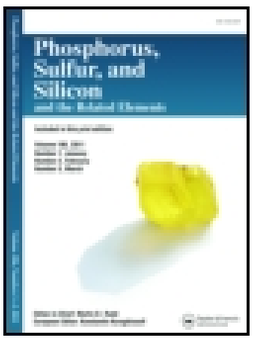

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Application of pentacoordinated spirophosphorane as a new organocatalyst for the Michael addition reaction

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ABSTRACT

Pentacoordinated spirophosphorane as a simple, effective and novel organocatalyst for the Michael addition reaction has been investigated. The bisaminoacyl spirophosphorane that possessed a thiourea-like moiety and an amine group was applied to the Michael addition reaction of 1, 3-dicarbonyl compound with β-nitrostyrene, affording the desired adduct in good yield. Furthermore, the mechanism of the Michael addition reaction catalyzed by spirophosphorane was proposed with the help of the analysis of single crystal structure, NMR experiments. It was identified that 1, 3-dicarbonyl compound and β-nitrostyrene formed hydrogen bonds with amine group and N-H groups of spirophosphorane catalyst, respectively. Then the two reactants approached each other, and the methylene of 1, 3-dicarbonyl compound attacked the olefin carbon of β-nitrostyrene to form nucleophilic addition product. This report is the first example of spirophosphorane as a novel organocatalyst to successfully catalyze the Michael addition reaction.

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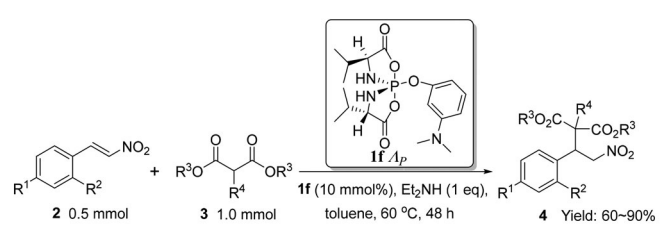
Pentacoordinated spirophosphorane; organocatalyst; Michael addition reaction; catalytic mechanism; hydrogen bonds

GRAPHICAL ABSTRACT



1. Introduction

Organocatalysis is a kind of catalysis reaction that can be accelerated by adding a small account of organic compounds.[1–4] In the past few decades, organocatalysis has become a very important synthetic tool, which is now a complement to organometallic catalysis, although organometallic catalysis has been widely applied in many fields. It is well known that the catalytic effect of some metal catalyst is greatly affected by water and oxygen, and enzyme catalysis is influenced by acid and base in the reaction system. However, organocatalysis typically has the advantages of mild reaction conditions, easy recovery of the catalyst and environmentally friendly processes. Therefore, organocatalyst becomes a third type of catalyst after metal and enzyme catalyst, and has been widely used in organic synthesis.

Hydrospirophosphorane (HSP) is a type of pentacoordinated phosphorus compound with P-H bond. The pentacoordinated bisaminoacyl spirophosphorane with a P-H bond is a special type of HSP, which is synthesized from amino acid, hereinafter abbreviated as AA-HSP.[5–8] It is well known that the thiourea catalyst with two N-H bonds as hydrogen bond donor is one of the most powerful system in organocatalytic field. AA-HSP as shown in Scheme 1 (**1a–1d**) has two N-H groups located on their rigid spiro skeleton, which is similar to the structure of thiourea, so it can be inferred to act as a hydrogen bond donor to activate substrate. Nowadays, most organic catalyst in use is bifunctional, usually with acid and Lewis base sites,[9] and a bifunctional catalyst leads to a considerable acceleration of reaction rate by the activation of donor and acceptor. Considering recent success using AA-HSPs to synthesize a series of spirophosphorane derivatives in our laboratory,[10–15] we envisaged that the P-H bond of AA-HSP was well suited for the introduction of new functional group containing activation sites. Therefore, spirophosphorane derivatives with bifunctional groups might be designed and synthesized to act as a prospective organocatalyst. Furthermore, different pentacoordinated phosphorus configurations of AA-HSP might provide more selectivity for

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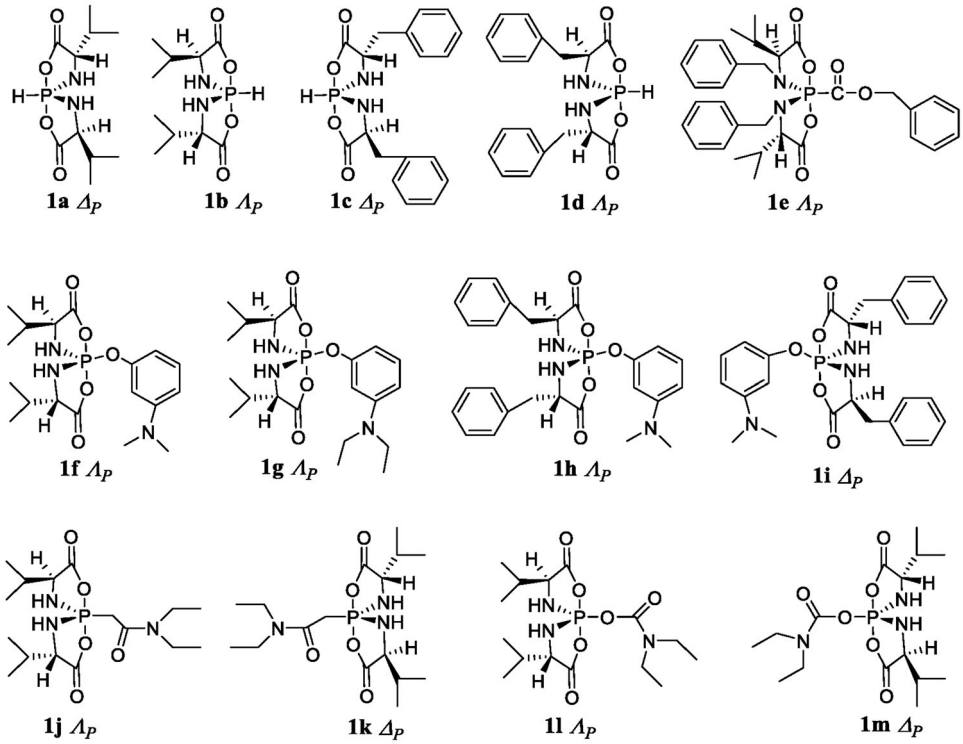


Scheme 1. Structures of pentacoordinated spirophosphorane catalyst.

catalytic processes. It is worthy to note that simple synthesis process, mild reaction condition and long-time stable storage of pentacoordinated spirophosphoranes make them attractive to be used as a potential organocatalyst.

Compared with the structure of thiourea catalyst, the feasibility of bisaminoacyl spirophosphorane derivatives as a new organocatalysis framework was investigated. Since thiourea derivatives are often used to catalyze the Michael addition reaction, the reaction of 1, 3-dicarbonyl compound and β-nitrostyrene catalyzed by bisaminoacyl spirophosphoranes was firstly studied. Moreover, the catalytic mechanism of the Michael addition reaction was proposed by the analysis of single crystal structure, NMR experiments. The investigation of pentacoordinated bisaminoacyl spirophosphorane as a new type of small molecular organocatalyst would enrich the type of organocatalyst and expand the application of pentacoordinated spirophosphorane.

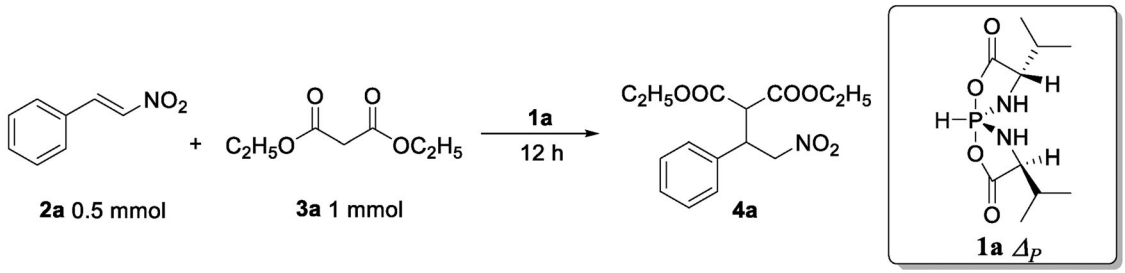
2. Results and discussion

2.1. Synthesis of pentacoordinated spirophosphorane organocatalysts

At present, a bifunctional thiourea catalyst is often used in the Michael addition reaction by dual functional activation of substrates. According to the mechanism of bifunctional thiourea catalysis, an effective catalyst needs not only two N-H sites as hydrogen bond donors, but also another activation site as a hydrogen bond receptor.[16–19] Based on this concept, a series of bifunctional spirophosphorane catalysts were designed and synthesized from AA-HSPs. Obviously, pentacoordinated spirophosphoranes have different structural characteristics from thiourea derivatives. In addition to analogous N-H functional group, they have two types of phosphorus configurations, which might bring unexpected selectivity and catalytic activity for the Michael addition reaction. Therefore, spirophosphorane molecules with different phosphorus configurations were also prepared.

