Efficient synthesis of pyridines *via* a sequential solventless aldol condensation and Michael addition †

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The aldol condensation of an enolisable ketone and a benzaldehyde followed by Michael addition of the enone with a second enolisable ketone under solvent free conditions leads to the quantitative formation of a diketone, which can be readily converted to a pyridine (typically >80% overall yield) *via* a double condensation in the presence of ammonium acetate in acetic acid, allowing access to a diverse range of oligopyridyls including bipyridyls and terpyridyls.

Introduction

Pyridine functionalities have been both widely studied,[1,2] and widely used,[3–6] but still generate much interest.[7–11] Kröhnke type pyridines,[1] and other substituted pyridines including the related terpyridines, are prominent building blocks in both organic and inorganic supramolecular chemistry,[6,7,12,13] with their π-stacking ability, directional H-bonding and coordination properties. The luminescence properties stemming from the conjugated aromatic cores of these molecules continue to be studied,[14] with varying applications including liquid crystals,[4] photosensitisers,[10] and studying biochemical DNA binding reaction mechanisms.[15] Studies into the possible medical applications of substituted terpyridines have shown promising results, attributed to their ability to form complexes with metals, although the toxicity of previously synthesised materials has hampered clinical trials.[16] The significance of being able to synthesise such substituted terpyridines for use in pharmacological testing is evident by observing the increasing number of associated international patents in recent years.[17] There is also a growing interest in utilizing the excellent thermal stability of aromatic pyridines as monomeric units in organic, inorganic and organometallic polymers.[3,18,19]

Despite the continual research surrounding such molecules, the methodologies used to synthesise these compounds has changed little since Kröhnke's review article in 1976.[1] In general, conventional methods used in the synthesis of substituted pyridines involve volatile organic solvents and display only moderate to low yields with low atom efficiency.[1] In developing a more versatile route to such compounds, where possible adopting the principles of 'Green Chemistry',[20] we have established that using solventless conditions for a sequential aldol (Knoevengel) and Michael addition reaction results in a dramatic improvement in yield, and indeed allows access to a range of compounds not accessible using conventional methods involving organic solvents. Overall, this versatile new approach can be applied to the synthesis of a range of symmetrical and unsymmetrical terpyridines, and pyridines in general bearing aryl groups in the 2, 4 and 6 positions.

† Electronic supplementary information (ESI) available: summary of the waste from the syntheses of 4,6-diphenyl-2,3′-bipyridine and 4′-phenyl-4,2′:6′,4″-terpyridyl by the conventional and green routes. See http://www.rsc.org/suppdata/p1/b1/b107302h/

The significance of our approach also relates to reducing the use of organic solvents as potentially toxic and hazardous materials,[20] as well as its simplicity and mild conditions, and inherent lower costs, with more likely downstream applications. Moreover, the findings are further evidence to challenge the conventional view of using organic solvents in synthesis even in the absence of reasons to do so.[21] The use of solventless reactions is gaining prominence with recent advances in solventless reactions under mild conditions including the aldol condensation,[21–24] and others recently reviewed by Tanaka and Toda.[21]

We recently published our preliminary results relating to this work, demonstrating its simplicity and potential diversity.[25] Herein we have extended our studies to include previously reported compounds in order to draw a qualitative comparison of procedures, together with the synthesis and characterisation of several new pyridines, and an improved technique to our original protocol for isolating the pure product. In keeping with our 'green' approach to organic chemistry we have also synthesised all non-commercially available starting alkoxybenzaldehydes and alkoxyacetophenones using recyclable polypropylene glycol as a low vapour pressure reaction medium.[26]

Results and discussion

The conventional synthesis of enones **3** from a benzaldehyde **1** and an aryl ketone **2** involves the preliminary synthesis of the enolate by solubilising the ketone in a basic alcohol solution. This is subsequently added to an alcoholic solution of the aldehyde, resulting in the formation of the product as a precipitate, which is collected and washed with water and ethanol to yield the enone product in *ca.* 90% yield.[4] By putting aside the time honoured prerequisite for solvent, we have found, by grinding/mixing the reactants together in the presence of a catalytic quantity of base, that the aldol condensation proceeds as in solution, however, the product forms essentially quantitatively (Scheme 1). The product was isolated without the need for recrystallisation, by washing with water to remove the catalyst. The efficiency of the solventless reaction can be seen from the ^{1}H NMR of the product formed by grinding/mixing equimolar quantities of benzaldehyde and acetophenone with NaOH, after being washed with water to remove the base (Fig. 1).

Benzaldehyde and acetophenone are both colourless liquids at room temperature (Fig. 2, part 1); upon the addition of the

