

The Aryne-Abramov Reaction as a 1,2-Benzdiyne Platform for the Generation and Solvent-Dependent Trapping of 3-Phosphonyl Benzyne

Brianna M. Bembenek, Maya M. S. Petersen, Julia A. Lilly, Amber L. Haugen, Naomi J. Jiter, Andrew J. Johnson, Ethan E. Ripp, Shelby A. Winchell, Alisha N. Harvat, Caitlin McNulty, Sierra A. Thein, Abigail M. Grieger, Brandon J. Lyle, Gabriella L. Mraz, Abigail M. Stitgen, Samuel Foss, Merranda L. Schmid, Joseph D. Scanlon, and Patrick H. Willoughby*

Cite This: *J. Org. Chem.* 2021, 86, 10724–10746

Read Online

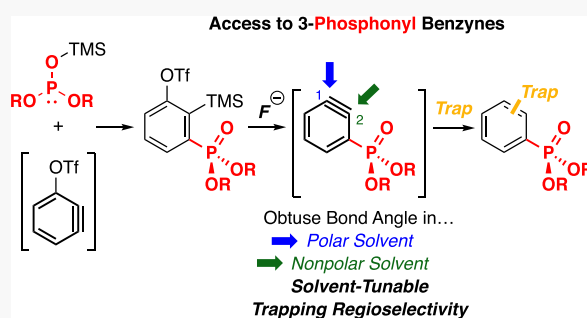
ACCESS |

Metrics & More

Article Recommendations

Supporting Information

ABSTRACT: Synthetic methodology utilizing two aryne intermediates (i.e., a formal benzdiyne) enables the rapid generation of structurally complex molecules with diverse functionality. This report describes the sequential generation of two *ortho*-benzyne intermediates for the synthesis of 2,3-disubstituted aryl phosphonates. Aryl phosphonates have proven useful in medicinal chemistry and materials science, and the reported methodology provides a two-step route to functionally dense variants by way of 3-phosphonyl benzyne intermediates. The process begins with regioselective trapping of a 3-trifloxybenzyne intermediate by an *O*-silyl phosphite in an Abramov-like reaction to bond the strained Csp carbons with phosphorus and silicon. Standard aryne-generating conditions follow to convert the resulting 2-silylphenyl triflate into a 3-phosphonyl benzyne, which readily reacts with numerous aryne trapping reactants to form a variety of 2,3-difunctionalized aryl phosphonate products. DFT computational studies shed light on important mechanistic details and revealed that 3-phosphonyl benzyne is highly polarizable. Specifically, the distortion in the internal bond angles at each of the Csp atoms was strongly influenced by both the electronegativity of the phosphonate ester groups as well as the dielectric of the computational solvation model. These effects were verified experimentally as the regioselectivity of benzyl azide trapping increased with more electronegative esters and/or increasingly polar solvents. Conversely, replacing the conventional solvent, acetonitrile, with nonpolar alternatives provided attenuated or even inverted selectivities. Overall, these studies showcase new reactivity of benzyne intermediates and extend the aryne relay methodology to include organophosphonates. Furthermore, this work demonstrates that the regioselectivity of aryne trapping reactions could be tuned by simply changing the solvent.



INTRODUCTION

Phosphonates have established roles in pharmaceutical, agrochemical, and materials industries,¹ where *P*-aryl phosphonates (e.g., **12**, Figure 1) have proven particularly versatile. Specifically, aryl phosphonates possess an array of interesting biological activities² and are synthetically useful where the phosphonate is both a precursor to other phosphorus moieties³ and a directing group for *ortho* C–H activation.⁴ Moreover, aryl phosphonates are important monomeric building blocks for flame-retardant polymers,⁵ and their use as tunable surface-modifying agents is beneficial to myriad technologies.⁶ The most widely used approach for the synthesis of aryl phosphonates includes transition-metal-catalyzed phosphorylation of arenes (e.g., Hirao reaction⁷).⁸ More recently, several impressive photomediated catalytic systems have been reported, greatly expanding arene phosphorylation methodologies.⁹ Benzyne and related aryne intermediates serve as a

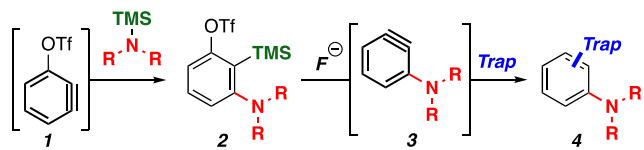
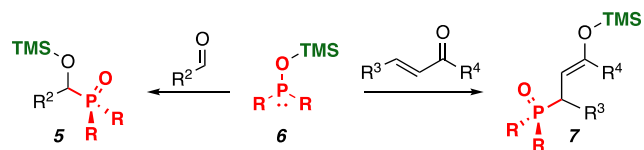
useful platform for the synthesis of aryl phosphonates,¹⁰ allowing for either trialkyl^{10a} or dialkyl phosphites^{10b,c,e} to serve as phosphorylating agents. Despite these impressive advances, the concise preparation of densely functionalized aryl phosphonates remains challenging and/or impractical.

Benzyne reactive intermediates are a versatile platform for generating molecular complexity through the use of various “trapping” agents, often enabling *ortho*-difunctionalization across the strained sp-hybridized carbon atoms.¹¹ Recently, multibenzene strategies have been reported, offering new

Received: June 11, 2021

Published: July 8, 2021



a) First Reported Aryne Relay Process (Hosoya, 2016)¹³b) Abramov Reactions (Abramov 1954 and Hata 1977)^{17,18}

c) This Work: Aryne-Abramov Reaction for Access to 3-Phosphonyl Benzyne via an Aryne Relay Process

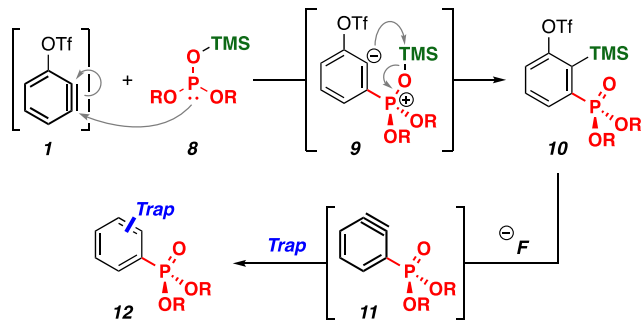


Figure 1. Comparison of previous studies to the work described in this report. (a) Hosoya's first report of aryne methodology for the synthesis of substituted anilines via 3-amino benzyne intermediates. (b) A general representation of the Abramov reactions. (c) A summary of the work described in this report. Structurally complex aryl phosphonates are available under aryne relay methodology by utilizing the aryne-Abramov reaction.

approaches for generating densely functionalized arenes.¹² Aryne relay processes provide a convenient approach for sequentially accessing two distinct aryne intermediates, which are formed under complementary benzyne-generating conditions (Figure 1a). The Hosoya lab first reported this strategy by generating 3-trifloxybenzynes (1) and trapping the highly electrophilic intermediate with an *N*-silyl amine via *N*-Si bond insertion to form a *C*-silyl aniline (cf. 2).¹³ This initial aryne process formed a 2-silylphenyl triflate moiety capable of readily generating a second aryne (cf. 3) under standard (i.e., Kobayashi¹⁴) fluoride-mediated conditions. Using a variety of established aryne trapping agents, several structurally diverse anilines (cf. 4) were readily prepared. Since this initial report, the Li¹⁵ and Hosoya¹⁶ laboratories have independently reported methods to extend aryne relay strategies for the synthesis of α -aryl carbonyls,^{15a,16a} 2-aryl pyridines,^{15b} and aryl sulfides.^{16b}

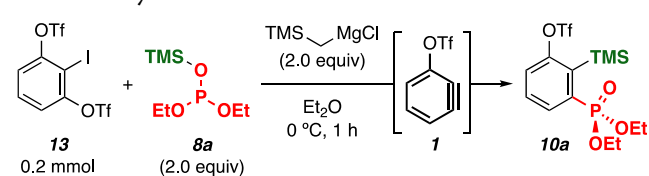
We envisioned that aryne relay methodology could be applied to the synthesis of aryl phosphonates using readily available silyl phosphites (cf. 8). In general, *O*-silyl organophosphorous agents (cf. 6) are best known for their role in the Abramov reaction (Figure 1b), where the P(III) center undergoes nucleophilic addition to an aldehyde or α,β -unsaturated carbonyl with subsequent silyl transfer to form α -siloxy (cf. 5) or silyl enol ether (cf. 7) products, respectively.^{17–19} With this in mind, it seemed viable that silyl phosphites could engage aryne 1 by regioselective²⁰

nucleophilic addition of 8, resulting in a zwitterionic intermediate like 9. Driven by the formation of a P=O π bond, intramolecular silyl transfer would follow to give arene 10, which is equipped with the requisite 2-silylphenyl triflate moiety for generating a second, 3-phosphonyl, benzyne (cf. 11) under fluoride-mediated conditions. Trapping 3-phosphonyl benzyne 11 with any of the multitude of possible aryne trapping reactants would afford aryl phosphonates with a range of functionality (cf. 12). Herein, we describe our efforts to evaluate this hypothesis by developing a benzyne variant on the classic Abramov reaction, which we term the aryne-Abramov reaction, allowing for the concomitant formation of arene C–P and C–Si bonds. Furthermore, we show that application of the aryne-Abramov reaction to a 3-trifloxybenzyne enables the subsequent generation of a 3-phosphonyl benzyne, which can engage numerous aryne trapping agents to form structurally complex aryl phosphonates. This multi-benzyne (i.e., formally 1,2-benzdienes¹²) strategy represents an extension of Hosoya's aryne relay methodology and provides a straightforward route to functionally dense 2,3-disubstituted aryl phosphonates that would otherwise require lengthy synthetic routes to prepare. Given the range of applications for aryl phosphonates discussed above, the reported methodology will enable preparation of structurally complex analogues to further enhance the utility of this versatile functional group. Additionally, access to 3-phosphonyl benzyne reveals that these unique intermediates engage lowly selective aryne trapping agents with *solvent-dependent regioselectivities*. This further demonstrates the utility of 3-phosphonyl benzyne by enabling tunable access to regioisomeric mixtures of aryl phosphonates. More broadly, these studies show that solvent generally influences benzyne distortion as this effect was observed for other strained alkyne intermediates. Overall, this report describes that the aryne-Abramov reaction provides (1) a new strategy for the synthesis of structurally complex aryl phosphonates, (2) an extension of aryne relay methodology, and (3) the opportunity to study the properties of 3-phosphonyl benzyne.

RESULTS AND DISCUSSION

Optimization of Reaction Conditions. We chose to evaluate the feasibility of the aryne-Abramov reaction using 3-trifloxy benzyne precursor 13 (Table 1) and diethyl trimethylsilyl phosphite (8a). Precursor 13 is readily prepared in decagram quantities over two steps from resorcinol via regioselective iodination followed by bis-triflation.²⁰ *O*-Silyl phosphites like 8a are readily prepared from silylation of the corresponding dialkyl phosphite with chlorotrimethylsilane.²¹ As first described by Hosoya and co-workers, 13 is capable of forming 3-trifloxybenzyne 1 when treated with either organolithium or Grignard reagents.^{20,22} Following guidance from these studies, we initially used (trimethylsilyl)-methylmagnesium chloride. Consistent with our hypothesis, when 1 was generated in the presence of silylphosphite 8a, 3-trifloxy-2-(trimethylsilyl)aryl phosphonate 10a was isolated in 52% yield (entry 1). Similar to prior reports involving 1,²⁰ phosphorus addition was highly regioselective, and the alternative regioisomer was not detected. In our hands, other conditions known^{16b,22} to promote efficient generation of aryne 1 from precursor 13 (entries 2–4) led to reduced yields. Screening other routine alterations to the reaction conditions (e.g., stoichiometry, solvent choice, solvent volume, reaction time, temperature, and rate of reactant addition) did not

Table 1. Aryne-Abramov Reaction Conditions Screen

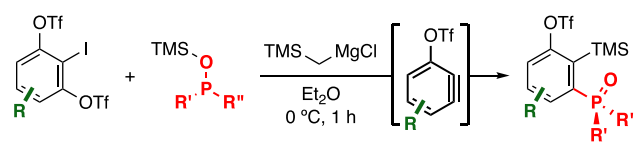


entry	variation from initial conditions	yield
1	none	52% ^a
2	toluene solvent	44% ^a
3	CH ₂ Cl ₂ solvent	53% ^a
4	TMSCH ₂ Li-MgCl ₂ with <i>n</i> -hexane solvent in place of TMSCH ₂ MgCl	14% ^b
5	OTs in place of OTf on 13	trace ^b
6	OSO ₂ (<i>p</i> -Cl)Ph in place of OTf on 13	trace ^b
7	substrate 13 added last ^c	77% ^a

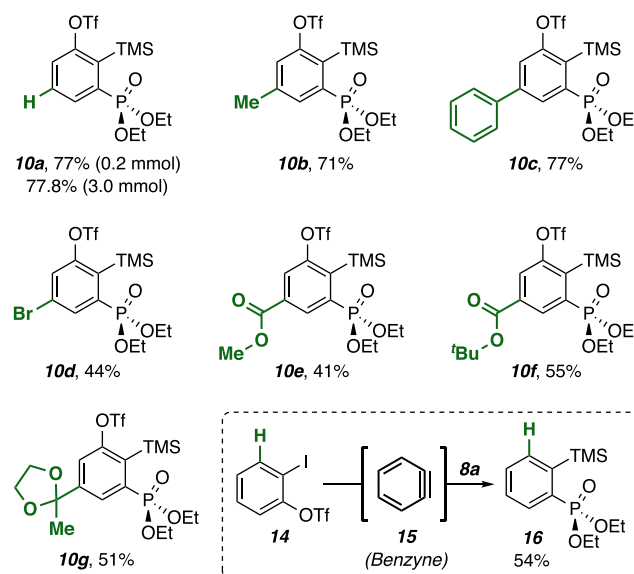
^aIsolated yield after flash chromatography purification. ^bYield determined from ¹H NMR by adding 1-bromo-4-nitrobenzene to the crude reaction mixture to serve as an internal standard. ^c13 added as a solution in Et₂O to a mixture of 8a and TMSCH₂MgCl also dissolved in Et₂O.

noticeably improve the reaction efficiency, and use of other 1,3-bis(sulfonates) failed to promote product formation (entries 5–6). However, the isolated yield increased to 77% when we changed the order of reactant addition such that a diethyl ether solution of precursor 13 was added last to a dilute mixture containing silyl phosphite 8a and the Grignard reagent (entry 7), suggesting that diluting both 13 and the Grignard reagent improves the efficiency of the transformation.

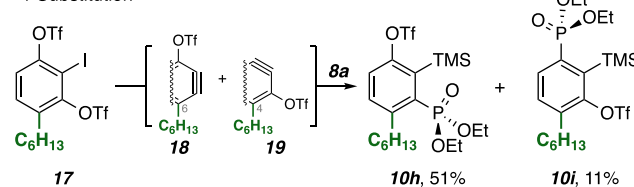
Evaluation of the Aryne-Abramov Reaction Substrate Scope. With suitable reaction conditions in hand, we evaluated the scope of iodophenyl bis(triflate) reactants amenable to the aryne-Abramov reaction (Figure 2a). Parent 10a was isolated in 77% yield on a 0.2 mmol scale, and the yield was unchanged when the reaction was scaled up to 3.0 mmol (i.e., 1.33 g of isolated product). Alkyl and aryl substituents at C5 were well-tolerated, providing good yields of products 10b and 10c. The yield of 5-bromo product 10d reduced to nearly half of that observed with the parent substrate. We saw no evidence that the additional halogen provided a competitive site for the Grignard reagent to engage. Rather, as reported by others,^{22–24} the inductively withdrawing bromine likely promotes a competitive thia-Fries rearrangement, preventing formation of the aryne intermediate. Lower yields were also observed in the formation of methyl ester 10e, which is likely due to a combination of undesired thia-Fries rearrangement along with competitive Grignard addition to the ester carbonyl. Replacing the methyl ester with a more electron-rich and sterically encumbered *tert*-butyl ester provided 10f with an improved isolated yield. Not surprisingly, complex mixtures were observed when trying to prepare the corresponding methyl ketone (not shown). However, the reaction proceeded smoothly with a cyclic ketal, which allowed for the preparation of aryl phosphonate 10g. Iodophenyl monotriflate 14 was amenable to the standard reaction conditions to give 2-silyl aryl phosphonate 16, demonstrating that benzyne itself (15) is able to participate in the aryne-Abramov reaction. This example also highlights that the reported conditions can form standard 2-silyl phosphonates, which are valuable ligands for iridium-catalyzed *ortho* borylation of arenes.²⁵ Unlike symmetric 5-substituted substrates, 4-hexyl aryne precursor 17 formed isomeric



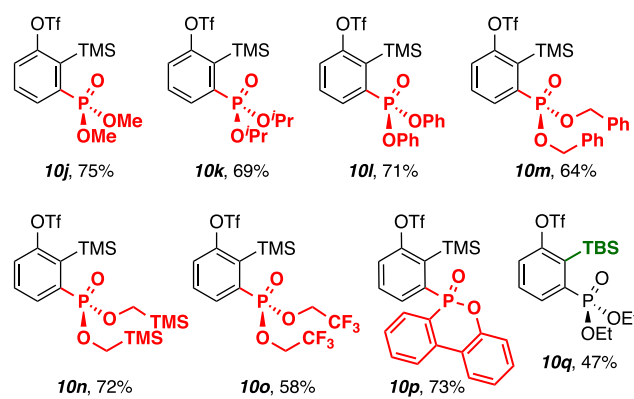
a) Scope of 3-Trifluorobenzene Precursors with 8a (i.e., R', R'' = OEt)



4-Substitution



b) Scope of Silyl Phosphites



c) Unproductive Silyl Phosphorus Substrates

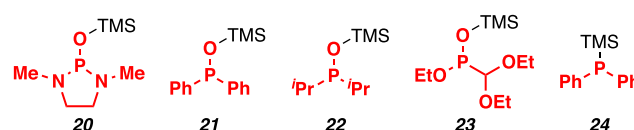


Figure 2. Studies related to the substrate scope of the aryne-Abramov reaction. (a) Scope of iodophenyl triflates found to participate in the aryne-Abramov reaction. (b) Scope of *O*-silyl phosphites found to participate in the aryne-Abramov reaction. (c) Attempted silyl phosphorus nucleophiles that failed to efficiently form aryne-Abramov products.

benzyne intermediates **18** and **19**, and each engaged phosphite **8a** to give aryl phosphonates **10h** and **10i** in a ~5:1 ratio.

The scope of silyl phosphorus nucleophiles was also assessed (Figure 2b), which demonstrated that a number of *O*-silyl phosphites are capable of readily forming product. Like the parent example, dimethyl, diisopropyl, diphenyl, and dibenzyl substrates afforded good yields of **10j–10m**, respectively. Trimethylsilyl-containing product **10n** was isolated in a similar yield, providing an opportunity to probe the influence of multiple silyl groups on fluoride-mediated benzyne generation. A slightly reduced yield was observed for trifluoroethyl-bearing product **10o**, which could be attributed to attenuated nucleophilicity of the corresponding phosphite or reduced stability of the phosphonate ester in the product. Aryl dibenzo[*c,e*][1,2]oxaphosphonate **10p** was readily prepared using the reported methodology and represents a novel DOPO derivative—a class of molecules with a multitude of flame-retardant applications.²⁶ Use of the *O*-TBS analogue of the parent silylphosphite provided product **10q**, albeit in reduced yields, suggesting that the larger TBS group impedes silyl transfer. Despite the ease with which numerous substrates were utilized under the reported conditions to provide products **10a–10q**, some silyl phosphorus nucleophiles proved unproductive (Figure 2c). Nitrogen analogue **20** seemingly participated in the aryne–Abramov reaction, but the corresponding product rapidly decomposed following chromatography purification.²⁷ Poor crude yields (0–10%) of the corresponding aryne–Abramov products were observed with *O*-silyl phosphine oxides **21** and **22** as well as *O*-silyl phosphonite **23** and *P*-silyl phosphine **24**. Benzyne *P*–Si bond insertion has been observed with **24** as substrate,²⁸ suggesting alternative conditions for generating 3-trifloxybenzyne will likely enable use of *P*-silyl phosphines as substrates.

DFT Computations of the Aryne–Abramov Reaction Mechanism. Computational investigation of the mechanism for the aryne–Abramov reaction was conducted using DFT (Figure 3) to evaluate the feasibility of the mechanism proposed in Figure 1c. Intermediates and transition states were located for the stepwise process in which silyl phosphite **8b** adds to 3-trifloxybenzyne (**1**) to form zwitterionic adduct **25**. A transition state corresponding to C1 addition was located (**TS1**), and the corresponding energy barrier was low (8.5 kcal·mol^{−1}), suggesting formation of **25** is rapid under the reaction conditions. Interestingly, the carbon-to-phosphorus atom distance was quite large (4.1 Å), indicating that the located structure corresponds to an early transition state. Numerous reports by Houk have demonstrated that nucleophile addition to aryne intermediates preferentially occurs at strained Csp atoms with internal bond angles that more closely resemble those of the transition state.²⁹ Consistent with these studies, the internal bond angle at C1 of **TS1** (136.4°) was similar to the angle at C1 in the optimized ground-state geometry for benzyne **1** (135.5°, see Supporting Information), whereas the angle at C2 of **1** was substantially more acute (117.4°). Formation of the intermediate zwitterionic adduct was substantially exergonic ($\Delta G = -21.5$ kcal·mol^{−1}), and the reaction continued downhill to form product **10j** ($\Delta G_{\text{rxn}} = -41.8$ kcal·mol^{−1}), likely driven by formation of the *P*=*O* π bond and neutralization of the zwitterion. The transition state for intramolecular silyl transfer (**TS2**) suggests the event is a low-barrier process ($\Delta G^\ddagger = 4.4$ kcal·mol^{−1}) that proceeds with a nearly planar arrangement of the five participating atoms,

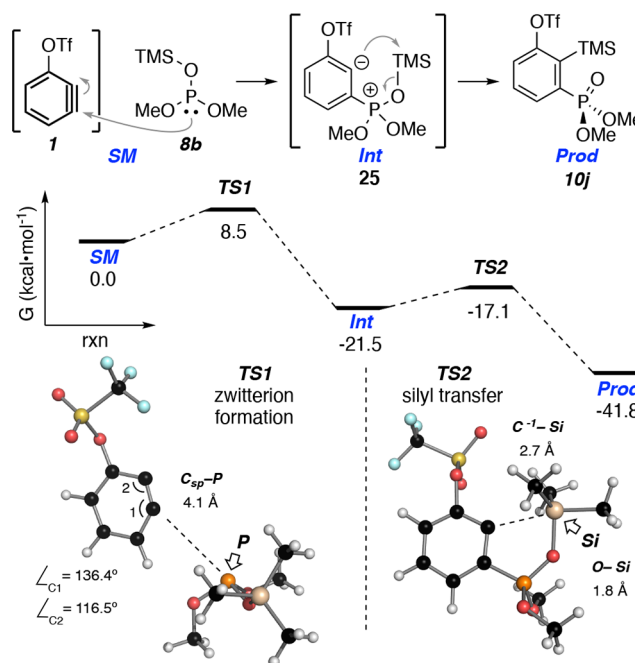


Figure 3. DFT computational [B3LYP/6-311+G(2d,p) with IEFPCM(Et₂O) solvation] studies of the mechanism for the aryne–Abramov reaction support a stepwise mechanism involving a zwitterionic intermediate.

which is aided by the longer carbanion-to-silicon atom distance (2.7 Å).

Generation of 3-Phosphonyl Benzyne and Scope of Trapping Reactants. To complete the aryne relay process, we needed to demonstrate that a second benzyne could be generated from products of the aryne–Abramov reaction. Using the conventional Kobayashi¹⁴ protocol for fluoride-mediated aryne generation, we studied the reaction of precursors **10a** and **10p** with several symmetric dienes (Figure 4a). Treating a mixture of **10a** and furan with CsF in MeCN provided 1,4-dihydro-1,4-epoxynaphthalene **12a** in excellent yield. Similar yields were observed with recently reported³⁰ conditions using a combination of 18-crown-6 and either KF or Cs₂CO₃. Precursor **10p** provided a similar outcome to give highly complex DOPO analogue **26**. *N*-Boc pyrrole and anthracene also provided cycloadducts with **10a** in good yields to give bicyclic aryl phosphonates **12b** and **12c**, respectively. The products observed from these diene trapping reactions strongly support the proposed intermediacy of a 3-phosphonyl benzyne like **11a**. Furthermore, tetraphenylcyclopentadienone (TPCP), another symmetric diene known³¹ to react with arynes, engaged **10a** in the presence of CsF to form naphthalene **12d**, presumably following decarbonylation of Diels–Alder adduct **27**.

