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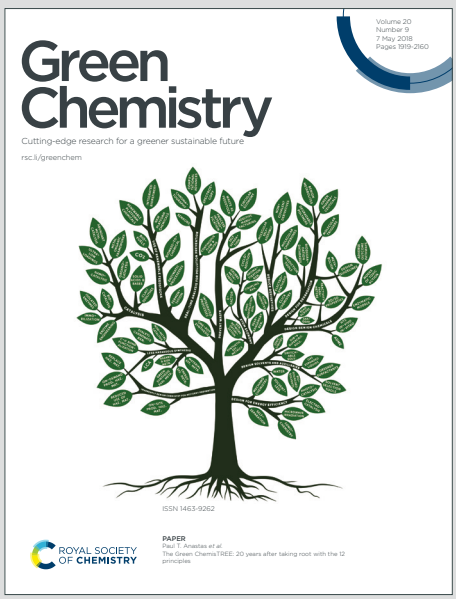

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ARTICLE

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

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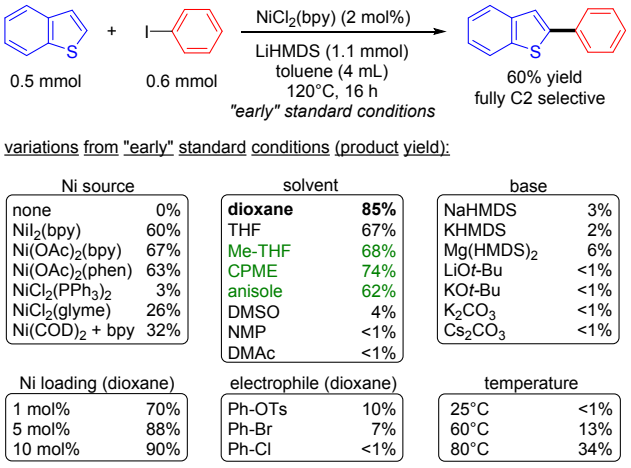
A nickel-based catalytic system for the regiospecific C2-H arylation of benzothiophene has been established. $NiCl_2$(bpy) is used as catalyst in combination with LiHMDS as base in dioxane. The catalytic system is applicable to a variety of funtionalized benzothiophenes, as well as other heteroarenes including thiophene, benzodithiophene, benzofuran and selenophene in combination with iodo aryl electrophiles. The role of LiHMDS as uniquely potent base and a postulated mechanism are discussed. The applicability of this system is finally demonstrated for the synthesis of an intermediate of an active pharmaceutical ingredient.

Introduction

In the quest of sustainable fine chemicals synthesis, the arylation reaction through C-H activation for (hetero)biaryl synthesis keeps attracting a wide interest for its advantageous atom economy and applicability in the synthesis of active pharmaceutical ingredients (API) and organic materials.[1–5] In parallel to transition metal-free biaryl synthesis,[6–9] non-noble metal catalysts attract a growing attention[2,10,11] with several successful advances made for the direct C-H arylation of heteroarenes using catalysts based on earth-abundant copper, nickel or iron.[11,12]

Among heterobiaryls, benzothiophenes are widely used as API[13,14] and optoelectronics building blocks.[15–18] In contrast to 30 years of literature on Pd[19–24] or Ir-catalyzed reactions,[25,26] the direct C-H arylation of benzothiophene using earth-abundant metal systems remains scarcely studied. For example, Daugulis and co-workers reported the C-H phenylation of benzothiophene catalyzed by the combination of 10 mol% CuI/phenanthroline and lithium 3-ethyl-3-pentanolate in *N*,*N*'-dimethylpropyleneurea.[27] More recently, Nakamura *et al.* reported the Fe-catalyzed direct oxidative C2 arylation of benzothiophene in the presence of a mixture of organozinc and organomagnesium reagents using an *N*,*N*'-bidentate permanent directing group on the phenyl electrophile.[28]

To the best of our knowledge, we report here the first example of a Ni-catalyzed direct C-H arylation of benzothiophenes.



Scheme 1 Discovery and optimisation of the Ni-catalyzed direct C-H arylation of benzothiophene. Solvents highlighted in green indicate sustainable alternatives to dioxane.[29]

This system is regiospecific, *i.e.* fully regioselective, towards 2-phenylbenzothiophene, as no detectable amounts of other regioisomers were formed. It is also shown to be applicable to various aryl electrophiles and to thiophene, benzofuran and selenophene.

Results and discussion

Discovery of Ni-catalyzed C2-H arylation of benzothiophene.

