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Chemoselectivity in the Kosugi-Migita-Stille coupling of bromophenyl triflates and bromo-nitrophenyl triflates with (ethenyl)tributyltin

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ABSTRACT

Kosugi-Migita-Stille cross coupling reactions of (ethenyl)tributyltin with all isomeric permutations of bromophenyl triflate and bromo-nitrophenyl triflate were examined in order to determine the chemoselectivity of carbon-bromine versus carbon-triflate bond coupling under different reaction conditions. In general, highly selective carbon-bromine bond cross couplings were observed using for example bis(triphenylphosphine)palladium dichloride (2 mol-%) in 1,4-dioxane at reflux. In contrast, reactions using the same pre-catalyst but in the presence of a three-fold excess of lithium chloride in *N,N*-dimethylformamide at ambient temperature were in most cases selective for coupling at the carbon-triflate bond. Overall, isolated yields and the selectivity for carbon-bromine bond coupling were significantly higher compared to carbon-triflate bond coupling.

1. Introduction

The reactivity order usually observed in palladium catalyzed coupling reactions of aromatic halides is I > Br ~ OTf > Cl > F[1,2] and it parallels the rate of oxidative addition of tetrakis(triphenylphosphine)palladium ($Pd(PPh_3)_4$) to aromatic halides as established by Fitton and Rick in 1971.[3] In Echavarren and Stille's seminal work on palladium catalyzed cross coupling reactions of organotin reagents with aromatic triflates, the chemoselectivity of carbon-bromine (C-Br) versus carbon-triflate (C-OTf) coupling of 4-bromophenyl triflate (**1**) with (ethenyl)tributyltin was dramatically modulated by proper choice of reaction conditions and additives.[4] For example, treatment of 4-bromophenyl triflate (**1**) with (ethenyl)tributyltin in 1,4-dioxane in the presence of $Pd(PPh_3)_4$ at reflux gave product **2** derived from a highly selective oxidative addition to the C-Br bond (Scheme 1).[5] In contrast, using bis(triphenylphosphine)palladium dichloride ($PdCl_2(PPh_3)_2$) as the catalyst precursor, in the presence of a three-fold excess of lithium chloride in *N,N*-dimethylformamide (DMF) at 24 °C, afforded selectively product **3** derived from oxidative addition to the C-OTf bond (Scheme 1).[6] Furthermore, a completely selective cross coupling at the iodine bearing carbon was observed for 4-iodophenyl triflate even in the presence of lithium chloride.[7]

Echavarren and Stille thus established the overall reactivity order for cross coupling reactions of organotin reagents in the absence of LiCl as I > Br > OTf > Cl and in the presence of LiCl as I > OTf > Br > Cl. This reactivity order should be used with some caution since the catalyst system can be tailored so that C-Cl coupling dominates over C-OTf. For example, treatment of 4-chlorophenyl triflate with (phenyl)tributyltin in the presence of tris(dibenzylideneacetone)dipalladium - bis(tri-*tert*-butylphosphine)palladium and cesium fluoride in 1,4-dioxane, at ambient temperature, gave exclusively the C-Cl coupling product **2**.[8,9]

The change in selectivity in the presence of added LiCl is most likely due to more than one factor. An increase in the rate of oxidative addition has been observed upon addition of LiCl. The apparent rate (K_{app}) of oxidative addition of $Pd(PPh_3)_4$ to phenyl triflate in DMF at 20 °C was shown to increase nineteen-fold going from 0 to 150 equivalents of LiCl.[10] In contrast, less than a two-fold change in K_{app} was observed using the more reactive 4-nitrophenyl triflate under the same reaction conditions. Thus, added LiCl accelerates the rate of oxidative addition but the magnitude of acceleration depends on additional functional groups present in the molecule.[11]

In addition to an increased rate of oxidative addition, the effect of added chloride ions has been attributed to a chloride – triflate metathesis of the intermediate Ar-Pd-OTf complex, i.e. Ar-Pd-OTf to Ar-Pd-Cl, followed by a rapid transmetallation and reductive elimination.[12] For example, Jutand and Maes et al. have shown that transmetallation of tin reagents are faster for pyridyl-Pd-Cl

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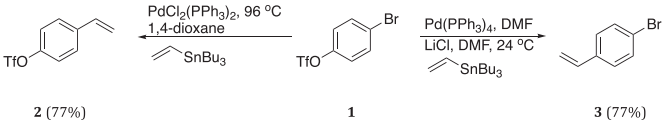


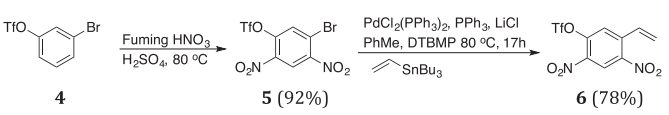
Scheme 1. Kosugi-Migita-Stille cross coupling of **1** with (ethenyl)tributyltin.

complexes compared to pyridyl-Pd-I complexes.[13] In a similar fashion, Casado and Espinet reported that transmetallation – reductive elimination from isolated *trans*-[3,5-dichloro-2,4,6-trifluorophenyl-Pd-X($AsPh_3$)$_2$] complexes were in the order X = Cl > Br > I.[14]

In addition to the group being replaced, the rate of reaction depends on the electronic nature of additional substituents on the aromatic ring. Milstein and Stille reported an almost ninety-fold difference in the relative reaction rate in reactions of tetramethyltin with 4-methoxy-1-bromobenzene (1) < 4-methyl-1-bromobenzene (1.46) < bromobenzene (2.18) < 4-trifluoromethyl-1-bromobenzene (19.5) < 3-nitro-1-bromobenzene (87.9) in hexamethylphophoramide (HMPA) at 63 °C using BnPd(PPh_3)$_2$Cl as the pre-catalyst.[15] These results clearly demonstrate the significant rate accelerating effect of the electron withdrawing nitro group even when not in conjugation with the site of the oxidative addition. In a similar fashion, the usually unreactive aryl fluorides can participate in Kosugi-Migita-Stille couplings in the presence of two electron withdrawing groups. For example, cross couplings of 4-fluoro-3-nitrobenzaldehyde and 4-fluoro-3-nitrobenzonitrile with (ethenyl)tributyltin have been reported.[16,17]

A chemoselective sequential introduction of two different alkenes was of interest to us for the synthesis of dinitrodialkenylbenzenes, substrates suitable for a palladium catalyzed double reductive cyclization en route to pyrroloindoles. It was envisioned that the chemoselectivity observed by Echavarren and Stille would enable us to prepare a variety of cyclization precursors containing two different alkenes. Thus, 2,4-dinitro-5-bromophenyl triflate (**5**) was prepared in good yield by dinitration of 3-bromophenyl triflate (**4**) (Scheme 2). Treatment of **5** with (ethenyl)tributyltin under the Echavarren-Stille conditions described above that should result in oxidative addition to the C-OTf bond did not afford any identifiable coupling product. The solvent was changed from DMF to toluene in order to simplify the work up and the analysis of the crude ^{1}H NMR spectrum. A small amount of 2,6-di-*tert*-butyl-4-methylphenol (DTBMP) was added as a radical inhibitor. No reaction occurred at ambient temperature, however the starting material was completely consumed within 17 h when the reaction temperature was increased to 80 °C. The ^{1}H NMR spectrum of the resulting crude reaction mixture contained three alkenyl proton resonances suggesting a single coupling product. Surprisingly, a quartet resonance in the ^{13}C NMR (J = 320 Hz) spectrum and a resonance at −72.9 ppm in the ^{19}F NMR spectrum indicated the presence of an intact triflate group. The crude product was purified by chromatography to afford **6** in good isolated yield.

The site selectivity of palladium catalyzed coupling reactions of benzenes having two electrophilic centers depends on the position of additional functional groups present in the substrate. However, the two potential coupling sites in **5** should be similar if not equally activated for oxidative addition by the two electron withdrawing nitro groups. In addition, the steric environments should be more or less equivalent since both sites have an *ortho*-nitro group and they are separated by an unsubstituted position. Thus, the absence of any apparent reaction at ambient temperature and the failure to obtain the expected C-OTf bond coupling product from **5**, under the reaction conditions reported to be selective for triflate coupling, were puzzling.



Scheme 2. Preparation and Kosugi-Migita-Stille reaction of **5**.

To the best of our knowledge, there is no reported systematic study on the chemoselectivity in Kosugi-Migita-Stille couplings of substituted bromophenyl triflates.

Herein is described a detailed study of the selectivity observed in palladium catalyzed coupling reactions of (ethenyl)tributyltin with all possible isomeric permutations of bromophenyl triflate and bromo-nitrophenyl triflate. Each isomeric compound was examined under bromide and triflate selective reaction conditions.

2. Results and discussion

In an attempt to corroborate the results reported by Echavarren and Stille, cross coupling reactions of 4-bromophenyl triflate (**1**) and (ethenyl)tributyltin were performed (Table 1). Under bromine selective conditions, a 33:1 ratio of C-Br to C-OTf (**2**:**3**) bond coupling was reported by the authors based on ^{1}H NMR of the crude reaction mixture (Table 1, entry 1). This reaction was repeated and in our hands only compound **2** was observed by ^{1}H NMR at 600 MHz (entry 2). The catalyst, Pd(PPh_3)$_4$, used in the initial study is not air stable and handling and extended storage of this compound often results in diminished catalytic activity. In order to minimize problems associated with Pd(PPh_3)$_4$, a combination of the significantly more stable precursor bis(dibenzylideneacetone)palladium (Pd(dba)$_2$) and triphenylphosphine (PPh_3) was used to generate Pd(PPh_3)$_4$ *in situ*. In the event, the same exclusive selectivity was observed using 2 mol% Pd(dba)$_2$ and 8 mol % PPh_3 in 1,4-dioxane at reflux (entry 3). Since the latter conditions gave the same selectivity as Pd(PPh_3)$_4$, the more convenient catalyst precursor Pd(dba)$_2$-PPh_3 was used in all subsequent reactions.

It is unclear why two different palladium catalyst precursors were used by Echavarren and Stille (Scheme 1). We found that $PdCl_2(PPh_3)_2$ without any added PPh_3 not only gave the same chemoselectivity as Pd(PPh_3)$_4$ in a reaction of **1** with (ethenyl) tributyltin and in the absence of LiCl, but this catalyst precursor also afforded a superior yield of product (entry 4). Under triflate selective conditions, employing $PdCl_2(PPh_3)_2$ in the presence of a three-fold excess of LiCl in DMF at 24 °C, Echavarren and Stille reported exclusive coupling derived from oxidative addition to the C-OTf bond (entry 5). In our hands, employing the same reaction conditions, a much lower selectivity C-Br/C-OTF = 1:6.7 (entry 6) was observed. This product ratio is similar to the ratio reported by Echavarren and Stille at a higher reaction temperature either in 1,4-dioxane (at reflux, entry 7) or DMF (70 °C, entry 8).[18] It should be noted that products **2**–**3** decompose/polymerize to varying extent upon chromatographic purification on silica gel.

In contrast to cross coupling of **1** with (ethenyl)tributyltin, carbonylative reactions of **1** with (2-phenylethenyl)tributyltin in the presence of 1,1′-bis(diphenylphosphinoferrocene)-palladium dichloride ($PdCl_2$(dppf)) was reported to afford exclusive C-OTf bond coupling with or without added LiCl (Scheme 3).[19,20] A C-OTf selectivite carbonylation of **1** using Pd(OAc)$_2$ - dppf in DMF to give an amide was very recently reported by Jiao and Wu et al.[21] Interestingly, switching the ligand to Xantphos and the solvent to toluene completely reversed the selectivity to C-Br. We assumed that the difference in site selectivity observed in the absence of LiCl when comparing Schemes 1 and 3 was the result of the $PdCl_2$(dppf) pre-catalyst and not the difference in tin reagents. Thus, **1** was

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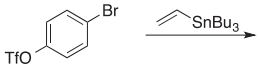
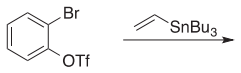
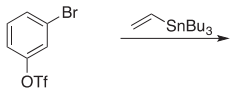
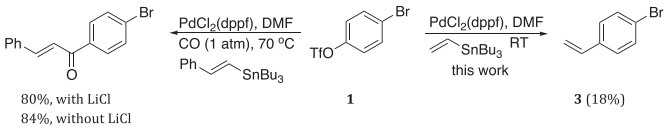
Table 1
Reaction of bromophenyl triflates with ethenyl tributyltin.

