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Convergent Synthesis of Polysubstituted Furans via Catalytic Phosphine Mediated Multicomponent Reactions

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Abstract: Tri- or tetrasubstituted furans have been prepared from terminal activated olefins and acyl chlorides or anhydrides by a multicomponental convergent synthesis mode. Instead of stoichiometric nBu$_3$P, only catalytic nBu$_3$P or nBu$_3$P=O is needed to furnish the furans in modest to excellent yields with a good functional group tolerance under the aid of reducing agent silane. This synthetic method features a silane-driven catalytic intramolecular Wittig reaction as a key annulation step and represents the first successful application of catalytic Wittig reaction in multicomponent cascade reaction.

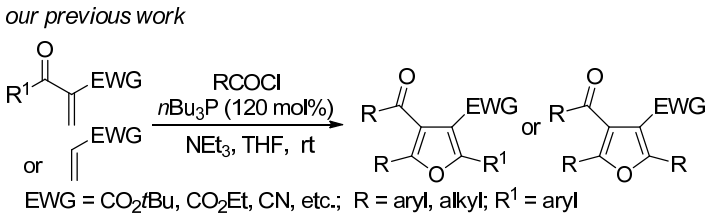
Keywords: polysubstituted furans; multicomponent reaction; silanes; phosphine oxides; catalytic Wittig reaction

1. Introduction

The Wittig reaction [1–4] provides a powerful tool for convenient construction of carbon-carbon double bonds in synthetic chemistry. Despite the popularity of this reaction, some major drawbacks are associated with the formation of stoichiometric phosphine oxides as by-products. The troublesome purification of the by-products [5] makes them valueless on an industrial scale [6–8]. Also, most well-designed phosphines, especially chiral phosphine reagents [9–15], are very expensive and high cost hampers their applications in asymmetric Wittig reaction [16–25]. In this context, it is highly desired to develop a catalytic version of phosphine-mediated Wittig reaction by in-situ recycling by-product phosphine oxide under the aid of a reducing agent. However, it is a challenging task to reuse phosphine oxides to effect a catalytic Wittig reaction [26–28]. First, phosphine oxides are not generally easy to be reduced into the corresponding phosphines at a substantially fast rate under mild conditions; second, the employed reducing agent should be safe for other functional groups of the substrates [29,30]. Consequently, although many new methods for reduction of phosphine oxides have emerged by using reducing agents such as DIBAL-H [31,32], $LiAlH_4$ [33,34], boron compounds [35–38], and others [39–45], applicable ones for catalytic Wittig reactions remain rare. Recently, silanes have been recognized as powerful reducing agents for in-situ deoxygenation of phosphine oxides with good functional tolerance after a series of successful applications of silanes in the transformation of a stoichiometric phosphine-mediated reaction into a catalytic one [46–52]. In 2009, O'Brien et al. [53] developed the first catalytic Wittig reaction for efficient synthesis of alkenes in moderate to high yields by using silanes such as diphenyl silane or trimethoxysilane to reuse in-situ by-product phosphine oxide [54–56]. In 2012, Beller and coworkers realized efficient and chemoselective reduction of tertiary and secondary

phosphine oxides to their corresponding phosphines by using silanes under the aid of catalytic copper complexes [57] or specific Brønsted acids [58]. Under the reported conditions, various reducible functional groups such as ketones, aldehydes, olefins, nitriles, and esters were well tolerated. Based on these encouraging findings, a number of important stoichiometric phosphine-involved reactions, including (aza-)Wittig [59–75], Mitsunobu [76–78], Staudinger [79–84], Appel [85,86], Cadogan [87], and others [88–93] have been successfully developed into the catalytic phosphine mediated ones.

Multicomponent reactions (MCRs) [94–96] have attracted much interest from organic chemists in recent years as a highly efficient synthetic strategy. In 2012, our group [97] realized a stoichiometric phosphine-mediated pseudo-three-component reaction between terminal activated olefins and acyl chlorides or anhydrides, leading to a convenient and convergent synthesis of tetra-substituted furans in moderate to excellent yields. The highly functionalized furan product was formed from one molecule of activated olefin and two or three molecules of acyl chloride or anhydride under the mediation of nBu$_3$P through a multiple domino sequence consisting of *C*-acylation, *O*-acylation, and intramolecular Wittig reaction (Scheme 1). A concomitant by-product nBu$_3$P=O was also formed [97]. Considering its high efficiency in synthesis of tetra-substituted furans and its characteristic of the multicomponent cascade reaction, we were interested in exploring a catalytic version of this reaction by using silanes as reducing agents. As mentioned above, although silanes have been successfully used as reducing agents in a series of catalytic versions of important phosphine-mediated reactions like the Wittig reaction [53–93], this silane-reduction strategy has never been applied to a stoichiometric phosphine mediated multicomponent cascade reaction before. Furthermore, the addition of reducing agent silane will certainly result in an increased complexity of a multiple domino reaction sequence. Herein we report the relevant results from such challenging studies.

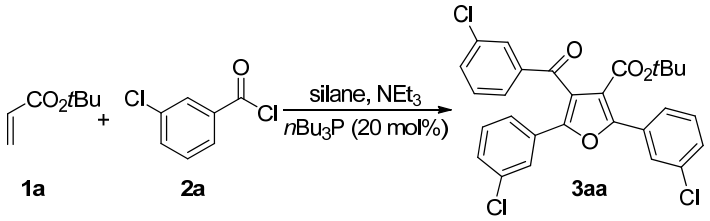


Scheme 1. Phosphine-mediated synthesis of tetra-substituted furans.

2. Results and Discussion

Our investigation started with a model reaction between *tert*-butyl acrylate **1a** and 3-chlorobenzoyl chloride **2a** (Table 1). Under the similar conditions of our previous work [97], *tert*-butyl acrylate (0.5 mmol) and 3-chlorobenzoyl chloride (1.8 mmol) were added to THF (2.0 mL) under N_2, followed by addition of catalytic nBu$_3$P (0.1 mmol), NEt$_3$ (2.7 mmol) and Ph_2SiH_2 (0.6 mmol), the resulting mixture was stirred at room temperature for 24 h. The desired product **3aa** was obtained, but only in 11% yield (entry 1). The reaction was then conducted at 60 °C and the yield of **3aa** was not substantially improved (entry 2). Although only a trace amount of the product was observed in a $PhSiH_3$ mediated reaction run at room temperature in toluene (entry 3), to our delight, tetra-substituted furan **3aa** was obtained in 74% yield when the temperature was raised to 110 °C in refluxing toluene (entry 4). Other silanes such as Ph_2SiH_2, $(MeO)_3SiH$, polymethylhydrosiloxane (PMHS) and Ph_3SiH were effective but offered inferior results (entries 5-9); $SiHCl_3$ were ineffective at all (entry 10). The loading amount of $PhSiH_3$ was studied and a decreased loading (0.4 mmol) could also smoothly offer a yield of 84% (entries 11-13). A lower reaction temperature (80 °C) resulted in a decreased yield (entry 14). Solvents like dioxane, xylene, and DMF only gave inferior results and acetonitrile was detrimental to the reaction (entries 15-18). A lowered loading amount of nBu$_3$P (0.05 mmol, 10 mol%) was investigated, only giving the product in a moderate yield (entry 19). Other phosphines such as PPh_3 and Ph_2PMe were totally ineffective as reported before [97]. Thus, the optimized conditions were established as those shown in Table 1, entry 12.

