JOC The Journal of Organic Chemistry



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*J. Org. Chem.*, **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b00830 • Publication Date (Web): 23 Jun 2017



## Just Accepted



ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

# Nitroalkenes as latent 1,2-biselectrophiles – A multicatalytic approach for the synthesis of 1,4-diketones and their application in a 4-step one-pot reaction to polysubstituted pyrroles

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*KEYWORDS multicatalysis, NHC catalysis, heterocycles, multicomponent reaction, domino reaction, pyrroles*

**ABSTRACT:** A NHC-catalyzed Nitro-Stetter/elimination/Stetter reaction sequence employs nitroalkenes as latent 1,2-dication synthons providing a novel access to highly useful symmetrical and unsymmetrical 2-aryl substituted 1,4-diketone building blocks from commercially available aldehyde precursors. For less activated (aliphatic) aldehydes a cooperative catalytic strategy has been developed *via* the merger of NHC and H-bonding catalysis. To further showcase the versatility of our approach a great variety of these unprecedented 1,4-diketones are used to efficiently synthesize polysubstituted pyrroles – including those with hetaryl substituents – in good to excellent yields in a multicatalytic metal-free, 4-step one–pot-cascade reaction under mild, yet robust conditions.

## INTRODUCTION

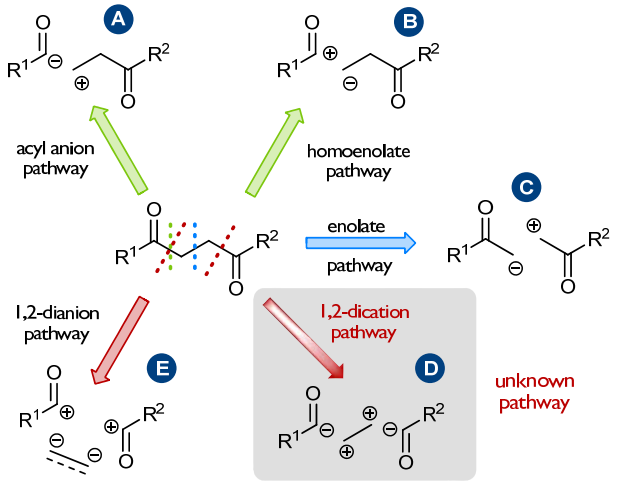
1,4-Diketones are highly important building blocks for a great variety of bioactive compounds. Apart from their abundant occurrence in natural products and their significance as synthetic precursors for 1,4-diols, they have witnessed great interest especially for the construction of heteroaryl subunits, which are privileged motifs in medicinal as well as material chemistry.[1] Following classical Paal-Knorr conditions[2] a wide range of 5-membered heterocycles,[3] such as furans, pyrroles, thiophenes can be conveniently accessed as other routes allow for the synthesis of cyclopentenones, benzenes[4] and biphenols.[5]

Due to this prevalence and to exploit the great versatility of this precursor numerous competent synthetic protocols have been developed,[6,7] albeit all of them with specific limitations.

As the dissonant connectivity of the 1,4-dicarbonyl motif is difficult to realize by classical reactivity,[8] umpolung approaches[9] or redox pathways have been followed to alter the original reactivity of the corresponding building blocks. However, especially the synthesis of un-symmetrically functionalized 1,4-dicarbonyl compounds can prove challenging and hence the development of new methods is highly desirable. As illustrated in Scheme 1 progress in the field may strongly rely on changes in the retrosynthetic analysis.

Probably one of the most famous examples of a traditional, conjugate addition approach is the Stetter reaction with catalytically generated acyl anions (pathway **A**).[10] Alternative nucleophilic acylations are reported with *in situ* generated acyl radicals[11] or *via* Pd-mediated carbonylative 1,4-additions.[12,13] The reverse approach (route **B**) using homoenolate equivalent synthons together with electrophilic acyl derivatives[14] has also been established. Coupling of two C2 subunits according to pathway **C**[15] requires the reactivity reversal of the carbonyl´s α-position, while functionalization of an 1,2-dianion (route **E**) can be achieved with alkynes[4] or as recently shown by the group of Bertus by a titanium mediated formal insertion of 1,2-dianions into acyl cyanohydrins.[16] However, the need of elaborate precursors, harsh reaction conditions as well as limitation to non-functionalized or only symmetrical 1,4-diketones are among the drawbacks of the current methodologies.

**Scheme 1. Different retrosynthetic strategies for 1,4-diketones.**

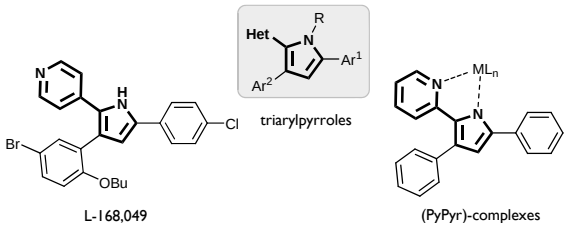



Based on this analysis and the attractiveness of a convergent three-component strategy we recently questioned whether an electronically reverse strategy of employing 1,2-biselectrophiles as a C2-carbon source (pathway **D**) together with two acyl anions, catalytically generated from simple aldehydes, could be used for the catalytic synthesis of 1,4-diketones. Moreover, we hoped that this approach would allow for direct integration in an one-pot Paal-Knorr-type sequence to access polysubstituted pyrroles.

Highly substituted pyrroles are known as a privileged class of nitrogen containing heterocycles,[17] being widespread in a variety of biological active substances such as pharmaceuticals, agrochemicals and natural products.[18] In addition, polysubstituted pyrrole derivatives are applied as versatile building blocks in modern organic chemistry[3,19] as well as in materials science.[20] Hence, the search for novel, broadly applicable pyrrole syntheses has triggered considerable attention.[21] Despite, even with these recent advances, current methods are unfortunately not without their limitations, particularly with regard to the application of advanced precursors which require time-consuming pre-synthesis and often costly additional steps.[22] Moreover, the common use of (often expensive) metal catalytic methods[23,24] may potentially cause well-known problems of product contamination, while rather rare, metal-free protocols suffer from harsh reaction conditions or advanced starting materials.[25] Addressing some of the mentioned drawbacks, the concept of multicomponent reactions (MCR) for pyrrole syntheses as a waste reducing, step and atom economic method has gained increasing interest.[26]

From a structural point of view current methodology often lacks the possibility to introduce hetaryl substituents at the pyrrole core; such triarylpyrrolo motifs, however, are important scaffolds in medicinal chemistry (Scheme 2), such as for p38 mitogen-activated protein kinases (MAS) inhibittors[27] or as glucagon receptor antagonist like L-168,049.[28]

**Scheme 2. Example applications of triarylpyrrolo compounds.**




Furthermore, 2-pyridylpyrroles (PyPyr) are interesting bidentate ligands for organometallic catalysts as they are known to stabilize high oxidation states.[29]

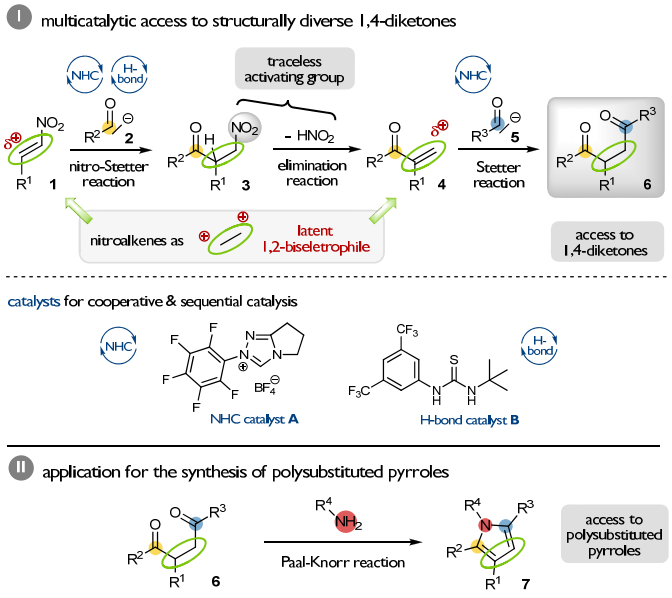
Herein, we report a novel multicatalytic MCR approach of using nitroalkenes as latent 1,2-biselectrophiles for the generation of 1,4-diketones. We further disclose the extension to a 4-step one-pot reaction to synthetically relevant 1,2,3,5-substituted pyrroles by employing only simple, commercially available starting materials.

*DESIGN PLAN*

Based on the synthetic power of NHC-catalyzed umpolung[30] of aldehydes we hypothesized that a multicomponent approach of catalytically generated acylanion equivalents together with a suitable bis-electrophilic alkene surrogate could lead to a large variety of 1,4-diketones **6** and their corresponding polysubstituted pyrroles **7** (Scheme 3).

It has been established that β-nitro carbonyl compounds can readily eliminate $HNO_2$ under mild acidic or basic conditions.[31] The electrophilic character of nitro alkenes allows for the attack of acyl anion **2**, generated by an *N*-heterocyclic carbene (NHC) catalyst (such as **A**) in a so-called nitro-Stetter reaction,[32] to furnish β-nitro ketone **3.** In combination with their ready commercial availability it renders nitro olefins attractive 1,2—dication synthons. Elimination of nitrous acid would lead to a subsequent Michael acceptor **4** with an electrophilic position at the former $NO_2$-substituted carbon atom; the nitro group hence serves as a traceless activating and directing group. Furthermore, the proposed latent 1,2-biselectrophilic nitroalkenes are well known to allow for additional activation with H-bond catalysts[33] such as thiourea catalyst **B** and therefore provide a further handle for tuning the reaction conditions of the nitro-Stetter reaction for less activated substrates.[34] The newly harnessed acceptor **4** could then be attacked by a second acyl anion equivalent **5** to form the desired 1,4-diketone **6** in a classical Stetter reaction.[10] Subsequent treatment with amines applying Paal-Knorr conditions would provide access to polysubstituted pyrroles **7**.