Other trapping agents were evaluated to expand upon the diversity of 2- and 3-substituted aryl phosphonates that can be prepared under this aryne relay protocol (Figures 4b–d). Using conditions described by Pérez and Guitián for Pd-catalyzed [2 + 2 + 2] cocyclization of benzyne with alkynes (Figure 4b),³² aryne precursor **10a** was converted into naphthalene **12e** when treated with dimethylacetylenedicarboxylate (DMAD), presumably via Pd-coordinated aryne **28**. Trapping **11a** with nitrogen-containing 1,3-dipoles allowed us to both prepare heterocycle-fused aryl phosphonates and probe the regioselectivity of nonsymmetric trapping reactions (Figure

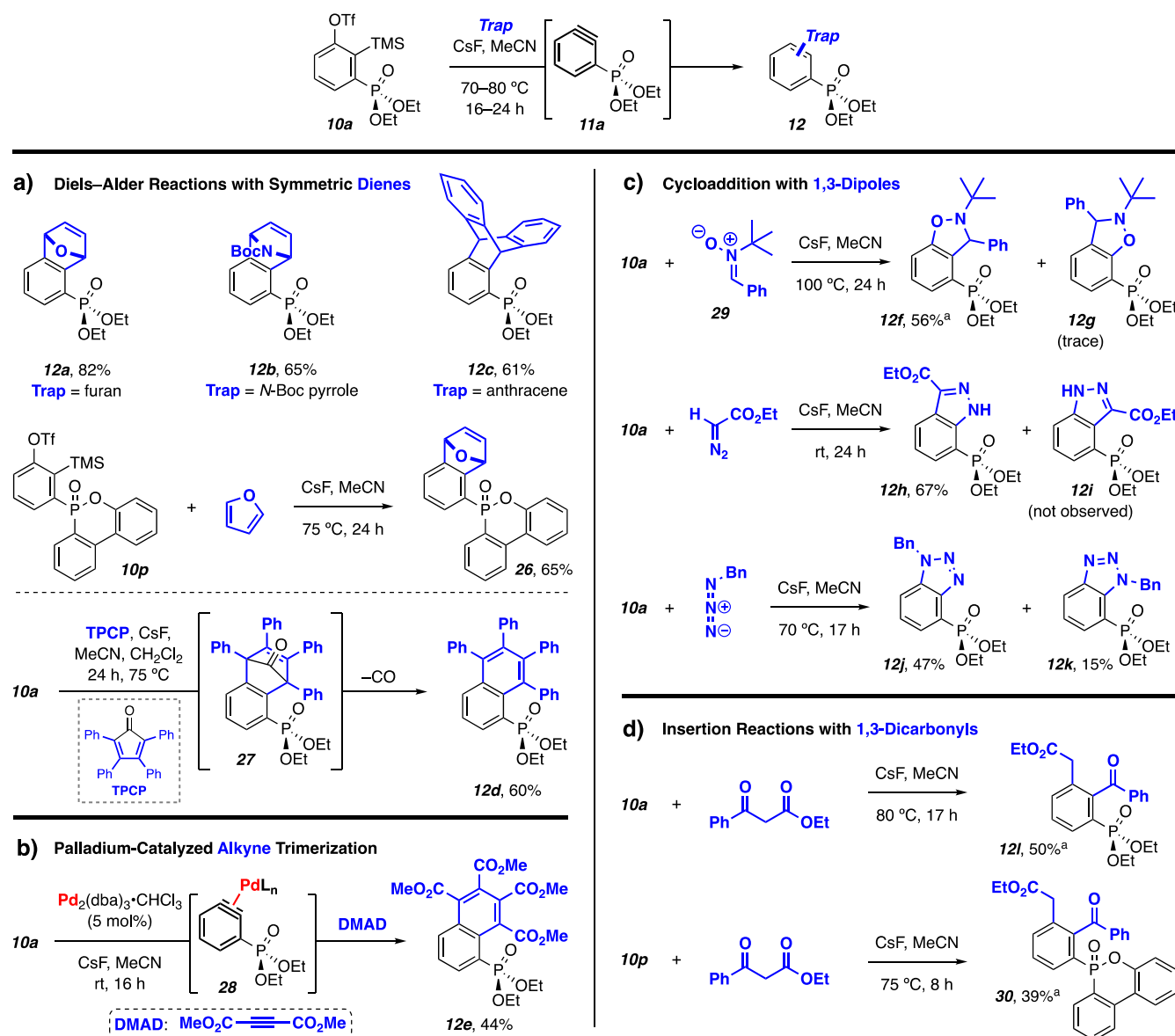


Figure 4. Scope studies of 3-phosphonyl benzyne generation and trapping reactions for the synthesis of structurally complex and functionally dense aryl phosphonates. (a) Products resulting from reaction of 3-phosphonyl benzyne with diene reactants. (b) Palladium-catalyzed alkyne trimerization involving a 3-phosphonyl benzyne. (c) Cycloaddition and observed regioselectivity of benzyne **11a** with several 1,3-dipoles. (d) Insertion of 3-phosphonyl benzyne into C–C σ bonds. “Trace amounts of regioisomeric products were observed in crude reaction mixtures but we were not able to isolate sufficient quantities to confirm their structure.”

4c). Nitroene **29** readily reacted under the usual conditions, providing dihydrobenzoxazole **12f** with trace amounts of regioisomer **12g**. Consistent with previous reports involving benzyne with 3-amino,¹³ 3-thionyl,^{16b} and 3-halo²⁴ substitution, the reaction led to preferential C–C bond formation at C2 of the aryne intermediate to give the seemingly more sterically congested product. The degree of observed regioselectivity was again large when the same aryne intermediate was trapped by ethyl diazoacetate to give 7-phosphonyl indazole **12h** without detectable formation of C4 isomer **12i**. However, reduced selectivity was observed in the aryne click reaction³³ with benzyl azide, providing triazole regioisomers **12j** and **12k** with an observed regioisomer ratio of ~3:1 in the crude reaction mixture. 3-Phosphonyl benzyne were also shown to engage 1,3-dicarbonyls to give products resulting from C–C σ bond insertion (Figure 4d) where both

10a and **10p** engaged ethyl benzoylacetate to form benzoylated phenylacetates **12l** and **30**, respectively.

Studies Related to the Regioselectivity of 3-Phosphonyl Benzyne Trapping Reactions. An important feature of aryne relay processes is the opportunity to study properties of otherwise inaccessible aryne intermediates. Several reports have demonstrated that the regioselectivity of azide cycloadditions with substituted benzyne is strongly influenced by the electronic nature of the aryne substituents.^{29,34} Specifically, electronegative groups at C3 direct the reaction to preferentially add the alkylated nitrogen of the azide to C1 of the aryne. This results in the *distal* benzotriazole regioisomer (e.g., **31a–c**, Figure 5a), where the *N*-alkyl is situated away from the C3-substituent. Conversely, reduced *distal* selectivity is observed with less electronegative groups at C3, providing an opportunity for formation of the *proximal* regioisomer (e.g., **32a–c**). We hypothesized that equipping the

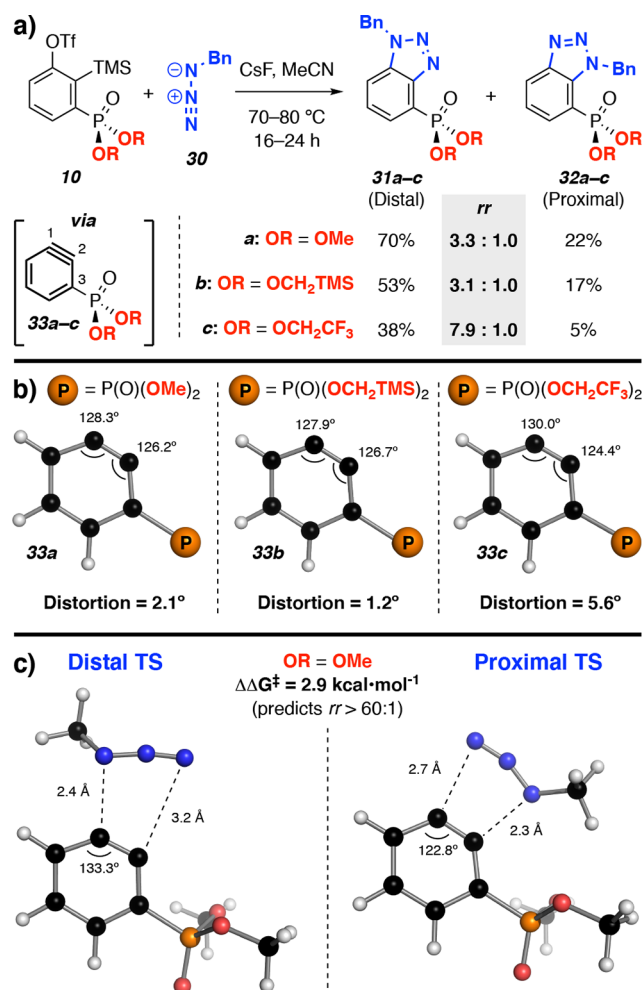


Figure 5. (a) Reactions of several 3-phosphonyl benzynes (33a–c) with benzyl azide. Electronegative phosphonate esters greatly influence trapping regioselectivity. Yields are isolated, and the regioisomeric ratios (i.e., rr values) correspond to the ratio of distal:proximal products observed in the ^1H NMR spectra of the crude reaction mixtures. (b) DFT-optimized [B3LYP/6-311+G(2d,p) with IEFPCM(MeCN) solvation] geometries, Csp internal bond angles, and benzyne distortion (i.e., difference in internal bond angle at C1 and C2) of 3-phosphonylbenzynes 33a–c. The degree of benzyne distortion in the computed structures is dependent on the phosphonate ester. (c) Computed [B3LYP/6-311+G(2d,p) with IEFPCM(MeCN) at 348.15 K] transition state geometries for formation of the distal and proximal products of benzyne 33a with methyl azide. The distal transition state is lower in energy, suggesting the distal product is preferentially formed, which is consistent with experimental regioselectivities using benzyl azide. However, the predicted regioselectivity based on the $\Delta\Delta G^\ddagger$ greatly exceeds that observed experimentally. The $\Delta\Delta G^\ddagger$ values were determined from the difference in free energies of the distal and proximal transition states.

3-phosphonyl benzynes with ester groups of varying electronegativities would influence the regioselectivities of azide trapping reactions. To test this, we carried out reactions of benzyl azide with precursors to dimethyl, bis-(trimethylsilylmethyl), and bis(trifluoroethyl) phosphonyl benzynes (33a–c, respectively). Consistent with the involvement of an aryne intermediate, a mixture of distal and proximal regioisomers was obtained in all cases. Contrary to our proposed hypothesis, there was no substantial difference in regioselectivity when using the seemingly electropositive silyl-

containing aryl phosphonate, where the distal:proximal ratio (31b:32b = 3.1:1) was similar to that of the dimethyl (31a:32a = 3.3:1) and diethyl (12j:12k = 3.1:1 in Figure 4c) analogues. However, the electronegative bis(trifluoroethyl) phosphonyl benzyne showed a nearly 3-fold increase in selectivity for distal regioisomer 31c, leading to minimal amounts of proximal product 32c (regioisomer ratio = 7.9:1). This demonstrates that distant inductive effects can influence the reactivity of 3-phosphonyl benzynes, which provides a straightforward approach to improving the regioselectivity obtained with unsymmetric trapping reactants.

We turned to DFT computations³⁵ to gain deeper insight into the influence of the phosphonyl esters on the ratios reported in Figure 5a. Numerous reports by Garg and Houk^{29,36} along with early studies by Buszek and Cramer³⁷ have demonstrated that the regioselectivity of aryne trapping reactions can be inferred from the relative internal bond angles of the sp^2 -hybridized carbons within the DFT-optimized geometries. These studies show that nucleophilic addition to the aryne intermediate is more likely to occur at the carbon with the greater (i.e., more obtuse) internal bond angle. Garg and Houk have rationalized this using the distortion-interaction model.³⁸ Namely, the more obtuse Csp atom better resembles the electrophilic site within the transition state, which must distort to a more linear geometry upon approaching the nucleophile. Nucleophilic addition to the Csp atom with the smaller internal bond angle requires additional distortion energy to reach the transition state geometry, thereby increasing the reaction barrier and decreasing the rate of regioisomer formation.^{29,36} Garg and Houk explain the role of substituent electronegativity on benzyne distortion in the context of Bent's rule.³⁹ Namely, increasing electronegativity at C3 encourages greater p -character on the in-plane (i.e., nonaromatic) π bond at C1, resulting in a larger internal bond angle.^{29,36} Given the ample precedence described above, benzyne distortion within the dimethyl, bis-(trimethylsilylmethyl), and bis(trifluoroethyl) phosphonyl benzynes (33a–c, Figure 5b) were determined from DFT-optimized geometries. All benzynes were distorted such that C1 was more obtuse than C2, suggesting that benzyl azide will react with each intermediate to preferentially form the distal regioisomer. These results are consistent with the experimentally observed regioselectivities. Furthermore, the enhanced distal selectivity observed in the case of the more electronegative benzyne 33c is reflected in a more pronounced distortion at C1 (5.6°). The computed geometry of the electron-rich trimethylsilyl-containing phosphonate, 33b, showed reduced distortion (1.2°) and a less obtuse C1 internal bond angle. This suggests that we should observe a reduced preference for distal product 31b in the reaction with benzyl azide. However, because the experimental regioselectivity was similar to that of the dimethyl and diethyl variants, sterics likely impede nucleophilic addition to C2. A similar steric effect has been observed by Garg and Houk in the case of the heavily C2 distorted triethylsilylbenzyne.⁴⁰

The experimental results and benzyne distortion computations suggest that the activation energy corresponding to distal product formation should be lower than that of the proximal isomer. DFT computations allowed us to locate geometries of both transition states (Figure 5c) for the reaction of dimethyl phosphonyl benzyne 33a with methyl azide, which showed that the transition state for forming the distal product was indeed lower in energy. However, the $\Delta\Delta G^\ddagger$ of 2.9 $\text{kcal}\cdot\text{mol}^{-1}$ predicts

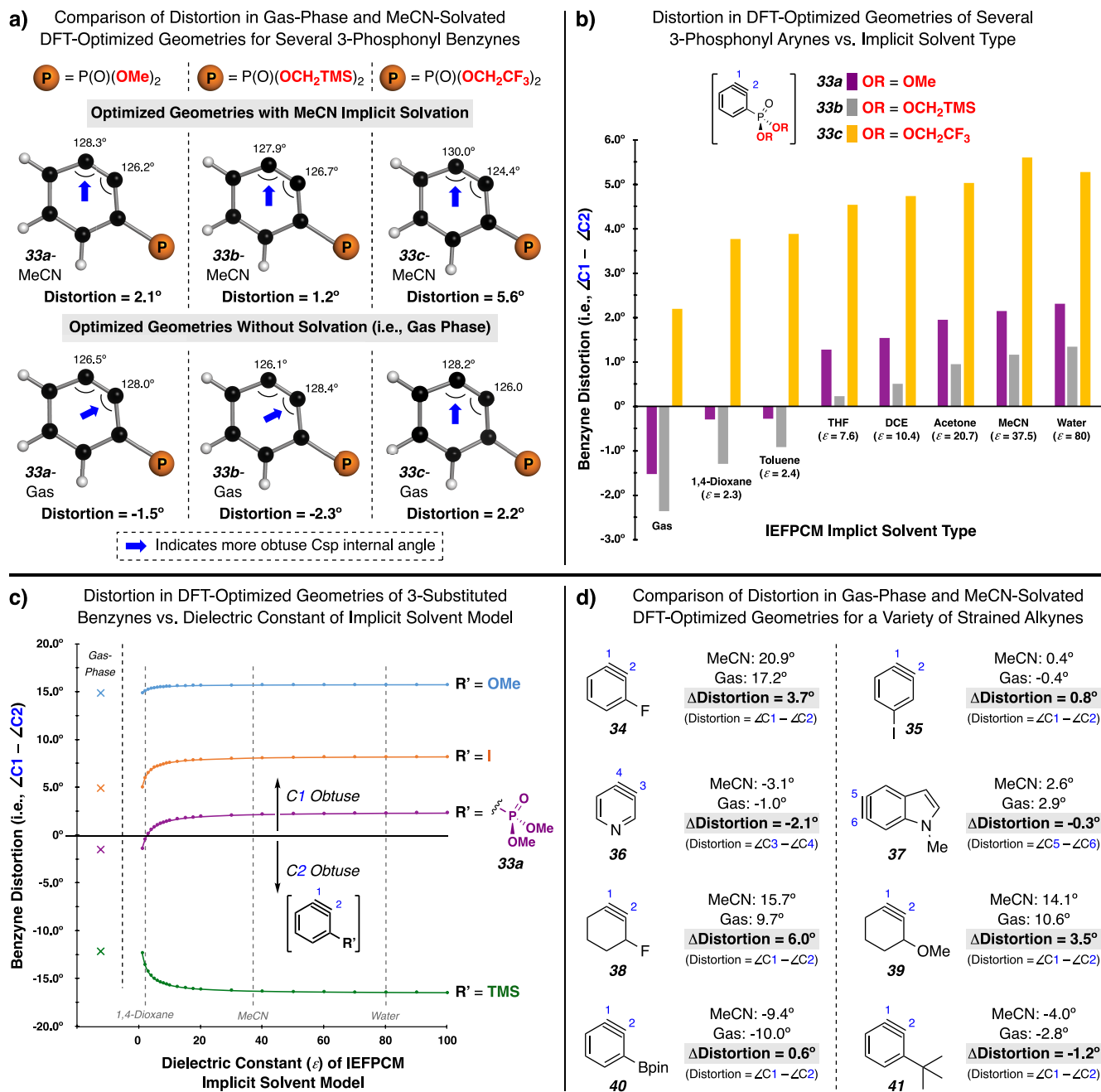


Figure 6. Influence of including a solvation model on the distortion of DFT geometry optimized [B3LYP/6-311G+(2d,p)] strained alkyne intermediates. Distortion is the difference in the internal bond angles at C1 and C2. (a) Comparison of DFT-optimized geometries for 3-phosphonyl arynes 33a–c with [IEFPCM(MeCN)] and without (i.e., gas phase) inclusion of an implicit solvation model. Including MeCN implicit solvation results in geometries with a more obtuse internal bond angle at C1 and more positive benzyne distortion. (b) A plot showing the influence of the type of implicit solvent on the distortion of 33a–c. Use of a solvent with a greater dielectric constant increases the observed benzyne distortion. The dielectric constants (ϵ) provided for each solvent refer to ambient temperature values. (c) A plot showing the influence of the dielectric constant of the IEFPCM implicit solvent model on the distortion of several 3-substituted benzyne. Aside from the dielectric constant, all other implicit solvent attributes are those of MeCN. (d) Comparison of distortion values of DFT-optimized geometries for several strained alkyne intermediates with [IEFPCM(MeCN)] and without (gas phase) inclusion of an implicit solvation model. The change in distortion (i.e., $\Delta\text{distortion}$) is the difference in distortion of the MeCN and gas-phase geometries. The iodinated benzyne were computed with LANL2DZ for the iodine atoms.

a regioselectivity $>60:1$,⁴¹ which greatly exceeds the experimentally observed 3:1 distal:proximal ratio which requires $\sim 0.8 \text{ kcal}\cdot\text{mol}^{-1}$. A similar overestimation of $\Delta\Delta G^\ddagger$ values for azide trapping reactions was observed by Garg and Houk.²⁹ To better represent the actual system, we repeated the transition state calculations with a single conformation of benzyl azide,

but the $\Delta\Delta G^\ddagger$ actually increased to $3.4 \text{ kcal}\cdot\text{mol}^{-1}$, predicting an even larger ($>130:1$)⁴¹ preference for the distal product (cf. the Supporting Information). Furthermore, despite considerable effort,⁴² we were not able to locate the distal transition state involving the more highly regioselective bis-(trifluoroethyl) phosphonyl benzyne 33c. Collectively, these

efforts suggest that structural complexities of the 3-phosphonyl arynes preclude efficient DFT transition state computations, further demonstrating the utility of benzyne distortion analysis to understand and predict experimental regioselectivities.

During the course of the computational studies, we noticed an interesting trend when comparing benzyne geometry optimizations performed with and without implicit solvation. Many previously reported computational studies of benzyne and aryne distortion have relied on calculations performed in the absence of solvation modeling (i.e., gas-phase calculations).^{29,34a,36,37,43} Following these reports, we initially computed the optimal geometries of the phosphonyl benzyne intermediates described above without including a solvation model (cf. gas structures in Figure 6a). In each case, the relative distortion was noticeably (3.4–3.6°) lower than those observed when including an implicit solvation model of acetonitrile (IEFPCM⁴⁴). Furthermore, the gas-phase calculations of the dimethyl and bis(trimethylsilyl)methyl phosphonyl benzyne gave structures with negative distortion values. These structures not only predict that the C2 internal bond angle of arynes **33a** and **33b** is more obtuse but also suggest that the intermediates are electronically predisposed toward formation of the proximal product in the reaction with benzyl azide, which is inconsistent with the experimental regioselectivities. The effect was also present when we performed the computations with alternative implicit solvation models (e.g., CPCM⁴⁴ or SMD⁴⁵) or different DFT methods (e.g., M06-2X⁴⁶ or M06L⁴⁷), and C1 was more obtuse when MeCN solvation was included, whereas C2 was more obtuse in the gas-phase structures (cf. the Supporting Information). Interestingly, the distortion measured with the MP2⁴⁸ *ab initio* method remained negative (−1.7° and −1.9°) both with and without inclusion of a solvation model for MeCN. Inspection of alternative conformations for each of the three phosphonyl arynes showed the effect was present across conformational space (cf. the Supporting Information).

The substantial impact of including an MeCN solvation model described above led us to consider if the degree of benzyne distortion was solvent-dependent. We computed the geometry of benzyne **33a–c** with an IEFPCM solvation model for a variety of common solvents (Figure 6b). Interestingly, benzyne distortion increases with the solvent dielectric constant where the distortion of **33a** and **33b** in 1,4-dioxane and toluene was actually negative—similar to that observed for the gas-phase calculations. Furthermore, the electronegativity of the ester group continued to influence the internal bond angles as electron-rich silyl-containing benzyne **33b** consistently possessed the lowest distortion value, whereas that observed in bis(trifluoroethyl)-containing **33c** was both positive and gave the largest C1 distortion with all solvents.⁴⁹ Because the influence of implicit continuum solvation models is largely due to the dielectric constant (i.e., epsilon value, ϵ),⁵⁰ we measured the degree of benzyne distortion in **33a** as the epsilon value was increased from 1.1 to 100, keeping all other solvation model parameters constant for MeCN (Figure 6c). While initially negative (i.e., C2 obtuse), the distortion sharply increased between 1.1–10 epsilon units before plateauing with minimal change from the MeCN distortion as epsilon approached 100. A similar study was conducted on 3-methoxy (R' = OMe), 3-iodo (R' = I), and 3-trimethylsilyl (R' = TMS) benzyne, all of which were similar in that the greatest change in distortion occurred at lower epsilon values. 3-Iodobenzyne had an overall more positive distortion than **33a** but otherwise

showed a similar trend as the phosphonyl aryne. Highly distorted 3-methoxybenzyne was minimally affected by the solvent dielectric, providing the smallest overall change in distortion (0.9°). Negatively distorted (i.e., C2 obtuse) 3-trimethylsilylbenzyne showed the largest dependence on epsilon, changing by 4.2°, and in contrast to the other benzyne, the distortion became more negative as the dielectric constant of the solvation model increased. It is interesting to note that while all benzyne intermediates were uniquely affected by the solvent dielectric, **33a** was the only example to cross the x -axis, providing C2 obtuse structures when $\epsilon < 3$ and C1 obtuse structures when $\epsilon \geq 3$.