Table 1. Survey of the model reaction conditions.[a]



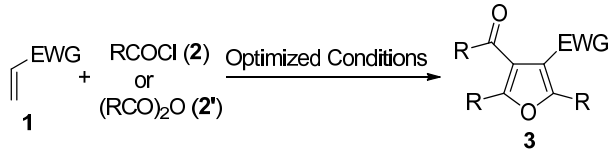
Entry	Silane (mmol)	Solvent	Temp (°C)	3 (%) [b]
1	Ph_2SiH_2 (0.6)	THF	rt	11
2	Ph_2SiH_2 (0.6)	THF	60	12
3	$PhSiH_3$ (0.6)	Toluene	rt	trace
4	$PhSiH_3$ (0.6)	Toluene	110	74
5	Ph_2SiH_2 (0.6)	Toluene	110	42
6	$(MeO)_3SiH$ (0.6)	Toluene	110	33
7	PMHS (0.034)	Toluene	110	26
8	PMHS (0.106)	Toluene	110	30
9	Ph_3SiH (1.2)	Toluene	110	18
10	$SiHCl_3$ (0.6)	Toluene	rt	trace
11	$PhSiH_3$ (0.25)	Toluene	110	65
12	$PhSiH_3$ (0.4)	Toluene	110	84
13	$PhSiH_3$ (0.75)	Toluene	110	49
14	$PhSiH_3$ (0.4)	Toluene	80	56
15	$PhSiH_3$ (0.4)	Dioxane	110	54
16	$PhSiH_3$ (0.4)	Xylene	110	60
17	$PhSiH_3$ (0.4)	DMF	110	11
18	$PhSiH_3$ (0.4)	CH_3CN	80	trace
19 [c]	$PhSiH_3$ (0.4)	Toluene	110	48

[a] Typical conditions: a mixture of **1a** (0.5 mmol), **2a** (1.8 mmol), nBu$_3$P (0.1 mmol), NEt_3 (2.7 mmol) and silane in the specified solvent (2.0 mL) under N_2 at indicated temperature for 24 h. [b] Isolated yield based on **1a**. [c] The loading amount of nBu$_3$P was 0.05 mmol.

Under the optimized conditions, the substrate scope of alkenes **1** and acyl chlorides **2** were further examined (Table 2). Gratifyingly, reducible functional groups such as ketone, acyl chloride, olefin, nitro, cyano, and ester were all well tolerated in this multicomponent reaction, and moderate to excellent yields were generally obtained when different substrates were employed (Table 2). When *tert*-butyl acrylate **1a** was employed, a series of substituted benzoyl chlorides **2**, except *o*-chlorobenzoyl chloride **2c** and 4-nitrobenzoyl chloride **2f**, readily afforded the corresponding tetra-substituted furans **3** in good yields (entries 1-6). Hetero-aryl acyl chloride like 2-thiofuroyl chloride (**2g**) was also effective in this transformation, furnishing the corresponding tetrasubstituted furan **3ag** in moderate yield (entry 7). Methyl, ethyl, *n*-butyl and benzyl acrylates (**1b**–**e**), acrylonitrile **1f** were all good candidates for this reaction and the expected products were readily delivered in moderate to good yields (entries 8-17). Aliphatic anhydride **2a'** was also found to be a suitable substrate, albeit giving a lower yield (entry 18).

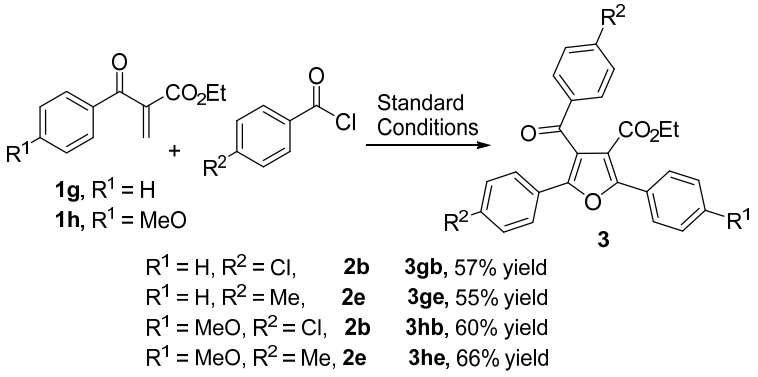
To further test the generality of the reaction, di-substituted alkene **1g** and **1h** were also studied (Scheme 2). We found that α,β-unsaturated ketones were well compatible under standard conditions, affording the corresponding tetra-substituted furans in satisfactory yields with different benzoyl chlorides (Scheme 2).

Table 2. Synthesis of tetra-substituted furans **3** from olefins **1** and acyl chlorides **2** or anhydride **2′**.[a]



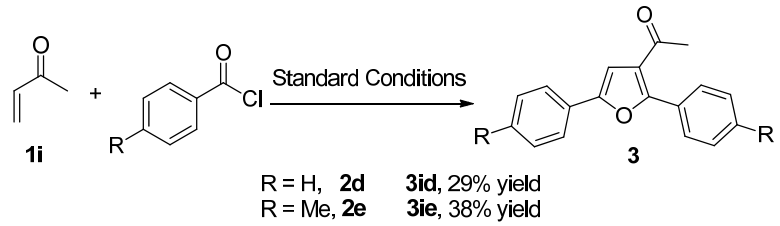
Entry	EWG in 1	R in 2 or 2′	3 (%) [b]
1	CO_2tBu (**1a**)	3-ClC_6H_4 (**2a**)	**3aa**, 84
2	CO_2tBu (**1a**)	4-ClC_6H_4 (**2b**)	**3ab**, 75
3	CO_2tBu (**1a**)	2-ClC_6H_4 (**2c**)	**3ac**, 33
4	CO_2tBu (**1a**)	Ph(**2d**)	**3ad**, 70
5	CO_2tBu (**1a**)	4-MeC_6H_4 (**2e**)	**3ae**, 90
6	CO_2tBu (**1a**)	4-$NO_2C_6H_4$ (**2f**)	**3af**, 37
7	CO_2tBu (**1a**)	2-thienyl (**2g**)	**3ag**, 46
8	CO_2Me (**1b**)	4-ClC_6H_4 (**2b**)	**3bb**, 81
9	CO_2Me (**1b**)	4-MeC_6H_4 (**2e**)	**3be**, 84
10	CO_2Et (**1c**)	4-ClC_6H_4 (**2b**)	**3cb**, 71
11	CO_2Et (**1c**)	4-MeC_6H_4 (**2e**)	**3ce**, 84
12	CO_2nBu (**1d**)	4-ClC_6H_4 (**2b**)	**3db**, 85
13	CO_2nBu (**1d**)	4-MeC_6H_4 (**2e**)	**3de**, 83
14	CO_2Bn (**1e**)	Ph (**2d**)	**3ed**, 87
15	CN (**1f**)	4-ClC_6H_4 (**2b**)	**3fb**, 38
16	CN (**1f**)	Ph (**2d**)	**3fd**, 57
17	CN (**1f**)	4-MeC_6H_4 (**2e**)	**3fe**, 44
18	CO_2tBu (**1a**)	Me (**2′a**)	**3aa′**, 27

[a] Optimized conditions: under a N_2 atmosphere and at 110 °C, alkenes **1** (0.5 mmol) and acyl chlorides **2** or anhydride **2′** (1.8 mmol) were added into toluene (2.0 mL), followed by additions of nBu$_3$P (0.1 mmol), NEt_3 (2.7 mmol) and $PhSiH_3$ (0.4 mmol), the resulting mixture was stirred for 24 h. [b] Isolated yield based on **1**.



