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Cobalt-Catalyzed Electrophilic Aminations with Anthranils: An Expedient Route to Condensed Quinolines

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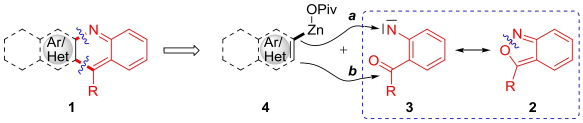
Supporting Information Placeholder

ABSTRACT: The reaction of various organozinc pivalates with anthranils provides anilines derivatives, which cyclize under acidic conditions providing condensed quinolines. Using alkenylzinc pivalates, electron-rich arylzinc pivalates or heterocyclic zinc pivalates produces directly the condensed quinolines of which several structures belong to new heterocyclic scaffolds. These N-heterocycles are of particular interest for organic light emitting diodes with their high photoluminescence quantum yields and long exciton lifetimes as well as for hole-transporting materials in methylammonium lead iodide perovskites solar cells due to an optimal band alignment for holes and a large bandgap.

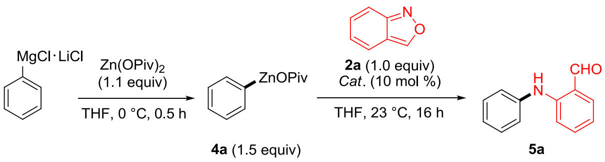
Condensed N-heterocycles are important molecules for material science applications.[1] Although, several synthetic methods have been developed for the preparation of condensed N-heterocycles, there is a lack of generality in such methods, especially for the preparation of condensed quinolines of type **1**, which are of interest as new materials.[1] Organometallics reagents are very useful for constructing heterocyclic scaffolds[2], especially organozinc reagents have found wide applications.[3] Organozinc pivalates are a class of zinc organometallics with enhanced air and moisture-stability, which can be stored for months as solids under argon.[4] Recently, we have reported a new cobalt-catalyzed electrophilic amination using the reaction of organozinc pivalates[5] with hydroxylamine benzoates.[6, 7] Compared to Pd- or Ni- catalysts, the use of cobalt salts[8] was preferred for toxicity and price considerations.[9] This amination had a broad reaction scope and proceeded under mild reaction conditions. Herein, we report an extension of this amination using readily accessible anthranils[10] of type **2** as electrophilic reaction partner.

We envision that anthranils **2** could react (formally via resonance structure **3**, eq. 1) with alkenyl-, aryl- or heteroaryl-zinc pivalates **4** (step a) to provide after a Friedel-Crafts reaction (step b) condensed quinoline structures of type **1**. Preliminary experiments show that PhZnOPiv (**4a**) reacts best with anthranil (**2a**) in the presence of 10 mol % of $CoCl_2$ at 23˚C for 16 h to provide the amino-aldehyde **5a** in 65% isolated yield. Other transition-metal salts, such as $CrCl_2$, $MnCl_2$, $FeCl_2$ or $Fe(acac)_3$ gave no product (Table 1, entries 1–7).[11] Using these conditions, we have prepared a range of amino-aldehydes (**5b**–**5f**) and amino-ketones (**5g**–**5k**) in 56–91% yields (Scheme 1). Organozinc pivalates were the best nucleophiles, although arylalanes of type $ArAlEt_2$ can also be used.[12] Also, heterocyclic zinc pivalates derived from the pyrazole and indole scaffolds produce the expected aniline derivatives **5l** and **5m** in 55–75% yields. Moreover, ferrocenylzinc pivalate, as well as methyl- or benzylzinc pivalates smoothly delivered the corresponding anilines **5n**–**5p** in 40–79% yields.



