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Triflic acid mediated functionalization of α-hydroxyphosphonates: route for sulfonamide phosphonates†

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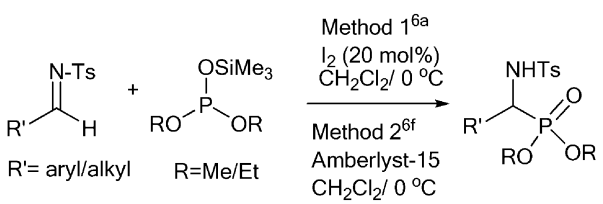
An operationally simple synthetic method for (±)-α-aryl/methylsulfonamidomethylphosphonates and new (±)-γ-aryl/methyl sulfonamidomethylvinylphosphonates has been developed through straightforward reactions of (±)-α-hydroxyphosphonates with sulfonamides in the presence of triflic acid (TfOH) at room temperature in a vessel open to air. For γ-dimethylallylhydroxyphosphonate, the (*E*)-1,3-butadienylphosphonate was formed quantitatively using TfOH while $FeCl_3$ afforded the expected product in moderate yield unpredictably. The favourable sulfonoamidation of benzyl alcohol is also observed when TfOH was used for α-hydroxyphosphonates having a benzyloxy group.

Introduction

The sulfonamide phosphonates form a class of distinct organophosphorus compounds where medicinally relevent sulfonamide bears the phosphonate unit.[1] These compounds are utilized as potential candidates for fluorescent β-lactamase[1b] and matrix metalloproteinase (MMPs) inhibitors as an analogue of known MMP inhibitors such as carboxylate and hydroxamate.[1c,d] In addition, these compounds are also well recognized as flame retardant materials[1a] along with their binding properties with selected lanthanides and actinides.[2] Moreover, sulfonamide phosphonates can be regarded as *N*-protected α- or γ-aminophosphonates, one of the most-desired structural motifs in bioorganic and medicinal chemistry due to its unique biological properties.[3] The related desulfonations are also well explored.[4] Thus, synthesis of protected or deprotected aminophosphonates has been pursued by several research groups.[3,5] The direct addition of imines with phosphites, preferably in the presence of metal salt, is the most common approach for synthesizing α-aminophosphonates[5] but synthesizing *N*-sulfonylimines requires special treatment due to the weak nucleophilicity of sulfonamides.[6c] Therefore, attempts for synthesis of specific α-sulfonamide phosphonates are sporadically mentioned in the literature[1,6] but γ-sulfonamide vinylphosphonates described herein are completely new. Most of these synthetic methods require freshly prepared imines (because of their instability) and metal salts (to activate the imines). Recently reported I_2 (ref. 6*a*) and Amberlyst-15 (ref. 6*h*) catalyzed methods explored the synthesis of sulfonamide phosphonates by reacting only *N*-tosylaldimines (freshly prepared) with expensive and moisture-sensitive dialkyl trimethylsilylphosphites at 0 °C under inert atmosphere (Scheme 1). It is again noteworthy that the syntheses of *N*-sulfonylimines prefer the induction of $TiCl_4$, $Si(OEt)_4$, BF_3[6e] *etc.* or multistep transformation along with special apparatus.[6a,1d]

The reported yields of related sulfonamide phosphonates obtained from tosylation reaction of α-aminophosphonate is also inadequate.[6f] The most recent synthetic method for γ-aminovinylphosphonates also required excess imines and Ti(II) complexes at very low temperature.[7] The γ-aminovinylphosphonates, thus synthesized, are already proved to be potent anti-inflammatory agents.[7a] In this regard, any simple synthetic method that avoids the use of imines, metals and also can be performed in open air at room temperature with water as a by-product would be attractive for medicinal/organic chemists. A synthetic method performed at room temperature is always beneficial as far as energy consumption is concerned. Hence, with our current interest on organophosphonates,[8] specifically in the umpolung reactivity of allyllic phosphonates,[8a] we present here an operationally simple, new and efficient



Scheme 1 Reported recent methods for α-sulfonamide phosphonates.[6a,f]

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† Electronic supplementary information (ESI) available: General informations and references for the synthesis of precursors, ^1H and ^{13}C NMR spectra. CCDC 934282 (**5a**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c3ra43823f

TfOH-mediated route to synthesize α-aryl/methylsulfonamidomethylphosphonates and more distinctively γ-aryl/methylsulfonamidomethylvinylphosphonates in moderate to high yield using cheap and easily accessible α-hydroxyphosphonates under mild conditions. We envisage that these new γ-aryl/methylsulfonamidomethylvinylphosphonates, described herein, will enhance the potential in the field of materials as well as biological sciences due the presence of sulfonamide at the γ-position for a useful vinylphosphonate.

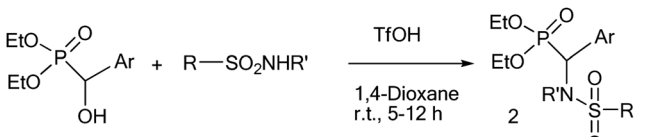
Results and discussion

Synthesis of (±)-α-aryl/methylsulfonamidomethylphosphonates

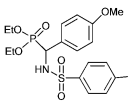
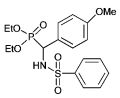
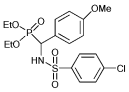
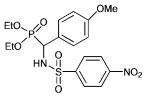
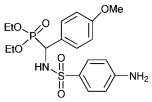
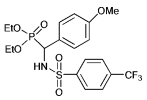
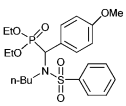
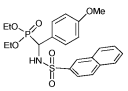
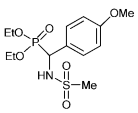
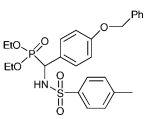
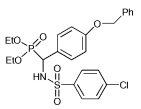
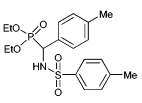
Initially, we preferred phosphonate (±)-**1a** and *p*-toluenesulfonamide ($TsNH_2$) as model substrates to optimize the suitable reaction conditions using different Lewis and Brønsted acids (see ESI† for details). The reported method of using $FeCl_3$ for this type of transformation could not offer a satisfactory result even under reflux in nitromethane.[9] With a possibility of hydrolyzing the alkoxy bonds of phosphonates, we tried the same reaction with TfOH, known to show a comparative effect as $FeCl_3$ in allylic amination reactions starting from allylic/benzylic alcohols.[10] Both $FeCl_3$ and TfOH worked very well as a catalyst for the reaction of benzylic/allylic alcohols with $TsNH_2$ (ref. 10) whereas sulfonamide phosphonate (±)-**2a** was isolated effectively from the reaction of hydroxyphosphonate (±)-**1a** with $TsNH_2$ only in the presence of TfOH. This different effect was observed probably due to the presence of phosphoryl group for (±)-**1a**. Moreover, TfOH and its salts are extensively used for amination reactions of alcohols.[10,11] Considering the generation of TfOH in the reaction medium using triflate salt,[12] efforts of treating $Yb(OTf)_3$ and $Cu(OTf)_2$ in place of TfOH were in vain. Screening with different stoichiometry (mol%) of TfOH showed that this reaction was mostly favoured with 60–100 mol% and it might be due to the presence of a strong coordinating group such as phosphonate for (±)-**1a**.[13] The only known direct approach from hydroxyphosphonates to only aminophosphonates with moderate yield was reported in the presence of acidic alumina using a kitchen-type microwave oven.[14] Using the same approach, we could isolate the product (±)-**2a** with only 25% yield whereas the γ-sulfonamide phosphonate was not formed even after 30 min by starting with phosphonate (±)-(*E*)-**4a**. Inspired by the report of Chan and co-workers on I_2-catalyzed allylic alkylation of sulfonamides,[15] our attempt to use I_2 for the synthesis of sulfonamide phosphonate failed under the present reaction conditions. There was no difference in the outcome even when the reaction was performed using LR grade 1,4-dioxane without exclusion of air/moisture at room temperature. Thus, TfOH/1,4-dioxane at room temperature appears to be the most suitable condition for the synthesis of sulfonamide phosphonates even in a vessel open to air.

