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Catalytic Phosphorus(V)-Mediated Nucleophilic Substitution Reactions: Development of a Catalytic Appel Reaction

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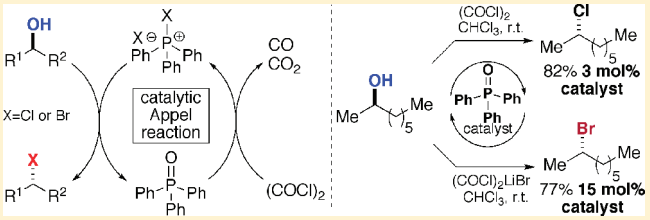
Supporting Information

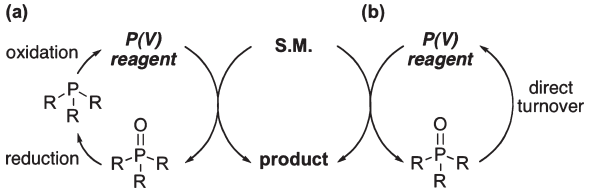
ABSTRACT: Catalytic phosphorus(V)-mediated chlorination and bromination reactions of alcohols have been developed. The new reactions constitute a catalytic version of the classical Appel halogenation reaction. In these new reactions oxalyl chloride is used as a consumable stoichiometric reagent to generate the halophosphonium salts responsible for halogenation from *catalytic* phosphine oxides. Thus, phosphine oxides have been transformed from stoichiometric waste products into catalysts and a new concept for catalytic phosphorus-based activation and nucleophilic substitution of alcohols has been validated. The present study has focused on a full exploration of the scope and limitations of phosphine oxide catalyzed chlorination reactions as well as the development of the analogous bromination reactions. Further mechanistic studies, including density functional theory calculations on proposed intermediates of the catalytic cycle, are consistent with a catalytic cycle involving halo- and alkoxyphosphonium salts as intermediates.



INTRODUCTION

During the past five decades phosphorus-mediated transformations such as the Wittig,[1] Mitsunobu,[2] and Appel[3] reactions have found widespread application in chemical synthesis. That these fundamental reactions have been so widely utilized is a testament to their reliability and generality as well as their strategic importance in synthesis.[4] However, despite being used on a daily basis, there remains a major limitation with this family of chemical reactions, namely, the generation of phosphine oxides as stoichiometric byproduct. The generation of these phosphine oxides and the problems inherent in their separation from the desired products impact heavily on the atom efficiency[5] and waste streams[6] of phosphorus-mediated transformations. Over the years many creative strategies have been developed to remove phosphine oxides from reaction mixtures and thereby eliminate purification issues.[7] However, the fundamental problem of phosphine oxide *generation* in this family of reactions remains. In order to tackle this problem new phosphorus-mediated reactions that generate the minimum amount of waste and consume the minimum amount of energy and raw materials[8] are required, and therefore, catalysis must be considered.[9] The development of such reactions poses a significant challenge to catalytic reaction design because the strong phosphorus−oxygen double bond, whose formation drives many of the stoichiometric reactions,[10] must be broken in order to convert the derived phosphine oxides into phosphorus(V) reagents and achieve turnover. Despite this and other difficulties, two potential catalytic cycles for the conversion of a generic starting material (SM) into product can be contemplated that differ with respect to how turnover is achieved (Scheme 1). The first (redox-driven catalysis, Scheme 1a) is predicated on the fact that most phosphorus(V) reagents are formed in situ from tervalent phosphorus compounds, e.g., phosphines.

Scheme 1. Hypothetical Catalytic Cycles for the Transformation of a Generic Starting Material (S.M.) into a Product by a P(V) Reagent[a]



[a] (a) Redox-driven cycle. (b) Redox-neutral cycle.

Therefore, closure of a catalytic cycle of this type could be achieved by reduction of the derived phosphine oxide to the corresponding phosphine. In the alternative strategy (redox-neutral catalysis, Scheme 1b), turnover is achieved by direct conversion of the phosphine oxide byproduct into the active phosphorus(V) reagent. Such an approach depends on the nontrivial conversion of phosphine oxides into synthetically useful phosphorus(V) reagents in the presence of starting materials and products. The redox-neutral strategy was pioneered by Marsden, who in 2008 disclosed the first examples of phosphine oxide-catalyzed aza-Wittig reactions.[11] In this work the catalytic cycle was closed by conversion of the phosphine oxide byproduct into the iminophosphorane required for the

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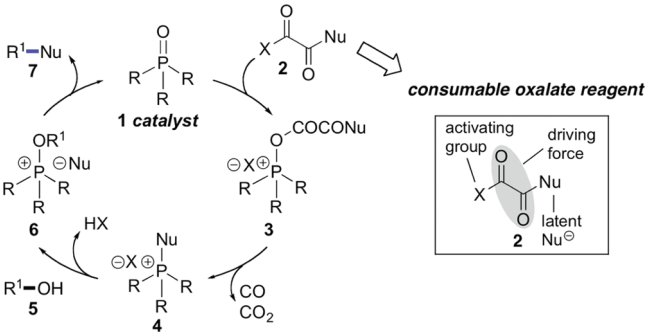
Scheme 2. Proposed General Catalysis Strategy for P(V)-Mediated Nucleophilic Substitution Reactions Using Consumable Oxalate Reagents

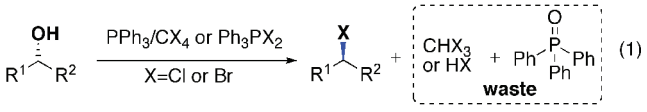


aza-Wittig reaction by a metathesis reaction with an isocyanate, the driving force being provided by the elimination of CO_2.[12] In 2009 the first example of catalysis in the redox-driven manifold (Scheme 1a) was reported by O'Brien in the form of the first phosphine-catalyzed Wittig reaction.[13] Catalytic turnover was achieved by reduction of the phosphine oxide byproduct followed by reformation of the required ylide from the derived phosphine. A further example of catalysis in this manifold followed from Woerpel, who described phosphine-catalyzed reductions of silyl peroxides in which turnover was again achieved via phosphine oxide reduction.[14] In this article we provide a detailed account of our studies on the development of catalytic phosphorus(V)-mediated nucleophilic substitution reactions of alcohols to afford alkyl chlorides and bromides.[15]

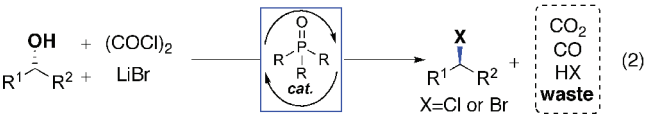
Reaction Design. Nucleophilic substitution reactions are fundamental transformations in organic chemistry and underpin a great deal of syntheses. Phosphorus-mediated reactions of this type, such as the Mitsunobu and related Appel halogenation reactions, are particularly attractive owing to their broad substrate scope and mild reaction conditions; however, their poor atom efficiency undermines their applicability in certain situations as mentioned above. The desire for *catalytic* activation/nucleophilic substitution reactions of alcohols is clear and has been well articulated.[16] The recent development of new methods for the activation of alcohols, for example, by Lambert,[17] as well as the catalytic halogenation reactions of alcohols developed by Stephenson[18a] along with other catalytic processes[18] exemplify the current drive toward the realization of efficient atom-economical catalytic nucleophilic substitution reactions. Our working plan for the design of catalytic transformations of this type is depicted in Scheme 2. In contemplating new catalytic reactions we reasoned that catalysis in a redox-neutral cycle might be possible if alkoxyphosphonium/nucleophile ion pairs such as **6**, the key intermediates in phosphorus(V)-mediated substitution reactions, could be accessed catalytically from phosphine oxides at the expense of a consumable stoichiometric reagent. The generic oxalate reagent **2** depicted in Scheme 2 contains an activating group X to facilitate the initial reaction with the phosphine oxide, a latent nucleophile (Nu), and importantly, the driving force to compensate for the cleavage of the phosphorus−oxygen double bond in the form of two carbonyl groups that will be converted into CO and CO_2 upon collapse of phosphonium salt **3**. We were attracted to this strategy because, in principle, it provides a general method for the catalytic activation and nucleophilic substitution of alcohols by varying the Nu group of the oxalate. The transformation of the phosphine oxide from stoichiometric waste product to organocatalyst was also an appealing aspect of this approach. Clearly, the successful implementation of this strategy depends on the conversion of phosphine oxides into phosphonium salts (e.g., **1** → **4**, Scheme 2); however, phosphine oxides are often regarded as unreactive due the strength of the phosphorus−oxygen double bond.

Nevertheless some interesting and potentially useful transformations of phosphine oxides have been documented; for example, the conversion of triphenylphosphine oxide to chlorotriphenylphosphonium chloride is possible using phosgene.[19] Less well-known and more useful is the analogous reaction with oxalyl chloride that was reported in the late 1970s.[20] This latter reaction provides a clear opportunity to validate the catalysis strategy outlined in Scheme 2 (where X = Nu = Cl) and,[21] therefore, we investigated the development of catalytic Appel chlorination reactions in which the pivotal halophosphonium salts[22] are accessed from substoichiometric amounts of phosphine oxides and stoichiometric oxalyl chloride. We reasoned that this would be a good starting point for our studies because the classical Appel reaction (eq 1) is used extensively for the conversion of alcohols into alkyl halides with inversion of configuration. These halides are fundamental building blocks in synthesis[23] as well as being valuable end products in their own right.[24] Halogenation of alcohols is most straightforwardly effected using haloacids; however, in general, these reactions are limited to alcoholic substrates that afford stabilized carbocations upon protonation and ionization.[25] Almost all of the other methods developed[26] rely on either stoichiometric covalent activation of the alcohol followed by nucleophilic displacement[27] or in situ stoichiometric activation.[28,29] For these reasons the development of a catalytic halogenation process of the type depicted in eq 2 and Scheme 1 was attractive.

Conventional Appel reaction



This work: *catalytic Appel reaction*



RESULTS AND DISCUSSION

Chlorination of Alcohols. We began our investigation by establishing that the conversion of triphenylphosphine oxide **1** to the desired chlorophosphonium salt **4a** occurred rapidly in $CDCl_3$. Effervescence began almost immediately upon mixing of the two reagents and continued for approximately 1.5 min. Analysis of the crude reaction mixture by NMR spectroscopy indicated complete conversion to the chlorophosphonium salt (^{31}P NMR δ 64.6 ppm). We next confirmed that the in situ generated phosphonium salt was effective in chlorinating decanol in $CDCl_3$ (eq 4). Again, NMR analysis indicated that the desired

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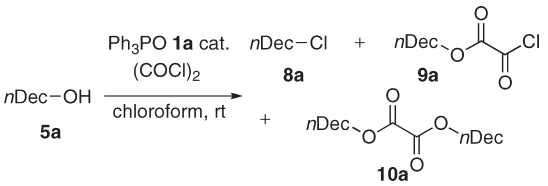
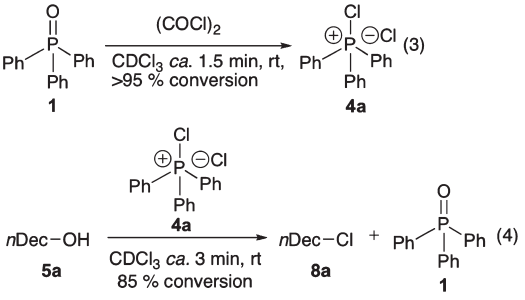
Table 1. Optimization of the Catalytic Chlorination of Decanol[a]



entry	Ph_3PO, mol %	addition protocol/addition time	product (yield, %)
1	0	**5a** added to $(COCl)_2$	**9a** (78) + **10a** (22)[b]
2	30	**5a** added to $(COCl_2)_2$ + Ph_3PO	**8a** (46) + **9a** (44) + **10a** (10)[b]
3	25	**5a** added to $(COCl)_2$ + Ph_3PO over 2 h	**8a** (65)[c]
4	18	$(COCl)_2$ added to **5a** + Ph_3PO over 0.5 h	**9a** (41) + **10a** (59)[b]
5	15	**5a** and $(COCl)_2$ added to $(COCl)_2$ + Ph_3PO over 7 h	**8a** (86)[b]

[a] Chloroform solutions of $(COCl)_2$ and **5a** were added simultaneously to a solution of $(COCl)_2$ and Ph_3PO in chloroform over the time indicated. The initial amount of $(COCl)_2$ used was equimolar with the catalyst; 1 equiv of $(COCl)_2$ was used in total. [b] Yield determined by ^1H NMR spectroscopy using $Cl_2CHCHCl_2$ as an internal standard. [c] Isolated yield after flash chromatography.

chloride was formed in high conversion along with the expected triphenylphosphine oxide byproduct (^{31}P NMR δ 29.0 ppm).[30]



Next we established the extent of the unwanted background reaction between oxalyl chloride and decanol (entry 1, Table 1). The rapid (<10 min) consumption of starting material and formation of chlorooxalate **9a** and bisester **10a** indicated a significant side reaction that could compete with the desired chlorination. However, an initial trial of the catalytic reaction using 30 mol % of triphenylphosphine oxide afforded a promising 46% of the desired product **8a** (entry 2, Table 1) along with **9a** and **10a**. Given that triphenylphosphine oxide is cheap and commercially available, we opted to conduct optimization experiments to suppress the formation of the esters using this catalyst. Addition of the alcohol to a solution of oxalyl chloride and triphenylphosphine oxide catalyst over 2 h afforded a 65% isolated yield of **8a** (entry 3, Table 1). However, addition of the oxalyl chloride to a solution of alcohol and the triphenylphosphine oxide catalyst over 0.5 h afforded no decyl chloride (entry 4, Table 1). A further modification involving simultaneous addition of both 85 mol % oxalyl chloride and decanol to a solution of 15 mol % catalyst and 15 mol % oxalyl chloride over 7 h afforded an excellent yield of **8a** (entry 5, Table 1). This protocol was therefore adopted for substrate screening studies.

The chlorination of a range of alcohols was then investigated using the optimal conditions indentified above (Table 1). The data in Table 2 indicate the scope and limitations of the catalytic chlorination reaction. Aliphatic primary and secondary alcohols are chlorinated very efficiently. Primary and secondary allylic, benzylic, and propargylic alcohols also are excellent substrates for the chlorination reaction. With regard to stereochemistry, in the case of entry 3, the specific rotation of the product ($[\alpha]^{22}_D$ +33.5, *c* 0.58, $CHCl_3$, lit.[31] $[\alpha]^{25}_D$ +33.7) indicated that the expected inversion of configuration had occurred. This was confirmed by GC analysis using a capillary column with a chiral stationary phase.[32] The stereochemical outcome of the chlorination of cholesterol was interesting: in this instance retention of configuration was observed and confirmed via X-ray analysis (Figure 1)[33] and is most likely the result of participation of the neighboring alkene.[34]

Because HCl is generated during the formation of the alkoxyphosphonium salt, we examined the possibility of conducting the reaction in the presence of base. In this regard both Hünig's base and 2,6-di-*tert*-butylpyridine were evaluated with substrates **5a** and **5c**, and each case the derived chlorides were obtained in excellent yield. In terms of substrates containing protected hydroxyl groups, the benzyl protecting group is tolerated (entry 18), and interesting results were obtained for substrates containing silyl ethers. For example, triethylsilylethers were unstable to the reaction conditions and afforded very high yields of chloride products as a result of in situ deprotection under the reaction conditions (entries 19 and 20), and a double chlorination reaction of bis-protected diol **8w** proceeded in good yield (entry 23). This is a useful observation since TES ethers are commonly used as protecting groups for alcohols and can be cleanly converted into the corresponding chlorides using this protocol. In contrast mono TBDPS-protected pentane diol underwent chlorination with retention of the protecting group in 60% yield in the presence of a non-nucleophilic pyridine base (entry 21). The catalytic reaction also proceeded smoothly with amidoalcohol **5v** that contains a potentially nucleophilic amide group (entry 22). Replacement of chloroform with ethyl acetate solvent was possible with only a small loss in yield (entries 1 and 13). The substrate limitations of the chlorination reaction are apparent from the data in Table 2. Sterically demanding alcohols such as cyclohexanol, menthol, and neopentyl alcohol are all poor substrates. The major products obtained from attempted chlorination reactions on these substrates are the oxalyl chloride derived chlorooxalates of type **9**. The failure of these substrates in the catalytic reactions indicates that the Arbuzov collapse

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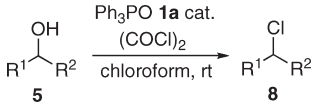
Table 2. Catalytic Chlorination of Alcohols under Appel Conditions[a]



entry	substrate	product	yield 8[b] (%)
1	decanol **5a**	**8a**	94 (85) 91[d] (80)[c] (85)[f]
2	benzyl alcohol **5b**	**8b**	80 (42)
3	(*R*)-(−)-2-octanol **5c**	**8c**	97 96[d] 88[e] (54)
4	(*S*)-ethyl lactate **5d**	**8d**	95 (87)
5	3-phenyl-1-propanol **5e**	**8e**	95 (72)
6	2-deyn-1-ol **5f**	**8f**	85 (82)
7	2-buten-1-ol **5g**	**8g**	70
8	1-octene-3-ol **5h**	**8h**	64
9	cinnamyl alcohol **5i**	**8i**	88 (70)
10	diphenyl methanol **5j**	**8j**	96
11	cyclohexenol **5k**	**8k**	88
12	cholesterol **5l**	**8l**	81 (66)
13	1-phenylethyl alcohol **5m**	**8m**	98 (95) (86)[c]
14	cyclohexanol **5n**	**8n**	7
15	(±)-menthol **5o**	**8o**	0
16	neopentyl alcohol **5p**	**8p**	0
17	*tert*-butanol **5q**	**8q**	37
18	$HO(CH_2)_5OBn$ **5r**	**8r**	88 (66)
19	$C_{10}H_{21}OTES$ **5s**	**8a**	89
20	2-triethylsiloxyoctanol **5t**	**8c**	99
21	$HO(CH_2)_5OTBDPS$ **5u**	**8u**	64[d] (58)[d]
22	$PhCONH(CH_2)_2OH$ **5v**	**8v**	(63)
23	$PhCH(OTES)CH_2OTES$ **5w**	**8w**	(68)[b]

[a] Chloroform solutions of the substrate (1 equiv) and $(COCl)_2$ (0.85 or 1.03 equiv) were added simultaneously to a solution of Ph_3PO (0.15 equiv) and $(COCl)_2$ (0.15 or 0.17 equiv) in chloroform over 7 h at rt. [b] Yield determined by ^1H NMR spectroscopy using $Cl_2CHCHCl_2$ as an internal standard; isolated yields in parentheses. [c] Ethyl acetate was used as solvent. [d] 1.8 equiv of 2,6-di-*tert*-butylpyridine was added with the alcohol. [e] 1.8 equiv of Hünig's base was added with the alcohol. [f] 10 mmol of alcohol substrate was used.

of the alkoxyphosphonium salt (e.g., **6** → **8** + **1**, Scheme 3) is slow and likely to be rate-limiting in these cases (vide infra). Finally, the repetition of three representative reactions with substrates **5a**, **5b**, and **5h** in the absence of triphenylphosphine oxide confirmed that the catalyst is required for chlorination.