Entry	Conditions[a]	Product(s) and Ratio[b]		Yield[c]
				
	1	**2**	**3**	
1[d]	*Pd(PPh$_3$)$_4$, 1,4-Dioxane (reflux)*	*33*	*1*	*77%*
2	Pd(PPh$_3$)$_4$, 1,4-Dioxane (reflux)	>30	1	Not determined
3	Pd(dba)$_2$, 4 PPh$_3$, 1,4-Dioxane (reflux)	>30	1	30%
4	PdCl$_2$(PPh$_3$)$_2$, 1,4-Dioxane (reflux)	>30	1	90%
5[d]	*PdCl$_2$(PPh$_3$)$_2$, LiCl, DMF (24 °C)*	*0*	*100*	*77%*
6	PdCl$_2$(PPh$_3$)$_2$, LiCl, DMF (24 °C)	1	6.7	Not determined
7[d]	*Pd(PPh$_3$)$_4$, LiCl, 1,4-Dioxane (reflux)*	*1*	*6*	*75%[e]*
8[d]	*PdCl$_2$(PPh$_3$)$_2$, LiCl, DMF (70 °C)*	*1*	*5*	*45%[e]*
				
	7	**9**	**10**	
10	Pd(dba)$_2$, PPh$_3$, 1,4-Dioxane (reflux)	>30	1	5%
11	PdCl$_2$(PPh$_3$)$_2$, LiCl, DMF (24 °C)	1	5.9	Not determined
				
	8	**11**	**12**	
12	Pd(dba)$_2$, 4 PPh$_3$, 1,4-Dioxane (reflux)	30	1[f]	34%[g]
13	PdCl$_2$(PPh$_3$)$_2$, 1,4-Dioxane (reflux)[h,i]	10	1[j,k]	47%
14	PdCl$_2$(PPh$_3$)$_2$, LiCl, DMF (24 °C)	1	6.3[l]	m
15[g]	*PdCl$_2$(dppp)$_2$, LiCl, DMF (25 °C)[n]*	*0*	*100*	*25%*

a) For experimental details see Experimental Section. b) Ratio of products from the crude mixture as determined by ^{1}H NMR at 600 MHz. c) Yield of pure major product after chromatography. d) Previously reported in ref 4. e) ~10% Dicoupling was also isolated. f) A 19:30:1:6 ratio of **8**/**11**/**12**/(ethenyl)tributyltin was observed in the crude ^{1}H NMR spectrum. g) Isolated as a mixture with **8**. Yield calculated from ^{1}H NMR spectrum. h) A significant amount of **8** still remained after 72 h. i) The reaction time was 39 h. j) The reaction time was 50 h. k) A ~10:1:4 ratio of **11**/**12**/(ethenyl)tributyltin was observed in the crude ^{1}H NMR spectrum. l) A 5.6:1:6.3 ratio of **8**/**11**/**12** was observed in the crude ^{1}H NMR spectrum. m) No product was isolated after chromatography. n) Previously reported reaction, see reference 23.



Scheme 3. Kosugi-Migita-Stille reaction of **1** using PdCl$_2$(dppf).

treated with (ethenyl)tributyltin in the presence of PdCl$_2$(dppf) in DMF at ambient temperature in the absence of LiCl. The starting material was almost completely consumed after 24 h and an exclusive formation of **3** was observed in the ^{1}H NMR of the crude reaction mixture. However, only a low isolated yield of product was obtained after chromatographic purification. Based on the result depicted in Scheme 3, it is plausible that other palladium catalysts and/or reaction conditions can be developed for selective C-OTf bond Kosugi-Migita-Stille cross-couplings even in the absence of added LiCl.[22]

To determine if the relative position of the bromide and the triflate would alter the chemoselectivity of the coupling reaction, the isomeric 2-bromophenyl and 3-bromophenyl triflates **7** and **8** were examined. Reactions of both **7** and **8** displayed the same high selectivity for C-Br coupling and a similar selectivity for C-OTf coupling as was observed in the reactions of **1** (Table 1, entries 10–14). In comparison to bromo-triflates **1** and **7**, reaction of **8** was slower and a significant amount of starting material was recovered after 24 h. It should be noted that cross-coupling of **8** with (ethenyl) tributyltin using PdCl$_2$(dppp) as the pre-catalyst has been described (entry 15).[23] Although only C-OTf coupling was reported in 25% yield after 39 h, it is unclear if the reported selectivity is based on the crude product or after purification.

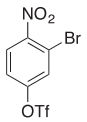
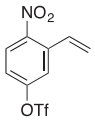
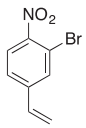
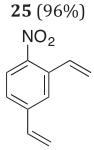
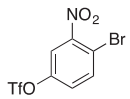
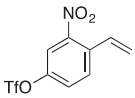
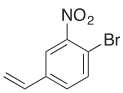
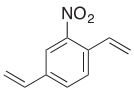
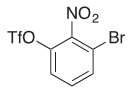
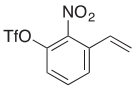
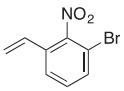
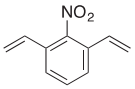
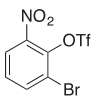
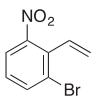
The following conclusions can be made based on the results presented in Table 1; a) a high selectivity for C-Br coupling is observed for all three substrates (**1**, **7**–**8**). b) PdCl$_2$(PPh$_3$)$_2$ and Pd(dba)$_2$ – PPh$_3$ are convenient, air stable, alternatives to Pd(PPh$_3$)$_4$. c) Although we were unable to repeat the results by Echavarren and Stille, a significantly lower but still synthetically very useful C-OTf selectivity can be realized. d) Reactions wherein the two substituents were either ortho or para to each other were faster.

Having established the general trends for cross coupling of bromophenyl triflates, the influence of a nitro group on the chemoselectivity of C-Br versus C-OTf coupling of the Kosugi-Migita-Stille reaction was examined next. All ten possible bromo-nitrophenyl triflate permutations (**13**–**22**) were prepared from the corresponding bromo-nitrophenols using triflic anhydride and pyridine. Compounds **13**–**22** were treated with (ethenyl)tributyltin under three different reaction conditions A - C. Conditions A consisted of a bis(dibenzylideneacetone)palladium (2-mol%) and triphenylphosphine (8-mol%) pre-catalyst system and the reactions

were performed in 1,4-dioxane at reflux temperature. Conditions B, employed bis(triphenylphosphine)palladium dichloride (2 mol%) in 1,4-dioxane at reflux temperature. Finally, for Condition C bis(-triphenylphosphine)palladium dichloride (2 mol%) and lithium chloride (300 mol%) was used and the reactions were performed in DMF at ambient temperature. Conditions A and B were anticipated to be bromo-selective conditions and Conditions C to be triflate-selective conditions. The reaction time was in all cases ~24 h regardless if all starting material had been consumed or not. The crude reaction mixtures were analyzed by ^{1}H NMR (400 or 600 MHz) to give the ratio of products prior to chromatographic purification. Unreacted starting material was observed in the crude reaction mixtures in some of the reactions. Although not seen prior to chromatography, phenols derived from hydrolysis of the triflate of the starting material were also obtained after purification. Since the aim of this study was to determine the chemoselectivity of the coupling reaction, i.e. C-Br versus C-OTf bond coupling, no attempts were made to optimize the yield of a given product for a particular substrate. The observed crude product ratios and the isolated yields of products after purification are seen in Table 2. Tin impurities may at times be problematic to remove by chromatography on silica gel. However, no trace of metal impurities was observed using a combination of silica gel and potassium carbonate (9:1 ratio) as described by Harrowven et al.[6]

Treatment of 2-bromo-3-nitrophenyl triflate (**13**) with (ethenyl) tributyltin under Conditions A gave the expected C-Br coupling product **23** in relatively low yield but with excellent chemoselectivity (Table 2, entry 1). The low yield can in part be explained by the observation of a fair amount of starting material. Under Conditions B, the isolated yield of **23** was more than doubled and the chemoselectivity remained the same (entry 2). The C-OTf coupling product was not observed by ^{1}H NMR in either of the reaction. It should be noted that cross coupling of **13** with (ethenyl) tributyltin in the presence of $Pd(PPh_3)_4$ in toluene at reflux has been reported to give C-Br coupling in 91% yield (entry 3).[24] While the reactions under Conditions A-B exhibited excellent chemoselectivities, a very disappointing 1:1.6 ratio of C-Br/C-OTf coupling was obtained under Conditions C (entry 5). In addition to the low

Table 2
Cross-coupling of **13**–**22** with (ethenyl)tributyltin.

Entry	Substrate	Br/OTf ratio[a]	C-Br coupling[b]	C-OTf coupling[b]	Other product(s)[b]	
						
1-A[c]	**13**	>30 - 1	**23** (36%)			([d])
2-B	**13**	>30 - 1	**23** (77%)			
3[e]	**13**		**23** (91%)			
4[f]	**13** (75%)					
5-C[g]	**13** (*~27%*)	1 - 1.6	**23** (20%)	**24** (38%)		(*~12%*)
6[h]	**13**	1 - 2.6	**23** (19%)	**24** (49%)	**25** (10%)	
7[i]	**13**				**25** (96%)	
						
8-A	**14**	>30 - 1	**26** (82%)		**27** (9%)	
9-B	**14**	57 - 1	**26** (68%)			
10[j]	**14**	90 - 1	**26** (69%)		**27** (4%)	
11-C	**14**	1 - 3	**26** (*~9%*)	**28** (*~37%*)	**27** (15%)	
						
12-A	**15**	32 - 1	**29** (68%)		**30** (2%)	
13-B	**15**	>30 -1	**29** (81%)		**30** (3%)	
14[j]	**15**	>30 -1	**29** (74%)		**30** (2%)	
15-C	**15** (*~17%*)	1 - 1	**29** (*~23%*)	**31** (36%)	**30** (3%)	
						
16-A	**16**	14 - 1	**32** (60%)	**33** (3%)	**34** (30%)	
17-B	**16**	19 - 1	**32** (68%)	**33** (1%)	**34** (23%)	
18-C	**16**	>1 - 30		**33** (61%)	**34** (trace)	
						
19-A[k]	**17** (9%)	3.2 - 1	**35** (24%)	**36** (*~5%*)	**25**(*~5%*)	(7%)
20-B	**17**	32 - 1	**35** (66%)	**36** (*~4%*)	**25** (*~8%*)	
21-C[l]	**17** (5%)	>1 - 30		**36** (43%)		(12%)

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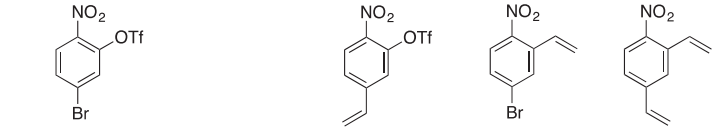
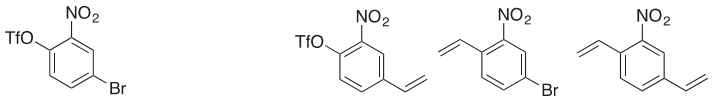
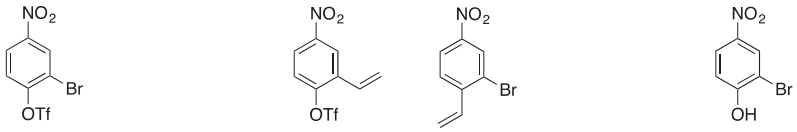


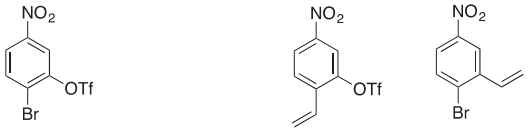
22-A	**18**	6 - 1	**37** (41%)		
23-B	**18**	16 - 1	**37** (74%)	**38** (*~14%*)	**27** (*~9%*)
24-C	**18** (22%)	1 - 1.3	**37** (23%)	**38** (17%)	



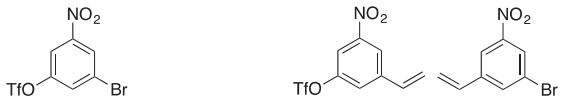
25-A[m]	**19**	13 - 1	**39** (*~41%*)[n]		
26-B	**19** (9%)	12 - 1	**39** (67%)	**40** (*~3%*)	**30** (*~8%*)
27-C	**19**	>1 - 30		**40** (78%)	



28-A[o]	**20** (7%)	>30 - 1	**41** (22%)		(7%)
29-B[p]	**20**	30 - 1	**41** (94%)		
30-C[q]	**20** (8%)	>1 - 30		**42** (57%)	(16%)



31-A	**21** (20%)	>30 - 1	**43** (48%)	
32-B	**21**	>30 - 1	**43** (89%)	
33-C	**21** (31%)	4 - 1	**43** (31%)	**44** (7%)



34-A	**22** (4%)	19 - 1	**45** (78%)	
35-B	**22**	24 - 1	**45** (89%)	
36-C	**22**	1 - 49		**46** (66%)

Catalyst system, reaction temperature and solvent for Conditions A-C:

A) $Pd(dba)_2$ (2 mol-%), PPh_3 (8 mol-%), 1,4-dioxane, at reflux
B) $PdCl_2(PPh_3)_2$ (2 mol-%), 1,4-dioxane, at reflux.
C) $PdCl_2(PPh_3)_2$ (2 mol-%), LiCl (300 mol-%), DMF, ambient temperature.

a) Calculated from the integration of the ^1H NMR of the crude reaction mixture. b) Isolated yields of pure products in parenthesis. Yields calculated from ^1H NMR spectra from inseparable mixtures are shown in italic. c) A ratio of **13/23** = 1:2 was observed by ^1H NMR of the crude reaction mixture. d) Isolated as a mixture with unknown impurities. e) $Pd(PPh_3)_4$ (2 mol-%), toluene, at reflux was used. Reference 25. f) $PdCl_2$(dppp) (2 mol-%), DMF, ambient temperature was used. g) A ratio of **13/23/24** = 1.14:1:1.93 was observed by ^1H NMR of the crude reaction mixture. h) $PdCl_2(dppp)_2$ (2 mol-%), LiCl (300 mol-%), DMF, ambient temperature was used. i) $PdCl_2(PPh_3)_2$ (4 mol-%), LiCl (120 mol-%), (ethenyl)tributyltin (300 mol-%), 1,4-dioxane, at reflux. j) $Pd(OAc)_2$ (2 mol-%), PPh_3 (8 mol-%), 1,4-dioxane, at reflux was used. k) A ratio of **17/35/36/25** = 3.22:3.55:1.10:1 was observed by ^1H NMR of the crude reaction mixture. l) A ratio of **17/36 =** 1:6.67 was observed by ^1H NMR of the crude reaction mixture. m) A ratio of **19/39** = 1:2.2 was observed by ^1H NMR of the crude reaction mixture. n) Calculated from a mixture of **39** and dibenzylideneacetone. o) A ratio of **20/41** = 1:2.58 was observed by ^1H NMR of the crude reaction mixture. p) Reaction time 36 h. q) A ratio of **20/42** = 1:5 was observed by ^1H NMR of the crude reaction mixture.

selectivity, the reaction did not go to completion.

