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Quinine-Derived Thiourea and Squaramide Catalyzed Conjugate Addition of α-Nitrophosphonates to Enones: Asymmetric Synthesis of Quaternary α-Aminophosphonates

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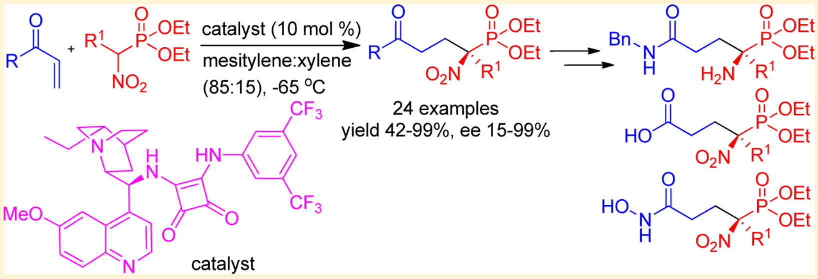
Supporting Information



ABSTRACT: Conjugate addition of α-nitrophosphonates to enones was carried out in the presence of two sets of organocatalysts, viz. a quinine-thiourea and a quinine-squaramide. The quinine-thiourea provided the products possessing an α-quaternary chiral center in high enantioselectivities only in the case of electron rich enones. On the other hand, the quinine-squaramide was more efficient in that a wide variety of electron rich and electron poor enones underwent Michael addition of nitrophosphonates to afford the quaternary α-nitrophosphonates in excellent yields and enantioselectivities. The hydrogen bonding donor ability of the bifunctional catalyst, as shown in the proposed transition states, appears primarily responsible for the observed selectivity. However, a favorable π-stacking between the aryl groups of thiourea/squaramide and aryl vinyl ketone also appeared favorable. The reaction was amenable to scale up, and the enantioenriched quaternary α-nitrophosphonates could be easily transformed to synthetically and biologically useful quaternary α-aminophosphonates and other multifunctional molecules.

INTRODUCTION

Aminophosphonic acids are regarded as transition state analogues of amino acids due to the ability of the phosphonate moiety to mimic the tetrahedral transition state of peptide bond hydrolysis.[1] The remarkable synthetic and biological profile of aminophosphonates has stimulated considerable research in this area.[2−4] The role of α-aminophosphonates, in particular, as various biological agents, viz. antibacterial, antifungal, antiviral, antitumor and as inhibitors of HIV protease and phosphatase has been extensively investigated.[5,6] α-Aminophosphonates have been successfully employed as proline surrogates in asymmetric aldol and Michael reactions.[7] The α-aminophosphonate moiety is a constituent of bioactive natural product K-26.[8] Since the biological and catalytic activities are dependent on the absolute configuration at the α-carbon, there have been many approaches to enantioenriched α-aminophosphonates including resolution and auxiliary based approaches.[9] However, catalytic asymmetric approaches have attracted tremendous attention in recent years.[10] These include hydrophosphonylation of imines,[11] nucleophilic addition to α-iminophosphonates,[12] electrophilic amination of α-phosphonate carbanion[13] and nucleophilic addition of phosphonate analogues of glycine to various electrophiles.[14]

In spite of the above-mentioned studies on the synthesis and applications of aminophosphonates, in general, and configurationally stable α-aminophosphonates, in particular, quaternary α-aminophosphonates have received only limited attention.[15] This is despite the potential of such α-aminophosphonates as prospective building blocks in the synthesis of novel protease inhibitors due to their configurational stability.[1]

As part of our ongoing research program concerned with the development of novel methods for the enantioselective synthesis of nitro- and aminophosphonates, we have reported the asymmetric synthesis of γ-nitrophosphonates via highly diastereo- and enantioselective Michael addition of α-lithiated phosphonates to nitroalkenes using cinchonine as the chiral catalyst.[16] Also β-nitrophosphonates were synthesized by (*S*)(−)−Li−Al-BINOL (ALB) catalyzed asymmetric Michael addition of dialkyl phosphites to nitroalkenes with excellent enantioselectivity.[17] We envisaged that the addition of α-substituted α-nitrophosphonates to a wide variety of electrophiles in the presence of suitable chiral catalysts would provide quaternary α-nitrophosphonates which are immediate precursors of quaternary α-aminophosphonates.[18] Very recently, we

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have reported the catalytic enantioselective synthesis of quaternary α-nitrophosphonates via Michael addition of α-nitrophosphonates to enones in the presence of a quinine-thiourea catalyst.[19] Similar addition of α-nitrophosphonates to vinyl sulfones under the catalytic influence of alkaloid-derived squaramide[20] and thiourea[21] has been reported. Herein we report the full version of our preliminary communication on the addition of α-nitrophosphonates to enones.[19] Our report describes not only the scope and applications of our methodology but a comparative study on possible hydrogen bonding and π-stacking interactions between the catalyst and the substrate by taking two different types of catalysts, viz. quinine-thiourea and quinine-squaramide. Our investigations also unravel the superior catalytic activity of squaramide vis-à-vis thiourea in catalyzing the reaction of a wide range of enones with α-nitrophosphonates.

■ RESULTS AND DISCUSSION

At the outset, several thiourea and other catalysts **C1**−**C8** were screened for the conjugate addition of α-nitrophosphonate **2a** to enone **1b** (Figure 1).[19] Among these, the quinine-thiourea catalyst **C8** was identified as the best to investigate the scope of the reaction (Table 1).[19] In fact, it was more suited for enones possessing electron donating aromatic rings **1b**−**1e** (ee 72−87%, Table 1, entries 2−5) with the exception of **1g**−**h** (ee 69−70%, entries 7−8). In the case of electroneutral and electron deficient aryl, heteroaryl and alkyl substituted enones **1a**, **1f** and **1i**−**k**, respectively, the enantioselectivities were moderate (ee 35−45%, entries 1, 6 and 9−11). Needless to mention, the chemical yields remained high (70−82%) in these reactions. A selected electron rich enone **1d** was later treated with different nitrophosphonates **2** to demonstrate the scope of the latter which led to the synthesis of a variety of nitrophosphonates **4** in excellent yield and enantioselectivity (Scheme 1). Possible applications of nitrophosphonates **3** and **4** as potential precursors for the synthesis of cyclic aminophosphonates **5** and **6** have also been investigated. Thus, nitrophosphonate **3b** has been converted to amidophosphonate **6** via Baeyer−Villiger oxidation followed by cascade nitro group reduction-lactamization. Similarly, nitrophosphonate **4a** (R = Et) has been subjected to cascade nitro group reduction-intramolecular condensation to afford cyclic iminophosphonate **5** (Scheme 1).[19]

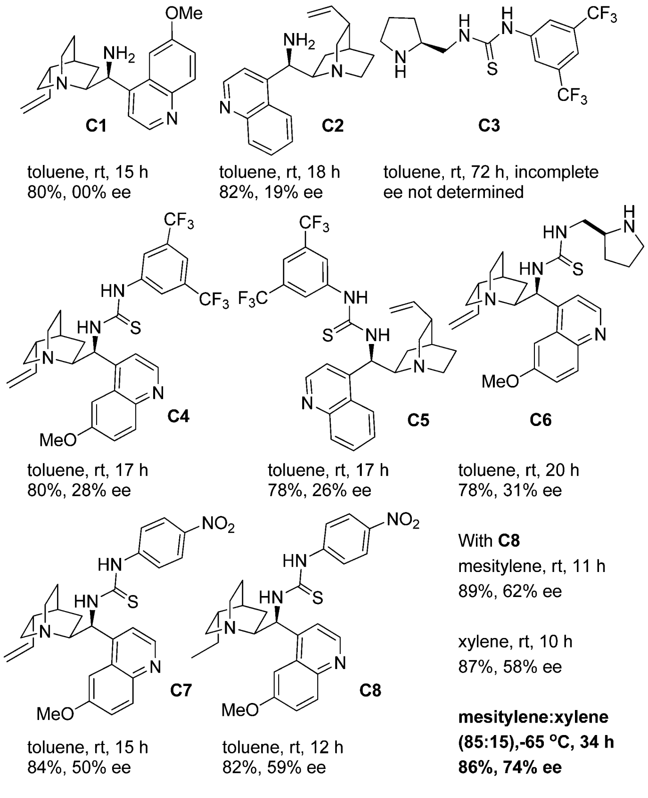
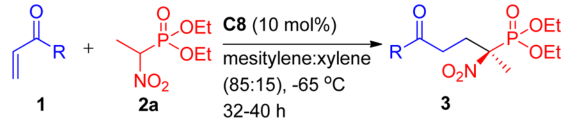


Figure 1. Catalysts screened for the reaction of vinyl ketone **1b** with nitrophosphonate **2a**.

Table 1. Scope of Enones 1

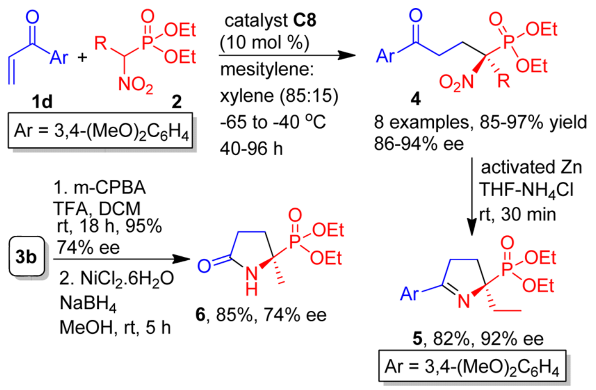


entry	R, 1	3	time (h)	% yield[a]	% ee[b]
1	Ph, **1a**	**3a**	34	81	45
2	4-MeC$_6$H$_4$, **1b**	**3b**	34	86	74
3	4-MeOC$_6$H$_4$, **1c**	**3c**	34	85	72
4	3,4-(MeO)$_2$C$_6$H$_3$, **1d**	**3d**	34	86	87
5	3,4,5-(MeO)$_3$C$_6$H$_2$, **1e**	**3e**	34	84	78
6	4-NO$_2$C$_6$H$_4$, **1f**	**3f**	30	75	35
7	4-CF$_3$C$_6$H$_4$, **1g**	**3g**	30	80	69
8	3-BrC$_6$H$_4$, **1h**	**3h**	32	83	70
9	2-furyl, **1i**	**3i**	40	78	42
10	2-thienyl, **1j**	**3j**	40	82	43
11	*c*-C$_6$H$_{11}$, **1k**	**3k**	32	70	44

[a] After silica gel column chromatography. [b] ee determined by chiral HPLC.