Having developed a catalytic chlorination reaction, we examined the feasibility of the analogous bromination reactions. Given that stoichiometric bromophosphonium salts generated from either the Ph_3P/CBr_4 or Ph_3P/NBS systems are used extensively for this purpose, a bromination reaction catalytic in the phosphorus component would clearly offer a substantial improvement in terms of atom efficiency and ease of purification of products. As suggested in Scheme 2 it appeared that reactions of this type would be simple to implement by substituting oxalyl chloride with oxalyl bromide; however, this was not the case (eq 5), and only a modest yield of decyl bromide was obtained,

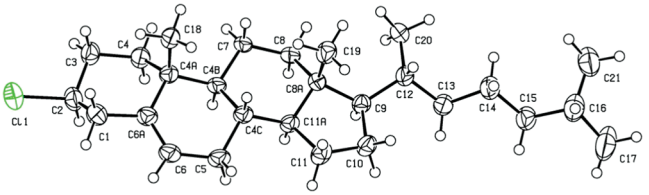
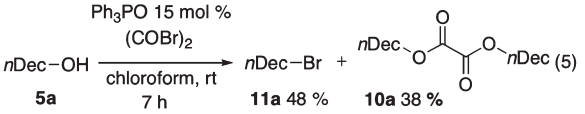


Figure 1. X-ray structure of **8l**.

with bis ester **10a** accounting for the majority of the remaining mass balance, when this was attempted. This initial poor result combined with the stability and availability issues associated with oxalyl bromide prompted us to examine an alternative strategy for bromination based on intercepting an alkoxyphosphonium chloride with a bromide ion.



For such an approach to be viable, attack by the bromide ion on the alkoxyphosphonium salt intermediate would have to be faster than the corresponding chlorination reaction in order for clean bromination to occur. We therefore examined the possibility of catalytic bromination using the $Ph_3PO/(COCl)_2$ system with hetero- and homogeneous sources of bromide ions (Table 3).

Initial experiments involving both sodium and lithium bromide (entries 1 and 2) were disappointing since in the first case the major product formed was the chloride while in the second it was the unwanted bis ester **10a**. Increasing the amount of oxalyl chloride to 1.3 equiv (entry 3) resulted in a promising 41% yield of the bromide and suppressed the formation of **10a**, but chloride **8a** was now obtained as a byproduct. Further optimization involved increasing both the amount of LiBr to 2.5 equiv (entry 4) and the addition time to 5 h (entry 5) and resulted in a decrease of chloride byproduct and an increase of the desired bromide to an acceptable 75%. At this juncture, in an attempt to improve on entry 6, we examined the use of tetrabutylammonium bromide as a homogeneous source of bromide ions (entry 7) with alcohol **5e**.

Our expectations that this would lead to a superior bromination reaction were not met; rather, a mixture of chloride and bromide products was obtained. In a direct comparison the corresponding reaction with lithium bromide (entry 6) produced no chloride.

These results indicate that, in addition to providing bromide ions, the lithium bromide is also sequestering chloride ions from solution through the formation of lithium chloride with the lattice energy of the latter presumably acting as the driving force. Given these results, we proceeded to examine the catalytic bromination of a range of alcohols using lithium bromide as the source of bromide ions (Table 4). In contrast to the catalytic chlorination reactions, we found it necessary to perform optimization reactions on several of the alcohol substrates in order to suppress the formation of chloride products that were difficult to separate from the desired bromides.

The catalytic bromination reactions are effective for aliphatic, benzylic, and propargylic primary alcohols as well as aliphatic, benzylic and allylic secondary alcohols. As was the case with the chlorination reactions, the bromination of cholesterol to afford **9l**

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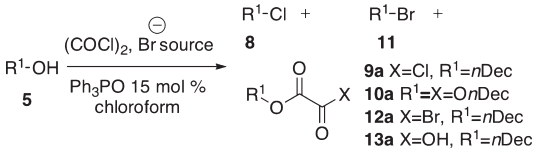
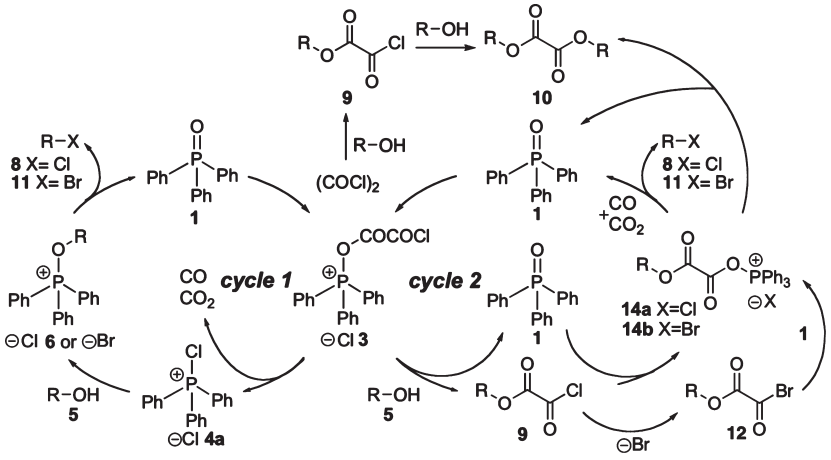
Table 3. Optimization of Catalytic Bromination Reactions[a]



entry	alcohol	$(COCl)_2$, mol %	Br source, mol %	addition time, h	product (yield, %)[b]
1	**5a**	100	NaBr, 300	7	**11a** (5), **8a** (44), **9a** (21), **10a** (30)
2	**5a**	100	LiBr, 200	2	**11a** (11), **10a** (43), **9a** + **12a** 1:2 (41), **13a** (5)
3	**5a**	130	LiBr, 200	2	**11a** (41), **8a** (19), **9a** (33), **13a** (7)
4	**5a**	130	LiBr, 250	2	**11a** (43), **8a** (7), **9a** (33), **10a** (8), **13a** (6)
5	**5a**	130	LiBr, 250	5	**11a** (74), **9a** + **12a** ca. 1:1 (21%)
6	**5e**	130	LiBr, 230	5	**11e** (66)
7	**5e**	130	nBu_4NBr, 230	5	**11e** (27), **8e** (47)

[a] Chloroform solutions of the alcohol (1 equiv) and $(COCl)_2$ were added simultaneously to a solution of Ph_3PO (0.15 equiv), LiBr, and $(COCl)_2$ in chloroform over the time indicated at rt. [b] Yield determined by ^1H NMR spectroscopy using $Cl_2CHCHCl_2$ as an internal standard.

Scheme 3. Possible Catalytic Cycles for Catalytic Chlorination and Bromination Reactions



took place with retention of configuration, while the bromination of (*R*)-(−)-2-octanol took place with the expected inversion of configuration, as confirmed by the specific rotation of the product ($[\alpha]^{22}_D$ +38.2, *c* 0.58, $CHCl_3$, lit.[35] $[\alpha]^{25}_D$ +40.2, *c* 5.8) and GC analysis.[32] The substrate scope is also similar to the chlorination reactions, i.e., sterically demanding alcohols do not undergo efficient catalytic bromination. The new catalytic protocol provides a valuable atom-economical alternative to the traditional NBS/triphenylphosphine system for bromination of unhindered primary and secondary alcohols.

Mechanistic Observations. Having established the substrate scope and limitations of the newly developed reactions, we sought a more detailed understanding of the nature of the catalytic cycle involved. We were particularly interested in understanding why certain catalytic reactions failed and in gaining an understanding of which step of the catalytic cycle is rate-limiting so that improved reactions could be developed in the future. Furthermore, we wished to probe the role of the phosphine oxide in the catalytic cycle and establish whether our catalytic reactions are indeed consistent with the Appel-type catalytic cycle as depicted in cycle 1 of Scheme 3 or if an alternative catalytic cycle, in which the phosphine oxide acts solely as a nucleophilic catalyst, intervenes (cycle 2, Scheme 3). In order to do this we studied the relative reactivity of the key intermediates in both possible catalytic cycles, namely, alkoxyphosphonium salts of type **6** and oxalylphosphonium salts of type **14**.

We began by looking in more detail at those reactions that had failed. As can be seen from entries 14−16, Table 2 and entry 12, Table 4, sterically demanding substrates are not tolerated. These unsuccessful reactions provide some insight into the turnover-limiting step of the catalytic cycle. If we assume that (a) the rate of reaction between oxalyl chloride and triphenylphosphine oxide will remain constant regardless of the alcohol substrate employed and (b) the rate of alkoxyphosphonium salt formation (**4a** → **6**, Scheme 3) and (c) the rate of the background reaction between alcohol and oxalyl chloride (**5** → **9**, Scheme 3) will also not be particularly sensitive to the steric demands of the alcohol,[36] then for successful catalytic reactions, the Arbuzov reaction of the alkoxyphosphonium salt (**6** → **8**, Scheme 3, cycle 1) needs to be

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Table 4. Catalytic Bromination of Alcohols under Appel Conditions[a]

entry	alcohol **5**	product	$(COCl)_2$, mol %	Ph_3PO, mol %	LiBr, mol %	time, h	yield **11**,[b] %
1	decanol **5a**	**11a**	130	15	250	5	75 (70)[c]
2	2-buten-1-ol **5g**	**11g**	130	15	300	5	73
3	3-phenyl-1-propanol **5e**	**11e**	130	15	230	5	67 (58)
4	benzyl alcohol **5b**	**11b**	130	15	300	5	71 (49)
5	2-decyn-1-ol **5f**	**11f**	130	15	250	5	75 (49)
6	(*R*)-(−)-2-octanol **5c**	**11c**	130	15	150	7	77
7	cholesterol **5l**	**11l**	130	25	250	7	44
8	1-phenylethyl alcohol **5m**	**11m**	130	15	250	5	74
9	cinnamyl alcohol **5i**	**11i**	130	15	300	5	69 (27)
10	2-cyclohexenol **5k**	**11k**	130	15	250	5	73 (14)
11	*tert*-butyl alcohol **5q**	**11q**	130	15	250	5	72
12	cyclohexanol **5n**	**11n**	130	15	250	5	0
13	decanol **5a**	**11a**	130	0	250	5	0
14	benzyl alcohol **5b**	**11b**	130	0	300	5	0

[a] Chloroform solutions of the substrate (1 equiv) and $(COCl)_2$ (1.11 equiv) were added simultaneously to a solution of Ph_3PO (0.15 equiv), LiBr, and $(COCl)_2$ (0.20 equiv) in chloroform over the time indicated at rt. [b] Yield determined by ^1H NMR spectroscopy using $Cl_2CHCHCl_2$ as an internal standard; isolated yields in parentheses. [c] 10 mmol of substrate was used.

relatively fast. We therefore examined the reactivity of alkoxyphosphonium chlorides derived from neopentyl alcohol, cyclohexanol, and decanol (Scheme 4, Table 5).

Given the failure of catalytic reactions with cyclohexanol and neopentyl alcohol, we were not surprised to observe that the derived alkoxyphosphonium salts **6n** and **6p** were relatively stable. For example, **6n** decomposed over 5 h to a mixture of chloride and cyclohexene. In the neopentyl case no chloride product was formed over this time period, and we were able to obtain X-ray quality crystals of the alkoxyphosphonium salt (Figure 2).[37]

With NMR data for **6n** and **6p** in hand, we examined NMR spectra taken at the end of failed catalytic reactions on cyclohexanol, neopentyl alcohol, and menthol. In each case peaks in the ^1H and ^{31}P NMR for the alkoxyphosphonium salts were observed. At the opposite end of the reactivity scale we attempted to prepare the alkoxyphosphonium salt derived from decanol. As we had found previously, stoichiometric chlorination of this substrate is very fast (eq 4), but we were able to observe **6a** by NMR if the spectrum was recorded within ca. 1.5 min. After this time the chlorination reaction is at 50% conversion and ca. 50% of the alkoxyphosphonium is visible by NMR. These results are consistent with alkoxyphosphonium salt collapse to product being turnover-limiting if the reaction proceeds in cycle 1 of Scheme 3. In a further experiment the catalytic chlorination of decanol was repeated, and aliquots of the reaction mixture were analyzed at 1, 3, 5, and 6 h intervals by multinuclear NMR. These experiments revealed that decyl chloride formed steadily over the course of the addition time along with a small amount of chlorooxalate **9a**. ^{31}P NMR analysis indicated the presence of chlorophosphonium salt **4a** and another signal (^{31}P δ 32−40 ppm) that we tentatively assign to protonated triphenylphosphine oxide.[22] At the end of the reaction a single peak corresponding to triphenylphosphine oxide was present in the ^{31}P NMR spectrum. These observations are consistent with a rapid chlorination reaction that is complete in the time that it takes to run the NMR spectra of the reaction mixture aliquot (typically 3−5 min). However, at this point, we could not rule out formation of the chloride product in cycle 2 of

Scheme 4. Formation and Reactivity of Alkoxyphosphonium Salts

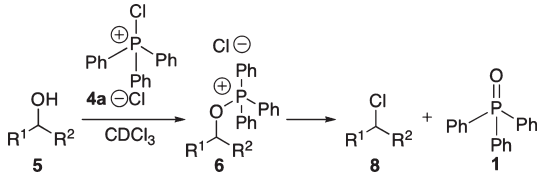

Table 5. Selected NMR Data and Reactivity of Alkoxyphosphonium Salts

entry	alcohol	product	selected NMR data	time	yield of **8**,[a] %
1	cyclohexanol	**8n**	^{31}P δ 59.2 ppm, $^2J_{CP}$ = 9.2, $^3J_{HP}$ = 4.4	5 h	14[b]
2	neopentyl alcohol	**8p**	^{31}P δ 61.9 ppm, $^2J_{CP}$ = 9.2, $^3J_{HP}$ = 8.4	5 h	0
3	decanol	**8a**	^{31}P δ 61.9 ppm, $^2J_{CP}$ = 9.2	ca. 1.5 min	50

[a] The yield was determined by ^1H NMR spectroscopy using $Cl_2CHCHCl_2$ as an internal standard. [b] The remainder of the mass balance in this reaction was cyclohexene (75%).

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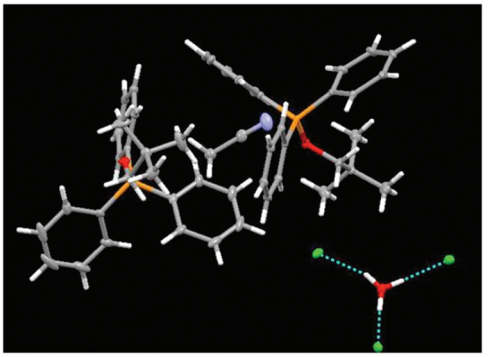


Figure 2. X-ray structure of **6p**.