Kamikawa and Hayashi have shown that the chemoselectivity of the oxidative addition of palladium(0) to 4-bromophenyl triflate (**1**) can be controlled by the proper choice of ligand.[25] Using the bidentate ligand 1,3-bis(diphenylphosphino)propane (dppp), a 95:5 C-OTf/C-Br ratio of oxidative addition products was observed in a stoichiometric reaction. In contrast, using PPh_3 as the ligand gave an almost reversed 15:85 ratio. When a catalytic amount of

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$PdCl_2$(dppp) was employed in a cross coupling of **1** with phenylmagnesium bromide, a rapid and highly triflate selective reaction was observed at 0 °C in diethyl ether. Based on this report, it may be possible to improve the C-OTf/C-Br coupling ratio of **13** by simply replacing PPh_3 with dppp as the ligand in Kosugi-Migita-Stille reactions. In the event, no reaction of **13** with (ethenyl)tributyltin was observed in DMF at ambient temperature in the presence of a catalytic amount of $PdCl_2$(dppp) (entry 4). The starting material was recovered in 75% yield. In contrast, reaction of **13** using $PdCl_2$(dppp) under Conditions C was faster compared to $PdCl_2(PPh_3)_2$ and the starting material was completely consumed after 24 h at ambient temperature (entry 6). Unfortunately, only a slight improvement of the product ratio was observed in addition to a fair amount of product derived from coupling at both positions (**25**). Excellent yield of **25** can be realized by treatment of **13** with a three-fold excess of (ethenyl)tributyltin in the presence of $PdCl_2(PPh_3)_2$ and LiCl in 1,4-dioxane at reflux (entry 7). It should be noted that di-coupling affording di(ethenyl)-nitrobenzenes was observed in several of the reactions seen in Table 2.

The results obtained from reactions of **14** and **15** parallels the cross couplings described above employing **13** as the starting material. A pre-catalyst system consisting of 2-mol% palladium diacetate ($Pd(OAc)_2$) and 4-mol% PPh_3 was also examined in reactions of (ethenyl)tributyltin with substrates **14** and **15**. Compared to the reactions using Conditions A-B, cross coupling experiments in the presence of $Pd(OAc)_2$-PPh_3 afforded similar yields of **26** and **29** (Table 2, entries 8–10 and 12–14). Not only were the isolated yields more or less the same, the crude ratios of **26**/**28** and of **29**/**31** were comparable using either $Pd(OAc)_2$ or $PdCl_2(PPh_3)_2$. Thus, there is a very minor, if any, effect on the C-Br/C-OTf selectivity from the chloride present when using $PdCl_2(PPh_3)_2$ as the catalyst.

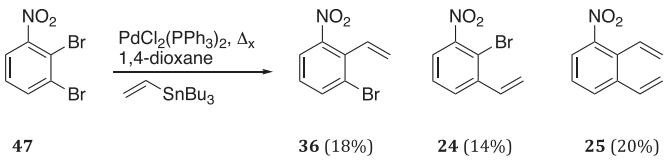
The remaining seven substrates were only treated with (ethenyl)tributyltin under Conditions A-C. Some general trends can be discerned from the result depicted in Table 2. For all substrates **13**–**22**, the C-Br/C-OTf coupling ratios were similar or better under Conditions B compared to Conditions A. The ratios under the former reaction conditions ranged from 12:1 to >30:1. Not only did the reactions under Conditions B exhibit better chemoselectivities, the isolated yields of C-Br cross coupling products were also superior. The yields under Conditions B ranged from 66 to 94% (average 77%) for the ten substrates and were in all but one case (compound **14**, Table 2) significantly higher compared to the yields obtained under Conditions A, which ranged from 22 to 82% (average 50%). Results from experiments employing Conditions C were inferior compared to Conditions A-B. The C-Br/C-OTf coupling ratios ranged from 4:1 to >1:30. It should be noted that cross coupling of compound **21** actually favored C-Br coupling under conditions presumed to favor C-OTf coupling (entry 33-C, Table 2). In addition to a lower chemoselectivity under Conditions C, the isolated yields of products were also lower ranging from 7 to 78% (average 44%).

For half of the substrates, compounds **16**–**17**, **19**–**20**, and **22**, highly selective C-OTf coupling reactions were observed under conditions C with C-Br/C-OTf ratios of >1:30. These substrates either have the bromide in an "unactivated" meta-position relative to the nitro group (entries 21, 27, and 30) or the triflate and the bromide were both ortho or meta to the nitro group (entries 18 and 36). For the other five substrates having the bromide ortho or para relative to the nitro group, compounds **13**–**15**, **18**, and **21**, a reversed or mediocre C-Br/C-OTf ratio (4:1–1:3) was observed (entries 5–6, 11, 15, 24, and 33).

Palladium catalyzed Sonogashira reactions of 3,4-dibromo-1-nitrobenzene and 2,3-dibromo-1-nitrobenzene (**47**) with 1-heptyne have been reported to occur exclusively at the more electrophilic site, that is ortho or para to the nitro group.[26,27] It was of interest to examine if a nitro group in a similar fashion activates the ortho position of **47** for cross coupling reactions using a tin reagent. Treatment of **47** under the published reaction conditions,[28] replacing 1-heptyne with (ethenyl)tributyltin, resulted in a 98% recovery of the starting material. In a second experiment, compound **47** was subjected to Conditions B. The starting material was completely consumed affording **36** and an inseparable mixture of **24** and **25**, all in similar yields (Scheme 4). Although cross-coupling at the ortho-position of **47** was slightly favored (1.3:1), it appears that the nitro group has only a very small effect on the site-selectivity in this case, in sharp contrast to the Sonagashira reaction.

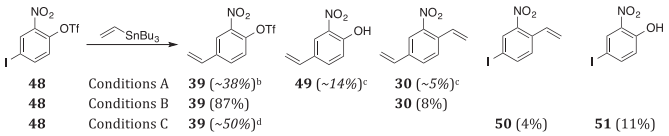
Aryl iodides undergo Kosugi-Migita-Stille coupling reactions significantly faster compared to aryl triflates even in the presence of a large excess of LiCl. Cross couplings of 4-iodo-2-nitrophenyl triflate (**48**) under conditions A-C were examined to determine if a nitro group is sufficiently ortho-activating for a triflate to react in the presence of an iodide in a less activated meta-position (Scheme 5). Compound **48** is the iodo-analog of **19** for which a relatively low C-Br selectivity and an excellent C-OTf selectivity were observed (Table 2, entry 25–27). In all three experiments employing **48**, the major product **39** was derived from oxidative addition to the C-I bond. In addition to **39**, di-coupled product **30** and compounds **49** and **51** derived from loss of triflate from **39** and **48**, respectively, were also isolated. Comparing the two pre-catalysts $Pd(dba)_2$-PPh_3 and $PdCl_2(PPh_3)_2$, the latter again proved to be superior, affording an excellent overall yield of coupling products (95%). The results shown in Scheme 5 illustrate the significantly higher reactivity of the carbon-iodide bond. Only under Conditions C was a small amount of the C-OTf coupling product **50** isolated. Although the yield of **50** was unimpressive it represents, to the best of our knowledge, the only example of a Kosugi-Migita-Stille coupling reaction wherein even a small fraction of C-Br or C-OTf coupling occurred on a benzene ring also containing an iodide.[29,30]

In order to examine if a similar chemoselectivity can be extended to benzene rings substituted with other electron withdrawing groups, 5-bromo-2-trifluoromethanesulfonylacetophenone (**52**) was prepared and treated with (ethenyl)tributyltin (Scheme 6). Under all reaction



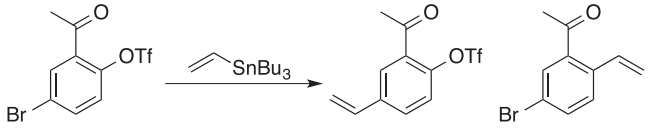
47 36 (18%) 24 (14%) 25 (20%)

Scheme 4. Kosugi-Migita-Stille reaction of **47**.



48	Conditions A	**39** (~38%)[b]	**49** (~14%)[c]	**30** (~5%)[c]	
48	Conditions B	**39** (87%)		**30** (8%)	
48	Conditions C	**39** (~50%)[d]			**50** (4%) **51** (11%)

Scheme 5. Kosugi-Migita-Stille cross-coupling of **48** with (ethenyl)tributyltin.[a].



52	Conditions A	**53** (14%)	
52	Conditions B	**53** (57%)	
52	Conditions C		**54** (58%)

Scheme 6. Kosugi-Migita-Stille cross-coupling of **52**.

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conditions (A-C), a single coupling product was observed in each case as determined by ^{1}H NMR (>30:1 ratio) of the crude reaction mixtures. The C-Br bond selectivity under Conditions A and B was significantly higher starting from **52** relative to the selectivity observed for the nitro substituted compound **19** (Table 3, entry 25–26) having the same relative substituent configuration. It is plausible, that the electron-withdrawing keto-functionality activates the ring toward oxidative addition of palladium(0) but does not sufficiently activate the ortho-position bearing the triflate to override the exclusive C-Br selectivity observed for the bromophenyl-triflate (**1**). As observed previously (Table 2), a significantly higher yield of cross-coupling product **53** was isolated using Conditions B in comparison to Conditions A.

Finally, the site-selectivity of a bromophenyl trifluoromethanesulfonate having an electron donating substituent on the aromatic ring was examined. Only a very limited number of palladium catalyzed coupling reactions of this type of substrate have been reported.[31–33] In no case was the effect of an electron donating group on the C-Br/C-OTf selectivity examined in detail. The known triflate **55** was selected as the starting material in order to minimize the effect of steric interactions between the bromide and triflate with the methoxy group. Two reactions were performed one under Conditions A and one under Conditions C (Scheme 7). The reactions were more sluggish and only low yields of products were obtained after purification. However, the site-selectivity remained the same, a selective C-Br bond coupling was seen under Conditions A and a relatively selective C-OTf bond coupling (~10:1 ratio) was realized under Conditions C. From these two experiments it appears that the only effect of the electron-donating group for this substrate is a somewhat lower reactivity.

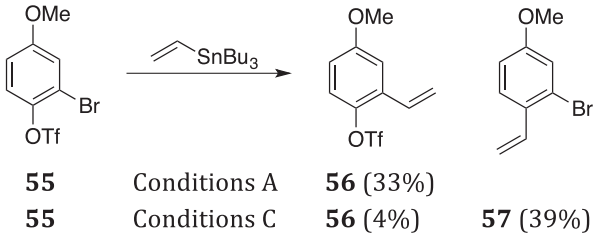
3. Conclusions

We have examined the chemoselectivity of carbon-bromine versus carbon-triflate bond coupling in Kosugi-Migita-Stille reactions of (ethenyl)tributyltin with bromophenyl triflates and bromo-nitrophenyl triflates. In general, highly selective carbon-bromine bond cross couplings were observed using bis(-triphenylphosphine)palladium dichloride in 1,4-dioxane at reflux. In contrast, reactions using the same pre-catalyst but in the presence of a three-fold excess of LiCl, in DMF at ambient temperature, were in most cases selective for coupling at the carbon-triflate bond. However, both isolated yields and the selectivity for carbon-bromine bond coupling were significantly higher compared to carbon-triflate bond coupling reactions.

4. Experimental Section

4.1. General procedures

NMR spectra were recorded in $CDCl_3$ at 400 and 600 MHz (^{1}H NMR), 100 and 150 MHz (^{13}C NMR), and 376 and 565 MHz (^{19}F NMR). The chemical shifts are expressed in δ values relative to $SiMe_4$ (0.0 ppm, ^{1}H and ^{13}C) or $CDCl_3$ (77.0 ppm, ^{13}C) internal standards. HRMS data were obtained via ESI with an orbitrap mass analyzer.



Scheme 7. Kosugi-Migita-Stille cross-coupling of **55**.

Anhydrous *N,N*-dimethylformamide was used as received. Hexanes and ethyl acetate were distilled prior to use. 1,4-Dioxane was purified/dried via two consecutive columns composed of activated alumina and Q5 catalyst on a Glass Contours solvent purification system. Dichloromethane and toluene was purified/dried via two consecutive columns composed of activated alumina on a Glass Contours solvent purification system. Chemicals prepared according to literature procedures have been footnoted the first time used; all other reagents were obtained from commercial sources and used as received. All reactions were performed under a nitrogen atmosphere in oven-dried glassware. Solvents were removed from reaction mixtures and products on a rotary evaporator at water aspirator pressure unless otherwise stated. Chromatography was performed on silica gel (SiO_2, 40–63 μm) if not otherwise stated. Melting points (uncorrected) were recorded from the pure products obtained by chromatography.