Starting from the "early" standard conditions, we first determined the most adequate reaction parameters for the phenylation of benzothiophene catalyzed by a molecular nickel salt (Scheme 1). After a screening of reaction parameters, we found that the Ni-based system requires the presence of a bipyridine (bpy) ligand and produces regioselectively 2-phenylbenzothiophene with 60% yield when combined with 2.2 eq of lithium hexamethyldisilazide (LiHMDS) as base in

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toluene at 120°C. A lower amount of base led to significantly reduced yield (Table S1). As shown in the scheme 1, the reaction does not proceed in the absence of nickel. Furthermore, *N*,*N*'-chelating ligands allow for higher yields (phenanthroline (phen): 63%, bipyridine: 67%) as compared to a labile ethereal (26%) or phosphine ligands (3%), while the nature of the counter ion (Cl^-, I^-, AcO^-) has no significant influence onto the reaction outcome (Scheme 1). Finally, employing a Ni(0) complex leads to a drop in activity (32%) as compared to Ni(II).

In toluene, when LiHMDS was replaced by other bases like *tert*-butoxides or carbonates, no targeted arylation product was observed. *Tert*-butoxide bases were also found not suitable in dioxane either, contrary to previous reports showing that similar nickel complexes catalyze the C-H arylation of azole-based heteroarenes, using 10 mol% of catalyst in the presence of lithium *tert*-butoxide.[30–32] However these catalytic systems proved to be unreactive towards benzothiophene derivatives (Table S1 and ref. 30).

Other hexamethyldisilazide bases like sodium hexamethyldisilazide (NaHMDS, 3%), potassium hexamethyldisilazide (KHMDS, 2%) or magnesium bis(hexamethyldisilazide) ($Mg(HMDS)_2$, 6%) allow for the benzothiophene arylation with only low yields.

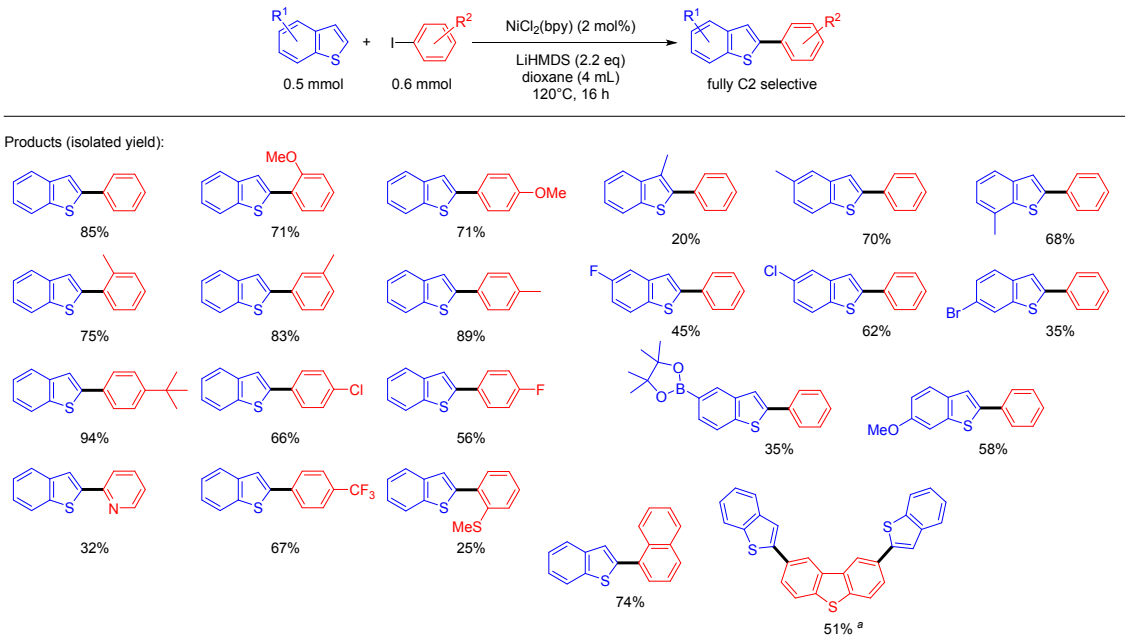
Compared to toluene, the $NiCl_2$(bpy) catalyst was found to be more active in ethereal solvents with the highest yield obtained using 1,4-dioxane (85%). Other ethers like 2-methyl-tetrahydrofuran (Me-THF, 68%), cyclopentyl methyl ether (CPME, 74%) and anisole (62%) are interesting sustainable alternatives to 1,4-dioxane.[29] Other polar solvents like dimethyl sulfoxide (DMSO, 4%), *N*-methyl-2-pyrrolidone (NMP, <1%) or *N*,*N*-dimethylacetamide (DMAc, <1%) showed negligible activity. Contrarily to toluene, in dioxane, the nickel dichloride catalyst gave a slightly higher yield in 2-phenylbenzothiophene formation as compared to the nickel diacetate analogue (Table S1).

