Syntheses of Three New Pyridyl Thienopyridine Ligands *via* the Hurtley Reaction

Robert O. Steen,* Lasse J. Nurkkala, and Simon J. Dunne

School of Sustainable Development of Society and Technology, Mälardalen University, Drottninggatan 12, 631 05 Eskilstuna, Sweden
*E-mail: robert.ove.steen@gmail.com

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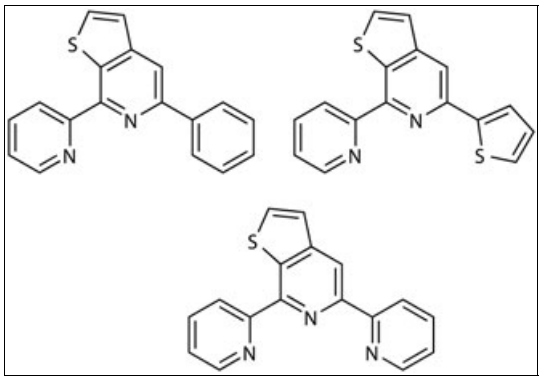

The tridentate pyridyl thienopyridines 5-phenyl-7-(pyridin-2-yl)thieno[2,3-*c*]pyridine (**L1**), 7-(pyridin-2-yl)-5-(thiophen-2-yl)-thieno[2,3-*c*]pyridine (**L2**) and 5,7-di(pyridin-2-yl)thieno[2,3-*c*]pyridine (**L3**) have been synthesized via the Hurtley reaction. **L1** and **L2** were synthesized by condensing 3-bromothiophene-2-carboxylic acid with phenyl-1,3-butanedione and 1-thienyl-1,3-butanedione respectively. **L3** was synthesized by condensing 3-bromothiophene-2-carboxylic acid with benzoylacetonitrile. Ring closure and a subsequent Negishi or Stille cross-coupling afforded **L1**, **L2**, and **L3** in an overall yield of 20, 3, and 6%, respectively.

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INTRODUCTION

In our studies into the use of oligothiophene substituted $[Ru(bpy)_3]^{2+}$ complexes as electron sources within molecular electronic devices, we have recently reported the effects of various modes of attachment of a thiophene unit onto a 2,2′-bipyridine ligand (L) and examined the electrochemical and photophysical properties of the resulting $[Ru(bpy)_2L]^{2+}$ complexes [1,2]. Pendant attachment in the 4-position led to the longest luminescence lifetimes (3000 ns), whilst fusion of a thiophene ring onto the *b* or *c* face of a bipyridine lead to complexes with lifetimes in the range 275–1510 ns and quantum yields ranging between 0.0047 and 0.014 [2].

$[Ru(tpy)_2]^{2+}$ complexes offer significant geometrical advantages over their tris-bipyridine analogs as linear arrays can be easily generated. However the photophysical properties of $[Ru(tpy)_2]^{2+}$ are vastly inferior to those of $[Ru(bpy)_3]^{2+}$. Results by the groups of Constable [3], Ferraudi [4], and Zeissel [5] have shown that introduction of thiophenyl and 2-ethynylthiophenyl substituents at the 4′-position of tpy greatly increases the lifetimes of the $[Ru(tpy)L]^{2+}$ complexes, from 0.25 ns for $[Ru(tpy)_2]^{2+}$ into the vicinity of 80–150 ns (depending upon the $[Ru(tpy)L]^{2+}$ complex) [3–5]. In light of these results and our recently reported photophysical and cyclic voltammetry studies upon $[Ru(bpy)_2L]^{2+}$ complexes [2] of several novel bidentate pyridyl thienopyridines [6], it was of interest to synthesize a range of tridentate ligands with a thiophene fused onto the *c* face of the central pyridine ring. We now report synthetic pathways to the compounds 5-phenyl-7-(pyridin-2-yl)thieno[2,3-*c*]pyridine (**L1**), 7-(pyridin-2-yl)-5-(thiophen-2-yl)thieno[2,3-*c*]pyridine (**L2**) and 5,7-di(pyridin-2-yl) thieno[2,3-*c*]pyridine (**L3**) (Fig. 1). **L1** can act as a cyclometallating ligand while **L2** has two possible binding modes, *S*-coordinated or cyclometallated [7]. Structural studies, together with electrochemical and photophysical measurements on the ruthenium(II)terpyridine complexes of these ligands are currently under investigation.