As the variations of substituents for sulfonamides reflect the activity of sulfonamide phosphonates,[1c,d] we have explored this reaction using different types of sulfonamides. The examples are shown in Table 1. The yield and duration of the reaction did not differ much when the substituent (electron donating/accepting)

Table 1 TfOH mediated reactions of sulfonamides with α-hydroxyphosphonates (±)-**1a–c**[a]

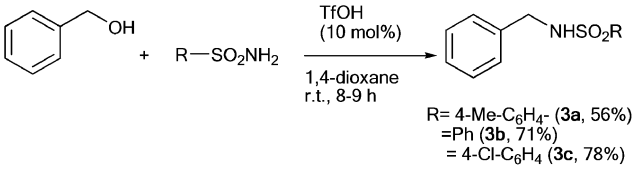


Ar= 4-OMe (1a)
= 4-OCH_2Ph (1b)
= 4-Me (1c)

Entry	**1**/R[b]	Product	(±)-**2**/Yield[c] (%)
1	**1a**/4-MeC_6H_4–		**2a**/94
2	**1a**/C_6H_5–		**2b**/90
3	**1a**/4ClC_6H_4–		**2c**/92
4	**1a**/4-$NO_2C_6H_4$–		**2d**/90
5	**1a**/4-$NH_2C_6H_4$–		**2e**/92
6	**1a**/4-$CF_3C_6H_4$–		**2f**/80
7	**1a**/R = Ph; R′ = *n*-Bu–		**2g**/88
8	**1a**/2-naphthyl–		**2h**/85
9	**1a**/Me–		**2i**/91
10	**1b**/4-MeC_6H_4–		**2j**/70
11	**1b**/4-ClC_6H_4–		**2k**/73
12	**1c**/4-MeC_6H_4–		**2l**/68[d]

[a] *Reaction conditions*: Phosphonate (1 mmol), sulfonamide (1 mmol) and TfOH (1 mmol) in 1,4-dioxane (3 mL) under open air at room temperature. [b] Except for entry 7, all R′ = H. [c] Isolated yield. [d] $FeCl_3$/dichloroethane (DCE) was used under nitrogen atmosphere at room temperature.

is changed in aryl groups for arylsulfonamides. The methanesulfonamide also worked very well to yield (±)-**2i** effectively. The yield was also good (Table 1, entry 7) when comparatively more electron rich *N*-butylsulfonamide was used. Notably, the yield was relatively poor (Table 2, entry 10) when the phosphonate (±)-**1b** was used. Interestingly, along with the expected compound (**2j**), we could also isolate the synthetically useful sulfonamide (**3a**, Scheme 2) from the reaction mixture of (±)-**1b**



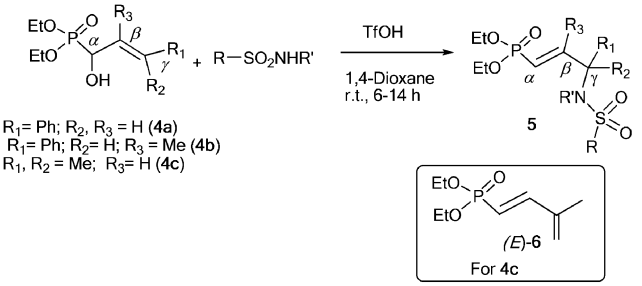
Scheme 2 TfOH catalyzed sulfonamidation of benzyl alcohol.

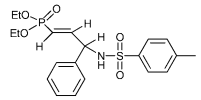
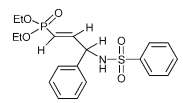
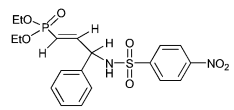
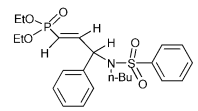
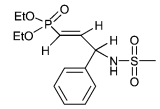
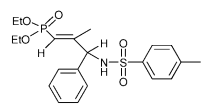
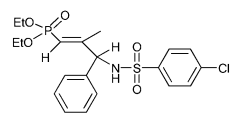
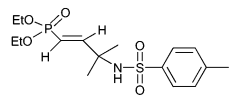
and $TsNH_2$. The compound **3a** was formed perhaps from the reaction of $TsNH_2$ with benzyl alcohol, generated by the partial acidic hydrolysis of phosphonate (±)-**1b** in the reaction mixture.

The known sulfonamide **3a** was synthesized recently using transition-metal (Ru, Mn *etc.*) catalyzed reactions.[16] It is also noteworthy that the primary benzylic alcohols did not react with $TsNH_2$ using $FeCl_3$ even on prolonged heating.[9] Inspired by these related reports and further to verify our result, we treated benzyl alcohol with only three sulfonamides separately in the presence of a catalytic amount of TfOH (10 mol%) at room temperature using 1,4-dioxane as solvent, which afforded compounds **3a–c** in moderate to good yield (Scheme 2). Even though a similar approach was reported with allylic alcohols, primary benzylic alcohol was not used in the literature using this method.[10] Thus, we believe that this facile metal-free process should be added to the existing methods for the synthesis of sulfonamides of type **3**.

Surprisingly, unlike (±)-**1a** and **1b**, the phosphonate (±)-**1c** reacted with $TsNH_2$ in the presence of $FeCl_3$/dichloroethane (DCE) in place of TfOH at room temperature. As expected, the presence of an electron donating group at the aryl part for phosphonates is needed for this method.

Table 2 TfOH mediated reactions of sulfonamides with α-hydroxyphosphonates (±)-**4a–c**[a]



Entry	**4**/R[b]	Product	(*E*)-**5**/Yield[c] (%)
1	**4a**/4-MeC_6H_4–		**5a**/92
2	**4a**/C_6H_5–		**5b**/90
3	**4a**/4-$NO_2C_6H_4$–		**5c**/86
4	**4a**/R = Ph; R′ = *n*-Bu–		**5d**/82
5	**4a**/Me–		**5e**/82
6	**4b**/4-MeC_6H_4		**5f**/88
7	**4b**/4ClC_6H_4–		**5g**/90
8	**4c**/4-MeC_6H_4		**5h**/56[d]

[a] *Reaction conditions*: Phosphonate (1 mmol), sulfonamide (1 mmol) and TfOH (1 mmol) in 1,4-dioxane (3 mL) in an open vessel. [b] Except entry 4, all R′ = H. [c] Isolated yield. [d] TfOH gave the diene and hence $FeCl_3$/DCE was used under nitrogen atmosphere.

