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A SHORT SYNTHESIS OF 2,3,5-TRISUBSTITUTED PYRROLES BY AN ALKYLATION/DEHYDROCYANATION SEQUENCE

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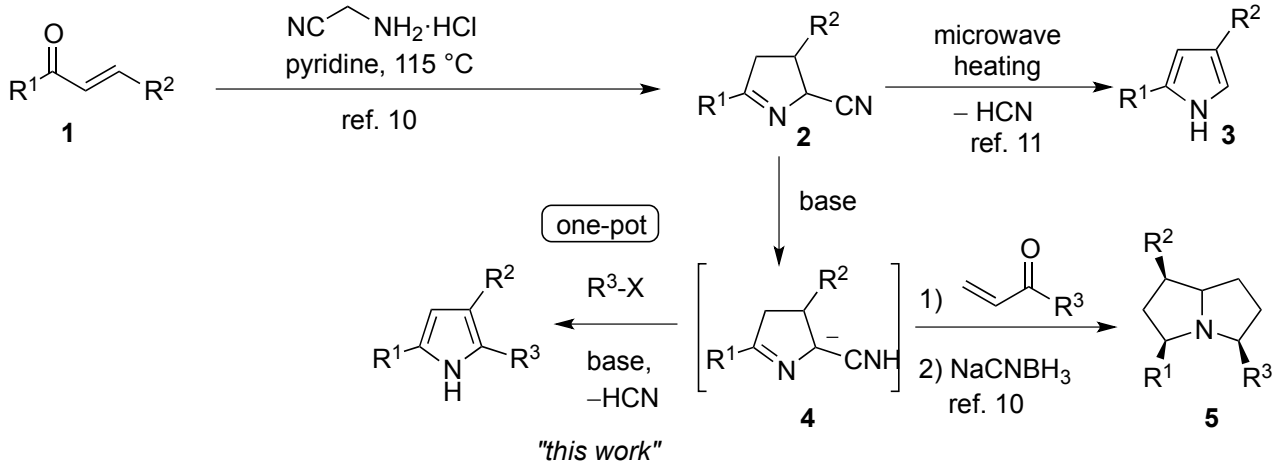
Abstract – 2,3,5-Trisubstituted pyrroles were prepared in a one-pot procedure from readily available 3,5-disubstituted 3,4-dihydro-2*H*-pyrrole-2-carbonitriles by an alkylation/dehydrocyanation sequence. The method was also applied to α,ω-dihaloalkanes to furnish dipyrroles tethered with an alkyl spacer.

The pyrrole ring is a frequently observed motif in various natural products,[1] many of which display pronounced biological activities, in particular antitumor activity and cytotoxicity.[2] Although many advances in the synthesis of pyrroles have been made, only few examples for the direct introduction of a 2-alkyl substituent into N-unsubstituted substrates have been reported so far.[3] The direct alkylation of pyrroles under Friedel-Crafts conditions is often limited due to the formation of polyalkylated products, polymerization or ring opening reactions mediated by the required Brønsted or Lewis acids.[4] Several approaches towards 2-alkylpyrroles therefore involve acylation of the heteroaromatic core with subsequent reduction[5] or the alkylation of 2-lithiated N-substituted pyrroles.[6] These strategies are usually of limited functional group tolerance due to harsh reaction conditions or they can only be applied to N-protected pyrroles.

α-Aminonitriles and α-(alkylideneamino)nitriles have been extensively applied in the preparation of nitrogen heterocycles due to their various modes of reactivity.[7] The carbanion-stabilizing effect of the nitrile group along with its leaving group capability makes such compounds versatile substrates for substitution or addition reactions with the option of late-stage modifications.[8] Herein, we report a one-pot synthesis of 2,3,5-trisubstituted pyrroles from 3,5-disubstituted-3,4-dihydro-2*H*-pyrrole-2-carbonitriles in an alkylation/dehydrocyanation sequence. Since the latter compounds are readily available in a single step from enones and aminoacetonitrile, the overall sequence represents a short modular approach to this

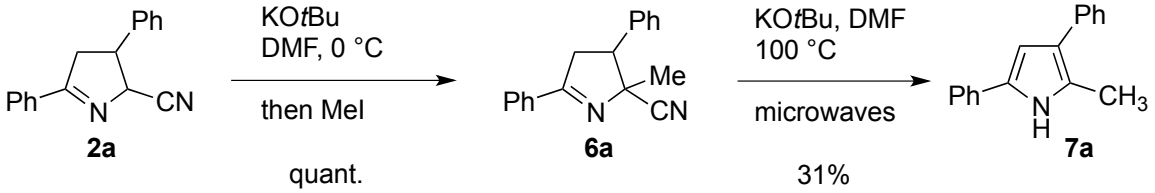
compound class. In contrast to related alkylation reactions of corresponding α-iminoesters providing 2-alkylpyrroline derivatives,[9] this method permits the conversion to pyrroles.

3,4-Dihydro-2*H*-pyrrole-2-carbonitriles **2** were obtained by cyclocondensation of aminoacetonitrile hydrochloride with enones **1** through a 6π-electrocyclization of intermediate 2-azapentadienyl anions.[10] Although the highly acidic proton at C2 prevents the base-induced dehydrocyanation, a microwave-induced thermal elimination of HCN can be used to transform them into the corresponding 2,4-disubstituted pyrroles **3**.[11] Alternatively, deprotonated cyanopyrrolines **4** can be reacted with enones furnish pyrrolizidines **5** by exhaustive reduction with $NaCNBH_3$.[10] Here, we demonstrate that cyanopyrrolines **4** can be reacted with carbon electrophiles to obtain 2-substituted intermediates prone to base-induced elimination of HCN to form 2,3,5-trisubstituted pyrroles in a one-pot sequence (Scheme 1).



Scheme 1. Synthesis and transformation of cyanopyrrolines 2

At first, the alkylation of cyanopyrroline **2a** was examined. A complete methylation with iodomethane could be effected when strong bases (KO*t*Bu, KHMDS, or LDA) were employed at low temperatures or –78 °C) while higher reaction temperatures resulted in the formation of unidentified by-products. However, microwave-induced dehydrocyanation[11] on cyanopyrroline **6a** in the presence of KO*t*Bu in gave only a disappointingly low yield of 31% of pyrrole **7a** over two separate steps (Scheme 2).