RESULTS AND DISCUSSION

The key step in the synthesis of **L1**–**L3** was the copper-catalysed condensation between 3-bromothiophene-2-carboxylic acid and a carbanion. This reaction is known as the Hurtley reaction. In 1929, Hurtley [8a] demonstrated that *o*-bromobenzoic acid could be condensed with carbanions under basic conditions through catalysis by Cu powder or $Cu(OAc)_2$. The reaction has been investigated several times, but quite a few details are still unclear. In its original incarnation the Hurtley reaction was

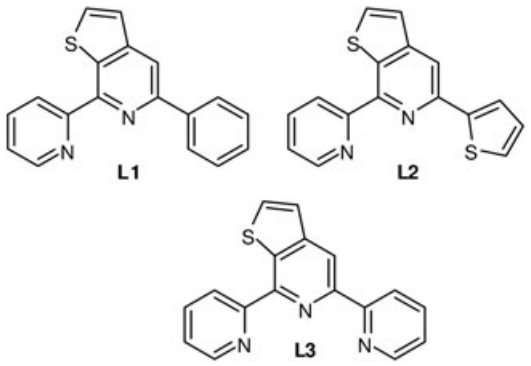


Figure 1. Three new tridentate thienopyridines, 5-phenyl-7-(pyridin-2-yl)thieno[2,3-*c*]pyridine (**L1**), 7-(pyridin-2-yl)-5-(thiophen-2-yl)thieno [2,3-*c*]pyridine (**L2**), and 5,7-di(pyridin-2-yl)thieno[2,3-*c*]pyridine (**L3**).

conducted in ethanol/NaOEt with copper powder as catalyst. Under these conditions the condensation between *o*-bromobenzoic acid and a β-dicarbonyl compound was usually followed by deacetylation through ethanolysis, which may be a complication or an advantage depending on the desired product. Bruggink and McKillop [8b] showed that it is possible to avoid the deacetylation and improve the yield by using the system toluene/NaH/CuBr instead. Bruggink and McKillop [8b] also showed that Cu(I) is almost certainly the catalytic species and proposed a mechanism for the reaction. Several other copper compounds have been used as catalysts in the Hurtley reaction, for example CuO [8c], CuCl [8c], and Cu(I)OAc [8b]. The necessity for a substituent *ortho* to the halogen capable of coordinating the intermediate copper species has been a limiting factor for the Hurtley reaction, but recently Ma *et al.* performed the condensation using arylbromides (both electron-rich and electron-deficient) and the catalytic system Cu(I)I/L-proline [8d]. *o*-Bromobenzoic acid and its derivatives are not the only bromo-acids that can be used in the Hurtley reaction, Ames and Dodds [8e] extended the scope of the Hurtley reaction and showed, using the ethanol/NaOEt system with Cu or $Cu(OAc)_2$, that the Hurtley reaction was applicable to bromopyridine carboxylic acids and bromothiophene carboxylic acids [8f].

SYNTHESIS OF L1–L3

In the first step of the synthesis of **L1** (Scheme 1) 3-bromothiophene-2-carboxylic acid (**1**) was condensed with 1-phenyl-1,3-butanedione using standard conditions for the Hurtley reaction, *i.e.* ethanol and NaOEt. According to Cirigottis and Taylor [8c], CuO would be a more efficient catalyst than $Cu(OAc)_2$. However, after reflux overnight with EtOH/NaOEt/CuO only starting material was recovered. The reaction was attempted again, this time using 10 mol% $Cu(OAc)_2$ as catalyst. After reflux overnight and subsequent workup the desired product 3-(2-oxo-2-phenylethyl)-2-thiophenecarboxylic acid [8f] (**2**) was obtained in moderate yield (64%).

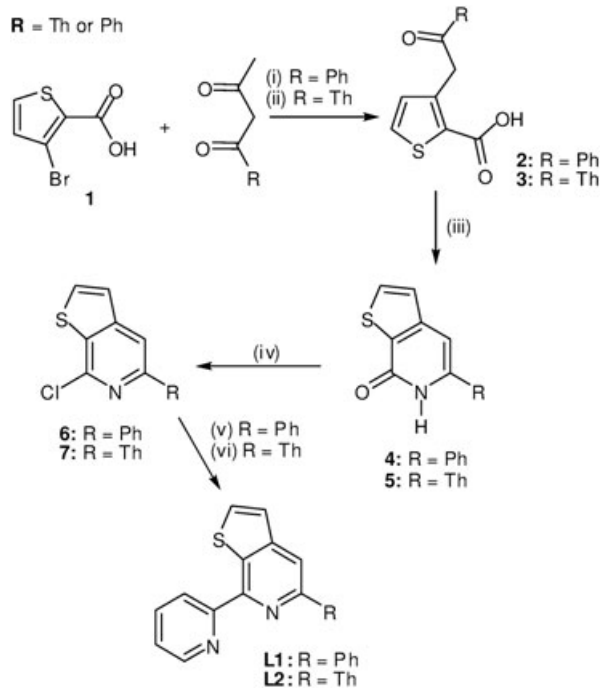
2 and NH_4OAc were refluxed in acetic acid overnight to yield 5-phenylthieno[2,3-*c*]pyridin-7(6H)-one [8f] (**4**) in good yield (81%).

