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FULL PAPER

Friedel-Crafts alkylation of arenes with carbenium ions generated by electrochemical oxidation of stannylmethylethers

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Abstract: The electrochemical activation of stannylmethylethers was exploited for Friedel-Crafts alkylation of arenes at near-neutral conditions. Single cell anodic oxidation of stannylmethylethers leads to oxonium ions which fragment to carbenium ions in the presence of electron rich arenes. Low oxidation potential of stannylmethylethers and buffered conditions enable the Friedel-Crafts reaction with a wide range of arenes including the substrates with acid-sensitive groups.

Introduction

The Friedel-Crafts alkylation is a fundamental organic reaction for functionalization of arenes in their reaction with in situ generated carbenium ions.[1] Products of this reaction have found wide application in drug discovery and material science.[2-4] Consequently, a number of Friedel-Crafts alkylation versions has been developed, including the alkylation of arenes with alcohols,[5-10] halogens,[11] ethers,[12,13] acetates,[14,15] phosphonates,[16] sulfones,[17,18] trichloroacetimidates,[12] tosylamides,[19] epoxides,[20] and olefins.[21] Typically, these reactions rely on Broensted or Lewis acid catalysis to promote the carbenium ion formation. Limited number of methods for Friedel-Crafts alkylation has been developed using weak or non-acidic conditions which offer wider substrate scope for this useful transformation.[22-28]
Electrochemical generation of carbenium ions avoids the use of acidic conditions because the protons formed during the reaction are reduced to hydrogen at the cathode.[27,28] This provides an option to perform reactions of carbenium ions at near-neutral conditions which are compatible with acid-sensitive functionalities in substrates.

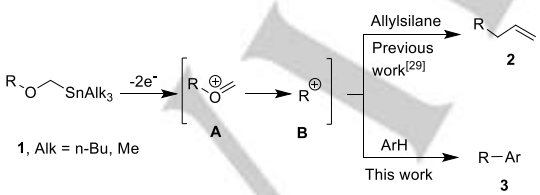


Figure 1 Electrochemical generation of carbenium ions from stannylmethylethers and their reaction with nucleophiles.

Recently, we have reported an operationally simple carbenium ion generation from stannylmethylethers **1** (Alk = *n*-Bu) in single cell electrolysis at relatively low potential (Figure 1).[29] The method is based on the oxidation of stannylmethyoxy group in substrates **1** to form oxonium ions **A** which fragment to carbenium ion **B**. The proof of the concept was demonstrated for the reaction of carbenium ions **B** with allylsilane providing olefins **2**. With an aim to complement the recent advances in electrochemical arene functionalization[30-32],we explored Friedel-Crafts reaction using stannylmethylethers **1** (Alk = *n*-Bu, Me) as precursors for electrochemical generation of carbenium ions **B** to form alkylated arenes **3** (Figure 1).

Results and Discussion

In a model reaction, stannylmethylether **1a** was subjected to anodic oxidation in the presence of *O*-TBS protected phenol **4** (Table 1, entry 1). Weekly nucleophilic HFIP was found as appropriate additive to secure the cathode reaction[33] without observable competition with arene.[27,28] The electrochemically induced reaction proceeded in a relatively short time providing the expected product **3.1** in good yield and high *para*-selectivity (*ortho*-product **5** formed <5% according to NMR: see Supporting Information). However, the control reaction without electric current was also productive, leading to observable formation of product **3.1** at longer reaction time (Table 1, entry 1).

Table 1. Reaction conditions for selective electrochemical substrate activation

Conditions A: I = 2.5 F/mol, 20 mA, graphite electrodes, r.t., 40 min
Conditions B: no current, r.t., 18 h

Entry	Additive	Cond. A Yield[a] of **3.1**,%	Cond. B Yield[a] of **3.1**,%
1	none	63	9
2	additional HFIP[b]	56	74
3	1 eq 2,6-lutidine	0	0
4	1 eq PivONa	38	0
5	1 eq $PhCO_2Li$	51	0
6	1 eq $NaHCO_3$	64 (55[c])	0

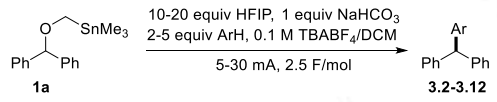
[a] NMR yield using ethyl acetate as an internal standard; [b] Solvent: HFIP/DCM, 1:1 [c] Isolated yield.

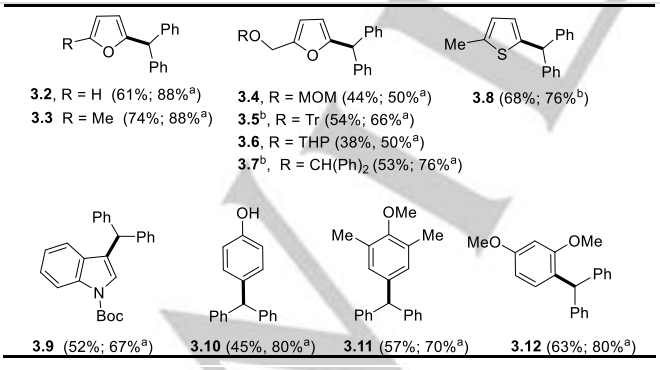
Notably, the increased amount of HFIP facilitated non-electrochemical reaction leading to product **3.1** formation in good yield (Table 1, entry 2). This indicated the susceptibility of trimethylstannylmethylether **1a** to undergo ionization in the presence of HFIP. Moreover, such a result implied that the reaction conditions are not compatible with acid-labile functional groups.