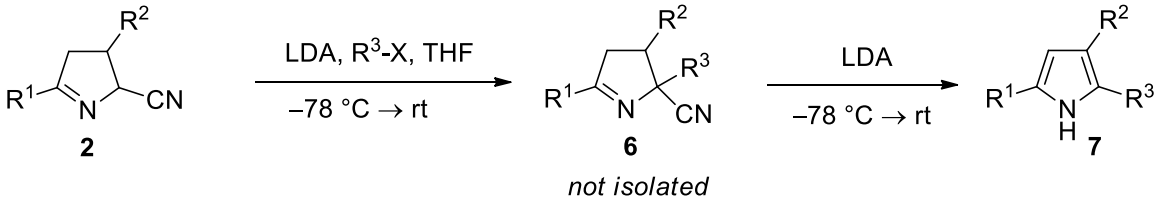


Scheme 2. Thermal dehydrocyanation

All attempts to improve the yield of pyrrole **7a** in analogy to the dehydrocyanation of compounds **2a** by microwave irradiation in the absence of solvent and base failed. The reaction also failed with KHMDS in THF at –78 °C or at elevated temperatures and only the starting material **6a** was recovered unchanged. On

the other hand, dehydrocyanation took place between –40 °C and ambient temperature when KHMDS replaced by LDA. The base strength appears to play a vital role in the course of reaction. While KHMDS (HMDS: pK_a of 26 in THF) is not strong enough to abstract the H3-proton of cyanopyrroline **6a**, LDA (*N*,*N*'-diisopropylamine: pK_a 36 in THF) is sufficiently basic to form pyrrole **7a**.[12]

Based on this finding, a one-pot procedure for alkylation and dehydrocyanation of cyanopyrrolines **2** LDA for both steps could be developed. The C-alkylation step was carried out in THF at –78 °C and alkyl halides were added immediately after deprotonating with LDA (1.2 equiv). Since the reaction did take place at that temperature, the mixture was allowed to warm to 25 °C. When the 2-alkylation was complete (as judged by TLC and/or LC-MS), the reaction mixture was cooled to –78 °C before the of LDA (2.0 equiv) to effect aromatization. The results obtained with this protocol are summarized in Table 1.



Scheme 3

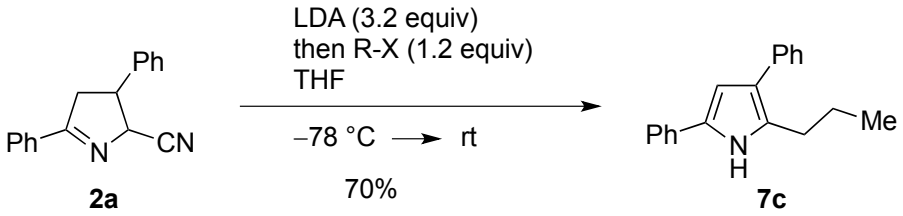
Table 1. Synthesis of 2-alkyl substituted pyrroles **7**

Entry	R^1	R^2	Cyanopyrroline	R^3-X	Pyrrole	Yield[a]
1	Ph	Ph	**2a**	MeI	**7a**	92%
2	Ph	Ph	**2a**	EtBr	**7b**	81%
3	Ph	Ph	**2a**	*n*PrBr	**7c**	90%
4	Ph	Ph	**2a**	$Me(CH_2)_{15}Br$	**7d**	97%
5	Ph	Ph	**2a**	$(Me)_2C{=}CHCH_2Br$	**7e**	81%
6	Ph	Ph	**2a**	$PhCH_2Br$	**7f**	61%[b]
7	2-Naph	Ph	**2b**	EtBr	**7g**	81%[c]
8	2-Naph	Ph	**2b**	*n*PrBr	**7h**	76%[c]
9	Ph	2,3-Cl_2-C_6H_3	**2c**	*n*PrBr	**7i**	72%[d]
10	Ph	4-CN-C_6H_4	**2d**	*n*PrBr	**7j**	68%[e]
11	Me	Ph	**2e**	MeI	**7k**	16%

[a] Isolated yields. [b] Extractive work-up of the intermediate. [c] Alkylation at –30 °C, dehydrocyanation at –20 °C. [d] Alkylation at –25 °C, dehydrocyanation at –40 °C. [e] Alkylation at –40 °C, dehydrocyanation at –20 °C.

The reaction works with primary alkyl iodides or bromides including 1-bromohexadecane (entry 4) and 1-bromo-3-methyl-but-2-ene (entry 5). However, the one-pot procedure failed in the case of benzyl bromide and the desired product **7f** could only be obtained in 61% yield (over two steps) when intermediate **6f** was isolated by an extractive work-up (entry 6). Possibly, the acidity of the benzylic methylene group accounts for this deviant behavior. In the case of the methyl-substituted substrate **2e**, the yield of pyrrole **7k** was low (entry 11). Presumably, deprotonation occurs at the methyl group and results in the formation of side products.

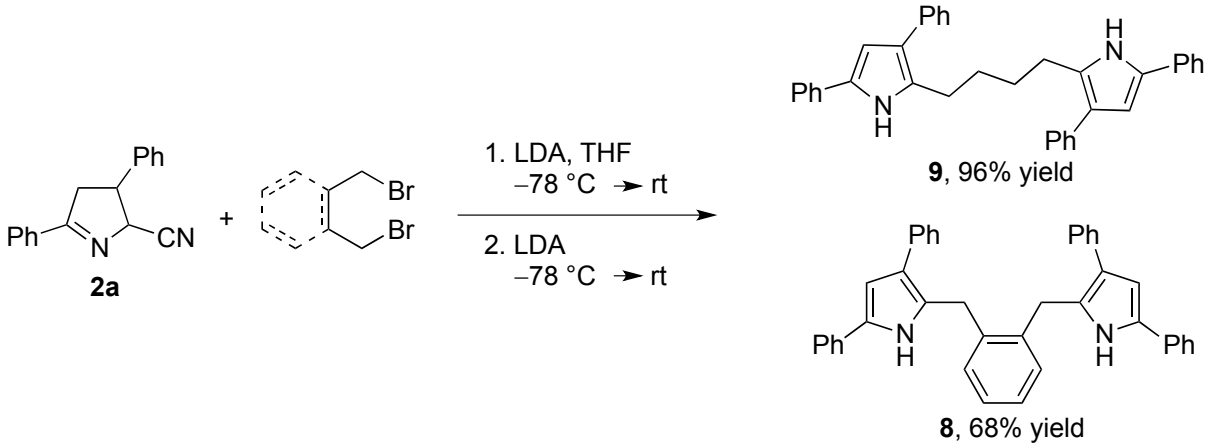
The two-step reaction procedure can also be simplified to a single operation by deprotonating substrates **2** with 3.2 equivalents of LDA prior to addition of the alkyl halide to effect the sequential C-alkylation and dehydrocyanation. With this protocol, cyanopyrroline **2a** could be directly converted to pyrrole **7c** in 70% yield (Scheme 4). Although the yield of pyrrole **7c** is lower compared to the two-step method (90%, see entry 3 in Table 1), the one-step method is more practical and monitoring of the formation of intermediate **6** is not required. During the investigation of reaction kinetics, it was found that the dehydrocyanation process is faster than the C-alkylation of deprotonated cyanopyrroline **2**. Thus, the N-alkylation of pyrrole **7** could be a potential side reaction but was not observed under these conditions.



