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3,4-Propylenedioxypyrrole-Based Conjugated Oligomers *via* Pd-Mediated Decarboxylative Cross Coupling

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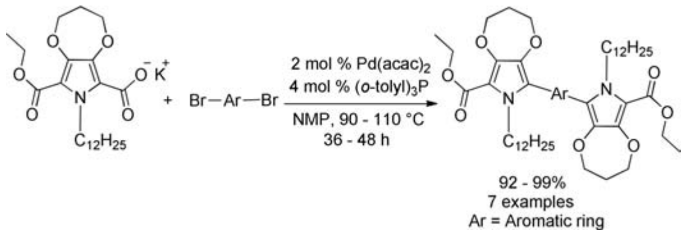
ABSTRACT



An effective decarboxylative cross-coupling involving a 3,4-dioxypyrrole is reported. Several conjugated oligomers were synthesized in high yields using various aryl bromides. No copper salt or other transmetalating agent was required. The reaction conditions employed displayed relatively low sensitivity toward the presence of water.

Dioxypyrroles (XDOPs) are interesting electron-rich molecules which yield polymers that combine low oxidation potential with intermediate to high band gaps to produce materials with high conductivity, electrochromism and fast optical switching.[1,2] 3,4-Dioxypyrrole monomers can be derivatized through N- or O-alkylation allowing the tuning of electronic properties and solubility of their resultant polymers.[1a] A wide number of 3,4-dioxypyrrole monomers can be prepared by Hinsberg condensation[3a] and other synthetic methodologies.[3b−d] Using these methodologies, our group has synthesized and studied a variety of XDOPs designed to yield polymers where the redox and optical properties are rationally controlled via the substituents.[1a−c,4]

Despite their interesting properties, most of the polymeric dioxypyrroles (PXDOPs) reported are restricted to homopolymers. Excluding a report by Merz et al.,[5a] organometallic coupling, commonly used for synthesis of many conjugated organic materials, is almost unknown for the XDOPs. The low stability of 2,5-dihaloXDOP derivatives, which can be seen as natural precursors for many organometallic coupling reactions, is one of the main drawbacks that hinders their utilization. Based on previous works reported by Merz,[5a] Wudl,[5b] and our group,[4d] we took advantage of this behavior to develop an efficient and convenient polymerization method of XDOPs via iododecarboxylation.[4c]

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(1) (a) Walczak, R. M.; Reynolds, J. R. *Adv. Mater.* **2006**, *18*, 1121. (b) Thomas, C. A.; Zong, K.; Schottland, P.; Reynolds, J. R. *Adv. Mater.* **2000**, *12*, 222. (c) Sonmez, G.; Schwendeman, I.; Schottland, P.; Zong, K.; Reynolds, J. R. *Macromolecules* **2003**, *36*, 639. (d) Dyer, A. L.; Reynolds, J. R. In *Handbook of Conducting Polymers*, 3rd ed.; Skotheim, T. A., Reynolds, J. R., Eds.; CRC Press: Boca Raton, 2007; Vol. 1; Chapter 20.

(2) (a) Darmanin, T.; Guittard, F. *J. Am. Chem. Soc.* **2009**, *131*, 7928. (b) Zotti, G.; Zecchin, S.; Schiavon, G.; Groenendaal, L. B. *Chem. Mater.* **2000**, *12*, 2996.

(3) (a) Hinsberg, O. *Ber. Dtsch. Chem. Ges.* **1910**, *43*, 901. (b) Merz, A.; Scnwarz, R.; Schropp, R. *Adv. Mater.* **1992**, *4*, 409. (c) Merz, A.; Meyer, T. *Synthesis* **1999**, *1*, 94. (d) Merz, A.; Schropp, R.; Dötterl, E. *Synthesis* **1995**, 1–795.

(4) (a) Schottland, P.; Zong, K.; Gaupp, C. L.; Thompson, B. C.; Thomas, C. A.; Giurgiu, I.; Hickman, R.; Abboud, K. A.; Reynolds, J. R. *Macromolecules* **2000**, *33*, 7051. (b) Walczak, R. M.; Jung, J.-H.; Cowart, J. S.; Reynolds, J. R. *Macromolecules* **2007**, *40*, 7777. (c) Walczak, R. M.; Leonard, J. K.; Reynolds, J. R. *Macromolecules* **2008**, *41*, 691. (d) Zong, K.; Reynolds, J. R. *J. Org. Chem.* **2001**, *66*, 6873.

