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Catalytic aza-Wittig Reaction of Acid Anhydride for the Synthesis of 4H-benzo[d][1,3]oxazin-4-ones and 4-benzylidene-2-aryloxazol-5(4H)-ones

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Abstract: Compared to the aza-Wittig reaction of aldehydes, ketones, amides and esters, the aza-Wittig reaction of acid anhydride was always overlooked, which should be important part of Wittig reactions. Here, aza-Wittig reaction of anhydride and catalytic aza-Wittig reaction of anhydride were both developed with high yields, which provides an efficient method to synthesize of 4H-benzo[d][1,3]oxazin-4-ones and 4-benzylidene-2-aryloxazol-5(4H)-ones. The strategy of copper-catalyzed reduction of phosphine oxide was used and found effective for this transformation. Additionally, the one-pot catalytic aza-Wittig reaction of carboxylic acids was achieved. Furthermore, NMR experiments and Hammett plot recorded the process of catalytic aza-Wittig reaction of anhydride, which provides direct proof that the copper-catalyzed reduction of waste phosphine oxide is the key step in this transformation.

Keywords: catalytic aza-Wittig reaction, anhydride, carboxylic acids

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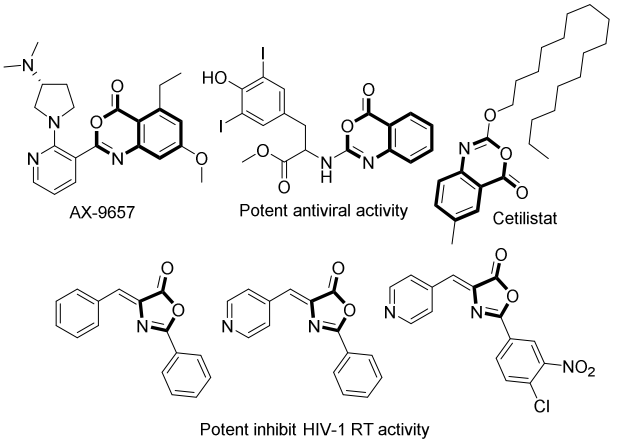
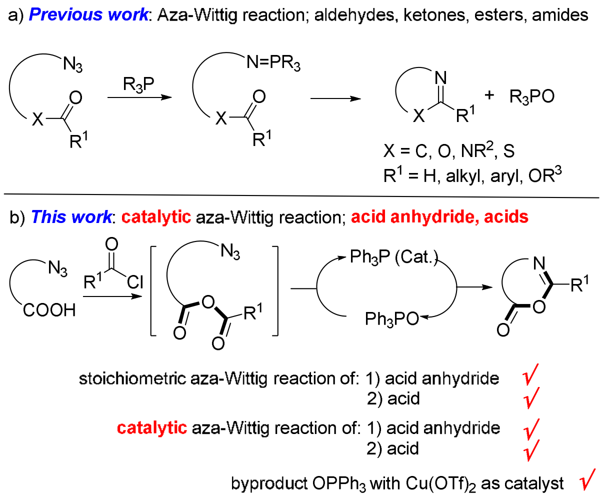
INTRODUCTION

4H-benzo[d][1,3]oxazin-4-ones and 4-benzylidene-2-aryloxazol-5(4H)-ones represent an important, widely used structural motif in natural products, drugs and biologically active compounds. For example, 4H-benzo[d][1,3]oxazin-4-one is the key pharmacophore in Cetilistat, which is a phase-III clinical trial drug.[1] Some others were found to display excellent antifungal, antibacterial, herbicidal activities.[2] Meanwhile, the substances of 4-benzylidene-2-aryloxazol-5(4H)-ones are considered to be the potent inhibitor of death-associated protein kinase (DAPK), which is a serine/threonine protein kinase implicated in diverse programmed cell death pathways. As the outstanding prospect target protein for dealing with ischemic diseases, DAPK is mainly adjusted cell death in response to external irritants, such as cytokines, activation, etc. (Scheme 1).[3] In 2010, Okamoto et al identified several potent and selective DAPK inhibitors efficiently by structure-based virtual screening and they pointed that 4-benzylidene-2-aryloxazol-5(4H)-ones have potential to contribute to the development of drug treatments for ischemic diseases.[3b] Moreover, Bourguignon et al. found that 4-benzylidene-2-aryloxazol-5(4H)-ones are very efficient fluorescence resonance energy transfer (FRET) and will be useful for a wide panel of biosensor applications.[3d] The Sampedro group showed that these compounds have good features that make them promising candidates for use as light-activated switches in different applications.[3a] Therefore, theirs synthesis has received extensive attention.[4]



Scheme 1. Several Bioactive Compounds.