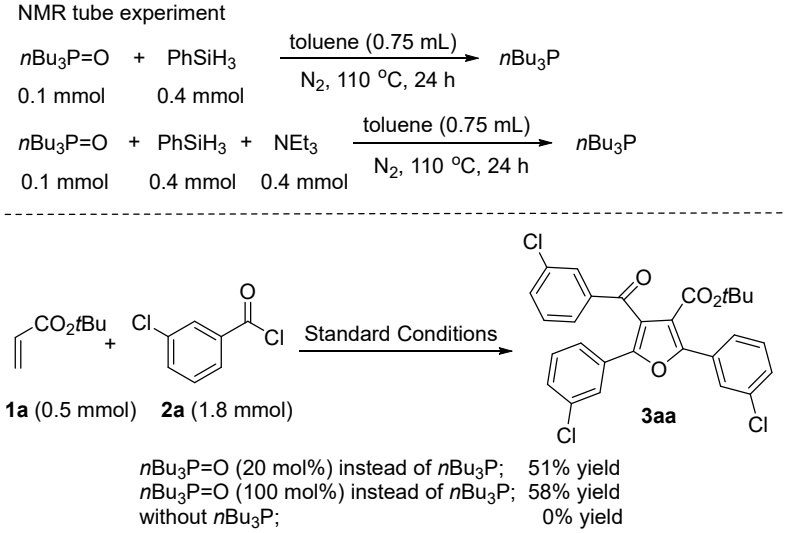
Scheme 2. Synthesis of tetra-substituted furans **3** from di-substituted alkene **1g** and **1h**.

To our surprise, methyl vinyl ketone (MVK) **1i** was also effective under the catalytic conditions, furnishing the corresponding tri-substituted furans **3id** and **3ie** in fair yields in the reactions with benzoyl chlorides (Scheme 3). It is worthy to note that, in our previous work [97], the more reactive alkene MVK **1i** failed to deliver the expected furans in appreciable yields under the mediation of stoichiometric nBu$_3$P. Presumably, under the silane-driven catalytic conditions, the instant concentration of nBu$_3$P would be kept at a relatively low level in the reaction mixture. The low concentration of nBu$_3$P may diminish the possible side reactions of the highly reactive olefin like **1i**.



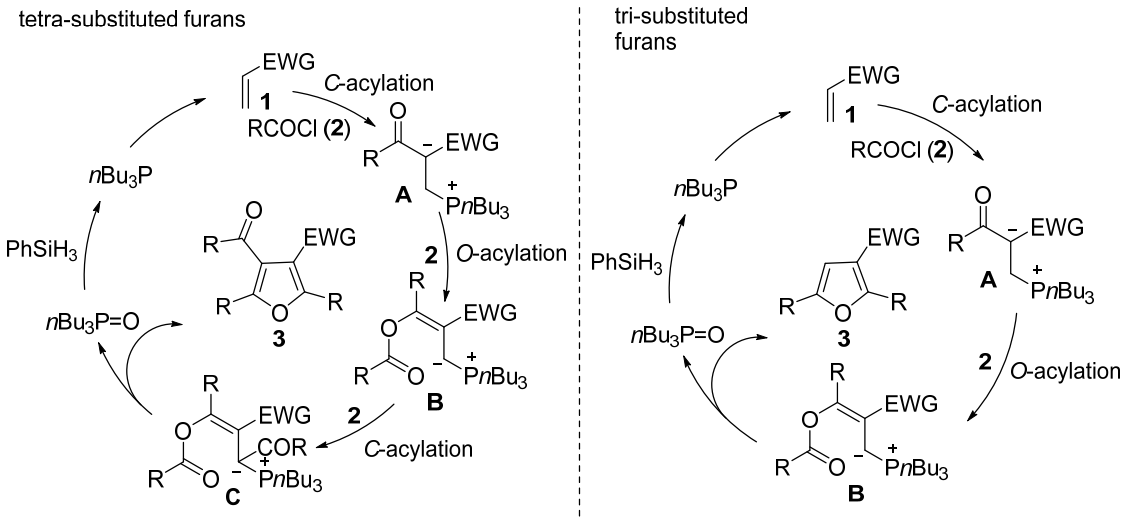
Scheme 3. Synthesis of tri-substituted furans **3** from methyl vinyl ketone **1i**.

In order to gain more insights about the reaction, some control experiments were conducted (Scheme 4). In a ^{31}P NMR tracking experiment (a sealed capillary containing C_6D_6 was used for field locking and shimming), a signal at δ −32.4 ppm was observed which was identified as nBu$_3$P when nBu$_3$P=O (0.1 mmol) and silane PhSiH$_3$ (0.4 mmol) were mixed with or without NEt$_3$ (0.4 mmol) in toluene in an NMR tube under N_2 for 24 h (for details, see Supporting Information). These results provided direct evidence for the regeneration of the nBu$_3$P catalyst. As expected, tetra-substituted furan **3aa** was readily obtained in 51% isolated yield when nBu$_3$P=O (20 mol%) was used instead of nBu$_3$P. In contrast, an increased loading of nBu$_3$P=O (100 mol%) only brought in a modestly improved yield (58%). The silane PhSiH$_3$ alone could not effect the domino reaction. These results indicated that nBu$_3$P=O was the equivalent catalyst of nBu$_3$P in the presence of silane PhSiH$_3$. It is noticeable that nBu$_3$P=O was inactive as a catalyst in Lin's report [68].



Scheme 4. Control experiments.

Based on the results of this work and previous reports [59–75,97], a multiple domino process is proposed to rationalize the formation of tetra-substituted furans **3** (Scheme 5, left). The catalytic cycle starts with the nucleophilic addition of nBu$_3$P to an activate alkene **1** like acrylates, the resulting intermediate undergoes a *C*-acylation reaction with acyl chloride **2** to give a phosphonium enolate A. The phosphorus ylide B, generated through the *O*-acylation reaction of intermediate A with acyl chloride 2 in the presence of NEt$_3$, engages in another *C*-acylation reaction to deliver an ylide C under the aid of base NEt$_3$. Finally, a polysubstituted furan is delivered through an intramolecular Wittig reaction of ylide C with the release of nBu$_3$P=O. The phosphine oxide nBu$_3$P=O is then in-situ reduced by silane PhSiH$_3$ into nBu$_3$P, which enters the next catalytic cycle. Regarding the formation of the tri-substituted furans **3id** and **3ie** from MVK **1i**, a similar triple domino sequence of *C*-acylation/*O*-acylation/intramolecular Wittig reaction presumably occurs (Scheme 5, right).



Scheme 5. Proposed mechanism.

3. Experimental Section

Unless otherwise noted, all reactions were carried out in a nitrogen atmosphere under anhydrous conditions. Solvents were purified prior to use according to standard procedures. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ with tetramethylsilane (TMS) as the internal standard. Column chromatography was performed on silica gel (200–300 mesh) using a mixture of petroleum ether (60–90 °C)/ethyl acetate as the eluant. 2-Acyl acrylates **1g–h** were prepared according to the reported procedure [98].

Typical procedure for synthesis of highly functionalized furans 3: Under a N_2 atmosphere, to a solution of activated olefins **1a–1i** (0.5 mmol), acylation agent **2** (1.8 mmol) in toluene (2.0 mL) were sequentially added nBu$_3$P (25 μL, 0.1 mmol), Et$_3$N (2.7 mmol) and silane (0.4 mmol) by means of microsyringe. The resulting reaction mixture was stirred at 110 °C for 24 h. After completion of the reaction as monitored by TLC, water (10 mL) was added. The mixture was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was washed with saturated brine (10 mL) and dried over anhydrous sodium sulfate. After filtration, the solvent was removed on a rotary evaporator under reduced pressure, and the residue was subjected to column chromatographic isolation on silica gel (eluted with petroleum ether/ ethyl acetate (40:1–20:1) to give furans **3**.

3aa–3de, **3fb–3he** are known compounds in our previous report [97]. NMR spectra of compounds **3** are available in Supplementary Materials.

3aa, 221 mg, 84% yield; as a yellow solid; m.p. 110–111 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 0.7 Hz, 1H), 7.98 (t, J = 1.7 Hz, 1H), 7.97–7.92 (m, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.67 (d, J = 1.7 Hz, 1H), 7.60–7.53 (m, 1H), 7.48–7.38 (m, 4H), 7.31–7.22 (m, 2H), 1.23 (s, 9H).