4.1.1. 2,4-Dinitro-5-bromophenyl trifluoromethanesulfonate (*5*)

To a solution of fuming HNO_3 (4.2 mL) in H_2SO_4 (4.2 mL) was added 3-bromophenyl trifluoromethanesulfonate (**4**)[34] (1.52 g, 4.98 mmol) and the mixture was heated at 60 °C for 15 h. The resulting mixture was poured onto ice, the ice was allowed to melt, and the resulting mixture was extracted with EtOAc (3 × 20 mL). The combined organic phases were dried ($MgSO_4$), filtered, and the solvents were removed under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 9:1) affording **5** (1.82 g, 4.60 mmol, 92%) as a pale yellow oil that solidified upon standing. Mp = 33–35 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.90 (s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.2, 142.7, 140.2, 131.2, 124.0, 122.1, 118.5 (q, J^{C-F} = 320 Hz); IR (ATR) 1591, 1541, 1436, 1337, 1213, 1130 cm^{-1}; HRMS (ESI, negative ion mode) calcd for $C_7HBrF_3N_2O_7S$ ($M\text{-}H^-$) 392.8640; found 392.8654.

4.1.2. 5-Ethenyl-2,4-dinitro trifluoromethanesulfonate (*6*)

A mixture of **5** (238 mg, 0.60 mmol), (ethenyl)tributyltin (187 mg, 0.59 mmol), 2,6-di-*t*-butyl-4-methylphenol (22 mg, 0.10 mmol), LiCl (87 mg, 2.05 mmol), PPh_3 (25.2 mg, 0.098 mmol), and $PdCl_2(PPh_3)_2$ (33.7 mg, 0.048 mmol) in toluene (4 mL) was heated at 80 °C for 17 h. The solvent was removed at reduced pressure and the crude product was purified by chromatography (hexane/EtOAc, 9:1) to give **6** (160 mg, 0.468 mmol, 78%) as a faint brown oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.81 (s, 1H), 7.69 (s, 1H), 7.26 (dd, J = 16.8, 10.8 Hz, 1H), 5.96 (d, J = 17.4 Hz, 1H), 5.86 (d, J = 10.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 145.3, 143.6, 140.5, 139.7, 129.8, 125.0, 124.4, 123.9, 118.5 (q, J^{C-F} = 321 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −72.9; IR (ATR) 1614, 1590, 1539, 1437, 1345, 1223, 1134 cm^{-1}; HRMS (ESI, negative ion mode) calcd for $C_9H_5F_3NO_7S$ (M^-) 341.9770; found 341.9787.

4.1.3. 4-Bromo-3-nitrophenyl trifluoromethanesulfonate (*15*)

To a solution of 4-bromo-3-nitrophenol[35] (269 mg, 1.23 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added pyridine (200 μL, 2.48 mmol) and trifluoromethanesulfonic anhydride (Tf_2O, 250 μL, 1.48 mmol). The mixture was removed from the cold bath and allowed to stir at ambient temperature for 30 min. The resulting mixture was filtered through a small plug of silica gel and the solvent was removed under reduced pressure from the filtrate. Purification by chromatography (hexane/EtOAc, 9:1) afforded **15** (391 mg, 1.12 mmol, 90%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 8.4 Hz, 1H), 7.81 (d, J = 2.8 Hz, 1H), 7.41 (dd, J = 8.8, 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1, 147.9, 136.8, 126.3, 119.3, 118.6 (q, J^{C-F} = 319 Hz), 114.6; IR (ATR) 3103, 1541, 1428, 1208, 1132 cm^{-1}; HRMS

(ESI) calcd for $C_7H_3BrNNaO_5F_3S$ (M + Na^+) 371.8765; found 371.8760.

4.1.4. 3-Bromo-2-nitrophenyl trifluoromethanesulfonate (**16**)

Treatment of 3-bromo-2-nitrophenol[36] (298 mg, 1.37 mmol) in CH_2Cl_2 (5 mL) with pyridine (250 μL, 3.10 mmol) and Tf_2O (300 μL, 1.77 mmol), as described for **15**, gave after chromatography (hexane/EtOAc, 8:2) **16** (394 mg, 1.13 mmol, 80%) as a red solid. Mp 52–53 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, J = 6.6, 3.0 Hz, 1H), 7.49 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.6, 136.2, 133.4, 132.1, 121.6, 118.3 (q, J^{C-F} =319 Hz), 115.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ −73.2; IR (ATR) 3099, 1538, 1434, 1360, 1219, 1132 cm^{-1}; HRMS (ESI) calcd for $C_7H_3BrNNaO_5F_3S$ (M + Na^+) 371.8765; found 371.8767.

4.1.5. 2-Bromo-6-nitrophenyl trifluoromethanesulfonate (**17**)

Treatment of 2-bromo-6-nitrophenol[37] (189 mg, 0.87 mmol) in CH_2Cl_2 (5 mL) with pyridine (150 μL, 1.85 mmol) and Tf_2O (200 μL, 1.18 mmol), as described for **15**, gave after chromatography (hexane/EtOAc, 7:3) **17** (299 mg, 0.85 mmol 98%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, J = 8.4, 1.6 Hz, 1H), 7.99 (dd, J = 8.4, 1.6 Hz, 1H), 7.45 (t, J = 8.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) d 143.6, 139.4, 139.1, 129.3, 125.6, 119.1, 118.4 (q, J^{C-F}=319 Hz);^{19}F NMR (376 MHz, $CDCl_3$) δ −73.2; IR (ATR) 3093, 1588, 1540, 1431, 1347, 1207 cm^{-1}; HRMS (ESI) calcd for $C_7H_3BrNNaO_5F_3S$ (M + Na^+) 371.8765; found 371.8761.

4.1.6. 4-Bromo-2-nitrophenyl trifluoromethanesulfonate (**19**).[38]

Treatment of 4-bromo-3-nitrophenol[39] (353 mg, 1.60 mmol) in CH_2Cl_2 (5 mL) with pyridine (260 μL, 3.22 mmol) and Tf_2O (330 μL, 1.95 mmol), as described for **15**, gave after chromatography (hexane/EtOAc, 7:3) **19** (540 mg, 1.54 mmol, 97%) as a yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30 (d, J = 2.4 Hz, 1H), 7.88 (dd, J = 9.0, 2.4 Hz, 1H), 7.36 (d, J = 9.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 141.9, 140.5, 138.2, 129.7, 125.6, 122.3, 118.5 (q, J^{C-F} = 319 Hz); IR (ATR) 3105, 1540, 1431, 1207, 1131 cm^{-1}.

4.1.7. 2-Bromo-5-nitrophenyl trifluoromethanesulfonate (**21**)

Treatment of 2-bromo-5-nitrophenol[40] (119 mg, 0.55 mmol) in CH_2Cl_2 (5 mL) with pyridine (90 μL, 1.12 mmol) and Tf_2O (120 μL, 0.71 mmol), as described for **15**, gave without further purification **21** (188 mg, 0.54 mmol, 98%) as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 2.8 Hz, 1H), 8.16 (dd, J = 8.4, 2.4 Hz, 1H), 7.93 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 146.9.0, 135.2, 124.0, 123.9, 118.5 (q, J^{C-F} = 320 Hz), 118.3; IR (ATR) 3104, 1534, 1431, 1348, 1211, 1134 cm^{-1}; HRMS (ESI) calcd for $C_7H_3BrNNaO_5F_3S$ (M + Na^+) 371.8765; found 371.8740.

4.1.8. 3-Bromo-5-nitrophenyl trifluoromethanesulfonate (**22**)

Treatment of 3-bromo-5-nitrophenol[41] (329 mg, 1.51 mmol) in CH_2Cl_2 (10 mL) with pyridine (250 μL, 3.10 mmol) and Tf_2O (300 μL, 1.78 mmol), as described for **15**, gave after chromatography (hexane/EtOAc, 7:3) **22** (316 mg, 0.90 mmol, 60%) as a red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (t, J = 1.8 Hz, 1H), 8.11 (t, J = 2.0 Hz, 1H), 7.80 (t, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.2, 130.8, 126.8, 123.9, 118.6 (q, J^{C-F} = 320 Hz), 116.0; IR (ATR) 3097, 1732, 1542, 1427, 1344, 1210, 1134 cm^{-1}; HRMS (ESI) calcd for $C_7H_3BrNNaO_5F_3S$ (M + Na^+) 371.8765; found 371.8764.

4.2. Table 1 - conditions A

4.2.1. Entry 3. 4-Ethenylphenyl trifluoromethanesulfonate (**2**).[4]

To a solution of PPh_3 (7.5 mg, 0.029 mmol) and $Pd(dba)_2$ (4.3 mg, 0.007 mmol) in dioxane (1.5 mL), stirred for 5 min under an atmosphere of N_2, was added 4-bromophenyl trifluoromethanesulphonate (**1**)[4] (102 mg, 0.34 mmol) followed by (ethenyl)tributyltin (128 mg, 0.40 mmol). The solution was heated at reflux for 24 h. The solvent was removed under reduced pressure and the residue was dissolved in EtOAc (10 mL) and washed with NH_4OH (10% aqueous, 3 × 20 mL), H_2O (20 mL), and brine (20 mL). The organic phase was dried ($MgSO_4$), filtered, and solvents were removed under reduced pressure. The crude product was purified by chromatography (hexane/EtOAc, 97:3) to give **2** (25.2 mg, 0.10 mmol, 30%) as a colorless oil. Only **2** was observed by ^{1}H NMR (600 MHz, $CDCl_3$) of the crude reaction mixture.

4.3. Conditions B

4.3.1. Entry 4. 4-Ethenylphenyl trifluoromethanesulfonate (**2**)

To a solution of $PdCl_2(PPh_3)_2$ (4.3 mg, 0.007 mmol) in dioxane (4 mL), stirred for 5 min under an atmosphere of N_2, was added **1** (310 mg, 1.02 mmol) followed by (ethenyl)tributyltin (340 mg, 1.07 mmol). The solution was heated at reflux for 24 h. The solvent was removed under reduced pressure and the resulting residue was purified by chromatography (SiO_2/K_2CO_3 = 9:1, hexane/EtOAc, 98:2) to give **2** (231 mg, 0.917 mmol, 90%) as a colorless oil. Only **2** was observed by ^{1}H NMR (600 MHz, $CDCl_3$) of the crude reaction mixture.

4.4. Conditions C

4.4.1. Entry 6. 4-Ethenylphenyl trifluoromethanesulfonate (**2**) and 4-ethenyl-1-bromobenzene (**3**).[4]

To a solution of LiCl (45.5 mg, 1.07 mmol) and $Pd(PPh_3)_2Cl_2$ (4.7 mg, 0.007 mmol) in DMF (1.5 mL), under an atmosphere of N_2, was added **1** (108 mg, 0.35 mmol) followed by (ethenyl)tributyltin (141 mg, 0.44 mmol). After stirring at ambient temperature for 24 h, the solvent was removed by bulb-to-bulb distillation. The resulting residue was dissolved in EtOAc (15 mL) and washed with NH_4OH (10% aqueous, 3 × 20 mL) and brine (20 mL). The organic phase was dried ($MgSO_4$), filtered, and solvents were removed under reduced pressure. The terminal *cis*-alkene protons were clearly resolved in the ^{1}H NMR spectrum at 600 MHz and these signals were used to determine the ratio of **2** (δ 5.35, d, J = 10.8 Hz, 1H) to **3** (δ 5.27, d, J = 10.8 Hz, 1H). A 6.7:1 ratio of **3**/**2** was observed by NMR. The products decomposed upon attempted purification on silica gel.

4.4.2. Entry 10. 2-Ethenylphenyl trifluoromethanesulfonate (**9**).[42]

Cross coupling of 2-bromophenyl trifluoromethanesulphonate (**7**)[43] (95.6 mg, 0.31 mmol) with (ethenyl)tributyltin (121 mg, 0.38 mmol) in the presence of PPh_3 (6.9 mg, 0.026 mmol) and $Pd(dba)_2$ (3.8 mg, 0.007 mmol) in dioxane (1.5 mL) was performed as described under Conditions A. Extractive work up and chromatography (hexane/EtOAc, 9:1) gave **9** (4.1 mg, 0.016 mmol, 5%) as a colorless oil. Only **9** was observed by ^{1}H NMR (600 MHz, $CDCl_3$) of the crude reaction mixture after work up.

4.4.3. Entry 11. 2-Ethenylphenyl trifluoromethanesulfonate (**9**) and 2-ethenyl-1-bromobenzene (**10**).[44]

Cross coupling of **7** (88.3 mg, 0.25 mmol) with (ethenyl)tributyltin (98.0 mg, 0.31 mmol) in the presence of LiCl (32.2 mg, 0.76 mmol) and $Pd(PPh_3)_2Cl_2$ (3.8 mg, 0.005 mmol) in DMF (1.0 mL) was performed as described under Conditions C. A 5.9:1 ratio of **10**/**9** was observed by ^{1}H NMR (600 MHz, $CDCl_3$) of the crude reaction mixture after extractive work up. The products decomposed upon attempted purification on silica gel. The terminal *cis*-alkene protons were clearly resolved in the ^{1}H NMR spectrum at 600 MHz and these signals were used to determine the ratios of **9** (δ 5.49, d, J = 11.1 Hz, 1H) to **10** (δ 5.37, dd, J = 10.9, 1.0 Hz, 1H).

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4.4.4. Entry 12. 3-Ethenylphenyl trifluoromethanesulfonate (**11**) and 3-Ethenylphenyl-1-bromobenzene (**12**).[50]

Cross coupling of 3-bromophenyl trifluoromethane sulphonate (**8**) (105 mg, 0.34 mmol) with (ethenyl)tributyltin (127 mg, 0.40 mmol) in the presence of PPh_3 (7.6 mg, 0.03 mmol) and $Pd(dba)_2$ (4.0 mg, 0.007 mmol) in dioxane (1.5 mL) was performed as described under Conditions A. Extractive work up and chromatography (hexane/EtOAc, 9:1) to give an inseparable mixture of **8** and **11** (49.2 mg, calculated from ^{1}H NMR spectrum: 20.2 mg **8** and 28.8 mg **11**, 34%) as a colorless oil. A ~30:1 ratio of **11**/**12** was observed by ^{1}H NMR (600 MHz, $CDCl_3$) of the crude reaction mixture. The terminal *cis*-alkene protons were clearly resolved in the ^{1}H NMR spectrum at 600 MHz and these signals were used to determine the ratios of **11** (δ 5.38, d, $J = 11.4$ Hz, 1H) to **12** (δ 5.30, d, $J = 10.8$ Hz, 1H).