**Scheme 3. Strategy of latent 1,2-biselectrophiles for the synthesis of 1,2,3,5 substituted pyrroles.**

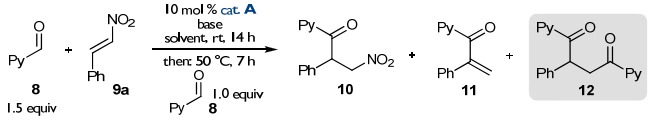



With water and $HNO_2$ as the only secondary reaction products this catalytic nitro-Stetter/elimination/Stetter/Paal-Knorr sequence would be additionally attractive due to its high atom economy.

## RESULTS AND DISCUSSION

We commenced our studies with β-nitrostyrene (**9a**) and pyridine carboxaldehyde (**8**) as our model substrates for the latent 1,2-biselectrophile generation (Table 1). Aryl substituted nitroalkenes were supposed to facilitate the crucial elimination of $HNO_2$.[35]

**Table 1. Optimization of the reaction conditions.**[a]



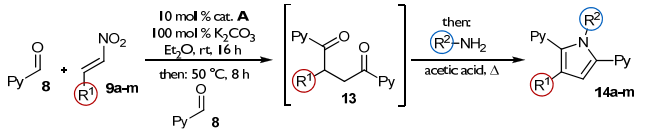

| Entry | Base | Solvent | Base loading [mol %] | Yield[b] **10** in % | Yield[b] **11** in % | Yield[b] **12** in % |
|---|---|---|---|---|---|---|
| 1 | NaOAc | $^t$AmOH | 40 | 32 | 12 | 54 |
| 2 | NaOAc | acetone | 40 | 26 | 16 | 58 |
| 3 | NaOAc | $Et_2O$ | 40 | 50 | 5 | 45 |
| 4 | DIPEA | $Et_2O$ | 40 | 39 | 28 | 19 |
| 5 | $K_2CO_3$ | $Et_2O$ | 40 | 31 | 0 | 69 |
| 6 | $K_2CO_3$ | $Et_2O$ | 70 | 3 | 0 | 97 |
| 7 | $K_2CO_3$ | $Et_2O$ | 100 | 0 | 0 | 100 (90)[c] |
| 8[d] | $K_2CO_3$ | $Et_2O$ | 100 | 0 | 0 | 85[c] |

[a] Conditions: Aldehyde **8** (Py = 2-pyridyl) (0.38 mmol), nitroalkene **9a** (0.25 mmol), cat. **A** (10 mol %), base (x mol %), solvent (2 mL) for 14 h at rt, then aldehyde **8** (0.25 mmol) for 7 h at 50 °C. [b] Yield determined by $^1$H NMR spectroscopy using dibromomethane (1 equiv) as internal standard. [c] Isolated yield. [d] Reaction was performed on a 1.5 mmol scale.

Our initial investigations were aimed to validate the general feasibility of our approach for a single aldehyde to furnish symmetrical substituted 1,4-diketones **12**. Based on these results we would then examine the scope of this reaction by employing two different aldehydes to generate unsymmetrical diketo products. It was apparent from the outset of our studies that - already for a single aldehyde - the mixture of possible products (nitro-Stetter adduct **10**, elimination product **11** and the desired 1,4-diketone **12**) would pose a major challenge. To find suitable conditions we started with reaction parameters typical for a nitro-Stetter reaction of aliphatic aldehydes,[32a] which we slightly modified by the use of achiral catalyst **A** and higher temperature (rt to 50 °C for 7 h) to promote the elimination and the sequential addition of a second equivalent of pyridyl aldehyde **8** (entry 1) as its NHC-derived acyl anion. All three products including diketone **12** were formed, therefore confirming the viability of β-nitrostyrenes as a latent 1,2-biselectrophiles. Furthermore, NHC-catalyst **A** proved to be competent to promote both the the nitro-Stetter and the Stetter reaction. An initial solvent screening with acetone (entry 2) and diethylether as a non-protic polar solvent (entry 3) revealed a slightly increased overall yield with a remarkable cut for elimination product **11**. As the rapid decomposition of Michael acceptor **11** was well-precedented, and also observed during work-up procedures[36] we selected diethylether as the solvent for further investigations. While an amine base (entry 4), was detrimental, changing to $K_2CO_3$ as alternative inorganic base showed promising results. With undetectable yields of Michael acceptor **11** the reaction was clean and reached full conversion (entries 5-7). Stepwise increasing amounts of base proved to favour the desired diketone **12** and the yield of the reaction could be raised to its quantitative formation (entries 6 and 7). Ultimately, we decided to use 1.0 equivalents of base to establish robust conditions that ensure complete elimination and would be applicable to a broad range of substrates. It is noteworthy, that this procedure is also amenable to efficient batch scale-up, providing diketone **12** in 85% yield on 1.5 mmol scale (entry 8).

With this optimized conditions for our novel 1,4-diketone synthesis in hand, we aimed to demonstrate the versatility of this approach by expanding the 3-step-one-pot-reaction to a 4-step-cascade with a terminal Paal-Knorr reaction to access tetrasubstituted pyrroles **14**. Next, we evaluated the scope of the reaction with respect to the substituted β-nitrostyrene fragments **9a-m** and different amines (Table 2). The extension to this one-pot pyrrole formation was successful for our initial model substrate **9a** providing pyrroles **14a** and **14b** in almost quantitative yields (entry 1,2).

**Table 2. 4-Step one-pot cascade to pyrroles - Scope of different β-nitrostyrene-derivatives.**[a]




| Entry | $R^1$ | $R^2$ | Product **14a-m** | Yield[b] in % |
|---|---|---|---|---|
| 1 | Ph (**9a**) | $CH_2$-Ph | **14a** | 97 |
| 2 | Ph (**9a**) | $(CH_2)_2$-Ph | **14b** | 95 |
| 3 | Ph (**9a**) | 4-OMe-Ph | **14c** | 95 |
| 4 | Ph (**9a**) | H | **14d** | 98 |
| 5 | 4-OMe-Ph (**9e**) | $CH_2$-Ph | **14e** | 94 |
| 6 | 4-Br-Ph (**9f**) | $CH_2$-Ph | **14f** | 77 |
| 7 | 3-Br-Ph (**9g**) | $CH_2$-Ph | **14g** | 92 |
| 8[c] | 3-CN-Ph (**9h**) | $CH_2$-Ph | **14h** | 59 |
| 9 | 2-F-Ph (**9i**) | $CH_2$-Ph | **14i** | 74 |
| 10 | 2-Me-Ph (**9j**) | $CH_2$-Ph | **14j** | 44 |
| 11 | 2,4,6-Me-Ph (**9k**) | $CH_2$-Ph | **14k** | nd |
| 12 | $CH_3(CH_2)_4$ (**9l**) | $CH_2$-Ph | **14l** | nd |
| 13 | Furyl (**9m**) | H | **14m** | 70 |

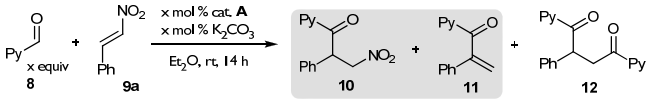
[a] Conditions: Aldehyde **8** (0.38 mmol), nitroalkene **9a-m** (0.25 mmol), cat. **A** (10 mol %), $K_2CO_3$ (0.25 mmol), $Et_2O$ (2 mL) for 16 h at rt, then aldehyde **8** (0.25 mmol) for 8 h at 50 °C, then amine (0.75 mmol) and acetic acid (2 mL) for 1.5 d at 70 °C in a screw-top reaction tube. [b] Yield of isolated product. [c] Milder conditions for the last step were used: benzylamine (1.4 mmol), acetic acid (0.75 mmol, 3.0 equiv) and heating overnight at 50 °C.

As expected the reaction is not limited to aliphatic amines and showed an excellent yield of 95% for the MCR using less nucleophilic aromatic amine (entry 3). Moreover, direct access to *N*-unsubstituted pyrroles is possible by employing ammonium acetate as a nitrogen source (95%; entry 4). Variations of the nitrostyrene´s aryl substituent with different electron donating and withdrawing groups were also well tolerated (entries 5-9). Notably, small *ortho*-substitutents had no influence on the product yield (74% yield for **14i**; entry 9). However, higher sterical demand as shown for the 2-methyl substituent results in lower yields, but still being useful for an operationally simple 4-step one-pot process (44% for pyrrole **14j**; entry 10). Two sterically demanding substituents at the *ortho*-position are the current limitation for this one-pot reaction (entry 11). Moreover, as 2-alkyl nitroalkenes hardly show any elimination[32b-e] to the corresponding Michael acceptors, no product formation was observed (entry 12). Finally, pyrrole formation also efficiently proceeds with heteroaryl substituted nitroalkenes, as shown for furyl derivative **14m** (entry 13).

As mentioned previously, the synthesis of unsymmetrical diketones has often proved challenging and lowering the scope of the corresponding methodology. After our promising results with a single aldehyde, we therefore aimed to further broaden the synthetic scope in order to provide access to unsymmetrically substituted 1,4-diketones by using two different aldehydes.

The key challenges for this cross-addition approach to the nitroalkene as our biselectrophile surrogate are rather manifold. As an excess of unreacted first aldehyde would unavoidably lead to the formation of the undesired symmetrical diketone, its full consumption during the nitro-Stetter catalysis needs to be guaranteed. Moreover, due to the lability of the intermediate Michael acceptor **11** (*vide supra*), $HNO_2$ elimination needs to be suppressed until the addition of the second aldehyde.

