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Synthesis of azafluorenones and related compounds using deprotocupration–aroylation followed by intramolecular direct arylation☆

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ABSTRACT

The efficiency of the deprotocupration–aroylation of 2-chloropyridine using lithiocuprates prepared from CuX (X=Cl, Br) and LiTMP (TMP=2,2,6,6-tetramethylpiperidido, 2 equiv) was investigated. CuCl was identified as a more suitable copper source than CuBr for this purpose. Different diaryl ketones bearing a halogen at the 2 position of one of the aryl groups were synthesized in this way from azines and thiophenes. These were then involved in palladium-catalyzed ring closure: substrates underwent expected CH-activation-type arylation to afford fluorenone-type compounds, and were also subjected to cyclization reactions leading to xanthones, notably in the presence of oxygen-containing substituents or reagents.

1. Introduction

Due to the biological interest of azafluorenones, for example, in relation to their antifungal,[1] antimicrobial,[2] antimalarial,[2b,3] and cytotoxic[2b,4] properties, or else for their role in the treatment of neurodegenerative disorders,[5] many studies have been devoted to their synthesis. Among modern synthetic methods by which to access them, lithiations[6] and multicomponent reactions[2d,4a,7] can be cited. In 2010, Kraus and Kempema developed an approach using 2-bromoaryl 3-pyridyl ketones, prepared by reaction of 3-pyridyllithiums with 2-bromobenzaldehydes followed by oxidation, in intramolecular Heck cyclization reactions.[2c] Facile oxidation of the corresponding α-aryl-α-(2-bromo-3-pyridyl)methanols led Ray and co-workers to successfully perform, within one step, both oxidation and cyclization reactions.[8]

In the course of the development of lithium 2,2,6,6-tetramethylpiperidido (LiTMP) bases for the deprotonative metallation of aromatic compounds,[9] we have developed the use of the lithiocuprates prepared in situ from CuCl and LiTMP (2 equiv).[10] Besides its possible use at rt, one main advantage of using the resulting bimetallic base is the possible trapping of the formed arylmetal species by aroyl chlorides to directly afford ketones. Applied to the synthesis of 2-chloro diaryl ketones, this method could be combined with direct arylation through C–H bond activation by intramolecular transition metal-catalysis,[11] to afford azafluorenones and related compounds. We have recently demonstrated the feasibility of this two-step access to such tricyclic heterocycles;[12] herein, the details of our investigations, including the testing of a large range of substrates, and the unexpected outcomes observed for the cyclization reactions are described.

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2. Results and discussion

Before embarking on a study aimed at using the deprotocupration–aroylation sequence as the main step in the synthesis of azafluorenones and related compounds, we sought to investigate what the best source of lithiocuprate base might be. This could conceivably involve preparation of the cuprate in situ from CuX (X=F, Cl, Br, I) and LiTMP (2 equiv) at 0 °C in THF containing TMEDA (1 equiv, TMEDA=*N*,*N*,*N*′,*N*′-tetramethylethylenediamine).[10c]

Prior work on the deprotometalation–iodination of benzoxazole involved the use of a $(TMP)_2Zn$–TMPLi mixture and afforded only a 2% difference in yield between the quenched products when the base was prepared from $ZnBr_2$ (58% yield) or $ZnCl_2$ (60% yield).[13] In a similar way, the putative base $(TMP)_3FeLi$ gave approximately equivalent yields (80% using $FeCl_2$ vs 86% with $FeBr_2$),[14] suggesting essentially equivalent reactivities for these two halides. In contrast, prior work with FeI_2 clearly gave a lower yield (62%) and it proved substantially worse with FeF_2 (27%).[14] On the back of these data we tested both CuCl and CuBr as potential substrates in the present study; 2-chloropyridine was reacted with bases generated using either copper(I) halide at rt for 2 h before interception of the corresponding arylmetal reagents with different benzoyl chlorides. In line with expectation, lithiocuprates generated using CuBr and CuCl achieved essentially similar yields (Table 1). However, it was noted that, reproducibly, chloride reagents performed slightly better and these were therefore selected for more detailed study (vide infra). This notwithstanding, the isolation and full characterization of Lipshutz-type $(TMP)_2CuLi\cdot LiBr$ (**B**) (Fig. 1) suggests that it is isostructural with the known chloride[12] analogue, so that the nominal differences observed in product yield are unlikely to be attributable to lithiocuprate structure based on the choice of bromide or chloride starting material.

Based on the prior work with CuF and CuI, and on the data in Table 1, CuCl was selected for preparing the lithiocuprate for use in subsequent deprotocupration-aroylation work. The technique to be used has previously been applied to the synthesis of the heterocyclic ketones **1**,[10b] **4**,[10c] **5**,[10b] **6**[10b] and **7**,[10b] and has been successfully used to reach the diaryl ketones **8**–**15**. All these

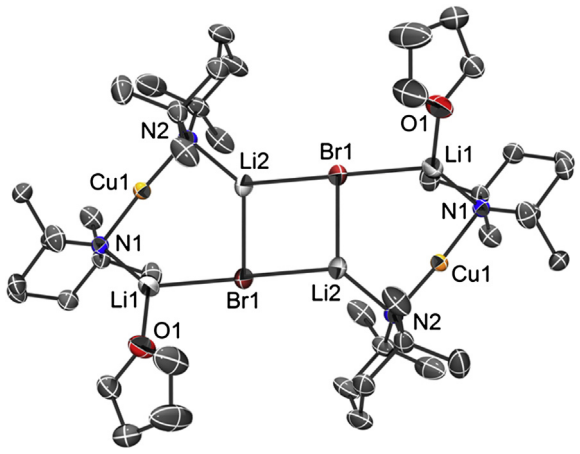
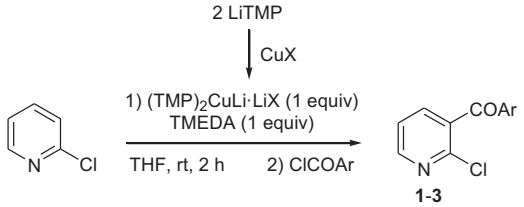


Fig. 1. ORTEP diagram (50% probability, H atoms omitted) of the dimer of $(TMP)_2Cu$-Li·LiBr (**B**).

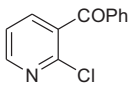
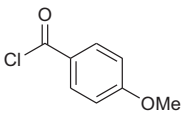
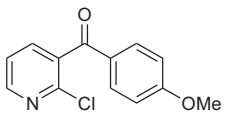
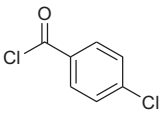
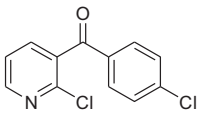
compounds, gathered in Table 2, could lead to heterocyclic tricycles (or tetracycle in the case of **4**) through cyclizing arylation. It is worth noting that the trapping step was improved in the thiophene series by raising the reaction temperature to 60 °C (entry 14).

We subsequently turned our attention to the cyclization of the halogeno diaryl ketones, using them to yield azafluorenones and related compounds through palladium-catalyzed intramolecular arylation. The synthesis of 4-azafluorenone (**16**) has previously been the subject of several studies,[6b,15] and harsh conditions are known to sometimes be required for its formation. For example, Stauffer and co-workers prepared it by heating 2-phenylnicotinic acid (obtained in two steps from 2-chloro-3-cyanopyridine) at 190 °C in polyphosphoric acid.[16] To attempt the conversion of 3-benzoyl-2-chloropyridine (**1**) to the tricycle **16**, we used a protocol previously described for the cyclization of 2-chloro diaryl aniline to carbazole as a basis for this.[17] The reactions were carried out in the presence of catalytic amounts of $Pd(OAc)_2$, an electron-

Table 1
Deprotocupration of 2-chloropyridine using in situ prepared $(TMP)_2CuLi\cdot LiCl$ (A) or $(TMP)_2CuLi\cdot LiBr$ (B) followed by benzoylation