4.4.5. Entry 13. 3-Ethenylphenyl trifluoromethanesulfonate (**11**)

Cross coupling of **8** (310 mg, 1.02 mmol) with (ethenyl)tributyltin (490 mg, 1.54 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (13.3 mg, 0.019 mmol) in dioxane (4 mL) was performed as described under Conditions B (50 h). A ~10:1:4 ratio of **11**/**12**:ethenyltributyltin was observed in the crude ^{1}H NMR spectrum. Solvent removal and chromatography (SiO_2/K_2CO_3 = 9:1, hexane/EtOAc, 98:2) gave **11** (121 mg, 0.480 mmol, 47%) as a colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42–7.40 (m, 2H), 7.29 (br s, 1H), 7.16 (dt, $J = 6.4$, 2.4 Hz, 1H), 6.70 (dd, $J = 17.2$, 10.8 Hz, 1H), 5.80 (d, $J = 17.6$ Hz, 1H), 5.38 (d, $J = 10.8$ Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.9, 140.3, 135.0, 130.3, 126.1, 120.2, 118.8, 118.7 (q, $J^{C-F} = 319$ Hz), 116.5; IR (ATR) 1574, 1420, 1205, 1136, 1117, 924, 825 cm^{-1}; HRMS (ESI) calcd for $C_9H_8F_3O_3S$ ($M + H^+$) 253.0146; found 253.0146.

4.4.6. Entry 14. 3-Ethenylphenyl trifluoromethanesulfonate (**11**) and 3-Ethenylphenyl-1-bromobenzene (**12**)

Cross coupling of **8** (108 mg, 0.36 mmol) with (ethenyl)tributyltin (140 mg, 0.44 mmol) in the presence of LiCl (45.6 mg, 1.08 mmol) and $Pd(PPh_3)_2Cl_2$ (5.4 mg, 0.008 mmol) in DMF (1.5 mL) was performed as described for **3** under Conditions C. A 5.3:6.3:1 ratio of **8**/**12**/**11** was observed by ^{1}H NMR (600 MHz, $CDCl_3$) of the crude reaction mixture after extractive work up. The products decomposed upon attempted purification on silica gel or basic alumina.

4.5. Table 2

4.5.1. Entry 1. 2-Ethenyl-3-nitrophenyl trifluoromethanesulfonate (**23**).[27]

Cross coupling of 2-bromo-3-nitrophenyl trifluoromethanesulfonate (**13**)[27] (105 mg, 0.30 mmol) with (ethenyl) tributyltin (119 mg, 0.38 mmol) in the presence of in the presence of PPh_3 (6.5 mg, 0.03 mmol) and $Pd(dba)_2$ (3.7 mg, 0.006 mmol) in dioxane (1.5 mL) was performed as described under Conditions A. Extractive work up and chromatography (hexane/EtOAc, 97:3) gave, in order of elution, **23** (32.3 mg, 0.11 mmol, 36%) as a white solid and impure 2-bromo-3-nitrophenol[50] (41 mg).

4.5.2. Entry 2. 2-Ethenyl-3-nitrophenyl trifluoromethanesulfonate (**23**)

Cross coupling of **13** (127 mg, 0.362 mmol) with (ethenyl)tributyltin (149 mg, 0.471 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (5.1 mg, 0.007 mmol) in dioxane (1 mL) was performed as described under Conditions B. Solvent removal and chromatography ($SiO_2/K_2CO_3 = 9:1$, hexane/EtOAc, 98:2) gave **23** (83 mg, 0.28 mmol, 77%) as a yellow oil.

4.5.3. Entry 5. 2-Ethenyl-3-nitrophenyl trifluoromethanesulfonate (**23**), 2-bromo-3-nitrophenol, and 2-bromo-3-ethenyl-nitrobenzene (**24**)

Cross coupling of **13** (110 mg, 0.32 mmol) with (ethenyl)tributyltin (123 mg, 0.39 mmol) in the presence of LiCl (40.9 mg, 0.96 mmol) and $Pd(PPh_3)_2Cl_2$ (4.8 mg, 0.007 mmol) in DMF (1.5 mL) was performed as described under Conditions C. Extractive work up and chromatography (hexane/EtOAc, 97:3) gave, in order of elution, **23** (18.5 mg, 0.06 mmol, 20%), **24** (27.6 mg, 0.12 mmol, 38%) as a colorless oil and an impure mixture of **13** and 2-bromo-3-nitrophenol (38.2 mg). Analytical data for **24**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.70 (d, $J = 7.8$ Hz, 1H), 7.58 (d, $J = 7.8$ Hz, 1H), 7.42 (t, $J = 7.8$ Hz, 1H), 7.10 (dd, $J = 16.8$, 11.4 Hz, 1H), 5.76 (d, $J = 17.4$ Hz, 1H), 5.52 (d, $J = 10.8$ Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 147.2, 128.9, 128.3, 126.2, 125.7, 124.8, 123.8, 119.5; IR (ATR) 3110, 1533, 1423, 1358, 1210, 1135 cm^{-1}; HRMS (ESI) calcd for $C_8H_6NNaO_2Br$ ($M + Na^+$) 249.9479; found 249.9473.

4.5.4. Entry 6. 2-Ethenyl-3-nitrophenyl trifluoromethanesulfonate (**23**), 1-bromo-2-ethenyl-nitrobenzene (**24**), and 2,3-diethenyl-nitrobenzene (**25**)

Cross coupling of **13** (143 mg, 0.41 mmol) with (ethenyl)tributyltin (123 mg, 0.39 mmol) in the presence of LiCl (53.8 mg, 1.27 mmol) and 1,3-bis(diphenylphosphino)propanepalladium dichloride (5.3 mg, 0.009 mmol) in DMF (2 mL) was performed as described under Conditions C. Extractive work up and chromatography (hexane/EtOAc, 97:3) gave in order of elution, **25** (7.0 mg, 0.04 mmol, 10%), **23** (22.9 mg, 0.077 mmol, 19%), and **24** (45.7 mg, 0.20 mmol, 49%) as a colorless oil. Spectral data for **25**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, $J = 8.0$ Hz, 1H), 7.71 (dd, $J = 8.0$, 1.2 HZ, 1H), 7.37 (t, $J = 7.6$ Hz, 1H), 6.96 (dd, $J = 17.2$, 11.2 Hz, 1H), 6.88 (dd, $J = 17.6$, 11.2 Hz, 1H), 5.71 (dd, $J = 17.6$, 0.8 Hz, 1H), 5.63 (dd, $J = 11.2$, 1.2 Hz, 1H), 5.37 (dd, $J = 11.2$, 0.8 Hz, 1H), 5.32 (d, $J = 18.0$, 1.2 Hz, 1H); ^{13}C NMR (100 MHZ, $CDCl_3$) δ 149.8, 138.7, 134.5, 131.4, 130.5, 130.0, 127.6, 122.8, 122.6, 117.3; IR (ATR) 1521, 1348, 985, 921, 810, 774, 753, 735 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{10}NO_2$ ($M + H^+$) 176.0711; found 176.0709.

4.5.5. Entry 7. 2,3-Diethenyl-nitrobenzene (**25**)

Treatment of **13** (70.2 mg, 0.201 mmol) with (ethenyl)tributyltin (203 mg, 0.641 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (6.0 mg, 0.008 mmol) and LiCl (6.0 mg, 0.008 mmol) in dioxane (1 mL, reflux, 24 h) was performed as described under Conditions B. Solvent removal and chromatography ($SiO_2/K_2CO_3 = 9:1$, hexane/EtOAc, 98:2) gave **25** (33.7 mg, 0.192 mmol, 96%) as a faint yellow oil.

4.5.6. Entry 8. 3-Ethenyl-4-nitrophenyl trifluoromethanesulfonate (**26**) and 2,4-diethenyl-nitrobenzene (**27**)

Cross coupling of 3-bromo-4-nitrophenyl trifluoromethanesulfonate (**14**)[45] (67.6 mg, 0.19 mmol) with (ethenyl) tributyltin (72.8 mg, 0.23 mmol) in the presence of in the presence of PPh_3 (4.5 mg, 0.02 mmol) and $Pd(dba)_2$ (2.2 mg, 0.004 mmol) in dioxane (1 mL) was performed as described under Conditions A. Extractive work up and chromatography (hexane/EtOAc, 97:3), gave in order of elution, **27** (3.0 mg, 0.02 mmol, 9%) and **26** (47.3 mg, 0.16 mmol, 82%) as a colorless oil. Analytical data for **26**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.06 (d, $J = 9.0$ Hz, 1H), 7.52 (d, $J = 2.4$ Hz, 1H), 7.34 (dd, $J = 9.0$, 3.0 Hz, 1H), 7.18 (dd, $J = 16.8$, 10.8 Hz, 1H), 5.81 (d, $J = 17.4$ Hz, 1H), 5.63 (d, $J = 10.8$ Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 151.7, 146.6, 136.4, 131.1, 127.0, 121.4, 121.3, 121.1, 118.7 (q, $J^{C-F} = 319$ Hz); IR (ATR) 3118, 1530, 1424, 1350, 1207, 1131 cm^{-1}; HRMS (ESI) calcd for $C_9H_6NNaO_5F_3S$ ($M + Na^+$) 319.9816; found 319.9809.

Analytical data for **27**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.96 (d, $J = 8.4$ Hz, 1H), 7.57 (d, $J = 1.8$ Hz, 1H), 7.44 (dd, $J = 9.0$, 1.8 Hz, 1H),

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7.23 (dd, $J = 17.4, 11.4$ Hz, 1H), 6.75 (dd, $J = 17.4, 10.8$ Hz, 1H), 5.92 (d, $J = 17.4$ Hz, 1H), 5.75 (dd, $J = 17.4$, 0.6 Hz, 1H), 5.50 (dd, $J = 10.8$, 0.6 Hz, 1H), 5.49 (d, $J = 10.8$ Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 146.6, 142.4, 134.9, 134.1, 133.0, 126.5, 125.5, 125.1, 118.9, 118.2; IR (ATR) 1600, 1575, 1509, 1337, 914, 835 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{10}NO_2$ ($M + H^+$) 176.0711; found 176.0709.

4.5.7. Entry 9. 3-Ethenyl-4-nitrophenyl trifluoromethanesulfonate (**26**)

Cross coupling of **14** (399 mg, 1.14 mmol) with (ethenyl)tributyltin (480 mg, 1.52 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (16 mg, 0.023 mmol) in dioxane (2.5 mL) was performed as described under Conditions B. Solvent removal and chromatography (SiO_2/K_2CO_3 = 9:1, hexane/EtOAc, 97:3) gave **26** (232 mg, 0.781 mmol, 68%) as a faint yellow oil.

4.5.8. Entry 10. 3-Ethenyl-4-nitrophenyl trifluoromethanesulfonate (**26**) and 2,4-diethenyl-nitrobenzene (**27**)

Cross coupling of **14** (206 mg, 0.587 mmol) with (ethenyl)tributyltin (248 mg, 0.782 mmol) in the presence of $Pd(OAc)_2$ (2.6 mg, 0.012 mmol) and PPh_3 (6.2 mg, 0.024 mmol) in dioxane (2 mL) was performed as described under conditions B. Solvent removal and chromatography (SiO_2/K_2CO_3 = 9:1, hexane/EtOAc, 97:3) gave, in order of elution, **27** (4.3 mg, 0.024 mmol, 4%) as a colorless oil and **26** (120.4 mg, 0.405 mmol, 69%) as a faint yellow oil.

4.5.9. Entry 11. 3-Ethenyl-4-nitrophenyl trifluoromethanesulfonate (**26**), 2,4-diethenyl-nitrobenzene (**27**), and 2-bromo-4-ethenyl-nitrobenzene (**28**)

Cross coupling of **14** (75.2 mg, 0.22 mmol) with (ethenyl)tributyltin (85.5 mg, 0.27 mmol) in the presence of LiCl (28.1 mg, 0.66 mmol) and $Pd(PPh_3)_2Cl_2$ (3.6 mg, 0.005 mmol) in DMF (1 mL) was performed as described under Conditions C. Extractive work up and chromatography (hexane/EtOAc, 97:3) gave, in order of elution, **27** (5.5 mg, 0.03 mmol, 15%) followed by a mixture of **28** and **26** (23.8 mg, calculated from ^{1}H NMR spectrum: 18.0 mg of **28**, 37%, 5.8 mg of **26**, 9%) as a yellow oil. Spectral data for **28** from the mixture: ^{1}H NMR δ 7.86 (d, $J = 7.8$ Hz, 1H), 7.74 (d, $J = 1.2$ Hz, 1H), 7.45 (dd, $J = 8.4, 1.8$ Hz, 1H), 6.69 (dd, $J = 18.0, 11.4$ Hz, 1H), 5.90, (d, $J = 17.4$ Hz, 1H), 5.52 (d, $J = 10.8$ Hz, 1H); ^{13}C NMR δ 142.9, 136.4, 133.7, 132.6, 126.1, 125.5, 119.3, 115.1; IR (ATR) 3095, 1573, 1526, 1346, 1217, 1139 cm^{-1}; HRMS (ESI) calcd for $C_8H_6NNaO_2Br$ ($M + Na^+$) 249.9480; found 249.9478.