To buffer the reaction media, various basic additives were tested. 2,6-Lutidine suppressed both electrochemically induced and solvolytic carbenium ion generation (Table 1, entry 3). Addition of sodium pivaloate and lithium benzoate to the reaction media gave Friedel-Crafts product **3.1** in medium yield and suppressed the solvolysis induced reaction (Table 1, entries 4,5). $NaHCO_3$ as additive induced the best yield of product **3.1** at electrochemical conditions and completely suppressed solvolytic carbenium ion generation (Table 1, entry 6).

With optimized conditions in hand, the stannylmethylether **1a** was subjected to electrochemically induced reaction with a range of arenes (Table 2). Alkylated furan derivatives **3.2** and **3.3** were prepared in good yield. Moreover, furfuryl alcohol derivatives bearing acid-labile *O*-protecting groups, such as MOM, Tr, THP and Ph_2CH, could also be alkylated with stannylmethylether **1a** to give the corresponding products **3.4-3.7**. To the best of our knowledge, these are the first examples of the compatibility of the acid-sensitive *O*-protecting groups with Friedel-Crafts alkylation conditions. Acid-sensitive heterocycles, such as thiophene and *N*-protected indole, also provided the desired alkylation products **3.8** and **3.9**. Electron rich phenols with low electrochemical potentials were also tested as substrates. Interestingly, unprotected phenol turned out to be a competent substrate to give *C*-alkylation product **3.10.** Anisole derivative and 1,3-dimethoxybenzene with low oxidation potentials were also successfully alkylated to give products **3.11** and **3.12** in good yields.

Table 2. Nucleophile scope for the electrochemically induced Friedel-Crafts reaction

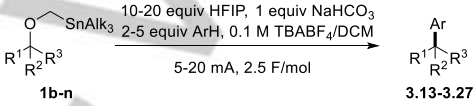


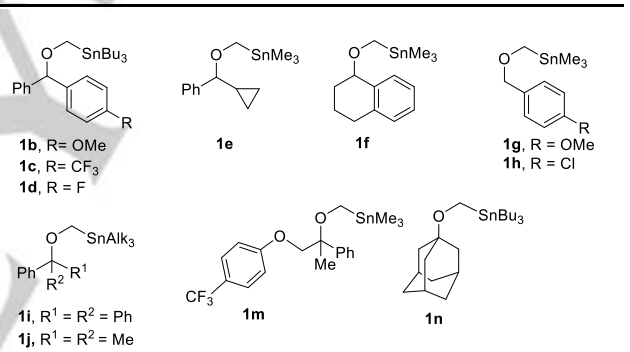


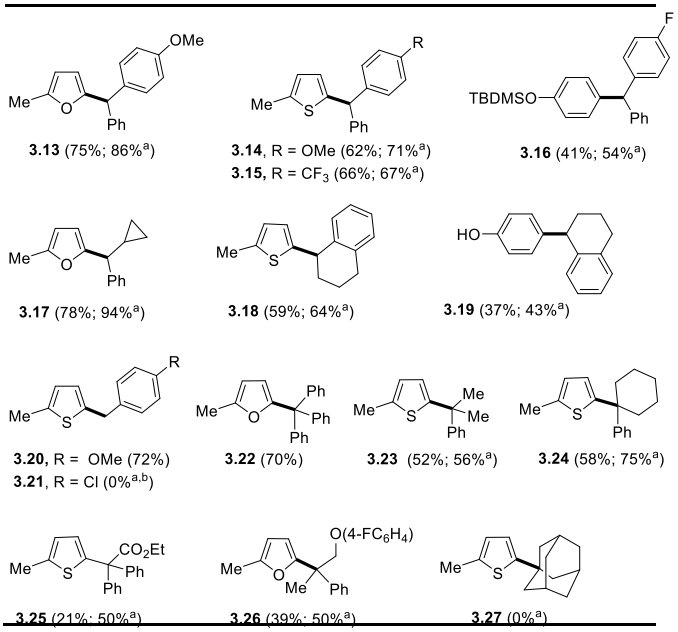
[a] NMR yield using ethyl acetate as an internal standard [b] 10 equiv HFIP

The scope of stannylmethylethers **1** for alkylation of arenes was also investigated (Table 3). Diarylmethyl cations generated from stannylmethylethers **1b,c** gave furan and thiophene alkylation products **3.13-3.15** in good yields. The reaction of fluorine-containing stannylmethylether **1d** provided alkylated protected phenol **3.16**, however, in slightly lower yield compared to non-fluorinated analogue **1a.** Alkylarylmethyl cations generated from stannylmethylethers **1e,f** gave furan, tiophene and phenol alkylation products **3.17-3.19**. Methoxy-substituted benzylic cation produced from substrate **1g** provided thiophene derivative **3.20** efficiently. However, chloro-substituted analogue **1h** failed to give the expected product **3.21**, likely due to the reduced stability of the intermediate carbenium ion. Tertiary carbenium ion precursors **1i-k** provided furan and tiophene alkylation products **3.22-3.24** in moderate yields. However, stannylmethylethers **1l,m** bearing EWG groups were considerably less productive, giving products **3.25, 3.26** in low yield. Also, the electrochemical activation of less stable adamantyl cation precursor **1n** failed to give the expected alkylation product **3.27**.