3ab, 199 mg, 75% yield; as a yellow solid; m.p. 198–199 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.7 Hz, 2H), 7.92 (d, J = 8.6 Hz, 2H), 7.53 (d, J = 8.7 Hz, 2H), 7.46 (dd, J = 8.7, 6.7 Hz, 4H), 7.30 (d, J = 8.7 Hz, 2H), 1.19 (s, 9H).

3ac, 87 mg, 33% yield; as a yellow solid; m.p. 118–120 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, J = 7.6, 1.5 Hz, 1H), 7.60 (dd, J = 7.4, 1.9 Hz, 1H), 7.53–7.46 (m, 2H), 7.42–7.34 (m, 2H), 7.34–7.27 (m, 3H), 7.27–7.24 (m, 1H), 7.23–7.16 (m, 2H), 1.22 (s, 9H).

3ad, 149 mg, 70% yield; as a white solid; m.p. 181–183 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.14–7.94 (m, 4H), 7.69–7.62 (m, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.53–7.41 (m, 5H), 7.37–7.26 (m, 3H), 1.16 (s, 9H).

3ae, 210 mg, 90% yield; as a white solid; m.p. 160–162 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.2 Hz, 2H), 7.79 (d, J = 8.1 Hz, 2H), 7.41 (d, J = 8.2 Hz, 2H), 7.15 (d, J = 8.1 Hz, 2H), 7.11 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.1 Hz, 2H), 2.27 (s, 3H), 2.25 (s, 3H), 2.15 (s, 3H), 1.06 (s, 9H).

3af, 102 mg, 37% yield; as a yellow solid; m.p. 178–180 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.37 (t, *J* = 9.6 Hz, 4H), 8.30 (d, *J* = 8.7 Hz, 2H), 8.23 (d, *J* = 8.6 Hz, 2H), 8.18 (d, *J* = 8.5 Hz, 2H), 7.79 (d, *J* = 8.6 Hz, 2H), 1.22 (s, 9H).

3ag, 101 mg, 46% yield; as a oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, *J* = 3.8, 1.0 Hz, 1H), 7.69 (dd, *J* = 4.9, 1.0 Hz, 1H), 7.61–7.59 (m, 1H), 7.48 (dd, *J* = 5.0, 1.0 Hz, 1H), 7.45 (dd, *J* = 3.7, 1.0 Hz, 1H), 7.32 (dd, *J* = 5.0, 1.0 Hz, 1H), 7.15 (dd, *J* = 5.0, 3.9 Hz, 1H), 7.09 (dd, *J* = 4.8, 3.9 Hz, 1H), 7.02 (dd, *J* = 5.0, 3.8 Hz, 1H), 1.25 (s, 9H).

3bb,196 mg, 81% yield; as a yellow solid; m.p. 185–186 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.4 Hz, 2H), 7.87 (d, *J* = 8.3 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.51–7.41 (m, 4H), 7.31 (d, *J* = 8.4 Hz, 2H), 3.50 (s, 3H).

3be, 190 mg, 84% yield; as a yellow solid; m.p. 185–186 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.0 Hz, 2H), 7.85 (d, *J* = 7.9 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 7.9 Hz, 2H), 7.22 (d, *J* = 7.8 Hz, 2H), 7.10 (d, *J* = 7.9 Hz, 2H), 3.46 (s, 3H), 2.41 (s, 3H), 2.37 (s, 3H), 2.29 (s, 3H).

3cb, 178 mg, 71% yield; as a white solid; m.p. 177–178 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.4 Hz, 2H), 7.90 (d, *J* = 8.3 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.45 (t, *J* = 9.2 Hz, 4H), 7.31 (d, *J* = 8.4 Hz, 2H), 4.00 (q, *J* = 7.1 Hz, 2H), 0.93 (t, *J* = 7.1 Hz, 3H).

3ce, 195 mg, 84% yield; as a white solid; m.p. 134–136 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.9 Hz, 2H), 7.88 (d, *J* = 7.8 Hz, 2H), 7.53 (d, *J* = 7.9 Hz, 2H), 7.28 (d, *J* = 7.9 Hz, 2H), 7.23 (d, *J* = 7.9 Hz, 2H), 7.10 (d, *J* = 7.9 Hz, 2H), 3.97 (q, *J* = 7.0 Hz, 2H), 2.41 (s, 3H), 2.38 (s, 3H), 2.29 (s, 3H), 0.90 (t, *J* = 7.1 Hz, 3H).

3db, 224 mg, 85% yield, as a yellow solid; m.p. 142–143 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.6 Hz, 2H), 7.90 (d, *J* = 8.5 Hz, 2H), 7.53 (d, *J* = 8.6 Hz, 2H), 7.44 (t, *J* = 8.6 Hz, 4H), 7.29 (d, *J* = 8.6 Hz, 2H), 3.96 (t, *J* = 6.6 Hz, 2H), 1.28–1.23 (m, 2H), 1.09–1.07 (m, 2H), 0.77 (t, *J* = 7.3 Hz, 3H).

3de, 193 mg, 83% yield, as a white solid; m.p. 120–121 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.1 Hz, 2H), 7.88 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 3.93 (t, *J* = 6.5 Hz, 2H), 2.40 (s, 3H), 2.37 (s, 3H), 2.28 (s, 3H), 1.35–1.15 (m, 2H), 1.07–1.05 (m, 2H), 0.74 (t, *J* = 7.3 Hz, 3H).

3ed, 200 mg, 87% yield, as a white solid; m.p. 124–126 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 6.5, 2.7 Hz, 2H), 7.92 (d, *J* = 7.6 Hz, 2H), 7.68 (d, *J* = 7.9 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.53–7.47 (m, 2H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.38–7.31 (m, 3H), 7.30–7.22 (m, 2H), 7.05 (d, *J* = 7.1 Hz, 2H), 5.00 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.2, 162.2, 156.3, 150.1, 137.3, 134.6, 133.4, 129.9, 129.3, 128.9, 128.8, 128.7, 128.6, 128.5, 128.3, 128.2, 128.2, 128.0, 125.9, 121.8, 115.1, 66.7. HRMS-ESI calcd. for $C_{31}H_{23}O_4$ $[M + H]^+$ 459.1591; found 459.1593.

3fb, 85 mg, 38% yield, as a yellow solid; m.p. 181–182 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) 8.03 (d, *J* = 8.6 Hz, 2H), 7.81 (d, *J* = 8.5 Hz, 2H), 7.52 (dd, *J* = 8.3, 6.2 Hz, 4H), 7.41 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.6 Hz, 2H).

3fd, 100 mg, 57% yield, as a white solid; m.p. 152–154 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.18–8.07 (m, 2H), 7.88 (d, *J* = 7.3 Hz, 2H), 7.62–7.48 (m, 6H), 7.39 (t, *J* = 7.7 Hz, 2H), 7.32 (t, *J* = 6.4 Hz, 3H).

3fe, 85 mg, 44% yield, as a yellow solid; m.p. 165–167 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.1 Hz, 2H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 7.9 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 2.42 (s, 3H), 2.37 (s, 3H), 2.31 (s, 3H).

3aa', 32 mg, 27% yield; as a oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 3H), 2.43 (s, 3H), 2.34 (s, 3H), 1.55 (s, 9H).

3gb, 133 mg, 57% yield; as a white solid; m.p. 135–137 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.06–8.00 (m, 2H), 7.94–7.89 (m, 2H), 7.59–7.53 (m, 2H), 7.52–7.46 (m, 3H), 7.46–7.42 (m, 2H), 7.33–7.28 (m, 2H), 4.00 (q, *J* = 7.1 Hz, 2H), 0.94 (t, *J* = 7.1 Hz, 3H).

3ge, 117 mg, 55% yield; as a white solid; m.p. 128–130 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.09–8.02 (m, 2H), 7.88 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 8.2 Hz, 2H), 7.51–7.41 (m, 3H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 8.1 Hz, 2H), 3.97 (q, *J* = 7.1 Hz, 2H), 2.40 (s, 3H), 2.31 (s, 3H), 0.90 (t, *J* = 7.1 Hz, 3H).

