Electronic Supplementary Material (ESI) for Green Chemistry.

Supporting Information

Nickel-catalyzed and Li-mediated regiospecific C-H arylation of benzothiophenes

Yorck Mohr, Gaëlle Hisler, Léonie Grousset, Yoann Roux, Elsje Alessandra Quadrelli, Florian M. Wisser, Jérôme Canivet*

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1. Abbreviations

Chemicals & Solvents

bis-BT	2,2'-bibenzothiophene
bpy	2,2’-bipyridine
CPME	cyclopentyl methyl ether
COD	1,5-cyclooctadiene
diglyme	1-methoxy-2-(2-methoxyethoxy)ethane
DMAc	*N,N*-dimethylacetamide
DMSO	dimethyl sulfoxide
glyme	1,2-dimethoxyethane
LDA	lithium diisopropylamide
LiHMDS	lithium bis(trimethylsilyl)amide
LiO*t*-Bu	lithium *tert*-butoxide
Me-THF	2-methyltetrahydrofuran
n-BuLi	*n*-butyl lithium
NMP	*N*-methyl-2-pyrrolidone
OMs	mesylate
OTs	tosylate
Ph-HMDS	*N*-phenyl-hexamethyldisilazane
phen	1,10-phenanthroline
THF	tetrahydrofuran

Other

APCI	atomic pressure chemical ionization
EI	electron ionization
ESI	electrospray ionization
FID	flame ionization detector
GC	gas chromatography
KIE	kinetic isotopic effect
(HR)MS	(high resolution) mass spectrometry
NMR	nuclear magnetic resonance

2. General remarks and technical data

Liquid nuclear magnetic resonance (NMR) spectra were recorded either on a Bruker Ascend 400 (^{1}H at 400.13 MHz, ^{13}C at 100.61 MHz) spectrometer using $CDCl_3$ as solvent. Chemical shifts for ^{1}H NMR and for ^{13}C NMR spectra are expressed in ppm relative to the residual solvent signal. Data are reported as follows: chemical shift, integration multiplicity (s = singlet, d = doublet, dd = doublet of doublets, ddd = doublet of doublets of doublets, dt = doublet of triplets, t = triplet, q = quartet, m = multiplet, br = broad signal) and coupling constant (*J* in Hz).

Gas Chromatography (GC) FID analysis was conducted on an Agilent Technologies 7890A instrument equipped with a HP-5 column (30 m × 0.320 mm × 0.25 µm, Agilent). GC-MS analysis was conducted on a Shimadzu GCMS-QP-2010 instrument equipped with a HP-5 column (30 m × 0.320 mm × 0.25 µm, Agilent). High Resolution Mass Spectra (HRMS) were recorded on a Bruker MicroTOFQ II using electrospray ionization (5 ppm error, Centre Commun de Spectrométrie de Masse, Université Lyon 1).

Liquid size-exclusion chromatography was performed using a LC-20AR Semi-Preparative Recycle System (Manual Injector) (Shimadzu) with two size-exclusion PLGel columns (10 µm, 50 Å, Agilent) in series and $CHCl_3$ (Merck, HPLC grade) as eluent.

3. Chemicals

Unless otherwise stated, all materials were obtained from commercial suppliers and used as received. All reaction solvents were purchased from Sigma Aldrich as anhydrous quality. If this quality was not available reagent grade purity was purchased and the solvent was degassed by three cycles of freeze-pump-thaw and then dried over molecular sieve (3 Å) prior to use.

The following compounds were purchased from Sigma Aldrich: 1-chloro-4-iodobenzene (99%), 1-iodo-2-methylbenzene (98%), 1-methylindole (97%), 1-iodonaphthalene (97%), 2,2′-bipyridine (99%), 2-iodopyridine (98%), 2-methylfuran (99%), 2-methylthiophene (98%), 4-iodobenzotrifluoride (97%), 4-*tert*-butyliodobenzene (98%), 6-bromobenzothiophene (97%), benzothiophene (98%), bromobenzene (99.5%), $CDCl_3$ (99%), chlorobenzene (99.8%), Cs_2CO_3 (99.9%), D_2O (99.99%), dodecane (99%), iodobenzene (98%), K_2CO_3 (99%), KHMDS (95%), KO^tBu (99.99%), $La(HMDS)_3$ (98%), LDA (97%), Li_2CO_3 (99.997%), LiHMDS (97%), LiO^tBu (97%), methanol-OD (99%), $Mg(HMDS)_2$ (97%), NaHMDS (95%), *n*-BuLi (2.5 M in hexane), $Ni(COD)_2$ (99%), $Ni(glyme)Cl_2$ (98%), $Ni(OAc)_2$ (99%), $Ni(PPh_3)_2Cl_2$ (99.99%), NiI_2 (99%), phenanthroline (99%), phenyl methanesulfonate (98%), selenophene (97%), $Sn(HMDS)_2$ (99%), thiophene (99%), $Zn(HMDS)_2$ (97%).

The following compounds were purchased from TCI Europe: 1-iodo-3-methylbenzene (98%), 1-iodo-4-methoxybenzene (99%), 1-iodo-4-methylbenzene (99%), 2-iodoanisole (98%), 2-methylbenzothiophene (98%), 2,8-diiododibenzothiophene (97%), 3-bromobenzothiophene (96%), 3-methylbenzothiophene (97%), 4-iodoanisole (99%), 5-methylbenzothiophene (98%), benzo[1,2-*b*:4,5-*b*']dithiophene (98%), benzofuran (99%), phenyl *p*-toluenesulfonate (99%).

The following compounds were purchased from AmBeed: 2-(benzothiophen-5-yl)-4,4,5,5-tetramethyl-1, 3,2-dioxaborolane (97%), 6-methoxybenzothiophene (95%).

The following compounds were purchased from Enamine: 5-fluorobenzothiophene (98%), 7-methylbenzothiophene (98%).

1-fluoro-4-iodobenzene (99%) was purchased from Alfa Aesar. 2-iodothioanisole (95%) was purchased from Combi-Blocks. 5-chlorobenzothiophene (97%) was purchased from abcr.

$Ni(OAc)_2$ was dried prior to use (90°C, 10^{-3} mbar, 4 h).[1] $Ni(bpy)Cl_2$ was synthesized according to literature.[2] $Ni(bpy)I_2$ was synthesized according to literature.[3] $Ni(bpy)(OAc)_2$ and $Ni(phen)(OAc)_2$ were synthesized according to literature.[4] Ph-HMDS was synthesized according to literature.[5] Benzothiophene-2-*d* was prepared according to literature.[6] Benzothiophene-3-*d* was prepared according to literature.[7]

4. Catalysis protocols

Unless otherwise stated, all coupling reactions were prepared in a glove box and conducted under argon atmosphere using 50 ml glass vessel tubes equipped with a Schlenk tap and heated in a Radleys® Carousel 12 Plus Reaction Station. Unless otherwise stated, all work-up and purification procedures were carried out with reagent grade solvents in air.

4.1. Screening

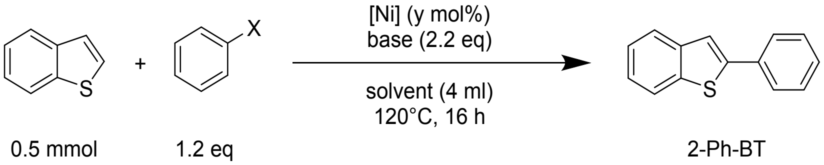
Catalyst screening: To a flame-dried Schlenk tube equipped with a magnetic stir bar were added benzothiophene 69.2 mg (0.5 mmol), LiHMDS (1.1 mmol, 189 mg, 2.2 eq), a defined amount of nickel complex and if indicated the same defined amount of a ligand. The flask was sealed with a silicon septum and transferred out of the glove box. Dry solvent (4 ml) was injected through the septum and the mixture was stirred for two minutes. Then iodobenzene (69 µl, 0.6 mmol, 1.2 eq) and dodecane (40 µl, 0.174 mmol) as an internal standard for GC-FID analysis were injected through the septum. The reaction was stirred and heated to 120°C. After 16 h the reaction mixture was quenched with 2 ml of methanol. The yield was determined using GC-FID analysis.

Base & Base equivalents: To a flame-dried Schlenk tube equipped with a magnetic stir bar were added benzothiophene 69.2 mg (0.5 mmol), $Ni(bpy)Cl_2$ (2.9 mg, 10 µmol, 2 mol%) and a defined amount of base inside a glove box. The flask was sealed with a silicon septum and transferred out of the glove box. Dry toluene or dioxane (4 ml) was injected through the septum and the mixture was stirred for two minutes. If the base is a liquid it was injected alongside the solvent through the septum. Then iodobenzene (69 µl, 0.6 mmol, 1.2 eq) and dodecane (40 µl, 0.174 mmol) as an internal standard for GC-FID analysis were injected through the septum. The reaction was stirred and heated to a given temperature. After 16 h, unless otherwise stated, the reaction mixture was quenched with 2 ml of methanol. The yield was determined using GC-FID analysis.

Solvent & temperature: To a flame-dried Schlenk tube equipped with a magnetic stir bar were added benzothiophene 69.2 mg (0.5 mmol), LiHMDS (1.1 mmol, 189 mg, 2.2 eq) and $Ni(bpy)Cl_2$ (2.9 mg, 10 µmol, 2 mol%) inside a glove box. The flask was sealed with a silicon septum and transferred out of the glove box. Dry solvent (4 ml) was injected through the septum and the mixture was stirred for two minutes. Then iodobenzene (69 µl, 0.6 mmol, 1.2 eq) and dodecane (40 µl, 0.174 mmol) as an internal standard for GC-FID analysis were injected through the septum. The reaction was stirred and heated to a given temperature. After 16 h, unless otherwise stated, the reaction mixture was quenched with 2 ml of methanol. The yield was determined using GC-FID analysis.