The AA-HSPs **1a–1d** (Scheme 1) were synthesized from L-valine and L-phenylalanine according to the literature.[5] They had two N-H bonds on the spiro-ring, which was similar to N-H bond of thiourea. Our group has investigated the reactivity of N-H bond of spirophosphoranes by H/D exchange and NMR experiments.[20] The results showed that the reactivity of N-H bond was influenced by steric hindrance and the substituents at phosphorus atom. In addition, when we investigated the CO_2 insertion reaction related to pentacoordinated P-C bond, the N-H bond of the product could participate in the reaction unexpectedly, and spirophosphorane **1e** was obtained. Here, it was used to explore the effect of N-H site in catalytic process. It was reported that bifunctional catalyst usually has both a thiourea moiety and an amine group on a chiral scaffold to achieve remarkably catalytic activity in the Michael addition reaction.[16–19] The bifunctional catalyst could activate both β-nitrostyrene and nucleophile, and sometimes even control the approach direction of nucleophile to β-nitrostyrene. On the basis of this concept, bifunctional spirophosphoranes **1f–1m** with an amine group as a hydrogen bond receptor were synthesized as shown in Scheme 1. The derivatives **1f–1i** with new P-O bond were produced by the Atherton-Todd-type reaction of AA-HSP **1a–1d** with 3-hydroxylanilines.[10,21] Spirophosphoranes **1j** and **1k** were synthesized by P-alkylation reaction following literature method.[11] Spirophosphorane derivatives **1l** and **1m** were prepared from diethylamine by a CO_2 insertion reaction into the

Table 1. Optimization of the reaction conditions.



Entry	Solvent	T (°C)	The amount of catalyst (mmol%)	Additive	The amount of additive (equ.)	Yield[a] (%)
1	CH_3OH	20	15	Et_3N	0.5	14
2	$CHCl_3$	20	15	Et_3N	0.5	25
3	CH_3CN	20	15	Et_3N	0.5	19
4	DMSO	20	15	Et_3N	0.5	26
5	THF	20	15	Et_3N	0.5	32
6	CH_2Cl_2	20	15	Et_3N	0.5	29
7	toluene	20	15	Et_3N	0.5	50
8	toluene	−15	15	Et_3N	0.5	28
9	toluene	10	15	Et_3N	0.5	30
10	toluene	30	15	Et_3N	0.5	51
11	toluene	40	15	Et_3N	0.5	53
12	toluene	80	15	Et_3N	0.5	32
13	toluene	60	15	Et_3N	0.5	55
14	toluene	60	5	Et_3N	0.5	34
15	toluene	60	30	Et_3N	0.5	28
16	toluene	60	20	Et_3N	0.5	38
17	toluene	60	25	Et_3N	0.5	32
18	toluene	60	10	Et_3N	0.5	56
19	toluene	60	10	Et_3N	0.25	47
20	toluene	60	10	Et_3N	1.5	45
21	toluene	60	10	Et_3N	2.0	32
22	toluene	60	10	Et_3N	2.5	24
23	toluene	60	10	Et_3N	1.0	58
24	toluene	60	10	Et_2NH	1.0	65
25	toluene	60	10	$CH_3(CH_2)_2NH_2$	1.0	41
26	toluene	60	10	DBU	1.0	34
27	toluene	60	10	K_2CO_3	1.0	35
28	toluene	60	10	Cs_2CO_3	1.0	32

[a]Isolated yield.

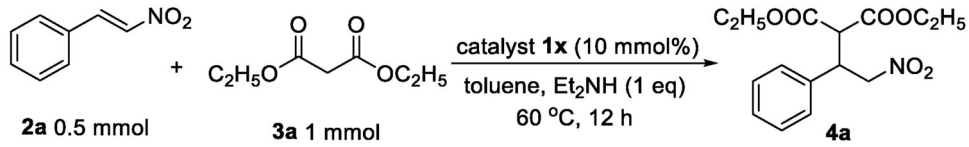
pentacoordinate P–N bond developed by our group.[12] Among them, spirophosphoranes **1f–1k** were first synthesized for the investigation of their catalytic effects.

2.2. Optimization of reaction conditions

In order to optimize the reaction conditions, **1a** as an organocatalyst was initially examined for the Michael addition reaction between *β*-nitrostyrene **2a** and diethyl malonate **3a**. Firstly, taking Et_3N as an additive, various solvents were screened. As shown in Table 1, the catalytic efficiency of **1a** significantly depended on the solvent used. Protic solvents and polar solvents, which might reduce the activity of **1a**, resulted in poor yields of product **4a**. It was presumed that the hydrogen bond interaction between spirophosphorane and nitro group of substrate might be weakened by H-bonding acceptor or donor solvent (entries 1–6).[22] As expected, toluene without H-bonding acceptor or donor sites efficiently promoted the reaction and gave a better yield (entry 7). Accordingly, toluene was chosen to be the best solvent for further investigation. By changing the reaction temperature from −15 °C to 80 °C, the yield of the desired adduct reached the maximum 55% at 60 °C (entries 7–13). Next, the influence of catalyst loading was examined, and the results showed that 10 mmol% of catalyst was the most suitable ratio (entries 13–18). Similarly, increasing or reducing the amount of Et_3N weakened activation ability of catalyst (entries 18–23). Moreover, it could be seen diethylamine was an ideal additive for the Michael addition reaction catalyzed by spirophosphorane (entries 23–28). Therefore, using 10 mmol% of catalyst and 1 equivalent amount of diethylamine as an additive provided the most suitable environment for this reaction.

Subsequently, the effect of different catalysts was investigated, and the results were listed in Table 2. The Michael addition reaction between *β*-nitrostyrene **2a** and diethyl malonate **3a** only gave 31% yield in the absence of spirophosphorane catalyst (entry 14). However, even using AA-HSP **1a–1d** as a catalyst, the target products were obtained with good yields (entries 1–4). It proved that the substrates could be actually activated by spirophosphorane AA-HSP, although AA-HSP only had N-H activation site. Considering the concept of bifunctional catalyst, organocatalysts **1f–1m** bearing an amine group achieved better yields as expected (entries 6–13). On the whole, the catalytic effect of bifunctional catalyst **1f–1m** was better than that of single

Table 2. The Michael addition reaction of **2a** and **3a** with various catalyst **1x**.



2a 0.5 mmol **3a** 1 mmol **4a**

Entry	Catalyst **1x**	Yield[a] (%)
1	**1a**	65
2	**1b**	55
3	**1c**	61
4	**1d**	48
5	**1e**	36
6	**1f**	90
7	**1g**	77
8	**1h**	60
9	**1i**	65
10	**1j**	66
11	**1k**	63
12	**1l**	71
13	**1m**	85
14	no catalyst	31

[a]Isolated yield.

functional catalyst **1a**–**1d**. Finally, the highest yield of the desired product was obtained utilizing catalyst **1f**. Therefore, the spirophosphorane skeleton with bifunctional activation sites proved to be more effective for the Michael addition reaction. Then, the optimal conditions of the Michael addition reaction were determined to be using 10 mmol% of **1f** as a catalyst, 1 equivalent amount of diethylamine as additive in toluene at 60 °C.