2a **7c**

Scheme 4. Single-step alkylation/dehydrocyanation

In addition to simple primary alkyl halides, α,ω-bis(pyrrol-2-yl)alkanes could be synthesized from α,ω-dibromoalkanes using the two-step one-pot protocol. Dipyrroles **8** and **9** were obtained from **2a** and



2a

Scheme 5. Synthesis of α,ω-bis(pyrrol-2-yl)alkanes

1,2-bis(bromomethyl)benzene or 1,4-dibromobutane in 68 and 96% yield, respectively (Scheme 5). Similar to the monopyrroles, the yield of dipyrroles was relatively low when they bear benzylic substituents since 2-benzylpyrroles are more prone to oxidize compared to 2-alkylpyrroles.

CONCLUSION

In summary, a highly efficient one-pot synthesis of 2,3,5-trisubstituted pyrroles from readily available 3,4-dihydro-2*H*-pyrrole-2-carbonitriles by an alkylation/dehydrocyanation sequence has been developed. The pyrroles can thus be obtained in a modular approach consisting of only two consecutive operations from enones, alkyl halides, and aminoacetonitrile hydrochloride. In addition to mononuclear products, the alkylation/dehydrocyanation sequence also permits the straightforward synthesis of symmetrical dipyrroles tethered by an alkyl chain. In combination with an improved preparation of intermediate **2a** (85% combined yield from chalcone), exceptionally high overall yields can be obtained which compare very favorably with other approaches.

EXPERIMENTAL

All reactions involving air or moisture sensitive reagents or intermediates were performed under an inert atmosphere of argon in glassware that was oven dried. THF was freshly distilled from potassium under argon. Melting points were determined in open capillary tubes using an electronic apparatus. NMR spectra were recorded on a 400 MHz spectrometer equipped with a 5 mm BBFO probe head with z-gradient and ATM capability. Chemical shifts were referenced to the deuterated solvent (e.g., for $CDCl_3$, δ = 7.26 ppm and 77.16 ppm, for DMSO-d_6, δ = 2.50 ppm and 39.52 ppm for ^{1}H and ^{13}C NMR, respectively). Infrared spectra were recorded as FT-IR spectra using a diamond ATR unit. MS spectra were recorded on a linear ion trap LC/MSD detector (ESI-MS). High-resolution masses were recorded on a QToF-Instrument with a dual electrospray source and a suitable external calibrant. Thin-layer chromatography (TLC) was carried out on 0.25 mm silica gel plates ($60F_{254}$) using UV light as visualizing agent and an ethanolic solution of diluted aqueous sulfuric acid, ammonium pentamolybdate and cerium(IV) sulfate (Seebach's reagent), and heat as developing agents. Chromatography was performed using flash chromatography of the indicated solvent system on 35–70 μm silica gel unless otherwise indicated.

Starting materials. Cyanopyrrolines **2** were prepared by previously reported procedures.[10] LDA solution was obtained from commercial suppliers and was titrated using *N*-benzylbenzamide prior to use.[13]

3,5-Diphenyl-3,4-dihydro-2*H*-pyrrole-2-carbonitrile (**2a**).

The title compound was prepared by heating a mixture of aminoacetonitrile hydrochloride (3.29 g, 35.6 mmol), chalcone (5.07 g, 24.3 mmol), and pyridine (150 mL) to reflux for 255 min. TLC indicated incomplete conversion, and a second portion of aminoacetonitrile hydrochloride (1.23 g, 13.3 mmol) was added. After another 2 h, the reaction mixture was filtered and partitioned between EtOAc (100 mL) and sat. aq $NaHCO_3$ (100 mL). The organic layer was washed with sat. aq $NaHCO_3$ (2 x 50 mL) and brine (50 mL) and the combined aqueous layers were extracted with EtOAc (2 x 50 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo to yield a dark residue which was purified by flash chromatography (cyclohexane/ EtOAc, 10:1) to give gave *trans*-**2a** as a yellow oil (4.00 g, 67%) which crystallized from hexanes/Et_2O; mp 68–70 °C (dec), (lit.[14] mp 74–76 °C); R_f = 0.42 (EtOAc /cyclohexane, 1:5), and *cis*-**2a** as yellow crystals (1.10 g, 18%); mp 111–113 °C (lit.[10] mp 103–104 °C, dec), R_f = 0.22 (EtOAc /cyclohexane, 1:5). *trans*-Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.97–7.83 (m, 2H, Ph), 7.57–7.50 (m, 1H, Ph), 7.50–7.44 (m, 2H, Ph), 7.41–7.35 (m, 2H, Ph), 7.34–7.23 (m, 3H, Ph), 4.94 (dt, J = 7.2, 1.9 Hz, 1H, H-2), 3.95 (d-pseudo-t, J_d = 9.5, $J_t \approx$ 7 Hz, 1H, H-3), 3.70 (ddd, J = 17.4, 9.5, 1.9 Hz, 1H, H-4a), 3.27 (ddd, J = 17.4, 7.5, 1.9 Hz, 1H, H-4b) ppm. *cis*-Isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.00–7.78 (m, 2H, Ph), 7.59–7.43 (m, 3H, Ph), 7.42–7.30 (m, 3H, Ph), 7.30–7.18 (m, 2H, Ph), 5.33 (dt, J = 8.3, 1.5 Hz, 1H, H-2), 3.96 (pseudo-t-d, $J_t \approx$ 8, J_d = 6.5 Hz, 1H, H-3), 3.53 (ddd, J = 17.3, 8.5, 1.5 Hz, 1H, H-4a), 3.43 (ddd, J = 17.3, 6.5, 1.5 Hz, 1H, H-4b) ppm. The spectroscopic data are in accordance with the literature.[10] Both diastereomers of the product are equally suitable for the alkylation reactions.

General Procedure for Alkylpyrroles 7. To a solution of cyanopyrroline **2** in THF (0.1 M) was added a solution of LDA (1.10–1.20 equiv) in THF/heptane/ethylbenzene at –78 °C. The reaction was stirred at this temperature for 3–5 min before the addition of the corresponding alkyl halide (1.10–1.20 equiv). Then the reaction mixture was allowed to warm up to between –40 °C and rt. Stirring was continued until the reaction was almost completed (LC-MS monitoring). The mixture was cooled to –78 °C and more LDA (2.00 equiv) was added. The mixture was stirred for 1–2 h at –20 °C or rt (LC-MS monitoring) before it was quenched by addition of water (10 mL/1.0 mmol cyanopyrroline) and the product was extracted with EtOAc (3 × 20 mL/1.0 mmol cyanopyrroline). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography.