Synthesis of (±)-γ-aryl/methyl sulfonamidovinylphosphonates

Further, we have extended our studies to synthesize new sulfonamide phosphonates regio- and stereoselectively where the sulfonamide is attached to a γ-carbon of a vinylphosphonate by choosing the easily-accessible cheap phosphonates (±)-(*E*)-**4a–c**. The newly synthesized sulfonamide phosphonates are shown in Table 2. The reaction of (±)-(*E*)-**4a** with $TsNH_2$ was not clean in the presence of $FeCl_3$/DCE or nitromethane whereas TfOH/1,4-dioxane gave almost quantitative yield of (±)-(*E*)-**5a**. Indeed, compounds (±)-(*E*)-**5a–c** were isolated and purified simply by crystallization from ethyl acetate. The phosphonate (±)-(*E*)-**4b** with an extra methyl group at β-C also afforded expected products (±)-(*E*)-**5e–f** in high yields. There was no evidence to account for the formation of γ-aminophosphonate from the reported reaction of (±)-(*E*)-**4a** with amines in the literature.[14] The TfOH-mediated method did not produce any other possible isomeric products either with a (*Z*)-configuration or sulfonamides attached at the α-carbon. It is important to note that the γ-aminovinylphosphonates were synthesized with mainly *E*-configuration [*Z*-isomers: (0–33%)] by Lu *et al.* using the umpolung reactivity of allylic phosphonates supported by expensive $Pd(PPh_3)_4$ starting from α-acetoxyallylic phosphonates and only amines under purified nitrogen.[17]

Using TfOH, attempted reactions of sulfonamides (mentioned here) with phosphonate (*E*)-**4c** led to the formation

of (*E*)-1,3-dienylphosphonate **6** quantitatively instead of forming sulfonamide phosphonates. Unpredictably, the expected product (*E*)-**5h** was obtained with moderate yield along with diene **6** by the employment of $FeCl_3$/DCE at room temperature. ^{31}P NMR for the reaction mixture showed that the ratio of product (*E*)-**5h** and diene (*E*)-**6** formed is 70/30, respectively. The formation of dienes could not be avoided even when the reaction was performed at −30 °C. It is worth noting that a similar type of observation to form an elimination product from 2-phenylpropan-2-ol was reported in the literature.[18] Moreover, the synthesis of 1,3-butadienylphosphonates is well demonstrated by Srebnik *et al. via* zirconation of 1-alkynylphosphonates.[19a] This diene compound (**6**) could also be used as a precursor to synthesize phosphorus based polymers, used in the biomedical field.[19b]

The sulfonamide phosphonates, synthesized herein, are characterized using multinuclear NMR ($^1H/^{13}C/^{31}P$) spectroscopy. The sulfonamide phosphonates (±)-**2a–l** (except **2g**) showed the characteristic doublet of doublet at ~δ 4.80 (dd, $J \sim$ 9.6 and 24.0 Hz) for P–C(α)*H* in ^1H NMR and a doublet at ~δ 54.9 (d, $J \sim$ 159.0 Hz) for P–*C*(α)H in ^{13}C NMR spectra. The stereochemistries for compounds (*E*)-(±)-**5a–h** including **6** are depicted by analysing the coupling constant ($^3J_{P-C}$ ~22.0–24.0 Hz) between the phosphorus and γ-carbon in ^{13}C NMR by comparing the values that are reported in the literature.[7,20] Moreover, single-crystal X-ray crystallographic studies for (±)-**5a** confirmed the (*E*)-configuration as well as the position (γ) of sulfonamide unequivocally (Fig. 1).[21]

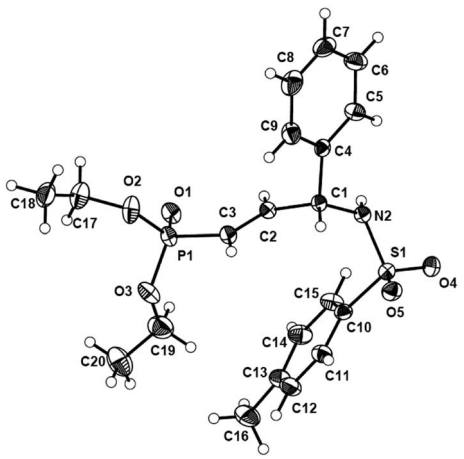
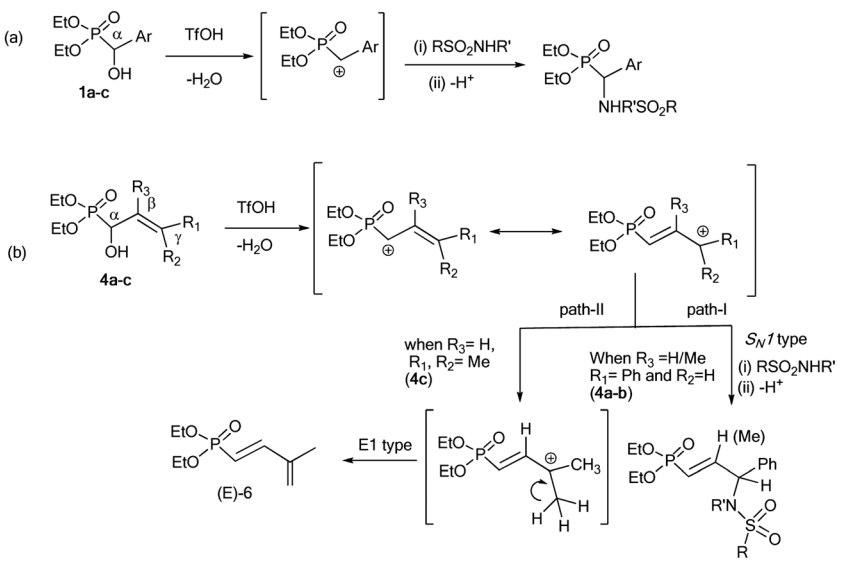


Fig. 1 ORTEP diagram (with 20%) probability labels for compound (*E*)-(±)-**5a**.

Thus, based on the observed experimental results and previous studies,[10–13,18] we believe that the reaction proceeds *via* a carbocation intermediate that will be stabilized by inductive/conjugation effect of adjacent substituents. Unlike other Lewis acids, TfOH promotes the formation of a carbocation from α-hydroxyphosphonate, which is relatively hard to achieve, without any other side reactions such as coordination with phosphoryl group, alkene and sulfonamide.

In case of simple α-hydroxy (aryl)phosphonates (**1a–c**), the intermediate carbocation is stabilized by electron donating substituents present in the aryl group (+I effect), followed by nucleophilic attack of sulfonamide to yield the desired (±)-α-aryl/methylsulfonamidomethylphosphonate (Scheme 3a). In case of α-hydroxy allylicphosphonates (**4a–b**; where R_1 = Ph and R_2 = H), it is expected that the generated carbocation at the α-carbon (to phosphonate moiety) is stabilized by an adjacent double bond *via* a resonance effect and thus generated a more stable carbocation at a γ-carbon (which is further stabilized by a +R effect of aryl groups), followed by nucleophilic attack of sulfonamide (SN1 type mechanism), which selectively leads to (±)-γ-aryl/methyl sulfonamidomethylvinylphosphonates in very good yields (Scheme 3b). In case of compound **4c** (where R_1 = R_2 = Me), the carbocation (at γ-carbon) undergoes elimination (E1 type) rather than nucleophilic substitution reaction, and yielded diene (*E*)-**6** as the sole product under this condition. Thus, we conclude that the reaction proceeds *via* carbocation



Scheme 3 A plausible mechanism for the formation of sulfonamide phosphonates and diene.

intermediate and selectively leads to the expected products in very good yields.

Conclusions

In conclusion, TfOH has been efficiently used to synthesize a variety of sulfonamide phosphonates (specifically new (±)-γ-aryl/methylsulfonamidomethylvinylphosphonates) starting from α-hydroxyphosphonates and directly sulfonamides (not sulfonylimines) using an operationally simple method at room temperature in a vessel open to air. Although the method appears very simple and obvious, it should be a metal-free facile alternative for highly demanding sulfonamide phosphonates including sulfonamides obtained from benzyl alcohol. The water as a by-product and the selectivities for (±)-γ-aryl/methylsulfonamidomethylvinylphosphonates are added advantages. A new method for the synthesis of 1,3-butadienylphosphonate is also described. Initial antibacterial and antifungal studies for these sulfonamide phosphonates has already been started with our collaborators.

