Journal Name

ARTICLE

Exploration and development of gold- and silver-catalyzed cross dehydrogenative coupling toward donor-acceptor π-conjugated polymer synthesis

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Lauren J. Kang,[a] Liwen Xing,[b] and Christine K. Luscombe[c]

π-Conjugated polymers are materials of interest for use in organic electronics. Within these polymers, donor-acceptor polymers are favorable for solar cell applications due to improved charge mobility, better absorption in the low energy region of the solar spectrum, and tunable band gaps. One of the barriers to commercializing these donor-acceptor materials is that their synthetic pathways are complex because of the alternating repeat units in the polymer. To address this, the application of cross dehydrogenative coupling (also called oxidative CH/CH cross-coupling) toward the synthesis of donor-acceptor polymers was explored. In this work, the roles of specific reagents in a one-pot gold- and silver-catalyzed cross dehydrogenative coupling and the factors that contribute to selectivity for cross-coupling rather than homo-coupling are analyzed. Based on our results, we postulate that the percentage of alternating repeat units in the final polymer is affected by the increased reactivity of the dimer that forms in the initial stages of the polymerization compared to the monomer, which ultimately may be exploited to control the ratio of electron-rich to electron-poor monomers.

Introduction

Donor-acceptor (D-A) polymers are a class of semiconducting polymers that have attracted interest in the organic electronics field, due to their favorable properties such as high charge mobility, solution-processability, and low band gaps.[1–3] One of the factors that has slowed down commercialization of such polymers in large scale applications is the lack of scalable synthetic methods. In general, D-A polymer syntheses rely on polycondensations that require halogenations and organometallic pre-functionalization steps, such as stannylations for Stille couplings (Figure 1A). Stille couplings are favored for synthesizing D-A polymers because of their high conversion and low catalyst requirements, but the hazardous by-products are undesirable for industrial scale syntheses. Recently, there has been growing use of direct heteroarylation polymerization (DHArP) for the synthesis of D-A polymers (Figure 1B).[4–7] DHArP involves C-H activation of just one of the aromatic coupling partners while the other is typically halogenated. Thus, DHArP reduces the number of monomer pre-functionalization steps required by eliminating the need for specific organometallic functionalization, but still requires halogenation to produce one of the monomers. The use of cross dehydrogenative coupling (CDC), or oxidative CH/CH cross-coupling, in which both coupling partners are selectively C-H activated and then cross-coupled would be far more appealing since neither monomer would have to be pre-functionalized (Figure 1C). Recently, Kanbara *et al.* demonstrated such a synthetic method with a palladium-catalyzed system in the presence of silver salts to synthesize a copolymer of 2,2′,3,3′,5,5′,6,6′-octafluorobiphenyl and 3,3′-dihexyl-2,2′-bithiophene.[8] Though a successful polymerization of an alternating copolymer was achieved, it remains unclear what the sources of selectivity and the roles of each additive were.

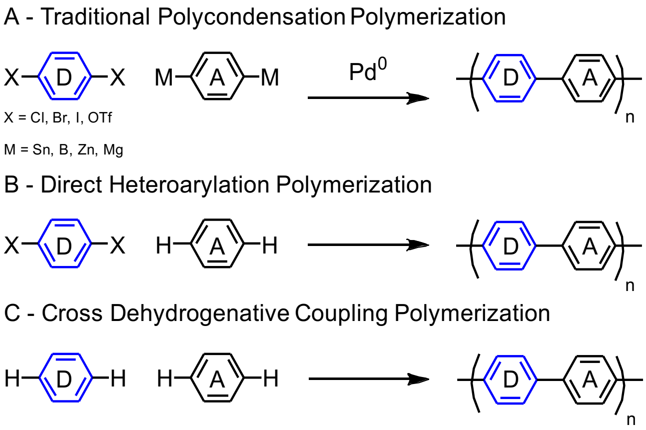


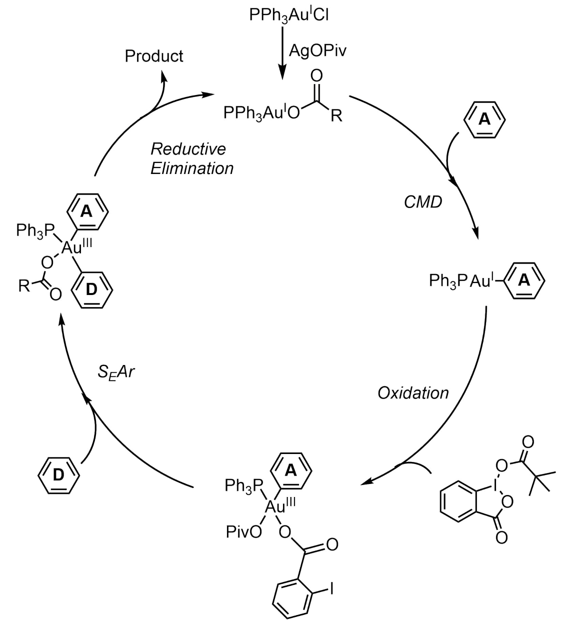
Figure 1 Synthetic pathways for donor-acceptor polymers.

---

[a] Department of Chemistry, University of Washington, Seattle, WA 98195.
Molecular Engineering and Sciences Institute, University of Washington, Seattle, WA 98195
Department of Material Science & Engineering, University of Washington, Seattle, WA 98195.