2-Methyl-3,5-diphenyl-1*H*-pyrrole (7a). The title compound was prepared according to the general procedure described from cyanopyrroline **2a** (123 mg, 0.50 mmol) and iodomethane (85 mg, 0.60 mmol, 1.20 equiv) using LDA (0.60 mmol, 1.20 equiv, –78 °C → rt, 1 h for alkylation; 1.00 mol, 2.00 equiv, –78 °C → rt, 1 h for dehydrocyanation). The crude product was purified by column chromatography

(EtOAc /cyclohexane 1:10) to obtain pyrrole **7a** (107 mg, 0.46 mmol, 92%) as a yellow oil. R_f = 0.19 (EtOAc /cyclohexane, 1:10); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 11.14 (br s, 1H, H-1), 7.66–7.62 (m, 2H, H-2'',6''), 7.46–7.43 (m, 2H, H-2',6'), 7.39–7.31 (m, 4H, H-3',5', H-3'',5''), 7.19–7.10 (m, 2H, H-4', H-4''), 6.70 (d, J = 2.8 Hz, 1H, H-4), 2.41 (s, 3H, CH_3) ppm. The data are in accordance with the literature.[10]

2-Ethyl-3,5-diphenyl-1*H*-pyrrole (7b). The title compound was prepared according to the general procedure described from cyanopyrroline **2a** (123 mg, 0.50 mmol) and bromoethane (60 mg, 0.55 mmol, 1.10 equiv) using LDA (0.60 mmol, 1.20 equiv, –78 °C → rt, 2 h for alkylation; 1.00 mol, 2.00 equiv, –78 °C → rt, 1 h for dehydrocyanation). The crude product was purified by column chromatography (EtOAc /cyclohexane 1:10) to obtain pyrrole **7b** (100 mg, 0.404 mmol, 81%) as a dark brown oil. R_f = 0.58 (EtOAc /cyclohexane, 1:5); IR (ATR) $\tilde{\nu}$ = 3426, 3058, 3028, 2966, 2928, 2871, 2855, 1712, 1523, 1450, 756, 696 cm^{-1}; ^{1}H NMR, COSY (400 MHz, DMSO-d_6) δ = 11.06 (br s, 1H, H-1), 7.67–7.64 (m, 2H, H-2'',6''), 7.42–7.39 (m, 2H, H-2',6'), 7.38–7.36 (m, 2H, H-3',5'), 7.35–7.32 (m, 2H, H-3'',5''), 7.20–7.16 (m, 1H, H-4'), 7.16–7.11 (m, 1H, H-4''), 6.64 (d, J = 2.8 Hz, 1H, H-4), 2.76 (q, J = 7.5 Hz, 2H, CH_2), 1.25 (t, J = 7.5 Hz, 3H, CH_3) ppm; ^{13}C NMR (101 MHz, DMSO-d_6) δ = 136.9 (C1'), 132.8 (C1''), 132.1 (C2), 129.5 (C5), 128.6 (2C, C3'',5''), 128.4 (2C, C3',5'), 127.0 (2C, C2',6'), 125.3 (C4''), 124.9 (C4'), 123.2 (2C, C2'',6''), 120.9 (C3), 105.5 (C4), 19.4 (*C*H$_2$), 15.1 (*C*H$_3$) ppm; HRMS (ESI-TOF): Calcd for [$C_{18}H_{17}N$+H]$^+$ 248.1439, found 248.1444.

3,5-Diphenyl-2-propyl-1*H*-pyrrole (7c). The title compound was prepared according to the general procedure described from cyanopyrroline **2a** (123 mg, 0.50 mmol) and 1-bromopropane (74 mg, . 0.60 mmol, 1.20 equiv) using LDA (0.60 mmol, 1.20 equiv, –78 °C → rt, 1 h for alkylation; 1.00 mol, 2.00 equiv, –78 °C → rt, 1 h for dehydrocyanation). The crude product was purified by column chromatography (EtOAc /cyclohexane 1:5) to obtain pyrrole **7c** (117 mg, 0.45 mmol, 90%) as a dark brown oil. R_f = 0.61 (EtOAc /cyclohexane, 1:4); IR (ATR) $\tilde{\nu}$ = 3427, 3057, 3026, 2967, 2928, 2869, 1604, 1493, 1450, 753, 692 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 11.04 (d, J = 2.8 Hz, 1H, H-1), 7.67–7.64 (m, 2H, H-2'',6''), 7.42–7.39 (m, 2H, H-2',6'), 7.38–7.35 (m, 2H, H-3',5'), 7.35–7.32 (m, 2H, H-3'',5''), 7.20–7.15 (m, 1H, H-4'), 7.15–7.11 (m, 1H, H-4''), 6.64 (d, J = 2.8 Hz, 1H, H-4), 2.74–2.69 (m, 2H, CH_2), 1.65 (sextet, J = 7.3 Hz, 2H, CH_2CH$_3$), 0.92 (t, J = 7.3 Hz, 3H, CH_3) ppm; ^{13}C NMR (101 MHz, DMSO-d_6) δ = 137.0 (C1'), 132,8 (C1''), 130.7 (C2), 129.5 (C5), 128.6 (2C, C3'',5''), 128.4 (2C, C3',5'), 127.0 (2C, C2',6'), 125.2 (C4''), 124.9 (C4'), 123.2 (2C, C2'',6''), 121.3 (C3), 105.6 (C4), 28.2 (*C*H$_2$), 23.3 (*C*H$_2$CH$_3$), 13.9 (*C*H$_3$) ppm; HRMS (ESI-TOF): Calcd for [$C_{19}H_{18}N$+H]$^+$ 262.1596, found 262.1585.

One-step procedure: To a solution of cyanopyrroline **2a** (123 mg, 0.50 mmol) in THF (0.1 M) was added a solution of LDA (1.60 mmol, 3.20 equiv) in THF/heptane/ethylbenzene at –78 °C. The mixture was stirred at this temperature for 3–5 min before the addition of 1-bromopropane (74 mg, 0.60 mmol, 1.20 equiv). Then the reaction mixture was allowed to warm up to rt and was stirred for 2 h before it was quenched by addition of water (5 mL) and the product was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (EtOAc /cyclohexane 1:5) to obtain pyrrole **7c** (91 mg, 0.35 mmol, 70%) as a dark brown oil.