4 was added to fresh $POCl_3$ and refluxed for 22 h. After flash chromatography the product 7-chloro-5-phenylthieno[2,3-*c*]pyridine (**6**) was recovered in moderate yield (56%).

For the final step a Negishi cross-coupling [9] was utilized. Under a nitrogen atmosphere, **6** was treated with 2-pyridylzinc bromide in refluxing dry THF with 3 mol% $[Pd(PPh_3)_4]$ to give **L1** as pale needles (68%). The overall yield of this four-step synthesis was 20%.

L2 was planned to be synthesized analogously to **L1** (Scheme 1). **1** and 1-thienyl-1,3-butanedione [10] were treated with NaOEt and 10 mol% $Cu(OAc)_2$ in EtOH in the same manner as in the synthesis of **2**. However, after reflux overnight and workup, only small amounts of **3** were found. The yield was only ~10% (calculated from ^{1}H-NMR). Different catalysts and catalyst loadings were

Scheme 1. General outline for the synthesis of **L1** and **L2**. Reagents and conditions: (i) 10 mol% $Cu(OAc)_2 \times H_2O$, 2.1 equiv. NaOEt, EtOH, 18 h, Δ; (ii) 10 mol% Cu(I)OAc, 2.1 equiv. NaOEt, EtOH, N_2-atmosphere, 72 h, Δ; (iii) NH_4OAc, AcOH, 16 h, Δ; (iv) $POCl_3$, 22 h, Δ; (v) 2-pyridylzinc bromide, 3 mol% $[Pd(PPh_3)_4]$, THF, N_2-atmosphere, 24 h, Δ; (vi) 2-(tributylstannyl) pyridine, 2 mol% $[Pd_2(dba)_3]$, 4 mol% $[(t\text{-}Bu)_3PH]BF_4$, 2.2 equiv. cesium fluoride, dioxane, N_2-atmosphere, 48 h, Δ.



tested (10–20 mol% CuBr, 10–20 mol% Cu) but no improvement was achieved. A slight increase in the yield (~15%) was however achieved by using 10 mol% Cu(I) OAc. In an attempt to increase the yield the reaction mixture was refluxed for 72 h under N_2 with Cu(I) OAc as catalyst. According to ^{1}H-NMR this increased the yield of **3** to 65%. However, it proved to be difficult to isolate **3** from starting materials and byproducts. Separation could not be achieved by either recrystallization or chromatography with a range of different mobile phases. In an attempt to investigate if separation actually was necessary the product mixture was dissolved in AcOH and refluxed with NH_4OAc for #16 h. After workup pure 5-(thiophen-2-yl)thieno [2,3-*c*]pyridin-7(6H)-one (**5**) was recovered in 26% yield (calculated from **1**).

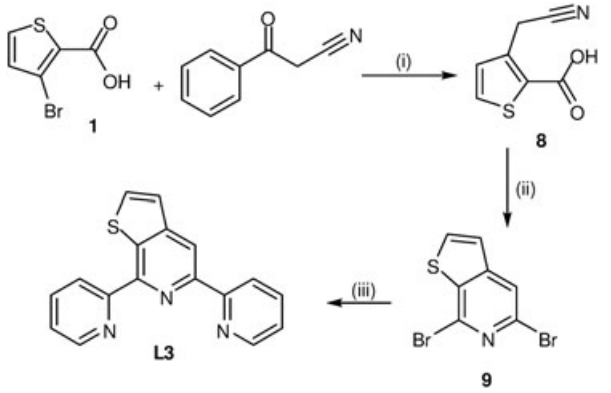
The pyridyl chloride (**7**) 7-chloro-5-(thiophen-2-yl) thieno[2,3-*c*]pyridine was synthesized in the same manner as **6**, albeit in a lower yield (29%).

In the final step **L2** was planned to be synthesized by a Negishi cross-coupling with 2-pyridylzinc bromide [6]. However, after refluxing for 24 h in THF only starting materials were recovered in nearly quantitative yield.

A Negishi cross-coupling requires expensive arylzinc reagents and rigorously dry conditions. Since stannyl reagents are readily available and due to the general robustness of the reaction, a Stille cross-coupling [11] was preferable for the final step in the synthesis of **L2**. Previously it has not been feasible to conduct Stille cross-couplings with aryl chlorides, but thanks to the work by Fu [12] this limitation has now been removed. Fu showed that by utilizing a catalytic mixture of $[Pd_2(dba)_3]$ and P(*t*-Bu)$_3$ with 2–3 equiv. of potassium fluoride or cesium fluoride it is possible to perform Stille cross-couplings with aryl chlorides in good yields and also allows Stille, Suzuki, and Heck reactions with aryl bromides and iodides to be performed at ambient temperature. As P(*t*-Bu)$_3$ is a fairly sensitive chemical to work with. Fu investigated the possibility of using stable phosphonium salts as replacements and showed that indeed, phosphonium tetrafluoroborate salts serve as direct replacement for P(*t*Bu)$_3$ [12]. Mixtures of $[Pd_2(dba)_3]/[(t\text{-}Bu)_3PH]BF_4$ are now commercially available.

