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## Novel Active Molybdenum-Based Anode for Dehydrogenative Coupling Reactions

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**Abstract:** A new and powerful active anode system that can be operated in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) was found. The molybdenum anode forms in HFIP a compact, conductive, and electroactive layer of higher-valent molybdenum species. This system can be used to replace powerful but stoichiometrically required Mo(V) reagents for dehydrogenative coupling of aryls. The performance of this electrolytic protocol is more sustainable and allows the conversion of a broad scope of activated arenes.

Active electrodes exhibit on their surface electrocatalytically active species, which represent immobilized mediators. Ideally, a compact and electrically conductive reagent is formed which is regenerated in-situ.<sup>[1]</sup> This does not only facilitate an electroconversion, but also represents a redox-filter since only the electrochemical potential of this redox-active layer is relevant and the experimental set-up is tremendously simplified.<sup>[1]</sup> Within the multitude of electrochemical transformations, only a few metals are known to perform as active anodes in protic media. Most commonly, nickel and lead systems perform well with their active and conductive surfaces, but represent harmful or environmentally less benign metals.<sup>[2]</sup> In the Simons process Ni electrodes and anhydrous hydrogen fluoride are utilized for electrochemical fluorination.<sup>[3]</sup> Furthermore, under alkaline conditions Ni forms NiOOH as an active and stable surface.<sup>[4]</sup> This anodic system is a versatile example for many transformations and even suitable for the selective degradation of bio-based and complex mixtures such as lignin.<sup>[5]</sup> By using the different alloys of nickel or cobalt the performance in alkaline media can be modulated.<sup>[6]</sup> With PbO<sub>2</sub> electrodes (on Pb), usually a significant concentration of sulfuric acid is required for the stability of the anode.<sup>[7]</sup> Nevertheless, also alkaline conditions are reported in the context of the degradation of

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biological waste flows.<sup>[8]</sup> Due to the limited solubility of organic molecules in aqueous media, alcohols are more versatile solvents for anodic conversions. In particular, fluorinated alcohols, such as 1,1,1,3,3,3-hexafluoroisopropanol (HFIP), offer a broad applicability and are known to stabilize radicals.<sup>[9]</sup> Such of significant importance intermediates are the in dehydrogenative coupling reaction employing Mo(V) reagents.<sup>[10]</sup> By a partial ligand exchange of HFIP and chloride, an improved reagent could be established.<sup>[11]</sup> We anticipated an electrochemical generation of an Mo(HFIP)5 reagent, which will either dissolve in the electrolyte or remain at the electrode to form an active surface layer (Scheme 1).



 $\label{eq:scheme1:Comparison} \begin{array}{l} \mbox{Scheme1: Comparison between stoichiometric } Mo(V) \mbox{ and electrocatalytic dehydrogenative coupling reactions.} \end{array}$ 

This approach is safer, since no highly reactive reagents are used and high amounts of waste are avoided. In addition, this method promises to be easily scalable combined with an inherently safe protocol.<sup>[12]</sup>

By serendipity, we found that using molybdenum as anode and platinum as inert cathode in a HFIP electrolyte already proved its utility in dehydrogenative coupling reactions. The effect of this two-electrode galvanostatic arrangement was monitored by the conversion of 4-methyl veratrole (1) to the respective dehydrodimer 2. By applying a constant current density of 7.5 mA/cm<sup>2</sup> different electrolyte systems were investigated (Table 1). With regards to the coordination ability of the anions, less coordinating and more stable anions turned out to be more beneficial (Table 1, Entries 1-5). Tetrabutylammonium hexafluorophosphate gave the highest conversion of 85%, which could neither be improved by altering the solvent nor by application of different cathode materials (Table 1, Entries 6-9). Recently, we found that the counter electrode can have a significant impact onto the electro-organic transformation since the hydrogen evolution is promoted and other cathodic processes suppressed.<sup>[13]</sup> Due to the inexpensive nature of graphite, this material was further applied as cathode. By the use of 3.0 F per mole of electricity the best conversion of 95% was achieved (Table 1, Entry 10). The addition of methanol or water to the electrolyte system resulted in a strong decrease in conversion (see SI). Using the optimized reaction conditions Table 1: Optimization of the electrolysis conditions to 2.