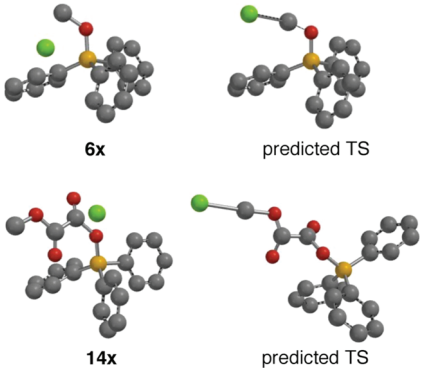
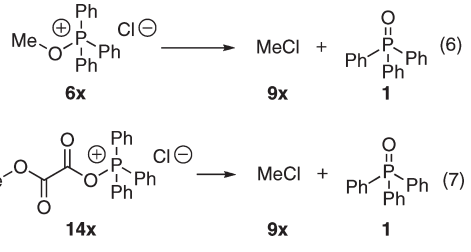


Figure 3. Ball and spoke representation of **6r** and **14r** and predicted transition structures (hydrogen atoms omitted for clarity).

Scheme 3 from either intermediate **9** or **14**, and therefore we examined the reactivity of these species.

We note first that the chlorooxalates of type **9** have received very little attention and oxalyl phosphonium salts of type **14** have not been reported; however, it is known that the former compounds are significantly more stable than analogous chloroformates and chlorosulfinates with respect to decomposition to chlorides.[31] For example, the chlorooxalate derived from oxalyl chloride and butanol was converted to the corresponding chloride only by conversion to the corresponding pyridinium salt and heating to 110 °C for 3 h.[31] For the present study we prepared chlorooxalates from substrates **6a**, **6b**, and **6h** by slow addition to oxalyl chloride and conducted a series of experiments with triphenylphosphine oxide in which we attempted to convert the chlorooxalates to chloride products of type **8**. The interested reader is referred to the Supporting Information for full details of these experiments. To summarize the results: our attempts to convert the oxalates to the corresponding chlorides **8**, either under the conditions used in the catalytic reactions or more forcing conditions involving stoichiometric amounts of triphenylphosphine oxide and elevated temperatures, were unsuccessful. Furthermore, we obtained no evidence for the formation of oxalyl phosphonium salts of type **14a** from chlorooxalates under the conditions of the catalytic reactions. In a parallel computational study, we modeled the Arbuzov reactions of truncated (methyl replaced *n*-decyl) alkoxyphosphonium salts of type **6** and oxalylphosphonium salts of type **14a** to chloride products **8** (eqs 6 and 7). Geometry optimizations on the ion pairs **6x** and **14x** were performed using the B3LYP model and 6-31G* basis set (Spartan '08 Macintosh).[38,39] We succeeded in locating transition structures for the both of the Arbuzov reactions using the same theoretical model (Figure 3).



Activation energies of 12.3 and 31.8 kcal/mol were obtained for the reactions depicted in eqs 6 and 7, respectively. These results indicate that decomposition of oxalylphosphonium salts to chloride products **8** is very much more difficult than decomposition of the analogous alkoxyphosphonium salts.

At this point we summarize the key features of the catalytic chlorination reactions: (a) The catalytic reactions work very well for primary and secondary alcohols that are not too sterically hindered. (b) With sterically demanding substrates the slow step in the catalytic cycle is the collapse of the alkoxyphosphonium salt (**6** → **8**, Scheme 4), which leads to alcohol and oxalyl chloride buildup in the absence of catalyst and, therefore, to formation of chlorooxalates of type **9**. This is corroborated by the slow stoichiometric chlorination reactions of problematic substrates and the observation of the alkoxyphosphonium salts **6** derived from such substrates at the end of failed catalytic reactions. (c) Chlorooxalates of type **9** are unreactive with respect to chloride formation, i.e., **9** → **8** and **14a** → **8** (Scheme 4) are not viable under the conditions of the catalytic reactions (or even under more forcing conditions, see Supporting Information). These data and observations are consistent with chlorination occurring in the "Appel-type" pathway (cycle 1, Scheme 3).

We now collate the results of similar investigations carried out on the catalytic bromination reactions described in Table 4. The interested reader is once again referred to Supporting Information for full details of the experiments relating to each of the following key points: (a) Alkyl bromides **11** do not form from alkyl chlorides and LiBr in chloroform under the reaction conditions. (b) LiBr is superior to homogeneous sources of bromide ions such as nBu$_4$Br, suggesting that the former is involved in counterion metathesis that sequesters chloride ions from the reaction mixture. (c) The conversion of chlorooxalates into bromooxalates (**9b** → **12**, Scheme 3) under the conditions of the catalytic reaction is viable; however, the bromooxalates **12** are not converted to bromide products **11** in the presence of triphenylphosphine oxide under the conditions of the catalytic reactions. It is, however, possible to obtain bromide products with activated substrates under more forcing conditions (e.g., **12b**, 1 equiv of Ph$_3$PO, 48 h, ca. 30%). Therefore, we conclude that the catalytic bromination reactions are also consistent with an "Appel-type" pathway as depicted in cycle 1, Scheme 3.

Further Optimization Studies. Having developed catalytic chlorination and bromination reactions for a wide range of alcohol substrates and having established that the reactions were consistent with a catalytic cycle involving halo- and alkoxyphosphonium salts as intermediates, we began a second series of

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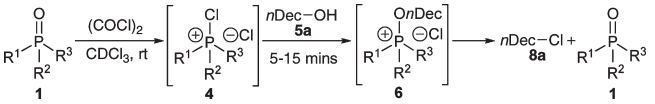
Table 6. Formation and Reactivity of Chlorophosphonium Salts 4[a]



entry	phosphine oxide	yield **8a**, %
1	**1a** $R^1 = R^2 = R^3$ = Ph	96[a]
2	**1b** $R^1 = R^2$ = Ph, R^3 = py	88[b]
3	**1c** $R^1 = R^2 = R^3$ = 4-fluorophenyl	94[c]
4	**1d** $R^1 = R^2 = R^3$ = 2-furyl	0[a]
5	**1e** $R^1 = R^2 = R^3$ = 2-tolyl	23[d]
6	**1f** $R^1 = R^2 = R^3$ = 4-methoxyphenyl	0[b]
7	**1g** $R^1 = R^2 = R^3$ = 2,6-dimethoxyphenyl	0[a]
8	**1h** $R^1 = R^2$ = Ph, R^3 = Me	8[a]
9	**1i** $R^1 = R^2 = R^3$ = Me	0[a]
10	**1j** $R^1 = R^2 = R^3$ = Bu	1[a]
11	**1k** $R^1 = R^2$ = 3-methylcyclopentenyl, R^3 = Ph	2[a]

[a] Phosphine oxide (1.2 equiv), $(COCl)_2$ (1.2 equiv), and $Cl_2CHCHCl_2$ internal standard were dissolved in $CDCl_3$ and stirred for 5 min. Decanol (1.0 equiv) was added and stirred for 10 min. [b] The phosphine oxide and $(COCl)_2$ were stirred for 10 min. [c] The phosphine oxide and oxalyl chloride were stirred for 15 min. [d] The phosphine oxide, 2,6-di-*tert*-butylpyridine (1.2 equiv), and $(COCl)_2$ were dissolved in $CDCl_3$ and stirred for 30 min.

optimization studies with a view to reducing both the catalyst loading and the addition time to more practical levels. However, we were also interested in exploring the reactivity of several other catalysts and we began with a survey of different phosphine oxides.

We selected a series of aryl- and alkyl-substituted phosphine oxides and investigated their reactivity with oxalyl chloride and the reactivity of the chlorophosphonium salts so obtained with decanol (Table 6). We were pleased to observe that most of the phosphine oxides reacted smoothly with oxalyl chloride to afford the desired chlorophosphonium salts **4**. It was immediately apparent that trialkyl-substituted phosphine oxides (e.g., entries 9−11) reacted more rapidly than their bi- and triaryl counterparts. With regard to the latter, electron-deficient triarylphosphine oxides reacted more slowly than triphenylphosphine oxide (entries 2 and 3), while those phosphine oxides bearing electron-rich arenes (entries 5−7) did not form a single species upon addition of oxalyl chloride. In the case of trifurylphosphine oxide (entry 4) no appreciable reaction with oxalyl chloride was observed after 5 or 10 min. We then reacted each of the derived chlorophosphonium salts with decanol in order to evaluate the relative rates of the chlorination reactions. From the studies described above it is clear that, for a given phosphine oxide to be a viable catalyst, its derived chlorophosphonium salt **4** must effect chlorination of the alcohol faster than, or at a similar rate to, the background reaction between the alcohol and oxalyl chloride (entry 1, Table 1). If the Arbuzov reaction is slow, for example, in the case of sterically hindered alcohols, the catalytic reactions fail.

Upon reaction of the derived chlorophosphonium salts **6** with decanol, it can be seen that the alkoxyphosphonium salts derived from aliphatic phosphine oxides underwent very slow Arbuzov decomposition to product. For example, after 10 min only 2% decyl chloride had been produced from the reaction of decanol with chlorophosphonium salt **4k**. Similar results were observed for salts **4i** and **4j**. These results indicate that the Arbuzov reaction is also highly sensitive to the nature of the substituents attached to phosphorus and that bis- and trialkyl phosphine oxides cannot be effective catalysts due to the low reactivity of their derived alkoxyphosphonium salts. The results for the electron-rich phosphine oxides were also poor: the chlorination reactions were slow, and therefore these phosphine oxides were also excluded. More promising were the electron-poor aryl phosphine oxides **1b** and **1c**: they gave results similar to those with triphenylphosphine oxide in the stoichiometric chlorination reaction, and therefore we took these forward, along with **1a**, into a second optimization study focused on reducing catalyst loading and addition time. We began by comparing the two new phosphine oxides to **1a** (Table 7) in catalytic chlorination reactions. The result with the pyridyl phosphine oxide **1b** was a moderate 53% (entry 9).

However, phosphine oxide **1c** was identical to **1a** in this test reaction and afforded an excellent 94% yield of product (entry 5). Therefore, we investigated lowering the loading of catalysts **1a** and **1c** to more practical levels with decanol and 2-octanol as representative nonsterically demanding primary and secondary alcohol substrates.

Lowering the loading of both **1a** and **1c** decreased the yield, and in both cases it fell off sharply at 2.5 mol %; however, good yields were still obtained at 5 mol % with **1a** and **1c** (entries 3 and 5). We were pleased to observe that **1c**, which catalyzed the chlorination of decanol in 81% yield, was an improvement on triphenylphosphine oxide. This constitutes a significant improvement to the original conditions described in Table 2. A similar series of experiments was then undertaken with 2-octanol, and similar results were obtained. Again, the loading of both catalyst **1a** and **1c** could be reduced significantly with only a small affect on the yield. For example, at 3 mol % **1a** and **1c** afforded the product in yields of 82% and 85%, respectively (entries 13 and 17). These results indicate that secondary alcohols are better substrates for the catalytic reaction than primary. During this and related work we have observed that alkoxyphosphonium salts form very rapidly from alcohols and the rate of this reaction is rather insensitive to the steric demands of the alcohol. On the other hand secondary alcohols react more slowly than primary alcohols with oxalyl chloride. This results in a slower background reaction for these substrates and allows lower catalyst loadings to be realized. To reach still lower catalyst loading we examined the TES-protected substrate **5t** since the background reaction here ought to be slower than that of 2-octanol. Our expectations were met: chlorination was achieved in 93% yield with 2.5 mol % catalyst and 77% yield with just 1 mol % of catalyst.

In a second series of experiments catalysts **1a** and **1c** were examined with varying addition times and different catalyst loadings (Table 8). As can be seen, decreasing the addition time resulted in a reduction in yield with both catalysts; however, catalyst **1c** provided superior results. For example, chlorination of decanol over 3 h with **1a** afforded a 77% yield, while the same reaction with **1c** gave a much-improved 95% (entries 3 and 7). In the case of 2-octanol yields of 48% and 82% were obtained for reactions carried out over 1 h with catalyst **1a** and **1c**, respectively (entries 12 and 20). These results clearly indicate the superiority of catalyst **1c** with respect to reaction addition times.

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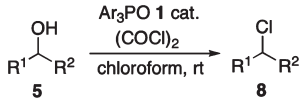
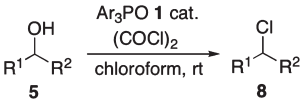
Table 7. Comparison of Phosphine Oxide Catalysts at Different Loadings in Catalytic Chlorination[a]



entry	substrate	catalyst	loading, mol %	yield of **8**, %[b]
1	**5a**	**1a** Ar = Ph	15	94
2	**5a**	**1a** Ar = Ph	10	86
3	**5a**	**1a** Ar = Ph	5	74
4	**5a**	**1a** Ar = Ph	2.5	42
5	**5a**	**1c** Ar = 4-fluorophenyl	15	(94)
6	**5a**	**1c** Ar = 4-fluorophenyl	10	91
7	**5a**	**1c** Ar = 4-fluorophenyl	5	81
8	**5a**	**1c** Ar = 4-fluorophenyl	2.5	45
9	**5a**	**1b** Ar = 2-pyridyl, Ph, Ph	15	53
10	**5c**	**1a** Ar = Ph	15	97
11	**5c**	**1a** Ar = Ph	10	93
12	**5c**	**1a** Ar = Ph	5	92
13	**5c**	**1a** Ar = Ph	3	82
14	**5c**	**1c** Ar = 4-fluorophenyl	15	94
15	**5c**	**1c** Ar = 4-fluorophenyl	10	94
16	**5c**	**1c** Ar = 4-fluorophenyl	5	88
17	**5c**	**1c** Ar = 4-fluorophenyl	3	85
18	**5t**	**1a** Ar = Ph	2.5	93
19	**5t**	**1a** Ar = Ph	1	77

[a] Chloroform solutions of the substrate (1 equiv) and $(COCl)_2$ (1.2 × [1-catalyst loading] equiv) were added simultaneously to a solution of Ar_3PO (amount indicated) and $(COCl)_2$ (1.2 × catalyst loading equiv) in chloroform over 7 h at rt. [b] Yield determined by ^1H NMR spectroscopy using $Cl_2CHCHCl_2$ as an internal standard; isolated yields in parentheses.

Table 8. Comparison of Phosphine Oxide Catalysts and Different Addition Times in Catalytic Chlorination[a]



entry	alcohol	catalyst	loading, mol %	addition time, h	yield of **8**, %[b]
1	**5a**	**1a** Ar = Ph	15	7	94
2	**5a**	**1a** Ar = Ph	15	5	86
3	**5a**	**1a** Ar = Ph	15	3	77
4	**5a**	**1a** Ar = Ph	15	1	36
5	**5a**	**1c** Ar = 4-fluorophenyl	15	7	94
6	**5a**	**1c** Ar = 4-fluorophenyl	15	5	95
7	**5a**	**1c** Ar = 4-fluorophenyl	15	3	95
8	**5a**	**1c** Ar = 4-fluorophenyl	15	1	49
9	**5c**	**1a** Ar = Ph	15	7	97
10	**5c**	**1a** Ar = Ph	15	5	92
11	**5c**	**1a** Ar = Ph	15	3	85
12	**5c**	**1a** Ar = Ph	15	1	48
13	**5c**	**1a** Ar = Ph	5	7	92
14	**5c**	**1a** Ar = Ph	5	5	74
15	**5c**	**1a** Ar = Ph	5	3	50
16	**5c**	**1a** Ar = Ph	5	1	22
17	**5c**	**1c** Ar = 4-fluorophenyl	15	7	94
18	**5c**	**1c** Ar = 4-fluorophenyl	15	5	92
19	**5c**	**1c** Ar = 4-fluorophenyl	15	3	89
20	**5c**	**1c** Ar = 4-fluorophenyl	15	1	82

[a] Chloroform solutions of the substrate (1 equiv) and $(COCl)_2$ (1.2 × [1-catalyst loading] equiv) were added simultaneously to a solution of Ar_3PO (amount indicated) and $(COCl)_2$ (1.2 × catalyst loading equiv) in chloroform over the time indicated at rt. [b] Yield determined by ^1H NMR spectroscopy using $Cl_2CHCHCl_2$ as an internal standard; isolated yields in parentheses.

Clearly, a low loading and short addition time would be desirable, and to this end, we examined reactions of 2-octanol run with 5 mol % **1a** with varying addition times. Entry 14 indicates that a good (74%) yield was obtained with a relatively short addition time and low catalyst loading.

Having developed improved protocols for catalytic chlorination, we revisited catalytic bromination reactions of decanol and 2-octanol (Table 9) to see if catalyst loading could be decreased and if improvements could be realized here with catalyst **1c**.

