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Transition-Metal-Free Synthesis of 1,2-Disubstituted Indoles

Gleb A. Chesnokov,[a,b] Alexandra A. Ageshina,[a] Maxim A. Topchiy,[a,b] Mikhail S. Nechaev,[a,b] and Andrey F. Asachenko*[a,b]

Abstract: Herein, we report a new transition-metal-free robust and cost-effective method for synthesis of 1,2-disubstituted indoles from easily available unactivated (i.e. without EWG, PPh_3 or SiR_3 groups) tertiary amides. Scope of synthetic applicability of the presented protocol was shown on 23 examples of 1,2-disubstituted indoles with different substitution patterns obtained in good to excellent yields. The reported method turned out to be especially effective for synthesis of *N*-arylated 2-CF_3-indoles. Moreover, this approach can be performed in one-pot two-step manner directly from commercially available secondary amines. Mechanistic studies showed that acyl transfer might be an important step in the course of the reaction. Viability of the presented approach for benzofurans and benzothiophenes synthesis was also discussed.

Introduction

The indole structural motif[1] is widespread in both natural and synthetic biologically active compounds.[2] For decades, this highly important heterocycle remains a privileged scaffold in medicinal chemistry and drug discovery research.[2b, 3] Therefore, a lot of new methods for indole system preparation are reported every year and most of them are usually based on transition metal catalysis.[4] It's also important to point out that in numerous applications indole core appears with different substitution patterns. However, most of the synthetic studies deal mainly with 1-unsubstituted indoles, leaving their substituted counterparts with much less attention from the researchers. Meanwhile, convenient methods of synthesis of 1,2-substituted indoles are also highly desired. Known-to-date methods for such indoles synthesis include direct arylation of 1-[5] or 2-substituted[6] indoles, coupling of imines with 1,2-dihalobenzenes[7], intramolecular hydroamination of alkynes[8] and several other routes.[9] But most of these methods are catalytic and make use of transition metals (Pd, Cu etc.), and often in considerable amounts. For example, Melkonyan et al. reported in 2013 an efficient one-pot two-step (titanium(IV) alkoxide mediated imine formation – copper-catalyzed *N*-arylation) method for preparation of 1,2-disubstituted indoles.[9e] In spite of generally high yields and broad scope this method is far from ideal from perspective of green chemistry[10] (10 mol% of CuI, 500% of Ti(O*t*-Bu)$_4$) and atom economy[11] (halogen-containing byproducts). And these features are generally common for other catalytic methods mentioned above. Furthermore, transition-metal-based catalysts are usually expensive and highly toxic[12] and, in addition, cause trace metal contamination of the products; the latter poses a serious practical problem in the pharmaceutical industry and organic electronics and require extra metal-removing steps, which are usually time demanding and expensive.

Another drawback of catalytic methods is almost inevitable use of halogenated compounds, e.g. aryl bromides, which implies additional synthetic steps for installation of the halogen atom in the substrate before catalytic step and formation of halide salts as byproducts after the catalytic reaction. The latter is especially undesirable in industry because of ecological (toxicity) and economic reasons (decreased reactors lifetime due to corrosion issues). Moreover, catalytic methods usually utilize elevated temperatures, which are another obstacle for industrial appliance of the reactions.

Therefore, transition-metal-free methods for 1,2-disubstituted indoles preparation might be more efficient from both economic and ecological points of view and search for such methods are highly desired. And intramolecular condensation approach to the indole core construction can be a viable solution of this task. The historically first reaction of this class is a base-mediated intramolecular condensation of acylated *ortho*-toluidines at elevated temperatures (200-300 °C) – Madelung reaction.[13] Then, this reaction was further developed by Houlihan *et al.* to afford *N*-unsubstituted indoles by the reaction of secondary amides with *n*-BuLi at RT.[14] Unfortunately, Madelung synthesis is unable to produce *N*-substituted indoles from tertiary amides. The indirect rationalization of this limitation was first provided in works by Houser *et al.*[15] The reason is in deprotonation step of Madelung reaction of secondary amides, which results in efficient suppression of nucleophilic addition to carbonyl group by the base. There is no such "antinucleophile protection" in case of tertiary amides. Other related condensation methods, Smith indole synthesis[16] and Clark approach[17], rely on utilization of *N*-protected *ortho*-toluidine derivatives, that excludes the possibility of *N*-substituted indoles synthesis.

In general, tertiary amides with *ortho*-toluidine moiety on nitrogen atom are unable to afford 1,2-disubstituted indoles.[1] That's why some other methods based on modified *ortho*-toludine moiety were devised. These methods make benefit from installation of some auxiliary groups on methyl group in *ortho*-toluidine moiety that increases acidity of the resulting -CH_2-fragment (**Scheme 1**). For example, *N*-substituted indoles are accessible via intramolecular Wittig reaction (**Scheme 1**, **A**).[18] But this method cannot be the number one choice for the preparation of 1,2-disubstituted indoles because of formation of equivalent amount of byproducts (halide salts and $OPPh_3$) that makes this method neither green nor atom efficient.

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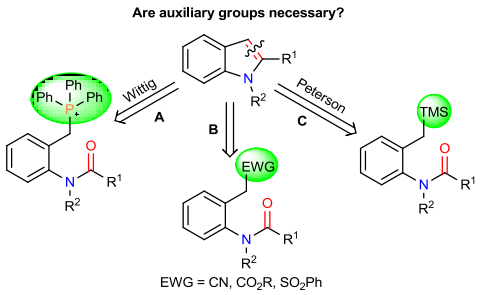


Scheme 1. Known intramolecular condensations for 1,2-disubstituted indoles synthesis.

In order to enable cyclization, an increase of proton acidity in the -CH_2- fragment can be achieved through introduction of different electron-withdrawing groups (EWG), such as cyano, phenylsulfo, or carboxy (**Scheme 1**, **B**).[19]

Intramolecular cyclization can also be promoted by the introduction of trimethylsilyl group to *ortho*-toluidine moiety. In such a case, indoles are obtained via intramolecular Peterson reaction (**Scheme 1**, **C**).[20] However, this approach implies laborious preparation of starting materials using rather expensive reagents, such as $TMSCH_2MgCl$.

Obviously, introduction (and in some cases further removal) of auxiliary groups to methyl substituent in *ortho*-toluidine moiety in order to facilitate intramolecular condensation of tertiary amides in the described methods requires additional and undesirable synthetic steps, which even can lead to more complex and less available starting materials. This consideration along with individual drawbacks of the methods described above make them almost unsuitable for industrial use.

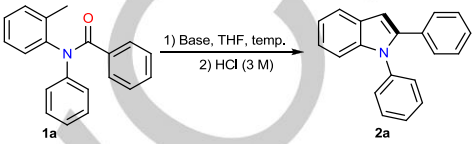
Therefore, we believe that it is highly important to know if it's possible for *ortho*-toluidine moiety-containing tertiary amides without any auxiliary groups (unactivated tertiary amides) to undergo intramolecular cyclization or not, because this may open a new more efficient transition-metal-free route to 1,2-disubstituted indoles from readily available starting materials – tertiary amides, which are usually much simpler than substrates in all the methods described above, making this approach more industrially preferred.

Herein, we report a thorough investigation of intramolecular cyclization of unactivated tertiary amides with *ortho*-toluidine moiety which resulted in and transition-metal-free, cost-effective and high-yielding approach towards 1,2-disubstituted indoles synthesis from easily-available tertiary amides using inexpensive popular and quite tolerant base – LDA. The reaction proceeds normally at RT which is another advantage of the presented method. This approach was further upgraded to one-pot two-step procedure for 1,2-disubstituted indoles preparation from corresponding commercially available secondary amines with almost the same yields as in the amide-based method. In addition, detection and isolation of the key intermediates in the course of the reaction allowed us to rationalize a mechanism and apply the reported approach to benzofurans and benzothiophenes synthesis.

Results and Discussion

Firstly, search for optimal conditions for cyclization of a model compound *N*-(phenyl)-*N*-(*o*-tolyl)benzamide (**1a**) into 1,2-diphenylindole (**2a**) was performed. The choice of amide **1a** as a model substrate was determined by the poorer synthetic availability of *N*-arylated indoles compared to *N*-alkylindoles.

Table 1. Optimization of the reaction conditions.

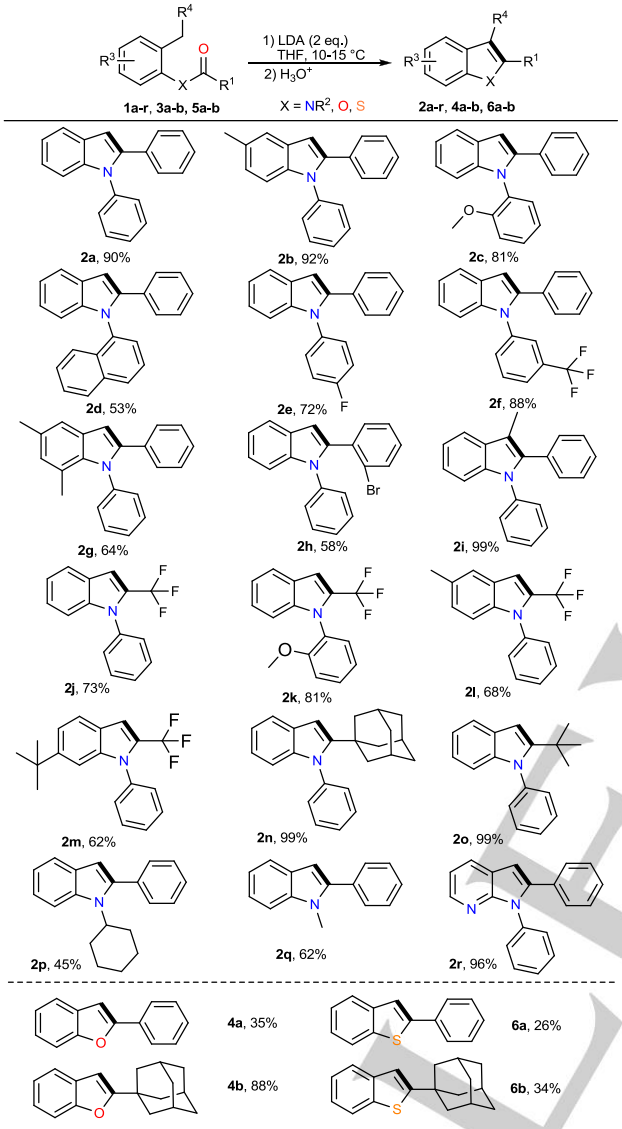


Entry	Base	Temp., °C	Yield, %[a]	Comments
1	*t*-BuLi	-78	-	No product
2	*t*-BuLi	0	-	No product
3	*t*-BuLi/TMEDA	-78	-	No product
4	*t*-BuLi/KO*t*-Bu	-78	-	No product
5	LDA (1 eq.)	-78	36	Neat **1a** in one portion
6	LDA (1 eq.)	10-15	65	Neat **1a** in small portions
7	LDA (**1** eq.)	10-15	79	Slow addition of **1a** solution
8	LDA (**2** eq.)	10-15	90	Slow addition of **1a** solution
9	LDA (**3** eq.)	10-15	90	Slow addition of **1a** solution

[a] All reactions were performed in THF at 0.25 M concentration. Isolated yields.