2.3. The Michael addition reaction of 1,3-dicarbonyl compound with β-nitrostyrene

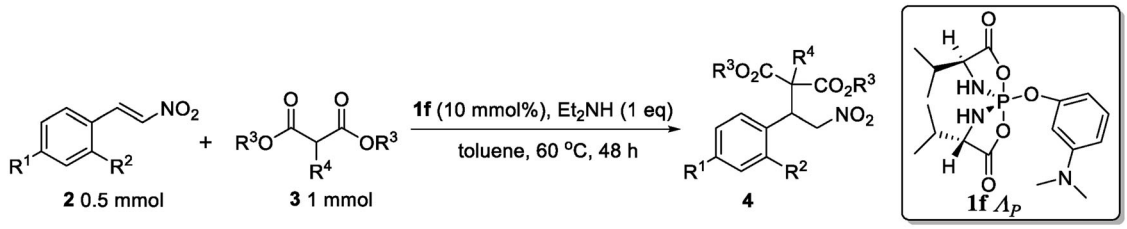
With the optimal conditions in hand, the substrate scope of the Michael addition reaction of 1, 3-dicarbonyl compound with *β*-nitrostyrene catalyzed by spirophosphorane **1f** was examined (Table 3). When a bulkier ester group was introduced to malonate, such as tert-butyl ester, the reaction exhibited lower yield (entries 1–4). The results revealed that the bulk of ester group of malonate apparently influenced the yield of addition adduct. If α-substituted malonate was employed as a nucleophile in the Michael reaction, various products bearing a quaternary carbon center would be obtained. For example, when dimethyl methylmalonate or diethyl 2-chloromalonate as a nucleophile was applied to the present catalytic system, the reaction proceeded smoothly to give the desired adduct in good yield (entries 5, 6). Furthermore, the results showed that the position and the electronic property of substituents on the aromatic ring of nitroalkene were well tolerated by the Michael addition reaction. Whether electron-withdrawing (entries 7–9, 13, 14), electron-donating (entries 10, 12), or electron-neutral (entry 11) groups were on the aromatic ring, the reactions provided the product **4a** in moderate to good yields (65–86%).

2.4. Proposed mechanism of the Michael addition reaction catalyzed by spirophosphorane

As reported in the literature,[17,23] diethyl malonate could be easily deprotonated by a tertiary amine moiety, and *β*-nitrostyrene could be activated by a thiourea moiety through hydrogen bond interaction simultaneously, furnishing the corresponding vinylogous carbanion. Through a subsequent cyclization sequence, the desired final product could be smoothly obtained. Based on this process, N-H group on five-membered ring of **1f**–**1m** was presumed to form a hydrogen bond with *β*-nitrostyrene, and amine group of **1f**–**1m** might activate diketone at the same time. Finally, spirophosphoranes **1f**–**1m** as a bifunctional catalyst, which possessed both two N-H groups and an amine group, were possible to be effective to catalyze the Michael addition reaction.

To verify our conjecture and evaluate the actual three-dimensional structure of spirophosphoranes **1f**–**1m**, the single crystal of spirophosphorane catalyst was cultivated by different methods. Although the single crystal of **1f** was not prepared, the single crystal structure of **1g** was obtained. (Tables S 1 – S 4, Supplemental Materials). Based on the X-ray analysis of **1g** (Figure 1), it could be seen that the orientation of two N-H bonds of **1g** was spatially pointing in the opposite directions. As shown in Figure 1, the direction of N(1)-H was approximately toward the front of the paper and the direction of N(2)-H was approximately toward the back of the paper. Furthermore, the angle of P(1)-O(5)-C(11) was determined to be 123.8°, and then tertiary amine group -N(3)Et_2 on the *meta* position of the benzene ring was closer to N(1)-H bond compared with the distance to N(2)-H bond. Therefore, as shown in Figure 1, a cavity composed of an N(1)-H bond, a P(1)-O(5) bond, a benzene ring, and a tertiary amine group -N(3)Et_2 was formed, which might provide an active region to catalyze

Table 3. The Michael addition reaction of nitroolefin **2** and malonate **3** catalyzed by **1f**.



Entry	R^1	R^2	R^3	R^4	Adduct	Yield[a](%)
1	H	H	Et	H	**4a**	85
2	H	H	Me	H	**4b**	70
3	H	H	^{i}Pr	H	**4c**	65
4	H	H	^{t}Bu	H	**4d**	60
5	H	H	Me	Me	**4e**	79
6	H	H	Et	Cl	**4f**	90
7	F	H	^{i}Pr	H	**4g**	67
8	Cl	H	^{i}Pr	H	**4h**	65
9	NO_2	H	^{i}Pr	H	**4i**	72
10	OCH_3	H	^{i}Pr	H	**4j**	68
11	CH_3	H	^{i}Pr	H	**4k**	65
12	H	OCH_3	^{i}Pr	H	**4l**	75
13	H	Cl	^{i}Pr	H	**4m**	71
14	H	NO_2	^{i}Pr	H	**4n**	86

[a]Isolated yield.

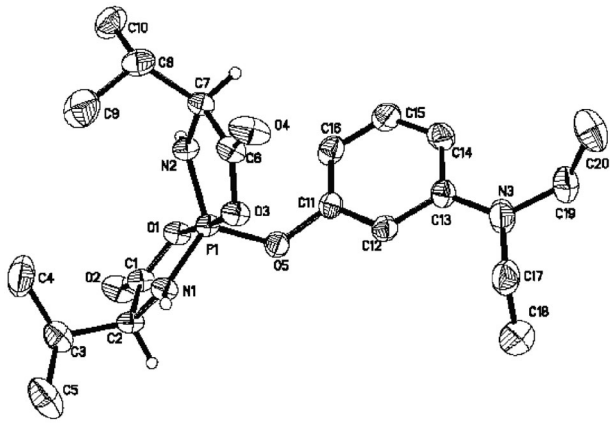


Figure 1. X-ray crystal structure of **1g** (Thermal ellipsoids are drawn at the 30% probability level).

the substrates simultaneously. Although the single-crystal of other catalyst had not been obtained, the analogues of **1h**,[21] **1j**,[11] **1l**[12] had been reported. The other catalysts were presumed to be structurally similar to **1g**. Therefore, they might also have an activating cavity in the spatial structures, which could catalyze the reaction substrates by N-H and amine site. In short, the X-ray analysis of catalyst **1g** further illustrated that the structures of **1f–1m** could provide two active sites in one cavity to catalyze the reaction substrates.

To obtain further information about the reaction mechanism, the reaction process catalyzed by spirophosphonane **1f** was monitored by ^{31}P NMR tracing experiments (Figure S 1, Supplemental Materials). The results showed that phosphorus signal did not change, so the structure of spirophosphonane **1f** should be well maintained during the reaction. The reaction was speculated to be indeed catalyzed through the weak interaction rather than the formation of new chemical bond. As previously mentioned, N-H groups and the tertiary amine group of **1f** might form hydrogen bonds to activate β-nitrostyrene and diketone, respectively. It was presumed that **1f** could act as a hydrogen bond donor and a hydrogen bond acceptor similar to thiourea derivatives. To identify the hydrogen bond between catalyst **1f** and reaction substrates, we collected the ^{1}H NMR spectrum of spirophosphonane **1f** in the presence of β-nitrostyrene **2a**, diethyl malonate **3a**, and additive diethylamine in DMSO-d^6 according to the reaction ratio. Then, the spectra of **1f** (Figure 2A) and **3a** (Figure 2B) were compared with the spectrum of reaction mixture (Figure 2C). Although there was only a little change in the ^{1}H NMR spectrum of reaction mixture, the change revealed some information about hydrogen bond interaction between **1f** and the substrates. It was observed that the chemical shift of N-H proton of **1f**, which was split by phosphorus atom and exhibited doublet, shifted from 6.11 to 6.17 ppm as shown in enlarged images, while other peaks did not change. It was speculated that N-H proton of catalyst **1f** was one of reaction sites, acting as a hydrogen bond donor to interact with the nitro group of **2a**, so the chemical shift of N-H proton changed. In addition, the chemical shift of methylene of **3a** shifted from 3.48 to 3.46 ppm after mixing with **1f** and **3a**. Although the chemical shift changed little, the peak width of methylene broadened significantly from 0.01 to 0.2 ppm as shown in enlarged images. This suggested that the methylene of **3a** might have a resonance structure between ketone form and enol form during the reaction. The result was consistent with our hypothesis that the enol form of **3a** formed a hydrogen bond with the nitrogen atom of tertiary amine group of catalyst **1f**.