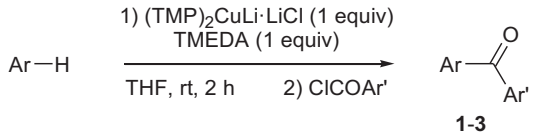


1-3

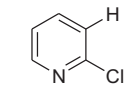
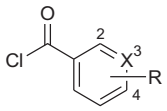
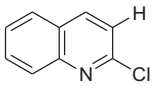
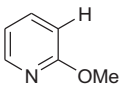
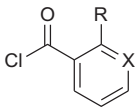
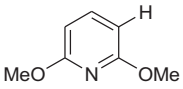
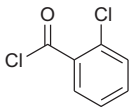
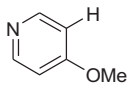
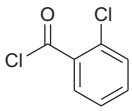
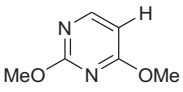
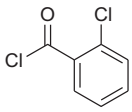
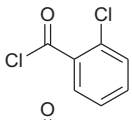
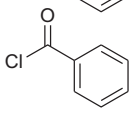
Entry	ClCOAr	CuX (base)		Product	Yield[a] (%)
1	ClCOPh	CuCl (A)	**1**		78–90[b,10]
2		CuBr (B)			60–70[b]
3		CuCl (A)	**2**		60–80[b]
4		CuBr (B)			49
5		CuCl (A)	**3**		56–80[b]
6		CuBr (B)			55–61[b]

[a] Yield after purification by column chromatography. The rest is starting material.
[b] Reaction performed at least twice.

Table 2
Synthesis of the diaryl ketones **1**–**15** by deprotocupration followed by aroylation



1-3

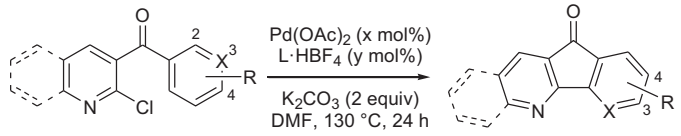
Entry	Ar—H	ClCOAr′	R and/or X	Product	Yield[a] (%)
1			H, CH	**1**	90[10b]
2			4-OMe, CH	**2**	80
3			4-Cl, CH	**3**	80
4			3-OMe, CH	**8**	66
5			2-Cl, CH	**9**	59
6			2-Cl, N	**10**	65
7		ClCOPh		**4**	44[10c]
8			Cl, CH	**11**	56
9			Br, CH	**12**	43
10			Cl, N	**13**	39
11				**5**	91[10b]
12				**6**	57[10b]
13				**7**	58[10b]
14				**14**	35, 57[b]
15				**15**	85[b]

[a] Yield after purification by column chromatography. The rest is starting material.
[b] Trapping step performed at 60 °C instead of rt.

rich and bulky trialkyl phosphine, and K_2CO_3 as a base. Different transition metal–ligand ratios were screened by using Cy_3P (Cy=cyclohexyl) in DMF at 130 °C, and the best result was observed using 5 mol % of $Pd(OAc)_2$ and 10 mol % of phosphine (incomplete conversion was noted using 20 mol % of $Pd(OAc)_2$ and 10 mol % of phosphine) (Table 3, entries 1–4). Using DMA or dioxane as solvent or even a tetraalkylammonium chloride, as recommended by Kraus and Kempema for the cyclization of bromo diaryl ketones,[2c] proved less suitable.

These optimized conditions in hand, the ketones **2** and **3** were involved in the reaction. Whereas the former led to the expected methoxy-substituted azafluorenone **17** in 69% yield (entry 5), only 4-azafluorenone (**16**, 19%) was isolated alongside unidentified side products using the latter (entry 6). Cyclization of 3-benzoyl-2-chloroquinoline (**4**) was achieved under the same reaction conditions, affording 11*H*-indeno[1,2-*b*]quinolin-11-one (**18**) in 63% yield (entry 8). In the case of 2-chloro-3-pyridyl 3-methoxyphenyl ketone (**8**), for which two cyclization products are possible, the reaction proved regioselective,[18] the C–H bond activation occurring *para* to the methoxy group in the course of the formation of the tricycle **19** (entry 9). The structures of both **16** and **19** were confirmed unambiguously by X-ray diffraction (Fig. 2). As was observed of its isomer **3**, the reagent **9**, expected to allow further coupling thanks to the presence of a chloro group, did not afford the corresponding chloro cyclized product. Indeed, 4-azafluorenone (**16**) was again the sole identifiable product obtained using Cy_3P or $^tBu_3P$ (entries 10 and 11). The use of **10**, in which the 2-chlorophenyl is replaced by a 2-chloro-3-pyridyl, also failed to lead to the isolation

Table 3
Synthesis of the azafluorenones **16**–**19** by intramolecular arylation



Entry	Substrate	*x*	L (*y*)	Product	Yield[a] (%)
1	**1**	5	Cy_3P (10)	**16**	87
2		5	Cy_3P (15)		82
3		10	Cy_3P (10)		81
4		20	Cy_3P (10)		64[b]
5	**2** (R=OMe)	5	Cy_3P (10)	**17**	69[c]
6	**3** (R=Cl)	5	Cy_3P (10)	—	—[d]
7		5	$^tBu_3P$ (10)	—	—[e]
8	**4**	5	Cy_3P (10)	**18**	63[b]
9	**8**	5	Cy_3P (10)	**19**	60[b]
10	**9**	5	Cy_3P (10)	—	—[f]
11		5	$^tBu_3P$ (10)	—	—[f]
12	**10**	5	Cy_3P (10)	—	—[g]

[a] After purification by column chromatography.
[b] Only organic product present in the crude.
[c] Compound **2** was also recovered in 10% yield.
[d] 8-Chloro-5*H*-indeno[1,2-*b*]pyridin-5-one was not obtained but **16** was isolated in 19% yield.
[e] 8-Chloro-5*H*-indeno[1,2-*b*]pyridin-5-one was not obtained but **16** was isolated in 8% yield.
[f] 6-Chloro-5*H*-indeno[1,2-*b*]pyridin-5-one was not obtained but **16** and 3-benzoylpyridine were isolated in 18 and 13% yields, respectively, among unidentified products.
[g] 6-Chloro-5*H*-pyrido[3′,4′:4,5]cyclopenta[1,2-*b*]pyridin-5-one was not obtained but 5*H*-pyrano[2,3-*b*:6,5-*b*′]dipyridin-5-one **20** was isolated in 70% yield (only organic product present in the crude), see Scheme 1.

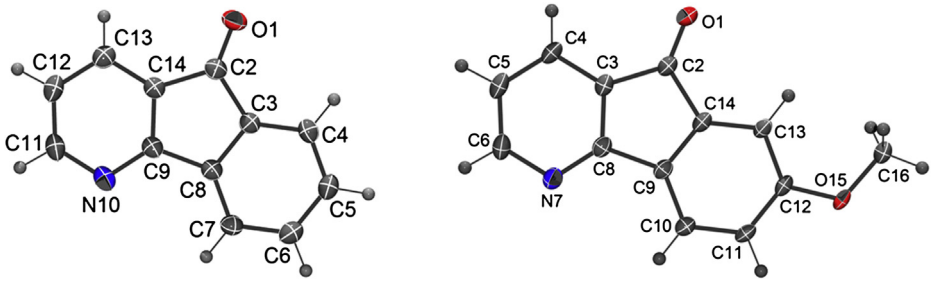
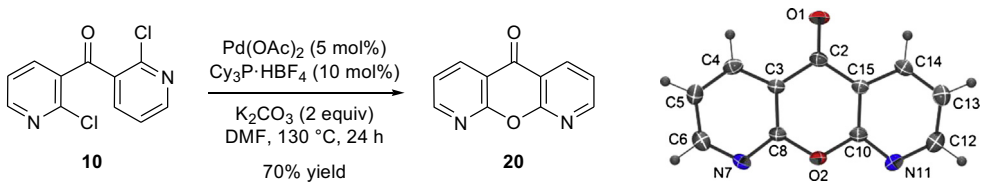


Fig. 2. ORTEP diagrams (50% probability) of compounds **16** and **19**.

of an azafluorenone (entry 12). Surprisingly, 5*H*-pyrano[2,3-*b*:6,5-*b*′]dipyridin-5-one (**20**) was isolated instead in 70% yield (Scheme 1), a result that could be attributed to the presence of a carbonate reagent (vide infra).