At first, *t*-BuLi in THF was chosen as a strong and sterically hindered organometallic base (**Table 1**, entry 1). Unfortunately, treatment of benzamide **1a** with *t*-BuLi resulted in the formation of complex mixture without any traces of indole **2a** at both –78 and 0 °C (**Table 1**, entries 1, 2). This result was obtained probably due to generally nucleophilic nature of organolithium species, which caused amide degradation.[15, 21] Utilization of stronger bases, such as *t*-BuLi/TMEDA and *t*-BuLi/KO*t*-Bu, was also ineffective (**Table 1**, entries 3, 4).[22] Therefore, we decided to test a considerably less nucleophilic amide-type base – LDA. It turned out that addition of tertiary amide **1a** to equimolar amount of freshly prepared LDA solution in one portion afforded 1,2-diphenylindole **2a** in 36% yield at –78 °C, whereas gradual addition of **1a** at 10–15 °C yielded 65% of **2a** (**Table 1**, entries 5, 6). These results encouraged us to try slow addition of **1a** in the form of THF solution; this approach gave **2a** in 79% yield (**Table 1**, entry 7). Conversions of the starting amide **1a** were not full in these examples (**Table 1**, entries 5-7). That's why the effect of LDA amount was evaluated. Slow addition of benzamide **1a** solution in THF to a solution of two-fold excess of LDA at 10–

15 °C provided the product in 90% yield (**Table 1**, entry 8). Further increase of LDA amount up to 3 eq. had no effect on the product yield (**Table 1**, entry 9).



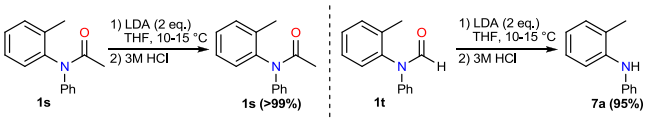
Scheme 2. Scope of the reaction of tertiary amides, esters and thioesters.

To determine the scope and limitations of the optimal conditions for unactivated tertiary amides cyclization, we performed a series of experiments with variously substituted tertiary amides **1**. It turned out that tertiary amides with substituents, that can tolerate LDA, generally afforded corresponding 1,2-diarylindoles in good to excellent isolated yields (**Scheme 2**, **2a**–**f**). In case of amide **1g,** presence of the second *ortho*-methyl group in *ortho*-toluidine moiety led to somewhat lower yield due to byproduct **2g'** (**Scheme 7**) formation presumably via double or sequential lithiation of **1g** (64%, **2g**).

Also, a good yield was observed in the reaction of 1-(2-bromophenyl)-2-phenylindole **2h** formation. Replacement of methyl group with ethyl in the *ortho*-toluidine moiety of tertiary amide **1i** led to quantitative formation of corresponding indole **2i**. Heterocyclic amide **1r** was successfully converted into 1,2-diphenyl-7- azaindole **2r** in excellent yield (96%). Preparation of azaindoles is a challenging task in organic synthesis, and most of the methods described in literature rely on transition-metal catalysis (intra- or intermolecular heteroannulations using alkynes, mostly), especially in case of *N*-arylated azaindoles.[23] Therefore, our result can be a valuable transition-metal-free alternative to catalytic methods. Moreover, our example is the first *N*-arylated azaindole synthesis via intramolecular condensation reaction.

Amides of tertiary aliphatic carboxylic acids, such as 1-adamantanecarboxylic **1n** and pivalic **1o**, also underwent successful cyclization affording products **2n** and **2o** in virtually quantitative yields. Amides of trifluoroacetic acid (**1j-m**) turned out to be great substrates for indole preparation under optimized conditions. Thus, corresponding indoles (**2j-m**) were obtained in good to high yields. It's important to point out that preparation of *N*-arylated 2-CF_3-indoles[24] is a challenging area in organic synthesis and, to the best of our knowledge, the methods proposed by Zhang and co-workers (Pd-catalyzed amination using 2-chloro-1-phenyl-3,3,3-trifluoroprop-1-ene prepared from corresponding benzaldehyde and CF_3CCl_3) are the only available synthetic tool towards such indoles.[25] Thus, it's clear that our method provides a valuable synthetic option for construction of such *N*-arylated 2-CF_3-indole with yields and scope comparable to Zhang's method. Moreover, our method utilizes readily-available trifluoroacetamides and makes use of no palladium against 10 mol% in the aforementioned method; that is, we believe, a significant achievement from both economic and ecological perspectives.

Replacement of an aryl group at nitrogen atom with an alkyl one was also successful. Thus, 1-methyl-2-phenylindole **2q** was isolated in 62 % yield, whereas more sterically hindered amide **1p** gave 1-cyclohexyl-2-phenylindole **2p** in 45 % yield. Such decrease in yield can be explained by formation of a byproduct **2p'** (**Scheme 7**).

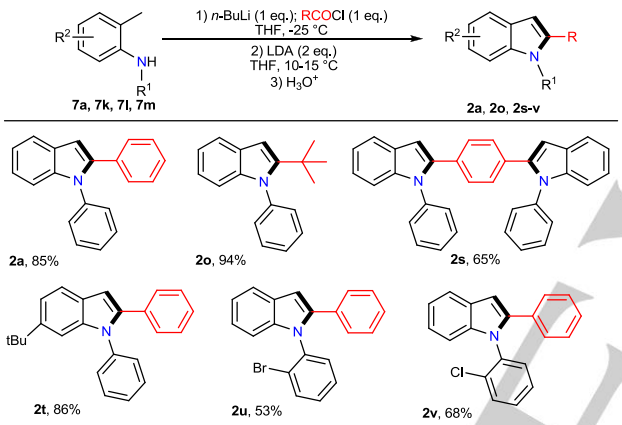


Scheme 3. Limitations of the method.

It should be mentioned that amides of enolizable acids did not undergo Madelung reaction under developed conditions. Thus, in case of *N*-phenyl-*N*-(*o*-tolyl)acetamide (**1s**), lithium enolate formation completely suppresses electrophilicity of amide group. Another interesting result was obtained with the formamide derivative **1t**. Treatment of *N*-phenyl-*N*-(*o*-tolyl)formamide (**1t**) with lithium diisopropylamide led to a smooth removal of formyl

group producing corresponding diarylamine **7a** in nearly quantitative yield (**Scheme 3**).

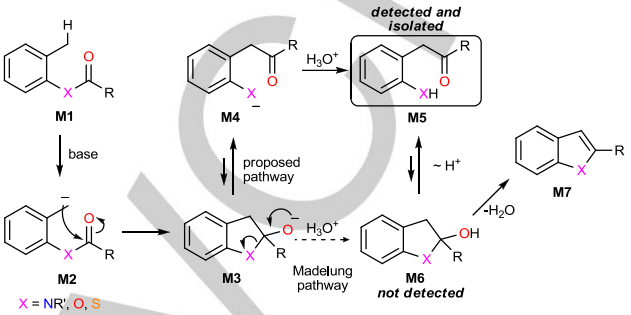
Successful intramolecular cyclization of substrates containing formally inert N–R fragment in their structure prompted us to evaluate the possibility of cyclization of substrates containing analogous formally inert O or S-fragments instead (e.g. esters and thioesters instead of amides). Such a replacement implies formation of benzofurans and benzothiophenes, respectively (**Scheme 2**). However, yields of the products in most cases were modest. Excellent yield was obtained only for transformation of *ortho*-tolyl adamantane-1-carboxylate (**3b**) into 2-(1-adamantyl)benzofuran (**4b**) (88%). In other cases, yields did not exceed 40% (**4a**, **6a**, **6b**). Nevertheless, it is worth mentioning that benzofurans (**4a**, **4b**) and benzothiophenes (**6a**, **6b**) were obtained from unactivated esters and thioesters by this approach for the first time, providing important conceptual expansion of presented cyclization to synthesis of five-membered benzo[*b*]heterocycles with one heteroatom.



Scheme 4. Results of one-pot implementation.

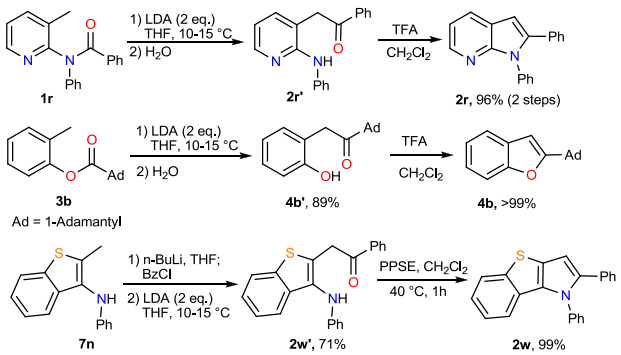
One of the main disadvantages of aforementioned intramlecular condensation methods (**Scheme 1**) is the necessity of preliminary amide synthesis in order to eventually get an indole from starting materials (e.g. substituted *ortho*-toluidines). Thus, synthesis of *N*,*N*-diarylamides of benzoic acids is a synthetic problem of its own. Lowered nucleophilicity and high steric bulk of diarylamines hinder their acylation into corresponding *N*,*N*-diarylbenzamides under conventional conditions. Looking for more robust and facile synthetic approach to indoles via intramolecular condensation we attempted a one-pot protocol. Results of one-pot experiments are presented in **Scheme 4**. We found that synthesis of amides from acyl chlorides and substituted lithium amides can be successfully followed by transformation of tertiary amides into corresponding indole in a one-pot two-step manner. Noteworthy, yield drops in cases of indoles **2a** and **2o** comparing to the amide cyclization were only about 5%, which is a considerable advantage, since it allows to save time significantly and reduce the number of synthetic steps with nearly the same yield.