Subsequent to the above report (Figure 1, Table 1 and Scheme 1),[19] the absolute configuration of nitrophosphonate **4a** (R = Et) was unambiguously assigned as *R* by single crystal X-ray structure analysis and that of the others by analogy (see the Supporting Information). The proposed transition state involving *Re*-face addition of nitrophosphonate **2** to vinyl ketone **1** adequately explains the stereochemical outcome (*R* configuration) of quaternary α-nitrophosphonates **3**−**4** (Figure 2). It involves deprotonation of nitrophosphonate **2** by the quinuclidine moiety of catalyst **C8** and activation of enone **1** by the thiourea moiety. Severe steric interaction between the phosphonate moiety and the quinuclidine moiety appears to disfavor the approach of enone **1** to the *Si*-face of nitro-

Scheme 1. Scope of Nitrophosphonates and Synthetic Applications of the Michael Adducts



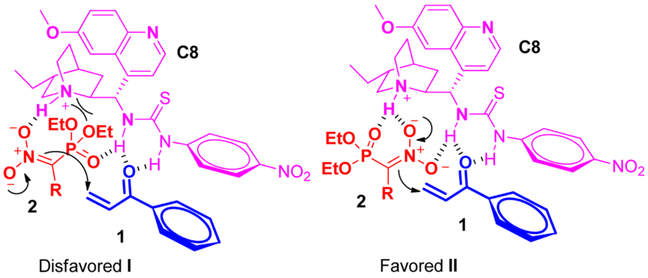


Figure 2. Proposed transition states for the thiourea catalyzed Michael addition of nitrophosphonates **2** to enones **1**.

phosphonate **2**. Absence of such steric interaction along with possible existence of a favorable $\pi-\pi$ interaction between the aryl group of enone **1** and the aryl group of catalyst **C8**, favored the approach of enone **1** to the *Re*-face of nitrophosphonate **2** and afforded nitrophosphonates **3** and **4** with *R* configuration (Figure 2).

We reasoned that as catalyst **C8** has an electron deficient aromatic ring attached to the thiourea moiety, the high enantioselectivities observed, in general, for electron rich enones could be due to excellent π-stacking between the electron deficient aromatic ring of the catalyst **C8** and the electron rich aromatic ring of the enones (e.g., **1b**−**e**, Table 1, entries 2−5). Similarly, the poor selectivities observed for electroneutral, electron deficient, and heteroaromatic enones as well as alkyl enones could be due to poor π-stacking between the two aromatic rings as a result of the electron poor nature (mismatch in electron density) of both aromatic rings (e.g., **1a**, **1f** and **1i**−**j**, respectively) or due to the absence of an aromatic ring in the enone (e.g., **1k**, Table 1, entries 1, 6 and 9−11).

In order to circumvent the poor enantioselectivities observed for enones possessing electron poor aromatic rings, it was anticipated that a catalyst possessing an electron rich aromatic ring attached to the thiourea moiety would offer better π-stacking and in turn improve the enantioselectivity of the conjugate adduct. Armed with this rationale, we employed several cinchona derived thiourea catalysts with a key electron rich aromatic ring in the conjugate addition of nitrophosphonate **2a** to electron deficient enone **1f** under otherwise identical conditions (mesitylene-xylene, 85:15, −65 °C, Figure 3 and Table 2).[22]

At the outset, conjugate addition of nitrophosphonate **2a** to enone **1f** was performed in the presence of catalyst **C9** to afford the desired adduct **3f** in 93% yield and enhanced enantioselectivity (35% to 44%, Table 2, entry 1, see also Table 1, entry 6). Later, catalysts **C10**−**C13** bearing aromatic rings with greater electron donating capabilities were screened (Table 2, entries 2−5; Figure 3). Surprisingly, catalyst **C10** with a strongly electron donating OMe group at the para-position of the aromatic ring decreased the enantioselectivity to 22% (entry 2) though it could enhance the $\pi-\pi$ interaction between the electron deficient aromatic ring of enone **1f** and the catalyst's electron rich aromatic ring. This observation suggested that the increase in the electron density of the aromatic ring in **C10**, though could enhance the π-stacking, caused an undesirable decrease in the acidity of thiourea moiety and in turn its hydrogen bonding ability leading to a dramatic drop in the ee of conjugate adduct **3f**.[23] This observation was further supported by employing catalysts **C11**−**C13** with electron donating groups at unhindered *meta*- and/or *para*-positions (entries 3−5). Thus, two Me groups at the 3 and 5 positions of the aromatic ring of catalyst **C11** increased the selectivity to 49% (entry 3). The ee was substantially higher with catalyst **C12** possessing a *meta*-OMe group as compared to **C10** (Table 2, entry 4) clearly indicating a direct correlation between the H-bonding ability of the thiourea moiety and the substitution on the aromatic ring. As expected, a 3,4-dimethoxyphenyl group attached to thiourea moiety as in catalyst **C13** decreased the ee to below 20% confirming the remarkable dependence of enantioselectivity on the electronic character of the aromatic ring attached to the thiourea moiety (Table 2, entry 5). These observations also unambiguously established that the primary factor that controls the enantioselectivity is H-bonding and not π-stacking, but when circumstances do permit, π-stacking offers an additional point of interaction that stabilizes the transition state and improves the enantioselectivity.

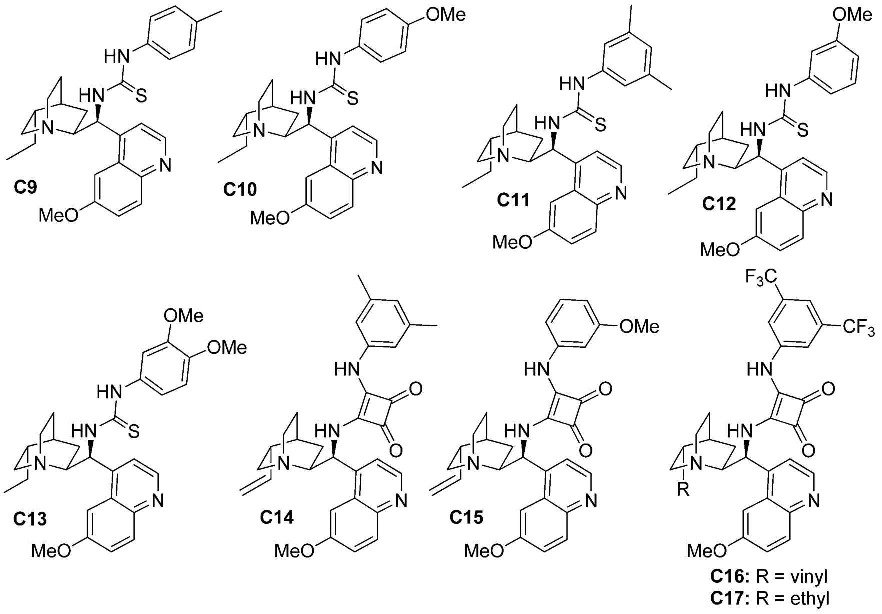
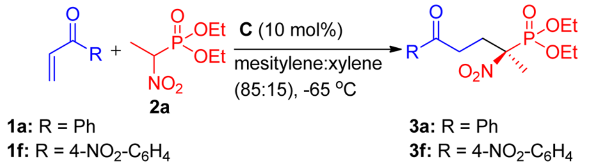


Figure 3. Thiourea and squaramide catalysts screened.

Table 2. Screening of Catalysts and Reaction Conditions



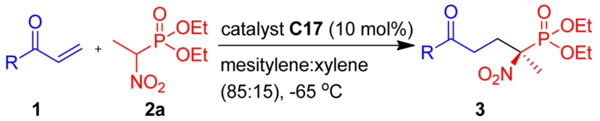
entry	1	C	solvent	*T* (°C)	time (h)	3	% yield[a]	% ee[b]
1	**1f**	**C9**	mesitylene:xylene[c]	−65	20	**3f**	93	44
2	**1f**	**C10**	mesitylene:xylene[c]	−65	20	**3f**	90	22
3	**1f**	**C11**	mesitylene:xylene[c]	−65	20	**3f**	92	49
4	**1f**	**C12**	mesitylene:xylene[c]	−65	20	**3f**	90	40
5	**1f**	**C13**	mesitylene:xylene[c]	−65	20	**3f**	89	19
6	**1f**	**C14**	mesitylene:xylene[c]	−65	10	**3f**	85	60
7	**1f**	**C15**	mesitylene:xylene[c]	−65	10	**3f**	87	70
8	**1f**	**C16**	mesitylene:xylene[c]	−65	7	**3f**	90	90
9	**1a**	**C16**	mesitylene:xylene[c]	−65	20	**3a**	90	91
10	**1a**	**C16**	DCM	rt	2	**3a**	88	67
11	**1a**	**C16**	EDC	rt	2	**3a**	89	62
12	**1a**	**C16**	$CHCl_3$	rt	2	**3a**	91	63
13	**1a**	**C16**	toluene	rt	2	**3a**	92	78
14	**1a**	**C16**	xylene	rt	2	**3a**	95	80
15	**1a**	**C16**	mesitylene	rt	2	**3a**	92	83
16	**1a**	**C16**	THF	rt	2	**3a**	88	74
17	**1a**	**C16**	MeCN	rt	2	**3a**	91	65
18	**1a**	**C17**	mesitylene:xylene[c]	−65	20	**3a**	90	92

[a] After silica gel column chromatography. [b] ee determined by chiral HPLC. [c] Ratio 85:15.

At this juncture, it became apparent that we needed a catalyst which could form stronger hydrogen bonding with the electrophile compared to the thiourea derivative and also possess an aromatic ring with optimum electron density. The recent success of chiral squaramides as strong hydrogen bond donor catalysts in asymmetric catalysis prompted us to employ a squaramide derivative as catalyst in our reaction.[24] Therefore, we screened the quinine-squaramide catalysts **C14**−**C16** in the conjugate addition of nitrophosphonate **2a** to enone **1f** (Table 2, entries 6−8). To our delight, 10 mol % of squaramide **C14** provided the quaternary α-nitrophosphonate **3f** in good yield (85%) and with 60% enantioselectivity (Table 2, entry 6). The enantioselectivity further improved to 70% when squaramide **C15** was employed (Table 2, entry 7). However, the best enantioselectivity (90%) was obtained with squaramide **C16** (Table 2, entry 8). Under the same reaction conditions, enone **1a** also provided quaternary nitrophosphonate **3a** in 90% yield and 91% selectivity (Table 2, entry 9). Screening of several solvents at two different temperatures confirmed the efficacy of our initially chosen solvent system (mesitylene:xylene, 85:15) and temperature (−65 °C) to get the best results (Table 2, entries 9−17). Finally, marginally higher selectivity was obtained in the presence of dihydroquinine-squaramide **C17** (Table 2, entry 18), which was chosen for further studies.