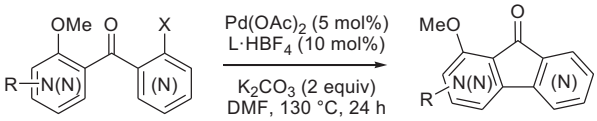
We next turned to the cyclization through intramolecular arylation of the ketones prepared from methoxypyridines (Table 4). The diaryl ketone **11**, in which the chloro group is connected to the phenyl component, led to the corresponding azafluorenone, but did so less

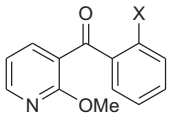
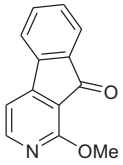
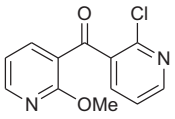
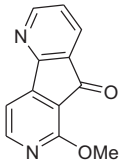
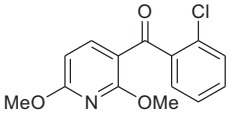
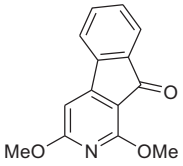
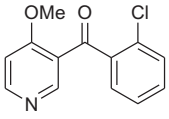
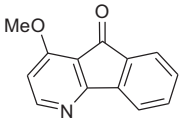
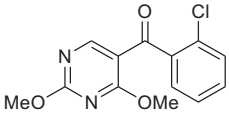
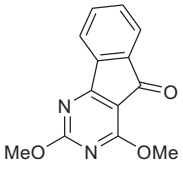


Scheme 1. Synthesis of 5*H*-pyrano[2,3-*b*:6,5-*b*′]dipyridin-5-one (**20**) from **10** and ORTEP diagram (50% probability) of compound **20**.

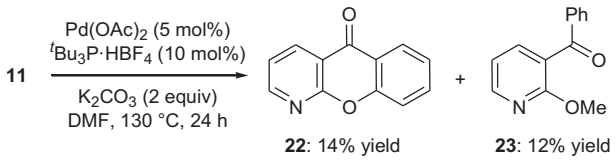
efficiently than either **1**, **2**, **4** or **8** (Table 3). Using a tetraalkylammonium chloride, as recommended by Kraus and Kempema for the cyclization of bromo diaryl ketones,[2c] we were able to isolate the expected methoxy-substituted 9*H*-indeno[2,1-*c*]pyridin-9-one **21** in 48% yield (Table 4, entry 1). Various attempts to increase the yield by recourse to cesium carbonate or sodium *tert*-butoxide as base or to toluene or DMA as solvent led to lower conversions. It is worth noting that using $^{t}Bu_3P$ in this case did not lead to an azafluorenone but only to the cyclized demethylated azaxanthone **22** together with the non-cyclized dechlorinated product **23** (entry 2, Scheme 2).

Table 4
Synthesis of the azafluorenones **21** and **24** by intramolecular arylation



Entry	Substrate		L	Product		Yield[a] (%)
1	**11** (X=Cl)		Cy_3P	**21**		48[b,c,d]
2			$^{t}Bu_3P$			—[e]
3	**12** (X=Br)		Cy_3P			40,[b,f] 61[f]
4			$^{t}Bu_3P$			81[b]
5	**13**		Cy_3P	—		—[g]
6	**5**		Cy_3P	**24**		30[h]
7			$^{t}Bu_3P$			21
8	**6**		Cy_3P	—		—[i]
9	**7**		Cy_3P	—		—[j]

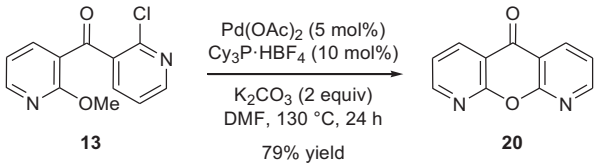
[a] After purification by column chromatography.
[b] Reaction performed in the presence of Pr_4NCl (2 equiv).
[c] Lower conversion without Pr_4NCl.
[d] Only organic product present in the crude.
[e] 1-Methoxy-9*H*-indeno[2,1-*c*]pyridin-9-one (**21**) was not obtained (see Scheme 2).
[f] The rest is starting material.
[g] 6-Methoxy-5*H*-pyrido[3′,4′:4,5]cyclopenta[1,2-*b*]pyridin-5-one was not obtained, see Scheme 3.
[h] Compound **5** (34%) was recovered; an unidentified product also formed.
[i] 4-Methoxy-5*H*-indeno[1,2-*b*]pyridin-5-one was not obtained, see Scheme 5.
[j] 2,4-Dimethoxy-5*H*-indeno[1,2-*d*]pyrimidin-5-one was not obtained, see Scheme 6.



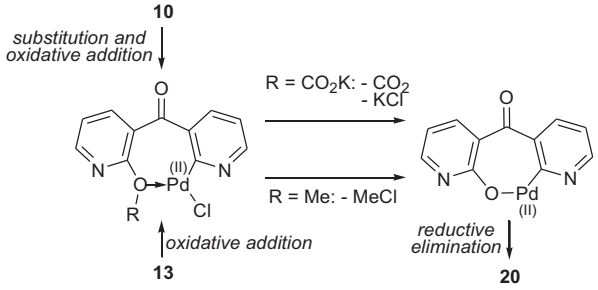
Scheme 2. Synthesis of 5*H*-benzopyrano[2,3-*b*]pyridin-5-one (**22**) from **11**.

The disappointing results obtained using **11** led us to also consider the diaryl ketone **12**, which bears a bromo group instead of a chloro one. Its cyclization in the presence of Pr_4NCl using either Cy_3P or $^tBu_3P$ afforded the methoxy-substituted azafluorenone **21** in 40 and 81% yields, respectively. It transpired that Pr_4NCl was not actually required since **21** could still be isolated in 61% yield using Cy_3P without this ammonium salt (entries 3 and 4). Replacing K_2CO_3 by Cs_2CO_3 also allowed us to isolate **21** using toluene as solvent (110 °C), but in a low 20% yield.

We next turned to the cyclization of the diaryl ketone **13**, which differs from **11** in that the 2-chlorophenyl ring is replaced by a 2-chloro-3-pyridyl one. As noted using **10**, no azafluorenone was obtained, but instead the same azaxanthone **20** was isolated in 79% yield (the crude also contained recovered **13** and unidentified products, entry 5, Scheme 3). The formation of **20** from both **10** (in this case, the substitution of a chloro group by a carbonate is considered to explain the presence of oxygen in the product) and **13** through a common intermediate can be explained by the mechanism depicted in Scheme 4.



Scheme 3. Synthesis of 5*H*-pyrano[2,3-*b*:6,5-*b*′]dipyridin-5-one (**20**) from **13**.



Scheme 4. Mechanism proposed to explain the formation of 5*H*-pyrano[2,3-*b*:6,5-*b*′] dipyridin-5-one (**20**) from **10** and **13** through a common intermediate (ligands omitted).

As observed for **11**, the cyclization of the dimethoxy ketone **5** furnished the expected 9*H*-indeno[2,1-*c*]pyridin-9-one **24** (Fig. 3). However, the yield proved to be lower in the case of **24** since it was isolated in 30 and 21% yields, respectively, using Cy_3P and $^tBu_3P$ as ligand. The presence of a second electron-donating methoxy group on the substrate **5** could be responsible for the reduced reactivity observed; indeed, the ketone **5** was recovered in 34% yield using Cy_3P as ligand (entries 6 and 7).

Compared with **11**, the ketone **6**, for which the methoxy group was moved from the 2- to the 4-position of the pyridine ring, gave a different result. Indeed, when treated under the general cyclization conditions using Cy_3P, no azafluorenone was obtained, but 10*H*-benzopyrano[3,2-*c*]pyridin-10-one (**25**) formed instead in 31%

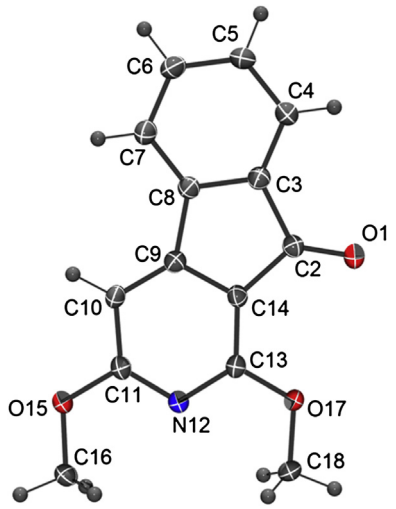


Fig. 3. ORTEP diagram (50% probability) of compound **24**.