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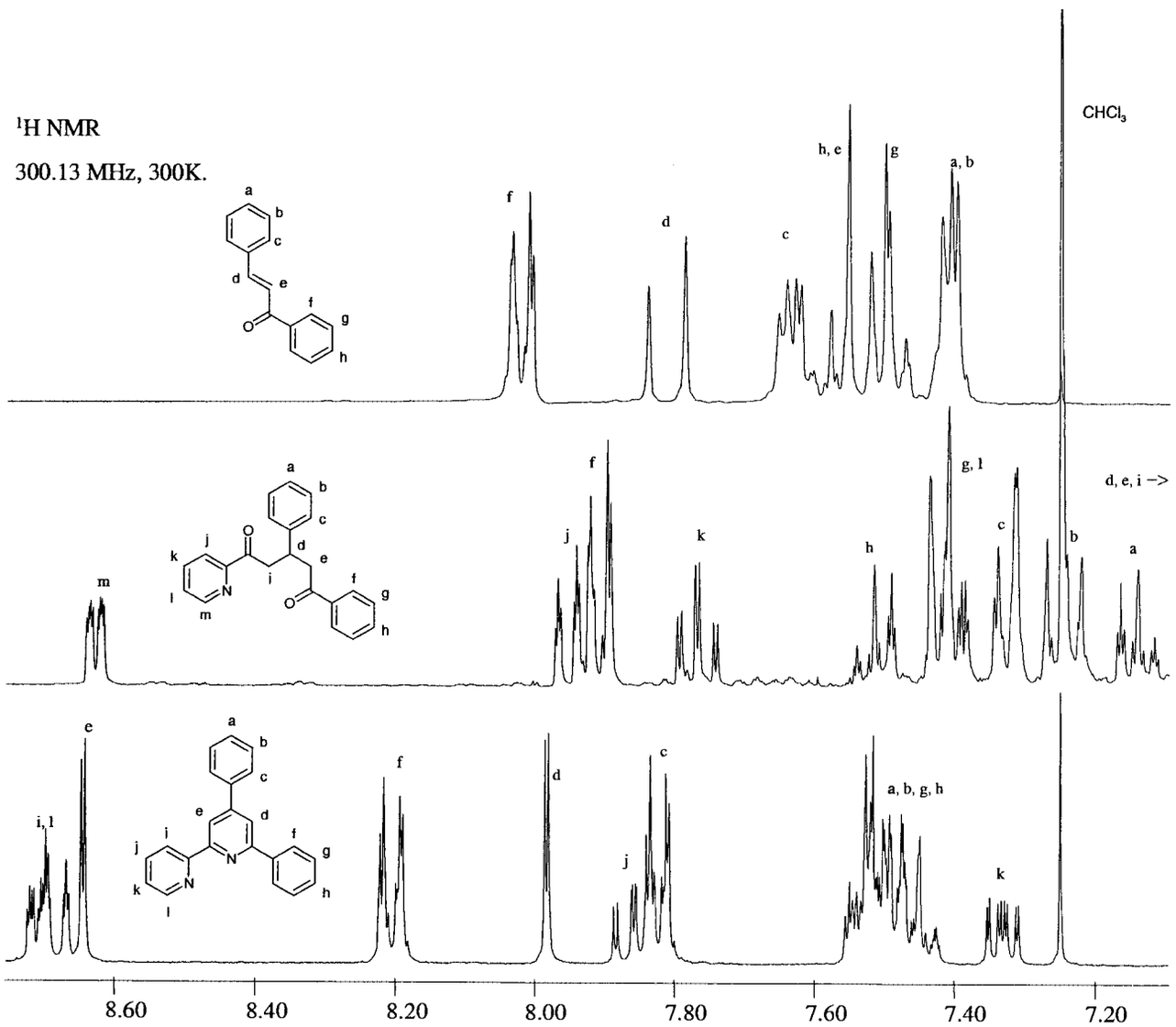


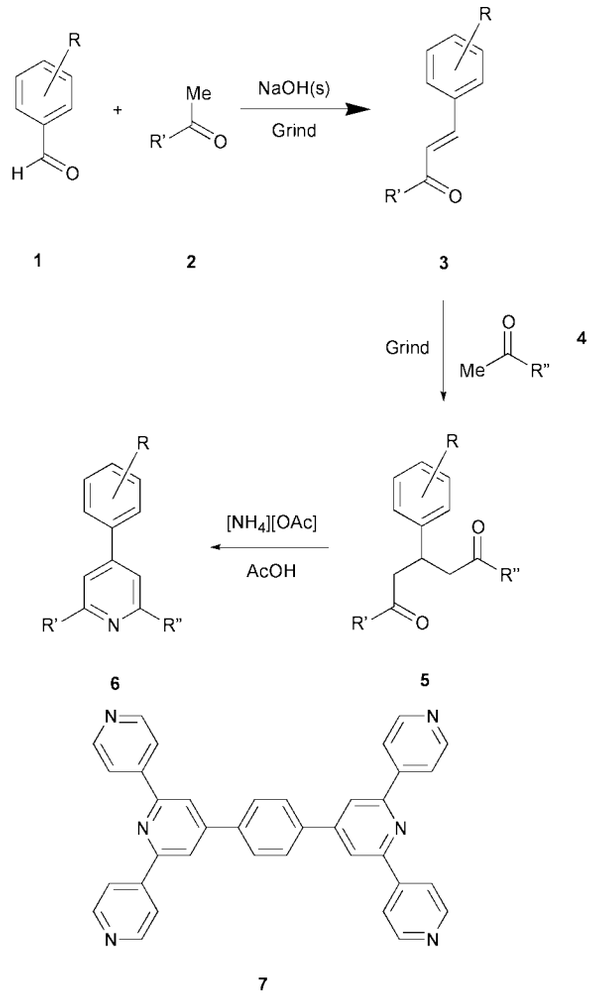
Fig. 1 ^{1}H NMR spectra of **3b** (top), **5b** (middle), **6b** (bottom).

NaOH the liquids immediately turn yellow indicating the formation of the enolate (Fig. 2, part 2). By aggregating the reaction mixture using a mortar and pestle, the viscosity rapidly increases to form a tacky solid after *ca.* 5 min of constant mixing (Fig. 2, part 3). The pliable solid can be left to harden (*ca.* 30 min) as the solid aldol product; this phase transition can be accelerated by continuing the grinding for a further 5 min, resulting in the formation of the aldol product, **3a**, as an amorphous powder (Fig. 2, part 4). These solventless aldol condensations from liquid–liquid, liquid–solid and solid–solid starting materials all proceed cleanly and demonstrate quantitative yields of the enone. During the reaction between two solids, the reaction mixture undergoes a phase transition into a eutectic melt (Fig. 2, part 5). We note that, by grinding the solid starting materials in the absence of the base catalyst, this eutectic phase can be reproduced; however, there is no observed conversion to the aldol product upon workup.