Experimental

The general experimental conditions and synthesis of the precursors are described in ESI.†

General procedure for the synthesis of sulfonamide phosphonate (±)-2a

To a stirred solution of (±)-**1a** (0.5 g, 1.824 mmol) and *p*-toluenesulfonamide (0.31 g, 1.824 mmol) in 1,4-dioxane (4 mL) open to the air, TfOH (0.16 mL, 1.824 mmol) was added. The reaction mixture was stirred for 5 h at room temperature. After completion of the reaction as indicated by TLC, the mixture was quenched with ice-cold water, and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic layer was dried over Na_2SO_4. After filtration and removal of solvent in vacuum, the crude product was purified by column chromatography using 65% ethyl acetate–petroleum ether as eluent to afford compound (±)-**2a** as a white solid. All the other compounds (±)-**2b–k** were prepared analogously unless stated otherwise.

(±)-Diethyl (4-methoxyphenyl)(4-methylphenylsulfonamido)-methylphosphonate (2a). Yield 0.733 g (94%); white solid; mp 144–148 °C; IR (KBr, cm^{-1}) 3120, 2911, 1398, 1325, 1229, 1159, 1094; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 and 1.35 (t, J = 7.1 Hz, 6H), 2.28 (s, 3H), 3.56–3.85 (m, 1H), 3.88 (s, 3H), 3.89–4.12 (m, 1H), 4.22–4.27 (m, 2H), 4.78 (dd, J = 9.6 and 24.0 Hz, 1H), 6.60 (d, J = 8.8 Hz, 2H), 6.95 (br, 1H), 6.98 (d, J = 8.1 Hz, 2H), 7.12 (dd, J = 8.7, 2.0, Hz, 2H), 7.46 (d, J = 8.3 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.1 and 16.4 (two sets of doublets, J = 5.8 Hz each), 21.3, 54.7 (d, J = 158.3 Hz), 55.2, 63.5 and 64.0 (two sets of doublets, J = 7.1 Hz each), 113.5, 125.7, 127.1, 128.9, 129.5 (d, J = 6.0 Hz), 138.1, 142.5, 159.2 (d, J = 2.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.8. Anal. Calc. for $C_{19}H_{26}NO_6PS$: C, 53.39; H, 6.13; N, 3.28. Found: C, 53.26; H, 6.19; N, 3.21%. This compound is known in the literature.[6g]

(±)-Diethyl (4-methoxyphenyl)(phenylsulfonamido)methylphosphonate (2b). The reaction was stirred for 6 h at room temp. Yield 0.679 g (90%); white solid; mp 132–135 °C; IR (KBr, cm^{-1}) 3117, 1611, 1516, 1460, 1394, 1325, 1232, 1157, 1029; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 and 1.36 (two sets of triplets, J = 7.1 Hz each, 6H), 3.58–3.81 (m, 1H), 3.85 (s, 3H), 3.87–3.91 (m, 1H), 4.23–4.28 (m, 2H), 4.56 (dd, J = 9.6 and 24.1 Hz, 1H), 6.59 (d, J = 8.5 Hz, 2H), 7.05–7.44 (m, 6H), 7.58 (d, J = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.2 and 16.5 (two sets of doublets, J = 5.5 Hz each), 54.8 (d, J = 159.3 Hz), 55.2, 63.5 and 64.1 (two sets of doublets, J = 7.1 Hz each), 113.5, 125.5, 126.9, 128.2, 129.6, 131.7, 141.2, 159.2; ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.7. Anal. Calc. for $C_{18}H_{24}NO_6PS$: C, 52.29; H, 5.85; N, 3.39. Found: C, 52.15; H, 5.92; N, 3.31%.

(±)-Diethyl (4-chlorophenylsulfonamido)(4-methoxyphenyl)-methylphosphonate (2c). This compound is synthesized in a manner analogous to compound **2b** by starting with **1a** (0.300 g, 1.094 mmol). Yield 0.450 g (92%); white solid; mp 163–165 °C; IR (KBr, cm^{-1}) 3092, 2930, 1614, 1516, 1470, 1394, 1333, 1237, 1023; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 and 1.40 (two sets of triplets, $J \sim$ 7.2 Hz each, 6H), 3.57–3.81 (m, 1H), 3.84 (s, 3H), 3.87–3.91 (m, 1H), 4.27–4.34 (m, 2H), 4.77 (dd, J = 9.6 and 25.6 Hz, 1H), 6.58 (d, J = 8.4 Hz, 2H), 7.08–7.12 (m, 4H), 7.37 (d, J = 8.8 Hz, 2H), 7.54–7.57 (br, m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.2 and 16.5 (two sets of doublets, J = 5.7 Hz each), 54.9 (d, J = 159.2 Hz), 55.3, 63.7 and 63.9 (two sets of doublets, J = 7.1 Hz each), 113.6, 125.2, 128.4, 128.5, 129.6 (d, J = 6.0 Hz), 138.1, 139.8 (d, J = 2.1 Hz), 159.4 (d, J = 2.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.5; LC/MS m/z 448 $[M + 1]^+$. Anal. Calc. for $C_{18}H_{23}ClNO_6PS$: C, 48.27; H, 5.18; N, 3.13. Found: C, 48.36; H, 5.08; N, 3.21%.

(±)-Diethyl (4-methoxyphenyl)(4-nitrophenylsulfonamido)-methylphosphonate (2d). This compound also was synthesized analogously by starting with **1a** (0.300 g, 1.094 mmol) by stirring the reaction mixture for 8 h.

Yield 0.450 g (90%); light yellow solid; mp 186–188 °C; IR (KBr, cm^{-1}) 3101, 1611, 1525, 1344, 1236, 1026; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 and 1.45 (two sets of triplets, J = 7.1 Hz each, 6H), 3.58–3.65 (m, 1H), 3.67 (s, 3H), 3.88–3.92 (m, 1H), 4.34–4.41 (m, 2H), 4.83 (dd, J = 24.2 and 10.1 Hz, 1H), 6.53 (d, J = 8.4 Hz, 2H), 7.09–7.12 (m, 2H), 7.71 (d, J = 9.0 Hz, 2H), 7.93 (d, J = 8.4 Hz, 2H), 8.21 (br, dd, J = 10.0, 4.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.2 and 16.5 (two sets of doublets, J = 5.5 Hz each), 55.1 (d, J = 160.8 Hz), 55.2, 63.8 and 64.3 (two sets of doublets, J = 7.3 Hz each), 113.6, 123.2, 124.8, 128.3, 129.7 (d, J = 5.9 Hz), 147.2 (d, J = 2.4 Hz), 149.2, 159.6 (d, J = 2.7 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.2; LC/MS m/z 459 $[M + 1]^+$. Anal. Calc. for $C_{18}H_{23}N_2O_8PS$: C, 47.16; H, 5.06; N, 6.11. Found: C, 47.23; H, 5.12; N, 6.21%.

