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Hydrophosphonylation of Aldimines under Catalysts-Free Conditions

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Trimethylsilyl phosphite reacted with aldimines efficiently under catalysts-free conditions, giving α-aminophosphonates in good to excellent yields. Furthermore, the reaction can be scaled-up easily and the high yield can be maintained.

Keywords trimethylsilyl phosphite, aldimines, α-aminophosphonates, catalysts-free

Introduction

α-Aminophosphoric acids and phosphonates have attracted considerable attention in recent years due to their intriguing biological and pharmaceutical activities.[1] Pudovik reaction,[2] coupling of phosphites with imines, is the most straight forward and efficient protocol for the synthesis of this type of important compound. Although considerable efforts have been made recently,[3] given the usefulness of Pudovik reaction in carbon-phosphorus bond constructions, the development of simple transformation which features in high efficiency is still clearly desirable. In contrast to dialkyl phosphites, an alternative strategy through nucleophilic addition of readily available trialkylsilyl phosphite to suitable electrophiles was farless examined.[4] Recently, the group of Das[5] used trialkylsilyl phosphites as nucleophilic reagents successfully in iodine molecular catalyzed aminophosphonylation of *N*-tosyl aldimines, obtained sulfonamide phosphonates in excellent yields. And more recently, we discovered that *N*-heterocyclic carbenes (NHCs)[6] can also promote the Pudovik reaction of trimethylsilyl phosphite with aldehydes efficiently, giving α-hydroxyphosphonates in good yields.[7b] As part of our ongoing studies of NHCs catalysis,[7] we evisioned that NHCs may be able to catalyze the addition of trimethylsilyl phosphites with imines. In this paper, we describe the direct coupling of trimethylsilyl phosphite with aldmines to produce α-aminophosphonates.

Results and Discussion

In our initial experiments, *N*-tosyl benzaldimine coupled with dimethyl trimethylsilyl phosphite smoothly in the presence of 2 mol% 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr, a stable NHC),[8] affording the corresponding adduct in excellent yield (Table 1, Entry 1). However, to our surprise, in the control experiments, we found that trimethylsilyl phosphite can react with *N*-tosyl benzaldimine directly in the absence of any catalysts, giving the desired α-aminophosphonate in impressive yield within 5 h (Table 1, Entry 2).[9] We then re-examined the reaction very carefully using freshly distilled trimethylsilyl phosphite and recrystallized *N*-tosyl benzaldimine in a new, dried and clean glassware for several times, but the same results were obtained. A brief survey of solvents indicated that ether, dichloromethane, toluene are all suitable reaction media, and gave the desired product in high yield (Table 1, Entries 3—5). Interestingly, when lowered reaction temperature to 0 ℃, no obvious effect on the reaction was observed (Table 1, Entry 6). However, when quenched the reaction within 2 h, the reaction was not completed under catalysts-free conditions and relatively low yield was obtained (Table 1, Entries 7, 8).[9] On the other hand, when alkyl phosphites such as $(MeO)_2P(O)H$, $(EtO)_2P(O)H$, $(MeO)_3P$ and $(EtO)_3P$ were used instead of dimethyl trimethylsilyl phosphite, no addition product was detected after long reaction time (Table 1, Entries 9—12).

With the optimal reaction conditions in hand, the scope of aldimine was then evaluated (Table 2). Tosyl arylimines with either electron-donating or withdrawing groups worked well to furnish α-aminophosphonates in excellent yields (Table 2, Entries 1—7). Additionally, the substitution at different position of the aromatic ring had no effect on the reaction (Table 2, Entries 8—12).