(eq. 1)

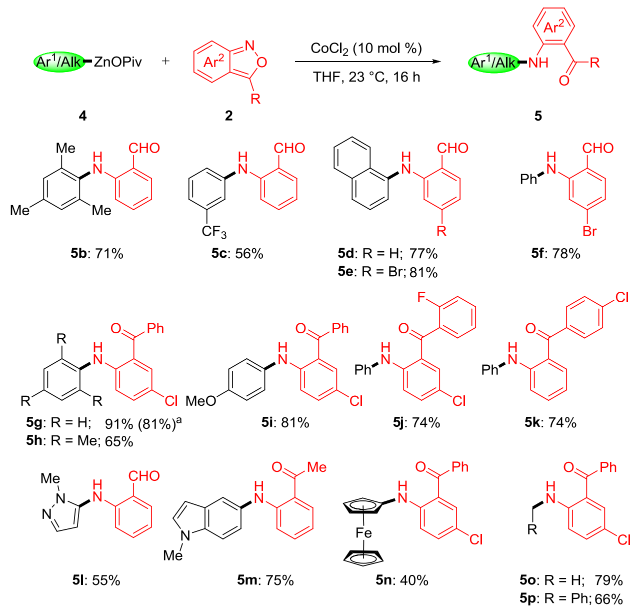
Table 1. Optimization for cobalt-catalyzed amination using anthranils (2a).[a]



entry	[met] (10 mol %)	yield (%)[b]
1	$CoCl_2$	65
2	$MnCl_2$	0
3	$CrCl_2$	0
4	$FeCl_2$	0
5	$Fe(acac)_3$	0
6	--	0
7	$CoCl_2$	0[c]

[a] Reaction conditions: **4a** (0.75 mmol), **2a** (0.50 mmol), [Cat.] (10 mol %), THF (2.0 mL), 23 °C, N_2, 16 h. [b] Isolated yields. [c] PhMgCl (1.5 equiv) was used.

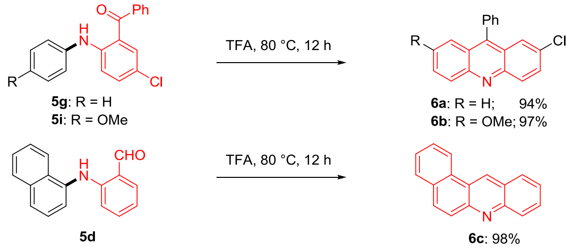
Scheme 1. Amino-aldehydes and amino-ketones of type 5 obtained by cobalt-catalyzed reaction of organozinc pivalates 4 with anthranils 2.



[a] $PhAl(Et)_2$ (1.5 equiv) was used as nucleophile.

The treatment of aniline derivatives of type **5** in TFA for 12 h at 80 ℃ provides the corresponding acridines (**6a**–**6c**) in excellent yields (Scheme 2).[10d]

Scheme 2. Condensed N-heterocycles prepared from anilines of type 5.



We have extended this preparation of quinoline derivatives by treating various anthranils (**2**) with alkenylzinc pivalates[13] under our standard conditions. To our delight, we observed after the electrophilic amination step, an cycloisomerisation which in a one-pot procedure provided the quinolines **8a**–**8n** in 62–96% yields (Scheme 3).

Furthermore, we have extended this new quinoline synthesis using aryl and heterocylic zinc pivalates **9**, which were prepared from the corresponding (hetero)aryl bromides by Mg- insertion in the presence of LiCl[14] (**9a**–**9g**), or by a directed metalation of heterocyclic substrates with TMP-bases (TMP = 2,2,6,6-tetramethylpiperidyl)[15] such as TMPZnOPiv·LiCl[16] or TMPMgCl·LiCl[17] (**9h**–**9n**), followed by transmetalation with $Zn(OPiv)_2$. By using especially electron-rich organozinc pivalates, we have observed using our standard conditions, that after amination a cyclization occurs (*via* **A** and **B** in Table 2) leading to various condensed N-heterocyclic derivatives **10a**–**10p**. In several cases, fully new types of heterocycles were obtained (**10l**–**10p**). Of special interest for material applications may be the TTF-derived heterocycle[18] **10m** (entry 13), as well as the related sulfur-contained heterocycles[19] **10n** to **10p** (entries 14–16).

Scheme 3. Cobalt-catalyzed amination of alkenylzinc pivalates (7) with anthranils (2).