The synthesis of pyridines bearing aryl groups in the *ortho* and *para* positions with respect to the nitrogen of the central pyridine ring *via* conventional Kröhnke syntheses proceeds by treating an unsaturated ketone with the pyridinium salt formed by reacting halogenated-methyl ketone with pyridine, to produce the Michael addition product **5**. Although this step is reported to be high yielding, the byproducts of the reaction generate significant waste and the reagents are expensive. Some researchers report that often the direct reaction of the enone with an enolisable aryl methyl ketone in a basic solution proceeds to the 1,5-diketone,[8] thus eliminating the preliminary pyridinium salt formation. By this rationale, we synthesised the 1,5-diketone by grinding the aldol product **3** with a second enolisable aryl ketone **4**, in the presence of NaOH, with complete conversion. The ^{1}H NMR of the washed (water) crude product formed by the solventless Michael addition of 2-acetylpyridine and 1,3-diphenylpropenone demonstrates clearly the efficiency of the reaction (Fig. 1, middle) to form the 1,5-diketone. As observed for the aldol condensation during the grinding process, the reaction medium forms as before, solidifying to form the pure 1,5-diketone (Fig. 2, part 5).

The complete conversion of the benzaldehyde **1** and aryl ketone **2** to the enone **3** enables the second ketone **4** to be added directly to the reaction mixture following the aldol condensation, thereby eliminating an intermediate purification step, and without the need for further addition of NaOH. When synthesising the symmetrical pyridines, *i.e.* **2** = **4**, it is possible to add two equivalents of the ketone to the aldehyde without first having to isolate the enone. During this process it is possible to see the transition from the enone intermediate to the 1,5-diketone by way of a colour change from cream/white to pink (Fig. 2, part 6). This protocol is also quantitative.

It is noteworthy that when the solvent based methods are adopted in an attempt to prepare 4′-(4-alkoxyphenyl)-4,2′:6′,4″-terpyridines, only the cyclohexyl product **8** (Fig. 3) could be isolated from the complex reaction mixture which is devoid of target molecules. Compound **8**, which was character-



Scheme 1

ised using NMR data, R = OC_4H_9,[25] and X-ray diffraction data,[27] R = H, does however, incorporate the expected diketone moiety. Indeed, a relatively recent paper describes the synthesis of **6h** under somewhat harsh conditions with a moderate 6% overall yield.[28]

The formation of the pyridine ring is achieved by reacting the 1,5-diketone with ammonium acetate in a minimum volume of boiling acetic acid over 1 to 2 h, which involves aerial oxidation. During this time, the reaction mixture turns from a pale yellow solution to a deep green or blue in colour. The final product can then be precipitated out of solution by the addition of water to the reaction mixture, collected and washed with ethanol to ate the pure product in high yield often as crystalline solids, *e.g.* **6m**, Fig. 4. Although this stage of the synthesis requires the use of a solvent, it should be noted that the low vapour-pressure of the acetic acid allows the use of an air condenser during the reflux. Following the workup process, the acetic acid can be efficiently regenerated and used as a batch process. The chosen solvent is also a naturally renewable source in alignment with the principles of green chemistry).

By utilising the above techniques, we have synthesised several novel building blocks (Table 1) which will potentially be used as supramolecular synthons, polymeric monomers, coordination ligands, mono- and di-cyclometallation ligands, and be tested for pharmacological properties. The added halogen functionality on the terminal carbon of the alkyl chains in compounds **6s**–**6v** also allows for great scope.

The elimination of volatile organic solvents in the synthesis of Kröhnke type pyridines has obvious environmental benefits in regard to the depletion of solvent waste; the simplicity and efficiency of the overall process also significantly reduces the quantities of solid waste. Previously reported synthesis generate

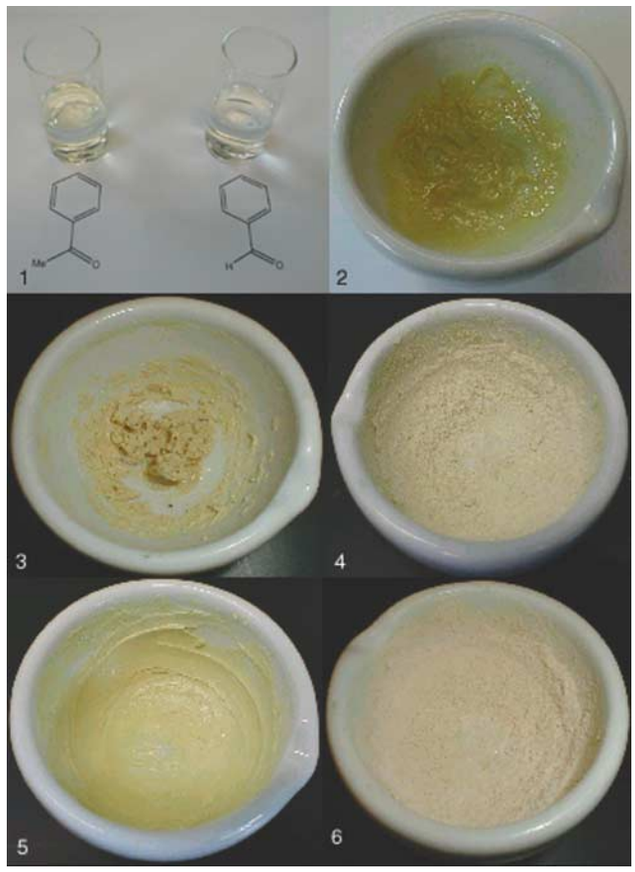


Fig. 2 Photographic plates. (1) Benzaldehyde and acetophenone liquids; (2) enolate, t = 0; (3) initial formation of aldol product as a tacky solid, t = 5 min; (4) complete conversion to enone, t = 10 min; (5) eutectic melt; (6) amorphous 1,5-diketone product.

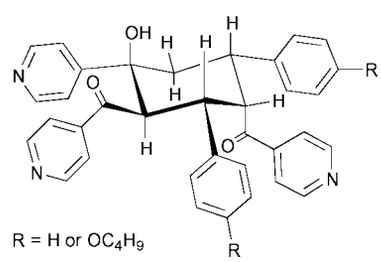


Fig. 3 Compound **8**, showing the Michael addition product **5h** moiety.