Under the optimized conditions, i.e., 10 mol % of squaramide **C17**, in mesitylene and xylene (85:15), at −65 °C, the scope of the above reaction was investigated by treating α-nitrophosphonate **2a** with various enones **1a**−**s** (Table 3). Although the steric and electronic properties and position of substituents on the aromatic ring of enones **1a-s** had no effect on the chemical yields of the Michael adducts **3a**−**s** (90−98% except in the case of **3k**), such factors influenced the selectivities and rate of the reaction (Table 3). Enones possessing electron donating substituents (Me and OMe, entries 2−4) and electron withdrawing substituents (NO_2, Br, Cl, CN, entries 5−6 and 10−12) at unhindered positions of the aromatic ring furnished the Michael adducts **3b**−**d**, **3f**, **3h**, **3l**−**n** in excellent yields (90−98%) and selectivities (88−97%) over a period of 7−30 h. However, the rate of the reaction was faster for electron deficient enones (7−10 h, entries 5−6 and 10−12) compared with their electron rich congeners (18−30 h, entries 2−4).

Table 3. Scope of Enones 1



entry	R, 1	time (h)	3	% yield[a]	% ee[b]
1	C_6H_5, **1a**	20	**3a**	90	92
2	4-MeC_6H_4, **1b**	18	**3b**	92	97
3	4-MeOC_6H_4, **1c**	25	**3c**	98	93
4	3,4-$(MeO)_2C_6H_3$, **1d**	30	**3d**	92	94
5	4-$NO_2C_6H_4$, **1f**	7	**3f**	90	92
6	3-BrC_6H_4, **1h**	10	**3h**	96	96
7	2-furyl, **1i**	10	**3i**	96	85
8	2-thienyl, **1j**	13	**3j**	93	93
9	*c*-C_6H_{11}, **1k**	25	**3k**	70	51
10	4-ClC_6H_4, **1l**	10	**3l**	94	92
11	4-CNC_6H_4, **1m**	8	**3m**	96	88
12	4-BrC_6H_4, **1n**	10	**3n**	95	90
13	2-ClC_6H_4, **1o**	20	**3o**	97	74
14	1-naphthyl, **1p**	18	**3p**	98	15
15	2-naphthyl, **1q**	12	**3q**	95	96
16	PhCH=CH, **1r**	15	**3r**	98	95
17	C_6H_5CH=CMe, **1s**	28	**3s**	91	90

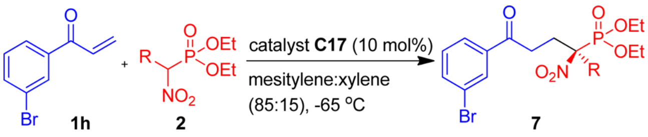
[a] Isolated yield after silica gel column chromatography. [b] ee determined by chiral HPLC.

Heteroaromatic enones **1i,j** reacted with nitrophosphonate **2a** in 10−13 h to provide the products **3i,j** in 93−96% yield and 85−93% ee (entries 7−8). Though the *ortho*-substituted aromatic enone **1o** provided Michael adduct **3o** in excellent yield (97%), the enantioselectivity surprisingly dropped to 74% (entry 13). Poor selectivity (15% ee) was observed also in case of 1-naphthyl vinyl ketone **1p** (entry 14). However, 2-naphthyl vinyl ketone **1q** furnished the Michael adduct **3q** in excellent yield 95% and selectivity 96% (entry 15). Notably, the regioselective Michael addition of α-nitrophosphonate **2a** to the β-unsubstituted olefin moiety over the β-substituted olefin moiety in enone **1r,s** was observed under the present reaction conditions (entries 16−17). An aliphatic enone **1k** also furnished the Michael adduct **3k** in moderate yield and selectivity which suggests that π-stacking interaction may be important for higher asymmetric induction (entry 9).

Further, we also explored the scope of the reaction with other sterically and electronically different nitrophosphonates **2b−g** (Table 4). Various alkyl, cycloalkyl, ester and benzyl substituted nitrophosphonates **2b−g** were treated with a representative enone **1h** under the optimal reaction conditions (Table 4). It is noteworthy that regardless of the length of the alkyl substituents and bulkiness of the nitrophosphonates, the Michael adducts **7a−f** were isolated in excellent yields (94−98%) and selectivities (91−98% ee) over a period of 10−22 h (Table 4, entries 1−6). Presumably, due to the bulkiness of the substituent, the rate of the reaction was very slow at −65 °C in case of cyclopropyl substituted nitrophosphonate **2d** and the reaction was performed at −40 °C (entry 3).

The absolute configuration of the Michael adduct **3n** was unambiguously assigned as *R* by single crystal X-ray structure analysis and that of the others was assigned by analogy (see the Supporting Information). The observed stereochemistry can be explained based on the transition state proposed in Figure 4. It involves deprotonation of nitrophosphonate **2** by the quinuclidine moiety of catalyst **C17** and activation of enone **1** by the squaramide moiety (Figure 4). Because of severe steric interaction between the phosphonate moiety and the quinuclidine moiety, approach of enone **1** toward the *Si* face of nitrophosphonate **2** to provide the product with *S* configuration appears disfavored. However, approach of enone **1** toward the *Re* face of nitrophosphonate **2** appears favored in the absence of such steric interactions affording nitrophosphonates **3** or **7** with *R* configuration. More importantly, the distance between the two N−H hydrogens is approximately 0.6 Å more in squaramide compared to that in thiourea and the acidity of squaramide hydrogens is approximately 2 orders of magnitude higher than that of thiourea.[23,24] This allows squaramide to simultaneously activate enone and nitrophosphonate via hydrogen bonding more effectively compared to thiourea and in turn provide better enantioselectivities.

Table 4. Scope of Nitrophosphonates 2



entry	R, **2**	time (h)	**7**	% yield[a]	% ee[b]
1	Et, **2b**	10	**7a**	96	92
2	*n*-Pr, **2c**	17	**7b**	97	96
3[c]	*c*-C_3H_5, **2d**	20	**7c**	94	92
4	*n*-C_9H_{19}, **2e**	20	**7d**	98	95
5	$EtO_2C(CH_2)_3$, **2f**	22	**7e**	95	91
6	$PhCH_2CH_2$, **2g**	20	**7f**	98	98

[a] After silica gel column chromatography. [b] ee determined by chiral HPLC. [c] Reaction performed at −40 °C.

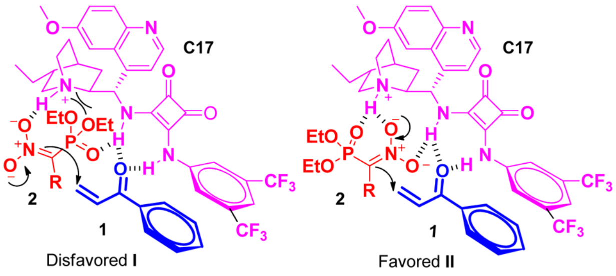


Figure 4. Proposed transition state.

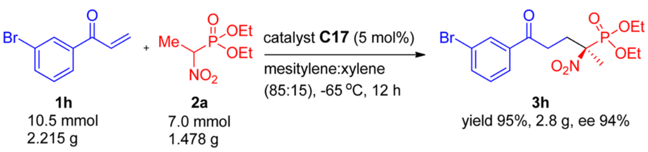
To demonstrate the practical utility of our method, the asymmetric Michael addition of nitrophosphonate **2a** to enone **1h** was carried out on multigram scale (Scheme 2). Gratifyingly, we observed that 5 mol % of catalyst **C17** was sufficient to catalyze the reaction without any appreciable drop in the yield or selectivity and the desired Michael adduct **3h** was obtained in 2.8 g (95%) with 94% ee.

Nitrophosphonylketones **3** and **7** in which the carbonyl group is at the δ-position of the nitro and the phosphonate groups are excellent precursors for the enantioselective synthesis of quaternary γ-phosphonylcarboxylic acid **9**, hydroxamic acid **12** and amides **10−11** (Scheme 3). Thus, a representative nitrophosphonylketone **3b** was subjected to Baeyer−Villiger oxidation using *m*-CPBA-TFA to afford nitrophosphonylester **8** in 95% yield. Subsequent lithium hydroxide mediated ester hydrolysis of **8** provided quaternary γ-nitro-γ-phosphonyl butaric acid **9** in 84% yield. Further, ester **8** was successfully transformed to hydroxamic acid **12** in 94% yield by treating with hydroxylamine hydrochloride in the presence of pyridine. Reaction of benzylamine with ester **8** led to the formation of amide **11** in 82% yield which was subjected to Zn-HCl-mediated selective reduction of nitro group to generate quaternary α-aminophosphonate **10** in 96% yield.

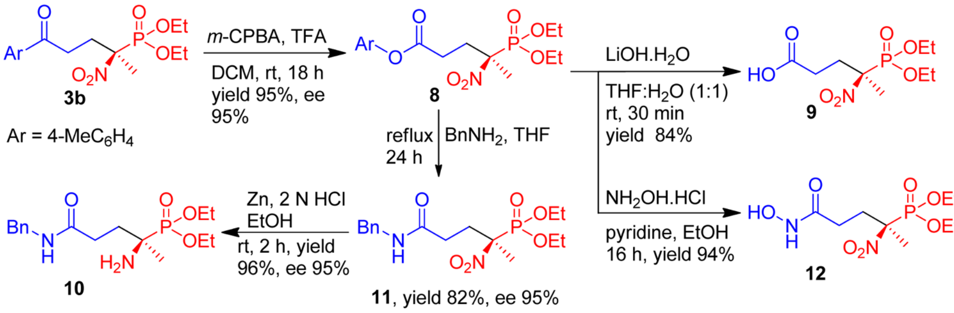
Finally, the effect phosphonate ester moiety on the rate of reaction and the enantioselectivity as well as the possible deprotection of the ester to obtain free phosphonic acid were investigated (Schemes 4 and 5). Surprisingly, the addition of di-isopropyl ester **2h** to vinyl ketone **1f** remained incomplete even after 3 days to afford the product **13** in moderate yield (42%) and selectivity (74% ee, Scheme 4).