4.5.10. Entry 12. 4-Ethenyl-3-nitrophenyl trifluoromethanesulfonate (**29**) and 2,5-diethenyl-nitrobenzene (**30**).[46]

Cross coupling of **15** (110 mg, 0.32 mmol) with (ethenyl)tributyltin (134 mg, 0.42 mmol) in the presence of in the presence of PPh_3 (6.9 mg, 0.03 mmol) and $Pd(dba)_2$ (3.6 mg, 0.006 mmol) in dioxane (1.5 mL) was performed as described under Conditions A. Extractive work up and chromatography (hexane/EtOAc, 97:3) gave, in order of elution, **30** (1.2 mg, 0.0068 mmol, 2%) and **29** (63.3 mg, 0.21 mmol, 68%) both as colorless oils. Spectral data for **30** were in accordance with literature values. Analytical data for **29**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, $J = 2.4$ Hz, 1H), 7.74 (d, $J = 9.0$ Hz, 1H), 7.53 (dd, $J = 9.0, 2.4$ Hz, 1H), 7.18 (dd, $J = 17.4, 10.8$ Hz, 1H), 5.79 (d, $J = 16.8$ Hz, 1H), 5.61 (d, $J = 10.8$ Hz, 1H); ^{13}C NMR (600 MHz, $CDCl_3$) δ 148.0, 147.7, 133.8, 131.1, 130.5, 126.2, 121.0, 118.6 (q, $J^{C\text{-}F} = 319$ Hz), 118.0; ^{19}F NMR (565 MHz, $CDCl_3$) δ −72.7; IR (ATR) 3110, 1533, 1426, 1351, 1208, 1133 cm^{-1}; HRMS (ESI) calcd for $C_9H_6NNaO_5F_3S$ ($M + Na^+$) 319.9816; found 319.9810.

4.5.11. Entry 13. 4-Ethenyl-3-nitrophenyl trifluoromethanesulfonate (**29**) and 2,5-diethenyl-nitrobenzene (**30**).[56]

Cross coupling of **15** (406 mg, 1.16 mmol) with (ethenyl)tributyltin (489 mg, 1.54 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (16.3 mg, 0.023 mmol) in dioxane (2.5 mL) was performed as described under Conditions B., Solvent removal and chromatography (SiO_2/K_2CO_3 = 9:1, hexane/EtOAc, 97:3) gave, in order of elution, **30** (5.4 mg, 0.031 mmol, 3%) and **29** (280 mg, 0.942 mmol, 81%) both as a colorless oil.

4.5.12. Entry 14. 4-Ethenyl-3-nitrophenyl trifluoromethanesulfonate (**29**) and 2,5-diethenyl-nitrobenzene (**30**)

Cross coupling of **15** (221 mg, 0.630 mmol) with (ethenyl)tributyltin (245 mg, 0.773 mmol) in the presence of $Pd(OAc)_2$ (2.8 mg, 0.012 mmol) and PPh_3 (6.6 mg, 0.025 mmol) in dioxane (2 mL) was performed as described under Conditions B (31 h). Solvent removal and chromatography (SiO_2/K_2CO_3 = 9:1, hexane/EtOAc, 97:3) gave, in order of elution, **30** (2.4 mg, 0.014 mmol, 2%) and **29** (139 mg, 0.468 mmol, 74%) both as a colorless oil.

4.5.13. Entry 15. 4-Ethenyl-3-nitrophenyl trifluoromethanesulfonate (**29**), 2,5-diethenyl-nitrobenzene (**30**), and 2-bromo-5-ethenyl-nitrobenzene (**31**).[47]

Cross coupling of **15** (120 mg, 0.34 mmol) with (ethenyl)tributyltin (135 mg, 0.43 mmol) in the presence of LiCl (48.2 mg, 1.13 mmol) and $Pd(PPh_3)_2Cl_2$ (4.8 mg, 0.007 mmol) in DMF (1.5 mL) was performed as described under Conditions C. Extractive work up and chromatography (hexane/EtOAc, 97:3) gave, in order of elution, **30** (1.7 mg, 0.0097 mmol, 3%), **31** (27.8 mg, 0.12 mmol, 36%) as a colorless oil and a mixture of **29** and **15** (42 mg, calculated from ^{1}H NMR spectrum: **29** 22 mg, 23% and **15** 20 mg, 17%). Spectral data for **31** were in accordance with literature values.

4.5.14. Entry 16. 3-Ethenyl-2-nitrophenyl trifluoromethanesulfonate (**32**), 2-bromo-6-ethenyl-nitrobenzene (**33**), and 2,6-diethenyl-nitrobenzene (**34**)

Cross coupling of **16** (104 mg, 0.30 mmol) with (ethenyl)tributyltin (121 mg, 0.38 mmol) in the presence of in the presence of PPh_3 (6.7 mg, 0.03 mmol) and $Pd(dba)_2$ (3.7 mg, 0.006 mmol) in dioxane (1.5 mL) was performed as described under Conditions A. Extractive work up and chromatography (hexane/EtOAc, 97:3) gave, in order of elution, **34** (16.0 mg, 0.09 mmol, 30%) as a colorless oil, **33** (2.3 mg, 0.01 mmol, 3%) and **32** (52.9 mg, 0.18 mmol, 60%) as faint yellow solids.

Analytical data for **32**: Mp = 38–39 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, $J = 8.4$ Hz, 1H), 7.57 (t, $J = 8.4$ Hz, 1H), 7.41 (dd, $J = 8.4, 1.2$ Hz, 1H), 6.68 (dd, $J = 17.4, 10.8$ Hz, 1H), 5.91 (d, $J = 17.4$ Hz, 1H), 5.61 (d, $J = 11.4$ Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.0, 140.2, 133.2, 131.6, 128.6, 126.4, 121.9, 121.4, 118.4 (q, $J^{C\text{-}F} = 321$ Hz); IR (ATR) 3090, 1533, 1427, 1361, 1211, 1138 cm^{-1}; HRMS (ESI) calcd for $C_9H_6NNaO_5F_3S$ ($M + Na^+$) 319.9816; found 319.9809.

Analytical data for **33**: Mp = 42–44 °C; ^{1}H NMR δ 7.57 (d, $J = 7.8$ Hz, 1H), 7.56 (d, $J = 7.8$ Hz, 1H), 7.33 (t, $J = 7.8$ Hz, 1H), 6.57 (dd, $J = 16.8$, 11.4 Hz, 1H), 5.85 (d, $J = 16.8$ Hz, 1H), 5.51 (d, $J = 10.8$ Hz, 1H); ^{13}C NMR δ 150.1, 132.6, 131.6, 130.9, 129.0, 125.6, 120.8, 112.9; IR (ATR) 3077, 1557, 1521, 1460, 1365, 1187 cm^1; HRMS (ESI) calcd for $C_8H_6NNaO_2Br$ ($M + Na^+$) 249.9479; found 249.9454.

Analytical data for **34**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, $J = 7.1$ Hz, 2H), 7.43 (dd, $J = 8.6$, 6.7 Hz, 1H), 6.62 (dd, $J = 17.2$, 10.9 Hz, 2H), 5.83 (d, $J = 17.2$ Hz, 2H), 5.47 (d, $J = 10.9$ Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.9, 130.4, 130.1, 129.8, 126.1, 119.8; IR (ATR) 1513, 1365, 926, 850, 809, 731 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{10}NO_2$ ($M + H^+$) 176.0711; found 176.0709.

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4.5.15. Entry 17. 3-Ethenyl-2-nitrophenyl trifluoromethanesulfonate (**32**), 2-bromo-6-ethenyl-nitrobenzene (**33**), and 2,6-diethenyl-nitrobenzene (**34**)

Cross coupling of **16** (105 mg, 0.300 mmol) with (ethenyl)tributyltin (140 mg, 0.442 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (4.2 mg, 0.006 mmol) in 1,4-dioxane (1 mL) was performed as described under Conditions B. Solvent removal and chromatography (SiO_2/K_2CO_3 = 9:1 hexane/EtOAc, 19:1) gave, in order of elution, **34** (11.9 mg, 0.068 mmol, 23%) a colorless oil, **33** (0.9 mg, 0.004 mmol, 1%) and **32** (60.6 mg, 0.204 mmol, 68%).

4.5.16. Entry 18. 2-Bromo-6-ethenyl-nitrobenzene (**33**)

Cross coupling of **16** (119 mg, 0.34 mmol) with (ethenyl)tributyltin (138 mg, 0.44 mmol) in the presence of LiCl (45.6 mg, 1.08 mmol) and $Pd(PPh_3)_2Cl_2$ (5.0 mg, 0.007 mmol) in DMF (1.5 mL) was performed as described under Conditions C. Extractive work up and chromatography (hexane/EtOAc, 97:3) gave **33** (47.1 mg, 0.21 mmol, 61%) as an off-white solid.

4.5.17. Entry 19. 6-Ethenyl-2-nitrophenyl trifluoromethanesulfonate (**35**), 3-bromo-6-ethenylnitrobenzene (**36**), and 2,3-diethenyl-nitrobenzene (**25**)

Cross coupling of **17** (135 mg, 0.39 mmol) with (ethenyl)tributyltin (129 mg, 0.41 mmol) in the presence of in the presence of PPh_3 (8.2 mg, 0.03 mmol) and $Pd(dba)_2$ (4.5 mg, 0.008 mmol) in dioxane (2 mL) was performed as described under Conditions A. Extractive work up and chromatography (hexanes/EtOAc, 97:3) gave, in order of elution, **36** and **25** (8.5 mg, 1:1 mixture), 2-bromo-6-nitrophenol[27] (22.7 mg mixed with dba), and a mixture of **17** and **35** (95.1 mg). The latter fraction was repurified by chromatograhy (hexane/EtOAc, 97:3) to give in order of elution, **35** as a colorless oil (27.8 mg, 0.09 mmol, 24%) and **17** (12.3 mg, 0.04 mmol, 9%). Analytical data for **35**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (dd, J = 8.4, 1.8 Hz, 1H), 7.91 (dd, J = 8.4, 1.8 Hz, 1H), 7.48 (t, J = 8.4 Hz, 1H), 6.99 (dd, J = 17.4, 10.8 Hz, 1H), 5.95 (d, J = 17.4 Hz, 1H), 5.67 (d, J = 10.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.0, 137.8, 134.4, 132, 128.5, 128.0, 125.5, 121.4, 118.3 (q, $J^{C\text{-}F}$ = 319 Hz); IR (ATR) 3103, 1539, 1429, 1351, 1210, 1131 cm^{-1}; HRMS (ESI) calcd for $C_9H_6NNaO_5F_3S$ ($M + Na^+$) 319.9816; found 319.9808.

4.5.18. Entry 20. 3-Ethenyl-6-nitrophenyl trifluoromethanesulfonate (**35**), 3-bromo-6-ethenylnitrobenzene (**36**), and 2,3-diethenyl-nitrobenzene (**25**)

Cross coupling of **17** (117 mg, 0.334 mmol) with (ethenyl)tributyltin (159 mg, 0.501 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (5.1 mg, 0.007 mmol) in 1,4-dioxane (1 mL) was performed as described under Conditions B. Solvent removal and chromatography on (SiO_2/K_2CO_3 = 9:1, hexane/EtOAc, 97:3) gave, in order of elution, a mixture of **36** and **25** (16.1 mg, 1:2 mixture, 8% and 4% respectively calculated from ^{1}H NMR spectrum) and **35** (65.3 mg, 0.220 mmol, 66%) as a yellow oil.

4.5.19. Entry 21. 3-Bromo-2-ethenyl-nitrobenzene (**36**).[48]

Cross coupling of **17** (99.8 mg, 0.29 mmol) with (ethenyl)tributyltin (97.5 mg, 0.31 mmol) in the presence of LiCl (36.6 mg, 0.86 mmol) and $Pd(PPh_3)_2Cl_2$ (4.1 mg, 0.006 mmol) in DMF (1.5 mL) was performed as described under Conditions C. Extractive work up and chromatography (hexane/EtOAc, 9:1) gave, in order of elution, **36** as a yellow oil (28.3 mg, 0.12 mmol, 43%), 2-bromo-6-nitrophenol (7.4 mg, 0.03 mmol, 12%), and **17** (5.0 mg, 0.01 mmol, 5%). Spectral data for **35** were in accordance with literature values.

4.5.20. Entry 22. 5-Ethenyl-2-nitrophenyl trifluoromethanesulfonate (**37**)

Cross coupling of 5-bromo-1-nitrophenyl trifluoromethanesulfonate (**18**)[49] (100 mg, 0.29 mmol) with (ethenyl)tributyltin (95.1 mg, 0.30 mmol) in the presence of in the presence of (6.0 mg, 0.02 mmol) and $Pd(dba)_2$ (3.3 mg, 0.006 mmol) in dioxane (1.5 mL) was performed as described under Conditions A. Extractive work up and chromatography (hexane/EtOAc, 97:3) gave, in order of elution, a mixture of **18** and dba (17.2 mg) followed by **37** (34.6 mg, 0.12 mmol, 41%) as a yellow oil. Analytical data for **37**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.16 (d, J = 8.4 Hz, 1H), 7.55 (dd, J = 8.4, 1.8 Hz, 1H), 7.41 (d, J = 1.8 Hz, 1H), 6.76 (dd, J = 17.4, 10.8 Hz, 1H), 5.97 (d, J = 17.4 Hz, 1H), 5.63 (d, J = 10.8 Hz, 1H); ^{13}C NMR δ 145.2, 141.9, 140.1, 133.4, 127.1, 126.2, 121.4, 120.9, 118.6 (q, $J^{C\text{-}F}$ = 319 Hz); IR (ATR) 3114, 1587, 1529, 1429, 1341, 1209 cm^{-1}; HRMS (ESI) calcd for $C_9H_7NO_5F_3S$ ($M + H^+$) 297.9997; found 297.9994.