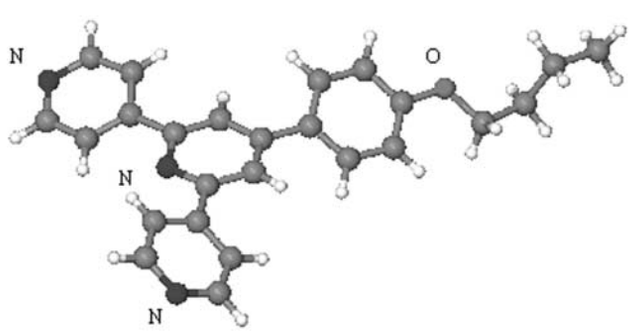


Fig. 4 A view of one of the two independent molecules of 4′-(4-butyloxyphenyl)-4,2′:6′,4″-terpyridine, **6m**.

over 29 times more solid waste than the 'greener' route to the same compound. We have calculated that even the most efficient synthetic protocols produce *ca.* 3.3 kg of waste per 1 kg of product. This novel method is also a cost effective alternative to commercially available products, and is estimated to be *ca.* 600% more cost effective than previously published procedures,[29] not taking into account the cost of waste disposal and energy usage.

Table 1 Summary of solventless reactions and conversion of the products to the pyridines (% yield)

	1	2	4	Method	Yield (%)	Lit. yield (%)
6a	Benzaldehyde	Acetophenone	Acetophenone	B	89	92[a] [1]
6b	Benzaldehyde	Acetophenone	2-Acetylpyridine	A	89	73[b] [1]
6c	Benzaldehyde	Acetophenone	3-Acetylpyridine	A	84	—
6d	Benzaldehyde	Acetophenone	4-Acetylpyridine	A	86	—
6e	Benzaldehyde	Acetophenone	4-Iodoacetophenone	A	78	—
6f	Benzaldehyde	Acetophenone	4-Bromoacetophenone	A	92	84[c] [32]
6g	Benzaldehyde	2-Acetylpyridine	2- Acetylpyridine	B	79	47[c] [33]
6h	Benzaldehyde	4-Acetylpyridine	4-Acetylpyridine	B	84	6[d] [21]
6i	Benzaldehyde	4-Octyloxyacetophenone	4-Octyloxyacetophenone	B	78	—
6j	Benzaldehyde	4-Nitroacetophenone	4-Nitroacetophenone	B	74	65[d] [18]
6k	4-Butyloxybenzaldehyde	Acetophenone	Acetophenone	B	85	—
6l	4-Butyloxybenzaldehyde	2-Acetylpyridine	2-Acetylpyridine	B	80	—
6m	4-Butyloxybenzaldehyde	4-Acetylpyridine	4-Acetylpyridine	B	76	—
6n	4-Butyloxybenzaldehyde	2-Hydroxyacetophenone	2-Hydroxyacetophenone	B	64	—
6o	4-Octyloxybenzaldehyde	4-Acetylpyridine	4-Acetylpyridine	B	86	—
6p	4-Octyloxybenzaldehyde	4-Iodoacetophenone	4-Iodoacetophenone	B	85	—
6q	4-Bromobenzaldehyde	2-Acetylpyridine	2-Acetylpyridine	B	75	19[d] [19]
6r	4-Bromobenzaldehyde	4-Acetylpyridine	4-Acetylpyridine	B	81	—
6s	4-(4′-Bromobutoxy)benzaldehyde	2-Acetylpyridine	2-Acetylpyridine	B	89	—
6t	4-(4′-Bromobutoxy)benzaldehyde	3-Acetylpyridine	3-Acetylpyridine	B	88	—
6u	4-(4′-Bromobutoxy)benzaldehyde	4-Acetylpyridine	4-Acetylpyridine	B	86	—
6v	4-(4′-Bromobutoxy)benzaldehyde	Acetophenone	Acetophenone	B	90	—
6w	4-Hydroxybenzaldehyde	3-Acetylpyridine	3-Acetylpyridine	B	67	—
7	Terephthalaldehyde	4-Acetylpyridine	4-Acetylpyridine	B	87	—

[a] Calculated from pyridinium salt. [b] Calculated from alkylphosphonate. [c] Calculated from diketone. [d] Calculated from aldehyde.

Experimental

General

All chemicals were used as supplied; unless noted otherwise. The benzaldehyde derivatives were prepared in polypropylene glycol, as previously reported.[27] NMR spectra were recorded on a Bruker DPX300 spectrometer and referenced to TMS. Mass spectra were recorded using Chemical Ionisation or Electrospray Ionisation techniques on a Bruker BioApex 47e FTMS (4.7 T) fitted with an Analytica electrospray source spectrometer. The infrared spectra were recorded on a Perkin Elmer 1610 FTIR in the range 4000–400 cm^{-1} as KBr discs. X-Ray data were recorded on an Enraf-Nonius KappaCCD diffractometer (123 K). All elemental analyses were performed by Chemical and Micro Analytical Services, Australia.

Method A

General procedure: 2,4,6-triphenylpyridine (6a). Acetophenone (2.345 g, 19.5 mmol), benzaldehyde (1.035 g 9.76 mmol) and NaOH (s) (0.82 g, 19.5 mmol) were combined using a mortar and pestle, and the yellow medium was aggregated until a yellow powder formed (*ca.* 10 min). The powder was transferred to a suspension of ammonium acetate (5 g, excess) in glacial acetic acid (25 cm^3, *ca.* 100%) and heated to reflux (2 h). The crude product was precipitated out of solution *via* the addition of water (10 cm^3), collected and washed with water and ethanol. Yield: 2.67 g (89%, 8.99 mmol). Anal. Found (calcd): C 89.50 (89.87), H 5.96 (5.57), N 4.95 (4.56)%. MS (EI^+, 70 eV, 200 °C) for $C_{23}H_{17}N$ ($[M]^+$): calcd: 307.39; found: 307. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.25 (d, 4H, ^3J = 8.5 Hz), 7.92 (s, 2H), 7.89–7.76 (m, 2H), 7.58–7.45 (m, 9H).^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 157.5, 150.2, 139.6, 139.1, 129.1, 129.0, 128.7, 127.1, 117.1.