Furthermore, the effects of solvent also elucidated the formation of hydrogen bonds between catalyst and substrates as shown in Table 1. In nonpolar toluene as the solvent, the catalyst efficiently promoted the reaction to afford

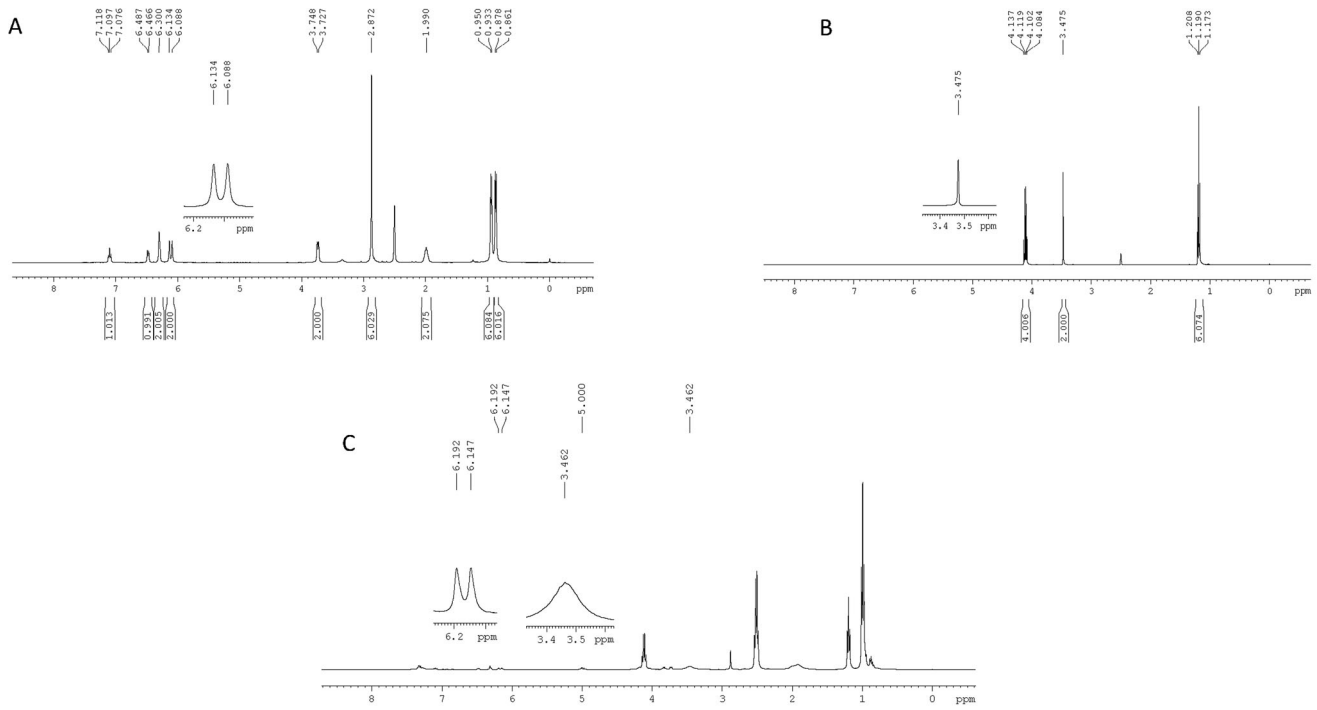


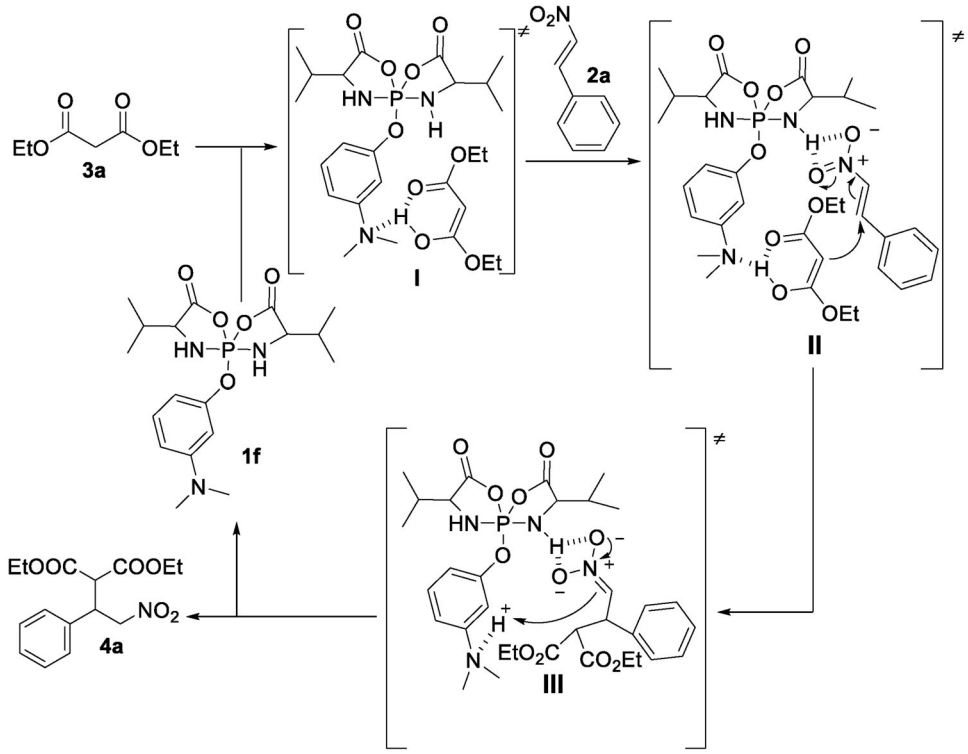
Figure 2. The ^{1}H NMR spectra of **1f** (A), **3a** (B) and the mixture (C) of **1f**, **2a**, **3a** and Et_2NH in DMSO.

adduct **4a** in moderate yield. In contrast, the yields of **4a** were apparently low in polar solvents (CH_3OH, CH_3CN), since the solvation of nitro group of **2a** might disturb the hydrogen bond between the catalyst and **2a**. Therefore, hydrogen bonds between catalyst and substrates were the main interaction mode in the Michael addition reaction. In the case of the effect of structure of spirophosphoranes as shown in Table 2, the results indicated that both N-H group and amine group were indispensable moieties for catalyst. On the whole, the catalytic effect of bifunctional catalyst **1f**–**1m** was better than that of single functional catalyst **1a**–**1d**. It implied that the amine group promoted the catalytic activity of spirophosphoranes. Moreover, spirophosphorane **1e** had a special structure, that the hydrogen attached to the nitrogen atom on five-membered ring was substituted by benzyl group. With **1e** as a catalyst, the reaction provided desired adduct **4a** in only 36% yield (Table 2, entry 5). Apparently, the result of **1e** indicated that the N-H group on five-membered ring was an essential factor for spirophosphorane catalyst to catalyze the Michael addition reaction. Comparing the catalytic result of **1f** and **1h** with the same tertiary amino group and phosphorus configuration, it was found that the substituent on five-membered ring also had a significant effect on the addition reaction (Table 2, entries 6, 8). When a bulkier benzyl group replaced an isopropyl group adjacent to the N-H group of catalyst, the yield of **4a** decreased from 90% to 60%. It implied that steric hindrance around the N-H group was indeed related to the catalytic activity of spirophosphorane. In this context, it could be concluded that the N-H sites and amine site of spirophosphorane catalysts played a vital role on this catalytic process. Subsequently, the catalytic results of spirophosphorane catalysts with different phosphorus configuration were also compared (entry 8/9, 10/11, 12/13), but no special effect on the yield was achieved. Although the effect of pentacoordinated phosphorus configuration on the Michael addition reaction was not clarified at this stage, we assumed that it might bring some selectivity for asymmetric Michael addition reaction in the future.

Based on the analysis of single crystal structure of **1g**, NMR experiments and the comparison of catalytic results by different spirophosphoranes, a plausible reaction cascade was proposed in Scheme 2.[24–26] Taking catalyst **1f** as an example, the tertiary amine group of **1f** could firstly deprotonate the acidic proton of diethyl malonate **3a** through hydrogen-bond interaction, generating the complex **I** of **3a** and **1f**. The enol form as a resonance structure of **3a** had been identified by NMR spectra as previously mentioned. At about the same time, *β*-nitrostyrene **2a** interacted with catalyst **1f** through the hydrogen bonding between nitro group and N-H proton on five-membered ring, and a ternary complex **II** was formed. Thus, the reactants **2a** and **3a** approached each other in one cavity composed by N-H bond, benzene ring and tertiary amine group. Next, the methylene of **3a** attacked the olefin carbon of *β*-nitrostyrene, forming the complex **III**. Finally, the hydrogen bond between N-H group of catalyst **1f** and nitro group of **2a** was cleaved, and the nitronate captured the proton from the amino group of catalyst to produce **4a** along with catalyst **1f**.

3. Conclusions

In summary, pentacoordinated spirophosphorane as a simple, effective and novel organocatalyst for the Michael addition reaction has been investigated. Firstly, a variety of novel bifunctional spirophosphorane catalysts that possess a thiourea-like moiety and an amine group were synthesized.



Scheme 2. The proposed mechanism of the Michael addition reaction catalyzed by spirophosphorane **1f**.

