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Palladium-Catalyzed Modular Assembly of Electron-Rich Alkenes, Dienes, Trienes, and Enynes from (*E*)-1,2-Dichlorovinyl Phenyl Ether

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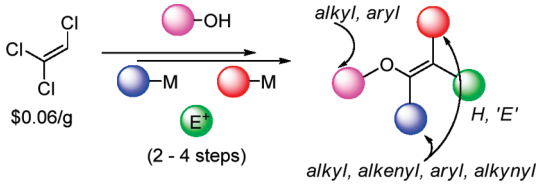

We have devised a modular construction of electron-rich alkene derivatives from trichloroethylene (TCE). The three C−Cl bonds of TCE have sufficiently different reactivities that they can be sequentially and selectively functionalized. Following the substitution of one chlorine by phenol to generate (*E*)-1,2-dichlorovinyl ether, the C^1-Cl group next participates in palladium-catalyzed cross-coupling reactions with a variety of organometallic reagents. Subsequently, the C^2-Cl group can engage in cross-couplings, while the C^2-H may be deprotonated and quenched with an electrophile. Thus, isomerically pure tri- and tetrasubstituted electron-rich alkenes may be accessed in as few as two steps from simple and inexpensive starting materials. This method is ideally suited for diversity-oriented synthesis of highly conjugated molecules of interest as chromophores or as potential molecular electronics. It also gives access to diverse building blocks for further synthetic elaboration into high-value compounds.

Introduction

Tri- and tetrasubstituted alkenes are ubiquitous structures in organic chemistry, being found in biologically active compounds such as the anticancer drug (*Z*)-tamoxifen.[1] A significant amount of research has gone into developing syntheses of tri- and tetrasubstituted alkenes.[2] Alkenes[3] and dienes[4] bearing electron-donating groups (e.g., enol ethers) have many uses in organic synthesis, and one would expect that methods for their efficient preparation would be common. However, there have been few reports on the metal-catalyzed synthesis of such electron-rich alkenes, in contrast to the plethora of methods for assembling fully carbon-substituted alkenes.[2a,b] Even so, this topic has begun to receive more attention in the recent literature.[5]

Organ has pointed out that while most chemists think of alkene synthesis in terms of forming the C=C bond, a potentially better approach would be to build outward from a suitable functionalized alkene unit.[6] Based on this idea, Organ et al. developed one-pot methods for selective and

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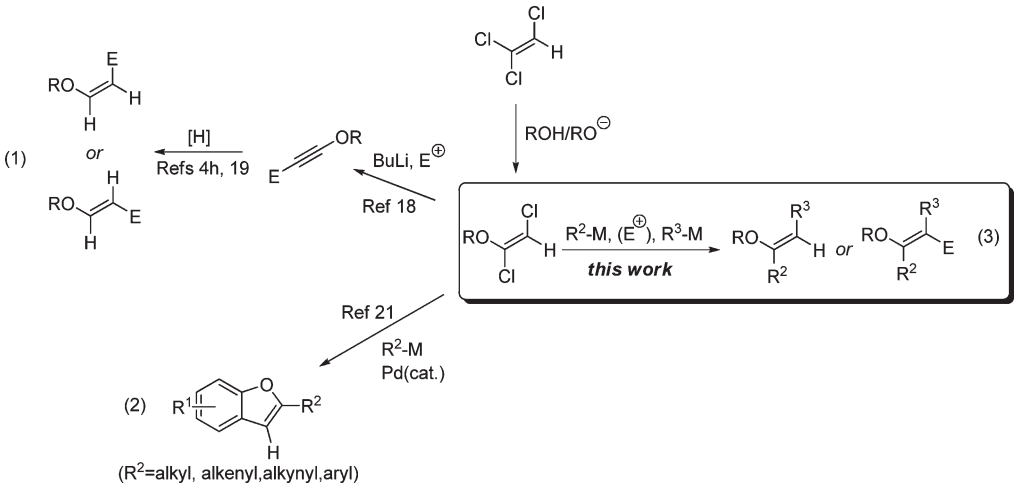
SCHEME 1. Uses of Dichlorovinyl Ethers Derived from Trichloroethylene and Alcohols



sequential C−C bond formation reactions of 2,3-dibromo- or 2,3-dichloropropene or (*E*)-2-chloro-1-iodoethylene and have explored the use of these "olefin templates" in target-oriented syntheses.[6,7] Others have likewise exploited the olefin template concept. Yoshida et al. devised a small library of tamoxifen analogues[8] employing a vinyl pyridylsilane template.[9] Nishihara and co-workers obtained tri- and tetrasubstituted alkenes from alkynyl pinacolatoboronates via zirconation and sequential cross-coupling reactions.[10] A series of papers by Ogilvie and co-workers has described the stepwise elaboration of α,β-dihalo-α,β-unsaturated esters leading to either tri- or tetrasubstituted alkenes.[11]

Many routes to electron-rich alkenes involve metal-promoted addition across an alkyne. Jiang et al. prepared 2-halo enol acetates via the silver-catalyzed reaction of terminal acetylenes with *N*-halosuccinimides in the presence of acetic anhydride.[12] 1,2-Disubstituted arylvinyl ethers[13] and sulfides[14] have been synthesized via the gold-catalyzed addition of phenol- or copper-catalyzed addition of thiophenol across an internal alkyne. Kato, Akita, and co-workers recently published the palladium-catalyzed carbonylative reaction of alkynes with methanol to give a variety of "push−pull alkenes" (β-alkoxy-substituted α,β-unsaturated esters).[15] These processes were generally high yielding and required as little as one step from commercially available materials. However, the reported regioselectivity was often highly substrate-dependent when the alkyne substrate was unsymmetrical.

Trichloroethylene is a very inexpensive two-carbon starting material.[16] Much of the interest in its chemistry derives from the ease with which it may be converted to dichloroacetylene.[17] Alcohols will add across dichloroacetylene, but the resultant (*E*)-dichlorovinyl ethers are generally treated in situ with excess *n*-butyllithium and quenched to give acetylenic ethers (Scheme 1, eq 1).[18] The alkynes in turn may be reduced or otherwise functionalized to give either (*E*)- or (*Z*)-enol ethers.[4hh,19] These methods, while both general and useful, "waste" the stereo- and regiochemical information inherent in the initial (*E*)-dichlorovinyl ethers.

A recent report noted that TCE underwent base-promoted elimination/addition in the presence of iodide, affording 1-iodo-1,2-dichloroethylene, which then underwent palladium-catalyzed methoxycarbonylation of the C−I group.[20] We reasoned that the three C−Cl bonds of TCE might

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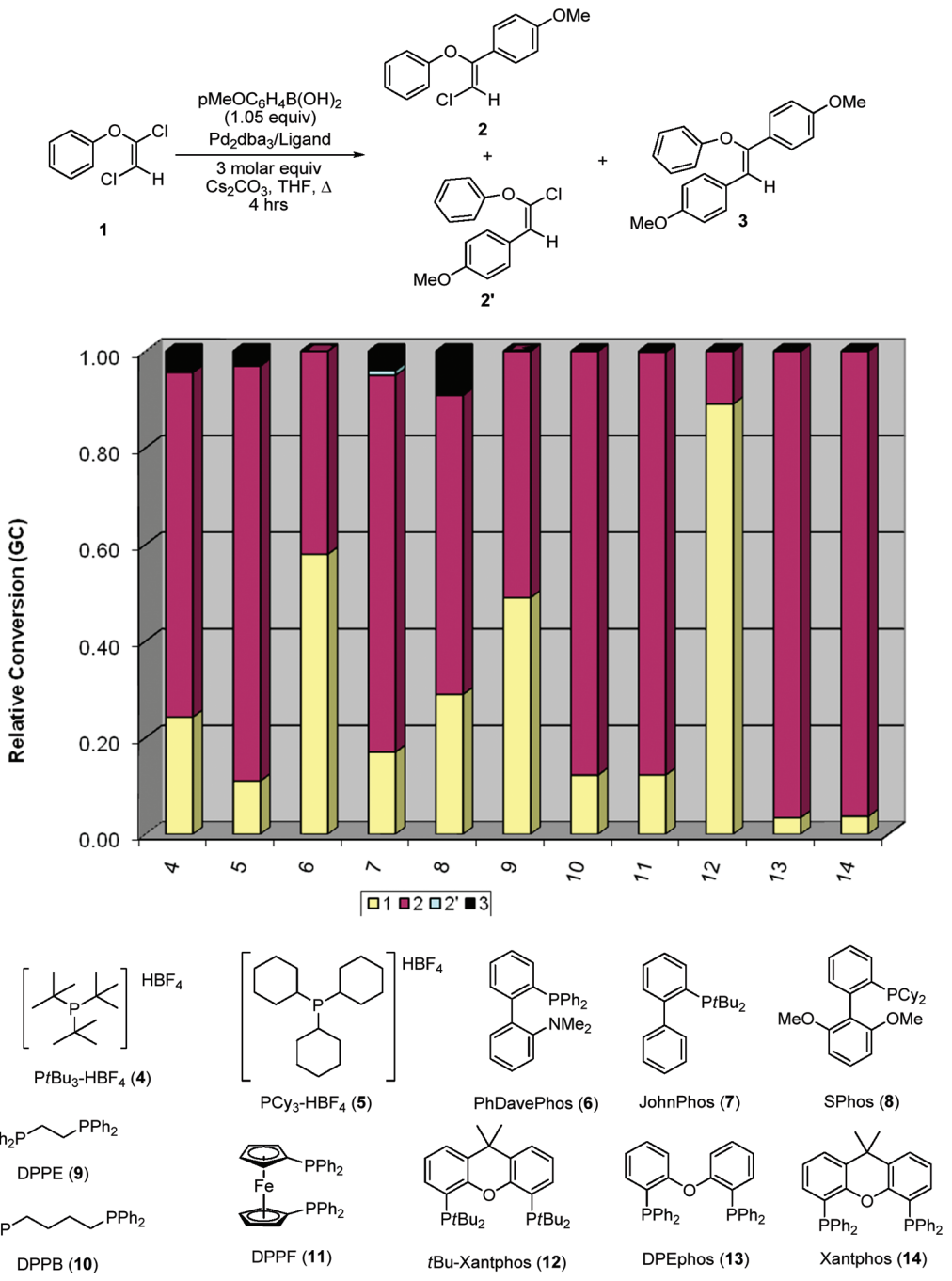
SCHEME 2. Ligand Screen for C[1]-Selective Cross-Coupling Reactions



Conditions: 0.2 M solution of **1** in THF, 65 °C, 1.05 equiv of boronic acid, 3.0 molar equiv of Cs_2CO_3, 2.5 mol % of Pd_2dba_3, 7.5 mol % of **4**−**6**, or 5 mol % of **7**−**14**, 4 h. The data for each experiment are normalized to 1.

actually be sufficiently different that they could be sequentially addressed by appropriately chosen chemistry and that the vinylic C−H could likewise be a handle for controlled synthetic elaboration. We found that benzofurans may be obtained by one-pot Suzuki coupling/direct arylation of dichlorovinyl ethers with organoboron compounds (Scheme 1, eq 2).[21] We now describe the simple, general, and modular assembly of both tri- and tetrasubstituted alkenes via an operationally simple combination of palladium-catalyzed cross-coupling reactions and vinyllithium chemistry (Scheme 1, eq 3). Our results demonstrate that trichloroethylene is an inexpensive and versatile tetrafunctionalizable two-carbon linchpin for the direct, rapid, and stereocontrolled synthesis of high-value products or molecular platforms for numerous[6,22] synthetic transformations.

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Results and Discussion

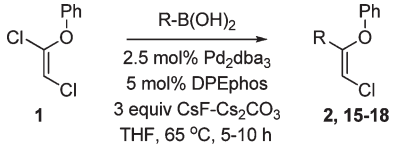
Dichlorovinyl ethers derived from aliphatic alcohols have been reported to be somewhat labile, even under the basic conditions required for cross-couplings,[23] so we decided to develop this chemistry using phenol-based vinyl ethers. We[21] and others[24] have previously reported the reactions of various phenols with TCE to obtain the corresponding aryl 1,2-dichlorovinyl ethers.

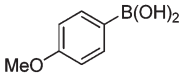
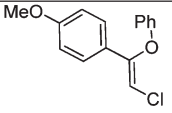
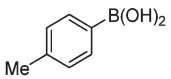
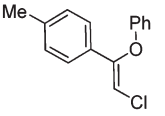
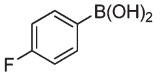
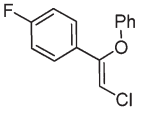
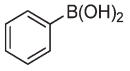
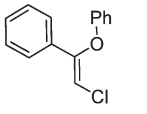
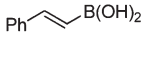
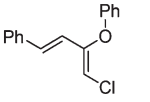
Selective C^1−Cl Cross Coupling. The selective functionalization of 1,1-dichloroalkenes[25] has been looked at by Minato and Tamao[26] and, more recently, by both Negishi[27] and Roulland.[28] The regioselective functionalization of 1,2-dihaloalkenes has been less explored,[25] likely because they are more challenging to prepare. Most examples of regioselective cross-coupling reactions of 1,2-dihaloalkenes involve α,β-unsaturated esters[25,29] with only a few exceptions.[30]

To find conditions for C^1 site-selective Suzuki−Miyaura cross-coupling of a dichlorovinyl ether, we exposed dichlorovinyl phenol ether **1**[31] and *p*-methoxyphenyl boronic acid to Pd_2dba_3 and Cs_2CO_3 in hot THF in the presence of one of several ligands (Scheme 2). Electron-rich monophosphines P-*t*-Bu_3 (**4**) and PCy_3 (**5**) as well as monodentate biarylphosphines JohnPhos (**7**) and S-Phos (**8**) led to unselective cross-coupling; while monoarylated material **2** was produced, substantial amounts of diarylated **6** also formed even before complete consumption of **1**. Additionally, the reactions involving either P-*t*-$Bu_3 \cdot HBF_4$ (**4**)[32] or JohnPhos (**7**) produced a second monoarylated product. Analysis of the product mixture by GC/MS suggested that this was an isomer of compound **2**, likely resulting from competing C^2 arylation and tentatively assigned the structure **2′**. The catalyst incorporating monodentate ligand PhDavePhos (**6**) was much more selective, leading only to product **2**, but it was rather inefficient giving only 42% conversion after 4 h.

The catalysts derived from either DPEphos (**13**) or Xantphos (**14**) were both extremely selective and were also the most active, giving about 96% conversion from **1** to monoarylated **2** after 4 h of reaction time. Curiously, the catalyst derived from *tert*-butyl-Xantphos (**12**) was the least active, showing only 11% conversion. Of the remaining bidentate ligands, DPPB (**10**) and DPPF (**11**) both afforded reasonably competent catalysts (~87% conversion), while the catalyst incorporating DPPE (**9**) only led to ~51% conversion.