3hb, 149 mg, 60% yield; as a yellow solid; m.p. 150–151 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.9 Hz, 2H), 7.91 (d, *J* = 8.5 Hz, 2H), 7.55 (d, *J* = 8.7 Hz, 2H), 7.43 (d, *J* = 8.6 Hz, 2H), 7.28 (d, *J* = 8.7 Hz, 2H), 7.00 (d, *J* = 8.9 Hz, 2H), 3.99 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 3H), 0.92 (t, *J* = 7.1 Hz, 3H).

3he, 150 mg, 66% yield; as a white solid; m.p. 132–133 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.6 Hz, 2H), 7.87 (d, *J* = 7.8 Hz, 2H), 7.52 (d, *J* = 7.9 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 2H), 7.00 (d, *J* = 8.8 Hz, 2H), 3.96 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 3H), 2.40 (s, 3H), 2.30 (s, 3H), 0.89 (t, *J* = 7.1 Hz, 3H).

3id, 38 mg, 29% yield; as a yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.77–7.73 (m, 2H), 7.58 (dd, *J* = 7.8, 1.7 Hz, 2H), 7.44–7.35 (m, 2H), 7.28 (dd, *J* = 13.2, 5.4 Hz, 2H), 7.21–7.15 (m, 2H), 6.21 (d, *J* = 0.8 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.9, 154.5, 151.1, 138.2, 132.6, 130.0, 129.7, 128.6, 128.2, 128.1(overlap), 127.2, 121.7, 109.7, 13.4; HRMS-ESI calcd. for $C_{18}H_{15}O_2$ $[M + H]^+$ 263.1067; found 263.1071.

3ie, 55 mg, 38% yield; as a yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 2H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 6.24 (d, *J* = 0.8 Hz, 1H), 2.38 (s, 6H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.7, 154.3, 150.6, 143.4, 138.5, 135.7, 129.8, 128.9 (overlap), 127.3, 127.0, 121.3, 109.7, 21.6, 21.3, 13.4; HRMS-ESI calcd. for $C_{20}H_{19}O_2$ $[M + H]^+$ 291.1380; found 291.1383.

4. Conclusions

In conclusion, a convergent synthetic method for tri- or tetra-substituted furans has been developed by catalytic phosphine mediated multicomponental cascade reactions. Instead of stoichiometric *n*Bu_3P, only catalytic *n*Bu_3P or *n*Bu_3P=O is needed to deliver the furans in modest to excellent yields. A broad scope of substrates, bearing various reducible functional groups including ketone, acyl chloride, olefin, nitro, cyano, and ester, are all well tolerated in the presence of reducing agent silane. This synthetic method features a silane-driven catalytic intramolecular Wittig reaction as a key step and represents the first successful application of catalytic Wittig reaction in a multicomponent cascade reaction. Future efforts in our laboratory will be directed toward exploring the asymmetric reactions involving catalytic chiral phosphine mediated Wittig reaction, the results of which will be reported in due course.

Supplementary Materials: The supplementary materials are available online.

Author Contributions: R.C. and Z.H. conceived and designed the experiments; X.F. performed the experiments; J.H. checked and analyzed the data; R.C. wrote the paper; Z.H. revised the manuscript.

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References

1. Byrne, P.A.; Gilheany, D.G. The modern interpretation of the Wittig reaction mechanism. *Chem. Soc. Rev.* **2013**, *42*, 6670–6696. [CrossRef]
2. Chelucci, G. Synthesis and Metal-Catalyzed Reactions of gem-Dihalovinyl Systems. *Chem. Rev.* **2012**, *112*, 1344–1462. [CrossRef]
3. Perin, G.; Lenardão, E.J.; Jacob, R.G.; Panatieri, R.B. Synthesis of Vinyl Selenides. *Chem. Rev.* **2009**, *109*, 1277–1301. [CrossRef]
4. Flynn, A.B.; Ogilvie, W.W. Stereocontrolled Synthesis of Tetrasubstituted Olefins. *Chem. Rev.* **2007**, *107*, 4698–4745. [CrossRef]
5. Batesky, D.C.; Goldfogel, M.J.; Weix, D.J. Removal of Triphenylphosphine Oxide by Precipitation with Zinc Chloride in Polar Solvents. *J. Org. Chem.* **2017**, *82*, 9931–9936. [CrossRef]
6. Bergbreiter, D.E.; Yang, Y.-C.; Hobbs, C.E. Polyisobutylene-Supported Phosphines as Recyclable and Regenerable Catalysts and Reagents. *J. Org. Chem.* **2011**, *76*, 6912–6917. [CrossRef]

7. Constable, D.J.C.; Dunn, P.J.; Hayler, J.D.; Humphrey, G.R.; Leazer, J.J.L.; Linderman, R.J.; Lorenz, K.; Manley, J.; Pearlman, B.A.; Wells, A.; et al. Key green chemistry research areas-a perspective from pharmaceutical manufacturers. *Green Chem.* **2007**, *9*, 411–420. [CrossRef]
8. Dandapani, S.; Curran, D.P. Separation-Friendly Mitsunobu Reactions: A Microcosm of Recent Developments in Separation Strategies. *Chem. Eur. J.* **2004**, *10*, 3130–3138. [CrossRef]
9. Dutartre, M.; Bayardon, J.; Juge, S. Applications and stereoselective syntheses of P-chirogenic phosphorus compounds. *Chem. Soc. Rev.* **2016**, *45*, 5771–5794. [CrossRef]
10. Wang, Z.; Xu, X.; Kwon, O. Phosphine catalysis of allenes with electrophiles. *Chem. Soc. Rev.* **2014**, *43*, 2927–2940. [CrossRef]
11. Wei, Y.; Shi, M. Applications of Chiral Phosphine-Based Organocatalysts in Catalytic Asymmetric Reactions. *Chem. Asian J.* **2014**, *9*, 2720–2734. [CrossRef] [PubMed]
12. Marinetti, A.; Voituriez, A. Enantioselective Phosphine Organocatalysis. *Synlett* **2010**, 174–194. [CrossRef]
13. Glueck, D.S. Catalytic asymmetric synthesis of chiral phosphanes. *Chem. Eur. J.* **2008**, *14*, 7108–7117. [CrossRef] [PubMed]
14. Li, Y.-M.; Kwong, F.-Y.; Yu, W.-Y.; Chan, A.S.C. Recent advances in developing new axially chiral phosphine ligands for asymmetric catalysis. *Coord. Chem. Rev.* **2007**, *251*, 2119–2144. [CrossRef]
15. Pietrusiewicz, K.M.; Zablocka, M. Preparation of Scalemic P-Chiral Phosphines and Their Derivatives. *Chem. Rev.* **1994**, *94*, 1375–1411. [CrossRef]
16. Rein, T.; Pedersen, T.M. Palladium-catalyzed reaction of olefins with $PhI(OAc)_2$-TBAB system: An efficient and highly selective bisfunctionalization strategy. *Synthesis* **2002**, *2002*, 579–594. [CrossRef]
17. Rein, T.; Reiser, O. Recent advances in asymmetric Wittig-type reactions. *Acta Chem. Scand.* **1996**, *50*, 369–379. [CrossRef]
18. Zhang, K.; Lu, L.-Q.; Yao, S.; Chen, J.-R.; Shi, D.-Q.; Xiao, W.-J. Enantioconvergent Copper Catalysis: In Situ Generation of the Chiral Phosphorus Ylide and Its Wittig Reactions. *J. Am. Chem. Soc.* **2017**, *139*, 12847–12854. [CrossRef]
19. Wong, G.W.; Landis, C.R. Iterative Asymmetric Hydroformylation/Wittig Olefination Sequence. *Angew. Chem. Int. Ed.* **2013**, *52*, 1564–1567. [CrossRef]
20. Enders, D.; Grossmann, A.; Gieraths, B.; Duezdemir, M.; Merkens, C. Organocatalytic One-Pot Asymmetric Synthesis of 4*H*,5*H*-Pyrano[2,3-*c*]pyrazoles. *Org. Lett.* **2012**, *14*, 4254–4257. [CrossRef]
21. Lin, A.; Wang, J.; Mao, H.; Ge, H.; Tan, R.; Zhu, C.; Cheng, Y. Organocatalytic Asymmetric Michael-Type/Wittig Reaction of Phosphorus Ylides: Synthesis of Chiral α-Methylene-δ-Ketoesters. *Org. Lett.* **2011**, *13*, 4176–4179. [CrossRef] [PubMed]
22. Gramigna, L.; Duce, S.; Filippini, G.; Fochi, M.; Franchini, M.C.; Bernardi, L. Organocatalytic asymmetric Wittig reactions: Generation of enantioenriched axially chiral olefins breaking a symmetry plane. *Synlett* **2011**, 2745–2749. [CrossRef]
23. Ye, L.-W.; Wang, S.-B.; Wang, Q.-G.; Sun, X.-L.; Tang, Y.; Zhou, Y.-G. Asymmetric tandem Michael addition-ylide olefination reaction for the synthesis of optically active cyclohexa-1,3-diene derivatives. *Chem. Commun.* **2009**, 3092–3094. [CrossRef] [PubMed]
24. Liu, Y.-k.; Ma, C.; Jiang, K.; Liu, T.-Y.; Chen, Y.-C. Asymmetric Tandem Michael Addition-Wittig Reaction to Cyclohexenone Annulation. *Org. Lett.* **2009**, *11*, 2848–2851. [CrossRef] [PubMed]
25. Hong, B.-C.; Jan, R.-H.; Tsai, C.-W.; Nimje, R.Y.; Liao, J.-H.; Lee, G.-H. Organocatalytic Enantioselective Cascade Michael-Michael-Wittig Reactions of Phosphorus Ylides: One-Pot Synthesis of the *all-cis* Trisubstituted Cyclohexenecarboxylates via the [1 + 2 + 3] Annulation. *Org. Lett.* **2009**, *11*, 5246–5249. [CrossRef] [PubMed]
26. Voituriez, A.; Saleh, N. From phosphine-promoted to phosphine-catalyzed reactions by in situ phosphine oxide reduction. *Tetrahedron Lett.* **2016**, *57*, 4443–4451. [CrossRef]
27. Xu, S.; Tang, Y. Catalytic approaches to stoichiometric phosphine-mediated organic reactions. *Lett. Org. Chem.* **2014**, *11*, 524–533. [CrossRef]
28. Van Kalkeren, H.A.; van Delft, F.L.; Rutjes, F.P.J.T. Organophosphorus Catalysis to Bypass Phosphine Oxide Waste. *ChemSusChem* **2013**, *6*, 1615–1624. [CrossRef]
29. Zhao, Q.; Curran, D.P.; Malacria, M.; Fensterbank, L.; Goddard, J.-P.; Lacôte, E. N-Heterocyclic Carbene-Catalyzed Hydrosilylation of Styryl and Propargylic Alcohols with Dihydrosilanes. *Chem. Eur. J.* **2011**, *17*, 9911–9914. [CrossRef]