4.5.21. Entry 23. 5-Ethenyl-2-nitrophenyl trifluoromethanesulfonate (**37**), 4-bromo-2-ethenyl-nitrobenzene (**38**),[50] and 2,4-diethenyl-nitrobenzene (**27**)

Cross coupling of **18** (96.8 mg, 0.277 mmol) with (ethenyl)tributyltin (114 mg, 0.360 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (4.0 mg, 0.006 mmol) in 1,4-dioxane (0.7 mL) was performed as described under Conditions B. Solvent removal and chromatography (SiO_2/K_2CO_3 = 9:1, hexanes/EtOAc, 19:1) gave, in order of elution, a 6:1 mixture of **27** and **38** (5.1 mg, 0.024 mmol, 9% of **27** and 0.9 mg, 0.004 mmol, 14% of **38**, calculated from ^{1}H NMR spectrum) and **37** (60.9 mg, 0.205 mmol, 74%).

4.5.22. Entry 24. 5-Ethenyl-2-nitrophenyl trifluoromethanesulfonate (**37**) and 4-bromo-2-ethenyl-nitrobenzene (**38**)

Cross coupling of **18** (99.5 mg, 0.29 mmol) with (ethenyl)tributyltin (98.1 mg, 0.31 mmol) in the presence of LiCl (37.0 mg, 0.87 mmol) and $Pd(PPh_3)_2Cl_2$ (4.0 mg, 0.006 mmol) in DMF (1.5 mL) was performed as described under Conditions C. Extractive work up and chromatography (hexane/EtOAc, 9:1) gave, in order of elution, **38** (11.0 mg, 0.05 mmol, 17%) as an off-white solid, **18** (22.9 mg, 0.07 mmol, 22%) and **37** (19.4 mg, 0.07 mmol, 23%). Spectral data for **38** were in accordance with literature values.

4.5.23. Entry 25. 4-Ethenyl-2-nitrophenyl trifluoromethanesulfonate (**39**)

Cross coupling of **19** (103 mg, 0.29 mmol) with (ethenyl)tributyltin (112 mg, 0.35 mmol) in the presence of in the presence of (6.8 mg, 0.03 mmol) and $Pd(dba)_2$ (3.4 mg, 0.006 mmol) in dioxane (1.5 mL) was performed as described under Conditions A. Extractive work up and chromatography (hexane/EtOAc, 9:1) gave, in order of elution, a mixture of **19** and 5-bromo-2-nitrophenol (11.3 mg) followed by **39** as a yellow oil mixed with dibenzylideneacetone (34.6 mg, 0.12 mmol, 41% of **39**, calculated from ^{1}H NMR spectrum).

4.5.24. Entry 26. 4-Ethenyl-2-nitrophenyl triflate (**39**), 5-bromo-2-ethenyl-nitrobenzene (**40**), and 2,5-diethenyl-nitrobenzene (**30**)

Cross coupling of **19** (122 mg, 0.348 mmol) with (ethenyl)tributyltin (162 mg, 0.512 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (4.9 mg, 0.007 mmol) in 1,4-dioxane (2.5 mL) was performed as described under Conditions B. Solvent removal and chromatography (SiO_2/K_2CO_3 = 9:1, hexane/EtOAc, 98:2) gave, in order of elution, an inseparable 1:1.4 mixture of **40** and **30** (7.0 mg; calculated from ^{1}H NMR spectrum: 2.4 mg of **40**, 3%; 4.6 mg of **30**, 8%), **20** (11.1 mg, 0.032 mmol, 9%), and **39** (69.6 mg, 0.236 mmol, 67%) as a colorless oil. Analytical data for **39**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.15 (d, J = 2.2 Hz, 1H), 7.72 (dd, J = 8.6, 2.6 Hz, 1H), 7.41 (d, J = 8.5 Hz, 1H), 6.74 (dd, J = 17.5, 10.9 Hz, 1H), 5.92 (d, J = 17.6 Hz, 1H), 5.55 (d, J = 10.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.7, 140.3, 139.2, 133.1, 132.2, 124.3, 123.8, 119.1, 118.5 (q, $J^{C\text{-}F}$ = 319 Hz); IR (ATR) 1526, 1425, 1345, 1209, 1134, 944, 836 cm^{-1}; HRMS (ESI) calcd for

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$C_9H_7NO_5F_3S$ ($M + H^+$) 297.9997; found 297.9994.

4.5.25. Entry 27. 5-Bromo-2-ethenyl-nitrobenzene (**40**)

Cross coupling of **20** (111 mg, 0.32 mmol) with (ethenyl)tributyltin (131 mg, 0.41 mmol) in the presence of LiCl (44.5 mg, 0.86 mmol) and $Pd(PPh_3)_2Cl_2$ (4.2 mg, 0.006 mmol) in DMF (1.5 mL) was performed as described under Conditions C. Extractive work up and chromatography (hexane/EtOAc, 9:1) gave **40** as a yellow solid (56.3 mg, 0.25 mmol, 78%). Analytical data for **40**: Mp = 40–41 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.07 (d, J = 2.4 Hz, 1H), 7.70 (dd, J = 8.4, 2.4 Hz, 1H), 7.51 (d, J = 8.4 Hz, 1H), 7.11 (dd, J = 17.4, 11.4 Hz, 1H), 5.76 (d, J = 17.4 Hz, 1H), 5.55 (d, J = 11.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.0, 136.1, 132.2, 131.5, 129.7, 127.3, 121.4, 119.7; IR (ATR) 3097, 1552, 1514, 1341, 1149 cm^{-1}; HRMS (ESI) calcd for $C_8H_6NNaO_2Br$ ($M + Na^+$) 249.9479; found 249.9455.

4.5.26. Entry 28. 2-Ethenyl-4-nitrophenyl trifluoromethanesulfonate (**41**)

Cross coupling of 2-bromo-4-nitrophenyl trifluoromethanesulfonate (**20**)[51] (102 mg, 0.29 mmol) with (ethenyl) tributyltin (116 mg, 0.37 mmol) in the presence of in the presence of PPh_3 (6.5 mg, 0.03 mmol) and $Pd(dba)_2$ (4.1 mg, 0.007 mmol) in dioxane (1.5 mL) was performed as described under Conditions A. Extractive work up and chromatography (hexane/EtOAc, 8:2) gave, in order of elution, a mixture of **20** and **41** (45.1 mg) followed by 2-bromo-4-nitrophenol[40] (5.2 mg, 0.02 mmol, 7%). The mixture was repurified by chromatographed (hexane/EtOAc, 97:3) to afford, in order of elution, **41** (19.3 mg, 0.06 mmol, 22%) as a light pink oil and **20** (7.0 mg, 0.02 mmol, 7%). Analytical data for **41**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.53 (d, J = 3.0 Hz, 1H), 8.21 (dd, J = 9.0, 2.4 Hz, 1H), 7.48 (d, J = 9.0 Hz, 1H), 6.94 (dd, J = 17.4, 11.4 Hz, 1H), 6.04 (d, J = 17.4 Hz, 1H), 5.70 (d, J = 11.4 Hz, 1H); ^{13}C (150 MHz, $CDCl_3$) δ 149.9, 147.2, 132.7, 127.3, 124.0, 122.9, 122.7, 121.7, 118.5 (q, J^{C-F} = 319 Hz); IR (ATR) 3107, 1536, 1424, 1347, 1209, 1134 cm^{-1}; HRMS (ESI) calcd for $C_9H_7NO_5F_3S$ ($M + H^+$) 297.9997; found 297.9994.

4.6. Entry 29 – conditions B

4.6.1. 2-Ethenyl-4-nitrophenyl trifluoromethanesulfonate (**41**)

Cross coupling of **20** (89.1 mg, 0.255 mmol) with (ethenyl)tributyltin (105 mg, 0.331 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (3.6 mg, 0.005 mmol) in 1,4-dioxane (0.8 mL) was performed as described under Conditions B. Solvent removal and chromatography (SiO_2/K_2CO_3 = 9:1, hexane/EtOAc, 98:2) gave **41** (71.4 mg, 0.240 mmol, 94%) as a yellow oil.

4.6.2. Entry 30. 3-Bromo-4-ethenyl-nitrobenzene (**42**)

Cross coupling of **20** (110 mg, 0.32 mmol) with (ethenyl)tributyltin (138 mg, 0.43 mmol) in the presence of LiCl (42.6 mg, 1.0 mmol) and $Pd(PPh_3)_2Cl_2$ (4.5 mg, 0.006 mmol) in DMF (1.5 mL) was performed as described under Conditions C. Extractive work up and chromatography (hexane/EtOAc, 85:15) gave a mixture of **20** and **42**. The mixture was repurified by chromatography (hexanes/EtOAc, 97:3) to afford in order of elution, **42** (40.7 mg, 0.18 mmol, 57%) as a yellow oil, **20** (8.7 mg, 0.02 mmol, 8%), and 3-bromo-4-nitrophenol (11.1 mg, 0.05 mmol, 16%). Analytical data for **42**: ^{1}H NMR δ 8.43 (d, J = 2.4 Hz, 1H), 8.14 (ddd, J = 8.4, 2.4, 0.6 Hz, 1H), 7.69 (d, J = 9.0 Hz, 1H), 7.09 (dd, J = 17.4, 11.4 Hz, 1H), 5.88 (d, J = 18.0 Hz, 1H), 5.60 (dd, J = 10.8, 0.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 147.2, 143.7, 134.3, 128.2, 127.1, 123.4, 122.4, 120.9; IR (ATR) 3099, 1520, 1342, 1116, 1035 cm^{-1}; HRMS (ESI) calcd for $C_8H_6NNaO_2Br$ ($M + Na^+$) 249.9479; found 251.9456.

4.6.3. Entry 31. 2-Ethenyl-5-nitrophenyl trifluoromethanesulfonate (**43**)

Cross coupling of **21** (74.7 mg, 0.21 mmol) with (ethenyl)tributyltin (83.2 mg, 0.26 mmol) in the presence of in the presence of PPh_3 (5.0 mg, 0.02 mmol) and $Pd(dba)_2$ (2.7 mg, 0.005 mmol) in dioxane (1.5 mL) was performed as described under Conditions A. Extractive work up and chromatography (hexane/EtOAc, 97:3) gave, in order of elution, **21** (14.8 mg, 0.04 mmol, 20%) and **43** (30.2 mg, 0.10 mmol, 48%) as a yellow oil. Analytical data for **43**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25 (dd, J = 8.4, 1.8 Hz, 1H), 8.17 (d, J = 1.8 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H), 6.98 (dd, J = 17.4, 10.8 Hz, 1H), 6.05 (d, J = 17.4 Hz, 1H), 5.75 (d, J = 10.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 147.4, 145.9, 137.4, 127.8, 127.5, 123.2, 122.9, 118.5 (q, J^{C-F}=319 Hz), 117.7; IR (ATR) 3118, 1528, 1425, 1346, 1210, 1132 cm^{-1}; HRMS (ESI) calcd for $C_9H_6NNaO_5F_3S$ ($M + Na^+$) 319.9816; found 319.9809.

4.6.4. Entry 32. 2-Ethenyl-5-nitrophenyl trifluoromethanesulfonate (**43**)

A solution of **21** (162 mg, 0.463 mmol) in dioxane (2 mL) was treated with (ethenyl)tributyltin (191 mg, 0.602 mmol) in the presence of $PdCl_2(PPh_3)_2$ (13.0 mg, 0.019 mmol), was performed as described under Conditions B. Solvent removal and chromatography (SiO_2/K_2CO_3 = 9:1, hexane/EtOAc, 19:1) **43** (122 mg, 0.412 mmol, 89%) as a pale yellow oil.

4.6.5. Entry 33. 2-Ethenyl-5-nitrophenyl trifluoromethanesulfonate (**43**) and 4-bromo-3-ethenyl-nitrobenzene (**44**)

Cross coupling of **21** (85.9 mg, 0.25 mmol) with (ethenyl)tributyltin (98.2 mg, 0.31 mmol) in the presence of LiCl (32.2 mg, 0.76 mmol) and $Pd(PPh_3)_2Cl_2$ (3.6 mg, 0.005 mmol) in DMF (1.5 mL) was performed as described under Conditions C. Extractive work up and chromatography (hexane/EtOAc, 97:3) gave, in order of elution, **44** (3.8 mg, 0.02 mmol, 7%) as an off-white solid, **21** (27.0 mg, 0.08 mmol, 31%) and **43** (22.4 mg, 0.08 mmol, 31%). Analytical data for **44**: Mp = 38–40 °C; ^{1}H NMR δ 8.39 (d, J = 2.4 Hz, 1H), 7.97 (dd, J = 8.4, 2.4 Hz, 1H), 7.74 (d, J = 9.0 Hz, 1H), 7.06 (dd, J = 17.4, 10.8 Hz, 1H), 5.99 (d, J = 17.4 Hz, 1H), 5.56 (d, J = 10.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.5, 139.1, 134.2, 133.9, 131.4, 123.1, 121.5, 119.7; IR (ATR) 3099, 2926, 1525, 1341, 1030 cm^1; HRMS (ESI) calcd for $C_8H_6NNaO_2Br$ ($M + Na^+$) 249.9479; found 249.9452.