TABLE 1. Regioselective Arylation and Vinylation at C^1 of Dichlorovinyl Ether 1



entry	R-B(OH)$_2$	product		yield (%)
1			**2**	92
2			**15**	95
3			**16**	87
4			**17**	60
5			**18**	60

The initial studies shown in Scheme 2 employed 3 molar equiv of Cs_2CO_3 as a base, but other experiments showed that 3 equiv of CsF were also moderately effective in many instances. We discovered that using a mixture of Cs_2CO_3 and CsF (3 equiv each) provided the most consistent results, and we therefore employed this base couple in our remaining studies without further optimization. While reactions employing either Xantphos or DPEphos ligands in THF (65 °C) generally required 5.5 h to reach completion, reactions in dioxane (100 °C) were complete in about 1 h, and so dioxane became our solvent of choice.

Having established workable reaction conditions, we set out to synthesize a number of C^1-functionalized vinyl ethers. As seen in Table 1, C^1-aryl vinyl ethers **2** and **15**−**18** were easily obtained using the Pd_2dba_3/DPEphos system. This regioselectivity is consistent with the expectation that C^1 would be relatively electron-poor, leading to preferential oxidative insertion of Pd at this site. Further, other observations in aryl and heteroaryl systems show a related preference for oxidative insertion adjacent to a heteroatom.[33]

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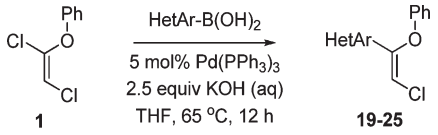
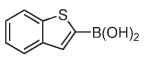
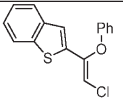
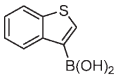
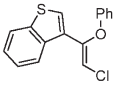
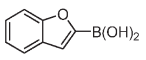
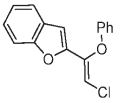
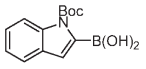
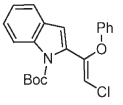
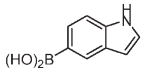
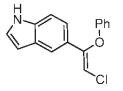
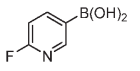
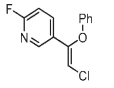
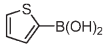
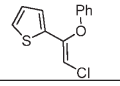
(31) The preparation of **1** is described in the Experimental Section.

(32) Similar unselectivity was noted in reactions using only CsF or KF, and the overall conversion was lower with KF.

(33) (a) Schweizer, S. A.; Bach, T. *Synlett* **2010**, 81–84. (b) Abid, O.-u.-R.; Ibad, M. F.; Nawaz, M.; Ali, A.; Sher, M.; Rama, N. H.; Villinger, A.; Langer, P. *Tetrahedron Lett*. **2010**, *51*, 1541–1544. (c) Schnürch, M.; Flasik, R.; Khan, A. F.; Spina, M.; Mihovilovic, M. D.; Stanetty, P. *Eur. J. Org. Chem*. **2006**, 3283–3307. (d) Schröter, S.; Stock, C.; Bach, T. *Tetrahedron* **2005**, *61*, 2245–2267.

TABLE 2. Regioselective C^1 Heteroarylation of Dichlorovinyl Ether 1



entry	boronic acid	product		yield (%)
1			**19**	30
2			**20**	68
3			**21**	40
4			**22**	52
5			**23**	49
6			**24**	54
7			**25**	73

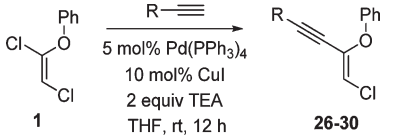
Curiously, the only other report we have found in which a 1,2-dichlorovinyl ether was the electrophile in a palladium-catalyzed cross-coupling stated that a Sonogashira coupling occurred at C^2.[23]

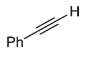
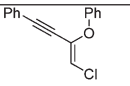
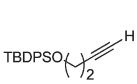
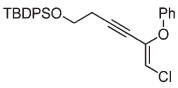
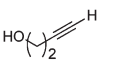
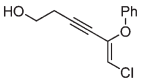
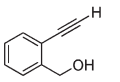
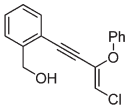
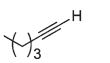
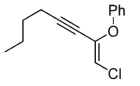
Most of the heteroarylboronic acids we tested were completely unreactive toward the Pd/DPEphos catalytic system. However, $Pd(PPh_3)_4$ in boiling THF and aqueous KOH[6] promoted the cross-coupling of these stubborn boronic acids, permitting us to prepare vinyl heteroaromatics **19**−**25** in modest to good yields (Table 2). This catalytic system also proved to be very effective for the C^1-selective Suzuki−Miyaura couplings shown in Table 1. The yields of these reactions were similar to those obtained using Pd_2dba_3/DPEphos but proceeded much faster, requiring only 1 h or less.

C^1-selective Sonogashira alkynylations were equally successful (Table 3), using an adaptation of the procedure of Tiano and Belmont[34] for the alkynylation of 2-halobenzofurans and indoles. These conditions afforded compounds **26**−**30** in good yields from **1**, although hydroxyl-substituted products **28** and **29** slowly decomposed at room temperature.

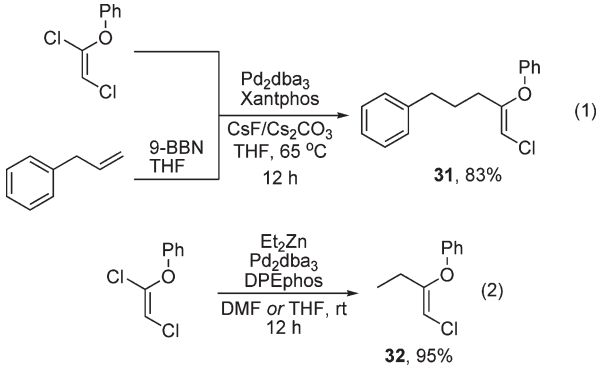
We have only examined a few couplings of aliphatic organometallic donors. Not surprisingly, attempts to cross-couple

TABLE 3. Regioselective C^1 Sonogashira Coupling Reactions of 1



entry	alkyne	product		yield (%)
1			**26**	78
2			**27**	56
3			**28**	90
4			**29**	95
5			**30**	77

SCHEME 3. C^1-Selective Alkylations of 1



*c*Hex-$B(OH)_2$ with **1** were unsuccessful.[35] On the other hand, **31** was readily obtained using Roulland's trialkylborane procedure (Scheme 3, eq 1).[28] Negishi cross-coupling with diethylzinc[27] likewise afforded C^1 ethyl vinyl ether **32** in excellent yield (Scheme 3, eq 2).

Cross-Couplings at C^2: Synthesis of Trisubstituted Alkenes. Elaboration of the remaining C^2-Cl group was the next goal we addressed. Treating compound **2** with 1.5 equiv of *p*-fluorophenylboronic acid in the presence of Pd_2dba_3/DPEphos formed the expected diarylated vinyl ether **33**, which was isolated in 56% yield (Scheme 4). However, 2-(4-methoxyphenyl)benzofuran **34**, formed via intramolecular C−H activation, was also isolated in 8% yield based on conversion from **2**. The development of this observation into a general method for benzofuran synthesis has been described elsewhere.[21] In the context of the present investigation, competition from intramolecular arylation was problematic.

(34) Tiano, M.; Belmont, P. *J. Org. Chem.* **2008**, *73*, 4101–4109.
(35) Doucet, H. *Eur. J. Org. Chem.* **2008**, 2013–2030.

SCHEME 4. Pd/DPEphos-Promoted Cross-Coupling between Arylvinyl Chloride 2 and a Boronic Acid

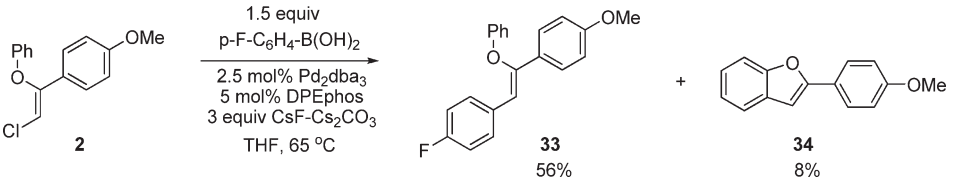
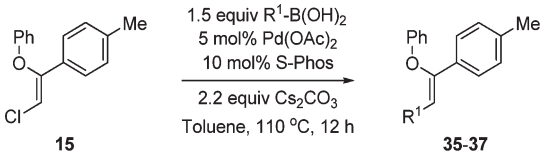
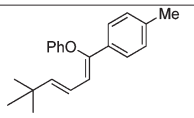
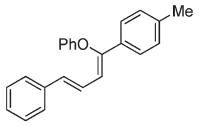
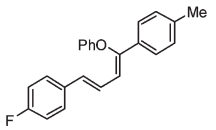


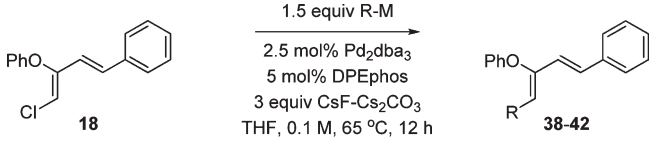
TABLE 4. Synthesis of a Vinyl Ether and 1-Phenoxy-1,3-butadienes from (*Z*)-2-Chloro-1-arylvinyl Ethers

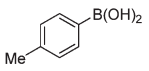
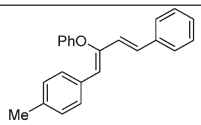
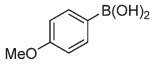
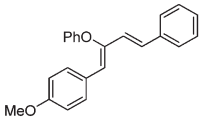
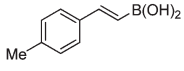
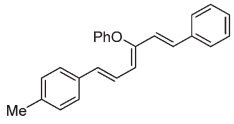
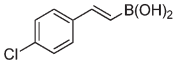
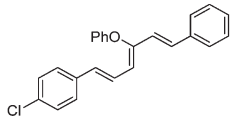
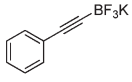
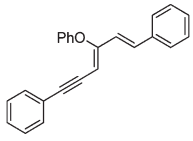


entry	product		yield (%)
1		**35**	87
2		**36**	65
3		**37**	15[a]

[a]The mass balance was recovered unreacted starting material (79%).

TABLE 5. Synthesis of 2-Phenoxy-1,3-butadienes, Hexatrienes, and a Dienyne from (*Z*)-1-Chloro-2-aryloxy-1,3-butadiene



entry	R-M		product		yield (%)
1				**38**	53
2				**39**	78
3				**40**	52
4				**41**	64
5				**42**	20[a]

[a]65% unreacted starting material recovered as well.

Our C^1 arylation ligand screen (Scheme 2) had indicated that the use of S-Phos (**8**) as a ligand in THF solution gave the most diarylated product with no evidence of intramolecular arylation, suggesting that these conditions might be appropriate for cross-coupling at C^2. We therefore treated **15** with three different vinylboronic acids in the presence of $Pd(OAc)_2$/S-Phos in hot toluene.[27] Electron-rich dienes **35** and **36** were obtained in this way in very good yields (Table 4), but the cross-coupling with *p*-fluorostyrylboronic acid to form diene **37** remained problematic.

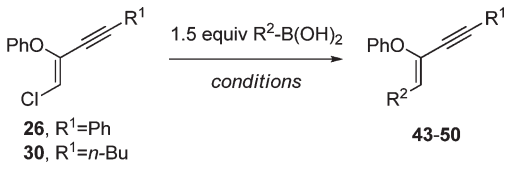
In contrast to the reactions of the C^1-arylated compounds shown in Table 4, Suzuki cross-coupling at C^2 of the C^1 alkenyl derivative **18** under Pd/DPEphos catalysis proceeded smoothly (Table 5). Good yields were obtained for C^2-arylated dienes **38** and **39** (entries 1 and 2). We also obtained electron-rich trienes **40** and **41** in good yields (entries 3 and 4); notably, the reaction tolerated the presence of an aryl chloride (**41**, entry 4), leaving a useful handle for further functionalization.[36] Additionally, while we have been unable to C^2-alkynylate via standard Sonogashira chemistry (in contrast to the ready formation of C^1-alkynyl derivatives **26**−**30**, and the single example reported previously by Schmidt et al.[23]), dienyne **42** could be generated from **18** and potassium phenylethynyl trifluoroborate, albeit in lower yield (entry 5). In all cases, no other isomers or the corresponding benzofuran could be detected, suggesting that for C^1 alkenyl derivatives, intermolecular Suzuki coupling is much faster than competing intramolecular arylation at this concentration.[37]

Despite the difficulties of C^2 alkynylation, reactions of electron-rich enynes **26** and **30** with a variety of aryl-, heteroaryl-, and alkenylboronic acids proved facile (Table 6). We observed that **30** was more labile under cross-coupling conditions than was the phenylacetylene compound **26**. However, **30** underwent cross-coupling in modest yields to give enynes **43**−**45** (entries 1−3). Notably, 2-thiopheneboronic

(36) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176–4211.

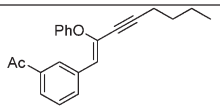
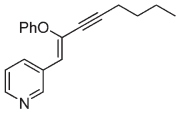
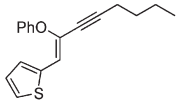
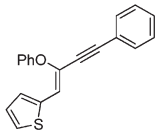
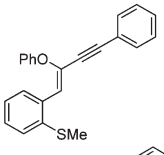
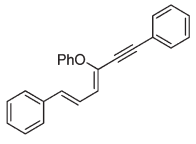
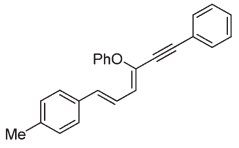
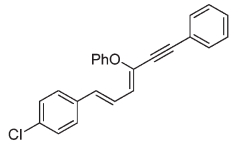
(37) Normally, the direct arylation to benzofurans is done at a concentration of 0.4 M in dioxane, and we have observed that this process is slowed at lower concentrations.

TABLE 6. Enynes and Dienynes from 1-Alkynyl Vinyl Ethers



26, R^1=Ph
30, R^1=*n*-Bu

43-50

entry	product		yield (%)[a]
1		**43**	54[a]
2		**44**	0[a] 60[b,c]
3[b]		**45**	29[d]
4[a]		**46**	28[e]
5[a]		**47**	69
6[a]		**48**	76
7[a]		**49**	65
8[a]		**50**	46

[a]1 equiv of vinyl chloride **26** or **30**, 1.5 equiv of R-B(OH)$_2$, 2.5 mol % of Pd_2dba_3, 5 mol % of DPEphos, 3 equiv of CsF, 3 equiv of Cs_2CO_3, 0.4 M in dioxane, heated at 100 °C overnight. [b]1 equiv of vinyl chloride **26** or **30**, 1.5 equiv of R-B(OH)$_2$, 5 mol % of $Pd(PPh_3)_4$, 2.5 equiv of KOH (aq), THF, 65 °C overnight. [c]15% recovered starting material. [d]40% recovered starting material. [e]Isolated 17% of 2-(phenylethynyl)-benzofuran as well.

acid could be cross-coupled using Pd/DPEphos, but 3-pyridylboronic acid could not. Nevertheless, 3-pyridylboronic acid did cross-couple with **22** under the aqueous $Pd(PPh_3)_4$ conditions.