(±)-Diethyl (4-aminophenylsulfonamido)(4-methoxyphenyl)-methylphosphonate (2e). The reaction was performed in manner similar to **2d** using similar molar quantities. No column chromatography was used. The product was isolated by crystallization method from ethyl acetate. Yield 0.430 g (92%); white solid; mp 197–199 °C; IR (KBr, cm^{-1}) 3089, 2992, 2875, 1614, 1514, 1461, 1328, 1230, 1164, 1023; ^{1}H NMR (400 MHz,

DMSO-d6) δ 1.01 and 1.21 (t, $J = 7.1$ Hz, 6H), 3.62–3.66 (m, 1H), 3.68 (s, 3H), 3.79–3.84 (m, 1H), 4.03–4.05 (m, 2H), 4.56 (dd, $J =$ 10.3 and 24.1 Hz, 1H), 5.78 (br, 2H), 6.33 (d, $J = 8.6$ Hz, 2H), 6.68 (d, $J = 8.6$ Hz, 2H), 7.14–7.16 (m, 2H), 7.18 (d, $J = 8.0$ Hz, 2H), 8.26 (dd, $J = 10.3$ and 1.7 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d6) δ 16.0 and 16.2 (two sets of doublets, $J = 5.6$ Hz each), 53.8 (d, $J = 158.3$ Hz), 54.9, 62.2 (d, $J = 6.9$ Hz), 62.7 (d, $J = 6.9$ Hz), 112.0, 113.1, 126.4, 126.6, 128.3, 129.4 (d, $J = 5.9$ Hz), 152.0, 158.4 (d, $J = 2.6$ Hz); ^{31}P NMR (162 MHz, DMSO-d6) δ 20.6; LC/MS m/z 429 $[M + 1]^+$. Anal. Calc. for $C_{18}H_{25}N_2O_6PS$: C, 50.46; H, 5.88; N, 6.54. Found: C, 50.61; H, 5.82; N, 6.61%.

(±)-Diethyl (4-methoxyphenyl)(4-(trifluoromethyl)phenylsulfonamido)methylphosphonate (2f). This reaction was performed using **1a** (0.200 g, 0.729 mmol) and reaction time was 8 h. Yield 0.280 g (80%); white solid; mp 154–156 °C; IR (KBr, cm^{-1}) 3087, 1615, 1516, 1462, 1321, 1235, 1172, 1027; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 and 1.43 (two sets of triplets, $J = 7.1$ Hz each, 6H), 3.57–3.63 (m, 1H), 3.68 (s, 3H), 3.82–3.91 (m, 1H), 4.30–4.38 (m, 2H), 4.80 (dd, $J = 10.1$ and 24.2 Hz, 1H), 6.52 (d, $J = 8.5$ Hz, 2H), 7.09 (d, $J = 10.4$ Hz, 2H), 7.36 (d, $J = 8.3$ Hz, 2H), 7.66 (d, $J = 8.4$ Hz, 2H), 7.96 (br, dd, $J = 9.9$, 3.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.2 and 16.5 (two sets of doublets, $J =$ 5.7 Hz each), 55.0, 54.9 (d, $J = 160.4$ Hz), 63.8 and 64.2 (two sets of doublets, $J = 7.1$ Hz each), 113.5, 124.8, 125.1, 125.2, 127.6, 129.7 (d, $J = 6.0$ Hz), 133.3 (q, $J = 32.8$ Hz), 144.8, 159.4 (d, $J =$ 2.6 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.3; LC/MS m/z 482 $[M +$ $1]^+$. Anal. Calc. for $C_{19}H_{23}F_3NO_6PS$: C, 47.40; H, 4.82; N, 2.91. Found: C, 47.56; H, 4.76; N, 2.98%.

(±)-Diethyl (*N*-butylphenylsulfonamido)(4-methoxyphenyl) methylphosphonate (2g). This reaction was performed using **1a** (0.500 g) and reaction time was 12 h.

Yield 0.750 g (88%), colorless gummy liquid; IR (KBr, cm^{-1}) 2960, 1610, 1513, 1445, 1348, 1252, 1159, 1026; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.79–0.82 (m, 3H), 1.06–1.09 (m, 3H), 1.15–1.18 (m, 2H), 1.25–1.31 (m, 5H), 3.397–3.422 (m, 2H), 3.79 (s, 3H), 3.94–4.21 (m, 4H), 5.43 (d, $J = 25.6$ Hz, 1H), 6.80 (d, $J = 8.8$ Hz, 2H), 7.40–7.78 (m, 5H), 7.79 (d, $J = 7.2$ Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 13.6, 16.2 and 16.4 (two sets of doublets, $J = 5.7$ Hz each), 20.2, 31.7, 46.6, 55.2, 56.8 (d, $J = 162.6$ Hz), 62.7 and 63.0 (two sets of doublets, $J = 7.4$ Hz each), 113.8, 125.3 (d, $J =$ 6.3Hz, 2H), 127.6, 128.7, 131.5 (d, $J = 8.6$ Hz, 2H), 132.3, 140.7, 159.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ 20.4; LC/MS m/z 492 $[M +$ $Na]^+$. Anal. Calc. for $C_{22}H_{32}NO_6PS$: C, 56.28; H, 6.87; N, 2.98. Found: C, 56.15; H, 6.93; N, 2.85%.

(±)-Diethyl (4-methoxyphenyl)(naphthalene-2-sulfonamido) methylphosphonate (2h). This reaction was performed using **1a** (0.300 g) and reaction time was 8 h.

Yield 0.430 g (85%); white solid; mp 142–144 °C; IR (KBr, cm^{-1}) 1614, 1514, 1461, 1328, 1230, 1023; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 and 1.35 (two sets of triplets, $J = 7.2$ Hz each, 6H), 3.43 (s, 3H), 3.53–3.81 (m, 1H), 3.87–3.91 (m, 1H), 4.22–4.29 (m, 2H), 4.82 (dd, $J = 9.7$ and 23.8 Hz, 1H), 6.35 (d, $J = 8.4$ Hz, 2H), 7.05–7.08 (m, 2H), 7.14–7.18 (br, m, 1H), 7.47–7.75 (m, 6H), 8.01 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.1 and 16.4 (two sets of doublets, $J = 5.8$ Hz each), 54.9 (d, $J = 158.2$ Hz), 54.9, 63.7 and 63.9 (two sets of doublets, $J = 7.1$ Hz each), 113.4 (d, $J = 2.1$ Hz), 122.5, 125.1, 126.9, 127.5, 128.3, 128.4, 128.6, 129.0, 129.5 (d, $J =$ 6.0 Hz), 131.8, 134.3, 137.8 (d, $J = 1.9$ Hz), 159.0 (d, $J = 2.6$ Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.7; LC/MS m/z 464 $[M + 1]^+$. Anal. Calc. for $C_{22}H_{26}NO_6PS$: C, 57.01; H, 5.65; N, 3.02. Found: C, 57.12; H, 5.58; N, 3.07%.

(±)-Diethyl (4-methoxyphenyl)(methylsulfonamido)methylphosphonate (2i). This reaction was performed using **1a** (0.400 g) and reaction time was 8 h. Yield 0.466 g (91%); white solid; mp 146–148 °C; IR (KBr, cm^{-1}) 3118, 1614, 1585, 1518, 1464, 1322, 1255, 1039; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 and 1.39 (two sets of triplets, $J \sim 7.1$ Hz each, 6H), 2.59 (S, 3H), 3.64–3.90 (m, 1H), 3.91 (s, 3H), 3.92–3.96 (m, 1H), 4.23–4.31 (m, 2H), 4.82 (dd, $J = 9.8$ and 23.8 Hz, 1H), 6.91 (d, $J = 8.4$ Hz, 2H), 7.48 (d, $J = 8.7$ Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.2 and 16.4 (two sets of doublets, $J = 5.8$ Hz each), 42.1, 54.5 (d, $J = 163.9$ Hz), 55.3, 63.7 and 64.0 (two sets of doublets, $J = 7.1$ Hz each), 114.3, 126.4, 129.6 (d, $J = 5.9$ Hz), 159.8 (d, $J = 2.2$ Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.9; LC/MS m/z 352 $[M + 1]^+$. Anal. Calc. for $C_{13}H_{22}NO_6PS$: C, 44.44; H, 6.31; N, 3.99. Found: C, 44.56; H, 6.38; N, 3.91%.

(±)-Diethyl (4-(benzyloxy)phenyl)(4-methylphenylsulfonamido)methylphosphonate (2j). This compound was synthesized by starting with **1b** (0.300 g, 0.856 mmol) using the same procedure as **2g**. Along with the product, compound **3a** was also isolated from column by using 10% EtOAc in petroleum ether.