30. Quin, L.D.; Caster, K.C.; Kisalus, J.C.; Mesch, K.A. Bridged ring systems containing phosphorus: Structural influences on the stereochemistry of silane reductions of P-oxides and on carbon-13 and phosphorus-31 NMR properties of phosphines. *J. Am. Chem. Soc.* **1984**, *106*, 7021–7032. [CrossRef]
31. Busacca, C.A.; Raju, R.; Grinberg, N.; Haddad, N.; James-Jones, P.; Lee, H.; Lorenz, J.C.; Saha, A.; Senanayake, C.H. Reduction of Tertiary Phosphine Oxides with DIBAL-H. *J. Org. Chem.* **2008**, *73*, 1524–1531. [CrossRef] [PubMed]
32. Busacca, C.A.; Lorenz, J.C.; Grinberg, N.; Haddad, N.; Hrapchak, M.; Latli, B.; Lee, H.; Sabila, P.; Saha, A.; Sarvestani, M.; et al. A Superior Method for the Reduction of Secondary Phosphine Oxides. *Org. Lett.* **2005**, *7*, 4277–4280. [CrossRef] [PubMed]
33. Imamoto, T.; Kikuchi, S.-i.; Miura, T.; Wada, Y. Stereospecific Reduction of Phosphine Oxides to Phosphines by the Use of a Methylation Reagent and Lithium Aluminum Hydride. *Org. Lett.* **2001**, *3*, 87–90. [CrossRef] [PubMed]
34. Henson, P.D.; Naumann, K.; Mislow, K. Stereomutation of phosphine oxide by lithium aluminum hydride. *J. Amer. Chem. Soc.* **1969**, *91*, 5645–5646. [CrossRef]
35. Sowa, S.; Stankevic, M.; Flis, A.; Pietrusiewicz, K.M. Reduction of Tertiary Phosphine Oxides by BH_3 Assisted by Neighboring Activating Groups. *Synthesis* **2018**, *50*, 2106–2118.
36. Provis-Evans, C.B.; Emanuelsson, E.A.C.; Webster, R.L. Rapid Metal-Free Formation of Free Phosphines from Phosphine Oxides. *Adv. Synth. Catal.* **2018**, *360*, 3999–4004. [CrossRef]
37. Elias, J.S.; Costentin, C.; Nocera, D.G. Direct Electrochemical P(V) to P(III) Reduction of Phosphine Oxide Facilitated by Triaryl Borates. *J. Am. Chem. Soc.* **2018**, *140*, 13711–13718. [CrossRef]
38. Mehta, M.; Garcia de la Arada, I.; Perez, M.; Porwal, D.; Oestreich, M.; Stephan, D.W. Metal-Free Phosphine Oxide Reductions Catalyzed by $B(C_6F_5)_3$ and Electrophilic Fluorophosphonium Cations. *Organometallics* **2016**, *35*, 1030–1035. [CrossRef]
39. Stepen, A.J.; Bursch, M.; Grimme, S.; Stephan, D.W.; Paradies, J. Electrophilic Phosphonium Cation-Mediated Phosphane Oxide Reduction Using Oxalyl Chloride and Hydrogen. *Angew. Chem. Int. Ed.* **2018**, *57*, 15253–15256. [CrossRef]
40. Li, P.; Wischert, R.; Metivier, P. Mild Reduction of Phosphine Oxides with Phosphites To Access Phosphines. *Angew. Chem. Int. Ed.* **2017**, *56*, 15989–15992. [CrossRef]
41. Kuroboshi, M.; Kita, T.; Aono, A.; Katagiri, T.; Kikuchi, S.; Yamane, S.; Kawakubo, H.; Tanaka, H. Reduction of phosphine oxides to the corresponding phosphine derivatives in Mg/Me_3SiCl/DMI system. *Tetrahedron Lett.* **2015**, *56*, 918–920. [CrossRef]
42. Pehlivan, L.; Metay, E.; Delbrayelle, D.; Mignani, G.; Lemaire, M. Reduction of phosphine oxides to phosphines with the $InBr_3$/TMDS system. *Tetrahedron* **2012**, *68*, 3151–3155. [CrossRef]
43. Rajendran, K.V.; Gilheany, D.G. Simple unprecedented conversion of phosphine oxides and sulfides to phosphine boranes using sodium borohydride. *Chem. Commun.* **2012**, *48*, 817–819. [CrossRef] [PubMed]
44. Kawakubo, H.; Kuroboshi, M.; Yano, T.; Kobayashi, K.; Kamenoue, S.; Akagi, T.; Tanaka, H. Electroreduction of triphenylphosphine oxide to triphenylphosphine in the presence of chlorotrimethylsilane. *Synthesis* **2011**, 4091–4098.
45. Yano, T.; Kuroboshi, M.; Tanaka, H. Electroreduction of triphenylphosphine dichloride and the efficient one-pot reductive conversion of phosphine oxide to triphenylphosphine. *Tetrahedron Lett.* **2010**, *51*, 698–701. [CrossRef]
46. Longwitz, L.; Werner, T. Recent advances in catalytic Wittig-type reactions based on P(III)/P(V) redox cycling. *Pure Appl. Chem.* **2019**, *91*, 95–102. [CrossRef]
47. Podyacheva, E.; Kuchuk, E.; Chusov, D. Reduction of phosphine oxides to phosphines. *Tetrahedron Lett.* **2019**, *60*, 575–582. [CrossRef]
48. Karanam, P.; Reddy, G.M.; Lin, W. Strategic Exploitation of the Wittig Reaction: Facile Synthesis of Heteroaromatics and Multifunctional Olefins. *Synlett* **2018**, *29*, 2608–2622.
49. Kovacs, T.; Keglevich, G. The Reduction of Tertiary Phosphine Oxides by Silanes. *Curr. Org. Chem.* **2017**, *21*, 569–585. [CrossRef]
50. Kovacs, T.; Keglevich, G. The deoxygenation of phosphine oxides under green chemical conditions. *Phosphorus Sulfur Silicon Relat. Elem.* **2016**, *191*, 359–366. [CrossRef]
51. Lao, Z.; Toy, P.H. Catalytic Wittig and aza-Wittig reactions. *Beilstein J. Org. Chem.* **2016**, *12*, 2577–2587. [CrossRef] [PubMed]

