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Organocatalyst and metal provide different products: a catalystcontrolled switchable phosphination of α -diazoesters has been developed by using DBU and copper as catalysts. It provided an efficient synthetic method for the construction of various phosphorus compounds *via* the formation of N–P and C–P bonds.

α-diazoesters†

and Chengjian Zhu*^{a,c}

The synthetic and biological importance of phosphorus compounds has stimulated increasing research on the construction of structurally sophisticated phosphorus compounds.¹ P–E bond-forming reactions have been extensively studied *via* transition-metal catalysed coupling with organohalides, addition to unsaturated C–C bonds, homo- and heterodehydro coupling or coupling through decarboxylation.^{1,2} However the search for economical, high yielding, and technically simple methods for the synthesis of useful phosphorus compounds remains a burgeoning field of synthetic research.

Much attention has been paid to α -diazocarbonyl compounds because of their extensive applications in synthetic chemistry,³ which includes cyclopropanation,⁴ cyclopropenation,⁵ X–H (X = C, O, S, N, Si) bond insertions⁶ and ylide formations.⁷ Although α -diazocarbonyl compounds have been studied extensively, the reactions between phosphorus compounds and α -diazocarbonyl compounds are rarely studied.⁸ The reported method was limited to high temperature, low yields and an excess of aliphatic phosphonates. For diversity reaction properties, the α -diazocarbonyl compounds can not only form carbenes but also can be used as nucleophiles under special conditions.⁹ To the best of our knowledge, the important chemoselective reaction of α -diazocarbonyl compounds with the same partners both at the carbon (C1) and



Scheme 1 The switchable phosphination of α-diazoesters.

Catalyst-controlled switchable phosphination of

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the terminal nitrogen (N1) has not been reported. It is particularly interesting for substrates with multiple reactive sites capable of undergoing different reactions switched by different catalysts. Furthermore, developing approaches that can construct different phosphorous compounds in an effective way is actively required, since the process can afford the desired products through rapid, easily obtained substrates and minimal synthetic manipulations.¹⁰ Herein we disclose a new methodology for chemoselectively constructing N–P and C–P bonds: organocatalyst- and copper-catalysed switchable reactions between α -diazoesters and phosphorus compounds (Scheme 1).

In our initial study, we observed that the reaction between dimethyl phosphonate **2a** and methyl 2-diazo-2-phenylacetate **1a** could be catalysed by K_2CO_3 and CuBr (Table 1, entry 1). To our surprise, the result was the phosphinamide from the phosphonate nucleophilic addition to the terminal nitrogen of α -diazoester rather than the P–H bond insertion into the carbene. Additionally, the metal CuBr was unnecessary during the process (Table 1, entry 2). To uncover this unprecedented, base-catalysed phosphinamide synthesis, we put our attention to studying the feasibility of this novel finding. No conversion of **1a** was observed in the absence of any catalyst (Table 1, entry 3). Meanwhile, Li₂CO₃ did not furnish the desired coupling product either (Table 1, entry 4). Intriguingly, DBU effectively catalysed the reaction even at ambient temperature, which indicated that inorganic salts usually gave unsatisfactory

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 $\label{eq:table_$



Entry	Cat (mol%)	R	Solvent	Yield ^c (%)
1	K ₂ CO ₃ -CuBr ^b	OMe	DMF	3a /20
2	$K_2 CO_3 (20)$	OMe	DMF	3a /20
3		OMe	DMF	3a /0
4	$Li_2CO_3(20)$	OMe	DMF	3a/trace
5	DBU (20)	OMe	DMF	3a /55
6	DMAP (20)	OMe	DMF	3a /0
7	DMEDA (20)	OMe	DMF	3a /0
8	DBU (20)	OMe	CH ₃ CN	3a/66
9	DBU (20)	OMe	DMSO	3a /45
10	DBU (20)	OMe	THF	3a /24
11	CuBr (5)	OMe	CH_2Cl_2	4a /0
12	CuBr (5)	OEt	CH_2Cl_2	4a /0
13	CuBr (5)	OPh	CH_2Cl_2	4a /45
14	CuBr (5)	OPh	ClCH ₂ CH ₂ Cl	4a/87
15	CuBr (5)	OPh	Toluene	4a /12
16	CuBr (5)	OPh	Hexane	4a /0

^{*a*} A mixture of **1a** (0.5 mmol), **2** (0.55 mmol) and catalyst in solvent (2 mL) was stirred at room temperature for 48 h (**3a**), 12 h (**4a**). ^{*b*} K₂CO₃ (20 mol%) and CuBr (5 mol%). ^{*c*} Yield of isolated product.

results. It is noteworthy that the reaction using DMAP and DMEDA gave no product (Table 1, entries 6–7). We further examined the efficacy of this transformation in the presence 20 mol% DBU as the catalyst by varying the solvents. Only acetonitrile provided a moderate result and produced the corresponding N–P bond formation product in 66% yield, whereas all other tested solvents gave unsatisfactory yields (Table 1, entries 9–10).