We suppose that the presented one-pot protocol of the reaction has the same features and limitations that were described above for the amide cyclization to 1,2-disubstituted indoles. Also, double cyclization producing 1,4-*bis*(2-(*N*-phenyl)indolyl)benzene **2s** in 65 % yield was quite effective under described conditions.



Scheme 5. Proposed mechanism of tertiary amide cyclization reaction.

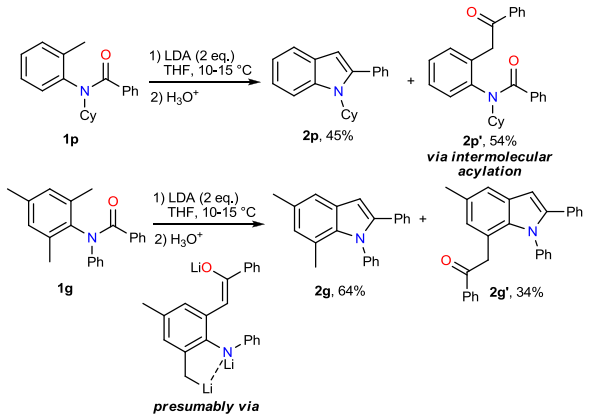
Proposed mechanism of the reaction is presented in **Scheme 5**. It includes initial deprotonation of methyl group in the starting material **M1** followed by intramolecular nucleophilic attack onto carbonyl group (intermediate **M2**) resulting in formation of intermediate **M3**. The latter one might undergo dehydrative aromatization into five-membered benzo[*b*]heterocycle **M7** during the acidic hydrolysis. This is a conventionally accepted mechanism of Madelung reaction,[26] closely related intramolecular cyclization process. However, intermediate **M3** can be unstable and subjected to further ring-opening into corresponding intermediate **M4**, protonation of which gives **M5**, which in turn can also undergo cyclization into corresponding five-membered benzo[*b*]heterocycle **M7** after treatment with acid. On the other hand, intermediate **M6** in acidic aqueous medium can also turn into ketone **M5** instead of aromatization.



Scheme 6. Mechanistic features of the reaction.

In our study, we tried to detect corresponding intermediates **M5** and **M6**. It turned out that in case of 1-phenyl-2-(1-adamantyl)indole **2n** mixture of indole **2n** and 1-(1-adamantyl)-2-

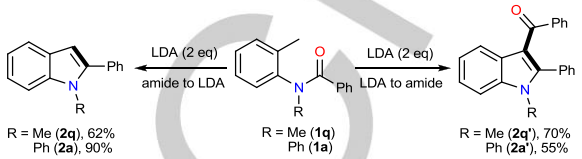
(2-hydroxyphenyl)ethanone **2n'** was observed after neutral work-up with water. However, pure intermediate **2n'** was not isolated due to its poor stability on silica. Considering 1,2-diphenyl-7-azaindole **2r** synthesis, reaction proceeds through formation of 1-phenyl-2-(2-(phenylamino)pyridin-3-yl)ethanone **2r'**, which was isolated and characterized after neutral work-up (**Scheme 6**).



Scheme 7. Byproduct formation in the course of the cyclization.

Cyclization of esters and thioesters to corresponding benzofurans and benzothiophenes presumably also proceeds through intermediate **M5** formation. Analogous 1-(1-adamantyl)-2-(2-hydroxyphenyl)ethanone (**4b'**) was isolated and characterized after neutral aqueous work-up. Subsequent treatment of this intermediate with TFA in DCM provided smooth cyclization to the corresponding benzofuran **4b** in quantitative yield (**Scheme 6**). Application of proposed above one-pot two-step protocol to the amine **7n** also resulted in keto product of the rearrangement (**2w'**). But unlike the case of product **2r'** cyclization into indole was not successful with TFA in DCM. However, trimethylsilyl polyphosphate (PPSE) in DCM was found to be the suitable reagent for the **2w'** cyclization into 1,2-diphenyl-1*H*-[1]benzothieno[3,2-*b*]pyrrole **2w**.[27] Therefore, it turned out that, unlike Madelung reaction, the reported reaction proceeds through the acyl transfer from heteroatom to the methyl carbon atom. And the resulting intermediate undergoes aromatization under acidic conditions.

Another question concerning mechanism: could intermediate **M2** undergo not intramolecular but intermolecular acylation by another molecule of the substrate **M1**? And analysis of byproducts in several studied cases clearly showed that this pathway might also be viable. Thus, during indole **2p** synthesis some of the starting material turned into byproduct **2p'**, which was presumably formed by intermolecular attack between **1p** and its deprotonated at Me site form (**Scheme 7**). The byproduct didn't undergo cyclization into 3-benzoyl indole under the reaction conditions. This might be due to steric reasons and Cy playing the role of conformational anchor. Another peculiar byproduct (**2g'**) was obtained during indole **2g** synthesis. This substance could be possibly formed by acyl transfer in **1g**, followed by lithiation at the second *ortho*-Me site with subsequent acylation by another molecule of the starting amide **1g**. An alternative is the reverse order of events: intermolecular acylation and subsequent rearrangement. However, the latter pathway would also lead to the formation of 3-benzoyl byproduct. But that's not the case. Anyway, formation of this byproduct (**2g'**) is hardly possible via Madelung type mechanism.



Scheme 8. Intramolecular and intermolecular processes compete.

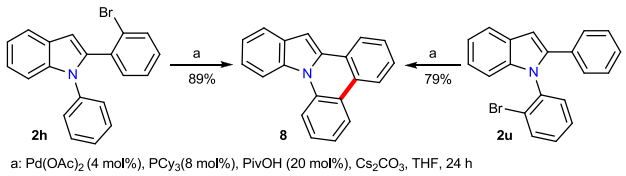
In transformations of tertiary amides **1a** and **1q** we were able to control the direction of the reaction (**Scheme 8**). Thus, optimized conditions of the cyclization reaction afforded corresponding indoles **2a** and **2q** in 90 and 62% yields, respectively. However, the reversed order of the reagent addition unexpectedly gave 3-benzoyl indoles **2a'** and **2q'** in 55 and 70% isolated yield (based on amide conversion). The role of the addition order can be explained as follows. During the reversed order addition small portions of deprotonated amide form in the solution full of non-deprotonated amide molecules, making intramolecular and intermolecular processes compete. On the contrary, during normal order addition quite fast deprotonation of incoming amide and large excess of LDA prevents the simultaneous presence of non-deprotonated and deprotonated amide species, favoring intramolecular nucleophilic attack.

Thus, all the pieces of evidence concerning mechanism of the reaction discussed above clearly show that acyl transfer, both intramolecular and intermolecular, seems to be an important step in the course of the reaction.

It's worth mentioning that indoles **2h** and **2u** containing 2-bromophenyl moiety are convenient starting materials in synthesis of indolo[1,2-*f*]phenanthridines through palladium-catalyzed intramolecular direct arylation via C–H activation.[8f] Indolo[1,2-*f*]phenanthridine (**8**) is a parent compound of the whole class of compounds having found various applications in technology, including organic light-emitting diodes (OLEDs)[28] and dye-sensitized solar cells (DSSCs)[29]. However, only few simple and efficient methods for indolo[1,2-*f*]phenanthridine synthesis have been reported so far.[28, 30] And all these methods rely on utilization of rather complex or unstable starting materials, such as *N*-(*o*-bromophenyl)indoles, 2,2'-dihalobiphenyls, and 2-(phenylethynyl)anilines, that undoubtedly limits potential areas of application thereof.

Previously, it was demonstrated that indolo[1,2-*f*]phenanthridine **8** could also be obtained by intramolecular palladium-catalyzed C–H/C–Br coupling of indole **2h**.[8f] The indole was produced in the course of copper-catalyzed arylation of 2-(2-phenylethynyl)aniline by phenylboronic acid followed by cyclization using $Pd(OAc)_2$/P(*p*-Tol)$_3$. This approach turns us back to 2-(2-phenylethynyl)aniline synthesis. On the other hand,

indole **2h**, similar to its isomer indole **2u**, can be obtained in one step from corresponding easily available diarylamines (**7a** and **7l**, respectively) via our one-pot protocol of the reaction.



Scheme 9. Synthesis of indolo[1,2-f]phenanthridine (**8**).

Intramolecular cyclization can be performed under conditions described previously in literature (**Scheme 9**).[31] Here, isomeric indoles **2h** and **2u** were transformed into indolophenanthridine **8** utilizing reported conditions in high yields (89 and 79%, respectively). To summarize, implementation of the devised method followed by Pd-catalyzed synthesis of indolo[1,2-*f*]phenanthridine **8** provides target compound faster, in a simpler manner, and with yields that are non-inferior to those described in the literature.

Conclusions

In this paper we report a systematic investigation of 1,2-disubstituted indole synthesis via intramolecular condensation of tertiary amides without any auxiliary anion-stabilizing groups in the *ortho*-toluidine moiety at Me site. It was found that LDA in THF successfully furnishes this transformation, providing transition-metal-free, robust and cost-effective method for synthesis of 1,2-disubstituted indoles from readily-available tertiary amides. Synthetic utility of the elaborated protocol was tested on 23 examples of different substitution patterns. Yields are from good to excellent. It's important from the synthetic point of view that *N*-arylated 2-CF_3-indoles are accessible by the proposed method in high yields from cheap and readily-available trifluoroacetamides. In order to increase the synthetic significance of the method a one-pot two-step high-yielding protocol for 1,2-disubstituted indoles synthesis directly from secondary amines was also devised. Rationalization of mechanistic features of the reaction allowed us to transfer this methodology to benzothiophenes and benzofurans synthesis. Other mechanistic experiments demonstrated that the reaction proceeds through acyl transfer with subsequent cyclization. Moreover, the presented protocol provides a simpler way to indolo[1,2-*f*]phenanthridines.

Experimental Section

General Information: NMR spectra were obtained on a Bruker "Avance 600" (600 MHz ^{1}H, 151 MHz ^{13}C). The chemical shifts are frequency referenced relative to the residual undeuterated solvent peaks. Coupling constants J are given in hertz as positive values regardless of their real individual signs. The multiplicity of the signals is indicated as ''s", ''d", "t" or ''m" for singlet, doublet, triplet or multiplet, respectively. The abbreviation ''br" is given for broadened signals. Analytical thin layer chromatography was performed using Merck TLC Silica gel 60 F254 plates, visualization under 254 nm UV light or iodine vapors. Merck Silica gel 60 (0.040-0.063 mm) was used for flash chromatography purification. All commercially available reagents and solvents were used without further purification.

