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Palladium-Catalyzed Synthesis of Heterocycle-Containing Diarylmethanes through Suzuki–Miyaura Cross-Coupling

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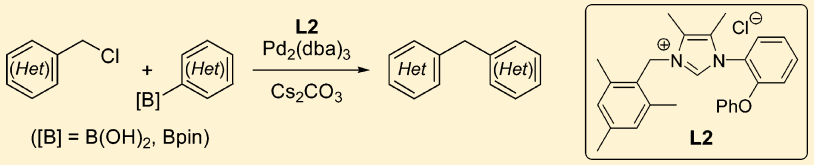
Supporting Information



ABSTRACT: The heterocycle-containing diarylmethane synthesis from chloromethyl(hetero)arenes with (hetero)arylboron reagents was attained using the palladium/ether-imidazolium chloride system. This coupling process tolerated a diverse range of heteroaromatic moieties with sufficient catalytic activity to achieve the efficient synthesis of various diheteroarylmethanes in good to excellent yields.

Diheteroarylmethanes are known as ubiquitous and important structures in naturally occurring and biologically active compounds.[1] Although transition metal-catalyzed C–C bond formation is one of the most powerful synthetic methods,[2,3] diheteroarylmethane synthesis through cross-coupling reactions with chloromethylheteroarenes has been limited to only two reports,[4] which are preferable to other halomethylheteroarenes in the light of cost, diversity, and stability.[5] In these methods, only a very few kinds of specific chloromethylheteroarenes and heteroarylboronic acids were applied to the preparation of diheteroarylmethanes. Therefore, the development of effective coupling reactions for diheteroarylmethane synthesis with broad scope of substrates is still desired, in which Suzuki–Miyaura reaction is highly suitable due to the superior features of organoboronic acids and their derivatives, such as low toxicity, easy manipulation, and ready availability.[6,7] However, the catalytic cross-coupling for heteroaryl derivative synthesis remains a challenging task on the grounds of detrimental influences of heterocyclic motifs on catalytic activity,[8] and substantial efforts have been made to find effective ligands for Suzuki–Miyaura reaction with heteroaryl substrates.[9,10] Recently, we developed the ether-imidazolium chlorides (Figure 1) as *N*-heterocyclic carbene precursors,[11−13] and found that the palladium/ether-imidazolium chloride system achieved high catalytic performance and broad substrate tolerance for heteroaryl moieties.[14]

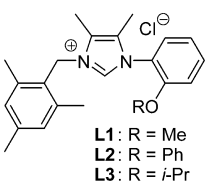


Figure 1. Ether-imidazolium chlorides.

Herein, we describe the palladium-catalyzed synthesis of heterocycle-containing diarylmethanes from chloromethyl(hetero)arenes through the Suzuki–Miyaura reaction with the ether-imidazolium chlorides.

First of all, optimization of reaction conditions was conducted using 2-chloro-5-(chloromethyl)pyridine (**1a**) and 3-thiopheneboronic acid (**2a**) as model substrates (Table 1). The cross-coupling with 1.0 mol % of catalysts (Pd/L = 1/2) formed in situ from carbene ligand precursors **L1**–**3** and allylpalladium(II) chloride dimer was carried out at 90 °C, and ether-imidazolium chloride **L2** proved to be a superior ligand precursor (entries 2–4), while the control experiment using no imidazolium chloride afforded no conversion (entry 1). A series of palladium sources were examined, and tris(dibenzylideneacetone)dipalladium(0) led to the highest catalytic activity to give 2-chloro-5-(thiophen-3-ylmethyl)-pyridine (**3aa**) in 86% yield (entries 3 and 5–8).[15] The screening of bases revealed that cesium carbonate was the reagent of choice (entries 8–12). The influence of solvents was investigated, and dioxane was found to be the most suitable (entries 8 and 13–16).

Investigation of heterocycle-containing diarylmethane synthesis was conducted with chloromethylheteroarenes and arylboronic acids (Scheme 1). In the cross-coupling using 2-chloro-5-(chloromethyl)pyridine (**1a**), a series of arylboronic acids was examined. The sterically hindered 2-methylphenylboronic acid (**2d**) as well as 3- and 4-methylphenylboronic acid (**2c** and **2b**) reacted smoothly to give desired products **3ab**–**ad** in high yields. The electron-rich arylboronic acids with a methoxy or methylsulfanyl group were also proved to be good reaction partners (**3ae**–**af**), while the electron-withdrawing substituents on aromatic rings led to slight

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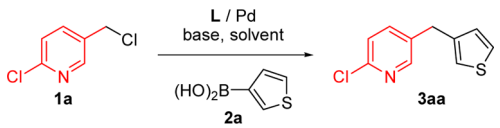
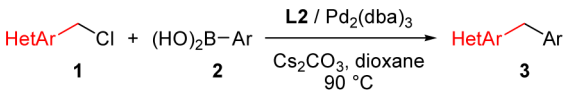
Table 1. Optimization of Reaction Conditions[a]

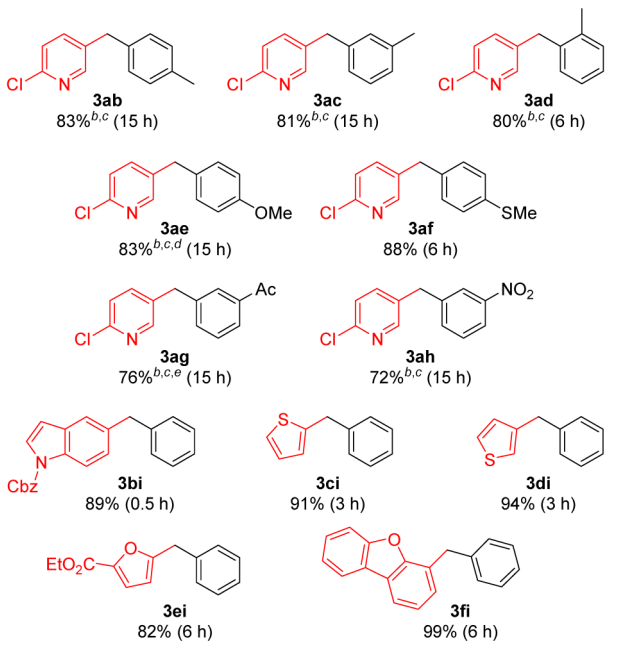


entry	L	Pd	base	solvent	yield (%)[b]
1	none	$[Pd(allyl)Cl]_2$	Cs_2CO_3	dioxane	0
2	**L1**	$[Pd(allyl)Cl]_2$	Cs_2CO_3	dioxane	80
3	**L2**	$[Pd(allyl)Cl]_2$	Cs_2CO_3	dioxane	84
4	**L3**	$[Pd(allyl)Cl]_2$	Cs_2CO_3	dioxane	79
5	**L2**	$Pd(OAc)_2$	Cs_2CO_3	dioxane	68
6	**L2**	$PdCl_2$	Cs_2CO_3	dioxane	23
7	**L2**	$Pd(dba)_2$	Cs_2CO_3	dioxane	81
8	**L2**	$Pd_2(dba)_3$	Cs_2CO_3	dioxane	86
9	**L2**	$Pd_2(dba)_3$	K_2CO_3	dioxane	23
10	**L2**	$Pd_2(dba)_3$	Na_2CO_3	dioxane	4
11	**L2**	$Pd_2(dba)_3$	CsF	dioxane	60
12	**L2**	$Pd_2(dba)_3$	K_3PO_4	dioxane	54
13	**L2**	$Pd_2(dba)_3$	Cs_2CO_3	toluene	45
14	**L2**	$Pd_2(dba)_3$	Cs_2CO_3	DMA	30
15	**L2**	$Pd_2(dba)_3$	Cs_2CO_3	DMF	19
16	**L2**	$Pd_2(dba)_3$	Cs_2CO_3	DMSO	0

[a]Reaction conditions: **1a** (1.0 mmol), **2a** (1.5 mmol), **L** (2.0 mol %), Pd (1.0 mol %), base (2.0 mmol), solvent (2.0 mL), 90 °C, 15 h. [b]Isolated yields.