Method B

General procedure: 1,3-diphenylpropenone (3). Acetophenone (1.17 g, 9.75 mmol), benzaldehyde (1.04 g 9.75 mmol) and NaOH (s) (0.41 g, 9.75 mmol) were combined using a mortar and pestle, and the yellow medium was aggregated until a pale yellow powder formed (*ca.* 10 min). The aldol product can be isolated by washing with water–ethanol, yielding the pure product as a white powder. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.02 (d, ^3J = 7.0 Hz, 2H), 7.81 (d, ^3J = 15.7 Hz, 1H), 7.63 (m, 2H), 7.52 (m, 4H), 7.40 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 191.9, 146.1, 139.6, 136.3, 134.1, 131.9, 130.3, 129.9, 129.8, 129.8, 123.5.

1,3-Diphenyl-5-pyridin-2-ylpentane-1,5-dione (5). 2-Acetylpyridine (1.18 g, 9.75 mmol), 1,3-diphenylpropenone (2.03 g, 9.75 mmol) and NaOH (s) (0.41g, 9.75 mmol) were mixed together using a mortar and pestle until a yellow powder was formed (*ca.* 10 min). The Michael addition product can be isolated by washing with water–ethanol, yielding the pure product as a white powder. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.55 (m, 1H), 7.88 (m, 1H), 7.83 (m, 2H), 7.69 (dt, ^3J = 7.65, ^4J = 1.73 Hz, 1H), 7.44 (m, 1H), 7.32 (m, 3H), 7.25 (m, 2H), 7.20 (t, ^3J = 7.48 Hz, 2H), 7.06 (m, 1H), 4.05 (m, 1H), 3.63 (m, 2H), 3.33 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 200.2, 198.7, 153.6, 149.0, 144.5, 137.3, 137.0, 133.1, 128.7, 128.5, 128.3, 127.8, 127.3, 126.7, 122.0, 45.4, 44.1, 36.8.

4,6-Diphenyl-2,2′-bipyridyl (6b). 1,3-Diphenyl-5-pyridin-2-ylpentane-1,5-dione (3.21 g, 9.75 mmol) and ammonium acetate (5 g, excess) were heated at reflux in acetic acid (25 cm^3, *ca.* 100%) (2 h) resulting in a colour change from colourless to dark green. The white product was precipitated out of solution *via* the addition of water (10 cm^3), collected and washed with water–ethanol. Overall yield: 2.66 g (89%, 8.64 mmol). Anal. Found (calcd): C 86.00 (85.69), H 5.55 (5.23), N 9.05 (9.08)%. MS (EI^+, 70 eV, 200 °C) for $C_{22}H_{16}N_2$ ($[M]^+$): calcd: 308.38; found: 308. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.63 (m, 2H), 8.57 (d, ^4J = 1.54 Hz, 1H), 8.13 (d, ^3J = 6.95 Hz, 2H), 7.91 (d, ^4J = 1.54 Hz, 1H), 7.75 (m, 3H), 7.42 (m, 6H), 7.26 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 157.2, 156.4, 156.3, 150.3, 149.1, 139.5, 138.8, 136.9, 129.1, 129.0, 128.9, 128.7, 127.3, 127.1, 123.8, 121.6, 118.5, 117.6.

4,6-Diphenyl-2,3′-bipyridyl (6c). The pure product was obtained as a white powder. Yield: 3.56 g, 84%. Anal. Found (calcd): C 85.70 (85.69), H 5.25 (5.23), N 9.00 (9.08)%. MS (EI^+, 70 eV, 200 °C) for $C_{22}H_{16}N_2$ ($[M]^+$): calcd: 308.38; found: 308. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 9.38 (d, ^4J = 1.8 Hz, 1H), 8.67 (dd, ^3J = 4.8, ^4J = 1.80 Hz, 1H), 8.51 (m, 1H), 8.19 (d, ^3J = 6.8 Hz, 2H), 7.93 (d, ^4J = 1.4 Hz, 1H), 7.88 (d,

^4J = 1.4 Hz, 1H), 7.37 (d, ^3J = 7.9 Hz, 2H), 7.50 (m, 7H). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 158.6, 155.5, 151.2, 150.5, 149.1, 139.8, 139.3, 135.7, 135.3, 129.9, 129.8, 129.7, 129.4, 127.8, 127.7, 124.2, 118.4, 117.7.

4,6-Diphenyl-2,4′-bipyridyl (6d). The pure product was obtained as a white powder. Yield: 3.56 g, 84%. Anal. Found (calcd): C 85.75 (85.69), H 5.30 (5.23), N 9.10 (9.08)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{22}H_{16}N_2$ ([M]$^+$): calcd: 308.38; found: 308. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.80 (AA′XX′, 2H), 8.19 (d, ^3J = 6.8 Hz, 2H), 8.09 (AA′XX′, 2H), 7.98 (d, ^4J = 1.4 Hz, 1H), 7.94 (d, ^4J = 1.4 Hz, 1H), 7.74 (d, ^3J = 6.6 Hz, 2H), 7.53 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 182.1, 165.9, 158.0, 154.8, 150.7, 150.4, 139.1, 138.6, 129.4, 129.3, 129.3, 128.8, 127.2, 127.1, 118.7, 117.4.

2-(4′-Iodophenyl)-4,6-diphenylpyridine (6e). The pure product was obtained as a white powder. Yield: 2.56 g, 78%. Anal. Found (calcd): C 64.05 (63.76), H 4.05 (3.72), N 2.95 (3.23)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{23}H_{16}NI$ ([M]$^+$): calcd: 433.28; found: 433. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.17 (d, ^3J = 6.8 Hz, 2H), 7.93 (AA′XX′, 2H), 7.87 (d, ^4J = 1.4 Hz, 1H), 7.83 (AA′XX′, 2H), 7.82 (d, ^4J = 1.4 Hz, 1H), 7.71 (d, ^3J = 8.3 Hz, 2H), 7.48 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 155.70, 154.44, 148.44, 137.44, 137.12, 136.91, 135.90, 127.26, 127.23, 127.17, 126.95, 126.82, 125.25, 125.21, 115.55, 115.18, 114.83.