General procedure for indole synthesis from tertiary amides (A): A solution of LDA was prepared by slow addition of *n*-BuLi (8 ml, 2.5M in hexanes, 20 mmol, 2 eq.) to *N,N*-diisopropylamine (2.9 ml, 2.094 g, 20.7 mmol, 2.07 eq.) in absolute THF (20 ml) under Ar at 0 °C. Then a solution of amide **1** (10 mmol, 1 eq.) in THF (20 ml) was added dropwise (1-2 drops per second) at 10-15 °C. The resulting mixture was allowed to stir overnight at RT. The reaction was quenched with 3M aqueous HCl (10 ml) and stirred for additional 0.5 h, then concentrated under reduced pressure. The resulting mixture was partitioned between DCM (30 ml) and water (30 ml). Layers were separated and aqueous phase was extracted twice with DCM (30 ml). Combined organic fractions were dried over Na_2SO_4 and concentrated *in vacuo*. Residual oil was purified by column chromatography in EtOAc/hexanes (1:10) to afford pure indole **2**.

General procedure for one-pot indole synthesis from diarylamines (B): A solution of secondary amine **7** (10 mmol, 1 eq.) in dry THF (20 ml) was cooled to -30 °C and then *n*-BuLi was added slowly (4 ml, 2.5M in hexanes, 10 mmol, 1 eq.). The resulting mixture was allowed to stir for 0.5 h at -30 °C and then slowly treated with acyl chloride (10 mmol, 1 eq.) and allowed to stir for additional 0.5 h. In a separate flask a solution of LDA was prepared by slow addition of *n*-BuLi (8 ml, 2.5M in hexanes, 20 mmol, 2 eq.) to *N,N*-diisopropylamine (2.9 ml, 2.094 g, 20.7 mmol, 2.07 eq.) in absolute THF (20 ml) under Ar at 0 °C. Then a solution of preformed amide was added dropwise (1-2 drops per second) at 10-15 °C. The resulting mixture was allowed to stir overnight at RT. The reaction was quenched with 3M aqueous HCl (10 ml) and stirred for additional 0.5 h, then concentrated under reduced pressure. The resulting mixture was partitioned between DCM (30 ml) and water (30 ml). Layers were separated and aqueous phase was extracted twice with DCM (30 ml). Combined organic fractions were dried over Na_2SO_4 and concentrated *in vacuo*. Residual oil was purified by column chromatography in EtOAc/hexanes (1:10) to afford pure indole **2**.

1,2-Diphenyl-1*H*-indole (2a): Following the general procedure A, **2a** was obtained as a white crystalline solid from 2.874 g of *N*-phenyl-*N*-*o*-tolylbenzamide (**1a**). Yield: 2.424 g (90%). Following the general procedure B, **2a** was obtained as a white crystalline solid from 1.833 g of 2-methyl-*N*-phenylanilin (**7a**) and 1.406 g of benzoyl chloride. Yield: 2.292 g (85%). MP 83-84 °C (lit. 83-84 °C).[8h] ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.73 – 7.69 (m, 1H), 7.45 – 7.40 (m, 2H), 7.39 – 7.34 (m, 1H), 7.34 – 7.31 (m, 1H), 7.31 – 7.24 (m, 7H, overlapping with residual $CHCl_3$), 7.20 (dq, *J* = 7.0, 3.9 Hz, 2H), 6.83 (s, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 140.9 , 139.1 , 138.7 , 132.7 , 129.4 , 129.1 , 128.4 , 128.3 , 128.2 , 127.4 , 127.3 , 122.5 , 120.8 , 120.7 , 110.8 , 103.8 . The ^{1}H, ^{13}C NMR spectra were identical to the previously reported in the literature.[8h]

(1,2-Diphenyl-1*H*-indol-3-yl)(phenyl)methanone (2a'): This compound can be obtained as a byproduct during 1,2-diphenyl-1*H*-indole (**2a**) synthesis, but only in 2-5% yield. But the reverse order of the reagents mixing allowed us to obtain **2a'** as a major product. A solution of LDA was prepared by slow addition of *n*-BuLi (8 ml, 2.5M in hexanes, 20 mmol, 2 eq.) to diisopropylamine (2.9 ml, 2.094 g, 20.7 mmol, 2.07 eq.) in absolute THF (20 ml) under Ar at 0 °C. Then this LDA solution was added dropwise (1-2 drops per second) to a solution of amide 1a (2.874

g, 10 mmol, 1 eq.) in minimum amount of THF (~5 ml) at 10-15 °C. The resulting mixture was allowed to stir overnight at RT. The reaction was quenched with 3M aqueous HCl (10 ml) and concentrated under reduced pressure. The resulting mixture was partitioned between DCM (30 ml) and water (30 ml). Layers were separated and aqueous phase was extracted twice with DCM (30 ml). Combined organic fractions were dried over Na_2SO_4 and concentrated *in vacuo*. Residual oil was purified by column chromatography in EtOAc/hexanes (1:10) to afford pure **2a'** as a white solid. Yield: 1,035 g (55%). MP 146-147 °C. HRMS (APCI) calcd for $C_{27}H_{19}NO$ [M+H$^+$]: 374.1545, found: 374.1545. IR (KBr) 3055, 1617, 1495, 1473, 1454, 1394, 1204, 886, 759, 753, 743, 696, 664, 591 cm^{-1}. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 7.5 Hz, 1H), 7.63 (d, *J* = 7.2 Hz, 2H), 7.42 – 7.33 (m, 3H), 7.33 – 7.24 (m, 4H, overlapping with residual $CHCl_3$), 7.21 (d, *J* = 7.4 Hz, 2H), 7.13 (t, *J* = 7.7 Hz, 2H), 7.04 (t, *J* = 8.4 Hz, 3H), 6.99 (t, *J* = 7.3 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 193.4 , 145.4 , 139.8 , 138.2 , 137.3 , 131.4 , 131.4 , 130.7 , 129.6 , 129.4 , 128.5 , 128.3 , 128.2 , 127.8 , 127.7 , 127.7 , 123.8 , 122.8 , 121.8 , 115.8 , 111.0 .

5-Methyl-1,2-diphenyl-1*H*-indole (2b): Following the general procedure A on 5 mmol scale, **2b** was obtained as a white crystalline solid from 1.507 g of *N*-(2,4-dimethylphenyl)-*N*-phenylbenzamide (**1b**). Yield: 1.308 g (92%). MP 135-136 °C (lit. 89-92 °C).[7c] ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.55 – 7.51 (m, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.35 – 7.22 (m, 8H, overlapping with residual $CHCl_3$ signal), 7.10 – 7.04 (m, 1H), 6.79 (s, 1H), 2.53 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 140.8 , 138.8 , 137.6 , 132.8 , 130.1 , 129.3 , 129.0 , 128.6 , 128.2 , 128.1 , 127.3 , 127.1 , 124.0 , 120.3 , 110.4 , 103.5 , 21.5 The ^{1}H, ^{13}C NMR spectra were identical to the previously reported in the literature.[32]

1-(2-Methoxyphenyl)-2-phenyl-1*H*-indole (2c): Following the general procedure A, **2c** was obtained as a white crystalline solid from 3.174 g of *N*-(2-methoxyphenyl)-*N*-*o*-tolylbenzamide (**1c**). Yield: 2.423 g (81%). MP 70-71 °C. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.72 – 7.68 (m, 1H), 7.38 (ddd, *J* = 8.3, 7.5, 1.7 Hz, 1H), 7.33 – 7.30 (m, 2H), 7.29 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.26 – 7.21 (m, 3H), 7.19 – 7.15 (m, 2H), 7.12 – 7.08 (m, 1H), 7.03 (td, *J* = 7.6, 1.3 Hz, 1H), 6.98 (dd, *J* = 8.3, 1.2 Hz, 1H), 6.82 (s, 1H), 3.52 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 155.7 , 141.8 , 139.2 , 133.3 , 130.2 , 129.4 , 128.4 , 128.3 , 128.1 , 127.5 , 127.3 , 122.1 , 121.0 , 120.5 , 120.5 , 112.5 , 110.9 , 102.7 , 55.5 . The ^{1}H, ^{13}C NMR spectra were identical to the previously reported in the literature.[8a]

1-(Naphthalen-1-yl)-2-phenyl-1*H*-indole (2d): Following the general procedure A, **2d** was obtained as a white crystalline solid from 3.374 g of *N*-(naphthalen-1-yl)-*N*-*o*-tolylbenzamide (**1d**). Yield: 1.682 g (53%). MP 103-104 °C (lit. 73-74 °C).[8h] ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.95 (d, *J* = 8.3 Hz, 1H), 7.93 (d, *J* = 8.3 Hz, 1H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.56 – 7.45 (m, 4H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 7.2 Hz, 1H), 7.27 – 7.23 (m, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.16 – 7.05 (m, 5H), 6.96 (s, 1H), 6.84 (d, *J* = 8.2 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 142.3 , 140.4 , 135.4 , 134.5 , 132.7 , 131.5 , 128.7 , 128.4 , 128.4 , 128.3 , 128.2 , 127.4 , 127.3 , 127.2 , 126.7 , 125.7 , 123.7 , 122.4 , 120.8 , 120.6 , 111.4 , 103.4 . The ^{1}H, ^{13}C NMR spectra were identical to the previously reported in the literature.[8h]

1-(4-Fluorophenyl)-2-phenyl-1*H*-indole (2e): Following the general procedure A, **2e** was obtained as a white crystalline solid from 3.054 g of *N*-(4-fluorophenyl)-*N*-*o*-tolylbenzamide (**1e**). Yield: 2.075 g (72%). MP 118-119 °C (lit. 123-124 °C).[33] ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.72 – 7.69 (m, 1H), 7.29 – 7.19 (m, 11H), 7.12 (t, *J* = 8.6 Hz, 2H), 6.82 (s, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 161.6 (d, *J* = 247.2 Hz), 140.9 , 139.2 , 134.7 (d, *J* = 2.9 Hz), 132.5 , 129.8 (d, *J* = 8.6 Hz), 129.4 , 129.1 , 128.4 , 127.6 , 122.6 , 121.0 , 120.8 , 116.4 (d, *J* = 22.6 Hz), 110.5 , 103.9 . ^{19}F NMR (188 MHz, Chloroform-*d*) δ -115.7 . The ^{1}H, ^{13}C NMR spectra were identical to the previously reported in the literature.[33]