Electrophile screening: To a flame-dried Schlenk tube equipped with a magnetic stir bar were added benzothiophene 69.2 mg (0.5 mmol), LiHMDS (1.1 mmol, 189 mg, 2.2 eq) and $Ni(bpy)Cl_2$ (2.9 mg, 10 µmol, 2 mol%) inside a glove box. The flask was sealed with a silicon septum and transferred out of the glove box. Dry toluene or dioxane (4 ml) was injected through the septum and the mixture was stirred for two minutes. Then a phenyl halide or phenol derivative (1.2 eq) and dodecane (40 µl, 0.174 mmol) as an internal standard for GC-FID analysis were injected through the septum. If the phenol derivative is a solid it was added alongside the other solids in the glove box. The reaction was stirred and heated to 120°C. After 16 h the reaction mixture was quenched with 2 ml methanol. The yield was determined using GC-FID analysis.

Table S1: Summary of catalyst, base, solvent & temperature and electrophile screening.



entry	*X*	*[Ni] catalyst*	*y / mol%*	*base*	*solvent*	*2-Ph-BT / % (GC-FID)*
1	I	none	-	LiHMDS	toluene	0
2	I	$Ni(glyme)Cl_2$	2	LiHMDS	toluene	26
3	I	$Ni(PPh_3)_2Cl_2$	2	LiHMDS	toluene	3
4	I	$Ni(bpy)Cl_2$	2	LiHMDS	toluene	60
5	I	$Ni(bpy)I_2$	2	LiHMDS	toluene	60
6	I	$Ni(bpy)(OAc)_2$	2	LiHMDS	toluene	67
7	I	$Ni(phen)(OAc)_2$	2	LiHMDS	toluene	63
8	I	$Ni(COD)_2$ + bpy	2	LiHMDS	toluene	32
9	I	$Ni(glyme)Cl_2$ + bpy	2	LiHMDS	toluene	58
10	I	$Ni(bpy)Cl_2$ + 2 bpy	2	LiHMDS	toluene	60
11	I	$Ni(bpy)Cl_2$ + 5 bpy	2	LiHMDS	toluene	62
12	I	$Ni(bpy)Cl_2$	2	LiO-*t*Bu	toluene	< 1
13	I	$Ni(bpy)Cl_2$	2	KO-*t*Bu	toluene	< 1
14	I	$Ni(bpy)Cl_2$	2	LDA	toluene	< 1
15	I	$Ni(bpy)Cl_2$	2	Li_2CO_3	toluene	< 1
16	I	$Ni(bpy)Cl_2$	2	K_2CO_3	toluene	< 1
17	I	$Ni(bpy)Cl_2$	2	Cs_2CO_3	toluene	< 1
18	I	$Ni(bpy)Cl_2$	2	NaHMDS	toluene	3
19	I	$Ni(bpy)Cl_2$	2	KHMDS	toluene	2
20	I	$Ni(bpy)Cl_2$	2	$Mg(HMDS)_2$	toluene	6
21	I	$Ni(bpy)Cl_2$	2	$Zn(HMDS)_2$	toluene	1
22	I	$Ni(bpy)Cl_2$	2	$Sn(HMDS)_2$	toluene	< 1
23	I	$Ni(bpy)Cl_2$	2	$La(HMDS)_2$	toluene	2
24	I	$Ni(bpy)Cl_2$	2	none	toluene	0
25	I	$Ni(bpy)Cl_2$	2	LiHMDS (1.0 eq)	toluene	19

26	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS (1.5 eq)	toluene	49
27	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS (2.0 eq)	toluene	58
28	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS (3.0 eq)	toluene	62
29	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	toluene (80°C)	34
30	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	toluene (60°C)	13
31	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	toluene (25°C)	< 1
32	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	NMP	< 1
33	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	DMAc	< 1
34	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	DMSO	4
35	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	diglyme	59
36	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	anisole	62
37	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	THF	67
38	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	Me-THF	68
39	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	CPME	74
40	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	dioxane	85
41	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	dioxane	85
42	I	$\mathrm{Ni(bpy)Cl_2}$	2	LiO-*t*Bu	dioxane	< 1
43	I	$\mathrm{Ni(bpy)Cl_2}$	10	LiO-*t*Bu	dioxane	< 1
44	I	$\mathrm{Ni(bpy)Cl_2}$	2	KO-*t*Bu	dioxane	< 1
45	I	none	-	LiHMDS	dioxane	0
46	I	$\mathrm{Ni(bpy)Cl_2}$	1	LiHMDS	dioxane	70
47	I	$\mathrm{Ni(bpy)Cl_2}$	5	LiHMDS	dioxane	87
48	I	$\mathrm{Ni(bpy)Cl_2}$	10	LiHMDS	dioxane	90
49	I	$\mathrm{Ni(bpy)(OAc)_2}$	2	LiHMDS	dioxane	79
50	Br	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	dioxane	7
51	Cl	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	dioxane	< 1
52	OMs	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	dioxane	< 1
53	OTs	$\mathrm{Ni(bpy)Cl_2}$	2	LiHMDS	dioxane	10

Please note: for reactions taking place in toluene with ligands other than bpy or phen (Table S1, entries 2 and 3), considerable amounts (> 50%, GC) of *N*-phenyl-hexamethyldisilazane (Ph-HMDS) were observed. The reaction is known and results from the nickel catalyzed coupling of iodobenzene and LiHMDS.[5] With the use of bpy or phen as ligands, the formation could be largely suppressed (ca. 10% formation of Ph-HMDS, GC). In ethereal solvents the formation of Ph-HMDS was negligible (< 2%, GC). Please note further that for entries 2-23, 25-44 and 46-53) small amounts (2-5%, GC) of 2,2'-bibenzothiophene (bis-BT) could be observed. Finally, entry 4 in Table S1 was repeated eight times in total. Based on these results the standard deviation of the reaction yield (including experimental and instrumental errors) was determined to be less than 2%.

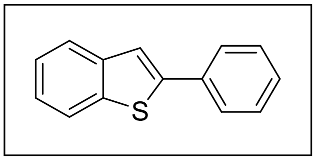
4.2. Synthesis of 2-arylbenzothiophenes and related compounds

For a typical arylation reaction were added benzothiophene or a benzothiophene derivative (0.5 mmol), LiHMDS (189 mg, 1.1 mmol, 2.2 eq) and $\mathrm{Ni(bpy)Cl_2}$ (2.9 mg, 10 µmol, 2 mol%) to a flame-dried Schlenk tube equipped with a magnetic stir bar inside a glove box. The flask was sealed with a silicon septum and transferred out of the glove box. Dry toluene or dioxane (4 ml) was injected through the septum and the mixture was stirred for two minutes. Then the corresponding aryl halide (0.6 mmol, 1.2 eq) was injected through the septum. If the aryl iodide is a solid, it was added alongside benzothiophene and LiHMDS in the glovebox. If the corresponding benzothiophene derivative is a liquid it was injected alongside iodobenzene through the septum outside of the glove box. The reaction was stirred and heated to 120°C. After 16 h the reaction mixture was quenched with 2 ml of methanol. After removal of the solvent by rotary evaporation, unless otherwise stated, the crude product was purified by liquid size exclusion chromatography. The characterization of isolated 2-arylbenzothiophenes is shown in section 4.3.

Variations: for bis-functional heteroarenes (thiophene, selenophene, benzo[1,2-*b*:4,5-*b*']dithiophene) different ratios of heteroarene to iodobenzene were applied; aiming for monoarylation 2.4 eq (1.2 mmol) of heteroarene and 1 eq (0.5 mmol) of iodobenzene were used; aiming for diarylation 1 eq of arylation site, *i.e.* 0.5 eq (0.25 mmol) of heteroarene, and 1.2 eq (0.6 mmol) of iodobenzene were used. The yield is always referenced to the amount of the reaction limiting compound.

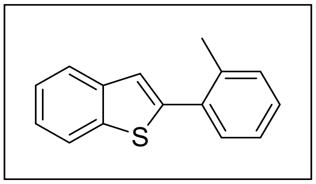
4.3. Characterization of 2-arylbenzothiophenes and related compounds

Unless otherwise stated, the synthesis and isolation of 2-arylbenzothiophenes and derivatives thereof was conducted according to the protocol described in section 4.2.



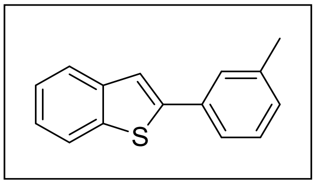
2-phenylbenzothiophene is obtained as a white solid from benzothiophene and iodobenzene in 60% or 85% isolated yield in toluene or dioxane, respectively.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.84 (1H, d, *J* = 7.6 Hz), 7.78 (1H, d, *J* = 7.3 Hz), 7.74 - 7.72 (2H, m), 7.55 (1H, s), 7.43 (2H, t, *J* = 7.3 Hz), 7.39 - 7.29 (3H, m). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 144.4, 140.8, 139.7, 134.5, 129.1, 128.4, 126.7, 124.7, 124.5, 123.7, 122.4, 119.6. **HRMS (APCI):** calculated for $C_{14}H_{11}S^+$: 211.0576 (m/z $[M+H]^+$), found 211.0571 (m/z $[M+H]^+$). Data is in accordance with the literature.[8]



2-(*o*-tolyl)benzothiophene is obtained as a white solid in 75% isolated yield from benzothiophene and 1-iodo-2-methylbenzene in dioxane.