Then, the Michael addition reaction of 1, 3-dicarbonyl compound and *β*-nitrostyrene in the presence of bifunctional catalyst **1f–1m** was investigated, obtaining the desired adduct in good yields ranging from 60% to 90%. Furthermore, the mechanism of the Michael addition reaction catalyzed by spirophosphorane catalysts was proposed by the analysis of single crystal structure and NMR experiments. The N-H sites and amine site of spirophosphorane were testified to be necessary for the catalytic process. The Michael addition reaction was catalyzed by spirophosphorane catalyst through hydrogen bonds between catalyst and substrates. It was identified that 1, 3-dicarbonyl compound and *β*-nitrostyrene formed hydrogen bond with amine group and N-H groups of spirophosphorane catalyst, respectively. Then two reactants approached each other in one cavity, and the methylene of 1, 3-dicarbonyl compound attacked the olefin carbon of *β*-nitrostyrene to form nucleophilic addition product. This report is a first example of the successful Michael addition reaction catalyzed by spirophosphorane as a novel organocatalyst in metal-free conditions. The investigation of pentacoordinated spirophosphorane as a new type of small molecular organocatalyst would enrich the type of organocatalyst and expand the application of pentacoordinated spirophosphorane.

4. Experimental

The ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ with tetramethylsilane (TMS) as the internal standard on a Bruker Avance 400 MHz spectrometer operating at 400.13 and 100.61 MHz, respectively. The ^{31}P NMR spectra were measured with a Bruker Avance 400 MHz spectrometer with 85% H_3PO_4 as the internal standard. Melting points were determined with a XT-4 micro melting point apparatus. ESI-HRMS was performed on a Q-TOF mass spectrometer (Waters, Manchester, UK). The crystal data was collected on an Oxford Gemini E diffractometer. The Supplemental Materials contains sample ^{1}H, ^{13}C and ^{31}P NMR spectra of novel products 1 and 4 (Figures S 2 – S 28).

4.1. Synthesis of spirophosphorane catalysts

The AA-HSP **1a**, **1b**, **1c**, **1d** and derivatives **1e**, **1l** and **1m** were prepared according to literature procedures.[5,12]

*General procedure Preparation of **1f**∼**1i**:* To a stirred solution of AA-HSP (0.5 mmol) and 3-(diamino) phenol (0.5 mmol) in CH_3CN (5 mL), CCl_4 (1 mmol) and Cs_2CO_3 (3 mmol) were added. The reaction mixture was stirred at room temperature until the ^{31}P NMR signal of reactant AA-HSP disappeared. Then the reaction solution was filtered and dried to obtain a crude product. The residue was purified by column chromatography (PE-EA) to afford the desired products **1f**, **1g**, **1h** and **1i**.[10]

*Preparation of (3S,8S)-5-(3-(dimethylamino)phenoxy)-3,8-diisopropyl-1,6-dioxa-4,9-diaza-5λ^5-phosphaspiro[4.4]nonane-2,7-dione **1f**:* The general procedure was followed using **1a** (131 mg, 0.5 mmol) and 3-(dimethylamino) phenol (68.6 mg, 0.5 mmol). The crude product was purified by column chromatography (silica gel/PE: EA = 8:1) to give **1f** as a white solid. MP 187–189 °C; FTIR: ν_{max} 3308 (N-H) , 2964, 1751 (C = O), 1598, 1454 (Ar-H) , 1281, 1227, 829, 657 cm^{-1}; ^{31}P

NMR (162 MHz, $CDCl_3$, H_3PO_4): δ − 54.77 ppm; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 0.96 (d, 6H, J = 6.7 Hz, 2 × CH_3), 1.02 (d, 6H, J = 6.9 Hz, 2 × CH_3), 2.18–2.21 (m, 2H, 2 × CH), 2.94 (s, 6H, 2 × CH_3), 3.68 (d, 2H, $^2J_{H\text{-}N\text{-}P}$ = 16.5 Hz, 2 × NH), 3.77 (dd, 2H, J = 8.5 Hz, J = 2.9 Hz, 2 × CH), 6.40–6.42 (2H, Ar-H), 6.52 (d, 1H, J = 8.4 Hz, Ar-H), 7.15 (t, 1H, J = 8.0 Hz, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 16.4, 19.0, 30.7 (d, J = 6.4 Hz), 40.4, 60.1 (d, $^2J_{C\text{-}N\text{-}P}$ = 3.3 Hz) , 105.3 (d, J = 5.1 Hz), 108.7, 109.2, 129.9 (d, J = 2.1 Hz), 151.8, 152.5 (d, J = 10.2 Hz), 169.3 (d, $^2J_{C(O)\text{-}O\text{-}P}$ = 11.5 Hz); HRMS (ESI): m/z $[M+H]^+$, calcd for $C_{18}H_{19}N_3O_5P^+$ 398.1839, found 398.1844.

Preparation of (3S,8S)-5-(3-(diethylamino)phenoxy)-3,8-diisopropyl-1,6-dioxa-4,9-diaza-5λ^5-phosphaspiro[4.4]nonane-2,7-dione ***1g****:* The general procedure was followed using **1b** (131 mg, 0.5 mmol) and 3-(diethylamino) phenol (82.6 mg, 0.5 mmol). The crude product was purified by column chromatography (silica gel/PE: EA = 5:1) to give **1g** as a white solid. MP 135–136 °C; FTIR: ν_{max} 3280 (N-H), 2963, 1732 (C = O), 1606, 1506, 1270, 836, 655 cm^{-1}; ^{31}P NMR (162 MHz, $CDCl_3$, H_3PO_4): δ − 54.47 ppm; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 0.96 (d, 6H, J = 6.8 Hz, 2 × CH_3), 1.02 (d, 6H, J = 7.0 Hz, 2 × CH_3), 1.16 (t, 6H, J = 7.04 Hz, 2 × CH_3), 2.18–2.22 (m, 2H, 2 × CH), 3.32 (q, 4H, J = 7.08 Hz, 2 × CH_2), 3.65 (d, 2H, $^2J_{H\text{-}N\text{-}P}$ = 15.96 Hz, 2 × NH), 3.77 (dd, 2H, J = 8.4 Hz, J = 2.6 Hz, 2 × CH), 6.32 (d, 2H, J = 6.5 Hz, Ar-H), 6.46 (d, 1H, J = 8.1 Hz, Ar-H), 7.11 (t, 1H, J = 8.4 Hz, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 12.5, 16.4, 19.1, 30.7 (d, J = 6.5 Hz), 44.4, 60.1 (d, $^2J_{C\text{-}N\text{-}P}$ = 3.4 Hz), 104.6, 107.7, 108.7, 130.1, 149.2, 152.7 (d, J = 10.2 Hz), 169.3(d, $^2J_{C(O)\text{-}O\text{-}P}$ = 11.2 Hz); HRMS (ESI): m/z $[M+H]^+$, calcd for $C_{20}H_{33}N_3O_5P^+$ 426.2152, found 426.2157.

Preparation of (3S,8S)-3,8-dibenzyl-5-(3-(dimethylamino)phenoxy)-1,6-dioxa-4,9-diaza-5λ^5-phosphaspiro[4.4]nonane-2,7-dione ***1h*** *and (3S,8S)-3,8-dibenzyl-5-(3-(dimethylamino)phenoxy)-1,6-dioxa-4,9-diaza-5λ^5-phosphaspiro[4.4]nonane-2,7-dione* ***1i****:* The general procedure was followed using **1d** (179 mg, 0.5 mmol) and 3-(dimethylamino) phenol (68.6 mg, 0.5 mmol). The crude products were purified by column chromatography (silica gel/PE: EA = 5:1) to give **1h** and **1i** as a white solid.

1h: MP 190–191 °C; FTIR: ν_{max} 3316 (N-H), 2918, 1741 (C = O), 1597, 1506 (Ar-H), 1270, 855, 682 cm^{-1}; ^{31}P NMR (162 MHz, $CDCl_3$, H_3PO_4): δ − 57.05 ppm; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 2.72 (dd, 2H, J = 8.4 Hz, J = 13.8 Hz, 1 × CH_2), 2.91 (s, 6H, 2 × CH_3), 3.16 (dd, 2H, J = 3.0 Hz, J = 13.8 Hz, 1 × CH_2), 3.54 (d, 2H, $^2J_{H\text{-}N\text{-}P}$ = 16.9 Hz, 2 × NH), 4.00 (dt, 2H, J = 3.6 Hz, J = 8.6 Hz, 2 × CH), 6.28–6.50 (m, 4H, Ar-H), 7.10–7.15 (m, 5H, Ar-H), 7.29–7.38 (m, 5H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 39.3 (d, J = 6.6 Hz), 40.4, 56.0 (d, $^2J_{C\text{-}N\text{-}P}$ = 4.9 Hz), 105.1, 109.3, 127.4, 128.9, 129.4, 129.9, 130.1, 135.9, 152.2, 156.7, 169.1 (d, $^2J_{C(O)\text{-}O\text{-}P}$ = 11.5 Hz); HRMS (ESI): m/z $[M+H]^+$, calcd for $C_{26}H_{29}N_3O_5P^+$ 484.1839, found 494.1846.