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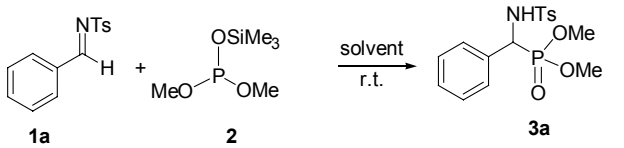
Table 1 Evaluation of reaction conditions[a]



1a **2** **3a**

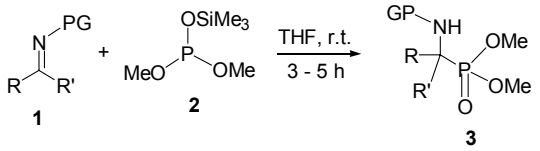
Entry	Phosphite	Solvent	Time/h	Yield[b]/%
1[c]	$Me_3SiOP(OMe)_2$	THF	5	90
2	$Me_3SiOP(OMe)_2$	THF	5	91
3	$Me_3SiOP(OMe)_2$	Et_2O	5	82
4	$Me_3SiOP(OMe)_2$	DCM	5	78
5	$Me_3SiOP(OMe)_2$	Toluene	5	88
6[d]	$Me_3SiOP(OMe)_2$	THF	5	87
7	$Me_3SiOP(OMe)_2$	THF	2	71
8[d]	$Me_3SiOP(OMe)_2$	THF	2	69
9	$HP(O)(OEt)_2$	THF	24	ND[e]
10	$HP(O)(OMe)_2$	THF	24	ND[e]
11	$P(OEt)_3$	THF	24	ND[e]
12	$P(OMe)_3$	THF	24	ND[e]

[a] Reaction conditions: *N*-tosyl benzaldimine (0.3 mmol), phosphite (0.45 mmol), solvent (2.0 mL), room temperature. [b] Isolated yield. [c] Using 2 mol% IPr. [d] The reaction was performed at 0 ℃. [e] the product was not detected.

Interestingly, *N*-tosyl-1-(2-furyl)methanimine and *N*-tosyl-1-(2-naphthyl)methanimine were also very good candidates for the reaction, and afforded the corresponding products in 99% and 92% yields respectively (Table 2, Entries 13, 14). On the other hand, *N*-tosyl alkylimines such as *N*-tosyl-1-butanimine and *N*-tosyl-1-cyclohexylmethanimine, can also couple with silylated reagent very smoothly (Table 2, Entries 15, 16). But it is worthwhile noting that the use of freshly prepared imine that derived from open chain aliphatic aldehyde is necessary for getting high yield.[10] Aldimines bearing different *N*-protecting groups other than tosyl were also investigated for the reaction. To our delight, *N*-*tert*-butoxycarbonyl and 4-nitrophenylsulfonyl aldimines were also proved to be very good reactants and gave the desired products in excellent yields (Table 2, Entries 17, 18). We also attempted hydrophosphonylation of tosyl-ketimines, but no product was obtained under catalysts-free conditions (Table 2, Entries 19, 20). Finally, the reaction was conducted on a one-gram scale and the α-aminophosphonate **3a** could be isolated in 93% yield (1.23 g, Table 2, Entry 21).

Based on the pioneering work of Lewis base promoted Pudovik type reaction,[7b] we propose the following reaction mechanism (Scheme 1). Firstly, the Schiff base attacks the silicon atom of trimethylsilyl phosphite to form a possible hypervalent intermediate, thus the Si—O bond is activated, which might trigger the addition of aldimine and after hydrolysis, could give the desired product.

Table 2 α-Aminophosphonylation of aldimines[a]