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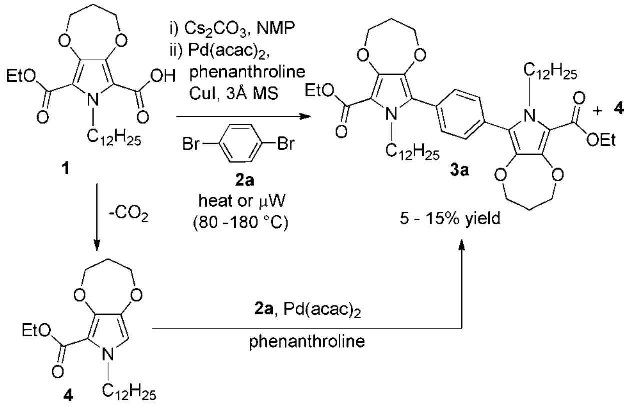
Palladium-mediated decarboxylative cross coupling is a relatively recent methodology which is being developed and optimized as a convenient alternative to traditional couplings.[6] The first decarboxylative coupling report, a copper-catalyzed Ullmann-like cross coupling, was reported by Nilsson in 1966.[7a] In 1997, Steglich and co-workers,[7b−d] and more recently Myers et al. in 2002,[7e] Bilodeau and Forgione et al. in 2006,[8] Goossen et al. in 2006,[9] and Lee et al. in 2008[10] reported new effective variants of this methodology using palladium catalysts. On the other hand, several research groups have also proposed that palladium complexes can be applied in the proto-decarboxylation of aromatic compounds.[11]

This report shows our efforts to apply the palladium-catalyzed decarboxylative cross coupling in the synthesis of *N*-alkyl-XDOP-based π-conjugated oligomers which can serve as precursors to conducting and electroactive polymers with Goossen's[9] and Bilodeau and Forgione's reports[8] serving as our starting point. It is known that 3,4-dioxypyyroles, 3,4-dioxythiophenes, and 3,4-dioxyfurans undergo proto-decarboxylation (loss of CO_2 and formation of a new C−H bond) catalyzed by copper salts,[12,13] and in the particular case of 3,4-dioxypyrroles, this decarboxylation can occur without copper catalyst at relatively high temperature.[1a] In our experiments, we used *N*-dodecyl-3,4-propylenedioxypyrrole (ProDOP-N-C_{12}) derivative **1** [*N*-dodecyl-5-(ethoxycarbonyl)-3,4-(propylene-1,3-dioxy)pyrrole-2-carboxylic acid] as a trial compound. Monoacid **1** was synthesized from its diester, diethyl *N*-dodecyl-3,4-(propylene-1,3-dioxy)pyrrole-2,5-dicarboxylate ((COOEt)$_2$ProDOP-N-C_{12}).

Initially, we decided to focus on Goossen's methodology[9,14a] since this seemed to be more general and efficient, having high conversion and yield, with the reaction conditions modified based on literature reports.[8,9,14b,c] These reaction conditions were unsuccessful for cross coupling of test compound **1**, yielding compound **4** as the major or only product (Scheme 1). In an attempt to reproduce Bilodeau and Folgione's conditions,[8] microwave radiation was also used, producing similar results. Yields of these initial experiments oscillated between 5 and 15%, and the proto-decarboxylation product **4** was obtained as the major product even when the anhydrous potassium carboxylate of **1** was used. Later, we found that the reaction yields for **1**, or its carboxylate salt **5**, under these conditions fit with a direct arylation mechanism[15] or a Heck-type reaction[6b] on proto-decarboxylation product **4** (Scheme 1 and entry 6, Table 1). Several base/solvent combinations (LiH, Cs_2CO_3, K_2CO_3, BuOK; TFH, MeOH, DMF, NMP) were used to synthesize the carboxylate salt **5** shown in Table 2, and in some cases, the solvent was partially or totally removed after salt formation. Anhydrous conditions were always assured, yet no improvement of reaction yields was achieved. Reaction temperature was also manipulated. High temperature, > 120 °C, resulted in increased proto-decarboxylation. Decreasing the amount of CuI/phenanthroline, which is the transmetalating agent used by Goossen and co-workers,[9] produced a slight increase in the reaction yield (25%). The reactivity of the copper salt was then decreased by adding KBr,[14c] but this had no effect on the reaction yield.