1i: MP 190–191 °C; FTIR: ν_{max} 3317 (N-H), 2937, 1751 (C = O), 1607, 1498 (Ar-H), 1263, 1001, 856, 693 cm^{-1}; ^{31}P NMR (162 MHz, $CDCl_3$, H_3PO_4): δ − 53.90 ppm; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 2.29 (dd, 2H, J = 11.3 Hz, J = 13.5 Hz, 1 × CH_2), 3.02 (s, 6H, 2 × CH_3), 3.18 (d, 2H, J = 13.6 Hz, 1 × CH_2), 3.56 (d, 2H, $^2J_{H\text{-}N\text{-}P}$ = 17.5 Hz, 2 × NH), 3.95–4.02 (m, 2H, 2 × CH), 6.54–6.62 (m, 3H, Ar-H), 7.14–7.15 (m, 4H, Ar-H), 7.28–7.37 (m, 7H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 39.6 (d, J = 3.6 Hz), 40.5, 56.2 (d, $^2J_{C\text{-}N\text{-}P}$ = 5.6 Hz), 109.7, 127.4, 129.0, 129.1, 129.4, 130.0, 136.5,152.1, 152.2, 169.2 (d, $^2J_{C(O)\text{-}O\text{-}P}$ = 11.9 Hz); HRMS (ESI): m/z $[M+H]^+$, calcd for $C_{26}H_{29}N_3O_5P^+$ 484.1839, found 494.1846.

Preparation of 2-((3S,8S)-3,8-diisopropyl-2,7-dioxo-1,6-dioxa-4,9-diaza-5λ^5-phosphaspiro[4.4]nonan-5-yl)-N,N-diethylacetamide ***1j*** *and 2-((3S,8S)-3,8-diisopropyl-2,7-dioxo-1,6-dioxa-4,9-diaza-5λ^5-phosphaspiro[4.4]nonan-5-yl)-N,N-diethylacetamide* ***1k****:* To a stirred solution of compounds **1a** (131 mg, 0.5 mmol) and 2-chloro-N, N-diethylacetamide (74.8 mg, 0.5 mmol) in CH_3CN (5 mL), TBAI (2 mmol) and Cs_2CO_3 (3 mmol) were added. The reaction mixture was stirred at room temperature until the ^{31}P NMR signal of reactant **1a** disappeared. Then the reaction solution was filtered and dried to obtain a crude product. The residue was purified by column chromatography (silica gel/PE: EA = 2:1) to give **1j** and **1k** as a white solid.[11]

1j: MP 130–132 °C; FTIR: ν_{max} 3361 (N-H), 2981, 2918, 1750 (C = O), 1642, 1506, 1270, 1235, 809 cm^{-1}; ^{31}P NMR (162 MHz, $CDCl_3$, H_3PO_4): δ − 50.66 ppm; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 0.94 (d, 6H, J = 6.8 Hz, 2 × CH_3), 1.01 (d, 6H, J = 7.0 Hz, 2 × CH_3), 1.11 (t, 3H, J = 7.0 Hz, 1 × CH_3), 1.21 (t, 3H, J = 7.2 Hz, 1 × CH_3), 2.13–2.20 (m, 2H, 2 × CH), 3.12–3.50 (m, 8H, 3 × CH_2, 2 × NH), 3.88 (ddd, 2H, J = 12.2 Hz, J = 3.4 Hz, J = 1.2 Hz), ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 12.8, 14.5, 16.7, 19.1, 30.8 (d, J = 3.5 Hz), 38.8, 40.6 (d, J = 23.35 Hz), 43.1, 60.3 (d, $^2J_{C\text{-}N\text{-}P}$ = 3.5 Hz), 166.0 (d, J = 6.3 Hz), 170.3 (d, J = 7.3 Hz); HRMS (ESI): m/z $[M+H]^+$, calcd for $C_{16}H_{31}N_3O_5P^+$ 376.1996, found 376.1995.

1k: MP 130–132 °C; FTIR: ν_{max} 3352 (N-H), 2963, 2918, 1750 (C = O), 1624, 1515, 1270, 1226, 800 cm^{-1}; ^{31}P NMR (162 MHz, $CDCl_3$, H_3PO_4): δ − 49.87 ppm; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 0.98 (d, 6H, J = 6.4 Hz, 2 × CH_3), 1.7 (d, 6H, J = 6.6 Hz, 2 × CH_3), 1.13 (t, 3H, J = 6.8 Hz, 1 × CH_3), 1.21 (t, 3H, J = 6.8 Hz, 1 × CH_3), 2.19–2.24 (m, 2H, 2 × CH), 3.19–3.67 (m, 10H, 3 × CH_2, 2 × NH, 2 × CH), ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 12.7, 14.4, 17.9, 19.4, 31.1 (d, J = 6.1 Hz), 40.4 (d, J = 15.4 Hz), 42.0, 42.9, 60.0 (d, $^2J_{C\text{-}N\text{-}P}$ = 2.9 Hz), 165.2 (d, J = 6.1 Hz), 170.3 (d, J = 5.9 Hz); HRMS (ESI): m/z $[M+Na]^+$, calcd for $C_{16}H_{30}N_3NaO_5P^+$ 398.1815, found 398.1831.

4.2. Synthesis of 4x by the Michael addition reaction

General procedure: To a stirred solution of nitroolefin **2a** (0.5 mmol), malonate **3a** (1 mmol) and Et_2NH (0.5 mmol) in toluene was added catalyst **1f** (10 mmol%). After being stirred

at 60 °C for 48 h, the reaction solution was extracted with dichloromethane and saturated NH_4Cl solution and dried with anhydrous Mg_2SO_4. The residue was purified by column chromatography (PE-EA) to afford the desired product.

Preparation of diethyl 2-(2-nitro-1-phenylethyl)malonate ***4a***:[27] The general procedure was followed using (E)-2-nitrovinyl) benzene (74.6 mg, 0.5 mmol) and diethyl malonate (152 μL, 1 mmol). The crude product was purified by column chromatography (silica gel/PE: EA = 15:1) to give **4a** (131.4 mg, 85% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 1.05 (t, 3H, J = 7.1 Hz, 1 × CH_3) 1.27 (t, 3H, J = 7.2 Hz, 1 × CH_3), 3.82 (d, 1H, J = 9.3 Hz, 1 × CH), 4.01 (q, 2H, J = 7.1 Hz, 1 × CH_2), 4.20–4.27 (m, 3H, 1 × CH, 1 × CH_2), 4.84–4.95 (m, 2H, 1 × CH_2), 7.23–7.34 (m, 5H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 13.7, 13.9, 42.9, 54.9, 61.8, 62.1, 77.6, 128.0, 128.3, 128.9, 136.2, 166.8, 167.5; HRMS (ESI): *m/z* $[M+H]^+$, calcd for $C_{15}H_{20}NO_6^+$ 310.1285, found 310.1287.

Preparation of dimethyl 2-(2-nitro-1-phenylethyl)malonate ***4b***:[27] The general procedure was followed using (E)-2-nitrovinyl)benzene (74.6 mg, 0.5 mmol) and dimethyl malonate (114 μL, 1 mmol). The crude product was purified by column chromatography (silica gel/PE: EA = 5:1) to give **4b** (98.4 mg, 70% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 3.56 (s, 3H, 1 × CH_3), 3.76 (s, 3H, 1 × CH_3), 3.86 (d, 1H, J = 9.0 Hz, 1 × CH), 4.25 (dt, 1H, J = 5.3 Hz, J = 8.9 Hz, 1 × CH), 4.85–4.95 (m, 2H, 1 × CH_2) 7.22–7.34 (m, 5H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 42.9, 52.8, 53.0, 54.8, 77.4, 127.9, 128.4, 129.0, 136.1, 167.2, 167.8; HRMS (ESI): *m/z* $[M+H]^+$, calcd for $C_{13}H_{16}NO_6^+$ 282.0972, found 282.0976.