Using $[Pd_2(dba)_3]/[(t\text{-}Bu)_3PH]BF_4$ (Pd:P = 1:2) as catalyst **7** was refluxed with 2-(tributylstannyl)pyridine and 2.2 equivalents cesium fluoride in 1,4-dioxane. **L2** was obtained in acceptable yield (44%). It should be noted that the actual yield of **L2** was higher (calculated from ^{1}H-NMR the yield was ~75%) but after flash chromatography only the fractions that contained pure **L2** were kept, resulting in a lower final yield. The overall yield of this four-step synthesis was 3%.

Scheme 2. General outline for the synthesis of **L3**. Reagents and conditions: (i) 10 mol% $Cu(OAc)_2 \times H_2O$, 2.1 equiv. NaOEt, EtOH, 18 h, Δ; (ii) PBr_3, 175°C, N_2-atmosphere, 5 h; (iii) 2.05 equiv. 2-(tributylstannyl)-pyridine, 5 mol% $[Pd(PPh_3)_4]$, toluene, N_2-atmosphere, 24 h, Δ.



The final ligand **L3** was also to be synthesized according to the general pathway outlined in Scheme 1. However, even though Ames and Dodds [8e] showed that 2-bromopyridine-3-carboxylic acid can be used as a starting material in the Hurtley reaction it would appear that the same is not true for the β-dicarbonyl compound 1-pyridyl-1,3-butanedione [13]. When **1** was reacted with 1-pyridyl-1,3-butanedione under the same reaction conditions as in the synthesis of **2** and with the workup as detailed by Ames and Dodds [8e] only starting materials were recovered in nearly quantitative yield. Different reaction times (24, 48, and 72 h) were tested as well as different catalysts (CuBr, CuO, Cu, Cu(I)OAc), and catalyst loadings, but in all cases only starting materials were recovered. A possible explanation is that the copper ions forms a complex with to 1-pyridyl-1,3-butanedione, removing them from the catalytic cycle. It would appear that **L3** is not accessible via the pathway shown in Scheme 1. A new pathway was devised (Scheme 2).

3-(Cyanomethyl)thiophene-2-carboxylic acid (**8**) had previously been synthesized by Ames and Dodds [8f] by the same general method used to synthesize **2**. By reacting **1** with benzoylacetonitrile in EtOH with NaOEt and 10 mol% $Cu(OAc)_2$, **8** was generated in moderate yield (69%).

Under a nitrogen atmosphere **8** was then refluxed with fresh PBr_3 at 175°C with vigorous stirring. Despite the intense stirring, black aggregates were formed during the reaction. These were carefully broken up by removing the condenser and crushing them with a glass rod. After workup 5,7-dibromothieno[2,3-*c*]pyridine [14] (**9**) was obtained in poor yield (11%). Even though the yield was poor, enough material was produced to proceed with the final step in the synthesis of **L3**.

In the final step of the synthesis of **L3** a Stille cross-coupling was used. Dibromopyridine **9** was reacted with

2-(tributylstannyl)pyridine in refluxing toluene with 5 mol% [$Pd(PPh_3)_4$] as catalyst. After flash chromatography and recrystallization from MeOH, **L3** was collected in good yield (80%). The overall yield of this three-step synthesis was 6%.

EXPERIMENTAL

All moisture and air sensitive reactions were performed in oven-dried (120°C, 12 h) glassware under nitrogen. Analytical TLC was performed on commercially prepared plates coated with 0.20 mm of Macherey-Nagel silica gel 60. The compounds were visualized by illumination with UV light (254 nm). Column chromatography was performed using Matrex Normal Phase Silica 60 (particle size 35–70 μm). All melting points were determined using an Electrothermal 9200 melting point apparatus and are uncorrected. Mass spectra (MS) were obtained with a Fisions Instrument Trio 1000 spectrometer equipped with a Hewlett Packard 5MS gas chromatography column. NMR spectra were recorded with a Bruker DPX Avance 300 MHz spectrometer and the chemical shifts are expressed in ppm from tetramethylsilane as internal standard. Abbreviations for signal coupling are as follows: s, singlet; d, doublet; tr, triplet; q, quartet; dd, doublet of doublets; ddd, doublet of doublets of doublets; dtr, doublet of triplets; m, multiplet; br, broad. The catalyst tris(dibenzylideneacetone) dipalladium(0)/tri-*t*-butylphosphonium tetrafluoroborate admixture (molar Pd:P = 1:2, Prod. No. 46-3020) was purchased from Strem Chemicals Inc. All commercially available chemicals were used as received unless otherwise noted. THF and 1,4-dioxane were distilled from sodium/benzophenone ketal directly prior to use.