The aza-Wittig reaction was accepted as an excellent tool in the construction of organic heterocycles by inter- or intramolecular processes under very mild conditions.[5] The aza-Wittig reaction of aldehydes, ketones, amides and esters were already used in the synthesis of many natural products and biologically active compounds,[6] however, aza-Wittig reaction of acid anhydride was always overlooked. As an important part of the aza-Wittig reaction, the expansion of the aza-Wittig reaction of acid anhydride is necessary and significant as a means to enrich the aza-Wittig reaction (Scheme 2).

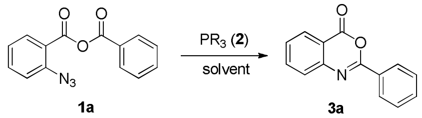


Scheme 2. The aza-Wittig Reaction of Aldehydes, Ketones, Amides and Esters *VS* Acid Anhydride.

Very recently, catalytic aza-Wittig reaction has gradually aroused people's interest because it only needs catalytic amount organophosphorus reagent, which shows high atom efficiency and solves the problem of the separation of the product from the byproduct triphenylphosphine oxide.[7] In 2008, Marsden and co-workers reported the first example of catalytic aza-Wittig reaction using carbonyl isocyanate derivatives that cyclize to produce benzoxazoles and phenanthridines with a special cyclic phosphorus oxide as the catalyst.[7a] Later, Delft developed the catalytic Staudinger/aza-Wittig sequence through in-situ phosphane oxide reduction.[7b] In 2009, O'Brien and Chass demonstrated the first catalytic Wittig reaction at moderate to high yields, also using a special cyclic phosphorus oxide as the catalyst.[7j] In 2010, Zhou group developed tandem catalytic Wittig reactions by using "waste as the catalyst/co-catalyst" strategy.[7s] In 2012, Ashfeld and coworkers reported a redox phosphine catalyzed Staudinger ligation that enables the direct conversion of carboxylic acids to amides, which is the first example PPh_3 used as a catalyst with a stoichiometric silane reductant for C–N bond formations.[7m] In addition, they also reported many other meaningful works about phosphonic catalytic.[7w-7z] In 2014, Krenske and O'Brien reported the first examples of catalytic Wittig reactions with semi-stabilized and non-stabilized yields.[7e] In 2015, Milstein developed a catalytic and oxidant-free coupling of alcohols with non-stabilized phosphorus ylides to form olefins using Wittig reagents.[7t] In 2015, Plietker found that dual [Fe+phosphine] catalyst could catalyze the Wittig reaction at moderate to high yields with Z/E mixtures in most cases.[7u] In 2015, Werner developed the first base-free catalytic Wittig reaction with available tributyl phosphate as the catalyst.[7v] In 2015, Radosevich designed a elegant phosphonic catalyst which is found to catalyze the deoxygenative condensation of α-keto esters and carboxylic acids via P^{III}/P^{V} =O redox cycling.[7q] Recently, we reported a catalytic classical aza-Wittig reaction by using the waste-byproduct triphenylphosphine oxide as the catalyst.[7c] A series of quinazolinone derivatives were very easily and convenient synthesized using ring–close reaction caused by catalytic aza-Wittig reaction. Herein, aza-Wittig reaction of anhydride and catalytic aza-Wittig reaction of anhydride were both developed with the strategy of copper-catalyzed reduction of phosphine oxide, which provides an efficient method for synthesis of 4H-benzo[d][1,3]oxazin-4-ones and 4-benzylidene-2-aryloxazol-5(4H)-ones (Scheme 2).

In the beginning, we found anhydrides (**1**) were very easily prepared from the corresponding carboxylic acids and acyl chlorides with high yields. Following their synthesis, 2-azidobenzoic benzoic anhydride (**1a**) was chosen as the model substrate for the reaction attempt. We firstly checked the effect of solvents on this reaction using common triphenylphosphine as the yield precursor. As shown in Table 1, the reaction was strongly solvent-dependent. Low yields and longer reaction time were obtained in DCM and THF. It was found that toluene was the best solvent. Next, various phosphine reagents were screened, with the results showing that nearly all the phosphines could promote this transformation with excellent yields.