2-(4′-Bromophenyl)-4,6-diphenylpyridine (6f). The pure product was obtained as a white powder. Yield: 2.68 g, 92%. Anal. Found (calcd): C 71.50 (71.51), H 4.10 (4.17), N 3.60 (3.63)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{23}H_{16}NBr$ ([M]$^+$): calcd: 386.28; found: 386. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.18 (d, ^3J = 6.9 Hz, 2H), 8.08 (AA′XX′, 2H), 7.89 (d, ^4J = 1.3 Hz, 1H), 7.84 (d, ^4J = 1.3 Hz, 1H), 7.73 (d, ^3J = 8.2 Hz, 2H), 7.63 (AA′XX′, 2H), 7.50 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 158.4, 156.9, 151.1, 140.1, 139.6, 139.2, 132.5, 129.9, 129.8, 129.5, 129.4, 127.9, 127.8, 124.2, 118.84, 118.1, 117.5.

4′-Phenyl-2,2′:6′,2″-terpyridine (6g). The pure product was obtained as a white powder. Yield: 4.05 g, 79%. Anal. Found (calcd): C 81.50 (81.53), H 4.25 (4.89), N 13.60 (13.58)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{21}H_{15}N_3$ ([M]$^+$): calcd: 309.36; found: 309. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.74 (s, 2H), 8.72 (m, 2H), 8.66 (d, ^3J = 7.9 Hz, 2H), 7.86 (m, 4H), 7.47 (m, 3H), 7.33 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 156.7, 156.4, 150.8, 149.6, 138.9, 137.2, 129.3, 127.8, 124.2, 121.8, 119.4, 119.3.

4′-Phenyl-4,2′:6′,4″-terpyridine (6h). The pure product was obtained as a white powder. Yield: 6.47 g, 84%. Anal. Found (calcd): C 81.65 (81.53), H 4.50 (4.89), N 13.55 (13.58)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{21}H_{15}N_3$ ([M]$^+$): calcd: 309.36; found: 309. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.76 (AA′XX′, 4H), 8.16 (AA′XX′, 4H), 8.06 (s, 2H), 7.71 (d, ^3J = 6.24 Hz, 2H), 7.49 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 154.9, 151.9, 148.8, 148.1, 137.9, 130.2, 129.8, 127.5, 122.29, 120.1.

2,6-Bis(4′-octyloxyphenyl)-4-phenylpyridine (6i). The pure product was obtained as a white powder. Yield: 1.45 g, 78%. Anal. Found (calcd): C 83.50 (83.08), H 8.35 (8.76), N 2.60 (2.48)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{39}H_{49}NO_2$ ([M]$^+$): calcd: 563.81; found: 564. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.17 (d, ^3J = 7.9 Hz, 2H), 7.90 (AA′XX′, 4H), 7.88 (s, 2H), 7.09 (m, 5H), 4.05 (t, 4H, ^3J = 7.6 Hz, 2H), 1.75 (m, 4H), 1.40 (m, 4H), 1.30 (m, 16H), 0.88 (t, ^3J = 7.4 Hz, 6H).

2,6-Bis(4′-nitrophenyl)-4-phenylpyridine (6j). The pure product was obtained as a yellow powder. Yield: 1.24 g, 74%. Anal. Found (calcd): C 70.00 (69.52), H 4.05 (3.80), N 10.65 (10.57)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{23}H_{15}N_3O_4$ ([M]$^+$): calcd: 397.38; found: 397. ^{1}H NMR (300 MHz, acetone-d_6, 300.0 K): δ = 8.22 (AA′XX′, 4H), 7.98 (s, 2H), 7.94 (d, ^3J = 7.3 Hz, 2H), 7.0 (m, 7H).

4-(4′-Butoxyphenyl)-2,6-diphenylpyridine (6k). The pure product was obtained as a white powder. Yield: 2.56 g, 85%. Anal. Found (calcd): C 85.50 (85.45), H 6.55 (6.64), N 3.60 (3.69)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{27}H_{25}NO$ ([M]$^+$): calcd: 379.49; found: 380. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.20 (d, ^3J = 6.7 Hz, 4H), 7.85 (s, 2H), 7.69 (AA′XX′, 2H), 7.51 (m, 6H), 7.04 (AA′XX′, 2H), 4.04 (t, ^3J = 6.5 Hz, 2H), 1.79 (m, 2H), 1.52 (m, 2H), 1.28 (t, ^3J = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 158.43, 155.79, 148.03, 138.08, 129.35, 127.26, 126.98, 126.74, 125.84, 114.01, 113.43, 66.23, 29.62, 17.46, 12.16.

4′-(4-Butyloxyphenyl)-2,2′:6′,2″-terpyridine (6l). The pure product was obtained as a white powder. Yield: 3.75 g, 80%. Anal. Found (calcd): C 78.75 (78.71), H 6.05 (6.08), N 11.00 (11.02)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{25}H_{23}N_3O$ ([M]$^+$): calcd: 381.47; found: 381. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.75 (s, 2H), 8.72 (m, 2H), 8.66 (d, ^3J = 7.9 Hz, 2H), 7.76 (m, 2H), 7.63 (AA′XX′, 2H), 7.33 (m, 2H), 7.14 (AA′XX′, 2H), 4.06 (t, ^3J = 6.5 Hz, 2H), 1.78 (m, 2H), 1.52 (m, 2H), 0.86 (t, ^3J = 7.4 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 157.5, 156.7, 150.8, 149.4, 139.5, 137.8, 129.9, 127.2, 124.2, 121.4, 119.4, 113.2, 66.6, 30.4, 17.3, 12.6.

