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Electrochemical *ipso*-Thiocyanation of Arylboron Compounds

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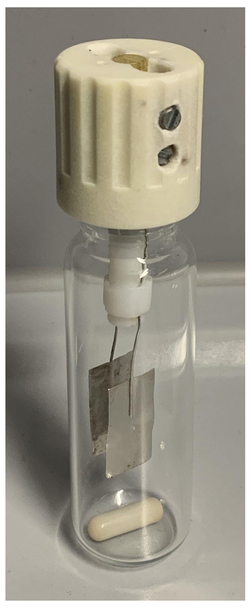
Abstract: Sustainable methods for the transformation of functional groups are in constant demand for synthesis of pharmaceuticals and agrochemicals. Organothiocyanates serve as versatile building blocks in the synthesis of various biologically active organosulfur compounds. In this work, an operationally simple, electrochemical synthesis of aryl thiocyanates from the corresponding arylboron compounds and a thiocyanate salt is presented. A key feature of the reaction is the solvent system, which contains acetic or formic acid as protic, but poorly nucleophilic (co)solvent. This allows cathodic H_2 evolution while stabilizing $(SCN)_2$, which is generated *in situ* by anodic oxidation. Electrophilic *ipso*-substitution of an arylboron compound with electrochemically generated $(SCN)_2$ affords the aryl thiocyanate in good yields and with high regioselectivity.

Electrochemical Synthesis

Electrochemistry is mostly considered a discipline within analytical or physical chemistry. However, in recent years, it has also attracted tremendous attention as a tool in synthetic organic chemistry.[1]



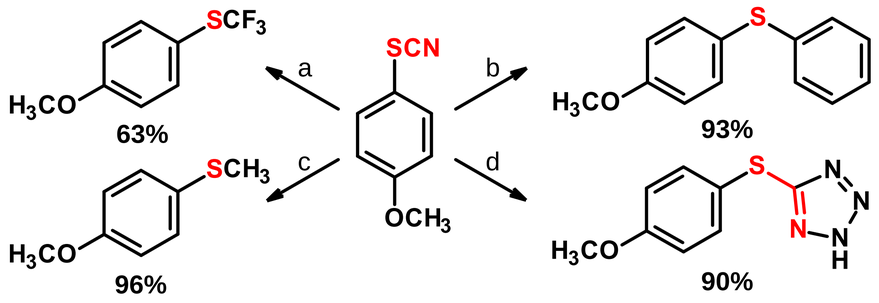
Advantages of electrochemical synthesis:

- ✓ Replaces stoichiometric hazardous reagents
- ✓ Lower costs and reduced waste
- ✓ Inherent safety: „switch on and off“
- ✓ Renewable sources for higher sustainability

The greatest drawback is the need for **specialised equipment**. We have developed specialised electrochemical cells, which allow **high-throughput screening** in constant current mode.

Organothiocyanates

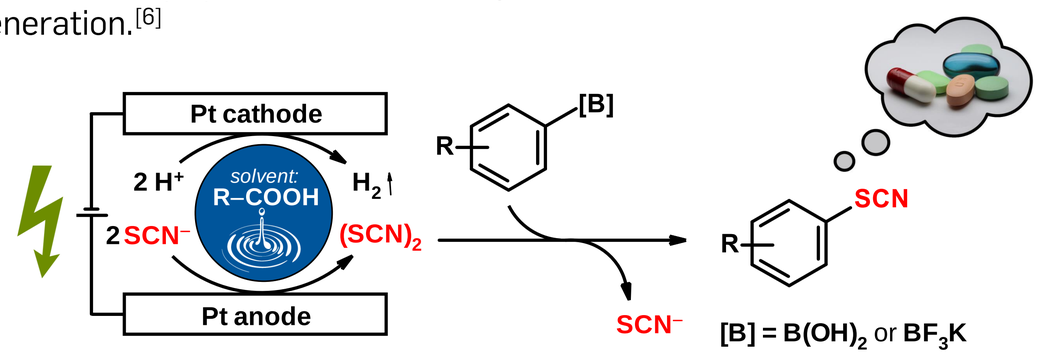
Organothiocyanates are valuable intermediates in the synthesis of organosulfur compounds, e.g. thioethers, thiols, disulfides, and various heterocycles, many of which are used as pharmaceuticals or agrochemicals.[2] Known syntheses of aryl thiocyanates include electrophilic C–H thiocyanation,[3] copper-catalysed Sandmeyer reaction starting from arenediazonium salts,[4] and Chan-Evans-Lam coupling starting from boronic acids.[5]



a) $TMSCF_3$, Cs_2CO_3; b) PhMgBr; c) MeMgCl; d) NaN_3, $ZnCl_2$.