Table 1. Screening of Reaction Conditions [a]

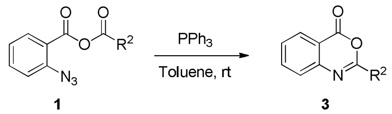


Entry	PR_3	Solvent	T	Yield [%][b]
1	PPh_3	CH_2Cl_2	rt	67
2	PPh_3	MeOH	rt	21
3	PPh_3	THF	rt	51
4	PPh_3	toluene	rt	98
5	$P(4\text{-}ClC_6H_4)_3$	toluene	rt	91
6	$P(4\text{-}MeOC_6H_4)_3$	toluene	rt	93
7	$P(4\text{-}MeC_6H_4)_3$	toluene	rt	95
8	$P(4\text{-}FC_6H_4)_3$	toluene	rt	90
9	$MePPh_2$	toluene	rt	93
10	Me_2PPh	toluene	rt	91
11	$P(n\text{-}Bu)_3$	toluene	rt	88
12	PPh_3	toluene	60 °C	98
13	PPh_3	toluene	reflux	98
14	none	toluene	rt	<5

[a] Conditions: **1a** (0.5 mmol, 1.0 equiv.), **2** (0.55 mmol, 1.1 equiv.), 1 h. [b] Isolated yields.

In the presence of triphenylphosphine and toluene, a variety of substituted substrates have been tested to examine the reaction scope (Table 2). In most cases, the anhydrides (**2**) were very smoothly converted to the corresponding 4H-benzo[d][1,3]oxazin-4-ones with moderate to high yields. However, the reaction of substrates with the electron-withdrawing group gave slightly high yields than those with the electron-donating group.

Table 2. aza-Wittig Reaction of Anhydride[a]

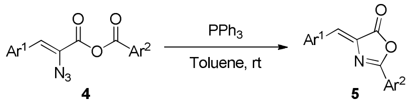


Entry	R^1	R^2	Yield[%][b]
1	H	Ph	98**(3a)**
2	H	*p*-Cl-C_6H_4	98**(3b)**
3	H	*p*-Br-C_6H_4	95**(3c)**
4	H	*o*-Me-C_6H_4	84**(3d)**
5	H	Me	73**(3e)**
6	H	*p*-Me-C_6H_4	88**(3f)**
7	H	*o*-MeO-C_6H_4	79**(3g)**
8	H	Et	71**(3h)**
9	H	*p*-MeO-C_6H_4	82**(3i)**
10	H	*p*-F-C_6H_4	94**(3j)**

[a] Conditions: **1** (0.5 mmol, 1.0 equiv.), PPh_3 (0.55 mmol, 1.1 equiv.), toluene (3 mL), 0.2-2 h. [b] Isolated yields.

The core of 4-benzylidene-2-aryloxazol-5(4H)-ones represents a typical skeleton in natural molecules that revealed excellent bioactivities, i.e. antifungal, herbicidal, antibacterial, HSV-1 protease inhibition, etc. Here, we also attempted the aza-Wittig reaction of anhydrides with 2-azido-3-arylacrylic benzoic anhydride derivatives under the upper conditions. The results were summarized in Table 3. Under the optimized reaction conditions, a variety of 2-azido-3-arylacrylic benzoic anhydride derivatives could successfully converted to their corresponding 4-benzylidene-2-aryloxazol-5(4H)-one derivatives. As illustrated in Table 3, moderate to high yields were achieved for most of the substrates.

Table 3. aza-Wittig Reaction of Anhydride[a]

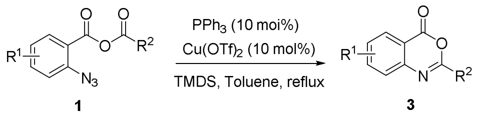


Entry	Ar^1	Ar^2	Yield[%][b]
1	*p*-Me-C_6H_4	Ph	81(**5a**)
2	*p*-Me- C_6H_4	*p*-Cl-C_6H_4	87(**5b**)
3	*p*-Me- C_6H_4	*o*-Cl-C_6H_4	72(**5c**)
4	*p*-Me- C_6H_4	*p*-Br-C_6H_4	85(**5d**)
5	*p*-Me- C_6H_4	*p*-Me-C_6H_4	76(**5e**)
6	*p*-Me- C_6H_4	*o*-F-C_6H_4	70(**5f**)
7	*p*-Me- C_6H_4	*o*-MeO-C_6H_4	62**(5g)**
8	*p*-Me- C_6H_4	*p*-MeO-C_6H_4	73**(5h)**
9	*p*-Me- C_6H_4	*o*-Me-C_6H_4	63**(5i)**
10	*p*-Me- C_6H_4	*p*-F-C_6H_4	83**(5j)**
11	Ph	Ph	85**(5k)**
12	Ph	*p*-Me-C_6H_4	81**(5l)**

[a] Conditions: **4** (0.5 mmol, 1.0 equiv.), PPh_3 (0.55 mmol, 1.1 equiv.), toluene (3 mL), 0.2-2 h. [b] Isolated yields.