2-Phenyl-1-(3-(trifluoromethyl)phenyl)-1*H*-indole (2f): Following the general procedure A, **2f** was obtained as a white crystalline solid from 3.554 g of *N*-*o*-tolyl-*N*-(3-(trifluoromethyl)phenyl)benzamide (**1f**). Yield: 2.972 g (88%). MP 91-92 °C (lit. 91-92 °C).[8h] ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.75 – 7.71 (m, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.60 (s, 1H), 7.54 (t, *J* = 7.9 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.33 – 7.24 (m, 8H), 6.86 (d, *J* = 0.8 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 140.8 , 139.3 , 138.8 , 132.1 , 131.9 (q, *J* = 32.8 Hz), 131.4 , 130.0 , 129.1 , 128.6 , 128.5 , 127.8 , 124.8 (q, *J* = 3.6 Hz), 123.9 (q, *J* = 3.6 Hz), 123.7 (q, *J* = 272.5 Hz), 123.0 , 121.4 , 121.0 , 110.3 , 104.8 . ^{19}F NMR (188 MHz, Chloroform-*d*) δ -64.3 . The ^{1}H, ^{13}C NMR spectra were identical to the previously reported in the literature.[8h]

5,7-Dimethyl-1,2-diphenyl-1*H*-indole (2g): Following the general procedure A, **2g** was obtained as a white crystalline solid from 3.154 g of *N*-mesityl-*N*-phenylbenzamide (**1g**). Yield: 1.905 g (64%). MP 124-126 °C. HRMS (APPI) calcd for $C_{22}H_{19}N$ [M$^+$]: 297.1517, found: 297.1517. IR (KBr) 3057, 3029, 2969, 1596, 1496, 1453, 1438, 1406, 1374, 1338, 1295, 1221, 1069, 1025, 842, 767, 758, 744, 705, 692, 628 cm^{-1}. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.40 – 7.31 (m, 6H), 7.27 – 7.19 (m, 5H), 6.79 (s, 1H), 6.69 (s, 1H), 2.46 (s, 3H), 1.93 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 142.3 , 140.6 , 136.1 , 133.2 , 130.6 , 129.7 , 129.4 , 129.2 , 128.4 , 128.2 , 128.0 , 127.3 , 127.0 , 121.7 , 118.3 , 103.2 , 21.3 , 19.6 .

2-(5-Methyl-1,2-diphenyl-1*H*-indol-7-yl)-1-phenylethanone (2g'): This compound can be obtained as a byproduct during 5,7-dimethyl-1,2-diphenyl-1*H*-indole (**2g**) synthesis after the column chromatography step as a yellow solid. Yield: 0.683 g (34%). MP 151-152 °C. HRMS (APCI) calcd for $C_{29}H_{23}NO$ [M+H$^+$]: 402.1858, found: 402.1851. IR (KBr) 3055, 3030, 1686, 1596, 1497, 1341, 1327, 1209, 1179, 997, 854, 756, 744, 699, 609 cm^{-1}. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.64 (d, *J* = 7.2 Hz, 2H), 7.50 (t, *J* = 6.5 Hz, 1H), 7.45 (s, 1H), 7.38 – 7.33 (m, 2H), 7.22 – 7.15 (m, 7H), 7.05 – 6.98 (m, 3H), 6.75 (s, 1H), 6.70 (s, 1H), 4.00 (s, 2H), 2.45 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 197.4 , 142.4 , 140.1 , 136.7 , 135.9 , 133.0 , 132.9 , 130.4 , 129.8 , 129.7 , 129.4 , 128.8 , 128.3 , 128.1 , 128.0 , 127.3 , 119.9 , 118.0 , 103.5 , 42.5 , 21.3 . The structure of **2g'** was unambiguously confirmed by 2D ^{1}H-^{1}H NOESY NMR.

2-(2-Bromophenyl)-1-phenyl-1*H*-indole (2h): Following the general procedure A, **2h** was obtained as yellow oil from 3.663 g of 2-bromo-*N*-phenyl-*N*-*o*-tolylbenzamide (**1h**). Yield: 2.031 g (58%). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 6.8 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.29 – 7.21 (m, 8H), 7.18 – 7.13 (m, 1H), 6.78 (s, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 139.0 , 138.0 , 137.8 , 134.2 , 133.1 , 132.9 , 129.7 , 129.0 , 128.0 , 127.8 , 127.1 , 126.9 , 124.8 , 122.6 , 121.0 , 120.8 , 110.8 , 105.3 . The ^{1}H, ^{13}C NMR spectra were identical to the previously reported in the literature.[8f]

3-Methyl-1,2-diphenyl-1*H*-indole (2i): Following the general procedure A, **2i** was obtained as a white crystalline solid from 3.014 g of *N*-(2-ethylphenyl)-*N*-phenylbenzamide (**1i**). Yield: 2.829 g (>99%). MP 115-116 °C (lit. 120 °C).[34] ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.72 – 7.66 (m, 1H), 7.38 – 7.33 (m, 3H), 7.32 – 7.27 (m, 3H), 7.27 – 7.25 (m, 1H, overlapping with residual $CHCl_3$), 7.25 – 7.22 (m, 4H), 7.21 – 7.19 (m, 2H), 2.44 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 138.8 , 137.7 , 137.0 , 132.2 , 130.7 , 129.2 , 129.1 , 128.1 , 128.0 , 127.2 , 126.7 , 122.6 , 120.2 , 119.0 , 110.8 , 110.5 , 9.7 . The ^{1}H, ^{13}C NMR spectra were identical to the previously reported in the literature. [34]

1-Phenyl-2-(trifluoromethyl)-1*H*-indole (2j): Following the general procedure A, **2j** was obtained as a light-yellow crystalline solid from 2.793 g of 2,2,2-trifluoro-*N*-phenyl-*N*-*o*-tolylacetamide (**1j**). Yield: 1.899 g (73%). MP 54-57 °C (lit. 53 °C).[25b] ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 7.9 Hz, 1H), 7.57 – 7.52 (m, 3H), 7.45 – 7.42 (m, 2H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.26 – 7.22 (m, 1H), 7.14 – 7.12 (m, 1H), 7.10 – 7.08 (m, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 140.2 , 137.1 , 129.5 , 129.1 , 128.7 , 128.5 (q, *J* = 37.3 Hz), 125.8 , 125.0 , 122.2 , 121.5 , 121.4 (q, *J* = 268.7 Hz), 111.4 , 105.9 (q, *J* = 3.7 Hz). ^{19}F NMR (188 MHz, Chloroform-*d*) δ -59.0 . The ^{1}H, ^{13}C NMR spectra were identical to the previously reported in the literature.[25b]

1-(2-Methoxyphenyl)-2-(trifluoromethyl)-1*H*-indole (2k): Following the general procedure A, **2k** was obtained as a colorless oil from 3.091 g of 2,2,2-trifluoro-*N*-(2-methoxyphenyl)-*N*-*o*-tolylacetamide (**1k**). Yield: 2.364 g (81%). HRMS (APPI) calcd for $C_{16}H_{12}F_3NO$ [M$^+$]: 291.0871, found: 291.0868. IR (KBr) 3060, 2966, 2947, 2842, 1599, 1556, 1507, 1465, 1414, 1318, 1271, 1194, 1162, 1121, 1046, 1026, 972, 808, 753, 674, 635, 445 cm^{-1}. ^{1}H NMR (600 MHz, Chloroform-d) δ 7.73 (d, J = 7.9 Hz, 1H), 7.51 (td, J = 8.3, 1.7 Hz, 1H), 7.37 (d, J = 7.6 Hz, 1H), 7.28 – 7.24 (m, 1H), 7.21 (td, J = 7.5, 7.1, 0.9 Hz, 1H), 7.13 – 7.06 (m, 4H), 6.98 – 6.93 (m, 1H), 3.70 (s, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 156.7, 139.8, 130.9, 130.7, 128.5 (q, *J* = 36.9 Hz), 125.6, 125.2, 124.7, 122.0, 121.3 (q, *J* = 268.5 Hz),121.1, 120.7, 118.6, 112.2, 111.2, 105.4 (q, *J* = 3.8 Hz), 55.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -59.2.

5-Methyl-1-phenyl-2-(trifluoromethyl)-1*H*-indole (2l): Following the general procedure A, **2l** was obtained as a yellow oil from 2.931 g of *N*-(2,4-dimethylphenyl)-2,2,2-trifluoro-*N*-phenylacetamide (**1l**). Yield: 1.882 g (68%). HRMS (APPI) calcd for $C_{16}H_{12}F_3N$ [M$^+$]: 275.0922, found: 275.0917. IR (KBr) 3030, 2923, 2862, 1598, 1556, 1500, 1415, 1304, 1271, 1221, 1204, 1166, 1120, 805, 761, 698 cm^{-1}. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.56 – 7.49 (m, 4H), 7.41 (d, *J* = 6.7 Hz, 2H), 7.11 (d, *J* = 8.5 Hz, 1H), 7.03 (s, 1H), 6.97 (d, *J* = 8.5 Hz, 1H), 2.48 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 138.5, 137.0, 130.8, 129.5, 129.0, 128.6, 128.2 (q, *J* = 36.9 Hz), 126.8, 125.9, 121.5, 121.4 (q, *J* = 268.4 Hz), 111.0, 150.4 (q, *J* = 3.8 Hz), 76.9, 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.4.

6-*tert*-Butyl-1-phenyl-2-(trifluoromethyl)-1*H*-indole (2m): Following the general procedure A, **2m** was obtained as a yellowish solid from 3.352 g of *N*-(5-*tert*-butyl-2-methylphenyl)-2,2,2-trifluoro-*N*-phenylacetamide (**1m**). Yield: 1.982 g (62%). MP 60-62 °C. HRMS (APPI) calcd for $C_{19}H_{18}F_3N$ [M$^+$]: 317.1391, found: 317.1389. IR (KBr) 3051, 2960, 2903, 2867, 1598, 1546, 1500, 1411, 1280, 1184, 1157, 1099, 828, 696 cm^{-1}. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.68 (d, *J* = 8.5 Hz, 1H), 7.59 – 7.53 (m, 3H), 7.45 (d, *J* = 7.2 Hz, 2H), 7.36 – 7.33 (m, 1H), 7.08 (s, 1H), 7.04 (s, 1H), 1.33 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 148.8, 140.1, 136.9, 129.5, 129.0, 128.7, 127.1 (q, *J* = 37.1 Hz), 123.3, 121.6, 121.4 (q, *J* = 268.3 Hz), 120.0, 107.1, 105.5 (q, *J* = 3.7 Hz), 35.2, 31.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -57.4.