4′-(4-Butyloxyphenyl)-4,2′:6′,4″-terpyridine (6m). The pure product was obtained as a white powder. Yield: 3.63 g, 76%. Anal. Found (calcd): C 78.60 (78.71), H 5.95 (6.08), N 10.85 (11.02)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{25}H_{23}N_3O$ ([M]$^+$): calcd: 381.47; found: 381. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.76 (AA′XX′, 4H), 8.04 (AA′XX′, 4H), 7.96 (s, 2H), 7.58 (AA′XX′, 2H), 7.04 (AA′XX′, 2H), 4.04 (t, ^3J = 6.5 Hz), 1.81 (m, 2H), 1.52 (m, 2H), 0.99 (t, ^3J = 7.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 159.6, 154.1, 149.6, 149.4, 145.2, 128.8, 127.3, 120.2, 117.3, 114.3, 67.0, 30.2, 18.2, 12.8.

2,6-Bis(2-hydroxyphenyl)-4-(4-butoxyphenyl)pyridine (6n). The pure product was obtained as a white powder. Yield: 0.24 g, 64%. Anal. Found (calcd): C 78.60 (78.81), H 5.90 (6.12), N 2.90 (3.40)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{27}H_{25}NO_3$ ([M]$^+$): calcd: 411.49; found: 411. ^{1}H NMR (300 MHz, methanol-d_4, 300.0 K): δ = 7.82 (m, 4H), 7.55 (AA′XX′, 2H), 7.31 (d, ^3J = 7.9 Hz, 2H), 6.96 (m, 2H), 6.84 (m, 4H), 3.95 (t, ^3J = 7.4 Hz, 2H), 1.70 (m, 2H), 1.42 (m, 2H), 0.89 (t, ^3J = 7.6 Hz, 3H). ^{13}C NMR (75 MHz, methanol-d_4, 300.0 K): δ = 192.7, 191.2, 162.6, 160.7, 144.4, 135.1, 129.5, 128.5, 126.7, 117.7, 117.1, 114.0, 113.8, 66.9, 30.3, 18.2, 12.8.

4′-(4-Octyloxyphenyl)-4,2′:6′,4″-terpyridine (6o). The pure product was obtained as a white powder. Yield: 5.45 g, 86%. Anal. Found (calcd): C 79.60 (79.60), H 7.20 (7.14), N 9.50 (9.60)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{29}H_{31}N_3O$ ([M]$^+$): calcd: 437.58; found: 438. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.76 (AA′XX′, 4H), 8.05 (AA′XX′, 4H), 7.99 (s, 2H), 7.67 (AA′XX′, 2H), 7.05 (AA′XX′, 2H), 4.04 (t, ^3J = 7.6 Hz, 2H), 1.83 (m, 2H), 1.35 (m, 10H), 0.89 (t, ^3J = 7.5 Hz, 2H).

2,6-Bis(4-iodophenyl)-4-(4-octyloxyphenyl)pyridine (6p). The pure product was obtained as a white powder. Yield: 2.56 g, 85%. Anal. Found (calcd): C 54.08 (54.17), H 4.67 (4.55), N 1.96 (2.04)%. MS (EI$^+$, 50 eV, 200 °C) for $C_{31}H_{31}NOI$ ([M]$^+$): calcd: 687.39; found: 688. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 7.89 (AA′XX′, 4H), 7.82 (AA′XX′, 4H), 7.79 (s, 2H),

7.64 (AA′XX′, 2H), 7.02 (AA′XX′, 2H), 4.02 (t, ^3J = 7.0 Hz, 2H), 1.85 (m, 2H), 1.43 (m, 10H), 0.90 (t, ^3J = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 198.7, 157.7, 137.9, 137.8, 136.2, 132.8, 129.4, 129.3, 128.8, 114.6, 100.9, 68.1, 40.6, 31.8, 29.4, 29.2, 26.1, 22.6, 14.1.

4′-(4-Bromophenyl)-2,2′:6′,2″-terpyridine (6q). The pure product was obtained as a white powder. Yield: 1.56 g, 75%. Anal. Found (calcd): C 64.05 (64.96), H 3.65 (3.63), N 10.95 (10.82)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{21}H_{14}N_3Br$ ([M]$^+$): calcd: 388.26; found: 388. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.64 (dd, ^3J = 7.7, ^4J = 1.7 Hz, 2H), 8.61 (s, 2H), 8.57 (d,^3J = 7.9 Hz, 2H), 7.79 (dt, ^3J = 7.9, ^4J = 1.7 Hz, 2H), 7.68 (AA′XX′, 2H), 7.55 (AA′XX′, 2H), 7.26 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 156.7, 156.6, 149.7, 149.6, 138.0, 137.5, 132.7, 129.4, 124.5, 124.0, 122.0, 119.1.

4′-(4-Bromophenyl)-4,2′:6′,4″-terpyridine (6r). The pure product was obtained as a white powder. Yield: 1.50 g, 81%. Anal. Found (calcd): C 64.15 (64.96), H 3.15 (3.63), N 10.55 (10.82)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{21}H_{14}N_3Br$ ([M]$^+$): calcd: 388.26; found: 388. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.79 (AA′XX′, 4H), 8.09 (AA′XX′, 4H), 7.98 (s, 2H), 7.67 (AA′XX′, 2H), 7.58 (AA′XX′, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 227.7, 173.2, 153.4, 148.2, 144.5, 134.8, 126.7, 122.4, 119.6, 116.9.

4′-[4-(4-Bromobutoxy)phenyl]-2,2′:6′,2″-terpyridine (6s). The pure product was obtained as a white powder. Yield: 2.38 g, 89%. Anal. Found (calcd): C 67.15 (67.57), H 5.25 (4.99), N 9.00 (9.46)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{25}H_{22}N_3Br$ ([M]$^+$): calcd: 444.37; found: 444. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.58 (m, 4H), 8.54 (d, ^3J = 7.9 Hz, 2H), 7.72 (m, 4H), 7.20 (m, 2H), 6.87 (AA′XX′, 2H), 3.94 (m, 4H), 1.76 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 170.1, 158.9, 155.3, 154.8, 148.6, 148.0, 135.85, 127.4, 122.8, 120.4, 117.2, 113.8, 66.4, 63.1, 24.4, 19.9.