Table 3. Scope of stannylmethylethers for the electrochemically induced Friedel-Crafts reaction







[a] NMR yield using ethyl acetate as an internal standard [b] oxonium ion reaction product in 35% by NMR

The proposed mechanism of electrochemically induced Friedel-Crafts reaction is shown in Figure 2. The cathode reaction involves the reduction of HFIP to generate the corresponding alkoxide and hydrogen. Stannate complex formed from substrate **1** undergoes anodic oxidation at low oxidation potential to form oxonium ion **A** with stannate $\mathbf{X}^-$ as the counterion. Fragmentation of oxonium ion **A** forms cation **B** which reacts with activated arene (**ArH**) providing Friedel-Crafts alkylation product **3** and non-acidic by-products (**HX**).

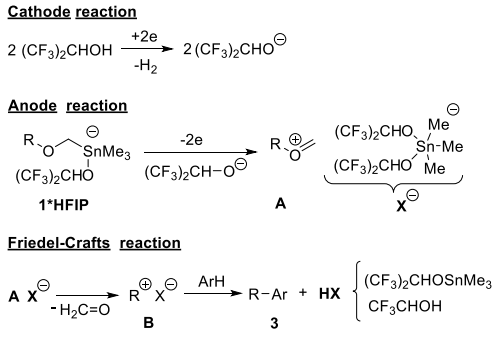


Figure 2. Proposed mechanism of electrochemically induced Friedel-Crafts reaction.

Conclusion

In summary, it was demonstrated that Friedel-Crafts reaction can be achieved by electrochemical activation of stannylmethylethers in the presence of electron rich arenes. The buffered electrolytic mixture contained HFIP as the cathode reactant and $NaHCO_3$ as proton scavenger. These conditions were found to be compatible with acid-labile *O*-protecting groups such as MOM, Tr, THP and Ph_2CH. We believe that electrochemical activation of substrates to form carbenium will expand the application of Friedel-Crafts reaction in the synthesis of useful products.

Experimental Section

General Remarks. All procedures were performed in oven-dried glassware under argon atmosphere unless noted otherwise. Reagents and starting materials were obtained from commercial sources and used as received unless otherwise noted. Tetrabutylammonium tetrafluoroborate (Fluorochem) was recrystallized from ethyl acetate and dried at 80 °C for 8 h before use. Solvents were purified and dried by standard procedures before use. Flash column chromatography was carried out using silica gel (230−400 mesh). Thin-layer chromatography (TLC) was performed on Merck TLC Silica gel 60 F254 Aluminium sheets and was visualized by UV lamp or staining with $KMnO_4$. NMR spectra were recorded on 300 or 400 MHz spectrometers with chemical shift values (δ) in parts per million using the residual solvent as an internal standard. HRMS analyses were performed on a hybrid quadrupole time-of-flight mass spectrometer equipped with an electrospray ion source. Electrochemical experiments were performed using electrochemical system Electrasyn 2.0.

Experimental Details. Synthesis of starting materials and characterization of side products is described in Supporting Information.

General Procedure for Electrochemical Friedel-Crafts Alkylation. Anodic oxidation was performed in Electrasyn beaker–type undivided cell (5 mL) equipped with two standard Electrasyn graphite plate electrodes (8×40 mm, ~15 mm submerged in the solution) in 0.1 M $TBABF_4$/dry DCM (2 mL) solution with the addition of HFIP (0.41 mL, 4.0 mmol unless noted otherwise) and $NaHCO_3$ (17.0 mg, 0.2 mmol). The trialkylstannylmethyl group bearing substrate (0.2 mmol) and nucleophile (2-5 equiv) were added to the solution. Constant current electrolysis (5-30 mA) was carried out in air at ambient temperature with magnetic stirring and change of polarization every minute until approx. 2.5 F/mol were consumed. After the electrolysis, the reaction mixture was concentrated *in vacuo* and purified by flash column chromatography on silica gel.