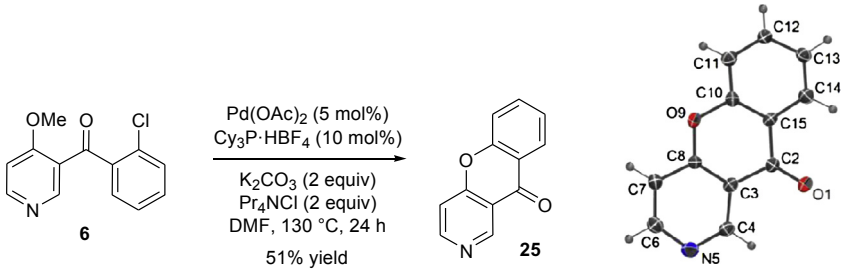
yield. The presence of Pr_4NCl improved this yield to 51% (**25** was the only organic product present in the crude, entry 8, Table 4, Scheme 5).

From the pyrimidyl ketone **7**, neither an azafluorenone nor an azaxanthone was formed, but a complex mixture resulted instead. Doubling the amount of catalyst led to a complete degradation of the substrate. Crystals suitable for X-ray diffraction were isolated in this case and therefore allowed the pyrimidine ring-opening product shown in Scheme 6 to be evidenced. To rationalize the unexpected formation of **26**, the plausible mechanistic sequence depicted in Scheme 7 was proposed.

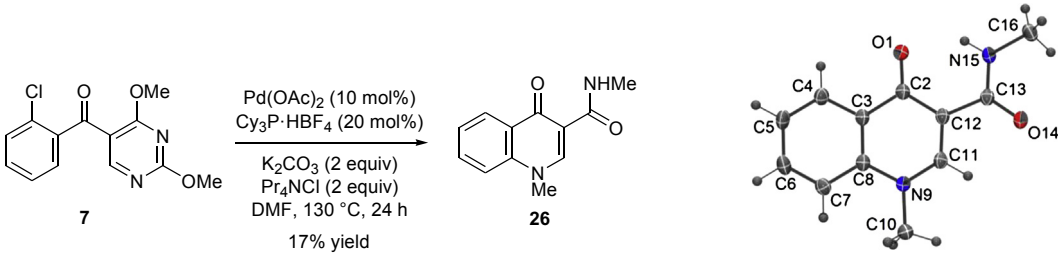
8*H*-Indeno[2,1-*b*]thiophen-8-one (**27**) has previously been efficiently synthesized by Campo and Larock from 3-(2-bromophenyl) thiophene using palladium-catalyzed cyclocarbonylation.[19] Starting from **14**, which bears the chloro group on the phenyl ring, both Cy_3P and $^tBu_3P$ were tested as ligand in DMF at 130 °C, affording **27** in 90 and 38% yields, respectively. Lower 35 and 17% yields were, respectively, obtained from **15**, for which the chloro group is present on the thiophene ring (Table 5).

3. Biological evaluation

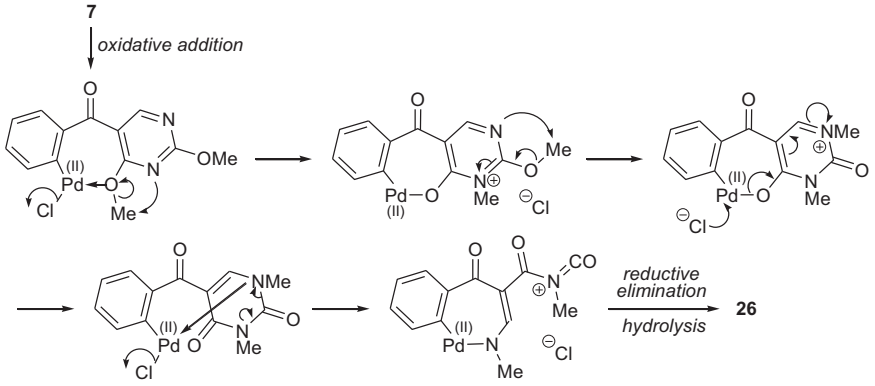
A preliminary study has been carried out to investigate the cytotoxic potential of the fluorenone derivatives **16**, **17**, **18**, **21**, **27** and the azaxanthones **20** and **25**. The anti-proliferative activity of the derivatives was determined using breast cancer cell lines: MCF-7, A549 human lung adenocarcinoma cells, and A2058 human melanoma cells. MCF-7 is an invasive differentiated mammary epithelial breast cancer cell line; A549 is an adenocarcinomic alveolar epithelial cell line, and A2058 is a highly invasive and tumorigenic epithelial melanoma cell line. These three cell lines are used worldwide to screen and compare the anti-proliferative activity of new molecules vs standard anticancer compounds. The molecules tested fell short of exhibiting moderate-to-strong activity at 10 mM with the selected cell lines, with none of the molecules causing more than a 10% inhibition of growth. Because of structural similarity with natural azafluorenone antimicrobial agents such as Onychine,[2b] the synthesized compounds **16**, **17**, **18**, **21**, and the thiofluorenone analogue **27** were then screened for their antibacterial activity against a panel of Gram-positive and Gram-negative reference strain bacteria (*Escherichia coli* ATCC25922, *Salmonella enterica serovar Typhimurium* CIP5858, *Pseudomonas aeruginosa* ATCC27853, *Staphylococcus aureus* ATCC25923, *Bacillus subtilis* CIP52.62), and for their antifungal activity against pathogenic strain



Scheme 5. Synthesis of 10*H*-benzopyrano[3,2-*c*]pyridin-10-one (**25**) from **6** and ORTEP diagram (50% probability) of compound **25**.

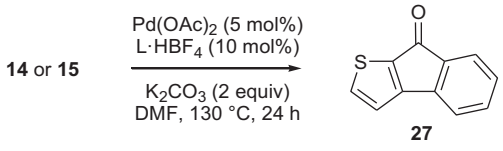


Scheme 6. Degradation of **7** under palladium catalysis and ORTEP diagram (50% probability) of compound **26**.



Scheme 7. Mechanistic sequence proposed for the formation of **26**.

Table 5
Synthesis of 8*H*-indeno[2,1-*b*]thiophen-8-one (**27**) by intramolecular arylation



Entry	Substrate	L	Yield[a] (%)
1	**14**	Cy_3P	90
2		$^tBu_3P$	38[b]
3	**15**	Cy_3P	35[c]
4		$^tBu_3P$	17[d]

[a] After purification by column chromatography.
[b] The rest corresponds to recovered **14** but also to the formation of an unidentified product.
[c] The formation of 2-benzoylthiophene was also noted.
[d] The rest corresponds to recovered **15** but also to the formation of unidentified products.

(*Candida glabrata* DSM6425). However, no antimicrobial activity was detected against bacteria or yeast.

4. Conclusion

In summary, different heterocyclic diaryl ketones have been synthesized by sequential deprotocupration–aroylation. For diaryl ketone reagents bearing a halogen at the 2-position of one of the aryl groups cyclization under palladium catalysis was considered. In the absence of a methoxy or a second chloro group at the position adjacent to the ketone function, fluorenones were obtained. The presence of a second chloro group was not tolerated, and resulted in mixtures containing dechlorinated products. The presence of a methoxy group led to lower yields of fluorenones, with unexpected xanthones being obtained in some cases. In the case of the dimethoxylated pyrimidyl ketone **7**, ring-opening of the pyrimidine ring was established. Lastly, efficient thiofluorenone formation was demonstrated, though the efficiency of this reaction proved to be strongly dependent on the location of the chloro-substituent.