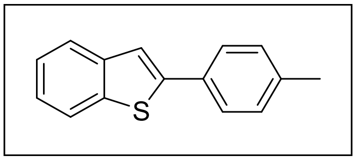
^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.86 (1H, d, *J* = 7.8 Hz), 7.80 (1H, d, *J* = 7.3 Hz), 7.48 (1H, d, *J* = 7.3 Hz), 7.41 - 7.23 (6H, m), 2.49 (3H, s). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 143.6, 140.3, 140.2, 136.6, 134.3, 130.9, 130.8, 128.5, 126.1, 124.5, 124.2, 123.6, 123.2, 122.2, 21.2. **HRMS (APCI):** calculated for $C_{15}H_{13}S^+$: 225.0732 (m/z $[M+H]^+$), found 225.0729 (m/z $[M+H]^+$). Data is in accordance with the literature.[8]



2-(*m*-tolyl)benzothiophene is obtained as a white solid in 83% isolated yield from benzothiophene and 1-iodo-3-methylbenzene in dioxane.

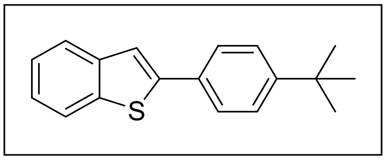
^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.84 (1H, d, *J* = 7.8 Hz), 7.77 (1H, d, *J* = 7.6 Hz), 7.56 - 7.50 (3H, m), 7.38 - 7.28 (3H, m), 7.17 (1H, d, *J* = 7.6 Hz), 2.43 (3H, s).

^{13}C{^{1}H} NMR (100.61 MHz, $CDCl_3$) δ: 144.6, 140.9, 139.6, 138.8, 134.4, 129.2, 129.0, 127.4, 124.6, 124.4, 123.8, 123.7, 122.4, 119.5, 21.6. **HRMS (APCI):** calculated for $C_{15}H_{13}S^+$: 225.0732 (m/z $[M+H]^+$), found 225.0733 (m/z $[M+H]^+$). Data is in accordance with the literature.[8]



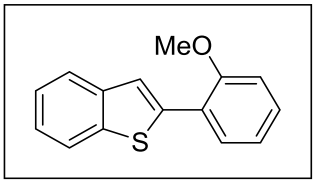
2-(*p*-tolyl)benzothiophene is obtained as a white solid in 89% isolated yield from benzothiophene and 1-iodo-4-methylbenzene in dioxane.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.82 (1H, d, *J* = 8.0 Hz), 7.76 (1H, d, *J* = 7.5 Hz), 7.64 - 7.59 (2H, m), 7.50 (1H, s), 7.34 - 7.27 (2H, m), 7.24 (1H, d, *J* = 8.0 Hz), 2.40 (3H, s). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 144.6, 140.9, 139.5, 138.4, 131.7, 129.8, 126.5, 124.6, 124.3, 123.5, 122.4, 119.0, 21.4. **HRMS (APCI):** calculated for $C_{15}H_{13}S^+$: 225.0732 (m/z $[M+H]^+$), found 225.0732 (m/z $[M+H]^+$). Data is in accordance with the literature.[8]



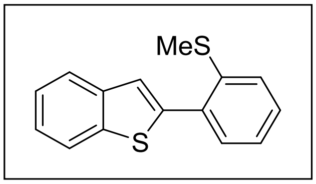
2-(4-(*tert*-butyl)phenyl)benzothiophene is obtained as a white solid in 94% isolated yield from benzothiophene and 1-(*tert*-butyl)-4-iodobenzene in dioxane.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.84 (1H, d, *J* = 7.8 Hz), 7.78 (1H, d, *J* = 7.8 Hz), 7.72 - 7.65 (2H, m), 7.53 (1H, s), 7.50 - 7.45 (2H, m), 7.40 - 7.28 (2H, m), 1.38 (9H, s). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 151.7, 144.5, 140.9, 139.5, 131.7, 126.4, 126.0, 124.6, 124.2, 123.6, 122.4, 119.1, 34.8, 31.4. **HRMS (EI):** calculated for $C_{18}H_{18}S^+$: 266.1124 (m/z $[M]^+$), found 266.1132 (m/z $[M]^+$). Data is in accordance with the literature.[9]



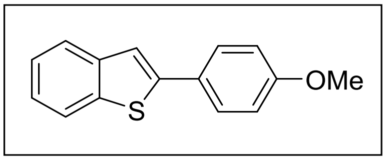
2-(2-methoxyphenyl)benzothiophene is obtained as a colorless oil in 71% isolated yield from benzothiophene and 1-iodo-2-methoxybenzene in dioxane.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.84 (1H, d, *J* = 7.7 Hz), 7.79 (1H, d, *J* = 7.7 Hz), 7.76 (1H, s), 7.72 (1H, dd, *J* = 7.7, 1.5 Hz), 7.37 - 7.27 (3H, m), 7.07 - 7.01 (2H, m), 3.97 (3H, s). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 156.5, 140.3, 140.2, 140.0, 129.7, 129.4, 124.3, 124.2, 123.6, 123.4, 122.6, 122.0, 121.1, 111.9, 55.8. **HRMS (APCI):** calculated for $C_{15}H_{13}OS^+$: 241.0682 (m/z $[M+H]^+$), found 241.0678 (m/z $[M+H]^+$). Data is in accordance with the literature.[8]



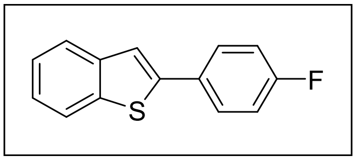
2-(2-(methylthio)phenyl)benzothiophene is obtained as an orange solid in 25% isolated yield from benzothiophene and 1-iodo-2-methylthiobenzene in dioxane.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.89 - 7.77 (2H, m), 7.52 - 7.29 (6H, m), 7.25 - 7.18 (1H, m), 2.44 (3H, s). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 141.7, 140.4, 140.1, 138.4, 133.3, 131.2, 129.0, 125.9, 124.9, 124.5, 124.4, 123.9, 122.2, 16.3. **HRMS (EI):** calculated for $C_{15}H_{12}S_2^+$: 256.0375 (m/z $[M]^+$), found 256.0374 (m/z $[M]^+$). Data is in accordance with the literature.[10]



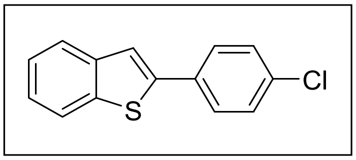
2-(4-methoxyphenyl)benzothiophene is obtained as a white solid in 71% isolated yield from benzothiophene and 1-iodo-4-methoxybenzene in dioxane.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.81 (1H, d, *J* = 7.8 Hz), 7.74 (1H, d, *J* = 7.8 Hz), 7.67 - 7.62 (2H, m), 7.43 (1H, s), 7.37 - 7.26 (2H, m), 6.99 - 6.93 (2H, m), 3.86 (3H, s). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 160.0, 144.3, 141.0, 139.3, 127.9, 127.2, 124.6, 124.1, 123.4, 122.3, 118.4, 114.5, 55.5. **HRMS (APCI):** calculated for $C_{15}H_{13}OS^+$: 241.0682 (m/z $[M+H]^+$), found 241.0682 (m/z $[M+H]^+$). Data is in accordance with the literature.[8]



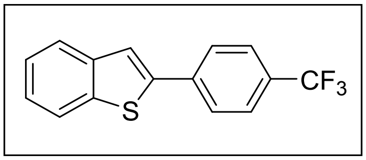
2-(4-fluorophenyl)benzothiophene is obtained as a white solid in 56% isolated yield from benzothiophene and 1-fluoro-4-iodobenzene in dioxane.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.83 (1H, d, *J* = 7.8 Hz), 7.77 (1H, d, *J* = 7.3 Hz), 7.71 - 7.65 (2H, m), 7.47 (1H, s), 7.39 - 7.28 (2H, m), 7.17 - 7.07 (2H, m). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 162.9 (*J* = 248.2 Hz), 143.2, 140.8, 139.6, 130.7 (*J* = 3.2 Hz), 128.3 (*J* = 8.1 Hz), 124.8, 124.5, 123.7, 122.4, 119.6, 116.1 (*J* = 22.0 Hz). **HRMS (APCI):** calculated for $C_{14}H_{10}FS^+$: 229.0482 (m/z $[M+H]^+$), found 229.0484 (m/z $[M+H]^+$). Data is in accordance with the literature.[8]



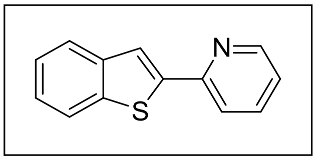
2-(4-chlorophenyl)benzothiophene is obtained as a white solid in 66% isolated yield from benzothiophene and 1-chloro-4-iodobenzene in dioxane.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.83 (1H, d, *J* = 7.6 Hz), 7.78 (1H, d, *J* = 7.3 Hz), 7.66 - 7.62 (2H, m), 7.52 (1H, s), 7.43 - 7.29 (4H, m). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 143.0, 140.7, 139.7, 134.3, 133.0, 129.3, 127.8, 124.8, 124.7, 123.8, 122.4, 120.0. **HRMS (APCI):** calculated for $C_{14}H_{10}ClS^+$: 245.0186 (m/z $[M+H]^+$), found 245.0183 (m/z $[M+H]^+$). Data is in accordance with the literature.[8]