Scheme 1. Cross-Coupling of Chloromethylheteroarenes with Arylboronic acids[a]





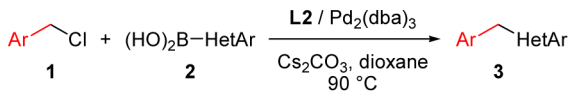
[a]Reaction conditions: **1** (1.0 mmol), **2** (1.5 mmol), **L2** (2.0 mol %), Pd (1.0 mol %), Cs_2CO_3 (2.0 mmol), dioxane (2.0 mL), 90 °C. [b]Organoboronic acid (2.0 mmol) was used. [c]100 °C. [d]$Pd(dba)_2$ (1.0 mol %) was used. [e]H_2O (0.2 mL) was added.

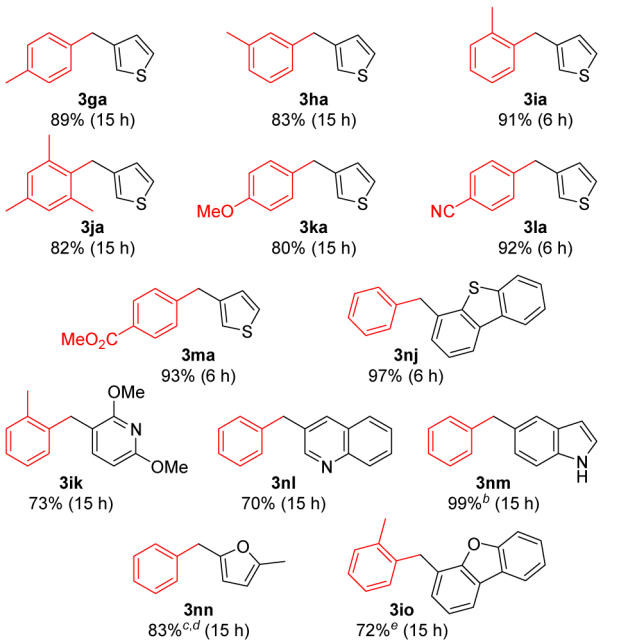
decrease in yield (**3ag–ah**). Then, the coupling reactions of a set of chloromethylheteroarenes with phenylboronic acid (**2i**) were carried out. In addition to indole-containing substrate **1b**, 2- and 3-(chloromethyl)thiophene (**1c–d**) afforded excellent yields (**3bi–di**). The cross-coupling using furan-type substrates **1e–f** proceeded with high efficiency (**3ei–fi**).

Influence of heteroarylboron reagents was investigated in heterocycle-containing diarylmethane synthesis with chloromethylarenes (Scheme 2). A series of chloromethylarenes was tested using 3-thiopheneboronic acid (**2a**) as a coupling partner. The benzyl chlorides bearing a methyl group at the 4- or 3-position were easily converted to give desired products **3ga–ha** with high yields. No significant decrease in yield was observed in the coupling reactions with sterically hindered chloromethylarenes (**3ia–ja**). Both the electron-rich and -poor benzyl chloride derivatives **1k–m** led to excellent yields of coupling products (**3ka–ma**). Subsequently, a set of heteroarylboron reagents were examined in the cross-coupling using benzyl chloride (**1n**) or 2-methylbenzyl chloride (**1i**). 4-Dibenzothienylboronic acid (**2j**) was also a good coupling partner to afford an excellent yield (**3nj**). The coupling reactions with heteroarylboronic acids bearing pyridine, quinoline, and indole moieties proceeded with sufficient efficiency (**3ik** and **3nl–nm**). In addition, furan derivative-containing organoboron reagents showed good reactivity (**3nn** and **3io**).

The catalytic synthesis of diheteroarylmethanes was examined with 1.0–3.0 mol % catalyst loading (Scheme 3). Sufficient catalytic activity for the cross-coupling with 2-chloro-5-(chloromethyl)pyridine (**1a**) was observed even in the use of organoboron reagents bearing an unprotected

Scheme 2. Cross-Coupling of Chloromethylarenes with Heteroarylboronic acids[a]





[a]Reaction conditions: **1** (1.0 mmol), **2** (1.5 mmol), **L2** (2.0 mol %), Pd (1.0 mol %), Cs_2CO_3 (2.0 mmol), dioxane (2.0 mL), 90 °C. [b]H_2O (0.2 mL) was added. [c]100 °C. [d]Pinacol boronate ester (1.5 mmol) was used. [e]Organoboronic acid (2.0 mmol) was used.

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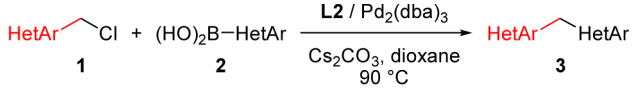
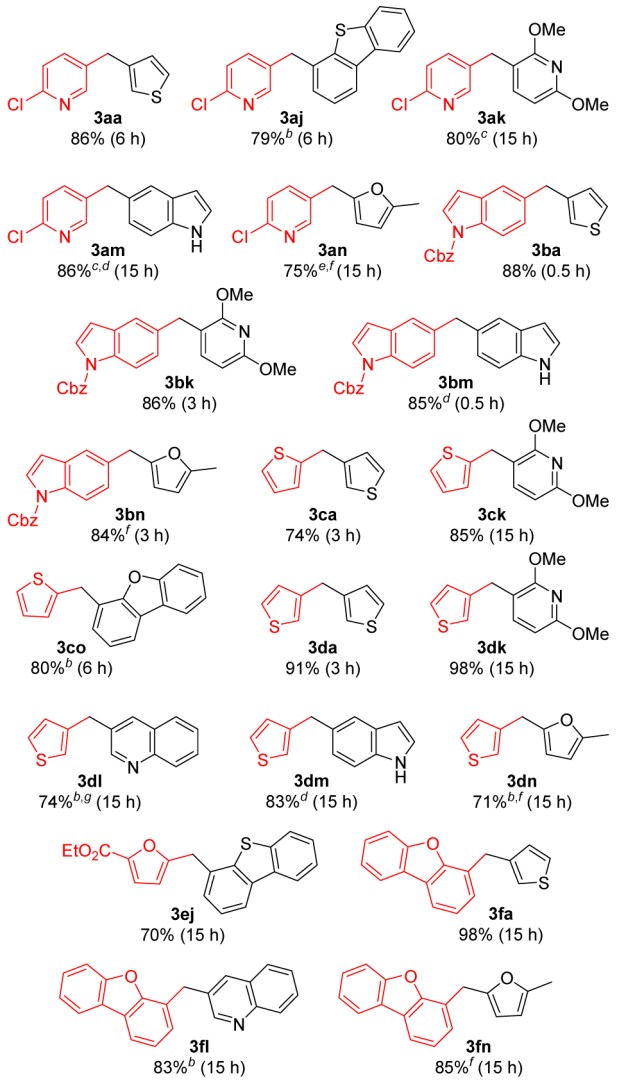
Scheme 3. Cross-Coupling of Chloromethylheteroarenes with Heteroarylboronic acids[a]





[a]Reaction conditions: **1** (1.0 mmol), **2** (1.5 mmol), **L2** (2.0 mol %), Pd (1.0 mol %), Cs_2CO_3 (2.0 mmol), dioxane (2.0 mL), 90 °C. [b]100 °C. [c]Organoboronic acid (2.0 mmol) was used. [d]H_2O (0.2 mL) was added. [e]**L2** (6.0 mol %) and Pd (3.0 mol %) were used. [f]Pinacol boronate ester (1.5 mmol) was used. [g]Cs_2CO_3 (2.5 mmol) was used.

indole (**3am**) in addition to thiophene, pyridine, and furan moieties (**3aa**, **3aj**–**ak**, and **3an**). *N*-Protected 5-(chloromethyl)-1*H*-indole **1b** was also applicable to the catalytic preparation of various diheteroarylmethanes, leading to high yields (**3ba**, **3bk**, and **3bm**–**bn**). In the coupling reactions with 2- and 3-(chloromethyl)thiophene (**1c**–**d**), broad substrate tolerance was achieved for sulfur-, nitrogen-, oxygen-containing heteroaromatic rings (**3ca**, **3ck**, **3co**, **3da**, and **3dk**–**dn**). Ethyl 5-(chloromethyl)furan-2-carboxylate (**1e**) as well as 4-(chloromethyl)dibenzofuran (**1f**) reacted with good to excellent efficiency in the presence of heteroaryl coupling partners (**3ej**, **3fa**, **3fl**, and **3fn**).

