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Low temperature Kumada–Corriu cross-coupling of polychlorinated acene derivatives and a synthesis of sterically demanding acenes

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ABSTRACT

Conditions for low-temperature Kumada–Corriu cross-coupling of polychlorinated acenes with Grignard reagents are reported. Our work was motivated by a search for cross-coupling reactions effective in the synthesis of functionalized linear acenes for organic materials applications. Treatment of polychlorinated acenes with the PEPPSI-IPr catalyst and MeMgBr undergo 6–8 concurrent coupling reactions to yield products such as octamethylnaphthalene, which is distorted out of planarity due to the steric interaction between the methyl groups. More sterically demanding Grignard reagents such as PhMgBr coupled cleanly with 9,10-dichloroanthracene to provide products such as 9,10-diphenylanthracene, a blue OLED component, in excellent yield.

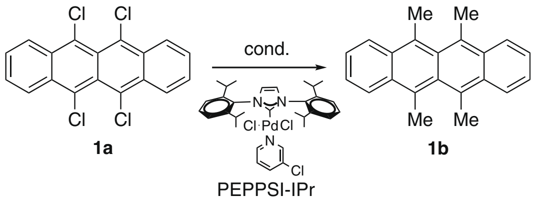
1. Introduction

Linear acene derivatives such as substituted anthracenes and tetracenes are well known for their properties as organic semiconductors and fluorophores.[1] 5,6,11,12-Tetraphenyltetracene (rubrene), in particular, has exceptional charge carrier mobility values of up to 20 cm^2/V s.[2] Traditional approaches for the synthesis of linear acenes often involve rearrangements and condensations with low yields and difficult purifications, complicating the synthesis of any derivatives.[3] More recent syntheses of substituted acenes via Grignard or organolithium additions into acene-quinones are quite effective, but require stoichiometric amounts of reducing agents to aromatize diol intermediates.[4]

An alternative to the above-mentioned methods are metal-catalyzed cross-couplings reactions, which are often reliable and powerful methods for forming carbon–carbon bonds.[5] The instability or low availability of iodo- and bromoacenes, however, makes their use difficult in cross-coupling reactions despite success in highly sterically demanding cross-coupling reactions with polyiodo- or polybromobenzenes.[6] On the other hand, chloroacenes are more readily available, but their use is complicated by difficulties in coupling sterically hindered aryl chlorides. The cross-coupling of aryl chloride electrophiles possessing two *ortho* substituents is notoriously difficult.[7,8] We are unaware of any cross-coupling reactions of linear acene-type aryl chlorides with *peri*-substitution, which adds an additional element of steric demand not often considered in cross coupling.

We now report a Kumada–Corriu coupling for hindered polychlorinated acenes containing two *ortho* substituents to produce linear acene derivatives. Optimized conditions allow the couplings to take place at room temperature, an improvement over higher temperature coupling conditions.[7] In some cases, even *peri*-substituted polychlorinated acenes undergo effective cross coupling. Moreover, our conditions enable late-stage diversification of known polychlorinated acenes and the synthesis of new organic electronic materials.

Table 1
Optimization of cross-coupling of polychlorinated acenes



Entry	Catalyst[a]	M–Me	Additive	Yield
1	PEPPSI-IPr	$(MeBO)_3$	K_2CO_3/4 Å MS	50%
2	PEPPSI-IPr	$(MeBO)_3$	Cs_2CO_3/4 Å MS	45%
3[c]	**PEPPSI-IPr**	**MeMgBr**	**None**	**98%**
4[d]	PEPPSI-IPr	MeMgBr	None	80%
5	$Pd(OAc)_2$/X-Phos[b]	MeMgBr	None	60%
6	$Pd(OAc)_2$/Ru-Phos[b]	MeMgBr	None	55%
7	SiPr·HCl/$FeCl_3·3H_2O$	MeMgBr	EtMgBr	Dec.
8	$NiCl_2$(dppf)	MeMgBr	None	Dec.