Both heteroaryl- and ortho-substituted aryl boronic acids underwent cross-coupling with enyne **26** using the Pd/DPEphos method, giving **46** and **47** (entries 4 and 5). The formation of the 2-substituted thiophene **46** was accompanied by production of 2-(phenylethynyl)benzofuran in 17% yield. This may reflect the known lower reactivity of many heteroaryl-2-boronic acids, permitting the intramolecular direct arylation to compete with the desired intermolecular Suzuki–Miyaura coupling. As demonstrated in Table 6, alkenyl boronic acids may be used as substrates, and substituted dienynes **48**–**50** were generated in good yield (entries 6–8); again, the tolerance for an aryl chloride group in this reaction is noteworthy (**50**, entry 8).

The cross-coupling of 3-phenylpropenylboronic acid with **26** led to an interesting "downstream" reaction (Scheme 5), affording biphenyl **52** as the sole identifiable product. We assume this reaction forms the adduct **51**, which then undergoes an isomerization/electrocyclization to **52**, although the mechanistic details are not clear. This process may prove useful for a modular and simple synthesis of highly substituted biaryl ethers, as an alternative to Buchwald–Hartwig coupling.

Cross-couplings at C^2 of C^1-alkyl compounds were much less facile than were the reactions shown in Tables 5 and 6. The Pd/DPEphos catalyst in dioxane proved ineffective in any attempted coupling of **31**, but we were gratified to find that **31** was smoothly converted to **53** in toluene using the $Pd(OAc)_2$/S-Phos catalyst (Table 7, entry 1). We were initially surprised to find that cross-coupling of **31** with potassium phenylethynyl trifluoroborate under these conditions afforded 2-alkylbenzofuran **55** as the major product (46%), and the desired enyne **54** was obtained in only 24% yield (entry 3). The recent results of Lloyd-Jones,[38] however, show that slow cross-coupling should be expected under conditions such as these, where only adventitious water is available to hydrolyze the potassium alkyltrifluoroborate. The Negishi coupling of **31** with diethyl zinc under the same catalytic conditions (entry 4) proceeded sluggishly, affording only 35% conversion after 23 h. The dialkylvinyl ether **56** was isolated in 33% yield.

Finally, we set out to see if the cross-couplings could be done in one pot, increasing the efficiency of the reaction. As the diarylated compounds could be synthesized fairly readily in two steps using the Pd/DPEphos catalytic system for both cross-couplings, our only concern for a one-pot process was competing against direct arylation to the benzofuran (cf. Scheme 4). With that in mind, we attempted the reaction using the dichlorovinyl ether **57** derived from benzyl alcohol rather than phenol.[39] The one-pot sequential Suzuki–Miyaura arylations proceeded very smoothly to give the fully elaborated product **58** (Scheme 6). Other observations suggest that even phenolic ethers should be able to participate in this one-pot diarylation because cyclization by direct arylation appears to be slower than cross-coupling provided that a second boronic acid is present in sufficient concentration.

C^2-H Functionalization Leading to Tetrasubstituted Alkenes. Our overall concept was that all four substituent groups of TCE were potential handles for synthetic elaboration.

(38) Butters, M.; Harvey, J. N.; Jover, J.; Lennox, A. J. J.; Lloyd-Jones, G. C.; Murray, P. M. *Angew. Chem., Int. Ed.* **2010**, *49*, 5156–5160.

(39) We have attempted sequential Suzuki coupling/direct arylation of benzyl alcohol derivative using the Pd/DPEphos conditions and have found that while Suzuki coupling is facile, intramolecular direct arylation to the six-membered ring fails under these conditions.

SCHEME 5. Production of Substituted Biaryl Ether 52 from the Reaction between Vinyl Chloride 26 and 3-Phenylpropenylboronic Acid

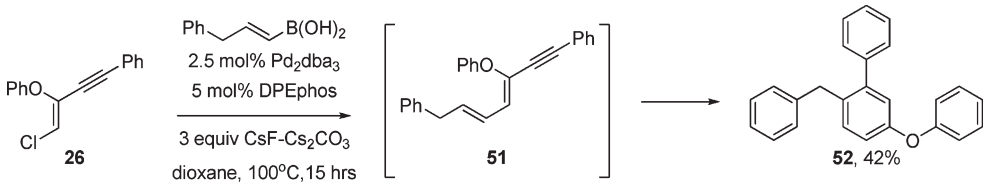
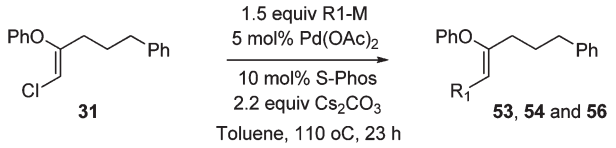
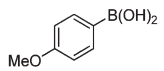
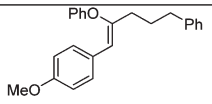
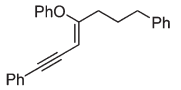
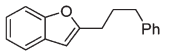
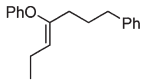


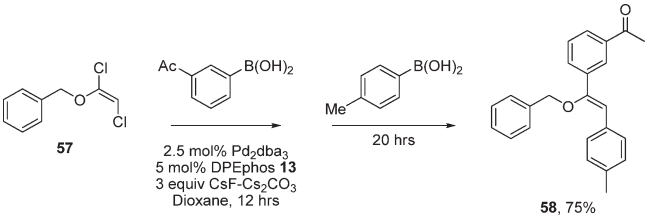
TABLE 7. Cross-Coupling at C^2 of the Alkyl Derivative 31



entry	R^1-M	product		yield (%)
1			**53**	85
2			**54**	24
			**55**	46
3	Et_2Zn		**56**	33 [a, b]

[a] No Cs_2CO_3 was added to this reaction. [b] Only 35% conversion from starting material by ^1H NMR.

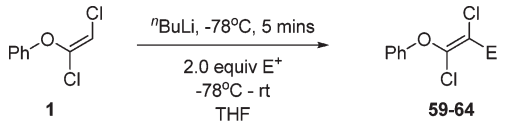
SCHEME 6. One-Pot Sequential Suzuki−Miyaura Cross-Couplings of 57

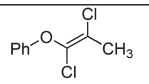
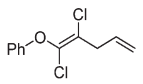
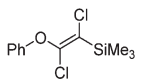
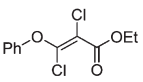
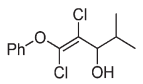
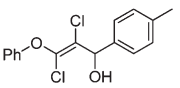


While deprotonation at C^2 was known to trigger elimination to form alkynyl ethers,[19n19n] appropriate control of the reaction conditions would permit us to trap the vinyl anion with various electrophiles. Indeed, Greene had reported one such example in 2008.[40]

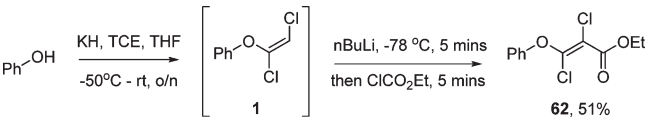
(*E*)-(1,2-Dichlorovinyloxy)benzene **1** was deprotonated with BuLi and quenched with either methyl iodide or allyl bromide to give adducts **59** or **60** in excellent yields (Table 8, entries 1 and 2). The vinyllithium could also add to TMSCl, giving vinylsilane **61** (entry 3), which is useful as a third

TABLE 8. Synthesis of (*E*)-2-Substituted 1,2-Dichlorovinyl Ethers



entry	electrophile	product		yield (%)
1	CH_3-I		**59**	76
2	Allyl bromide		**60**	66
3	$Si(CH_3)_3Cl$		**61**	89
4	$ClCO_2Et$		**62**	56
5	*i*PrCHO		**63**	92
6	*p*-CH_3-C_6H_4-CHO		**64**	94

SCHEME 7. One-Pot Alcohol Addition/Alkylation



and orthogonal handle in subsequent palladium-catalyzed chemistry[41] and other processes.[42] Ethyl chloroformate was also a useful electrophile, giving 1,2-dichloro-1,2-unsaturated ethyl ester **62** in good yield (entry 4). Quenching the anion with aldehydes (entries 5 and 6) gave allyl alcohols **63** and **64** in excellent yields; the tolerance of an acidic α-proton is notable (entry 5). This opens yet another pathway for further synthetic transformation, as allyl alcohols are useful substrates for Tsuji−Trost substitution reactions.[43] We

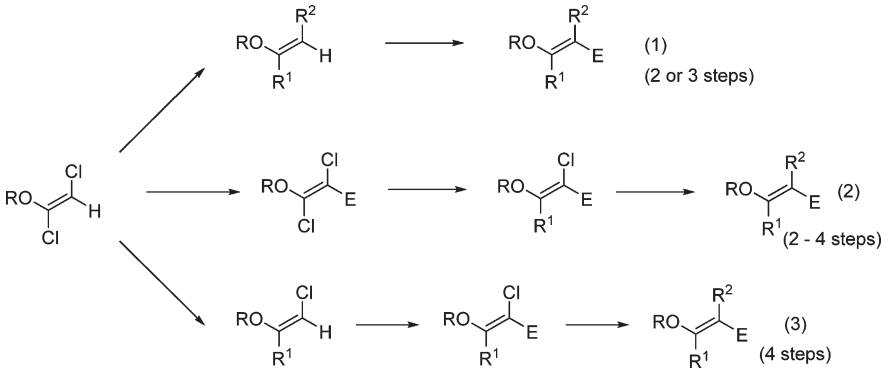
(40) Darses, B.; Milet, A.; Philouze, C.; Greene, A. E.; Poisson, J.-F. *Org. Lett*. **2008**, *10*, 4445–4447.

(41) Denmark, S. E.; Sweis, R. F. In *Metal-Catalyzed Cross-Coupling Reactions*; de Meijere, A., Diederich, F., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 1, pp 163−216.

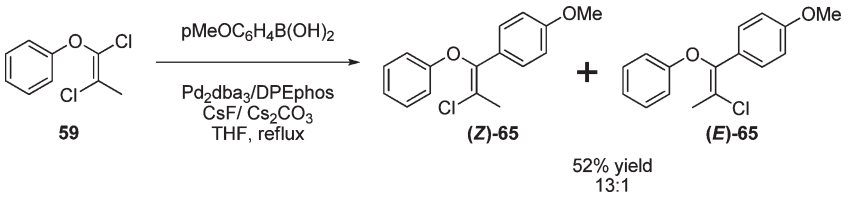
(42) (a) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev*. **1997**, *97*, 2063–2192. (b) Blumenkopf, T. A.; Overman, L. E. *Chem. Rev*. **1986**, *86*, 857–873.

(43) Kazmaier, U.; Pohlman, M. In *Metal-Catalyzed Cross-Coupling Reactions*; de Meijere, A., Diederich, F., Eds.; Wiley-VCH: Weinheim, 2004; Vol. 2, pp 531−584.

SCHEME 8. Reaction Sequences Leading to Highly Substituted Ethylene Derivatives



SCHEME 9. Cross Coupling on C^2-Methylated Compound



also found that while **1** added easily and cleanly to DMF, the resultant α,β-unsaturated aldehyde (provisionally identified from NMR spectra of the crude product) was unstable and decomposed upon attempted column chromatography.

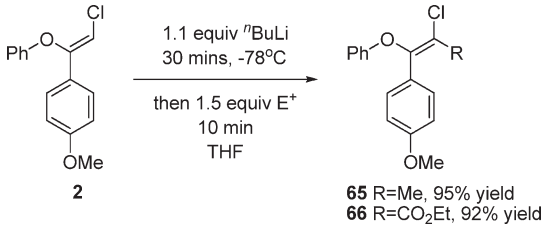
We have also found that the elimination/addition reaction of a phenolate with TCE and deprotonation of the dichlorovinyl ether followed by electrophilic quench with ethyl chloroformate can be done in one pot with no significant change in the overall yield of α,β-unsaturated ester **62** (Scheme 7).

With the knowledge that anion chemistry at C^2 was feasible, we envisaged three possible sequences leading to fully elaborated alkenes (Scheme 8). We ruled out the pathway of eq 1 in Scheme 8 after preliminary experiments showed that deprotonation of the trisubstituted ethylene intermediate (R^1, R^2 = aryl) was problematic.

The route depicted in eq 2 (Scheme 8) also encountered difficulties. The cross-coupling between C^2-methylated compound **59** and *p*-methoxyphenylboronic acid catalyzed by Pd_2dba_3/DPEphos (Scheme 9) produced a mixture of what appeared to be two isomers in an approximate 13:1 ratio (52% yield). The major product was determined to be (*Z*)-**65**. Given that Pd_2dba_3/DPEphos is unable to effect cross-coupling between isolated (*Z*)-**65** and boronic acids (vide infra), it is unlikely that arylation is occurring at C^2 here, and we have a mixture of (*E*)-**65** and (*Z*)-**65** isomers. An analogous cross coupling between **59** and (*E*)-styrylboronic acid gave a similar mixture of products with incomplete conversion. We were unable to induce Sonogashira cross-coupling between the alkylated derivative **59** and terminal alkynes.

We also explored cross-coupling reactions between the dichlorovinyl ester **62** and arylboronic acids. Cross-coupling is known to favor the β position in α,β-unsaturated esters (i.e., C^1 in **62**).[11c11c] Furthermore, we have already noted the directing effect of the C^1-phenoxy substituent for selective

SCHEME 10. Functionalization of 2-Chloro-1-aryl-1-phenoxyethylene



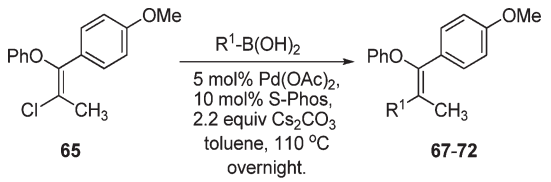
C^1−Cl cross-coupling. We therefore thought that the C^1−Cl should be activated by *both* substituents in a "push−pull" fashion,[44] and expected that cross-coupling of **62** should be rapid and selective. We were surprised to find that cross-coupling between **62** and *p*-$MeOC_6H_4B(OH)_2$ gave mixtures of products, similar the outcome observed with the 2-methyl-substituted **59** (Scheme 9). We are currently trying to understand the source of this difficultly and exploring alternative catalytic systems.