5. Experimental section

5.1. General

All reactions were performed in Schlenk tubes under an argon atmosphere. THF was distilled over sodium/benzophenone. DMF was dried over CaH_2 and distilled before use. Liquid chromatography separations were achieved on silica gel Merck-Geduran Si 60 (63–200 μm). Nuclear magnetic resonance spectra were acquired using Bruker AC-300 spectrometer (300 MHz and 75 MHz for ^1H and ^{13}C, respectively). ^1H chemical shifts (δ) are given in parts per million (ppm) relative to the residual solvent peak, and ^{13}C chemical shifts relative to the central peak of the solvent signal. High-resolution mass spectrometry measurements were performed at the Centre Régional de Mesures Physiques de l'Ouest (CRMPO) in Rennes.

X-ray crystallography. The samples **16**, **19**, **20** and **24**–**26** were studied with graphite monochromatized Mo-Kα radiation (λ=0.71073 Å). X-ray diffraction data were collected at T=150(2) K using APEXII, Bruker-AXS diffractometer. All structures were solved by direct methods using the SIR97 program,[20] and then refined with full-matrix least-square methods based on F^2 (SHELX-97)[21] with the aid of the WINGX program.[22] All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. H atoms were finally included in their calculated positions. Molecular diagrams were generated by ORTEP-3 (version 2.02).[22] For B a Nonius Kappa-CCD and an Oxford Cryostream low-temperature device were used. Structure solution used direct methods,[23] with full-matrix least-squares refinement based on F^2.[24] Non-hydrogen atoms were refined anisotropically and a riding model with idealized geometry employed for the refinement of H atoms.

5.2. General procedure 1: deprotonation using the lithium–copper base prepared from CuCl (1 equiv) and LiTMP (2 equiv) before trapping with an aroyl chloride

A stirred cooled (0 °C) solution of LiTMP prepared at 0 °C in THF (6 mL) from 2,2,6,6-tetramethylpiperidine (1.7 mL, 10 mmol) and BuLi (1.6 M hexanes solution, 10 mmol) was treated with TMEDA (0.77 mL, 5.0 mmol) and CuCl (495 mg, 5.0 mmol). The mixture was stirred for 15 min at 0 °C before introduction of the required substrate (5 mmol). After 2 h at rt, a solution of the required aroyl chloride (10 mmol) in THF (3 mL) was added. The mixture was stirred at rt or 60 °C overnight before addition of a 1 M aqueous solution of NaOH (20 mL) and extraction with Et_2O (2×20 mL). After washing the organic phase with an aqueous saturated solution of NH_4Cl (10 mL) and drying over anhydrous Na_2SO_4, the solvent was evaporated under reduced pressure, and the product was isolated after purification by flash chromatography on silica gel (the eluent is given in the product description).

*5.2.1. 2-Chloro-3-pyridyl phenyl ketone (**1**).*[10b] Compound **1** was prepared from 2-chloropyridine (using benzoyl chloride) and was isolated (eluent: 9:1 heptane/AcOEt) as a yellow oil (yield: 90%): ^1H NMR (300 MHz, $CDCl_3$) δ 7.38 (dd, 1H, J=7.5 and 4.9 Hz), 7.42–7.50 (m, 2H), 7.61 (tt, 1H, J=7.4 and 1.3 Hz), 7.72 (dd, 1H, J=7.5 and 2.0 Hz), 7.75–7.81 (m, 2H), 8.52 ppm (dd, 1H, J=4.9 and 2.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ 122.3 (CH), 128.9 (2CH), 130.0 (2CH), 134.3 (CH), 134.9 (C), 135.7 (C), 138.0 (CH), 147.7 (C), 150.9 (CH), 193.3 ppm (C=O).

*5.2.2. 2-Chloro-3-pyridyl 4-methoxyphenyl ketone (**2**).* Compound **2** was prepared from 2-chloropyridine (using 4-methoxybenzoyl chloride) and was isolated (eluent: 8:2 heptane/AcOEt) as a yellow powder (yield: 80%): mp 79 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 3.89 (s, 3H), 6.96 (d, 2H, J=9.0 Hz), 7.38 (dd, 1H, J=7.5 and 4.8 Hz), 7.72 (dd, 1H, J=7.5 and 1.9 Hz), 7.78 (d, 2H, J=4.8 Hz), 8.54 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.8 (CH_3), 114.3 (2CH), 122.4 (CH), 128.9 (C), 132.7 (2CH), 135.5 (C), 137.8 (CH), 147.8 (C), 150.7 (CH), 164.6 (C), 192.0 ppm (C=O). These NMR data are analogous to those described previously.[25]

*5.2.3. 4-Chlorophenyl 2-chloro-3-pyridyl ketone (**3**).* Compound **3** was prepared from 2-chloropyridine (using 4-chlorobenzoyl chloride) and was isolated (eluent: 8:2 heptane/AcOEt) as a yellow powder (yield: 80%): mp 56 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40 (dd, 1H, J=7.5 and 4.8 Hz), 7.44–7.48 (m, 2H), 7.71–7.76 (m, 3H), 8.57 (dd, 1H, J=4.8 and 1.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 122.5 (CH), 129.4 (2CH), 131.4 (2CH), 134.2 (C), 134.6 (C), 138.1 (CH), 141.0 (C), 147.8 (C), 151.2 (CH), 192.3 ppm (C=O). These NMR data are analogous to those described previously.[26]

*5.2.4. 2-Chloro-3-benzoylquinoline (**4**).*[10c] Compound **4** was prepared from 2-chloroquinoline (using benzoyl chloride) and was isolated (eluent: 7:3 heptane/AcOEt) as a beige powder (yield: 44%): mp 98 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.43–7.48 (m, 2H), 7.55–7.61 (m, 2H), 7.77–7.84 (m, 4H), 8.05 (d, 1H, J=8.5 Hz), 8.18 ppm (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 126.0 (C), 127.9 (CH), 128.1 (CH), 128.5 (CH), 128.8 (2CH), 130.1 (2CH), 131.9 (CH), 132.4 (C), 134.1 (CH), 136.2 (C), 138.5 (CH), 146.5 (C), 147.9 (C), 193.3 ppm (C=O).

*5.2.5. 2-Chlorophenyl 2,6-dimethoxy-3-pyridyl ketone (**5**).*[10b] Compound **5** was prepared from 2,6-dimethoxypyridine (using 2-chlorobenzoyl chloride) and was isolated (eluent: 9:1 heptane/AcOEt) as a yellow powder (yield: 91%): mp 55 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 3.81 (s, 3H), 3.98 (s, 3H), 6.37 (d, 1H, J=8.4 Hz), 7.31–7.37 (m, 4H), 7.98 ppm (d, 1H, J=8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 54.0 (CH_3), 54.2 (CH_3), 102.7 (CH), 113.1 (C), 126.8 (CH), 128.7 (CH), 129.6 (CH), 130.6 (CH), 130.9 (C), 141.1 (C), 144.1 (CH), 163.0 (C), 166.3 (C), 192.1 ppm (C=O).

*5.2.6. 2-Chlorophenyl 4-methoxy-3-pyridyl ketone (**6**).*[10b] Compound **6** was prepared from 4-methoxypyridine (using 2-chlorobenzoyl chloride) and was isolated (eluent: 2:8 heptane/AcOEt) as a yellow powder (yield: 57%): mp 107 °C; ^1H NMR (300 MHz, C_6D_6) δ 3.76 (s, 3H), 6.95–7.05 (m, 1H), 7.31–7.43 (m, 3H), 7.45–7.49 (m, 1H), 8.42–9.76 (br m, 2H); ^{13}C NMR (75 MHz, C_6D_6) δ 55.0 (CH_3), 108.8 (C), 126.7 (CH), 128.3 (CH), 130.1 (CH), 130.1 (CH), 131.3 (CH), 132.1 (C), 140.8 (C), 152.7 (CH), 154.5 (CH), 164.1 (C), 192.3 ppm (C=O).

*5.2.7. 2-Chlorophenyl 2,4-dimethoxypyrimidin-5-yl ketone (**7**).*[10b] Compound **7** was prepared from 2,4-dimethoxypyrimidine (using 2-chlorobenzoyl chloride) and was isolated (eluent: 8:2 heptane/

AcOEt) as an orange powder (yield: 58%): mp 74 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.91 (s, 3H), 4.06 (s, 3H), 7.31–7.44 (m, 4H), 8.62 ppm (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 54.7 (CH_3), 55.7 (CH_3), 114.1 (C), 127.0 (CH), 129.4 (CH), 129.9 (CH), 131.3 (C), 131.6 (CH), 139.4 (C), 163.4 (CH), 167.0 (C), 169.6 (C), 190.8 ppm (C=O).