Electronic Supplementary Information (ESI) available: Characterization data such as ^{1}H NMR, ^{2}H NMR, MALDI-TOF and calculation of % alt, M_n, and DP. See DOI: 10.1039/x0xx00000x

Recently, Larossa *et al.* developed a gold-catalyzed aromatic CDC method for small molecules and observed selectivity in the reactivity of TIPS-protected indoles toward fluorinated benzenes.[9] This methodology achieved direct cross-coupling of simple electron-poor and electron-rich (hetero)arenes with selectivity for the cross-coupled product over the two possible homo-coupled products (Scheme 1). Additionally, the method did not require the use of directing groups and retained selectivity for the cross-coupling product at close to stoichiometric ratios of the arenes, which has been a challenge for similar Pd-catalyzed systems where typically a large excess of one of the coupling partners is used.[10,11] With seemingly orthogonal reactivity based on substrate electronics, these conditions appeared promising for synthesizing D-A polymers. To this end, the use of the aforementioned method for D-A polymer synthesis was explored, and small molecule model studies were used to elucidate the factors that contribute to the selectivity in the polymerization.

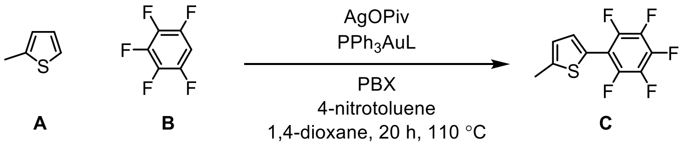


Scheme 1 Proposed mechanism for Au(I) and Au(III) catalyzed CDC. A represents the electron-poor (acceptor) monomer and D represents the electron-rich (donor) monomer.

Results and Discussion

Preliminary small molecule screening

Our work began by exploring reaction conditions to use for our polymerizations that would maximize cross-coupling. While significant optimization work had been carried out previously,[9] the optimization was primarily performed using TIPS-protected indoles or 1,3-dimethoxybenzene as the electron-rich arene. As such, we chose to use a model system comprising of 2-methylthiophene (**A**) and pentafluorobenzene (**B**), serving as the electron-rich and electron-poor coupling partners, respectively (Scheme 2) to mimic the subsequent synthesis of conjugated D-A polymers (poly(thiophene-*alt*-fluorobenzene)). Both reagents were selected to prevent any trimer formation, which was observed when the same reactions were run with 1,2,4,5-tetrafluorobenzene as the electron-poor arene. Although trimer formation is promising in the context of polymerization, we elected to block additional reactive sites for this study in order to observe the extent of cross-coupling selectivity between the two coupling partners. These two aromatic compounds were cross-coupled in the presence of AgOPiv, triphenylphosphinegold(I) catalyst (PPh_3AuL), and PBX as the oxidant (Table 1, representative ^{1}H NMR spectrum used for analysis shown in ESI Figure S1). Overall, cross-coupling yields increased with increasing AgOPiv loading (Table 1, compare Entries 2, 4, 5 and 7, 9, 10) regardless of the **A**:**B** ratio used, which was also observed previously although the use of AgOPiv beyond 0.35 eq was not reported.[9] There was no measurable presence of homo-coupled product of **B** by GC-MS for all entries.

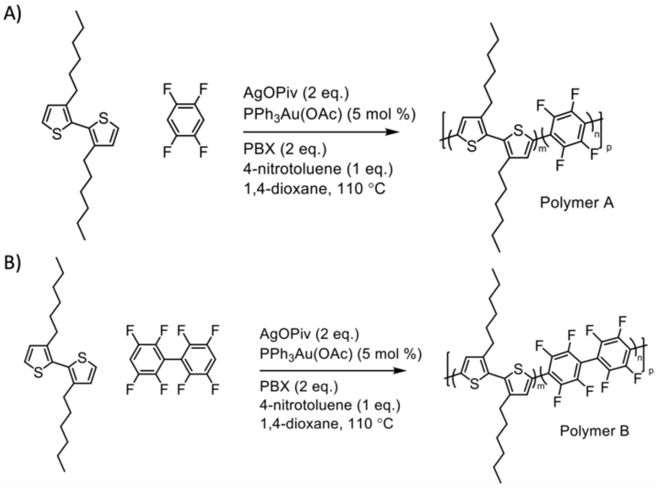


Scheme 2 Small molecule CDC model reaction using 2-methythiophene (**A**) and pentafluorobenzene (**B**).

Table 1 Optimization of small molecule cross-coupling reaction. Reactions were run on 0.1 mmol scale of **A**, using 5 mol % Au-catalyst and PBX (1.5 eq). Reported yields are averages of 3 runs per reaction. The yields were determined by ^{1}H NMR using 4-nitrotoluene as an internal standard following reported procedures.[9] There was no measurable presence of homo-coupled product of **B**. Yields of homo-coupled product of **A** were up to 13 % for entries 6-11 and 5 % for entries 1-5.

Entry	Eq. of **A**	Eq. of **B**	L	Eq. of AgOPiv	% yield of **C**	Rxn time (h)
1	1	5	Cl	0.35	36±7	20
2	1	5	OAc	0.35	59±5	20
3	1	5	OAc	0.35	82±2	40
4	1	5	OAc	0.7	87±2	20
5	1	5	OAc	1	94±6	20
6	1	1	Cl	0.35	27±8	20
7	1	1	OAc	0.35	20±7	20
8	1	1	OAc	0.35	52±5	40
9	1	1	OAc	0.7	41±9	20
10	1	1	OAc	1	66±12	20
11	1	1	OAc	1	66±3	40

Using optimized conditions with increased AgOPiv loading, polymerizations were attempted using 3,3’-dihexyl-2,2’-bithiophene as the electron-rich monomer and 1,2,4,5-tetrafluorobenzene (Scheme 3A) or 2,2’,3,3’,5,5’,6,6’-octafluorobiphenyl (Scheme 3B) as the electron-poor monomer. 3,3’-dihexyl-2,2’-bithiophene was chosen to increase polymer solubility as the polymer grew by incorporating alkyl chains along the polymer backbone, and to eliminate any regioselectivity issues by using a symmetrical monomer that would otherwise arise by the use of a 3-alklythiophene monomer. ^{1}H NMR assignment (ESI Figure S5 and Figure 2) of the peaks were made following literature[8] and our small molecule model studies (discussed further in Scheme 7, ESI Figure S9). Previous work had indicated that the aromatic peak from the terminal fluorinated aromatic group could be observed at 7.3 ppm. However, in our spectra (Figure 2), we observe a doublet in this region, which we assign to terminal thiophenes suggesting that our polymer chains are terminated by thiophene units on both chain ends. For polymer B, there are overlapping signals in the nearby region. As such, we cannot entirely eliminate the possibility of fluorinated aromatic end-groups. However, given the greater incorporation of the bithiophene monomer into the polymer chain (discussed further below), statistically, there is a greater probability that the polymers are terminated by thiophenes.