[a] GC conversion determined by referencing to hexadecane as internal standard. [b] HFIP: 1,1,1,3,3,3-hexafluoroisopropanol. [c] Isolated yield: 67%.

(Table 1, Entry 10), product **2** could be obtained in 67% isolated yield. We found by ICP-OES measurements, that only 0.74 $\pm$ 0.01 mg/g molybdenum is found upon electrolysis in the final mixture (for details see SI). This clearly corresponds to a very low amount of 0.53 mol% molybdenum which is dissolved during electrolysis. We attribute this to a slight and undesired corrosion. The very low Mo concentration and the effect of surface make an active species in the electrolyte unlikely.

To further prove the molybdenum-effect of this anode material a variety of other metals or commonly used anode materials were tested. Therefore, 4-bromo veratrole (3) was used as test substrate, since dehalogenation might occur as a common side reaction.<sup>[14]</sup> Besides the isolated yields of the respective dehydrodimer 4 also the GC data for the conversion are provided. For the active molybdenum anode an isolated yield of 75% was obtained (Table 2, Entry 1). Commonly used materials like Pt, Au, and boron-doped diamond (BDD)<sup>[15]</sup> provided the product in high yields of up to 81%, but are significantly more expensive materials and therefore less attractive for simple laboratory applications and upscaling, respectively (Table 2, Entries 2-4). In addition, these materials gave 4 in high yields, but significantly lower purity, because unselective coupling processes occur. Such by-products have to be removed by expensive and/or time-consuming purification protocols. Electroanalytical studies reveal that the first oxidation peak of 3 directly correlates with the yield of 4, which is visible in cyclic voltammetry (see SI).

Since commonly  $CuCl_2$ ,  $AlCl_3$  and  $FeCl_3$  are used stoichiometrically in reagent-mediated dehydrogenative coupling reactions,<sup>[16]</sup> we also investigated Cu, Al, and Fe as anode materials. All of them performed this transformation with a poor

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or even no conversion and are undesirable (Table 2, Entries 5-7). Group 5 and 6 elements located near molybdenum in the periodic table were also investigated with regards to their applicability. Of the group 5 elements only vanadium gave 4 in a moderate yield of 57%, whereas niobium and tantalum only resulted in decomposition of the substrate (Table 2, Entries 8-10). This finding corresponds to an expected crossrelation between molybdenum and vanadium. Interestingly, chromium gave product 4 in a high conversion and a reasonable yield, however, during the electrolysis tremendous corrosion took place. Besides the dissolution of chromium, it results in the formation of a thick green film at the anode. In addition, this fouling suppresses the conductivity almost completely (Table 2, Entry 11). The heavier congener tungsten gave poor conversion and isolated yield of 4 and is non-favored due to the challenging machinability of tungsten (Table 2, Entry 12).

Table 2: Investigation of anode material onto the yield of 4.

anode || graphite 0.1 M NBu<sub>4</sub>PF<sub>6</sub> in HFIP Q = 3.0 F, j = 7.5 mA/cm<sup>2</sup> 0 Br

		•		4	
E	Entry	Anode	<b>3</b> (GC-%) <sup>[a]</sup>	<b>4</b> (GC-%) <sup>[a]</sup>	Yield (%) <sup>[b]</sup>
	1	Мо	-	100	75
	2	BDD <sup>[c]</sup>	-	91	81
	3	Pt	13	84	69
	4	Au	1	90	72
	5	Cu	93	-	-
	6	AI	92	1	5
	7	Fe	99	-	-
	8	V	-	79	57
	9	Nb	87	-	-
	10	Та	88	1	-
	11	Cr	29	60	80 <sup>[d]</sup>
	12	W	43	38	26

[a] Absolute GC integral values; if **3** and **4** do not sum to 100% by-products are formed. [b] Isolated yield. [c] BDD: boron-doped diamond. [d] Strong corrosion.