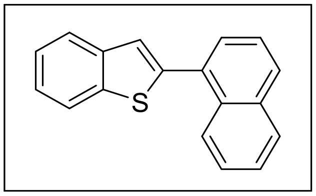
2-(4-(trifluoromethyl)phenyl)benzothiophene is obtained as a white solid in 67% isolated yield from benzothiophene and 4-iodobenzotrifluoride in dioxane. Note: after quenching the reaction with 2 ml of methanol, the resulting precipitate was filtered off and washed with a cold mixture of dioxane and methanol (2:1, v/v) to yield the title compound as a white powder.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.88 - 7.76 (4H, m), 7.68 (2H, d, *J* = 8.3 Hz), 7.64 (1H, s), 7.42 - 7.32 (2H, m). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 142.5, 140.6, 140.0, 137.9, 130.0 (q, *J* = 32.8 Hz) 126.8, 126.1 (q, *J* = 3.8 Hz), 125.1, 125.0, 124.9 (q, *J* = 272.6 Hz) 124.1, 122.5, 121.2. **HRMS (EI):** calculated for $C_{15}H_9F_3S^+$: 278.0372 (m/z $[M]^+$), found 278.0372 (m/z $[M]^+$). Data is in accordance with the literature.[8]



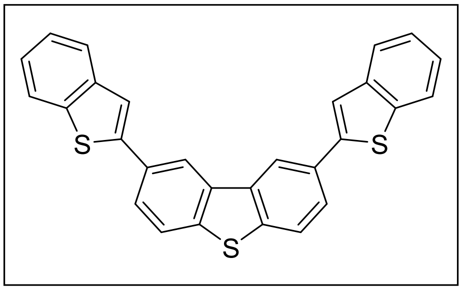
2-(2-pyridyl)benzothiophene is obtained as a white solid in 32% isolated yield from benzothiophene and 2-iodopyridine in dioxane.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 8.64 (1H, d, *J* = 4.5 Hz), 7.91 - 7.77 (4H, m), 7.77 - 7.70 (1H, m), 7.40 - 7.30 (2H, m), 7.25 - 7.17 (1H, m). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 152.7, 149.9, 145.0, 140.8, 140.6, 136.8, 125.2, 124.7, 124.2, 122.8, 122.7, 121.2, 119.7. **HRMS (EI):** calculated for $C_{13}H_9NS^+$: 211.0450 (m/z [M]$^+$), found 211.0444 (m/z [M]$^+$). Data is in accordance with the literature.[11]



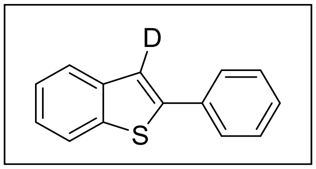
2-(naphthalen-1-yl)benzothiophene is obtained as a white solid in 74% isolated yield from benzothiophene and 1-iodonaphthalene in dioxane.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 8.35 - 8.28 (1H, m), 7.99 - 7.83 (4H, m), 7.68 (1H, dd, *J* = 7.1, 1.1 Hz), 7.58 - 7.50 (3H, m), 7.48 (1H, s), 7.47 - 7.36 (2H, m). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 142.2, 140.4, 140.3, 133.8, 132.4, 131.8, 129.0, 128.6, 128.3, 126.7, 126.3, 125.8, 125.3, 124.6, 124.4, 124.2, 123.6, 122.2. **HRMS (EI):** calculated for $C_{18}H_{12}S^+$: 260.0654 (m/z [M]$^+$), found 260.0657 (m/z [M]$^+$). Data is in accordance with the literature.[8]



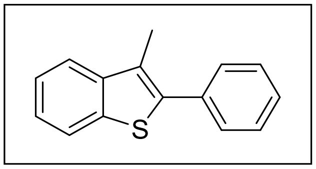
2,8-bis(benzo[*b*]thiophen-2-yl)dibenzo[*b*,*d*]thiophene is obtained as a grey solid in 51% isolated yield from benzothiophene (69.2 mg, 0.5 mmol) and 2,8-diiododibenzothiophene (89.9 mg, 0.2 mmol) in dioxane. Note: after quenching the reaction with 2 ml of methanol, the resulting precipitate was filtered off and washed with a cold mixture of dioxane and methanol (2:1, v/v) to yield the title compound as a grey powder.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 8.53 (2H, s), 7.95 - 7.79 (8H, m), 7.71 (2H, s), 7.43 - 7.31 (4H, m). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 144.2, 141.0, 140.0, 139.7, 136.0, 131.4, 125.8, 124.8, 124.6, 123.8, 123.5, 122.5, 119.9, 119.6. **HRMS (APCI):** calculated for $C_{28}H_{17}NS_3^+$: 449.0487 (m/z [M+H]$^+$), found 449.0484 (m/z [M+H]$^+$).



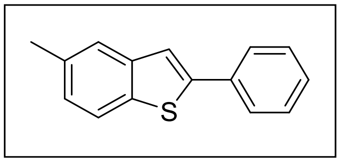
2-phenylbenzothiophene-3-*d* is obtained as a white solid in 81% isolated yield and full deuterium retention from benzothiophene-3-*d* and iodobenzene in dioxane.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.87 - 7.82 (1H, m), 7.81 - 7.76 (1H, m), 7.74 - 7.72 (2H, m), 7.47 - 7.40 (2H, m), 7.39 - 7.29 (3H, m). **HRMS (EI):** calculated for $C_{14}H_9DS^+$: 211.0560 (m/z [M]$^+$), found 211.0567 (m/z [M]$^+$). Data is in accordance with the literature.[12]



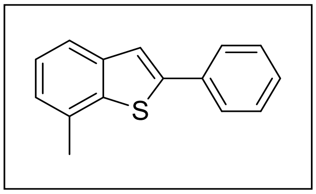
3-methyl-2-phenylbenzothiophene is obtained as a white solid in 20% isolated yield from 3-methylbenzothiophene and iodobenzene in dioxane.

^{1}H NMR (400.13 MHz, CDCl$_3$) δ: 7.84 (1H, d, J = 7.8 Hz), 7.73 (1H, 7.9 Hz), 7.59 - 7.52 (2H, m), 7.51 - 7.31 (5H, m), 2.47 (3H, s). **^{13}C{^{1}H} NMR** (100.61 MHz, CDCl$_3$) δ: 141.4, 139.1, 138.1, 134.8, 129.9, 128.7, 128.5, 127.9, 127.6, 124.3, 122.3, 122.3, 12.6. **HRMS (EI):** calculated for C$_{15}$H$_{12}$S$^+$: 224.0654 (m/z [M]$^+$), found 224.0645 (m/z [M]$^+$). Data is in accordance with the literature.[13]



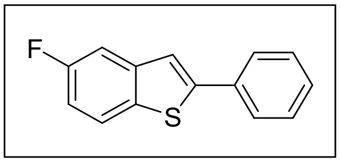
5-methyl-2-phenylbenzothiophene is obtained as a white solid in 70% isolated yield from 5-methylbenzothiophene and iodobenzene in dioxane.

^{1}H NMR (400.13 MHz, CDCl$_3$) δ: 7.76 - 7.66 (3H, m), 7.58 (1H, s), 7.48 (1H, s), 7.46 - 7.38 (2H, m), 7.37 - 7.30 (1H, m), 7.19 - 7.11 (1H, m), 2.47 (3H, s). **^{13}C{^{1}H} NMR** (100.61 MHz, CDCl$_3$) δ: 144.5, 141.2, 136.8, 134.6, 134.4, 129.0, 128.3, 126.6, 126.2, 123.7, 122.0, 119.3, 21.6. **HRMS (EI):** calculated for C$_{15}$H$_{12}$S$^+$: 224.0654 (m/z [M]$^+$), found 224.0650 (m/z [M]$^+$).



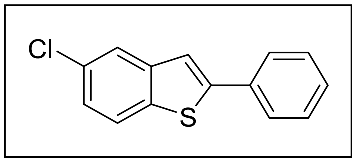
7-methyl-2-phenylbenzothiophene is obtained as a white solid in 68% isolated yield from 7-methylbenzothiophene and iodobenzene in dioxane.

^{1}H NMR (400.13 MHz, CDCl$_3$) δ: 7.76 (2H, d, J = 7.5 Hz), 7.65 (1H, d, J = 7.9 Hz), 7.59 (1H, s), 7.48 - 7.41 (2H, m), 7.39 - 7.27 (2H, m), 7.14 (1H, d, J = 7.2 Hz), 2.60 (3H, s). **^{13}C{^{1}H} NMR** (100.61 MHz, CDCl$_3$) δ: 143.9, 140.7, 139.9, 134.6, 132.0, 129.1, 128.3, 126.6, 125.0, 124.7, 121.3, 120.3, 20.5. **HRMS (EI):** calculated for C$_{15}$H$_{12}$S$^+$: 224.0654 (m/z [M]$^+$), found 224.0644 (m/z [M]$^+$).



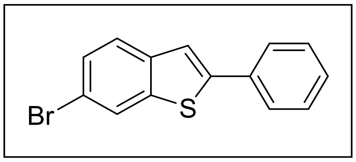
5-fluoro-2-phenylbenzothiophene is obtained as a white solid in 45% isolated yield from 5-fluorobenzothiophene and iodobenzene in dioxane.

^{1}H NMR (400.13 MHz, CDCl$_3$) δ: 7.78 - 7.67 (3H, m), 7.49 (1H, s), 747- 7.40 (3H, m), 7.39 - 7.33 (1H, m), 7.07 (1H, dt, J = 8.8, 2.4 Hz). **^{13}C{^{1}H} NMR** (100.61 MHz, CDCl$_3$) δ: 161.1 (d, J = 241.6 Hz), 147.0, 141.8 (d, J = 9.5 Hz), 135.0, 134.1, 129.2, 128.7, 126.7, 123.5 (d, J = 9.4 Hz), 119.3 (d, J = 4.4 Hz), 113.2 (d, J = 24.9 Hz), 109.1 (d, J = 22.8 Hz). **HRMS (EI):** calculated for C$_{14}$H$_9$FS$^+$: 228.0404 (m/z [M]$^+$), found 228.0401 (m/z [M]$^+$).