Scheme 3 Polymerization scheme with 1,2,4,5-tetrafluorobenzene (polymerization A) and with 2,2′,3,3′,5,5′,6,6′-octafluorobiphenyl (polymerization B) as the electron-poor monomer. All polymerizations were run on a 1 mmol scale with 1:1 comonomer ratios

The degree of polymerization (DP) and thus number-average molecular weight (M_n) values were determined using end-group analysis *via* ^{1}H NMR spectroscopy (ESI Equations S1 and S2, respectively), and dispersity ($Đ$) values were determined using size-exclusion chromatography (SEC). The resonances of a thiophene positioned between two thiophenes (e.g., T**T**-**T**T, where T = thiophene) appear at 7.01-7.09 ppm for Polymer A and 7.04-7.10 ppm for Polymer B (labelled H_h in Figure 2), while the resonance of a thiophene located between a fluorinated benzene and a thiophene (e.g., -F-**TT**-F-, where F = tetrafluorobenzene) appears at 7.50-7.59 ppm for Polymer A and 7.59-7.63 ppm for Polymer B (labelled H_c in Figure 2). The presence of the H_h peaks indicate that there is a higher degree of homo-coupling observed in the polymerization than was observed in the small molecule studies. We also see two different thiophene end-group peaks depending on whether or not the end-group is adjacent to a fluorinated benzene or a bithiophene as a result of homo-coupling. Specifically, the proton signals from the end-groups of bithiophenes adjacent to a fluorinated benzene appear as doublets at ~7.35 (H_a) and ~7.00 ppm (H_b), while those adjacent to another bithiophene appear as doublets at ~7.3 ($H_{a'}$) and ~6.98 ppm ($H_{b'}$). The ratio between the H_c peaks *vs*. all end-group peaks gives us the number of alternating units along the polymer backbone, and multiplying this value by two provides the total number of both bithiophene and fluorinated benzene units that make up the alternating units. Furthermore, the ratio between the H_h peaks *vs*. all end-group peaks gives us the number of additional bithiophene units that were incorporated into the polymer chain. The sum of these provides a value for DP and the equation is shown in the ESI as Equation S1. This analysis can then be used to calculate M_n (Equation S2).

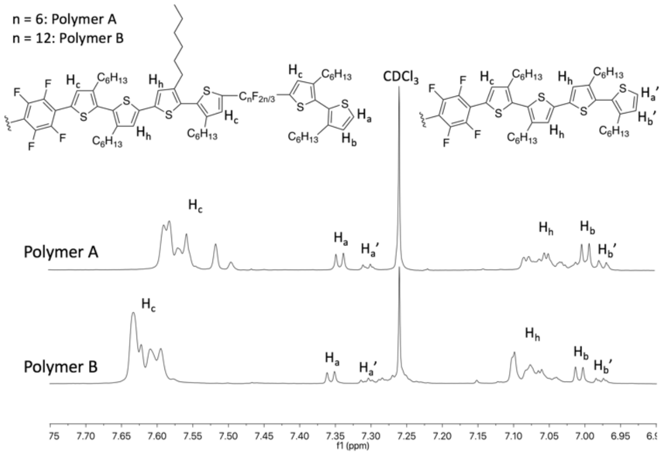


Figure 2 Example ^{1}H NMR showing the region used for M_n, DP, and % alt calculation. The ^{1}H NMR corresponds to aliquots at 168 h time point.

Based on this analysis, the resulting M_n of Polymers A and B were calculated to be 5.1 kg/mol and 9.4 kg/mol, respectively, with DPs of 18 and 28, respectively. The yields for Polymers A and B were 47% and 63%, respectively, with the $Đ$ for both measured to be 1.2. The percentage of alternating units in the polymer sequence (% alt) was calculated by comparing the ratio of the number of alternating units (H_c) *vs*. all repeat unit peaks in the aromatic region of the ^{1}H NMR (ESI Equation S3 and Figure 2). A perfectly alternating polymer would have a % alt of 100 %. Noticeably, the % alt of both polymers remained constant at around 70 % throughout the polymerization process (Table 2, ESI Table S3) regardless of reaction time. These % alt values are supported by the MALDI data (ESI Tables S1 and S2, Figure S4) that show that more bithiophene units are incorporated into the polymer compared to the fluorinated benzene units. The presence of multiple peaks in the ^{19}F NMR (ESI Figure S6) of the polymers also reflect the fact that 100% alternation was not achieved.[8] The lower than expected % alt showed that the selectivity observed in the small molecule reaction did not transfer to the polymer synthesis suggesting three possibilities: (i) the terminal protons at the polymer chain-ends would become more electronically similar due to increased conjugation thereby reducing selectivity as the polymer grew; (ii) the previously proposed mechanism as shown in Scheme 1 was not occurring and required further investigation; (iii) the dimers generated at the early stages of the polymerization are more reactive than the monomers. We believe that the first possibility can be ruled out for two reasons. First of all, the two adjacent hexyl groups of the bithiophene unit in polymers would cause the polymer backbone to twist, which would lead to ineffective π-conjugation along the polymer backbone. Secondly, for Polymer B, the twist between the two benzene rings in the octafluorobiphenyl unit would reduce the effective conjugation length even more.[13] If the extended conjugation as the polymer grew was indeed detrimental to the selectivity of the CDC reaction, higher % alt in Polymer B than in Polymer A should have been observed, and % alt should have decreased with increasing chain length. However, as summarized in Table 2, it can be seen that the % alt remain similar for both systems and does not change significantly as the polymerization proceeds.