Under the optimized conditions based on $NiCl_2$(bpy) combined with LiHMDS in dioxane, phenyl tosylate (Ph-OTs, 10%) and phenyl bromide (Ph-Br, 7%) can be used as aryl electrophiles leading however to low conversions, in contrast to unreactive phenyl chloride (Ph-Cl, <1%). Moreover, the catalytic system is operational at loadings as low as 1 mol% of nickel, but giving rise to a lower yield after 16 hours (70% with 1 mol% and 85% with 2 mol%). Increasing the Ni loading from 2 mol% to 5 or 10 mol% resulted in only limited improvement (88% and 90%, respectively).

Scope of applicable substrates.

A series of electronically and structurally diverse aryl iodides was evaluated under the optimized conditions (*i.e.* 2 mol% $NiCl_2$(bpy) with LiHMDS in dioxane, see Scheme 2). Both electron donating (*p*-Me: 89%, *p*-*t*-Bu: 94%, *p*-OMe: 71%) and electron withdrawing functional groups (*p*-Cl: 66%, *p*-F: 56%, *p*-CF_3: 67%) are tolerated, resulting in good to excellent yields. Sterically congested *ortho*-substituted aryl electrophiles can be used without major restriction (*o*-Me: 75%, *o*-OMe: 71%, *o*-SMe: 25%). Hetero- and polyaromatics, like pyridyl (32%), naphtyl (74%) and dibenzothienyl (51%), can also be efficiently applied to obtain π-delocalized molecular organic backbones with moderate to good yields.

Similarly, benzothiophenes functionalized at various positions were also studied under optimized conditions (Scheme 2). Substitution at the C5, C6 and C7 position is well tolerated regardless of the functional group being electron donating or electron withdrawing. The capacity to obtain 6-bromo and 5-pinacolboronate substituted benzothiophenes is noteworthy as much as these products allow for further functionalization. The 3-methylbenzothiophene can be phenylated with, however, a low yield (20%), presumably due to the steric hindrance reducing the accessibility of the C2 position.



Scheme 2 Scope of applicable aryl electrophiles and substituted benzothiophenes ([a] 0.2 mmol of 2,8-diiododibenzothiophene is used).

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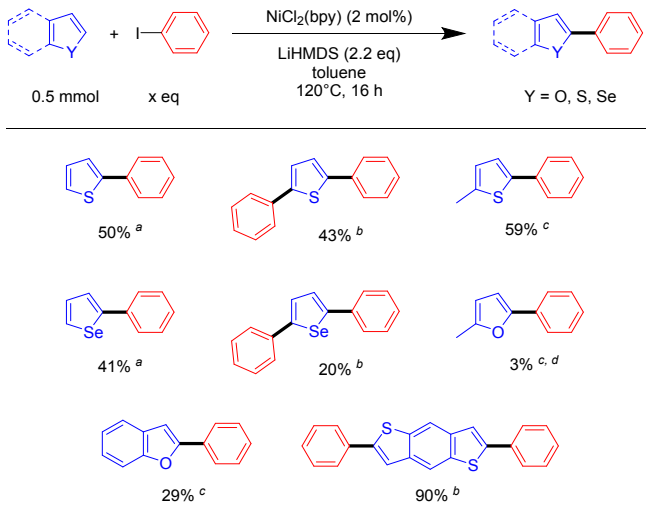
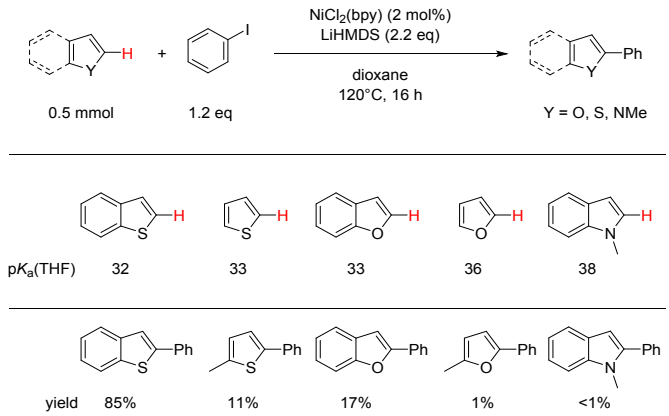


Scheme 3 Scope of other applicable heteroarenes. Isolated yields are determined based on the limiting reactant ([a] x = 0.4; [b] x = 2.4; [c] x = 1.2). [d] GC-FID yield.