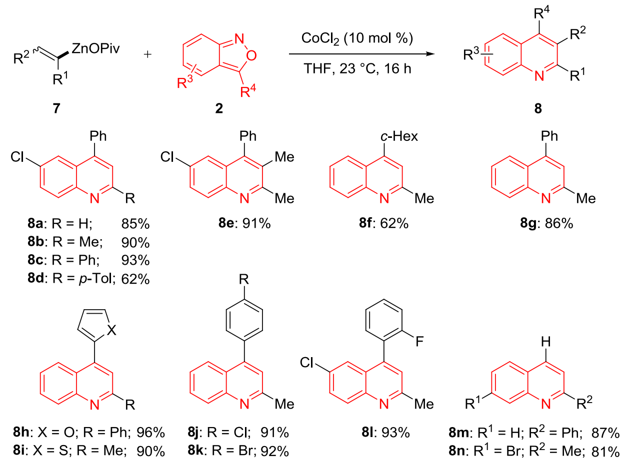
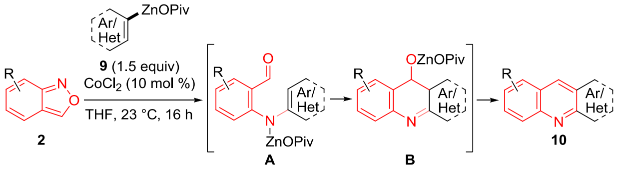
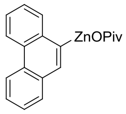
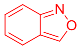
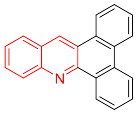
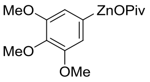
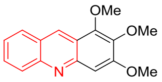
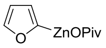
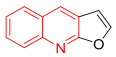
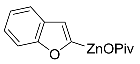
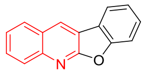
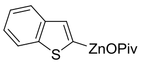
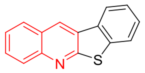
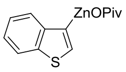
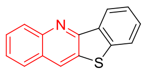
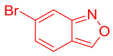
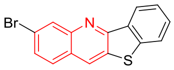
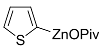
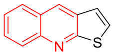
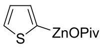
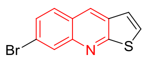
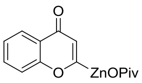
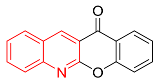
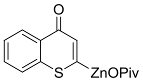
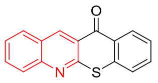
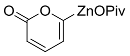
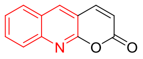
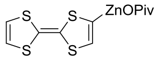
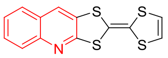
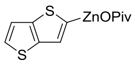
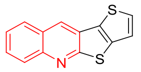
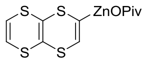
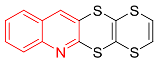
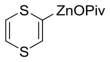
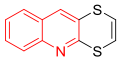


***Table 2*. Substrate scope of (hetero)arylzinc pivalates 9 leading to condensed N-heterocycles type 10.**

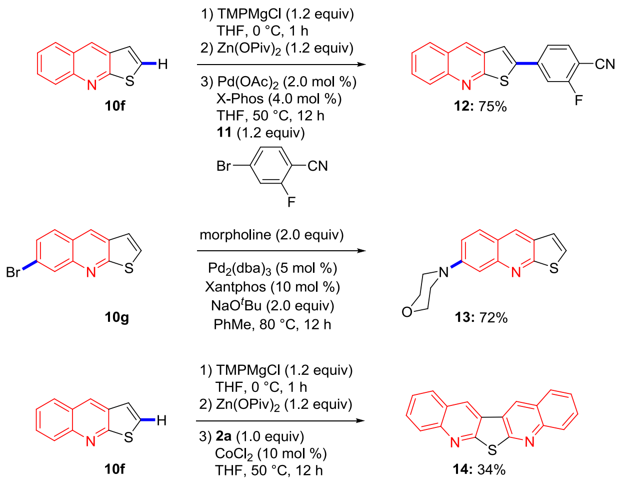


entry	(hetero) arylzinc pivalate of type 9	anthranil 2	product of type 10[b]
1	 **9a**	 **2a**	 **10a**: 61%
2	 **9b**	**2a**	 **10b**: 55%
3	 **9c**	**2a**	 **10c**: 61%