In summary, the catalytic synthesis of heterocycle-containing diarylmethanes through Suzuki–Miyaura cross-coupling was achieved with 1.0–3.0 mol % of the palladium/ether-imidazolium chloride system. This coupling process proceeded with sufficient catalytic activity and high substrate tolerance. The substrate combination of chloromethylarenes and heteroarylboron reagents as well as chloromethylheteroarenes and arylboronic acids gave desired coupling products with high efficiency. In addition, a variety of diheteroarylmethanes were successfully prepared from chloromethylheteroarenes and heteroarylboron reagents to afford good to excellent yields.

EXPERIMENTAL SECTION

General. All melting points are not corrected. IR spectra were expressed in cm^{-1}. ^1H and ^{13}C NMR spectra were taken at 400 and 100 MHz, respectively. Chemical shift values are expressed in ppm relative to internal or external TMS. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. A double-focusing magnetic sector mass spectrometer was used for low- and high-resolution EIMS. The products were isolated by silica gel column chromatography. All reagents were used as received. Dioxane was distilled from sodium benzophenone ketyl under argon. The preparations of 2-(chloromethyl)thiophene (**1c**)[16] and 3-(chloromethyl)thiophene (**1d**)[17] were conducted as reported before.

Benzyl 5-(Chloromethyl)-1*H*-indole-1-carboxylate (1b). This substrate was prepared using a reported method.[18] A stock solution (1.5 M) was prepared by mixing up $SOCl_2$ (1.43 g, 12 mmol) and 1*H*-benzotriazole (1.43 g, 12 mmol) in CH_2Cl_2 (8.0 mL). To the solution of benzyl 5-(hydroxylmethyl)-1*H*-indole-1-carboxylate (1.46 g, 5.2 mmol) in CH_2Cl_2 (52 mL), was added the stock solution (1.5 equiv) intermittently. The reaction mixture was stirred for 10 min at room temperature. The solid was filtered off and washed with CH_2Cl_2. The filtrate was washed with 10% HCl and H_2O followed by 2% NaOH solution. The organic layer was separated and dried over $MgSO_4$. Concentration and purification through silica gel column chromatography (hexane/AcOEt = 10/1) gave 1.26 g of **1b** (4.20 mmol, 81%) as white solids of mp 107–108 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 4.70 (s, 2H), 5.46 (s, 2H), 6.58 (d, J = 3.6 Hz, 1H), 7.35 (d, J = 8.8 Hz, 1H), 7.38–7.44 (m, 3H), 7.48 (d, J = 6.8 Hz, 2H), 7.59 (s, 1H), 7.65 (d, J = 3.6 Hz, 1H), 8.16 (d, J = 6.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 46.8 (CH_2), 68.8 (CH_2), 108.1 (CH), 115.5 (CH), 121.2 (CH), 125.3 (CH), 126.4 (CH), 128.5 (CH), 128.8 (CH), 130.7 (C), 132.3 (C), 134.9 (C), 135.1 (C), 150.7 (C). IR (ATR): 690, 720, 1390, 1740 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{17}H_{14}{}^{35}ClNO_2$: 299.0713; Found: 299.0708.

4-(Chloromethyl)dibenzofuran (1f). This substrate was prepared using a reported method.[19] To the solution of 4-(hydroxylmethyl)dibenzofuran (1.98 g, 10 mmol) in CH_2Cl_2 (15 mL), was added $SOCl_2$ (21.4 g, 180 mmol) slowly at room temperature. The reaction mixture was refluxed for 1 h. Then, concentration and purification through silica gel column chromatography (hexane/AcOEt = 100/1) gave 1.63 g of **1f** (7.52 mmol, 75%) as white solids of mp 74–75 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 4.99 (s, 2H), 7.34 (t, J = 7.4 Hz, 1H), 7.36 (t, J = 7.4 Hz, 1H), 7.46–7.51 (m, 2H), 7.62 (d, J = 8.4 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 40.3 (CH_2), 111.9 (CH), 120.8 (CH), 121.1 (CH), 121.5 (C), 123.0 (CH), 124.0 (C), 124.6 (C), 127.4 (CH), 127.6 (CH), 153.9 (C), 156.1 (C). IR (ATR): 690, 750, 1190 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{13}H_9{}^{35}ClO$: 216.0342; Found: 216.0341.

Typical Procedure for Catalytic Synthesis of Heterocycle-Containing Diarylmethanes through Suzuki–Miyaura Cross-Coupling. Under argon atmosphere, a reaction tube was charged with **L2** (8.66 mg, 0.02 mmol), $Pd_2(dba)_3$ (4.58 mg, 0.005 mmol), and Cs_2CO_3 (652 mg, 2.0 mmol). Then, dioxane (2.0 mL) was added. The mixture was stirred for 15 min at 80 °C. Then, 2-chloro-5-(chloromethyl)pyridine (**1a**) (162 mg, 1.0 mmol) and 3-

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thiopheneboronic acid (**2a**) (192 mg, 1.5 mmol) were added at room temperature. The reaction mixture was stirred at 90 °C for 6 h. Water and saturated Na_2CO_3 were added, and then the resulting mixture was extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4. Concentration and purification through silica gel column chromatography gave desired product **3aa**.

2-Chloro-5-(4-methylbenzyl)pyridine (3ab). Column chromatography (hexane/EtOAc = 20/1) gave 181 mg of the product (0.83 mmol, 83%) as white solids of mp 73−74 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.32 (s, 3H), 3.90 (s, 2H), 7.04 (d, J = 7.8 Hz, 2H), 7.12 (d, J = 7.8 Hz, 2H), 7.22 (d, J = 8.1 Hz, 1H), 7.41 (dd, J = 2.2, 8.1 Hz, 1H), 8.27 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.9 (CH_3), 37.7 (CH_2), 124.0 (CH), 128.6 (CH), 129.4 (CH), 135.7 (C), 136.1 (C), 136.3 (C), 139.1 (CH), 149.2 (C), 149.7 (CH). IR (ATR): 800, 1100, 1460 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{13}H_{12}{}^{35}ClN$: 217.0658; Found: 217.0651.

2-Chloro-5-(3-methylbenzyl)pyridine (3ac). Column chromatography (hexane/EtOAc = 20/1) gave 176 mg of the product (0.81 mmol, 81%) as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.32 (s, 3H), 3.91 (s, 2H), 6.95−6.96 (m, 2H), 7.05 (d, J = 7.5 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 7.23 (d, J = 8.3 Hz, 1H), 7.42 (dd, J = 2.4, 8.3 Hz, 1H), 8.27 (d, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.3 (CH_3), 38.0 (CH_2), 124.0 (CH), 125.7 (CH), 127.4 (CH), 128.6 (CH), 129.4 (CH), 135.5 (C), 138.5 (C), 139.0 (C), 139.1 (CH), 149.2 (C), 149.7 (CH). IR (ATR): 750, 780, 1020, 1100, 1460 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{13}H_{12}{}^{35}ClN$: 217.0658; Found: 217.0643.

2-Chloro-5-(2-methylbenzyl)pyridine (3ad). Column chromatography (hexane/EtOAc = 20/1) gave 174 mg of the product (0.80 mmol, 80%) as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.22 (s, 3H), 3.95 (s, 2H), 7.06−7.08 (m, 1H), 7.15−7.23 (m, 4H), 7.34 (dd, J = 2.4, 8.3 Hz, 1H), 8.23−8.24 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.5 (CH_3), 35.8 (CH_2), 123.9 (CH), 126.2 (CH), 127.0 (CH), 129.7 (CH), 130.6 (CH), 134.8 (C), 136.3 (C), 137.0 (C), 138.9 (CH), 149.1 (C), 149.7 (CH). IR (ATR): 740, 1100, 1460 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{13}H_{12}{}^{35}ClN$: 217.0658; Found: 217.0643.

2-Chloro-5-(4-methoxylbenzyl)pyridine (3ae). Column chromatography (hexane/EtOAc = 20/1) gave 194 mg of the product (0.83 mmol, 83%) as white solids of mp 46−47 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.79 (s, 3H), 3.89 (s, 2H), 6.83−6.87 (m, 2H), 7.05−7.09 (m, 2H), 7.22 (d, J = 8.3 Hz, 1H), 7.41 (dd, J = 2.4, 8.3 Hz, 1H), 8.25 (d, J = 2.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 37.3 (CH_2), 55.2 (CH_3), 114.2 (CH), 124.0 (CH), 129.7 (CH), 131.2 (C), 135.9 (C), 139.1 (CH), 149.2 (C), 149.6 (CH), 158.4 (C). IR (ATR): 800, 1100, 1250, 1510 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{13}H_{12}{}^{35}ClNO$: 233.0607; Found: 233.0606.