**Table 3. Optimization of reaction conditions.**[a]



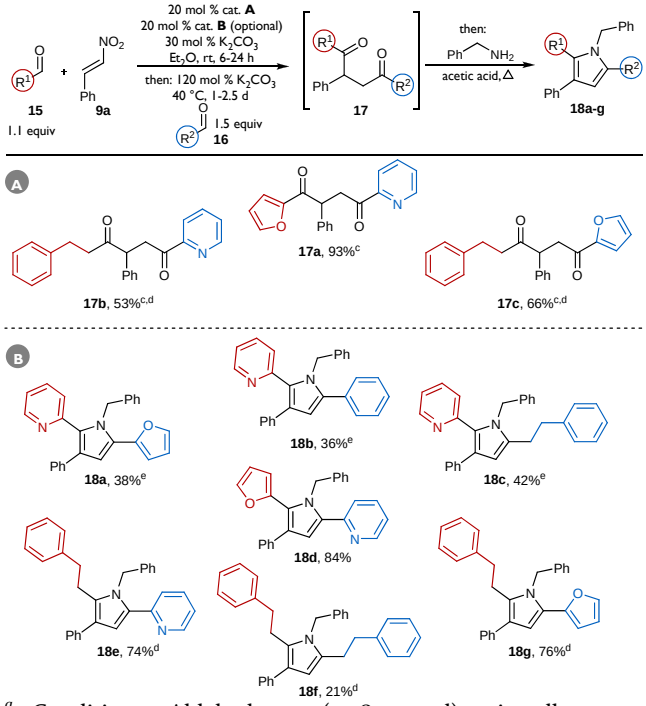

| Entry | $K_2CO_3$ loading [mol %] | Aldehyde loading [equiv] | Catalyst loading [mol %] | Yield[b] **10** in % | Yield[b] **11** in % | Yield[b] **12** in % |
|---|---|---|---|---|---|---|
| 1 | 40 | 1.5 | 10 | 61 | 7 | 30 |
| 2 | 30 | 1.5 | 10 | 68 | 1 | 30 |
| 3 | 30 | 1.1 | 10 | 68 | 12 | traces |
| 4 | 30 | 1.1 | 20 | 74 | 17 | 8 |

[a] Conditions: Aldehyde **8** (x equiv), nitroalkene **9a** (0.25 mmol), cat. **A** (x mol %), $K_2CO_3$ (x mol %), $Et_2O$ (2 mL) for 14 h at rt. [b] Yield determined by $^1$H NMR spectroscopy using dibromomethane (1 equiv) as internal standard.

Table 3 shows the further optimization of step 1 and illustrates the influence of base on the observed product distribution (entries 1-3). We began this screening with conditions similar to entry 5 of our first screening (Table 1, entry 5), but now stopped the reaction before heating and addition of the second aldehyde amount. Lowering the aldehyde amount (entry 3) together with increased catalyst loading to ensure full conversion (entry 4) nicely favoured formation of the targeted nitro-Stetter product **10**. Finally, upon sequential addition of the second aldehyde altered reaction conditions (base, temperature) are required to then promote the eliminative formation of Michael acceptor **11** thus avoiding further (NHC-catalyzed) side reactions.

With these further optimized conditions in hand we finally examined the generality of our approach to both synthesize unsymmetrically substituted 1,4-diketones **17** and to carry out their straightforward conversion into the corresponding pyrroles **18a-g**. Scheme 4 shows representative examples for each new class of substituents. As illustrated in part A, formation of 1,4-diketones is achieved with good efficiency, albeit partly with lower yields as for the corresponding pyrrole products further highlighting the benefits of our cascade approach.

**Scheme 4. Unsymmetric polysubstituted pyrroles – Scope of different aldehydes.**[a,b]




[a] Conditions: Aldehyde **15** (0.28 mmol), nitroalkene **9a** (0.25 mmol), cat. **A** (20 mol %), thiourea cat. **B** (20 mol %), $K_2CO_3$ (30 mol %), $Et_2O$ (2 mL) for 6-24 h at rt, then aldehyde **16** (0.38 mmol) and $K_2CO_3$ (120 mol %) for 1-2.5 d at 40 °C (diketone formation, part A), then benzylamine (1.4 mmol) and acetic acid (0.75 mmol) for 16 h at 50 °C (pyrroles, part B). [b] Yield of isolated product. [c] For diketones (part A): the reaction was stopped before the addition of the amine and acetic acid. [d] 1.5 equiv of aldehyde **15** and different amounts of $K_2CO_3$ (40 mol % + 110 mol %) were added. [e] No thiourea cat. **B** was required; toluene was used as solvent and the final step was performed with benzylamine (0.75 mmol) and acetic acid (2 mL) for 2.5 d at 100 °C (70 °C for **18c**).

Starting with 2-pyridine carboxaldehyde as the initial aldehyde heteroaromatic, aromatic and aliphatic aldehydes were competent reaction partners providing the corresponding pyrrole products **18a-c** with overall yields of around 40% (approx. 80% for each step) and offering convenient access to hetaryl substituted triarylpyrrolo motifs. Longer reaction times for the second Stetter reaction (2.5 days instead of overnight reaction, see Table 2) paired with the fast decomposing 2-pyridyl substituted Michael acceptor **11** may contribute to the partly observed lower yields. To further broaden the scope to allow the implementation of other starting aldehydes of lower reactivity, we built on the initially proposed concurrent activation of nitroalkene **9a** with thiourea **B** as H-bonding catalyst. This synergistic catalytic strategy allowed us to employ other heteroaromatic aldehydes like furfural with a very good yield (84%; **18d**). Moreover, we were able to expand the scope to aliphatic aldehydes with high yields (74-76%; **18e**, **18g**). The here obtained higher yields as compared to the corresponding 1,4-diketones **17b** and **17c** (*vide supra*) exemplify the advantage of the cascade procedure. Side reactions, e. g. caused by the aliphatic aldehydes′ α-acidity or homobenzoin formation, can lead to tricky separation problems at the diketone stage. Notably, despite these challenges even pyrrole **18f**, bearing two aliphatic substituents, could be synthesized, albeit with a lower overall yield of 21%; however, still highly useful with respect to the operational simplicity of the method and the readily available starting materials.

Given the generality of this approach and the possibility to easily integrate heterocyclic arenes, which are common scaffolds in targets relevant to medicine and material sciences, we expect this protocol to be useful for a wide range of complex molecules.

## CONCLUSION

In summary, we have developed a highly convergent access to symmetrical and unsymmetrical 1,4-diketones using nitrostyrenes as simple latent 1,2-biselectrophilic building blocks in combination with commercially available aldehydes as acylanion precursors *via* NHC catalysis. Our multicatalytic metal-free, 4-step one–pot Nitro-Stetter/elimination/Stetter/Paal-Knorr reaction sequence provides access to polysubstituted pyrroles, including up-to-date difficult to synthesize heteroaryl substituted scaffolds, under mild conditions.

## EXPERIMENTAL SECTION

**General Information.** Unless otherwise noted, all commercially available compounds were used as provided without further purification. NMR spectra were recorded on a Bruker Avance 300 (300.13 MHz), Varian MERCURY plus (300.08 MHz), Bruker Avance III 400 (400.13 MHz) and Varian MERCURY plus (399.95 MHz) using the solvent peak as internal reference ($CDCl_3$: δ H 7.26; δ C 77.16). Multiplicities are indicated, s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sept (septet), m (multiplet); coupling constants (*J*) are given in Hertz (Hz). High resolution mass was recorded on an Agilent Q-TOF 6540 UHD, Finnigan MAT95 or Bruker APEX II. All reactions were monitored by thin-layer chromatography; visualization was accomplished with UV light and/or appropriate stains ($KMnO_4$, anisaldehyde or vanillin). Standard flash chromatography procedures ($SiO_2$, size 40–63 μm) were followed. All reactions were carried out under a protective atmosphere of dry nitrogen using oven-dried glassware unless otherwise stated. Solvents for the catalytic reactions were purchased at absolute quality. Solvents for chromatography (acetone, $Et_2O$, DCM, EtOAc, hexanes) were technical grade and distilled prior to use. $K_2CO_3$, in the text referred as "predried", was finely ground in a mortar and then heated for at least 20 minutes at 650 °C at high vacuum. All aldehydes are commercially available and were distilled under reduced pressure prior to use. All nitroalkenes are commercially available, however nitroalkenes **9e-h**,**k**,**m**,[37] **9i**,**j**[38] and **9l**[39] were prepared according to published protocols. Triazolium salt **A** is commercially available. Thiourea **B** was synthesized according to a known procedure described by Wang.[40]

**Experimental Details.**

***General Procedure A:*** *Screening Experiments for Optimized Conditions***.** An oven-dried screw-capped schlenk tube equipped with a magnetic stir bar was heated up to 650 °C (using a heat gun). After cooling to room temperature 38.4 mg nitroalkene **9a** (0.250 mmol, 1.00 equiv), a base and 9.07 mg catalyst **A** (0.0250 mmol, 0.100 equiv) were added under a nitrogen atmosphere. The tube was then evacuated and purged four times with nitrogen and dissolved in 2 mL solvent (0.125 m). 40.2 mg 2-pyridine carbaldehyde **8** (0.380 mmol, 1.50 equiv) was added; the reaction mixture was stirred at room temperature for 14 h. Then a second amount of 26.8 mg 2-pyridine carbaldehyde **8** (0.250 mmol, 1.00 equiv) was added to the mixture which was heated then to 50 °C for 7 h. The yield was determined by NMR using dibromomethane as internal standard.