Scheme 1. Initial Experiments for Decarboxylative Cross-Coupling of Compound **1**



Several experiments were carried out to understand some of the initial results and to set the reaction conditions. Thermogravimetric analysis (TGA) was used to measure the decarboxylation temperature for **1** (entry 1, Table 1), where the results showed that the decarboxylation temperature in bulk is higher than the temperatures used to run the reactions in presence of the palladium catalyst. Experiments in entries 2 and 3 (Table 1) showed that Pd(acac)/(*o*-tolyl)$_3$P was able to decarboxylate **1** and also the anhydrous potassium salt **5** in *N*-methylpyrrolidone (NMP) producing **4**. Here, the NMP is a possible proton source for proto-decarboxylation of **5**. CuI/phenanthroline produced similar results (entry 4). The experiment in entry 5 showed that potassium salt **5** does not decompose or react under same conditions used in entries 2−4 in the absence of palladium or copper catalysts. We

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(5) (a) Merz, A.; Kronberger, J.; Dunsch, L.; Neudeck, A.; Petr, A.; Parkanyi, L. *Angew. Chem., Int. Ed.* **1999**, *38*, 1442. (b) Meng, H.; Perepichka, D. F.; Bendikov, M.; Wudl, F.; Pan, G. Z.; Yu, W.; Dong, W.; Brown, S. *J. Am. Chem. Soc.* **2003**, *125*, 15151.

(6) (a) Baudoin, O. *Angew. Chem., Int. Ed.* **2007**, *46*, 1373. (b) Goossen, Lukas, J.; Rodríguez, N.; Goossen, K. *Angew. Chem., Int. Ed.* **2008**, *47*, 3100.

(7) (a) Nilsson, M. *Acta Chem. Scand.* **1966**, *20*, 423. (b) Heim, A.; Terpin, A.; Steglich, W. *Angew. Chem., Int. Ed.* **1997**, *109*, 158. (c) Heim, A.; Terpin, A.; Steglich, W. *Angew. Chem., Int. Ed.* **1997**, *36*, 155. (d) Peschko, C.; Winklhofer, C.; Steglich, W. *Chem.*−*Eur. J.* **2000**, *6*, 1147. (e) Myers, A. G.; Tanaka, D.; Mannion, M. R. *J. Am. Chem. Soc.* **2002**, *124*, 11250.

(8) Forgione, P.; Brochu, M.-C.; St-Onge, M.; Thesen, K. H.; Bailey, M. D.; Bilodeau, F. *J. Am. Chem. Soc.* **2006**, *128*, 11350.

(9) Goossen, L. J.; Deng, G.; Levy, L. M. *Science* **2006**, *313*, 662.

(10) Moon, J.; Jeong, M.; Nam, H.; Ju, J.; Moon, J. H.; Jung, H. M.; Lee, S. *Org. Lett.* **2008**, *10*, 945.

(11) (a) Dickstein, J. S.; Mulrooney, C. A.; O'Brien, E. M.; Morgan, B. J.; Kozlowski, M. C. *Org. Lett.* **2007**, *9*, 2441. (b) Magro, A. A.; Eastham, G. R.; Cole-Hamilton, D. J. *Dalton Trans.* **2009**, 4683.

(12) (a) Heywang, G.; Jonas, F.; Merten, R. German Patent DE 3903973, 1990. (b) Rauchschwalbe, G.; Jonas, F. Eur. Patent EP 1142888, 2001. (c) Turnbull, S. G., Jr. Patent 2453103, 1948.

(13) Fager, E. W. *J. Am. Chem. Soc.* **1945**, *67*, 2217.

(14) (a) Goossen, L. J.; Zimmermann, B.; Knauber, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 7103. (b) Goossen, L. J.; Rodríguez, N.; Melzer, B.; Linder, C.; Deng, G.; Levy, L. M. *J. Am. Chem. Soc.* **2007**, *129*, 4824. (c) Goossen, L. J.; Thiel, W. R.; Rodríguez, N.; Linder, C.; Melzer, B. *Adv. Synth. Catal.* **2007**, *349*, 2241.

(15) Miura, M.; Nomura, M. *Top. Curr. Chem.* **2002**, *219*, 211.

also found that $Pd(acac)_2/(o\text{-tolyl})_3P/K_2CO_3$ produced the desired product **3a** using ProDOP-N-C_{12} ester **4** (entry 6, Table 1) in 21% yield at the same temperature used for the decarboxylative coupling, which explains the initial results using $CuI/Phen/Pd(acac)_2$ (Scheme 1).