Preparation of diisopropyl 2-(2-nitro-1-phenylethyl)malonate ***4c***:[28] The general procedure was followed using (E)-2-nitrovinyl) benzene (74.6 mg, 0.5 mmol) and diisopropyl malonate (190 μL, 1 mmol). The crude product was purified by column chromatography (silica gel/PE: EA = 15:1) to give **4c** (109.6 mg, 65% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 1.02 (d, 3H, J = 6.2 Hz, 1 × CH_3), 1.07 (d, 3H, J = 6.2 Hz, 1 × CH_3), 1.24 (d, 3H, J = 6.3 Hz, 1 × CH_3), 1.25 (d, 3H, J = 6.3 Hz, 1 × CH_3), 3.76 (d, 1H, J = 9.6 Hz, 1 × CH), 4.23 (dt, 1H, J = 4.6 Hz, J = 9.4 Hz, 1 × CH), 4.80–4.87 (m, 2H, 1 × CH, 0.5 × CH_2), 4.93 (dd, 1H, J = 4.6 Hz, J = 12.9 Hz, 0.5 × CH_2), 5.05–5.12 (m, 1H, 1 × CH), 7.23–7.33 (m, 5H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 21.3, 21.3, 21.5, 21.6, 42.9, 55.2, 69.5, 69.9, 77.9, 128.1, 128.3, 128.8, 136.3, 166.3, 167.1; HRMS (ESI): *m/z* $[M+H]^+$, calcd for $C_{17}H_{24}NO_6^+$ 338.1598, found 338.1597.

Preparation of di-tert-butyl 2-(2-nitro-1-phenylethyl)malonate ***4d***:[17] The general procedure was followed using (E)-2-nitrovinyl) benzene (74.6 mg, 0.5 mmol) and di-tert-butyl malonate (223.7 μL, 1 mmol). The crude product was purified by column chromatography (silica gel/PE: EA = 15:1) to give **4d** (109.6 mg, 60% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 1.22 (s, 9H, 3 × CH_3), 1.47 (s, 9H, 3 × CH_3), 3.62 (d, 1H, J = 9.8 Hz, 1 × CH), 4.12 (dt, 1H, J = 4.3 Hz, J = 9.7 Hz, 1 × CH), 4.80 (dd, 1H, J = 9.8 Hz, J = 12.7 Hz, 0.5 × CH_2), 4.93 (dd, 1H, J = 4.3 Hz, J = 12.7 Hz, 0.5 × CH_2), 7.23–7.32 (m, 5H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 27.5, 27.9, 43.1, 56.5, 78.3, 82.3, 82.9, 128.2, 128.3, 128.8, 136.6, 166.0, 166.9; HRMS (ESI): *m/z* $[M+Na]^+$, calcd for $C_{19}H_{27}NNaO_6^+$ 388.1731, found 388.1731.

Preparation of dimethyl 2-methyl-2-(2-nitro-1-phenylethyl)-malonate ***4e***:[18] The general procedure was followed using (E)-2-nitrovinyl) benzene (74.6 mg, 0.5 mmol) and dimethyl methylmalonate (133 μL, 1 mmol). The crude product was purified by column chromatography (silica gel/PE: EA = 10:1) to give **4e** (116.6 mg, 79% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 1.35 (s, 3H, 1 × CH_3), 3.73 (s, 3H, 1 × CH_3), 3.78 (s, 3H, 1 × CH_3), 4.18 (dd, 1H, J = 4.8 Hz, J = 9.6 Hz, 1 × CH), 5.01–.09 (m, 2H, 1 × CH_2) 7.15–7.31 (m, 5H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 20.3, 48.4, 52.8, 53.0, 56.8, 77.5, 128.5, 128.8, 128.9, 135.0, 170.7, 171.4; HRMS (ESI): *m/z* $[M+H]^+$, calcd for $C_{14}H_{18}NO_6^+$ 296.1129, found 296.1131.

Preparation of diethyl 2-chloro-2-(2-nitro-1-phenylethyl)malonate ***4f***:[29] The general procedure was followed using (E)-2-nitrovinyl) benzene (74.6 mg, 0.5 mmol) and diethyl 2-chloromalonate (162.8 μL, 1 mmol). The crude product was purified by column chromatography (silica gel/PE: EA = 10:1) to give **4f** (154.4 mg, 90% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 1.11 (t, 3H, J = 7.2 Hz, 1 × CH_3) 1.29 (t, 3H, J = 7.1 Hz, 1 × CH_3), 3.96–4.11 (m, 2H, 1 × CH_2), 4.26–4.35 (m, 2H, 1 × CH_2), 4.63 (dd, 1H, J = 3.4 Hz, J = 10.4 Hz, 1 × CH), 4.99 (dd, 1H, J = 10.4 Hz, J = 13.5 Hz, 0.5 × CH_2), 5.23 (dd, 1H, J = 3.4 Hz, J = 13.5 Hz, 0.5 × CH_2), 7.30–7.39 (m, 5H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 13.6, 13.7, 48.2, 63.5, 63.6, 71.8, 77.3, 128.7, 129.1, 129.3, 133.5, 164.3, 166.0; HRMS (ESI): *m/z* $[M+H]^+$, calcd for $C_{15}H_{19}ClNO_6^+$ 344.0895, found 344.0898.

Preparation of diisopropyl 2-(1-(4-fluorophenyl)-2-nitroethyl)-malonate ***4g***: The general procedure was followed using (E)-1-fluoro-4-(2-nitrovinyl)benzene (83.5 mg, 0.5 mmol) and diisopropyl malonate (190 μL, 1 mmol). The crude product was purified by column chromatography (silica gel/PE: EA = 20:1) to give **4g** (119.0 mg, 67% yield) as a white solid. MP 82–84 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 1.04 (d, 3H, J = 6.2 Hz, 1 × CH_3), 1.08 (d, 3H, J = 6.3 Hz, 1 × CH_3), 1.24–1.26 (m, 6H, 2 × CH_3), 3.72 (d, 1H, J = 9.6 Hz, 1 × CH), 4.20 (dt, 1H, J = 4.5 Hz, J = 9.6 Hz, 1 × CH), 4.77–4.88 (m, 2H, 0.5 × CH_2, 1 × CH), 4.91 (dd, 1H, J = 4.5 Hz, J = 12.9 Hz, 0.5 × CH_2) 5.05–5.12 (m, 1H, 1 × CH), 6.99–7.03 (m, 2H, Ar-H), 7.21–7.25 (m, 2H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 21.3, 21.4, 21.6, 42.2, 55.1, 69.7, 70.0, 77.9, 115.7, 115.9, 129.9 (d, J = 8.2 Hz), 132.1, 166.2, 166.9; HRMS (ESI): *m/z* $[M+H]^+$, calcd for $C_{17}H_{23}FNO_6^+$ 356.1504, found 356.1507.

*Preparation of diisopropyl 2-(1-(4-chlorophenyl)-2-nitroethyl)-malonate **4h**:* The general procedure was followed using (E)-1-chloro-4-(2-nitrovinyl)benzene (91.5 mg, 0.5 mmol) and diisopropyl malonate (190 μL, 1 mmol). The crude product was purified by column chromatography (silica gel/PE: EA = 15:1) to give **4h** (120.6 mg, 65% yield) as a white solid. MP 80–81 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 1.05 (d, 3H, J = 6.2 Hz, 1 × CH_3), 1.09 (d, 3H, J = 6.2 Hz, 1 × CH_3), 1.24–1.26 (m, 6H, 2 × CH_3), 3.71 (d, 1H, J = 9.5 Hz, 1 × CH), 4.18 (dt, 1H, J = 4.5 Hz, J = 9.5 Hz, 1 × CH), 4.78–4.87 (m, 2H, 0.5 × CH_2, 1 × CH), 4.91 (dd, 1H, J = 4.6 Hz, J = 13.0 Hz, 0.5 × CH_2), 5.03–5.13 (m, 1H, 1 × CH), 7.18–7.20 (m, 2H, Ar-H), 7.28–7.30 (m, 2H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 21.3, 21.3, 21.4, 21.6, 42.3, 55.0, 69.8, 70.1, 77.7, 129.1, 129.5, 134.3, 134.9, 166.1, 166.8; HRMS (ESI): m/z $[M+H]^+$, calcd for $C_{17}H_{23}ClNO_6^+$ 372.1208, found 372.1210.