***General Procedure B:*** *Preparation of 2,5-Dipyridyl Substituted Pyrroles.* An oven-dried screw-capped schlenk tube equipped with a magnetic stir bar was heated up to 650 °C (using a heat gun). After cooling to room temperature a nitroalkene (0.250 mmol, 1.00 equiv), 34.6 mg "predried" $K_2CO_3$ (0.250 mmol, 1.00 equiv) and 9.07 mg catalyst **A** (0.0250 mmol, 0.100 equiv) were added under a nitrogen atmosphere. The tube was then evacuated and purged four times with nitrogen and dissolved in 2 mL $Et_2O$ (0.125 m). 40.2 mg 2-pyridine carbaldehyde **8** (0.380 mmol, 1.50 equiv) was added followed by four freeze-pump-thaw cycles. The reaction mixture was stirred at room temperature overnight. Then a second amount of 26.8 mg 2-pyridine carbaldehyde **8** (0.250 mmol, 1.00 equiv) was added to the mixture and was heated to 50 °C for 8 hours. Upon complete consumption an amine (0.750 mmol, 3.00 equiv) and 2 mL acetic acid were added successively and heated for 1.5 days at 70 °C. The crude reaction mixture was

transferred to a separating funnel and 15 mL of a 3 m NaOH solution was added. The aqueous layer was extracted four times with DCM (10 mL). The organic layers were combined and dried over anhydrous $NaSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography to obtain the corresponding pyrrole.

***General Procedure C:*** *Preparation of Unsymmetrical 1,4-Diketones.* An oven-dried screw-capped schlenk tube equipped with a magnetic stir bar was heated up to 650 °C (using a heat gun). After cooling to room temperature nitroalkene **9a**, "predried" $K_2CO_3$, thiourea derivative **B** and catalyst **A** were added under a nitrogen atmosphere. The tube was then evacuated and purged four times with nitrogen and dissolved in 2 mL $Et_2O$ followed by the addition of the first aldehyde and a sequence of four freeze-pump-thaw cycles. The reaction mixture was stirred at room temperature until complete conversion of the nitroalkene **9a** (6 h to 1 d, TLC control). For consecutive elimination-Stetter reaction sequence a second amount of "predried" $K_2CO_3$ and the second aldehyde were added to the mixture. The resulting mixture was heated to 40 °C until complete formation of the respective Stetter product (1 d, TLC control). The crude products were purified by column chromatography to obtain the 1,4-diketones.

***General Procedure D:*** *Preparation of Unsymmetrical 2,5-Substituted Pyrroles.* An oven-dried screw-capped schlenk tube equipped with a magnetic stir bar was heated up to 650 °C (using a heat gun). After cooling to room temperature nitroalkene **9a**, "predried" $K_2CO_3$ and catalyst **A** were added under a nitrogen atmosphere. Furthermore, if the first aldehyde is not 2-pyridine carbaldehyde, the thiourea derivative **B** was added as cocatalyst. The tube was then evacuated and purged four times with nitrogen and dissolved in 2 mL $Et_2O$ or toluene (0.125 m), followed by the addition of the first aldehyde and a sequence of four freeze-pump-thaw cycles. The reaction mixture was stirred at room temperature until complete conversion of the nitroalkene **9a** (6 h to 1 d, TLC control). For consecutive elimination-Stetter reaction sequence a second amount of "predried" $K_2CO_3$ and the second aldehyde were added to the mixture. The resulting mixture was heated to 40 °C until complete formation of the respective Stetter product (1 d to 2.5 d, TLC control). To generate the corresponding pyrroles benzylamine and acetic acid were added successively and heated until completion (16 h to 2.5 d, TLC control). The crude reaction mixture was either directly purified by column chromatography or transferred in a separating funnel followed by adding 15 mL of a 3 M NaOH solution. The aqueous layer was extracted four times with DCM (10 mL). The combined organic layers were dried over anhydrous $NaSO_4$, filtered, and concentrated under reduced pressure. The crude products were purified by column chromatography to obtain the corresponding pyrroles.

*3-Nitro-2-phenyl-1-(pyridin-2-yl)propan-1-one (**10**).* For the synthesis of nitro-Stetter product **10** an oven-dried screw-capped schlenk tube equipped with a magnetic stir bar was heated up to 650 °C (using a heat gun). After cooling to room temperature 38.4 mg nitroalkene **9a** (0.250 mmol, 1.0 equiv), 8.20 mg sodium acetate (0.100 mmol, 0.40 equiv) and 9.07 mg catalyst **A** (0.0250 mmol, 0.10 equiv) were added under a nitrogen atmosphere. The tube was then evacuated and purged four times with nitrogen and dissolved in 2 mL *tert*-amyl alcohol (0.125 M). Then 40.2 mg 2-pyridine carbaldehyde **8** (0.375 mmol, 1.5 equiv) was added. The resulting reaction mixture was stirred at room temperature for 20 h. The crude product was purified by column chromatography. Yield after column chromatography (flash gel (2-25 µm); hexanes/ethyl acetate 33/1 to 4/1): 21.5 mg (0.0840 mmol, 34%), colorless oil. $R_f$ (hexanes/ethyl acetate 4:1): 0.49. $^1$H NMR (400 MHz, $CDCl_3$): 8.70 (d, *J* = 4.9 Hz, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.82 (td, *J* = 7.7, 1.7 Hz, 1H), 7.49 – 7.39 (m, 3H), 7.36 – 7.24 (m, 3H), 6.26 (dd, *J* = 10.2, 5.0 Hz, 1H), 5.38 (dd, *J* = 14.6, 10.2 Hz, 1H), 4.72 (dd, *J* = 14.6, 5.0 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): 197.1, 151.6, 149.2, 137.2, 133.5, 129.3 (2C), 129.1 (2C), 128.4, 127.7, 123.2, 75.9, 48.6. HRMS (ESI): Exact mass calculated for $C_{14}H_{12}N_2NaO_3$ ($[M+Na]^+$): 279.0740, mass found: 279.0738.

*2-Phenyl-1-(pyridin-2-yl)prop-2-en-1-one (**11**).* For the synthesis of elimination product **11** an oven-dried screw-capped schlenk tube equipped with a magnetic stir bar was heated up to 650 °C (using a heat gun). After cooling to room temperature 38.4 mg nitroalkene **9a** (0.250 mmol, 1.0 equiv), 34.6 mg "predried" $K_2CO_3$ (0.250 mmol, 1.0 equiv) and 9.07 mg catalyst **A** (0.0250 mmol, 0.10 equiv) were added under a nitrogen atmosphere. The tube was then evacuated and purged four times with nitrogen and dissolved in 2 mL $Et_2O$ (0.125 M). 28.1 mg 2-pyridine carbaldehyde **8** (0.260 mmol, 1.05 equiv) was added followed by a sequence of four freeze-pump-thaw cycles. The reaction mixture was stirred for one day at room temperature. The crude product was purified by column chromatography. Yield after column chromatography (flash gel; hexanes/ethylacetate 4/1): 20.0 mg (0.0980 mmol, 38%), colorless oil. $R_f$ (hexanes/ethyl acetate 4:1): 0.37. $^1$H NMR (400 MHz, $CDCl_3$): 8.65 (d, *J* = 4.8 Hz, 1H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.84 (td, *J* = 7.7, 1.7 Hz, 1H), 7.45 – 7.38 (m, 3H), 7.37 – 7.29 (m, 3H), 6.19 (s, 1H), 5.95 (s, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): 196.2, 154.9, 149.2, 147.8, 137.4, 137.1, 128.5 (2C), 128.3, 127.6 (2C), 126.5, 124.9, 124.3. HRMS (ESI): Exact mass calculated for $C_{14}H_{12}NO$ ($[M+H]^+$): 210.0913, mass found: 210.0914.

*2-Phenyl-1,4-di(pyridin-2-yl)butane-1,4-dione (**12**).* 1,4-Diketone **12** was prepared according to **general procedure A** using 34.6 mg "predried" $K_2CO_3$ (0.250 mmol, 1.00 equiv) and $Et_2O$ as a solvent. The crude product was purified by column chromatography. Yield after column chromatography (flash gel; hexanes/ethyl acetate 2/1): 71.4 mg (0.230 mmol, 90%), yellowish oil. $R_f$ (hexanes/ethyl acetate 4:1): 0.26. $^1$H NMR (400 MHz, $CDCl_3$): 8.74 (d, *J* = 4.9 Hz, 1H), 8.69 (d, *J* = 4.9 Hz, 1H), 8.06 (d, *J* = 7.9 Hz, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.83 – 7.74 (m, 2H), 7.55 – 7.49 (m, 2H), 7.49 – 7.44 (m, 1H), 7.43 – 7.38 (m, 1H), 7.32 – 7.25 (m, 2H), 7.23 – 7.16 (m, 1H), 6.07

(dd, *J* = 11.2, 3.6 Hz, 1H), 4.46 (dd, *J* = 19.1, 11.1 Hz, 1H), 3.80 (dd, *J* = 19.1, 3.6 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$): 200.3, 200.0, 153.1, 152.8, 149.1, 149.0, 138.3, 136.9, 136.9, 129.1 (2C), 128.7 (2C), 127.3, 127.1, 127.0, 122.9, 121.9, 46.0, 42.9. HRMS (ESI): Exact mass calculated for $C_{20}H_{17}N_2O_2$ ($[M+H]^+$): 317.1285, mass found: 317.1281.