Table 2 Results of polymerization comparing 1,2,4,5-tetrafluorobenzene (polymerization A) to 2,2',3,3',5,5',6,6'-octafluorobiphenyl (polymerization B) as the electron-poor monomer. Co-monomer ratio loading was 1:1. M_n shown in ESI Table S3.

Timepoint (h)	% alt for polymerization A	% alt for polymerization B
24	71	67
48	73	71
96	72	68
120	72	69
144	76	70
168	67	69
192	69	69

Cross-coupling mechanism studies

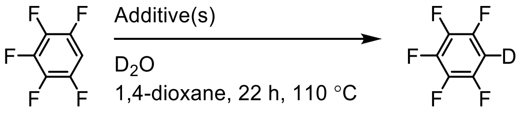
In order to understand the source of selectivity loss in polymerization, the mechanism of the polymerization was explored further. No reaction was observed when control polymerizations were performed in the absence of Ag and Au showing that the decline in selectivity is not due to oxidative homo-coupling of the bithiophene caused by PBX. We propose that there are two possible mechanisms for this CDC cross-coupling based on previous work: (i) where Au(I) is responsible for activating the electron-poor species, and Au(III) is activating the electron-rich species as shown in Scheme 1; or (ii) where Ag was mainly responsible for the C-H activation of the electron-poor arene, and Au(III) activated the electron-rich arene, which was suggested as a possibility previously but not experimentally confirmed.[9] To this end, a series of experiments were run using slightly altered conditions to Scheme 2 (Table 3) in an attempt to elucidate the role of silver salts in this reaction. Silver salts have been the subject of increased studies in recent reports in in Pd-catalyzed C-H activation.[12–14] It has been proposed that the silver salt could act as an oxidant, as a ligand source, halide scavengers and/or a C-H activating agent.[14] Similarly, for this gold-catalyzed method, AgOPiv could be playing multiple roles. From Table 3 and previous work,[9] it is clear that AgOPiv was not simply a ligand or base source, or a halide scavenger as the reaction still required the presence of Ag to proceed no matter whether PPh_3AuOAc or PPh_3AuCl was used (Table 3, Entries 3, 4, 8, and 9) and even when a stoichiometric amount of pivalate was added in the absence of Ag (Table 3, Entry 13). It was also shown that the AgOPiv was not a sufficient oxidant, as the reaction did not proceed without PBX, even in the presence of excess AgOPiv (Table 3, Entries 5 and 10). There was also an observed decrease in yield with the reduction of the **B** to **A** ratio (Table 3, Entries 1, 2, 6, and 7). In combination with the observed increase in yield with increased AgOPiv loading (Table 1, Entries 4, 5, 9, and 10), we speculate that both AgOPiv and **B** may play a role in the rate-determining step of the reaction. However, more detailed kinetic studies are required to confirm this.

Table 3 Control experiments for CDC reaction. Reactions were run on 0.1 mmol scale of **A** (1 eq) for 20 h using 5 mol % Au-catalyst. Reported yields are averages of 3 runs per reaction. The yields were determined by ^{1}H NMR using 4-nitrotoluene as an internal standard, as reported by Larrosa *et al.*[9] There was no measurable presence of homo-coupled product of **B**.

Entry	Eq. of **B**	L	Eq. of PBX	Additive (eq)	% yield of **C**	% yield of homo-coupled product of **A**
1	5	Cl	1.5	AgOPiv (0.35)	36±7	2.3±1.5
2	5	OAc	1.5	AgOPiv (0.35)	59±5	3.0±1.0
3	5	Cl	1.5	None	<1	<1
4	5	OAc	1.5	None	<1	<1
5	5	OAc	0	AgOPiv (0.7)	<1	<1
6	1	Cl	1.5	AgOPiv (0.35)	27±8	2.3±0.6
7	1	OAc	1.5	AgOPiv (0.35)	20±7	3.7±1.2
8	1	Cl	1.5	None	<1	<1
9	1	OAc	1.5	None	1.1±0.6	<1
10	1	OAc	0	AgOPiv (0.7)	<1	<1
11	1	OAc	1.5	AgOPiv (0.7)	41±9	6.7±1.5
12	1	OAc	1.5	AgOPiv (1)	66±12	13.0±1.0
13	1	OAc	1.5	NaOPiv (1)	<1	4.7±0.8