3-(2-Oxo-2-phenylethyl)-2-thiophene-carboxylic acid (2). EtOH (99.7%, 30 mL) and NaOEt (0.78 g, 11.5 mmol) were added to a dry round-bottomed flask. The mixture was stirred until all NaOEt was dissolved. 1-Phenyl-1,3-butanedione (1.0 g, 6 mmol), 3-bromothiophene-2-carboxylic acid (**1**) (0.93 g, 4.5 mmol) and Cu(II)OAc × H_2O (10 mol%, 0.12 g, 0.6 mmol) were then added in that order. A spiral condenser and a drying tube filled with $CaCl_2$ were fitted and the mixture was refluxed over 18 h. The solution was then poured into H_2O (200 mL) and the resulting solution was acidified with HCl (aq, 2 M). The solution was extracted with Et_2O (2 × 75 mL). The organic phases were combined and extracted with Na_2CO_3 (aq, 1 M, 2 × 75 mL). The aqueous phases were combined and washed with Et_2O (50 mL) and subsequently acidified with HCl (aq, 2 M). The acidified solution was extracted with $CHCl_3$ (2 × 50 mL). The organic phases were combined and dried over $MgSO_4$. After evaporation under reduced pressure **2** was obtained as a pale brown powder which was subsequently recrystallized from EtOH/H_2O.

Yield: 0.71 g (64%); pale needles. mp. 198–200°C (lit. 199–201°C) [8f]. ^{1}H-NMR (DMSO-d_6, 300 MHz) δ: 7.97–8.07 (m, 2H), 7.77 (d, 1H, J = 5.0 Hz), 7.65 (dd, 1H, J = 7.3, 1.3 Hz), 7.50–7.60 (m, 2H), 7.09 (d, 1H, J = 5.0 Hz), 4.75 (s, 2H) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz) δ: 196.3, 163.4, 142.4, 136.6, 133.3, 132.3, 130.7, 129.1, 128.8, 128.0, and 39.3 ppm. MS (m/z): 246 (M^+).

5-Phenylthieno[2,3-*c*]pyridin-7(6H)-one (4). **2** (0.38 g, 1.54 mmol) and NH_4OAc (3.9 g, 51 mmol) were transferred to a round-bottomed flask after which AcOH (15 mL) was added. The mixture was heated to reflux overnight, after which the solution was allowed to cool to r.t. and was poured into H_2O (100 mL), resulting in the formation of a precipitate. The precipitate was recovered by suction filtration and washed with water until it was free of acetic acid. The precipitate was dried by suction after which it was subsequently recrystallized from EtOH/H_2O.

Yield: 0.26 g (81%); off-white crystals. mp. 197.5–199.5°C (lit. 195–197.5°C).[7] ^{1}H-NMR (DMSO-d_6, 300 MHz) δ: 11.70 (br s, 1H), 8.60 (d, 1H, J = 5.1 Hz), 7.70–7.89 (m, 2H), 7.54–7.43 (m, 3H), 7.41 (d, 1H, J = 5.1 Hz), 7.03 (s, 1H) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz) δ: 159.0, 146.4, 141.9, 134.2, 133.9, 129.2, 128.8, 127.9, 126.8, 125.2, and 100.9 ppm. MS (*m*/*z*): 227 (M^+).

5-(Thiophen-2-yl)thieno[2,3-*c*]pyridin-7(6H)-one (5). EtOH (99.7%, 450 mL) was added to a dry round-bottomed flask and the system was flushed with N_2. Sodium (2.77 g, 0.12 mol) was then added over *ca.* 30 min. When all the sodium had dissolved 1-thienyl-1,3-butanedione (10.4 g, 61.8 mmol), **1** (12.1 g, 58.7 mmol) and Cu(I)OAc (10 mol%, 0.75 g, 6 mmol) were added in that order and the mixture was refluxed for 72 h under nitrogen. The resulting dark solution was allowed to cool to r.t. after which it was concentrated to ~1/3 of the original volume. The residue was poured into H_2O (500 mL) and the resulting solution was acidified with HCl (aq, 2 M). The acidified solution was extracted with Et_2O (3 × 150 mL) and the organic phases were combined and extracted with Na_2CO_3 (aq, 1 M, 3 × 100). The aqueous phases were combined and washed with Et_2O (100 mL). The aqueous phase was separated and acidified with HCl (aq, 2 M) resulting in the formation of a brown precipitate which was recovered by suction filtration and dried on the filter. Compound **3** was not isolated from starting materials and byproducts, instead the precipitate (14.5 g) was dissolved in AcOH (300 mL) and NH_4OAc (140 g) was added. The resulting mixture was refluxed for 16 h, after which the solution was cooled to r.t. and poured into H_2O (500 mL), resulting in the formation of a precipitate. The mixture was transferred to a separatory funnel and was extracted with Et_2O (3 × 100 mL). The organic phases were combined and washed with Na_2CO_3 (aq, 1 M, 2 × 100 mL). The organic phase was separated, dried over $MgSO_4$ and evaporated under reduced pressure, yielding **5** as a pale white powder, which was subsequently recrystallized from EtOH/H_2O.