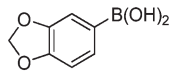
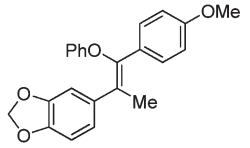
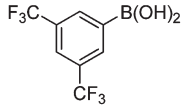
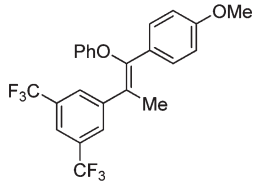
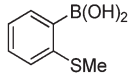
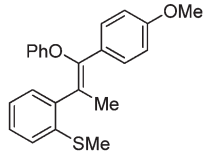
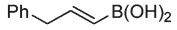
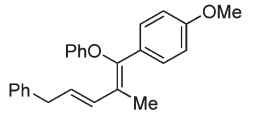
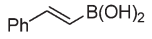
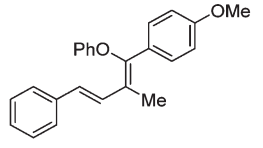
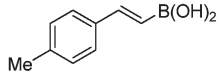
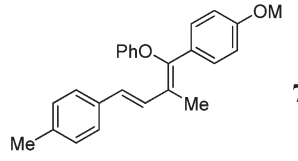
As these results ruled out the route according to Scheme 8, eq 2, we next examined C^2-H functionalization from C^1 arylated substrates. Deprotonation of vinyl ether **1** was facile, and quenching with either iodomethane (to give **65**) or ethyl chloroformate (to give **66**) proceeded smoothly (Scheme 10).

The results of cross-couplings of relatively electron-rich **65** and electron-poor **66** are summarized in Tables 9 and 10. The electron-rich alkene **65** did not participate in any Suzuki−Miyaura cross-coupling in hot dioxane in the presence of Pd/DPEphos. However, the $Pd(OAc)_2$/S-Phos catalyst in toluene proved able to promote Suzuki−Miyaura couplings of **65**, and adducts **67**−**69** were obtained in good yields (Table 9). Cross-coupling occurred

(44) Kleinpeter, E. *J. Serb. Chem. Soc.* **2006**, *71*, 1–17.

TABLE 9. Tetrasubstituted Alkenes from Cross-Coupling with Electron-Rich Alkene 65

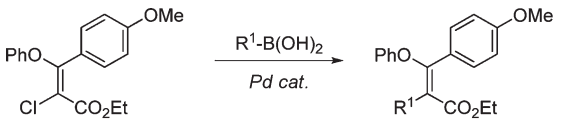


entry	R^1-B(OH)$_2$	product		yield (%)
1			**67**	76
2			**68**	83
3			**69**	55
4			**70**	92
5			**71**	74
6			**72**	47

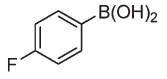
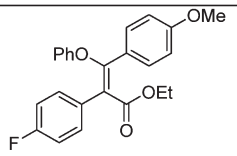
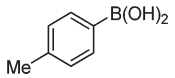
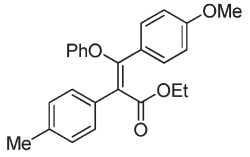
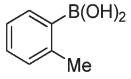
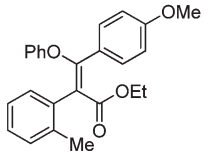
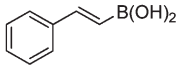
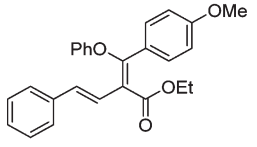
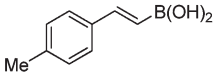
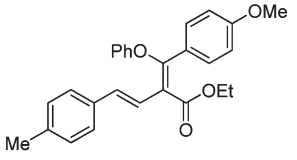
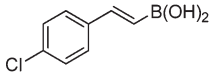
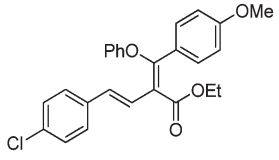
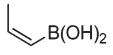
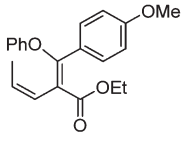
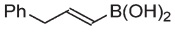
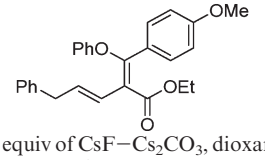
readily with an electron-rich (entry 1), an electron-deficient (entry 2), and an ortho-substituted (entry 3) arylboronic acid. Similarly, electron-rich tetrasubstituted dienes **70**−**72** were easily assembled in high yields (entries 4−6).

Analogous reactions of α-chloro-α,β-unsaturated ester **65** catalyzed by Pd/DPEphos typically gave the tetrasubstituted unsaturated esters **73**−**78** in good yields (Table 10, conditions A, entries 1, 3, 5, 7, 9, and 11). However, in some cases 2-(4-methoxyphenyl)-3-carboxyethylbenzofuran was also produced in competition, as detected by TLC and ^{1}H NMR analysis of the crude products. Generally, the Pd(OAc)$_2$/S-Phos/toluene conditions gave higher yields of these adducts (Table 10, conditions B, entries 2, 4, 6, 8, and 10). Cross-coupling with vinylboronic acids provided butadienes **76**−**80**. As in the synthesis of trisubstituted alkenes (Tables 5 and 6), an aryl chloride substituent was tolerated by either catalyst examined (entries 11 and 12) giving butadiene **78** in excellent yields. Finally, alkyl-substituted vinyl boronic acids could be utilized, giving butadienes **79** and **80** in moderate to good yield (entries 13 and 14). In all cases, only one isomer could be detected in the ^{1}H NMR spectra of the crude material and the pure isolated product. Unsaturated esters **73**−**80** are also generally referred to as

TABLE 10. Push−Pull Alkenes from Cross-Coupling with 65



66 **73-80**

entry	R^1-B(OH)$_2$	Pd cat.[a]	yield (%)	product
1		**A**	70	 **73**
2		**B**	72	
3		**A**	75	 **74**
4		**B**	87	
5		**A**	59	 **75**
6		**B**	89	
7		**A**	82	 **76**
8		**B**	69	
9		**A**	36	 **77**
10		**B**	91	
11		**A**	62	 **78**
12		**B**	73	
13		**B**	34	 **79**
14		**B**	65	 **80**

[a] **A**: 1 equiv of **66**, 1.5 equiv of RB(OH)$_2$, 2.5 mol % of Pd_2dba_3, 5 mol % of DPEphos, 3 equiv of CsF−Cs_2CO_3, dioxane, 100 °C, overnight. **B**: 1 equiv of **66**, 1.5 equiv of RB(OH)$_2$, 5 mol % of Pd(OAc)$_2$, 10 mol % of S-Phos, 2.2 equiv of Cs_2CO_3, toluene, 110 °C, overnight.

push−pull alkenes[45] and are reactive to both electrophiles and nucleophiles,[45] making them highly useful targets. The method described here provides a nice complement to the published procedures for the synthesis of trisubstituted unsaturated esters.[46]

(45) Lloyd, D.; McNab, H. *Angew. Chem., Int. Ed.* **1976**, *15*, 459–468.

(46) (a) Nakatsuji, H.; Nishikado, H.; Ueno, K.; Tanabe, Y. *Org. Lett.* **2009**, *11*, 4258–4261. (b) Nakatsuji, H.; Ueno, K.; Misaki, T.; Tanabe, Y. *Org. Lett.* **2008**, *10*, 2131–2134.

Conclusions

We have developed a modular and efficient synthesis of tri- and tetrasubstituted electron-rich alkenes from the two-carbon building block trichloroethylene. In general, C−C bond formation at C^1 was best accomplished using a DPEphos-based catalyst in dioxane, while C^2 functionalization could be achieved using an S-Phos-based catalyst in toluene solution. Cross-coupling heteroaryl boronic acids was the exception to those generalizations, and $Pd(PPh_3)_4$ in THF/KOH (aq) was the most efficient catalyst for cross-coupling heteroarylboronic acids at either C^1 or C^2. This method efficiently installs alkyl, alkenyl, alkynyl, and (hetero)aryl groups at C^1 and C^2 of TCE. This is one of the most general approaches we know of to access alkoxy-substituted stilbenes, dienes, trienes, enynes, and related conjugated structural motifs.

Experimental Section

General Considerations. All glassware was oven-dried and cooled in a desiccator before use. All reactions were carried out under argon using standard syringe techniques. THF and toluene were purified by passage through two columns of activated alumina under argon pressure[47] and degassed via sparging with argon before use. Anhydrous dioxane was degassed via sparging with argon before use. Boronic acids were generally used as received, but *trans*-2-phenylvinylboronic acid and 2-thiopheneboronic acid were recrystallized before use. Alkynes were generally used as purchased, or in the case of phenylacetylene, were passed through a short column of activated alumina first. All palladium reagents, as well as phosphine ligands, cesium fluoride, and cesium carbonate, were used as received. Flash chromatography employed 230−400 mesh silica gel. R_f values refer to TLC on precoated 0.2 mm silica gel plates obtained using the eluent indicated. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were recorded in $CDCl_3$ solutions. Chemical shifts for ^{1}H and ^{13}C are reported in parts per million (ppm) downfield from TMS, using residual $CDCl_3$ (7.27 ppm and triplet at 77.0 ppm, respectively) as an internal standard.

(*E*)-1,2-Dichloro-1-phenoxyethylene (1). This compound was prepared according to our published procedure.[21a21a] KH (2.05 equiv) was weighed into a round-bottom flask and washed with three portions of either pentane or petroleum ether. The KH was then suspended in THF (ca. 2.4 mL per mmol of KH). A solution of the phenol (1.0 equiv) in THF (ca. 1.25 mL per mmol of phenol) was added dropwise (vigorous gas evolution was noted), and the reaction was allowed to stir for 30−120 min. The suspension was cooled to approximately −50 °C ($CHCl_3$/CO_2(s) bath). Trichloroethylene (1.5 equiv) was then added dropwise. The reaction was allowed to warm gradually to room temperature overnight. The reaction was diluted with petroleum ether and quenched with ice-cold water. The phases were separated, and the aqueous phase was extracted once more with petroleum ether. The organic layers were combined, dried with sodium sulfate, filtered, and concentrated to give a yellow to dark brown oil. The crude oil was applied to a silica column pretreated with triethylamine (ca. 2.5 vol% with respect to the volume of dry silica) and eluted with petroleum ether: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.36 (m, 2H), 7.22−7.17 (m, 1H), 7.13−7.08 (m, 2H), 5.97 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 140.1, 129.8, 124.5, 117.1, 103.8.

Representative Procedure A for Suzuki−Miyaura Cross-Coupling Reactions Using Pd/DPEphos: Synthesis of (*Z*)-1-Chloro-2-phenoxy-2-(4-methoxyphenyl)ethylene (2). The boronic acid (1.3550 g, 8.9 mmol, 1.05 equiv), Pd_2dba_3 (194.6 mg, 0.212 mmol, 2.5 mol %), DPEphos (228.8 mg, 0.425 mmol, 5 mol %), CsF (3.87 g, 25.5 mmol, 3 equiv), and Cs_2CO_3 (8.31 g, 25.5 mmol, 3 equiv) were placed into a one-piece, round-bottom flask/condenser, sealed with a septum, and purged with argon for 20−30 min. A solution of the 1,2-dichlorovinyl ether **1** (1.6068 g, 8.5 mmol) in dioxane (25 mL) was added. The solution was vigorously stirred and brought to reflux. When complete (6 h), the reaction was cooled and partitioned between water and dichloromethane. The layers were separated, and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were dried with magnesium sulfate, filtered, and concentrated onto silica gel, applied to a column, and eluted with 9:1 hexanes/dichloromethane. NMR were consistent with previously published data:[21] R_f = 0.29 (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, CDCl3) δ 7.40 (d, 2H), 7.28−7.21 (m, 2H), 7.00−6.95 (m, 3H), 6.83 (d, 2H), 6.30 (s, 1H), 3.78 (s, 3H); ^{13}C NMR (75 MHz, CDCl3) δ 160.3, 156.1, 151.1, 129.6, 127.7, 127.1, 125.7, 122.2, 115.9, 114.2, 105.1, 55.3.

(*Z*)-1-Chloro-2-phenoxy-2-(4-methylphenyl)ethylene (15). This compound was prepared according to representative procedure A on a 5.4 mmol scale to give 1.26 g of **15** (95% yield). Purified via flash chromatography using a gradient of hexanes to 14:1 hexanes/dichloromethane as an eluent: R_f = 0.62 (9:1 hexanes/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, 2H, J = 8 Hz), 7.34−7.29 (m, 2H), 7.19 (d, 2H, J = 8 Hz), 7.08−7.02 (m, 3H), 6.54 (s, 1H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.2, 151.4, 139.3, 130.4, 129.6, 129.5, 125.6, 122.3, 116.0, 106.2, 21.3; HRMS calcd for $C_{15}H_{13}ClO$ 244.0655, found 244.0659.

(*Z*)-1-Chloro-2-phenoxy-2-(4-fluorophenyl)ethylene (16). This compound was prepared according to representative procedure A on a 5 mmol scale. NMR were consistent with previously published data:[21] R_f = 0.5 (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (m, 2H), 7.31 (m, 2H), 7.07−7.00 (m, 5H), 6.41 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8, 161.5, 155.9, 150.5, 129.7, 129.4, 122.5, 116.1, 115.9, 115.8, 106.8, 106.8.

(*Z*)-1-Chloro-2-phenoxy-2-phenylethylene (17). Viscous, colorless oil prepared according to Representative Procedure A on a 0.38 mmol scale. Purified via flash chromatography on TEA-treated silica using 9:1 hexanes/dichloromethane as an eluent to give 75.5 mg of **17** (60% yield): R_f = 0.57 (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52−7.49 (m, 2H), 7.36−7.25 (m, 5H), 7.04−7.00 (m, 3H), 6.47 (s, 1H). The structure of this compound has been confirmed by its transformation into the known compound 2-phenylbenzo[*b*]furan.[21]

(1*Z*,3*E*)-1-Chloro-2-phenoxy-4-phenylbuta-1,3-diene (18). This compound is a clear oil and was prepared according to representative procedure A. NMR were consistent with previously published data:[21] R_f = 0.49 (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.27 (m, 7H), 7.12−7.06 (m, 3H), 6.83 (d, 1H, J = 16 Hz), 6.72 (d, 1H, J = 16 Hz), 6.22 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ156.5, 151.1, 136.0, 131.1, 129.7, 128.8, 128. 5, 126.9, 122.3, 120.3, 115.2, 110.6.

Representative Procedure B for Suzuki−Miyaura Cross-Coupling Using $Pd(PPh_3)_4$: (*Z*)-2-(2-Chloro-1-phenoxyvinyl)-benzo[*b*]thiophene (19). The boronic acid (308.4 mg, 1.73 mmol, 1.05 equiv) and tetrakis(triphenylphosphine)palladium(0) (95.3 mg, 82.5 μmol, 5 mol %) were placed into a one-piece, round-bottom flask-condenser, sealed with a septum, and purged with argon for 20 min. A 1.0 equiv portion of the dichlorovinyl ether **1** (311.9 mg, 1.65 mmol, 1 equiv) in THF (5 mL) was added, and then a degassed 1.0 M aqueous solution of KOH (3.5 mL, 3,5 mmol, 2.1 equiv) was added. The solution was vigorously stirred and brought to reflux. When complete (14 h), the reaction was cooled and partitioned between water and dichloromethane. The layers were separated, and the aqueous layer was extracted

(47) Pangborn, A. B.; Giardello, M.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.

with dichloromethane once more. The combined organic layers were washed with brine, dried with sodium sulfate, filtered, and concentrated. The crude residue was purified via flash chromatography using 14:1 hexanes/dichloromethane as an eluent to give 0.50 g of **19**: $R_f = 0.65$ (9:1 hexanes/diethyl ether). This material could not be separated from traces of 2,2′-dibenzo[*b*]thiophene arising from homocoupling of benzothiophene-2-boronic acid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80−7.67 (m, 2H), 7.42−7.29 (m, 10H), 7.13−7.05 (m, 3H), 6.57 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.2, 146.9, 139.4, 135.9, 133.9, 133.6, 129.7, 128.7, 128.6, 128.5, 125.5, 124.8, 124.2, 122.8, 122.7, 122.2, 115.5, 108.6; HRMS calcd for $C_{16}H_{11}ClOS$ 286.0219, found 286.0227.