In the case of decanol and catalyst **1a** we were unable to reduce the catalyst loading below 15 mol % and maintain an acceptable yield (entries 2 and 3). However, as expected, the secondary alcohol was a better substrate, and the loading of **1a** could be decreased to 5 mol % while maintaining a reasonable 60% yield of bromide product (entry 6). Finally, we evaluated the fluorinated catalyst **1c** in the bromination of decanol at loadings of 15 and 10 mol % (entries 7 and 8). At 15 mol % chloride **8c** was formed in addition to the bromide product, while at 10 mol % no chloride was formed but the yield of bromide **11c** was not acceptable. A range of other bromination experiments were conducted with this catalyst; however, in contrast to the chlorination reactions, we were unable to realize an improved protocol.

We now summarize the results of our studies on catalyst structure, catalyst loading, and addition time: (a) The Arbuzov reaction of decanol with stoichiometric chlorophosphonium salts derived from a variety of alkyl and aryl phosphine oxides provided a convenient means to screen potential catalysts. the very slow Arbuzov collapse of alkyl alkoxyphosphonium chlorides rule these species out; however, other triarylphosphine oxides were identified as viable catalysts. (b) The catalyst loading and the addition time can be lowered compared to the original protocol, resulting in more practical catalytic reactions. (c) In most cases the use of catalyst **1c** provides higher yields at a given catalyst loading and addition time for decanol and 2-octanol. (d) The benefits associated with catalyst **1c** unfortunately do not translate to the more complex catalytic bromination reactions of decanol and 2-octanol. (e) Whereas the Arbuzov reaction of alkoxyphosphonium chloride **6c** is fast, the reaction of the parent phosphine oxide **1c** with oxalyl chloride is significantly slower than that of triphenylphosphine oxide, and therefore the rate-limiting step in reactions catalyzed by **1c** may be the conversion of the phosphine oxide into the chlorophosphonium salt (**1c** → **4c**).

CONCLUSIONS

In this article we have outlined a new general strategy for catalytic phosphorus(V)-based activation and nucleophilic substitution reactions of alcohols that involves accessing phosphonium

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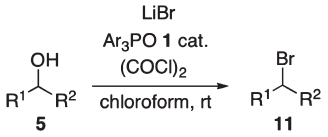
Table 9. Catalytic Bromination of Alcohols under Appel Conditions: Effect of Catalyst Structure and Loading[a]



entry	alcohol	catalyst	loading, mol %	**11** (yield, %)[b]
1	**5a**	**1a** Ar = Ph	15	**11c** (75)
2	**5a**	**1a** Ar = Ph	10	**11c** (51)
3	**5a**	**1a** Ar = Ph	5	**11c** (35)
4	**5c**	**1a** Ar = Ph	15	**11c** (77)
5	**5c**	**1a** Ar = Ph	10	**11c** (66)
6	**5c**	**1a** Ar = Ph	5	**11c** (60)
7	**5a**	**1c** Ar = 4-fluorophenyl	15	**11c** (52) **8c** (34)
8	**5a**	**1c** Ar = 4-fluorophenyl	10	**11c** (56)

[a] Chloroform solutions of the substrate (1 equiv) and $(COCl)_2$ (1.3 × [1-catalyst loading] equiv) were added simultaneously to a solution of Ar_3PO (amount indicated), LiBr (2.5 equiv), and $(COCl)_2$ (1.3 × catalyst loading equiv) in chloroform over the time indicated at rt. [b] Yield determined by ^1H NMR spectroscopy using $Cl_2CHCHCl_2$ as an internal standard.

salts with established reactivity catalytically at the expense of consumable oxalate reagents. This new mode of catalysis has been validated through the development of catalytic Appel halogenation reactions in which the halophosphonium salts responsible for chlorination and bromination are derived from catalytic phosphine oxides and stoichiometric oxalyl chloride. The new reactions, which take place at rt, represent a highly efficient and atom-economical alternative to the traditional PPh_3/CX_4 system for the chlorination and bromination unhindered primary and secondary alcohols. This work demonstrates that catalysis of reactions in which phosphine oxides are produced as byproduct is possible at rt using a cheap and low molecular weight reagent to induce phosphine oxide turnover. Finally, this study provides a platform for a range of further catalytic Mitsunobu-type C−C and C−heteroatom bond-forming reactions to be developed by adjusting the structure of the oxalate reagents used. These studies are currently in progress in our laboratory.

EXPERIMENTAL SECTION

General. Glassware was dried in an oven overnight before use. Thin layer chromatography was carried out on silica-aluminum plates, and plates were visualized using ultraviolet light (254 nm) and $KMnO_4$ solution. For flash column chromatography silica gel 60, 35−70 μm was used. NMR data was collected at either 270 or 400 MHz. All samples were analyzed in $CDCl_3$ unless otherwise stated. Reference values for residual solvent was taken as δ = 7.27 ($CDCl_3$) for ^1H NMR; δ = 77.1 ($CDCl_3$) for ^{13}C NMR. Multiplicities for coupled signals designated using the abbreviations s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sex = sextet, br = broad signal, ap = apparent and are given in Hz. ^{13}C multiplicities were assigned using a DEPT sequence. Where appropriate, COSY, HMQC, and HMBC experiments were performed to aid assignment. ^{31}P NMR was recorded with decoupling. High-resolution mass spectrometric data were quoted to four decimal places (0.1 mDa) with error limits for acceptance of ±5.0 ppm (defined as calcd/found mass 10-6). Infrared spectra were recorded on a FTIR instrument as dilute chloroform solutions. Single crystal X-ray diffraction was carried out by the X-ray crystallography department at the University of Nottingham. All solvents and reagents were used as supplied.

Determination of Yield by ^1H NMR. The crude reaction mixture was dissolved in $CDCl_3$ and transferred to a volumetric flask (two washings of the original flask were done after transfer) that was subsequently made up to the correct volume with further $CDCl_3$. To a 1 mL aliquot of this solution was added 1,1,2,2-tetrachlorethane (accurately approximately 15−80 mg). The ^1H NMR spectrum was recorded, and the mass of the product was calculated according to the equation below:

$$mass_{product} = \left(\frac{area_{product}}{area_{standard}}\right)\left(\frac{MW_{product}}{MW_{standard}}\right) \cdot mass_{standard} \cdot purityfactor_{standard} \cdot n \cdot \frac{m}{purityfactor_{alcohol}}$$

where n corrects for the amount of the crude reaction mixture used, and m corrects for the number of protons associated with the resonance used.

General Procedure 1. To a solution of triphenylphosphine oxide (42 mg, 0.15 mmol) in either $CHCl_3$ or $CDCl_3$ (1.5 mL) was added oxalyl chloride (12.0 μL, 0.142 mmol), and the reaction mixture was stirred for 5 min. The appropriate alcohol (1.00 equiv) and oxalyl chloride (73.0 μL, 0.863 mmol) as solutions in either $CHCl_3$ or $CDCl_3$ (1.0 mL) were then added simultaneously over 7 h via syringe pump at rt. The solvent was removed in vacuo. Purification by flash chromatography (silica, 5−10% Et_2O/petroleum ether) gave the pure chlorides.

General Procedure 2. To a solution of triphenylphosphine oxide (42 mg, 0.15 mmol) in either $CHCl_3$ or $CDCl_3$ (1.5 mL) was added oxalyl chloride (15.0 μL, 0.177 mmol), and the reaction mixture was stirred for 5 min. The appropriate alcohol (1.00 equiv) and oxalyl chloride (87.0 μL, 1.03 mmol) as solutions in either $CHCl_3$ or $CDCl_3$ (1.0 mL) were then added simultaneously over 7 h via syringe pump at rt. The solvent was removed in vacuo. Purification by flash chromatography (silica, 5−100% Et_2O/petroleum ether) gave the pure chlorides.

1-Chlorodecane (8a).[40] The following reagents were combined in the amounts and method indicated according to general procedure 2. Decanol (158 mg, 1.00 mmol), oxalyl chloride (102 μL, 1.21 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **8a** 166 mg, 94% by ^1H NMR. Purification by flash column chromatography (silica, 10% Et_2O/petroleum ether) afforded **8a** as a colorless oil (150 mg, 85%). ^1H NMR (400 MHz, $CDCl_3$) δ 3.55 (t, J = 6.8 Hz, 2H, C$\mathbf{H_2}$Cl), 1.79 (m, 2H, $\mathbf{H_2}$CCH$_2$Cl), 1.50−1.23 (m, 14H, 7 × C$\mathbf{H_2}$), 0.91 (t, J = 6.8, 3H, C$\mathbf{H_3}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.1, 32.7, 31.9, 29.5, 29.5, 29.3, 28.9, 26.9, 22.7, 14.1.

Benzylchloride (8b).[17] The following reagents were combined in the amounts and method indicated according to general procedure 1. Benzyl alcohol (108 mg, 1.00 mmol), oxalyl chloride (85 μL, 1.0 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **8b** 101 mg, 80% by ^1H NMR. Purification by flash column chromatography (silica, 5% Et_2O/petroleum ether) afforded **8b** as a colorless oil (53 mg, 42%). ^1H NMR (270 MHz, $CDCl_3$) δ 7.30−7.43 (m, 5H, Ar**H**), 4.62 (s, 2H, C$\mathbf{H_2}$); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ137.6, 128.9, 128.7, 128.5, 46.3.

(*S*)-2-Chlorooctane (8c).[41] The following reagents were combined in the amounts and method indicated according to general procedure 2. (*R*)-(−)-2-Octanol (130 mg, 1.00 mmol), oxalyl chloride (102 μL, 1.21 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **8c** (144 mg, 97%) by ^1H NMR. **8c** $[\alpha]^{22}_D$ +32.8 (*c* 0.58, $CHCl_3$), alcohol $[\alpha]^{22}_D$ −7.4 (*c* 0.97, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 4.03 (m, 1H, C**H**Cl), 1.71 (m, 2H, $\mathbf{H_2}$CCHCl), 1.51 (d, J = 6.6 Hz, 3H, ClCHC$\mathbf{H_3}$), 1.45−1.24 (m, 8H, 4 × C$\mathbf{H_2}$), 0.9 (t, J = 6.9 Hz, 3H, C$\mathbf{H_3}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 59.0, 40.0, 31.8, 28.9, 26.7, 25.4, 22.7, 14.1.

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(*R*)-2-Chloropropanoic Acid Ethyl Ester (8d).[42] The following reagents were combined in the amounts and method indicated according to general procedure 2. Ethyl-(*s*)-(−)-lactate (118 mg, 1.00 mmol), oxalyl chloride (102 μL, 1.21 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **8d** 130 mg, 95% by ^{1}H NMR. Purification by flash column chromatography (silica, 100% Et_2O) afforded **8d** as a colorless oil (119 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.37 (q, *J* = 7.0 Hz, 1H, ClC**H**), 4.21 (q, *J* = 7.2 Hz, 2H, $\mathbf{H_2}CCH_3$), 1.67 (d, *J* = 7.0 Hz, 3H, $\mathbf{H_3}CCHCl$), 1.29 (t, *J* = 7.2 Hz, 2H, $\mathbf{H_2}CCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 62.0, 52.6, 21.5, 14.0.

3-Phenylpropylchloride (8e).[43] The following reagents were combined in the amounts and method indicated according to general procedure 2. 3-Phenyl-1-propanol (136 mg, 1.00 mmol), oxalyl chloride (102 μL, 1.21 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **8e** 147 mg, 95% by ^{1}H NMR. Purification by flash column chromatography (silica, 5% Et_2O/petroleum ether) afforded **8e** as a colorless oil (112 g, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.28 (m, 2H, Ar**H**), 7.26−7.19 (m, 3H, Ar**H**), 3.54 (t, 2H, *J* = 6.4 Hz, $PhCH_2CH_2C\mathbf{H_2}Cl$), 2.80 (t, J= 6.4 Hz, 2H, $PhC\mathbf{H_2}CH_2CH_2Cl$), 2.10 (m, 2H, $PhCH_2C\mathbf{H_2}CH_2Cl$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7, 128.7, 128.6, 126.2, 44.2, 34.1, 32.8.

1-Chloro-2-decyne (8f).[43] The following reagents were combined in the amounts and method indicated according to general procedure 2. 2-Deyn-1-ol (154 mg, 1.00 mmol), oxalyl chloride (102 μL, 1.21 mmol), triphenylphosphine oxide (42.0 mg, 0.15 mmol). Gave **8f** 147 mg, 85% by ^{1}H NMR. Purification by flash column chromatography (silica, 5% Et_2O/petroleum ether) afforded **8f** as a colorless oil (142 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.15 (t, *J* = 2.4 Hz, 2H, $CCC\mathbf{H_2}Cl$), 2.22 (m, 2H, $H_2CC\mathbf{H_2}CC$), 1.50 (m, 2H, $H_2CC\mathbf{H_2}CH_2CC$), 1.44−1.22 (m, 8H, 4 × $C\mathbf{H_2}$), 0.91 (t, *J* = 6.8 Hz, 3H, $C\mathbf{H_3}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 87.8, 75.0, 31.8, 31.4, 28.9, 28.9, 28.5, 22.7, 18.9, 14.2.

1-Chloro-2-butene (8g).[44] The following reagents were combined in the amounts and method indicated according to general procedure 1. 2-buten-1-ol (72 mg, 1.00 mmol), oxalyl chloride (85 μL, 1.0 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **8g** 64 mg, 70% by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.80 (m, 1H, H_3C-$CHC\mathbf{H}CH_2Cl$), 5.64 (m, 1H, $H_3CC\mathbf{H}CHCH_2Cl$), 4.02 (dt, *J* = 7.0 and 0.9 Hz, 2H, $C\mathbf{H_2}Cl$), 1.73 (m, 3H, $C\mathbf{H_3}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 130.1, 129.1, 45.4, 17.7.

2-Chloro-1-octene (8h).[45] The following reagents were combined in the amounts and method indicated according to general procedure 1. 1-Octene-3-ol (128 mg, 1.00 mmol), oxalyl chloride (85 μL, 1.0 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **8h** (94 mg, 64%) by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89 (ddd, *J* =17.0 Hz, 10.1 and 7.3 Hz, 1H, $H_2CC\mathbf{H}CHCl$), 5.26 (d, *J* = 17.0 Hz, 1H, $\mathbf{H_2}CC$-$HCHCl$), 5.13 (d, *J* = 10.1 Hz, 1H, $\mathbf{H_2}CCHCHCl$), 4.34 (m, 1H, ClC**H**), 1.87−1.74 (m, 2H, $ClCHC\mathbf{H_2}CH_2$), 1.61−1.10 (m, 6H, 3 × $C\mathbf{H_2}$), 0.91 (t, *J* = 6.8 Hz, 3H, $C\mathbf{H_3}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 114.4, 63.2, 45.5, 31.2, 26.1, 22.6, 14.0. Also gave 1-chloro-2-octene (25 mg, 17%) by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (dt, *J* = 15.2 and 7.1 Hz, 1H, $ClCH_2C\mathbf{H}$), 5.62 (m, 1H, $ClCH_2CHC\mathbf{H}$), 4.04 (dd, *J* = 7.1 and 0.8 Hz, 2H, $ClC\mathbf{H_2}CH$), 2.06 (dt, *J* = 7.1 and 6.8 Hz, 2H, $ClCH_2CHCHC\mathbf{H_2}$), 1.42−1.28 (m, 6H, $C\mathbf{H_2}C\mathbf{H_2}C\mathbf{H_2}CH_3$), 0.88 (t, *J* = 6.4 Hz, 3H, $C\mathbf{H_3}$); ^{13}C NMR (100 MHz, $CDCl_3$)δ 136.4, 125.9, 45.6, 32.1, 31.4, 28.6, 22.6, 14.0.

Cinnamylchloride (8i).[17] The following reagents were combined in the amounts and method indicated according to general procedure 1. Cinnamyl alcohol (134 mg, 1.00 mmol), oxalyl chloride (85 μL, 1.0 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **8i** 134 mg, 88% by ^{1}H NMR. Purification by flash column chromatography (silica, 5% Et_2O/petroleum ether) afforded **8i** as a colorless oil (106 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.49 (m, 5H, Ar**H**), 6.69 (d, *J* = 15.6 Hz, 1H, PhC**H**CH), 6.36 (dt, *J* = 15.6 and 7.2 Hz, 1H, $\mathbf{H}CCH_2Cl$), 4.28 (dd, *J* = 7.2 Hz, 2H, $C\mathbf{H_2}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4, 134.2, 128.7, 128.5, 126.7, 125.0, 45.5.

Diphenylmethyl Chloride (8j).[46] The following reagents were combined in the amounts and method indicated according to general procedure 1. Diphenyl methanol (184 mg, 1.00 mmol), oxalyl chloride (85 μL, 1.0 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **8j** 195 mg, 96% by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.29 (m, 6H, Ar**H**), 7.47−7.42 (m, 4H, Ar**H**), 6.17 (s, 1H, C**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.1, 128.6, 128.1, 127.8, 64.3.