To determine which metal species was responsible for the CH-activation of both the electron-rich and electron-poor species, deuterium studies were performed. By reacting each of the starting materials (i.e., **A** and **B**) separately with different combinations of additives in the presence of deuterium oxide, the degree of deuteration was quantified (Schemes 4 and 5, ESI Figure S7, Equation S4). For both **A** and **B**, NaOPiv yielded no C-H activation confirming that pivalate on its own could not deprotonate the starting arenes (Table 4, Entry 2; Table 5, Entry 2). In the case of pentafluorobenzene **B**, results in Table 4 indicate that AgOPiv itself can act as a C-H activating agent with a deuterium conversion of 23 % (Table 4, Entry 3), whereas no deuterium conversion in the presence of $PPh_3Au(I)OAc$ or Au(III) chloride ($AuCl_3$) (Table 4, Entry 4-7) was detected. In the case of 2-methylthiophene (**A**), while some deuterium conversion was observed in the presence of AgOPiv or PPh_3AuOAc, 10 % and 4 % respectively (Table 5, Entries 3 and 7), while significantly higher conversion of 42 % was observed in the presence of $AuCl_3$ (Table 5, Entry 4). Upon the addition of pivalic acid, there was an increase in deuterated product, 69 %, showing that the addition of a carboxylate ligand to the gold catalyst increases its ability to C-H activate **A** (Table 5, Entry 5). A surprising observation was made in both reactions with **A** and **B** separately, in that the combination of $AuCl_3$ and AgOPiv resulted in reduced C-H activation (Tables 4 and 5, Entry 6). Furthermore, these reactions also exhibited the formation of silver mirrors on the reaction vessels, indicating a decomposition pathway resulting in the formation of elemental silver. Silver mirror formation was not observed in the overall cross-coupling reactions, in which the Au(III) species would have carboxylate anions in place of chloride anions. Therefore, we believe that such a decomposition pathway is unique to the highly halogenated Au(III) chloride and is not occurring in the cross-coupling reaction. These deuterium studies show that Ag is capable of activating both the electron-poor and electron-rich arenes and that the activation of the electron-poor arene is more favourable (23 % *vs*. 10 %). They also suggest that Au(III) has a high reactivity for the C-H activation of the electron-rich species but low reactivity for the electron-poor species. However, these studies cannot definitively show that Au(I) does not participate in the CH-activation. Specifically, if the Au(I)-C_6F_5 complex is stable under the reaction conditions shown in Scheme 4, then the deuterium studies would provide an inaccurate representation of the degree of CH-activation. Indeed, when the Au(I)-C_6F_5 complex was synthesized independently and subjected to reaction conditions shown in Scheme 4 without additives, the formation of C_6F_5D was not observed by NMR suggesting that the reason for the lack of deuterium incorporation shown in Tables 4 and 5, Entry 7 could be a result of the stability of the Au(I)-arene complexes rather than the inability of Au(I) to perform CH-activation under the cross-coupling reaction conditions.

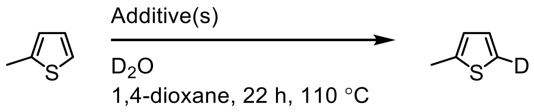
To overcome this issue, we chose to directly monitor the formation of the Au(I)-C_6F_5 complex (ESI Figure S8) by ^{1}H NMR using similar conditions used for the cross-coupling but in the absence of PBX, AgOPiv, and the cross-coupling partner, while using a stoichiometric amount of PPh_3AuOAc. The formation of Au(I)-C_6F_5 complex was not observed unless a strong base, such as sodium *tert*-butoxide (ESI Figure S8) was added, which has been shown previously.[15] This suggests that Au(I) can not activate the CH-bond under the cross-coupling reaction conditions used, leading us to conclude that AgOPiv likely activates the C-H bond of the electron-poor arene, while the electron-rich species is CH activated by Au(III).



Scheme 4 Deuterium study of pentafluorobenzene.

Table 4 Deuterium study results of pentafluorobenzene. Reactions were run on 0.1 mmol scale of **B**. Reported yields are averages of 3 runs per reaction. The yields were determined by using an internal standard of DMSO-d^6, using similar conditions as those previously reported by Sanford *et al.*[12]

Entry	Additive	Deuterium Incorporation (%)
1	None	0
2	0.35 eq. NaOPiv	0
3	0.35 eq. AgOPiv	23.1
4	0.05 eq. $AuCl_3$	0
5	0.05 eq. $AuCl_3$, 0.05 eq. PivOH	0
6	0.05 eq. $AuCl_3$, 0.35 eq AgOPiv	1.9
7	0.05 eq. PPh_3AuOAc	0
8	0.05 eq. PPh_3AuOAc, 0.35 eq. AgOPiv	17.7



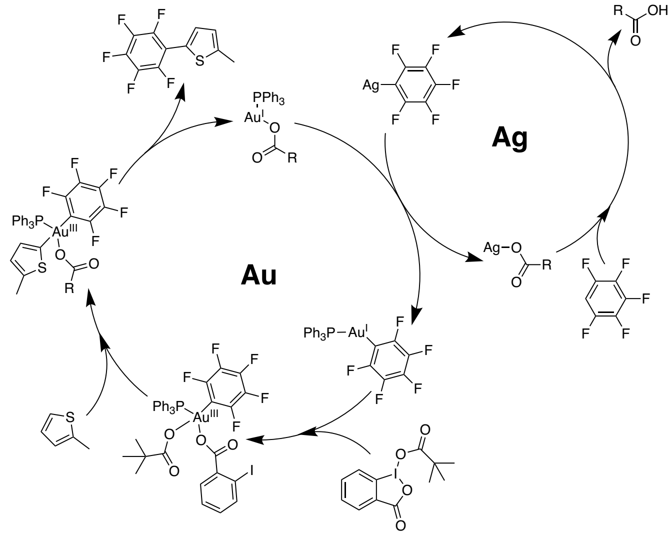
Scheme 5 Deuterium study of 2-methylthiophene.