*5.2.8. 2-Chloro-3-pyridyl 3-methoxyphenyl ketone (**8**).* Compound **8** was prepared from 2-chloropyridine (using 3-methoxybenzoyl chloride) and was isolated (eluent: 8:2 heptane/AcOEt) as an orange powder (yield: 66%): mp 62 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.72 (s, 3H), 7.05 (ddd, 1H, J=8.1, 2.6 and 1.0 Hz), 7.13 (ddd, 1H, J=7.6, 2.6 and 1.3 Hz), 7.22–7.30 (m, 3H), 7.63 (dd, 1H, J=7.5 and 1.9 Hz), 8.41 (d, 1H, J=4.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.6 (CH_3), 113.6 (CH), 120.9 (CH), 122.3 (CH), 123.3 (CH), 129.9 (CH), 135.0 (C), 137.2 (CH), 137.9 (C), 147.8 (C), 150.9 (CH), 160.1 (C), 193.2 ppm (C=O); HRMS (ESI): m/z calcd for $C_{13}H_{10}^{35}ClNaNO_2$ [(M+Na)$^+$•] 270.0298, found 270.0298.

*5.2.9. 2-Chlorophenyl 2-chloro-3-pyridyl ketone (**9**).*[12] Compound **9** was prepared from 2-chloropyridine (using 2-chlorobenzoyl chloride) and was isolated (eluent: 9:1 heptane/AcOEt) as an orange oil (yield: 59%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.51 (m, 4H), 7.57 (dd, 1H, J=7.6 and 1.7 Hz), 7.88 (dd, 1H, J=7.6 and 2.0 Hz), 8.52 ppm (dd, 1H, J=4.8 and 2.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 122.7 (CH), 127.3 (CH), 130.9 (CH), 131.2 (CH), 132.8 (C), 133.3 (CH), 134.9 (C), 137.1 (C), 139.5 (CH), 148.6 (C), 151.8 (CH), 193.1 ppm (C=O); HRMS (ESI): m/z calcd for $C_{12}H_7^{35}Cl_2NNaO$ [(M+Na)$^+$•] 273.9802, found 273.9805.

*5.2.10. Bis(2-chloro-3-pyridyl) ketone (**10**).* Compound **10** was prepared from 2-chloropyridine (using 2-chloronicotinoyl chloride) and was isolated (eluent: 7:3 heptane/AcOEt) as a yellow powder (yield: 65%): mp 109 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (dd, 2H, J=7.5 and 4.8 Hz), 7.98 (dd, 2H, J=7.5 and 1.8 Hz), 8.59 ppm (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 122.8 (2CH), 134.1 (2C), 139.8 (2CH), 148.5 (2C), 152.3 (2CH), 192.2 ppm (C=O). These NMR data are analogous to those described previously.[27]

*5.2.11. 2-Chlorophenyl 2-methoxy-3-pyridyl ketone (**11**).*[12] Compound **11** was prepared from 2-methoxypyridine (using 2-chlorobenzoyl chloride) and was isolated (eluent: 9:1 heptane/AcOEt) as a yellow powder (yield: 56%): mp 65 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.81 (s, 3H), 7.01 (dd, 1H, J=7.5 and 4.9 Hz), 7.31–7.41 (m, 3H), 7.44–7.47 (m, 1H), 7.99 (dd, 1H, J=7.5 and 2.0 Hz), 8.34 ppm (dd, 1H, J=4.9 and 2.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 53.9 (CH_3), 117.1 (CH), 121.8 (C), 126.9 (CH), 129.7 (CH), 129.9 (CH), 131.5 (CH), 131.6 (C), 139.7 (C), 140.6 (CH), 151.3 (CH), 162.2 (C), 193.7 ppm (C=O); HRMS (ESI): m/z calcd for $C_{13}H_{11}^{35}ClNO_2$ [(M+H)$^+$•] and $C_{13}H_{10}^{35}ClNNaO_2$ [(M+Na)$^+$•] 248.0478 and 270.0298, found 248.0483 and 270.0298, respectively.

*5.2.12. 2-Bromophenyl 2-methoxy-3-pyridyl ketone (**12**).* Compound **12** was prepared from 2-methoxypyridine (using 2-bromobenzoyl chloride) and was isolated (eluent: 9:1 heptane/AcOEt) as a yellow powder (yield: 43%): mp 80 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.82 (s, 3H), 6.94 (dd, 1H, J=7.5 and 4.9 Hz), 7.28–7.35 (m, 1H), 7.38–7.40 (m, 2H), 7.62 (dd, 1H, J=7.5 and 0.9 Hz), 8.03 (dd, 1H, J=7.5 and 2.0 Hz), 8.38 ppm (dd, 1H, J=4.9 and 2.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 53.9 (CH_3), 117.1 (CH), 119.6 (C), 121.2 (C), 127.4 (CH), 129.5 (CH), 131.5 (CH), 133.1 (CH), 140.9 (CH), 141.7 (C), 151.5 (CH), 162.2 (C), 194.3 ppm (C=O); HRMS (ESI): m/z calcd for $C_{13}H_{10}^{79}BrNNaO_2$ [(M+Na)$^+$•] 313.9793, found 313.9795.

*5.2.13. 2-Chloro-3-pyridyl 2-methoxy-3-pyridyl ketone (**13**).* Compound **13** was prepared from 2-methoxypyridine (using 2-chloronicotinoyl chloride) and was isolated (eluent: 8:2 heptane/AcOEt) as a yellow powder (yield: 39%): mp 87 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.79 (s, 3H), 7.08 (dd, 1H, J=7.5 and 4.9 Hz), 7.38 (br m, 1H), 7.82 (dd, 1H, J=7.5 and 1.4 Hz), 8.14 (dd, 1H, J=7.5 and 2.0 Hz), 8.40 (dd, 1H, J=4.9 and 2.0 Hz), 8.52 ppm (br m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 54.1 (CH_3), 117.5 (CH), 120.9 (C), 122.5 (CH), 136.6 (C), 138.2 (CH), 140.7 (CH), 147.7 (C), 150.7 (CH), 152.1 (CH), 162.1 (C), 192.0 ppm (C=O); HRMS (ESI): m/z calcd for $C_{12}H_9^{35}ClN_2NaO_2$ [(M+Na)$^+$•] 271.0250, found 271.0251.

*5.2.14. 2-Chlorophenyl 2-thienyl ketone (**14**).* Compound **14** was prepared from thiophene (using 2-chlorobenzoyl chloride, trapping step at 60 °C) and was isolated (eluent: 97:3 heptane/AcOEt) as an orange oil (yield: 57%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12 (dd, 1H, J=4.9 and 3.8 Hz), 7.33–7.49 (m, 5H), 7.76 ppm (dd, 1H, J=4.9 and 1.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 126.7 (CH), 128.4 (CH), 128.0 (CH), 130.4 (CH), 131.3 (C), 131.4 (CH), 135.8 (CH), 136.1 (CH), 138.5 (C), 143.8 (C), 187.2 ppm (C=O). These NMR data are analogous to those described previously.[28]

*5.2.15. 3-Chloro-2-thienyl phenyl ketone (**15**).*[12] Compound **15** was prepared from 3-chlorothiophene (using benzoyl chloride, trapping step at 60 °C) and was isolated (eluent: 9:1 heptane/AcOEt) as a yellow viscous oil (yield: 85%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.99 (d, 1H, J=5.2 Hz), 7.43–7.46 (m, 2H), 7.54–7.60 (m, 2H), 7.81–7.83 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 128.4 (2CH), 129.6 (2CH), 130.1 (CH), 130.7 (CH), 133.0 (CH), 134.3 (C), 137.8 (C), 187.8 ppm (C=O), one C not seen; HRMS (ESI): m/z calcd for $C_{11}H_8^{35}ClOS$ [(M+H)$^+$•] and $C_{11}H_7^{35}ClNaOS$ [(M+Na)$^+$•] 222.9984 and 244.9804, found 222.9999 and 244.9803, respectively.