2-Cyclohexenyl Chloride (8k).[17] The following reagents were combined in the amounts and method indicated according to general procedure 1. Cyclohexanol (98.1 mg, 1.00 mmol), oxalyl chloride (85 μL, 1.0 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **8k** 103 mg, 88% by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.91−5.85 (m, 1H, HC=C**H**CHCl), 5.85−5.79 (m, 1H, **H**C=CHCHCl), 4.62 (m, 1H, HC=CHC**H**Cl), 2.18−1.97 (m, 4H, $\mathbf{H_2}CCH_2C\mathbf{H_2}CH$=CH), 1.96−1.85 (m, 1H, $H_2CC\mathbf{H_2}CH_2CH$=CH), 1.70−1.61 (m, 1H, $H_2CC\mathbf{H_2}CH_2CH$=CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.4, 128.1, 55.6, 32.5, 24.7, 18,4.

3*β*-Chloro-5-cholestene (8l).[47] The following reagents were combined in the amounts and method indicated according to general procedure 1. Cholesterin (193 mg, 0.499 mmol), oxalyl chloride (42 μL, 0.50 mmol), triphenylphosphine oxide (21 mg, 0.075 mmol). Gave **8l** (156 mg, 81%) by ^{1}H NMR. Purification by flash column chromatography (silica, 5% Et_2O/petroleum ether) followed by recrystallization (EtOAc/petroleum ether) afforded **8l** as a white solid (128 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.38 (m, 1H), 3.77 (m, 1H), 2.62−2.46 (m, 2H), 2.11−1.79 (m, 6H), 1.64−0.83 (m, 32H), 0.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.9, 122.6, 60.5, 56.9, 56.8, 50.2, 43.6, 42.5, 39.9,39.7, 39.2, 36.5, 36.3, 36.0, 33.5, 32.0, 31.9, 28.4, 28.1, 24.4, 24.0, 23.0, 22.7, 21.1, 19.4, 18.9, 12.0.

(1-Chloroethyl)benzene (8m).[17] The following reagents were combined in the amounts and method indicated according to general procedure 2. 1-Phenylethyl alcohol (122 mg, 1.00 mmol,) oxalyl chloride-(102 μL, 1.21 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **8m** 138 mg, 98% by ^{1}H NMR. Purification by flash column chromatography (silica, 5% Et_2O/petroleum ether) afforded **8m** as a colorless oil (134 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47−7.30 (m, 5H, Ar**H**), 5.12 (q, *J* = 6.7 Hz, 1H, C**H**Cl), 1.88 (d, *J* = 6.7 Hz, 3H, $C\mathbf{H_3}$); ^{13}C NMR (100 MHz, $CDCl_3$); δ 142.9, 128.7, 128.3, 126.6, 58.8, 26.6.

(*R*)-(1-Chloroethyl)benzene (8m).[17] To a solution of triphenylphosphine oxide (42 mg, 0.15 mmol) in EtOAc (1.5 mL) was added oxalyl chloride (15.0 μL, 0.177 mmol), and the reaction mixture was stirred for 5 min. (*S*)-1-Phenylethyl alcohol (122 mg, 1.00 mmol) and oxalyl chloride (87.0 μL, 1.03 mmol) as solutions in EtOAc (1.0 mL) were then added simultaneously over 7 h via syringe pump at rt. The solvent was removed in vacuo. Gave **8m** 121 mg, 86% by ^{1}H NMR.

***tert*-Butyl Chloride (8q).**[48] The following reagents were combined in the amounts and method indicated according to general procedure 1. *tert*-Butyl chloride (74.1 mg, 1.00 mmol), oxalyl chloride (85 μL, 1.0 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **8q** (34 mg, 37%) by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.62 (s, 9H, $CCl(C\mathbf{H_3})_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 67.6, 34.5.

5-(Benzyloxy)pentan-1-ol (5r).[49] A solution of pentane-1,5-diol (1.57 mL, 15.0 mmol) in THF (5 mL) was added dropwise to a suspension of NaH (600 mg, 15.0 mmol, 60% in oil) in THF (15 mL) at 0 °C, and the mixture was stirred at 0 °C for 30 min. Then a solution of benzyl chloride (0.584 mL, 5.00 mmol) in THF (5 mL) was added dropwise, and the mixture was stirred at rt for 16 h. The reaction mixture was diluted with EtOAc (60 mL). The organic layer was washed with water (5 × 30 mL), brine (2 × 30 mL), dried over $MgSO_4$, and filtered. The solvent was removed in vacuo. Purification by flash column chromatography (silica, 40% EtOAc/petroleum ether) afforded **5r** as a

colorless oil (463 mg, 48%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.28 (m, 5H, Ar**H**), 4.54 (s, 2H, C**H$_2$**Ph), 3.66 (t, J = 6.5 Hz, 2H, C**H$_2$**OH), 3.52 (t, J = 6.5 Hz, 2H, C**H$_2$**OCHPh), 1.73−1.57 (m, 4H, OHCH$_2$C**H$_2$**C**H$_2$**), 1.53−1.44 (m, 2H, C**H$_2$**CH$_2$OCH$_2$Ph); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 128.4, 127.7, 127.6, 73.0, 70.4, 62.8, 32.6, 29.5, 22.5.

((5-Chloropentyloxy)methyl)benzene (8r).[50] To a solution of triphenylphosphine oxide (21 mg, 0.075 mmol) in $CDCl_3$ (0.75 mL) was added oxalyl chloride (7.5 μL, 0.089 mmol), and the reaction mixture was stirred for 5 min. **5r** (97 mg, 0.050 mmol) and oxalyl chloride (43.5 μL, 0.514 mmol) as solutions in $CDCl_3$ (0.5 mL) were then added simultaneously over 7 h via syringe pump at rt. The solvent was removed in vacuo. Gave **8r** 94 mg, 88% by ^{1}H NMR. Purification by flash chromatography (silica, 10% Et_2O/petroleum ether) afforded **8r** as a white solid (70 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.26 (m, 5H, Ar**H**), 4.52 (s, 2H, C**H$_2$**Ph), 3.55 (t, J = 6.7 Hz, 2H, C**H$_2$**Cl), 3.50 (t, J = 6.3 Hz, 2H, C**H$_2$**OCHPh), 1.86−1.77 (m, 2H, ClCH$_2$-C**H$_2$**CH$_2$), 1.71−1.62 (m, 2H, ClCH$_2$CH$_2$CH$_2$C**H$_2$**), 1.61−1.50 (m, 2H, ClCH$_2$CH$_2$C**H$_2$**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 128.4, 127.7, 127.6, 73.0, 70.1, 45.0, 32.5, 29.1, 23.7.

Decyloxytriethylsilane (5s).[51] To a solution of decanol (791 mg, 5.00 mmol) in DCM (25 mL) at 0 °C was added imidazole (1.36 g, 20.0 mmol), followed by TESCl (1.70 mL, 10.0 mmol). The mixture was stirred for 1.5 h at 0 °C and 1 h at rt. Then Et_2O (100 mL) was added, and the organic layer was washed with water (3 × 50 mL) and brine (50 mL), dried over $MgSO_4$, and filtered. The solvent was removed in vacuo. Purification by flash chromatography (silica, 10% EtOAc/petroleum ether) gave **5s** as a colorless oil (1.03 g, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 (t, J = 6.8 Hz, 2H, C**H$_2$**OTES), 1.53 (m, 2H, **H$_2$**CCH$_2$OTES), 1.37−1.20 (m, 14H, 7 × C**H$_2$**), 0.97 (t, J = 7.9 Hz, 9H, Si(CH$_2$C**H$_3$**)$_3$), 0.89 (t, J = 6.9 Hz, 3H, C**H$_3$**), 0.61 (q, J = 7.9 Hz, 6H, Si(C**H$_2$**CH$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 63.1, 33.1, 32.0, 29.8, 29.7, 29.6, 29.4, 25.9, 22.8, 14.2, 6.9, 4.5.

1-Chlorodecane (8a).[40] To a solution of triphenylphosphine oxide (7.0 mg, 0.025 mmol) in $CDCl_3$ (0.75 mL) was added oxalyl chloride (3.0 μL, 0.035 mmol), and the reaction mixture was stirred for 5 min. Decyloxytriethylsilane **5s** (136 mg, 0.499 mmol) and oxalyl chloride (48.0 μL, 0.567 mmol) as solutions in $CDCl_3$ (0.5 mL) were then added simultaneously over 7 h via syringe pump at rt. Gave **8a** 79 mg, 89% by ^{1}H NMR.

Triethyl(octan-2-yloxy)silane (5t).[52] To a solution of 2-octanol (651 mg, 5.00 mmol) in DCM (25 mL) at 0 °C was added imidazole (1.36 g, 20.0 mmol), followed by TESCl (1.70 mL, 10.0 mmol). The mixture was stirred for 1.0 h at 0 °C and 16 h at rt. Then Et_2O (100 mL) was added, and the organic layer was washed with water (3 × 50 mL) and brine (50 mL), dried over $MgSO_4$, and filtered. The solvent was removed in vacuo. Purification by flash chromatography (silica, 10% EtOAc/petroleum ether) gave **5t** as a colorless oil (0.91 g, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (m, 1H, C**H**OTES), 1.52−1.20 (m, 10H, 5 × C**H$_2$**), 1.14 (d, J = 6.1 Hz, 3H, ClCHC**H$_3$**), 0.97 (t, J = 7.9 Hz, 9H, Si(CH$_2$C**H$_3$**)$_3$), 0.89 (t, J = 6.8 Hz, 3H, C**H$_3$**), 0.60 (q, J = 7.9 Hz, 6H, Si(C**H$_2$**CH$_3$)$_3$; ^{13}C NMR (100 MHz, $CDCl_3$) δ 68.6, 39.9, 32.0, 29.5, 25.9, 23.9, 22.7, 14.2, 7.0, 5.0

(±)-2-Chlorooctane (8c).[43] To a solution of triphenylphosphine oxide (14 mg, 0.50 mmol) in $CDCl_3$ (1.5 mL) was added oxalyl chloride (5.0 μL, 0.059 mmol), and the reaction mixture was stirred for 5 min. Triethyl(octan-2-yloxy)silane **5t** (244 mg, 0.998 mmol) and oxalyl chloride (97.0 μL, 1.15 mmol) as solutions in $CDCl_3$ (1.0 mL) were then added simultaneously over 7 h via syringe pump at rt. Gave **8c** 147 mg, 99% by ^{1}H NMR.

5-(*tert*-Butyldiphenylsilyloxy)pentan-1-ol (5u).[53] TBDPSCl (2.60 mL, 10.0 mmol) was added to a cooled (−25 °C) solution of pentane-1,5-diol (2.62 mL, 25.0 mmol) and imidazole (1.36 g, 20.0 mmol) in DMF (10 mL) over 1 h via syringe pump. Then the mixture was warmed to 0 °C and stirred for 6 h. The reaction mixture was diluted with Et_2O (50 mL), washed with water (6 × 50 mL), dried over $MgSO_4$, and filtered. The solvent was removed in vacuo. Purification by flash chromatography (silica, 33% EtOAc/petroleum ether) gave **5u** as colorless oil (1.75 g, 51%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71−7.65 (m, 4H, Ar**H**), 7.46−7.36 (m, 6H, Ar**H**), 3.69 (t, J = 6.4 Hz, 2H, C**H$_2$**OH), 3.63 (t, J = 6.4 Hz, 2H, C**H$_2$**OTBDPS), 1.65−1.52 (m, 4H, CH$_2$C**H$_2$**CH$_2$C**H$_2$**CH$_2$), 1.48−1.39 (m, 2H, CH$_2$CH$_2$C**H$_2$**-CH$_2$CH$_2$), 1.06 (s, 9H, C(C**H$_3$**)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.7, 134.2, 129.6, 127.7, 63.9, 63.1, 32.5, 32.3, 27.0, 22.1, 19.3.

***tert*-Butyl (5-Chloropentyloxy)diphenylsilane (8u).**[54] To a solution of triphenylphosphine oxide (42 mg, 0.15 mmol) in $CDCl_3$ (1.5 mL) was added oxalyl chloride (15.0 μL, 0.177 mmol), and the reaction mixture was stirred for 5 min. Then 1.0 mL of a solution of 5-(*tert*-butyldiphenylsilyloxy)pentan-1-ol **5u** (343 mg, 1.00 mmol) and 2,6-di-*tert*-butyl pyridine (344 mg, 1.80 mmol) in $CDCl_3$ and 1.0 mL of a solution of oxalyl chloride (87.0 μL, 1.03 mmol) in $CDCl_3$ were added via syringe pump over 7 h at rt. The solvent was removed in vacuo. Gave **8u** 231 mg, 64% by ^{1}H NMR. Purification by flash chromatography (silica, 17% Et_2O/petroleum ether) gave **8u** as a colorless oil (208 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73−7.69 (m, 4H, Ar**H**), 7.49−7.39 (m, 6H, Ar**H**), 3.71 (t, J = 6.1 Hz, 2H, C**H$_2$**Cl), 3.54 (t, J = 6.7 Hz, 2H, C**H$_2$**OTBDPS), 1.79 (m, 2H, ClCH$_2$CH$_2$-CH$_2$C**H$_2$**CH$_2$), 1.66−1.51 (m, 2H, ClCH$_2$CH$_2$C**H$_2$**C**H$_2$**CH$_2$), 1.10 (s, 9H, C(C**H$_3$**)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.6, 134.1, 129.6, 127.7, 63.6, 45.1, 32.4, 31.8, 27.0, 23.3, 19.3.

***N*-(2-hydroxyethyl)benzamide (5v).**[55] To a solution of ethanolamine (4.55 mL, 75.0 mmol) and triethylamine (15.7 mL, 113 mmol) in DCM (75 mL) was added benzoyl chloride (4.35 mL, 37.5 mmol) via syringe pump over 1 h, and the mixture was stirred at rt for another 0.5 h. The reaction mixture was then hydrolyzed with water (50 mL), and the aqueous phase was extracted with DCM (3 × 50 mL). The combined organic phase was dried over $MgSO_4$ and filtered. The solvent was removed in vacuo, and the crude product was crystallized (EtOAc/Et_2O), affording **5v** as a white crystal (4.82 g, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80−7.74 (m, 2H, Ar**H**), 7.52−7.46 (m, 1H, Ar**H**), 7.43−7.37 (m, 2H, Ar**H**), 6.90 (br, 1H, N**H**), 3.84−3.77 (m, 2H, C**H$_2$**NH), 3.64−3.56 (m, 2H, C**H$_2$**OH), 3.00 (br, 1H, O**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 134.2, 131.7, 128.6, 127.1, 62.2, 42.9.

***N*-(2-chloroethyl) Benzamide (8v).**[56] The following reagents were combined in the amounts and method indicated according to general procedure 1. *N*-(2-Hydroxyethyl)benzamide **5v** (165 mg, 0.995 mmol), oxalyl chloride (85.0 μL, 1.00 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Purification by flash column chromatography (silica, 50% EtOaC/petroleum ether) afforded **8v** as a white solid (115 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83−7.77 (m, 2H, Ar**H**), 7.55−7.49 (m, 1H, Ar**H**), 7.48−7.41 (m, 2H, Ar**H**), 6.70 (br, 1H, N**H**), 3.84−3.77 (m, 2H, C**H$_2$**NH), 3.76−3.71 (m, 2H, C**H$_2$**Cl); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 134.2, 131.9, 128.7, 127.0, 44.3, 41.7.

(*S*)-3,3,8,8-Tetraethyl-5-phenyl-4,7-dioxa-3,8-disiladecane (5w). Styrene (573 μL, 5.00 mmol) was added to a cooled (0 °C) suspension of AD-mix-α (7.00 g) in *t*BuOH/H_2O (25 mL/25 mL) at once, and the heterogeneous slurry was stirred vigorously at 0 °C for 6 h. While the mixture was stirred at 0 °C, solid sodium sulfite (7.5 g) was added, and the mixture was allowed to warm to room temperature and stirred for 16 h. Ethyl acetate (50 mL) was added to the reaction mixture, and after separation of the layers, the aqueous phase was further extracted with ethyl acetate (3 × 25 mL). The combined organic extracts were dried over $MgSO_4$ and filtered. The solvent was removed in vacuo. Purification by flash chromatography (silica, 50% EtOAc/petroleum ether) gave (*S*)-1-phenylethane-1,2-diol as a white solid (658 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.29 (m, 5H, Ar**H**), 4.84 (dd, J = 8.1 and 3.6 Hz, 1H, PhC**H**OH), 3.79 (dd, J = 11.3 and 3.6 Hz, 1H, C**H$_2$**OH), 3.68 (dd, J = 11.3 and 8.1 Hz, 1H, C**H$_2$**OH);

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^{13}C NMR (100 MHz, $CDCl_3$). δ 140.6, 128.7, 128.1, 126.1, 74.8, 68.2. To a solution of (*S*)-1-phenylethane-1,2-diol (207 mg, 1.50 mmol) in DCM (5 mL) at 0 °C was added imidazole (613 mg, 9.00 mmol), followed by TESCl (766 μL, 4.50 mmol). The mixture was stirred for 2.0 h at 0 °C and 16 h at rt. Then Et_2O (20 mL) was added, and the organic layer was washed with water (4 × 10 mL) and brine (10 mL), dried over $MgSO_4$, and filtered. The solvent was removed in vacuo. Purification by flash chromatography (silica, 10% EtOAc/petroleum ether) gave **5w** as a colorless oil (502 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.22 (m, 5H, Ar**H**), 4.72 (dd, *J* = 7.1 and 5.1 Hz, 1H, PhC**H**OTES), 3.69 (dd, *J* = 10.2 and 7.1 Hz, 1H, C$\mathbf{H}_2$OTES), 3.57 (dd, *J* = 10.2 and 5.1 Hz, 1H, C$\mathbf{H}_2$OTES), 0.95−0.88 (m, 18H, 2 × Si($CH_2C\mathbf{H}_3$)$_3$), 0.61−0.51 (m. 12H, 2 × Si($C\mathbf{H}_2CH_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$). δ 142.9, 128.0, 127.3, 126.5, 76.0, 69.6, 6.8, 6.8, 4.9, 4.4; IR ν_{max} ($CHCl_3$) 2957, 2912, 2877, 1492, 1241, 1124, 1098, 1075, 1006, 962 cm^{-1}; HRMS (EI+) $C_{20}H_{38}NaO_2Si_2$ calcd 389.2303, found 389.2302.