*2,2′-(1-Benzyl-3-phenyl-1H-pyrrole-2,5-diyl)dipyridine (**14a**).* Pyrrole **14a** was prepared according to **general procedure B** using 37.3 mg nitroalkene **9a** and 80.0 mg benzylamine. Yield after column chromatography (flash gel; first DCM, then hexanes/acetone 30/1 to 20/1): 94.3 mg (0.243 mmol, 97%), colorless solid. mp: 161–162 °C. $R_f$ (hexanes/acetone 4:1): 0.24. $^1$H NMR (300 MHz, $CDCl_3$): 8.71 (d, *J* = 4.8 Hz, 1H), 8.58 (d, *J* = 4.8 Hz, 1H), 7.69 – 7.53 (m, 2H), 7.39 (td, *J* = 7.8, 1.8 Hz, 1H), 7.25 – 6.94 (m, 11H), 6.81 (s, 1H), 6.74 – 6.67 (m, 2H), 6.02 (s, 2H). $^{13}$C NMR (75.5 MHz, $CDCl_3$): 152.5, 152.3, 149.5, 148.9, 139.7, 136.5, 136.1, 136.1, 134.3, 132.9, 128.5 (2C), 128.3 (2C), 128.0 (2C), 127.2, 126.5, 126.5 (2C), 125.9, 125.8, 122.7, 121.9, 121.1, 112.2, 48.9. HRMS (ESI): Exact mass calculated for $C_{27}H_{21}N_3Na$ ($[M+Na]^+$): 410.1628, mass found: 410.1631.

*2,2′-(1-Phenethyl-3-phenyl-1H-pyrrole-2,5-diyl)dipyridine (**14b**).* Pyrrole **14b** was prepared according to **general procedure B** using 37.3 mg nitroalkene **9a** and 90.9 mg phenethylamine. Yield after column chromatography (flash gel; hexanes/ethyl acetate 33/1 to 2.5/1): 94.7 mg (0.237 mmol, 95%), colorless oil. $R_f$ (hexanes/ethyl acetate 4:1): 0.26. $^1$H NMR (400 MHz, $CDCl_3$): 8.84 (dd, *J* = 4.8 Hz, 1H), 8.73 (d, *J* = 4.8 Hz, 1H), 7.72 (td, *J* = 7.7, 1.9 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.54 (td, *J* = 7.7, 1.9 Hz, 1H), 7.30 – 7.14 (m, 10H), 7.09 (d, *J* = 7.8 Hz, 1H), 7.03 – 6.96 (m, 2H), 6.82 (d, *J* = 2.0 Hz, 1H), 4.95 – 4.83 (m, 2H), 3.08 – 2.96 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$): 152.7, 152.5, 149.5, 148.8, 139.4, 136.4, 136.3, 136.1, 133.2, 132.3, 128.8 (2C), 128.5 (2C), 128.29 (2C), 128.28 (2C), 127.2, 126.1, 125.8, 125.1, 122.5, 121.9, 120.9, 111.6, 47.4, 38.1. HRMS (ESI): Exact mass calculated for $C_{28}H_{24}N_3$ ($[M+H]^+$): 402.1964, mass found: 402.1960.

*2,2′-(1-(4-Methoxyphenyl)-3-phenyl-1H-pyrrole-2,5-diyl)dipyridine (**14c**).* Pyrrole **14c** was prepared according to **general procedure B** using 37.3 mg nitroalkene **9a** and 92.4 mg 4-methoxyanillin. Yield after column chromatography (flash gel; first DCM, then hexanes/acetone 30/1 to 7/1): 95.9 mg (0.238 mmol, 95%), colorless oil. $R_f$ (hexanes/acetone 4:1): 0.21. $^1$H NMR (400 MHz, $CDCl_3$): 8.52 (t, *J* = 4.4 Hz, 2H), 7.47 – 7.38 (m, 2H), 7.32 – 7.27 (m, 2H), 7.25 – 7.17 (m, 2H), 7.17 – 7.08 (m, 4H), 7.08 – 7.00 (m, 3H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.75 – 6.67 (m, 2H), 3.74 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): 158.6, 152.2, 151.2, 149.3, 149.1, 136.1, 135.77, 135.7, 134.6, 133.8, 132.2, 130.1 (2C), 128.4 (2C), 128.2 (2C), 127.1, 125.9, 125.5, 122.4, 121.9, 120.9, 113.6 (2C), 112.6, 55.4. HRMS (ESI): Exact mass calculated for $C_{27}H_{22}N_3O$ ($[M+H]^+$): 404.1757, mass found: 404.1754.

*2,2′-(3-Phenyl-1H-pyrrole-2,5-diyl)dipyridine (**14d**).* Pyrrole **14d** was prepared according to **general procedure B** using 37.3 mg nitroalkene **9a** and 57.8 mg ammonium acetate. Yield after column chromatography (flash gel; hexanes/ethyl acetate 99/1 to 5/1): 72.6 mg (0.244 mmol, 98%), colorless oil. $R_f$ (hexanes/ethyl acetate 4:1): 0.26. $^1$H NMR (400 MHz, $CDCl_3$): 10.66 (bs, 1H), 8.56 – 8.51 (m, 2H), 7.65 – 7.58 (m, 1H), 7.58 – 7.53 (m, 1H), 7.52 – 7.46 (m, 2H), 7.43 – 7.30 (m, 4H), 7.27 – 7.23 (m, 1H), 7.08 – 6.98 (m, 2H), 6.75 (s, 1H).$^{13}$C NMR (101 MHz, $CDCl_3$): 150.5, 150.0, 149.3 (2C), 137.1, 136.5, 136.0, 132.0, 129.4 (2C), 128.7 (3C), 126.9, 126.6, 121.1, 121.0, 120.2, 118.6, 111.0. HRMS (ESI): Exact mass calculated for $C_{20}H_{16}N_3$ ($[M+H]^+$): 298.1339, mass found: 298.1334.

*2,2′-(1-Benzyl-3-(4-methoxyphenyl)-1H-pyrrole-2,5-diyl) dipyridine (**14e**).* Pyrrole **14e** was prepared according to **general procedure B** using 44.8 mg nitroalkene **9e** and 80.0 mg benzylamine. Yield after column chromatography (flash gel; first DCM, then hexanes/acetone 25/1 to 20/1): 98.0 mg (0.240 mmol, 94%), yellowish solid. mp: 141–143 °C. $R_f$ (hexanes/acetone 4:1): 0.24. $^1$H NMR (300 MHz, $CDCl_3$): 8.70 (d, *J* = 4.9 Hz, 1H), 8.57 (d, *J* = 4.9, 1H), 7.66 – 7.53 (m, 2H), 7.39 (td, *J* = 7.7, 1.9 Hz, 1H), 7.17 – 6.94 (m, 8H), 6.80 – 6.73 (m, 3H), 6.72 – 6.65 (m, 2H), 6.00 (s, 2H), 3.77 (s, 3H). $^{13}$C NMR (75.5 MHz, $CDCl_3$): 158.0, 152.6, 152.5, 149.5, 149.0, 139.9, 136.4, 136.0, 134.3, 132.6, 129.6 (2C), 128.8, 128.0 (2C), 127.1, 126.5 (2C), 126.5, 125.4, 122.6, 121.8, 121.0, 113.8 (2C), 112.1, 55.3, 48.8. HRMS (ESI): Exact mass calculated for $C_{28}H_{24}N_3O$ ($[M+H]^+$): 418.1914, mass found: 418.1914.

*2,2′-(1-Benzyl-3-(4-bromophenyl)-1H-pyrrole-2,5-diyl) dipyridine (**14f**).* Pyrrole **14f** was prepared according to **general procedure B** using 57.0 mg nitroalkene **9f** and 80.0 mg benzylamine. Yield after column chromatography (flash gel; first DCM, then hexanes/acetone 30/1 to 20/1): 89.8 mg (0.190 mmol, 77%), yellowish solid. mp: 160–162 °C. $R_f$ (hexanes/acetone 4:1): 0.39. $^1$H NMR (300 MHz, $CDCl_3$): 8.71 (d, *J* = 4.9, 1H), 8.58 (d, *J* = 4.9, 1H), 7.69 – 7.52 (m, 2H), 7.42 (td, *J* = 7.7, 1.9 Hz, 1H), 7.35 – 7.27 (m, 2H), 7.18 – 6.93 (m, 8H), 6.76 (s, 1H), 6.72 – 6.64 (m, 2H), 5.98 (s, 2H). $^{13}$C NMR (75.5 MHz, $CDCl_3$): 152.4, 152.1, 149.7, 149.0, 139.6, 136.5, 136.2, 135.2, 134.5, 133.1, 131.4 (2C), 130.0 (2C), 128.1 (2C), 127.1, 126.6, 126.5 (2C), 124.4, 122.7, 122.1, 121.2, 119.7, 111.8, 48.9. HRMS (ESI): Exact mass calculated for $C_{27}H_{21}BrN_3$ ($[M+H]^+$): 466.0914, mass found: 466.0913.

*2,2′-(1-Benzyl-3-(3-bromophenyl)-1H-pyrrole-2,5-diyl) dipyridine (**14g**).* Pyrrole **14g** was prepared according to **general procedure B** using 57.0 mg nitroalkene **9g** and 80.0 mg benzylamine. Yield after column chromatography (flash gel; first DCM, then hexanes/acetone 30/1 to 20/1): 89.8 mg (0.23 mmol, 92%), brownish solid. mp: 96–97 °C. $R_f$ (hexanes/acetone 4:1): 0.40. $^1$H NMR (400 MHz, $CDCl_3$): 8.74 (m, 1H), 8.60 (m, 1H), 7.70 – 7.54 (m, 2H), 7.53 – 7.40 (m, 2H), 7.35 – 7.22 (m, 1H), 7.17 (m, 1H), 7.06 (m, 7H), 6.85 – 6.78 (m, 1H), 6.73 (m, 2H), 6.02 (s, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$): 152.3, 151.8, 149.7, 149.0, 139.5, 138.3, 136.5, 136.1, 134.4, 133.2, 131.1, 129.7, 128.7, 128.0 (2C), 127.0, 126.9, 126.5, 126.4 (2C), 123.9, 122.6, 122.4, 122.2, 121.2, 111.7, 48.8. HRMS (ESI): Exact mass calculated for $C_{27}H_{21}BrN_3$ ($[M+H]^+$): 466.0914, mass found: 466.0913.