1-Phenyl-2-(1-adamantyl)-1*H*-indole (2n): Following the general procedure A, **2n** was obtained as a white crystalline solid from 3.455 g of *N*-phenyl-*N*-*o*-tolyladamantane-1-carboxamide (**1n**). Yield: 3.253 g (99%). MP 143-144 °C. HRMS (APPI) calcd for $C_{24}H_{25}N$ [M$^+$]: 327.1987, found: 327.1981. IR (KBr) 3043, 2905, 2850, 1595, 1495, 1455, 1355, 1304, 781, 749, 699, 669, 608 cm^{-1}. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 7.7 Hz, 1H), 7.56 – 7.48 (m, 3H), 7.42 – 7.37 (m, 2H), 7.10 (t, *J* = 7.3 Hz, 1H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.65 (d, *J* = 8.1 Hz, 1H), 6.48 (s, 1H), 2.02 – 1.92 (m, 9H), 1.68 (d, *J* = 11.9 Hz, 3H), 1.58 (d, *J* = 12.0 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 151.2 , 140.9 , 140.7 , 130.8 , 129.1 , 128.7 , 127.0 , 121.2 , 119.8 , 119.7 , 110.3 , 99.3 , 42.3 , 36.7 , 35.9 , 28.6 . When the reaction mixture was quenched with water instead of aqueous HCl with subsequent passing through a pad of silica, corresponding 1-(1-adamantyl)-2-(2-(phenylamino)phenyl)ethanone (**2n'**) in mixture with 1-phenyl-2-(1-adamantyl)-1*H*-indole (**2n**) was observed in ^{1}H NMR spectrum in 1:1.8 ratio. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.40 (s, 1H), 7.26 – 7.22 (m, 2H), 7.22 – 7.13 (m, 2H), 7.00 – 6.93 (m, 4H), 6.87 (t, *J* = 7.1 Hz, 1H), 3.84 (s, 2H), 2.10 (s, 3H), 1.91 (s, 6H), 1.80 (d, *J* = 12.6 Hz, 3H), 1.73 (d, *J* = 12.5 Hz, 3H).

2-*tert*-Butyl-1-phenyl-1*H*-indole (2o): Following the general procedure A, **2o** was obtained as a white crystalline solid from 2.673 g of *N*-phenyl-*N*-*o*-tolylpivalamide (**1o**). Yield: 2.478 g (>99%). Following the general procedure D, 2-*tert*-butyl-1-phenyl-1*H*-indole (**2o**) was obtained as a white crystalline solid from 1.833 g of 2-methyl-*N*-phenylaniline (**7a**) and 1.206 g of pivaloyl chloride. Yield: 2.344 g (94%). MP 74-76 °C. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 7.7 Hz, 1H), 7.55 – 7.50 (m, 3H), 7.43 – 7.38 (m, 2H), 7.11 (t, *J* = 7.4 Hz, 1H), 7.07 – 7.03 (m, 1H), 6.67 (d, *J* = 8.1 Hz, 1H), 6.50 (s, 1H), 1.29 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 150.8 , 141.0 , 140.4 , 130.9 , 129.1 , 128.7 , 127.0 , 121.3 , 119.9 , 119.7 , 110.3 , 99.3 , 33.4 , 31.2 . The ^{1}H, ^{13}C NMR spectra were identical to the previously reported in the literature.[32]

1-Cyclohexyl-2-phenyl-1H-indole (2p): Following the general procedure A, **2p** was obtained as a white crystalline solid from 2.934 g of *N*-cyclohexyl-*N*-*o*-tolylbenzamide (**1p**). Yield: 1.246 g (45%). MP 105-106 °C (lit. 104 °C).[7c] ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.68 (d, *J* = 8.3 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.51 – 7.41 (m, 5H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 6.49 (s, 1H), 4.23 (tt, *J* = 12.5, 3.8 Hz, 1H), 2.45 – 2.35 (m, 2H), 1.96 – 1.88 (m, 4H), 1.76 – 1.71 (m, 1H), 1.33 – 1.27 (m, 3H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 141.7 , 136.0 , 134.0 , 129.7 , 129.1 , 128.5 , 128.0 , 121.0 , 120.9 , 119.5 , 112.8 , 102.4 , 56.5 , 31.6 , 26.4 , 25.7 . The ^{1}H, ^{13}C NMR spectra were identical to the previously reported in the literature.[7c]

***N*-Cyclohexyl-*N*-(2-(2-oxo-2-phenylethyl)phenyl)benzamide (2p'):** This compound can be obtained as a byproduct during **2p** synthesis after the column chromatography step as yellow crystals. Yield: 1.071 g (54%). MP 112-114 °C. HRMS (APCI) calcd for $C_{27}H_{27}NO_2$ [M+H$^+$]: 398.2120, found: 398.2118. IR (KBr) 3064, 3031, 2934, 2856, 1693, 1630, 1599, 1578, 1494, 1446, 1377, 1364, 1326, 1263, 1214, 989, 893, 750, 738, 728, 709, 695, 686, 669, 652, 638, 583, 569 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.98 (d, *J* = 7.5 Hz, 2H), 7.67 (t, *J* = 7.2 Hz, 1H), 7.56 (t, *J* = 7.2 Hz, 2H), 7.39 – 7.01 (m, 9H), 4.38 (d, *J* = 17.5 Hz, 1H), 4.23 (d, *J* = 15.7 Hz, 1H), 4.08 (s, 1H), 1.99 (d, *J* = 11.7 Hz, 1H), 1.72 – 1.54 (m, 4H), 1.51 (d, *J* = 11.8 Hz, 1H), 1.17 (s, 3H), 1.01 – 0.88 (m, 1H). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.84 (s, 2H), 7.58 (t, *J* = 7.3 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.33 – 7.16 (m, 6H), 7.08 (s, 3H), 4.54 (s, 1H), 4.20 (d, *J* = 17.6 Hz, 1H), 3.99 (d, *J* = 16.3 Hz, 1H), 2.16 (s, 1H), 1.79 (d, *J* = 10.6 Hz, 1H), 1.73 – 1.52 (m, 4H), 1.46 – 1.27 (m, 2H), 1.15 (d, *J* = 11.8 Hz, 1H), 1.02 (d, *J* = 11.5 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 196.1 , 170.3 , 139.7 , 137.0 , 136.8 , 133.5 , 132.2 , 130.9 , 129.5 , 128.8 , 128.4 , 128.2 , 127.9 , 127.7 , 127.2 , 57.9 , 40.4 , 32.4 , 30.1 , 26.1 , 26.0 , 25.5 .

1-Methyl-2-phenyl-1*H*-indole (2q): Following the general procedure A, **2q** was obtained as a white crystalline solid from 2.253 g of *N*-methyl-*N*-*o*-tolylbenzamide (**1q**). Yield: 1.277 g (62%). MP 99-100 °C (lit. 99-100 °C).[35] ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 7.8 Hz, 1H), 7.57 (dd, *J* = 8.1, 1.2 Hz, 2H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.48 – 7.39 (m, 2H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 7.4 Hz, 1H), 6.62 (s, 1H), 3.79 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 141.7 , 138.5 , 133.0 , 129.5 , 128.6 , 128.1 , 128.0 , 121.8 , 120.6 , 120.0 , 109.7 , 101.8 , 31.3 . The ^{1}H, ^{13}C NMR spectra were identical to the previously reported in the literature.[36]

(1-Methyl-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone (2q'): This compound can be obtained as a byproduct during **2q** synthesis in 20-25% yield. But the reverse order of mixing of reagents allowed us to obtain **2q'** as a major product. A solution of LDA was prepared by slow addition of *n*-BuLi (8 ml, 2.5M in hexanes, 20 mmol, 2 eq.) to diisopropylamine (2.9 ml, 2.094 g, 20.7 mmol, 2.07 eq.) in absolute THF (20 ml) under Ar at 0 °C. Then this LDA solution was added dropwise (1-2 drops per second) to a solution of amide **1q** (2.253 g, 10 mmol, 1 eq.) in minimum amount of THF (~5 ml) at 10-15 °C. The resulting mixture was allowed to stir overnight at RT. The reaction was quenched with 3M aqueous HCl (10 ml) and concentrated under reduced pressure. The resulting mixture was partitioned between DCM (30 ml) and water (30 ml). Layers were separated and aqueous phase was extracted twice with DCM (30 ml). Combined organic fractions were dried over Na_2SO_4 and concentrated *in vacuo*. Residual oil was purified by column chromatography in EtOAc/hexanes (1:10) to afford pure **2q'** as a white crystalline solid. Yield: 1,088 g (70%). MP 127-128 °C. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.02 (d, *J* = 7.9 Hz, 1H), 7.53 (d, *J* = 7.1 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 1H), 7.38 – 7.35 (m, 1H), 7.32 – 7.26 (m, 1H), 7.25 (d, *J* = 4.8 Hz, 6H, overlapping with residual $CHCl_3$), 7.12 (t, *J* = 7.7 Hz, 2H), 3.68 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 193.0 , 146.5 , 140.3 , 137.3 , 131.1 , 131.0 , 130.9 , 129.3 , 128.8 , 128.1 , 127.7 , 127.7 , 123.4 , 122.4 , 122.0 , 114.8 , 109.9 , 31.4 . The ^{1}H, ^{13}C NMR spectra were identical to the previously reported in the literature.[37]

1,2-Diphenyl-1*H*-pyrrolo[2,3-*b*]pyridine (2r): Following the general procedure A with subsequent treatment with TFA in DCM, **2r** was obtained on 5 mmol scale as a white crystalline solid from 1.442 g of *N*-(3-methylpyridin-2-yl)-*N*-phenylbenzamide (**1r**). Yield: 1.298 g (96%). MP 131-132 °C (lit. 130-131 °C).[38] ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.39 – 8.33 (m, 1H), 7.98 (d, *J* = 7.6 Hz, 1H), 7.48 – 7.40 (m, 2H), 7.40 – 7.24 (m, 8H, overlapping with residual $CHCl_3$), 7.19 – 7.12 (m, 1H), 6.75 (s, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 150.0 , 143.7 , 141.3 , 137.1 , 132.2 , 129.2 , 129.1 , 128.6 , 128.5 , 128.4 , 127.9 , 127.5 , 121.0 , 117.2 , 101.6 . The ^{1}H, ^{13}C NMR spectra were identical to the previously reported in the literature.[38]