(*R*)-(1,2-Dichloroethyl)benzene (8w).[15] To a solution of triphenylphosphine oxide (21 mg, 0.075 mmol) in $CDCl_3$ (0.75 mL) was added oxalyl chloride (8.0 μL, 0.095 mmol), and the reaction mixture was stirred for 5 min. **5w** (183 mg, 0.499 mmol) and oxalyl chloride (94.0 μL, 1.11 mmol) as solutions in $CDCl_3$ (0.5 mL) were then added simultaneously over 7 h via syringe pump at rt. Gave **8w** 60 mg, 68% by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.35 (m, 5H, Ar**H**), 5.02 (dd, *J* = 7.9 and 6.5 Hz, 1H, PhC**H**Cl), 4.01 (dd, *J* = 11.3 and 6.5 Hz, 1H, C$\mathbf{H}_2$Cl), 3.94 (dd, *J* = 11.3 and 7.9 Hz, 1H, C$\mathbf{H}_2$Cl); ^{13}C NMR (100 MHz, $CDCl_3$). δ 138.1, 129.2, 128.9, 127.5, 61.8, 48.4.

1,8-Dichlorooctane (8x).[57] To a solution of triphenylphosphine oxide (42 mg, 0.15 mmol) in $CDCl_3$ (1.5 mL) was added oxalyl chloride (15.0 μL, 0.177 mmol), and the reaction mixture was stirred for 5 min. **5x** (73 mg, 0.499 mmol) as a solution in THF (1.0 mL) and oxalyl chloride (87.0 μL, 1.03 mmol) as solution in $CDCl_3$ (1.0 mL) were then added simultaneously over 7 h via syringe pump at rt. The solvent was removed in vacuo. Purification by flash chromatography (silica, 100% petroleum ether) afforded **8x** as a colorless oil (65 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.54 (t, *J* = 6.8 Hz, 4H, 2 × C$\mathbf{H}_2$Cl), 1.78 (m, 4H, 2 × ClCH_2C$\mathbf{H}_2$), 1.45 (m, 4H, 2 × ClCH_2CH_2C$\mathbf{H}_2$), 1.34 (m, 4H, 2 × ClCH_2CH_2CH_2C$\mathbf{H}_2$); ^{13}C NMR (100 MHz, $CDCl_3$). δ 45.2, 32.6, 28.8, 26.8.

Synthesis of Bromides

General Procedure 3. To a solution of triphenylphosphine oxide (42 mg, 0.15 mmol) in either $CHCl_3$ or $CDCl_3$ (1.5 mL) were added oxalyl chloride (16.5 μL, 0.195 mmol) and LiBr (130−304 mg, 1.50−3.50 mmol), and the reaction mixture stirred for 5 min. The appropriate alcohol (1.00 equiv) and oxalyl chloride (93.5 μL, 1.11 mmol) as solutions in either $CHCl_3$ or $CDCl_3$ (1.0 mL) were then added simultaneously over 5 h via syringe pump at rt. The reaction mixture was filtered. The solvent was removed in vacuo. Further purification by flash chromatography (silica, 5−10% Et_2O/petroleum ether) gave the pure bromides.

General Procedure 4. To a solution of triphenylphosphine oxide (42 mg, 0.15 mmol) in either $CHCl_3$ or $CDCl_3$ (1.5 mL) was added oxalyl bromide (14 μL, 0.15 mmol), and the reaction mixture stirred for 5 min. The appropriate alcohol (1.00 equiv) and oxalyl bromide (80 μL, 0.85 mmol) as solutions in either $CHCl_3$ or $CDCl_3$ (1.0 mL) were then added simultaneously over 7 h via syringe pump at rt. The solvent was removed in vacuo. Further purification by flash chromatography (silica, 5−10% Et_2O/petroleum ether) gave the pure bromides.

1-Bromodecane (11a).[58] The following reagents were combined in the amounts and method indicated according to general procedure 4. Decanol (158 mg, 1.00 mmol), oxalyl bromide (94 μL, 1.0 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **11a** 106 mg, 48% by ^{1}H NMR. Purification by flash column chromatography (silica, 5% Et_2O/petroleum ether) afforded **11a** as a colorless oil (52 mg, 24%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.40 (t, *J* = 6.9 Hz, 2H, BrC$\mathbf{H}_2$), 1.86 (m, 2H, $\mathbf{H}_2$CCH_2Br),1.48−1.20 (m,14 H, 7 × C$\mathbf{H}_2$), 0.89 (t, *J* = 6.9 Hz, 3H, C$\mathbf{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.0, 32.9, 31.9, 29.5, 29.5, 29.3, 28.8,28.2, 22.7, 14.1.

1-Bromodecane (11a).[58] The following reagents were combined in the amounts and method indicated according to general procedure 3. Decanol (158 mg, 1.00 mmol), oxalyl chloride (110 μL, 1.30 mmol), LiBr (217 mg, 2.50 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **11a** 166 mg, 75% by ^{1}H NMR. Purification by flash column chromatography (silica, 5% Et_2O/petroleum ether) afforded **11a** as a colorless oil (135 mg, 61%).

1-Bromomethylbenzene (11b).[59] The following reagents were combined in the amounts and method indicated according to general procedure 3. Benzyl alcohol (108 mg, 1.00 mmol), oxalyl chloride (110 μL, 1.30 mmol), LiBr (261 mg, 3.01 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **11b** 121 mg, 71% by ^{1}H NMR. Purification by flash column chromatography (silica, 5% Et_2O/petroleum ether) afforded **11b** as a colorless oil (84 mg, 49%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.30 (m, 5H, Ar**H**), 4.52 (s,2H, C$\mathbf{H}_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 129.1, 128.9, 128.5, 33.6.

(*S*)-2-Bromooctane (11c).[59] The following reagents were combined in the amounts and method indicated according to general procedure 3 (the alcohol and oxalyl chloride was added over 7 h). (*R*)-(−)-2-Octanol (130 mg, 1.00 mmol), oxalyl chloride (110 μL, 1.30 mmol), LiBr (127 mg, 1.46 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **11c** 149 mg, 77% by ^{1}H NMR. **11c** $[\alpha]^{22}_D$ +38.2 (*c* 0.58, $CHCl_3$), alcohol $[\alpha]^{22}_D$ −7.42, (*c* 0.97, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.14 (m, 1H, ClC**H**), 1.89−1.73 (m, 2H, $\mathbf{H}_2$CCHCl), 1.71 (d, *J* = 6.6 Hz,3H, C$\mathbf{H}_3$), 1.57−1.24 (m, 8H, 4 × C$\mathbf{H}_2CH_3$), 0.90 (t, *J* = 6.7 Hz, 3H, C$\mathbf{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 52.1, 41.3, 31.8, 28.7, 27.8, 26.5, 22.7, 14.1.

3-Phenyl-1-bromopropane (11e).[60] The following reagents were combined in the amounts and method indicated according to general procedure 3. 3-Phenyl-1-propanol (136 mg, 1.00 mmol), oxalyl chloride (110 μL, 1.30 mmol), LiBr (200 mg, 2.30 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **11e** 133 mg, 67% by ^{1}H NMR. Purification by flash column chromatography (silica, 5% Et_2O/petroleum ether) afforded **11e** as a colorless oil (116 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.30 (m, 2H, Ar**H**), 7.27−7.20 (m, 3H, Ar**H**), 3.43 (t, *J* = 6.5 Hz, 2H, PhCH_2CH_2C$\mathbf{H}_2$Cl), 2.82 (t, *J* = 7.3 Hz, 2H, PhC$\mathbf{H}_2$CH_2CH_2Cl), 2.21 (m, 2H, PhCH_2C$\mathbf{H}_2$CH_2Cl); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 128.6, 128.6, 126.2, 34.2, 34.0, 33.1.

1-Bromodec-2-yne (11f).[61] The following reagents were combined in the amounts and method indicated according to general procedure 3. 2-Deyn-1-ol (154 mg, 1.00 mmol), oxalyl chloride (110 μL, 1.30 mmol), LiBr (217 mg, 2.50 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **11f** 163 mg, 75% by ^{1}H NMR. Purification by flash column chromatography (silica, 5% Et_2O/petroleum ether) afforded **11f** as a colorless oil (106 mg, 49%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.93 (t, *J* = 2.3 Hz, 2H, CCC$\mathbf{H}_2$Cl), 2.24 (m, 2H, H_2CC$\mathbf{H}_2$CC), 1.51 (m, 2H, H_2CC$\mathbf{H}_2$CH_2CC), 1.41−1.24 (m, 8H, 4 × C$\mathbf{H}_2CH_3$), 0.89 (t, *J* = 7.0 Hz, 3H, C$\mathbf{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 88.4, 75.3, 31.7, 28.8, 28.8, 28.4, 22.7, 19.0, 15.9, 14.1.

1-Bromo-2-butene (11g).[62] The following reagents were combined in the amounts and method indicated according to general procedure 3. 2-Buten-1-ol (72 mg, 1.0 mmol), oxalyl chloride (110 μL, 1.30 mmol), LiBr (261 mg, 3.01 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **11g** 100 mg, 73% by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.85−5.61 (m, 2H, **H**C═C**H**), 3.95 (d, *J* = 7.4 Hz, 2H, BrC$\mathbf{H}_2$), 1.74 (d, *J* = 5.9 Hz, 3H, C$\mathbf{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.5, 127.6, 33.6, 17.7.

Cinnamyl Bromide (11i).[63] The following reagents were combined in the amounts and method indicated according to general procedure 3. Cinnamyl alcohol (134 mg, 1.00 mmol), oxalyl chloride (110 μL, 1.30 mmol), LiBr (261 mg, 3.01 mmol), triphenylphosphine

oxide (42 mg, 0.15 mmol). Gave **11i** 136 mg, 69% by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.28 (m, 5H, Ar**H**), 6.68 (d, J = 15.5 Hz, 1H, PhC**H**CH), 6.44 (dt, J = 15.5 and 7.7 Hz, 1H, **H**CCH$_2$Cl), 4.19 (d, J =7.7 Hz, 2H, C**H$_2$**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5, 134.3, 128.4, 123.1, 126.5, 124.9, 33.4.

Bromocyclohexene (11k).[64] The following reagents were combined in the amounts and method indicated according to general procedure 3. Cyclohexanol (98.1 mg, 1.00 mmol), oxalyl chloride (110 μL, 1.30 mmol), LiBr (217 mg, 2.50 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **11k** 118 mg, 73% by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95−5.89 (m, 1H, HC=C**H**CHCBr), 5.85−5.79 (m, 1H, **H**C=CHCHBr), 4.85 (m, 1H, HC=CHC**H**Br), 2.28−1.61 (m, 6H, C**H$_2$**C**H$_2$**C**H$_2$**CH=CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.1, 128.9, 49.1, 32.7, 24.7, 18.6.

3β-Bromo-5-cholestene (11l).[47] To a solution of triphenylphosphine oxide (35 mg, 0.13 mmol) in $CHCl_3$ were added oxalyl chloride (14 μL, 0.17 mmol) and LiBr (109 mg, 1.26 mmol), and the reaction mixture was stirred for 5 min. Cholesterin (193 mg, 0.499 mmol) and oxalyl chloride (41 μL, 0.49 mmol) as solutions in $CHCl_3$ (1.0 mL) were then added simultaneously over 7 h via syringe pump at rt. The reaction mixture was filtered. The solvent was removed in vacuo. Gave **11l** 99 mg, 44% by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.37 (m, 1H), 3.92 (m, 1H), 2.75 (m,1H), 2.58 (m,1H), 2.20−0.85 (m, 38H), 0.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 122.4, 56.7, 56.2, 52.6, 50.2, 44.3, 42.3, 40.4, 39.7, 39.6, 36.4, 36.2, 35.8, 34.4, 31.8, 31.8, 28.3, 28.0, 24.3, 23.9, 22.9, 22.6, 20.9, 19.3, 18.8, 11.9.

1-Bromoethyl Benzene (11m).[65] The following reagents were combined in the amounts and method indicated according to general procedure 3. 1-Phenylethyl alcohol (122 mg, 1.00 mmol, oxalyl chloride (110 μL, 1.30 mmol), LiBr (217 mg, 2.50 mmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **11m** 137 mg, 74% by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48−7.28 (m, 5H, Ar**H**), 5.25 (q, J = 6.9 Hz, 1H, ClC**H**), 2.08 (d, J = 6.9 Hz, 3H, C**H$_3$**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.3, 128.7, 128.4, 126.9, 49.6, 26.9.

***tert*-Butyl Bromide (11q).**[59] The following reagents were combined in the amounts and method indicated according to general procedure 3. *tert*-Butyl chloride (74.1 mg, 1.00 mmol), oxalyl chloride (110 μL, 1.30 mmol), LiBr (217 mg, 2.50 mmmol), triphenylphosphine oxide (42 mg, 0.15 mmol). Gave **11q** 99 mg, 72% by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.80 (s, 9H, CBr(C**H$_3$**)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 63.0, 36.5.

Synthesis of Intermediates and Oxalates

Alkoxyphosphonium Salt (6a). To a solution of triphenylphosphine oxide (28 mg, 0.10 mmol) in $CDCl_3$ (0.35 mL) was added oxalyl chloride (8.8 μL, 0.10 mmol), and the reaction mixture was stirred for 5 min. Decanol (16 mg, 0.10 mmol) was then added. The NMR spectrum was acquired <2 min. ^{31}P NMR (162 MHz, $CDCl_3$) δ 61.7.

Alkoxyphosphonium Salt (6n). To a solution of triphenylphosphine oxide (139 mg, 0.499 mmol) in $CDCl_3$ (2.0 mL) was added oxalyl chloride (0.0423 mL, 0.500 mmol), and the reaction mixture was stirred for 5 min. Cyclohexanol (50.0 mg, 0.499 mmol) was then added, and the reaction mixture was stirred for 2 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89−7.69 (m, 15H, Ar**H**), 4.58 (m, $^3J_{HP}$ = 8.0 Hz, 1H, **H**CO), 1.95−1.20 (m, 10H, 5 × C**H$_2$**), ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4 (d, J = 3.1 Hz), 133.2 (d, J = 11.5 Hz), 130.6 (d, J = 13.8 Hz), 119.5 (d, J = 106.6 Hz), 84.3 (d, J = 9.2 Hz), 33.2 (d, J = 3.1 Hz), 24.2, 23.1; ^{31}P NMR (162 MHz, $CDCl_3$) δ 59.2.

Alkoxyphosphonium Salt (6p).[66] To a solution of triphenylphosphine oxide (278 mg, 1.00 mmol) in $CDCl_3$ (3.0 mL) was added oxalyl chloride (85 μL, 1.0 mmol), and the reaction mixture was stirred for 5 min. Neopentanol (88.1 mg, 1.00 mmol) was added, and the reaction mixture was stirred for 5 min. The crude reaction mixture was concentrated in vacuo, and the crude product was crystallized (MeCN/Et$_2$O), affording **4p** as white crystals. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90−7.84 (m, 3H, Ar**H**), 7.79−7.68 (m, 12H, Ar**H**), 3.89 (d, $^3J_{HP}$ = 4.4 Hz, 2H, OC**H$_2$**), 0.95 (s, 9H, CO(C**H$_3$**)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.6 (d, J = 3.1 Hz), 133.3 (d, J = 11.5 Hz), 130.7 (d, J = 13.8 Hz), 118.5 (d, J = 106.6 Hz), 80.6 (d, J = 9.2 Hz), 32.8 (d, J = 6.9 Hz), 25.9; ^{31}P NMR (162 MHz, $CDCl_3$) δ 61.9.