In all cases, only C2 arylated benzothiophenes were obtained without any traces of other regioisomers, thus confirming the regiospecific nature of this reaction protocol.

The scope of applicable heteroarenes was further evaluated with the $NiCl_2$(bpy)/LiHMDS catalytic system (Scheme 3). Trials in dioxane led to only low activity in most cases (see Supplementary Information, section 4.3 for details). Nevertheless, by employing toluene as solvent, thiophenes and selenophene could be arylated at the C2 (and/or C5) position with moderate to good yields. 2-Methylfuran was found to react only poorly (3%), whereas benzofuran could be arylated in moderate yield (29%). It is worth noting that the direct arylation of selenophene is only scarcely documented and was until now entirely limited to Pd-based catalysts.[33–35]



Scheme 4 C2-H pK_a of various heteroarenes determined in THF[39] and corresponding Ni-catalyzed C2-H phenylation yield in dioxane.

Mechanistic insights.

Role of LiHMDS and dynamic equilibrium. As shown in Scheme 1, while LiHMDS successfully promotes the Ni-catalyzed direct arylation of benzothiophene, other related systems give poor yields: most of the other bases tested did not allow reaching yields higher than 3%, except for Mg^{2+} (6%, see Table S1). Similarly to previous studies on Pd[36] and Ni-catalyzed C-H arylation reactions,[30,32,37] lithium seems to be a key element for the reactivity of this benzothiophene-nickel system.

The unique role of LiHMDS is not solely due to its capacity to generate the lithiated benzothiophene (BT-Li) in solution. The use of a stronger lithiated base than LiHMDS, lithium diisopropylamide (LDA, pK_a ~ 36 in THF),[38] led to degradation of the benzothiophene under the catalytic conditions, without formation of the arylated product.

LiHMDS is expected to yield small amounts of lithiated substrate BT-Li in solution (BT-H: pK_a ~ 32 in THF[39] *versus* hexamethyldisilazane: pK_a ~ 30 in THF[38], see Scheme 4).

In order to get deeper insight into the deprotonation step of benzothiophene, we designed different deuterium scrambling experiments (Scheme 5 and Supplementary Information).

First, after letting react benzothiophene with LiHMDS under conditions similar to those of catalysis (dioxane, 120°C), and quenching the reaction mixture with deuterated methanol, only traces of deuterated benzothiophene were detected (Scheme 5a). This shows that almost no lithiated benzothiophene is present in the solution under conditions similar to those of catalysis. In a second set of experiments, benzothiophene was allowed to react with LiHMDS (2.2 eq) in the presence of *N*-deuterated hexamethyldisilazane (D-HMDS, 1 eq). The solution was then quenched with either MeOH or MeOD (Scheme 5b). Liquid state ^{1}H NMR analysis of the organic solution revealed a deuterium incorporation of *ca.* 43-44% in the two cases (Scheme 5b). Repeating the same experiment in toluene led to a similar result (Figure S2). This evidences the existence of a dynamic equilibrium between the protonated and lithiated benzothiophene species, in favor of the protonated (deuterated) form. The same deuterium scrambling experiments as in Scheme 5b were performed with lithium *tert*-butoxide as base. These tests yielded only minor deuterium incorporation (ca. 4%) which shows the inability of LiO*t*-Bu to sufficiently generate lithiated benzothiophene (Figure S6), in line with a negligible catalytic activity (Scheme 1). Finally, parallel experiments were performed for proton-deuterium exchange starting from benzothiophene in the presence of LiHMDS and D-HMDS, for a H-to-D exchange, or starting from (2-^{2}H)-benzothiophene in the presence of LiHMDS and hexamethyldisilazane (H-HMDS), for a D-to-H exchange (Scheme 5c).