52. Herault, D.; Nguyen, D.H.; Nuel, D.; Buono, G. Reduction of secondary and tertiary phosphine oxides to phosphines. *Chem. Soc. Rev.* **2015**, *44*, 2508–2528. [CrossRef] [PubMed]
53. O'Brien, C.J.; Tellez, J.L.; Nixon, Z.S.; Kang, L.J.; Carter, A.L.; Kunkel, S.R.; Przeworski, K.C.; Chass, G.A. Recycling the Waste: The Development of a Catalytic Wittig Reaction. *Angew. Chem. Int. Ed.* **2009**, *48*, 6836–6839. [CrossRef] [PubMed]
54. O'Brien, C.J.; Lavigne, F.; Coyle, E.E.; Holohan, A.J.; Doonan, B.J. Breaking the Ring through a Room Temperature Catalytic Wittig Reaction. *Chem. Eur. J.* **2013**, *19*, 5854–5858.
55. O'Brien, C.J.; Nixon, Z.S.; Holohan, A.J.; Kunkel, S.R.; Tellez, J.L.; Doonan, B.J.; Coyle, E.E.; Lavigne, F.; Kang, L.J.; Przeworski, K.C. Part I: The Development of the Catalytic Wittig Reaction. *Chem. Eur. J.* **2013**, *19*, 15281–15289. [CrossRef]
56. Coyle, E.E.; Doonan, B.J.; Holohan, A.J.; Walsh, K.A.; Lavigne, F.; Krenske, E.H.; O'Brien, C.J. Catalytic Wittig Reactions of Semi- and Nonstabilized Ylides Enabled by Ylide Tuning. *Angew. Chem. Int. Ed.* **2014**, *53*, 12907–12911. [CrossRef]
57. Li, Y.; Das, S.; Zhou, S.; Junge, K.; Beller, M. General and Selective Copper-Catalyzed Reduction of Tertiary and Secondary Phosphine Oxides: Convenient Synthesis of Phosphines. *J. Am. Chem. Soc.* **2012**, *134*, 9727–9732. [CrossRef]
58. Li, Y.; Lu, L.-Q.; Das, S.; Pisiewicz, S.; Junge, K.; Beller, M. Highly Chemoselective Metal-Free Reduction of Phosphine Oxides to Phosphines. *J. Am. Chem. Soc.* **2012**, *134*, 18325–18329. [CrossRef]
59. Cai, L.; Zhang, K.; Chen, S.; Lepage, R.J.; Houk, K.N.; Krenske, E.H.; Kwon, O. Catalytic Asymmetric Staudinger-aza-Wittig Reaction for the Synthesis of Heterocyclic Amines. *J. Am. Chem. Soc.* **2019**, *141*, 9537–9542. [CrossRef]
60. Longwitz, L.; Spannenberg, A.; Werner, T. Phosphetane Oxides as Redox Cycling Catalysts in the Catalytic Wittig Reaction at Room Temperature. *ACS Catal.* **2019**, *9*, 9237–9244. [CrossRef]
61. Lorton, C.; Castanheiro, T.; Voituriez, A. Catalytic and Asymmetric Process via P^{III}/P^{V}=O Redox Cycling: Access to (Trifluoromethyl)cyclobutenes via a Michael Addition/Wittig Olefination Reaction. *J. Am. Chem. Soc.* **2019**, *141*, 10142–10147. [CrossRef]
62. Fianchini, M.; Maseras, F. DFT characterization of the mechanism for Staudinger/aza-Wittig tandem organocatalysis. *Tetrahedron* **2019**, *75*, 1852–1859. [CrossRef]
63. Han, X.; Saleh, N.; Retailleau, P.; Voituriez, A. Phosphine-Catalyzed Reaction between 2-Aminobenzaldehydes and Dialkyl Acetylenedicarboxylates: Synthesis of 1,2-Dihydroquinoline Derivatives and Toward the Development of an Olefination Reaction. *Org. Lett.* **2018**, *20*, 4584–4588. [CrossRef] [PubMed]
64. Wang, L.; Sun, M.; Ding, M.-W. Catalytic Intramolecular Wittig Reaction Based on a Phosphine/Phosphine Oxide Catalytic Cycle for the Synthesis of Heterocycles. *Eur. J. Org. Chem.* **2017**, 2568–2578. [CrossRef]
65. Wang, L.; Xie, Y.-B.; Huang, N.-Y.; Yan, J.-Y.; Hu, W.-M.; Liu, M.-G.; Ding, M.-W. Catalytic aza-Wittig Reaction of Acid Anhydride for the Synthesis of 4*H*-Benzo[*d*][1,3]oxazin-4-ones and 4-Benzylidene-2-aryloxazol-5(4*H*)-ones. *ACS Catal.* **2016**, *6*, 4010–4016. [CrossRef]
66. Saleh, N.; Voituriez, A. Synthesis of 9*H*-Pyrrolo[1,2-a]indole and 3*H*-Pyrrolizine Derivatives via a Phosphine-Catalyzed Umpolung Addition/Intramolecular Wittig Reaction. *J. Org. Chem.* **2016**, *81*, 4371–4377. [CrossRef]
67. Schirmer, M.-L.; Adomeit, S.; Spannenberg, A.; Werner, T. Novel Base-Free Catalytic Wittig Reaction for the Synthesis of Highly Functionalized Alkenes. *Chem. Eur. J.* **2016**, *22*, 2458–2465. [CrossRef]
68. Lee, C.-J.; Chang, T.-H.; Yu, J.-K.; Madhusudhan Reddy, G.; Hsiao, M.-Y.; Lin, W. Synthesis of Functionalized Furans via Chemoselective Reduction/Wittig Reaction Using Catalytic Triethylamine and Phosphine. *Org. Lett.* **2016**, *18*, 3758–3761. [CrossRef]
69. Schirmer, M.-L.; Adomeit, S.; Werner, T. First Base-Free Catalytic Wittig Reaction. *Org. Lett.* **2015**, *17*, 3078–3081. [CrossRef]
70. Tsai, Y.-L.; Lin, W. Synthesis of Multifunctional Alkenes from Substituted Acrylates and Aldehydes via Phosphine-Catalyzed Wittig Reaction. *Asian J. Org. Chem.* **2015**, *4*, 1040–1043. [CrossRef]
71. Rommel, S.; Belger, C.; Begouin, J.-M.; Plietker, B. Dual [Fe+Phosphine] Catalysis: Application in Catalytic Wittig Olefination. *Chemcatchem* **2015**, *7*, 1292–1301. [CrossRef]
72. Werner, T.; Hoffmann, M.; Deshmukh, S. First Enantioselective Catalytic Wittig Reaction. *Eur. J. Org. Chem.* **2014**, 6630–6633. [CrossRef]