2-Hexadecyl-3,5-diphenyl-1*H*-pyrrole (7d). The title compound was prepared according to the general procedure described from cyanopyrroline **2a** (123 mg, 0.50 mmol) and 1-bromohexadecane (183 mg, 0.60 mmol, 1.20 equiv) using LDA (0.60 mmol, 1.20 equiv, –78 °C → rt, 1 h for alkylation; 1.00 mol, 2.00 equiv, –78 °C → rt, 2 h for dehydrocyanation). The crude product was purified by column chromatography (EtOAc /cyclohexane 1:5) to obtain pyrrole **7d** (216 mg, 0.487 mmol, 97%) as a colorless solid. mp 51–52 °C; R_f = 0.29 (EtOAc/cyclohexane, 1:5); IR (ATR) $\tilde{\nu}$ = 3448, 3405, 2921, 2851, 1606, 1495, 1465, 1452, 1264, 755, 738, 697 cm^{-1}; ^1H NMR, COSY (400 MHz, DMSO-d_6) δ = 11.01 (d, J = 2.8 Hz, 1H, H-1), 7.67–7.59 (m, 2H, H2’’’,6’’’), 7.41–7.37 (m, 2H, H-2’’,6’’), 7.37–7.30 (m, 4H, H-3’’,5’’, H-3’’’,5’’’), 7.20–7.10 (m, 2H, H-4’’, H-4’’’), 6.62 (d, J = 2.8 Hz, 1H, H-4), 2.72 (t, J = 7.8 Hz, 2H, H-1’), 1.62 (quintet, J = 7.8 Hz, 2H, H-2’), 1.33–1.15 (m, 26H, H-3’–17’), 0.84 (t, J = 7.2 Hz, 3H, H-16’) ppm; ^{13}C NMR, HSQC, HMBC (101 MHz, DMSO-d_6) δ = 137.1 (C1’’), 132.8 (C1’’’), 130.8 (C2), 129.5 (C4), 128.6 (2C, C3’’’,5’’’), 128.3 (2C, C3’’,5’’), 127.0 (2C, C2’’,6’’), 125.2 (C4’’’), 124.8 (C4’’), 123.1 (2C, C2’’’,6’’’), 121.3 (C3), 105.6 (C4), 31.3, 29.8, 29.1, 29.0, 28.8, 28.7, 26.1, 22.1, 14.0 ppm; HRMS (ESI-TOF): Calcd for $[C_{32}H_{45}N+H]^+$ 444.3630, found 444.3634.

2-(3-Methylbut-2-en-1-yl)-3,5-diphenyl-1*H*-pyrrole (7e). The title compound was prepared according to the general procedure described from cyanopyrroline **2a** (123 mg, 0.50 mmol) and 1-bromo-3-methylbut-2-ene (89 mg, 0.60 mmol, 1.20 equiv) using LDA (0.60 mmol, 1.20 equiv, –78 °C → rt, 1 h for alkylation; 1.00 mol, 2.00 equiv, –78 °C → rt, 1 h for dehydrocyanation). The crude product was purified by column chromatography (EtOAc/cyclohexane 1:10) to obtain pyrrole **7e** (117 mg, 0.405 mmol, 81%) as a dark brown oil. R_f = 0.51 (EtOAc/cyclohexane, 1:5); IR (ATR) $\tilde{\nu}$ = 3424, 3354, 3058, 3027, 2966, 2924, 1606, 1494, 1450, 754 cm^{-1}; ^1H NMR, COSY (400 MHz, DMSO-d_6) δ = 11.90 (d, J = 2.9 Hz, 1H, H-1), 7.67–7.64 (m, 2H, H2’’’,6’’’), 7.41–7.37 (m, 2H, H-2’’,6’’), 7.36–7.33 (m, 4H, H-3’’,5’’, H-3’’’,5’’’), 7.19–7.12 (H-4’’, H-4’’’), 6.66 (d, J = 2.9 Hz, 1H, H-4), 5.30–5.26 (m, 1H, H-2’), 3.44 (d, J = 6.7 Hz, 2H, H-1’), 1.67 (d, ^4J = 1.5 Hz, 3H, CH_3), 1.66 (d, ^4J = 1.3 Hz, 3H, CH_3) ppm; ^{13}C

NMR, HSQC, HMBC (101 MHz, DMSO-d_6) δ = 136.8 (C1''), 132.7 (C1'''), 131.1 (C3'), 129.6 (C4), 129.5 (C2), 128.6 (2C, C3''',5'''), 128.4 (2C, C3'',5''), 127.0 (2C, C2'',6''), 125.3 (C4'''), 124.9 (C4''), 123.2 (2C, C2''',6'''), 122.7 (C2'), 121.3 (C3), 105.6 (C4), 25.5 (2C, C1, CH_3 *trans* to H-2'), 17.8 (CH_3 *cis* to H-2') ppm; HRMS (ESI-TOF): Calcd for $[C_{21}H_{21}N+H]^+$ 288.1752, found 288.1753.

2-Benzyl-3,5-diphenyl-1*H*-pyrrole (7f). The title compound was prepared according to the general procedure described from cyanopyrroline **2a** (123 mg, 0.50 mmol) and benzyl bromide (103 mg, 0.60 mmol, 1.20 equiv) using LDA (0.60 mmol, 1.20 equiv, –78 °C → rt, 2 h for alkylation). After an extractive work-up, the residue was dissolved in THF (5 mL) and LDA (1.00 mol, 2.00 equiv) was added at –78 °C. The solution was allowed to warm up to rt and stirred 1 h. The crude product was purified by column chromatography (EtOAc/cyclohexane 1:10) to obtain pyrrole **7f** (94 mg, 0.305 mmol, 61%) as a dark brown oil. R_f = 0.53 (EtOAc/cyclohexane, 1:5); IR (ATR) $\tilde{\nu}$ = 3425, 3059, 3027, 2925, 1606, 1495, 1452, 1074, 757, 731 cm^{-1}; ^1H NMR, COSY (400 MHz, DMSO-d_6) δ = 11.34 (d, J = 2.8 Hz, 1H, H-1), 7.70–7.66 (m, 2H, H-2''',6'''), 7.39–7.33 (m, 4H, H-2'',6'', H-3''',5'''), 7.33–7.25 (m, 4H, H-3',5', H-3'',5''), 7.20–7.12 (5H, H-2',6', H-4', H-4'', H-4'''), 6.78 (d, J = 2.8 Hz, H-4), 4.15 (s, 2H, CH_2) ppm; ^{13}C NMR, HSQC, HMBC (101 MHz, DMSO-d_6) δ = 140.5 (C1'), 136.6 (C1''), 132.6 (C1'''), 130.2 (C5), 128.7 (2C, C3''',5'''), 128.4 (4C, C3',5', C3'',5''), 127.92 (C2), 127.87 (2C, C2',6'), 126.7 (2C, C2'',6''), 126.0 (C4'), 125.5 (C4'''), 125.1 (C4''), 123.2 (2C, C2''',6'''), 122.4 (C3), 105.7 (C4), 31.8 (CH$_2$) ppm; HRMS (ESI-TOF): Calcd for $[C_{23}H_{19}N+H]^+$ 310.1596, found 310.1608.