4.6.6. Entry 34. 3-Ethenyl-5-nitrophenyl trifluoromethanesulfonate (**45**)

Cross coupling of **22** (106 mg, 0.30 mmol) with (ethenyl)tributyltin (130 mg, 0.41 mmol) in the presence of in the presence of (6.4 mg, 0.02 mmol) and $Pd(dba)_2$ (3.4 mg, 0.006 mmol) in dioxane (1.5 mL) was performed as described under Conditions A. Extractive work up and chromatography (hexane/EtOAc, 97:3) gave, in order of elution, **22** (4.1 mg, 0.01 mmol, 4%) and **45** (70.0 mg, 0.24 mmol, 78%) as a colorless oil. Analytical data for **45**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30 (t, J = 1.8 Hz, 1H), 8.02 (t, J = 1.8 Hz, 1H), 7.61 (t, J = 1.8 Hz, 1H), 6.78 (dd, J = 17.4, 10.8 Hz, 1H), 5.98 (d, J = 17.4 Hz, 1H), 5.61 (d, J = 10.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.4, 149.2, 141.7, 133.2, 124.6, 120.6, 119.8, 118.6 (q, J^{C-F} = 319 Hz), 115.6; IR (ATR) 3103, 1540, 1425, 1348, 1213, 1132 cm^{-1}; HRMS (ESI) calcd for $C_9H_7NO_5F_3S$ ($M + H^+$) 297.9997; found 297.9997.

4.6.7. Entry 35. 3-Ethenyl-5-nitrophenyl trifluoromethanesulfonate (**45**)

Cross coupling of **22** (104 mg, 0.296 mmol) with (ethenyl)tributyltin (122 mg, 0.385 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (4.3 mg, 0.006 mmol) in 1,4-dioxane (1 mL) was performed as described under Conditions B. Solvent removal and chromatography (SiO_2/K_2CO_3 = 9:1, hexane/EtOAc, 98:2) gave **45** (78.5 mg, 0.264 mmol, 89%) as a yellow oil.

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*4.6.8. Entry 36. 3-Bromo-5-ethenyl-nitrobenzene (**46**)*

Cross coupling of **22** (109 mg, 0.31 mmol) with (ethenyl)tributyltin (139 mg, 0.44 mmol) in the presence of LiCl (45.0 mg, 1.1 mmol) and $Pd(PPh_3)_2Cl_2$ (4.7 mg, 0.007 mmol) in DMF (1.5 mL) was performed as described under Conditions C. Extractive work up and chromatography (hexane/EtOAc, 97:3) gave **46** (47.1 mg, 0.21 mmol, 66%) as an off-white solid. Analytical data for **46**: Mp = 37–39 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 (t, J = 1.8 Hz, 1H), 8.17 (t, J = 1.8 Hz, 1H), 7.83 (t, J = 1.8 Hz, 1H), 6.71 (dd, J = 17.4, 10.8 Hz, 1H), 5.91 (d, J = 17.4 Hz, 1H), 5.50 (d, J = 11.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.0, 140.8, 134.8, 133.6, 125.3, 122.9, 119.6, 118.5; IR (ATR) 3079, 1531, 1339, 1301, 1214 cm^1; HRMS (ESI) calcd for $C_8H_6NNaO_2Br$ ($M + Na^+$) 249.9479; found 249.9452.

*4.6.9. 2-Bromo-3-ethenyl-nitrobenzene (**24**), 2,3-Diethenyl-nitrobenzene (**25**), 3-bromo-2-ethenyl-nitrobenzene (**36**)*

Cross coupling of 2,3-dibromo-1-nitrobenzene (**47**)[29] (83.0 mg, 0.296 mmol) with (ethenyl)tributyltin (126 mg, 0.397 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (0.004 mg, 0.006 mmol) in dioxane (2 mL) was performed as described under Conditions B. Solvent removal and chromatography (SiO_2/K_2CO_3 = 9:1, hexane/EtOAc, 98:2) gave, in order of elution, an inseparable 1.0:0.9 mixture of **25** and **36** (23.2 mg, calculated from ^{1}H NMR spectrum: 10.2 mg **25**, 20% and 13.0 mg **36**, 18%) as a colorless oil and **24** (10.0 mg, 0.040 mmol, 14%) as a colorless oil.

*4.6.10. 4-Ethenyl-2-nitrophenyl trifluoromethanesulfonate (**39**), 4-Ethenyl-2-nitrophenol (**49**),[52] and 2,5-diethenyl-1-nitrobenzene (**30**)*

Cross coupling of 4-iodo-6-nitrophenyl trifluoromethane sulfonate (**48**)[53] (102 mg, 0.26 mmol) with (ethenyl)tributyltin (106 mg, 0.33 mmol) in the presence of in the presence of PPh_3 (5.8 mg, 0.02 mmol) and $Pd(dba)_2$ (3.5 mg, 0.006 mmol) in dioxane (1.5 mL) was performed as described under Conditions A. Extractive work up and chromatography (hexane/EtOAc, 97:3) gave, in order of elution, a mixture of **49** and **30** (8.2 mg; 5.8 mg, 0.035 mmol, 14% of **49** and 2.4 mg, 0.014 mmol, 5% of **30**, calculated from ^{1}H NMR spectrum) followed by **39** (29.5 mg, 0.099 mmol, 38%) as a yellow oil.

*4.6.11. 4-Ethenyl-2-nitrophenyl trifluoromethanesulfonate (**39**) and 2,5-diethenyl-1-nitrobenzene (**30**)*

Cross coupling of **48** (205 mg, 0.517 mmol) with (ethenyl)tributyltin (213 mg, 0.671 mmol) in the presence of $PdCl_2(PPh_3)_2$ (7.3 mg, 0.010 mmol) in dioxane (2 mL) was performed as described under Conditions B. Solvent removal and chromatography on (SiO_2/K_2CO_3 = 9:1, hexane/EtOAc, 19:1) gave, in order of elution, **30** (10.0 mg, 0.057 mmol, 8%) and **39**(133 mg, 0.449 mmol, 87%) as a faint yellow oil.

*4.6.12. 4-Ethenyl-2-nitrophenyl trifluoromethanesulfonate (**39**), 5-iodo-2-ethenyl-nitrobenzene (**50**) and 5-iodo-2-hydroxynitrobenzene (**51**)*

Cross coupling of **48** (116 mg, 0.29 mmol) with (ethenyl)tributyltin (120 mg, 0.38 mmol) in the presence of LiCl (39.7 mg, 0.94 mmol) and $Pd(PPh_3)_2Cl_2$ (4.1 mg, 0.006 mmol) in DMF (1.5 mL) was performed as described under Conditions C. Extractive work up and chromatography (hexane/EtOAc, 97:3) gave in order of elution, **50** (3.2 mg, 0.01 mmol, 4%) as a brown oil, **51** (8.7 mg, 0.03 mmol, 11%), and a mixture of **39** and **48** (67.1 mg; 43.7 mg, 0.147 mmol, 50% of **39** and 23.3 mg, 0.059 mmol, 20% of **48**, calculated from ^{1}H NMR spectrum). Analytical data for **50**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25 (d, J = 1.8 Hz, 1H), 7.89 (dd, J = 7.8, 1.8 Hz, 1H), 7.35 (d, J = 7.8 Hz, 1H), 7.10 (dd, J = 16.8, 10.8 Hz, 1H), 5.77 (d, J = 16.8 Hz, 1H), 5.52 (d, J = 10.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.0, 142.0, 133.0, 132.8, 131.6, 129.8, 119.7, 91.8; IR (ATR) 3094, 2925, 1519, 1341, 1261, 1086 cm^{-1}; HRMS (ESI) calcd for $C_8H_6NNaO_2I$ ($M + Na^+$) 297.9341; found 297.9333.

*4.6.13. 5-Bromo-2-trifluoromethanesulfonylacetophenone (**52**).[54]*

To a solution of 5-bromo-1-hydroxyacetophenone[50] (381 mg, 1.77 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added pyridine (275 μL, 3.41 mmol) and Tf_2O (325 μL, 1.92 mmol). The mixture was removed from the cold bath and allowed to stir at ambient temperature for 1 h. The resulting mixture was filtered through a small plug of silica gel and the solvent was removed under reduced pressure from the filtrate to give **52** (590 mg, 1.70 mmol, 96%) as a pale orange oil. The compound was used as such without further purification. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (d, J = 2.3 Hz, 1H), 7.69 (dd, J = 8.8 Hz, 2.3 Hz, 1H), 7.21 (d, J = 8.8 Hz, 1H), 2.60 (s, 3H); ^{13}C NMR NMR (150 MHz, $CDCl_3$) δ 195.1, 145.5, 136.4, 133.5, 133.4, 124.3, 122.0, 118.4 (d, J^{C-F} = 319 Hz) 29.2; IR (ATR) 1701, 1424, 1202, 1133, 879, 796 cm^{-1}; HRMS (ESI) calcd for $C_9H_7BrO_4F_3S$ ($M + H^+$) 346.9200; found 346.9177.

*4.6.14. 5-Ethenyl-2-trifluoromethanesulfylacetophenone (**53**)*

Cross coupling of **52** (101 mg, 0.29 mmol) with (ethenyl)tributyltin (116 mg, 0.37 mmol) in the presence of in the presence of PPh_3 (6.4 mg, 0.02 mmol) and $Pd(dba)_2$ (3.8 mg, 0.007 mmol) in dioxane (1.5 mL) was performed as described under Conditions A. Extractive work up and chromatography (hexane/EtOAc, 9:1) gave **53** (11.6 mg, 0.04 mmol, 14%) as a colorless oil. ^{1}H NMR δ 7.78 (d, J = 2.4 Hz, 1H), 7.61 (dd, J = 8.4, 2.4 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 6.73 (dd, J = 17.4, 10.8 Hz, 1H), 5.83 (d, J = 17.4 Hz, 1H), 5.44 (d, J = 10.8 Hz, 1H), 2.65 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.6, 145.9, 138.1, 134.3, 132.3, 130.7, 128.3, 122.9, 118.5 (q, J^{C-F} = 319 Hz), 117.3, 29.6; IR (ATR) 3096, 1698, 1421, 1202, 1134 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_{10}F_3O_4S$ ($M + H^+$) 295.0252; found 295.0249.

*4.6.15. 5-Ethenyl-2-trifluoromethanesulfonylacetophenone (**53**)*

Cross coupling of **52** (70.2 mg, 0.202 mmol) with (ethenyl)tributyltin (83.4 mg, 0.263 mmol) in the presence of $PdCl_2(PPh_3)_2$ (3.0 mg, 0.004 mmol) in dioxane (0.6 mL) was performed as described under Conditions B. Solvent removal and chromatography (SiO_2/K_2CO_3 = 9:1, hexane/EtOAc, 19:1) **53** (33.8 mg, 0.115 mmol, 57%) as a colorless oil.

*4.6.16. 5-Bromo-2-ethenylacetophenone (**54**)*

Cross coupling of **52** (112 mg, 0.32 mmol) with (ethenyl)tributyltin (129 mg, 0.41 mmol) in the presence of LiCl (43.5 mg, 1.03 mmol) and $Pd(PPh_3)_2Cl_2$ (4.8 mg, 0.007 mmol) in DMF (1.5 mL) was performed as described under Conditions C. Extractive work up and chromatography (hexane/EtOAc, 8:2) gave **54** (42.6 mg, 0.19 mmol, 58%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 2.0 Hz, 1H), 7.57 (dd, J = 8.0, 1.6 Hz, 1H), 7.43 (d, J = 8.8 Hz, 1H), 7.09 (dd, J = 17.2, 11.2 Hz, 1H), 5.64 (dd, J = 17.2, 0.8 Hz, 1H), 5.37 (dd, J = 11.2, 1.2 Hz, 1H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.5, 138.9, 136.4, 134.7, 134.4, 131.3, 129.1, 121.1, 117.4, 29.8; IR (ATR) 3088, 1686, 1472, 1355, 1235, 830 cm^{-1}; HRMS (ESI) calcd for $C_{10}H_{10}BrO$ ($M + H^+$) 224.9915; found 224.9914.

*4.6.17. 2-Ethenyl-4-methoxyphenyl trifluoromethanesulfonate (**56**).[55]*

Cross coupling of 2-bromo-4-methoxyphenyl trifluoromethane sulfonate (**55**)[56] (106 mg, 0.32 mmol) with (ethenyl)tributyltin (126 mg, 0.40 mmol) in the presence of PPh_3 (7.0 mg, 0.03 mmol) and $Pd(dba)_2$ (3.7 mg, 0.006 mmol) in dioxane (1.5 mL) was performed as described under Conditions A. Extractive work up and chromatography (hexane/EtOAc, 9:1) gave **56** (29.6 mg, 0.10 mmol, 33%) as a colorless oil. Spectral data for **56** were in accordance with

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literature values.

*4.6.18. 2-Ethenyl-4-methoxyphenyl trifluoromethanesulfonate (**56**) and 3-bromo-4-ethenylanisole (**57**).*[57]

Cross coupling of **55** (103 mg, 0.31 mmol) with (ethenyl)tributyltin (119 mg, 0.38 mmol) in the presence of LiCl (38.9 mg, 0.92 mmol) and $Pd(PPh_3)_2Cl_2$ (4.5 mg, 0.006 mmol) in DMF (2 mL) was performed as described under Conditions C. Extractive work up and chromatography (hexanes/EtOAc, 9:1) gave, in order of elution, **56** (26.3 mg, 0.12 mmol, 39%) as a faint orange oil and **57** (3.3 mg, 0.01 mmol, 4%). Spectral data for **57** were in accordance with literature values.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.tet.2018.02.051.

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