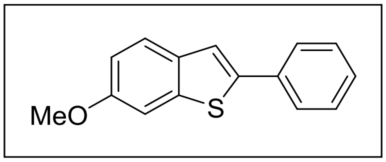
5-chloro-2-phenylbenzothiophene is obtained as a white solid in 62% isolated yield from 5-chlorobenzothiophene and iodobenzene in dioxane.

^{1}H NMR (400.13 MHz, CDCl$_3$) δ: 7.78 - 7.65 (4H, m), 7.50 - 7.32 (4H, m), 7.30 - 7.23 (1H, m). **^{13}C{^{1}H} NMR** (100.61 MHz, CDCl$_3$) δ: 146.5, 141.9, 137.7, 134.0, 130.9, 129.2, 128.8, 126.7, 124.9, 123.4, 123.2, 118.8. **HRMS (EI):** calculated for C$_{14}$H$_9$ClS$^+$: 244.0108 (m/z [M]$^+$), found 244.0107 (m/z [M]$^+$). Data is in accordance with the literature.[14]



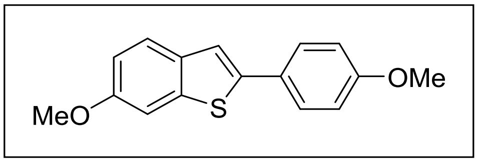
6-bromo-2-phenylbenzothiophene is obtained as a white solid in 35% isolated yield from 6-bromobenzothiophene and iodobenzene in dioxane.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.96 (1H, s), 7,70 (2H, d, *J* = 7.4 Hz), 7.62 (1H, d, *J* = 8.4 Hz), 7.52 - 7.32 (5H, m). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 145.1, 141.1, 139.6, 134.0, 129.2, 128.7, 128.1, 126.6, 124.9, 124.8, 119.1, 118.2. **HRMS (EI):** calculated for $C_{14}H_9BrS^+$: 287.9603 (m/z [M]$^+$), found 287.9612 (m/z [M]$^+$). Data is in accordance with the literature.[14]



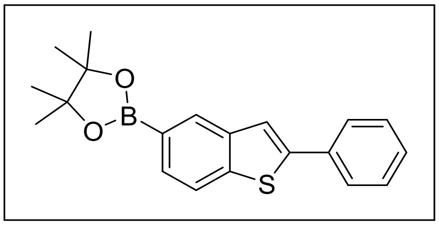
6-methoxy-2-phenylbenzothiophene is obtained as a white solid in 58% isolated yield from 6-methoxybenzothiophene and iodobenzene in dioxane.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.72 - 7.62 (3H, m), 7.49 - 7.38 (3H, m), 7.35 - 7.28 (2H, m), 6.99 (1H, dd, *J* = 8.7, 2.2 Hz), 3.89 (3H, s). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 157.6, 141.8, 141.1, 134.9, 134.6, 129.0, 128.0, 126.3, 124.4, 119.1, 114.7, 105.0, 55.8. **HRMS (EI):** calculated for $C_{15}H_{12}OS^+$: 240.0603 (m/z [M]$^+$), found 240.0614 (m/z [M]$^+$). Data is in accordance with the literature.[14]



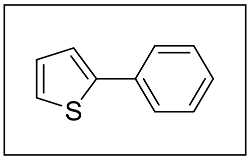
6-methoxy-2-(4-methoxyphenyl)benzothiophene is obtained from 6-methoxybenzothiophene and 1-iodo-4-methoxybenzene in dioxane in 60% and 83% isolated yield with 2 mol% and 5 mol% of nickel catalyst, respectively. With 5 mol% of nickel catalyst in 2-methyltetrahydrofuran, the title product could be isolated in 85% yield. Note: after quenching the reaction with 2 ml of methanol, the resulting precipitate was filtered off and washed with a cold mixture of the respective solvent and methanol (2:1, v/v) to yield the title compound as a white powder.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.64 - 7.57 (3H, m), 7.36 - 7.32 (1H, m), 7.31 - 7.27 (1H, m), 7.00 - 6.91 (3H, m), 3.88 (3H, s), 3.85 (3H, s). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 159.6, 157.4, 141.7, 140.8, 135.1, 127.6, 127.4, 124.0, 117.9, 114.5, 114.5, 105.1, 55.8, 55.5. **HRMS (APCI):** calculated for $C_{16}H_{15}O_2S^+$: 271.0787 (m/z [M+H]$^+$), found 271.0782 (m/z [M+H]$^+$). Data is in accordance with the literature.[14]



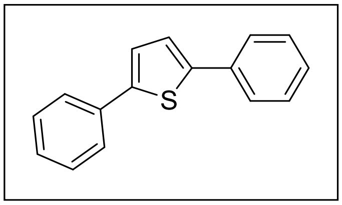
4,4,5,5-tetramethyl-2-(2-phenylbenzothiophen-5-yl)-1,3,2-dioxaborolane is obtained as a white solid in 35% isolated yield from 2-(benzo[b]thiophen-5-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane and iodobenzene in dioxane. Note: the reaction was not quenched with methanol, but directly evaporated to dryness and the residue subjected to liquid size exclusion chromatography.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 8.26 (1H, s), 7.84 (1H, d, *J* = 8.0 Hz), 7.77 - 7.68 (3H, m), 7.54 (1H, s), 7.48 - 7.38 (2H, m), 7.38 - 7.31 (1H, m), 1.39 (12H, s). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 144.1, 142.7, 140.5, 134.4, 130.8, 130.1, 129.1, 128.4, 126.7, 121.7, 119.8, 84.0, 25.1. **HRMS (APCI):** calculated for $C_{20}H_{22}BO_2S^+$: 337.1428 (m/z [M+H]$^+$), found 337.1428 (m/z [M+H]$^+$).



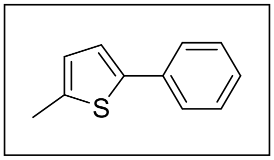
2-phenylthiophene is obtained as a colorless oil from thiophene (97 µl, 1.2 mmol) and iodobenzene (57 µl, 0.5 mmol) in 50% isolated yield in toluene. As a side product 2,5-diphenylthiophene was obtained as a white solid in 9% isolated yield.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.65 - 7.60 (2H, m), 7.42 - 7.35 (2H, m), 7.34 - 7.26 (3H, m), 7.11 - 7.06 (1H, m). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 144.6, 134.6, 129.0, 128.1, 127.6, 126.1, 124.9, 123.2. **HRMS (APCI):** calculated for $C_{10}H_9S^+$: 161.0419 (m/z $[M+H]^+$), found 161.0423 (m/z $[M+H]^+$). Data is in accordance with the literature.[11]



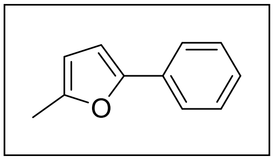
2,5-diphenylthiophene is obtained as a white solid from thiophene (20 µl, 0.25 mmol) and iodobenzene (69 µl, 0.6 mmol) in 43% and 11% isolated yield in toluene and dioxane, respectively. As a side product 2-phenylthiophene was obtained as a colorless oil in 7% isolated yield (toluene).

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.70 - 7.58 (4H, m), 7.44 - 7.36 (4H, m), 7.33 - 7.27 (4H, m). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 143.8, 134.6, 129.0, 127.7, 125.7, 124.2. **HRMS (EI):** calculated for $C_{16}H_{12}S^+$: 236.0654 (m/z $[M]^+$), found 236.0656 (m/z $[M]^+$). Data is in accordance with the literature.[15]



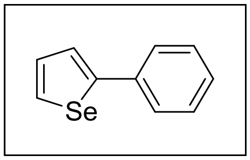
2-methyl-5-phenylthiophene is obtained as a white solid from 2-methylthiophene and iodobenzene in 59% and 11% isolated yield in toluene and dioxane, respectively.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.61 - 7.53 (2H, m), 7.40 - 7.33 (2H, m), 7.29 - 7.23 (1H, m), 7.15 - 7.09 (1H, m), 6.78 - 6.70 (1H, m), 2.52 (3H, s). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 141.9, 139.4, 134.6, 128.7, 126.9, 126.0, 125.4, 122.8, 15.4. **HRMS (EI):** calculated for $C_{11}H_{10}S^+$: 174.0498 (m/z $[M]^+$), found 174.0506 (m/z $[M]^+$). Data is in accordance with the literature.[16]



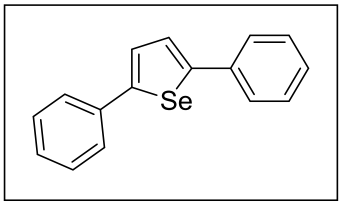
2-methyl-5-phenylfuran is obtained from 2-methylfuran in 3% and 1% GC-FID yield in toluene and dioxane, respectively. Due to the low yield, no other characterization than GC-MS can be indicated.

MS (GC-MS): calculated for $C_{11}H_{10}O$: 158.1 (m/z $[M]^+$), found 158.0 (m/z $[M]^-$).



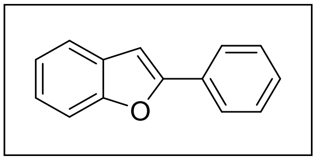
2-phenylselenophene is obtained as a white solid from selenophene (114 µl, 1.2 mmol) and iodobenzene (57 µl, 0.5 mmol) in 41% isolated yield in toluene. As a side product 2,5-diphenylselenophene was obtained in 3% yield (GC-FID).