Considering the potential of free phosphonic acids to behave as Bronsted acids in catalysis and also to exhibit biological activity due to the presence of additional co-ordinating sites as compared to phosphonate esters, a representative phosphonate ester **3f** was subjected to acid hydrolysis to afford phosphonic acid **14** in good yield (75%, Scheme 5).

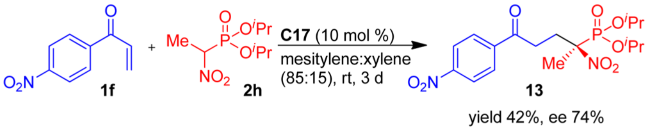
Scheme 2. Scaled-up Reaction



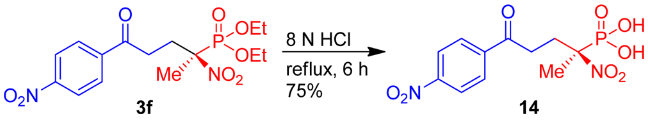
Scheme 3. Synthetic Transformations of α-Nitrophosphonates



Scheme 4. Effect of Ester Group on the Rate of Reaction and Enantioselectivity



Scheme 5. Acid Mediated Hydrolysis of Phosphonate Ester to Phosphonic Acid



■ CONCLUSIONS

The quinine-thiourea catalyzed Michael addition of tertiary α-nitrophosphonates to vinyl ketones proceed with high enantioselectivity in the case of electron rich aromatic enones and low to moderate enantioselectivity in the case of electron poor aromatic enones. On the other hand, both types of enones undergo the Michael addition with high enantioselectivity in the presence of a quinine-squaramide catalyst suggesting the superior catalytic activity of squaramide vis-à-vis thiourea in this transformation. This is attributed primarily to the ability of squaramide to form strong H-bonding when compared with thiourea though the catalyst-substrate interaction via π-stacking that supplements the former also appears probable. Scale up of the reaction to multigram scale and synthetic transformations of the Michael adducts, α-nitro-δ-ketophosphonates, to carboxylic acid, amide, hydroxamic acid and phosphonic acid with a key quaternary chiral center have been successfully carried out.

■ EXPERIMENTAL SECTION

General Experimental Details. The melting points recorded are uncorrected. NMR spectra (^{1}H, ^{1}H decoupled ^{13}C and ^{31}P) were recorded with TMS as the internal standard for ^{1}H and ^{13}C and phosphoric acid as the external standard for ^{31}P. The coupling constants (J values) are given in Hz. The J values reported as part of ^{13}C NMR data are only for C−P couplings. High resolution mass spectra were recorded under ESI Q-TOF conditions. Enantioselectivities were determined using an HPLC equipped with a PDA detector and a chiral column. Specific rotations were measured for solutions of samples of known concentrations in $CHCl_3$ using a polarimeter equipped with a sodium vapor lamp. X-ray data were collected on a diffractometer equipped with graphite monochromated Mo Kα radiation. The structure was solved by direct methods shelxs97 and refined by full-matrix least-squares against F^2 using shelxl97 software. Catalysts **C1−C2** and **C4−C5**,[25] **C3**,[26] **C6**,[27] **C7−C8**,[19] **C10**,[28] **C16**[29] and **C17**[30] were prepared by literature methods. Enones **1**[19] and nitrophosphonates **2**[19,20] were known in the literature and prepared following the literature procedures.

General Procedure for the Synthesis of Thiourea Catalysts C9−C13. To a solution of dihydroquinineamine (500 mg, 1.54 mmol) in dry THF (5 mL) was slowly added a solution of aryl isothiocyanate (1.7 mmol) in dry THF (5 mL) at 0 °C. Then the reaction mixture was brought to rt and stirred for 12 h. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography using EtOAc−MeOH (98:2) as eluent.

*Catalyst **C9**.* Colorless solid; Yield 440 mg, 60%; mp 116−119 °C; IR (film, cm^{-1}) 3264 (br m), 2955 (m), 2930 (m), 2866 (w), 1622 (m), 1589 (w), 1512 (vs), 1475 (m), 1337 (w), 1314 (w), 1297 (w), 1261 (w), 1241 (m), 1229 (m), 1032 (w), 853 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.75 (t, J = 7.3 Hz, 3H), 0.92 (dd, J = 13.0, 6.4 Hz, 1H), 1.08−1.28 (m, 3H), 1.36−1.45 (br m, 1H), 1.46−1.56 (br m, 1H), 1.57−1.62 (br m, 1H), 1.62−1.72 (br m, 1H), 2.36 (s, 3H), 2.36−2.43 (m, overlaps with singlet, 1H), 2.58−2.69 (m, 1H), 3.08 (dd, J = 13.5, 10.0 Hz, 1H), 3.12−3.17 (br m, 1H), 3.27−3.38 (br m, 1H), 3.93 (s, 3H), 5.90 (br s, 1H), 7.07, 7.16 (ABq, J = 8.1 Hz, 4H), 7.16 (br s overlap with ABq, 1H), 7.34 (dd, J = 9.2, 2.6 Hz, 1H), 7.78 (br s, 1H), 7.96 (d, J = 9.2 Hz, 1H), 8.27 (br s, 1H, D_2O exchangeable), 8.44 (s, 1H), 8.98 (br s, 1H, D_2O exchangeable); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1, 21.2, 25.2, 25.6, 27.4, 28.4, 37.1, 41.6, 55.8, 57.0, 60.8, 102.6, 119.9, 122.0, 125.6, 128.4, 130.2, 131.7, 135.1, 136.7, 144.8, 145.6, 147.7, 157.9, 180.7; MS (ES$^+$, Ar) m/z (rel intensity) 477 ([MH + 2]$^+$, 13), 476 ([MH + 1]$^+$, 36), 475 (MH$^+$, 100), 458 (12), 368 (17); HRMS (ES$^+$, Ar) calcd for $C_{28}H_{35}N_4OS$ (MH$^+$) 475.2532, found 475.2523; $[\alpha]^{25}_{D}$ = −224.0° (c = 0.5, $CHCl_3$).

*Catalyst **C11**.* Colorless solid; Yield 820 mg, 68%; mp 117−120 °C; IR (film, cm^{-1}) 3194 (br s), 2930 (vs), 2865 (s), 1622 (s), 1590 (s), 1511 (vs), 1475 (s), 1346 (m), 1313 (m), 1296 (m), 1228 (s), 1136 (vw), 1082 (w), 1032 (m), 853 (m), 736 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74 (t, J = 7.3 Hz, 3H), 0.94 (dd, J = 13.2, 6.7 Hz, 1H), 1.07−1.27 (m, 3H), 1.35−1.44 (br m, 1H), 1.46−1.55 (br m, 1H), 1.57−1.62 (br m, 1H), 1.62−1.72 (br m, 1H), 2.31 (s, 6H), 2.37 (dd, J = 13.8, 3.0 Hz, 1H), 2.64−2.73 (m, 1H), 2.99−3.08 (m, 1H), 3.10 (dd, J = 13.5, 10.0 Hz, 1H), 3.25−3.38 (br m, 1H), 3.91 (s, 3H), 5.81 (br s, 1H), 6.81 (s, 2H), 6.91 (s, 1H), 7.12 (br s, 1H), 7.33 (dd, J = 9.2, 2.3 Hz, 1H), 7.75 (br s, 1H), 7.96 (d, J = 9.2 Hz, 1H), 8.25 (br s, 1H, D_2O exchangeable), 8.47 (s, 1H), 8.76 (br s, 1H, D_2O exchangeable); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1, 21.4, 25.2, 25.8, 27.4, 28.6, 37.2, 41.6, 55.7, 57.2, 60.9, 102.5, 119.9, 121.9, 123.1, 128.3, 131.6, 137.3, 139.4, 144.8, 145.8, 147.6, 157.7, 180.3; MS (ES$^+$, Ar) m/z (rel intensity) 491 ([MH + 2]$^+$, 13), 490 ([MH + 1]$^+$, 38), 489 (MH$^+$, 100), 311 (45), 290 (22); HRMS (ES$^+$, Ar) calcd for $C_{29}H_{37}N_4OS$ (MH$^+$) 489.2688, found 489.2689; $[\alpha]^{25}_{D}$ = −150.1° (c = 0.5, $CHCl_3$).

*Catalyst **C12**.* Colorless solid; Yield 870 mg, 72%; mp 109−112 °C; IR (film, cm^{-1}) 3277 (br m), 2927 (s), 2864 (m), 1621 (m), 1602 (m), 1557 (s), 1509 (vs), 1433 (w), 1302 (m), 1266 (s), 1228 (s), 1034 (m), 854 (w), 739 (m); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74 (t, J = 7.3 Hz, 3H), 0.90 (dd, J = 13.0, 6.5 Hz, 1H), 1.08−1.28 (m, 3H), 1.34−1.44 (br m, 1H), 1.45−1.55 (br m, 1H), 1.56−1.70 (br m, 2H), 2.39 (br d, J = 10.9 Hz, 1H), 2.58−2.69 (m, 1H), 3.05 (dd, J = 13.3, 10.2 Hz, 1H), 3.08 (br s, 1H), 3.27−3.38 (br m, 1H), 3.74 (s, 3H), 3.93 (s, 3H), 5.91 (br s, 1H), 6.69 (d, J = 7.7 Hz, 1H), 6.79 (dd, J = 8.2, 2.2 Hz, 1H), 6.84 (s, 1H), 7.15 (br s, 1H), 7.24 (t, J = 8.2 Hz, 1H), 7.34 (dd, J = 9.2, 2.2 Hz, 1H), 7.79 (br s, 1H), 7.96 (d, J = 9.2 Hz, 1H), 8.32 (br s, 1H, D_2O exchangeable), 8.46 (br s, 1H), 9.16 (br s, 1H, D_2O exchangeable); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1, 25.1, 25.7, 27.4, 28.5, 37.2, 41.7, 55.6, 55.8, 57.0, 60.8, 102.5, 110.7, 112.9, 117.4, 119.9, 122.0, 128.4, 130.2, 131.6, 138.8, 144.8, 145.6, 147.7, 157.8, 160.5, 180.3; MS (ES^+, Ar) m/z (rel intensity) 493 ($[MH + 2]^+$, 12), 492 ($[MH + 1]^+$, 37), 491 (MH^+, 100), 368 (19), 310 (12); HRMS (ES^+, Ar) calcd for $C_{28}H_{35}N_4O_2S$ (MH^+) 491.2481, found 491.2462; $[\alpha]^{25}_D$ = −183.0° (c = 0.5, $CHCl_3$).