(*Z*)-3-(2-Chloro-1-phenoxyvinyl)benzo[*b*]thiophene (20). Viscous, colorless oil prepared according to representative procedure B on a 1.59 mmol scale. Purified via flash chromatography on TEA-treated silica using 14:1 hexanes/dichloromethane as an eluent to give 0.31 g of **20** (68% yield): $R_f = 0.53$ (9:1 hexanes/diethyl ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (d, 1H, J = 8 Hz), 7.86 (d, 1H, J = 8 Hz), 7.62 (s, 1H), 7.51−7.38 (m, 2H), 7.30−7.22 (m, 2H), 7.07 (m, 2H), 7.00 (m, 1H), 6.44 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.8, 147.9, 140.4, 136.2, 129.7, 129.6, 127.2, 125.0, 123.1, 123.0, 122.7, 116.3, 107.8; HRMS calcd for $C_{16}H_{11}ClOS$ 286.0219, found 286.0207.

(*Z*)-2-(2-Chloro-1-phenoxyvinyl)benzo[b]furan (21). Viscous, colorless oil prepared according to representative procedure B on a 1.62 mmol scale. Purified via flash chromatography on TEA-treated silica using 14:1 hexanes/dichloromethane as an eluent to give 175.8 mg of **21** (40% yield): $R_f = 0.28$ (14:1 hexanes/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70−7.59 (m, 1H), 7.51 (m, 2H), 7.41−7.33 (m, 4H), 7.28−7.22 (m, 1H), 7.13−7.08 (m, 3H), 6.90 (s, 1H), 6.71 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.4, 155.0, 149.5, 143.2, 129.8, 128.6, 128.1, 125.5, 125.1, 123.4, 123.4, 122.8, 121.6, 121.4, 115.3, 111.3, 111.2, 109.7, 105.2, 103.7; HRMS calcd for $C_{16}H_{11}ClO_2$ 270.0448, found 270.0447.

(*Z*)-1-(*tert*-Butoxycarbonyl)-2-(2-chloro-1-phenoxyvinyl)indole (22). Viscous, colorless oil prepared according to representative procedure B on a 2.75 mmol scale. Purified via flash chromatography on TEA-treated silica using 4:1 hexanes/dichloromethane as an eluent to give 524.5 mg of **22** (52% yield): $R_f = 0.36$ (9:1 hexanes/diethyl ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, 1H, J=8 Hz), 7.56 (d, 1H, J = 7.5 Hz), 7.41−7.34 (m, 2H), 7.25 (m, 3H), 7.03 (m, 3H), 6.80 (s, 1H), 6.28 (s, 1H), 1.78 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3, 149.4, 146.2, 137.4, 131.3, 129.4, 128.0, 125.6, 123.2, 123.1, 121.0, 117.2, 115.4, 115.4, 114.2, 108.0, 84.4, 28.0; HRMS calcd for $C_{21}H_{20}ClNNaO_3$ 392.1024, found 392.0989.

(*Z*)-5-(2-Chloro-1-phenoxyvinyl)indole (23). Viscous, colorless oil prepared according to representative procedure B on a 0.53 mmol scale. Purified via flash chromatography on TEA-treated silica using 4:1 hexanes/ethyl acetate as an eluent to give 65.7 mg of **23** (49% yield): $R_f = 0.15$ (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (br s, 1H), 7.80 (s, 1H), 7.35−7.23 (m, 4H), 7.20 (t, 1H, J = 2.8 Hz), 7.07 (m, 2H), 6.98 (m, 1H), 6.54 (br t, 1H, J = 2.4 Hz), 6.39 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.4, 152.6, 136.2, 129.6, 127.9, 125.2, 125.2, 122.1, 120.0, 118.8, 116.1, 111.4, 104.6, 103.3. This compound gradually decomposes at room temperature, and we were unable to get satisfactory HRMS.

(*Z*)-2-Fluoro-5-(2-chloro-1-phenoxyvinyl)pyridine (24). This compound was a colorless oil prepared according to representative procedure B on a 0.38 mmol scale. NMR were consistent with previously published data:[21a21a] $R_f = 0.10$ (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.38 (d, 1H, J = 2 Hz), 7.85 (ddt, 1H, J = 1 Hz, 2 Hz, 7 Hz), 7.32−7.26 (m, 2H), 7.04 (dt, 1H, J = 1 Hz, 7 Hz), 6.97 (dd, 1H, J = 1 Hz, 8 Hz), 6.90 (dd, 1H, J = 3 Hz, 8 Hz), 6.46 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3, 162.09, 155.4, 148.0, 145.3, 145.1, 138.4, 138.3, 129.9, 127.6, 127.5, 123.0, 116.0, 110.1, 109.6, 108.4, 108.4.

(*Z*)-2-(2-Chloro-1-phenoxyvinyl)thiophene (25). This compound was prepared according to representative procedure B. It decomposes at room temperature. NMR were consistent with previously reported data:[21a21a] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33−7.24 (m, 3H), 7.13 (m, 1H), 7.07−7.02 (m, 3H), 6.96 (m, 1H), 6.42 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.1, 146.7, 136.4, 129.7, 127.6, 126.2, 125.9, 122.6, 115.8, 106.1 (also contains a trace of decomposed material).

Representative Procedure C for Sonogashira Cross-Coupling: Synthesis of (*Z*)-1-Chloro-2-phenoxy-4-phenylbut-1-en-3-yne (26). $Pd(PPh_3)_4$ (286.0 mg, 0.25 mmol, 5 mol %) and CuI (95.2 mg, 0.5 mmol, 10 mol %) were placed into an oven-dried one-piece, round-bottom flask/condenser, sealed with a septum, and purged with argon for 20 min. A dichlorovinyl ether **1** (946.3 mg, 4.95 mmol, 1 equiv) in THF (5 mL) was added, followed by TEA (1.4 mL, 9.9 mmol, 2.0 equiv) and phenylacetylene (0.61 mL, 5.4 mmol, 1.1 equiv). The solution was stirred at room temperature for 12 h, after which it was diluted with ethyl acetate, filtered through Celite, concentrated, and purified via flash chromatography using 9:1 hexanes/ethyl acetate as an eluant. NMR were consistent with previously published data.[21a21a] $R_f = 0.48$ (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41−7.26 (m, 7H), 7.18−7.13 (m, 3H), 6.21 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 136.5, 131.5, 129.4, 129.2, 128.4, 123.8, 121.4, 118.4, 111.3, 94.0, 81.3.

(*Z*)-1-Chloro-2-phenoxy-6-(*tert*-butyldiphenylsilyloxy)hex-1-en-3-yne (27). This compound is a colorless oil and was prepared according to representative procedure C. NMR were consistent with previously published data:[21a21a] $R_f = 0.61$ (9:1 hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72−7.67 (m, 4H), 7.51−7.40 (m, 6H), 7.34−7.28 (m, 2H), 7.12−7.05 (m, 3H), 6.04 (s, 1H), 3.71 (t, 2H), 2.51 (t, 2H), 1.09 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 136.2, 135.6, 135.6, 133.5, 129.8, 129.3, 127.8, 123.5, 117.9, 111.0, 92.8, 74.0, 61.8, 26.8, 23.4, 19.2.

(*Z*)-1-Chloro-2-phenoxy-6-hydroxyhex-1-ene-3-yne (28). This compound is a colorless oil and was prepared according to representative procedure C. NMR were consistent with previously published data:[21a21a] $R_f = 0.17$ (9:1 hexane/ethyl acetate; dec at room temperature; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39−7.32 (m, 2H), 7.17−7.12 (m, 1H), 7.10−7.05 (m, 2H), 6.04 (s, 1H), 3.56 (t, 2H), 2.47 (t, 2H), 1.61 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.1, 136.3, 129.3, 123.9, 118.5, 110.5, 92.4, 74.7, 60.5, 23.6.

(*Z*)-1-Chloro-2-phenoxy-4-(2-hydroxymethylphenyl)but-1-en-3-yne (29). Viscous, colorless oil prepared on a 0.8 mmol scale according to representative procedure C. Purified via flash chromatography on TEA-treated silica using hexanes as an eluent to give 171.8 mg of **29**: $R_f = 0.33$ (hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45−7.32 (m, 5H), 7.28−7.16 (m, 4H), 6.22 (s, 1H), 4.39 (s, 2H), 1.57 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 142.8, 136.5, 132.1, 129.6, 129.6, 127.4, 127.2, 124.2, 119.3, 118.8, 111.2, 91.7, 85.7, 63.2; HRMS calcd for $C_{17}H_{13}ClO_2$ 284.0604, found 284.0601.

(*Z*)-1-Chloro-2-phenoxyoct-1-en-3-yne (30). This compound is a colorless oil and was prepared according to representative procedure C. NMR were consistent with previously published data:[21a21a] $R_f = 0.63$ (9:1 hexane/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.31 (m, 2H), 7,15−7.06 (m, 3H), 6.01 (s, 1H), 2.22 (t, 2H), 1.44−1.34 (m, 2H), 1.30−1.18 (m, 2H), 0.84 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 136.5, 129.2, 123.5, 118.3, 109.9, 95.9, 73.0, 30.0, 21.7, 18.8, 13.5.

(*Z*)-1-Chloro-2-phenoxy-5-phenylpent-1-ene (31). An oven-dried one piece round-bottom flask/condenser was sealed with a septum and purged with argon for 20−30 min. Allylbenzene (0.64 mL, 4.8 mmol, 1.2 equiv) was added followed by a 0.5 M solution of 9-BBN in THF (9.6 mL, 4.8 mmol, 1.2 equiv) and the mixture stirred at room temperature. After 1 h, Pd_2dba_3 (91.7 mg,

0.10 mmol, 2.5 mol %), Xantphos (115.7 mg, 0.20 mmol, 5 mol %), CsF (1.82 g, 12 mmol, 3 equiv), and Cs_2CO_3 (3.91 g, 12 mmol, 3 equiv) were added as solids, followed by 1.0 equiv of vinyl chloride **1** (0.7561 g, 4 mmol) in THF (8 mL). The suspension was brought to reflux and stirred for 12 h. When complete, the reaction was cooled and partitioned between water and dichloromethane. The layers were separated, and the aqueous layer was extracted with dichloromethane once more. The combined organic layers were dried with magnesium sulfate, filtered and concentrated onto silica gel for purification via flash chromatography using 14:1 hexanes/ethyl acetate as an eluant: R_f = 0.62 (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.00 (m, 10H), 5.81 (s, 1H), 2.70 (m, 2H), 2.33 (s, 2H), 1.90 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 152.9, 141.5, 129.7, 128.5, 126.0, 122.7, 116.7, 104.3, 35.0, 30.9, 27.9; HRMS calcd for $C_{17}H_{17}ClO$ 272.0968, found 272.0956.

Representative Procedure D for Negishi Cross-Coupling with Et_2Zn: Synthesis of (*Z*)-1-Chloro-2-phenoxybut-1-ene (32). Pd_2dba_3 (14.2 mg, 15.5 μmol, 2.5 mol %) and DPEphos (17.0 mg, 31 μmol, 5 mol %) were placed into an oven-dried, one-piece, round-bottom flask condenser, sealed with a septum, and purged with Ar for 20 min. A 1.0 equiv portion of dichlorovinyl ether **1** (118.5 mg, 0.62 mmol) as a solution in DMF or THF (2 mL) was added, followed by Et_2Zn as a 1.0 M solution in hexanes (0.68 mL, 0.68 mmol, 1.1 equiv). The resulting solution was stirred at room temperature for 12 h. When complete, water was added to the reaction and extracted three times with diethyl ether. The organic layers were combined, washed with brine, dried with magnesium sulfate, filtered, and concentrated. The crude oil obtained was applied to a silica gel column that was pretreated with 2.5 vol % of triethylamine and eluted with 14:1 hexanes/diethyl ether to yield the corresponding 1-ethyl-2-chlorovinyl ether **32** as a colorless oil: R_f = 0.71 (9:1 hexanes/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.31 (m, 2H), 7.11−7.05 (m, 1H), 7.03−6.99 (m, 2H), 5.77 (t, 1H, J = 1.2 Hz), 2.28 (dd, 2H, J^1 = 7.5 Hz, J^2 = 1.2 Hz), 1.11 (t, 3H, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3, 154.7, 129.6, 122.6, 116.7, 103.4, 24.9, 11.2. We were unable to get satisfactory HRMS of this compound.

(*Z*)-1-Phenoxy-1-(4-methoxyphenyl)-2-(4-fluorophenyl)ethylene (33). Colorless solid prepared according to representative procedure A on 0.38 mmol scale. Purified via flash chromatography using 9:1 hexanes/dichloromethane as an eluent to give 68.9 mg of **33**: R_f = 0.45 (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66−7.60 (m, 2H), 7.56−7.52 (m, 2H), 7.30−7.23 (m, 2H), 7.06−6.96 (m, 5H), 6.90−6.85 (m, 2H), 6.55 (s, 1H), 3.81 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.3, 160.0, 159.9, 156.3, 149.2, 131.3, 131.2, 130.4, 130.3, 129.7, 128.3, 127.4, 122.1, 116.3, 115.6, 115.3, 114.1, 113.8, 55.3; HRMS calcd for $C_{21}H_{17}FO_2$ 321.1284, found 321.1285.

Representative Procedure E for Suzuki−Miyaura Cross-Coupling with Pd/S-Phos Catalytic System: Synthesis of (1*Z*,3*E*)-1-Phenoxy-1-(4-methylphenyl)-5,5-dimethylhexa-1,3-diene (35). The boronic acid (50.2 mg, 0.39 mmol, 1.5 equiv), $Pd(OAc)_2$ (2.9 mg, 0.013 mmol, 5 mol %), S-Phos (10.7 mg, 0.026 mmol, 10 mol %), and Cs_2CO_3 (187.6 mg, 0.58 mmol, 2.2 equiv) were placed in a one-piece, round-bottom flask/condenser, sealed with a septum and purged with argon for 20 min. A solution of the vinyl chloride **15** (64.0 mg, 0.26 mmol, 1 equiv) in toluene (2.5 mL) was added and the suspension was refluxed overnight. When complete, the reaction was cooled and partitioned between dichloromethane and water. The layers were separated, and the water layer was extracted twice more with dichloromethane. The organic layers were combined, dried with magnesium sulfate, filtered, and concentrated onto silica gel, which was applied to a silica gel column and eluted with 14:1 hexanes/dichloromethane to give 66.7 mg of **35**: R_f = 0.25 (9:1 hexanes/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, 2H), 7.29 (t, 2H), 7.14 (d, 2H), 7.06−6.97 (m, 3H), 6.48−6.34 (m, 2H), 5.96 (d, 1H), 2.36 (s, 3H), 1.08 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.8, 147.7, 147.0, 137.9, 132.5, 129.5, 129.3, 125.3, 121.5, 119.2, 116.9, 115.9, 33.6, 29.6, 21.2; HRMS calcd for $C_{21}H_{24}O$ 292.1827, found 292.1827.