			
4	**9d**	**2a**	**10d**: 75%
			
5	**9e**	**2a**	**10e**: 60%
			
6	**9f**	**2a**	**10f**: 45%
			
7	**9f**	**2b**	**10g**: 40%
			
8	**9g**	**2a**	**10h**: 58%
			
9	**9g**	**2b**	**10i**: 38%
			
10	**9h**	**2a**	**10j**: 50%
			
11	**9i**	**2a**	**10k**: 61%
			
12	**9j**	**2a**	**10l**: 54%
			
13	**9k**	**2a**	**10m**: 51%
			
14	**9l**	**2a**	**10n**: 53%
			
15	**9m**	**2a**	**10o**: 55%
			
16	**9n**	**2a**	**10p**: 80%

Furthermore, we have shown that some of these heterocycles can be further functionalized by metalation. Thus, the condensed heterocycles **10m** and **10f** were treated with TMPMgCl·LiCl at 23°C for 16 h to give complete magnesiation (as shown by iodolysis).[12, 17] Addition of Zn(OPiv)$_2$ followed by a Negishi cross-coupling using X-Phos[20] gave the arylated N-heterocycle **12**.[5d] Also a Buchwald-Hartwig amination[21] of **10g** provided the aminated thieno[2,3-*b*]quinoline **13** in 72% yield. Interestingly, the zinc pivalate derived from thieno[2,3-*b*]quinoline (**10f**) reacted again with anthranil (**4a**) in the presence of CoCl$_2$ (10 mol %) furnishing the new heterocycle **14** in 34% yield (Scheme 4).

Scheme 4. Late-stage functionalizations of N-heterocycles.



In order to gain insights about the electronic structures of these heterocycles, we analysed the optical properties and performed in some cases additional cyclovoltammetry measurements. Studies about the optical features of these N-heterocycles can allow for the preparation of tailor-made molecules with optimum optical properties. All compounds showed a strong absorption in the UV region whereas careful tuning or functionalization of the quinoline backbone allowed extending the absorption towards the visible range.[12] This was achieved by simply increasing the size of the chromophore, exchanging the heteroatoms or inserting functional groups such as a methoxy group. In the case of **6a** and **6b**, it was noticed that the insertion of a methoxy group at the acridine body leads to a small redshift and an increased absorption of wavelengths longer than 300 nm (Fig. 1a). When comparing **10d**, **10e** and **10f** or **10j** and **10k**, it was observed that the exchange of oxygen heteroatoms with sulfur leads to a redshift of the absorption which results in a

0.3 eV reduced bandgap (see Supporting Information).[22,23] This was explained by the higher electronegativity of oxygen which led to a more localized electron density and subsequently a loss of aromaticity of the heterocycles. For the sulfur containing heterocycles, the better aromaticity led to larger π-systems and thus absorption of longer wavelengths.

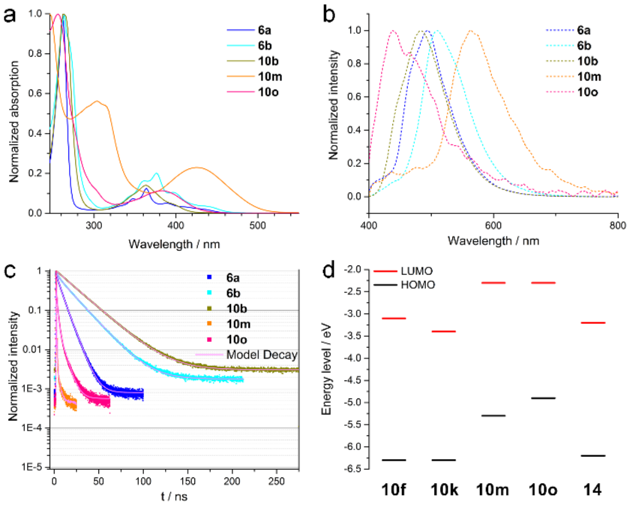


Figure 1: (a) Absorption spectra, (b) photoluminescence spectra and (c) time-correlated single photon counting in solution (50 µM in DCM). (d) Energy levels of selected condensed N-heterocycles obtained by CV measurements and optical bandgap.