(4-Benzhydrylphenoxy)(tert-butyl)dimethylsilane (3.1). Electrochemical oxidation of ((benzhydryloxy)methyl)trimethylstannane (**1a**) (72.6 mg, 0.20 mmol) in the presence of *tert*-butyldimethyl(phenoxy)-silane (**4**) (84.0 mg, 0.40 mmol) according to the general procedure at 30 mA and purification by column chromatography on silica gel (eluent petroleum ether/Et_2O 40:1) afforded 41.5 mg (55%) of product as a white solid (m.p. 80–82 °C).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.25 (m, 4H), 7.24 – 7.16 (m, 2H), 7.14 – 7.07 (m, 4H), 6.99 – 6.92 (m, 2H), 6.78 – 6.72 (m, 2H), 5.49 (s, 1H), 0.98 (s, 9H), 0.19 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 154.12, 144.46, 136.70, 130.46, 129.55, 128.38, 126.33, 119.86, 56.23, 25.83, 18.32, -4.25.
HR-MS (ESI-TOF) m/z: calcd. for $C_{25}H_{29}OSi$ $[M-1]^+$ 373.1988; found: 373.1972.
Anal. calcd. for $C_{25}H_{30}OSi$: C, 80.16; H, 8.07. Found: C, 79.17; H, 8.08.

2-Benzhydrylfuran (3.2) Electrochemical oxidation of ((benzhydryloxy)methyl)trimethylstannane (**1a**) (71.9 mg, 0.2 mmol) in the presence of furan (0.1 mL, 1 mmol) according to the general procedure at 5 mA and purification twice by column chromatography on silica gel (eluent petroleum ether/diethyl ether 20:1) afforded 28.4 mg (61%) of product as a colourless oil. This compound has been reported in the literature.[30]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 1.8 Hz, 1H), 7.31 (dd, J = 8.2, 6.6 Hz, 4H), 7.27 – 7.22 (m, 2H), 7.18 (dd, J = 7.0, 1.9 Hz, 4H), 6.31 (dd, J = 3.3, 1.9 Hz, 1H), 5.92 (d, J = 3.2 Hz, 1H), 5.46 (s, 1H).

2-Benzhydryl-5-methylfuran (3.3) Electrochemical oxidation of ((benzhydryloxy)methyl)trimethylstannane (**1a**) (72.6 mg, 0.20 mmol) was carried out in the presence of 2-methylfuran (0.09 mL, 1.00 mmol) according to the general procedure at 5 mA until 2.87 F/mol has been consumed. Purification by column chromatography on silica gel (eluent petroleum ether/Et_2O 20:1) afforded 36.7 mg (74%) of product as an yellowish oil. This compound has been reported in literature.[31]
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 – 7.12 (m, 10H), 5.88 (m, 1H), 5.74 (m, 1H), 5.39 (s, 1H), 2.25 (m, 3H).

2-Benzhydryl-5-((methoxymethoxy)methyl)furan (3.4) Electrochemical oxidation of ((benzhydryloxy)methyl)trimethylstannane (**1a**) (71.8 mg, 0.20 mmol) was performed in the presence of 2-((methoxymethoxy)methyl)furan (56.5 mg, 0.40 mmol) according to the general procedure at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/EtOAc 10:1) afforded 27.2 mg (44%) of product as an yellowish oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (dd, J = 8.1, 6.5 Hz, 4H), 7.22 – 7.13 (m, 2H), 7.12 (dd, J = 7.0, 1.9 Hz, 4H), 6.21 (d, J = 3.1 Hz, 1H), 5.82 – 5.76 (m, 1H), 5.40 (s, 1H), 4.60 (s, 2H), 4.43 (s, 2H), 3.30 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 157.36, 150.90, 141.81, 128.90, 128.54, 126.84, 110.24, 109.33, 95.34, 77.36, 61.15, 55.46, 51.08.

HR-MS (ESI-TOF) m/z: calcd. for $C_{29}H_{19}O_3$ $[M-1]^+$ 307.1334; found: 307.1341.

2-Benzhydryl-5-((trityloxy)methyl)furan (3.5) Electrochemical oxidation of ((benzhydryloxy)methyl)trimethylstannane (**1a**) (71.4 mg, 0.20 mmol) was performed in the presence of 2-((trityloxy)methyl)furan (135.0 mg, 0.40 mmol) in a modified general procedure using 0.2 mL of HFIP at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/EtOAc 20:1 with 3% triethylamine) afforded 54.1 mg (54%) of product as a white solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 7.7 Hz, 8H), 7.27 (m, 22H), 6.19 (d, J = 3.1 Hz, 1H), 5.87 (d, J = 3.3 Hz, 1H), 5.46 (s, 1H), 4.02 (s, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 156.43, 151.92, 144.06, 142.10, 128.97, 128.85, 128.53, 127.98, 127.14, 126.81, 109.08, 108.70, 87.15, 59.57, 51.13.
HR-MS (ESI-TOF) m/z: calcd. for $C_{37}H_{29}O$ $[M-1]^+$ 505.2168; found: 505.2180.