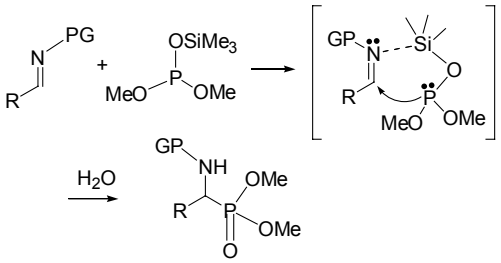


1 **2** **3**

Entry	R	R'	PG	Time/h	Product	Yield[b]/%
1	C_6H_5	H	Ts	5	**3a**	91
2	4-MeC_6H_4	H	Ts	5	**3b**	95
3	4-$MeOC_6H_4$	H	Ts	5	**3c**	86
4	4-FC_6H_4	H	Ts	5	**3d**	83
5	4-ClC_6H_4	H	Ts	5	**3e**	82
6	4-$CF_3C_6H_4$	H	Ts	4	**3f**	99
7[c]	4-$NO_2C_6H_4$	H	Ts	4	**3g**	98
8	2-$MeOC_6H_4$	H	Ts	5	**3h**	86
9	3-$MeOC_6H_4$	H	Ts	5	**3i**	78
10	2-ClC_6H_4	H	Ts	5	**3j**	91
11	2,4-$Cl_2C_6H_4$	H	Ts	5	**3k**	82
12	3-$NO_2C_6H_4$	H	Ts	4	**3l**	98
13	2-Furyl	H	Ts	5	**3m**	99
14	2-Naphthyl	H	Ts	5	**3n**	92
15	$CH_3CH_2CH_2$	H	Ts	2	**3o**	91
16	Cyclohexyl	H	Ts	5	**3p**	95
17	C_6H_5	H	Boc	5	**3q**	94
18	C_6H_5	H	Ns	3	**3r**	95
19	C_6H_5	CH_3	Ts	24	—	—
20	C_6H_5	C_6H_5	Ts	24	—	—
21[d]	C_6H_5	H	Ts	24	**3a**	93

[a] Reaction conditions: aldimine (0.3 mmol), phosphite (0.45 mmol), THF (2.0 mL), room temperature, 5 h. [b] Isolated yield. [c] Using 5 mL THF. [d] Using 3.6 mmol *N*-tosyl aldimine and 5.4 mmol phosphite.

Scheme 1 Proposed reaction mechanism



Conclusions

In summary, we have demonstrated an efficient approach for hydrophosphonylation of aldimines using commercially available dimethyl trimethylsilyl phosphite. The mild and catalysts-free conditions, simple procedure, easy scale-up and impressive yield provides a valuable method for the preparation of various α-aminophosphonates. Further improvements and ap-

plications are on going in our laboratory.

Experimental

General

Unless otherwise indicated, all reactions were conducted under nitrogen atmosphere in oven-dried glassware with magnetic stirring bar. Column chromatograph was performed with silica gel (200—300 mesh) and analytical TLC on silica gel 60-F254. ^{1}H NMR (300 or 400 MHz), ^{13}C NMR (75 or 100 MHz) spectra were recorded on a 400 MHz or 300 MHz spectrometer in $CDCl_3$ or DMSO-d_6, with tetramethylsilane as an internal standard. Infrared spectra were reported as wave number (cm^{-1}). Dimethyl trimethylsilyl phosphite **2** was distilled before use. Other starting materials were obtained from commercial supplies and used as received. Anhydrous THF, toluene and Et_2O were distilled from sodium and imines were synthesized according to literatures. Petroleum ether (PE), where used, had a boiling range of 60—90 ℃.

General procedure for preparation of *α*-aminophosphonates

Aldimine (0.3 mmol) was dissolved in 2 mL of dry THF, then cooled to 0 ℃ and dimethyl trimethylsilyl phosphite (0.45 mmol, 86 μL) was added via syringe under N_2. Subsequently, the reaction solution was stirred at room temperature for 5 h, 1 mL of H_2O was added at this moment and the mixture was continued stirring for 0.5 h, then the mixture was extracted by CH_2Cl_2 (20 mL×3). The combined organic phase was filtered after drying over anhydrous Na_2SO_4, and concentrated under vacuum. The crude product was purified through flash column chromatography (silica gel, PE-EtOAc, 1∶1) to give desired product.