Catalyst ***C13***. Colorless solid; Yield 490 mg, 61%; mp 108−110 °C; IR (film, cm^{-1}) 3208 (br m), 2999 (w), 2954 (m), 2931 (m), 2870 (w), 1622 (m), 1591 (w), 1512 (vs), 1465 (m), 1348 (w), 1296 (w), 1262 (m), 1238 (s), 1135 (w), 1028 (m), 854 (w); ^1H NMR (400 MHz, $CDCl_3$) δ 0.75 (t, J = 7.3 Hz, 3H), 0.89 (dd, J = 14.6, 6.9 Hz, 1H), 1.10−1.28 (m, 3H), 1.35−1.44 (br m, 1H), 1.45−1.55 (br m, 1H), 1.59 (br s, 1H), 1.60−1.70 (br m, 1H), 2.38 (d, J = 11.5 Hz, 1H), 2.58−2.68 (br m, 1H), 3.05, 3.09 (ABq, J = 10.1 Hz, 2H), 3.35 (br s, 1H), 3.78 (s, 3H), 3.90 (s, 3H), 3.93 (s, 3H), 5.91 (br s, 1H), 6.68 (d, J = 7.7 Hz, 1H), 6.79 (d, J = 1.9 Hz, 1H), 6.82 (d, J = 8.5 Hz, 1H), 7.11 (br s, 1H), 7.35 (dd, J = 9.2, 2.4 Hz, 1H), 7.79 (br s, 1H), 7.96 (d, J = 9.2 Hz, 1H), 8.10 (br s, 1H, D_2O exchangeable), 8.43 (br s, 1H), 8.90 (br s, 1H, D_2O exchangeable); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1, 25.2, 25.7, 27.5, 28.6, 37.2, 41.8, 55.9, 56.2, 57.3, 60.8, 102.6, 110.1, 111.4, 118.2, 119.6, 122.0, 128.4, 130.6, 131.7, 144.9, 145.8, 147.7, 148.0, 149.6, 157.9, 180.7; MS (ES^+, Ar) m/z (rel intensity) 523 ($[MH + 2]^+$, 12), 522 ($[MH + 1]^+$, 38), 521 (MH^+, 100), 369 (15), 368 (55), 309 (14), 297 (9); HRMS (ES^+, Ar) calcd for $C_{29}H_{37}N_4O_3S$ (MH^+) 521.2586, found 521.2573; $[\alpha]^{25}_D$ = −187.50° (c = 0.25, $CHCl_3$).

General Procedure for the Synthesis of Squaramide Catalysts C14−C15. To a solution of 3-methoxy-4-(arylamino)-cyclobut-3-ene-1,2-dione (3.09 mmol) in dry DCM (10 mL) was slowly added a solution of quinineamine (1.0 g, 3.09 mmol) in dry DCM (10 mL) at rt. The reaction mixture was stirred for 48 h, and the resulting precipitate was isolated by filtration. The residue was washed with ether (10 mL) and dried in vacuo to afford catalyst **C14** or **C15** as white solid.

Catalyst ***C14***. Colorless solid; Yield 1.325 g, 80%; mp 256−258 °C; IR (film, cm^{-1}) 3244 (br s), 2945 (br s), 1793 (m), 1678 (s), 1583 (vs), 1472 (vs), 1230 (m), 1172 (w), 1029 (w), 915 (w), 842 (m), 689 (w);^1H NMR (400 MHz, DMSO-d_6) δ 0.62 (br s, 1H), 1.45−1.55 (br m, 4H), 2.18 (s, 6H), 2.25 (br s, 1H), 2.57−2.64 (m, 1H), 2.65−2.73 (m, 1H), 3.17 (dd, J = 13.4, 10.2 Hz, 1H), 3.25−3.37 (br m, 1H), 3.46 (q, J = 8.9 Hz, 1H), 3.94 (s, 3H), 4.97 (d, J = 10.7 Hz, 1H), 5.01 (d, J = 17.3 Hz, 1H), 5.97 (td, J = 17.3, 10.7 Hz, 1H), 6.04 (br s, 1H), 6.63 (s, 1H), 6.94 (s, 2H), 7.44 (dd, J = 9.2, 2.5 Hz, 1H), 7.66 (d, J = 4.6 Hz, 1H), 7.78 (s, 1H), 7.98 (d, J = 9.2 Hz, 1H), 8.10 (br s, 1H, D_2O exchangeable), 8.81 (d, J = 4.6 Hz, 1H), 9.58 (br s, 1H, D_2O exchangeable); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.1 (q), 26.2 (t), 27.3 (t), 27.4 (d), 39.4 (d), 40.1 (t), 53.3 (d), 55.7 (t), 55.7 (q), 58.8 (d), 101.5 (d), 114.3 (t), 116.0 (d), 119.6 (d), 122.0 (d), 124.5 (d), 127.5 (s), 131.6 (d), 138.5 (s), 142.3 (d), 143.3 (s), 144.3 (s), 147.8 (d), 157.9 (s), 163.7 (s), 167.9 (s), 180.0 (s), 184.0 (s); MS (ES^+, Ar) m/z (rel intensity) 525 ($[MH + 2]^+$, 8), 524 ($[MH + 1]^+$, 38), 523 (MH^+, 100), 309 (10), 192 (14); HRMS (ES^+, Ar) calcd for $C_{32}H_{35}N_4O_3$ (MH^+) 523.2709, found 523.2707; $[\alpha]^{25}_D$ = −69.07° (c = 0.25, DMSO).

Catalyst ***C15***. Colorless solid; Yield 1.240 g, 75%; mp 167−169 °C; IR (film, cm^{-1}) 3265 (br m), 2927 (m), 1672 (m), 1627 (m), 1606 (m), 1547 (m), 1435 (s), 1224 (w), 1027 (w), 923 (w), 823 (w), 684 (w); ^1H NMR (400 MHz, DMSO-d_6) δ 0.63 (br s, 1H), 1.46−1.59 (br m, 4H), 2.25 (br s, 1H), 2.56−2.73 (m, 2H), 3.17 (t, J = 11.4 Hz, 1H), 3.25−3.35 (br m, 1H), 3.47 (q, J = 9.3 Hz, 1H), 3.70 (s, 3H), 3.94 (s, 3H), 4.97 (d, J = 9.5 Hz, 1H), 5.02 (d, J = 17.2 Hz, 1H), 5.98 (td, J = 17.2, 9.5 Hz, 1H), 6.01 (br s, overlaps with td, 1H), 6.56 (d, J = 8.1 Hz, 1H), 6.85 (d, J = 7.9 Hz, 1H), 7.14 (br s, 1H), 7.18 (t, J = 8.1 Hz, 1H), 7.44 (d, J = 9.2 Hz, 1H), 7.66 (d, J = 4.6 Hz, 1H), 7.77 (br s, 1H), 7.96 (d, J = 9.2 Hz, 1H), 8.19 (br s, 1H, D_2O exchangeable), 8.82 (d, J = 4.6 Hz, 1H), 9.64 (br s, 1H, D_2O exchangeable); ^{13}C NMR (100 MHz, DMSO-d_6) δ 26.2 (t), 27.3 (t), 27.4 (d), 39.4 (d), 40.1 (t), 53.3 (d), 55.1 (q), 55.7 (t), 55.8 (q), 58.9 (d), 101.6 (d), 103.9 (d), 108.6 (d), 110.3 (d), 114.4 (t), 119.5 (d), 122.0 (d), 127.6 (s), 130.2 (d), 131.6 (d), 140.0 (s), 142.2 (d), 143.3 (s), 144.4 (s), 147.9 (d), 158.0 (s), 160.2 (s), 163.7 (s), 168.1 (s), 179.9 (s), 184.0 (s); MS (ES^+, Ar) m/z (rel intensity) 527 ($[MH + 2]^+$, 34), 526 ($[MH + 1]^+$, 85), 525 ($[MH]^+$, 100), 309 (44), 263 (62); HRMS (ES+, Ar) calcd for $C_{31}H_{33}N_4O_4$ (MH^+) 525.2502, found 525.2502; $[\alpha]^{25}_D$ = −52.45° (c = 0.25, DMSO).

General Procedure for the Addition of Dialkyl 1-Nitroethylphosphonate 2 to Enones 1. To a solution of dialkyl-1-nitroethylphosphonate **2** (0.2 mmol) and catalyst **C17** (10 mol %, 0.02 mmol) in mesitylene:xylene (85:15, 0.2 mL) was added enone **1** (0.3 mmol, dissolved in mesitylene:xylene (85:15, 0.2 mL) at −65 °C. The reaction mixture was stirred at the same temperature and monitored by TLC. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography using EtOAc−pet ether as eluent (30−45% gradient elution).

Diethyl 2-nitro-5-oxo-5-phenylpentan-2-ylphosphonate ***(3a)***.[19] Colorless solid; Yield 62 mg, 90%; mp 72−74 °C; $[\alpha]^{25}_D$ = −8.40° (c = 1.00, $CHCl_3$); HPLC Chiralcel OD-H (pet ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm), t_R (major) = 29.0 min, t_R (minor) = 33.7 min; 92% ee.

Diethyl 2-nitro-5-oxo-5-p-tolylpentan-2-ylphosphonate ***(3b)***.[19] Light yellow liquid; Yield 66 mg, 92%; $[\alpha]^{25}_D$ = −8.0° (c = 0.5, $CHCl_3$); HPLC Chiralcel OD-H (pet ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 230 nm), t_R (major) = 27.6 min, t_R (minor) = 30.8 min; 97% ee.

Diethyl 5-(4-methoxyphenyl)-2-nitro-5-oxopentan-2-ylphosphonate ***(3c)***.[19] Colorless liquid; Yield 73 mg, 98%; $[\alpha]^{25}_D$ = −10.62° (c = 1.00, $CHCl_3$); HPLC Chiralpak IA (pet ether/i-PrOH = 90/10, flow rate 1 mL/min, λ = 268 nm), t_R (major) = 17.5 min, t_R (minor) = 19.9 min; 93% ee.