2-Chloro-5-[4-(methylthio)benzyl]pyridine (3af). Column chromatography (hexane/EtOAc = 10/1) gave 220 mg of the product (0.88 mmol, 88%) as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.47 (s, 3H), 3.91 (s, 2H), 7.07 (d, J = 8.3 Hz, 2H), 7.19−7.24 (m, 3H), 7.41 (dd, J = 2.4, 8.3 Hz, 1H), 8.26 (d, J = 2.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.9 (CH_3), 37.5 (CH_2), 124.0 (CH), 127.0 (CH), 129.2 (CH), 135.3 (C), 136.0 (C), 136.7 (C), 139.1 (CH), 149.3 (C), 149.6 (CH). IR (ATR): 790, 1090, 1460 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{13}H_{12}{}^{35}ClNS$: 249.0379; Found: 249.0365.

5-(3-Acetylbenzyl)-2-chloropyridine (3ag). Column chromatography (hexane/EtOAc = 5/1) gave 187 mg of the product (0.76 mmol, 76%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.59 (s, 3H), 4.02 (s, 2H), 7.24−7.26 (m, 1H), 7.35 (d, J = 7.6 Hz, 1H), 7.40−7.44 (m, 2H), 7.79 (s, 1H), 7.83 (d, J = 7.6 Hz, 1H), 8.28 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.6 (CH_3), 38.0 (CH_2), 124.1 (CH), 127.0 (CH), 128.3 (CH), 129.0 (CH), 133.4 (CH), 134.8 (C), 137.5 (C), 139.1 (CH), 139.8 (C), 149.6 (C), 149.7 (CH), 198.0 (C). IR (ATR): 790, 1100, 1270, 1460, 1680 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{14}H_{12}{}^{35}ClNO$: 245.0607; Found: 245.0618.

2-Chloro-5-(3-nitrobenzyl)pyridine (3ah). Column chromatography (hexane/EtOAc = 5/1) gave 179 mg of the product (0.72 mmol, 72%) as yellow solids of mp 82−83 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.08 (s, 2H), 7.29 (d, J = 8.3 Hz, 1H), 7.45 (dd, J = 2.2, 8.3 Hz, 1H), 7.50−7.53 (m, 2H), 8.05 (s, 1H), 8.11−8.14 (m, 1H), 8.29 (d, J = 2.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 37.7 (CH_2), 121.9 (CH), 123.5 (CH), 124.4 (CH), 129.8 (CH), 133.8 (C), 134.9 (CH), 139.1 (CH), 141.2 (C), 148.4 (C), 149.7 (CH), 150.0 (C). IR (ATR): 730, 1100, 1340, 1460, 1520 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{12}H_9{}^{35}ClN_2O_2$: 248.0353; Found: 248.0353.

5-Benzyl-1-(benzyloxycarbonyl)indole (3bi). Column chromatography (hexane/EtOAc = 20/1) gave 304 mg of the product (0.89 mmol, 89%) as white solids of mp 70−71 °C. ^{1}H NHR (400 MHz, $CDCl_3$): δ 4.06 (s, 2H), 5.44 (s, 2H), 6.52 (d, J = 3.6 Hz, 1H), 7.15−7.20 (m, 4H), 7.25−7.29 (m, 2H), 7.36−7.43 (m, 4H), 7.46−7.48 (m, 2H), 7.60 (d, J = 3.6 Hz, 1H), 8.07 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 41.7 (CH_2), 68.5 (CH_2), 108.0 (CH), 115.0 (CH), 121.0 (CH), 125.7 (CH), 125.8 (CH), 126.0 (CH), 128.3 (CH), 128.4 (CH), 128.6 (CH), 128.7 (CH), 128.9 (CH), 130.7 (C), 133.8 (C), 135.1 (C), 136.0 (C), 141.5 (C), 150.7 (C). IR (ATR): 690, 720, 760, 1730 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{23}H_{19}NO_2$: 341.1416; Found: 341.1421.

2-Benzylthiophene (3ci).[20] Column chromatography (hexane/Et_2O = 200/1) gave 159 mg of the product (0.91 mmol, 91%) as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.15 (s, 2H), 6.79−6.81 (m, 1H), 6.91−6.93 (m, 1H), 7.14 (d, J = 4.9 Hz, 1H), 7.21−7.32 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.9 (CH_2), 123.9 (CH), 125.1 (CH), 126.4 (CH), 126.8 (CH), 128.55 (CH), 128.60 (CH), 140.3 (C), 144.0 (C). IR (ATR): 690, 850, 1450, 1490 cm^{-1}. EIMS m/z: 174 (M^+).

3-Benzylthiophene (3di).[20] Column chromatography (hexane/Et_2O = 200/1) gave 164 mg of the product (0.94 mmol, 94%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.98 (s, 2H), 6.90−6.91 (m, 2H), 7.19−7.31 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 36.5 (CH_2), 121.2 (CH), 125.6 (CH), 126.1 (CH), 128.47 (CH), 128.50 (CH), 128.7 (CH), 140.5 (C), 141.4 (C). IR (ATR): 700, 830, 1450, 1490 cm^{-1}. EIMS m/z: 174 (M^+).

2-Benzyl-5-(ethoxycarbonyl)furan (3ei).[21] Column chromatography (hexane/EtOAc = 20/1) gave 189 mg of the product (0.82 mmol, 82%) as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (t, J = 7.1 Hz, 3H), 4.04 (s, 2H), 4.34 (q, J = 7.1 Hz, 2H), 6.04−6.06 (m, 1H), 7.08 (d, J = 3.4 Hz, 1H), 7.23−7.27 (m, 3H), 7.30−7.34 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2 (CH_3), 34.6 (CH_2), 60.6 (CH_2), 108.7 (CH), 118.9 (CH), 126.7 (CH), 128.5 (CH), 128.7 (CH), 136.6 (C), 143.6 (C), 158.7 (C), 159.4 (C). IR (ATR): 760, 1130, 1300, 1520, 1710 cm^{-1}. EIMS m/z: 230 (M^+).

4-Benzyldibenzofuran (3fi). Column chromatography (hexane/Et_2O = 200/1) gave 257 mg of the product (0.99 mmol, 99%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.34 (s, 2H), 7.18−7.35 (m, 8H), 7.45 (dt, J = 1.2, 8.4 Hz, 1H), 7.59 (d, J = 8.4 Hz, 1H), 7.81 (dd, J = 1.2, 7.3 Hz, 1H), 7.93−7.95 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.6 (CH_2), 111.7 (CH), 118.6 (CH), 120.7 (CH), 122.6 (CH), 122.8 (CH), 124.0 (C), 124.5 (C), 125.1 (C), 126.2 (CH), 126.9 (CH), 127.6 (CH), 128.4 (CH), 128.9 (CH), 140.0 (C), 154.6 (C), 156.1 (C). IR (ATR): 910, 1180, 1450 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{19}H_{14}O$: 258.1045; Found: 258.1032.

3-(4-Methylbenzyl)thiophene (3ga).[4a] Column chromatography (hexane/Et_2O = 200/1) gave 168 mg of the product (0.89 mmol, 89%) as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.32 (s, 3H), 3.94 (s, 2H), 6.90−6.91 (m, 2H), 7.09−7.11 (m, 4H), 7.23−7.25 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0 (CH_3), 36.1 (CH_2), 121.0 (CH), 125.5 (CH), 128.4 (CH), 128.6 (CH), 129.1 (CH), 135.6 (C), 137.5 (C), 141.7 (C). IR (ATR): 740, 770, 1510 cm^{-1}. EIMS m/z: 188 (M^+).

3-(3-Methylbenzyl)thiophene (3ha).[4a] Column chromatography (hexane/Et_2O = 200/1) gave 156 mg of the product (0.83 mmol, 83%) as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.31 (s, 3H), 3.94 (s, 2H), 6.91−6.92 (m, 2H), 6.99−7.03 (m, 3H), 7.16−7.20 (m, 1H), 7.23−7.25 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.4 (CH_3), 36.4 (CH_2), 121.1 (CH), 125.5 (CH), 125.7 (CH),

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126.9 (CH), 128.3 (CH), 128.4 (CH), 129.5 (CH), 138.0 (C), 140.5 (C), 141.6 (C). IR (ATR): 710, 730, 770, 1490, 1610 cm^{-1}. EIMS *m/z*: 188 (M^+).