Table 5 Deuterium study results of 2-methylthiophene. Reactions were run on 0.1 mmol scale of **A**. Reported yields are averages of 3 runs per reaction. The yields were determined by using an internal standard of DMSO-d^6, using similar conditions as those previously reported by Sanford *et al.*[12]

Entry	Additive	Deuterium Incorporation (%)
1	None	0
2	0.35 eq. NaOPiv	0
3	0.35 eq. AgOPiv	10.0
4	0.05 eq. $AuCl_3$	41.8
5	0.05 eq. $AuCl_3$, 0.05 eq. PivOH	69.3
6	0.05 eq. $AuCl_3$, 0.35 eq. AgOPiv	0
7	0.05 eq. PPh_3AuOAc	4.4
8	0.05 eq. PPh_3AuOAc, 0.35 eq. AgOPiv	6.6

Based on the results from the above studies, we propose that the cross-coupling mechanism consists of two overlapping cyclic pathways (Scheme 6). To the extent of our knowledge, there is only one case of polymerization method for a semiconducting polymer that utilizes a dual catalytic mechanism and this was used to synthesize a homopolymer of poly(3-hexylthiophene).[16]

We also hypothesize that transmetalation likely occurs between Ag and Au(I) rather than Ag with Au(III), the latter requiring Au(I) to be oxidized to Au(III) first. This hypothesis is based on the yields observed for homo-coupling of the thiophene species (Table 3 and ESI Scheme S1). The homo-coupling product could arise *via* three pathways: (i) activation of two thiophene species by Ag followed by transmetalation; (ii) oxidation of Au(I) to Au(III), followed by activation of two thiophenes species by Au(III) and subsequent transmetalation; (iii) pathway shown in Scheme 6 but where pentafluorobenzene is replaced by thiophene. While we cannot completely eliminate the possibility of all three pathways since homo-coupling is observed in the absence of Ag (Table 3, Entry 13), we believe that pathway (i) is not a dominant pathway because the homo-coupling of pentafluorobenzene is never observed. Additionally, since the yield for homo-coupling of thiophene increases with silver loading (Table 3, Entries 7,11, and 12), we believe that a pathway involving silver is more dominant (pathway (iii)) than pathway (ii). It should be noted that we see a similar trend in homo-coupling in the polymerization as well where a %alt of 77% was achieved when 1 eq of AgOPiv was used instead of 2 eq of AgOPiv, although M_n decreased significantly because of overall lower monomer conversion, which is also seen in the small molecule studies.

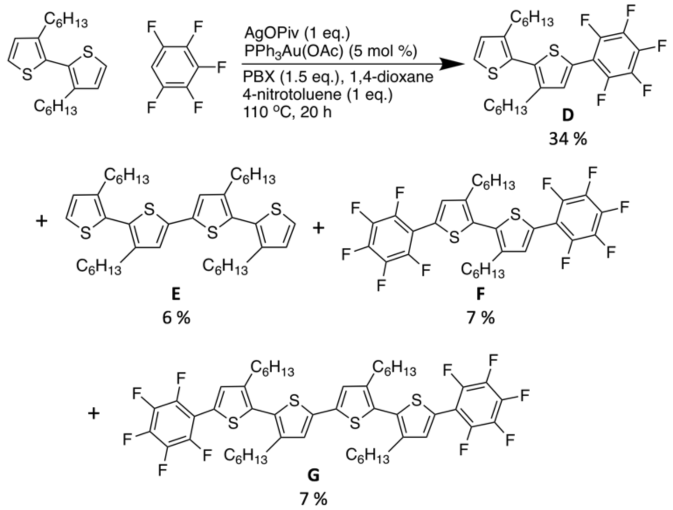


Scheme 6 Simplified proposed mechanism of gold- and silver-catalyzed dehydrogenative cross-coupling.

Consequence of the dual cycle on the polymerization

The newly proposed mechanism presents a challenge for transitioning the gold- and silver-catalyzed CDC method from a small molecule synthesis to a polymer synthesis, as observed by the increase in amount of homo-coupling occurring in the polymerization compared to the small molecule coupling reactions. Polymer chain growth in a perfectly alternating manner in a dual cyclic mechanism would require both cycles to turn over in synchrony or for one of the intermediates to be a persistent intermediate, while also ensuring that each metal can only selectively activate one monomer over the other.[17] The deuterium exchange studies indicated that Ag can activate both the electron-rich and electron-poor species giving rise to the homo-coupling of the electron-rich species in the small molecule studies, but our polymerizations indicated that the selectivity worsened in the polymerization mixture. We hypothesized that this was because once a thiophene coupled with the electron-poor species, the thiophene end could show increased reactivity towards Ag because of the electron-withdrawing effect from the fluorinated benzene, and/or that the generated M-bithiophene-fluorinated benzene species, where M = Au or Ag, was more reactive than M-bithiophene.

To test this hypothesis, we performed a CDC reaction of 3,3'-dihexyl-2,2'-bithiophene with **B** using similar reaction conditions to Scheme 2 and measured the mol % of the different products in the reaction mixture (Scheme 7). A 1:1 ratio of 3,3'-dihexyl-2,2'-bithiophene to **B** was used to mimic the polymerization conditions as much as possible, while preventing a polymerization from taking place by using pentafluorobenzene **B**. We observed the formation of four products by GC-MS, and the conversion of 3,3'-dihexyl-2,2'-bithiophene in this reaction was 67 % as observed by ^{1}H NMR (ESI Figure S9). While the primary product was the cross-coupled product **D**, the mol % of product **G** was as high as that of product **F** supporting our hypothesis that **D** or M-**D** is more reactive than the bithiophene or M-bithiophene, and shows similar reactivity as pentafluorobenzene of M-pentafluorobenzene, thereby increasing the amount of homo-coupling in the polymerization. We believe that the electron-withdrawing effect from the fluorinated benzene is limited to two bithiophene units because of the twist in the monomer units, thus allowing one to maintain % alt of ~70% throughout the polymerization. This new understanding of the selectivity in D-A polymer synthesis via CDC provides us with a potential for controlling the incorporation ratio of donor *vs.* acceptor monomers. For example, choosing and designing monomers with larger differences in their electronic properties could enhance the selectivity of Ag. Also, since we had observed that increased loading of electron-poor species resulted in higher yields of the cross-coupled product for the small molecule reactions, using different feed ratios of the two monomers would be another way to adjust % alt of the polymers leading to the development of synthetic methodologies to achieve sequence-specific polymers.