Yield: 3.8 g (26%); pale white needles. mp. 243–244.5°C. ^{1}H-NMR (DMSO-d_6, 300 MHz) δ: 11.80 (br s, 1H, exchangable with deuterium), 8.05 (d, 1H, J = 5.1 Hz), 7.82 (dd, 1H, J = 3.7, 1.1 Hz), 7.65 (dd, 1H, J = 5.1, 1.1 Hz), 7.41 (d, 1H, J = 5.1 Hz), 7.17 (dd, 1H, J = 5.1, 3.7 Hz), 7.03 (br s, 1H) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz) δ: 158.7, 146.3, 136.4, 135.8, 134.5, 128.5, 127.8, 127.5, 126.5, 125.3, and 100.0 ppm. MS (*m*/*z*): 233 (M^+). Anal. Calcd. (%) for $C_{11}H_7NOS_2$: C, 56.63; H, 3.02; N, 6.00. Found C, 56.84; H, 2.73; N, 6.27.

7-Chloro-5-phenylthieno[2,3-*c*]pyridine (6). The pyridone **4** (1.8 g, 8 mmol) was transferred to a dry round-bottomed flask. Fresh $POCl_3$ (40 mL) was then added in one portion. The mixture was refluxed for 22 h. The reaction mixture was then cooled to r.t., after which it was carefully poured into a H_2O/ice-slurry with vigorous stirring. After the exothermic reaction had subsided, the pH of the solution was adjusted to 10 with NaOH (aq, 1 M). The solution was extracted with CH_2Cl_2 (3 × 100 mL), the organic phase were combined, dried over $MgSO_4$ and evaporated under reduced pressure, yielding

a dark oil. The oil was purified by flash chromatography (silica, hexane:EtOAc 3:2). The fractions containing product (R_f = 0.95) were combined and the solvent was removed under reduced pressure, yielding a yellow oil that solidified upon standing into a pale powder, which was recrystallized from MeOH.

Yield: 1.1 g (56%); pale white crystals.mp. 72–75°C ^{1}H-NMR (DMSO-d_6, 300 MHz) δ: 8.46 (s, 1H), 8.23 (d, 1H, J = 5.4 Hz), 8.06–8.13 (m, 2H), 7.66 (d, 1H, J = 5.4 Hz), 7.40–7.44 (m, 3H) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz) δ: 151.2, 148.6, 143.3, 137.4, 135.3, 133.3, 129.1, 128.9,126.6, 124.9, and 114.0 ppm. MS (*m*/*z*): 245 (M^+). Anal. Calcd. (%) for $C_{13}H_8ClNS$: C, 63.54; H, 3.28; N, 5.70. Found C, 63.85; H, 3.43; N, 6.0.

7-Chloro-5-(thiophen-2-yl)thieno[2,3-*c*]pyridine (7). This compound was synthesized analogously to **6** [8e].

Yield: 29%; colourless crystals. mp. 81–84°C. ^{1}H-NMR (DMSO-d_6, 300 MHz) δ: 8.40 (br s, 1H), 8.24 (d, 1H, J = 5.4 Hz), 7.83 (dd, 1H, J = 3.7, 1.1 Hz), 7.66 (dd, 1H, J = 5.1, 1.1 Hz), 7.63 (d, 1H, J = 5.4 Hz), 7.18 (dd, 1H, J = 5.1 Hz) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz) δ: 148.4, 147.0, 142.9, 142.8, 135.8, 132.8, 128.6, 128.3, 125.3, 124.7, and 112.3 ppm. MS (*m*/*z*): 251 (M^+). Anal. Calcd. (%) for $C_{11}H_6ClNS_2$: C, 52.48; H, 2.40; N, 5.56. Found C, 52.31; H, 2.23; N, 5.71.