Assuming the epsilon value for the gas-phase structures was that of free space ($\epsilon = 1$), the distortion values from the gas-phase optimizations of each benzyne shown in Figure 6c actually fit the trend observed when implicit solvation is included. This indicates that the gas-phase calculations provide a practical lower limit of distortion, and the overall influence of the solvent dielectric can be readily assessed by comparing the gas-phase and MeCN-solvated DFT-optimized geometries. With this in mind, we determined the difference in benzyne distortion, Δ distortion, of the MeCN and gas-phase geometries for a variety of strained alkynes (Figure 6d). Overall, the Δ distortion values ranged from negligible (e.g., −0.3° for **37**) to 6° (i.e., cyclohexyne **38**), demonstrating that benzyne intermediates possess variable polarizabilities that are highly substituent-dependent. 3-Fluorobenzyne (**34**) exhibited a larger distortion than the 3-OMe analogue (data in Figure 6c) and showed a much greater solvent dependence (Δ distortion = 3.7°), similar to that of 3-iodobenzyne (Δ distortion = 3.2°, data in Figure 6c). In contrast, the C4 substitution of iodobenzyne **35** led to a substantially reduced Δ distortion, but of the several benzyne we studied, **35** was the only example like the 3-phosphonyl benzyne where the distortion in the gas-phase and MeCN-solvated structures had opposite signs. The gas-phase structure of 3,4-pyridyne (**36**) is weakly distorted, suggesting this intermediate is minimally predisposed to favor nucleophile addition to C4. It is then interesting to note that including an MeCN implicit solvation model led to greater distortion, approaching the 4° threshold considered necessary to provide highly regioselective aryne trapping reactions.⁴³ 3-Substituted cyclohexynes were also considered where, similar to **34**, fluoride-substituted **38** had a large Δ distortion. However, in contrast to 3-methoxybenzyne (R' = OMe in Figure 6c), 3-methoxycyclohexyne (**39**) had a large Δ distortion, suggesting substituted cyclohexynes are more polarizable than their aromatic counterparts. The unusual polarizability observed with 3-trimethylsilylbenzyne (R' = TMS in Figure 6c) led us to evaluate electropositive-substituted benzyne **40** and **41**. Interestingly, neither of these structures showed as significant solvent dependence as that of the silylated benzyne (Δ distortion = 4.2°), and their distortions varied by only ~1°. Furthermore, the change in distortion was also inconsistent, and the Δ distortion of boron-substituted **40** increased, whereas *tert*-butyl benzyne **41** behaved like the silyl variant and was more strongly C2 distorted when solvent was included in the calculation. Collectively, these data indicate that it is likely necessary to include a solvation model when computing structures of strained alkyne intermediates. Furthermore, as is shown in Figure 5, the solvated structures likely serve as a better predictor of regioselectivity for weakly selective trapping reactions.

The computational studies of benzyne distortion discussed in Figures 5 and 6 suggest that the regioselectivity observed in benzyne trapping reactions could be solvent-dependent. To test this experimentally, we carried out benzyne trapping reactions with several phosphonyl benzyne precursors in a variety of common solvents (Figure 7). Consistent with the

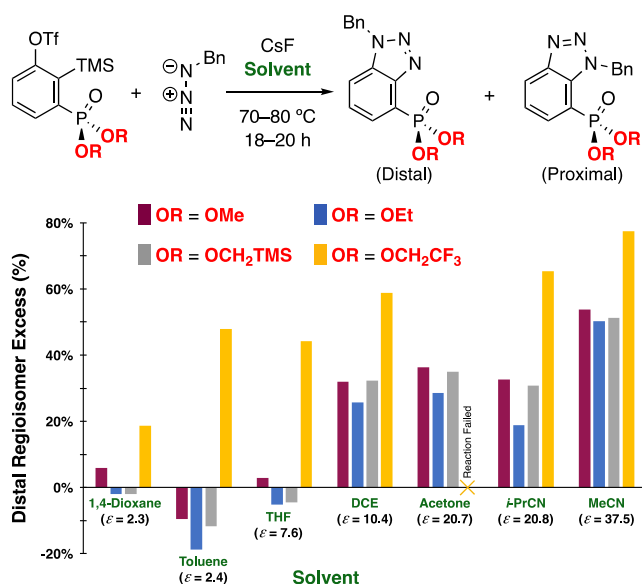


Figure 7. Plot depicting the influence of solvent on the observed distal regioisomer excess for the reaction of several 3-phosphonyl benzyne precursors with benzyl azide. Regioselectivity increases with solvent polarity, and use of low dielectric solvents substantially attenuates the distal selectivity observed in higher dielectric solvents like acetonitrile. The dielectric constants (ϵ) provided for each solvent refer to ambient temperature values.

computational results shown in Figure 6b,c, conducting the reaction in solvents with a dielectric constant less than 10 (i.e., 1,4-dioxane, toluene, and THF) gave attenuated regioselectivities for all substrates. Solvents with a larger dielectric (i.e., DCE, acetone, and *i*-PrCN) provided a preference for the distal isomer similar to that observed with MeCN. While experimental solvent effects certainly extend far beyond polarity, especially for substrates capable of participating in π -stacking interactions, it is remarkable the extent to which the observed selectivities agree with the distortion measured in the computed geometries. Furthermore, the regioisomer preference of all except for the CF₃-containing substrate *inverted in toluene*, and the proximal product was formed as the major regioisomer. Additionally, the influence of ester electronegativity emerged to a larger extent in the ethereal solvents, where ethyl and trimethylsilylmethyl aryl phosphonates showed the greatest preference for the proximal product. The electronegative CF₃-containing phosphonyl benzyne had the largest distal selectivity in all cases, but it is noteworthy that the observed regioisomer excess in 1,4-dioxane approached that of the dimethyl analogue. Collectively, these results clearly demonstrate that solvent choice can greatly influence the regioselectivity in the reaction of azides with benzyne, providing a practical approach to tune the product ratio and improve access to minor regioisomers. Additionally, to the best of our knowledge, this represents the first reported example of solvent choice leading to inversion of regioselectivity in an aryne trapping reaction.

CONCLUSION

This report provides the first account of an Abramov-like reaction of *O*-silyl phosphites with benzyne intermediates. Under straightforward conditions, this “aryne-Abramov” reaction proceeded with a number of benzyne precursors and *O*-silyl phosphites to provide 2-silyl aryl phosphonates via concomitant C–P and C–Si bond formation. Moreover, by engaging a 3-trifloxyaryne intermediate, the resulting product was capable of fluoride-mediated formation of a second (3-phosphonyl) benzyne intermediate. This extension of aryne relay methodology proved useful as the 3-phosphonyl benzyne readily engaged a number of aryne trapping agents to provide a variety of structurally complex 2,3-disubstituted aryl phosphonates. The trapping reaction with benzyl azide provided a mixture of regioisomers, and DFT computations of benzyne distortion with MeCN implicit solvation accounted for the observed preference for nucleophile addition at C1. Appending electronegative ester groups onto the 3-phosphonyl benzyne led to increased distortion in the computed structure and enhanced regioselectivity in the reaction with benzyl azide. Furthermore, an extensive probe of the influence of solvation on benzyne distortion and trapping regioselectivity revealed that 3-substituted benzyne intermediates are somewhat polarizable. Specifically, these aryne intermediates showed variable degrees of computed distortion and experimental regioselectivity depending on the polarity of the solvent, and the formerly minor isomer was favored when reactions were conducted in nonpolar solvents. Collectively, the results summarized in this report (1) demonstrate the versatility of the aryne-Abramov process for the preparation of aryl phosphonates and (2) underscore the numerous opportunities in synthesis and physical organic chemistry available from studies into the aryne relay methodology.

EXPERIMENTAL SECTION

General. NMR Spectra were recorded on a 300 MHz NMR. ¹H NMR chemical shifts in CDCl₃ are referenced to TMS (δ 0.00 ppm). ¹³C NMR data were acquired with ¹H decoupling, and chemical shifts in CDCl₃ are referenced to chloroform (δ 77.16 ppm). ¹⁹F NMR data were acquired with ¹³C decoupling, and chemical shifts are referenced to hexafluorobenzene added (ca. 0.05% v/v) as an internal standard (δ –163.00 ppm). ³¹P NMR data were acquired with ¹H decoupling, and chemical shifts are referenced using a phosphoric acid external standard (δ 0.00 ppm). High-resolution mass spectrometry (HRMS) measurements were performed on an Agilent 6230 LC/MS accurate-mass time-of-flight (TOF) instrument, using electrospray ionization (ESI) calibrated against purine ([M+H]⁺ requires 121.0509 *m/z*) and hexakis(1H,1H,3H-perfluoropropoxy)-phosphazene ([M+H]⁺ requires 922.0098 *m/z*). Reactions needing anhydrous conditions were performed in glassware that had been dried in an oven. Reactions performed with less than 5 mmol of starting material were carried out in screw cap vials or culture tubes fitted with a Teflon-lined cap.

General Procedure A: Synthesis of *o*-Silyl Triflate-Containing Aryl Phosphonates via Aryne Abramov Reaction with (Trimethylsilyl)methyl Magnesium Chloride. A solution of 2-iodophenyl bis(triflate) (e.g., 13, 0.2 mmol, 1 equiv) in Et₂O (1.0 mL) was added dropwise to a solution of silyl phosphite (0.4 mmol, 2 equiv) and (trimethylsilyl)methyl magnesium chloride (0.4 mL, 2 equiv, 1.0 M solution in Et₂O) in Et₂O (1.0 mL, excluding volume from Grignard reagent) at 0 °C with stirring. To ensure quantitative transfer of the 2-iodophenyl bis(triflate), the vial containing the 2-iodophenyl bis(triflate) solution was rinsed with Et₂O (3 \times 0.1 mL). The overall reaction concentration was \sim 0.07 M in 2-iodophenyl bis(triflate) (i.e., 0.2 mmol in \sim 2.7 mL of Et₂O). After 1 h, the mixture was quenched with aqueous 1 M HCl and extracted with

EtOAc. The organic extract was washed with brine, dried (MgSO₄), and concentrated. The crude product was purified by flash chromatography.

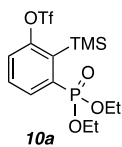
General Procedure B: Synthesis of Silyl Phosphites.

Chlorotrimethylsilane (1.4 equiv) was added to a solution of phosphorus substrate (1.0 equiv) and triethylamine (1.2 equiv) in CH₂Cl₂ (0.2 M) at 0 °C with stirring. After 60 min, the mixture was concentrated under reduced pressure to remove dichloromethane and excess chlorotrimethylsilane, and the residue was diluted with hexanes and filtered through a plug of Celite (hexanes eluent). The resulting solution was concentrated under reduced pressure to give crude silyl phosphite with between ~75% and >99% purity, where the major impurity is the starting phosphorus agent.

If the residue contained visible amounts of triethylammonium chloride (i.e., white crystalline solids), the product was again diluted in hexanes and filtered through a cotton plug. The filtrate was concentrated to give the silyl phosphite product.

Because of the sensitivity of most silyl phosphites to convert into the starting dialkyl phosphites, all steps in the aforementioned procedure should be carried out in the same day. Additionally, the resulting silyl phosphite should be used immediately or diluted in benzene and frozen for long-term storage.

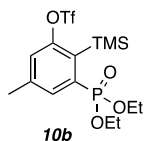
3-(Diethoxyphosphoryl)-2-(trimethylsilyl)phenyl Trifluoromethanesulfonate (10a).



[0.1 g Scale] Aryl phosphonate **10a** was prepared according to General Procedure A from a solution of 2-iodophenyl bis(triflate) **13**⁵² (109 mg, 0.218 mmol) in Et₂O (1 mL) and a mixture of diethyl trimethylsilyl phosphite (**8a**, 91 mg, 0.433 mmol) and (trimethylsilyl)methyl magnesium chloride (0.4 mL, 0.4 mmol, 1.0 M in Et₂O) in Et₂O (1 mL). Purification by flash chromatography (SiO₂, hexanes:EtOAc 7:3) gave aryl phosphonate **10a** (73 mg, 0.168 mmol, 77%) as a clear, colorless oil.

[1.0 g Scale] Aryl phosphonate **10a** was prepared according to General Procedure A from a solution of 2-iodophenyl bis(triflate) **13** (1.97 g, 3.94 mmol) in Et₂O (20 mL) and a mixture of diethyl trimethylsilyl phosphite (**8a**, 1.7 g, 8.1 mmol) and (trimethylsilyl)methyl magnesium chloride (8.0 mL, 8.0 mmol, 1.0 M in Et₂O) in Et₂O (20 mL). Purification by gradient flash chromatography (SiO₂, hexanes:EtOAc 4:1 to 7:3) gave aryl phosphonate **10a** (1.33 g, 3.06 mmol, 77.7%) as a clear, colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.93 (ddd, *J* = 0.96, 7.0, 14 Hz, 1H), 7.43–7.55 (m, 2H), 4.04–4.24 (m, 4H), 1.35 (t, *J* = 7.1 Hz, 6H), and 0.52 (s, 9H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 155.6 (d, *J* = 28.8 Hz), 138.6 (d, *J* = 23.1 Hz), 137.7 (d, *J* = 191.9 Hz, C_{aryl}-P), 133.2 (d, *J* = 10.3 Hz), 130.4 (d, *J* = 16.4 Hz), 124.0 (d, *J* = 3 Hz), 118.6 (q, *J* = 320.2 Hz, CF₃), 62.5 (d, *J* = 6.2 Hz), 16.3 (d, *J* = 6.1 Hz), and 2.4. ¹⁹F{¹³C} NMR (282 MHz, CDCl₃): δ -74.8. ³¹P{¹H} NMR (121 MHz, CDCl₃): δ 17.6. IR (neat): 2987, 2907, 1586, 1552, 1423, 1405, 1249, 1215, 1143, 1113, 1053, 1025, 968, 910, 850, 800, and 767 cm⁻¹. HRMS (ESI) *m/z*: [M + Na⁺] calcd for C₁₄H₂₂F₃NaO₆PSSi⁺ requires 457.0488; found 457.0478.

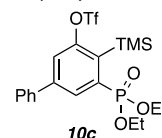
3-(Diethoxyphosphoryl)-5-methyl-2-(trimethylsilyl)phenyl Trifluoromethanesulfonate (10b).



Aryl phosphonate **10b** was prepared according to General Procedure A from a solution of 2-iodo-5-methyl-1,3-phenylene bis-(trifluoromethanesulfonate) **15a** (115 mg, 0.224 mmol) in Et₂O (1 mL) and a mixture of diethyl trimethylsilyl phosphite (**8a**, 94 mg, 0.448 mmol) and (trimethylsilyl)methyl magnesium chloride (0.4 mL, 0.4 mmol, 1.0 M in Et₂O) in Et₂O (1 mL). Purification by flash

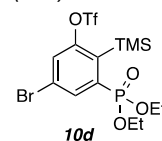
chromatography (SiO₂, hexanes:EtOAc 7:3) gave aryl phosphonate **10b** (70 mg, 0.16 mmol, 71%) as a clear, colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.77 (d, *J* = 14.2 Hz, 1H), 7.26 (s, 1H), 4.03–4.24 (m, 4H), 2.42 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 6H), and 0.49 (s, 9H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 155.7 (d, *J* = 29.9 Hz), 141.3 (d, *J* = 17.2 Hz), 137.1 (d, *J* = 191.3 Hz, C_{aryl}-P), 134.6 (d, *J* = 23.1 Hz), 134.3 (d, *J* = 10.3 Hz), 124.5 (d, *J* = 3 Hz), 118.6 (q, *J* = 320.2 Hz, CF₃), 62.4 (d, *J* = 5.8 Hz), 21.2, 16.4 (d, *J* = 6.9 Hz), and 2.4. ¹⁹F{¹³C} NMR (282 MHz, CDCl₃): δ -74.9. ³¹P{¹H} NMR (121 MHz, CDCl₃): δ 18.2. IR (neat): 2985, 2907, 1602, 1421, 1247, 1216, 1143, 1098, 1054, 1024, 959, 890, 850, 812, and 765 cm⁻¹. HRMS (ESI) *m/z*: [M + Na⁺] calcd for C₁₅H₂₄F₃NaO₆PSSi⁺ requires 471.0645; found 471.0645.

5-(Diethoxyphosphoryl)-4-(trimethylsilyl)-[1,1'-biphenyl]-3-yl Trifluoromethanesulfonate (10c).



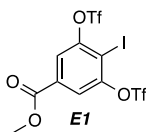
Aryl phosphonate **10c** was prepared according to General Procedure A from a solution of 4-iodo-[1,1'-biphenyl]-3,5-diyl bis-(trifluoromethanesulfonate) **15a** (113 mg, 0.196 mmol) in Et₂O (1 mL) and a mixture of diethyl trimethylsilyl phosphite (**8a**, 83 mg, 0.40 mmol) and (trimethylsilyl)methyl magnesium chloride (0.4 mL, 0.4 mmol, 1.0 M in Et₂O) in Et₂O (1 mL). Purification by gradient flash chromatography (SiO₂, hexanes:EtOAc 9:1 to 7:3) gave aryl phosphonate **10c** (77 mg, 0.15 mmol, 77%) as a white solid. ¹H NMR (300 MHz, CDCl₃): δ 8.16 (dd, *J* = 1.9, 14.5 Hz, 1H), 7.66 (d, *J* = 1.8 Hz, 1H), 7.59 (br d, *J* = 7 Hz, 2H), 7.41–7.53 (m, 3H), 4.07–4.27 (m, 4H), 1.37 (t, *J* = 7.1 Hz, 6H), and 0.54 (s, 9H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 156.1 (d, *J* = 29.9 Hz), 143.7 (d, *J* = 17.2 Hz), 138.1 (d, *J* = 192.0 Hz, C_{aryl}-P), 138.0 (d, *J* = 1.6 Hz), 136.5 (d, *J* = 23.0 Hz), 131.8 (d, *J* = 10.6 Hz), 129.4 (2xC), 129.0, 127.2 (2xC), 122.2 (br), 118.6 (q, *J* = 320.2 Hz, CF₃), 62.6 (d, *J* = 6.2 Hz), 16.4 (d, *J* = 6.1 Hz), and 2.4. ¹⁹F{¹³C} NMR (282 MHz, CDCl₃): δ -74.7. ³¹P{¹H} NMR (121 MHz, CDCl₃): δ 17.8. IR (neat): 2985, 2905, 1596, 1421, 1248, 1215, 1143, 1088, 1053, 1024, 967, 925, 851, 811, and 764 cm⁻¹. HRMS (ESI) *m/z*: [M + Na⁺] calcd for C₂₀H₂₆F₃NaO₆PSSi⁺ requires 533.0801; found 533.0811. mp: 60–63 °C.

5-Bromo-3-(diethoxyphosphoryl)-2-(trimethylsilyl)phenyl Trifluoromethanesulfonate (10d).



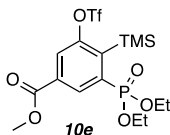
Aryl phosphonate **10d** was prepared according to General Procedure A from a solution of 5-bromo-2-iodo-1,3-phenylene bis-(trifluoromethanesulfonate) **15a** (111 mg, 0.192 mmol) in Et₂O (1 mL) and a mixture of diethyl trimethylsilyl phosphite (**8a**, 88 μL, 0.385 mmol) and (trimethylsilyl)methyl magnesium chloride (0.4 mL, 0.4 mmol, 1.0 M in Et₂O) in Et₂O (1 mL). Purification by flash chromatography (SiO₂, hexanes:EtOAc 6:1) gave aryl phosphonate **10d** (44 mg, 0.86 mmol, 44%) as a clear, colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 8.05 (dd, *J* = 1.7, 14.2 Hz, 1H), 7.60 (d, *J* = 1.5 Hz, 1H), 4.06–4.26 (m, 4H), 1.36 (t, *J* = 7.1 Hz, 6H), and 0.50 (s, 9H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 155.1 (d, *J* = 30.0 Hz), 139.4 (d, *J* = 191.8 Hz, C_{aryl}-P), 137.5 (d, *J* = 22.7 Hz), 136.1 (d, *J* = 10.5 Hz), 127.0, 123.7 (d, *J* = 23 Hz), 118.5 (q, *J* = 320.1 Hz, CF₃), 62.9 (d, *J* = 6.0 Hz), 16.4 (d, *J* = 6.6 Hz), and 2.2. ¹⁹F{¹³C} NMR (282 MHz, CDCl₃): δ -74.7. ³¹P{¹H} NMR (121 MHz, CDCl₃): δ 15.7. IR (neat): 2986, 2907, 1567, 1533, 1426, 1366, 1250, 1216, 1144, 1052, 1023, 969, 922, 851, 802, and 761 cm⁻¹. HRMS (ESI) *m/z*: [M + Na⁺] calcd for C₁₄H₂₁BrF₃NaO₆PSSi⁺ requires 534.9593; found 534.9592.

Methyl 4-Iodo-3,5-bis(((trifluoromethyl)sulfonyl)oxy)benzoate (E1).



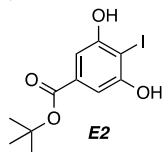
Trifluoromethanesulfonic anhydride (1.5 mL, 8.9 mmol) was added dropwise over 15 min to a mixture of methyl 3,5-dihydroxy-4-iodobenzoate⁵³ (1.26 g, 4.29 mmol), *N,N*-diisopropylethylamine (1.6 mL, 9.1 mmol), and CH₂Cl₂ (10 mL) at −78 °C with stirring. After 1 h, the cooling bath was removed. The mixture was allowed to warm at room temperature over 30 min, and water was added (3 mL). The resulting mixture was diluted with NaHCO₃ and extracted three times with CH₂Cl₂. The organic extracts were combined, dried (MgSO₄), and concentrated. Purification by gradient flash chromatography (SiO₂, hexanes:EtOAc 19:1 to 9:1) gave 2-iodophenyl bis(triflate) **E1** (1.39 g, 2.49 mmol, 58%) as a yellow oil, which partially solidified on standing. ¹H NMR (300 MHz, CDCl₃): δ 7.96 (s, 2H) and 3.99 (s, 3H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 163.4, 151.8, 133.8, 122.1, 118.8 (q, *J* = 321.2 Hz, CF₃), 94.1, and 53.5. ¹⁹F{¹³C} NMR (282 MHz, CDCl₃): δ −74.0. IR (neat): 3103, 2961, 1720, 1428, 1301, 1251, 1217, 1142, 1135, 999, 988, 846, 796, and 768 cm^{−1}. HRMS (ESI) *m/z*: [M+Na⁺] calcd for C₁₀H₅F₆INaO₈S₂⁺ requires 580.8267; found 580.8280.

Methyl 3-(Diethoxyphosphoryl)-5-(((trifluoromethyl)sulfonyl)oxy)-4-(trimethylsilyl)benzoate (10e).



Aryl phosphonate **10e** was prepared according to General Procedure A from a solution of 2-iodophenyl bis(triflate) **E1** (124 mg, 0.222 mmol) in Et₂O (1 mL) and a mixture of diethyl trimethylsilyl phosphite (**8a**, 93 mg, 0.44 mmol) and (trimethylsilyl)methyl magnesium chloride (0.45 mL, 0.45 mmol, 1.0 M in Et₂O) in Et₂O (1.25 mL). Purification by flash chromatography (SiO₂, hexanes:EtOAc 4:1) gave aryl phosphonate **10e** (45 mg, 0.091 mmol, 41%) as a clear, colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 8.51 (d, *J* = 14.0 Hz, 1H), 8.04 (s, 1H), 4.08–4.24 (m, 4H), 3.97 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 6H), and 0.54 (s, 9H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 164.7 (d, *J* = 1.9 Hz), 155.4 (d, *J* = 28.0 Hz), 144.8 (d, *J* = 23.2 Hz), 138.7 (d, *J* = 193.5 Hz, C_{aryl}-P), 133.4 (d, *J* = 11.4 Hz), 132.4 (d, *J* = 17.1 Hz), 124.4 (br s), 118.6 (q, *J* = 320.3 Hz, CF₃), 62.8 (d, *J* = 6.4 Hz), 53.0, 16.4 (d, *J* = 6.2 Hz), and 2.2. ¹⁹F{¹³C} NMR (282 MHz, CDCl₃): δ −74.7. ³¹P{¹H} NMR (121 MHz, CDCl₃): δ 16.4. IR (neat): 2988, 2958, 2907, 1735, 1439, 1426, 1375, 1290, 1247, 1217, 1142, 1053, 1023, 995, 971, 930, 852, 809, and 770 cm^{−1}. HRMS (ESI) *m/z*: [M+Na⁺] calcd for C₁₆H₂₄F₃NaO₈PSSi⁺ requires 515.0543; found 515.0541. TLC: R_f 0.4 (SiO₂, 4:1 hexanes:EtOAc).

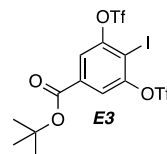
tert-Butyl 3,5-Dihydroxy-4-iodobenzoate (E2).