1-Phenyl-2-(2-(phenylamino)pyridin-3-yl)ethanone (1r'): Following the general procedure A on 5 mmol scale but with neutral aqueous work-up instead of aqueous HCl and without column chromatography and subsequent treatment with TFA in DCM, **1r'** was obtained as a yellow-orange solid from 1.442 g of *N*-(3-methylpyridin-2-yl)-*N*-phenylbenzamide (**1r**). Yield: 1.391 g (96%). Treatment of **1r'** (1.00 g, 3.5 mmol) with TFA (0.1 ml) in DCM (10 ml) gave 1,2-diphenyl-1*H*-pyrrolo[2,3-*b*]pyridine (**2r**) after 30 min stirring. Yield: 0.935 g (>99%). HRMS (ESI) calcd for $C_{19}H_{16}N_2O$ [M+H$^+$]: 289.1341, found: 289.1331. IR (KBr) 3395, 1673, 1592, 1529, 1497, 1440, 1323, 1213, 1159, 772, 749, 695, 686 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.08 (d, *J* = 8.0 Hz, 3H), 8.04 (s, 1H), 7.67 (t, *J* = 7.2 Hz, 1H), 7.57 (t, *J* = 7.7 Hz, 4H), 7.46 (d, *J* = 7.1 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 2H), 6.88 (t, *J* = 7.2 Hz, 1H), 6.81 – 6.76 (m, 1H), 4.56 (s, 2H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 196.8 , 154.5 , 145.5 , 141.7 , 139.5 , 136.6 , 133.2 , 128.6 , 128.3 , 128.1 , 120.7 , 119.6 , 117.1 , 114.9 , 40.6 .

1,4-Bis(1-phenyl-1*H*-indol-2-yl)benzene (2s): Following the general procedure B, **2s** was obtained on 2.5 mmol scale as a yellow crystalline solid from 0.916 g (5 mmol) of 2-methyl-*N*-phenylaniline (**7a**) and 0.508 g (2.5 mmol) of terephthaloyl chloride. Yield: 0.753 g (65%). MP >230 °C. HRMS (APPI) calcd for $C_{34}H_{24}N_2$ [M$^+$]: 460.1939, found: 460.1934. IR (KBr) 3057, 1594, 1497, 1457, 1450, 1353, 1314, 845, 784, 751, 695, 624 cm^{-1}. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.70 – 7.66 (m, 2H), 7.41 (t, *J* = 7.5 Hz, 4H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.31 – 7.27 (m, 2H), 7.25 – 7.22 (m, 4H), 7.20 – 7.16 (m, 4H), 7.13 (s, 4H), 6.81 (s, 2H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 140.3 , 139.3 , 138.6 , 131.4 , 129.4 , 128.7 , 128.4 , 128.2 , 127.3 , 122.6 , 120.9 , 120.7 , 110.7 , 104.0 .

6-*tret*-Butyl-1,2-diphenyl-1*H*-indole (2t): Following the general procedure B, **2t** was obtained on 5 mmol scale as a white crystalline solid from 1.197 g of 5-*tert*-butyl-2-methyl-*N*-phenylaniline (**7k**) and 0.703 g of benzoyl chloride. Yield: 1.404 g (86%). MP 145-146 °C. HRMS (APPI) calcd for $C_{24}H_{23}N$ [M$^+$]: 325.180, found: 325.1828. IR (KBr) 3063, 3036, 2962, 1595, 1500, 1490, 1427, 1378, 1346, 1329, 1245, 831, 824, 763, 699 cm^{-1}. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.65 (d, *J* = 8.1 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.35 – 7.20 (m, 9H, overlapping with residual $CHCl_3$), 6.78 (s, 1H), 1.37 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 146.1 , 140.8 , 139.2 , 138.8 , 133.0 , 129.4 , 129.0 , 128.3 , 128.2 , 127.2 , 126.1 , 120.1 , 119.2 , 106.8 , 103.6 , 35.1 , 31.9 .

1-(2-Bromophenyl)-2-phenyl-1*H*-indole (2u): Following the general procedure B, **2u** was obtained on 5 mmol scale as yellow oil from 1.311 g of 2-bromo-*N*-*o*-tolylaniline (**7l**) and 0.703 g of benzoyl chloride. Yield: 0.930 g (53%). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.77 – 7.69 (m, 2H), 7.37 (td, *J* = 7.6, 1.3 Hz, 1H), 7.33 (dd, *J* = 7.9, 1.7 Hz, 2H), 7.30 – 7.20 (m, 7H, overlapping with residual $CHCl_3$ signal), 7.02 – 6.96 (m, 1H), 6.86 (s, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 141.3 , 138.9 , 138.3 , 133.8 , 132.5 , 131.5 , 129.9 , 128.6 , 128.5 , 128.4 , 128.4 , 127.6 , 124.1 , 122.5 , 120.9 , 120.7 , 111.1 , 103.5 . The ^{1}H, ^{13}C NMR spectra were identical to the previously reported in the literature.[8e]

1-(2-Chlorophenyl)-2-phenyl-1*H*-indole (2v): Following the general procedure B, **2v** was obtained on 5 mmol scale as yellow oil from 1.088 g of 2-chloro-*N*-*o*-tolylaniline (**7m**) and 0.703 g of benzoyl chloride. Yield: 1.029 g (68%). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.74 – 7.68 (m, 1H), 7.54 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.37 (td, *J* = 7.7, 1.7 Hz, 1H), 7.34 – 7.22 (m, 7H, overlapping with residual $CHCl_3$ signal), 7.21 – 7.17 (m, 2H), 7.02 – 6.98 (m, 1H), 6.85 (s, 1H). ^{13}C{^{1}H} NMR (151 MHz, Chloroform-*d*) δ 141.5 , 139.1 , 136.7 , 133.9 , 132.6 , 131.4 , 130.7 , 129.6 , 128.6 , 128.5 , 128.4 , 127.8 , 127.6 , 122.6 , 121.0 , 120.7 , 110.9 , 103.6 . The ^{1}H, ^{13}C NMR spectra were identical to the previously reported in the literature.[7c]

1-Phenyl-2-(3-(phenylamino)benzo[*b*]thiophen-2-yl)ethanone (2w'): Following the general procedure B, **2w'** was obtained on 5 mmol scale as an orange solid from 1.197 g of 2-methyl-*N*-phenylbenzo[*b*]thiophen-3-amine (**7n**) and 0.703 g of benzoyl chloride. Yield: 1.157 g (71%). MP 192-194 °C. HRMS (APCI) calcd for $C_{22}H_{17}NOS$ [M+H$^+$]: 344.1109, found: 344.1104. IR (KBr) 3367, 3050, 1685, 1603, 1593, 1573, 1501, 1450, 1366, 1332, 1305, 1251, 1216, 992, 747, 731, 691, 684 cm^{-1}. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.98 (d, *J* = 7.7 Hz, 2H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.56 (t, *J* = 7.1 Hz, 1H), 7.50 (d, *J* = 7.9 Hz, 1H), 7.44 (t, *J* = 7.2 Hz, 2H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.27 (d, *J* = 9.0 Hz, 1H), 7.15 (t, *J* = 7.0 Hz, 2H), 6.78 (t, *J* = 6.9 Hz, 1H), 6.65 (d, *J* = 7.7 Hz, 2H), 4.47 (s, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 196.3 , 146.0 , 137.6 , 136.4 , 136.1 , 133.8 , 132.3 , 129.4 , 129.2 , 128.9 , 128.7 , 128.6 , 124.7 , 124.2 , 122.8 , 122.2 , 118.9 , 114.3 , 37.6 .

1,2-Diphenyl-1*H*-[1]benzothieno[3,2-*b*]pyrrole (2w): Phosphorus pentoxide (100 mg, 0.704 mmol, 3.1 eq.) and dry DCM (2 ml) were placed into Schlenk tube under Ar. To the resulting vigorously stirred suspension TMS_2O (0.5 ml, 382 mg, 2.353 mmol, 10.3 eq.) was added. The mixture was allowed to stay at 40 °C for 0.5h (suspension turned into clear solution). After that solid **2w'** (77.2 mg, 0.225 mmol, 1.0 eq.) was added in one portion and the reaction was stirred for additional 1h at 40 °C. Then it was cooled down to RT and poured into KOH solution (25 ml, 20%). The resulting mixture was extracted with DCM. Combined organic phase was dried over anhydrous Na_2SO_4 and condensed under

reduced pressure. The residue was filtered through a small pad of silica (DCM/PE, 1:1). The product **2w** was obtained as colorless crystals. Yield: 72.4 mg (99%). MP 186-187 °C. HRMS (APPI) calcd for $C_{22}H_{15}NS$ [M^+]: 325.0925, found: 325.0922. IR (KBr) 3048, 1594, 1504, 1492, 1461, 1352, 1071, 1057, 1019, 788, 751, 695, 632 cm^{-1}. ^1H NMR (600 MHz, Chloroform-*d*) δ 7.80 (d, *J* = 8.0 Hz, 1H), 7.53 – 7.46 (m, 3H), 7.46 – 7.40 (m, 2H), 7.26 – 7.16 (m, 6H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.07 (d, *J* = 7.9 Hz, 1H), 6.77 (s, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, Chloroform-*d*) δ 142.3 , 140.3 , 139.0 , 134.7 , 132.7 , 129.5 , 128.6 , 128.4 , 128.3 , 127.5 , 127.0 , 124.2 , 123.9 , 123.3 , 122.9 , 118.9 , 102.9 .

General procedure for benzofuran and benzofuran synthesis (C): A solution of LDA was prepared by slow addition of *n*-BuLi (8 ml, 2.5M in hexanes, 20 mmol, 2 eq.) to diisopropylamine (2.9 ml, 2.094 g, 20.7 mmol, 2.07 eq.) in absolute THF (20 ml) under Ar at 0 °C. Then a solution of ester **3** (10 mmol, 1 eq.) in THF (20 ml) was added dropwise (1-2 drops per second) at 10-15 °C. The resulting mixture was allowed to stir overnight at RT. The reaction was quenched with 3M aqueous HCl (10 ml) and stirred for additional 0.5 h, then concentrated under reduced pressure. The resulting mixture was partitioned between DCM (30 ml) and water (30 ml). Layers were separated and aqueous phase was extracted twice with DCM (30 ml). Combined organic fractions were dried over Na_2SO_4 and concentrated *in vacuo*. Residual oil was redissolved in DCM (20 ml) and allowed to stir with 1 ml of TFA for 1 h at RT. Then it was concentrated again and purified by column chromatography in EtOAc/hexanes (1:40) affording pure benzofuran **4**.