2-((5-Benzhydrylfuran-2-yl)methoxy)tetrahydro-2*H*-pyran (3.6) Electrochemical oxidation of ((benzhydryloxy)methyl)trimethyl-stannane (**1a**) (72.5 mg, 0.20 mmol) was performed in the presence of 2-(furan-2-ylmethoxy)tetrahydro-2*H*-pyran (73.2 mg, 0.40 mmol) according to the general procedure at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/Et_2O 5:1) afforded 22.2 mg (38%) of product as an yellowish oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 4H), 7.26 – 7.15 (m, 6H), 6.25 (d, J = 3.0 Hz, 1H), 5.84 (d, J = 3.0 Hz, 1H), 5.45 (s, 1H), 4.69 (d, J = 3.3 Hz, 1H), 4.61 & 4.47 (d & d, J = 12.9 Hz, 1H, 3.86 (m, 1H), 3.53 – 3.42 (m, 1H), 1.60 (m, 8H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 157.11, 151.33, 141.90, 128.93, 128.51, 126.81, 110.04, 109.26, 97.29, 62.16, 60.87, 51.08, 30.53, 25.55, 19.37.
HR-MS (ESI-TOF) m/z: calcd. for $C_{23}H_{24}O_3Na$ $[M+Na]^+$ 371.1623; found: 371.1622.

2-Benzhydryl-5-((benzhydryloxy)methyl)furan (3.7) Electrochemical oxidation of ((benzhydryloxy)methyl) trimethylstannane (**1b**) (72.2 mg, 0.20 mmol) was performed in the presence of 2-((benzhydryloxy)methyl)furan (105.8 mg, 0.40 mmol) in a modified general procedure using 0.2 mL of HFIP at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/Et_2O 9:1) afforded 45.5 mg (53 %) of product as an yellowish oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.15 (m, 21H), 6.21 (d, J = 3.1 Hz, 1H), 5.85 (dd, J = 3.0, 0.9 Hz, 1H), 5.43 (s, 1H), 5.41 (s, 1H), 4.42 (s, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 157.14, 151.38, 141.90, 141.88, 128.95, 128.57, 128.48, 127.58, 127.45, 127.36, 126.85, 110.36, 109.17, 81.71, 62.63, 51.12.
HR-MS (ESI-TOF) m/z: calcd. for $C_{31}H_{26}O_2Na$ $[M+Na]^+$ 453.1830; found: 453.1832.

2-Benzhydryl-5-methylthiophene (3.8) Electrochemical oxidation of ((benzhydryloxy)methyl)trimethylstannane (**1a**) (72.5 mg, 0.20 mmol) was performed in the presence of 2-methylthiophene (0.1 mL, 1.00 mmol) according to the general procedure at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/DCM 9:1) afforded 36.4 mg (68%) of product as a colourless oil. Product has been reported in literature.[32]
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (d, J = 6.7 Hz, 4H), 7.26 – 7.18 (m, 6H), 6.57 (d, J = 3.3 Hz, 1H), 6.45 (d, J = 3.3 Hz, 1H), 5.59 (s, 1H), 2.42 (s, 3H).

***t*-Butyl-3-benzhydryl-1*H*-indole-1-carboxylate (3.9)** Electrochemical oxidation of ((benzhydryloxy)methyl)trimethyl-stannane (**1b**) (75.7 mg, 0.21 mmol) was performed in the presence of 1-Boc-*1H*-indole (43.4 mg, 0.20 mmol) and $NaHCO_3$ (16.8 mg, 0.2 mmol) according to the general procedure at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/Et_2O 9:1) afforded 40.0 mg (52%) of product as an yellowish oil. Product has been reported in literature. [33]
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (d, J = 8.2 Hz, 1H), 7.32 (s, 9H), 7.22 (m, 2H), 7.19 – 7.06 (m, 2H), 7.02 (s, 1H), 5.57 (s, 1H), 1.64 (s, 9H).

4-Benzhydrylphenol (3.10) Electrochemical oxidation of ((benzhydryloxy)methyl)trimethylstannane (**1a**) (72.9 mg, 0.20 mmol) in the presence of phenol (45.6 mg, 0.48 mmol) according to the general procedure at 20 mA and purification by column chromatography on silica gel (eluent DCM) afforded 23.8 mg (45%) of product as a white solid. Product has been reported in literature.[34]
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 – 7.11 (m, 7H), 7.12 – 7.00 (m, 4H), 6.98 – 6.85 (m, 2H), 6.76 – 6.61 (m, 2H), 5.44 (s, 1H), 4.65 (br.s, 1H).

((4-Methoxy-3,5-dimethylphenyl)methylene)dibenzene (3.11) Electrochemical oxidation of ((benzhydryloxy)methyl)trimethyl-stannane (**1a**) (72.7 mg, 0.20 mmol) in the presence of 2,6-dimethylanisole (0.14 mL, 1.00 mmol) according to the general procedure at 30 mA and purification by column chromatography on silica gel (eluent petroleum ether/Et_2O 20:1) afforded 34.9 mg (57%) of product as a colourless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 4H), 7.26 – 7.20 (m, 2H), 7.19 – 7.11 (m, 4H), 6.78 (s, 2H), 5.46 (s, 1H), 3.73 (s, 3H), 2.24 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 155.49, 144.33, 139.11, 130.58, 129.86, 129.53, 128.37, 126.31, 59.78, 56.46, 16.33.
HR-MS (ESI-TOF) m/z: calcd. for $C_{22}H_{21}O$ $[M-1]^+$ 301.1592; found: 301.1593.