3,5-Diacetoxybenzoyl chloride⁵⁴ (5.00 g, 19.5 mmol) was diluted in dichloromethane (28 mL), set to stir at room temperature, and sequentially treated with pyridine (1.7 mL, 21 mmol) and *tert*-butanol (3.4 mL, 36 mmol). After 24 h, the mixture was diluted with dichloromethane, washed with 1 M HCl (4×), dried (MgSO₄), and concentrated. The crude material (5.14 g, ~17 mmol) was dissolved in MeOH (35 mL) and treated with K₂CO₃ (12.1 g, 87 mmol) at room temperature with stirring. After 1 h, the mixture was filtered, and the filtrate was concentrated. The residue was diluted with EtOAc, sequentially washed with 1 M HCl and brine, dried (Na₂SO₄), and concentrated. The crude *tert*-butyl ester (2.84 g,

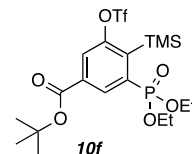
~13.5 mmol) was added to a mixture of NaHCO₃ (3.4 g, 41 mmol), water (23 mL), and THF (7 mL) and cooled to 0 °C with stirring. After 5 min, a solution of iodine (6.9 g, 27 mmol) in THF (16 mL) was added by syringe pump over 30 min with stirring. One hour after complete addition of the iodine solution, the resulting mixture was diluted with diethyl ether, washed with 10% aqueous Na₂S₂O₃ and brine, dried (Na₂SO₄), and concentrated to give the crude iodo resorcinol **E2** (3.21 g, 9.55 mmol, 49% crude over three steps) as a brown solid. The crude material was sufficiently pure for subsequent experiments. ¹H NMR (300 MHz, CDCl₃): δ 7.18 (s, 2H), 6.02 (br s, 2H), and 1.58 (s, 9H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 165.3, 156.0, 134.3, 107.9, 82.6, 82.2, and 28.3. IR (neat): 3424, 3207, 3183, 3001, 2973, 1672, 1603, 1586, 1422, 1375, 1288, 1258, 1211, 1157, 1126, 1040, 1023, 975, 867, 842, and 775 cm^{−1}. HRMS (ESI) *m/z*: [M+Na⁺] calcd C₁₁H₁₃INaO₄⁺ requires 358.9751; found 358.9750. mp: 148–153 °C.

tert-Butyl 4-Iodo-3,5-bis(((trifluoromethyl)sulfonyl)oxy)benzoate (E3).



Trifluoromethanesulfonic anhydride (0.85 mL, 5.0 mmol) was added dropwise over 15 min to a mixture of the crude iodo resorcinol **E2** (0.807 g, 2.40 mmol), *N,N*-diisopropylethylamine (0.89 mL, 5.1 mmol), and CH₂Cl₂ (8.00 mL) at −78 °C with stirring. After complete addition of trifluoromethanesulfonic anhydride, the cooling bath was removed. After the mixture was stirred for an additional hour, water was added (2.5 mL). The resulting mixture was diluted with NaHCO₃ and extracted three times with CH₂Cl₂. The organic extracts were combined, dried (MgSO₄), and concentrated. The crude material was dissolved in an Et₂O:hexanes solution (100 mL, 1:1); silica gel (10 g) was added, and the mixture was set to stir. After 10 min, the mixture was filtered through a plug of silica gel (1:1 Et₂O:hexanes eluent), and the filtrate was concentrated to give bis(trifloxy)arene **E3** (1.38 g, 2.30 mmol, 96%) as an off-white crystalline solid, which was sufficiently pure for subsequent reactions. White crystals could be obtained by recrystallization with hexanes. On smaller scales, the material can be purified by gradient flash chromatography (SiO₂, hexanes:EtOAc 39:1 to 19:1). ¹H NMR (300 MHz, CDCl₃): δ 7.90 (s, 2H) and 1.61 (s, 9H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 161.8, 151.7, 135.8, 122.0, 118.8 (q, *J* = 321 Hz, CF₃), 93.5, 84.0, and 28.1. ¹⁹F{¹³C} NMR (282 MHz, CDCl₃): δ −74.1. IR (neat): 2991, 1713, 1560, 1431, 1402, 1308, 1226, 1135, 984, 842, 794, 753, 714, and 665 cm^{−1}. HRMS (ESI) *m/z*: [M+Na⁺] calcd for C₁₃H₁₁F₆INaO₈S₂⁺ requires 622.8736; found 622.8733. mp: 90–94 °C.

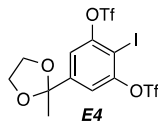
tert-Butyl 3-(Diethoxyphosphoryl)-5-(((trifluoromethyl)sulfonyl)oxy)-4-(trimethylsilyl)benzoate (10f).



Aryl phosphonate **10f** was prepared according to General Procedure A from a solution of 2-iodophenyl bis(triflate) **E3** (274 mg, 0.457 mmol) in Et₂O (2.3 mL) and a mixture of diethyl trimethylsilyl phosphite (**8a**, 192 mg, 0.913 mmol) and (trimethylsilyl)methyl magnesium chloride (0.91 mL, 0.91 mmol, 1.0 M in Et₂O) in Et₂O (2.3 mL). Purification by flash chromatography (SiO₂, hexanes:EtOAc 6:1) gave aryl phosphonate **10f** (134 mg, 0.251 mmol, 55%) as a clear, colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 8.45 (dd, *J* = 1.5, 14.2 Hz, 1H), 7.99 (d, *J* = 1 Hz, 1H), 4.06–4.26 (m, 4H), 1.60 (s, 9H), 1.36 (t, *J* = 7.1 Hz, 6H), and 0.53 (s, 9H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 163.2 (d, *J* = 3 Hz), 155.5 (d, *J* = 27.8 Hz), 144.0 (d, *J* = 23.2 Hz), 138.3 (d, *J* = 193.5 Hz, C_{aryl}-P), 134.4 (d, *J* = 17.1 Hz),

133.2 (d, $J = 11.3$ Hz), 124.4, 118.6 (q, $J = 320.3$ Hz, CF_3), 82.8, 62.7 (d, $J = 6.6$ Hz), 28.2, 16.4 (d, $J = 6.4$ Hz), and 2.2. $^{19}\text{F}\{^{13}\text{C}\}$ NMR (282 MHz, CDCl_3): $\delta -74.7$. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): $\delta 16.3$. IR (neat): 2984, 2928, 2853, 1723, 1428, 1370, 1297, 1247, 1215, 1144, 1053, 1023, 956, 848, 811 cm^{-1} . HRMS (ESI) m/z : $[\text{M} + \text{Na}^+]$ calcd for $\text{C}_{19}\text{H}_{30}\text{F}_3\text{NaO}_8\text{PSSi}^+$ requires 557.1013; found 557.1012.

2-Iodo-5-(2-methyl-1,3-dioxolan-2-yl)-1,3-phenylene Bis(trifluoromethanesulfonate) (E4).

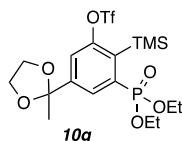


Tetrabutylammonium tribromide (0.073 g, 0.16 mmol) was added to a mixture of 3',5'-dihydroxyacetophenone (1.01 g, 6.64 mmol), trimethylorthoformate (1.68 mL, 15.4 mmol), and ethylene glycol (3.7 mL, 66 mmol) at room temperature and with stirring. After 1 h, the mixture was diluted with water and extracted with EtOAc (3 \times). The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated to give the crude ketal [5-(2-methyl-1,3-dioxolan-2-yl)benzene-1,3-diol, 1.02 g], which underwent partial deketalization on silica gel and so was used directly in subsequent experiments.

N-Iodosuccinimide (1.15 g, 5.10 mmol) was added to a mixture of crude 5-(2-methyl-1,3-dioxolan-2-yl)benzene-1,3-diol (1.00 g) in acetonitrile (12 mL) at 0 $^\circ\text{C}$ and with stirring. After 10 min, the mixture was diluted with ethyl acetate and washed with 10% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ and brine, dried (Na_2SO_4), and concentrated to give the crude iodo resorcinol [2-iodo-5-(2-methyl-1,3-dioxolan-2-yl)benzene-1,3-diol, 0.882 g], which underwent partial deketalization on silica gel and so was used directly in subsequent experiments.

Trifluoromethanesulfonic anhydride (1.0 mL, 5.9 mmol) was added dropwise over 30 min to a mixture of crude 2-iodo-5-(2-methyl-1,3-dioxolan-2-yl)benzene-1,3-diol (0.882 g), *N,N*-diisopropylethylamine (1.4 mL, 8.2 mmol), and CH_2Cl_2 (9.1 mL) at -78 $^\circ\text{C}$ with stirring. After complete addition of trifluoromethanesulfonic anhydride, the cooling bath was removed and the mixture was stirred for an additional hour; water was added (3.2 mL). The resulting mixture was diluted with NaHCO_3 and extracted three times with CH_2Cl_2 . The organic extracts were combined, dried (MgSO_4), and concentrated. Purification by flash chromatography (SiO_2 , hexanes:EtOAc 19:1) gave 2-iodophenyl bis(triflate) **E4** (0.644 g, 1.10 mmol, 17% over three steps) as a pale brown solid. ^1H NMR (300 MHz, CDCl_3): δ 7.47 (s, 2H), 4.03–4.15 (m, 2H), 3.71–3.83 (m, 2H), and 1.64 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 151.6, 149.0, 118.9, 118.8 (q, $J = 320.3$ Hz, CF_3), 107.4, 86.6, 65.0 (2C), and 27.4. $^{19}\text{F}\{^{13}\text{C}\}$ NMR (282 MHz, CDCl_3): $\delta -74.1$. IR (neat): 3090, 2995, 2898, 1709, 1564, 1433, 1415, 1400, 1377, 1277, 1247, 1217, 1139, 1038, 982, 883, 856, 796, 757, 712, and 671 cm^{-1} . HRMS (ESI) m/z : $[\text{M} + \text{Na}^+]$ calcd for $\text{C}_{12}\text{H}_{10}\text{F}_6\text{INaO}_8\text{S}_2^+$ requires 608.8580; found 608.8592. mp: 66–69 $^\circ\text{C}$.

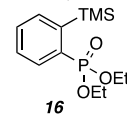
3-(Diethoxyphosphoryl)-5-(2-methyl-1,3-dioxolan-2-yl)-2-(trimethylsilyl)phenyl Trifluoromethanesulfonate (10g).



Aryl phosphonate **10g** was prepared according to General Procedure A from a solution of 2-iodophenyl bis(triflate) **E4** (62 mg, 0.11 mmol) in Et_2O (0.53 mL) and a mixture of diethyl trimethylsilyl phosphite (**8a**, 44 mg, 0.21 mmol) and (trimethylsilyl)methyl magnesium chloride (0.21 mL, 0.21 mmol, 1.0 M in Et_2O) in Et_2O (0.53 mL). Purification by gradient flash chromatography (SiO_2 , hexanes:EtOAc 4:1 to 7:3) gave aryl phosphonate **10g** (29 mg, 0.056 mmol, 51%) as a clear, colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 8.00 (dd, $J = 1.1, 14.2$ Hz, 1H), 7.55 (s, 1H), 4.02–4.23 (m, 6H), 3.72–3.79 (m, 2H), 1.64 (s, 3H), 1.36 (t, $J = 7.1$ Hz, 6H), and 0.51

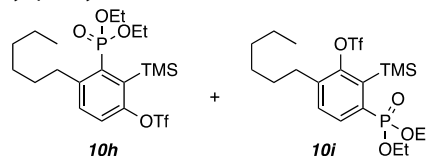
(s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 155.6 (d, $J = 28.9$ Hz), 146.9 (d, $J = 15.3$ Hz), 137.9 (d, $J = 195.0$ Hz, $\text{C}_{\text{aryl}}\text{-P}$), 138.0 (d, $J = 23.5$ Hz), 130.1 (d, $J = 11.0$ Hz), 121.1 (br s), 118.6 (q, $J = 320.0$ Hz, CF_3), 107.8, 64.8, 62.6 (d, $J = 6.4$ Hz), 27.4, 16.4 (d, $J = 6.7$ Hz), and 2.3. $^{19}\text{F}\{^{13}\text{C}\}$ NMR (282 MHz, CDCl_3): $\delta -74.8$. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): $\delta 17.6$. IR (neat): 2988, 2902, 1422, 1374, 1213, 1141, 1051, 1033, 1023, 941, 950, 807, and 762 cm^{-1} . HRMS (ESI) m/z : $[\text{M} + \text{Na}^+]$ calcd for $\text{C}_{18}\text{H}_{28}\text{F}_3\text{NaO}_8\text{PSSi}^+$ requires 543.0856; found 543.0878.

Diethyl (2-(Trimethylsilyl)phenyl)phosphonate (16).



Aryl phosphonate **16** was prepared according to General Procedure A from a solution of 2-iodophenyl bis(triflate) **14**⁵⁵ (103 mg, 0.292 mmol) in Et_2O (1.5 mL) and a mixture of diethyl trimethylsilyl phosphite (**8a**, 132 μL , 120 mg, 0.58 mmol) and (trimethylsilyl)methyl magnesium chloride (0.58 mL, 0.58 mmol, 1.0 M in Et_2O) in Et_2O (1.5 mL). The mixture was stirred for 20 h. Purification by gradient flash chromatography (SiO_2 , hexanes:EtOAc 4:1 to 7:3) gave aryl phosphonate **16** (69 mg, 0.16 mmol, 54%) as a clear, pale brown oil. ^1H NMR (300 MHz, CDCl_3): δ 7.89 (ddd, $J = 1.8, 7.4, 14$ Hz, 1H), 7.74 (ddd, $J = 1.6, 4.7, 6.8$ Hz, 1H), 7.39–7.53 (m, 2H), 4.01–4.21 (m, 4H), 1.33 (t, $J = 7.1$ Hz, 6H), and 0.41 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 145.2 (d, $J = 21.5$ Hz), 135.9 (d, $J = 19.6$ Hz), 133.5 (d, $J = 188.9$ Hz, $\text{C}_{\text{aryl}}\text{-P}$), 133.3 (d, $J = 11.5$ Hz), 131.2 (d, $J = 3.4$ Hz), 128.4 (d, $J = 14.2$ Hz), 61.9 (d, $J = 5.7$ Hz), 16.4 (d, $J = 6.7$ Hz), and 1.0. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): $\delta 20.8$. IR (neat): 2983, 2956, 2903, 1424, 1392, 1250, 1139, 1026, 963, 846, and 755 cm^{-1} . HRMS (ESI) m/z : $[\text{M} + \text{Na}^+]$ calcd for $\text{C}_{14}\text{H}_{22}\text{F}_3\text{NaO}_6\text{PSSi}^+$ requires 309.1046; found 309.1063. TLC: Rf 0.45 (SiO_2 , 30% EtOAc in hexanes).

3-(Diethoxyphosphoryl)-6-hexyl-2-(trimethylsilyl)phenyl Trifluoromethanesulfonate (10h) and 3-(Diethoxyphosphoryl)-4-hexyl-2-(trimethylsilyl)phenyl Trifluoromethanesulfonate (10i).

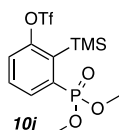


A ~4:8:1 mixture of isomeric aryl phosphonates **10h** and **10i** was prepared according to General Procedure A from a solution of 2-iodophenyl bis(triflate) **17** (528 mg, 0.904 mmol) in Et_2O (4.5 mL) and a mixture of diethyl trimethylsilyl phosphite (**8a**, 380 mg, 1.8 mmol) and (trimethylsilyl)methyl magnesium chloride (1.8 mL, 1.8 mmol, 1.0 M in Et_2O) in Et_2O (4.5 mL). Purification by gradient flash chromatography (SiO_2 , hexanes:EtOAc 9:1 to 7:3) gave faster-eluting aryl phosphonate **10h** (240 mg, 0.46 mmol, 51%) and slower-eluting aryl phosphonate **10i** (50 mg, 0.096 mmol, 11%), each as a clear, pale-yellow oil. Structures for **10h** and **10i** were assigned by comparing the aromatic regions of the ^1H NMR spectra. Specifically, minor isomer **10h** exhibited a downfield signal with a dd splitting ($J = 7.8, 13.1$ Hz) that is characteristic of a $\text{C}_{\text{aryl}}\text{-H}$ hydrogen *ortho* to a phosphonyl group.

Spectral data for **10h** (faster-eluting major isomer). ^1H NMR (300 MHz, CDCl_3): δ 7.24–7.37 (m, 2H), 3.94–4.20 (m, 4H), 2.92 (br t, $J = 8$ Hz, 2H), 1.53–1.66 (m, 2H), 1.47–1.22 (m, 12H), 0.90 (br t, $J = 6.7$ Hz, 3H), and 0.48 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 153.0 (d, $J = 28.1$ Hz), 148.4 (d, $J = 11.5$ Hz), 142.4 (d, $J = 23.9$ Hz), 136.1 (d, $J = 192.3$ Hz, $\text{C}_{\text{aryl}}\text{-P}$), 132.8 (d, $J = 17.2$ Hz), 124.0 (br s), 118.7 (q, $J = 326.4$ Hz, CF_3), 62.3 (d, $J = 6.0$ Hz), 34.8 (d, $J = 3.0$ Hz), 32.3, 31.9, 29.8, 22.8, 16.3 (d, $J = 5.9$ Hz), 14.2, and 3.6. $^{19}\text{F}\{^{13}\text{C}\}$ NMR (282 MHz, CDCl_3): $\delta -74.8$. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): $\delta 19.0$. IR (neat): 2984, 2960, 2932, 2861, 1422, 1249, 1213, 1165, 1144, 1111, 1049, 1023, 964, 919, 848, and 790 cm^{-1} . HRMS (ESI) m/z : $[\text{M} + \text{Na}^+]$ calcd for $\text{C}_{20}\text{H}_{34}\text{F}_3\text{NaO}_6\text{PSSi}^+$ requires 541.1427; found 541.1425.

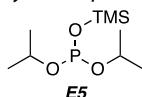
Spectral data for **10i** (slower-eluting minor isomer). ^1H NMR (300 MHz, CDCl_3): δ 7.78 (dd, $J = 7.9, 13.1$ Hz, 1H, $J^{\text{P-H}}$ ^{31}P – ^1H), 7.38 (dd, $J = 4.5, 7.7$ Hz, 1H), 3.97–4.25 (m, 4H), 2.73 (br t, $J = 8$ Hz, 2H), 1.49–1.66 (m, 2H), 1.40–1.24 (m, 12H), 0.89 (br t, $J = 6$ Hz, 3H), and 0.51 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 150.6 (d, $J = 28.9$ Hz), 141.5 (d, $J = 24.3$ Hz), 140.7 (d, $J = 3.2$ Hz), 135.5 (d, $J = 19.4$ Hz, $\text{C}_{\text{aryl}}\text{-P}$), 133.7 (d, $J = 9.4$ Hz), 131.7 (d, $J = 17.0$ Hz), 118.7 (q, $J = 320.0$ Hz, CF_3), 62.3 (d, $J = 5.8$ Hz), 31.7, 30.7, 29.8, 29.2, 22.7, 16.4 (d, $J = 6.2$ Hz), 14.2, and 2.9. $^{19}\text{F}\{^{13}\text{C}\}$ NMR (282 MHz, CDCl_3): δ –74.6. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 18.7. IR (neat): 2958, 2932, 2861, 1403, 1247, 1215, 1165, 1142, 1094, 1053, 1025, 965, 911, 872, 852, 829, 766, and 667 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{Na}^+]$ calcd for $\text{C}_{20}\text{H}_{34}\text{F}_3\text{NaO}_6\text{PSSi}^+$ requires 541.1427; found 541.1427.

3-(Dimethoxyphosphoryl)-2-(trimethylsilyl)phenyl Trifluoromethanesulfonate (**10j**).



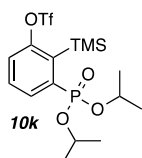
Aryl phosphonate **10j** was prepared according to General Procedure A from a solution of 2-iodophenyl bis(triflate) **13**⁵² (228 mg, 0.456 mmol) in Et_2O (2 mL) and a mixture of dimethyl trimethylsilyl phosphite (**8b**, 191 mg, 1.05 mmol) and (trimethylsilyl)methyl magnesium chloride (0.8 mL, 0.8 mmol, 1.0 M in Et_2O) in Et_2O (2 mL). Purification by flash chromatography (SiO_2 , hexanes: EtOAc 2:1) gave aryl phosphonate **10j** (139 mg, 0.342 mmol, 75%) as a clear, colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 7.90 (ddd, $J = 1.4, 7, 13.5$ Hz, 1H), 7.45–7.57 (m, 2H), 3.78 (d, $J = 11.1$, 6H), and 0.51 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 155.6 (d, $J = 28.5$ Hz), 138.8 (d, $J = 23.6$ Hz), 136.3 (d, $J = 193.4$ Hz, $\text{C}_{\text{aryl}}\text{-P}$), 133.3 (d, $J = 10.3$ Hz), 130.6 (d, $J = 16.9$ Hz), 124.3 (d, $J = 3$ Hz), 118.5 (q, $J = 320.3$ Hz, CF_3), 52.9 (d, $J = 6.7$ Hz) and 2.1. $^{19}\text{F}\{^{13}\text{C}\}$ NMR (282 MHz, CDCl_3): δ –74.9. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 20.3. IR (neat): 2956, 2906, 2853, 1586, 1423, 1408, 1249, 1215, 1142, 1113, 1057, 1032, 916, 850, 812, 771, and 719 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{Na}^+]$ calcd for $\text{C}_{12}\text{H}_{18}\text{F}_3\text{NaO}_6\text{PSSi}^+$ requires 429.0175; found 429.0173. TLC: Rf 0.3 (SiO_2 , 30% EtOAc in hexanes).

Diisopropyl (Trimethylsilyl) Phosphite (**E5**).



Silyl phosphite **E5** was prepared according to General Procedure B from diisopropyl phosphite (1.0 mL, 6.0 mmol), TMSCl (1.1 mL, 8.7 mmol), Et_3N (1.0 mL, 7.2 mmol), and CH_2Cl_2 (30 mL). The resulting product (**E5**, 1.2 g, 5.0 mmol, 83% crude yield) was obtained as a clear, colorless oil with starting phosphite contamination. The ratio of product to starting phosphite was found to be 82:18 as determined by ^1H and ^{31}P NMR, and this mixture was used directly without further purification. ^1H NMR (300 MHz, CDCl_3): δ 4.32–4.49 (m, 2H), 1.21 (br d, $J = 6.2$ Hz, 12H), and 0.20 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 65.2 (d, $J = 11.4$ Hz), 24.4 (dd, $J = 2.9, 3.0$ Hz), and 1.60 (d, $J = 2.3$ Hz). $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 129.2. IR (neat): 2976, 2937, 2898, 2879, 1467, 1454, 1385, 1351, 1251, 1178, 1139, 1109, 1051, 1001, 952, 844, 759, 721, and 688 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{H}^+]$ calcd for $\text{C}_9\text{H}_{24}\text{O}_3\text{PSi}^+$ requires 239.1227; found 239.1231.

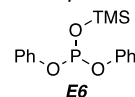
3-(Diisopropoxyphosphoryl)-2-(trimethylsilyl)phenyl Trifluoromethanesulfonate (**10k**).



Aryl phosphonate **10k** was prepared according to General Procedure A from a solution of 2-iodophenyl bis(triflate) **13**⁵² (207 mg, 0.414

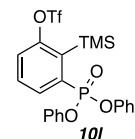
mmol) in Et_2O (2.1 mL) and a mixture of silyl phosphite **E5** (198 mg, 0.832 mmol) and (trimethylsilyl)methyl magnesium chloride (0.83 mL, 0.83 mmol, 1.0 M in Et_2O) in Et_2O (2.1 mL). Purification by flash chromatography (SiO_2 , hexanes: EtOAc 4:1) gave aryl phosphonate **10k** (133 mg, 0.288 mmol, 69%) as a clear, colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 7.90 (ddd, $J = 1.3, 7.1, 13.4$ Hz, 1H), 7.40–7.53 (m, 2H), 4.64–4.80 (m, 2H), 1.38 (d, $J = 6.2$ Hz, 6H), 1.24 (d, $J = 6.2$ Hz, 6H), and 0.53 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 155.3 (d, $J = 28.8$ Hz), 139.4 (d, $J = 193.4$ Hz, $\text{C}_{\text{aryl}}\text{-P}$), 138.5 (d, $J = 24.1$ Hz), 133.3 (d, $J = 9.4$ Hz), 130.2 (d, $J = 16.5$ Hz), 123.8 (d, $J = 1.8$ Hz), 118.6 (q, $J = 320.2$ Hz, CF_3), 71.7 (d, $J = 6.1$ Hz), 24.1 (d, $J = 4.4$ Hz), 23.8 (d, $J = 4.7$ Hz), and 2.6. $^{19}\text{F}\{^{13}\text{C}\}$ NMR (282 MHz, CDCl_3): δ –74.7. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 15.2. IR (neat): 2982, 2937, 2904, 1424, 1405, 1387, 1375, 1258, 1249, 1213, 1142, 1105, 1005, 982, 913, 882, 848, 811, 796, 766, 718, and 665 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{Na}^+]$ calcd for $\text{C}_{16}\text{H}_{26}\text{F}_3\text{NaO}_6\text{PSSi}^+$ requires 485.0801; found 485.0811.