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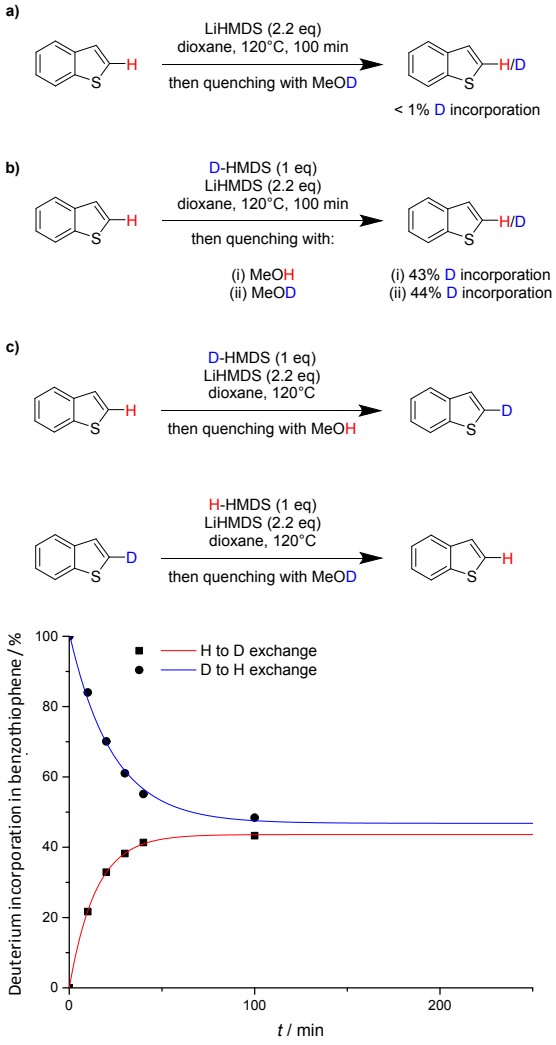

Scheme 5 Deuterium scrambling experiments and evidence for a LiHMDS-mediated dynamic deprotonation/lithiation equilibrium.

The comparison of the kinetic profiles of the H-to-D and D-to-H exchange shows a small difference depending on the isotope used ($k_{H\text{-to-}D}/k_{D\text{-to-}H}$ = 1.2, see Supplementary Information, section 5.6).

We thus propose that, despite its lower pK_a value, LiHMDS is able to deprotonate benzothiophene to a certain extent and that this deprotonation/lithiation reaction displays a dynamic equilibrium. The resulting lithiated benzothiophene species (BT-Li) seems to be present in solution in only a very small amount. However, with its consumption over the course of catalysis, BT-Li should be continuously reformed thanks to the dynamic deprotonation/lithiation equilibrium. Moreover this dynamic equilibrium is much favoured in dioxane than in toluene (Figures S2 and S9).

This proposal is corroborated by the fact that when acids weaker than benzothiophene (namely thiophene, benzofuran, furan and *N*-methylindole) are used, a drop in the yields of the C2-H phenylation is observed that follows the trend expected from the respective pK_a values (Scheme 4).

Catalytic pathway. To get deeper insight into the possible reaction mechanism, deuterium-labelled substrates were subjected to catalysis.

First, when (3-^{2}H)-benzothiophene was used as a substrate, the final product was obtained with complete deuterium retention (2-phenyl-(3-^{2}H)-benzothiophene), which excludes any C-H activation on the C3 position (see Supplementary Information, section 4.3).

This is further supported by the fact that 3-methylbenzothiophene can be C2-arylated (Scheme 2). Conversely, the use of 2-methylbenzothiophene led to no reaction at all, further supporting the absence of reactivity of the C3 position (Table S2).

Further, comparing the direct arylation of benzothiophene and (2-^{2}H)-benzothiophene as substrates in parallel reactions, a kinetic isotopic effect (KIE) could be observed (KIE = k_H/k_D = 1.5; see Figure S7). This small value points towards a mechanism in which the C-H bond cleavage is reversible, in line with the above-described deprotonation/lithiation equilibrium, and not rate-determining, but takes place before the rate-determining step.[40]

We also investigated the role of the nickel oxidation state. Reactions were performed under stoichiometric conditions using Ni(II) and Ni(0) precursors. The use of Ni(II)Cl_2(bpy) gave rise to a yield of 74% for bis-benzothiophene, resulting from homocoupling of benzothiophene, and 16% of 2-phenyl-benzothiophene. Contrarily, Ni(0)$(COD)_2$ in combination with bpy led to no homocoupling of benzothiophene and only traces of 2-phenylbenzothiophene (see Figure S1). We could thus conclude that (i) the initial reduction of the Ni(II) most likely occurs *via* the formation of bis-benzothiophene, similar to the Ni-catalyzed direct arylation of azoles,[30,32] and that (ii) Ni(0) is unlikely to be the active species in the present case. This latter mechanistic aspect differs from previously published nickel-catalyzed Li-mediated C-H arylation of heteroarenes.[31] It is worth noting that on a catalytic scale, *i.e.* few mol% of metal, redox reactions could occur to generate some active nickel species from Ni(0) explaining the moderate yield obtained using a Ni$(COD)_2$ precatalyst (Scheme 1). In contrast to more common Ni(0)/Ni(II) mechanisms, we postulate here a polar redox pathway involving the odd oxidation states Ni(I) and Ni(III) for this reaction.[41,42]

Noteworthy in the reported transition metal-free systems, C-H arylation involved aryne intermediates.[43,44] Here the existence of such aryne species can be ruled out because *ortho*-substituted aryl electrophiles led to single *ortho*-substituted products.