5.3. General procedure used for the cyclization step

A degassed mixture of K_2CO_3 (0.28 g, 2.0 mmol), $Pd(OAc)_2$ (the amount is given in the product description), the ligand (its nature and the amount is given in the product description), the required ketone (1.0 mmol), and in some cases Pr_4NCl (0.44 g, 2 mmol), in DMF (4 mL) was heated at 130 °C for 24 h. After filtration over a Celite pad, washing using CH_2Cl_2 (3×10 mL), and removal of the solvent under reduced pressure, the product was isolated after purification by flash chromatography on silica gel (the eluent is given in the product description).

*5.3.1. 5H-Indeno[1,2-b]pyridin-5-one (**16**).* Compound **16** was obtained from **1** (using $Pd(OAc)_2$ (5 mol %, 50 μmol, 11 mg) and $Cy_3P{\cdot}HBF_4$ (10 mol %, 0.10 mmol, 37 mg)) and was isolated (eluent: 8:2 heptane/AcOEt) as a yellow powder (yield: 87%): mp 138 °C (lit.[29] 137–138 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 (1H, dd, J=7.4 and 5.1 Hz), 7.44 (1H, td, J=7.5 and 0.9 Hz), 7.61 (1H, td, J=7.5 and 1.1 Hz), 7.73 (1H, ddd, J=7.5, 1.1 and 0.9 Hz), 7.86 (1H, dt, J=7.5 and 0.9 Hz), 7.90 (1H, dd, J=7.4 and 1.6 Hz), 8.61 ppm (1H, dd, J=5.1 and 1.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 121.0 (CH), 123.4 (CH), 124.3 (CH), 128.5 (C), 131.1 (CH), 131.4 (CH), 134.8 (C), 135.4 (CH), 143.6 (C), 154.0 (CH), 165.1 (C), 191.8 ppm (C=O). These NMR data are analogous to those described previously.[30]

*X-ray data for compound **16***: $C_{12}H_7NO$, M=181.19, monoclinic, $P2_1/c$, a=12.068(3), b=5.1986(15), c=14.465(3) Å, β=108.686(13)°, V=859.7(4) Å^3, Z=4, ρ_c=1.4 g cm^{-3}, μ=0.090 mm^{-1}. A final refinement on F^2 with 1964 unique intensities and 128 parameters converged at $\omega R(F^2)$=0.0996 ($R(F)$=0.0452) for 1460 observed reflections with $I>2\sigma(I)$. CCDC 944094.

*5.3.2. 8-Methoxy-5H-indeno[1,2-b]pyridin-5-one (**17**).*[12] Compound **17** was prepared from **2** (using $Pd(OAc)_2$ (5 mol %, 50 μmol, 11 mg) and $Cy_3P{\cdot}HBF_4$ (10 mol %, 0.10 mmol, 37 mg)) and was isolated (eluent: 8:2 heptane/AcOEt) as a yellow powder (yield: 69%): mp

113 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.96 (s, 3H), 6.92 (dd, 1H, J=8.3 and 2.3 Hz), 7.24 (dd, 1H, J=7.4 and 5.1 Hz), 7.41 (d, 1H, J=2.3 Hz), 7.7 (d, 1H, J=8.3 Hz), 7.89 (dd, 1H, J=7.4 and 1.6 Hz), 8.62 ppm (dd, 1H, J=5.1 and 1.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.1 (CH_3), 106.4 (CH), 116.7 (CH), 123.7 (CH), 126.4 (CH), 127.8 (C), 129.8 (C), 131.2 (CH), 146.5 (C), 153.4 (CH), 164.2 (C), 166.1 (C), 190.3 ppm (C=O); HRMS (ESI): m/z calcd for $C_{13}H_9NNaO_2$ [$(M+Na)^{+\bullet}$] 234.0531, found 234.0534.

*5.3.3. 11H-Indeno[1,2-b]quinolin-11-one (**18**).* Compound **18** was obtained from **4** (using $Pd(OAc)_2$ (5 mol %, 50 μmol, 11 mg) and $Cy_3P{\cdot}HBF_4$ (10 mol %, 0.10 mmol, 37 mg)) and was isolated (eluent: 8:2 heptane/AcOEt) as a yellow powder (yield: 63%): mp 173 °C (lit.[29] 176 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49–7.56 (2H, m), 7.69 (1H, td, J=7.5 and 1.1 Hz), 7.82 (1H, td, J=7.0 and 1.4 Hz), 7.84 (1H, dt, J=7.5 and 0.7 Hz), 7.88 (1H, dd, J=8.2 and 1.2 Hz), 8.11–8.16 (2H, m), 8.4 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 121.9 (CH), 124.2 (CH), 127.1 (C), 127.3 (CH), 127.7 (C), 129.9 (CH), 130.6 (CH), 131.6 (CH), 132.1 (CH), 132.5 (CH), 135.6 (CH), 137.5 (C), 143.9 (C), 150.7 (C), 162.1 (C), 190.9 ppm (C=O). The ^{1}H NMR data are analogous to those described previously.[31]

*5.3.4. 7-Methoxy-5H-indeno[1,2-b]pyridin-5-one (**19**).* Compound **19** was prepared from **8** (using $Pd(OAc)_2$ (5 mol %, 50 μmol, 11 mg) and $Cy_3P{\cdot}HBF_4$ (10 mol %, 0.10 mmol, 37 mg)) and was isolated (eluent: 8:2 heptane/AcOEt) as an orange powder (yield: 60%): mp 190 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.82 (s, 3H), 7.07–7.15 (m, 2H), 7.18 (d, 1H, J=2.4 Hz), 7.79 (d, 1H, J=8.2 Hz), 7.84 (dd, 1H, J=7.4 and 1.6 Hz), 8.53 (dd, 1H, J=5.2 and 1.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.9 (CH_3), 109.4 (CH), 120.9 (CH), 122.3 (CH), 122.5 (CH), 128.6 (CH), 131.4 (CH), 135.9 (C), 136.8 (C), 153.8 (CH), 162.5 (C), 165.5 (C), 191.7 (C=O); HRMS (ESI): m/z calcd for $C_{13}H_9NNaO_2$ [$(M+Na)^{+\bullet}$] 234.0531, found 234.0531.

*X-ray data for compound **19***: $C_{13}H_9NO_2$, M=211.21, monoclinic, $P2_1/a$, a=15.323(3), b=3.8645(7), c=17.224(3) Å, β=112.183(6)°, V=944.4(3) Å^3, Z=4, ρ_c=1.485 g cm^{-3}, μ=0.102 mm^{-1}. A final refinement on F^2 with 2082 unique intensities and 147 parameters converged at $\omega R(F^2)$=0.1524 ($R(F)$=0.0569) for 1532 observed reflections with $I>2\sigma(I)$. CCDC 944095.

*5.3.5. 5H-Pyrano[2,3-b:6,5-b′]dipyridin-5-one (**20**).* Compound **20** was prepared from **10** or **13** (using $Pd(OAc)_2$ (5 mol %, 50 μmol, 11 mg) and $Cy_3P{\cdot}HBF_4$ (10 mol %, 0.10 mmol, 37 mg)) and was isolated (eluent: 7:3 heptane/AcOEt) as a yellow powder (yield: 70 or 79%, respectively): mp 240 °C (lit.[27] 240 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (dd, 2H, J=7.8 and 4.6 Hz), 8.70 (dd, 2H, J=7.8 and 2.1 Hz), 8.83 ppm (dd, 2H, J=4.6 and 2.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 116.7 (2C), 121.8 (2CH), 137.4 (2CH), 155.1 (2CH), 160.3 (2C), 178.0 ppm (C=O). The ^{1}H NMR data are analogous to those described previously.[27]

*X-ray data for compound **20***: $2(C_{11}H_6N_2O_2)$, M=396.36, monoclinic, Pc, a=3.7934(8), b=20.911(4), c=10.908(2) Å, β=97.678(10)°, V=857.5(3) Å^3, Z=2, ρ_c=1.535 g cm^{-3}, μ=0.109 mm^{-1}. A final refinement on F^2 with 2910 unique intensities and 271 parameters converged at $\omega R(F^2)$=0.0876 ($R(F)$=0.0416) for 2263 observed reflections with $I>2\sigma(I)$. CCDC 944096.