Diethyl 5-(3,4-dimethoxyphenyl)-2-nitro-5-oxopentan-2-ylphosphonate ***(3d)***.[19] Light yellow solid; Yield 74 mg, 92%; mp 58.5−61 °C; $[\alpha]^{25}_D$ = −8.97° (c = 1.00, $CHCl_3$); HPLC Chiralpak IA (pet ether/i-PrOH = 95/5, flow rate 1 mL/min, λ = 230 nm), t_R (major) = 50.6 min, t_R (minor) = 56.5 min; 94% ee.

Diethyl 2-nitro-5-(4-nitrophenyl)-5-oxopentan-2-ylphosphonate ***(3f)***.[19] Light yellow solid; Yield 70 mg, 90%; mp 79−82 °C; $[\alpha]^{25}_D$ = −10.67° (c = 1.00, $CHCl_3$); HPLC Chiralpak IC (pet ether/i-PrOH = 60/40, flow rate 1 mL/min, λ = 216 nm), t_R (major) = 32.7 min, t_R (minor) = 50.1 min; 92% ee.

Diethyl 5-(3-bromophenyl)-2-nitro-5-oxopentan-2-ylphosphonate ***(3h)***.[19] Light yellow oil; Yield 81 mg, 96%; $[\alpha]^{25}_D$ = −6.03° (c = 1.00, $CHCl_3$); HPLC Chiralcel OD-H (pet ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 230 nm), t_R (major) = 30.4 min, t_R (minor) = 33.9 min; 96% ee.

Diethyl 5-(furan-2-yl)-2-nitro-5-oxopentan-2-ylphosphonate ***(3i)***.[19] Light yellow oil; Yield 63 mg, 95%; $[\alpha]^{25}_D$ = −8.25° (c = 1.00, $CHCl_3$); HPLC Chiralcel OD-H (pet ether/i-PrOH = 95/5, flow rate 1 mL/min, λ = 268 nm), t_R (major) = 24.9 min, t_R (minor) = 29.1 min; 85% ee.

Diethyl 2-nitro-5-oxo-5-(thiophen-2-yl)pentan-2-ylphosphonate ***(3j)***.[19] Colorless solid; Yield 65 mg, 93%; mp 60−61 °C; $[\alpha]^{25}_D$ = −6.92° (c = 1.00, $CHCl_3$); HPLC Chiralcel OD-H (pet ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 260 nm), t_R (major) = 44.2 min, t_R (minor) = 49.5 min; 93% ee.

Diethyl 5-cyclohexyl-2-nitro-5-oxopentan-2-ylphosphonate ***(3k)***.[19] Colorless liquid; Yield 49 mg, 70%; $[\alpha]^{25}_D$ = −1.08 (c = 1.00, $CHCl_3$); HPLC Chiralcel OD-H (pet ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 254 nm), t_R (major) = 18.5 min, t_R (minor) = 20.3 min; 51% ee.

Diethyl 5-(4-chlorophenyl)-2-nitro-5-oxopentan-2-ylphosphonate ***(3l)***. Colorless solid; Yield 71 mg, 94%; mp 56−58 °C; IR (film, cm^{-1}) 2984 (m), 2925 (m), 2854 (m), 1689 (s), 1590 (m), 1572 (m), 1547 (s), 1488 (w), 1445 (w), 1400 (w), 1370 (w), 1336 (w), 1258 (s), 1213 (m), 1177 (w), 1163 (w), 1092 (m), 1048 (vs), 1021 (vs), 979 (s), 863 (w), 790 (w), 761 (w); ^1H NMR (400 MHz, $CDCl_3$) δ 1.35 (t, J = 7.0 Hz, 3H), 1.37 (t, J = 7.0 Hz, 3H), 1.84 (d, J =

14.2 Hz, 3H), 2.57 (dtd, J = 15.2, 10.2, 5.0 Hz, 1H), 2.75 (dtd, J = 15.2, 10.2, 5.0 Hz, 1H), 3.05, 3.13 (ABqdd, J = 17.7, 10.2, 5.0 Hz, 2H), 4.19−4.31 (m, 4H), 7.43 (d, J = 8.6 Hz, 2H), 7.88 (d, J = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.5, 16.6, 20.8, 30.2, 33.1 (d, J = 7.0 Hz), 64.4 (d, J = 7.0 Hz), 64.7 (d, J = 8.0 Hz), 89.4 (d, J = 151.0 Hz), 129.2, 129.6, 134.7, 140.1, 196.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ 16.4; MS (ES$^+$, Ar) m/z (rel intensity) 380 ([MH + 2]$^+$, 43), 379 ([MH + 1]$^+$, 20), 378 (MH$^+$, 100), 333 (20), 332 (15), 331 (54), 201 (19), 179 (15); HRMS (ES$^+$, Ar) calcd for $C_{15}H_{22}NO_6PCl$ (MH$^+$) 378.0873, found 378.0878; $[\alpha]^{25}_D$ = −10.38° (c = 0.50, $CHCl_3$); HPLC Chiralcel OD-H (pet ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 230 nm), t_R (major) = 32.9 min, t_R (minor) = 35.6 min; 92% ee.

*Diethyl 5-(4-cyanophenyl)-2-nitro-5-oxopentan-2-ylphosphonate (**3m**).* Colorless solid; Yield 71 mg, 96%; mp 103−105 °C; IR (film, cm^{-1}) 3097 (w), 2988 (w), 2934 (w), 2228 (m), 1693 (s), 1546 (s), 1439 (w), 1388 (w), 1334 (w), 1300 (w), 1256 (m), 1213 (m), 1164 (w), 1048 (s), 1018 (s), 967 (m), 864 (m), 838 (w), 792 (w), 741 (w), 589 (w), 575 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (t, J = 7.0 Hz, 3H), 1.36 (t, J = 7.0 Hz, 3H), 1.83 (d, J = 14.2 Hz, 3H), 2.57 (dtd, J = 15.2, 10.2, 5.1 Hz, 1H), 2.74 (dtd, J = 15.2, 10.2, 5.1 Hz, 1H), 3.10, 3.20 (ABqdd, J = 17.8, 10.2, 5.1 Hz, 2H), 4.17−4.31 (m, 4H), 7.76, 8.02 (ABq, J = 8.4 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.5, 16.6, 21.1, 30.0, 33.6 (d, J = 7.0 Hz), 64.4 (d, J = 8.0 Hz), 64.8 (d, J = 7.0 Hz), 89.2 (d, J = 151.0 Hz), 116.8, 118.0, 128.6, 132.7, 139.3, 196.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ 16.2; MS (ES$^+$, Ar) m/z (rel intensity) 371 ([MH + 2]$^+$, 4), 370 ([MH + 1]$^+$, 20), 369 (MH$^+$, 100), 323 (12), 322 (35); HRMS (ES$^+$, Ar) calcd for $C_{16}H_{22}N_2O_6P$ (MH$^+$) 369.1216, found 369.1224; $[\alpha]^{25}_D$ = −9.42° (c = 0.50, $CHCl_3$); HPLC Chiralpack IC (pet ether/i-PrOH = 60/40, flow rate 1.0 mL/min, λ = 216 nm), t_R (major) = 35.3 min, t_R (minor) = 56.4 min; 88% ee.

*Diethyl 5-(4-bromophenyl)-2-nitro-5-oxopentan-2-ylphosphonate (**3n**).* Colorless solid; Yield 80 mg, 95%; mp 74−75 °C; IR (film, cm^{-1}) 2985 (w), 1689 (m), 1586 (w), 1545 (s), 1443 (w), 1397 (w), 1337 (w), 1257 (m), 1210 (w), 1163 (w), 1019 (vs), 983 (m), 863 (w); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.36 (t, J = 7.0 Hz, 3H), 1.37 (t, J = 6.5 Hz, 3H), 1.84 (d, J = 14.3 Hz, 3H), 2.57 (dtd, J = 15.0, 10.2, 5.0 Hz, 1H), 2.76 (dtd, J = 15.0, 10.2, 5.0 Hz, 1H), 3.05, 3.14 (ABqdd, J = 17.4, 10.2, 5.0 Hz, 2H), 4.20−4.32 (m, 4H), 7.60 (d, J = 8.3 Hz, 2H), 7.80 (d, J = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.5, 16.5, 20.8, 30.2, 33.0 (d, J = 7.5 Hz), 64.4 (d, J = 5.0 Hz), 64.6 (d, J = 6.3 Hz), 89.4 (d, J = 152.2 Hz), 128.8, 129.7, 132.1, 135.1, 196.8; ^{31}P NMR (202 MHz, $CDCl_3$) δ 16.4; LRMS (ES$^+$, Ar) 446 (M+2]$^+$, 100), 444 (M$^+$, 98); HRMS (ES$^+$, Ar) calcd for $C_{15}H_{21}BrNO_6PNa$ (MNa$^+$) 444.0182, found 444.0181; $[\alpha]^{25}_D$ = −9.42° (c = 1.00, $CHCl_3$); HPLC Chiralpack IA (pet ether/i-PrOH = 90/10, flow rate 0.5 mL/min, λ = 216 nm), t_R (major) = 100.3 min, t_R (minor) = 112.6 min; 90% ee. Selected X-ray data: $C_{15}H_{21}BrNO_6P$, M = 422.21, Monoclinic, space group $P2(1)$, a = 10.158(5) Å, b = 6.593(5) Å, c = 13.228(5) Å, α = 90.000(4)°, β = 98.716(5)°, γ = 90.000(5)°, V = 875.7(9) Å^3, Z = 2, ρcald = 1.601 Mg/m^3, F(000) = 432, λ = 0.71073 Å, μ = 2.469 mm^{-1}, total/unique reflections = 12316/4035. Final R [$I > 2\sigma(I)$]: $R1$ = 0.0533, $wR2$ = 0.1002. R (all data): $R1$ = 0.0657, $wR2$ = 0.1094. Absolute structure parameter 0.011(9).