Diphenyl (Trimethylsilyl) Phosphite (**E6**).



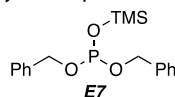
Silyl phosphite **E6** was prepared according to General Procedure B from diphenyl phosphite (1.0 mL, 5.2 mmol), TMSCl (0.93 mL, 7.3 mmol), Et_3N (0.87 mL, 6.3 mmol), and CH_2Cl_2 (26 mL). The resulting product (**E6**, 1.1 g, 3.6 mmol, 69% crude yield) was obtained as a clear, colorless oil with less than 25 mol % starting phosphite contamination as determined by ^1H and ^{31}P NMR. Given the instability of related *O*-silyl phosphites, purification was not attempted. ^1H NMR (300 MHz, CDCl_3): δ 7.25–7.36 (m, 4H), 7.03–7.12 (s, 6H), and 0.23 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 152.0 (d, $J = 3.3$ Hz), 129.6, 123.8, 120.9 (d, $J = 7.9$ Hz), and 1.6. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 124.6. IR (neat): 3066, 3040, 2958, 2898, 1590, 1487, 1254, 1223, 1191, 1163, 992, 839, 755, 706, and 688 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{H}^+]$ calcd for $\text{C}_{15}\text{H}_{20}\text{O}_3\text{PSi}^+$ requires 307.0914; found 307.0921.

3-(Diphenoxyphosphoryl)-2-(trimethylsilyl)phenyl Trifluoromethanesulfonate (**10l**).



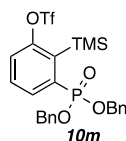
Aryl phosphonate **10l** was prepared according to General Procedure A from a solution of 2-iodophenyl bis(triflate) **13**⁵² (169 mg, 0.34 mmol) in Et_2O (1.7 mL) and a mixture of silyl phosphite **E6** (207 mg, 0.68 mmol) and (trimethylsilyl)methyl magnesium chloride (0.70 mL, 0.70 mmol, 1.0 M in Et_2O) in Et_2O (1.7 mL). To remove phenol impurities from the crude reaction mixture, the workup was modified from the general procedure. Namely, after stirring for 1 h, the reaction mixture was diluted in 1 M HCl (10 mL) and ethyl acetate (50 mL), and the phases were separated. The organic phase was sequentially washed with 1 M NaOH (3 \times 25 mL) and brine, dried (MgSO_4), and concentrated. Purification by flash chromatography (SiO_2 , hexanes: EtOAc 19:1) gave aryl phosphonate **10l** (130 mg, 0.24 mmol, 71%) as a clear, colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 8.14 (ddd, $J = 2, 6.7, 14.2$ Hz, 1H), 7.52–7.62 (m, 2H), 7.27–7.35 (m, 4H), 7.11–7.20 (m, 6H), and 0.57 (s, 9H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 155.5 (d, $J = 31.1$ Hz), 150.5 (d, $J = 8.7$ Hz), 139.5 (d, $J = 25.6$ Hz), 136.4 (d, $J = 198.1$ Hz, $\text{C}_{\text{aryl}}\text{-P}$), 133.8 (d, $J = 10.3$ Hz), 130.7 (d, $J = 17.7$ Hz), 130.0, 125.4, 124.9 (d, $J = 2.4$ Hz), 120.5 (d, $J = 4.6$ Hz), 118.6 (q, $J = 320.6$ Hz, CF_3), and 2.5. $^{19}\text{F}\{^{13}\text{C}\}$ NMR (282 MHz, CDCl_3): δ –74.6. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 10.1. IR (neat): 3071, 2958, 2906, 1592, 1491, 1424, 1405, 1280, 1251, 1213, 1187, 1161, 1142, 1113, 1072, 1049, 1025, 1006, 934, 900, 848, 811, 796, 764, 718, and 688 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{Na}^+]$ calcd for $\text{C}_{22}\text{H}_{22}\text{F}_3\text{NaO}_6\text{PSSi}^+$ requires 553.0488; found 553.0487.

Dibenzyl (Trimethylsilyl) Phosphite (E7).



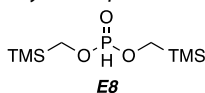
Silyl phosphite E7 was prepared according to General Procedure B from dibenzyl phosphite (1.0 mL, 4.5 mmol), TMSCl (0.87 mL, 6.8 mmol), Et₃N (0.94 mL, 6.8 mmol), and CH₂Cl₂ (23 mL). The resulting product (E7, 1.3 g, 3.9 mmol, 87% crude yield) was obtained as a clear, colorless oil with ca. 10 mol % starting phosphite contamination as determined by ¹H and ³¹P NMR. Given the instability of related *O*-silyl phosphites, purification was not attempted. ¹H NMR (300 MHz, CDCl₃): δ 7.25–7.37 (m, 10H), 4.82 (d, *J* = 7.9 Hz, 4H), and 0.22 (s, 9H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 138.6 (d, *J* = 4.6 Hz), 128.5, 127.7, 127.6, 63.0 (d, *J* = 9.1 Hz), and 1.5 (d, *J* = 2.3 Hz). ³¹P{¹H} NMR (121 MHz, CDCl₃): δ 128.0. IR (neat): 3092, 3068, 3034, 2958, 1498, 1456, 1254, 1213, 1047, 982, 952, 848, 781, 760, 732, and 695 cm⁻¹. HRMS (ESI) *m/z*: [M+H]⁺ calcd for C₁₇H₂₄O₃PSi⁺ requires 335.1227; found 335.1243.

3-(Bis(benzyloxy)phosphoryl)-2-(trimethylsilyl)phenyl Trifluoromethanesulfonate (10m).



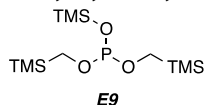
Aryl phosphonate 10m was prepared according to General Procedure A from a solution of 2-iodophenyl bis(triflate) 13⁵² (204 mg, 0.408 mmol) in Et₂O (2.0 mL) and a mixture of silyl phosphite E7 (296 mg, 0.818 mmol) and (trimethylsilyl)methyl magnesium chloride (0.82 mL, 0.82 mmol, 1.0 M in Et₂O) in Et₂O (2.0 mL). Purification by flash chromatography (SiO₂, hexanes:EtOAc 7:3) gave aryl phosphonate 10m (154 mg, 0.262 mmol, 64%) as a clear, colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.86 (ddd, *J* = 2.6, 6.0, 13.8 Hz, 1H), 7.38–7.45 (m, 2H), 7.28–7.38 (m, 10H), 5.06 (ddd, *J* = 7.5, 11.6, 11.6 Hz, 2H), 5.05 (ddd, *J* = 8.1, 11.7, 11.7 Hz, 2H), and 0.50 (s, 9H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 155.6 (d, *J* = 28.8 Hz), 138.8 (d, *J* = 24.1 Hz), 137.2 (d, *J* = 192.5 Hz, C_{aryl}-P), 135.7 (d, *J* = 6.9 Hz), 133.4 (d, *J* = 10.1 Hz), 130.4 (d, *J* = 16.9 Hz), 128.69, 128.66, 128.4, 124.2 (br s), 118.6 (q, *J* = 320.2 Hz, CF₃), 68.1 (d, *J* = 5.8 Hz), and 2.3. ¹⁹F{¹³C} NMR (282 MHz, CDCl₃): δ -74.8. ³¹P{¹H} NMR (121 MHz, CDCl₃): δ 18.8. IR (neat): 3068, 3034, 2956, 2900, 1422, 1405, 1249, 1215, 1142, 1113, 1049, 992, 917, 848, and 811 cm⁻¹. HRMS (ESI) *m/z*: [M+Na]⁺ calcd for C₂₄H₂₆F₃NaO₆PSSi⁺ requires 581.0801; found 581.0809. TLC: R_f 0.6 (SiO₂, 30% EtOAc in hexanes).

Bis(trimethylsilyl)methyl Phosphonate (E8).



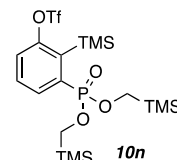
Diphenyl phosphite (400 μL, 2.1 mmol) was added to a solution of (trimethylsilyl)methanol (560 μL, 4.4 mmol) in pyridine (2.10 mL) with stirring. After 24 h, pyridine was removed by azeotropic distillation with cyclohexane, and the resulting material was diluted in ethyl acetate (100 mL) and sequentially washed with 1 M NaOH (3 × 100 mL) and brine. The organic phase was dried (MgSO₄) and concentrated to give phosphite E8 (416 mg, 1.64 mmol, 78%) as a clear, colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 6.69 (d, *J* = 684 Hz, 1H), 3.70 (d, *J* = 7.2 Hz, 4H), and 0.11 (s, 18H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 58.7 (d, *J* = 9.9 Hz) and -3.4. ³¹P{¹H} NMR (121 MHz, CDCl₃): δ 14.3. IR (neat): 2958, 2900, 1422, 1292, 1249, 1060, 1031, 977, 837, 759, 699, and 677 cm⁻¹. HRMS (ESI) *m/z*: [M+Na]⁺ calcd for C₈H₂₃NaO₃PSi⁺ requires 277.0816; found 277.0817.

Trimethylsilyl Bis(trimethylsilyl)methyl Phosphite (E9).



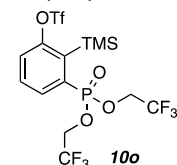
Silyl phosphite E9 was prepared according to General Procedure B from phosphite E8 (507 mg, 2.00 mmol), TMSCl (0.51 mL, 4.0 mmol), Et₃N (0.47 mL, 3.4 mmol), and CH₂Cl₂ (10 mL). The resulting product (E9, 628 mg, 1.9 mmol, 95% crude yield) was obtained as a clear, colorless oil with less than 5 mol % starting phosphite contamination as determined by ¹H and ³¹P NMR. Further purification was not attempted. ¹H NMR (300 MHz, CDCl₃): δ 3.31 (ap d, *J* = 6.9 Hz, 4H), 0.21 (s, 9H), and 0.06 (s, 18H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 52.6 (d, *J* = 4.7 Hz), 1.68, and -2.99. ³¹P{¹H} NMR (121 MHz, CDCl₃): δ 128.9. IR (neat): 2958, 2898, 2820, 1420, 1293, 1247, 1031, 986, 960, 837, 773, 757, 742, and 697 cm⁻¹. HRMS (ESI) *m/z*: [M+H]⁺ calcd for C₁₁H₃₂O₃PSi⁺ [M+H]⁺ requires 327.1391; found 327.1388.

3-(Bis(trimethylsilyl)methoxy)phosphoryl)-2-(trimethylsilyl)-phenyl Trifluoromethanesulfonate (10n).



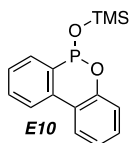
Aryl phosphonate 13 was prepared according to General Procedure A from a solution of 2-iodophenyl bis(triflate) 13⁵² (456 mg, 0.912 mmol) in Et₂O (4.6 mL) and a mixture of silyl phosphite E9 (0.52 g, 1.6 mmol) and (trimethylsilyl)methyl magnesium chloride (1.8 mL, 1.8 mmol, 1.0 M in Et₂O) in Et₂O (4.6 mL). Purification by flash chromatography (SiO₂, hexanes:EtOAc 6:1) gave aryl phosphonate 10n (367 mg, 0.66 mmol, 72%) as a clear, colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.80 (ddd, *J* = 1.5, 6.9, 13.0 Hz, 1H), 7.41–7.54 (m, 2H), 3.74 (dd, *J* = 6.6, 13.4 Hz, 2H), 3.60 (dd, *J* = 5.1, 13.4 Hz, 2H), 0.51 (s, 9H), and 0.09 (s, 18H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 155.6 (d, *J* = 27.8 Hz), 139.1 (d, *J* = 23.0 Hz), 137.2 (d, *J* = 188.2 Hz, C_{aryl}-P), 133.4 (d, *J* = 9.4 Hz), 130.3 (d, *J* = 16.2 Hz), 123.9 (br d, *J* = 2.6 Hz), 118.6 (q, *J* = 320.1 Hz, CF₃), 59.5 (d, *J* = 9.3 Hz), 2.4, and -3.2. ¹⁹F{¹³C} NMR (282 MHz, CDCl₃): δ -74.9. ³¹P{¹H} NMR (121 MHz, CDCl₃): δ 21.2. IR (neat): 2958, 2902, 1426, 1405, 1251, 1213, 1144, 1113, 1031, 1013, 989, 848, 818, 764, 703, and 680 cm⁻¹. HRMS (ESI) *m/z*: [M+Na]⁺ calcd for C₁₈H₃₄F₃NaO₆PSSi₃⁺ requires 573.0966; found 573.0957.

3-(Bis(2,2,2-trifluoroethoxy)phosphoryl)-2-(trimethylsilyl)phenyl Trifluoromethanesulfonate (10o).



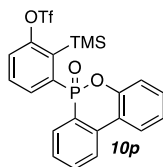
Aryl phosphonate 10o was prepared according to General Procedure A from a solution of 2-iodophenyl bis(triflate) 13⁵² (206 mg, 0.412 mmol) in Et₂O (2 mL) and a mixture of bis(2,2,2-trifluoroethyl) (trimethylsilyl) phosphite⁵⁶ (303 mg, 0.95 mmol) and (trimethylsilyl)methyl magnesium chloride (0.8 mL, 0.8 mmol, 1.0 M in Et₂O) in Et₂O (2 mL). Purification by flash chromatography (SiO₂, hexanes:EtOAc 9:1) gave aryl phosphonate 10o (128 mg, 0.238 mmol, 58%) as a clear, colorless oil, which solidified to a white solid upon standing. ¹H NMR (300 MHz, CDCl₃): δ 7.94 (ddd, *J* = 1.6, 6.9, 14.2 Hz, 1H), 7.52–7.63 (m, 2H), 4.27–4.57 (m, 4H), and 0.52 (s, 9H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 155.4 (d, *J* = 34.3 Hz), 139.7 (d, *J* = 26.5 Hz), 133.8 (d, *J* = 199.8 Hz, C_{aryl}-P), 133.6 (d, *J* = 10.9 Hz), 131.0 (d, *J* = 17.5 Hz), 125.6 (br s), 122.6 (dq, *J* = 9.7, 277 Hz, CF₃), 118.5 (q, *J* = 319.8 Hz, CF₃), 62.6 (dq, *J* = 5.5, 38.2 Hz, CCF₃), and 2.0. ¹⁹F{¹³C} NMR (282 MHz, CDCl₃): δ -74.7 (s, 3F) and -76.0 (t, *J* = 8.0 Hz, 6F). ³¹P{¹H} NMR (121 MHz, CDCl₃): δ 19.9. IR (neat): 3004, 2971, 2907, 1586, 1556, 1456, 1428, 1416, 1407, 1295, 1252, 1219, 1176, 1142, 1116, 1100, 1068, 964, 923, 878, 848, 828, 805, 790, 760, 718, and 662 cm⁻¹. HRMS (ESI) *m/z*: [M+Na]⁺ calcd for C₁₄H₁₆F₉NaO₆PSSi⁺ requires 564.9923; found 564.9926. mp: 68–72 °C. TLC: R_f 0.4 (SiO₂, 10% EtOAc in hexanes).

6-((Trimethylsilyl)oxy)-6H-dibenzo[c,e][1,2]oxaphosphinine (E10).



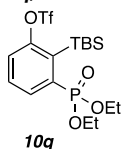
Silyl phosphite E10 was prepared according to General Procedure B from 9,10-dihydro-9-oxa-10-phosphaphenanthrene 10-oxide (1.50 g, 6.9 mmol), TMSCl (1.2 mL, 9.7 mmol), Et₃N (1.2 mL, 8.3 mmol), and CH₂Cl₂ (35 mL). The resulting product (E10, 1.6 g, 5.7 mmol, 82% crude yield) was obtained as a clear, colorless oil with less than 5 mol % starting phosphite contamination as determined by ¹H and ³¹P NMR. Given the instability of related O-silyl phosphites, purification was not attempted. ¹H NMR (300 MHz, CDCl₃): δ 7.94–8.01 (m, 2H), 7.68 (dd, *J* = 7.3, 11.5 Hz, 1H), 7.59 (dd, *J* = 7.5, 7.7 Hz, 1H), 7.45 (br t, *J* = 7 Hz, 1H), 7.34 (ddd, *J* = 1.7, 8.8, 8.8 Hz, 1H), 7.15–7.27 (m, 2H), and –0.04. ¹³C{¹H} NMR (75 MHz, CDCl₃): 149.2 (d, *J* = 9.1 Hz), 135.3 (d, *J* = 24.0 Hz), 131.5, 131.3, 130.6, 129.5, 127.5 (d, *J* = 12.9 Hz), 124.9, 123.6, 123.3, 122.9 (d, *J* = 6.9 Hz), 121.0, and 1.0 (d, *J* = 2.2 Hz). ³¹P{¹H} NMR (121 MHz, CDCl₃): δ 119.7. IR (neat): 3060, 2958, 2898, 1603, 1592, 1582, 1560, 1491, 1474, 1444, 1429, 1252, 1230, 1200, 1137, 1115, 1087, 1042, 978, 937, 919, 872, 837, 768, 751, 731, 714, 684, and 667 cm^{–1}. HRMS (ESI) *m/z*: [M+H⁺] calcd for C₁₅H₁₈O₂PSi⁺ requires 289.0808; found 289.0826.

3-(6-Oxidodibenzo[c,e][1,2]oxaphosphinin-6-yl)-2-(trimethylsilyl)phenyl Trifluoromethanesulfonate (10p).



Aryl phosphonate 10p was prepared according to General Procedure A from a solution of 2-iodophenyl bis(triflate) 13⁵² (200 mg, 0.400 mmol) in Et₂O (2.0 mL) and a mixture of silyl phosphite E10 (231 mg, 0.800 mmol) and (trimethylsilyl)methyl magnesium chloride (0.8 mL, 0.8 mmol, 1.0 M in Et₂O) in Et₂O (2 mL). Purification by flash chromatography (SiO₂, 6:1 EtOAc:hexanes) gave aryl phosphonate 10p (149 mg, 0.29 mmol, 73%) as a white solid. ¹H NMR (300 MHz, CDCl₃): δ 8.04 (dd, *J* = 5.1, 8.1 Hz, 1H), 7.98 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.74 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.66 (dd, *J* = 7.5, 13.6 Hz, 1H), 7.16–7.53 (m, 7H), and 0.63 (s, 9H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 155.9, 155.6, 148.8, 148.7, 139.7, 139.4, 137.8, 136.4, 136.3, 134.24, 134.20, 134.0, 133.6, 133.5, 132.7, 132.5, 131.5, 131.4, 131.3, 130.9, 130.8, 130.3, 130.1, 129.1, 128.9, 128.82, 128.78, 128.64, 128.59, 126.2, 125.3, 124.9, 124.8, 124.5, 124.1, 124.0, 123.8, 122.5, 122.3, 120.8, 120.7, 120.6, 120.5, 116.5, and 2.9. Because of complex *J*_{CP} coupling and overlapping multiplets, the chemical shift of each peak is provided without further interpretation. ¹⁹F{¹³C} NMR (282 MHz, CDCl₃): δ –74.7. ³¹P{¹H} NMR (121 MHz, CDCl₃): δ 28.0. IR (neat): 3070, 2954, 2904, 1595, 1584, 1478, 1422, 1403, 1249, 1239, 1213, 1141, 1118, 1108, 1046, 902, 848, 809, 796, 755, and 716 cm^{–1}. HRMS (ESI) *m/z*: [M+Na⁺] calcd for C₂₂H₂₀F₃NaO₃PSSi⁺ requires 535.0383; found 535.0386. mp: 166–168 °C. TLC: Rf 0.6 (SiO₂, 50% EtOAc in hexanes).

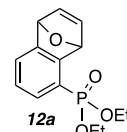
2-(*tert*-Butyldimethylsilyl)-3-(diethoxyphosphoryl)phenyl Trifluoromethanesulfonate (10q).



Aryl phosphonate 10q was prepared according to General Procedure A from a solution of 2-iodophenyl bis(triflate) 13⁵² (117 mg, 0.234 mmol) in Et₂O (1 mL) and a mixture of *tert*-butyldimethylsilyl diethyl

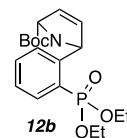
phosphite⁵⁷ (120 mg, 0.48 mmol) and (trimethylsilyl)methyl magnesium chloride (0.4 mL, 0.4 mmol, 1.0 M in Et₂O) in Et₂O (1 mL). Purification by flash chromatography (SiO₂, hexanes:EtOAc 4:1) gave aryl phosphonate 10q (51 mg, 0.11 mmol, 47%) as a clear, colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.98 (ddd, *J* = 1, 7.5, 14.0 Hz, 1H), 7.62 (br d, *J* = 8.3 Hz, 1H), 7.52 (ddd, *J* = 4.3, 7.6, 8.5 Hz, 1H), 4.04–4.29 (m, 4H), 1.36 (t, *J* = 7.1 Hz, 6H), 1.00 (s, 9H), and 0.56 (s, 6H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 157.6 (d, *J* = 28.8 Hz), 138.2 (d, *J* = 192.2 Hz, C_{aryl}-P), 135.2 (d, *J* = 23.1 Hz), 132.8 (d, *J* = 9.4 Hz), 130.4 (d, *J* = 17.1 Hz), 121.6 (m), 118.8 (q, *J* = 321.2 Hz, CF₃), 62.5 (d, *J* = 6.7 Hz), 28.5, 18.5, 16.4 (d, *J* = 6.6 Hz), and 0.8. ¹⁹F{¹³C} NMR (282 MHz, CDCl₃): δ –74.5. ³¹P{¹H} NMR (121 MHz, CDCl₃): δ 17.4. IR (neat): 2982, 2933, 2906, 2861, 1426, 1403, 1366, 1258, 1249, 1215, 1142, 1115, 1053, 1023, 967, 926, 852, 826, 813, 798, 766, 719, and 688 cm^{–1}. HRMS (ESI) *m/z*: [M+Na⁺] calcd for C₁₇H₂₈F₃NaO₆PSSi⁺ requires 499.0958; found 499.0962. TLC: Rf 0.6 (SiO₂, 30% EtOAc in hexanes).

Diethyl (1,4-Dihydro-1,4-epoxynaphthalen-5-yl)phosphonate (12a).



Cesium fluoride (320 mg, 2.1 mmol) was added to an oven-dried screw cap vial containing a mixture of aryl phosphonate 10a (314 mg, 0.72 mmol), furan (150 μL, 2.1 mmol), and acetonitrile (3.5 mL). Argon was blown over the headspace of the mixture; the vial was sealed with a Teflon-lined cap, and the reaction mixture was heated at 80 °C in a sand bath. After 24 h, the mixture was cooled to rt, diluted in ethyl acetate, sequentially washed with water and brine, dried (MgSO₄), and concentrated. Purification by gradient flash chromatography (SiO₂, hexanes:EtOAc 1:2 to 0:1) gave aryl phosphonate 12a (165 mg, 0.59 mmol, 82%) as a clear, colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.39 (ap d, *J* = 6.5 Hz, 1H), 7.35 (dd, *J* = 7.5, 12.0 Hz, 1H), 7.02–7.10 (m, 3H), 6.19 (s, 1H), 5.76 (s, 1H), 4.00–4.22 (m, 4H), and 1.33 (t, *J* = 7.1 Hz, 6H). ¹³C{¹H} NMR (75 MHz, CDCl₃): δ 154.5 (d, *J* = 10.6 Hz), 149.9 (d, *J* = 12.6 Hz), 143.6, 142.8, 127.4 (d, *J* = 10.6 Hz), 125.1 (d, *J* = 12.7 Hz), 123.6 (d, *J* = 3.3 Hz), 121.1 (d, *J* = 190.0 Hz, C_{aryl}-P), 82.6, 82.1, 62.2 (d, *J* = 5.2 Hz), 62.1 (d, *J* = 5.5 Hz), 16.5 (d, *J* = 6.3 Hz), and 16.4 (d, *J* = 6.5 Hz). ³¹P{¹H} NMR (121 MHz, CDCl₃): δ 17.7. IR (neat): 2984, 2907, 1771, 1249, 1234, 1159, 1044, 1016, 965, 874, 855, 818, 794, 781, 751, 714, and 665 cm^{–1}. HRMS (ESI) *m/z*: [M+Na⁺] calcd for C₁₄H₁₇NaO₄P⁺ requires 303.0757; found 303.0767. TLC: Rf 0.4 (SiO₂, 67% EtOAc in hexanes).