3-(2-Methylbenzyl)thiophene (3ia).[4a] Column chromatography (hexane/Et_2O = 200/1) gave 171 mg of the product (0.91 mmol, 91%) as yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 2.26 (s, 3H), 3.95 (s, 2H), 6.81 (d, *J* = 1.5 Hz, 1H), 6.88 (d, *J* = 4.1 Hz, 1H), 7.12−7.16 (m, 4H), 7.24−7.26 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.4 (CH_3), 34.2 (CH_2), 121.0 (CH), 125.4 (CH), 126.0 (CH), 126.4 (CH), 128.3 (CH), 129.5 (CH), 130.2 (CH), 136.3 (C), 138.7 (C), 140.8 (C). IR (ATR): 740, 840, 1460, 1490 cm^{-1}. EIMS *m/z*: 188 (M^+).

3-(2,4,6-Trimethylbenzyl)thiophene (3ja).[22] Column chromatography (hexane/Et_2O = 200/1) gave 177 mg of the product (0.82 mmol, 82%) as yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 2.23 (s, 6H), 2.28 (s, 3H), 3.94 (s, 2H), 6.63 (s, 1H), 6.86−6.88 (m, 3H), 7.22 (dd, *J* = 2.9, 4.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.9 (CH_3), 20.8 (CH_3), 30.0 (CH_2), 120.1 (CH), 125.2 (CH), 128.0 (CH), 128.9 (CH), 134.0 (C), 135.5 (C), 136.5 (C), 140.6 (C). IR (ATR): 760, 830, 850, 1440, 1480 cm^{-1}. EIMS *m/z*: 216 (M^+).

3-(4-Methoxybenzyl)thiophene (3ka).[4a] Column chromatography (hexane/Et_2O = 200/1) gave 163 mg of the product (0.80 mmol, 80%) as yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 3.79 (s, 3H), 3.92 (s, 2H), 6.82−6.86 (m, 2H), 6.89 (d, *J* = 3.9 Hz, 2H), 7.10−7.14 (m, 2H), 7.23−7.25 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.6 (CH_2), 55.1 (CH_3), 113.8 (CH), 120.9 (CH), 125.5 (CH), 128.3 (CH), 129.6 (CH), 132.7 (C), 142.0 (C), 158.0 (C). IR (ATR): 780, 1030, 1240, 1510 cm^{-1}. EIMS *m/z*: 204 (M^+).

3-(4-Cyanobenzyl)thiophene (3la). Column chromatography (hexane/EtOAc = 10/1) gave 183 mg of the product (0.92 mmol, 92%) as orange oil. ^1H NMR (400 MHz, $CDCl_3$): δ 4.04 (s, 2H), 6.87 (dd, *J* = 1.2, 4.8 Hz, 1H), 6.95−6.96 (m, 1H), 7.28−7.31 (m, 3H), 7.58 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 36.3 (CH_2), 109.9 (C), 118.8 (C), 121.8 (CH), 126.1 (CH), 128.0 (CH), 129.3 (CH), 132.1 (CH), 139.3 (C), 146.1 (C). IR (ATR): 780, 1410, 1610, 2230 cm^{-1}. HRMS (EI) *m/z*: (M^+) Calcd for $C_{12}H_9NS$: 199.0456; Found: 199.0442.

3-(4-Methoxycarbonylbenzyl)thiophene (3ma). Column chromatography (hexane/EtOAc = 10/1) gave 216 mg of the product (0.93 mmol, 93%) as colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 3.90 (s, 3H), 4.03 (s, 2H), 6.89 (d, *J* = 4.6 Hz, 1H), 6.93 (s, 1H), 7.26−7.28 (m, 3H), 7.97 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 36.4 (CH_2), 51.9 (CH_3), 121.5 (CH), 125.8 (CH), 128.1 (C), 128.2 (CH), 128.7 (CH), 129.7 (CH), 140.2 (C), 145.9 (C), 166.9 (C). IR (ATR): 710, 1270, 1710 cm^{-1}. HRMS (EI) *m/z*: (M^+) Calcd for $C_{13}H_{12}O_2S$: 232.0558; Found: 232.0555.

4-Benzyldibenzothiophene (3nj). Column chromatography (hexane/Et_2O = 200/1) gave 266 mg of the product (0.97 mmol, 97%) as white solids of mp 104−105 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 4.25 (s, 2H), 7.20−7.30 (m, 6H), 7.40−7.46 (m, 3H), 7.82−7.84 (m, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 8.13−8.16 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 41.0 (CH_2), 119.7 (CH), 121.7 (CH), 122.8 (CH), 124.4 (CH), 124.8 (CH), 126.5 (CH), 126.6 (CH), 127.1 (CH), 128.5 (CH), 129.1 (CH), 135.4 (C), 135.9 (C), 136.0 (C), 139.0 (C), 139.2 (C), 139.4 (C). IR (ATR): 700, 750, 1400, 1440 cm^{-1}. HRMS (EI) *m/z*: (M^+) Calcd for $C_{19}H_{14}S$: 274.0816; Found: 274.0802.

2,6-Dimethoxy-3-(2-methylbenzyl)pyridine (3ik). Column chromatography (hexane/benzene = 1/1) gave 178 mg of the product (0.73 mmol, 73%) as colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 2.24 (s, 3H), 3.81 (s, 2H), 3.90 (s, 3H), 3.96 (s, 3H), 6.18 (d, *J* = 8.0 Hz, 1H), 7.01 (d, *J* = 8.0 Hz, 1H), 7.04−7.06 (m, 1H), 7.11−7.17 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.4 (CH_3), 31.9 (CH_2), 53.3 (CH_3), 53.4 (CH_3), 100.0 (CH), 113.5 (C), 125.9 (CH), 126.3 (CH), 129.6 (CH), 130.1 (CH), 136.6 (C), 138.2 (C), 140.5 (CH), 160.1 (C), 161.4 (C). IR (ATR): 1020, 1590, 1600 cm^{-1}. HRMS (EI) *m/z*: (M^+) Calcd for $C_{15}H_{17}NO_2$: 243.1259; Found: 243.1254.

3-Benzylquinoline (3nl). Column chromatography (hexane/EtOAc = 5/1) gave 153 mg of the product (0.70 mmol, 70%) as brown solids of mp 64−65 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 4.17 (s, 2H), 7.22−7.26 (m, 3H), 7.30−7.34 (m, 2H), 7.51 (t, *J* = 7.3 Hz, 1H), 7.64−7.69 (m, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.88 (d, *J* = 0.7 Hz, 1H), 8.08 (d, *J* = 8.1 Hz, 1H), 8.82 (d, *J* = 1.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 39.2 (CH_2), 126.5 (CH), 126.6 (CH), 127.4 (CH), 128.1 (C), 128.7 (CH), 128.8 (CH), 128.9 (CH), 129.1 (CH), 133.8 (C), 134.8 (CH), 139.6 (C), 146.9 (C), 152.1 (CH). IR (ATR): 710, 740, 1490 cm^{-1}. HRMS (EI) *m/z*: (M^+) Calcd for $C_{16}H_{13}N$: 219.1048; Found: 219.1053.

5-Benzylindole (3nm). Column chromatography (hexane/EtOAc = 10/1) gave 205 mg of the product (0.99 mmol, 99%) as yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 4.08 (s, 2H), 6.48−6.49 (m, 1H), 7.03 (dd, *J* = 1.5, 8.5 Hz, 1H), 7.16−7.31 (m, 7H), 7.45 (d, *J* = 0.7 Hz, 1H), 8.05 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 42.0 (CH_2), 102.2 (CH), 111.0 (CH), 120.5 (CH), 123.4 (CH), 124.4 (CH), 125.8 (CH), 128.0 (C), 128.3 (CH), 128.9 (CH), 132.4 (C), 134.3 (C), 142.3 (C). IR (ATR): 700, 720, 1470, 1490, 3410 cm^{-1}. HRMS (EI) *m/z*: (M^+) Calcd for $C_{15}H_{13}N$: 207.1048; Found: 207.1044.