*Diethyl 5-(2-chlorophenyl)-2-nitro-5-oxopentan-2-ylphosphonate (**3o**).* Colorless oil; Yield 73 mg, 97%; IR (neat, cm^{-1}) 3064 (w), 2986 (s), 2934 (s), 2914 (s), 1704 (s), 1590 (m), 1547 (s), 1471 (m), 1435 (m), 1388 (w), 1338 (w), 1290 (w), 1259 (s), 1210 (w), 1163 (m), 1096 (w), 1049 (s), 1025 (s), 975 (m), 861 (m), 791 (w), 758 (s), 588 (m), 567 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, J = 7.1 Hz, 6H), 1.79 (d, J_{C-P} = 14.3 Hz, 3H), 2.46−2.60 (m, 1H), 2.69−2.82 (m, 1H), 3.04 (t, J = 7.9 Hz, 2H), 4.15−4.29 (m, 4H), 7.25−7.32 (m, 1H), 7.34−7.40 (m, 2H), 7.41−7.45 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.4, 16.5, 20.3, 30.0, 37.2 (d, J = 8.0 Hz), 64.4 (d, J = 7.0 Hz), 64.5 (d, J = 7.0 Hz), 89.2 (d, J = 150.0 Hz), 127.1, 129.1, 130.7, 131.0, 132.2, 138.6, 200.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ 16.4; MS (ES$^+$, Ar) m/z (rel intensity) 380 ([MH + 2]$^+$, 41), 379 ([MH + 1]$^+$, 19), 378 (MH$^+$, 100), 333 (7), 332 (6), 331 (20); HRMS (ES$^+$, Ar) calcd for $C_{15}H_{22}NO_6PCl$ (MH$^+$) 378.0873, found 378.0886; $[\alpha]^{25}_D$ = −4.07° (c = 1.00, $CHCl_3$); HPLC Chiralpack IC (pet ether/i-PrOH = 80/20, flow rate 1.0 mL/min, λ = 216 nm), t_R (major) = 35.3 min, t_R (minor) = 37.7 min; 74% ee.

*Diethyl 5-(naphthalen-1-yl)-2-nitro-5-oxopentan-2-ylphosphonate (**3p**).* Colorless oil; Yield 77 mg, 98%; IR (neat, cm^{-1}) 3051 (w), 2985 (s), 2934 (m), 1683 (s), 1545 (s), 1509 (m), 1443 (m), 1388 (m), 1368 (w), 1336 (m), 1258 (s), 1176 (m), 1164 (m), 1100 (m), 1044 (s), 975 (s), 861 (m), 803 (s), 780 (s), 681 (w), 588 (w), 570 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (t, J = 7.1 Hz, 3H), 1.37 (t, J = 7.1 Hz, 3H), 1.85 (d, J = 14.3 Hz, 3H), 2.65 (dddd, J = 15.4, 12.7, 9.7, 5.8 Hz, 1H), 2.87 (dtd, J = 15.4, 9.7, 5.8 Hz, 1H), 3.16, 3.23 (ABqdd, J = 17.4, 9.7, 5.8 Hz, 2H), 4.18−4.33 (m, 4H), 7.47 (t, J = 8.3 Hz, 1H), 7.52 (td, J = 8.2, 1.2 Hz, 1H), 7.58 (td, J = 8.2, 1.2 Hz, 1H), 7.85 (dd, J = 8.2, 1.2 Hz, 1H), 7.87 (dd, J = 8.2, 1.2 Hz, 1H), 7.98 (d, J = 8.3 Hz, 1H), 8.60 (d, J = 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.5, 16.5, 20.5 (d, J = 1.0 Hz), 30.5, 36.1 (d, J = 8.0 Hz), 64.5 (d, J = 7.0 Hz), 64.5 (d, J = 7.0 Hz), 89.5 (d, J = 150.0 Hz), 124.5, 125.7, 126.6, 128.1, 128.2, 128.6, 130.2, 133.3, 134.1, 135.0, 201.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 16.6; MS (ES$^+$, Ar) m/z (rel intensity) 396 ([MH + 2]$^+$, 4), 395 ([MH + 1]$^+$, 23), 394 (MH$^+$, 100), 370 (6), 369 (15), 348 (14), 347 (51), 209 (25), 201 (34), 179 (9); HRMS (ES$^+$, Ar) calcd for $C_{19}H_{25}NO_6P$ (MH$^+$) 394.1420, found 394.1433; $[\alpha]^{25}_D$ = −0.70° (c = 1.00, $CHCl_3$); HPLC Chiralcel OD-H (pet ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 230 nm), t_R (major) = 53.3 min, t_R (minor) = 66.7 min; 15% ee.

*Diethyl 5-(naphthalen-2-yl)-2-nitro-5-oxopentan-2-ylphosphonate (**3q**).* Colorless solid; Yield 75 mg, 95%; mp 63−65 °C; IR (film, cm^{-1}) 3053 (w), 2985 (m), 2931 (w), 1685 (m), 1546 (s), 1509 (w), 1443 (w), 1388 (w), 1336 (w), 1258 (s), 1176 (w), 1164 (w), 1100 (w), 1049 (s), 1021 (s), 975 (w), 861 (w), 803 (m), 780 (m), 588 (w), 570 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (t, J = 7.0 Hz, 3H), 1.39 (t, J = 7.0 Hz, 3H), 1.89 (d, J = 14.2 Hz, 3H), 2.65 (dddd, J = 15.2, 10.5, 13.5, 5.2 Hz, 1H), 2.86 (dtd, J = 15.2, 10.0, 5.1 Hz, 1H), 3.22 (ddd, J = 17.4, 10.0, 5.2, Hz, 1H), 3.31 (ddd, J = 17.4, 10.5, 5.1 Hz, 1H), 4.22−4.36 (m, 4H), 7.56 (dt, J = 8.4, 1.4 Hz, 1H), 7.61 (dt, J = 8.4, 1.4 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.90 (dd, J = 8.4, 1.4 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 8.01 (dd, J = 8.4, 1.4 Hz, 1H), 8.46 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.4, 16.4, 20.4, 30.2, 32.9 (d, J = 8.0 Hz), 64.3 (d, J = 7.0 Hz), 64.4 (d, J = 8.0 Hz), 89.4 (d, J = 150.0 Hz), 123.6, 126.9, 127.7, 128.5, 128.6, 129.6, 129.8, 132.4, 133.6, 135.6, 197.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 16.6; MS (ES$^+$, Ar) m/z (rel intensity) 395 ([MH + 1]$^+$, 23), 394 (MH$^+$, 100), 370 (14), 369 (24), 348 (32), 347 (92), 209 (28), 201 (52), 179 (17); HRMS (ES$^+$, Ar) calcd for $C_{19}H_{25}NO_6P$ (MH$^+$) 394.1420, found 394.1423; $[\alpha]^{25}_D$ = −15.92° (c = 0.50, $CHCl_3$); HPLC Chiralpack IC (pet ether/i-PrOH = 60/40, flow rate 1.0 mL/min, λ = 216 nm), t_R (major) = 20.3 min, t_R (minor) = 22.9 min; 96% ee.

*(E)-Diethyl 2-nitro-5-oxo-7-phenylhept-6-en-2-ylphosphonate (**3r**).* Colorless oil; Yield 72 mg, 98%; IR (neat, cm^{-1}) 3058 (w), 2986 (m), 2934 (w), 2913 (w), 1692 (m), 1665 (m), 1613 (m), 1577 (w), 1546 (s), 1496 (w), 1450 (m), 1388 (w), 1370 (w), 1335 (w), 1258 (s), 1185 (m), 1163 (w), 1097 (m), 1048 (vs), 1022 (vs), 977 (s), 857 (w), 793 (w), 752 (m), 692 (m), 587 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, J = 7.1 Hz, 3H), 1.34 (t, J = 7.1 Hz, 3H), 1.79 (d, J = 14.3 Hz, 3H), 2.41−2.55 (m, 1H), 2.63−2.74 (m, 1H), 2.74−2.86 (m, 2H), 4.16−4.30 (m, 4H), 6.69 (d, J = 16.3 Hz, 1H), 7.31−7.42 (m, 3H), 7.47−7.54 (m, 2H), 7.53 (d, J = 16.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.4, 16.5, 20.4, 30.0, 34.9 (d, J = 8.0 Hz), 64.4 (d, J = 7.0 Hz), 64.5 (d, J = 7.0 Hz), 89.5 (d, J = 150.0 Hz), 125.7, 128.4, 129.1, 130.8, 134.3, 143.4, 197.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ 16.5; MS (ES$^+$, Ar) m/z (rel intensity) 372 ([MH + 2]$^+$, 4), 371 ([MH + 1]$^+$, 20), 370 (MH$^+$, 100), 324 (5), 323 (9), 266 (18), 228 (6), 214 (14), 158 (7); HRMS (ES$^+$, Ar) calcd for $C_{17}H_{25}NO_6P$ (MH$^+$) 370.1420, found 370.1431; $[\alpha]^{25}_D$ = −10.92° (c = 1.00, $CHCl_3$); HPLC Chiralpack IC (pet ether/i-PrOH = 60/40, flow rate 1.0 mL/min, λ = 260 nm), t_R (major) = 24.3 min, t_R (minor) = 41.2 min; 95% ee.

*(E)-Diethyl 6-methyl-2-nitro-5-oxo-7-phenylhept-6-en-2-ylphosphonate (**3s**).* Colorless oil; Yield 70 mg, 91%; IR (neat, cm^{-1}) 3055 (m), 2871 (m), 2986 (s), 2932 (s), 1668 (s), 1627 (m), 1546 (s), 1491 (w), 1444 (s), 1388 (m), 1369 (m), 1335 (w), 1259 (s),

1204 (w), 1162 (w), 1049 (s), 1025 (s), 974 (m), 925 (w), 861 (m), 793 (m), 754 (s), 700 (m), 679 (w), 588 (m), 511 (w); ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.37 (t, J = 7.0 Hz, 3H), 1.37 (t, J = 7.0 Hz, 3H), 1.84 (d, J = 14.3 Hz, 3H), 2.06 (d, J = 1.1 Hz, 3H), 2.50 (dddd, J = 15.2, 12.7, 10.5, 5.0 Hz, 1H), 2.74 (ddt, J = 15.2, 10.0, 5.3 Hz, 1H), 2.89 (ddd, J = 16.7, 10.0, 5.0 Hz, 1H), 2.97 (ddd, J = 16.7, 10.5, 5.3 Hz, 1H), 4.20−4.32 (m, 4H), 7.31−7.38 (m, 1H), 7.39−7.44 (m, 4H), 7.50 (q, J = 1.1 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 13.1, 16.3, 16.4, 20.2, 30.6, 31.7 (d, J = 8.0 Hz), 64.3, 64.3, 89.4 (d, J = 149.0 Hz), 128.4, 128.7, 129.7, 135.5, 136.6, 139.3, 199.5; ^{31}P NMR (162 MHz, CDCl$_3$) δ 16.6; MS (ES$^+$, Ar) m/z (rel intensity) 386 ([MH + 2]$^+$, 4), 385 ([MH + 1]$^+$, 22), 384 (MH$^+$, 100), 359 (13), 338 (12), 337 (36), 266 (30), 238 (12), 201 (25), 200 (11), 199 (50), 179 (14); HRMS (ES$^+$, Ar) calcd for $\mathrm{C_{18}H_{27}NO_6P}$ (MH$^+$) 384.1576, found 384.1557; $[\alpha]^{25}_{D}$ = −19.79° (c = 1.00, CHCl$_3$); HPLC Chiralcel OD-H (pet ether/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 280 nm), t_R (major) = 18.0 min, t_R (minor) = 21.2 min; 90% ee.