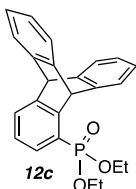
tert-Butyl 5-(Diethoxyphosphoryl)-1,4-dihydro-1,4-epimino-naphthalene-9-carboxylate (12b).



Cesium fluoride (320 mg, 2.1 mmol) was added to an oven-dried screw cap vial containing a mixture of aryl phosphonate 10a (296 mg, 0.68 mmol), *N*-Boc pyrrole (346 mg, 2.1 mmol), and acetonitrile (3.5 mL). Argon was blown over the headspace of the mixture; the vial was sealed with a Teflon-lined cap, and the reaction mixture was heated at 75 °C in a sand bath. After 15 h, the mixture was cooled to rt and diluted in ethyl acetate and water. The phases were separated, and the aqueous mixture was extracted twice more with ethyl acetate. The organic phases were combined, washed with brine, dried (MgSO₄), and concentrated. Purification by gradient flash chromatography (SiO₂, hexanes:EtOAc 1:2 to 0:1) gave aryl phosphonate 12b (169 mg, 0.45 mmol, 65%) as a clear, colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.31–7.47 (br m, 2H), 6.97 (m, 3H), 6.00 (s, 1H), 5.53 (s, 1H), 3.99–4.26 (m, 4H), 1.38 (s, 9H), and 1.33 (t, *J* = 6.9 Hz, 6H). ¹³C{¹H} NMR (75 MHz, CDCl₃, 19 °C): δ 154.9, 153.5 (d, *J* = 10.5 Hz), 149.4 (d, *J* = 13.0 Hz), 144.2 (br), 143.2 (br), 142.5 (br), 127.8

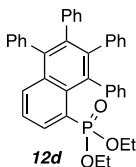
(br), 125.0 (d, $J = 3.9$ Hz), 124.4 (br), 80.9, 66.6 (br), 66.0 (br), 62.3 (d, $J = 4.7$ Hz), 62.1 (d, $J = 5.5$ Hz), 28.2, 16.52 (d, $J = 6.6$ Hz), and 16.48 (d, $J = 6.6$ Hz). $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 17.6. IR (neat): 2980, 2933, 2907, 1709, 1392, 1366, 1331, 1254, 1161, 1092, 1051, 1021, 964, 861, 841, 787, 762, 746, and 723 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{Na}^+]$ calcd for $\text{C}_{19}\text{H}_{26}\text{NNaO}_5\text{P}^+$ requires 402.1441; found 402.1447. TLC: Rf 0.3 (SiO_2 , 2:1 EtOAc:hexanes).

Diethyl (9,10-Dihydro-9,10-[1,2]benzenoanthracen-1-yl)-phosphonate (12c).



Cesium fluoride (315 mg, 2.1 mmol) was added to an oven-dried screw cap vial containing a mixture of aryl phosphonate **10a** (305 mg, 0.70 mmol), anthracene (370 mg, 2.1 mmol), and acetonitrile (3.5 mL). Argon was blown over the headspace of the mixture; the vial was sealed with a Teflon-lined cap, and the reaction mixture was heated at 80 °C in a sand bath. After 15 h, the mixture was cooled to rt and diluted in ethyl acetate and saturated aqueous NH_4Cl . The phases were separated, and the aqueous mixture was extracted twice more with ethyl acetate. The organic phases were combined, washed with brine, dried (MgSO_4), and concentrated. Purification by gradient flash chromatography (SiO_2 , hexanes:EtOAc 2:1 to 1:2) gave aryl phosphonate **12c** (169 mg, 0.43 mmol, 61%) as a white solid. ^1H NMR (300 MHz, CDCl_3): δ 7.52–7.62 (m, 2H), 7.35–7.48 (m, 4H), 7.08 (dd, $J = 3.8$, 7.6 Hz, 1H), 6.97–7.05 (m, 4H), 6.26 (s, 1H), 5.47 (s, 1H), 3.93–4.26 (m, 4H), 1.36 (t, $J = 7.1$ Hz, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 149.0 (d, $J = 10.6$ Hz), 146.8 (d, $J = 13.0$ Hz), 145.2, 144.4, 129.9 (d, $J = 10.8$ Hz), 128.0 (d, $J = 3.3$ Hz), 125.5, 124.9, 124.7, 124.2, 123.7, 122.9 (d, $J = 184.5$ Hz, $\text{C}_{\text{aryl}}\text{-P}$), 62.2 (d, $J = 5.1$ Hz), 54.1 (d, $J = 1.6$ Hz), 52.0 (d, $J = 3.4$ Hz), and 16.6 (d, $J = 6.9$ Hz). $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 19.5. IR (neat): 3070, 2980, 2902, 1457, 1424, 1390, 1366, 1249, 1197, 1156, 1098, 1047, 1019, 965, 837, 798, 749, and 695 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{Na}^+]$ calcd for $\text{C}_{24}\text{H}_{23}\text{NaO}_5\text{P}^+$ requires 413.1277; found 413.1289. mp: 122–127 °C. TLC: Rf 0.4 (SiO_2 , 2:1 EtOAc:hexanes).

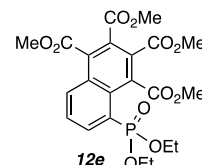
Diethyl (5,6,7,8-Tetraphenylnaphthalen-1-yl)phosphonate (12d).



Cesium fluoride (315 mg, 2.1 mmol) was added to an oven-dried screw cap vial containing a mixture of aryl phosphonate **10a** (285 mg, 0.66 mmol), tetraphenylcyclopentadienone (746 mg, 1.9 mmol), dichloromethane (1.7 mL), and acetonitrile (3.5 mL). Argon was blown over the headspace of the mixture; the vial was sealed with a Teflon-lined cap, and the reaction mixture was heated at 75 °C in a sand bath. After 15 h, the mixture was cooled to rt, concentrated, diluted in dichloromethane, and loaded onto a flash column. Elution of the material via gradient flash chromatography (SiO_2 , hexanes:EtOAc 9:1 to 0:1) achieved partial separation of the desired aryl phosphonate from the unreacted tetraphenylcyclopentadienone. Purification with a second flash column (SiO_2 , hexanes:EtOAc 9:1 to 1:2) gave aryl phosphonate **12d** (227 mg, 0.40 mmol, 60%) as a white solid. ^1H NMR (300 MHz, CDCl_3): δ 8.10 (ddd, $J = 1.4$, 7.1, 17.5 Hz, 1H), 7.75 (ddd, $J = 1.5$, 1.6, 8.5 Hz, 1H), 7.32–7.41 (m, 1H), 7.09–7.25 (m, 7H), 7.02–7.09 (m, 3H), 6.77–6.86 (m, 6H), 6.71–6.77 (m, 2H), 6.23–6.68 (m, 2H), 3.74–3.90 (m, 2H), 3.47–3.64 (m, 2H), and 1.17 (t, $J = 7.0$ Hz, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 142.0, 140.4 (d, $J = 8.0$ Hz), 140.2, 139.6, 139.5, 139.0 (d, $J = 2.2$ Hz), 138.9, 138.8, 135.6 (d, $J = 7.0$ Hz), 134.5, 133.7 (d, $J = 12.7$ Hz), 133.0 (d, $J = 11.4$ Hz), 132.3 (d, $J = 3.4$ Hz), 131.4, 131.0,

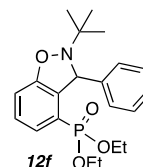
130.9, 127.6, 126.7, 126.5 (d, $J = 13.8$ Hz), 126.3, 125.9, 125.41, 125.1, 124.2 (ap s), 123.9, 123.7, 61.9 (d, $J = 6.7$ Hz), and 16.2 (d, $J = 6.9$ Hz). The 124.2 (ap s) is likely part of a $\text{C}_{\text{aryl}}\text{-P}$ doublet, but the other peak was not observed because of coincidental overlap. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 20.2. IR (neat): 3058, 3023, 2982, 2928, 2902, 1442, 1251, 1161, 1146, 1096, 1055, 1025, 965, 777, and 697 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{H}^+]$ calcd for $\text{C}_{38}\text{H}_{34}\text{O}_3\text{P}^+$ requires 569.2240; found 569.2243. mp: 73–77 °C.

Tetramethyl 5-(Diethoxyphosphoryl)naphthalene-1,2,3,4-tetracarboxylate (12e).



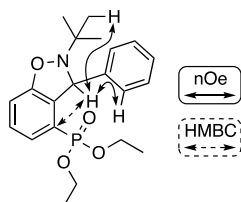
The supply of acetonitrile used in this experiment was sparged with N_2 for 20 min and used immediately. A solution of aryl phosphonate **10a** (264 mg, 0.61 mmol) in acetonitrile (6.1 mL) was added to screwcap vial containing a mixture of dimethyl acetylenedicarboxylate (374 μL , 3.0 mmol), CsF (185 mg, 1.2 mmol), and $\text{Pd}_2(\text{dba})_3\cdot\text{CHCl}_3$ (31 mg, 30 μmol) in acetonitrile (6.1 mL) at room temperature with stirring. The headspace of the mixture was exchanged with Ar, and the vial was sealed with a Teflon-lined cap. After 15 h, the mixture was filtered through a plug of silica gel (EtOAc eluent) and concentrated. Purification by gradient flash chromatography (SiO_2 , hexanes:EtOAc 2:1 to 1:2 to 0:1) gave aryl phosphonate **12e** (134 mg, 0.27 mmol, 44%) as a clear, yellow oil. ^1H NMR (300 MHz, CDCl_3): δ 8.33 (ddd, $J = 1.1$, 7.2, 16.5 Hz, 1H), 8.16 (ddd, $J = 1.3$, 1.4, 8.6, 1H), 7.72 (ddd, $J = 2.4$, 7.3, 8.4 Hz, 1H), 3.95–4.22 (m, 4H), 4.02 (s, 3H), 3.95 (s, 3H), 3.93 (s, 3H), 3.92 (s, 3H), and 1.33 (t, $J = 7.1$ Hz, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 167.7, 167.4, 166.7, 165.8, 138.8 (d, $J = 5.7$ Hz), 136.0 (d, $J = 2.4$ Hz), 132.5, 132.1 (d, $J = 3.3$ Hz), 131.5 (d, $J = 11.7$ Hz), 131.2 (d, $J = 3.0$ Hz), 130.6 (d, $J = 13.7$ Hz), 127.5 (d, $J = 15.0$ Hz), 127.0 (d, $J = 190.9$ Hz, $\text{C}_{\text{aryl}}\text{-P}$), 126.2, 62.8 (d, $J = 6.1$ Hz), 53.5, 53.4, 53.1, 52.9, and 16.3 (d, $J = 6.7$ Hz). $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 16.6. IR (neat): 2984, 2954, 2902, 1735, 1439, 1392, 1375, 1355, 1338, 1236, 1167, 1094, 1083, 1051, 1021, 973, 824, 796, and 762 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{Na}^+]$ calcd for $\text{C}_{22}\text{H}_{25}\text{NaO}_{11}\text{P}^+$ requires 519.1027; found 519.1032.

Diethyl (2-(tert-Butyl)-3-phenyl-2,3-dihydrobenzo[d]isoxazol-4-yl)phosphonate (12f).

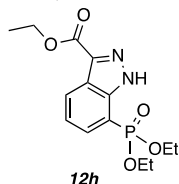


Cesium fluoride (470 mg, 3.1 mmol) was added to an oven-dried screw cap vial containing a mixture of aryl phosphonate **10a** (387 mg, 0.892 mmol), nitron **29** (260 mg, 1.5 mmol), and acetonitrile (9.0 mL). Argon was blown over the headspace of the mixture; the vial was sealed with a Teflon-lined cap, and the reaction mixture was heated at 100 °C in a sand bath. After 24 h, the mixture was cooled to rt and diluted in ethyl acetate and water. The phases were separated, and the aqueous mixture was extracted twice more with ethyl acetate. The organic phases were combined, washed with brine, dried (MgSO_4), and concentrated. Inspection of the crude ^1H NMR did not reveal evidence for the presence of regioisomer **12g**. Purification by gradient flash chromatography (SiO_2 , CH_2Cl_2 :Acetone 39:1 to 29:1) gave dihydrobenzo[d]isoxazole **12f** (194 mg, 0.498 mmol, 56%) as a clear, colorless oil. These chromatography solvents were required as the product partially coelutes with excess nitron **29**. ^1H NMR analysis of the impure chromatography fractions suggests that an additional ~7% yield of product (ca. 25 mg leading to ~220 mg total) could be obtained with subsequent purifications. ^1H NMR (300 MHz, CDCl_3): δ 7.07–7.37 (m, 8H), 5.98 (s, 1H), 3.87–4.02 (m, 1H), 3.42–3.80 (m, 3H), 1.17 (s, 9H), 1.11 (t, $J = 7.1$ Hz, 3H), and 1.02 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 158.4 (d, $J = 19.8$ Hz),

143.2, 132.7 (d, $J = 11.6$ Hz), 129.1 (d, $J = 15.1$ Hz), 128.4, 128.2, 127.3, 125.2 (d, $J = 9.0$ Hz), 123.9 (d, $J = 188.8$ Hz, $C_{\text{aryl}}\text{-P}$), 111.0 (d, $J = 2.7$ Hz), 66.4 (d, $J = 2.2$ Hz), 61.8 (d, $J = 4.7$ Hz), 61.7, 61.6 (d, $J = 5.0$ Hz), 25.5, 16.18, and 16.08. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 16.6. IR (neat): 2978, 2937, 2907, 1577, 1497, 1478, 1437, 1392, 1366, 1256, 1206, 1172, 1098, 1053, 1025, 971, 874, 781, 721, and 697 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{H}^+]$ calcd for $\text{C}_{21}\text{H}_{29}\text{NO}_4\text{P}^+$ requires 390.1829; found 390.1816. The proposed structure of **12f** was supported by an observed HMBC correlation between the methine C–H and $C_{\text{aryl}}\text{-P}$ (cf. structure below). Furthermore, 2D NOESY and numerous 1D NOE experiments (DPFGSE) failed to provide evidence for NOE correlation between the methine C–H and the $C_{\text{aryl}}\text{-H}$ *para* to phosphorus. Rather, the methine C–H only demonstrated NOE correlation with the *tert*-butyl C–H and *ortho* $C_{\text{phenyl}}\text{-H}$ atoms.



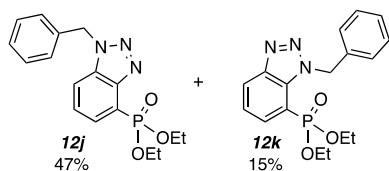
Ethyl 7-(Diethoxyphosphoryl)-1H-indazole-3-carboxylate (**12h**).



12h

Cesium fluoride (400 mg, 2.6 mmol) was added to an oven-dried screw cap vial containing a mixture of aryl phosphonate **10a** (304 mg, 0.700 mmol), ethyl diazoacetate (370 μL , 3.5 mmol), and acetonitrile (14 mL). Argon was blown over the headspace of the mixture; the vial was sealed with a Teflon-lined cap, and the reaction mixture was stirred at room temperature. After 18 h, the mixture was diluted in ethyl acetate and washed with brine. The organic phase was dried (MgSO_4) and concentrated. Purification by gradient flash chromatography (SiO_2 , hexanes:EtOAc 7:3 to 1:2) gave indazole phosphonate **12h** (153 mg, 0.469 mmol, 67%) as a pale yellow solid. The ^1H NMR spectrum of the crude (i.e., prior to flash chromatography) mixture suggested a single indazole isomer of product formed. The proposed structure was supported by the absence of observed NOE correlation between NH and $C_{\text{aryl}}\text{-H}$, which would be present in the case of indazole isomer **12i**. ^1H NMR (300 MHz, CDCl_3): δ 11.76 (br s, 1H), 8.48 (d, $J = 8.1$ Hz, 1H), 7.75 (ddd, $J = 0.79, 7.1, 14.7$ Hz, 1H), 7.39–7.48 (m, 1H), 4.54 (q, $J = 7.2$ Hz, 2H), 4.01–4.30 (m, 4H), 1.50 (t, $J = 7.1$ Hz, 3H), and 1.33 (t, $J = 7.0$ Hz, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 162.6, 141.9 (d, $J = 8.0$ Hz), 137.2, 131.4 (d, $J = 6.8$ Hz), 127.2 (d, $J = 3.3$ Hz), 123.0 (d, $J = 13.7$ Hz), 122.9 (ap s), 110.2 (d, $J = 191.4$ Hz, $C_{\text{aryl}}\text{-P}$), 62.9 (d, $J = 5.4$ Hz), 61.4, 16.4 (d, $J = 6.8$ Hz), and 14.5. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 17.0. IR (neat): 3179, 2984, 2935, 2907, 1735, 1713, 1457, 1387, 1329, 1245, 1219, 1157, 1135, 1083, 1049, 1019, 969, and 749 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{H}^+]$ calcd for $\text{C}_{14}\text{H}_{20}\text{N}_2\text{O}_5\text{P}^+$ requires 327.1104; found 327.1104. mp: 74–76 $^\circ\text{C}$.

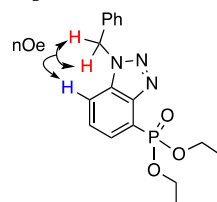
Diethyl (1-Benzyl-1H-benzo[d][1,2,3]triazol-4-yl)phosphonate (**12j**) and Diethyl (1-Benzyl-1H-benzo[d][1,2,3]triazol-7-yl)phosphonate (**12k**).



Cesium fluoride (406 mg, 2.7 mmol) was added to an oven-dried screw cap vial containing a mixture of aryl phosphonate **10a** (387 mg, 0.89 mmol), benzyl azide (346 mg, 2.1 mmol via 0.74 mL of a 3.6 M

solution in CH_2Cl_2), and acetonitrile (8.9 mL). Argon was blown over the headspace of the mixture; the vial was sealed with a Teflon-lined cap, and the reaction mixture was heated at 75 $^\circ\text{C}$ in a sand bath. After 15 h, the mixture was cooled to rt and diluted in ethyl acetate and water. The phases were separated, and the aqueous mixture was extracted twice more with ethyl acetate. The organic phases were combined, washed with brine, dried (MgSO_4), and concentrated. ^1H NMR analysis of the crude reaction mixture indicated that the ratio of isomers **12k** and **12j** was 1.0 to 3.1. Purification by gradient flash chromatography (SiO_2 , hexanes:EtOAc 1:1 to 1:2 to 0:1) gave faster-eluting triazole **12k** (44 mg, 0.13 mmol, 15%) as a clear, colorless oil and slower-eluting triazole **12j** (145 mg, 0.42 mmol, 47%) as a clear, colorless oil.

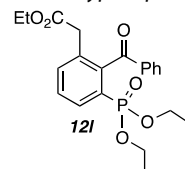
Structural assignment for both isomers was determined from 1D NOE analysis of the ^1H NMR spectrum of both isomers. Specifically, the benzylic position of both isomers (δ 6.39 ppm for **12k** and δ 5.89 ppm for **12j**) was irradiated. In the case of **12j**, enhancement was observed for the resonance corresponding to H_{aryl} *para* to the phosphonyl group (multiplet at δ 7.54–7.60 ppm).



Analytical data for **12j** (slower-eluting major isomer): ^1H NMR (300 MHz, CDCl_3): δ 7.96 (ddd, $J = 1, 6.9, 15.2$ Hz, 1H), 7.54–7.60 (m, 1H), 7.47 (ddd, $J = 2.8, 7.0, 8.4$ Hz, 1H), 7.28–7.40 (m, 5H), 5.89 (s, 2H), 4.19–4.42 (m, 4H), and 1.37 (t, $J = 7.1$ Hz, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 145.6 (d, $J = 8.1$ Hz), 134.3, 132.9 (d, $J = 12.7$ Hz), 130.5 (d, $J = 8.0$ Hz), 129.2, 128.8, 127.8, 126.8 (d, $J = 14.6$ Hz), 120.5 (d, $J = 190.9$ Hz, $C_{\text{aryl}}\text{-P}$), 114.8 (d, $J = 3.3$ Hz), 63.0 (d, $J = 5.6$ Hz), 52.6, and 16.5 (d, $J = 6.8$ Hz). $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 14.7. IR (neat): 3066, 3034, 2984, 2935, 2906, 2872, 1601, 1497, 1457, 1418, 1392, 1368, 1295, 1251, 1217, 1163, 1098, 1053, 1025, 984, 971, 859, 792, 762, 729, and 699 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{H}^+]$ calcd for $\text{C}_{17}\text{H}_{21}\text{N}_3\text{O}_3\text{P}^+$ requires 346.1315; found 346.1316.

Analytical data for **12k** (faster-eluting minor isomer): ^1H NMR (300 MHz, CDCl_3): δ 8.34 (ap d, $J = 8.2$ Hz, 1H), 8.10 (dd, $J = 7.1, 15.4$ Hz, 1H), 7.47 (ddd, $J = 2.9, 7.8, 7.8$ Hz, 1H), 7.22–7.32 (m, 3H), 7.04 (br d, $J = 6.7$ Hz, 2H), 6.39 (s, 2H), 3.84–4.13 (m, 4H), and 1.13 (t, $J = 7.0$ Hz, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 146.9 (d, $J = 8.5$ Hz), 137.0, 135.1 (d, $J = 7.8$ Hz), 128.6, 127.7, 126.6, 125.5 (d, $J = 3.4$ Hz), 123.3 (d, $J = 13.9$ Hz), 111.6 (d, $J = 193.4$ Hz, $C_{\text{aryl}}\text{-P}$), 63.0 (d, $J = 5.7$ Hz), 52.8, and 16.2 (d, $J = 6.1$ Hz). One resonance was not observed. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 15.1. IR (neat): 3064, 3034, 2979, 2906, 1457, 1418, 1389, 1251, 1163, 1096, 1046, 1019, 990, 971, 952, 861, 796, 753, 727, 695, and 665 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{Na}^+]$ calcd for $\text{C}_{17}\text{H}_{20}\text{N}_3\text{NaO}_3\text{P}^+$ requires 368.1134; found 368.1157.

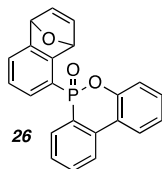
Ethyl 2-(2-Benzoyl-3-(diethoxyphosphoryl)phenyl)acetate (**12l**).



Cesium fluoride (300 mg, 2.0 mmol) was added to an oven-dried screw cap vial containing a mixture of aryl phosphonate **10a** (310 mg, 0.714 mmol), ethyl benzoylacetate (150 μL , 0.87 mmol), and acetonitrile (13 mL). Argon was blown over the headspace of the mixture; the vial was sealed with a Teflon-lined cap, and the reaction mixture was heated at 80 $^\circ\text{C}$ in a sand bath. After 17 h, the mixture was cooled to rt and diluted in ethyl acetate and water. The phases were separated, and the aqueous mixture was extracted twice more with ethyl acetate. The organic phases were combined, washed with

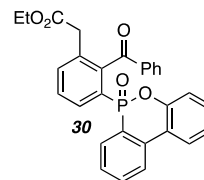
brine, dried (MgSO_4), and concentrated. Purification by gradient flash chromatography (SiO_2 , hexanes:EtOAc 6:1 to 7:3 to 0:1) gave 197 mg of an inseparable mixture of **12l**, the C2/C3 regioisomer, and an isomer resulting from C2 incorporation of hydrogen instead of benzoyl with mole fractions of 0.76, 0.14, and 0.10, respectively. From the relative mole fractions we could assume a 76% purity by mass of **12l** (150 mg, 0.37 mmol, 50%). Subsequent purification by gradient flash chromatography (SiO_2 , hexanes:EtOAc 7:3 to 1:1 to 1:2) enabled partial resolution of **12l**, providing a sample with sufficient purity to confirm structure assignment of **12l**, which was a clear, colorless oil. The proposed structure of **12l** was supported by 1D NOE ^1H NMR experiments (DPFGSE), which showed a correlation between the methylene alpha to the ester and the $\text{C}_{\text{aryl}}\text{-H}$ *para* to phosphorus. ^1H NMR (300 MHz, CDCl_3): δ 7.96 (ddd, $J = 1.7, 7.1, 13.8$ Hz, 1H), 7.70–7.86 (m, 2H), 7.50–7.64 (m, 3H), 7.34–7.50 (m, 2H), 3.69–4.18 (m, 6H), 3.48 (s, 2H), 1.06 (t, $J = 7.1$ Hz, 3H), and 0.80–1.30 (m, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 197.3 (d, $J = 3.6$ Hz), 170.4, 143.1 (d, $J = 11.4$ Hz), 137.5, 135.1 (d, $J = 2.5$ Hz), 133.6, 132.6 (d, $J = 8.9$ Hz), 131.9 (d, $J = 15.0$ Hz), 130.7 (d, $J = 193.1$ Hz, $\text{C}_{\text{aryl}}\text{-P}$), 130.0 (br), 128.9 (d, $J = 15.0$ Hz), 128.4, 62.3 (d, $J = 4.6$ Hz), 61.1, 38.4, 16.0 (br), and 14.0. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 16.5. IR (neat): 3062, 2984, 2935, 2907, 2872, 1735, 1674, 1597, 1582, 1450, 1370, 1330, 1316, 1252, 1198, 1165, 1098, 1051, 1025, 971, 926, 794, 775, 710, and 673 cm^{-1} . HRMS (ESI) m/z : $[\text{M} + \text{Na}^+]$ calcd for $\text{C}_{21}\text{H}_{25}\text{NaO}_6\text{P}^+$ requires 427.1281; found 427.1280.