Thus the benzothiophene arylation most likely occurs through (i) the oxidative addition of Ni(I) to the aryl electrophile (Ar-X) *in-situ* resulting in an Ar-Ni(III)-X intermediate, followed by (ii) the transmetallation with the lithiated benzothiophene (BT-Li) giving rise to Ar-Ni(III)-BT, and ending with (iii) the reductive elimination of a heterobiaryl (BT-Ar) with the regeneration of the Ni(I) species. A plausible reaction mechanism summarizing these steps is depicted in Scheme 6.

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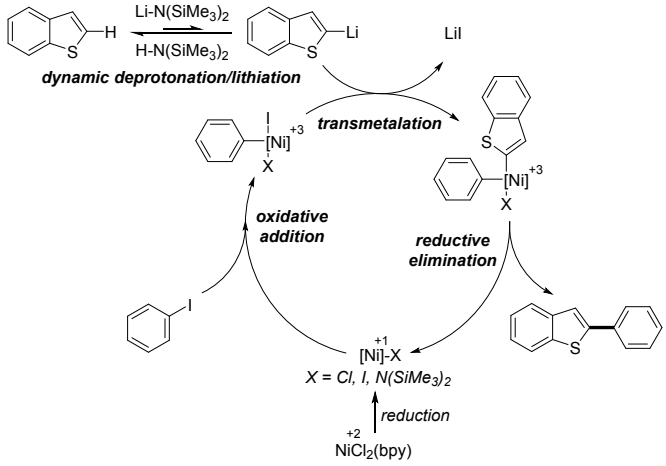


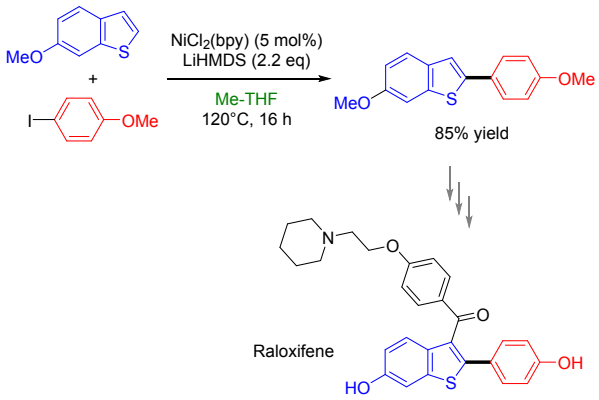
Scheme 6 Postulated mechanism for the Ni-catalyzed C-H arylation of benzothiophene. Neutral ligands on Ni are omitted for clarity.

Application to API intermediate.

To demonstrate its synthetic potential, the reported Ni-catalyzed C-H arylation has been applied to the synthesis of a Raloxifene intermediate in 2-methyltetrahydrofuran (Me-THF) as sustainable solvent (Scheme 6). Raloxifene is a selective estrogen receptor modulator used for the treatment and prevention of postmenopausal disorders, osteoporosis and breast cancer.[45] This API is based on a substituted 2-arylbenzothiophene unit. The formation of this unit classically requires multistep cyclization[46–48] or palladium-catalyzed cross-coupling reactions.[49,50]

Here, under Ni-catalyzed C-H arylation, the commercially available 6-methoxybenzothiophene and *p*-iodo-methoxybenzene underwent cross-coupling in Me-THF to give the corresponding 6-methoxy-2-(4-methoxyphenyl)-benzothiophene regiospecifically with 85% yield (Scheme 7).

Compared to the Pd-catalyzed Suzuki-Miyaura cross-coupling synthesis of this intermediate (81% yield),[50] a higher yield could be reached in our case, while replacing palladium with nickel, omitting the use of a boronic acid prefunctionalized benzothiophene and carrying out the reaction through C-H activation instead.



Scheme 7 Synthesis of Raloxifene intermediate *via* Li-mediated nickel catalysis in 2-methyltetrahydrofuran as sustainable solvent.

Experimental

In a typical catalysis experiment, benzothiophene (69.2 mg, 0.5 mmol), LiHMDS (189 mg, 1.1 mmol, 2.2 eq) and a nickel complex (2 mol%) were added 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 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 crude product was purified by liquid size exclusion chromatography equipped with PLGel columns (10 µm, 50 Å) and using chloroform as eluent to obtain the isolated product.