2-Ethyl-5-(naphthalen-2-yl)-3-phenyl-1*H*-pyrrole (7g). The title compound was prepared according to the general procedure described from cyanopyrroline **2b** (148 mg, 0.50 mmol) and bromoethane (65 mg, 0.60 mmol, 1.20 equiv) using LDA (0.60 mmol, 1.20 equiv, –78 °C → –30 °C, 2 h for alkylation; 1.00 mol, 2.00 equiv, –78 °C → –20 °C, 2 h for dehydrocyanation). The crude product was purified by column chromatography (EtOAc/cyclohexane 1:10) to obtain pyrrole **7g** (121 mg, 0.407 mmol, 81%) as a yellow oil. R_f = 0.20 (EtOAc/cyclohexane, 1:10); IR (ATR) $\tilde{\nu}$ = 3428, 3054, 3026, 2967, 2929, 2871, 1627, 1446, 805, 762, 699 cm^{-1}; ^1H NMR, COSY (400 MHz, DMSO-d_6) δ = 11.26 (d, J = 2.8 Hz, 1H, H-1), 8.13 (s, 1H, H-1''), 7.88–7.81 (m, 4H, H_{Naphth}), 7.51–7.46 (m, 1H, H_{Naphth}), 7.45–7.40 (m, 3H, H_{Naphth}, H-2',6'), 7.40–7.36 (m, 2H, H-3',5'), 7.22–7.17 (m, 1H, H-4'), 6.81 (d, J = 2.8 Hz, 1H, H-4), 2.79 (q, J = 7.4 Hz, 2H, CH_2), 1.28 (t, J = 7.4 Hz, 3H, CH_3) ppm; ^{13}C NMR, HSQC, HMBC (101 MHz, DMSO-d_6) δ = 136.9 (C1'), 133.5(C_{Naphth}), 132.7 (C2), 131.3 (C_{Naphth}), 130.2 (C_{Naphth}), 129.5 (C5), 128.5 (2C, C3',5'), 128.1 (C_{Naphth}), 127.6 (C_{Naphth}), 127.4 (C_{Naphth}), 127.0 (2C, C2',6'), 126.4 (C_{Naphth}), 125.0 (C4'), 124.9 (C_{Naphth}), 123.1 (C_{Naphth}), 121.2 (C3), 119.8 (C1''), 106.5 (C4), 19.5 (CH$_2$) 15.0 (CH$_3$) ppm; HRMS (ESI-TOF): Calcd for $[C_{22}H_{19}N+H]^+$ 298.1596, found 298.1593.

5-(Naphthalen-2-yl)-3-phenyl-2-propyl-1*H*-pyrrole (7h). The title compound was prepared according to the general procedure described from cyanopyrroline **2b** (148 mg, 0.50 mmol) and 1-bromopropane (55 µL, 0.60 mmol, 1.20 equiv) using LDA (0.60 mmol, 1.20 equiv, –78 °C → –30 °C, 2 h for alkylation; 1.00 mol, 2.00 equiv, –78 °C → –20 °C, 1 h for dehydrocyanation). The crude product was purified by column chromatography (EtOAc/cyclohexane 1:14) to obtain pyrrole **7h** (119 mg, 0.38 mmol, 76%) as a yellow oil. R_f = 0.29 (EtOAc/cyclohexane, 1:14); IR (ATR) $\tilde{\nu}$ = 3431, 3054, 3026, 2958, 2929, 2869, 1628, 1604, 1490, 1444, 1146, 805, 763, 699 cm^{-1}; ^{1}H NMR, COSY (400 MHz, DMSO-d_6) δ = 11.23 (d, J = 2.8 Hz, 1H, H-1), 8.13 (s, 1H, H-1''), 7.91–7.78 (m, 4H, H_{Naphth}), 7.53–7.44 (m, 1H, H_{Naphth}), 7.47–7.41 (m, 3H, H_{Naphth}, H-2',6'), 7.40–7.33 (m, 2H, H-3',5'), 7.20 (m, 1H, H-4'), 6.81 (d, J = 2.8 Hz, 1H, H-4), 2.75 (t, J = 7.4 Hz, 2H, CH_2), 1.69 (sept, 2H, J = 7.4 Hz, CH_2CH$_3$), 0.94 (t, J = 7.4 Hz, 3H, CH_3) ppm; ^{13}C NMR, HSQC, HMBC (101 MHz, DMSO-d_6) δ = 137.0 (C1'), 133.5(C_{Naphth}), 131.3 (C2), 131.26 (C_{Naphth}) 130.2 (C_{Naphth}), 129.5 (C5), 128.5 (2C, C3',5'), 128.1 (C_{Naphth}), 127.6 (C_{Naphth}), 127.3 (C_{Naphth}), 127.0 (2C, C2',6') 126.4 (C_{Naphth}), 125.0 (C4'), 124.9 (C_{Naphth}), 123.1 (C_{Naphth}), 121.6 (C3), 119.8 (C1''), 106.6 (C4), 28.3 (CH$_2$), 23.3 (CH$_2$CH$_3$), 13.9 (CH$_3$) ppm; HRMS (ESI-TOF): Calcd for $[C_{23}H_{21}N+H]^+$ 312.1752, found 312.1759.

3-(2,3-Dichlorophenyl)-5-phenyl-2-propyl-1*H*-pyrrole (7i). The title compound was prepared according to the general procedure described from cyanopyrroline **2c** (158 mg, 0.50 mmol) and 1-bromopropane (74 mg, 0.60 mmol, 1.20 equiv) using LDA (0.60 mmol, 1.20 equiv, –78 °C → –25 °C, 2 h for alkylation; 1.00 mol, 2.00 equiv, –78 °C → –40 °C, 30 min for dehydrocyanation). The crude product was purified by column chromatography (EtOAc/cyclohexane 1:10) to obtain pyrrole **7i** (118 mg, 0.36 mmol, 72%) as an orange oil. R_f = 0.28 (EtOAc/cyclohexane, 1:10); IR (ATR) $\tilde{\nu}$ = 3442, 2959, 2929, 2870, 1606, 1480, 1450, 1405, 1149, 1052, 784, 755, 722 cm^{-1}; ^{1}H NMR, COSY (400 MHz, $CDCl_3$) δ = 8.21 (br s, 1H, H-1), 7.50–7.47 (m, 2H, H-2''',6'''), 7.41 (dd, J = 7.8, 1.9 Hz, 1H, H-4''), 7.39–7.35 (m, 2H, H-3''',5'''), 7.25 (dd, J = 7.6, 1.9 Hz, 1H, H-6''), 7.22 (pseudo-t, J_{app} ≈ 8 Hz, 1H, H-5''), 7.22–7.18 (m, 1H, H-4'''),6.53 (d, J = 2.9 Hz, 1H, H-4), 2.60–2.56 (m, 2H, H-1'), 1.66–1.57 (m, 2H, H-2'), 0.92 (t, J = 7.3 Hz, 3H, H-3') ppm; ^{13}C NMR, HSQC, HMBC (101 MHz, $CDCl_3$) δ = 138.6 (C1''), 133.4 (C3''), 132.6 (C1'''), 132.5 (C2''), 131.5 (C2), 130.5 (C6''), 129.9 (C5), 129.0 (2C, C3''',5'''), 128.7 (C4''), 126.8 (C5''), 126.2 (C4'''), 123.5 (2C, C2''',6'''), 120.5 (C3), 107.9 (C4), 28.7 (C1'), 23.2 (C2'), 14.0 (C3') ppm; HRMS (ESI-TOF): Calcd for $[C_{19}H_{17}NCl_2]^+$ 329.0738, found 329.0739.