*2-(1-Benzyl-2,5-di(pyridin-2-yl)-1H-pyrrol-3-yl)benzonitrile (**14h**).* Pyrrole **14h** was initially prepared according to **general**

**procedure B** using 43.5 mg nitroalkene **9h**. However, milder conditions were used for the Paal-Knorr reaction by adding first 147 mg benzylamine (1.4 mmol, 5.5 equiv) then 45.0 mg acetic acid (0.75 mmol, 3.0 equiv) and heating the reaction overnight at 50 °C. Yield after column chromatography (hexanes/ethyl acetate 2/1): 60.3 mg (0.17 mmol, 59%), yellowish oil. $R_f$ (hexanes/ethyl acetate 2:1): 0.26. $^1$H NMR (300 MHz, $CDCl_3$): 8.72 (d, *J* = 4.9 Hz, 1H), 8.58 (d, *J* = 4.9 Hz, 1H), 7.69 – 7.62 (m, 1H), 7.56 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.52 – 7.43 (m, 2H), 7.42 – 7.36 (m, 2H), 7.29 – 7.22 (m, 1H), 7.22 – 7.16 (m, 1H), 7.15 – 7.09 (m, 1H), 7.05 – 6.95 (m, 4H), 6.80 (s, 1H), 6.72 – 6.65 (m, 2H), 5.94 (s, 2H). $^{13}$C NMR (101 MHz, CDCl3): 151.9, 151.4, 149.9, 148.8, 139.2, 137.4, 136.8, 136.4, 134.4, 133.5, 132.6, 131.6, 129.3, 129.1, 128.1 (2C), 126.9, 126.7, 126.4 (2C), 123.2, 122.8, 122.6, 121.4, 119.1, 112.4, 111.7, 49.0. HRMS (ESI): Exact mass calculated for $C_{28}H_{21}N_4$ ([M+H]$^+$): 413.1760, mass found: 413.1750.

*2,2′-(1-Benzyl-3-(2-fluorophenyl)-1H-pyrrole-2,5-diyl) dipyridine (**14i**).* Pyrrole **14i** was prepared according to **general procedure B** using 41.8 mg nitroalkene **9i** and 80.0 mg benzylamine. Yield after column chromatography (flash gel; first DCM, then hexanes/acetone 30/1 to 20/1): 75.3 mg (0.19 mmol, 74%), brownish solid. mp: 140–141 °C. $R_f$ (hexanes/acetone 4:1): 0.33. $^1$H NMR (300 MHz, $CDCl_3$): 8.68 (d, *J* = 4.9 Hz, 1H), 8.58 (d, *J* = 4.9 Hz, 1H), 7.67 – 7.54 (m, 2H), 7.42 – 7.34 (m, 1H), 7.19 – 7.05 (m, 4H), 7.05 – 6.92 (m, 6H), 6.83 (d, *J* = 1.8 Hz, 1H), 6.75 – 6.67 (m, 2H), 6.11 (s, 2H). $^{13}$C NMR (75.5 MHz, $CDCl_3$): 160.0 (d, $^1J_{CF}$ = 245 Hz), 152.6, 152.3, 149.5, 149.0, 139.8, 136.4, 136.0, 134.3, 134.2 (d, $^2J_{CF}$ = 14 Hz), 131.8 (d, $^3J_{CF}$ = 4 Hz), 128.0 (2C), 127.8 (d, $^3J_{CF}$ = 8 Hz), 126.50 (2C), 126.47, 126.2, 124.0 (d, $^3J_{CF}$ = 14 Hz), 123.8 (d, $^4J_{CF}$ = 4 Hz), 122.7, 121.8, 121.0, 119.1, 115.8 (d, $^2J_{CF}$ = 22 Hz), 113.3 (d, $^4J_{CF}$ = 3 Hz), 48.9. $^{19}$F NMR (377 MHz, $CDCl_3$): -114.8. HRMS (ESI): Exact mass calculated for $C_{27}H_{21}FN_3$ ([M+H]$^+$): 406.1714, mass found: 406.1709.

*2,2′-(1-Benzyl-3-o-tolyl-1H-pyrrole-2,5-diyl)dipyridine (**14j**).* Pyrrole **14j** was prepared according to **general procedure B** using 40.8 mg nitroalkene **9j** and 80.0 mg benzylamine. Yield after column chromatography (flash gel; first DCM, then hexanes/acetone 30/1 to 20/1): 44.2 mg (0.11 mmol, 44%), colorless solid. mp: 153–155 °C. $R_f$ (hexanes/acetone 4:1): 0.45. $^1$H NMR (300 MHz, $CDCl_3$): 8.67 – 8.56 (m, 2H), 7.66 – 7.52 (m, 2H), 7.31 – 7.18 (m, 2H), 7.17 – 7.06 (m, 4H), 7.06 – 6.97 (m, 4H), 6.76 – 6.68 (m, 3H), 6.67 – 6.63 (m, 1H), 6.19 (s, 2H), 2.08 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): 152.4, 152.1, 149.0, 148.9, 140.2, 136.9, 136.5, 136.3, 136.0, 134.6, 133.5, 131.2, 130.1, 128.0 (2C), 126.8, 126.4, 126.3 (2C), 126.0, 125.8, 125.6, 122.8, 121.2, 121.1, 113.7, 49.1, 20.5. HRMS (ESI): Exact mass calculated for $C_{28}H_{24}N_3$ ([M+H]$^+$): 402.1965, mass found: 402.1965.

*2,2′-(3-(Furan-2-yl)-1H-pyrrole-2,5-diyl)dipyridine (**14m**).* Pyrrole **14m** was prepared according to **general procedure B** using 34.8 mg nitroalkene **9m** and 57.8 mg ammonium acetate. Yield after column chromatography (flash gel; hexanes/ethyl acetate 99/1 to 2/1): 50.1 mg (0.174 mmol, 70%), colorless oil. $R_f$ (hexanes/ethyl acetate 4:1): 0.29. $^1$H NMR (300 MHz, $CDCl_3$): 10.68 (s, 1H), 8.62 – 8.49 (m, 2H), 7.75 – 7.46 (m, 5H), 7.17 – 6.94 (m, 2H), 6.88 (d, *J* = 2.7 Hz, 1H), 6.51 (d, *J* = 1.3 Hz, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$): 150.3, 150.0, 149.8, 149.32, 149.25, 141.2, 136.5, 136.3, 132.2, 129.6, 121.4, 121.3, 120.5, 118.6, 115.3, 111.4, 109.8, 107.2. HRMS (ESI): Exact mass calculated for $C_{18}H_{14}N_3O$ ([M+H]$^+$): 288.1131, mass found: 288.1128.

*1-(Furan-2-yl)-2-phenyl-4-(pyridin-2-yl)butane-1,4-dione (**17a**).* 1,4-Diketone **17a** was prepared according to **general procedure C** using 37.3 mg nitroalkene **9a** (0.250 mmol, 1.0 equiv), 10.4 mg $K_2CO_3$ (0.0750 mmol, 0.30 equiv), thiourea **B** (0.0500 mmol, 0.20 equiv), 18.1 mg catalyst **A** (0.0500 mmol, 0.20 equiv) and 17.2 mg 26.4 mg furfural (0.280 mmol, 1.1 equiv). For the elimination-Stetter reaction sequence 41.5 mg $K_2CO_3$ (0.300 mmol, 1.2 equiv) and 40.3 mg 2-pyridine carbaldehyde (0.38 mmol, 1.5 equiv) were used. Yield after column chromatography (flash gel; hexanes/EtOAc 33/1 to 3/1): 70.5 mg (0.231 mmol, 93%), colorless oil. $R_f$ (hexanes/EtOAc 4/1): 0.19. $^1$H NMR (400 MHz, $CDCl_3$): 8.66 (d, *J* = 4.8 Hz, 1H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.79 (td, *J* = 7.7, 1.8 Hz, 1H), 7.56 – 7.52 (m, 1H), 7.48 – 7.38 (m, 3H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.25 – 7.19 (m, 2H), 6.49 – 6.44 (m, 1H), 5.07 (dd, *J* = 10.5, 3.8 Hz, 1H), 4.39 (dd, *J* = 19.1, 10.5 Hz, 1H), 3.62 (dd, *J* = 19.1, 3.8 Hz, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): 199.7, 187.9, 153.0, 152.4, 149.1, 146.5, 138.4, 136.9, 129.0 (2C), 128.5 (2C), 127.43, 127.39, 121.9, 118.1, 112.3, 48.9, 42.3. HRMS (ESI): Exact mass calculated for $C_{19}H_{16}NO_3$ ([M+H]$^+$): 306.1124, mass found: 306.1117.