*Preparation of diisopropyl 2-(2-nitro-1-(4-nitrophenyl)ethyl)-malonate **4i**:*[30] The general procedure was followed using (E)-1-nitro-4-(2-nitrovinyl)benzene (97.0 mg, 0.5 mmol) and diisopropyl malonate (190 μL, 1 mmol). The crude product was purified by column chromatography (silica gel/PE: EA = 10:1) to give **4i** (137.6 mg, 72% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 1.07 (d, 3H, J = 6.2 Hz, 1 × CH_3), 1.10 (d, 3H, J = 6.3 Hz, 1 × CH_3), 1.24–1.26 (m, 6H, 2 × CH_3), 3.77 (d, 1H, J = 9.2 Hz, 1 × CH), 4.34 (dt, 1H, J = 4.5 Hz, J = 9.4 Hz, 1 × CH), 4.84–4.92 (m, 2H, 0.5 × CH_2, 1 × CH), 4.97 (dd, 1H, J = 4.5 Hz, J = 13.4 Hz, 0.5 × CH_2), 5.06–5.13 (m, 1H, 1 × CH), 7.47 (d, 2H, J = 8.7 Hz, Ar-H), 8.20 (d, 2H, J = 8.7 Hz, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 21.3, 21.4, 21.4, 21.6, 42.5, 54.6, 70.1, 70.5, 77.1, 124.1, 129.3, 143.8, 147.8, 165.9, 166.5; HRMS (ESI): m/z $[M+Na]^+$, calcd for $C_{17}H_{22}N_2NaO_8^+$ 405.1268, found 405.1270.

*Preparation of diisopropyl 2-(1-(4-methoxyphenyl)-2-nitroethyl)malonate **4j**:*[30] The general procedure was followed using (E)-1-methoxy-4-(2-nitrovinyl)benzene (89.5 mg, 0.5 mmol) and diisopropyl malonate (190 μL, 1 mmol). The crude product was purified by column chromatography (silica gel/PE: EA = 15:1) to give **4j** (124.8 mg, 68% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 1.04 (d, 3H, J = 6.2 Hz, 1 × CH_3), 1.08 (d, 3H, J = 6.2 Hz, 1 × CH_3), 1.24–1.26 (m, 6H, 2 × CH_3), 3.72 (d, 1H, J = 9.7 Hz, 1 × CH), 3.76 (s, 3H, 1 × CH_3), 4.15 (dt, 1H, J = 4.6 Hz, J = 9.5 Hz, 1 × CH), 4.76–4.91 (m, 3H, 1 × CH_2, 1 × CH), 5.05–5.11 (m, 1H, 1 × CH), 6.82–6.84 (m, 2H, Ar-H), 7.15–7.17 (m, 2H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 21.3, 21.4, 21.5, 21.6, 42.3, 55.2, 55.3, 69.5, 69.9, 78.2, 114.2, 128.1, 129.3, 159.4, 166.4, 167.1; HRMS (ESI): m/z $[M+H]^+$, calcd for $C_{18}H_{26}NO_7^+$ 368.1698, found 368.1707.

*Preparation of diisopropyl 2-(2-nitro-1-(p-tolyl)ethyl)malonate **4k**:*[30] The general procedure was followed using (E)-1-methyl-4-(2-nitrovinyl)benzene (81.5 mg, 0.5 mmol) and diisopropyl malonate (190 μL, 1 mmol). The crude product was purified by column chromatography (silica gel/PE: EA = 15:1) to give **4k** (114.1 mg, 65% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 1.03 (d, 3H, J = 6.2 Hz, 1 × CH_3), 1.08 (d, 3H, J = 6.2 Hz, 1 × CH_3), 1.24–1.26 (m, 6H, 2 × CH_3), 2.29 (s, 3H, 1 × CH_3), 3.73 (d, 1H, J = 9.6 Hz, 1 × CH), 4.16 (dt, 1H, J = 4.6 Hz, J = 9.4 Hz, 1 × CH), 4.78–4.92 (m, 3H, 1 × CH_2, 1 × CH), 5.05–5.11 (m, 1H, 1 × CH), 7.09–7.13 (m, 4H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 21.1, 21.3, 21.3, 21.5, 21.6, 42.6, 55.2, 69.5, 69.9, 78.1, 127.9, 129.5, 133.2, 138.0, 166.4, 167.1; HRMS (ESI): m/z $[M+H]^+$, calcd for $C_{18}H_{26}NO_6^+$ 352.1755, found 352.1758.

*Preparation of diisopropyl 2-(1-(2-methoxyphenyl)-2-nitroethyl)malonate **4l**:* The general procedure was followed using (E)-1-methoxy-2-(2-nitrovinyl)benzene (89.5 mg, 0.5 mmol) and diisopropyl malonate (190 μL, 1 mmol). The crude product was purified by column chromatography (silica gel/PE: EA = 15:1) to give **4l** (137.7 mg, 75% yield) as a white solid. MP 55–57 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 0.97 (d, 3H, J = 6.2 Hz, 1 × CH_3), 1.03 (d, 3H, J = 6.2 Hz, 1 × CH_3), 1.24–1.26 (m, 6H, 2 × CH_3), 3.86 (s, 3H, 1 × CH_3), 4.09 (d, 1H, J = 10.5 Hz, 1 × CH), 4.34 (dt, 1H, J = 4.2 Hz, J = 9.8 Hz, 1 × CH), 4.73–4.79 (m, 1H, 1 × CH), 4.86 (dd, 1H, J = 4.2 Hz, J = 12.7 Hz, 0.5 × CH_2), 4.98–5.11 (m, 2H, 1 × CH, 0.5 × CH_2), 6.85–6.87 (m, 2H, Ar-H), 7.13–7.26 (m, 2H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 21.2, 21.3, 21.5, 21.6, 40.6, 52.9, 55.4, 69.1, 69.7, 76.4, 111.0, 120.7, 123.7, 129.6, 131.2, 157.5, 166.7, 167.5; HRMS (ESI): m/z $[M+H]^+$, calcd for $C_{18}H_{26}NO_7^+$ 368.1704, found 368.1706.

*Preparation of diisopropyl 2-(1-(2-chlorophenyl)-2-nitroethyl)-malonate **4m**:* The general procedure was followed using (E)-1-chloro-2-(2-nitrovinyl)benzene (91.5 mg, 0.5 mmol) and diisopropyl malonate (190 μL, 1 mmol). The crude product was purified by column chromatography (silica gel/PE: EA = 10:1) to give **4m** (131.7 mg, 71% yield) as a white solid. MP 52–54 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 1.09 (t, 6H, J = 6.1 Hz, 2 × CH_3), 1.21 (d, 3H, J = 6.3 Hz, 1 × CH_3), 1.24 (d, 3H, J = 6.2 Hz, 1 × CH_3), 4.05 (d, 1H, J = 9.2 Hz, 1 × CH), 4.71 (dt, 1H, J = 4.3 Hz, J = 8.6 Hz, 1 × CH), 4.85–4.94 (m, 2H, 1 × CH_2), 5.04–5.12 (m, 2H, 2 × CH), 7.21–7.26 (m, 3H, Ar-H), 7.39–7.41 (m, 1H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 21.2, 21.3, 21.5, 21.6, 39.4, 53.4, 69.7, 70.0, 76.0, 127.2, 129.1, 129.4, 130.4, 133.8, 134.2, 166.3, 167.0; HRMS (ESI): m/z $[M+H]^+$, calcd for $C_{17}H_{22}ClNNaClO_6^+$ 394.1031, found 394.1028.

*Preparation of diisopropyl 2-(2-nitro-1-(2-nitrophenyl)ethyl)-malonate **4n**:* The general procedure was followed using (E)-1-nitro-2-(2-nitrovinyl)benzene (97.0 mg, 0.5 mmol) and diisopropyl malonate (190 μL, 1 mmol). The crude product was purified by column chromatography (silica gel/PE: EA = 15:1) to give **4n** (164.3 mg, 86% yield) as a white solid. MP 50–51 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ (ppm) 1.04 (d, 3H, J = 6.2 Hz, 1 × CH_3), 1.09 (d, 3H, J = 6.3 Hz,

$1 \times CH_3$), 1.23–1.26 (m, 6H, $2 \times CH_3$), 4.14 (d, 1H, $J = 8.8$ Hz, $1 \times CH$), 4.70 (dt, 1H, $J = 4.2$ Hz, $J = 8.1$ Hz, $1 \times CH$), 4.84–4.90 (m, 1H, $1 \times CH$), 5.02–5.18 (m, 3H, $1 \times CH_2$, $1 \times CH$), 7.46 (dd, 2H, $J = 7.8$ Hz, $J = 18.6$ Hz, Ar-H), 7.58 (t, 1H, $J = 7.6$ Hz, Ar-H), 7.93 (d, 1H, $J = 8.1$ Hz, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ (ppm) 21.2, 21.3, 21.5, 21.6, 37.8, 53.8, 70.0, 70.2, 76.6, 125.4, 129.2, 129.4, 131.5, 133.2, 150.0, 166.2, 166.9; HRMS (ESI): m/z $[M + H]^+$, calcd for $C_{17}H_{23}N_2O_8^+$ 383.1449, found 383.1447.

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