Bold conditions in entry 3 were used for the remainder of the study; Dec. = decomposition and multiple products.
[a] 12 mol % catalyst unless otherwise noted.
[b] 1:2 metal to ligand ratio.
[c] Solvent: dioxane/Et_2O (10:1).
[d] Solvent: MTBE/Et_2O (10:1).

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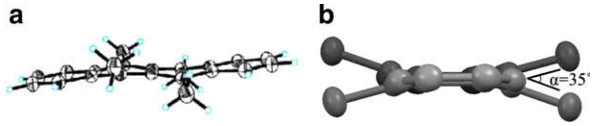


Figure 1. X-ray structure of tetramethyltetracene **1b**. (a) Thermal ellipsoid picture obtained with program SHELXTL. Distortion from planarity in tetracene core can clearly be seen. (b) Thermal ellipsoid plot obtained using program Mercury. Side view, angle between neighboring methyl groups α = 35°. No hydrogen atoms are shown for the simplicity.

2. Results and discussion

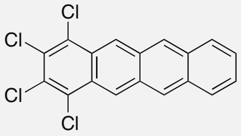
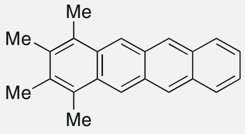
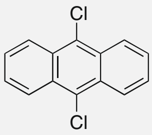
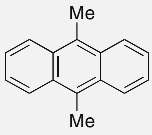
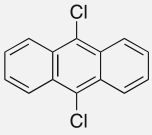
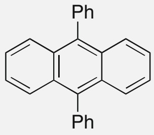
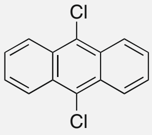
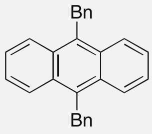
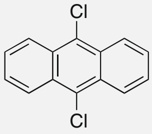
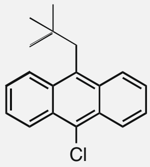
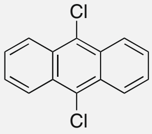
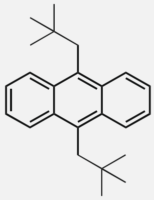
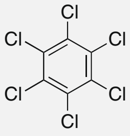
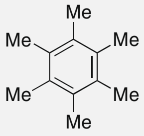
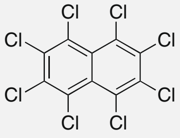
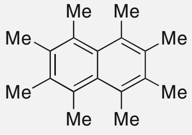
2.1. Optimization of Kumada–Corriu cross-coupling

Our studies began with 5,6,11,12-tetrachlorotetracene **1a** (Table 1),[9] which possesses organic semiconducter properties and is easy to synthesize on a large scale. Each chlorinated site contains two *ortho* substituents. Suzuki coupling of tetrachlorotetracene **1a** with Organ's PEPPSI-IPr catalyst[7a] provided tetramethyltetracene **1b** albeit in a modest yield (entries 1 and 2).[10] By substituting the methyl boroxine, carbonate base, and mol sieves for all in one MeMgBr (3 equiv per chlorine) we were able to generate tetramethyltetracene **1b** in excellent yield (98%, entry 3). A brief solvent screen involving MTBE and dioxane showed that dioxane gave better results (entries 3 and 4). Using more traditional cross-coupling catalysts $Pd(OAc)_2$ with X-Phos and Ru-Phos ligands[11] also gave **1b**, although in a modest yield (entries 5 and 6). Utilization of iron[12] and nickel[13] cross-coupling systems gave decomposition and multiple products (entries 7 and 8).