4′-[4-(4-Bromobutoxy)phenyl]-3,2′:6′,3″-terpyridine, (6t). The pure product was obtained as a white powder. Yield: 2.20 g, 88%. Anal. Found (calcd): C 67.30 (67.57), H 5.05 (4.99), N 9.20 (9.46)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{25}H_{22}N_3Br$ ([M]$^+$): calcd: 444.37; found: 444. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 9.24 (s, 2H), 8.56 (d, ^3J = 7.9 Hz, 2H), 8.39 (d, ^3J = 7.9 Hz, 2H), 7.78 (s, 2H), 7.56 (AA′XX′, 2H), 7.34 (m, 2H), 6.91 (AA′XX′, 2H), 4.01 (m, 4H), 1.77 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 171.5, 160.6, 155.3, 150.6, 150.0, 148.3, 135.1, 130.5, 128.7, 124.1, 117.5, 115.6, 67.9, 64.4, 25.7, 21.3.

4′-[4-(4-Bromobutoxy)phenyl]-4,2′:6′,4″-terpyridine (6u). The pure product was obtained as a white powder. Yield: 2.47 g, 86%. Anal. Found (calcd): C 67.45 (67.57), H 4.85 (4.99), N 9.00 (9.46)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{25}H_{22}N_3Br$ ([M]$^+$): calcd: 444.37; found: 444. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.66 (AA′XX′, 4H), 8.00 (AA′XX′, 4H), 7.93 (s, 2H), 7.61 (AA′XX′, 2H), 7.00 (AA′XX′, 2H), 4.02 (t, ^3J = 7.4 Hz, 2H), 3.63 (t, ^3J = 7.4 Hz, 2H), 1.76 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$, 300.0 K): δ = 171.5, 163.6, 155.4, 150.6, 146.9, 128.7, 121.7, 121.1, 118.9, 115.7, 68.5, 62.6, 26.1, 25.0.

4-(4′-Bromobutoxy)phenyl-2,6-diphenylpyridine (6v). The pure product was obtained as a white powder. Yield: 1.54 g, 90%. Anal. Found (calcd): C 73.05 (73.30), H 4.95 (5.47), N 3.00 (3.17)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{27}H_{24}NBr$ ([M]$^+$): calcd: 442.39; found: 442. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.1 (d, ^3J = 7.9 Hz, 4H), 7.75 (s, 2H), 7.55 (AA′XX′, 2H), 7.35 (t, ^3J = 7.9 Hz, 2H), 7.32 (m, 4H), 6.91 (AA′XX′, 2H), 4.05 (m, 4H), 2.05 (m, 4H).

4-(3,2′:6′,3″-Terpyridin-4′-yl)phenol (6w). The pure product was obtained as a blue powder. Yield: 0.64 g, 67%. Anal. Found (calcd): C 77.60 (77.52), H 5.95 (4.65), N 12.85 (12.91)%. MS (EI$^+$, 70 eV, 200 °C) for $C_{21}H_{15}N_3O$ ([M]$^+$): calcd: 325.36; found: 325. ^{1}H NMR (300 MHz, DMSO-d_6, 300.0 K): δ = 9.53 (s, 2H), 8.70 (m, 4H), 8.30 (s, 2H), 7.99 (AA′XX′, 2H), 7.59 (m, 2H), 6.99 (AA′XX′, 2H), 3.61 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6, 300.0 K): δ = 159.7, 154.8, 150.3, 150.2, 148.6, 134.7, 134.5, 129.1, 127.7, 124.0, 116.8, 116.3.

4′,4′′′′-(1,4-Phenylene)bis(4,2′:6′,4″-terpyridine) (7). The product was synthesised as described above using terephthalaldehyde (1.00 g, 7.46 mmol) and 4-acetylpyridine (3.61 g, 29.82 mmol). Yield: 3.49 g (87%, 6.46 mmol). Anal. Found (calcd): C 9.50 (79.98), 3.96 (4.47), N 14.95 (15.55)%. MS (EI$^+$, 50 eV, 200 °C) for $C_{36}H_{24}N_6$ ([M]$^+$): calcd: 540.62; found: 541. ^{1}H NMR (300 MHz, $CDCl_3$, 300.0 K): δ = 8.55 (AA′XX′, 8H), 8.41 (s, 4H), 7.48 (AA′XX′, 4H), 6.94 (s, 4H).

Crystallographic data for 4′-(4-butyloxyphenyl)-4,2′:6′,4″-terpyridine

Crystals suitable for structural analysis were grown from EtOH. A yellow prism (dimensions 0.20 × 0.16 × 0.12 mm) was mounted with oil on a thin quartz fiber. The molecular structure is largely unexceptional with an absence of both directional H-bonding and π-stacking of the aromatics. Triclinic, space group $P\bar{1}$, a = 10.8889(2), b = 14.1687(8), c = 14.6071(2) Å, α = 117.946(1), β = 91.825(1), γ = 96.606(1)°, V = 1968.13 Å^3, D_c = 1.287 g cm^{-3}, Z = 4, 28835 data collected, of which 9549 unique (R_{int} = 0.0507), least-squares refinement gave final R_1 = 0.0577 [for 6158 observed data with $I_{net} > 2\sigma(I_{net})$], wR_2 = 0.1920 (all data). The intensity data were collected on a Enraf-Nonius KappaCCD diffractometer using Mo-Kα radiation (λ = 0.71073 Å) at 123(1) K. The structure was solved by direct methods using SHELXS[30] and refined using SHELXL[31] software.

CCDC reference number 168943. See http://www.rsc.org/suppdata/p1/b1/b107302h/ for crystallographic files in .cif format.

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