Decyl 2-Chloro-2-oxoacetate (9a). To a solution of oxalyl chloride (127 mg, 1.00 mmol) in $CHCl_3$ (1.5 mL) was added decanol (158 mg, 1.00 mmol) as a solution in $CHCl_3$ (1.0 mL) via syringe pump over 0.5 h. The solvent was removed in vacuo, affording chlorooxalate **9a** (229 mg, 92%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.35 (t, J = 6.8 Hz, 2H, **H$_2$**CO), 1.76 (m, 2H, **H$_2$**CCH$_2$O), 1.44−1.20 (m, 14H, 7 × C**H$_2$**), 0.88 (t, J= 6.4 Hz, 3H, C**H$_3$**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 155.9, 69.2, 31.9, 29.5, 29.5, 29.3, 29.1, 28.3, 25.7, 22.7, 14.1; IR ν_{max} ($CDCl_3$) 2909 (CH), 1780 (CO), 1467, 1378 cm^{-1}; HRMS (EI+) (of the CH_3OH derived methylesters) $C_{13}H_{24}NaO_4$ calcd 267.1567, found 267.1560.

Didecyl Oxalate (10a). To a solution of oxalyl chloride (63 mg, 0.50 mmol) in $CHCl_3$ (2.5 mL) was added decanol (158 mg, 1.00 mmol). The reaction mixture was stirred at rt for 2 h. The solvent was removed in vacuo, affording oxalate **10a** (175 mg, 94%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.30 (t, J = 6.8 Hz, 2H, **H$_2$**CO), 1.75 (m, 2H, **H$_2$**CCH$_2$O), 1.23−1.49 (m, 14H, 7 × C**H$_2$**), 0.90 (t, J = 6.9 Hz, 3H, C**H$_3$**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 67.2, 31.9, 29.6, 29.5, 29.3, 29.2, 28.3, 25.8, 22.7, 14.2; IR ν_{max} ($CDCl_3$) 2928 (CH), 1763 (CO), 1739, (CO), 1467, 1318, 1185 cm^{-1}; HRMS (EI+) $C_{22}H_{42}O_4$ calcd 370.3083, found 370.3077.

Decyl 2-Bromo-2-oxoacetate (12a). To a solution of oxalyl bromide (94 μL, 1.0 mmol) in $CHCl_3$ (1.5 mL) was added decanol (158 mg, 1.00 mmol) as a solution in $CHCl_3$ (1.0 mL) via syringe pump over 0.5 h. The solvent was removed in vacuo, affording **12a** (249 mg, 85%) as an orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.35 (t, J = 6.7 Hz, 2H, **H$_2$**CO), 1.76 (m, 2H, **H$_2$**CCH$_2$O), 1.44−1.21 (m, 14H, 7 × C**H$_2$**), 0.88 (t, J = 7.0 Hz, 3H, C**H$_3$**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 155.8, 69.3, 31.9, 29.5, 29.4, 29.3, 29.1, 28.2, 25.6, 22.7, 14.1; IR ν_{max} ($CHCl_3$) 2928 (CH), 1793 (CO), 1755 (CO),1466, 1261 cm^{-1}; HRMS (EI+) (of the CH_3OH derived methylester) $C_{13}H_{24}NaO_4$ calcd 267.1567, found 267.1560.

2-(Decyloxy)-2-oxoacetic Acid (13a). To a solution of oxalyl chloride (127 mg, 1.00 mmol) in $CHCl_3$ (1.5 mL) was added decanol (158 mg, 1.00 mmol) as a solution in $CHCl_3$ (1.0 mL) via syringe pump over 0.5 h. Water (100 μL) was then added, and the reaction mixture was stirred for 2 h. The solvent was removed in vacuo, affording **13a** (184 mg, 80%) by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.29 (t, J = 6.8 Hz, 2H, **H$_2$**CO), 1.72 (m, 2H, **H$_2$**CCH$_2$O), 1.41−1.17 (m, 14H, 7 × C**H$_2$**), 0.86 (t, J= 7.2 Hz, 3H, C**H$_3$**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 158.2, 68.0, 31.9, 29.5, 29.4, 29.3, 29.1, 28.2, 25.6, 22.7, 14.1; IR ν_{max} ($CHCl_3$) 2922 (CH), 1732 (CO), 1755 (CO),1466, 1377 cm^{-1}; HRMS (EI+) (of the CH_3OH derived methylester) $C_{13}H_{24}NaO_4$ calcd 267.1567, found 267.1560.

Benzyl 2-Chloro-2-oxoacetate (9b).[67] To a solution of oxalyl chloride (85 μL, 1.0 mmol) in $CHCl_3$ (1.5 mL) was added benzyl alcohol (108 mg, 1.00 mmol) as a solution in $CHCl_3$ (1.0 mL) via syringe pump over 0.5 h. The solvent was removed in vacuo, affording chlorooxalate **9b** (146 mg, 79%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.36 (m, 5H, Ar**H**), 5.38 (s, 2H, C**H$_2$**O); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 155.6, 133.4, 129.4, 129.0, 128.8, 70.4.

Dibenzyl Oxalate (10b)[68]. To a solution of oxalyl chloride (0.042 mL, 0.50 mmol) in $CHCl_3$ (2.5 mL) was added benzyl alcohol (108 mg, 1.00 mmol). The reaction mixture was stirred at rt for 2 h. The solvent was removed in vacuo, affording oxalate **10b** (214 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.36 (m, 10H, Ar**H**), 5.32 (s, 4H, **H$_2$**COCOCOOC**H$_2$**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 134.2, 128.9, 128.8, 128.7, 68.7.

2-(Benzyloxy)-2-oxoacetic Acid (13b).[69] To a solution of oxalyl chloride (102 μL, 1.21 mmol) in $CDCl_3$ (1.0 mL) was added benzyl alcohol (108 mg, 1.00 mmol) as a solution in $CDCl_3$ (1.0 mL) via syringe pump over 0.5 h. Water (100 μL) was then added, and the reaction mixture was stirred for 16 h. The organic phase was separated, affording **13b** (168 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ8.16 (br, 1H, COO**H**), 7.44−7.33 (m, 5H, Ar**H**), 5.31 (s, 2H, C**H**$_2$O); ^{13}C NMR (100 MHz, $CDCl_3$) δ158.7, 157.9, 133.7, 129.1, 128.9, 128.8, 69.3.

Benzyl 2-Bromo-2-oxoacetate (12b). To a solution of oxalyl bromide (113 μL, 1.20 mmol) in $CHCl_3$ (1.5 mL) was added benzyl alcohol (108 mg, 1.00 mmol) as a solution in $CHCl_3$ (1.0 mL) via syringe pump over 0.5 h. The solvent was removed in vacuo, affording bromooxalate **12b** (208 mg, 91%) as an orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47−7.40 (m, 5H, Ar**H**), 5.38 (s, 2H, **H**$_2$CO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.7, 155.6, 133.3, 129.4, 129.0, 128.8, 70.6; IR ν_{max} ($CHCl_3$) 1786 (CO), 1758 (CO),1456, 1263 cm^{-1}.

Oct-1-en-3-yl 2-Chloro-2-oxoacetate (9h). To a solution of oxalyl chloride (102 μL, 1.19 mmol) in $CHCl_3$ (1.5 mL) was added 1-octen-3-ol (128 mg, 1.00 mmol) as a solution in $CHCl_3$(1.0 mL) via syringe pump over 0.5 h. The solvent was removed in vacuo, affording chlorooxalate **9h** (146 mg, 79%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (ddd, *J* = 17.1 Hz, 10.5 Hz and 7.2 Hz, 1H, H_2CC**H**CHO), 5.41−5.28 (m, 3H, **H**$_2$CCHC**H**O), 1.86−1.66 (m, 2H, OCHC**H**$_2$), 1.43−1.24 (m, 6H, 3 × C**H**$_2$), 0.89 (t, *J* = 6.7, 3H, C**H**$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 155.2, 134.3, 119.5, 80.9, 33.8, 31.4, 24.6, 22.5, 14.0; IR ν_{max} ($CHCl_3$) 1791 (CO), 1754 (CO),1467, 1267 cm^{-1}. We were unable to determine the HRMS of either **9h** or its derived methyl ester.

5-(*tert*-Butyldiphenylsilyloxy)pentyl 2-Chloro-2-oxoacetate (9u). To a solution of oxalyl chloride (32.0 μL, 0.378 mmol) in $CHCl_3$ (0.75 mL) was added 5-(*tert*-butyldiphenylsilyloxy)pentan-1-ol **5u** (100 mg, 0.292 mmol) as a solution in $CHCl_3$ (0.75 mL) via syringe pump over 1 h. The solvent was removed in vacuo, affording **9u** (119 mg, 95%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72−7.66 (m, 4H, Ar**H**), 7.48−7.38 (m, 6H, Ar**H**), 4.36 (t, *J* = 6.7 Hz, 2H, C**H**$_2$OCO), 3.71 (t, *J* = 6.1 Hz, 2H, C**H**$_2$OTBDPS), 1.78 (m, 2H, OCOCH$_2$-C**H**$_2$CH$_2$CH$_2$CH$_2$), 1.67−1.58 (m, 2H, OCOCH$_2$CH$_2$CH$_2$C**H**$_2$CH$_2$), 1.57−1.47 (m, 2H, OCOCH$_2$CH$_2$C**H**$_2$CH$_2$CH$_2$), 1.08 (s, 9H, C-(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 155.8, 135.6, 134.0, 129.7, 127.7, 69.0, 63.4, 31.9, 28.0, 26.9, 22.1, 19.3; IR νmax ($CHCl_3$) 3011, 1788 (CO), 1758 (CO), 1272, 1111, 989 cm^{-1}. HRMS was obtained on the corresponding acid (ESI−) $C_{23}H_{29}O_5Si_1$ [M − 1]$^-$ calcd 413.1790, found 413.1808.

2-(5-(*tert*-Butyldiphenylsilyloxy)pentyloxy)-2-oxoacetic Acid (13u). To a solution of oxalyl chloride (32.0 μL, 0.378 mmol) in $CHCl_3$ (0.75 mL) was added 5-(*tert*-butyldiphenylsilyloxy)pentan-1-ol **5u** (100 mg, 0.292 mmol) as a solution in $CHCl_3$ (0.75 mL) via syringe pump over 0.5 h. Water (1.00 mL) was then added, and the reaction mixture was stirred for 2 h. The reaction mixture was diluted with EtOAc (10 mL), washed with brine (10 mL), dried over $MgSO_4$, and filtered, The solvent was removed in vacuo. Gave **13u** as a white solid (89.6 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70−7.65 (m, 4H, Ar**H**), 7.46−7.36 (m, 6H, Ar**H**), 4.31 (t, *J* = 6.7 Hz, 2H, C**H**$_2$OCO), 3.68 (t, *J* = 6.2 Hz, 2H, C**H**$_2$OTBDPS), 1.75 (m, 2H, OCOCH$_2$C**H**$_2$-CH$_2$CH$_2$CH$_2$), 1.65−1.56 (m, 2H, OCOCH$_2$CH$_2$CH$_2$C**H**$_2$CH$_2$), 1.53−1.43 (m, 2H, OCOCH$_2$CH$_2$C**H**$_2$CH$_2$CH$_2$), 1.06 (s, 9H, C-(C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 158.3, 135.6, 134.0, 129.7, 127.7, 68.0, 63.6, 32.0, 28.0, 26.9, 22.1, 19.3; IR ν_{max} ($CHCl_3$) 3446, 2933 (CH), 1802 (CO), 1737 (CO), 1187, 1111, 909 cm^{-1}; HRMS (ESI−) $C_{23}H_{29}O_5Si_1$ [M − 1]$^-$ calcd 413.1790, found 413.1808.

Synthesis of Phosphine Oxides

General Procedure 5. To a solution of phosphine (1.00 equiv) in THF (5 mL/1 mmol phosphine) was added H_2O_2 (5.00 equiv, 12% in water) via syringe pump over 30 min, and the mixture was stirred for another 2 h. The THF was removed in vacuo. The reaction mixture was diluted with water and extracted with EtOAc. The extract was dried over $MgSO_4$ and filtered. The solvent was removed in vacuo. Give pure phosphine oxide.

2-(Diphenylphosphoryl)pyridine (1b).[70] The following reagents were combined in the amounts and method indicated according to general procedure 5. Diphenyl-2-pyridyl-phosphine (1.32 g, 5.01 mmol), H_2O_2 (7.08 mL, 25.0 mmol, 12% in water). Gave **1b** 1.22 g, 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (m, 1H, Ar**H**), 8.31 (m, 1H, Ar**H**), 7.93−7.83 (m, 5H, Ar**H**), 7.56−7.37 (m,7H, Ar**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3 (d, *J* = 131.9 Hz), 150.2 (d, *J* = 19.9 Hz), 136.3 (d, *J* = 9.2 Hz), 132.2 (d, *J* = 9.2 Hz), 132.0 (d, *J* = 2.3 Hz), 132.0 (d, *J* = 103.6 Hz), 128.6, 128.5 (d, *J* = 12.3 Hz), 125.4 (d, *J* = 3.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 21.4.

Tris(4-fluorophenyl)phosphine Oxide (1c).[71] The following reagents were combined in the amounts and method indicated according to general procedure 5. Tris(4-fluorophenyl)phosphine (1.00 g, 3.16 mmol), H_2O_2 (4.48 mL, 15.8 mmol, 12% in water). Gave **1c** 909 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (m, 6H, Ar**H**), 7.18 (m, 6H, Ar**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.6 (d, *J* = 8.4 Hz), 134.5 (d, *J* = 8.4 Hz), 116.3 (d, *J* = 13.0 Hz), 116.1 (d, *J* = 13 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 26.9.

Tri-2-furylphosphine Oxide (1d).[72] The following reagents were combined in the amounts and method indicated according to general procedure 5. Tri(2-furyl)phosphine (1.00 g, 4.31 mmol), H_2O_2 (6.12 mL, 21.6 mmol, 12% in water). Gave **1d** 884 mg, 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (m, 1H, CHCHC**H**O), 7.18 (m, 1H, C**H**CHCHO), 6.56 (m, 1H, CHC**H**CHO); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0 (d, *J* = 9.2 Hz), 145.9 (d, *J* = 145.9 Hz), 123.7 (d, *J* = 22.1 Hz), 111.2 (d, *J* = 9.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ −11.4.

Tri(*o*-tolyl)phosphine Oxide (1e).[73] The following reagents were combined in the amounts and method indicated according to general procedure 5. Tri(*o*-tolyl)phosphine (2.44 g, 8.02 mmol), H_2O_2 (11.3 mL, 39.9 mmol, 12% in water). Gave **1e** 2.54 g, 99%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48−7.41 (m, 3H, Ar**H**), 7.35−7.30 (m, 3H, Ar**H**), 7.21−7.06 (m, 6H, Ar**H**), 2.50 (s, 9H, 3 × C**H**$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.6 (d, *J* = 7.7 Hz), 133.0 (d, *J* = 13.0 Hz), 132.1 (d, *J* = 10.7 Hz), 132.0 (d, *J* = 2.3 Hz), 130.5 (d, *J* = 101.4 Hz), 125.6 (d, *J* = 12.3 Hz), 22.1 (d, *J* = 3.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 37.6.

Tris(4-methoxyphenyl)phosphine Oxide (1f).[74] The following reagents were combined in the amounts and method indicated according to general procedure 5. Tris(4-methoxyphenyl)phosphine (2.82 g, 8.00 mmol), H_2O_2 (11.3 mL, 39.9 mmol, 12% in water). Gave **1f** 2.84 g, 96%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (m, 6H, Ar**H**), 6.95 (m, 6H, Ar**H**), 3.83 (s, 9H, 3 × C**H**$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5 (d, *J* = 2.3 Hz), 134.0 (d, *J* = 11.5 Hz), 124.2 (d, *J* = 111.2 Hz), 114.1 (d, *J* = 13.8 Hz), 55.4; ^{31}P NMR (162 MHz, $CDCl_3$) δ 29.9.

Tris(2,6-dimethoxyphenyl)phosphine Oxide (1g).[74] The following reagents were combined in the amounts and method indicated according to general procedure 5. Tris (2,6-dimethoxyphenyl)phosphine (2.21 g, 4.99 mmol), H_2O_2 (7.08 mL, 25.0 mmol, 12% in water). Gave **1g** 2.07 g, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, *J* = 8.3 Hz, 3H, Ar**H**), 6.50 (dd, *J* = 8.4 and 4.9 Hz, 6H, Ar**H**), 3.52 (s, 18H, 6 × C**H**$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 132.5, 113.6 (d, *J* = 113.6), 104.5 (d, *J* = 6.9 Hz), 55.9; ^{31}P NMR (162 MHz, $CDCl_3$) δ 17.0.