2-Phenylbenzofuran (4a): Following the general procedure C, **4a** was obtained as a white solid from 2.122 g of *o*-tolyl benzoate (**3a**). Yield: 0.684 g (35%). MP 119-120 °C (lit. 119-120 °C).[39] ^1H NMR (600 MHz, Chloroform-*d*) δ 7.90 (d, *J* = 7.4 Hz, 2H), 7.61 (d, *J* = 7.5 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.47 (t, *J* = 7.3 Hz, 2H), 7.38 (t, *J* = 7.3 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.29 – 7.23 (m, 1H), 7.05 (s, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, Chloroform-*d*) δ 156.1 , 155.0 , 130.6 , 129.4 , 128.9 , 128.7 , 125.1 , 124.4 , 123.1 , 121.0 , 111.3 , 101.4 . The ^1H, ^{13}C NMR spectra were identical to the previously reported in the literature.[40]

2-(1-Adamantyl)benzofuran (4b): Following the general procedure C, **4b** was obtained as a white solid from 2.704 g of *o*-tolyl adamantane-1-carboxylate (**3b**). Yield: 2.223 g (88%). MP 105-106 °C. HRMS (APPI) calcd for $C_{18}H_{20}O$ [M^+]: 252.1514, found: 252.1511. IR (KBr) 2931, 2913, 2851, 2361, 2343, 1581, 1454, 1256, 1102, 1031, 929, 793, 750, 737, 683 cm^{-1}. ^1H NMR (600 MHz, Chloroform-*d*) δ 7.50 (d, *J* = 6.9 Hz, 1H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.23 - 7.14 (m, 2H), 6.32 (s, 1H), 2.11 (s, 3H), 2.03 (s, 6H), 1.84 – 1.78 (m, 6H). $^{13}C\{^1H\}$ NMR (151 MHz, Chloroform-*d*) δ 167.7 , 154.5 , 129.0 , 123.1 , 122.4 , 120.5 , 110.9 , 98.6 , 41.1 , 36.9 , 35.0 , 28.3 .

1-(1-Adamantyl)-2-(2-hydroxyphenyl)ethanone (4b'): Following the general procedure C but with aqeouos work-up and without subsequent treatment with TFA in DCM, **4b'** was obtained as a white crystalline solid from 2.704 g of *o*-tolyl adamantane-1-carboxylate (**3b**). Yield: 2.382 g (88%). Treatment of **4b'** (2.00 g, 7.4 mmol) with TFA (0.2 ml) in DCM (20 ml) gave **4b** after 30 min stirring. Yield: 1.865 g (>99%). MP 140-141 °C. HRMS (APCI) calcd for $C_{18}H_{22}O_2$ [M^+-H_2]: 268.1463, found: 268.1461. IR (KBr) 3423, 3302, 2905, 2850, 1682, 1608, 1598, 1457, 1347, 1272, 1230, 1095, 1018, 750, 715 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) δ 9.23 (s, 1H), 7.02 (t, *J* = 7.7 Hz, 1H), 6.96 – 6.92 (m, 1H), 6.74 (d, *J* = 8.0 Hz, 1H), 6.69 (t, *J* = 7.4 Hz, 1H), 3.71 (s, 2H), 2.01 (s, 3H), 1.83 (d, *J* = 2.3 Hz, 6H), 1.69 (q, *J* = 12.3 Hz, 6H). $^{13}C\{^1H\}$ NMR (151 MHz, DMSO-d_6) δ 211.8 , 155.0 , 131.4 , 127.3 , 122.5 , 118.5 , 114.61 , 45.9 , 37.8 , 37.1 , 36.1 , 27.5 .

General procedure for benzothiofene synthesis (D): A solution of LDA was prepared by slow addition of *n*-BuLi (8 ml, 2.5M in hexanes, 20 mmol, 2 eq.) to diisopropylamine (2.9 ml, 2.094 g, 20.7 mmol, 2.07 eq.) in absolute THF (20 ml) under Ar at 0 °C. Then a solution of thioester **5** (10 mmol, 1 eq.) in THF (20 ml) was added dropwise (1-2 drops per second) at 10-15 °C. The resulting mixture was allowed to stir overnight at RT. The reaction was quenched with 3M aqueous HCl (10 ml) and stirred for additional 0.5 h, then concentrated under reduced pressure. The resulting mixture was partitioned between DCM (30 ml) and water (30 ml). Layers were separated and aqueous phase was extracted twice with DCM (30 ml). Combined organic fractions were dried over Na_2SO_4 and concentrated *in vacuo*. Residual oil was redissolved in DCM (20 ml) and allowed to stir with 1 ml of TFA for 1 h at RT. Then it was concentrated again and purified by column chromatography in EtOAc/hexanes (1:40) affording pure benzothiofene **6**.

2-Phenylbenzo[*b*]thiophene (6a): Following the general procedure D, **6a** was obtained as a white solid from 2.283 g of *S*-*o*-tolyl benzothioate (**5a**). Yield: 0.551 g (26%). MP 169-170 °C (lit. 168-169 °C).[41] ^1H NMR (600 MHz, Chloroform-*d*) δ 7.84 (d, *J* = 7.8 Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.74 (d, *J* = 7.3 Hz, 2H), 7.56 (s, 1H), 7.44 (t, *J* = 6.9 Hz, 2H), 7.35 (dd, *J* = 17.9, 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, Chloroform-*d*) δ 144.4 , 140.8 , 139.7 , 134.5 , 129.1 , 128.4 , 126.6 , 124.7 , 124.5 , 123.7 , 122.4 , 119.6 . The ^1H, ^{13}C NMR spectra were identical to the previously reported in the literature.[42]

2-(1-Adamantyl)benzo[*b*]thiophene (6b): Following the general procedure D, **6b** was obtained as a white solid from 2.864 g of *S*-*o*-tolyl adamantane-1-carbothioate (**5b**). Yield: 0.922 g (34%). MP 150-151 °C. HRMS (APPI) calcd for $C_{18}H_{20}S$ [M^+]: 268.1286, found: 268.1283. IR (KBr) 2907, 2845, 1457, 1445, 1435, 1344, 825, 809, 739, 725, 586 cm^{-1}. ^1H NMR (600 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 7.7 Hz, 1H), 7.69 (d, *J* = 7.7 Hz, 1H), 7.34 – 7.22 (m, 2H), 7.03 (s, 1H), 2.16 – 2.10 (m, 3H), 2.06 (s, 6H), 1.86 – 1.77 (m, 6H). $^{13}C\{^1H\}$ NMR (151 MHz, Chloroform-*d*) δ 158.9 , 140.2 , 138.6 , 124.0 , 123.4 , 123.0 , 122.4 , 116.9 , 44.8 , 36.8 , 29.0 .

Indolo[1,2-*f*]phenanthridine (8): A screw-capped vial was charged with 2-(2-bromophenyl)-1-phenyl-1*H*-indole (**2h**) (150 mg, 0.43 mmol 1 eq.), $Pd(OAc)_2$ (4 mg, 0.017mmol, 0.04 eq.), PCy_3 (10 mg, 0.034 mmol, 0.08 eq.), pivalic acid (9 mg, 0.086 mmol, 0.2 eq.), Cs_2CO_3 (280 mg, 0.86, 2 eq.) and THF (3 ml). Then it was purged with Ar, immersed into preheated oil bath (110 °C) and stirred for 24 h. After being cooled to RT it was submitted to column chromatography with DCM/PE mixture (1:5), which provided the product as a pale yellow solid. Yield: 102 mg (89%). Exploitation of the same procedure but with isomeric 1-(2-bromophenyl)-2-phenyl-1*H*-indole (**2u**) also afforded the product. Yield: 91 mg (79%). MP 145-147 °C. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.55 (d, *J* = 8.2 Hz, 1H), 8.39 (d, *J* = 8.1 Hz, 1H), 8.32 (d, *J* = 7.7 Hz, 1H), 8.26 – 8.19 (m, 1H), 8.17 – 8.12 (m, 1H), 7.88 – 7.82 (m, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.54 – 7.46 (m, 2H), 7.43 – 7.33 (m, 3H), 7.33 – 7.19 (m, 1H, overlapping with residual $CHCl_3$). $^{13}C\{^1H\}$ NMR (151 MHz, Chloroform-*d*) δ 136.1 , 135.4 , 134.1 , 130.5 , 128.9 , 128.3 , 128.0 , 127.0 , 126.3 , 124.3 , 124.2 , 123.2 , 122.6 , 122.3 , 122.2 , 121.9 , 121.2 , 116.5 , 114.4 , 96.4 . The ^1H, ^{13}C NMR spectra were identical to the previously reported in the literature.[43]

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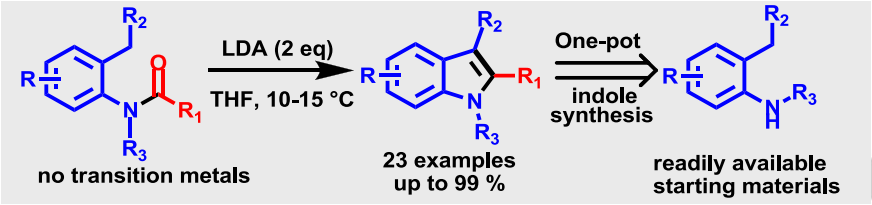

A new robust transition-metal-free method for synthesis of 1,2-disubstituted indoles from easily available tertiary amides is presented. This approach can be performed in one-pot two-step manner directly from secondary amines. Mechanistic studies showed that acyl transfer might be an important step in the course of the reaction. Viability of the presented approach for benzofurans and benzothiophenes synthesis is also demonstrated.

Indole synthesis*

*Gleb A. Chesnokov, Alexandra A. Ageshina, Maxim A. Topchiy, Mikhail S. Nechaev and Andrey F. Asachenko **

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Transition-Metal-Free Synthesis of 1,2-Disubstituted Indoles