Yield 0.300 g (70%); white solid; mp 147–149 °C; IR (KBr, cm^{-1}) 3117, 2872, 1609, 1509, 1332, 1234, 1161, 1052; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04 and 1.35 (two sets of triplets, $J = 7.2$ Hz each, 6H), 2.28 (s, 3H), 3.55–3.65 (m, 1H), 3.84–3.90 (m, 1H), 4.18–4.26 (m, 2H), 4.74 (dd, $J = 23.9$ and 9.6 Hz, 1H), 4.97 (s, 2H), 6.69 (d, $J = 8.5$ Hz, 2H), 6.83–6.87 (m, br, 1H), 6.97 (d, $J =$ 8.0 Hz, 2H), 7.12 (dd, $J = 8.7$ and 2.0 Hz, 2H), 7.33–7.39 (m, 5H), 7.46 (d, $J = 8.3$ Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.1 and 16.5 (two sets of doublets, $J = 5.8$ Hz each), 21.4, 54.7 (d, $J =$ 158.2 Hz), 63.5 and 64.0 (two sets of doublets, $J = 7.1$ Hz each), 69.9, 114.5, 126.0, 127.1, 127.4, 128.0, 128.6, 128.9, 129.5 (d, $J =$ 8.5 Hz), 136.7, 138.1, 142.6, 158.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.8; LC/MS m/z 504 $[M + 1]^+$. Anal. Calc. for $C_{25}H_{30}NO_6PS$: C, 59.63; H, 6.01; N, 2.78. Found: C, 59.48; H, 6.08; N, 2.71%.

N-Benzyl-4-methylbenzenesulfonamide (**3a**), mp = 115–117 °C; yield 0.045 g (20%); white solid; IR (KBr, cm^{-1}) 3272, 1598, 1496, 1319, 1167, 1089; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 4.11 (d, $J = 6.2$ Hz, 2H), 4.87 (br t, $J = 6.1$ Hz, 1H), 7.18–7.31 (m, 7H), 7.75 (d, $J = 8.3$ Hz, 2H); LC/MS m/z 262 $[M + 1]^+$. This compound is known.[7]

(±)-Diethyl (4-(benzyloxy)phenyl)(4-chlorophenylsulfonamido)methylphosphonate (2k). This compound was synthesized using similar procedure and molar quantities as **2j** for 12 h.

Yield 0.320 g (73%); white solid; mp 138–142 °C; IR (KBr, cm^{-1}) 3122, 1609, 1513, 1455, 1335, 1243, 1165, 1024; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 and 1.39 (two sets of triplets, $J = 7.1$ Hz each, 6H), 3.58–3.64 (m, 1H), 3.85–3.90 (m, 1H), 4.73–4.81 (m, 2H), 4.77 (dd, $J = 24.0$ and 9.7 Hz, 1H), 4.99 (s, 2H), 6.68 (d, $J =$ 8.4 Hz, 2H), 7.11 (d, $J = 8.6$ Hz, 4H), 7.34–7.42 (m, br, 6H), 7.48 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.2 and 16.5 (two sets of doublets, $J = 5.7$ Hz each), 54.8 (d, $J = 157.9$ Hz), 63.7 and 64.0 (two sets of doublets, $J = 7.1$ Hz each), 70.1, 114.6 (d, $J = 1.9$ Hz), 125.4, 127.5, 128.1, 128.5, 128.6, 129.6

(d, $J = 6.0$ Hz), 136.6, 138.3, 139.6 (d, $J = 1.9$ Hz), 158.7 (d, $J = 2.7$ Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.5; LC/MS m/z 524 $[M + 1]^+$. Anal. Calc. for $C_{24}H_{27}ClNO_6PS$: C, 55.01; H, 5.19; N, 2.67. Found: C, 55.16; H, 5.08; N, 2.58%.

(±)-Diethyl (4-methyphenylsulfonamido)(*p*-tolyl)methylphosphonate (2l). Anhydrous $FeCl_3$ (0.188 g, 1.161 mmol) was added to a stirred solution of **1c** (0.3 g, 1.161 mmol) and *p*-toluenesolfonamide (0.19 g, 1.161 mmol) in 1,2-dichloroethane (3.0 mL) and then the reaction mixture was stirred at room temperature under N_2 for 12 h. After completion of the reaction as indicated by TLC, the reaction mixture was quenched with saturated NH_4Cl solution, and the aqueous layer was extracted with ethyl acetate (2 × 15 mL). The combined organic layer was dried over Na_2SO_4. After filtration and removal of solvent in vacuum, the crude product was purified by column chromatography using 70% ethyl acetate–petroleum ether as the eluent to afford the product.

Yield 0.320 g (68%); white solid; mp 152–154 °C; IR (KBr, cm^{-1}) 3142, 2889, 1598, 1459, 1341, 1241, 1162, 1050; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.05 and 1.35 (two sets of triplets, $J = 7.2$ Hz each, 6H), 2.24 (s, 3H), 2.28 (s, 3H), 3.56–3.64 (m, 1H), 3.86–3.90 (m, 1H), 4.19–4.26 (m, 2H), 4.74 (dd, $J = 24.0$ and 9.7 Hz, 1H), 6.89–6.97 (m, 5H), 7.08 (dd, $J = 8.1$, 2.0 Hz, 2H), 7.45 (d, $J = 8.3$ Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.1 and 16.5 (two sets of doublets, $J = 5.8$ Hz each), 21.0, 21.3, 55.1 (d, $J = 157.5$ Hz), 63.5 and 64.0 (two sets of doublets, $J = 7.0$ Hz each), 127.0, 128.2 (d, $J = 6.0$ Hz), 128.6, 128.7 (d, $J = 2.1$ Hz), 130.6, 137.4 (d, $J = 3.1$ Hz), 138.1 (d, $J = 1.8$ Hz), 142.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.7; LC/MS m/z 412 $[M + 1]^+$. Anal. Calc. for $C_{19}H_{26}NO_5PS$: C, 55.46; H, 6.37; N, 3.40. Found: C, 55.38; H, 6.32; N, 3.51%.

General procedure for the TfOH catalyzed sulfonamidation of benzyl alcohol

To a stirred solution of benzyl alcohol (0.500 g, 4.629 mmol), *p*-toluenesolfonamide (0.790 g, 4.629 mmol) in 1,4-dioxane (5.0 mL), TfOH (0.04 mL, 0.4629 mmol) was added under N_2 at room temperature and the reaction mixture was stirred for 8 h. After completion of the reaction as indicated by TLC, the mixture was quenched with ice cold water, and the aqueous layer was extracted with ethyl acetate (2 × 100 mL). The combined organic layer was dried over Na_2SO_4. After filtration and removal of solvent in vacuum, the crude product was purified by column chromatogram using 30% ethyl acetate–petroleum ether) as the eluent to afford the product. All the other compounds were prepared analogously using similar molar quantities unless stated otherwise. All these compounds are known in literature.