Scheme 7 CDC reaction between 3,3’-dihexyl-2,2’-bithiophene and **B** (1:1 ratio), and the resultant products as well as their mol % in the reaction mixture as determined by ^{1}H NMR (ESI Figure S9).

Conclusions

In conclusion, we applied the gold- and silver-catalyzed CDC method to D-A polymer synthesis which, to the best of our knowledge, is the first example where a dual-catalytic system being applied to the synthesis of D-A conjugated polymers via CDC method. Through small molecule model studies, the roles of the various reagents in the reaction were elucidated. Specifically, we provide further experimental support to the suggestion that Ag is playing a role in the CH-activation.[9] Our control experiments also suggest that the Ag-mediated C-H activation of the electron-poor species may be the rate-limiting step, but kinetic studies need to be carried out to confirm this which are currently ongoing in our lab. By performing the CDC reaction between 3,3’-dihexyl-2,2’-bithiophene and pentafluorobenzene, we suggest that the selectivity loss when applying this reaction to polymer synthesis is primarily due to the increased reactivity of the bithiophene-fluorinated benzene species compared to the bithiophene monomer. The originally proposed monometallic Au(I)/Au(III)-catalyzed mechanism may have appeared ideal for an $(\text{-AB-})_n$ alternating copolymer synthesis, but ultimately these studies show that the multimetallic nature of the mechanism may provide a new tool for the facile synthesis of sequence-controlled polymers. Ongoing studies in our lab include development of ligands on Ag and Au to increase their selectivity and turnover, use of different metal combinations to improve selectivity, and the exploration of the use of monomer with greater differences in electron density to achieve a higher % alternation as well as higher MWs.

Experimental

General procedures and materials

All manipulation of air- and/or moisture-sensitive compounds were carried out using standard Schlenk and glovebox techniques under a dry nitrogen atmosphere. Anhydrous 1,4-dioxane, chloro(triphenylphosphine)gold(I), deuterium oxide, 3,3’-dihexyl-2,2’-bithiophene, gold(III) chloride, 2-methylthiophene, 4-nitrotoluene, 2,2’,3,3’,5,5’,6,6’-octafluorobiphenyl, pentafluorobenzene, pivalic acid, sodium trimethylacetate hydrate, and 1,2,4,5-tetrafluorobenzene were used as purchased. Pivaloyloxy-1,2-benziodoxol-3(1H)-one (PBX),[9] silver pivalate (AgOPiv),[18] and acetate(triphenylphosphine)gold(I) (PPh_3AuOAc)[19] were synthesized using previously reported methods.

Cross-coupling studies

A 4 mL amber vial and an acid-washed stir bar were oven dried overnight. PPh_3AuOAc (2.59 mg, 5.00 µmol), silver pivalate (14.6 mg, 70.0 µmol), 4-nitrotoluene (13.7 mg, 100 µmol), and PBX (52.2 mg, 150 µmol) were added to the previously mentioned vial and sealed with a septa cap. Vial was evacuated and refilled with nitrogen three times. Under nitrogen pressure, anhydrous 1,4-dioxane (0.5 mL), pentafluorobenzene (16.8 mg, 100 µmol), and 2-methylthiophene (9.82 mg, 100 µmol) were injected into the reaction flasks in succession. The reactions were heated at 110 °C overnight. The resulting mixtures were passed through a celite plug using hexanes, washed with 1 M HCl, followed by 1 M NaOH aqueous solution, and then the organic layer was dried using anhydrous Na_2SO_4. The remaining solvent was removed under reduced pressure. The resulting mixtures were analyzed by NMR.

Deuterium studies

A 4 mL amber vial and an acid-washed stir bar were oven dried overnight. Varied combinations of additives were added and then the vial was evacuated and refilled with nitrogen three times. Under nitrogen pressure, anhydrous 1,4-dioxane (0.5 mL), 2-methylthiophene (9.82 mg, 100 µmol) or pentafluorobenzene (16.8 mg, 100 µmol), and deuterium oxide (10.0 mg, 500 µmol) were injected into the reaction flasks in succession. The reactions were heated at 110 °C overnight. d_6-DMSO (10.0 µL, 141 µmol) were added. The reaction mixtures were passed through a celite plug. The mixture was analyzed using ^{2}H NMR, by comparing the deuterated aryl peak against the d_6-DMSO peak.

Cross Dehydrogenative Coupling Polymerization

A 20 mL amber vial and an acid-washed stir bar were oven dried overnight. PPh_3AuOAc (25.9 mg, 50.0 µmol), silver pivalate (418 mg, 2.00 mmol), 4-nitrotoluene (137 mg, 1.00 mmol), and PBX (696 mg, 2.00 mmol) were added to the previously mentioned vial and sealed with a septa cap. Vial was evacuated and refilled with nitrogen three times. Under nitrogen pressure, anhydrous 1,4-dioxane (5 mL), 2,2’,3,3’,5,5’,6,6’-octafluorobiphenyl (298 mg, 1.00 mmol) or 1,2,4,5-tetrafluorobenzene (150 mg, 1.00 mmol), and 3,3’-dihexyl-2,2’-bithiophene (334 mg, 1.00 mmol) were injected into the reaction flasks in succession. The reactions were heated at 110 °C. The reaction was quenched with 1 M HCl. The resulting mixture was washed with saturated EDTA solution, and then precipitated into excess MeOH. Then the resulting polymer was Soxhlet extracted with MeOH, then collected in chloroform. The remaining solvent was removed under reduced pressure. The resulting mixtures were analyzed by NMR, GPC, MALDI.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This work was supported by the NSF under the CCI Center for Selective C–H Functionalization, CHE-1700982.