((2,4-Dimethoxyphenyl)methylene)dibenzene (3.12) Electrochemical oxidation of ((benzhydryloxy)methyl)trimethylstannane (**1a**) (72.2 mg, 0.20 mmol) in the presence of 1,3-dimethoxybenzene (0.13 mL, 1.00 mmol) according to the general procedure at 20 mA and purification by column chromatography on silica gel (eluent petroleum ether/EtOAc 20:1) afforded 38.3 mg (63%) of product as a white solid. This compound has been reported in literature.[30]
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13 – 7.05 (m, 4H), 6.74 (d, J = 8.4 Hz, 1H), 6.47 (m, 1H), 6.40 (m, 1H), 5.83 (s, 1H), 3.79 (s, 3H), 3.70 (s, 3H).
HR-MS (ESI-TOF) m/z: calcd. for $C_{21}H_{19}O_2$ $[M-1]^+$ 303.1385; found: 303.1382

2-((4-Methoxyphenyl)(phenyl)methyl)-5-methylfuran (3.13) Electrochemical oxidation of tributyl(((4-methoxyphenyl)(phenyl)methoxy)methyl)stannane (**1b**) (103.5 mg, 0.20 mmol) was performed in the presence of 2-methylfuran (0.09 mL, 1.0 mmol) according to the general procedure at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/Et_2O 20:1) afforded 41.5 mg (75%) of product as an yellowish oil. Product has been reported in literature.[32]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 2H), 7.25 – 7.19 (m, 1H), 7.17 (m, 2H), 7.13 – 7.06 (m, 2H), 6.90 – 6.80 (m, 2H), 5.87 (m, 1H), 5.77 – 5.70 (m, 1H), 5.34 (s, 1H), 3.79 (s, 3H), 2.25 (m, 3H).

2-((4-Methoxyphenyl)(phenyl)methyl)-5-methylthiophene (3.14) Electrochemical oxidation of tributyl(((4-methoxyphenyl)(phenyl)-methoxy)methyl)stannane (**1b**) (104.1 mg, 0.20 mmol) was performed in the presence of 2-methylthiophene (0.1 mL, 1.0 mmol) according to

the general procedure at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/EtOAc 20:1) afforded 36.5 mg (62%) of product as a colourless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.28 (m, 2H), 7.28 – 7.21 (m, 3H), 7.20 – 7.11 (m, 2H), 6.93 – 6.81 (m, 2H), 6.59 (dq, J = 3.5, 1.1 Hz, 1H), 6.47 (dd, J = 3.4, 1.1 Hz, 1H), 5.57 (s, 1H), 3.81 (s, 3H), 2.44 (d, J = 1.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.39, 146.08, 144.31, 139.04, 136.25, 129.92, 128.87, 128.45, 126.67, 126.08, 124.64, 113.82, 55.34, 51.61, 15.46.
HR-MS (ESI-TOF) m/z: calcd. for $C_{19}H_{17}OS$ $[M-1]^+$ 293.1000; found: 293.1009.

2-Methyl-5-(phenyl(4-(trifluoromethyl)phenyl)methyl)thiophene (3.15) Electrochemical oxidation of tributyl((phenyl(4-(trifluoro-methyl)phenyl)methoxy)methyl)stannane (**1c**) (111.9 mg, 0.20 mmol) was performed in the presence of 2-methylthiophene (0.1 mL, 1.0 mmol) according to the general procedure at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/EtOAc 10:1) afforded 44.0 mg (66%) of product as an yellowish oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.0 Hz, 2H), 7.43 – 7.33 (m, 4H), 7.33 – 7.27 (m, 1H), 7.27 – 7.21 (m, 2H), 6.63 (m, 1H), 6.51 (m, 1H), 5.69 (s, 1H), 2.47 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 148.0 (q, $^1J_{CF}$ = 1 Hz), 144.29, 143.06, 139.65, 129.31, 129.1 (q, $^2J_{CF}$ = 32 Hz), 28.92, 128.70, 127.15, 126.60, 125.5 (q, $^3J_{CF}$ = 4 Hz), 124.3 (q, $^2J_{CF}$ = 272 Hz),124.83, 52.18, 15.45.
^{19}F NMR (376 MHz, $CDCl_3$) δ -62.36.
HR-MS (ESI-TOF) m/z: calcd. for $C_{19}H_{14}F_3S$ $[M-1]^-$ 331.0768; found: 331.0778.