Table 1. Test Reactions for ProDOP-N-C_{12} Derivatives

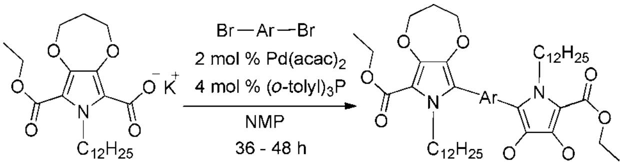
entry	dioxy-pyrrole	substrate	reaction conditions	product	yield (%)
1	**1**	none	melt, 123 °C	**4**	>99[a]
2	**1**	none	$Pd(acac)_2$, $(o\text{-tolyl})_3P$, NMP, 95 °C, 24 h	**4**	>99[b,c]
3	**5**	none	$Pd(acac)_2$, $(o\text{-tolyl})_3P$, NMP, 95 °C, 24 h	**4**	93[b,c]
4	**5**	none	10 mol % of CuI, 10 mol %, 1,10-phenanthroline, 100 °C, 24 h	**4**	97[b]
5	**5**	none	NMP, 105 °C, 36 h	none	
6	**4**	**2a**	K_2CO_3, $Pd(acac)_2$, $(o\text{-tolyl})_3P$, NMP, 95 °C, 48 h	**3a**	21[b,c]

[a] Measured by TGA. [b] Chromatographic column purification. [c] 2 mol % of $Pd(acac)_2$, 4 mol % of $(o\text{-tolyl})_3P$.

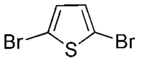
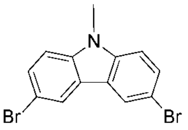
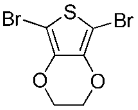
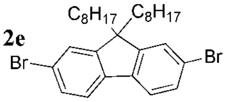
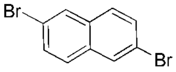
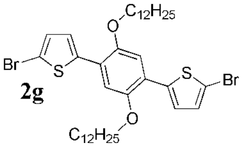
With these latest results, we found that when no copper salt is used and phenanthroline is replaced by a phosphine ligand and the temperature is lower than 110 °C, the reaction proceeds more effectively. Modification of the Goossen methodology led to a clean and efficient palladium-mediated decarboxylative cross coupling for ProDOP-N-C_{12} derivative **1**. Although these reaction conditions might work only for 3,4-dioxypyrrole derivatives which are easily decarboxylable molecules, the results should prove practical and useful in creating conjugated systems containing this moiety. The methodology was quite effective for several aryl dibromides that were tested (entries 1−7, Table 2).

High yields with relatively low catalyst load (less than 2 mol %) were obtained and low, or no, side reactions were observed. Relatively low temperatures were used (90−110 °C). The fact that there is no need for a transmetalating agent, such as copper salts, offers some advantages. The reaction is less sensitive toward the presence of water negating the need for molecular sieves (MS)[8,9] or water removal after salt formation with K_2CO_3. Also, reducing the amount of metals which might contaminate the final product is favorable. The oligomeric products are highly fluorescent under UV light, so their formation was easily confirmed by UV illumination. This was not possible when Cu(I) was present since this quenched the fluorescence.

Table 2. Decarboxylative Cross-Coupling of the Potassium Salt of **1** with Several Aryl Dibromides



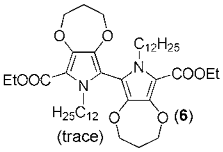
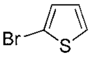
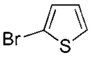
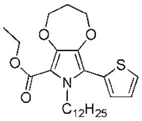
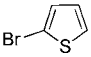
5 **3a-g**

entry	Br-Ar-Br	product	*temp.* (°C)	yield (%) of **3**
1	**2a** 	**3a**	95	99[a](96)[b]
2	**2b** 	**3b**	95	99[a](95)[b]
3	**2c** 	**3c**	110	92[a]
4	**2d** 	**3d**	90	99[a]
5	**2e** 	**3e**	105	97[a]
6	**2f** 	**3f**	105	95[b]
7	**2g** 	**3g**	105	96[b]

[a] Purification by chromatographic column. [b] Purification by recrystallization.