To demonstrate the advantages of this reaction, we challenged catalytic aza-Wittig reaction together with the upper two transformations, which could be great breakthrough in atom efficiency.[7] The key question in regard to catalytic aza-Wittig reaction is the reduction of the byproduct phosphine oxide. According to the literature, phosphine oxide could be reduced to phosphine by trichlorosilane,[8] lithium aluminum hydride,[9] phosgene[10] and silanes.[11] Among these reducing agents, silane is a much better choice as a mild and economic reason.[12] We attempted the catalytic aza-Wittig reaction with the TMDS(tetramethyldisiloxane, $Me_2HSiOSiMe_2H$), which is easily obtained as an inexpensive byproduct from the organo-silicon industry as a reduction. To our surprise, we found that the reaction occurred smoothly over a longer time (4h) with 95% yield obtained (Table 4, entry 1). Generally, all the 2-azidobenzoic benzoic anhydrides could be converted to the corresponding 4H-benzo[d][1,3]oxazin-4-ones with very good yields (Table 4). However, there are only 9% yield was obtained in the absence of $Cu(OTf)_2$ (Table 4, entry 10), and no 4H-benzo[d][1,3]oxazin-4-one **3a** was produced without PPh_3 (Table 4, entry 11).

Table 4. Catalytic aza-Wittig Reaction[a]



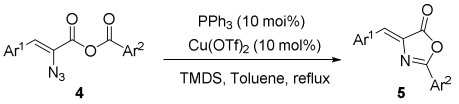
Entry	R^1	R^2	Yield[%][b]
1	H	Ph	95**(3a)**
2	H	*m*-Cl-C_6H_4	95**(3k)**
3	H	*i*-Pr	66**(3l)**
4	4-Cl	Ph	92**(3m)**
5	4-Cl	*p*-Cl-C_6H_4	93**(3n)**
6	4-Cl	*o*-MeO-C_6H_4	76**(3o)**
7	4-Cl	*p*-Me-C_6H_4	85**(3p)**
8	4-Cl	*p*-F-C_6H_4	90**(3q)**
9	4-Cl	*p*-MeO-C_6H_4	79**(3r)**

10	H	Ph	9 **(3a)** [c]
11	H	Ph	0 **(3a)** [d]

[a] Conditions: **1** (0.5 mmol, 1.0 equiv.), PPh_3 (0.05 mmol, 0.1 equiv.), $Cu(OTf)_2$ (0.05 mmol, 0.1 equiv.), TMDS (3 equiv.), toluene (3 mL), 2-6 h. [b] Isolated yields. [c] Without copper salt. [d] Without PPh_3 .

Concurrently, we conducted the catalytic aza-Wittig reaction of 2-azido-3-arylacrylic benzoic anhydrides and the results were summarized in Table 5. Under those conditions, the reaction proceeded well and the corresponding 4-benzylidene-2-aryloxazol-5(4H)-ones were obtained with moderate to high yields (Table 5).

Table 5. Catalytic aza-Wittig Reaction [a]

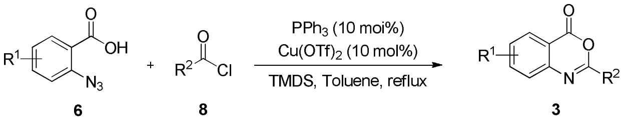


Entry	Ar^1	Ar^2	Yield[%][b]
1	*p*-Me-C_6H_4	Ph	62(**5a**)
2	Ph	*p*-MeO-C_6H_4	69(**5m**)
3	Ph	*p*-F-C_6H_4	63(**5n**)
4	*p*-F-C_6H_4	Ph	72(**5o**)
5	*p*-F-C_6H_4	*p*-MeO-C_6H_4	62(**5p**)
6	*p*-F-C_6H_4	*p*-Me-C_6H_4	63(**5q**)
7	*p*-F-C_6H_4	*p*-F-C_6H_4	67(**5r**)
8	*p*-MeO-C_6H_4	Ph	60(**5s**)
9	*p*-MeO-C_6H_4	*p*-Me-C_6H_4	54(**5t**)
10	*p*-MeO-C_6H_4	*p*-MeO-C_6H_4	58(**5u**)
11	*p*-MeO-C_6H_4	*p*-F-C_6H_4	73(**5v**)
12	*o*-F-C_6H_4	Ph	70(**5w**)
13	*o*-F-C_6H_4	*p*-Me-C_6H_4	66(**5x**)
14	*o*-F-C_6H_4	*p*-MeO-C_6H_4	56(**5y**)
15	*o*-F-C_6H_4	*p*-F-C_6H_4	71(**5z**)