6-(1,4-Dihydro-1,4-epoxynaphthalen-5-yl)dibenzo[*c,e*][1,2]-oxaphosphinine 6-oxide (26).



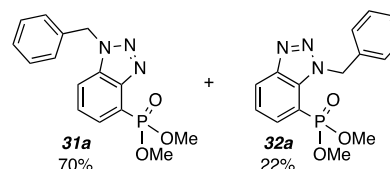
Cesium fluoride (235 mg, 1.4 mmol) was added to an oven-dried screw cap vial containing a mixture of aryl phosphonate **10p** (235 mg, 0.46 mmol), furan (170 μL , 2.3 mmol), and acetonitrile (5.0 mL). Argon was blown over the headspace of the mixture; the vial was sealed with a Teflon-lined cap, and the reaction mixture was heated at 75 $^\circ\text{C}$ in a sand bath. After 24 h, the mixture was cooled to rt, diluted in ethyl acetate, sequentially washed with water and brine, dried (MgSO_4), and concentrated. Purification by gradient flash chromatography (SiO_2 , hexanes:EtOAc 7:3 to 1:1) gave an inseparable 1:1 mixture of racemic diastereomers (i.e., four stereoisomers total) of aryl phosphonate **26** (106 mg, 0.30 mmol, 65%) as a white solid. ^1H NMR (300 MHz, CDCl_3): δ 7.97–8.11 (m, 4H), 7.64–7.73 (m, 2H), 7.21–7.64 (m, 14H), 7.00–7.11 (m, 3H), 6.93–6.99 (m, 2H), 6.57 (d, $J = 1.7, 5.5$ Hz, 1H), 5.99 (br s, 1H), 5.78 (br s, 1H), 5.73 (s, 1H), and 5.72 (s, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 155.8, 155.6, 155.3, 155.2, 150.25, 150.21, 150.11, 150.06, 149.0, 148.91, 148.86, 148.75, 143.6, 143.4, 142.73, 142.64, 135.6, 135.5, 135.42, 135.35, 135.1, 133.38, 133.36, 133.24, 133.22, 131.2, 131.10, 131.05, 130.9, 130.7, 129.9, 128.7, 128.5, 128.4, 128.3, 128.1, 127.9, 127.80, 127.75, 127.69, 127.5, 126.3, 125.8, 125.35, 125.30, 125.20, 125.16, 124.9, 124.8, 124.6, 124.26, 124.24, 124.20, 124.14, 123.88, 123.84, 123.76, 123.71, 123.5, 123.3, 122.0, 121.9, 121.8, 121.6, 121.5, 121.4, 120.9, 120.8, 120.7, 120.6, 82.23, 82.21, 82.04, 82.00, 81.9, and 81.8. Because the sample is a mixture of diastereomers with complex J_{CP} coupling and overlapping multiplets, the chemical shift of each peak is provided without further interpretation. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 23.3 and 22.0. IR (neat): 3068, 3021, 2958, 2932, 2868, 2240, 1595, 1582, 1560, 1478, 1448, 1431, 1405, 1347, 1279, 1236, 1204, 1157, 1118, 1083, 1044, 1008, 919, 876, 855, 814, 777, 757, 729, 718, and 688 cm^{-1} . HRMS (ESI) m/z : $[\text{M} + \text{H}^+]$ calcd for $\text{C}_{22}\text{H}_{16}\text{O}_3\text{P}^+$ requires 359.0832; found 359.0829. mp: 57–60 $^\circ\text{C}$.

Ethyl 2-(2-Benzoyl-3-(6-oxidodibenzo[*c,e*][1,2]oxaphosphinin-6-yl)phenyl)acetate (30).



Cesium fluoride (120 mg, 0.79 mmol) was added to an oven-dried screw cap vial containing a mixture of aryl phosphonate **10p** (145 mg, 0.282 mmol), ethyl benzoylacetate (60 μL , 0.35 mmol), and acetonitrile (3.0 mL). Argon was blown over the headspace of the mixture; the vial was sealed with a Teflon-lined cap, and the reaction mixture was heated at 75 $^\circ\text{C}$ in a sand bath. After 8 h, the mixture was cooled to rt and diluted in ethyl acetate and water. The phases were separated, and the aqueous mixture was extracted twice more with ethyl acetate. The organic phases were combined, washed with brine, dried (MgSO_4), and concentrated. Purification by gradient flash chromatography (SiO_2 , hexanes:EtOAc 7:3 to 1:1) gave aryl phosphonate **30** (52 mg, 0.11 mmol, 39%) as a clear, colorless oil. Structural assignment for **30** was made based on comparison with diethyl ester variant **12l**. ^1H NMR (300 MHz, CDCl_3 , 20 $^\circ\text{C}$): δ 7.06–8.33 (br m, 16H), 3.89 (br q, $J = 7.03$ Hz, 2H), 3.44 (br s, 2H), and 1.03 (t, $J = 7.11$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 197.0, 170.3, 148.7, 143.8, 136.8, 135.89, 135.86, 135.04, 134.97, 133.6, 133.3, 133.0, 132.5, 132.3, 132.1, 131.5, 131.3, 130.7, 130.2 (br), 129.7 (br), 129.2, 129.0, 128.7, 128.4, 128.24, 128.16, 127.5, 127.2, 125.6, 125.1, 124.6, 124.5, 123.9, 123.3, 123.2, 121.3, 121.1, 120.4 (br), 61.1, 38.3, and 14.0. Because of complex J_{CP} coupling, overlapping multiplets, and peak broadening from hindered rotation, the chemical shift of each peak is provided without further interpretation. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 21.2. IR (neat): 3064, 2984, 2935, 1735, 1672, 1597, 1478, 1448, 1433, 1370, 1331, 1316, 1273, 1243, 1206, 1159, 1120, 1027, 924, 759, 706, and 671 cm^{-1} . HRMS (ESI) m/z : $[\text{M} + \text{Na}^+]$ calcd for $\text{C}_{29}\text{H}_{23}\text{NaO}_5\text{P}^+$ requires 505.1175; found 505.1170.

Dimethyl (1-Benzyl-1H-benzod[1,2,3]triazol-4-yl)phosphonate (31a) and Dimethyl (1-Benzyl-1H-benzod[1,2,3]triazol-7-yl)phosphonate (32a).



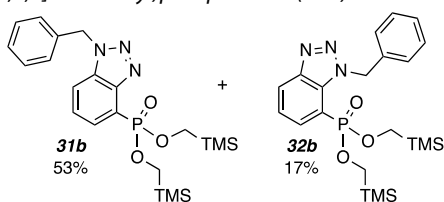
Cesium fluoride (151 mg, 1.0 mmol) was added to an oven-dried screw cap vial containing a mixture of aryl phosphonate **10j** (135 mg, 0.33 mmol), benzyl azide (130 mg, 1.0 mmol via 0.28 mL of a 3.6 M solution in CH_2Cl_2), and acetonitrile (3.3 mL). Argon was blown over the headspace of the mixture; the vial was sealed with a Teflon-lined cap, and the reaction mixture was heated at 70 $^\circ\text{C}$ in a sand bath. After 17 h, the mixture was cooled to rt and diluted in ethyl acetate and water. The phases were separated, and the aqueous mixture was extracted twice more with ethyl acetate. The organic phases were combined, washed with brine, dried (MgSO_4), and concentrated. ^1H NMR analysis of the crude reaction mixture indicated that the ratio of isomers **32a** and **31a** was 1.0 to 3.3. Purification by gradient flash chromatography (SiO_2 , hexanes:EtOAc 1:1 to 1:2 to 0:1) gave faster-eluting triazole **32a** (23 mg, 0.073 mmol, 22%) as a clear, colorless oil and slower-eluting triazole **31a** (73 mg, 0.23 mmol, 70%) as a clear, colorless oil. Structural assignment for both isomers was made based on comparison with diethyl ester variants **12j** and **12k**.

Spectral data for **31a** (slower-eluting major isomer). ^1H NMR (300 MHz, CDCl_3): δ 7.97 (ddd, $J = 0.9, 6.9, 15.3$ Hz, 1H), 7.57–7.62 (m, 1H), 7.49 (ddd, $J = 2.9, 7.0, 8.5$ Hz, 1H), 7.27–7.39 (m, 5H), 5.90 (s, 2H), 3.94 (s, 3H), and 3.90 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 145.6 (d, $J = 8.1$ Hz), 134.3, 132.9 (d, $J = 12.8$ Hz), 130.9 (d, $J = 8.1$ Hz), 129.2, 128.8, 127.8, 126.9 (d, $J = 14.9$ Hz), 119.1 (d, J

= 191.6 Hz, $C_{\text{aryl}}-\text{P}$), 114.8 (d, $J = 3.4$ Hz), 53.5 (d, $J = 5.6$ Hz), and 52.7. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 17.9. IR (neat): 3066, 2954, 2851, 1599, 1456, 1258, 1059, and 1032 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{Na}^+]$ calcd for $\text{C}_{15}\text{H}_{16}\text{N}_3\text{NaO}_3\text{P}^+$ requires 340.0821; found 340.0823.

Spectral data for **32a** (faster-eluting minor isomer). ^1H NMR (300 MHz, CDCl_3): δ 8.36 (br d, $J = 8.4$ Hz, 1H), 8.08 (dd, $J = 7.2$, 15.4 Hz, 1H), 7.48 (ddd, $J = 2.6$, 7.4, 8.3 Hz, 1H), 7.22–7.33 (m, 3H), 7.01 (br d, $J = 7.6$ Hz, 2H), 6.35 (s, 2H), 3.57 (s, 3H), and 3.53 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 147.0 (d, $J = 9.4$ Hz), 136.9, 135.4 (d, $J = 7.7$ Hz), 128.6, 127.6, 126.5, 125.8 (d, $J = 2.7$ Hz), 123.3 (d, $J = 17.0$ Hz), 110.2 (d, $J = 194.4$ Hz, $C_{\text{aryl}}-\text{P}$), 53.1 (d, $J = 5.8$ Hz), and 52.7. One resonance was not observed. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 17.8. IR (neat): 2948, 2848, 1578, 1245, 1047, and 1023 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{H}^+]$ calcd for $\text{C}_{15}\text{H}_{17}\text{N}_3\text{O}_3\text{P}^+$ requires 318.1002; found 318.0991.

Bis(trimethylsilyl)methyl (1-Benzyl-1H-benzo[d][1,2,3]triazol-4-yl)phosphonate (31b) and **Bis(trimethylsilyl)methyl (1-Benzyl-1H-benzo[d][1,2,3]triazol-7-yl)phosphonate (32b)**.

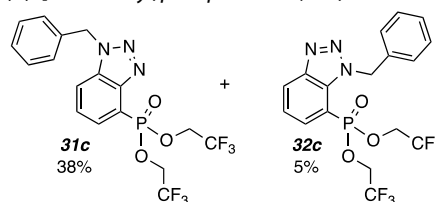


Cesium fluoride (146 mg, 0.96 mmol) was added to an oven-dried screw cap vial containing a mixture of aryl phosphonate **10n** (176 mg, 0.32 mmol), benzyl azide (130 mg, 0.98 mmol via 0.27 mL of a 3.6 M solution in CH_2Cl_2), and acetonitrile (3.2 mL). Argon was blown over the headspace of the mixture; the vial was sealed with a Teflon-lined cap, and the reaction mixture was heated at 70 $^\circ\text{C}$ in a sand bath. After 17 h, the mixture was cooled to rt and diluted in ethyl acetate and water. The phases were separated, and the aqueous mixture was extracted twice more with ethyl acetate. The organic phases were combined, washed with brine, dried (MgSO_4), and concentrated. ^1H NMR analysis of the crude reaction mixture indicated that the ratio of isomers **32b** and **31b** was 1.0 to 3.1. Purification by gradient flash chromatography (SiO_2 , hexanes:EtOAc 7:3 to 1:1) gave faster-eluting triazole **32b** (25 mg, 0.055 mmol, 17%) as a clear, colorless oil and slower-eluting triazole **31b** (76 mg, 0.17 mmol, 53%) as a clear, colorless oil. Structural assignment for both isomers was made based on comparison with diethyl ester variants **12j** and **12k**.

Spectral data for **31b** (slower-eluting major isomer). ^1H NMR (300 MHz, CDCl_3): δ 7.92 (dd, $J = 6.8$, 14.7 Hz, 1H), 7.50–7.57 (m, 1H), 7.46 (ddd, $J = 2.7$, 6.8, 8.8 Hz, 1H), 7.25–7.42 (m, 5H), 5.89 (s, 2H), 3.94 (dd, $J = 6.5$, 13.4 Hz, 2H), 3.83 (dd, $J = 6.1$, 13.4 Hz, 2H), and 0.07 (s, 18H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 145.8 (d, $J = 10.5$ Hz), 134.5, 132.8 (d, $J = 12.8$ Hz), 130.6 (d, $J = 7.2$ Hz), 129.2, 128.7, 127.7, 126.8 (d, $J = 14.0$ Hz), 120.5 (d, $J = 187.3$ Hz, $C_{\text{aryl}}-\text{P}$), 114.1 (d, $J = 3.3$ Hz), 60.0 (d, $J = 10.0$ Hz), 52.6, and –3.2. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 18.7. IR (neat): 2958, 2902, 1416, 1370, 1288, 1249, 1215, 1144, 1094, 1016, and 854 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{Na}^+]$ calcd for $\text{C}_{21}\text{H}_{32}\text{N}_3\text{NaO}_3\text{PSi}_2^+$ requires 484.1612; found 484.1616.

Spectral data for **32b** (faster-eluting minor isomer). ^1H NMR (300 MHz, CDCl_3): δ 8.33 (ddd, $J = 1.2$, 2.0, 8.3 Hz, 1H), 7.99 (ddd, $J = 1.1$, 7.2, 14.8 Hz, 1H), 7.46 (ddd, $J = 2.5$, 7.2, 8.4 Hz, 1H), 7.23–7.32 (m, 3H), 7.11–7.16 (m, 2H), 6.40 (s, 2H), 3.67 (dd, $J = 7.3$, 13.5 Hz, 2H), 3.48 (dd, $J = 6.2$, 13.5 Hz, 2H), and 0.02 (s, 18H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 146.8 (d, $J = 9.4$ Hz), 136.8, 135.0 (d, $J = 6.7$ Hz), 133.1 (d, $J = 7.0$ Hz), 128.7, 127.8, 127.2, 125.3 (d, $J = 3.1$ Hz), 123.2 (d, $J = 13.7$ Hz), 111.1 (d, $J = 190.0$ Hz, $C_{\text{aryl}}-\text{P}$), 60.3 (d, $J = 9.3$ Hz), 53.0, and –3.3. $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 18.8. IR (neat): 2954, 2894, 1416, 1249, 1033, 1008, and 854 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{H}^+]$ calcd for $\text{C}_{21}\text{H}_{33}\text{N}_3\text{O}_3\text{PSi}_2^+$ requires 462.1793; found 462.1802.

Bis(2,2,2-trifluoroethyl) (1-Benzyl-1H-benzo[d][1,2,3]triazol-4-yl)phosphonate (31c) and **Bis(2,2,2-trifluoroethyl) (1-Benzyl-1H-benzo[d][1,2,3]triazol-7-yl)phosphonate (32c)**.



Cesium fluoride (360 mg, 2.4 mmol) was added to an oven-dried screw cap vial containing a mixture of aryl phosphonate **10o** (429 mg, 0.79 mmol), benzyl azide (320 mg, 2.4 mmol via 0.66 mL of a 3.6 M solution in CH_2Cl_2), and acetonitrile (7.9 mL). Argon was blown over the headspace of the mixture; the vial was sealed with a Teflon-lined cap, and the reaction mixture was heated at 70 $^\circ\text{C}$ in a sand bath. After 17 h, the mixture was cooled to rt and diluted in ethyl acetate and water. The phases were separated, and the aqueous mixture was extracted twice more with ethyl acetate. The organic phases were combined, washed with brine, dried (MgSO_4), and concentrated. ^1H NMR analysis of the crude reaction mixture indicated that the ratio of isomers **32c** and **31c** was 1.0 to 7.9, respectively. Purification by gradient flash chromatography (SiO_2 , hexanes:EtOAc 4:1 to 1:1) gave faster-eluting triazole **32c** (17 mg, 0.037 mmol, 5%) as a clear, colorless oil and slower-eluting triazole **31c** (134 mg, 0.30 mmol, 38%) as a clear, colorless oil. Structural assignment for both isomers was made based on comparison with diethyl ester variants **12j** and **12k**.

Spectral data for **31c** (slower-eluting major isomer). ^1H NMR (300 MHz, CDCl_3): δ 7.88 (dd, $J = 7.0$, 16.0 Hz, 1H), 7.63 (dd, $J = 2.7$, 8.3 Hz, 1H), 7.51 (ddd, $J = 3.4$, 6.9, 8.6 Hz, 1H), 7.23–7.40 (m, 5H), 5.90 (s, 2H), and 4.64–4.85 (m, 4H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 145.5 (d, $J = 9.3$ Hz), 134.1, 133.0 (d, $J = 14.0$ Hz), 129.8 (d, $J = 8.0$ Hz), 129.3, 129.0, 127.8, 127.0 (d, $J = 16.0$ Hz), 122.7 (dq, $J = 9.0$, 277.6 Hz, CF_3), 117.6 (d, $J = 201.1$ Hz, $C_{\text{aryl}}-\text{P}$), 115.7 (d, $J = 3.5$ Hz), 63.0 (dq, $J = 4.7$, 38.0), and 52.9. $^{19}\text{F}\{^{13}\text{C}\}$ NMR (282 MHz, CDCl_3): δ –76.4 (t, $J = 8.1$ Hz). $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 16.7. IR (neat): 3066, 3030, 2973, 1601, 1584, 1497, 1457, 1420, 1293, 1262, 1219, 1174, 1100, 1070, 982, 964, 867, 844, 796, 760, 729, 699, and 662 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{Na}^+]$ calcd for $\text{C}_{17}\text{H}_{14}\text{F}_6\text{N}_3\text{NaO}_3\text{P}^+$ requires 476.0569; found 476.0569.

Spectral data for **32c** (faster-eluting minor isomer). ^1H NMR (300 MHz, CDCl_3): δ 8.46 (ddd, $J = 1.1$, 2.0, 8.3 Hz, 1H), 8.09 (ddd, $J = 1.1$, 7.3, 16.2 Hz, 1H), 7.54 (ddd, $J = 3.0$, 7.3, 8.3 Hz, 1H), 7.27–7.35 (m, 3H), 7.00 (m, 2H), 6.38 (s, 2H), 4.20–4.36 (m, 2H), and 3.88–4.06 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 136.3, 135.3 (d, $J = 7.9$ Hz), 128.9, 128.0, 127.3 (d, $J = 3.4$ Hz), 126.4, 123.5 (d, $J = 15.0$ Hz), 108.9 (d, $J = 186.6$ Hz, $C_{\text{aryl}}-\text{P}$), 62.6 (dq, $J = 5.3$, 38.7 Hz), and 53.1. Because of the low amount of material that was formed, three resonances were not observed. $^{19}\text{F}\{^{13}\text{C}\}$ NMR (282 MHz, CDCl_3): δ –76.3 (t, $J = 7.9$ Hz). $^{31}\text{P}\{^1\text{H}\}$ NMR (121 MHz, CDCl_3): δ 17.9. IR (neat): 3077, 3034, 1603, 1580, 1420, 1295, 1258, 1172, 1094, 1062, 962, 865, and 801 cm^{-1} . HRMS (ESI) m/z : $[\text{M}+\text{H}^+]$ calcd for $\text{C}_{17}\text{H}_{15}\text{F}_6\text{N}_3\text{O}_3\text{P}^+$ requires 454.0750; found 454.0747.

Computational Methods. All computed structures were optimized using Gaussian16.³⁵ Specific functionals, basis sets, and solvation models are provided in the corresponding figure captions for each data set. Tight convergence criteria were used for geometry optimizations. Vibrational frequency calculations were used to confirm minima or transition state computations, where minima had no imaginary frequencies and transition states had one imaginary frequency. Vibrational frequency calculations also provided the thermochemical information (i.e., Free Energy values) used to determine relative free energies.

■ ASSOCIATED CONTENT

■ Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.joc.1c01382>.

Expanded experimental details; expanded computational details; raw computational data used to construct the plots shown Figures 3, 5, and 6; coordinates of all optimized geometries; raw NMR data used to construct the plot shown in Figure 7; and copies of NMR spectral data (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Patrick H. Willoughby – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States;
orcid.org/0000-0001-5163-0502; Email: willoughby@ripn.edu

Authors

Brianna M. Bembeneck – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Maya M. S. Petersen – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Julia A. Lilly – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Amber L. Haugen – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Naomi J. Jiter – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Andrew J. Johnson – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Ethan E. Ripp – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Shelby A. Winchell – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Alisha N. Harvat – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Caitlin McNulty – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Sierra A. Thein – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Abigail M. Grieger – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Brandon J. Lyle – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Gabriella L. Mraz – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Abigail M. Stitgen – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Samuel Foss – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Merranda L. Schmid – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States
Joseph D. Scanlon – Chemistry Department, Ripon College, Ripon, Wisconsin 54971, United States

Complete contact information is available at:
<https://pubs.acs.org/doi/10.1021/acs.joc.1c01382>

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Acknowledgement is made to the Donors of the American Chemical Society Petroleum Research Fund for support of this research. Additional funding was provided by the Ripon College Knop and Oyster Funds. The NSF Major Research Instrumentation Grant Program supported acquisition of both high-resolution mass spectrometry instrumentation (CHE-1429616) as well as the computational chemistry resources from the Midwest Computational Chemistry Consortium (MU3C, CHE-1039925). The authors are grateful to Jonathan M. Ellis and Andrew R. Buller at the University of Wisconsin—Madison for helpful conversations during the later stages of these studies.