Procedure for preparation of *N*-tosyl *α*-aminophosphonates on a one-gram scale (3a)

Tosylimine (3.6 mmol) was dissolved in 24 mL of dry THF, then cooled to 0 ℃ and dimethyl trimethylsilyl phosphite (5.4 mmol, 1.03 mL) was added via syringe under N_2. Subsequently the reaction solution was stirred at room temperature for 24 h, 5 mL of H_2O was added at this moment and the mixture was continued stirring for 0.5 h, then the mixture was extracted by CH_2Cl_2 (60 mL×3). The combined organic phase was filtered after drying over anhydrous Na_2SO_4, and concentrated under vacuum. The crude product was purified through flash column chromatography (silica gel, PE-EtOAc, 1∶1) to give desired product as a white solid, 1.23 g (93%).

Dimethyl (4-methylphenylsulfonamido) (phenyl) methyl phosphonate (3a)[5] White solid, 101 mg (91%); m.p. 163—164 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 7.53—7.38 (m, 3H), 7.32—7.18 (m, 2H), 7.17—7.02 (m, 3H), 6.94 (d, *J*=7.9 Hz, 2H), 4.85 (dd, *J*=24.2, 9.9 Hz, 1H), 3.89 (d, *J*=10.7 Hz, 3H), 3.39 (d, *J*=10.5 Hz, 3H), 2.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ*: 142.7, 137.9, 133.3, 128.9, 128.3, 128.2, 127.8 (d, *J*=3.0 Hz), 127.0, 54.9 (d, *J*=156.7 Hz), 54.6 (d, *J*=6.7 Hz), 53.9 (d, *J*=6.7 Hz), 21.3.

Dimethyl (4-methylphenyl) (4-methylphenylsulfonamido) methyl phosphonate (3b)[5] White solid, 110 mg (95%); m.p. 187—189 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.47 (d, *J*=8.2 Hz, 2H), 7.19—6.86 (m, 6H), 6.82 (br s, NH), 4.78 (dd, *J*=23.9, 9.8 Hz, 1H), 3.84 (d, *J*=10.8 Hz, 3H), 3.41 (d, *J*=10.6 Hz, 3H), 2.29 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 142.7, 137.8 (d, *J*=4.0 Hz), 130.2, 128.97, 128.94, 128.0 (d, *J*=6.0 Hz), 127.0, 54.6 (d, *J*=156.0 Hz), 54.4 (d, *J*=7.0 Hz), 53.9 (d, *J*=7.0 Hz), 21.3, 21.0.

Dimethyl (4-methoxyphenyl) (4-methylphenylsulfonamido) methyl phosphonate (3c)[5] White solid, 103 mg (86%); m.p. 160—161 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.47 (d, *J*=8.3 Hz, 2H), 7.12 (dd, *J*=8.6, 1.8 Hz, 2H), 7.00 (d, *J*=8.0 Hz, 2H), 6.72 (br s, NH), 6.63 (d, *J*=8.5 Hz, 2H), 4.77 (dd, *J*=24.6, 10.1 Hz, 1H), 3.85 (d, *J*=10.8 Hz, 3H), 3.73 (s, 3H), 3.42 (d, *J*=10.6 Hz, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 159.3 (d, *J*=3.0 Hz), 142.8, 137.8 (d, *J*=2.0 Hz), 129.3 (d, *J*=6.0 Hz), 129.0, 127.0, 125.3, 113.7 (d, *J*=2.0 Hz), 55.2, 54.4 (d, *J*=7.0 Hz), 54.2 (d, *J*=157.0 Hz), 53.9 (d, *J*=7.0 Hz), 21.3.

Dimethyl (4-fluorophenyl) (4-methylphenylsulfonamido) methyl phosphonate (3d)[3i] White solid, 96 mg (83%); m.p. 209—210 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.48 (s, 1H), 7.46 (s, 1H), 7.23—7.16 (m, 3H), 7.00 (d, *J*=8.0 Hz, 2H), 6.78 (t, *J*=8.5 Hz, 2H), 4.83 (dd, *J*=24.2, 9.8 Hz, 1H), 3.90 (d, *J*=10.8 Hz, 3H), 3.46 (d, *J*=10.7 Hz, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 162.4 (dd, *J*=246.0, 3.0 Hz), 143.1, 137.8 (d, *J*=1.0 Hz), 129.9 (dd, *J*=8.0, 5.0 Hz), 129.2 (d, *J*=4.0 Hz), 129.0, 127.0, 115.2 (dd, *J*=22.0, 2.0 Hz), 54.8 (d, *J*=8.0 Hz), 54.2 (dd, *J*=157.0 Hz), 53.9 (d, *J*=7.0 Hz), 21.4.