The PEPPSI-IPr and MeMgBr system (entry 3) gave tetramethyltetracene **1b** cleanly and could be performed at low temperatures

Table 2

Kumada–Corriu coupling of polychlorinated acene derivatives[a]

Entry	Chloride	R–MgBr	Product	Temp	Yield (%)
1	 **2a**	Me	 **2b**	rt	64[c]
2	 **3a**	Me	 **3b**	rt	95[b]
3	 **3a**	Ph	 **3c**	rt	95[b]
4	 **3a**	Bn	 **3d**	rt	81[c]
5	 **3a**	Neopentyl	 **3e**	rt	80[c]
6	 **3a**	Neopentyl	 **3f**	70 °C	55[c]
7	 **4a**	Me	 **4b**	rt 80 °C	30[d] 64[c]
8	 **5a**	Me	 **5b**	rt to 80 °C	52[c]

[a] Conditions: 3 mol % PEPPSI-IPr per chlorine, dioxane, 24 h. R-MgBr reagents were used as solutions in Et_2O.

[b] After workup without additional purification. Appears pure by ^1H NMR.

[c] After flash chromatography and/or recrystallization.

[d] Based on recovered starting material.

and catalyst loadings. The high conversion allowed for isolation of oxygen-sensitive tetramethyltetracene **1b** with minimal purification. Lowering the temperature to 5 °C using the PEPPSI-IPr catalyst and MeMgBr also gave **1b** cleanly after 24 h. At larger scales (2 g of **1a**), catalyst loadings could be lowered to 0.5 mol % per chlorine atom to give **1b** at 83% yield after recrystallization from degassed toluene. Crystals of **1b** suitable for X-ray crystallography were also grown from degassed toluene. The structure clearly shows distortion from planarity (Fig. 1), a likely consequence of the steric interaction between the *peri*-methyl groups on the acene backbone.

2.2. Scope of Kumada–Corriu cross-coupling

Using the conditions developed during our optimization study (Table 1, entry 3), we explored the scope of reactivity using five polychlorinated acenes (**2a** through **5a**, Table 2), and six different coupling partners (MeMgBr, PhMgBr, BnMgBr, neopentyl-MgBr, EtMgBr, and vinyl-MgBr). Coupling using EtMgBr and vinyl-MgBr with **1a** through **5a** gave a mixture of byproducts after cross-coupling attempts with the polychlorinated acenes (not shown).

Every polychlorinated acene we examined cross-coupled with MeMgBr, giving yields ranging from 52% to 95% (entries 1, 2, 7, and 8). Acenes possessing less chlorines gave higher yields and required lower temperatures: 9,10-dichloroanthracene **3a** coupled with MeMgBr at room temperature to give dimethylanthracene **3b** in excellent yield (95%, entry 2), while 1,2,3,4-tetrachlorotetracene **2a**[14] gave the tetramethyltetracene **2b** in modest yield (64%, entry 1), also at room temperature. Compounds with more chlorines required higher temperatures: exhaustive methylation of hexachlorobenzene **4a** required temperatures of 80 °C to form hexamethylbenzene **4b**[15] (entry 7), while octachloronaphthalene **5a** required a gradual temperature increase to 80 °C to generate the octamethylnaphthalene **5b**[16] (52%, entry 8). Our synthesis of octamethylnaphthalene **5b** is particularly remarkable given the steric-induced strain in the product: the presence of eight methyl groups causes the naphthalene backbone to distort from planarity to a twisted acene.[17] Indeed, when the reaction of octachloronaphthalene **5a** and MeMgBr was conducted at 70 °C for 24 h, sextamethyl- and septamethylnaphthalene isomers (identified by GC–MS) were produced. This is possible due to MgBr exchange with the chlorides in competition with continued methylation of already hindered polymethylnaphthalenes. Our synthesis of octamethylnaphthalene **5b** is a much more direct than the circuitous Diels–Alder route typically used.[16]