5-Phenyl-7-(pyridin-2-yl)thieno[2,3-*c*]pyridine (L1). The chloropyridine **6** (0.49 g, 2 mmol) and [Pd(PPh$_3$)$_4$] (3 mol%, 0.066 g, 0.06 mmol) were transferred to a three-necked round-bottomed flask. The system was flushed with N_2, after which dry THF (20 mL) was added via a syringe. 2-Pyridylzinc bromide (0.5 M in THF, 6 mL, 3 mmol) was then added via a syringe. The reaction mixture was refluxed for 24 h with stirring, resulting in the formation of a grey precipitate. The reaction was quenched by pouring into a solution of Na_2CO_3/EDTA (150 mL H_2O, 150 mmol Na_2CO_3, 20 mmol EDTA). The aqueous phase was extracted with Et_2O (2 × 50 mL). The organic extracts were washed with brine, dried over $MgSO_4$ and evaporated. After recrystallisation from MeOH **L1** was obtained as pale needles.

Yield: 0.39 g (68%); pale needles. mp. 98–101°C. UV (EtOH): λ_{max}/nm (log ε/dm^3 mol^{-1} cm^{-1}) = 255 (4.51), 265 (4.53), 288 (4.19), 298 (4.13), 309 (4.05), and 342 (4.14). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 8.92 (dd, 1H, J = 8.0, 1.0 Hz), 8.85 (m, 1H), 8.23–8.3 (m, 2H), 8.21 (s, 1H) 7.92 (dd, 1H, J = 7.9, 1.8 Hz), 7.84 (d, 1H, J = 5.6 Hz), 7.52–7.6 (m, 2H), 7.58 (d, 1H, J = 5.5 Hz), 7.57 (d, 1H, J = 6.1 Hz), 7.39 (dd, 1H, J = 4.8, 1.2 Hz) ppm. ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 156.0, 150.9, 149.4, 148.3, 148.1, 139.8, 136.9, 136.4, 131.6, 128.9, 128.7, 127.2, 123.8, 122.8, 121.9, and 114.9 ppm. MS (*m*/*z*): 288 (M^+). Anal. Calcd. (%) for $C_{18}H_{12}N_2S$: C, 74.97; H, 4.19; N, 9.71. Found C, 75.15; H, 4.37; N, 9.56.

7-(Pyridin-2-yl)-5-(thiophen-2-yl)thieno[2,3-*c*]pyridine (L2). **7** (0.40 g, 1.6 mmol), 2-(tributylstannyl)pyridine (0.70 g, 1.9 mmol) and cesium fluoride (0.53 g, 3.5 mmol) were added to dry 1,4-dioxane (20 mL) in a round-bottomed flask. The resulting mixture was purged with N_2 for 15 min. The catalyst [Pd$_2$(dba)$_3$]/[(*t*-Bu)$_3$PH]BF$_4$ admixture (Pd:P 1:2, 50 mg, 2 mol% Pd, 4 mol% P) was then added and the resulting solution was heated to 100°C under N_2. The reaction was monitored by TLC (silica, hexane: EtOAc 7:3). After 48 h the reaction was deemed complete and the reaction mixture was cooled to r.t. after which it was diluted with Et_2O (100 mL) and filtered through celite. The filtrate was concentrated yielding an oily residue which was purified by flash chromatography (silica, hexane:EtOAc 7:3). The fractions containing pure product were combined and evaporated under reduced pressure, yielding **L2** as a pale solid. An analytical sample was acquired by recrystallization from MeOH/H_2O.

Yield: 0.21 g (44%); off-white needles. mp: 131–133°C. UV (EtOH): λ_{max}/nm (log ε/dm^3 mol^{-1} cm^{-1}) = 255 (4.47), 280 (4.53), 286 (4.56), 308 (4.37), 320 (4.36), and 354 (4.16). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 8.8–8.89 (m, 2H), 8.10 (s, 1H), 7.92 (dtr, 1H, J = 7.6, 1.6 Hz), 7.82 (d, 1H, J = 5.5 Hz), 7.72, (dd, 1H, J = 3.7, 1.1 Hz) 7.43 (d, 1H, J = 5.5 Hz), 7.35–7.43 (m, 2H), 7.17 (dd, 1H, J = 3.7 Hz) ppm. ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 155.6, 149.2, 148.1 (2 signals overlapping), 146.4, 145.8, 137.0, 136.8, 131.3, 128.3, 126.9, 124.0, 123.8, 122.6, 122.1, and 113.0 ppm. MS (m/z): 294 (M^+). Anal. Calcd. (%) for $C_{16}H_{10}N_2S_2$: C, 65.28; H, 3.42; N, 9.52. Found C, 65.41; H, 3.67; N, 9.17.

3-(Cyanomethyl)thiophene-2-carboxylic acid [8f] (8). This compound was synthesized analogously to **2**, using benzoylacetonitrile instead of 1-phenyl-1,3-butanedione as starting material.