Upon excitation at 378 nm the compounds showed photoluminescence (PL) in the range of 400 nm to 570 nm. The strongest emission was found for **6b** at 510 nm followed by **10b**, **10a**, **6a** and **14** with their maxima at 482 nm, 398 nm, 494 nm and 434 nm respectively. Additionally, a significant red-shift was observed for the PL maxima of **10m** compared to **10o** which was attributed to the larger π-system and the TTF-scaffold (Fig 1b). We measured the photoluminescence quantum yields (PLQY) of the heterocycles whereby the highest PLQY of 37% was observed for compound **6b**, followed by the other acridine containing heterocycles **10b** (26%) and **6a** (15%). The other heterocycles showed only moderate PLQY below 5%.[12] Interestingly, the compounds with the strongest PL were all containing an acridine core unit. Furthermore, by just flipping a thiophene unit in compound **10e**, i.e. the sulfur and nitrogen heteroatoms were not in neighbouring position but on opposite sites (**10f**), the PL position and intensity as well as the lifetimes did drastically change. In this fashion, it is possible to tune PL properties without changing the absorption bands and bandgap considerably.[12] The longest PL decay times were measured on **10b** with an acridine core and three methoxy groups. Furthermore, the PL lifetimes of **6b** were more than doubled compared to **6a** which is missing a methoxy group. Also interesting was the that the TTF-scaffold in **10m** resulted in one of the fastest PL decays (Fig. 1c). These results give an indication that the inserted methoxy groups are of great advantage to increase PL lifetimes. Regarding the overall emission properties of the studied N-heterocycles, applications in the field of OLEDs are promising. Materials for OLEDs require, among other properties, a long PL lifetime and high PL quantum yield, i.e. low non-radiative recombination loss, in order to provide high device efficiencies.[24,25] In our study, compound **6b** was found to be a promising candidate for OLEDs with a high PL quantum yield and long lifetimes. Our values are comparable with reports in the literature, particularly for materials based on singlet emission (fluorescence).[24,26–28] Based on these results, one can even improve or tailor-design the desired features by adding new or different functional groups, such as methoxy groups, which would be part of further studies.

In order to investigate the energy levels of compounds **10f**, **10k**, **10m**, **10o** and **14**, we performed cyclic voltammetry (CV) measurements. The energy for the highest occupied molecular orbital (HOMO) was extracted from forward scans in an acetonitrile solution using the internal standard ferrocene with a potential of $E(Fc/Fc^{+}) = -4.8$ eV vs. E_{vac}.[29] The HOMO levels for **10f**, **10k** and **14** were found to be in the same region around −6.3 eV, whereas **10m** and **10o** exhibit significantly higher HOMO energies with −4.9 eV and −5.3 eV, respectively. The TTF-derived heterocycle displayed the highest HOMO which is in good agreement with results from the literature (Fig. 1d).[18c] Solely from the energy level of compound **10m** and **10o** the alignment would be suitable for an application as hole transporting material in organic photovoltaics (OPVs) or in the case of **10o** for perovskite solar cells. For the latter, not only the HOMO is in good alignment with the commonly used methylammonium lead iodide (MAPI) perovskite, but also the LUMO value is high enough to effectively block electrons. The large bandgap also implies that no visible light is absorbed which will hence not diminish the light to be absorbed by the active layer.[30]

In summary, we have reported a convenient cobalt-catalyzed amination using various anthranils and functionalized aryl-, heteroaryl-, alkenyl- and alkyl-zinc pivalates under mild reaction conditions. This method gives an access to condensed N-heterocycles, of which several are new heterocyclic scaffolds. The optical characterization of the condensed N-heterocycles revealed promising properties for applications such as organic light emitting diodes or hole-transporting materials e.g. in perovskite solar cells. Further extensions of the method are currently underway in our laboratory and will provide a broad set of potential building blocks for new materials.

ASSOCIATED CONTENT

Supporting Information

The supporting information is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interests.

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