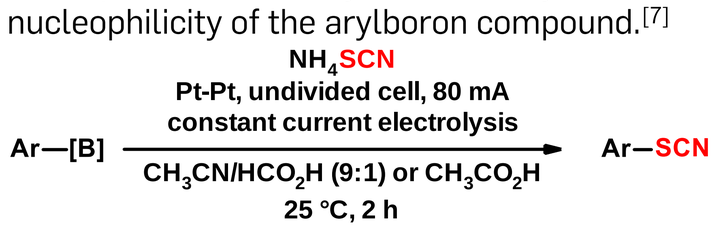
Thiocyanation of Arylboron Compounds

Electrochemical oxidation of thiocyanate ions was used to generate the reactive pseudohalogen $(SCN)_2$, which undergoes an *ipso*-substitution of an arylboron group. Carboxylic acids such as acetic acid or formic acid were chosen as (co)solvents, whose protic nature facilitates cathodic H_2 generation.[6]

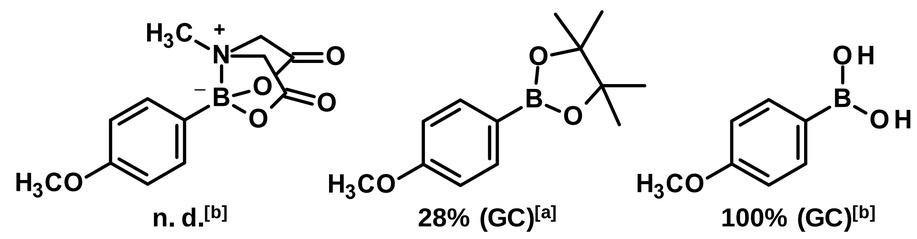


Scope of the Thiocyanation

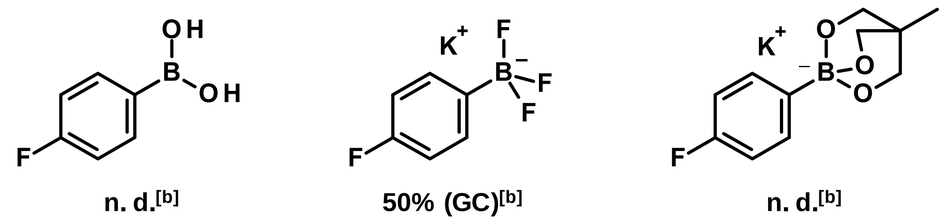
Various arylboronic acids and aryl trifluoroborates with electron-donating and electron-neutral substituents can be thiocyanated in moderate to good yields. With the exception of sterically hindered aryl triolborates, the yields scale with the nucleophilicity of the arylboron compound.[7]



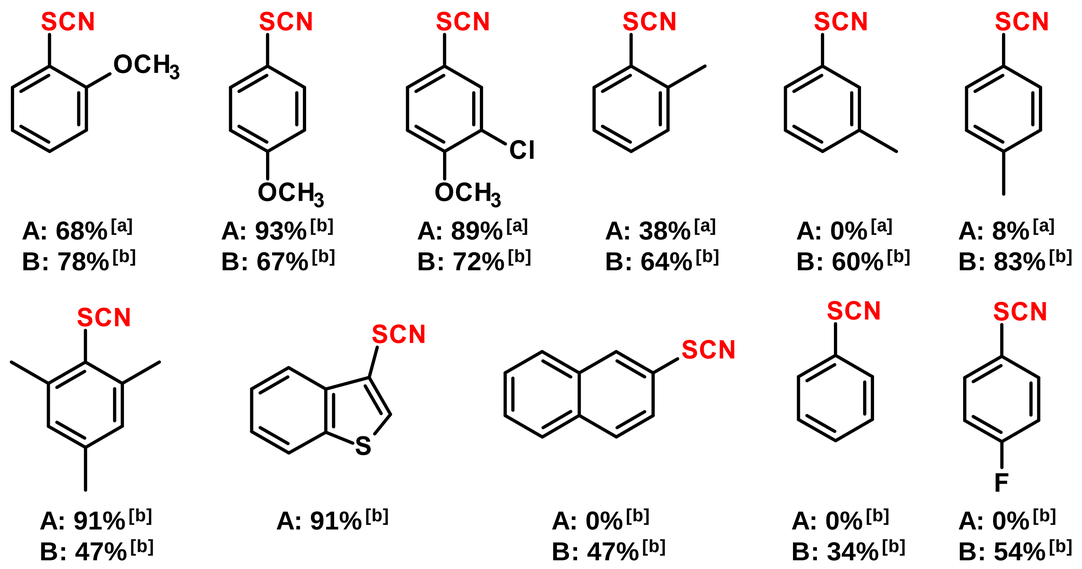
Variation of **Ar–[B]**:



NUCLEOPHILICITY



Scope of substituents – **A**: from $Ar–B(OH)_2$; **B**: from $Ar–BF_3K$:



[a] 10 mL of acetic acid as solvent; [b] 9 mL of CH_3CN and 1 mL of formic acid as solvent. Isolated yields, if not stated otherwise. GC: yield determined by gas chromatography; n. d.: not detected.

Conclusion and Outlook

We have developed a transition-metal-free, electrochemically enabled thiocyanation of arylboronic acids and aryl trifluoroborates. The underlying strategy consists of oxidation of pseudohalides to generate electrophilic reagents, which undergo facile nucleophilic substitution reactions with organometallic reagents. We are currently investigating whether this strategy can also be applied for deborylative couplings with other pseudohalides such as trifluoromethylthiolate (SCF_3^-).

References

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We gratefully acknowledge financial support from:

SFB/TRR 88
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