2-Benzyl-5-methylfuran (3nn).[23] After the reaction mixture was stirred for 15 h at 100 °C and cooled to room temperature, CH_2Cl_2 and 1 M NaOH were added. The resulting mixture was stirred for 1 h at room temperature and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4. Concentration and purification through column chromatography (hexane/EtOAc = 200/1) gave 143 mg of the product (0.83 mmol, 83%) as colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 2.24 (s, 3H), 3.91 (s, 2H), 5.85−5.87 (m, 2H), 7.20−7.32 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.5 (CH_3), 34.5 (CH_2), 106.0 (CH), 106.9 (CH), 126.3 (CH), 128.4 (CH), 128.7 (CH), 138.5 (C), 151.0 (C), 152.7 (C). IR (ATR): 690, 710, 1450, 1490 cm^{-1}. EIMS *m/z*: 172 (M^+).

4-(2-Methylbenzyl)dibenzofuran (3io). Column chromatography (hexane/Et_2O = 200/1) gave 196 mg of the product (0.72 mmol, 72%) as white solids of mp 74−75 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 2.32 (s, 3H), 4.34 (s, 2H), 7.03 (d, *J* = 7.8 Hz, 1H), 7.13−7.25 (m, 5H), 7.34 (t, *J* = 7.8 Hz, 1H), 7.44−7.48 (m, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.96 (d, *J* = 7.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.6 (CH_3), 32.9 (CH_2), 111.7 (CH), 118.5 (CH), 120.7 (CH), 122.6 (CH), 122.8 (CH), 123.8 (C), 124.4 (C), 124.6 (C), 126.0 (CH), 126.6 (CH), 127.0 (CH), 127.2 (CH), 129.9 (CH), 130.3 (CH), 136.8 (C), 137.7 (C), 154.6 (C), 156.1 (C). IR (ATR): 740, 1190, 1420 cm^{-1}. HRMS (EI) *m/z*: (M^+) Calcd for $C_{20}H_{16}O$: 272.1201; Found: 272.1204.

2-Chloro-5-(thiophen-3-ylmethyl)pyridine (3aa). Column chromatography (hexane/EtOAc = 20/1) gave 180 mg of the product (0.86 mmol, 86%) as yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 3.96 (2H, s), 6.87 (dd, *J* = 1.2, 4.9 Hz, 1H), 6.93−6.95 (m, 1H), 7.25 (d, *J* = 8.6 Hz, 1H), 7.29 (dd, *J* = 2.9, 4.9 Hz, 1H), 7.45 (dd, *J* = 2.4, 8.6 Hz, 1H), 8.27 (dd, *J* = 0.5, 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 32.6 (CH_2), 121.6 (CH), 123.8 (CH), 126.2 (CH), 127.8 (CH), 134.8 (C), 138.9 (CH), 139.3(C), 149.1 (C), 149.4 (CH). IR (ATR): 780, 1020, 1100, 1460 cm^{-1}. HRMS (EI) *m/z*: (M^+) Calcd for $C_{10}H_8{}^{35}ClNS$: 209.0066; Found: 209.0046.

2-Chloro-5-(dibenzothiophen-4-ylmethyl)pyridine (3aj). Column chromatography (hexane/EeOAc = 20/1) gave 245 mg of the product (0.79 mmol, 79%) as yellow solids of mp 101−103 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 4.20 (s, 2H), 7.22 (t, *J* = 8.4 Hz, 2H), 7.42−7.50 (m, 4H), 7.82−7.85 (m, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 8.13−8.16 (m, 1H), 8.39 (d, *J* = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 37.3 (CH_2), 120.2 (CH), 121.8 (CH), 122.7 (CH), 124.0 (CH), 124.6 (CH), 125.0 (CH), 126.9 (CH), 127.0 (CH), 133.4 (C), 135.7 (C), 136.1 (C), 138.9 (C), 139.1 (CH), 149.7 (C), 150.0 (CH). IR (ATR): 740, 1100, 1460 cm^{-1}. HRMS (EI) *m/z*: (M^+) Calcd for $C_{18}H_{12}ClNS$: 309.0379; Found: 309.0362.

3-[(6-Chloropyridin-3-yl)methyl]-2,6-dimethoxypyridine (3ak). Column chromatography (hexane/EtOAc = 20/1) gave 212 mg of the product (0.80 mmol, 80%) as colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 3.79 (s, 2H), 3.90 (s, 3H), 3.92 (s, 3H), 6.25 (d, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.44 (dd, *J* = 2.4, 8.0 Hz, 1H), 8.26 (d, *J* = 2.4 Hz, 1H). ^{13}C NMR

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(100 MHz, $CDCl_3$): δ 31.5 (CH_2), 53.3 (CH_3), 53.5 (CH_3), 100.5 (CH), 112.5 (C), 123.8 (CH), 135.1 (C), 138.9 (CH), 141.0 (CH), 149.0 (C), 149.7 (CH), 160.1 (C), 162.0 (C). IR (ATR): 800, 1020, 1250, 1320 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{13}H_{13}{}^{35}ClN_2O_2$: 264.0666; Found: 264.0664.

5-[(6-Chloropyridin-3-yl)methyl]indole (3am). Column chromatography (hexane/EtOAc = 10/1) gave 209 mg of the product (0.86 mmol, 86%) as pink solids of mp 140−141 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 4.04 (s, 2H), 6.49−6.51 (m, 1H), 6.97 (dd, J = 1.7, 8.3 Hz, 1H), 7.19−7.22 (m, 2H), 7.33 (d, J = 8.3 Hz, 1H), 7.42−7.43 (m, 1H), 7.45 (dd, J = 2.4, 8.3 Hz, 1H), 8.23 (brs, 1H), 8.30−8.31 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 38.3 (CH_2), 102.3 (CH), 111.3 (CH), 120.6 (CH), 123.0 (CH), 124.0 (CH), 124.8 (CH), 128.2 (C), 130.6 (C), 134.6 (C), 136.7 (C), 139.3 (CH), 149.0 (C), 149.6 (CH). IR (ATR): 730, 760, 1090, 1100, 3240 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{14}H_{11}ClN_2$: 242.0611; Found: 242.0597.

2-Chloro-5-[(5-methylfuran-2-yl)methyl]pyridine (3an). After the reaction mixture was stirred for 15 h at 90 °C and cooled to room temperature, CH_2Cl_2 and 1 M NaOH were added. The resulting mixture was stirred for 1 h at room temperature and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4. Concentration and purification through column chromatography (hexane/EtOAc = 20/1) gave 156 mg of the product (0.75 mmol, 75%) as orange oil. ^1H NMR (400 MHz, $CDCl_3$): δ 2.24 (s, 3H), 3.89 (s, 2H), 5.86−5.87 (m, 1H), 5.90 (d, J = 2.9 Hz, 1H). 7.26 (d, J = 8.1 Hz, 1H), 7.52 (dd, J = 2.4, 8.1 Hz, 1H), 8.28 (d, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.3 (CH_3), 30.8 (CH_2), 106.0 (CH), 107.4 (CH), 123.8 (CH), 132.8 (C), 139.0 (CH), 149.3 (C), 149.5 (CH), 150.3 (C), 151.4 (C). IR (ATR): 780, 1020, 1100, 1460 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{11}H_{10}ClNO$: 207.0451; Found: 207.0449.

1-Benzyloxycarbonyl-5-(thiophen-3-ylmethyl)indole (3ba). Column chromatography (hexane/EtOAc = 20/1) gave 305 mg of the product (0.88 mmol, 88%) as white solids of mp 60−61 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 4.06 (s, 2H), 5.44 (s, 2H), 6.53 (d, J = 3.4 Hz, 1H), 6.90−6.92 (m, 2H), 7.17 (d, J = 8.6 Hz, 1H), 7.23−7.25 (m, 1H), 7.37−7.42 (m, 4H), 7.47 (d, J = 6.4 Hz, 2H), 7.60 (d, J = 3.4 Hz, 1H), 8.09 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 36.4 (CH_2), 68.6 (CH_2), 108.1 (CH), 115.0 (CH), 120.8 (CH), 121.1 (CH), 125.5 (CH), 125.6 (CH), 125.7 (CH), 128.45 (CH), 128.47 (CH), 128.7 (CH), 128.8 (CH), 130.8 (C), 133.8 (C), 135.1 (C), 135.4 (C), 142.0 (C), 150.8 (C). IR (ATR): 750, 1030, 1730 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{21}H_{17}NO_2S$: 347.0980; Found: 347.0983.