[a] Conditions: **4** (0.5 mmol, 1.0 equiv.), PPh_3 (0.05 mmol, 0.1 equiv.), $Cu(OTf)_2$ (0.05 mmol, 0.1 equiv.), TMDS (3 equiv.), toluene (3 mL), 2-8 h. [b] Isolated yields.

Subsequently, we selected carboxylic acids as substrate to check this methodology for the reason that they aremuch cheaper and common reagents than anhydrides. For another reason is that carboxylic acids are easier to store and transport than the corresponding anhydrides. the catalytic aza-Wittig reaction of 2-azidobenzoic acid was then carried on. To our disappointment, it was found that no desired product was generated. However, when acyl chloride was added to the reaction, a nearly quantitative product was separated with only 10% triphenylphosphine used as the catalyst. Most of carboxylic acids reacted easily to give the 4H-benzo[d][1,3]oxazin-4-ones inhigh yields (Table 6).

Table 6. Direct One-Pot Catalytic aza-Wittig Reaction of Carboxylic Acids [a]

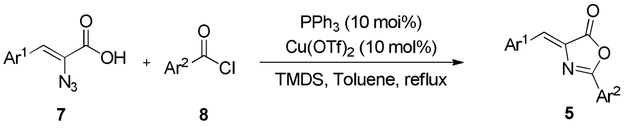


Entry	R^1	R^2	Yield[%][b]
1	H	Ph	98**(3a)**
2	H	*p*-Cl-C_6H_4	98**(3b)**
3	H	*p*-Br-C_6H_4	95**(3c)**
4	H	*o*-Me-C_6H_4	84**(3d)**
5	H	Me	73**(3e)**
6	H	*p*-Me-C_6H_4	88**(3f)**
7	H	*o*-MeO-C_6H_4	79**(3g)**
8	H	Et	71**(3h)**
9	H	*p*-MeO-C_6H_4	82**(3i)**
10	H	*p*-F-C_6H_4	94**(3j)**
11	H	*m*-Cl-C_6H_4	95**(3k)**
12	H	*i*-Pr	67**(3l)**
13	4-Cl	Ph	94**(3m)**
14	4-Cl	*p*-Cl-C_6H_4	95**(3n)**
15	4-Cl	*o*-MeO-C_6H_4	77**(3o)**
16	4-Cl	*p*-Me-C_6H_4	87**(3p)**
17	4-Cl	*p*-F-C_6H_4	91**(3q)**
18	4-Cl	*p*-MeO-C_6H_4	78**(3r)**

[a] Conditions: **6** (0.5 mmol, 1.0 equiv.), acyl chloride **8** (0.55 mmol, 1.1 equiv.), NEt_3 (0.55 mmol, 1.1 equiv.), PPh_3 (0.05 mmol, 0.1 equiv.), $Cu(OTf)_2$ (0.05 mmol, 0.1 equiv.), TMDS (3 equiv.), toluene (3 mL), 2-6 h. [b] Isolated yields.

Additionally, we conducted the catalytic aza-Wittig reaction of (Z)-2-azido-3-phenylacrylic acid and found that the reaction also took place smoothly. Under the above optimal conditions, we explored the scope of the triphenylphosphine-catalyzed one-pot aza-Wittig reaction of (Z)-2-azido-3-phenylacrylic acids and the results were summarized in Table 7. Various (Z)-2-azido-3-phenylacrylic acids could be used in this one-pot cyclization to produce 4-benzylidene-2-aryloxazol-5(4H)-ones.