(1*Z*,3*E*)-1-Phenoxy-1-(4-methylphenyl)-4-phenylbuta-1,3-diene (36). Colorless solid prepared according to representative procedure E on a 0.26 mmol scale. Purified via flash chromatography using 14:1 hexanes/dichloromethane as an eluent to give 53.1 mg of **36**: R_f = 0.10 (14:1 hexanes/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (m, 2H), 7.43 (m, 2H), 7.36−7.14 (m, 8H), 7.09−6.98 (m, 3H), 6.78−6.66 (m, 2H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.9, 149.8, 138.4, 137.5, 132.7, 132.0, 129.7, 129.4, 128.6, 127.6, 126.5, 125.5, 123.2, 121.8, 116.6, 115.2, 21.3; HRMS calcd for $C_{23}H_{20}O$ 312.1514, found 312.1517.

(1*Z*,3*E*)-1-Phenoxy-1-(4-methylphenyl)-4-(4-fluorophenyl)buta-1,3-diene (37). Colorless solid prepared according to representative procedure E on a 0.26 mmol scale. Purified via flash chromatography using 14:1 hexanes/dichloromethane to give 12.7 mg of **37**: R_f = 0.10 (14:1 hexanes/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (d, 2H), 7.38 (m, 2H), 7.31−7.25 (m, 3H), 7.15 (d, 2H), 7.09−6.97 (m, 6H), 6.71−6.62 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9, 160.7, 157.9, 149.8, 138.5, 133.7, 132.0, 131.4, 129.7, 129.4, 128.0, 127.9, 125.5, 122.89, 122.86, 121.8, 116.4, 116.4, 115.9 115.7 115.4, 21.3; HRMS calcd for $C_{23}H_{19}FO$ 330.1420, found 330.1427.

(1*Z*,3*E*)-1-(4-Methylphenyl)-2-phenoxy-4-phenylbuta-1,3-diene (38). Pale yellow solid prepared according to representative procedure A on a 0.38 mmol scale. Purified via flash chromatography using 14:1 hexanes/dichloromethane as an eluent to give 64.7 mg of **38**: R_f = 0.14 (14:1 hexanes/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, 2H, J = 8 Hz), 7.42 (m, 2H), 7.38−7.24 (m, 5H), 7.16−7.10 (m, 4H), 7.03 (m, 1H), 6.87 (d, 1H, J = 16 Hz), 6.71 (d, 1H, J = 16 Hz), 6.40 (s, 1H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.5, 148.5 137.6, 136.7, 131.8, 130.1 129.7, 129.3, 129.1, 128.7 127.8, 126.7 124.6, 121.8, 121.3 115.3, 21.3; HRMS calcd for $C_{23}H_{20}O$ 312.1514, found 312.1514.

(1*Z*,3*E*)-1-(4-Methoxyphenyl)-2-phenoxyl-4-phenylbuta-1,3-diene (39). Pale yellow solid prepared according to representative procedure A on a 0.38 mmol scale. Purified via flash chromatography using 9:1 hexanes/ethyl acetate as an eluent to give 100.4 mg of **39**: R_f = 0.38 (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, 2H, J = 8 Hz), 7.43−7.23 (m, 7H), 7.14 (d, 2H, J = 8 Hz), 7.03 (t, 1H), 6.86 (m, 3H), 6.68 (d, 1H, J = 16 Hz), 6.37 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 156.5, 147.5, 136.8, 130.6, 129.8, 129.5, 128.6, 127.7, 127.4, 126.6, 124.6, 121.8, 120.9, 115.3, 114.1, 55.2; HRMS calcd for $C_{23}H_{20}O_2$ 328.1463 found 328.1465.

(1*E*,3*Z*,5*E*)-1-Phenyl-3-phenoxy-6-(4-methylphenyl)hexa-1,3,5-triene (40). Colorless solid prepared according to representative procedure A on a 0.21 mmol scale. Purified via flash chromatography using 9:1 hexanes/ethyl acetate as an eluent to give 27.7 mg of **40**: R_f = 0.50 (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39−7.17 (m, 13H), 7.09 (m, 2H), 7.04−6.98 (m, 2H), 6.81−6.62 (m, 3H), 6.28 (d, 1H, J = 11 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.2, 149.7, 137.3, 136.6, 133.3, 130.3, 129.7, 128.6, 128.6, 127.9, 127.8, 126.7, 123.3, 122.9, 122.1, 121.8, 115.3; HRMS calcd for $C_{25}H_{22}O$ 338.1671, found 338.1672.

(1*E*,3*Z*,5*E*)-1-Phenyl-3-phenoxy-6-(4-chlorophenyl)hexa-1,3,5-triene (41). Pale yellow solid prepared according to representative procedure A on a 0.19 mmol scale. Purified via flash chromatography using 9:1 hexanes/dichloromethane as an eluent to give 44.6 mg of **41**: R_f = 0.14 (hexanes/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.25 (m, 12H), 7.13−6.98 (m, 4H), 6.83−6.70 (m, 2H), 6.62 (d, 1H, J = 16 Hz), 6.29 (d, 1H, J = 11 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.2, 150.2, 136.5, 135.8, 133.3, 131.8, 130.7, 129.8, 128.8, 128.7, 128.1, 127.7, 126.8, 123.5, 123.2, 121.9, 121.7, 115.3; HRMS calcd for $C_{24}H_{19}ClO$ 358.1124, found 358.1126.

(1*E*,3*Z*)-1,6-Diphenyl-3-phenoxyhexa-1,3-dien-5-yne (42). Pale yellow solid prepared according to representative procedure A on a 0.19 mmol scale. Purified via flash chromatography using 9:1 hexanes/dichloromethane as an eluent to give 13.2 mg of **42**: R_f = 0.10 (9:1 hexanes/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (m, 2H), 7.41−7.06 (m, 14H), 7.02 (d, 1H, J = 16 Hz), 6.84 (d, 1H, J = 16 Hz), 5.70 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 157.3, 136.1, 132.0, 131.3, 129.5, 128.8, 128.5, 128.1, 127.1, 123.3, 123.0, 122.2, 116.4, 99.7, 98.9, 85.5; HRMS calcd for $C_{24}H_{18}O$ 322.1358, found 322.1373.

(*Z*)-1-(3-Acetylphenyl)-2-(phenoxy)oct-1-ene-3-yne (43). Colorless solid prepared according to representative procedure A on a 85 μmol scale. Purified via flash chromatography using 10:1 hexanes/ethyl acetate to give 11.3 mg of **43**: R_f = 0.19 (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (m, 1H), 7.84 (m, 1H), 7.78 (m, 1H), 7.40−7.31 (m, 3H), 7.14−7.08 (m, 3H), 6.23 (s, 1H), 2.54 (s, 3H), 2.23 (t, 2H), 1.42−1.32 (m, 2H), 1.29−1.17 (m, 2H), 0.82 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.0, 155.3, 137.3, 135.8, 135.2, 133.2, 129.3, 129.0, 128.7, 126.8, 123.4, 118.9, 118.5, 94.4, 76.3, 30.1, 26.6, 21.7, 18.9, 13.5; HRMS calcd for $C_{22}H_{22}O_2$ 318.1620, found 318.1625.

(*Z*)-1-(3-Pyridinyl)-2-(phenoxy)oct-1-ene-3-yne (44). Colorless oil prepared according to representative procedure B on 0.28 mmol scale. Purified via flash chromatography on TEA-treated silica using 4:1 hexanes/ethyl acetate as an eluent: R_f = 0.33 (2:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73 (d, 1H, J = 2.2 Hz), 8.44 (dd, 1H, J^1 = 1.5 Hz, J^2 = 5 Hz), 8.08 (dt, 1H, J^1 = 2 Hz, J^2 = 8 Hz), 7.40−7.34 (m, 2H), 7.25−7.21 (m, 1H), 7.18−7.12 (m, 2H), 6.17 (s, 1H), 2.26 (t, 2H, J = 7 Hz), 1.44−1.35 (m, 2H), 1.31−1.19 (m, 2H), 0.85 (t, 2H, J = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.11 150.0, 147.9, 137.0, 135.4, 130.9, 129.2, 123.7, 123.4, 118.8, 115.8, 94.9, 76.0, 30.1, 21.7, 18.9, 13.5; HRMS calcd for $C_{19}H_{19}NO$ 277.1467, found 277.1476.

(*Z*)-1-(2-Thiophene-yl)-2-(phenoxy)oct-1-ene-3-yne (45). Colorless oil prepared according to representative procedure B on a 0.28 mmol scale. Purified via flash chromatography using 9:1 hexanes/dichloromethane as an eluent to give 23.2 mg of **45**: R_f = 0.18 (9:1 hexanes/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.32 (m, 2H), 7.28−7.25 (m, 1H), 7.18−7.09 (m, 4H), 7.02−6.98 (m, 1H), 6.58 (s, 1H), 2.27 (t, 2H), 1.47−1.37 (m, 2H), 1.34−1.23 (m, 2H), 0.85 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.1, 137.4, 132.4, 129.2, 127.1, 126.9, 126.4, 123.2, 118.1, 115.1, 94.9, 75.9, 30.2, 21.7, 19.0, 13.5; HRMS calcd for $C_{18}H_{18}OS$ 282.1078, found 282.1072.

(*Z*)-1-(2-Thiophene-yl)-2-phenoxy-4-phenylbut-1-en-3-yne (46). Colorless solid prepared according to representative procedure A on a 0.28 mmol scale. Purified via flash chromatography using 20:1 hexanes/dichloromethane to give 24.3 mg of **46**: R_f = 0.55 (20:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.36 (m, 2H), 7.33−7.13 (m, 11H), 7.04 (m, 1H), 6.77 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 137.2, 132.2, 131.4, 129.3, 128.7, 128.3, 127.8, 127.6, 126.6, 123.5, 122.1, 118.3, 116.3, 93.4, 84.6. We were unable to obtain satisfactory HRMS of this compound.

(*Z*)-1-[2-(Methylthio)phenyl]-2-phenoxy-4-phenylbut-1-en-3-yne (47). Colorless solid prepared according to representative procedure A on a 0.20 mmol scale. Purified via flash chromatography using 3% diethyl ether in hexanes to give 27.7 mg of **47**: R_f = 0.26 (24:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (m, 1H), 7.43−7.14 (m, 13H), 6.89 (s, 1H), 2.55 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.6, 137.1, 135.4, 133.2, 131.5, 129.8, 129.3, 128.7, 128.3, 128.1, 127.2, 125.5, 123.5, 118.7, 117.8, 92.4, 85.2, 16.9. We were unable to obtain satisfactory HRMS of this compound.

(3*Z*,5*E*)-1,6-Diphenyl-3-phenoxyhex-1-yne-3,5-diene (48). Pale yellow solid prepared according to representative procedure A on a 0.18 mmol scale. Purified via flash chromatography using 20:1 hexanes/dichloromethane as an eluent to give 45.2 mg of **48**: R_f = 0.10 (20:1 hexanes/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (m, 2H), 7.43−7.12 (m, 14H), 6.71 (d, 1H, J = 16 Hz), 6.41 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.3, 137.2, 134.0, 133.2, 131.5, 129.4, 128.7, 128.7, 128.4, 128.0, 126.8, 123.8, 123.2, 122.1, 118.1, 93.3, 85.2; HRMS calcd for $C_{24}H_{18}O$ 322.1358, found 322.1359.

(3*Z*,5*E*)-1-Phenyl-3-phenoxy-6-(4-methylphenyl)hex-1-yne-3,5-diene (49). Pale yellow solid prepared according to representative procedure A on a 0.18 mmol scale. Purified via flash chromatography using 20:1 hexanes/dichloromethane as an eluent to give 39.1 mg of **49**: R_f = 0.10 (20:1 hexanes/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.35 (m, 4H), 7.32−7.25 (m, 6H), 7.22−7.11 (m, 5H), 6.68 (d, 1H, J = 16 Hz), 6.40 (m, 1H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.4, 138.0, 134.4, 133.5, 133.3, 131.5, 129.43, 129.37, 128.7, 128.3, 126.7, 124.2, 123.1, 122.2, 121.2, 118.0, 93.1, 85.3, 21.4; HRMS calcd for $C_{25}H_{20}O$ 336.1514, found 336.1515.

(3*Z*,5*E*)-1-Phenyl-3-phenoxy-6-(4-chlorophenyl)hex-1-yne-3,5-diene (50). Pale yellow solid prepared according to representative procedure A on a 0.18 mmol scale. Purified via flash chromatography using 20:1 hexanes/dichloromethane as an eluent to give 29.5 mg of **50**: R_f = 0.40 (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.12 (m, 15H), 6.63 (d, 1H, J = 16 Hz), 6.36 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.2, 135.7, 134.5, 133.5, 131.6, 131.5, 129.4, 128.9, 128.8, 128.4, 127.9, 123.3, 123.2, 122.7, 122.0, 118.2, 93.6, 85.0; HRMS calcd for $C_{24}H_{17}ClO$ 356.0968, found 356.0962.

3-Benzyl-5-phenoxybiphenyl (52). Colorless solid prepared according to representative procedure A on a 0.18 mmol scale. Purified via flash chromatography using 20:1 hexanes/dichloromethane as an eluent to give 25.7 mg of **52**: R_f = 0.13 (20:1 hexanes/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.25 (m, 8H), 7.20−7.06 (m, 5H), 7.03−6.98 (m, 2H), 6.95−6.90 (m, 3H), 4.05 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.3, 155.7, 144.7, 141.3, 141.2, 129.9, 129.7, 129.4, 128.4, 128.1, 128.0, 127.2, 127.1, 125.48, 125.45, 123.0, 118.5, 117.9, 33.0; HRMS calcd for $C_{25}H_{20}O$ 336.1514, found 336.1517.

(*Z*)-1-(4-Methoxyphenyl)-2-phenoxy-5-phenylpent-1-ene (53). Colorless oil prepared according to representative procedure E on a 0.34 mmol scale. Purified via flash chromatography using 24:1 hexanes/ethyl acetate as an eluent to give 48.3 mg of **53**: R_f = 0.18 (24:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (m, 2H), 7.37−7.28 (m, 5H), 7.25−7.18 (m, 3H), 7.10−7.04 (m, 3H), 6.84 (m, 2H), 5.94 (s, 1H), 3.81 (s, 3H), 2.70 (t, 2H), 2.36 (t, 2H), 1.92 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.3, 155.5, 150.5, 142.1, 129.7, 128.5, 128.3, 127.8, 125.8, 122.2, 117.0, 115.1, 113.8, 55.2, 35.1, 32.7, 28.7. We were unable to obtain satisfactory HRMS of this compound.