73. Wang, L.; Wang, Y.; Chen, M.; Ding, M.-W. Reversible P(III)/P(V) Redox: Catalytic Aza-Wittig Reaction for the Synthesis of 4(3*H*)-Quinazolinones and the Natural Product Vasicinone. *Adv. Synth. Catal.* **2014**, *356*, 1098–1104. [CrossRef]
74. Werner, T.; Hoffmann, M.; Deshmukh, S. First Microwave-Assisted Catalytic Wittig Reaction. *Eur. J. Org. Chem.* **2014**, 6873–6876. [CrossRef]
75. Van Kalkeren, H.A.; te Grotenhuis, C.; Haasjes, F.S.; Hommersom, C.A.; Rutjes, F.P.J.T.; van Delft, F.L. Catalytic Staudinger/aza-Wittig sequence by in situ phosphane oxide reduction. *Eur. J. Org. Chem.* **2013**, 7059–7066. [CrossRef]
76. Beddoe, R.H.; Sneddon, H.F.; Denton, R.M. The catalytic Mitsunobu reaction: A critical analysis of the current state-of-the-art. *Org. Biomol. Chem.* **2018**, *16*, 7774–7781. [CrossRef]
77. Hirose, D.; Gazvoda, M.; Košmrlj, J.; Taniguchi, T. The "Fully Catalytic System" in Mitsunobu Reaction Has Not Been Realized Yet. *Org. Lett.* **2016**, *18*, 4036–4039. [CrossRef]
78. Buonomo, J.A.; Aldrich, C.C. Mitsunobu Reactions Catalytic in Phosphine and a Fully Catalytic System. *Angew. Chem. Int. Ed.* **2015**, *54*, 13041–13044. [CrossRef]
79. Lenstra, D.C.; Wolf, J.J.; Mecinovic, J. Catalytic Staudinger Reduction at Room Temperature. *J. Org. Chem.* **2019**, *84*, 6536–6545. [CrossRef]
80. Zhang, K.; Cai, L.; Yang, Z.; Houk, K.N.; Kwon, O. Bridged [2.2.1] bicyclic phosphine oxide facilitates catalytic γ-umpolung addition-Wittig olefination. *Chem. Sci.* **2018**, *9*, 1867–1872. [CrossRef]
81. Lenstra, D.C.; Lenting, P.E.; Mecinovic, J. Sustainable organophosphorus-catalysed Staudinger reduction. *Greem Chem.* **2018**, *20*, 4418–4422. [CrossRef]
82. Andrews, K.G.; Denton, R.M. A more critical role for silicon in the catalytic Staudinger amidation: Silanes as non-innocent reductants. *Chem. Commun.* **2017**, *53*, 7982–7985. [CrossRef] [PubMed]
83. Saleh, N.; Blanchard, F.; Voituriez, A. Synthesis of Nitrogen-Containing Heterocycles and Cyclopentenone Derivatives via Phosphine-Catalyzed Michael Addition/Intramolecular Wittig Reaction. *Adv. Synth. Catal.* **2017**, *359*, 2304–2315. [CrossRef]
84. Van Kalkeren, H.A.; Bruins, J.J.; Rutjes, F.P.J.T.; van Delft, F.L. Organophosphorus-catalyzed Staudinger reduction. *Adv. Synth. Catal.* **2012**, *354*, 1417–1421. [CrossRef]
85. Longwitz, L.; Jopp, S.; Werner, T. Organocatalytic Chlorination of Alcohols by P(III)/P(V) Redox Cycling. *J. Org. Chem.* **2019**, *84*, 7863–7870. [CrossRef] [PubMed]
86. Van Kalkeren, H.A.; Leenders, S.; Hommersom, C.R.A.; Rutjes, F.; van Delft, F.L. In situ phosphine oxide reduction: A catalytic Appel reaction. *Chem. Eur. J.* **2011**, *17*, 11290–11295. [CrossRef]
87. Nykaza, T.V.; Ramirez, A.; Harrison, T.S.; Luzung, M.R.; Radosevich, A.T. Biphilic Organophosphorus-Catalyzed Intramolecular Csp^2-H Amination: Evidence for a Nitrenoid in Catalytic Cadogan Cyclizations. *J. Am. Chem. Soc.* **2018**, *140*, 3103–3113. [CrossRef]
88. White, P.B.; Rijpkema, S.J.; Bunschoten, R.P.; Mecinovic, J. Mechanistic Insight into the Catalytic Staudinger Ligation. *Org. Lett.* **2019**, *21*, 1011–1014.
89. Nykaza, T.V.; Cooper, J.C.; Li, G.; Mahieu, N.; Ramirez, A.; Luzung, M.R.; Radosevich, A.T. Intermolecular Reductive C-N Cross Coupling of Nitroarenes and Boronic Acids by P^{III}/P^{V}=O Catalysis. *J. Am. Chem. Soc.* **2018**, *140*, 15200–15205. [CrossRef]
90. Hamstra, D.F.J.; Lenstra, D.C.; Koenders, T.J.; Rutjes, F.P.J.T.; Mecinovic, J. Poly(methylhydrosiloxane) as a green reducing agent in organophosphorus-catalyzed amide bond formation. *Org. Biomol. Chem.* **2017**, *15*, 6426–6432. [CrossRef]
91. Fourmy, K.; Voituriez, A. Catalytic Cyclization Reactions of Huisgen Zwitterion with α-Ketoesters by in Situ Chemoselective Phosphine Oxide Reduction. *Org. Lett.* **2015**, *17*, 1537–1540. [CrossRef]
92. Zhao, W.; Yan, P.K.; Radosevich, A.T. A Phosphetane Catalyzes Deoxygenative Condensation of α-Keto Esters and Carboxylic Acids via P^{III}/P^{V}=O Redox Cycling. *J. Am. Chem. Soc.* **2015**, *137*, 616–619. [CrossRef] [PubMed]
93. Kosal, A.D.; Wilson, E.E.; Ashfeld, B.L. Phosphine-Based Redox Catalysis in the Direct Traceless Staudinger Ligation of Carboxylic Acids and Azides. *Angew. Chem. Int. Ed.* **2012**, *51*, 12036–12040. [CrossRef] [PubMed]
94. Rotstein, B.H.; Zaretsky, S.; Rai, V.; Yudin, A.K. Small Heterocycles in Multicomponent Reactions. *Chem. Rev.* **2014**, *114*, 8323–8359. [CrossRef] [PubMed]
95. Estevez, V.; Villacampa, M.; Menendez, J.C. Recent advances in the synthesis of pyrroles by multicomponent reactions. *Chem. Soc. Rev.* **2014**, *43*, 4633–4657. [CrossRef]

96. Cioc, R.C.; Ruijter, E.; Orru, R.V.A. Multicomponent reactions: Advanced tools for sustainable organic synthesis. *Green Chem.* **2014**, *16*, 2958–2975. [CrossRef]
97. Wang, J.; Zhou, R.; He, Z.-R.; He, Z. Phosphane-Mediated Domino Synthesis of Tetrasubstituted Furans from Simple Terminal Activated Olefins. *Eur. J. Org. Chem.* **2012**, 6033–6041. [CrossRef]
98. Lawrence, N.J.; Crump, J.P.; McGown, A.T.; Hadfield, J.A. Reaction of Baylis–Hillman products with Swern and Dess–Martin oxidants. *Tetrahedron Lett.* **2001**, *42*, 3939–3941. [CrossRef]

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