*3,6-Diphenyl-1-(pyridin-2-yl)hexane-1,4-dione (**17b**).* 1,4-Diketone **17b** was prepared according to **general procedure C** using 37.3 mg nitroalkene **9a** (0.25 mmol, 1.0 equiv), 13.8 mg $K_2CO_3$ (0.100 mmol, 0.40 equiv), 17.2 mg thiourea **B** (0.0500 mmol, 0.20 equiv), 18.1 mg catalyst **A** (0.0500 mmol, 0.20 equiv) and 50.3 mg 3-phenylpropionaldehyde (0.380 mmol, 1.5 equiv). For the elimination-stetter reaction sequence 38.0 mg $K_2CO_3$ (0.280 mmol, 1.1 equiv) and 40.3 mg 2-pyridine carbaldehyde (0.380 mmol, 1.5 equiv) were used. Yield after column chromatography (flash gel; hexanes/EtOAc 50/1 to 4/1): 45.3 mg (0.132 mmol, 53%), yellowish oil. $R_f$ (hexanes/ethyl acetate 4:1): 0.50. $^1$H NMR (400 MHz, $CDCl_3$): 8.67 (d, *J* = 4.7 Hz, 1H), 8.01 (d, *J* = 7.9 Hz, 1H), 7.82 (td, *J* = 7.7, 1.7 Hz, 1H), 7.50 – 7.42 (m, 1H), 7.34 – 7.19 (m, 7H), 7.19 – 7.14 (m, 1H), 7.12 – 7.06 (m, 2H), 4.44 – 4.25 (m, 2H), 3.42 (dd, *J* = 18.5, 3.3 Hz, 1H), 3.01 – 2.87 (m, 2H), 2.87 – 2.75 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$): 208.4, 200.0, 153.1, 149.1, 141.2, 138.0, 136.9, 129.1 (2C), 128.5 (2C), 128.4 (2C), 128.3 (2C), 127.6, 127.4, 126.0, 121.9, 53.7, 43.3, 41.7, 29.8. HRMS (ESI): Exact mass calculated for $C_{23}H_{22}NO_2$ ([M+H]$^+$): 344.1645, mass found: 344.1640.

*1-(Furan-2-yl)-3,6-diphenylhexane-1,4-dione (**17c**).* 1,4-Diketone **17c** was prepared according to **general procedure C** using 37.3 mg nitroalkene **9a** (0.250 mmol, 1.0 equiv), 13.8 mg $K_2CO_3$ (0.100 mmol, 0.40 equiv), 17.2 mg thiourea **B** (0.0500 mmol, 0.20 equiv), 18.1 mg catalyst **A** (0.0500 mmol, 0.20 equiv) and 50.3 mg 3-phenylpropionaldehyde (0.380 mmol, 1.5 equiv). For the elimination-Stetter reaction sequence 38.0 mg $K_2CO_3$ (0.275 mmol, 1.1 equiv) and 36.0 mg furfural (0.380 mmol, 1.5 equiv)

were used. Yield after column chromatography (flash gel; hexanes/EtOAc 33/1 to 3/1, hexanes/$Et_2O$ 33/1 to 2.5/1): 54.7 mg (0.165 mmol, 66%), yellowish oil. $R_f$ (hexanes/EtOAc 4/1): 0.47. $^1$H NMR (400 MHz, $CDCl_3$): 7.59 (d, *J* = 1.6 Hz, 1H), 7.40 – 7.14 (m, 9H), 7.14 – 7.07 (m, 2H), 6.55 (dd, *J* = 3.6, 1.7 Hz, 1H), 4.43 (dd, *J* = 10.1, 4.1 Hz, 1H), 3.92 (dd, *J* = 17.8, 10.0 Hz, 1H), 3.05 (dd, *J* = 17.8, 4.1 Hz, 1H), 3.00 – 2.74 (m, 4H). $^{13}$C NMR (101 MHz, $CDCl_3$): 208.2, 187.3, 152.4, 146.5, 141.0, 137.7, 129.2 (2C), 128.42 (2C), 128.41 (2C), 128.3 (2C), 127.7, 126.0, 117.3, 112.3, 53.0, 43.2, 41.7, 29.8. HRMS (ESI): Exact mass calculated for $C_{22}H_{20}NaO_3$ ([M+Na]$^+$): 355.1305, mass found: 355.1301.

*2-(1-Benzyl-5-(furan-2-yl)-3-phenyl-1H-pyrrol-2-yl)pyridine (**18a**).* Pyrrole **18a** was prepared according to **general procedure D** using 37.3 mg nitroalkene **9a** (0.250 mmol, 1.0 equiv), 10.4 mg $K_2CO_3$ (0.075 mmol, 0.3 equiv), 18.1 mg catalyst **A** (0.0500 mmol, 0.2 equiv), 29.5 mg 2-pyridine carbaldehyde (0.280 mmol, 1.1 equiv) and toluene as the solvent. For the elimination-Stetter reaction sequence 41.5 mg $K_2CO_3$ (0.300 mmol, 1.2 equiv) and 36.0 mg furfural (0.380 mmol, 1.5 equiv) were used. Initially 80.0 mg benzylamine (0.750 mmol, 3.0 equiv), then 2 mL acetic acid were added for the Paal-Knorr reaction. Moreover, the reaction vessel was heated at 100 °C. The crude reaction mixture was extracted as described in **general procedure D**. Yield after column chromatography (flash gel; DCM): 36.0 mg (0.0960 mmol, 38%), yellowish solid. mp: 135–136 °C. $R_f$ (DCM): 0.37. $^1$H NMR (400 MHz, $CDCl_3$): 8.68 (d, *J* = 5.0 Hz, 1H), 7.45 – 7.42 (m, 1H), 7.39 (td, *J* = 7.7, 1.8 Hz, 1H), 7.25– 7.19 (m, 4H), 7.18 – 7.06 (m, 5H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.79 (d, *J* = 7.9 Hz, 2H), 6.69 (s, 1H), 6.43– 6.36 (m, 1H), 6.31 (d, *J* = 3.3 Hz, 1H), 5.63 (s, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$): 151.9, 149.2, 147.1, 141.8, 138.9, 136.2, 136.0, 130.7, 128.5 (2C), 128.24 (2C), 128.22 (2C), 127.0, 126.8, 126.7, 126.1 (2C), 125.9, 125.8, 121.7, 111.2, 110.3, 107.4, 48.9. HRMS (ESI): Exact mass calculated for $C_{26}H_{21}N_2O$ ([M+H]$^+$): 377.1648, mass found: 377.1646.

*2-(1-Benzyl-3,5-diphenyl-1H-pyrrol-2-yl)pyridine (**18b**).* Pyrrole **18b** was prepared according to **general procedure D** using 37.3 mg nitroalkene **9a** (0.250 mmol, 1.0 equiv), 10.4 mg $K_2CO_3$ (0.0750 mmol, 0.30 equiv), 18.1 mg catalyst **A** (0.0500 mmol, 0.20 equiv), 29.5 mg 2-pyridine carbaldehyde (0.280 mmol, 1.1 equiv) and toluene as the solvent. For the elimination-Stetter reaction sequence 41.5 mg $K_2CO_3$ (0.300 mmol, 1.2 equiv) and 39.8 mg benzaldehyde (0.380 mmol, 1.5 equiv) were used. Initially 80.0 mg benzylamine (0.750 mmol, 3.0 equiv), then 2 mL acetic acid were added for the Paal-Knorr reaction. Moreover, the reaction vessel was heated at 100 °C. The crude reaction mixture was extracted as described in **general procedure D**. Yield after column chromatography (flash gel; DCM): 35.2 mg (0.091 mmol, 36%), yellowish solid. mp: 96–97 °C. $R_f$ (DCM): 0.39. $^1$H NMR (400 MHz, $CDCl_3$): 8.68 (d, *J* = 5.1 Hz, 1H), 7.51 – 7.46 (m, 2H), 7.41 – 7.30 (m, 4H), 7.25 – 7.19 (m, 4H), 7.18 – 7.13 (m, 1H), 7.10 – 7.05 (m, 1H), 7.04 – 6.99 (m, 3H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.62 – 6.54 (m, 2H), 6.47 (s, 1H), 5.52 (s, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$): 152.3, 149.0, 139.2, 137.8, 136.3 (2C), 133.3, 130.1, 129.6 (2C), 128.6 (4C), 128.3 (2C), 128.1 (2C), 127.6, 127.1, 126.7, 126.3, 126.2 (2C), 125.9, 121.5, 110.6, 48.7. HRMS (ESI): Exact mass calculated for $C_{28}H_{23}N_2$ ([M+H]$^+$): 387.1856, mass found: 387.1848.

*2-(1-Benzyl-5-phenethyl-3-phenyl-1H-pyrrol-2-yl)pyridine (**18c**).* Pyrrole **18c** was prepared according to **general procedure D** using 37.3 mg nitroalkene **9a** (0.250 mmol, 1.0 equiv), 10.4 mg $K_2CO_3$ (0.0750 mmol, 0.30 equiv), 18.1 mg catalyst **A** (0.0500 mmol, 0.20 equiv), 29.5 mg 2-pyridine carbaldehyde (0.28 mmol, 1.1 equiv) and toluene as the solvent. For the elimination-Stetter reaction sequence 41.5 mg $K_2CO_3$ (0.300 mmol, 1.2 equiv) and 50.3 mg 3-phenylpropionaldehyde (0.380 mmol, 1.5 equiv) were used. Initially 80.0 mg benzylamine (0.750 mmol, 3.0 equiv), then 2 mL acetic acid were added for the Paal-Knorr reaction. Moreover, the reaction vessel was heated at 70 °C. The crude reaction mixture was extracted as described in **general procedure D**. Yield after column chromatography (flash gel; DCM): 43.2 mg (0.10 mmol, 42%), yellowish oil. $R_f$ (DCM): 0.42. $^1$H NMR (400 MHz, $CDCl_3$): 8.67 (d, *J* = 5.1 Hz, 1H), 7.48 – 7.40 (m, 1H), 7.34– 7.28 (m, 3H), 7.26 – 7.10 (m, 11H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.90 – 6.83 (m, 2H), 6.29 (s, 1H), 5.50 (s, 2H), 3.02 – 2.94 (m, 2H), 2.94 – 2.84 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$): 152.3, 148.9, 141.6, 139.1, 136.8, 136.5, 135.6, 128.62 (2C), 128.55 (2C), 128.53 (2C), 128.47, 128.46 (2C), 128.3 (2C), 127.0, 126.9, 126.2, 126.0 (2C), 125.7, 125.2, 121.4, 107.9, 47.6, 35.2, 28.7. HRMS (ESI): Exact mass calculated for $C_{30}H_{27}N_2$ ([M+H]$^+$): 415.2169, mass found: 415.2165.