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.94 (1H, dd/ddd, *J* = 47.6, 5.6, 1.1 Hz), 7.59 - 7.54 (2H, m), 7.49 - 7.45 (1H, m), 7.39 - 7.26 (4H, m). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 151.0, 136.6, 130.7, 130.1, 129.0, 127.7, 126.5, 125.4. **HRMS (EI):** calculated for $C_{10}H_8Se^+$: 207.9786 (m/z $[M]^+$), found 207.9788 (m/z $[M]^+$). Data is in accordance with the literature.[17]



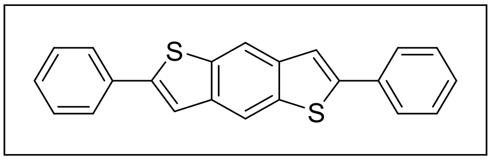
2,5-diphenylselenophene is obtained as a white solid from selenophene (24 µl, 0.25 mmol) and iodobenzene (69 µl, 0.6 mmol) in 23% isolated yield in toluene. As a side product 2-phenylselenophene was obtained as a grey solid in 20% isolated yield, as well as diphenylselenid in 11% yield (GC-MS/GC-FID).

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.60 - 7.55 (4H, m), 7.46 (1H, s), 7.40 - 7.35 (4H, m), 7.31 - 7.26 (2H, m). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 150.0, 136.5, 129.1, 127.8, 126.4, 126.2. **HRMS (EI):** calculated for $C_{16}H_{12}Se^+$: 284.0099 (m/z $[M]^+$), found 284.0120 (m/z $[M]^+$). Data is in accordance with the literature.[17]



2-phenylbenzofuran is obtained as a white solid from benzofuran and iodobenzene in 29% and 17% isolated yield from toluene and dioxane, respectively.

^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.88 (2H, d, *J* = 7.4 Hz), 7.59 (1H, d, *J* = 7.3 Hz), 7.53 (1H, d, *J* = 8.0 Hz), 7.46 (2H, t, *J* = 7.6 Hz), 7.39 - 7.20 (3H, m), 7.03 (1H, s). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 156.1, 155.0, 130.6, 129.4, 128.9, 128.7, 125.1, 124.4, 123.1, 121.0, 111.3, 101.4. **HRMS (APCI):** calculated for $C_{14}H_{11}O^+$: 195.0804 (m/z $[M+H]^+$), found 195.0801 (m/z $[M+H]^+$). Data is in accordance with the literature.[18]



2,6-diphenylbenzo[1,2-*b*:4,5-*b*']dithiophene is obtained as a yellow solid from benzo[1,2-*b*:4,5-*b*']dithiophene (48 mg, 0.25 mmol) and iodobenzene (69 µl, 0.6 mmol) in 90% and 85% isolated yield from toluene and dioxane, respectively. Note: the reaction was quenched with 2 ml of anhydrous methanol. The resulting precipitate is washed with a cold mixture of dioxane and methanol (2:1, v/v) to yield the title compound as a yellow powder. Due to the title compound's insolubility in common solvents no liquid NMR spectrum could be recorded.

HRMS (APCI): calculated for $C_{22}H_{15}S_2^+$: 343.0610 (m/z $[M+H]^+$), found 343.0606 (m/z $[M+H]^+$). **mp** > 300°C. Data is in accordance with the literature.[19]

5. Mechanistic studies

5.1. Catalytic trial with 2-methylbenzothiophene

To a flame-dried Schlenk tube equipped with a magnetic stir bar were added 2-methylbenzothiophene 76.4 mg (0.5 mmol), LiHMDS (1.1 mmol, 189 mg, 2.2 eq) and Ni(bpy)Cl_2 (2.9 mg, 10 µmol, 2 mol%) inside a glove box. The flask was sealed with a silicon septum and transferred out of the glove box. Dry toluene or dioxane (4 ml) was injected through the septum and the mixture was stirred for two minutes. Then iodobenzene (69 µl, 0.6 mmol, 1.2 eq) and dodecane (40 µl, 0.174 mmol) as an internal standard for GC-FID analysis were injected through the septum. The reaction was stirred and heated to 120°C. After 16 h the reaction mixture was quenched with 2 ml methanol. The yield was determined using GC-FID analysis.

Table S2: Summary of catalytic trials with 2-methylbenzothiophene

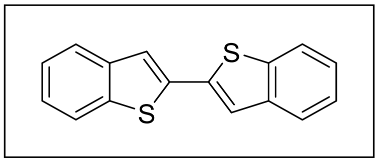
entry	*solvent*	*2-Me-BT conversion / % (GC-FID)*
1	toluene	< 1
2	dioxane	< 1

5.2. Stoichiometric trials

To a flame-dried Schlenk tube (A) equipped with a magnetic stir bar was added benzothiophene 68.2 mg (0.5 mmol) inside a glove box. The flask was sealed with a silicon septum and transferred out of the glove box. Dry THF (3 ml) was injected through the septum and the solution was stirred for two minutes and then cooled down to -78°C. Then 200 µl (0.5 mmol) of a solution of *n*-BuLi in hexane (2.5 M) was slowly injected through the septum. The mixture was stirred for 2 h at -78°C. To a second flame-dried Schlenk tube (B) equipped with a magnetic stir bar was added either 71.4 mg of Ni(bpy)Cl_2 (0.25 mmol) or 68.8 mg of Ni$(COD)_2$ (0.25 mmol) together with 39.0 mg of bpy (0.25 mmol) inside a glove box. Then 2.5 ml of dry THF, iodobenzene (35 µl, 0.3 mmol) and dodecane (40 µl, 0.174 mmol) as an internal standard for GC-FID analysis were injected through the septum and the solution was stirred for two minutes. To this mixture (B) 1.5 ml of solution A was added and the mixture was stirred and heated to 120°C. After 2 h the reaction mixture was quenched with 2 ml of methanol. The yield was determined using GC-FID analysis.

In the case of Ni(bpy)Cl_2 the mixture was then evaporated to dryness and subjected liquid size exclusion chromatography. 2,2'-bibenzo[*b*]thiophene (bis-BT) is obtained as a pale yellow solid in 74% isolated yield and 2-phenylbenzothiophene (2-Ph-BT) is obtained in 16% isolated yield. In the case of Ni$(COD)_2$/bpy, only traces of bis-BT and 2-Ph-BT are observed (GC-FID).

Characterization of 2,2'-bibenzo[*b*]thiophene:



^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 7.86 - 7.73 (4H, m), 7.52 (2H, s), 7.40 - 7.30 (4H, m). **^{13}C{^{1}H} NMR** (100.61 MHz, $CDCl_3$) δ: 140.2, 139.5, 137.4, 125.0, 124.9, 123.7, 122.3, 121.5. **HRMS (EI):** calculated for $C_{16}H_{10}S_2^+$: 266.0218 (m/z $[M]^+$), found 266.0217 (m/z $[M]^+$). Data is in accordance with the literature.[20]

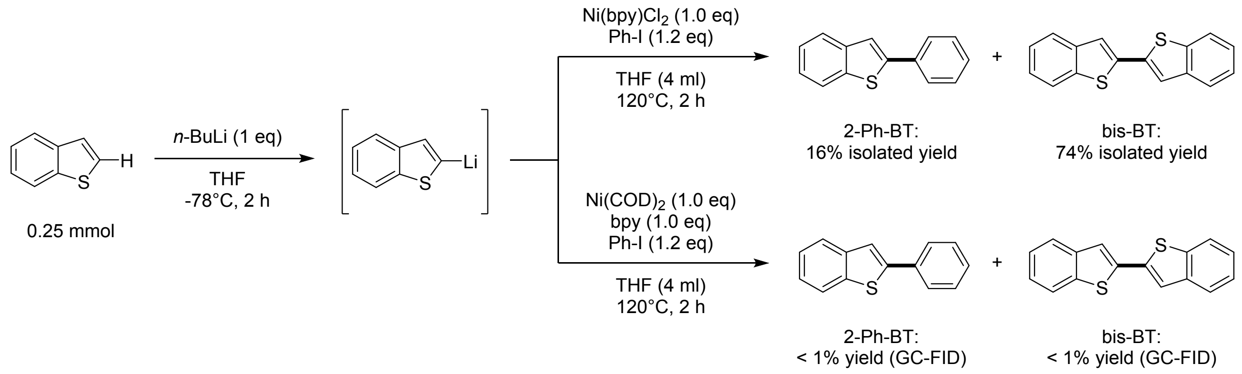


Figure S1: Overview of conditions for the stoichiometrical trials with Ni(II) and Ni(0).

5.3. Direct arylation trials of heteroarenes with varying pK_a values

To a flame-dried Schlenk tube equipped with a magnetic stir bar were added the corresponding heteroarene (0.5 mmol), Ni(bpy)Cl_2 (2.9 mg, 10 µmol, 2 mol%) and 189 mg of LiHMDS (1.1 mmol, 2.2 eq), inside a glove box. The flask was sealed with a silicon septum and transferred out of the glove box. Dry toluene (4 ml) was injected through the septum and the mixture was stirred for two minutes. Then iodobenzene (69 µl, 0.6 mmol, 1.2 eq) and dodecane (40 µl, 0.174 mmol) as an internal standard for GC-FID analysis were injected through the septum. If the heteroarene is a liquid it was injected alongside iodobenzene and dodecane through the septum. The reaction was stirred and heated to 120°C. After 16 h the reaction mixture was quenched with 2 ml methanol. The yield of the phenylated heteroarene was determined using GC-FID analysis.