Table 7. Direct One-Pot Catalytic aza-Wittig Reaction of Carboxylic Acids [a]

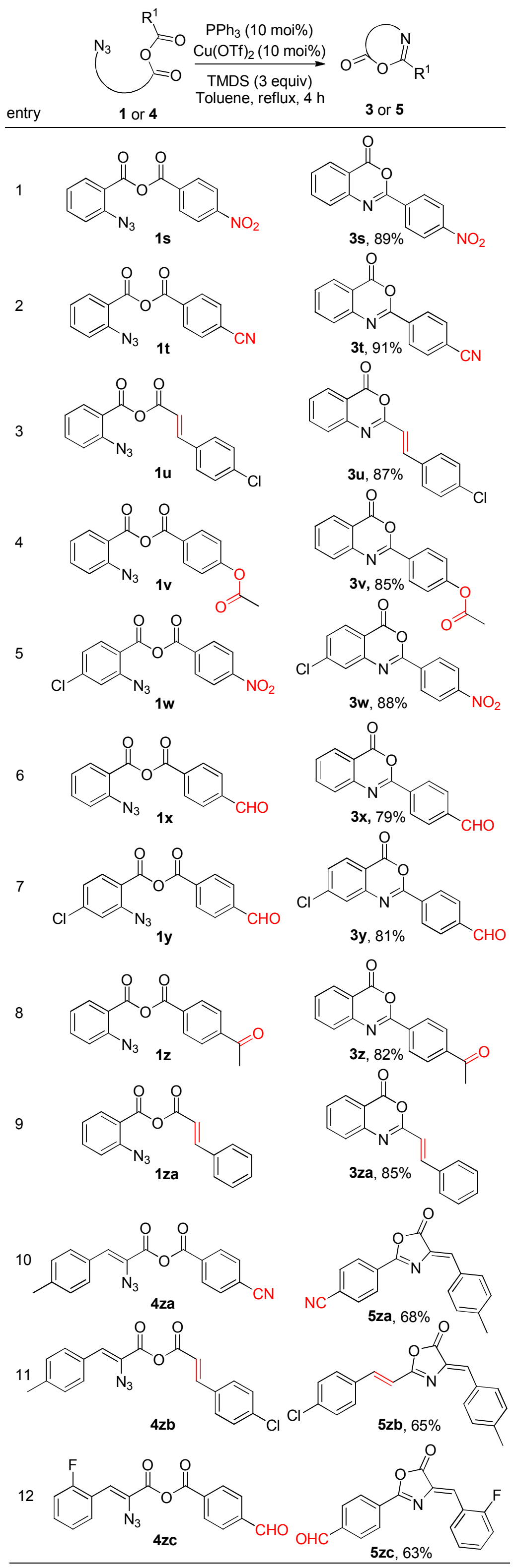


Entry	Ar^1	Ar^2	Yield[%] [b]
1	p-Me-C_6H_4	Ph	62(**5a**)
2	p-Me-C_6H_4	p-Cl-C_6H_4	72**(5b)**
3	p-Me-C_6H_4	o-Cl-C_6H_4	54**(5c)**
4	p-Me-C_6H_4	p-Br-C_6H_4	68**(5d)**
5	p-Me-C_6H_4	p-Me-C_6H_4	61**(5e)**
6	p-Me-C_6H_4	o-F-C_6H_4	55**(5f)**
7	p-Me-C_6H_4	o-MeO-C_6H_4	49**(5g)**
8	p-Me-C_6H_4	p-MeO-C_6H_4	56**(5h)**
9	p-Me-C_6H_4	o-Me-C_6H_4	47**(5i)**
10	p-Me- C_6H_4	p-F-C_6H_4	71**(5j)**
11	Ph	Ph	67**(5k)**
12	Ph	p-Me-C_6H_4	64**(5l)**
13	Ph	p-MeO-C_6H_4	69**(5m)**
14	Ph	p-F-C_6H_4	63**(5n)**
15	p-F-C_6H_4	Ph	72**(5o)**
16	p-F-C_6H_4	p-MeO-C_6H_4	62**(5p)**
17	p-F-C_6H_4	p-Me-C_6H_4	63**(5q)**
18	p-F-C_6H_4	p-F-C_6H_4	67**(5r)**
19	p-MeO-C_6H_4	Ph	60**(5s)**
20	p-MeO-C_6H_4	p-Me-C_6H_4	54**(5t)**
21	p-MeO-C_6H_4	p-MeO-C_6H_4	58**(5u)**
22	p-MeO-C_6H_4	p-F-C_6H_4	73**(5v)**
23	o-F-C_6H_4	Ph	70**(5w)**
24	o-F-C_6H_4	p-Me-C_6H_4	66**(5x)**
25	o-F-C_6H_4	p-MeO-C_6H_4	56**(5y)**
26	o-F-C_6H_4	p-F-C_6H_4	71**(5z)**