***N*-Benzyl-4-methylbenzenesulfonamide (3a).**[16b] Yield 0.68 g (56%); data is given before.

***N*-Benzylbenzenesulfonamide (3b).** The reaction was stirred for 9 h at room temp. Yield 0.810 g, (71%), as a white solid. IR (KBr, cm^{-1}): 3332, 2926, 1967, 1895, 1447, 1325, 1221, 1157, 1065; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.14 (d, $J = 6.0$ Hz, 2H), 4.87 (br t, $J \sim 6.0$ Hz, 1H), 7.18–7.25 (m, 5H), 7.49–7.60 (m, 3H), 7.87 (d, $J = 8.4$ Hz, 2H); LC/MS m/z 246 $[M - 1]^+$. This compound is known.[16b]

***N*-Benzyl-4-chlorobenzenesulfonamide (3c).** The reaction was stirred for 8 h at room temp. Yield 1.020 g (78%), as a white solid. IR (KBr, cm^{-1}): 3248, 2643, 1916, 1575, 1475, 1331, 1177, 1092; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.16 (d, $J = 6.4$ Hz, 2H), 4.81 (br t, $J \sim 6.0$ Hz, 1H), 7.18–7.29 (m, 5H), 7.47 (d, $J = 8.4$ Hz, 2H), 7.78 (d, $J = 8.4$ Hz, 2H); LC/MS m/z 280 $[M - 1]^+$. This compound is known.[16a]

General procedure for the synthesis of (±)-γ-aminophosphonates 5a–g

To a stirred solution of **4a** (0.200 g, 0.740 mmol), *p*-toulenesulfonamide (0.120 g, 0.740 mmol) and 1,4-dioxane (3.0 mL), in a round-bottom flask open to air at room temperature TfOH (0.06 mL, 0.740 mmol) was added. The reaction mixture was stirred for 6–7 h. After completion of the reaction as indicated by TLC, the reaction mixture was quenched with ice cold water, and the aqueous layer was extracted with ethyl acetate (2 × 10 mL). The combined organic layer was dried over Na_2SO_4. After filtration and removal of solvent in vacuum, the crude product was washed with ethyl acetate (2 × 5 mL). The resulting solid was recrystallized from ethyl acetate to yield compound **5a**. Compounds **5b–c** were prepared analogously using similar molar quantities unless stated otherwise. In the case of **5d–g**, the crude product was purified by column chromatography using 80% ethyl acetate–petroleum ether as the eluent.

(*E*)-Diethyl 3-(4-methylphenylsulfonamido)-3-phenylprop-1-enylphosphonate (5a). This compound was sparingly soluble in $CDCl_3$. Yield 0.288 g (92%); white solid; mp 155–160 °C; IR (KBr, cm^{-1}) 3118, 2911, 1477, 1398, 1325, 1229, 1159, 1094; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26–1.32 (m, 6H), 2.39 (s, 3H), 3.98–4.05 (m, 4H), 5.05 (br, 1H), 5.81–5.90 (m, 2H), 6.72–6.83 (m, 1H), 7.05–7.20 (m, 7H), 7.62 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.3 and 16.4 (d, $J = 6.3$ Hz each), 21.5, 59.6 (d, $J = 23.3$ Hz), 61.9 and 62.0 (d, $J = 5.2$ Hz), 118.5 (d, $J = 187.6$ Hz), 127.2 (d, $J = 16.4$ Hz), 128.2, 128.9, 129.5, 137.6, 137.8, 137.9, 143.3, 150.1 (d, $J = 6.2$ Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 17.1; LC/MS m/z 424 $[M + 1]^+$. Anal. Calc. for $C_{20}H_{26}NO_5PS$: C, 56.73; H, 6.19; N, 3.31. Found: C, 56.61; H, 6.07; N, 3.45%; X-ray structural analysis was done on this sample to confirm the stereochemistry.

(*E*)-Diethyl 3-(phenylsulfonamido)-3-phenylprop-1-enylphosphonate (5b). This compound was also moderately soluble in $CDCl_3$. Yield 0.274 g (90%); white solid; mp 178–184 °C; IR (KBr, cm^{-1}) 3108, 2903, 1476, 1395, 1325, 1234, 1162, 1020; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24–1.31 (m, 6H), 3.99–4.05 (m, 4H), 5.07 (br, 1H), 6.71–6.82 (m, 1H), 7.03–7.04 (m, 2H), 7.15–7.18 (m, 3H), 7.35–7.38 (m, 2H), 7.46–7.49 (m, 1H), 7.71–7.74 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.3 and 16.4 (d, $J = 6.3$ Hz each), 59.6 (d, $J = 23.1$ Hz), 61.9 and 62.0 (d, $J = 5.2$ Hz), 118.6 (d, $J = 187.1$ Hz), 126.9, 127.2, 128.3, 128.9, 132.5 (two peaks are merged), 137.7, 140.6, 149.9 (d, $J = 6.2$ Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 17.1; LC/MS m/z 410 $[M + 1]^+$. Anal. Calc. for $C_{19}H_{24}NO_5PS$: C, 55.74; H, 5.91; N, 3.42. Found: C, 55.61; H, 5.98; N, 3.49%.

(*E*)-Diethyl 3-(4-nitrophenylsulfonamido)-3-phenylprop-1-enylphosphonate (5c). Reaction was performed for 10 h at room temperature using **4a** (0.300 g). Yield 0.434 g (86%); light yellow solid; mp 162–164 °C; IR (KBr, cm^{-1}) 3113, 1525, 1468, 1350,

1221, 1166, 1039; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 and 1.31 (two sets of triplets, J = 7.1 Hz each, 6H), 3.96–4.07 (m, 4H), 5.14–5.18 (m, br, 1H), 5.76 (ddd, J = 18.8 Hz, 17.2 Hz, 1.6 Hz, 1H), 6.78 (ddd, J = 21.9 Hz, 17.1 Hz, 5.5 Hz, 1H), 7.05–7.78 (m, 5H), 7.78 (d, J = 8.8 Hz, 2H), 7.83–7.89 (m, 1H), 8.06 (d, J = 8.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.2 and 16.3 (d, J = 6.2 Hz each), 60.1 (d, J = 23.5 Hz), 62.3 and 62.4 (d, J = 5.7 Hz), 118.4 (d, J = 188.0 Hz), 123.7, 127.3, 128.1, 128.3, 128.8, 137.4, 147.1, 149.4, 149.9 (d, J = 5.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 16.6; LC/MS m/z 455 $[M + 1]^+$. Anal. Calc. for $C_{19}H_{23}N_2O_7PS$: C, 50.22; H, 5.10; N, 6.16. Found: C, 50.32; H, 5.06; N, 6.23%.

(*E*)-Diethyl 3-(*N*-butylphenylsulfonamido)-3-phenylprop-1-enylphosphonate (5d). Reaction was performed with **4a** (0.500 g) for 12 h at room temperature. Yield 0.706 g (82%), gummy colorless liquid; IR (KBr, cm^{-1}) 2985, 1634, 155, 1324, 1031, 974; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.66–0.69 (m, 3H), 0.991–1.04 (m, 3H), 1.28–1.34 (m, 7H), 3.03–3.05 (m, 2H), 3.99–4.08 (m, 4H), 5.71–5.79 (m, 2H), 6.82–6.94 (m, 1H), 7.12–7.13 (m, 2H), 7.27–7.28 (m, 3H), 7.46–7.58 (m, 3H), 7.79–7.82 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 13.4, 16.3 and 16.4 (d, J = 6.3 Hz each), 19.9, 32.3, 45.6, 61.8 and 61.9 (d, J = 5.7 Hz each), 62.9 (d, J = 23.3 Hz), 121.1 (d, J = 186.7 Hz), 127.2, 128.4, 128.5, 128.7, 129.1, 132.5, 136.7, 140.7, 148.1 (d, J = 5.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 16.9. a small peak (~8%) which appeared at δ 18.7 might be due to other isomers. LC/MS m/z 466 $[M + 1]^+$. Anal. Calc. for $C_{23}H_{32}NO_5PS$: C, 59.34; H, 6.93; N, 3.01. Found: C, 59.42; H, 6.85; N, 3.08%.