*2-(1-Benzyl-5-(furan-2-yl)-4-phenyl-1H-pyrrol-2-yl)pyridine (**18d**).* Pyrrole **18d** was prepared according to **general procedure D** using 37.3 mg nitroalkene **9a** (0.250 mmol, 1.0 equiv), 10.4 mg $K_2CO_3$ (0.0750 mmol, 0.30 equiv), 18.1 mg catalyst **A** (0.0500 mmol, 0.20 equiv), 17.2 mg thiourea **B** (0.0500 mmol, 0.20 equiv), 26.4 mg furfural (0.280 mmol, 1.1 equiv) and $Et_2O$ as the solvent. For the elimination-Stetter reaction sequence 41.5 mg $K_2CO_3$ (0.300 mmol, 1.2 equiv) and 40.3 mg 2-pyridine carbaldehyde (0.38 mmol, 1.5 equiv) were used. Initially 147 mg benzylamine (1.38 mmol, 5.5 equiv), then 45 mg acetic acid (0.75 mmol, 3.0 equiv) were added for the Paal-Knorr reaction. Moreover, the reaction vessel was heated at 50 °C. The crude reaction mixture was directly submitted to column chromatography. Yield after column chromatography (2x; flash gel; DCM): 78.8 mg (0.21 mmol, 84%), yellowish solid. mp: 103–162 °C. $R_f$ (DCM): 0.56. $^1$H NMR (400 MHz, $CDCl_3$): 8.59 (d, *J* = 5.1 Hz, 1H), 7.71 – 7.62 (m, 1H), 7.61 – 7.54 (m, 1H), 7.54 – 7.48 (m, 1H), 7.37 – 7.28 (m, 4H), 7.26 – 7.07 (m, 5H), 6.96 – 6.86 (m, 3H), 6. 48 – 6.37 (m, 1H), 6. 32 – 6.27 (m, 1H), 5.81 (s, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$): 152.2, 148.7, 145.6, 142.9, 139.6, 136.8, 135.7, 133.8, 128.3 (2C), 128.2 (2C), 127.6 (2C), 126.7 (2C), 126.4 (2C), 126.0, 124.1, 122.4, 121.2, 112.3, 111.6, 111.1, 49.4. HRMS (ESI): Exact mass calculated for $C_{26}H_{21}N_2O$ ([M+H]$^+$): 377.1643, mass found: 377.1648.

*2-(1-Benzyl-5-phenethyl-4-phenyl-1H-pyrrol-2-yl)pyridine (**18e**).* Pyrrole **18e** was prepared according to **general procedure D** using 37.3 mg nitroalkene **9a** (0.25 mmol, 1.0 equiv), 13.8 mg $K_2CO_3$ (0.100 mmol, 0.40 equiv),

18.1 mg catalyst **A** (0.0500 mmol, 0.20 equiv), 17.2 mg thiourea **B** (0.0500 mmol, 0.20 equiv), 50.3 mg 3-phenylpropionaldehyde (0.380 mmol, 1.5 equiv) and $Et_2O$ as the solvent. For the elimination-stetter reaction sequence 38.0 mg $K_2CO_3$ (0.280 mmol, 1.1 equiv) and 40.3 mg 2-pyridine carbaldehyde (0.380 mmol, 1.5 equiv) were used. Initially 147 mg benzylamine (1.40 mmol, 5.5 equiv), then 45.0 mg acetic acid (0.750 mmol, 3.0 equiv) were added for the Paal-Knorr reaction. Moreover, the reaction vessel was heated at 50 °C. The crude reaction mixture was directly submitted to column chromatography. Yield after column chromatography (flash gel; hexanes/EtOAc 50/1): 76.5 mg (0.19 mmol, 74%), yellowish oil. $R_f$ (hexanes/ethyl acetate 4:1): 0.67. $^1$H NMR (400 MHz, $CDCl_3$): 8.65 – 8.51 (m, 1H), 7.71– 7.65 (m, 1H), 7.63 – 7.58 (m, 1H), 7.58 – 7.53 (m, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.37 – 7.27 (m, 5H), 7.27 – 7.20 (m, 2H), 7.14 – 7.07 (m, 3H), 7.07 – 7.00 (m, 2H), 6.90 (s, 1H), 5.93 (s, 2H), 3.12 – 2.99 (m, 2H), 2.89 – 2.76 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$): 152.0, 148.0, 141.3, 139.6, 137.2, 136.9, 134.0, 131.3, 128.6 (2C), 128.5 (4C), 128.3 (2C), 128.1 (2C), 127.0, 126.2, 126.0 (2C), 125.9, 123.8, 122.1, 120.6, 112.5, 48.4, 36.6, 27.5. HRMS (ESI): Exact mass calculated for $C_{30}H_{27}N_2$ ($[M+H]^+$): 415.2169, mass found: 415.2169.

*1-Benzyl-2,5-diphenethyl-3-phenyl-1H-pyrrole (**18f**).* Pyrrole **18f** was prepared according to **general procedure D** using 37.3 mg nitroalkene **9a** (0.25 mmol, 1.0 equiv), 13.8 mg $K_2CO_3$ (0.100 mmol, 0.40 equiv), 18.1 mg catalyst **A** (0.0500 mmol, 0.20 equiv), 17.2 mg thiourea **B** (0.0500 mmol, 0.20 equiv), 50.3 mg 3-phenylpropionaldehyde (0.380 mmol, 1.5 equiv) and $Et_2O$ as the solvent. For the elimination-Stetter reaction sequence 38.0 mg $K_2CO_3$ (0.280 mmol, 1.1 equiv) and 50.3 mg 3-phenylpropionaldehyde (0.380 mmol, 1.5 equiv) were used. Initially 147 mg benzylamine (1.40 mmol, 5.5 equiv), then 45.0 mg acetic acid (0.750 mmol, 3.0 equiv) were added for the Paal-Knorr reaction. Moreover, the reaction vessel was heated at 50 °C. The crude reaction mixture was directly submitted to column chromatography. Yield after column chromatography (flash gel; DCM): 23.1 mg (0.0520 mmol, 21%)[41], yellowish oil. $R_f$ (DCM): 0.94. $^1$H NMR (400 MHz, $CDCl_3$): 7.54 – 7.49 (m, 2H), 7.46 – 7.40 (m, 2H), 7.39 – 7.17 (m, 12H), 7.12 – 7.04 (m, 2H), 6.98 – 6.91 (m, 2H), 6.27 (s, 1H), 5.04 (s, 2H), 3.02 – 2.92 (m, 4H), 2.85 – 2.75 (m, 4H). $^{13}$C NMR (101 MHz, $CDCl_3$): 141.8, 141.5, 138.7, 137.7, 132.4, 128.9 (2C), 128.53 (2C), 128.52 (2C), 128.50 (4C), 128.42, 128.37 (2C), 127.9 (2C), 127.3, 126.19, 126.16, 125.7 (2C), 125.4, 121.8, 106.2, 46.8, 37.3, 35.4, 28.8, 27.6. HRMS (ESI): Exact mass calculated for $C_{33}H_{32}N$ ($[M+H]^+$): 442.2529, mass found: 442.2534.

*1-Benzyl-5-(furan-2-yl)-2-phenethyl-3-phenyl-1H-pyrrole (**18g**).* Pyrrole **18g** was prepared according to **general procedure D** using 37.3 mg nitroalkene **9a** (0.250 mmol, 1.0 equiv), 13.8 mg $K_2CO_3$ (0.100 mmol, 0.40 equiv), 18.1 mg catalyst **A** (0.0500 mmol, 0.20 equiv), 17.2 mg thiourea **B** (0.0500 mmol, 0.20 equiv), 50.3 mg 3-phenylpropionaldehyde (0.380 mmol, 1.5 equiv) and $Et_2O$ as the solvent. For the elimination-Stetter reaction sequence 38.0 mg $K_2CO_3$ (0.275 mmol, 1.1 equiv) and 36.0 mg furfural (0.380 mmol, 1.5 equiv) were used. Initially 147 mg benzylamine (1.38 mmol, 5.5 equiv), then 45.0 mg acetic acid (0.75 mmol, 3.0 equiv) were added for the Paal-Knorr reaction. Moreover, the reaction vessel was heated at 50 °C. The crude reaction mixture was directly submitted to column chromatography. Yield after column chromatography (flash gel; DCM): 76.7 mg (0.19 mmol, 76%), yellowish oil. $R_f$ (DCM): 0.95. $^1$H NMR (400 MHz, $CDCl_3$): 7.58 – 7.52 (m, 2H), 7.50 – 7.41 (m, 3H), 7.41 – 7.19 (m, 7H), 7.14 – 7.02 (m, 4H), 6.73 (s, 1H), 6.44 – 6.39 (m, 1H), 6.28 – 6.22 (m, 1H), 5.32 (s, 2H), 3.07 – 2.97 (m, 2H), 2.81 – 2.71 (m, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$): 147.6, 141.5, 141.3, 138.8, 137.0, 131.2, 128.9 (2C), 128.6 (4C), 128.4 (2C), 128.1 (2C), 127.3, 126.2, 125.9 (2C), 125.8, 124.5, 123.3, 111.2, 109.5, 106.3, 48.4, 36.7, 27.6. HRMS (ESI): Exact mass calculated for $C_{29}H_{26}NO$ ($[M+H]^+$): 404.2009, mass found: 404.2006.

## ASSOCIATED CONTENT

**Supporting Information**. Additional data for screening of best conditions and copies of $^1$H NMR, $^{13}$C, NMR and $^{19}$F NMR spectra for all new compounds (PDF).
This material is available free of charge via the Internet at http://pubs.acs.org.

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### Funding Sources

Generous funding by the Deutsche Forschungsgemeinschaft (DFG, FOR 1296) is gratefully acknowledged.

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