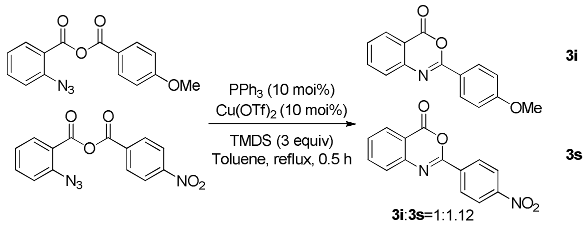
[a] Conditions: **7** (0.5 mmol, 1.0 equiv.), acyl chloride **8** (0.55 mmol, 1.1 equiv.), NEt_3 (0.55 mmol, 1.1 equiv.), PPh_3 (0.05 mmol, 0.1 equiv.), $Cu(OTf)_2$ (0.05 mmol, 0.1 equiv.), TMDS (3 equiv.), toluene (3 mL), 2-8 h. [b] Isolated yields.

Most of the natural products or pharmaceuticals contained 4H-benzo[d][1,3]oxazin-4-ones and 4-benzylidene-2-aryloxazol-5(4H)-ones are functionalized molecules. Therefore, substrates containing other functional groups occurred in this catalytic aza-Wittig reaction of anhydride (Table 8). In fact, functionalized anhydrides were very smoothly converted to the corresponding 4H-benzo[d][1,3]oxazin-4-ones and 4-benzylidene-2-aryloxazol-5(4H)-ones at good yields. Notably, ester, nitrile, nitro, alkene, ketone and even aldehyde are well tolerated in this reaction.

Table 8. Evaluation of the Chemoselectivity in the Catalytic aza-Wittig Reaction of Anhydride.

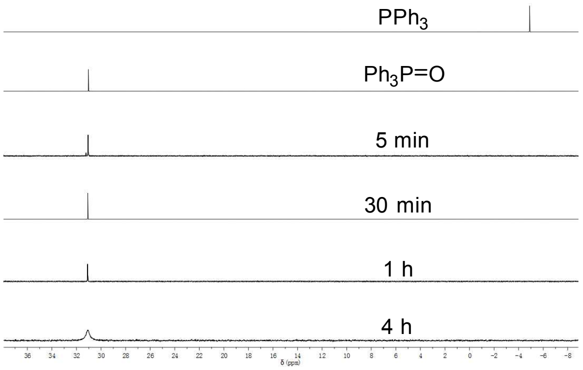


In order to obtain more information of this reaction, the competition experiments of 2-azido-3-phenylacrylic benzoic anhydride with the electron-withdrawing group and that with the electron-donating group were carried on. Interestingly, we found that there is certain product rate was observed in this transformation (Scheme 3).



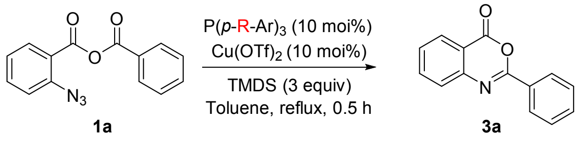
Scheme 3. Intermolecular Competition Reaction.

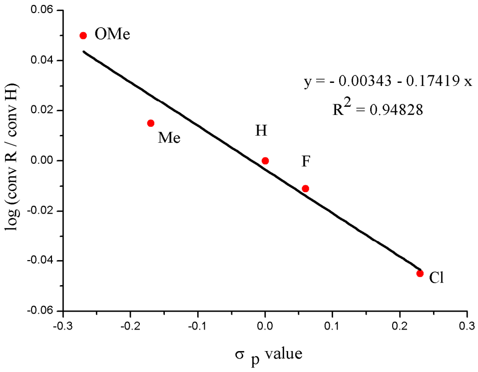
To better understand this catalytic process of aza-Wittig reaction, the ^{31}P NMR experiments were carried on since phosphine ligands were involved in this transformation, and the results are shown in Scheme 4. It was showed that chemical shift of reaction mixture was appeared in 28.91 ppm, which is due to triphenylphosphine oxide. No signal of triphenylphosphine was checked, which might means that once triphenylphosphine is generated it will immediately be consumed in the next aza-Wittig reaction.



Scheme 4. The ^{31}P NMR Spectra of Reaction Process.