Subsequently, we focused onto the synthetic application of this improved methodology using molybdenum as active anode material. Initially, we subjected anisole derivatives **5** to this electrolytic protocol. The para-coupled dimers **6** were obtained in moderate to high yields of up to 67% (Table 3). The chloroand bromo-substituted derivatives **6a-g** resulted in the highest yields and only fluoro and iodo substituents gave lower yields. In general, substrates involving the heavier halogens (Br or I) exhibited a decreased solubility and therefore a trend to lower conversion due to product precipitation at the anode. Beside halogenated substrates, also alkylated ones were suitable, but provided the products **6h-i** in moderate yields. When the 4-

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**10e** in a moderate yield of 39%. This involves a second dehydrogenation process. Triphenylene **10f** was isolated in an excellent yield of 82%.

In general, the formation of six-membered rings is favored over five-membered cycles, since dibenzothiophene **10g** and carbazole **10h** were obtained in poor yields. Benzothiophene functionalized spirocyclic product **10i** gave a slightly higher yield of 31%. By this method, also seven- and eight-membered rings (**10j** and **10k**) are accessible in high yields of 67% and 59%, respectively. Interestingly, micro-structured molybdenum, which was prepared by laser-grafting (see SI for details), resulted in an additionally increased yield of biaryl **8b** and phenanthrene **10a** compared to the planar anode (Figure 3). Due to a larger anodic area and therefore, an increased active electrode an excellent yield of 83% was obtained in both cases.



Figure 3: Micro-structured molybdenum resulted in an increased yield of 8b and 10a.

[a] Isolated yields.

position was blocked, *ortho*-coupling was observed in reasonable yield (**6j**).

In particular, tetra-halogenated products **6a-f**, which were accessible by this method, are valuable platform molecules for graphene substructures and can be applied to further functionalization by simultaneous or orthogonal cross-coupling functionalization.<sup>[17]</sup>

In addition to anisole substrates **5**, veratrole derivatives **7** gave higher yields in this established electrochemical active molybdenum anode system (Table 4). Alkylated, halogenated, and methoxylated derivatives **7a-f** were coupled in excellent isolated yields of up to 87% (Table 4). Also up-scaling to a 5 mmol scale gave **8b** in 69% yield (1.49 g, 3.45 mmol). Again fluoro substituted substrate resulted in significantly diminished yield (**8d**). In addition, para-dimethoxy arenes could be applied, in a yield of 54% (**8g**) and 15% (**8h**) respectively. Excellent yields were achieved for bromo- and iodo-functionalized biaryls **8b** and **8c** demonstrating the superior performance of this methodology compared to classical methods, which employ graphene oxide, transition metal catalysts or hypervalent iodine(III) reagents.<sup>[18]</sup>

In our ongoing study we subjected a variety of substrates to cyclization reactions, which are known to be converted by classical MoCl<sub>5</sub>-mediated reactions.<sup>[19]</sup> Phenanthrenes were synthesized in high yields of up to 80% (Table 5, **10a-d**) and even free carboxylic acids do not interfere in the course of the reaction (**10c**). This is of particular interest, since molybdenum chloride reagents do not tolerate free carboxylic acids. Ethyl-tethered biaryls reacted directly to the respective phenanthrene

In conclusion, we found an innovative active anodic system. The protocol is extremely simple to conduct by applying molybdenum

 Table 4: Scope of dehydrogenative coupling reactions of veratrole substrates

 7.<sup>[a]</sup> Newly formed bond indicated in bold.



[a] Isolated yields.

as anode and HFIP as protic solvent. The active anode characteristic is unique for molybdenum and can be even enhanced by structured anode surfaces. A broad scope of substrates was successfully converted demonstrating the utility of this system for electro-organic synthesis. This active anode system tolerates all halo substituents, which can be used for further functionalization since dehalogenation was never observed. This procedure can easily compete with classical Mo(V)-mediated conversions, but is more environmentally friendly since large amounts of reagent waste are avoided.

Table 5: Scope of dehydrogenative coupling reactions of tethered substrates 9.<sup>[a]</sup> Newly formed bond indicated in bold.



[a] Isolated yields.

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#### Entry for the Table of Contents (Please choose one layout)

Layout 1:

### COMMUNICATION

**Electrically driven** and with a comparable reactivity as Mo(V) reagents in the dehydrogenative coupling is achieved by the novel active anode system based on 1,1,1,3,3,3-hexafluoroisopropanol and molybdenum.



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