***Tert*-butyl(4-((4-fluorophenyl)(phenyl)methyl)phenoxy)dimethyl-silane (3.16)** Electrochemical oxidation of tributyl(((4-fluorophenyl)-(phenyl)methoxy)methyl)stannane (**1d**) (101.0 mg, 0.20 mmol) was performed in the presence of *t*-butyldimethyl(phenoxy)silane (83.3 mg, 0.4 mmol) according to the general procedure at 20 mA. Purification by column chromatography on silica gel (eluent petroleum ether/DCM 9:1) afforded 32.2 mg (41%) of product as an yellowish oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 2H), 7.25 – 7.19 (m, 1H), 7.12 – 7.04 (m, 4H), 7.01 – 6.91 (m, 4H), 6.80 – 6.73 (m, 2H), 5.47 (s, 1H), 0.98 (s, 9H), 0.19 (s, 6H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.51 (d, $^1J_{CF}$ = 244.8 Hz), 154.24, 144.28, 140.21, 136.51, 130.93 (d, $^3J_{CF}$ = 7.8 Hz), 130.37, 129.44, 128.47, 126.47, 119.95, 115.15 (d, $^2J_{CF}$ = 21.3 Hz), 55.43, 25.81, 18.32, -4.26.
^{19}F NMR (376 MHz, $CDCl_3$) δ -117.04.
HR-MS (ESI-TOF) m/z: calcd. for $C_{25}H_{28}OFSi$ $[M-1]^+$ 391.1893; found: 391.1888.

2-(Cyclopropyl(phenyl)methyl)-5-methylfuran (3.17) Electrochemical oxidation of ((cyclopropyl(phenyl)methoxy)methyl)trimethyl-stannane (**1d**) (64.8 mg, 0.20 mmol) was performed in the presence of 2-methylfuran (0.09 mL, 1.0 mmol) according to the general procedure at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/Et_2O 20:1) afforded 30.8 mg (78%) of product as a colourless oil.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 – 7.21 (m, 5H), 6.09 (m, 1H), 5.91 (m, 1H), 3.23 (d, J = 9.3 Hz, 1H), 2.25 (m, 3H), 1.38 – 1.28 (m, 1H), 0.73 – 0.64 (m, 1H), 0.61 – 0.52 (m, 1H), 0.43 – 0.22 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 156.18, 151.07, 142.95, 128.41, 128.07, 126.59, 106.55, 105.86, 49.91, 16.02, 13.76, 5.30, 4.43.
HR-MS (ESI-TOF) m/z: calcd. for $C_{15}H_{17}O$ $[M+1]^+$ 213.1279; found: 213.1281.

2-Methyl-5-(1,2,3,4-tetrahydronaphthalen-1-yl)thiophene (3.18) Electrochemical oxidation of trimethyl(((1,2,3,4-tetrahydronaphthalen-1-yl)oxy)methyl)stannane (**1f**) (65.1 mg, 0.20 mmol) was performed in the presence of 2-methylthiophene (0.10 mL, 1.0 mmol) according to the general procedure at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/EtOAc 20:1) afforded 27.2 mg (59%) of product as a colourless oil. Product has been reported in literature.[35]
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 – 7.06 (m, 4H), 6.61 – 6.53 (m, 1H), 6.50 (d, J = 3.3 Hz, 1H), 4.34 (t, J = 6.1 Hz, 1H), 2.98 – 2.75 (m, 2H), 2.45 (s, 3H), 2.26 – 2.11 (m, 1H), 2.07 – 2.00 (m, 2H), 1.88 – 1.71 (m, 1H).

4-(1,2,3,4-Tetrahydronaphthalen-1-yl)phenol (3.19) Electrochemical oxidation of trimethyl(((1,2,3,4-tetrahydronaphthalen-1-yl)oxy)-methyl)stannane (**1f**) (65.4 mg, 0.20 mmol) was performed in the presence of phenol (40.0 mg, 0.4 mmol) according to the general procedure at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/EtOAc 20:1) afforded 16.9 mg (37%) of product as a white solid. Product has been reported in literature.[38]
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 – 6.90 (m, 5H), 6.84 (d, J = 7.7 Hz, 1H), 6.74 (d, J = 8.4 Hz, 2H), 4.56 (s, 1H), 4.05 (t, J = 6.5 Hz, 1H), 3.00 – 2.74 (m, 2H), 2.14 (m, 1H), 2.01 – 1.65 (m, 3H).

2-(4-Methoxybenzyl)-5-methylthiophene (3.20) Electrochemical oxidation of (((4-methoxybenzyl)oxy)methyl)trimethylstannane (**1g**) (63.5 mg, 0.20 mmol) was performed in the presence of 2-methylthiophene (0.1 mL, 1.0 mmol) according to the general procedure at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/EtOAc 10:1) afforded 31.5 mg (72%) of product as a colourless oil. Product has been reported in literature.[31]
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.16 (m, 2H), 6.84 (m, 2H), 6.55 (s, 2H), 4.01 (s, 2H), 3.79 (s, 3H), 2.41 (s, 3H).

2-Methyl-5-tritylfuran (3.22) Electrochemical oxidation of tributyl((trityloxy)methyl)stannane (**1i**) (112.9 mg, 0.20 mmol) was performed in the presence of 2-methylfuran (0.09 mL, 1.0 mmol) according to the general procedure at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/DCM 9:1) afforded 45.6 mg (70%) of product as a white solid. Product has been reported in literature.[30]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.25 (m, 10H including residual $CHCl_3$), 7.18 – 7.11 (m, 6H), 5.95 – 5.90 (m, 1H), 5.88 (d, J = 3.2 Hz, 1H), 2.31 (s, 3H).