5.4. Probing of lithiated benzothiophene under catalytic conditions and evidence for a dynamic deprotonation/lithiation equilibrium

Deuterium scrambling and probing for lithiated benzothiophene in toluene: To a flame-dried Schlenk tube equipped with a magnetic stir bar were added 69.2 mg of benzothiophene (0.5 mmol) and 276 mg of LiHMDS (1.6 mmol, 3.2 eq) inside a glove box. The flask was sealed with a silicon septum and transferred out of the glove box. Dry toluene (4 ml) was injected through the septum and the mixture was stirred for two minutes. Then MeOD (20.5 µl, 0.5 mmol, 1 eq) was injected through the septum and the mixture was stirred for two minutes. The reaction was stirred and heated to 120°C. After 100 min the reaction mixture was quenched with 0.5 ml of deionized water (a) or D_2O (b). The organic phase was separated and the solvent removed by rotary evaporation. The residue was solubilized in $CDCl_3$ and the deuterium incorporation into benzothiophene was determined by ^{1}H NMR analysis.

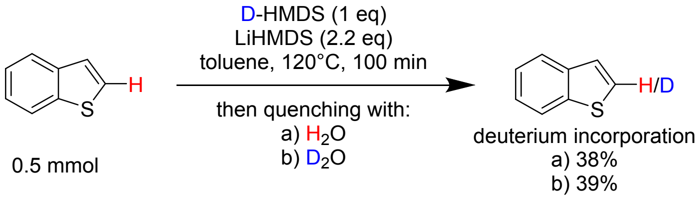


Figure S2: Overview of deuterium scrambling and probing for lithiated benzothiophene in toluene.

Deuterium scrambling and probing for lithiated benzothiophene in dioxane: To a flame-dried Schlenk tube equipped with a magnetic stir bar were added 69.2 mg of benzothiophene (0.5 mmol) and 276 mg of LiHMDS (1.6 mmol, 3.2 eq) inside a glove box. The flask was sealed with a silicon septum and transferred out of the glove box. Dry dioxane (4 ml) was injected through the septum and the mixture was stirred for two minutes. Then MeOD (20.5 µl, 0.5 mmol, 1 eq) was injected through the septum and the mixture was stirred for two minutes. The reaction was stirred and heated to 120°C. After 100 min the reaction mixture was quenched with 0.5 ml of MeOH (a) or MeOD (b). The solvent was removed by rotary evaporation and the residue was solubilized in $CDCl_3$. The deuterium incorporation into benzothiophene was determined by ^{1}H NMR analysis.

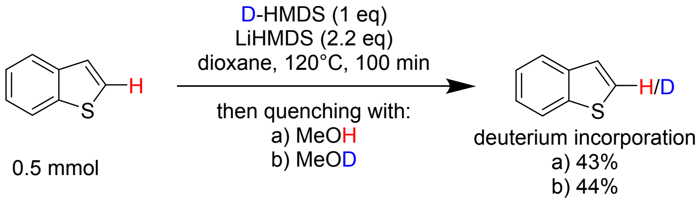


Figure S3: Overview of deuterium scrambling and probing for lithiated benzothiophene in dioxane.

Probing for lithiated benzothiophene in dioxane: To a flame-dried Schlenk tube equipped with a magnetic stir bar were added 69.2 mg of benzothiophene (0.5 mmol) and 189 mg of LiHMDS (1.1 mmol, 2.2 eq) inside a glove box. The flask was sealed with a silicon septum and transferred out of the glove box. Dry dioxane (4 ml) was injected through the septum and the mixture was stirred for two minutes. The mixture was stirred for two minutes. The reaction was stirred and heated to 120°C. After 100 min the reaction mixture was quenched with 0.5 ml of MeOD. The solvent was removed by rotary evaporation and the residue was solubilized in $CDCl_3$. The deuterium incorporation into benzothiophene was determined by ^{1}H NMR analysis.

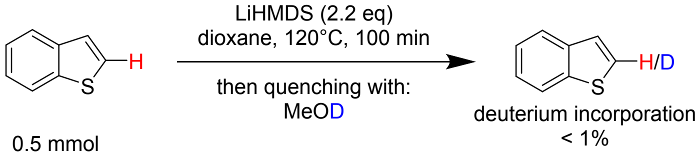


Figure S4: Overview of deuterium scrambling and probing for lithiated benzothiophene in dioxane.

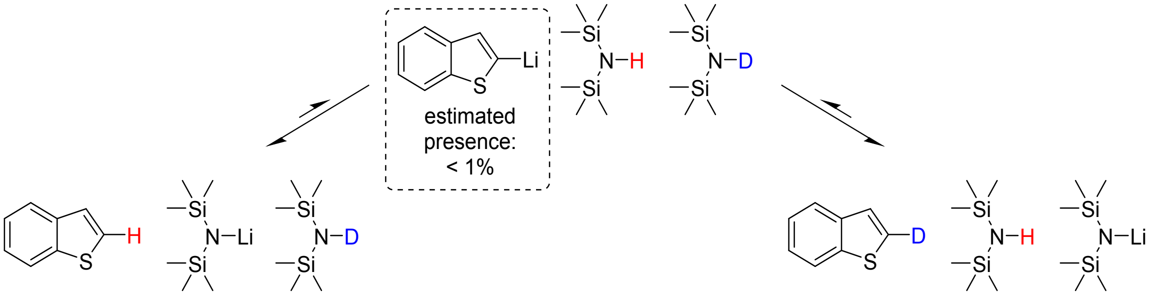


Figure S5: Summary of postulated dynamic deprotonation/lithiation deuteration equilibrium as evidenced in Figure S2 to Figure S4.

Deuterium scrambling and probing for lithiated benzothiophene in dioxane using LiO-tBu: To a flame-dried Schlenk tube equipped with a magnetic stir bar were added 69.2 mg of benzothiophene (0.5 mmol) and 132 mg of LiO-*t*Bu (1.6 mmol, 3.2 eq) inside a glove box. The flask was sealed with a silicon septum and transferred out of the glove box. Dry dioxane (4 ml) was injected through the septum and the mixture was stirred for two minutes. Then MeOD (20.5 µl, 0.5 mmol, 1 eq) was injected through the septum and the mixture was stirred for two minutes. The reaction was stirred and heated to 120°C. After 100 min the reaction mixture was quenched with 0.5 ml of MeOH (a) or MeOD (b). The solvent was removed by rotary evaporation and the residue was solubilized in $CDCl_3$. The deuterium incorporation into benzothiophene was determined by ^1H NMR analysis.

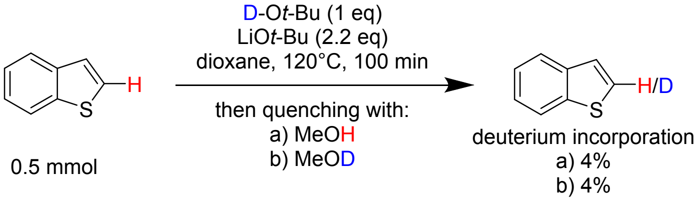


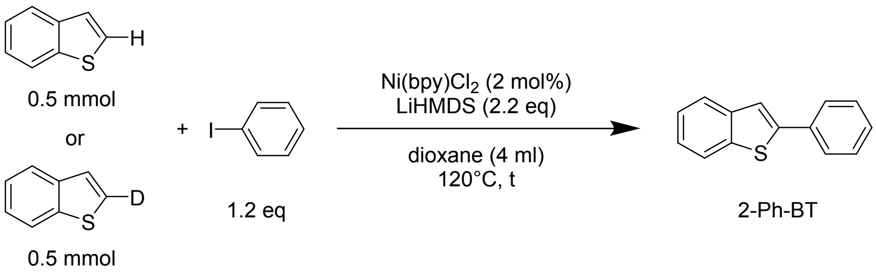
Figure S6: Overview of deuterium scrambling and probing for lithiated benzothiophene with LiO*t*-Bu/D-O*t*-Bu.

Note: LiO*t*-Bu as a weaker base (pK_a of HO*t*-Bu ~ 18) is not capable of ensuring a sufficient dynamic deprotonation/lithiation equilibrium.

5.5. Kinetic profile of catalysis and determination of the kinetic isotopic effect (KIE)

To a flame-dried Schlenk tube equipped with a magnetic stir bar were added benzothiophene (62.2 mg, 0.5 mmol) or benzothiophene-2-*d* (62.7 mg, 0.5 mmol), LiHMDS (189 mg, 1.1 mmol, 2.2 eq) and Ni(bpy)Cl_2 (2.9 mg, 10 µmol, 2 mol%) inside a glove box. The flask was sealed with a silicon septum and transferred out of the glove box. Dry dioxane (4 ml) was injected through the septum and the mixture was stirred for two minutes. Then iodobenzene (69 µl, 0.6 mmol, 1.2 eq) and dodecane (40 µl, 0.174 mmol) as an internal standard for GC-FID analysis were injected through the septum. The reaction was stirred and heated to

120°C. Samples of the reaction mixture were taken at defined points in time (10, 20, 30, 40, 50, 60, 120, 240, 360 and 1380 minutes). The respective yields were determined by GC-FID analysis.



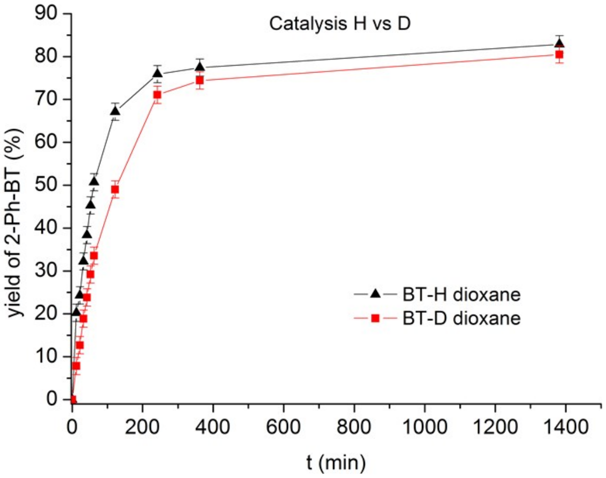


Figure S7: Kinetic profile of the nickel catalyzed direct arylation of benzothiophene (BT-H, black triangles) and benzothiophene-2-*d* (BT-D, red squares) in dioxane.