1-Benzyloxycarbonyl-5-[(2,6-dimethoxypyridin-3-yl)-methyl]indole (3bk). Column chromatography (hexane/EtOAc = 20/1) gave 346 mg of the product (0.86 mmol, 86%) as white solids of mp 105−106 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 3.89 (s, 3H), 3.92 (s, 2H), 3.94 (s, 3H), 5.44 (s, 2H), 6.20 (d, J = 8.0 Hz, 1H), 6.52 (d, J = 3.7 Hz, 1H), 7.16 (d, J = 8.0 Hz, 1H), 7.22 (d, J = 8.0 Hz, 1H), 7.35 (s, 1H), 7.37−7.43 (m, 3H), 7.46−7.48 (m, 2H), 7.59 (d, J = 3.7 Hz, 1H), 8.05 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 34.4 (CH_2), 53.3 (CH_3), 53.4 (CH_3), 68.6 (CH_2), 100.1 (CH), 108.1 (CH), 114.9 (C), 115.0 (CH), 120.8 (CH), 125.7 (CH), 128.4 (CH), 128.6 (CH), 128.7 (CH), 130.7 (C), 133.7 (C), 135.1 (C), 135.5 (C), 141.1 (CH), 150.9 (C), 160.1 (C), 161.5 (C). IR (ATR): 760, 1030, 1250, 1740 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{24}H_{22}N_2O_4$: 402.1580; Found: 402.1576.

1-Benzyloxycarbonyl-5-(indol-5-ylmethyl)indole (3bm). Column chromatography (hexane/EtOAc = 10/1) gave 323 mg of the product (0.85 mmol, 85%) as pink solids of mp 140−141 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 4.16 (s, 2H), 5.42 (s, 2H), 6.46−6.47 (m, 1H), 6.50 (d, J = 3.6 Hz, 1H), 7.03 (d, J = 8.3 Hz, 1H), 7.15 (t, J = 2.8 Hz, 1H), 7.20 (d, J = 8.3 Hz, 1H), 7.28 (d, J = 8.3 Hz, 1H), 7.34−7.41 (m, 4H), 7.45−7.46 (m, 3H), 7.58 (d, J = 3.6 Hz, 1H), 8.05 (brs, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 41.8 (CH_2), 68.5 (CH_2), 102.2 (CH), 108.2 (CH), 110.9 (CH), 114.9 (CH), 120.4 (CH), 121.0 (CH), 123.4 (CH), 124.3 (CH), 125.5 (CH), 125.8 (CH), 128.0 (C), 128.3 (CH), 128.6 (CH), 128.7 (CH), 130.7 (C), 132.9 (C), 133.6 (C), 134.3 (C), 135.1 (C), 137.2 (C), 150.9 (C). IR (ATR): 720, 1720, 3380 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{25}H_{20}N_2O_2$: 380.1525; Found: 380.1526.

1-Benzyloxycarbonyl-5-(5-methylfuran-2-ylmethyl)indole (3bn). After the reaction mixture was stirred for 3 h at 90 °C and cooled to room temperature, CH_2Cl_2 and 1 M NaOH were added. The resulting mixture was stirred for 1 h at room temperature and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4. Concentration and purification through column chromatography (hexane/EtOAc = 20/1) gave 290 mg of the product (0.84 mmol, 84%) as yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 2.24 (s, 3H), 4.00 (s, 2H), 5.44 (s, 2H), 5.84−5.86 (m, 2H), 6.54 (d, J = 3.4 Hz, 1H), 7.20 (d, J = 8.0 Hz, 1H), 7.35−7.43 (m, 4H), 7.47 (d, J = 6.4 Hz, 2H), 7.60 (d. J = 3.4 Hz, 1H), 8.08 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.4 (CH_3), 34.3 (CH_2), 68.4 (CH_2), 105.9 (CH), 106.7 (CH), 108.0 (CH), 114.9 (CH), 120.7 (CH), 125.4 (CH), 125.6 (CH), 128.2 (CH), 128.5 (CH), 128.6 (CH), 130.6 (C), 133.1 (C), 133.9 (C), 135.0 (C), 150.6 (C), 150.7 (C), 153.1 (C). IR (ATR): 700, 750, 1730 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{22}H_{19}NO_3$: 345.1365; Found: 345.1375.

2-(Thiophen-3-ylmethyl)thiophene (3ca). Column chromatography (hexane/Et_2O = 200/1) gave 133 mg of the product (0.74 mmol, 74%) as yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 4.17 (s, 2H), 6.81−6.82 (m, 1H), 6.91−6.93 (m, 1H), 6.98 (d, J = 4.6 Hz, 1H), 7.02 (s, 1H), 7.14 (d, J = 5.1 Hz, 1H), 7.25−7.27 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.6 (CH_2), 121.4 (CH), 123.8 (CH), 125.0 (CH), 125.7 (CH), 126.8 (CH), 128.1 (CH), 140.6 (C), 143.4 (C). IR (ATR): 690, 850 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_9H_8S_2$: 180.0067; Found: 180.0056.

2,6-Dimethoxy-3-(thiophen-2-ylmethyl)pyridine (3ck). Column chromatography (hexane/benzene = 1/1) gave 200 mg of the product (0.85 mmol, 85%) as colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 3.90 (s, 3H), 3.96 (s, 3H), 4.02 (s, 2H), 6.24 (d, J = 8.0 Hz, 1H), 6.80−6.81 (m, 1H), 6.91 (dd, J = 3.4, 5.2 Hz, 1H), 7.11 (dd, J = 1.0, 5.2 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.8 (CH_2), 53.2 (CH_3), 53.4 (CH_3), 100.2 (CH), 113.8 (C), 123.6 (CH), 124.9 (CH), 126.7 (CH), 140.8 (CH), 143.5 (C), 160.1 (C), 161.7 (C). IR (ATR): 690, 1020, 1250, 1420 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{12}H_{13}NO_2S$: 235.0667; Found: 235.0662.

4-(Thiophen-2-ylmethyl)dibenzofuran (3co). Column chromatography (hexane/Et_2O = 200/1) gave 211 mg of the product (0.80 mmol, 80%) as yellow oil. ^1H NMR (400 MHz, $CDCl_3$): δ 4.53 (s, 2H), 6.92−6.94 (m, 2H), 7.14 (dd, J = 1.5, 4.9 Hz, 1H), 7.26−7.36 (m, 3H), 7.44−7.48 (m, 1H), 7.60 (d, J = 8.3 Hz, 1H), 7.84 (dd, J = 2.4, 6.4, Hz, 1H), 7.95 (d, J = 8.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 29.7 (CH_2), 111.7 (CH), 119.0 (CH), 120.7 (CH), 122.6 (CH), 122.9 (CH), 123.9 (CH), 124.1 (C), 124.46 (C), 124.51 (C), 125.6 (CH), 126.8 (CH), 127.0 (CH), 127.3 (CH), 142.5 (C), 154.2 (C), 156.1 (C). IR (ATR): 760, 830, 1420, 1450 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{17}H_{12}OS$: 264.0609; Found: 264.0587.

3-(Thiophen-3-ylmethyl)thiophene (3da). Column chromatography (hexane/Et_2O = 200/1) gave 164 mg of the product (0.91 mmol, 91%) as colorless solids of mp 29−30 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 3.99 (s, 2H), 6.93−6.96 (m, 4H), 7.25−7.27 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.0 (CH_2), 121.1 (CH), 125.6 (CH), 128.3 (CH), 141.0 (C). IR (ATR): 770, 800, 830 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_9H_8S_2$: 180.0067; Found: 180.0055.

2,6-Dimethoxy-3-(thiophen-3-ylmethyl)pyridine (3dk). Column chromatography (hexane/benzene = 1/1) gave 231 mg of the product (0.98 mmol, 98%) as colorless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 3.84 (s, 2H), 3.90 (s, 3H), 3.95 (s, 3H), 6.22 (d, J = 7.8 Hz, 1H), 6.92−6.93 (m, 2H), 7.22−7.26 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 29.2 (CH_2), 53.2 (CH_3), 53.4 (CH_3), 100.1 (CH), 113.9 (C), 121.0 (CH), 125.3 (CH), 128.4 (CH), 140.9 (CH), 160.1 (C), 161.5 (C). IR (ATR): 770, 1020, 1240, 1420 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{12}H_{13}NO_2S$: 235.0667; Found: 235.0654.