References

(1) Müllen, K.; Pisula, W. Donor–Acceptor Polymers. *J. Am. Chem. Soc.* **2015**, *137* (30), 9503–9505.

(2) Holliday, S.; Li, Y.; Luscombe, C. K. Recent Advances in High Performance Donor-Acceptor Polymers for Organic Photovoltaics. *Prog. Polym. Sci.* **2017**, *70*, 34–51.

(3) Hou, J.; Chen, H.-Y.; Zhang, S.; Chen, R. I.; Yang, Y.; Wu, Y.; Li, G. Synthesis of a Low Band Gap Polymer and Its Application in Highly Efficient Polymer Solar Cells. *J. Am. Chem. Soc.* **2009**, *131* (43), 15586–15587.

(4) Hendsbee, A.D.; Li, Y. Performance Comparisons of Polymer Semiconductors Synthesized by Direct (Hetero)Arylation Polymerization (DHAP) and Conventional Methods for Organic Thin Film Transistors and Organic Photovoltaics. *Molecules* **2018**, *23*, 1255.

(5) Bura, T.; Blaskovits, J. T.; Leclerc, M. Direct (Hetero)Arylation Polymerization: Trends and Perspectives. *J. Am. Chem. Soc.* **2016**, *138* (32), 10056–10071.

(6) Lai, Y.-Y.; Tung, T.-C.; Liang, W.-W.; Cheng, Y.-J. Synthesis of Poly(3-Hexylthiophene), Poly(3-Hexylselenophene), and Poly(3-Hexylselenophene-Alt-3-Hexylthiophene) by Direct C–H Arylation Polymerization via N-Heterocyclic Carbene Palladium Catalysts. *Macromolecules* **2015**, *48* (9), 2978–2988.

(7) Roy, C.; Bura, T.; Beaupré, S.; Légaré, M.-A.; Sun, J.-P.; Hill, I. G.; Leclerc, M. Fluorinated Thiophene-Based Synthons: Polymerization of 1,4-Dialkoxybenzene and Fluorinated Dithieno-2,1,3-Benzothiadiazole by Direct Heteroarylation. *Macromolecules* **2017**, *50* (12), 4658–4667.

(8) Aoki, H.; Saito, H.; Shimoyama, Y.; Kuwabara, J.; Yasuda, T.; Kanbara, T. Synthesis of Conjugated Polymers Containing Octafluorobiphenylene Unit via Pd-Catalyzed Cross-Dehydrogenative-Coupling Reaction. *ACS Macro Lett.* **2018**, *7* (1), 90–94.

(9) Cambeiro, X. C.; Ahlsten, N.; Larrosa, I. Au-Catalyzed Cross-Coupling of Arenes via Double C–H Activation. *J. Am. Chem. Soc.* **2015**, *137* (50), 15636–15639.

(10) Stuart, D. R.; Fagnou, K. The Catalytic Cross-Coupling of Unactivated Arenes. *Science* **2007**, *316* (5828), 1172–1175.

(11) He, C.-Y.; Min, Q.-Q.; Zhang, X. Palladium-Catalyzed Aerobic Dehydrogenative Cross-Coupling of Polyfluoroarenes with Thiophenes: Facile Access to Polyfluoroarene–Thiophene Structure. *Organometallics* **2012**, *31* (4), 1335–1340.

(12) Lotz, M. D.; Camasso, N. M.; Canty, A. J.; Sanford, M. S. Role of Silver Salts in Palladium-Catalyzed Arene and Heteroarene C–H Functionalization Reactions. *Organometallics* **2017**, *36* (1), 165–171.

(13) Whitaker, D.; Burés, J.; Larrosa, I. Ag(I)-Catalyzed C–H Activation: The Role of the Ag(I) Salt in Pd/Ag-Mediated C–H Arylation of Electron-Deficient Arenes. *J. Am. Chem. Soc.* **2016**, *138*, 8384–8387.

(14) Bay, K. L.; Yang, Y.-F.; Houk, K. N. Multiple Roles of Silver Salts in Palladium-Catalyzed C–H Activations. *J. Organomet. Chem.* **2018**, *864*, 19–25.

(15) Ahlsten, N.; Perry, G. J. P.; Cambeiro, X. C.; Boorman, T. C.; Larrosa, I. A Silver-Free System for the Direct C–H Auration of Arenes and Heteroarenes from Gold Chloride Complexes. *Catal. Sci. Technol.* **2013**, *3* (11), 2892–2897.

(16) Lee, J. A.; Luscombe, C. K. Dual-Catalytic Ag–Pd System for Direct Arylation Polymerization to Synthesize Poly(3-Hexylthiophene). *ACS Macro Lett.* **2018**, *7* (7), 767–771.

(17) Ackerman, L. K. G.; Lovell, M. M.; Weix, D. J. Multimetallic Catalysed Cross-Coupling of Aryl Bromides with Aryl Triflates. *Nature* **2015**, *524* (7566), 454–457.

(18) Edwards, D. A.; Harker, R. M.; Mahon, M. F.; Molloy, K. C. Aerosol-Assisted Chemical Vapour Deposition (AACVD) of Silver Films from Triorganophosphine Adducts of Silver Carboxylates, Including the Structure of [Ag(O2CC3F7)(PPh3)2]. *Inorganica Chim. Acta* **2002**, *328* (1), 134–146.

(19) García-Domínguez, P.; Nevado, C. Au−Pd Bimetallic Catalysis: The Importance of Anionic Ligands in Catalyst Speciation. *J. Am. Chem. Soc.* **2016**, *138* (10), 3266–3269.