Dimethyl (4-chlorophenyl) (4-methylphenylsulfonamido) methyl phosphonate (3e)[5] White solid, 99 mg (82%); m.p. 198—199 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.45 (d, *J*=8.3 Hz, 2H), 7.20 (br s, NH), 7.17—7.10 (m, 2H), 7.04 (d, *J*=8.3 Hz, 2H), 6.99 (d, *J*=8.0 Hz, 2H), 4.82 (dd, *J*=24.4, 9.9 Hz, 1H), 3.91 (d, *J*=10.8 Hz, 3H), 3.47 (d, *J*=10.7 Hz, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 143.2, 137.6 (d, *J*=2.0 Hz), 134.0 (d, *J*=4.0 Hz), 131.9, 129.5 (d, *J*=5.0 Hz), 129.0, 128.4 (d, *J*=2.0 Hz), 127.0, 54.3 (d, *J*=157.0 Hz), 54.8 (d, *J*=7.0 Hz), 53.9 (d, *J*=7.0 Hz), 21.3.

Dimethyl (4-methylphenylsulfonamido) (4-trifluoromethylphenyl) methyl phosphonate (3f) White solid, 139 mg (99%); m.p. 228—230 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) *δ*: 8.91 (dd, *J*=10.6, 2.4 Hz, 1H), 7.41 (s, 4H), 7.40 (s, 1H), 7.01 (d, *J*=8.0 Hz, 2H), 4.98 (dd, *J*=24.9, 10.6 Hz, 1H), 3.70 (d, *J*=10.7 Hz, 3H), 3.49 (d, *J*=10.7 Hz, 3H), 3.35 (br s, NH, 1H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) *δ*: 142.3, 138.6, 137.7 (d, *J*=1.0 Hz), 128.9 (d, *J*=5.0 Hz), 128.8, 127.7

(dd, J=31.0, 3.0 Hz), 126.5, 124.4, 124.0 (d, J=271.0 Hz), 53.9 (d, J=7.0 Hz), 53.3 (d, J=155.0 Hz), 53.2 (d, J=7.0 Hz), 20.5.

Dimethyl (4-methylphenylsulfonamido) (4-nitrophenyl) methyl phosphonate (3g)[5] White solid, 121 mg (98%); m.p. 207—208 ℃; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.98 (d, J=8.3 Hz, 1H), 7.94 (d, J=8.7 Hz, 2H), 7.50 (dd, J=8.8, 2.0 Hz, 2H), 7.44 (d, J=8.3 Hz, 2H), 7.07 (d, J=8.3 Hz, 2H), 5.09 (dd, J=25.4, 10.3 Hz, 1H), 3.69 (d, J=10.7 Hz, 3H), 3.49 (d, J=10.8 Hz, 3H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 146.7 (d, J=3.0 Hz), 142.8, 142.2, 138.0, 129.7 (d, J=5.0 Hz), 129.2, 126.8, 122.9, 54.2 (d, J=7.0 Hz), 53.6 (d, J=7.0 Hz), 53.4 (d, J=142.0 Hz), 20.9.