Diphenylmethylphosphine Oxide (1h).[75] The following reagents were combined in the amounts and method indicated according to general procedure 5. Tri(2-furyl)phosphine (0.963 g, 4.81 mmol), H_2O_2 (6.80 mL, 24.0 mmol, 12% in water). Gave **1h** 777 mg, 75%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77−7.70 (m, 4H, Ar**H**), 7.56−7.44 (m, 6H, Ar**H**), 2.03 (d, *J* = 13.2 Hz, C**H**$_3$); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 134.0 (d, J = 101.6 Hz), 131.9 (d, J = 3.1 Hz), 130.6 (d, J = 10.0 Hz), 128.7 (d, J = 11.5 Hz), 16.6 (d, J = 73.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 30.2.

Synthesis of Chlorophosphonium Chlorides

Chlorophosphonium Chloride (3a).[76] To a solution of triphenylphosphine oxide (139 mg, 0.499 mmol) in $CDCl_3$ (2.0 mL) was added oxalyl chloride (63 μL, 0.74 mmol), and the reaction mixture was stirred for 5 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88−7.81 (m, 3H, Ar**H**), 7.76−7.68 (m, 6H, Ar**H**), 7.67−7.58 (m, 6H, Ar**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.2 (d, J = 3.1 Hz), 133.3 (d, J = 13.0 Hz), 130.8 (d, J = 15.3 Hz), 118.3 (d, J = 93.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 64.5.

Chlorophosphonium Chloride (3b). To a solution of 2--(diphenylphosphoryl)pyridine (42 mg, 0.15 mmol) in $CDCl_3$ (0.6 mL) was added oxalyl chloride (44 μL, 0.52 mmol), and the reaction mixture was stirred for 30 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96−8.90 (m, 1H, Ar**H**), 8.42−8.26 (m, 2H, Ar**H**), 7.94−7.81 (m, 7H, Ar**H**), 7.80−7.72 (m, 4H, Ar**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3 (d, J = 24.6 Hz), 143.6 (d, J = 134.2 Hz), 139.5 (d, J = 11.5 Hz), 137.2 (d, J = 3.1 Hz), 133.8 (d, J = 13.0 Hz), 131.6 (d, J = 29.2 Hz), 130.7 (d, J = 15.3 Hz), 129.7 (d, J = 4.6 Hz), 118.3 (d, J = 92.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 51.8.

Chlorophosphonium Chloride (3c).[77] To a solution of tris (4-fluorophenyl)phosphine oxide (66 mg, 0.20 mmol) in $CDCl_3$ (0.8 mL) was added oxalyl chloride (22 μL, 0.26 mmol), and the reaction mixture was stirred for 20 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (m, 6H, Ar**H**), 7.46 (m, 6H, Ar**H**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7 (dd, J = 263.8 and 3.8 Hz), 137.0 (dd, J = 15.7 and 10.4 Hz), 118.8 (dd, J = 23.0 and 16.8 Hz), 114.9 (dd, J = 102.0 and 3.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 59.9.

Chlorophosphonium Chloride (3e).[78] To a solution of tri (*o*-tolyl)phosphine oxide (96 mg, 0.30 mmol) and 2,6-di-*tert*-butylpyridine (101 μL, 0.450 mmol) in $CDCl_3$ (1.0 mL) was added oxalyl chloride (38 μL, 0.45 mmol), and the reaction mixture was stirred for 2 h. ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8 (d, J = 10.0 Hz), 137.2 (d, J = 3.1 Hz), 134.4 (d, J = 1.5 Hz), 134.3 (d, J = 2.3 Hz), 127.8 (d, J = 15.3 Hz), 115.8 (d, J = 88.4 Hz), 22.2 (d, J = 5.4 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 63.5.

Chlorophosphonium Chloride (3f).[79] To a solution of tris (4-methoxyphenyl)phosphine oxide (111 mg, 0.301 mmol) in $CDCl_3$ (1.0 mL) was added oxalyl chloride (38 μL, 0.45 mmol), and the reaction mixture was stirred for 10 min. ^{31}P NMR (162 MHz, $CDCl_3$) δ 64.0.

Chlorophosphonium Chloride (3g). To a solution of tris(2,6-dimethoxyphenyl)phosphine oxide (230 mg, 0.502 mmol) in $CDCl_3$ (2.0 mL) was added oxalyl chloride (42 μL, 0.50 mmol), and the reaction mixture was stirred for 5 min. Complex mixture of products formed. See NMR spectrum.

Chlorophosphonium Chloride (3h).[77] To a solution of diphenylmethylphosphine oxide (100 mg, 0.499 mmol) in $CDCl_3$ (2.0 mL) was added oxalyl chloride (63 μL, 0.74 mmol), and the reaction mixture was stirred for 5 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14−8.05 (m, 4H, Ar**H**), 7.81−7.75 (m, 2H, Ar**H**), 7.71−7.64 (m, 4H, Ar**H**), 3.58 (d, J = 12.9 Hz, 3H, C**H**$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4 (d, J = 3.1 Hz), 132.5 (d, J = 13.0 Hz), 130.5 (d, J = 15.3 Hz), 120.3 (d, J = 89.7 Hz), 17.2 (d, J = 52.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 71.5.

Chlorophosphonium Chloride (3i).[80] To a solution of trimethylphosphine oxide (23 mg, 0.25 mmol) in CD_3CN (1.0 mL) was added oxalyl chloride (28 μL, 0.33 mmol), and the reaction mixture was stirred for 5 min. ^{1}H NMR (400 MHz, CD_3CN) δ 2.5 (d, J = 14.0 Hz, 9H, 3 × C**H**$_3$); ^{13}C NMR (100 MHz, CD_3CN) δ 17.1 (d, J = 51.4 Hz); ^{31}P NMR (162 MHz, CD_3CN) δ 93.7.

Chlorophosphonium Chloride (3j).[77] To a solution of tributylphosphine oxide (109 mg, 0.499 mmol) in $CDCl_3$ (2.0 mL) was added oxalyl chloride (63 μL, 0.74 mmol), and the reaction mixture was stirred for 5 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.11 (m, 6H, P(C**H**$_2$CH$_2$CH$_2$CH$_3$)$_3$), 1.69−1.57 (m, 6H, P(CH$_2$C**H**$_2$CH$_2$CH$_3$)$_3$), 1.47 (m, 6H, P(CH$_2$CH$_2$ C**H**$_2$CH$_3$)$_3$), 0.90 (t, J = 7.3 Hz, 9H, P(CH$_2$CH$_2$ CH$_2$C**H**$_3$)$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.1 (d, J = 40.6 Hz), 23.5 (d, J = 6.1 Hz), 23.3 (d, J = 17.6 Hz), 13.3; ^{31}P NMR (162 MHz, $CDCl_3$) δ 106.6.

Chlorophosphonium Chloride (3k).[81] To a solution of tributylphosphine oxide (109 mg, 0.499 mmol) in $CDCl_3$ (2.0 mL) was added oxalyl chloride (63 μL, 0.74 mmol), and the reaction mixture was stirred for 5 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19−8.11 (m, 2H, Ar**H**), 7.74−7.69 (m, 1H, Ar**H**), 7.66−7.59 (m, 2H, Ar**H**), 6.54 (m, 1H, PC**H**=C), 3.64−3.56 (m, 2H, PC**H**$_2$), 3.48−3.38 (m, 2H, PCH$_2$C**H**$_2$), 2.33 (s, 3H, C**H**$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.6 (d, J = 30.6 Hz), 136.1 (d, J = 3.1 Hz), 132.2 (d, J = 13.8 Hz), 130.2 (d, J = 15.3 Hz), 120.8 (d, J = 91.3 Hz), 109.5 (d, J = 85.9 Hz), 37.3 (d, J = 8.4 Hz), 28.9 (d, J = 52.2 Hz), 22.4 (d, J = 19.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 97.7.

Experimental Details of Control Experiments Tabulated in Supporting Information.

Table 1, entry 1; Table 2 entries 1, 10, and 11. To $CDCl_3$ (1.5 mL) was added oxalyl chloride (12 μL, 0.14 mmol), and the mixture was stirred for 5 min. Decanol (158 mg, 1.00 mmol) and oxalyl chloride (73 μL, 0.86 mmol) as solutions in $CDCl_3$ (1.0 mL) were then added simultaneously over 7 h via syringe pump. Gave **8a** (0%), **9a** (88%), **10a** (12%) by ^{1}H NMR. The material was used without purification in the next step. Triphenylphosphine oxide (278 mg, 1.00 mmol) was added, and the reaction mixture was stirred at rt for 16 h. Gave **8a** 0% by ^{1}H NMR. The reaction mixture was then heated at reflux for a further 2 h. Gave **8a** 0% by 1H NMR. Then $CDCl_3$ was removed in vacuo. The reaction mixture was dissolved in toluene-d_8 (2 mL) and heated at reflux under N_2 for 5 h. Gave **8a** 0% by ^{1}H NMR.

Table 1, entry 2 and Table 2, entry 2. To $CDCl_3$ (1.5 mL) was added oxalyl chloride (12 μL, 0.14 mmol), and the mixture was stirred for 5 min. Benzyl alcohol (108 mg, 1.00 mmol) and oxalyl chloride (73 μL, 0.86 mmol) as solutions in $CDCl_3$ (1.0 mL) were then added simultaneously over 7 h via syringe pump. Gave **8b** (0%), **9b** (80%), **10b** (20%) by ^{1}H NMR. The material was used without purification in the next step. Triphenylphosphine oxide (278 mg, 1.00 mmol) was added. The reaction mixture was stirred at rt for 16 h. Gave **8b** 0% by ^{1}H NMR.

Table 1, entry 3 and Table 2, entry 3. To $CDCl_3$ (1.5 mL) was added oxalyl chloride (12 μL, 0.14 mmol), and the mixture was stirred for 5 min. 1-Octen-3-ol (128 mg, 1.00 mmol) and oxalyl chloride (73 μL, 0.86 mmol) as solutions in $CDCl_3$ (1.0 mL) were then added simultaneously over 7 h via syringe pump. Gave **8h** (0%), **9h** (100%), **10h** (0%) by ^{1}H NMR. The material was used without purification in the next step. Triphenylphosphine oxide (278 mg, 1.00 mmol) was added, and the reaction mixture was stirred at rt for 16 h. Gave **8h** (0%) by ^{1}H NMR.

Table 2, entry 4. To a solution of triphenylphosphine oxide (42 mg, 0.15 mmol) in $CDCl_3$ (1.5 mL) were added simultaneously **9a** (249 mg, 1.00 mmol) in $CDCl_3$ (1.0 mL) and $CDCl_3$ (1.0 mL) over 7 h via syringe pump. Gave **8a** (0%) by ^{1}H NMR.

Table 2, entry 5. To a solution of triphenylphosphine oxide (42 mg, 0.15 mmol) in $CDCl_3$ (1.5 mL) were added simultaneously **9b** (199 mg, 1.00 mmol) in $CDCl_3$ (1.0 mL) and $CDCl_3$ (1.0 mL) over 7 h via syringe pump. Gave **8b** (0%) by ^{1}H NMR.

Table 2, entry 6. To a solution of triphenylphosphine oxide (42 mg, 0.15 mmol) in $CDCl_3$ (1.5 mL) were added simultaneously **9h** (219 mg, 1.00 mmol) in $CDCl_3$ (1.0 mL) and $CDCl_3$ (1.0 mL) over 7 h via syringe pump. Gave **8h** (0%) by ^{1}H NMR.

Table 2, entry 7. To a solution of triphenylphosphine oxide (42 mg, 0.15 mmol) in $CDCl_3$ (1.5 mL) was added oxalyl chloride (12.0 μL,

0.142 mmol), and the reaction mixture was stirred for 5 min. **9a** (249 mg, 1.00 mmol) as a solution in $CDCl_3$ (1.0 mL) and $CDCl_3$ (1.0 mL) were added simultaneously over 7 h via syringe pump. Gave **8a** (0%) by ^{1}H NMR.

Table 2, entry 8. To a solution of triphenylphosphine oxide (42 mg, 0.15 mmol) in $CDCl_3$ (1.5 mL) was added oxalyl chloride (12 μL, 0.14 mmol), and the reaction mixture was stirred for 5 min. **9b** (199 mg, 1.00 mmol) as a solution in $CDCl_3$ (1.0 mL) and $CDCl_3$ (1.0 mL) were added simultaneously over 7 h via syringe pump. Gave **8b** (0%) by ^{1}H NMR.

Equation 1, R1 = C_9H_{21}. To a solution of 1-chlorodecane 8a (88.0 mg, 0.500 mmol) in $CDCl_3$ (1.75 mL) was added LiBr (109 mg, 1.26 mmol), and the reaction mixture stirred for 16 h at rt. Gave **11a** (0%) by ^{1}H NMR.

Equation 1, R1 = Ph. To a solution of benzylchloride **8b** (63.0 mg, 0.498 mmol) in $CDCl_3$ (1.75 mL) was added LiBr (109 mg, 1.26 mmol), and the reaction mixture stirred for 16 h at rt. Gave **11** (0%) by ^{1}H NMR.

Table 2, entry 2 and Table 4, entries 2 and 3. To $CDCl_3$ (1.5 mL) was added oxalyl bromide (13 μL, 0.14 mmol). Benzyl alcohol (108 mg, 1.00 mmol) and oxalyl bromide (81 μL, 0.86 mmol) as solutions in $CDCl_3$ (1.0 mL) were then added simultaneously over 7 h via syringe pump. Gave **11b** (30%), **10b** (69%) by ^{1}H NMR. The material was used in the next step without purification. Triphenylphosphine oxide (278 mg, 1.00 mmol) was added. The reaction mixture was stirred at rt for 16 h. Gave **11b** (38%), **12b** (50%), **13b** (13%) by ^{1}H NMR. Then the reaction mixture was stirred at rt for 48 h. Gave **11b** (63%), **12b** (25%), **13b** (13%) by ^{1}H NMR.

Table 3, entry 1 and Table 4, entry 1. To $CDCl_3$ (1.5 mL) was added oxalyl bromide (13 μL, 0.14 mmol). Decanol (158 mg, 1.00 mmol) and oxalyl bromide (81 μL, 0.86 mmol) as solutions in $CDCl_3$ (1.0 mL) were then added simultaneously over 7 h via syringe pump. Gave **12a** (90%) by ^{1}H NMR. The material was used in the next step without purification. Then triphenylphosphine oxide (278 mg, 1.00 mmol) was added. The reaction mixture was stirred at rt for 16 h. Gave **11a** (0%), **12a** (15%), **13a** (85%) by ^{1}H NMR.

Table 5, entry 1. To $CDCl_3$ (1.5 mL) were added oxalyl chloride (16.5 μL, 0.20 mmol) and LiBr (217 mg, 2.5 mmol), and the reaction mixture stirred for 5 min. The decanol (158 mg, 1.00 mmol) and oxalyl chloride (93.5 μL, 1.11 mmol) as solutions in $CDCl_3$ (1.0 mL) were then added simultaneously over 5 h via syringe pump. Gave **11a** (0%), **9a** and **12a** (86%) by ^{1}H NMR.

Table 5, entry 2. To $CDCl_3$ (1.5 mL) were added oxalyl chloride (16.5 μL, 0.20 mmol) and LiBr (261 mg, 3.01 mmol), and the reaction mixture stirred for 5 min. The benzyl alcohol (108 mg, 1.00 mmol) and oxalyl chloride (93.5 μL, 1.11 mmol) as solutions in $CDCl_3$ (1.0 mL) were then added simultaneously over 5 h via syringe pump. Gave **11b** (0%), **9b** and **12b** (82%) by ^{1}H NMR.

Equation 2, substrate 9a. To a solution of triphenylphosphine oxide (42 mg, 0.15 mmol) in $CDCl_3$ (1.5 mL) was added LiBr (217 mg, 2.50 mmol) followed by **9a** (249 mg, 1.00 mmol) as a solution in $CDCl_3$ (1.0 mL) and $CDCl_3$ (1.0 mL) simultaneously over 5 h via syringe pump. Gave **11a** (0%) by ^{1}H NMR.

Equation 2, substrate 9b. To a solution of triphenylphosphine oxide (42 mg, 0.15 mmol) in $CDCl_3$ (1.5 mL) was added LiBr (261 mg, 3.00 mmol) followed by **9b** (198 mg, 1.00 mmol) as a solution in $CDCl_3$ (1.0 mL) and $CDCl_3$ (1.0 mL) simultaneously over 7 h via syringe pump. Gave **11a** (0%) by ^{1}H NMR.

Equation 3, substrate 12a. To a solution of triphenylphosphine oxide (42 mg, 0.15 mmol) in $CDCl_3$ (1.5 mL) was added simultaneously **12a** (293 mg, 1.00 mmol) as a solution in $CDCl_3$ (1.0 mL) and $CDCl_3$ (1.0 mL) over 7 h via syringe pump. Gave **11a**, 0% by ^{1}H NMR.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. Experimental procedures for the synthesis and reactions of chlorooxalates; details of computations; X-ray crystallographic data in CIF format; and spectral data This material is available free of charge via the Internet at http://pubs.acs.org.

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