Yield: 69%; off-white crystals. mp. 133–135°C (lit. 134–136°C). [8f] ^{1}H-NMR (DMSO-d_6, 300 MHz) δ: 13.45 (br s, 1H), 7.89 (d, 1H, J = 5.1 Hz), 7.24 (d, 1H, J = 5.1 Hz), 4.25 (s, 2H) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz) δ: 162.9, 136.8, 132.2, 130.4, 129.5, 118.4, and 17.5 ppm. MS (*m*/*z*): 167 (M^+).

5,7-Dibromothieno[2,3-*c*]pyridine [14] (9). The carboxylic acid **8** (6.5 g, 39 mmol) was transferred to a dry round-bottomed flask. Fresh PBr_3 (100 g, 0.37 mol) was then added in one portion and the system was flushed with N_2. With vigorous stirring the mixture was heated to 175°C under N_2. After 6 h the reaction mixture was allowed to cool to r.t. Residual PBr_3 was hydrolyzed by slow dropwise addition of ice-water (200 mL) through the condenser with the round-bottomed flask submerged in an ice-bath. When the addition was complete the resulting solution was made alkaline with NaOH (aq, 1 M). The resulting solution was divided into five portions and each portion was extracted with EtOAc (2 × 100 mL). The organic phase were, washed with brine and dried over $MgSO_4$. Evaporation under reduced pressure yielded a brown powder (1.59 g). The product was purified by column chromatography (silica, EtOAc:hexane 9:1). The fractions containing product (R_f = 0.95) were evaporated under reduced pressure, yielding **9**, which was recrystallized from MeOH.

Yield: 1.59 g (11%); pale yellow needles. mp. 125–127.5°C. ^{1}H-NMR (DMSO-d_6, 300 MHz) δ: 8.29 (d, 1H, J = 5.4 Hz), 8.22 (s, 1H), 7.65 (d, 1H, J = 5.4 Hz) ppm. ^{13}C-NMR (DMSO-d_6, 75 MHz) δ: 148.6, 138.0, 137.1, 133.3, 132.8, 124.2, and 121.7 ppm. MS (*m*/*z*): 293 (M^+). Anal. Calcd. (%) for $C_7H_3Br_2NS$: C, 28.70; H, 1.03; N, 4.78. Found C, 28.96; H, 1.22; N, 4.61.

5,7-Di(pyridin-2-yl)thieno[2,3-*c*]pyridine (L3). The dibromo compound **9** (0.58 g, 2 mmol), 2-(tributylstannyl)pyridine (80%, 1.89 g, 4.1 mmol) and [Pd(PPh$_3$)$_4$] (5 mol%, 0.11 g) were added to toluene (25 mL) in a round-bottomed flask and the system was flushed with N_2. The mixture was refluxed under N_2 and monitored by TLC (hexane:EtOAc 7:3). After 24 h, no additional product appeared to have formed and the reaction mixture was allowed to cool to r.t. The solution was washed with potassium fluoride (aq, 1 M, 2 × 50 mL) and brine (50 mL). The organic phase was separated, dried over $MgSO_4$ and evaporated under reduced pressure, yielding a brown oily substance which was purified by flash chromatography (silica, hexane:EtOAc 7:3). The fractions containing product

(R_f = 0.55) were combined and evaporated under reduced pressure, yielding **L3** as an off-white powder which was recrystallized from MeOH.

Yield: 0.46 g (80%); white needles. mp. 134–136°C. UV (EtOH): λ_{max} /nm (log ε/dm^3 mol^{-1} cm^{-1}) = 254 (4.53), 277 (4.45), 286 (4.44), 301 (4.25), 313 (4.24), 334 (4.22), and 346 (4.20). ^{1}H-NMR ($CDCl_3$, 300 MHz) δ: 8.92 (s, 1H), 8.90 (dd, 1H, *J* = 8.0, 1.1 Hz), 8.85 (m, 1H), 8.71–8.76 (m, 2H), 7.86–7.97 (m, 2H), 7.84 (d, 1H, *J* = 5.6 Hz), 7.54 (d, 1H, *J* = 5.6 Hz), 7.39 (dd, 1H, *J* =4.8, 1.2 Hz), 7.33 (dd, 1H, *J* = 2.7, 1.0 Hz) ppm. ^{13}C-NMR ($CDCl_3$, 75 MHz) δ: 156.6, 155.9, 149.4, 149.2, 149.1, 148.3, 148.2, 137.4, 136.9, 136.5, 133.1, 123.9, 123.5, 123.4, 121.8, 121.5, and 115.8 ppm. MS (*m*/*z*): 289 (M^+). Anal. Calcd. (%) for $C_{17}H_{11}N_3S$: C, 70.56; H, 3.83; N, 14.52. Found C, 70.79; H, 4.15; N, 14.27.

SUPPORTING INFORMATION

^{1}H-NMR of compounds **2**, **4–9** and **L1–L3** and UV spectra of **L1–L3** is provided as Supporting Information in the online version of this article.

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