835, 1161, 1173, 1317, 1370, 1466, 1496, 1587, 1644, 2853, 2924, 2956, 3300 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{19}H_{25}NO$ $[M]^{+}$ 285.1936; found 283.1906.

2,6-Dimethyl-4-(1′-octylpyridinio)phenolate (4c): Compound **4c** was obtained from **26c** (30 mg, 0.07 mmol), following procedure H as an orange solid (20 mg, 85%). M.p. 120–125 °C (decomp.). ^1H NMR (CD_3OD): δ = 0.90 (t, J = 6.5 Hz, 3 H), 1.31–1.41 (m, 10 H), 2.04 (m, 6 H), 2.04 (m, 2 H), 4.56 (t, J = 7.3 Hz, 2 H), 6.46 (s, 2 H), 7.84 (d, J = 6.5 Hz, 2 H), 8.79 (d, J = 6.5 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 14.4, 21.2, 23.6, 27.2, 30.0, 30.1, 32.3, 32.8, 62.0, 120.6, 122.6, 131.2, 137.1, 144.2, 162.5, 170.6 ppm. IR (KBr): $\tilde{\nu}$ = 597, 694, 864, 1167, 1327, 1344, 1466, 1575, 1635, 2856, 2926, 2954, 3026, 3040, 3272, 3338 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{21}H_{29}NO$ $[M]^{+}$ 311.2249; found 311.2228.

2,6-Diethyl-4-(1′-octylpyridinio)phenolate (4d): Compound **4d** was obtained from **26d** (65 mg, 0.14 mmol) following procedure H. After reaction and removal of the solvents, CH_2Cl_2/AcOEt (7:13, 15 mL per 1 mmol) was added to the crude material. The precipitate was filtered and washed with a mixture of CH_2Cl_2/AcOEt (7:13) and dried to give **4d** as an orange solid (34 mg, 67%). M.p. 100 °C (decomp.). ^1H NMR (CD_3OD): δ = 0.90 (t, J = 6.8 Hz, 3 H), 0.99 (t, J = 7.3 Hz, 6 H),1.31–1.40 (m, 10 H), 2.00–2.08 (m, 2 H), 2.28 (q, J = 7.3 Hz, 4 H), 4.60 (t, J = 7.3 Hz, 2 H), 6.52 (s, 2 H), 7.85 (d, J = 6.3 Hz, 2 H), 8.84 (d, J = 6.3 Hz, 2 H) ppm. ^{13}C NMR (CD_3OD): δ = 14.4, 16.0, 23.6, 27.2, 27.7, 30.0, 30.2, 32.3, 32.8, 62.2, 118.1, 122.2, 131.7, 143.2, 144.5, 162.8, 169.6 ppm. IR (KBr): $\tilde{\nu}$ = 860, 1109, 1159, 1286, 1306, 1340, 1353, 1457, 1576, 1635, 2856, 2871, 2926, 2964, 3036, 3247, 3448 cm^{-1}. HRMS (ESI-Q-Tof): calcd. for $C_{23}H_{33}NO$ $[M]^{+}$ 339.2562; found 339.2536.

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