Conclusions

For the first time a Ni-based catalytic system is reported for the direct C2-H arylation of benzothiophenes, benzofuran and selenophene. This reaction is fully regioselective without any directing group. Mechanistic investigations unravelled that LiHMDS plays a key role in this reaction, ensuring the C-H arylation of these heteroarenes in the C2 position. The applicability of this earth-abundant metal catalytic system for C-H activation in a sustainable solvent has been demonstrated and underlines its strong potential for the synthesis of fine chemicals.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Notes and references

1 J. Yamaguchi, A. D. Yamaguchi and K. Itami, *Angew. Chem. Int. Ed.*, 2012, **51**, 8960–9009.
2 P. Gandeepan, T. Müller, D. Zell, G. Cera, S. Warratz and L. Ackermann, *Chem. Rev.*, 2019, **119**, 2192–2452.
3 T. Gensch, M. J. James, T. Dalton and F. Glorius, *Angew. Chem. Int. Ed.*, 2018, **57**, 2296–2306.
4 J. Wencel-Delord and F. Glorius, *Nat. Chem.*, 2013, **5**, 369–375.

5 Y. Segawa, T. Maekawa and K. Itami, *Angew. Chem. Int. Ed.*, 2015, **54**, 66–81.
6 R. Budhwan, S. Yadav and S. Murarka, *Org. Biomol. Chem.*, 2019, **17**, 6326–6341.
7 S. Lips, D. Schollmeyer, R. Franke and S. R. Waldvogel, *Angew. Chem. Int. Ed.*, 2018, **57**, 13325–13329.
8 Z. He, H. J. Shrives, J. A. Fernández-Salas, A. Abengózar, J. Neufeld, K. Yang, A. P. Pulis and D. J. Procter, *Angew. Chem. Int. Ed.*, 2018, **57**, 5759–5764.
9 R. Rossi, M. Lessi, C. Manzini, G. Marianetti and F. Bellina, *Adv. Synth. Catal.*, 2015, **357**, 3777–3814.
10 Y.-F. Zhang and Z.-J. Shi, *Acc. Chem. Res.*, 2019, **52**, 161–169.
11 G. Pototschnig, N. Maulide and M. Schnürch, *Chem. – Eur. J.*, 2017, **23**, 9206–9232.
12 R. Shang, L. Ilies and E. Nakamura, *Chem. Rev.*, 2017, **117**, 9086–9139.
13 S. Dadiboyena, *Eur. J. Med. Chem.*, 2012, **51**, 17–34.
14 R. S. Keri, K. Chand, S. Budagumpi, S. Balappa Somappa, S. A. Patil and B. M. Nagaraja, *Eur. J. Med. Chem.*, 2017, **138**, 1002–1033.
15 H. Ebata, T. Izawa, E. Miyazaki, K. Takimiya, M. Ikeda, H. Kuwabara and T. Yui, *J. Am. Chem. Soc.*, 2007, **129**, 15732–15733.
16 M. R. Reddy, H. Kim, C. Kim and S. Seo, *Synth. Met.*, 2018, **235**, 153–159.
17 H. Yao, L. Ye, H. Zhang, S. Li, S. Zhang and J. Hou, *Chem. Rev.*, 2016, **116**, 7397–7457.
18 C. Wang, H. Dong, W. Hu, Y. Liu and D. Zhu, *Chem. Rev.*, 2012, **112**, 2208–2267.
19 A. Ohta, Y. Akita, T. Ohkuwa, M. Chiba, R. Fukunaga, A. Miyafuji, T. Nakata, N. Tani and Y. Aoyagi, *Heterocycles*, 1990, **31**, 1951–1958.
20 B. Liégault, D. Lapointe, L. Caron, A. Vlassova and K. Fagnou, *J. Org. Chem.*, 2009, **74**, 1826–1834.
21 C. Colletto, A. Panigrahi, J. Fernández-Casado and I. Larrosa, *J. Am. Chem. Soc.*, 2018, **140**, 9638–9643.
22 C. B. Bheeter, L. Chen, J.-F. Soulé and H. Doucet, *Catal. Sci. Technol.*, 2016, **6**, 2005–2049.
23 S. E. Kazzouli, J. Koubachi, N. E. Brahmi and G. Guillaumet, *RSC Adv.*, 2015, **5**, 15292–15327.