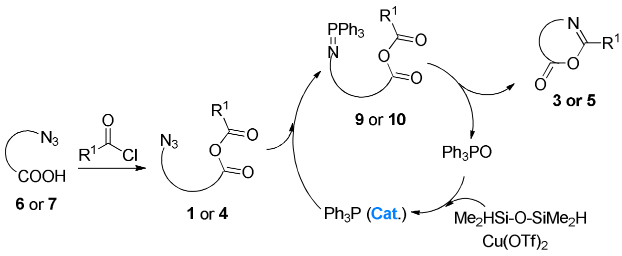
Furthermore, the Hammett plot was considered as the means to more fully describe this transformation, because the Hammett plot is a useful technique for checking reaction process and mechanism. Therefore, we explored the effect of different phosphine catalysts, and the equation was built in Scheme 5. The experiments revealed that election-rich phosphine catalysts resulted in faster reaction rate, which is consistent with the results reported by Beller.[12a]





Scheme 5. Hammett Pot of Various Phosphines.

A possible mechanism for the catalytic aza-Wittig reaction can be proposed (Scheme 6). (i) in situ formation of the anhydride via nucleophilic substitution reaction of carboxylic acids and acyl chloride (ii) a Staudinger reaction of anhydride **1** or **4** with triphenylphosphine to get the iminophosphorane **9** or **10** (iii) intramolecular aza-Wittig reaction of iminophosphorane **9** or **10** to produce the products **3** or **5** and triphenylphosphine oxide; (iv) reduction of triphenylphosphine oxide by the TMDS/Cu(OTf)$_2$ system to regenerate triphenylphosphine, which enters a new catalytic cycle.



Scheme 6. A possible mechanism for the catalytic aza-Wittig reaction.

CONCLUSION

In conclusion, the aza-Wittig reaction and catalytic aza-Wittig reaction of anhydride based on a phosphine(III)/ phosphine(V) oxide catalytic cycle were developed with the strategy of copper-catalyzed reduction of phosphine oxide, providing efficient methods for the synthesis of 4H-benzo[d][1,3]oxazin-4-ones and 4-benzylidene-2-aryloxazol-5(4H)-ones. Additionally, the one-pot catalytic aza-Wittig reaction of carboxylic acids was achieved with good yields. The NMR experiments and Hammett plot tested the process for the catalytic aza-Wittig reaction of anhydride, thereby offering direct proof that the reduction of waste phosphine oxide is the key step in this transformation.

EXPERIMENTAL DETAILS

Representative Procedure: Preparation of 3a via catalytic aza-Wittig reaction of carboxylic acids in one-pot. 2-azidobenzoic acid **6a** (0.326 g, 2.0 mmol) was dissolved in toluene (10 mL), and then NEt$_3$ (0.242 g, 2.4 mmol), acyl chloride (2 mmol), Cu(OTf)$_2$ (0.072 g, 0.2 mmol), TMDS (0.804 g, 6 mmol) and PPh$_3$ (0.052 g, 0.2 mmol) were added in the solution in order. The reaction mixture was then stirred at 110 ^{o}C and monitored by TLC (petroleum ether/ethyl acetate 6:1). After the reaction was completed (6 h), the solvent was removed under reduced pressure and the residue was purified by column chromatography with petroleum ether/ethyl acetate (6:1) as eluent to give **3a** with 98% yield. White solid (yield 0.437 g 98%), mp 183-186 ^{o}C; ^{1}H NMR (CDCl$_3$, 600 MHz) δ (ppm) 8.32 (d, *J* = 7.8 Hz, 2H, Ar-H), 8.25 (d, *J* = 7.8 Hz, 1H, Ar-H), 7.83 (t, *J* = 7.8 Hz, 1H, Ar-H), 7.70 (d, *J* = 7.8 Hz, 1H, Ar-H), 7.58 (d, *J* = 7.2 Hz, 1H, Ar-H), 7.52 (t, *J* = 7.2 Hz, 3H, Ar-H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ (ppm) 159.4, 156.9, 146.8, 136.4, 132.5, 130.0, 128.6, 128.4, 128.1, 127.1, 116.8.

ASSOCIATED CONTECT

Supporting Information

Detailed experimental procedures, ^{1}H NMR, ^{13}C NMR data for **3**, **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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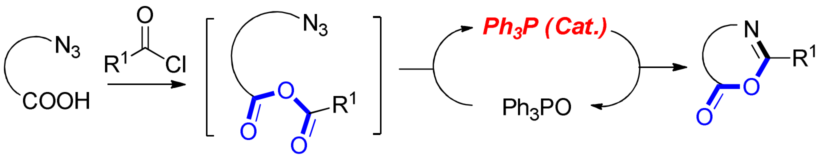

1) **catalytic** aza-Wittig reaction of **acid anhydride, acids**
2) **The common PPh$_3$ as catalyst under Cu/TMDS**
3) **102** examples; up to **98**% yield **and one-pot reaction**
4) **broad functional group tolerance**