Dimethyl (2-methoxyphenyl) (4-methylphenylsulfonamido) methyl phosphonate (3h) White solid, 103 mg (86%); m.p. 189—190 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.48 (s, 1H), 7.46 (s, 1H), 7.25 (dt, J=9.6, 1.9 Hz, 1H), 7.02—7.06 (m, 1H), 6.95 (d, J=8.0 Hz, 2H), 6.70 (t, J=7.5 Hz, 1H), 6.64 (br d, J=7.8 Hz, 1H), 6.61 (d, J=8.3 Hz, 1H), 5.30 (dd, J=24.6, 10.5 Hz, 1H), 3.87 (d, J=10.7 Hz, 3H), 3.74 (s, 3H), 3.44 (d, J=10.6 Hz, 3H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 156.4 (d, J=6.0 Hz), 142.8, 137.3 (d, J=2.0 Hz), 129.5 (d, J=5.0 Hz), 129.2 (d, J=3.0 Hz), 128.8, 127.0, 121.8, 127.0 (d, J=2.0 Hz), 110.5 (d, J=2.0 Hz), 55.6, 54.4 (d, J=7.0 Hz), 53.8 (d, J=7.0 Hz), 49.0 (d, J=161.0 Hz), 21.3.

Dimethyl (3-methoxyphenyl) (4-methylphenylsulfonamido) methyl phosphonate (3i) White solid, 92 mg (78%); m.p. 163—164 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.48 (s, 1H), 7.46 (s, 1H), 7.39 (d, J=6.4 Hz, 1H), 7.00 (t, J=7.7 Hz, 1H), 6.95 (d, J=8.0 Hz, 2H), 6.78 (d, J=7.5 Hz, 1H), 6.73 (s, 1H), 6.64 (d, J=8.2 Hz, 1H), 4.85 (dd, J=24.5, 10.2 Hz, 1H), 3.93 (d, J=10.8 Hz, 3H), 3.52 (s, 3H), 3.43 (d, J=10.6 Hz, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.5 (d, J=2.0 Hz), 142.8, 137.9, 134.5, 129.2 (d, J=2.0 Hz), 128.8, 127.1, 120.7 (d, J=6.0 Hz), 114.2, 113.0 (d, J=5.0 Hz), 55.1 (d, J=157.0 Hz), 54.9, 54.8 (d, J=7.0 Hz), 53.9 (d, J=7.0 Hz), 21.3.

Dimethyl (2-chlorophenyl) (4-methylphenylsulfonamido) methyl phosphonate (3j) White solid, 110 mg (91%); m.p. 223—224 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.52 (d, J=8.2 Hz, 2H), 7.47 (d, J=7.8 Hz, 1H), 7.18 (d, J=7.9 Hz, 2H), 7.05 (t, J=7.4 Hz, 3H), 6.96 (d, J=8.0 Hz, 2H), 5.50 (dd, J=24.6, 10.1 Hz, 1H), 3.95 (d, J=10.8 Hz, 3H), 3.44 (d, J=10.7 Hz, 3H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.9, 137.2, 133.3 (d, J=7.0 Hz), 131.6, 129.6 (d, J=4.0 Hz), 129.1 (d, J=2.0 Hz), 129.0, 126.9, 126.8 (d, J=3.0 Hz), 54.8 (d, J=7.0 Hz), 54.0 (d, J=7.0 Hz), 50.5 (d, J=158.0 Hz), 21.3; IR (KBr) v: 3152, 2954, 1449, 1334, 1239, 1156, 1065, 1033 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{19}ClNO_5PSNa$ (MNa^+) 426.0308, found 426.0313.

Dimethyl (2,4-dichlorophenyl) (4-methylphenylsulfonamido) methyl phosphonate (3k)[7d] White solid, 107 mg (82%); m.p. 185—187 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.51 (d, J=8.3 Hz, 2H), 7.32 (dd, J=8.4, 2.4 Hz, 1H), 7.22 (dd, J=2.1, 1.1 Hz, 1H), 7.03 (d, J=8.4 Hz, 2H), 6.94 (dd, J=8.5, 2.0 Hz, 1H), 6.77 (br s, 1H), 5.40 (dd, J=24.5, 9.8 Hz, 1H), 3.93 (d, J=10.9 Hz, 3H), 3.51 (d, J=10.8 Hz, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.6, 137.0, 134.5 (d, J=3.0 Hz), 134.1 (d, J=8.0 Hz), 130.5 (d, J=4.0 Hz), 130.3, 129.2, 128.9 (d, J=2.0 Hz), 127.2 (d, J=3.0 Hz), 126.9, 54.9 (d, J=7.0 Hz), 54.0 (d, J=7.0 Hz), 50.1 (d, J=158.0 Hz), 21.4; IR (KBr) v: 3152, 2958, 2883, 1588, 1477, 1342, 1247, 1164, 1061, 1033, 903, 871, 807, 720 cm^{-1}.