(*Z*)-1,7-Diphenyl-4-phenoxyhept-1-yne-3-ene (54). Colorless oil prepared according to representative procedure E on a 0.34 mmol scale. Purified via flash chromatography using 24:1 hexanes/ethyl acetate as an eluent to give 27.8 mg of **54**: R_f = 0.28 (20:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.05 (m, 15H), 5.32 (d, 1H, J = 0.6 Hz), 2.72 (t, 2H, J = 7.5 Hz), 2.37 (t, 2H, J = 7.5 Hz), 1.94 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.2, 156.0, 141.7, 131.3, 129.4, 128.44, 128.40, 127.7, 125.9, 123.6, 122.8, 118.0, 94.3, 93.1, 84.3, 35.1, 33.2, 28.4. We were unable to obtain satisfactory HRMS of this compound.

(*Z*)-4-Phenoxy-7-phenylhept-3-ene (56). Colorless oil prepared according to representative procedure E on a 0.34 mmol scale. Purified via flash chromatography using a gradient of hexanes to 4:1 hexanes/dichloromethane as an eluent to give 30.2 mg of **56**: R_f = 0.20 (9:1 hexanes/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.29 (m, 4H), 7.24−7.19

(m, 3H), 7.05−6.98 (m, 3H), 5.08 (t, 1H, J = 7.2 Hz), 2.67 (t, 2H, J = 7.6 Hz), 2.22 (t, 2H, J = 8 Hz), 2.09 (t, 2H, J = 7 Hz), 1.84 (m, 2H), 1.00 (t, 3H, J = 8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.8, 149.7, 142.2, 129.5, 128.5, 128.3, 125.8, 121.4, 118.3, 115.9, 35.2, 31.9, 28.5, 18.7, 14.1. We were unable to obtain satisfactory HRMS of this compound.

(*E*)-1-Benzyloxy-1,2-dichloroethylene (57). KH (2.74 g, 20.5 mmol, 2.05 equiv) was weighed into a round-bottom flask and washed with three portions of petroleum ether. The KH was then suspended in 40 mL THF, benzyl alcohol (1.0 mL, 10 mmol) was added dropwise, and the reaction was allowed to stir for 15 min. The suspension was cooled to approximately −50 °C ($CHCl_3/CO_2$ (s) bath). Trichloroethylene (1.35 mL, 15 mmol, 1.5 equiv) was then added dropwise. The reaction was allowed to warm gradually to room temperature overnight. The reaction was cooled to 0 °C, diluted with petroleum ether, and then quenched with ice-cold water. The phases were separated, and the aqueous phase was extracted once more with petroleum ether. The organic layers were combined, dried with sodium sulfate, filtered, and concentrated to give a yellow to dark brown oil. The crude oil was applied to a silica column pretreated with triethylamine (ca. 2.5 vol % with respect to the volume of dry silica) and eluted with hexanes to give 1.00 g of **57**: R_f = 0.55 (9:1 hexanes/ethyl acetate). ^{1}H and ^{13}C NMR data are consistent with literature values:[48] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48−7.37 (m, 5H), 5.53 (s, 1H), 5.07 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.4, 134.7, 128.8, 128.6, 128.6, 98.9, 73.4.

One-Pot Double Suzuki Coupling: Synthesis of (*Z*)-1-[3-[1-(Benzyloxy)-2-*p*-tolylvinyl)phenyl]ethanone (58). Pd_2dba_3 (3.6 mg, 3.9 μmol, 2.5 mol %), DPEphos (4.3 mg, 7.8 μmol, 5 mol %), 3-acetylphenylboronic acid (22.7 mg, 0.137 mmol, 1.05 equiv), CsF (59.5 mg, 0.39 mmol, 3 equiv), and Cs_2CO_3 (127.6 mg, 0.39 mg, 3 equiv) were added to an oven-dried test tube and sealed with a septum. The test tube was purged with argon for 10 min. A solution of benzyl dichlorovinyl ether **57** (26.5 mg, 0.13 mmol, 1 equiv) in 0.65 mL of THF was added to the test tube, and the reaction mixture was brought to reflux. When the first cross-coupling was deemed complete as judged by TLC (approximately 12 h), the reaction mixture was cooled to room temperature, and 4-methylphenylboronic acid (26.9 mg, 0.19 mmol, 1.5 equiv) was added as a solid. The reaction mixture reheated to reflux. After 20 h, the reaction mixture was cooled and partitioned between dichloromethane and water. The layers were separated, and the aqueous layer was reextracted with dichloromethane twice more. The organic layers were combined, dried with magnesium sulfate, filtered, and concentrated. The crude residue was applied to a silica gel column eluted with 9:1 hexanes/ethyl acetate to give 33.4 mg **58** (75% yield): R_f = 0.40 (4:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (m, 1H), 7.93 (m, 1H), 7.81 (m, 1H), 7.67 (d, 2H), 7.51 (t, 1H), 7.42−7.33 (m, 5H), 7.17 (m, 2H), 6.29 (s, 1H), 4.79 (s, 2H), 2.62 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.0, 153.2, 137.5, 137.5, 137.1, 136.9, 132.6, 130.8, 129.2, 128.9, 128.6, 128.1, 127.98, 127.95, 126.3, 114.8, 26.7, 21.3; HRMS calcd for $C_{24}H_{22}O_2$ 342.1620, found 342.1622.

Representative Procedure F for Synthesis of 2-Substituted 1,2-Dichlorovinyl Ethers from Dichlorovinyl Ether 1: Synthesis of (*E*)-1,2-Dichloro-1-phenoxypropene (59). A solution of the dichlorovinyl ether **1** (149.3 mg, 0.79 mmol, 1 equiv) in 4 mL of THF was cooled to −78 °C. *n*-BuLi as a 1.6 M solution in hexanes (0.56 mL, 0.89 mmol, 1.13 equiv) was added dropwise and stirred for 5 min. Iodomethane (98 μL, 1.58 mmol, 2 equiv) was added dropwise. The solution was allowed to stir at −78 °C for 1 h and allowed to warm to room temperature. The reaction was quenched with NH_4Cl, extracted twice with dichloromethane, dried with magnesium sulfate, filtered, and concentrated. The crude residue was applied to a silica gel column pretreated with 2.5 volume% of triethylamine and eluted with hexanes to yield 1.21 mg of **59** as a colorless oil: R_f = 0.7 (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ7.41−7.34 (m, 2H), 7.19−7.13 (m, 1H), 7.09−7.04 (m, 2H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.5, 134.9, 129.7, 124.0, 116.6, 116.5, 21.6; HRMS calcd for $C_9H_8Cl_2O$ 201.9952, found 201.9944.

(*E*)-1,2-Dichloro-1-phenoxy-1,4-pentadiene (60). Clear oil prepared according to representative procedure F on a 0.80 mmol scale using 2.5 equiv of allyl bromide. Purified via flash chromatography using 9:1 hexanes/dichloromethane as an eluent to give 107.11 mg of **60** (66% yield). R_f = 0.55 (9:1 hexanes/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41−7.34 (m, 2H), 7.19−7.13 (m, 1H), 7.08−7.03 (m, 2H), 5.97−5.83 (m, 1H), 5.32−5.22 (m, 2H), 3.33 (dd, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 135.5, 129.8, 124.1, 118.7, 118.1, 116.5, 39.0. We were unable to obtain satisfactory HRMS for this compound.

(*E*)-1,2-Dichloro-1-(trimethylsilyl)-2-phenoxyethylene (61). Clear oil prepared according to representative procedure F on a 0.88 mmol scale using 2.0 equiv of chlorotrimethylsilane as the electrophile. Purified via flash chromatography using 17:1 hexanes: ethyl acetate as an eluent to give 205.8 mg of **61** (89% yield): R_f = 0.55 (9:1 hexanes/dichloromethane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.36 (m, 2H), 7.21−7.15 (m, 1H), 7.09−7.05 (m, 2H), 0.41 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 143.6, 129.8, 124.2, 117.9, 117.0, −0.97; HRMS calcd for $C_{11}H_{14}Cl_2OSi$ 260.0191, found 260.0194.

Ethyl (*E*)-2,3-Dichloro-3-phenoxyacrylate (62). Clear oil prepared according to representative procedure F on 1.2 mmol scale using 2.5 equiv of ethylchloroformate. Purified via flash chromatography using 9:1 hexanes/dichloromethane as an eluent to give 174.4 mg of **62** (56% yield): R_f = 0.50 (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.35 (m, 2H), 7.25−7.19 (m, 1H), 7.09−7.04 (m, 2H), 4.35 (m, 2H), 1.38 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.8, 153.4, 145.7, 129.9, 125.4, 118.6, 109.8, 62.6, 14.1; HRMS calcd for $C_{11}H_{10}Cl_2O_3$ 260.0007, found 260.0006.

(*E*)-1,2-Dichloro-1-phenoxy-3-hydroxy-4-methylpentene (63). Clear oil prepared according to representative procedure F on a 0.83 mmol scale using 2.0 equiv of isobutyraldehyde. Purified via flash chromatography using 9:1 hexanes/ethyl acetate as an eluent to give 200.1 mg of **63** (92% yield): R_f = 0.21 (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.33 (m, 2H), 7.19−7.13 (m, 1H), 7.07−7.02 (m, 2H), 4.43 (m, 1H), 2.07 (br d, 1H), 2.04−1.94 (m, 1H), 1.16 (d, 3H, J = 6.6 Hz), 0.98 (d, 3H, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 136.5, 129.8, 124.3, 122.3, 116.9, 76.3, 32.8, 19.0, 18.5; HRMS calcd for $C_{12}H_{14}Cl_2O_2$ 260.0371, found 260.0362.

(*E*)-1,2-Dichloro-1-phenoxy-3-(4-methylphenyl)propen-3-ol (64). Clear oil prepared according to representative procedure F on a 0.70 mmol scale using 1.5 equiv of *p*-tolualdehyde. Purified via flash chromatography using 9:1 hexanes/ethyl acetate as an eluent to give 203.1 mg of **64** (94% yield): R_f = 0.18 (9:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47−7.38 (m, 4H), 7.28 (d, 2H, J = 8 Hz), 7.25−7.19 (m, 1H), 7.12−7.08 (m, 2H), 6.11 (br s, 1H), 2.61 (br s, 1H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1, 138.1, 136.7, 136.5, 129.9, 129.4, 125.6, 124.5, 122.5, 117.0, 71.5, 21.2; HRMS calcd for $C_{16}H_{14}Cl_2O_2$ 308.0371, found 308.0373.

Procedure for the One-Pot Synthesis of 62 from Phenol. KH (2.74 g, 20.5 mmol, 2.05 equiv) was weighed into a round-bottom flask and washed with three 5 mL portions of petroleum ether. The KH was then suspended in 20 mL of THF. A solution of phenol (0.9411 g, 10 mmol, 1.0 equiv) in 5 mL of THF was added dropwise, and the reaction was allowed to stir at room

(48) Dudley, G. B.; Takaki, K. S.; Cha, D. D.; Danheiser, R. L. *Org. Lett.* **2000**, *2*, 3407–3410.

temperature for 60 min. The suspension was cooled to approximately −50 °C ($CHCl_3/CO_2$ (s) bath), and trichloroethylene (TCE) (1.35 mL, 15 mmol, 1.5 equiv) was then added dropwise. The reaction was allowed to warm gradually to room temperature overnight. The solution of the dichlorovinyl ether was cooled to −78 °C. *n*-BuLi (7.5 mL of 1.6 M solution in hexanes, 1.13 equiv) was added dropwise and stirred for 5 min. Ethyl chloroformate (2.0 mL, 20 mL, 2.0 equiv) was added dropwise. The solution was allowed to stir at −78 °C for 5 h before being quenched with H_2O. The mixture was extracted twice with dichloromethane, and the combined organic extracts were dried with magnesium sulfate, filtered, and concentrated. The crude residue was applied to a silica gel column pretreated with 2.5 vol % of triethylamine, which was then eluted with 14:1 hexanes/diethyl ether to yield 1.32 g of adduct **62**.

Cross-Coupling between Vinyl Chloride 59 and *p*-Methoxyphenylboronic Acid. This reaction was performed according to representative procedure A on a 0.37 mmol scale. The product was purified via flash chromatography using 9:1 hexanes/dichloromethane as an eluent to give 54.1 mg of (*Z*)-**65** and 4.0 mg of a minor product identified by its ^1H and ^{13}C NMR spectra as (*E*)-**65**.

(*Z*)-1-(2-Chloro-1-phenoxyprop-1-enyl)-4-methoxybenzene ((*Z*)-65): R_f = 0.48 (9:1 hexanes/ethyl acetate); ^1H NMR (300 MHz, $CDCl_3$) δ 7.37 (m, 2H), 7.24−7.18 (m, 2H), 6.97−6.92 (m, 3H), 6.84 (m, 2H), 3.77 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 156.2, 145.4, 130.5, 129.4, 125.8, 122.1, 119.5, 116.5, 113.8, 55.2, 22.1; HRMS calcd for $C_{16}H_{15}ClO_2$ 274.0761, found 274.0767.

(*E*)-1-(2-Chloro-1-phenoxyprop-1-enyl)-4-methoxybenzene ((*E*)-65): ^1H NMR (300 MHz, $CDCl_3$) δ 7.33−7.26 (m, 5H), 7.09−7.04 (m, 1H), 7.02−6.98 (m, 1H), 6.80 (m, 2H), 3.76 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.6, 155.3, 135.2, 130.5, 130.4, 129.5, 129.4, 128.8, 116.7, 113.5, 55.2, 20.2.

Representative Procedure G for Lithiation and Electrophilic Quenching of 1-Aryl-2-chlorovinyl Ethers: Synthesis of (*Z*)-1-(2-Chloro-1-phenoxyprop-1-enyl)-4-methoxybenzene (65) from 2. This procedure is similar to representative procedure F for the alkylation of 1,2-dichlorovinyl ethers. A solution of the chlorovinyl ether **2** (800 mg, 3.06 mmol, 1 equiv) in 46 mL of THF was cooled to −78 °C. *n*-BuLi as a 1.6 M solution in hexanes (2.2 mL, 3.47 mmol, 1.13 equiv) was added dropwise, and the mixture was stirred for 30 min. The iodomethane (0.38 mL, 6.1 mmol, 2 equiv) was then added dropwise. The solution was allowed to stir at −78 °C for 10 min and then was quenched with water. It was then extracted twice with dichloromethane, dried with magnesium sulfate, filtered, and concentrated. The crude residue was applied to a silica gel column pretreated with 2.5 vol % of triethylamine and eluted with 9:1 hexanes/ethyl acetate to yield 832.1 mg of **65**. NMR data are listed above.