24 S. Mao, H. Li, X. Shi, J.-F. Soulé and H. Doucet, *ChemCatChem*, 2019, **11**, 269–286.
25 B. Join, T. Yamamoto and K. Itami, *Angew. Chem. Int. Ed.*, 2009, **48**, 3644–3647.
26 G. Tan, Q. You and J. You, *ACS Catal.*, 2018, **8**, 8709–8714.
27 H.-Q. Do, R. M. K. Khan and O. Daugulis, *J. Am. Chem. Soc.*, 2008, **130**, 15185–15192.
28 T. Doba, T. Matsubara, L. Ilies, R. Shang and E. Nakamura, *Nat. Catal.*, 2019, **2**, 400–406.
29 C. M. Alder, J. D. Hayler, R. K. Henderson, A. M. Redman, L. Shukla, L. E. Shuster and H. F. Sneddon, *Green Chem.*, 2016, **18**, 3879–3890.
30 J. Canivet, J. Yamaguchi, I. Ban and K. Itami, *Org. Lett.*, 2009, **11**, 1733–1736.
31 T. Yamamoto, K. Muto, M. Komiyama, J. Canivet, J. Yamaguchi and K. Itami, *Chem.- Eur. J.*, 2011, **17**, 10113–10122.
32 H. Hachiya, K. Hirano, T. Satoh and M. Miura, *Org. Lett.*, 2009, **11**, 1737–1740.
33 D. S. Rampon, L. A. Wessjohann and P. H. Schneider, *J. Org. Chem.*, 2014, **79**, 5987–5992.
34 A. Skhiri, R. Ben Salem, J.-F. Soulé and H. Doucet, *ChemCatChem*, 2017, **9**, 2895–2913.
35 D. Taguchi, T. Nakamura, H. Horiuchi, M. Saikawa and T. Nabeshima, *J. Org. Chem.*, 2018, **83**, 5331–5337.
36 Y. Mohr, M. Renom-Carrasco, C. Demarcy, E. A. Quadrelli, C. Camp, F. M. Wisser, E. Clot, C. Thieuleux and J. Canivet, *ACS Catal.*, 2020, **10**, 2713–2719.
37 D. K. Pandey, S. B. Ankade, A. Ali, C. P. Vinod and B. Punji, *Chem. Sci.*, 2019, **10**, 9493–9500.
38 R. R. Fraser and T. S. Mansour, *J. Org. Chem.*, 1984, **49**, 3442–3443.
39 R. R. Fraser, T. S. Mansour and S. Savard, *Can. J. Chem.*, 1985, **63**, 3505–3509.
40 E. M. Simmons and J. F. Hartwig, *Angew. Chem. Int. Ed.*, 2012, **51**, 3066–3072.
41 T. Sperger, I. A. Sanhueza, I. Kalvet and F. Schoenebeck, *Chem. Rev.*, 2015, **115**, 9532–9586.
42 K. D. Vogiatzis, M. V. Polynski, J. K. Kirkland, J. Townsend, A. Hashemi, C. Liu and E. A. Pidko, *Chem. Rev.*, 2019, **119**, 2453–2523.
43 T. Truong and O. Daugulis, *J. Am. Chem. Soc.*, 2011, **133**, 4243–4245.
44 C. Demangeat, T. Saied, R. Ramozzi, F. Ingrosso, M. Ruiz-Lopez, A. Panossian, F. R. Leroux, Y. Fort and C. Comoy, *Eur. J. Org. Chem.*, 2019, **2019**, 547–556.
45 P. Y. Maximov, T. M. Lee and V. C. Jordan, *Curr. Clin. Pharmacol.*, 2013, **8**, 135–155.
46 S.-M. Wen, C.-H. Lin, C.-C. Chen and M.-J. Wu, *Tetrahedron*, 2018, **74**, 2493–2499.
47 B. L. Flynn, E. Hamel and M. K. Jung, *J. Med. Chem.*, 2002, **45**, 2670–2673.
48 T. A. Grese, S. Cho, D. R. Finley, A. G. Godfrey, C. D. Jones, C. W. Lugar, M. J. Martin, K. Matsumoto, L. D. Pennington, M. A. Winter, M. D. Adrian, H. W. Cole, D. E. Magee, D. L. Phillips, E. R. Rowley, L. L. Short, A. L. Glasebrook and H. U. Bryant, *J. Med. Chem.*, 1997, **40**, 146–167.
49 E. David, J. Perrin, S. Pellet-Rostaing, J. Fournier dit Chabert and M. Lemaire, *J. Org. Chem.*, 2005, **70**, 3569–3573.
50 P. S. Shinde, S. S. Shinde, A. S. Renge, G. H. Patil, A. B. Rode and R. R. Pawar, *Lett. Org. Chem.*, 2009, **6**, 8–10.