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3-(Thiophen-3-ylmethyl)quinoline (3dl). Column chromatography (hexane/EtOAc = 2/1) gave 167 mg of the product (0.74 mmol, 74%) as white solids of mp 60−61 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.18 (s, 2H), 6.95 (dd, J= 1.2, 4.8 Hz, 1H), 6.99−7.00 (m, 1H), 7.30 (dd, J = 2.9, 4.8 Hz, 1H), 7.50−7.55 (m, 1H), 7.65−7.70 (m, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.91 (d, J = 1.2 Hz, 1H), 8.09 (d, J = 8.1 Hz, 1H), 8.83 (d, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 33.8 (CH_2), 121.8 (CH), 126.1 (CH), 126.6 (CH), 127.4 (CH), 128.1 (C), 128.2 (CH), 128.8 (CH), 129.1 (CH), 133.2 (C), 134.6 (CH), 140.0 (C), 147.0 (C), 152.0 (CH). IR (ATR): 750, 1490 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{14}H_{11}NS$: 225.0612; Found: 225.0590.

5-(Thiophen-3-ylmethyl)indole (3dm). Column chromatography (hexane/EtOAc = 5/1) gave 177 mg of the product (0.83 mmol, 83%) as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.07 (s, 2H), 6.49 (s, 1H), 6.92−6.94 (m, 2H), 7.05 (d, J = 8.3 Hz, 1H), 7.19 (t, J = 2.7 Hz, 1H), 7.23 (dd, J = 2.7, 4.6 Hz, 1H), 7.31 (d, J = 8.3 Hz, 1H), 7.46 (s, 1H), 8.07 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 36.6 (CH_2), 102.3 (CH), 110.9 (CH), 120.3 (CH), 120.9 (CH), 123.2 (CH), 124.4 (CH), 125.3 (CH), 128.1 (C), 128.6 (CH), 132.0 (C), 134.4 (C), 142.8 (C). IR (ATR): 730, 750, 3410 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{13}H_{11}NS$: 213.0612; Found: 213.0592.

2-Methyl-5-(thiophen-3-ylmethyl)furan (3dn). After the reaction mixture was stirred for 15 h at 100 °C and cooled to room temperature, CH_2Cl_2 and 1 M NaOH were added. The resulting mixture was stirred for 1 h at room temperature and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4. Concentration and purification through column chromatography (hexane/Et_2O = 200/1) gave 127 mg of the product (0.71 mmol, 71%) as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26 (s, 3H), 3.93 (s, 2H), 5.86−5.88 (m, 2H), 6.98 (d, J = 4.8 Hz, 1H), 7.02 (d, J = 1.5 Hz, 1H), 7.24−7.26 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.5 (CH_3), 29.2 (CH_2), 106.0 (CH), 106.6 (CH), 121.4 (CH), 125.4 (CH), 128.3 (CH), 138.6 (C), 150.8 (C), 152.2 (C). IR (ATR): 740, 780, 1570 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{10}H_{10}OS$: 178.0452; Found: 178.0435.

4-(2-Ethoxycarbonylfuran-5-ylmethyl)dibenzothiophene (3ej). Column chromatography (hexane/EtOAc = 20/1) gave 235 mg of the product (0.70 mmol, 70%) as yellow solids of mp 104−105 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.36 (t, J = 7.2 Hz, 3H), 4.31 (s, 2H), 4.34 (q, J = 7.2 Hz, 2H), 6.13 (d, J = 3.2 Hz, 1H), 7.08 (d, J = 3.2 Hz, 1H), 7.32 (d, J = 7.6 Hz, 1H), 7.42−7.46 (m, 3H), 7.83−7.85 (m, 1H), 8.08 (d, J = 7.6 Hz, 1H), 8.13−8.15 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.3 (CH_3), 33.9 (CH_2), 60.8 (CH_2), 109.6 (CH), 118.9 (CH), 120.4 (CH), 121.7 (CH), 122.8 (CH), 124.5 (CH), 125.0 (CH), 126.8 (CH), 127.1 (CH), 131.1 (C), 135.8 (C), 136.1 (C), 139.0 (C), 139.2 (C), 144.0 (C), 157.2 (C), 158.8 (C). IR (ATR): 750, 1140, 1720 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{20}H_{16}O_3S$: 336.0820; Found: 336.0822.

4-(Thiophen-3-ylmethyl)dibenzofuran (3fa). Column chromatography (hexane/Et_2O = 200/1) gave 259 mg of the product (0.98 mmol, 98%) as white solids of mp 62−63 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.34 (s, 2H), 7.03−7.04 (m, 2H), 7.23−7.29 (m, 3H), 7.34 (t, J = 7.4 Hz, 1H), 7.43−7.47 (m, 1H), 7.59 (d, J = 7.4 Hz, 1H), 7.82 (dd, J = 1.2, 7.4 Hz, 1H), 7.94 (d, J = 7.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.2 (CH_2), 111.7 (CH), 118.7 (CH), 120.7 (CH), 121.5 (CH), 122.6 (CH), 122.8 (CH), 124.0 (C), 124.5 (C), 124.7 (C), 125.5 (CH), 127.0 (CH), 127.5 (CH), 128.5 (CH), 140.1 (C), 154.4 (C), 156.1 (C). IR (ATR): 740, 750, 1190 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{17}H_{12}OS$: 264.0609; Found: 264.0605.

3-(Dibenzofuran-4-ylmethyl)quinoline (3fl). Column chromatography (hexane/EtOAc = 4/1) gave 257 mg of the product (0.83 mmol, 83%) as white solids of mp 117−118 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.52 (s, 2H), 7.27−7.36 (m, 3H), 7.44−7.51 (m, 2H), 7.58 (d, J = 8.1 Hz, 1H), 7.63−7.67 (m, 1H), 7.71 (d, J = 8.1 Hz, 1H), 7.85 (dd, J = 2.2, 6.6 Hz, 1H), 7.95 (d, J = 8.1 Hz, 1H), 7.98 (s, 1H), 8.07 (d, J = 8.1 Hz, 1H), 8.99 (d, J = 2.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 33.1 (CH_2), 111.7 (CH), 119.1 (CH), 120.7 (CH), 122.7 (CH), 123.0 (CH), 123.7 (C), 124,2 (C), 124.3 (C), 126.5 (CH), 127.1 (CH), 127.4 (CH), 127.5 (CH), 128.0 (C), 128.7 (CH), 129.1 (CH), 132.7 (C), 134.7 (CH), 146.9 (C), 152.0 (CH), 154.4 (C), 156.1 (C). IR (ATR): 750, 1180, 1500, 1590 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{22}H_{15}NO$: 309.1154; Found: 309.1159.

4-(2-Methylfuran-5-ylmethyl)dibenzofuran (3fn). After the reaction mixture was stirred for 15 h at 90 °C and cooled to room temperature, CH_2Cl_2 and 1 M NaOH were added. The resulting mixture was stirred for 1 h at room temperature and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4. Concentration and purification through column chromatography (hexane/Et_2O = 200/1) gave 223 mg of the product (0.85 mmol, 85%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26 (s, 3H), 4.30 (s, 2H), 5.87−5.88 (m, 1H), 5.94 (d, J = 2.8 Hz, 1H), 7.28−7.31 (m, 2H), 7.32−7.36 (m, 1H), 7.46 (dt, J = 1.2, 8.3 Hz, 1H), 7.58 (d, J = 8.3 Hz, 1H), 7.81−7.86 (m, 1H), 7.95 (dd, J = 0.5, 8.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6 (CH_3), 28.2 (CH_2), 106.1 (CH), 107.2 (CH), 111.7 (CH), 118.8 (CH), 120.6 (CH), 122.5 (C), 122.6 (CH), 122.8 (CH), 124.0 (C), 124.5 (C), 127.0 (CH), 127.5 (CH), 151.1 (C), 151.3 (C), 154.4 (C), 156.1 (C). IR (ATR): 750, 1180, 1570 cm^{-1}. HRMS (EI) m/z: (M^+) Calcd for $C_{18}H_{14}O_2$: 262.0994; Found: 262.0995.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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