For convenience, we decided to use the anhydrous potassium salt of **1**, but one-pot formation of **5** using either potassium carbonate or cesium carbonate produced similar results (entry 1, Table 3). Since water formation cannot be avoided using carbonate salts, this demonstrated that the reaction sensitivity toward water is low. As in Goossen's coupling,[9] palladium(II) acetylacetonate [$Pd(acac)_2$] was a good source for palladium and NMP an ideal solvent. The reaction can be run without an added ligand, but the use of tri(*o*-tolyl)phosphine produced optimal results. The reaction is highly temperature dependent; product formation was not observed under 85 °C and the optimal reaction temperature varied for each aryl dibromide. For some aryl dibromides, such as **2b** and **2d**, the reaction proceeds to completion in less than 12 h, even though reaction times spanned 36−48 h to ensure high conversion. The reaction was also run with triphenylphosphine (entry 1, Table 3) and without a phosphine ligand (entry 2, Table 3); decrease in the reaction yields was observed and **6** was also isolated in both cases. Reduction of Pd(II) to Pd(0) might be carried out either by the solvent[14b] or phosphine,[16] or via homocoupling of two ProDOP-N-*C*$_{12}$ carboxylates **5**. Small amounts of compound **6** were observed in several reactions, especially when less than 2 equiv of phosphine ligand per palladium was used.

Table 3. Alternative Reaction Conditions for Decarboxylative Cross-Coupling of ProDOP-N-*C*$_{12}$ Derivatives

entry	dioxy-pyrrole	substrate	product	yield (%)
1	**1**	**2a**	**3a**	98[a] 89[b]
2	**5**	**2e**	**3e** +  (trace) **(6)**	69[c]
3	**5**	**2a**	none	0[d]
4	**5**		none	0[d]
5	**1**	**2a**	**3a**	93[e]
6	**1**		 **(7)**	87[e]
7	**4**		none	0[e]

[a] Conditions: (i) K_2CO_3, NMP, (ii) 2 mol % of Pd(acac)$_2$, 4 mol % of (*o*-tolyl)$_3$P, 100 °C, one pot. [b] Conditions: (i) K_2CO_3, NMP, (ii) 2 mol % of Pd(acac)$_2$, 4 mol % of Ph$_3$P, 100 °C, one pot. A small amount of compound **6** was also observed. [c] Conditions: 2 mol % of Pd(acac)$_2$, NMP, 105 °C, 48 h, yield for fluorene oligomer **3e**, same product as in entry 5 (Table 2). [d] Conditions: THF or toluene, reflux, 2 mol % of Pd(acac)$_2$, 4 mol % of (*o*-tolyl)$_3$P, 48 h. [e] Conditions: *t*-BuOK, 2 mol % of Pd(acac)$_2$, 4 mol % of (*m*-NaSO$_3$Ph)Ph$_2$P, (*n*-Bu)$_4$NBr, toluene/water, 110 °C 48 h.

Anhydrous toluene and THF were tested as solvents for the coupling of potassium salt **5** with 1,4-dibromobenzene and 2-bromothiophene (entries 3 and 4, Table 3). No reactions were observed, and the starting materials were recovered in both cases. Interestingly, product formation was observed after addition of degassed water to the reaction using toluene; in this last case, 4 days of reaction yielded 67% of the expected product **3a**, but reaction conditions were not reproducible neither for 1,4-dibromobenzene nor others substrates. We decided to optimize these reaction conditions.

Using reaction conditions similar to those used for some Suzuki−Miyaura couplings,[17] toluene/water mixture was employed as the solvent and sodium biphenylphosphinobenzene-3-sulfonate, (*m*-NaSO$_3$−Ph)Ph$_2$P, as the ligand, produced **3a** and **7** in high yields (entries 5 and 6, Table 3). In this case the carboxylate salt of **1** was formed in situ using potassium *tert*-butoxide (*t*-BuOK), and tetrabutylammonium bromide (*n*-Bu$_4$NBr) was used as a phase-transfer agent. These conditions may provide a good alternative for the synthesis of 3,4-dioxypyrrole derivatives without using NMP. It also clearly demonstrates the low sensitivity of the reaction toward the presence of water; in fact, water is needed to increase the carboxylate salt solubility and the reaction to proceed under these reaction conditions. To rule out a possible product formation via compound **4** the reaction presented in entry 7 was also run, no product formation was seen.

In summary, experimental conditions for an efficient decarboxylative cross coupling of an *N*-alkylpropylenedioxypyrrole have been optimized. High reaction yields (92−99%) were observed for several aryl bromides that were tested. It was also demonstrated that these reaction conditions have relatively low sensitivity toward the presence of water and might be considered for synthesis of conjugated system involving 3,4-dioxypyrroles.

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Supporting Information Available: Experimental procedures and full spectroscopic data for all new compounds. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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(16) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.

(17) (a) Miyaura, N.; Suzuki, A. *J. Chem. Soc., Chem. Commun.* **1979**, *19*, 866. (b) Miyaura, N.; Yamada, K.; Suzuki, A. *Tetrahedron Lett.* **1979**, *20*, 3437. (c) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633.