4-(5-Phenyl-2-propyl-1*H*-pyrrol-3-yl)benzonitrile (7j). The title compound was prepared according to the general procedure described from cyanopyrroline **2d** (136 mg, 0.50 mmol) and 1-bromopropane

(74 mg, 0.60 mmol, 1.20 equiv) using LDA (0.60 mmol, 1.20 equiv, –78 °C → –40 °C, 1 h for alkylation; 1.00 mol, 2.00 equiv, –78 °C → –20 °C, 30 min for dehydrocyanation). The crude product was purified by column chromatography (EtOAc/cyclohexane 1:10) to obtain pyrrole **7j** (97 mg, 0.34 mmol, 68%) as a colorless solid. mp 163–164 °C; R_f = 0.17 (EtOAc/cyclohexane, 1:10); IR (ATR) $\tilde{\nu}$ = 3318, 3053, 2955, 2928, 2868, 2226, 1601, 1499, 1265, 804, 758, 735 cm^{-1}; ^{1}H NMR, COSY (400 MHz, DMSO-d_6) δ = 11.27 (br s, 1H, H-1'), 7.80–7.77 (AA' part of AA'–BB' system, 2H, H-2,6), 7.68–7.66 (m, 2H, H-2''',6'''), 7.62–7.58 (BB' part of AA'–BB' system, 2H, H-3,5), 7.38–7.34 (m, 2H, H3''',5'''), 7.18–7.15 (m, 1H, H-4'''), 6.79 (d, J = 2.8 Hz, 1H, H-4'), 2.79–2.75 (m, 2H, H-1''), 1.69–1.60 (m, 2H, H-2''), 0.92 (t, J = 7.3 Hz, 3H, H-3'') ppm; ^{13}C NMR, HSQC, HMBC (101 MHz, DMSO-d_6) δ = 141.9 (C4), 132.6 (C2'), 132.4 (2C, C2,6), 132.3 (C1'''), 130.3 (C5'), 128.7 (2C, C3''',5'''), 127.0 (2C, C3,5), 125.6 (C4'''), 123.4 (2C, C2''',6'''), 119.6 (C3'), 119.4 (CN), 106.7 (C1), 105.6 (C4'), 28.4 (C1''), 23.0 (C2''), 13.8 (C3'') ppm; HRMS (ESI-TOF): Calcd for $[C_{20}H_{18}N_2+H]^+$ 287.1548, found 287.1550.

2,5-Dimethyl-3-phenyl-1*H*-pyrrole (7k). The title compound was prepared according to the general procedure described from cyanopyrroline **2e** (144 mg, 0.78 mmol) and iodomethane (133 mg, 0.94 mmol, 1.20 equiv) using LDA (0.94 mmol, 1.20 equiv, –78 °C → rt, 1 h for alkylation; 1.56 mmol, 2.00 equiv, –78 °C → rt, 1 h for dehydrocyanation). The crude product was purified by column chromatography (EtOAc/cyclohexane 1:10) to obtain pyrrole **7k** (21 mg, 0.12 mmol, 16%) as an orange oil. R_f = 0.17 (EtOAc/cyclohexane, 1:10); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.64 (br s, 1H, H-1), 7.44–7.34 (m, 4H, H-2',6', H-3',5'), 7.23–7.17 (m, 1H, H-4'), 6.01 (d, J = 2.4 Hz, 1H, H-4), 2.39 (s, 3H, CH_3), 2.29 (s, 3H, CH_3) ppm. The data are in accordance with the literature.[15]

1,2-Bis[(3,5-diphenyl-1*H*-pyrrol-2-yl)methyl]benzene (8). The title compound was prepared according to the general procedure described from cyanopyrroline **2a** (123 mg, 0.50 mmol, 2.00 equiv) and 1,2-bis(bromomethyl)benzene (79 mg, 0.30 mmol, 1.20 equiv) using LDA (0.60 mmol, 2.40 equiv, –78 °C → rt, 2 h for alkylation; 1.00 mmol, 4.00 equiv, –78 °C → rt, 2 h for dehydrocyanation). The crude product was purified by column chromatography (EtOAc/cyclohexane 1:5) to obtain dipyrrole **8** (92 mg, 0.17 mmol, 68%) as a colorless solid. mp 76–78 °C (dec.); R_f = 0.43 (EtOAc/cyclohexane, 1:10); IR (ATR) $\tilde{\nu}$ = 3427, 3058, 3026, 1606, 1495, 1451, 756 cm^{-1}; ^{1}H NMR, COSY (400 MHz, DMSO-d_6) δ = 11.32 (d, J = 2.8 Hz, 2H, H-1'), 7.72–7.68 (m, 4H, H-2''',6'''), 7.40–7.34 (m, 4H, H-3''',5'''), 7.34–7.30 (m, 4H, H-2'',6''), 7.30–7.25 (m, 4H, H-3'',5''), 7.20–7.12 (m, 4H, H-4'', H-4'''), 7.11–7.07 (AA' part of AA'–BB' system, 2H, H-3), 6.90–6.87 (BB' part of AA'–BB' system, 2H, H-4), 6.83 (d, J = 2.8 Hz, 2H, H-4'), 4.14 (s, 4H, CH_2) ppm; ^{13}C NMR, HSQC, HMBC (101 MHz, DMSO-d_6) δ = 138.1 (2C, C1,2),

136.6 (2C, C1''), 132.6 (2C, C1'''), 130.4 (2C, C5') 127.1 (2C, C2'), 128.7 (4C, C3''',5'''), 128.5 (4C, C3'',5''), 127.6 (2C, C4,5), 126.6 (4C, C2'',6''), 126.2 (2C, C3,6), 125.5 (2C, C4'''), 125.1 (2C, C4''), 123.3 (4C, C2''',6'''), 122.9 (2C, C3'), 105.8 (2C, C4'), 29.4 (2C, *C*H_2) ppm; HRMS (ESI-TOF): Calcd for $[C_{40}H_{32}N_2+H]^+$ 541.2644, found 541.2626.