During our research on the α -diazoesters, we also investigated the C-P bond formation reactions since C-P bond construction is highly important in the synthesis of phosphinecontaining compounds. Although X-H (X = C, O, S, N, Si) bond insertions⁶ and copper-catalysed synthesis of alkylphosphonates from phosphonates and N-tosylhydrazones have been reported,¹¹ C-P bond formation by P-H insertion into the carbene has hardly been developed.8 To our disappointment, we found that P-H insertion into the carbene did not happen when the α-diazoester and aliphatic phosphonate was treated with copper-catalyst (Table 1, entries 11-12). Realizing it may due to its low activity,¹² we turned our attention to diphenyl phosphonate which has high activity. As anticipated, the C-P bond formation reaction did occur under copper(1) bromide (5 mol%) catalysis with dry CH_2Cl_2 as solvent, affording the product in 45% yield (Table 1, entry 13). Among the solvents screened, toluene and hexane decreased the yields dramatically, while the utilization of ClCH₂CH₂Cl gave an excellent yield, and the yield can be improved to 87% (Table 1, entries 14-16). Consequently, the optimal reaction conditions for C-P



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^a Reaction conditions: 1 (0.5 mmol), 2 (0.55 mmol), DBU (20 mol%, 0.1 mmol), CH₃CN (2.0 mL), room temperature, yield of isolated product.

bond formation included 5 mol% of copper(I) bromide at room temperature in the presence of $ClCH_2CH_2Cl$ as solvent. Therefore, chemoselective phosphination can be easily obtained through the selective N–P and C–P bond formation by controlling the DBU and copper catalyst.

With the optimized reaction conditions in hand, the scope of the phosphination *via* N–P bond formation between various α -diazoesters and phosphorous compounds was investigated. As described in Table 2, a broad range of α -diazoesters are compatible with this operationally simple DBU-catalysed phosphination. When the methyl ester group of the α -diazoester was switched to ethyl or isopropyl ester, a satisfactory yield was obtained (Table 2, **3a–3c**). Notably, the ester group of the α -diazoesters had a limited effect on the yield. Moreover, substrates with various electron-withdrawing and electron-donating functional groups were well tolerated, and gave the





^{*a*} Reaction conditions: **1** (0.5 mmol), **2** (0.55 mmol), copper (5 mol%, 0.025 mmol), ClCH₂CH₂Cl (2.0 mL), room temperature, yield of isolated product.

corresponding products in moderate to high yields (Table 2, 3d-3k). Meanwhile, some other phosphonates and the aliphatic α -diazoester were also applied under the standard conditions; they furnished the product smoothly with good results (Table 2, 3l-3n). Notably, diphenylphosphine oxide was also good substrate for the coupling reactions, and gave the product 3o with high yield.

Then, the scope of the copper catalysed P–H insertion into the carbene formed from α -diazoesters *in situ* under the optimal reaction conditions (entry 7, Table 3) was also investigated. The substrate scope of the C–P bond formation reaction is broad, different substituted groups on the α -diazoesters could be well tolerated and provide the desired products **4a–i** in excellent yields (85–98%). In addition, the aliphatic α -diazoester was also good substrate for this protocol and afforded the corresponding product **4j**. Intriguingly, when diphenylphosphine oxide was used, the desired products **4k–4l** were effectively obtained. However, the reaction did not work with aliphatic phosphonates under the standard reaction conditions, no products were detected, which may due to its low activity.

In summary, we have uncovered a switchable catalytic reaction between phosphorus compounds and α -diazoesters by using an organomolecule (DBU) and copper as catalysts. Selective N–P bond formation was achieved when DBU was applied as organocatalyst, while C–P bond was formed with the copper catalyst. The process demonstrated the diverse reactivity of α -diazoesters that could be controlled by organomolecule and metal. The new methodology offered facile access to various phosphorus compounds and provided an excellent option

toward establishing a new horizon for controlling reactions *via* different catalysts types.

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