The KIE for the direct arylation at the C2 position of benzothiophene (BT-H vs BT-D) was calculated from the initial rate constants (k_H and k_D) for short reaction time (< 60 min):

KIE = k_H/k_D = 0.0090/0.0060 = **1.5**

5.6. Qualitative correlation of the kinetic profiles of H/D exchange and catalysis

H/D exchange for benzothiophene in dioxane: To a flame-dried Schlenk tube equipped with a magnetic stir bar were added 69.2 mg of benzothiophene (0.5 mmol) or benzothiophene-2-*d* (62.7 mg, 0.5 mmol) and 276 mg of LiHMDS (1.6 mmol, 3.2 eq) inside a glove box. The flask was sealed with a silicon septum and transferred out of the glove box. Dry dioxane (4 ml) was injected through the septum and the mixture was stirred for two minutes. Then MeOD (20.5 µl, 0.5 mmol, 1 eq) or MeOH (20.5 µl, 0.5 mmol, 1 eq) was injected through the septum. The reaction was stirred and heated to 120°C. Samples of the reaction mixture were taken at defined points in time (10, 20, 30, 40, and 100 minutes) and quenched with either MeOH or MeOD. The solvent was removed by rotary evaporation and the respective residues were solubilized in $CDCl_3$. The deuterium (proton) incorporation into benzothiophene (benzothiophene-2-*d*) was determined by ^{1}H NMR analysis.

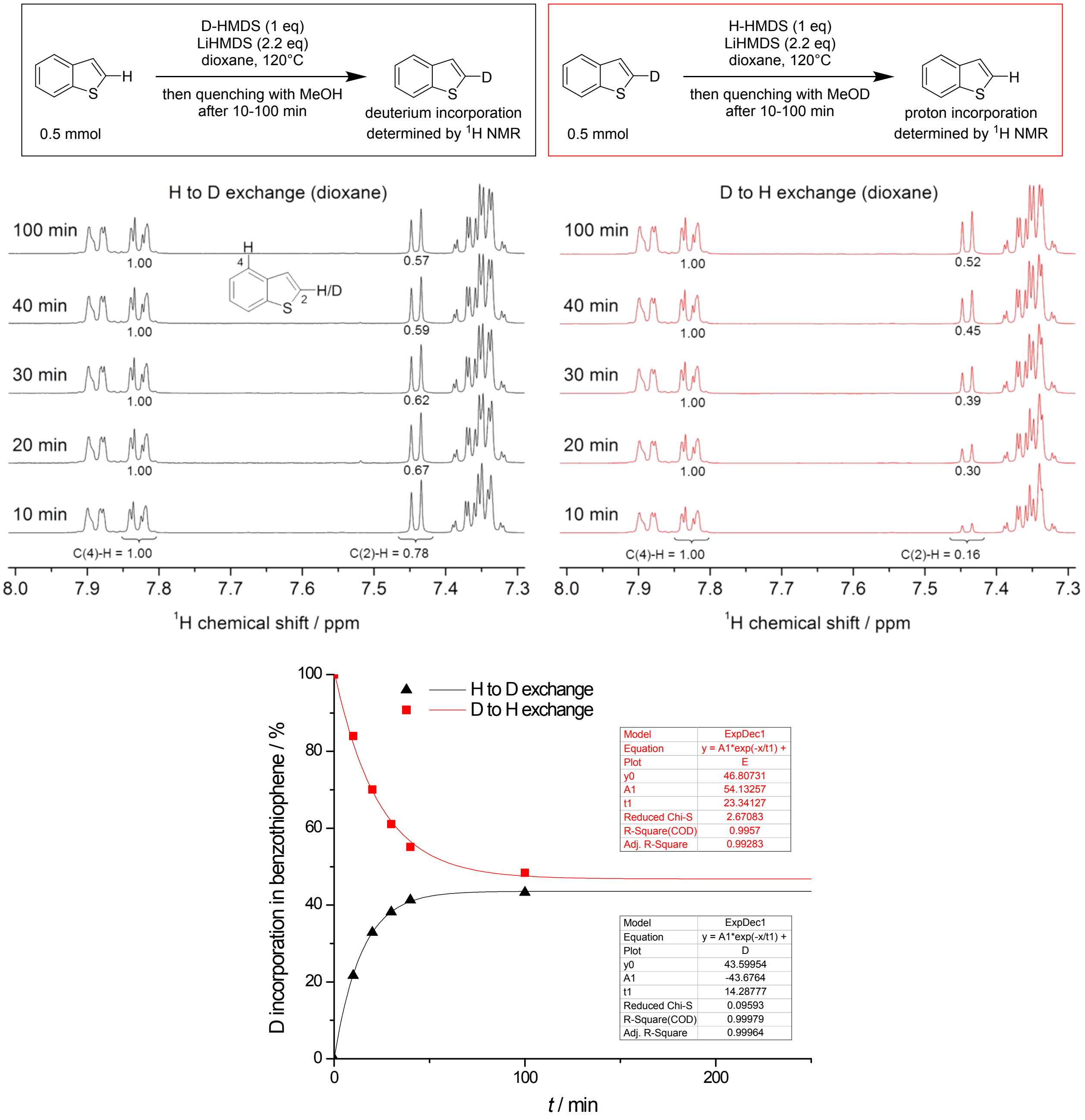


Figure S8: Time-dependent evolution of the LiHMDS mediated H/D exchange of benzothiophene (BT-H, black) and benzothiophene-2-*d* (BT-D, red) in dioxane. The deuterium incorporation was determined using ^{1}H-NMR (400.13 MHz, $CDCl_3$). In the depicted ^{1}H-NMR spectra the section of δ: 8.0 - 7.3 ppm is shown covering all benzothiophene resonances. The integral of the C(2)-H resonance is expressed relative to the integral of C(4)-H.

Similarly to the direct arylation of benzothiophene(-2-*d*) (Figure S7) also the LiHMDS mediated H/D exchange shows a different reaction rate depending on the starting isotope used (Figure S8). The ratio of the initial rate constants ($k_{\text{H-to-D}}$ and $k_{\text{D-to-H}}$) was calculated for a short reaction time (< 20 min):

$$\boldsymbol{k_{\text{H-to-D}}/k_{\text{D-to-H}}} = 0.0175/0.150 = \mathbf{1.2}$$

H/D exchange for benzothiophene in toluene: To a flame-dried Schlenk tube equipped with a magnetic stir bar were added 69.2 mg of benzothiophene (0.5 mmol) and 276 mg of LiHMDS (1.6 mmol, 3.2 eq) inside a glove box. The flask was sealed with a silicon septum and transferred out of the glove box. Dry toluene (4 ml) was injected through the septum and the mixture was stirred for two minutes. Then MeOD (20.5 µl, 0.5 mmol, 1 eq) was injected through the septum. The reaction was stirred and heated to 120°C. Samples of the reaction mixture were taken at defined points in time (10, 20, 30, 40, and 100 minutes) and quenched with MeOH. The solvent was removed by rotary evaporation and the respective residues were solubilized in $CDCl_3$. The deuterium incorporation into benzothiophene was determined by ^1H NMR analysis.

Catalysis with benzothiophene in toluene: the same protocol as in section 5.5 was applied by using benzothiophene (62.2 mg, 0.5 mmol) and dry toluene (4 ml) instead of dioxane.

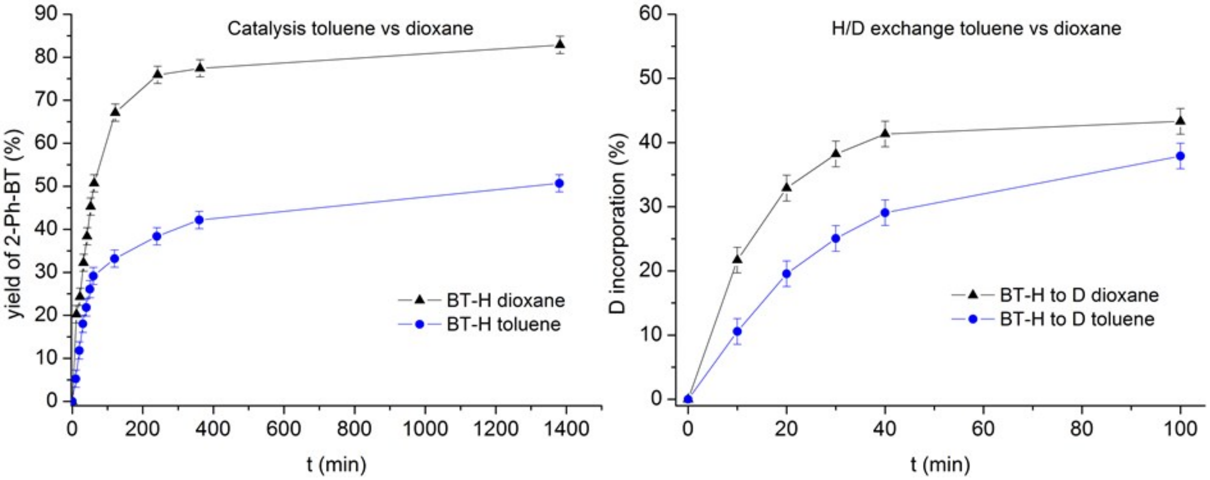


Figure S9: Left, comparison of the kinetic profiles for the catalysis with benzothiophene in dioxane (black triangle) and toluene (blue circle); right, comparison of the kinetic profiles for deuterium incorporation into benzothiophene in dioxane (black triangle) and toluene (blue circle).

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