1,4-Bis(3,5-diphenyl-1*H*-pyrrol-2-yl)butane (9). The title compound was prepared according to the general procedure described from cyanopyrroline **2a** (246 mg, 1.00 mmol, 2.00 equiv) and 1,4-dibromobutane (108 mg, 0.50 mmol, 1.00 equiv) using LDA (1.20 mmol, 2.40 equiv, –78 °C → rt, 1 h for alkylation; 2.00 mmol, 4.00 equiv, –78 °C → rt, 2 h for dehydrocyanation). The crude product was purified by column chromatography (EtOAc/cyclohexane 1:10) to obtain dipyrrole **9** (235 mg, 0.48 mmol, 96%) as a colorless solid. mp 199–201 °C; R_f = 0.22 (EtOAc/cyclohexane, 1:10); IR (ATR) $\tilde{\nu}$ = 3410, 3057, 3026, 2929, 2854, 1604, 1494, 755, 694 cm^{-1}; ^{1}H NMR, COSY (400 MHz, DMSO-d_6) δ = 11.04 (d, *J* = 2.8 Hz, 2H, H-1), 7.66–7.62 (m, 4H, H-2'',6''), 7.40–7.31 (m, 12H, H-2',6', H-3',5', H-3'',5''), 7.19–7.09 (m, 4H, H-4', H-4''), 6.64 (d, *J* = 2.8 Hz, 2H, H-4), 2.76 (t, *J* = 6.8 Hz, 4H, 2-CH_2) 1.74–1.68 (m, 4H, C$H_2$$CH_2$-2) ppm; ^{13}C NMR, HSQC, HMBC (101 MHz, DMSO-d_6) δ = 137.0 (2C, C1'), 132.7 (2C, C1''), 130.7 (2C, C2) 129.5 (2C, C5), 128.6 (4C, C3'',5''), 128.4 (4C, C3',5'), 126.9 (4C, C2',6'), 125.2 (2C, C4''), 124.9 (2C, C4'), 123.2 (4C, C2'',6''), 121.2 (2C, C3), 105.7 (2C, C4), 30.1 (2C, β-CH_2) 26.1 (2C, α-CH_2) ppm; HRMS (ESI-TOF): Calcd for $[C_{36}H_{32}N_2+H]^+$ 493.2644, found 493.2638.

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REFERENCES

1. (a) C. T. Walsh, S. Garneau-Tsodikova, and A. R. Howard-Jones, *Nat. Prod. Rep.*, 2006, **23**, 517; (b) I. S. Young, P. D. Thornton, and A. Thompson, *Nat. Prod. Rep.*, 2010, **27**, 1801; (c) H. Fan, J. Peng, M. T. Hamann, and J.-F. Hu, *Chem. Rev.*, 2008, **108**, 264.
2. (a) J. Gupton, in *Heterocyclic Antitumor Antibiotics, Vol. 2*, ed. by M. Lee, Springer Berlin Heidelberg, 2006, p 53; (b) V. Bhardwaj, D. Gumber, V. Abbot, S. Dhiman, and P. Sharma, *RSC Adv.*, 2015, **5**, 15233.
3. (a) X. Han and J. Wu, *Angew. Chem. Int. Ed.*, 2013, **52**, 4637; (b) L. Jiao and T. Bach, *Angew. Chem. Int. Ed.*, 2013, **52**, 6080; (c) H. Felkin and J. Zakrzewski, *J. Am. Chem. Soc.*, 1985, **107**, 3374; (d) Y. R. Jorapur, C.-H. Lee, and D. Y. Chi, *Org. Lett.*, 2005, **7**, 1231.
4. (a) A. D. Abell, B. K. Nabbs, and A. R. Battersby, *J. Org. Chem.*, 1998, **63**, 8163; (b) E. Díez-Barra,

A. De La Hoz, A. Sánchez-Migallón, and A. Loupy, *J. Heterocycl. Chem.*, 1994, **31**, 1715; (c) R. A. Jones and G. P. Bean, *The Chemistry of Pyrroles*, *Vol. 34*, Academic. Press, New York, 1977; (d) J. Leppin, C. Förster, and K. Heinze, *Inorg. Chem.*, 2014, **53**, 12416; (e) S. Nunomoto, Y. Kawakami, Y. Yamashita, H. Takeuchi, and S. Eguchi, *J. Chem. Soc., Perkin Trans. 1*, 1990, 111; (f) G. F. Smith, in *Advances in Heterocyclic Chemistry, Vol. 2*, ed. by A. R. Katritzky, Academic Press, 1963, pp. 287.

5. (a) D. O. A. Garrido, G. Buldain, and B. Frydman, *J. Org. Chem.*, 1984, **49**, 2619; (b) K. Papireddy, M. Smilkstein, J. X. Kelly, Shweta, S. M. Salem, M. Alhamadsheh, S. W. Haynes, G. L. Challis, and K. A. Reynolds, *J. Med. Chem.*, 2011, **54**, 5296.
6. (a) J. M. Brittain, R. A. Jones, J. S. Arques, and T. A. Saliente, *Synth. Commun.*, 1982, **12**, 231; (b) A. Thurner, F. Faigl, B. Ágai, and L. Tőke, *Synth. Commun.*, 1998, **28**, 443.
7. (a) N. Otto and T. Opatz, *Chem. Eur. J.*, 2014, **20**, 13064; (b) D. Enders and J. P. Shilvock, *Chem. Soc. Rev.*, 2000, **29**, 359.
8. (a) T. Opatz, *Synthesis*, 2009, 1941; (b) R. Achini, *Helv. Chim. Acta*, 1981, **64**, 2203; (c) A. Jończyk and Z. Pakulski, *Tetrahedron Lett.*, 1996, **37**, 8909; (d) K. Takahashi, T. Aihara, and K. Ogura, *Chem. Lett.*, 1987, **16**, 2359; (e) I. Netz, M. Kucukdisli, and T. Opatz, *J. Org. Chem.*, 2015, **80**, 6864; (f) I. Schäfer and T. Opatz, *Synthesis*, 2011, 1691.
9. (a) D. S. C. Black, G. L. Edwards, and S. M. Laaman, *Synthesis*, 2006, 1981; (b) M. Lee, Y.-J. Lee, E. Park, Y. Park, M. W. Ha, S. Hong, Y.-J. Lee, T.-S. Kim, M.-h. Kim, and H.-g. Park, *Org. Biomol. Chem.*, 2013, **11**, 2039; (c) N. Ningsanont, D. S. C. Black, R. Chanphen, and Y. Thebtaranonth, *J. Med. Chem.*, 2003, **46**, 2397; (d) Z.-Y. Xue, Z.-M. Song, and C.-J. Wang, *Org. Biomol. Chem.*, 2015, **13**, 5460.
10. I. Bergner, C. Wiebe, N. Meyer, and T. Opatz, *J. Org. Chem.*, 2009, **74**, 8243.
11. M. Kucukdisli, D. Ferenc, M. Heinz, C. Wiebe, and T. Opatz, *Beilstein J. Org. Chem.*, 2014, **10**, 466.
12. (a) R. R. Fraser, T. S. Mansour, and S. Savard, *J. Org. Chem.*, 1985, **50**, 3232; (b) R. R. Fraser, M. Bresse, N. Chuaqui-Offermanns, K. N. Houk, and N. G. Rondan, *Can. J. Chem.*, 1983, **61**, 2729.
13. A. F. Burchat, J. M. Chong, and N. Nielsen, *J. Organomet. Chem.*, 1997, **542**, 281.
14. D. Tasheva, A. Petrova, and S. Simova, *Synth. Commun.*, 2007, **37**, 3971.
15. M. Mori, M. Akashi, M. Hori, K. Hori, M. Nishida, and Y. Sato, *Bull. Chem. Soc. Jpn.*, 2004, **77**, 1655.