■ REFERENCES

- (1) (a) Quin, L. D. *A Guide to Organophosphorus Chemistry*; Wiley-Interscience: New York, 2000. (b) Savignac, P.; Iorga, B. *Modern Phosphonate Chemistry*; CRC Press: New York, 2003. (c) Svava, J.; Weferling, N.; Hofmann, T. Phosphorus Compounds, Organic. In *Ullmann's Encyclopedia of Industrial Chemistry*; Wiley-VCH: Weinheim, 2006. (d) Iaroshenko, V. *Organophosphorus Chemistry: From Molecules to Applications*; Wiley-VCH: Weinheim, 2019.
- (2) For representative examples, see: (a) Yoshino, K.; Kohno, T.; Morita, T.; Tsukamoto, G. *Organic Phosphorus Compounds. 2. Synthesis and Coronary Vasodilator Activity of (Benzothiazolylbenzyl)Phosphonate Derivatives*. *J. Med. Chem.* **1989**, *32*, 1528–1532. (b) Veale, C. A.; Damewood, J. R.; Steelman, G. B.; Bryant, C.; Gomes, B.; Williams, J. Non-Peptidic Inhibitors of Human Leukocyte Elastase. 4. Design, Synthesis, and *in Vitro* and *in Vivo* Activity of a Series of β -Carbolinone-Containing Trifluoromethyl Ketones. *J. Med. Chem.* **1995**, *38*, 86–97. (c) Heidebrecht, R. W.; Chenard, M.; Close, J.; Dahlberg, W. K.; Fleming, J.; Grimm, J. B.; Hamill, J. E.; Harsch, A.; Haines, B. B.; Hughes, B.; Kral, A. M.; Middleton, R. E.; Mushti, C.; Ozerova, N.; Szwczak, A. A.; Wang, H.; Wilson, K.; Witter, D. J.; Secrist, J. P.; Miller, T. A. Exploring the Pharmacokinetic Properties of Phosphorus-Containing Selective HDAC 1 and 2 Inhibitors (SHI-1:2). *Bioorg. Med. Chem. Lett.* **2009**, *19*, 2053–2058. (d) Dang, Q.; Brown, B. S.; Liu, Y.; Rydzewski, R. M.; Robinson, E. D.; Van Poelje, P. D.; Reddy, M. R.; Erion, M. D. Fructose-1,6-Bisphosphatase Inhibitors. 1. Purine Phosphonic Acids as Novel AMP Mimics. *J. Med. Chem.* **2009**, *52*, 2880–2898. (e) Lassaux, P.; Hamel, M.; Gulea, M.; Delbrück, H.; Mercuri, P. S.; Horsfall, L.; Dehareng, D.; Kupper, M.; Frère, J. M.; Hoffmann, K.; Galleni, M.; Bebrone, C. Mercapto-phosphonate Compounds as Broad-Spectrum Inhibitors of the Metallo- β -Lactamases. *J. Med. Chem.* **2010**, *53*, 4862–4876. (f) McGrath, J. W.; Chin, J. P.; Quinn, J. P. Organophosphonates Revealed: New Insights into the Microbial Metabolism of Ancient Molecules. *Nat. Rev. Microbiol.* **2013**, *11*, 412–419. (g) Nandre, K. P.; Bhosale, S. V.; Bhosale, R. S.; Pombala, S.; Kumar, C. G.; Latham, K.; Bhosale, S. V. Organogelation and Cytotoxic Evolution of Phosphonate Ester Functionalised Hydrophobic Alkanediamide Motifs. *Supramol. Chem.* **2014**, *26*, 873–881. (h) Németh, G.; Greff, Z.; Sipos, A.; Varga, Z.; Székely, R.; Sebestyén, M.; Jászay, Z.; Béni, S.; Nemes, Z.; Pirat, J. L.; Volle, J. N.; Virieux, D.; Gyuris, A.; Kelemenics, K.; Ay, E.; Minarovits, J.; Szathmary, S.; Kéri, G.; Orfi, L. Synthesis and Evaluation of Phosphorus Containing, Specific CDK9/CycT1 Inhibitors. *J. Med. Chem.* **2014**, *57*, 3939–3965. (i) Kim, T. W.; Yong, Y.; Shin, S. Y.; Jung, H.; Park, K. H.; Lee, Y. H.; Lim, Y.; Jung, K. Y. Synthesis and Biological Evaluation of Phenyl-1H-1,2,3-Triazole Derivatives as Anti-Inflammatory Agents. *Bioorg. Chem.* **2015**, *59*, 1–11.
- (3) For representative examples, see: (a) Kendall, A. J.; Salazar, C. A.; Martino, P. F.; Tyler, D. R. Direct Conversion of Phosphonates to Phosphine Oxides: An Improved Synthetic Route to Phosphines Including the First Synthesis of Methyl JohnPhos. *Organometallics* **2014**, *33*, 6171–6178. (b) Xu, G.; Li, M.; Wang, S.; Tang, W.

Efficient Synthesis of P-Chiral Biaryl Phosphonates by Stereoselective Intramolecular Cyclization. *Org. Chem. Front.* **2015**, *2*, 1342–1345. (c) Szabó-Szentjóni, H.; Majoros, I.; Márton, A.; Leveles, I.; Vértessy, B. G.; Dékány, M.; Tóth, T.; Huszthy, P. Synthesis of New Chiral Crown Ethers Containing Phosphine or Secondary Phosphine Oxide Units. *Synthesis* **2020**, *52*, 2870–2882.

(4) Xu, F.; Duke, O. M.; Rojas, D.; Eichelberger, H. M.; Kim, R. S.; Clark, T. B.; Watson, D. A. Arylphosphonate-Directed Ortho C-H Borylation: Rapid Entry into Highly-Substituted Phosphoarenes. *J. Am. Chem. Soc.* **2020**, *142*, 11988–11992.

(5) Chen, L.; Wang, Y.-Z. Aryl Polyphosphonates: Useful Halogen-Free Flame Retardants for Polymers. *Materials* **2010**, *3*, 4746–4760.

(6) Queffelec, C.; Petit, M.; Janvier, P.; Knight, D. A.; Bujoli, B. Surface Modification Using Phosphonic Acids and Esters. *Chem. Rev.* **2012**, *112*, 3777–3807.

(7) (a) Hirao, T.; Masunaga, T.; Ohshiro, Y.; Agawa, T. A Novel Synthesis of Dialkyl Arenephosphonates. *Synthesis* **1981**, *1981*, 56–57. (b) Belabassi, Y.; Alzghari, S.; Montchamp, J. L. Revisiting the Hirao Cross-Coupling: Improved Synthesis of Aryl and Heteroaryl Phosphonates. *J. Organomet. Chem.* **2008**, *693*, 3171–3178. (c) Jablonkai, E.; Keglevich, G. Advances and New Variations of the Hirao Reaction. *Org. Prep. Proced. Int.* **2014**, *46*, 281–316.

(8) Demmer, C. S.; Krogsgaard-Larsen, N.; Bunch, L. Review on Modern Advances of Chemical Methods for the Introduction of a Phosphonic Acid Group. *Chem. Rev.* **2011**, *111*, 7981–8006.

(9) For recent reviews see: (a) Cai, B. G.; Xuan, J.; Xiao, W. J. Visible Light-Mediated C–P Bond Formation Reactions. *Sci. Bull.* **2019**, *64*, 337–350. (b) Ung, S. P. M.; Mechrouk, V. A.; Li, C. J. Shining Light on the Light-Bearing Element: A Brief Review of Photomediated C–H Phosphorylation Reactions. *Synthesis* **2021**, *53*, 1003–1022. (c) Rout, L.; Punniyamurthy, T. Recent Advances in Transition-Metal-Mediated C_{sp^2} -B and C_{sp^2} -P Cross-Coupling Reactions. *Coord. Chem. Rev.* **2021**, *431*, 213675.

(10) (a) Dhokale, R. A.; Mhaske, S. B. P-Arylation: Arynes to Aryl-Phosphonates, -Phosphinates, and -Phosphine Oxides. *Org. Lett.* **2013**, *15*, 2218–2221. (b) Chen, Q.; Yan, X.; Du, Z.; Zhang, K.; Wen, C. P-Arylation of Dialkyl Phosphites and Secondary Phosphine Oxides with Arynes. *J. Org. Chem.* **2016**, *81*, 276–281. (c) Yang, G.; Shen, C.; Quan, M.; Zhang, W. Preparation of Organophosphorus Compounds from P-H Compounds Using *o*-(Trimethylsilyl)Aryl Triflates as Aryne Precursors. *Tetrahedron* **2016**, *72*, 333–337. (d) Chen, J.; Fan, R.; Liu, Z.; Tan, J. Reactions of Organophosphorus Compounds with Arynes: Reactivity and Mechanism. *Adv. Synth. Catal.* **2021**, *363*, 657–667. (e) Huang, Y.; Hu, Y.; Han, Y.; Ou, Y.; Huo, Y.; Li, X.; Chen, Q. Direct Synthesis of *ortho*-Halogenated Arylphosphonates via a Three-Component Reaction Involving Arynes. *J. Org. Chem.* **2021**, *86*, 7010–7018. (f) Yoshida, S.; Hosoya, T. Synthesis of Diverse Aromatic Oxophosphorus Compounds by the Michaelis-Arbuzov-Type Reaction of Arynes. *Chem. Lett.* **2013**, *42*, 583–585.

(11) (a) Wenk, H. H.; Winkler, M.; Sander, W. One Century of Aryne Chemistry. *Angew. Chem., Int. Ed.* **2003**, *42*, 502–528. (b) Gampe, C. M.; Carreira, E. M. Arynes and Cyclohexyne in Natural Product Synthesis. *Angew. Chem., Int. Ed.* **2012**, *51*, 3766–3778. (c) Tadross, P. M.; Stoltz, B. M. A Comprehensive History of Arynes in Natural Product Total Synthesis. *Chem. Rev.* **2012**, *112*, 3550–3577. (d) Takikawa, H.; Nishii, A.; Sakai, T.; Suzuki, K. Aryne-Based Strategy in the Total Synthesis of Naturally Occurring Polycyclic Compounds. *Chem. Soc. Rev.* **2018**, *47*, 8030–8056. (e) Fluegel, L. L.; Hoye, T. R. Hexadehydro-Diels-Alder Reaction: Benzyne Generation via Cycloisomerization of Tethered Triynes. *Chem. Rev.* **2021**, *121*, 2413–2444.

(12) Two recent reviews include: (a) Shi, J.; Li, Y.; Li, Y. Aryne Multifunctionalization with Benzyne and Benztriyne Equivalents. *Chem. Soc. Rev.* **2017**, *46*, 1707–1719. (b) He, J.; Qiu, D.; Li, Y. Strategies toward Aryne Multifunctionalization via 1,2-Benzdiyne and Benzyne. *Acc. Chem. Res.* **2020**, *53*, 508–519.

(13) Yoshida, S.; Nakamura, Y.; Uchida, K.; Hazama, Y.; Hosoya, T. Aryne Relay Chemistry En Route to Aminoarenes: Synthesis of 3-

Aminoaryne Precursors via Regioselective Silylamination of 3-(Triflyloxy)Arynes. *Org. Lett.* **2016**, *18*, 6212–6215.

(14) Himeshima, Y.; Sonoda, T.; Kobayashi, H. Fluoride-Induced 1,2-Elimination of *O*-Trimethylsilylphenyl Triflate to Benzyne Under Mild Conditions. *Chem. Lett.* **1983**, *12*, 1211–1214.

(15) (a) Shi, J.; Xu, H.; Qiu, D.; He, J.; Li, Y. Selective Aryne Formation via Grob Fragmentation from the [2 + 2] Cycloadducts of 3-Triflyloxyarynes. *J. Am. Chem. Soc.* **2017**, *139*, 623–626. (b) Lv, C.; Wan, C.; Liu, S.; Lan, Y.; Li, Y. Aryne Trifunctionalization Enabled by 3-Silylaryne as a 1,2-Benzdiyne Equivalent. *Org. Lett.* **2018**, *20*, 1919–1923.

(16) (a) Uchida, K.; Yoshida, S.; Hosoya, T. Three-Component Coupling of Triflyloxy-Substituted Benzocyclobutenones, Organolithium Reagents, and Arynophiles Promoted by Generation of Aryne via Carbon-Carbon Bond Cleavage. *Org. Lett.* **2017**, *19*, 1184–1187. (b) Nakamura, Y.; Miyata, Y.; Uchida, K.; Yoshida, S.; Hosoya, T. 3-Thioaryne Intermediates for the Synthesis of Diverse Thioarenes. *Org. Lett.* **2019**, *21*, 5252–5258.

(17) (a) Abramov, V. S. O reaktsii al'degidov s fosforistykhn efirov [Reaction of Aldehydes with Phosphite Esters]. *Dokl. Akad. Nauk SSSR* **1954**, *95*, 991–992. (b) Woźniak, L.; Chojnowski, J. Silyl Esters of Phosphorous-Common Intermediates in Synthesis. *Tetrahedron* **1989**, *45*, 2465–2524.

(18) Sekine, M.; Yamamoto, I.; Hashizume, A.; Hata, T. Silyl Phosphites V. the Reactions of Tris(Trimethylsilyl) Phosphite With Carbonyl Compounds. *Chem. Lett.* **1977**, *6*, 485–488.

(19) For recent reports related to the Abramov reaction, see: (a) Guin, J.; Wang, Q.; Van Gemmeren, M.; List, B. The Catalytic Asymmetric Abramov Reaction. *Angew. Chem., Int. Ed.* **2015**, *54*, 355–358. (b) Dussart, J.; Deschamp, J.; Migianu-Griffoni, E.; Lecouvey, M. From Industrial Method to the Use of Silylated P(III) Reagents for the Synthesis of Relevant Phosphonylated Molecules. *Org. Process Res. Dev.* **2020**, *24*, 637–651.

(20) Yoshida, S.; Uchida, K.; Igawa, K.; Tomooka, K.; Hosoya, T. An Efficient Generation Method and Remarkable Reactivities of 3-Triflyloxybenzyne. *Chem. Commun.* **2014**, *50*, 15059–15062.

(21) Debrouwer, W.; Hertsen, D.; Heugebaert, T. S. A.; Boydas, E. B.; Van Speybroeck, V.; Catak, S.; Stevens, C. V. Tandem Addition of Phosphite Nucleophiles Across Unsaturated Nitrogen-Containing Systems: Mechanistic Insights on Regioselectivity. *J. Org. Chem.* **2017**, *82*, 188–201.

(22) Uchida, K.; Yoshida, S.; Hosoya, T. Controlled Generation of 3-Triflyloxyarynes. *Synthesis* **2016**, *48*, 4099–4109.

(23) Hall, C.; Henderson, J. L.; Ernouf, G.; Greaney, M. F. Tandem Thia-Fries Rearrangement – Cyclisation of 2-(Trimethylsilyl)Phenyl Trifluoromethanesulfonate Benzyne Precursors. *Chem. Commun.* **2013**, *49*, 7602–7604.

(24) Yoshioka, E.; Kakigi, K.; Miyoshi, S.; Kawasaki, Y.; Miyabe, H. Aryne Precursors for Selective Generation of 3-Haloarynes: Preparation and Application to Synthetic Reactions. *J. Org. Chem.* **2020**, *85*, 13544–13556.

(25) Ghaffari, B.; Preshlock, S. M.; Plattner, D. L.; Staples, R. J.; Maligres, P. E.; Krska, S. W.; Maleczka, R. E.; Smith, M. R. Silyl Phosphorus and Nitrogen Donor Chelates for Homogeneous Ortho Borylation Catalysis. *J. Am. Chem. Soc.* **2014**, *136*, 14345–14348.

(26) (a) Salmeia, K. A.; Gaan, S. An Overview of Some Recent Advances in DOPO-Derivatives: Chemistry and Flame Retardant Applications. *Polym. Degrad. Stab.* **2015**, *113*, 119–134. (b) Kim, W.; Hoang, D.; Vothi, H.; Nguyen, C.; Giang, T.; An, H.; Kim, J. Synthesis, Flame Retardancy, and Thermal Degradation Behaviors of Novel Organo-Phosphorus Compounds Derived from 9,10-Dihydro-9-oxa-10-phosphaphenanthrene-10-oxide (DOPO). *Macromol. Res.* **2016**, *24*, 66–73. (c) Min, Y.; Li, P.; Yin, X.-G.; Ban, D.-M. Synthesis and Characterization of an Novel Flame Retardant Based on Phosphaphenanthrene for Epoxy Resin. *Polym. Bull.* **2017**, *74*, 1–10.

(27) Several attempts were made to characterize the corresponding diazaphospholidine, which rapidly decomposed ($t_{1/2} = 4$ h) to an unknown product. Despite our several attempts (1 h aryne-Abramov reaction, 1 h workup and flash chromatography), substantial amounts

of decomposition were present in the “purified” product. Future studies will probe the fate of these types of products in hopes of preventing unwanted loss of product.

(28) (a) Li, Y.; Chakrabarty, S.; Mück-Lichtenfeld, C.; Studer, A. *Ortho*-Trialkylstannyl Arylphosphanes by C-P and C-Sn Bond Formation in Arynes. *Angew. Chem., Int. Ed.* **2016**, *55*, 802–806. (b) Mesgar, M.; Nguyen-Le, J.; Daugulis, O. New Hindered Amide Base for Aryne Insertion into Si-P, Si-S, Si-N, and C-C Bonds. *J. Am. Chem. Soc.* **2018**, *140*, 13703–13710.

(29) Medina, J. M.; MacKey, J. L.; Garg, N. K.; Houk, K. N. The Role of Aryne Distortions, Steric Effects, and Charges in Regioselectivities of Aryne Reactions. *J. Am. Chem. Soc.* **2014**, *136*, 15798–15805.

(30) Yoshida, S.; Hazama, Y.; Sumida, Y.; Yano, T.; Hosoya, T. An Alternative Method for Generating Arynes from *ortho*-Silylaryl Triflates: Activation by Cesium Carbonate in the Presence of a Crown Ether. *Molecules* **2015**, *20*, 10131–10140.

(31) For recent examples, see: (a) Pozo, I.; Cobas, A.; Peña, D.; Guitián, E.; Pérez, D. 1,7-Naphthodiyne: A New Platform for the Synthesis of Novel, Sterically Congested PAHs. *Chem. Commun.* **2016**, *52*, 5534–5537. (b) Xu, F.; Hershey, K. W.; Holmes, R. J.; Hoye, T. R. Blue-Emitting Arylalkynyl Naphthalene Derivatives via a Hexadehydro-Diels–Alder Cascade Reaction. *J. Am. Chem. Soc.* **2016**, *138*, 12739–12742.

(32) Pena, D.; Pérez, D.; Guitián, E.; Castedo, L. Palladium-Catalyzed Cocyclization of Arynes with Alkynes: Selective Synthesis of Phenanthrenes and Naphthalenes. *J. Am. Chem. Soc.* **1999**, *121*, 5827–5828.

(33) Shi, F.; Waldo, J. P.; Chen, Y.; Larock, R. C. Benzyne Click Chemistry: Synthesis of Benzotriazoles from Benzyne and Azides. *Org. Lett.* **2008**, *10*, 2409–2412.

(34) (a) Ikawa, T.; Takagi, A.; Goto, M.; Aoyama, Y.; Ishikawa, Y.; Itoh, Y.; Fujii, S.; Tokiwa, H.; Akai, S. Regioselective Cycloaddition Reactions of Boryl- and Silylbenzyne with 1,3-Dipoles: Selective Synthesis of Benzo-Fused Azole Derivatives. *J. Org. Chem.* **2013**, *78*, 2965–2983. (b) Ikawa, T.; Kaneko, H.; Masuda, S.; Ishitsubo, E.; Tokiwa, H.; Akai, S. Trifluoromethanesulfonyloxy-Group-Directed Regioselective (3 + 2) Cycloadditions of Benzyne for the Synthesis of Functionalized Benzo-Fused Heterocycles. *Org. Biomol. Chem.* **2015**, *13*, 520–526.

(35) Gaussian16 was used for all computations: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. *Gaussian 16*, rev. B.01; Gaussian, Inc.: Wallingford, CT, 2016.

(36) (a) Cheong, P. H. Y.; Paton, R. S.; Bronner, S. M.; Im, G.-Y. J.; Garg, N. K.; Houk, K. N. Indolyne and Aryne Distortions and Nucleophilic Regioselectivities. *J. Am. Chem. Soc.* **2010**, *132*, 1267–1269. (b) Goetz, A. E.; Bronner, S. M.; Cisneros, J. D.; Melamed, J. M.; Paton, R. S.; Houk, K. N.; Garg, N. K. An Efficient Computational Model to Predict the Synthetic Utility of Heterocyclic Arynes. *Angew. Chem., Int. Ed.* **2012**, *51*, 2758–2762. (c) Picazo, E.; Houk, K. N.; Garg, N. K. Computational Predictions of Substituted Benzyne and Indolyne Regioselectivities. *Tetrahedron Lett.* **2015**, *56*, 3511–3514.

(37) Garr, A. N.; Luo, D.; Brown, N.; Cramer, C. J.; Buszek, K. R.; VanderVelde, D. Experimental and Theoretical Investigations into the

Unusual Regioselectivity of 4,5-, 5,6-, and 6,7-Indole Aryne Cycloadditions. *Org. Lett.* **2010**, *12*, 96–99.

(38) Bickelhaupt, F. M.; Houk, K. N. Analyzing Reaction Rates with the Distortion/Interaction-Activation Strain Model. *Angew. Chem., Int. Ed.* **2017**, *56*, 10070–10086.

(39) Bent, H. A. An Appraisal of Valence-bond Structures and Hybridization in Compounds of the First-row elements. *Chem. Rev.* **1961**, *61*, 275–311.

(40) Bronner, S. M.; MacKey, J. L.; Houk, K. N.; Garg, N. K. Steric Effects Compete with Aryne Distortion to Control Regioselectivities of Nucleophilic Additions to 3-Silylarynes. *J. Am. Chem. Soc.* **2012**, *134*, 13966–13969.

(41) Using the Boltzmann equation at 75 °C, a $\Delta\Delta G^\ddagger$ of 2.88 and 3.38 kcal·mol^{−1} provides distal Boltzmann factors of 0.985 and 0.993, respectively.

(42) In addition to routine techniques for computing transition state structures (e.g., gas-phase calculations and multiple phosphonate conformations), numerous attempts to locate the distal transition state involving the bis(trifluoroethyl) phosphonyl benzyne by scanning relevant nitrogen to carbon bond distances failed.

(43) Goetz, A. E.; Garg, N. K. Regioselective Reactions of 3,4-Pyridynes Enabled by the Aryne Distortion Model. *Nat. Chem.* **2013**, *5*, 54–60.

(44) Tomasi, J.; Mennucci, B.; Cammi, R. Quantum Mechanical Continuum Solvation Models. *Chem. Rev.* **2005**, *105*, 2999–3093.

(45) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. *J. Phys. Chem. B* **2009**, *113*, 6378–6396.

(46) Zhao, Y.; Truhlar, D. G. The M06 Suite of Density Functionals for Main Group Thermochemistry, Thermochemical Kinetics, Noncovalent Interactions, Excited States, and Transition Elements: Two New Functionals and Systematic Testing of Four M06-Class Functionals and 12 Other Functionals. *Theor. Chem. Acc.* **2008**, *120*, 215–241.

(47) Wang, Y.; Jin, X.; Yu, H. S.; Truhlar, D. G.; He, X. Revised M06-L Functional for Improved Accuracy on Chemical Reaction Barrier Heights, Noncovalent Interactions, and Solid-State Physics. *Proc. Natl. Acad. Sci. U. S. A.* **2017**, *114*, 8487–8492.

(48) Head-Gordon, M.; Head-Gordon, T. Analytic MP2 Frequencies without Fifth-Order Storage. Theory and Application to Bifurcated Hydrogen Bonds in the Water Hexamer. *Chem. Phys. Lett.* **1994**, *220*, 122–128.

(49) Unlike benzyne **33a** and **33b**, the relative energy of the lowest-energy conformers of **33c** was different when solvation was omitted. With this in mind, the lowest-energy conformation from both the gas-phase and MeCN-solvated computations were used as the starting geometry for the optimizations of **33c** in various solvents. The distortion of the lower-energy conformer was used to prepare the plot in Figure 6b. Additional details are provided in the [Supporting Information](#).

(50) Zhang, J.; Zhang, H.; Wu, T.; Wang, Q.; Van Der Spoel, D. Comparison of Implicit and Explicit Solvent Models for the Calculation of Solvation Free Energy in Organic Solvents. *J. Chem. Theory Comput.* **2017**, *13*, 1034–1043.

(51) Shirman, T.; Arad, T.; van der Boom, M. E. Halogen Bonding: A Supramolecular Entry for Assembling Nanoparticles. *Angew. Chem., Int. Ed.* **2010**, *49*, 926–929.

(52) Hamura, T.; Hosoya, T.; Yamaguchi, H.; Kuriyama, Y.; Tanabe, M.; Miyamoto, M.; Yasui, Y.; Matsumoto, T.; Suzuki, K. Facile Access to Versatile Polyaromatic Building Blocks: Selectively Protected Benzocyclobutenedione Derivatives via Regioselective [2 + 2] Cycloaddition of α -Alkoxybenzyne and Ketene Silyl Acetal. *Helv. Chim. Acta* **2002**, *85*, 3589–3604.

(53) Gao, L.; Han, J.; Lei, X. Enantioselective Total Syntheses of Kuwanon X, Kuwanon Y, and Kuwanol A. *Org. Lett.* **2016**, *18*, 360–363.

(54) Andrus, M. B.; Liu, J. Synthesis of Polyhydroxylated Ester Analogs of the Stilbene Resveratrol Using Decarbonylative Heck Couplings. *Tetrahedron Lett.* **2006**, 47, 5811–5814.

(55) Huang, Z.; Yang, Y.; Xiao, Q.; Zhang, Y.; Wang, J. Auto-Tandem Catalysis: Synthesis of Acridines by Pd-Catalyzed C = C Bond Formation and C(sp²)-N Cross-Coupling. *Eur. J. Org. Chem.* **2012**, 6586–6593.

(56) Imai, K.; Ito, T.; Kondo, S.; Takaku, H. A New Phosphorylating Agent, Di(2,2,2-Trifluoroethyl) Trimethylsilyl Phosphite. Its Application in DNA Synthesis by the Phosphotriester Approach. *Nucleosides Nucleotides* **1985**, 4, 669–679.

(57) Kondoh, A.; Aoki, T.; Terada, M. Organocatalytic Arylation of α -Ketoesters Based on Umpolung Strategy: Phosphazene-Catalyzed SNAr Reaction Utilizing [1,2]-Phospha-Brook Rearrangement. *Chem. - Eur. J.* **2018**, 24, 13110–13113.