Ethyl (*Z*)-3-Phenoxy-3-(4-methoxyphenyl)-2-chloroacrylate (66). Clear oil prepared on a 3.06 mmol scale according to representative procedure G. Purified via flash chromatography using 9:1 hexanes/ethyl acetate as an eluent to give 938.8 mg of **66**: R_f = 0.25 (9:1 hexanes/ethyl acetate); ^1H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, 2H), 7.21 (m, 2H), 6.98 (m, 1H), 6.92 (m, 2H), 6.80 (m, 2H), 4.15 (q, 2H), 3.77 (s, 3H), 1.13 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.1. 160.9, 158.8, 155.0, 131.1, 129.5, 124.9, 123.4, 118.5, 113.5, 113.5, 110.7, 61.9, 55.2, 13.8; HRMS calcd for $C_{18}H_{17}ClO_4$ 332.0815, found 332.0815.

Representative Procedure H for the Synthesis of Tetrasubstituted Alkenes: (*Z*)-1-Phenoxy-1-(4-methoxylphenyl)-2-(3,4-methylenedioxyphenyl)propene (67). The boronic acid (77.5 mg, 0.46 mmol, 1.5 equiv), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 5 mol %), S-Phos (12.5 mg, 0.031 mmol, 10 mol %), and Cs_2CO_3 (218.8 mg, 0.67 mmol, 2.2 equiv) were placed in a one-piece, round-bottom flask/condenser, sealed with a septum, and purged with argon for 20 min. A solution of the vinyl chloride **65** (83.8 mg, 0.31 mmol, 1 equiv) in toluene (0.75 mL) was added, and the suspension was refluxed overnight. When complete, the reaction was cooled, partitioned between dichloromethane and water. The layers were separated, and the water layer was extracted twice more with dichloromethane. The organic layers were combined, dried with magnesium sulfate, filtered, and concentrated onto silica gel, which was applied to a silica gel column and eluted with 14:1 hexanes/dichloromethane to give 83.6 mg of **67**: R_f = 0.24 (9:1 hexanes/ethyl acetate); ^1H NMR (300 MHz, $CDCl_3$) δ 7.46 (m, 2H), 7.17 (t, 2H, J = 7.5 Hz), 7.05−6.85 (m, 7H), 6.77 (m, 1H), 5.93 (s, 2H), 3.81 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 157.3, 147.2, 146.2, 145.0, 134.5, 131.0, 129.2, 128.0, 122.5, 121.3, 121.2, 117.0, 113.5, 108.6, 108.0, 100.8, 55.2, 20.2; HRMS calcd for $C_{23}H_{20}O_4$ 360.1362, found 360.1362.

(*Z*)-1-Phenoxy-1-(4-methoxyphenyl)-2-[3,5-bis(trifluoromethyl)-phenyl]propene (68). This compound was prepared according to representative procedure H on a 0.30 mmol scale. Purified via flash chromatography using 14:1 hexanes to ethyl acetate as an eluent to give 115.2 mg of **68**: R_f = 0.32 (14:1 hexanes/ethyl acetate); ^1H NMR (300 MHz, $CDCl_3$) δ 7.94 (s, 2H), 7.72 (s, 1H), 7.50 (m, 2H), 7.16 (m, 2H), 6.95−6.82 (m, 5H), 3.83 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7, 156.7, 147.7, 142.7, 131.3, 131.0, 129.3, 128.3, 128.3, 126.9, 125.6, 121.9, 121.6, 120.3, 120.3, 119.8, 116.7, 113.7, 55.2, 19.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ −62.92; HRMS calcd for $C_{24}H_{18}F_6O_2$ 452.1211, found 452.1216.

(*Z*)-1-Phenoxy-1-(4-methoxyphenyl)-2-[2-(methylthio)phenyl]-propene (69). This compound was prepared according to representative procedure H on a 0.30 mmol scale. Purified via flash chromatography using 12:1 hexanes to ethyl acetate as an eluent to give 78.5 mg of **69**: R_f = 0.31 (12:1 hexanes/ethyl acetate); ^1H NMR (300 MHz, $CDCl_3$) δ 7.51 (m, 2H), 7.23−7.04 (m, 6H), 6.90−6.84 (m, 4H), 6.79 (m, 1H), 3.80 (s, 3H), 2.48 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 157.3, 146.3, 140.3, 136.7, 130.9, 128.8, 128.5, 127.4, 127.3, 125.6, 124.7, 122.7, 121.1, 117.3, 113.5, 55.2, 19.6, 15.9; HRMS calcd for $C_{23}H_{22}O_2S$ 362.1341, found 362.1348.

(1*Z*,3*E*)-1-Phenoxy-1-(4-methoxyphenyl)-2-methyl-5-phenyl-penta-1,3-diene (70). This compound was prepared according to representative procedure H on a 0.30 mmol scale. Purified via flash chromatography using a gradient of neat hexanes to 14:1 hexanes to ethyl acetate as an eluent to give 100.9 mg of **70**: R_f = 0.34 (14:1 hexanes/ethyl acetate); ^1H NMR (300 MHz, $CDCl_3$) δ 7.42 (m, 2H), 7.36−7.31 (m, 7H), 7.00−6.84 (m, 7H), 6.03−5.92 (m, 1H), 3.81 (s, 3H), 3.52 (d, 2H, J = 7.7 Hz), 2.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 157.5, 146.0, 140.8, 131.0, 129.6, 129.4, 128.6, 128.6, 128.5, 128.3, 127.7, 126.1, 121.5, 121.0, 116.7, 113.4, 55.2, 39.9, 14.5. We were unable to obtain satisfactory HRMS for this compound.

(1*Z*,3*E*)-1-Phenoxy-1-(4-methoxyphenyl)-2-methyl-4-phenyl-buta-1,3-diene (71). This compound was prepared according to representative procedure H on a 0.30 mmol scale. Purified via flash chromatography using a gradient of neat hexanes to 9:1 hexanes to ethyl acetate as an eluent to give 78.5 mg of **71**: R_f = 0.25 (9:1 hexanes/ethyl acetate); ^1H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, 1H, J = 16 Hz), 7.47−7.41 (m, 4H), 7.34−7.28 (m, 2H), 7.25−7.19 (m, 3H), 7.00−6.83 (m, 5H), 6.71 (d, 1H, J = 16 Hz), 3.80 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 157.5, 147.9, 138.0, 131.2, 129.4, 128.7, 128.6, 127.6, 127.3, 126.5, 126.1, 121.8, 121.2, 117.0, 113.5, 55.2, 14.6; HRMS calcd for $C_{24}H_{22}O_2$ 342.1620, found 342.1625.

(1*Z*,3*E*)-1-Phenoxy-1-(4-methoxyphenyl)-2-methyl-4-(4-methyl-phenyl)-buta-1,3-diene (72). This compound was prepared according to representative procedure H on a 0.30 mmol scale. Purified via flash chromatography using a gradient of neat hexanes to 9:1 hexanes/ethyl acetate as an eluent to give 78.5 mg of **72**: R_f = 0.25 (9:1 hexanes/ethyl acetate); ^1H NMR (300 MHz, $CDCl_3$) δ7.49−6.81 (m, 14H) 6.68 (d, 1H, J = 16 Hz),3.79 (s, 3H), 2.34

(s, 3H), 2.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 157.6, 147.5, 137.1, 135.2, 131.1, 129.6, 129.4, 129.3, 128.9, 127.7, 126.4, 125.1, 121.7, 121.3, 117.0, 113.5, 55.2, 21.2, 14.4; HRMS calcd for $C_{25}H_{24}O_2$ 356.1776, found 136.1780.

Ethyl (*E*)-3-Phenoxy-3-(4-methoxyphenyl)-2-(4-fluorophenyl)-acrylate (73). This compound was prepared according to representative procedure H on a 0.30 mmol scale. Purified via flash chromatography using a gradient of 12:1 to 9:1 hexanes/ethyl acetate as an eluent to give 85.0 mg of **73**: R_f = 0.35 (4:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.36 (m, 4H), 7.19−7.13 (m, 2H), 7.00−6.86 (m, 5H), 6.82−6.78 (m, 2H), 4.10 (q, 2H), 3.77 (s, 3H), 1.06 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 163.7, 160.5, 156.2, 154.6, 130.6, 130.4, 129.4, 126.8, 122.6, 121.0, 117.9, 115.4, 115.1, 113.7, 61.2, 55.2, 13.9; HRMS calcd for $C_{24}H_{21}FO_4$ 392.1424, found 392.1437.

Ethyl (*E*)-3-Phenoxy-3-(4-methoxyphenyl)-2-(4-methylphenyl)-acrylate (74). This compound was prepared according to representative procedure H on a 0.30 mmol scale. Purified via flash chromatography using a 10:1 hexanes to ethyl acetate as an eluent to give 102.1 mg of **74**: R_f = 0.36 (4:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (m, 2H), 7.35 (m, 2H), 7.23−7.11 (m, 4H), 6.97−6.92 (m, 3H), 6.83 (m, 2H), 4.14 (q, 2H), 3.80 (s, 3H), 2.35 (s, 3H), 1.11 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 160.3, 156.5, 153.5, 137.4, 131.6, 130.3, 129.3, 129.0, 128.4, 127.1, 122.4, 122.3, 118.0, 113.7, 61.1, 55.2, 21.3, 13.9; HRMS calcd for $C_{25}H_{24}O_4$ 388.1675, found 388.1674.

Ethyl (*E*)-3-Phenoxy-3-(4-methoxyphenyl)-2-(2-methylphenyl)-acrylate (75). This compound was prepared according to representative procedure H on a 0.30 mmol scale. Purified via flash chromatography using 9:1 hexanes/ethyl acetate as an eluent to give 104.5 mg of **75**: R_f = 0.36 (4:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, 2H), 7.30 (m, 1H), 7.19−7.07 (m, 5H), 6.89−6.79 (m, 5H), 4.08 (q, 2H), 3.80 (s, 3H), 2.35 (s, 3H), 1.06 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 160.5, 157.8, 156.3, 137.1, 134.8, 130.9, 130.0, 129.9, 129.1, 127.7, 126.8, 125.5, 122.4, 120.5, 118.3, 113.5, 60.8, 55.3, 20.0, 13.9; HRMS calcd for $C_{25}H_{24}O_4$ 388.1675, found 388.1676.

(1*E*,3*E*)-1-Phenoxy-1-(4-methoxyphenyl)-2-(carboxyethyl)-4-phenylbuta-1,3-diene (76). This compound was prepared according to representative procedure H on a 0.30 mmol scale. Purified via flash chromatography using 9:1 hexanes/ethyl acetate as an eluent to give 93.7 mg of **76**: R_f = 0.38 (4:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44−7.40 (m, 4H), 7.33−7.19 (m, 7H), 7.01−6.94 (m, 3H), 6.82−6.72 (m, 2H), 4.21 (q, 2H), 3.78 (s, 3H), 1.12 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.5, 160.4, 156.6, 152.1, 137.4, 130.8, 130.0, 129.6, 128.6, 127.7, 126.7, 122.6, 122.4, 121.2, 117.5, 113.8, 61.3, 55.2, 13.9; HRMS calcd for $C_{26}H_{24}O_4$ 400.1675, found 400.1674.

(1*E*,3*E*)-1-Phenoxy-1-(4-methoxyphenyl)-2-(carboxyethyl)-4-(4-methylphenyl)buta-1,3-diene (77). This compound was prepared according to representative procedure H on a 0.30 mmol scale. Purified via flash chromatography using 7:1 hexanes/ethyl acetate as an eluent to give 113.4 mg of **77**: R_f = 0.38 (4:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (m, 2H), 7.31−7.12 (m, 6H), 7.02−6.87 (m, 6H), 6.64 (d, 1H, J = 16 Hz), 4.33 (q, 2H), 3.83 (s, 3H), 2.37 (s, 3H), 1.21 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 160.4, 156.8, 151.6, 137.6, 134.5, 131.6, 131.1, 129.4, 129.2, 126.4, 125.1, 122.6, 122.4, 121.3, 117.8, 113.9, 61.2, 55.3, 21.3, 14.1; HRMS calcd for $C_{27}H_{26}O_4$ 414.1831, found 414.1835.

(1*E*,3*E*)-1-Phenoxy-1-(4-methoxyphenyl)-2-(carboxyethyl)-4-(4-chlorophenyl)buta-1,3-diene (78). This compound was prepared according to representative procedure H on a 0.30 mmol scale. Purified via flash chromatography using 7:1 hexanes/ethyl acetate as an eluent to give 81.4 mg of **78**: R_f = 0.35 (4:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (m, 2H), 7.32−7.28 (m, 5H), 7.21 (m, 3H), 7.00−6.88 (m, 6H), 6.60 (d, 1H, J = 16 Hz), 4.33 (q, 2H), 3.83 (s, 3H), 1.21 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.8, 160.6, 156.6, 152.8, 135.8, 133.2, 131.6, 129.6, 129.2, 128.8, 127.6, 124.8, 122.9, 122.5, 122.1, 117.9, 114.0, 61.2, 55.3, 14.1; HRMS calcd for $C_{26}H_{23}ClO_4$ 434.1285, found 434.1287.

(1*E*,3*Z*)-1-Phenoxy-1-(4-methoxyphenyl)-2-(carboxyethyl)-penta-1,3-diene (79). This compound was prepared according to representative procedure H on a 0.30 mmol scale. Purified via flash chromatography using 7:1 hexanes/ethyl acetate as an eluent to give 81.4 mg of **79**: R_f = 0.35 (4:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (m, 2H), 7.24−7.18 (m, 2H), 7.00−6.91 (m, 3H), 6.81 (m, 2H), 6.24 (m, 1H), 5.78−5.67 (m, 1H), 4.14 (q, 2H), 3.79 (s, 3H), 1.70 (dd, 3H, J^1 = 2 Hz, J^2 = 7 Hz), 1.14 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.5, 160.4, 156.0, 154.4, 130.4, 129.4, 128.9, 126.5, 122.5, 122.4, 119.3, 117.6, 113.6, 61.1, 55.2, 14.9, 13.8; HRMS calcd for $C_{21}H_{22}O_4$ 338.1518, found 338.1527.

(1*E*,3*E*)-1-Phenoxy-1-(4-methoxyphenyl)-2-(carboxyethyl)-5-phenylpenta-1,3-diene (80). This compound was prepared according to representative procedure H on a 0.30 mmol scale. Purified via flash chromatography using a gradient of 9:1 to 7:1 hexanes/ethyl acetate as an eluent to give 81.4 mg of **80**: R_f = 0.28 (4:1 hexanes/ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45−7.19 (m, 10H), 7.02−6.93 (m, 3H), 6.82 (m, 2H). 6.66 (m, 2H), 6.09−5.98 (m, 1H), 4.15 (q, 2H), 3.79 (s, 3H), 3.52 (d, 2H, J = 7.2 Hz), 1.09 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.6, 160.3, 156.6, 150.8, 140.0, 132.1, 130.8, 129.9, 129.5, 128.6, 128.5, 126.8, 126.2, 126.1, 123.7, 122.4, 122.0, 117.9, 113.7, 113.3, 61.1, 55.2, 39.7, 13.9; HRMS calcd for $C_{27}H_{26}O_4$ 414.1831, found 414.1828.

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Supporting Information Available: Original ^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.