Dimethyl (4-methylphenylsulfonamido) (3-nitrophenyl) methyl phosphonate (3l) White solid, 121 mg (98%); m.p. 162—164 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 (d, J=1.8 Hz, 1H), 7.92 (d, J=8.1 Hz, 1H), 7.84 (br s, 1H), 7.54 (d, J=7.4 Hz, 1H), 7.44 (d, J=8.3 Hz, 2H), 7.31 (t, J=8.0 Hz, 1H), 6.88 (d, J=8.3 Hz, 2H), 5.00 (dd, J=25.0, 10.9 Hz, 1H), 4.03 (d, J=10.8 Hz, 3H), 3.57 (d, J=10.8 Hz, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 147.9, 143.2, 137.6, 135.3, 134.3 (d, J=6.0 Hz), 129.0 (d, J=2.0 Hz), 128.9, 126.9, 123.1 (d, J=6.0 Hz), 122.6 (d, J=3.0 Hz), 55.4 (d, J=3.0 Hz), 54.4 (d, J=148.0 Hz), 54.1 (d, J=7.0 Hz), 21.1; IR (KBr) v: 3105, 2954, 2883, 1532, 1465, 1358, 1334, 1243, 1168, 1085, 1057 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{19}N_2O_7PSNa$ (MNa^+) 437.0548, found 437.0538.

Dimethyl furan-2-yl (4-methylphenylsulfonamido) methyl phosphonate (3m)[5] White solid, 106 mg (99%); m.p. 163—164 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57 (d, J=8.4 Hz, 2H), 7.19—7.07 (m, 3H), 6.32—6.01 (m, 3H), 4.92 (dd, J=24.1, 10.1 Hz, 1H), 3.85 (d, J=10.8 Hz, 3H), 3.58 (d, J=10.8 Hz, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.5, 143.1, 142.6 (d, J=3.0 Hz), 137.3, 129.2, 126.9, 110.6 (d, J=2.0 Hz), 109.7 (d, J=7.0 Hz), 54.6 (d, J=7.0 Hz), 53.9 (d, J=7.0 Hz), 48.5 (d, J=163.0 Hz), 21.4.

Dimethyl (4-methylphenylsulfonamido) (naphth) methyl phosphonate (3n) White solid, 116 mg (92%); m.p. 172—173 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.71 (d, J=8.0 Hz, 1H), 7.60 (s, 1H), 7.54 (d, J=8.5 Hz, 2H), 7.50 (d, J=8.0 Hz, 2H), 7.46—7.34 (m, 5H), 7.29 (br s, NH), 6.69 (d, J=8.0 Hz, 2H), 5.02 (dd, J=24.2, 10.0 Hz, 1H), 3.96 (d, J=10.8 Hz, 3H), 3.43 (d, J=10.6 Hz, 3H), 1.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.8, 137.7 (d, J=2.0 Hz), 132.8 (d, J=2.0 Hz), 132.7 (dd, J=6.0, 2.0 Hz), 130.3, 128.7, 128.1 (d, J=1.0 Hz), 127.9, 127.8 (d, J=8 Hz), 127.3, 126.9, 126.2, 126.0, 125.6 (d, J=4.0 Hz), 55.3 (d, J=157.0 Hz), 54.8 (d, J=7.0 Hz), 54.0 (d, J=7.0 Hz), 20.9; IR (KBr) v: 3437, 3108, 2950, 1457, 1326, 1235, 1164, 1057, 1029 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{22}NO_5PSNa$ (Mna^+) 442.0854, found 442.0871.