2-Methyl-5-(2-phenylpropan-2-yl)thiophene (3.23) Electrochemical oxidation of trimethyl(((2-phenylpropan-2-yl)oxy)methyl)stannane (**1j**) (62.4 mg, 0.20 mmol) was performed in the presence of 2-methylthiophene (0.10 mL, 1.0 mmol) according to the general procedure at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/EtOAc 20:1) afforded 22.5 mg (52%) of product as a colourless oil. Product has been reported in literature.[37]
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 4H), 7.23 – 7.14 (m, 1H), 6.60 (d, J = 3.4 Hz, 1H), 6.56 (m, 1H), 2.41 (d, J = 1.1 Hz, 3H), 1.74 (s, 6H).

2-Methyl-5-(1-phenylcyclohexyl)thiophene (3.24) Electrochemical oxidation of tributyl(((1-phenylcyclohexyl)oxy)methyl)stannane (**1k**) (96.6 mg, 0.20 mmol) was performed in the presence of 2-methylthiophene (0.1 mL, 1.0 mmol) according to the general procedure at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/DCM 9:1) afforded 30.0 mg (58%) of product as a colourless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.27 (m, 4H), 7.21 – 7.16 (m, 1H), 6.63 – 6.53 (m, 2H), 2.42 (d, J = 1.2 Hz, 3H), 2.38 – 2.18 (m, 4H), 1.74 – 1.38 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.79, 148.32, 137.83, 128.38, 126.70, 125.92, 124.47, 123.30, 45.50, 38.76, 26.23, 23.03, 15.44.
HR-MS (ESI-TOF) m/z: calcd. for $C_{17}H_{21}S$ $[M+1]^+$ 257.1364; found: 257.1356.

Ethyl 2-(5-methylthiophen-2-yl)-2,2-diphenylacetate (3.25) Electrochemical oxidation of (80 mg, 0.18 mmol) was performed in the presence of 2-methylthiophene (0.1 mL, 1.0 mmol) according to the general procedure at 5 mA. Purification by twice column chromatography on silica gel (eluent petroleum) afforded 13.2 mg (21%) of product as an yellowish oil.
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 6H), 7.17 – 7.06 (m, 4H), 6.58 (dd, J = 3.6, 1.1 Hz, 1H), 6.43 (d, J = 3.6 Hz, 1H), 4.33 (q, J = 7.1 Hz, 2H), 2.44 (d, J = 1.1 Hz, 3H), 1.28 (t, J = 7.1 Hz, 3H).
HR-MS (ESI-TOF) m/z: calcd. for $C_{21}H_{21}O_2S$ $[M+1]^+$ 337.1262; found: 337.1245.

2-Methyl-5-(2-phenyl-1-(4-(trifluoromethyl)phenoxy)propan-2-yl)furan (3.26) Electrochemical oxidation of trimethyl(((2-phenyl-1-(4-(trifluoromethyl)phenoxy)propan-2-yl)oxy)methyl)stannane (94.8 mg, 0.20 mmol) was performed in the presence of 2-methylfuran (0.09 mL, 1.0 mmol) according to the general procedure at 5 mA. Purification by column chromatography on silica gel (eluent petroleum ether/Et_2O 20:1) afforded 28.0 mg (39%) of product as an yellowish oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.7 Hz, 2H), 7.26 (s, 6H), 6.98 (d, J = 8.5 Hz, 2H), 6.65 (d, J = 3.5 Hz, 1H), 6.59 (m, 1H), 4.37 (s, 2H), 2.43 (s, 3H), 1.91 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.33, 148.71, 145.62, 138.86, 128.37, 127.07, 127.01 (q, J = 3.8 Hz), 126.90, 124.5 (q, J = 271 Hz), 123.3 (q, J = 32.8 Hz), 114.85, 46.13, 26.69, 15.38.
Unstable under the conditions of HR-MS.

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Keywords: Friedel-Crafts reaction • electrochemistry • carbenium ion • anodic oxidation • stannylmethylethers

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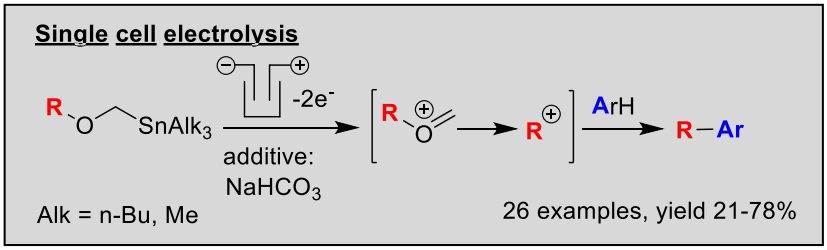

Friedel-Crafts alkylation of electron rich arenes can be achieved by stabilized carbenium ions which are generated by single cell anodic oxidation of stannylmethylethers at low potential. The use of $NaHCO_3$ as an additive ensures close-to-neutral conditions enabling the reaction with arenes bearing acid-sensitive groups such as *O*-TBS, *O*-Tr, *O*-MOM, *O*-THP.

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