In addition to coupling with MeMgBr in an excellent yield (entry 2), 9,10-dichloroanthracene **3a** coupled with PhMgBr, BnMgBr, and neopentyl-MgBr to produce products **3c** through **3f** in modest to excellent yields (55–95%). We were able to generate the well-known blue organic light emitted diode (OLED) component 9,10-diphenylanthracene **3c** in 95% at room temperature (entry 3), an improvement over previously disclosed cross-coupling routes to **3c**.[18] Similar transformations described in the literature[19] with the more electronically activated 9,10-dichlorooctafluoroanthracene also required elevated temperatures. Coupling with BnMgBr also proceeded in good yield at room temperature (entry 4). We were able to control single and double coupling of neopentyl-MgBr using slight changes in reaction conditions: our standard conditions (3 equiv per chlorine of neopentyl-MgBr, room temperature) gave product **3e** in 80% yield resulting from a single cross-coupling (entry 5), while increasing the reaction temperature to 80 °C and doubling the equivalents of neopentyl-MgBr gave product **3f**, resulting from both possible cross-coupling events (55%, entry 6). Unfortunately, more sterically hindered polychlorinated acenes **1a**, **2a**, **4a**, and **5a** did not cross-couple cleanly with PhMgBr, BnMgBr, or neopentyl-MgBr, yielding multiple products and in some cases recovered starting material even with elevated temperatures, resulting in no desired product formation. Based on our results, we will continue to explore conditions that allow different Grignard reagents to be used for the synthesis of rubrene derivatives.

3. Conclusion

In conclusion, we have developed a Kumada–Corriu cross-coupling method for linear polychlorinated acenes containing two *ortho* substituents. Cross-coupling could often be achieved with low catalyst loadings at room temperature. These conditions were successful even with sterically crowded substrates and can be used to prepare ‘twisted acenes’[20] such as octamethylnaphthalene.

4. Experimental section

*General procedure for low-temperature Kumada–Corriu couplings: synthesis of 5,6,11,12-tetramethyltetracene (**1b**).* In a 50-mL Schlenk flask, dried, and flushed with nitrogen, were added 5,6,11,12-tetrachlorotetracene[4] (50 mg, 0.137 mmol), PEPPSI-IPr (11 mg, 0.0165 mmol) and 6 mL 1,4-dioxane (freshly distilled from CaH_2). MeMgBr (3 M solution in diethyl ether, 0.6 mL, 1.65 mmol) was slowly added at room temperature. After the addition, white precipitate was formed and the solution was slightly warm. The Schlenk flask was sealed and allowed to stir at room temperature for 24 h. The reaction was quenched by pouring into a mixture of EtOAc (30 mL) and water (30 mL). Water (300 mL) was added and the mixture was extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with water (150 mL) and sat aq NaCl (150 mL), dried over Na_2SO_4, and filtered through cotton. Concentration of the resulting solution provided the title compound as bright red crystals (37 mg, 0.13 mmol, 95%) in >95% purity as judged by ^{1}H NMR: mp 191–192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 3.2, 6.8 Hz, 4H), 7.40 (dd, *J* = 3.2, 6.8 Hz, 4H), 3.12 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.2, 130.4, 128.2, 125.4, 125.2, 21.7; IR (thin film) 3067, 2961, 2917, 2849, 1698, 1589, 1540, 1455; LRMS (EI) *m*/*z* 284.1 (M^+), 269.1 $(M-CH_3)^+$; HRMS (EI) calcd for $C_{22}H_{21}{}^+$, 285.1638; found 285.1620. The structure was confirmed by X-Ray crystallography.

In a larger scale experiment, 5,6,11,12-tetrachlorotetracene (2 g, 5.49 mmol) and PEPPSI-IPr (80 mg, 0.11 mmol, 2 mol %) were used. The resulting red product was recrystallized from toluene (degassed with nitrogen purge for 20 min prior to use), providing the title compound (1.2 g, 4.22 mmol, 83%).

Caution: The final product is sensitive to light and air so the extraction and recrystallization should be done quickly and with as little exposure to light as possible.

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Supplementary data

Supplementary data (experimental procedures, tabulated data, copies of NMR spectra for all numbered products) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.03.121.

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