Dimethyl 1-(4-methylphenylsulfonamido) butyl phosphonate (3o)[5] White solid, 63 mg (63%); m.p. 117—118 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.76 (d,

J=8.2 Hz, 2H), 7.29 (d, J=8.2 Hz, 2H), 5.40 (br s, NH), 3.66 (d, J=1.3 Hz, 3H), 3.63 (d, J=1.1 Hz, 3H), 2.42 (s, 3H), 1.77—1.60 (m, 1H), 1.58—1.32 (m, 2H), 1.31—1.18 (m, 2H), 0.79 (dt, J=7.3, 1.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.3, 138.3, 129.4, 127.0, 53.5 (d, J=7.0 Hz), 52.9 (d, J=7.0 Hz), 49.7 (d, J=157.0 Hz), 32.5 (d, J=3.0 Hz), 21.5, 18.7 (d, J=10.0 Hz), 13.6.

Dimethyl cyclohexyl (4-methylphenylsulfonamido) methyl phosphonate (3p)[7d] White solid, 108 mg (95%); m.p. 160—161 ℃; IR (KBr) ν: 3152, 2950, 2922, 2847, 1465, 1322, 1235, 1152, 1105, 1057, 1013 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.75 (d, J=8.0 Hz, 2H), 7.39—7.18 (m, 2H), 3.59 (d, J=10.7 Hz, 3H), 3.53 (d, J=10.7 Hz, 3H), 2.42 (s, 3H), 1.80—1.55 (m, 6H), 1.22—1.00 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.2, 138.4, 129.3, 127.1, 54.8 (d, J=151.0 Hz), 52.8 (d, J=7.0 Hz), 52.7 (d, J=6.0 Hz), 39.2 (d, J=4.0 Hz), 30.4 (d, J=11.0 Hz), 28.0 (d, J=3.0 Hz), 26.1 (d, J=1.0 Hz), 26.0, 25.7, 21.5; IR (KBr) ν: 3152, 2950, 2922, 2847, 1465, 1322, 1235, 1152, 1105, 1057, 1013 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{26}NO_5PSNa$ (MNa^+) 398.1167, found 398.1142.

Dimethyl (*tert*-butoxycarbonylationamido) (phenyl)methyl phosphonate (3q)[3d] White solid, 88 mg (94%); m.p. 110—113 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.44—7.30 (m, 5H), 5.54 (br s, NH, 1H), 5.15 (dd, J=21.4, 9.9 Hz, 1H), 3.77 (d, J=10.7 Hz, 3H), 3.50 (d, J=10.6 Hz, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.8 (d, J=9.0 Hz), 135.1, 128.7, 128.1 (d, J=3.0 Hz), 127.7 (d, J=5.0 Hz), 80.5, 53.7 (d, J=7.0 Hz), 53.6 (d, J=7.0 Hz), 51.4 (d, J=153.0 Hz), 28.2.

Dimethyl (4-nitrophenylsulfonamido) (phenyl) methyl phosphonate (3r)[7d] Yellow solid, 114 mg (95%); m.p. 240—241 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.28 (d, J=6.4 Hz, 1H), 7.96—7.90 (m, 2H), 7.76—7.69 (m, 2H), 7.23 (br s, NH), 7.21 (d, J=1.7 Hz, 1H), 7.16—7.02 (m, 3H), 4.94 (dd, J=24.4, 10.2 Hz, 1H), 4.02 (d, J=10.9 Hz, 3H), 3.42 (d, J=10.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 149.3, 146.8 (d, J=2.0 Hz), 132.5, 128.5 (d, J=3.0 Hz), 128.4 (d, J=2.0 Hz), 128.3 (d, J=6.0 Hz), 128.2, 123.3, 55.2 (d, J=158.0 Hz), 54.8 (d, J=7.0 Hz), 54.3 (d, J=8.0 Hz).

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References and Notes

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(Pan, B.; Qin, X.)