(*E*)-Diethyl 3-(methylsulfonamido)-3-phenylprop-1-enylphosphonate (5e). This reaction was performed using **4a** (0.200 g, 0.740 mmol), methanesulfonamide (0.14 g, 1.48 mmol) and TfOH (0.065 mL, 0.740 mmol) in 1,4-dioxane (3.0 mL) under air at room temperature for 14 h. Yield 0.21 g (82%), white solid; mp 93–95 °C; IR (KBr, cm^{-1}) 3133, 1625, 1464, 1317, 1151, 1043; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26–1.33 (m, 6H), 2.70 (s, 3H), 4.02–4.11 (m, 4H), 5.21–5.23 (br, 1H), 5.89–5.98 (m, 1H), 6.13 (d, J = 8.2 Hz, 1H), 6.88 (ddd, J = 21.8, 17.1, 5.3 Hz, 1H), 7.32–7.38 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.3 and 16.4 (d, J = 6.2 Hz each), 41.9, 59.7 (d, J = 23.2 Hz), 62.1 and 62.2 (d, J = 5.7 Hz each), 118.4 (d, J = 187.4 Hz), 127.4, 128.5, 129.2, 138.5, 150.4 (d, J = 5.9 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 16.9; LC/MS m/z 348 $[M + 1]^+$. Anal. Calc. for $C_{14}H_{22}NO_5PS$: C, 48.41; H, 6.38; N, 4.03. Found: C, 48.29; H, 6.31; N, 4.07%.

(*E*)-Diethyl 2-methyl-3-(4-methylphenylsulfonamido)-3-phenylprop-1-enylphosphonate (5f). This compound was synthesized by using **4b** (0.300 g, 1.055 mmol), *p*-toulenesolfonamide (0.18 g, 1.055 mmol) and 1,4-dioxane (3.0 mL) in the open air at room temperature for 10 h in the presence of TfOH (0.09 mL, 1.055 mmol). Yield 0.410 g (88%); white solid; mp 140–142 °C; IR (KBr, cm^{-1}) 3122, 1628, 1476, 1325, 1224, 1163, 1020; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.29–1.33 (m, 6H), 1.90–1.91 (m, 3H), 2.41 (s, 3H), 3.98–4.07 (m, 4H), 4.80 (d, J = 7.0 Hz, 1H), 5.05 (d, J = 6.9 Hz, 1H), 5.88 (d, J = 17.5 Hz, 1H), 6.99 (dd, J = 7.5, 1.9 Hz, 2H), 7.22–7.24 (m, 5H), 7.65 (d, J = 8.3 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 16.5 and 16.6 (d, J ~ 5.8 Hz each), 18.0 (d, J = 6.8 Hz), 21.7, 61.6 and 61.8 (d, J = 5.6 Hz), 64.7 (d, J = 23.0 Hz), 114.4 (d, J = 188.4 Hz), 127.3, 127.4, 128.7, 129.2, 129.8, 137.4, 137.8, 143.8, 158.4 (d, J = 8.5 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 17.4; LC/MS m/z 438 $[M + 1]^+$. Anal. Calc. for $C_{21}H_{28}NO_5PS$: C, 57.65; H, 6.45; N, 3.20. Found: C, 57.73; H, 6.41; N, 3.12%.

(*E*)-Diethyl 2-methyl-3-(4-chlorophenylsulfonamido)-3-phenylprop-1-enylphosphonate (5g). The reaction mixture was stirred for 12 h starting with **4b** (0.500 g, 1.759 mmol). Yield 0.73 g (90%); white solid; mp 120–125 °C; IR (KBr, cm^{-1}) 3102, 2897, 1643, 1478, 1327, 1218, 1163, 1026; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.28–1.33 (m, 6H), 1.91 (s, 3H), 3.98–4.07 (m, 4H), 4.87 (d, J = 8.0 Hz, 1H), 5.79–5.83 (m, 2H), 7.01–7.02 (m, 2H), 7.19–7.24 (m, 3H), 7.35–7.36 (m, 2H), 7.64–7.67 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 16.5 and 16.6 (d, J ~ 5.8 Hz each), 18.2 (d, J = 6.8 Hz), 61.8 and 61.9 (d, J = 5.6 Hz), 64.7 (d, J = 22.9 Hz), 114.4 (d, J = 189.1 Hz), 127.5, 128.6, 128.7, 129.2, 129.4, 137.5, 139.1, 139.2, 158.3 (d, J = 8.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 17.2; LC/MS m/z 458 $[M + 1]^+$. Anal. Calc. for $C_{20}H_{25}NClO_5PS$: C, 52.46; H, 5.50; N, 3.06. Found: C, 52.36; H, 5.58; N, 3.12%.

$FeCl_3$-mediated reaction of 4c with $TsNH_2$

Anhydrous $FeCl_3$ (0.218 g, 1.35 mmol) was added to a stirred solution of **4c** (0.300 g, 1.35 mmol) and $TsNH_2$ (0.230 g, 1.35 mmol) in 1,2-dichloroethane (4.0 mL) and the reaction mixture was stirred at room temperature under N_2 for 6 h. The crude product was purified by column chromatography using EtOAc–petroleum ether as the eluent to afford the diene **6** (using 20% EtOAc in petroleum ether) followed by compound **5h** (70% EtOAc in petroleum ether).

(*E*)-Diethyl 3-methyl-3-(*N*-butylphenylsulfonamido)-3-phenylprop-1-enylphosphonate (5h). Anhydrous $FeCl_3$ (0.218 g, 1.35 mmol) was added to a stirred solution of **4c** (0.300 g, 1.35 mmol) and *p*-toulenesolfonamide (0.230 g, 1.35 mmol) in 1,2-dichloroethane (4.0 mL) and the reaction mixture was stirred at room temperature under N_2 for 6 h. The crude product was purified by column chromatography using (70% ethyl acetate–petroleum ether) as the eluent to afford **5h**.

Yield 0.285 g (56%); white solid; mp 92–95 °C; IR (KBr, cm^{-1}): 3114, 1631, 1322, 1222, 1144, 1030; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31–1.34 (m, 12H), 2.42 (m, 3H), 4.03–4.09 (m, 4H), 5.06 (s, br, 1H), 5.79 (dd → t, J = 17.6 Hz each, 1H), 6.69 (dd, J = 22.4 and 17.6 Hz, 1H), 7.28 (d, J = 8.0 Hz, 2H), 7.75 (d, J = 8.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.4 (d, J = 6.3 Hz), 21.5, 27.3, 57.4 (d, J = 21.9 Hz), 61.9 (d, J = 5.4 Hz), 114.9 (d, J = 187.0 Hz), 126.9, 129.6, 140.1, 143.1, 156.6 (d, J = 4.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 18.2; LC/MS m/z 376 $[M + 1]^+$. Anal. Calc. for $C_{16}H_{26}NO_5PS$: C, 51.19; H, 6.98; N, 3.73. Found: C, 51.26; H, 6.91; N, 3.65%.

(*E*)-Diethyl 3-methylbuta-1,3-dienylphosphonate (6). Yield 0.055 g (20%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, J = 7.2 Hz each, 6H), 1.79 (s, 3H), 3.88–4.12 (m, 4H), 5.24–5.25 (br, 2H), 5.55–5.64 (m, 1H), 7.09 (dd, J ~ 18 and 21.8 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 16.2 (d, J = 6.3 Hz each), 17.6, 61.6 (d, J = 5.6 Hz), 114.6 (d, J = 191.6 Hz), 123.6, 140.6 (d, J = 23.8 Hz), 151.0 (d, J = 6.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 19.9; LC/MS m/z 205 $[M + 1]^+$. This compound is known in the literature.[19c] In the presence of TfOH, the phosphonate **4c** gives this diene **6** with a quantitative yield at room temperature within 2 h under nitrogen atmosphere using 1,4-dioxane as solvent.

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