*5.3.6. 1-Methoxy-9H-indeno[2,1-c]pyridin-9-one (**21**).*[12] Compound **21** was prepared from **12** (using $Pd(OAc)_2$ (5 mol %, 50 μmol, 11 mg) and ^{t}Bu$_3$P·HBF$_4$ (10 mol %, 0.10 mmol, 29 mg)) and was isolated (eluent: 8:2 heptane/AcOEt) as a yellow powder (yield: 81%): mp 160 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.13 (s, 3H), 7.15 (d, 1H, J=5.0 Hz), 7.44 (td, 1H, J=7.2 and 1.6 Hz), 7.49–7.60 (m, 2H), 7.71 (ddd, 1H, J=7.2, 1.1 and 0.8 Hz), 8.37 (d, 1H, J=5.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 54.4 (CH_3), 109.8 (CH), 113.4 (C), 121.5 (CH), 124.3 (CH), 131.5 (CH), 134.1 (C), 134.2 (CH), 141.1 (C), 155.0 (CH), 156.4 (C), 161.0 (C), 191.5 (C=O); HRMS (ESI): m/z calcd for $C_{13}H_9NNaO_2$ [$(M+Na)^{+\bullet}$] 234.0531, found 234.0532.

*5.3.7. 5H-Benzopyrano[2,3-b]pyridin-5-one (**22**).* Compound **22** was prepared from **11** (using $Pd(OAc)_2$ (5 mol %, 50 μmol, 11 mg) and ^{t}Bu$_3$P·HBF$_4$ (10 mol %, 0.10 mmol, 29 mg)) and was isolated (eluent: 8:2 heptane/AcOEt) as a yellow powder (yield: 14%): mp 180 °C (lit.[32] 178–179 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45–7.57 (m, 2H), 7.62 (dd, 1H, J=8.4 and 0.6 Hz), 7.79 (ddd, 1H, J=8.4, 6.9 and 1.5 Hz), 8.32 (dd, 1H, J=8.1 and 1.8 Hz), 8.72 (dd, 1H, J=7.8 and 1.8 Hz), 8.75 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 116.9 (C), 118.7 (CH), 121.3 (CH), 121.7 (C), 124.8 (CH), 126.8 (CH), 135.8 (CH), 137.5 (CH), 154.3 (CH), 155.9 (C), 160.5 (C), 177.8 (C). These NMR data are analogous to those described previously.[32]

*5.3.8. 2-Methoxy-3-pyridyl phenyl ketone (**23**).* Compound **23** was prepared from **11** (using $Pd(OAc)_2$ (5 mol %, 50 μmol, 11 mg) and ^{t}Bu$_3$P·HBF$_4$ (10 mol %, 0.10 mmol, 29 mg)) and was similarly isolated (yield: 12%). The analyses are analogous to those described previously.[10b]

*5.3.9. 1,3-Dimethoxy-9H-indeno[2,1-c]pyridin-9-one (**24**).* Compound **24** was prepared from **5** (using $Pd(OAc)_2$ (5 mol %, 50 μmol, 11 mg) and $Cy_3P{\cdot}HBF_4$ (10 mol %, 0.10 mmol, 37 mg)) and was isolated (eluent: 8:2 heptane/AcOEt) as a yellow powder (yield: 30%): mp 166 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.02 (s, 3H), 4.1 (s, 3H), 6.52 (s, 1H), 7.36–7.51 (m, 3H), 7.70 (d, 1H, J=7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 54.2 (CH_3), 54.6 (CH_3), 96.1 (CH), 106.8 (C), 121.3 (CH), 123.7 (CH), 131.1 (CH), 133.4 (CH), 136.3 (C), 140.3 (C), 158 (C), 160.5 (C), 168.3 (C), 189.3 (C=O); HRMS (ESI): m/z calcd for $C_{14}H_{11}NNaO_3$ [$(M+Na)^{+\bullet}$] 264.0637, found 264.0635.

*X-ray data for compound **24***: $C_{14}H_{11}NO_3$, M=241.24, monoclinic, $P2_1/n$, a=5.2623(4), b=17.1350(9), c=12.1808(9) Å, β=93.170(3)°, V=1096.66(13) Å^3, Z=4, ρ_c=1.461 g cm^{-3}, μ=0.104 mm^{-1}. A final refinement on F^2 with 2506 unique intensities and 166 parameters converged at $\omega R(F^2)$=0.0962 ($R(F)$=0.0397) for 2049 observed reflections with $I>2\sigma(I)$. CCDC 944097.

*5.3.10. 10H-Benzopyrano[3,2-c]pyridin-10-one (**25**).* Compound **25** was prepared from **6** (using $Pd(OAc)_2$ (5 mol %, 50 μmol, 11 mg) and $Cy_3P{\cdot}HBF_4$ (10 mol %, 0.10 mmol, 37 mg)) and was isolated (eluent: 1:1 heptane/AcOEt) as a white powder (yield: 51%): mp 185 °C (lit.[33] 184 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.54 (m, 3H), 7.79 (dt, 1H, J=7.2 and 1.7 Hz), 8.34 (dd, 1H, J=7.8 and 1.7 Hz), 8.82 (d, 1H, J=5.2 Hz), 9.52 (s, 1H). These data are in accordance with the literature.[33] ^{13}C NMR (75 MHz, $CDCl_3$) δ 112.8 (CH), 118.3 (CH), 123.1 (C), 125.2 (CH), 126.9 (CH), 135.8 (CH), 150.6 (CH), 153.8 (CH), 156.0 (C), 161.3 (C), 176.3 (C), 191.3 ppm (C=O).

*X-ray data for compound **25***: $C_{12}H_7NO_2$, M=197.19, orthorhombic, $Pc2_1b$, a=5.1389(5), b=8.3386(7), c=20.173(2) Å, V=864.44(14) Å^3, Z=4, ρ_c=1.515 g cm^{-3}, μ=0.105 mm^{-1}. A final refinement on F^2 with 1664 unique intensities and 136 parameters converged at $\omega R(F^2)$=0.1816 ($R(F)$=0.0645) for 1509 observed reflections with $I>2\sigma(I)$. CCDC 944098.

*5.3.11. 1,4-Dihydro-N,1-dimethyl-4-oxo-3-quinolinecarboxamide (**26**).* Compound **26** was obtained from **7** (using $Pd(OAc)_2$ (10 mol %, 0.1 mmol, 22 mg) and $Cy_3P{\cdot}HBF_4$ (20 mol %, 0.20 mmol, 74 mg)).

*X-ray data for compound **26***: $C_{12}H_{12}N_2O_2$, M=216.24, monoclinic, $P2_1/n$, a=4.7522(4), b=13.1688(12), c=16.4679(14) Å, β=96.766(4)°, V=1023.40(15) Å^3, Z=4, ρ_c=1.403 g cm^{-3}, μ=0.098 mm^{-1}. A final refinement on F^2 with 2305 unique intensities and 147 parameters converged at $\omega R(F^2)$=0.1047 ($R(F)$=0.0372) for 1962 observed reflections with $I>2\sigma(I)$. CCDC 944099.

*5.3.12. 8H-Indeno[2,1-b]thiophen-8-one (**27**).*[12] Compound **27** was prepared from **14** (using $Pd(OAc)_2$ (5 mol %, 50 μmol, 11 mg) and

$Cy_3P{\cdot}HBF_4$ (10 mol %, 0.10 mmol, 37 mg)) and was isolated (eluent: 8:2 heptane/AcOEt) as an orange powder (yield: 38%): mp 106 °C (lit.[34] 107–109 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11–7.19 (m, 3H), 7.31–7.36 (m, 1H), 7.46–7.49 (m, 1H), 7.73 ppm (d, 1H, J=4.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 119.7 (CH), 120.3 (CH), 124.2 (CH), 128.3 (CH), 133.8 (CH), 137.2 (C), 138.0 (C), 139.4 (CH), 139.8 (C), 158.9 (C), 185.7 ppm (C=O).

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.09.030.

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