*Diethyl 6-(3-bromophenyl)-3-nitro-6-oxohexan-3-ylphosphonate (**7a**).* Colorless oil; Yield 84 mg, 96%; IR (neat, cm^{-1}) 2984 (m), 2942 (w), 1692 (s), 1546 (vs), 1442 (w), 1421 (w), 1257 (s), 1207 (w), 1163 (w), 1049 (vs), 1023 (vs), 976 (m), 791 (m), 757 (m), 681 (m); ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.97 (t, J = 7.4 Hz, 3H), 1.29 (t, J = 7.1 Hz, 3H), 1.31 (t, J = 7.1 Hz, 3H), 2.16 (ddq, J = 14.8, 11.8, 7.4 Hz, 1H), 2.31 (ddq, J = 14.8, 12.2, 7.4 Hz, 1H), 2.41 (dtd, J = 15.5, 10.8, 4.9 Hz, 1H), 2.65 (dtd, J = 15.5, 10.8, 4.9 Hz, 1H), 3.17, 3.25 (ABqdd, J = 15.9, 10.9, 4.9 Hz, 2H), 4.10−4.28 (m, 4H), 7.28 (t, J = 7.9 Hz, 1H), 7.62 (ddd, J = 7.9, 1.8, 1.0 Hz, 1H), 7.83 (ddd collapsed to dt, J = 7.9, 1.4 Hz, 1H), 8.02 (dd collapsed to t, J = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 8.4 (d, J = 7.0 Hz), 16.5 (d, J = 5.0 Hz), 16.5 (d, J = 5.0 Hz), 27.7, 29.7, 33.9 (d, J = 4.0 Hz), 63.9 (d, J = 7.0 Hz), 64.7 (d, J = 7.0 Hz), 93.5 (d, J = 150.0 Hz), 123.2, 126.8, 130.4, 131.2, 136.3, 138.3, 197.0; ^{31}P NMR (162 MHz, CDCl$_3$) δ 16.2; MS (ES$^+$, Ar) m/z (rel intensity) 439 ([MH + 3]$^+$, 20), 438 ([MH + 2]$^+$, 97), 437 ([MH + 1]$^+$, 20), 436 (MH$^+$, 100), 391 (35), 390 (34), 253 (19), 251 (18), 193 (23); HRMS (ES$^+$, Ar) calcd for $\mathrm{C_{16}H_{24}NO_6BrP}$ (MH$^+$) 436.0525, found 436.0532; $[\alpha]^{25}_{D}$ = −9.06° (c = 1.00, CHCl$_3$); HPLC Chiralcel OD-H (pet ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 216 nm), t_R (major) = 24.6 min, t_R (minor) = 26.3 min; 92% ee.

*Diethyl 1-(3-bromophenyl)-4-nitro-1-oxoheptan-4-ylphosphonate (**7b**).* Colorless oil; Yield 87 mg, 97%; IR (neat, cm^{-1}) 2973 (s), 2934 (m), 2876 (w), 1692 (s), 1547 (s), 1468 (w), 1443 (w), 1422 (w), 1338 (vw), 1295 (w), 1255 (s), 1208 (m), 1163 (w), 1096 (w), 1048 (vs), 1026 (vs), 976 (s), 855 (vw), 790 (m), 765 (m); ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.95 (t, J = 7.3 Hz, 3H), 1.35 (t, J = 7.1 Hz, 3H), 1.37 (t, J = 7.1 Hz, 3H), 1.42−1.58 (m, 1H), 2.09−2.22 (m, 1H), 2.21−2.34 (m, 1H), 2.47 (dtd, J = 15.5, 10.2, 5.2 Hz, 1H), 2.71 (dtd, J = 15.5, 10.2, 5.2 Hz, 1H), 3.22, 3.29 (ABqdd, J = 17.9, 10.2, 5.2 Hz, 2H), 4.16−4.35 (m, 4H), 7.34 (t, J = 7.9 Hz, 1H), 7.68 (ddd, J = 7.9, 1.7, 0.9 Hz, 1H), 7.88 (ddd collapsed to dt, J = 7.9, 1.3 Hz, 1H), 8.08 (dd collapsed to t, J = 1.3 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 14.1, 16.5 (d, J = 5.0 Hz), 16.6 (d, J = 5.0 Hz), 17.2 (d, J = 7.0 Hz), 28.1, 34.0 (d, J = 4.0 Hz), 38.3, 64.0 (d, J = 7.0 Hz), 64.7 (d, J = 7.0 Hz), 93.2 (d, J = 150.0 Hz), 123.2, 126.8, 130.4, 131.2, 136.3, 138.3, 197.0; ^{31}P NMR (162 MHz, CDCl$_3$) δ 16.1; MS (ES$^+$, Ar) m/z (rel intensity) 453 ([MH + 3]$^+$, 21), 452 ([MH + 2]$^+$, 99), 451 ([MH + 1]$^+$, 22), 450 (MH$^+$, 100), 406 (11), 405 (49), 404 (11), 403 (54), 377 (9), 375 (9), 359 (10), 357 (11), 267 (22), 265 (22), 207 (23); HRMS (ES$^+$, Ar) calcd for $\mathrm{C_{17}H_{26}NO_6PBr}$ (MH$^+$) 450.0681, found 450.0684; $[\alpha]^{25}_{D}$ = −9.70° (c = 1.00, CHCl$_3$); HPLC Chiralcel OD-H (pet ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 216 nm), t_R (major) = 20.2 min, t_R (minor) = 23.0 min; 96% ee.

*Diethyl 4-(3-bromophenyl)-1-cyclopropyl-1-nitro-4-oxobutylphosphonate (**7c**).* Colorless oil; Yield 84 mg, 94%; IR (neat, cm^{-1}) 3065 (m), 2983 (vs), 2931 (s), 2913 (s), 2871 (m), 1691 (vs), 1547 (vs), 1474 (m), 1441 (s), 1335 (w), 1256 (s), 1210 (m), 1163 (m), 1097 (m), 1047 (s), 974 (m), 842 (w), 788 (s), 758 (s), 737 (m), 603 (m), 567 (s); ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.62−0.71 (m, 2H), 0.72−0.82 (m, 2H), 1.34 (t, J = 7.4 Hz, 3H), 1.39 (t, J = 7.1 Hz, 3H), 1.74 (sextet, J = 7.1 Hz, 1H), 2.23 (ddt, J = 15.4, 11.1, 4.4 Hz, 1H), 2.41 (dtd, J = 15.4, 11.2, 4.4 Hz, 1H), 3.10 (ddd, J = 18.2, 11.1, 4.4 Hz, 1H), 3.48 (ddd, J = 18.2, 11.2, 4.4 Hz, 1H), 4.16−4.28 (m, 2H), 4.31−4.41 (m, 2H), 7.32 (t, J = 7.9 Hz, 1H), 7.67 (ddd, J = 7.9, 1.8, 1.0 Hz, 1H), 7.86 (ddd collapsed to dt, J = 7.9, 1.0 Hz, 1H), 8.06 (dd collapsed to t, J = 1.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 2.9 (d, J = 6.0 Hz), 3.9 (d, J = 3.0 Hz), 16.5 (d, J = 6.0 Hz), 16.6 (d, J = 6.0 Hz), 18.2, 25.8, 33.8 (d, J = 2.0 Hz), 63.7 (d, J = 8.0 Hz), 64.8 (d, J = 6.0 Hz), 92.9 (d, J = 156.0 Hz), 123.1, 126.8, 130.4, 131.1, 136.3, 138.3, 197.1; ^{31}P NMR (162 MHz, CDCl$_3$) δ 15.8; MS (ES$^+$, Ar) m/z (rel intensity) 451 ([MH + 3]$^+$, 24), 450 ([MH + 2]$^+$, 88), 449 ([MH + 1]$^+$, 25), 448 (MH$^+$, 100), 404 (22), 403 (93), 402 (27), 401 (81), 265 (30), 263 (40); HRMS (ES$^+$, Ar) calcd for $\mathrm{C_{17}H_{24}NO_6PBr}$ (MH$^+$) 448.0525, found 448.0523; $[\alpha]^{25}_{D}$ = −2.10° (c = 1.00, CHCl$_3$); HPLC Chiralcel OD-H (pet ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 230 nm), t_R (major) = 24.1 min, t_R (minor) = 31.8 min; 92% ee.

*Diethyl 1-(3-bromophenyl)-4-nitro-1-oxotridecan-4-ylphosphonate (**7d**).* Colorless oil; Yield 105 mg, 98%; IR (neat, cm^{-1}) 3064 (m), 2930 (vs), 2860 (vs), 1692 (vs), 1548 (vs), 1467 (s), 1444 (s), 1393 (w), 1369 (w), 1340 (w), 1263 (m), 1207 (m), 1163 (m), 1096 (m), 1067 (s), 951 (m), 904 (w), 864 (w), 790 (s), 761 (s), 739 (s), 700 (m), 682 (m), 566 (m); ^{1}H NMR (400 MHz, CDCl$_3$) δ 0.87 (t, J = 6.9 Hz, 3H), 1.18−1.32 (m, 13H), 1.35 (t, J = 7.1 Hz, 3H), 1.37 (t, J = 7.1 Hz, 3H), 1.41−1.54 (m, 1H), 2.05−2.20 (m, 1H), 2.23−2.37 (m, 1H), 2.46 (dtd, J = 15.4, 10.0, 5.4 Hz, 1H), 2.72 (dtd, J = 15.4, 10.0, 5.4 Hz, 1H), 3.26 (ABqdd, J = 17.9, 10.0, 5.4 Hz, 2H), 4.11−4.35 (m, 4H), 7.34 (t, J = 7.9 Hz, 1H), 7.69 (ddd, J = 7.9, 1.8, 1.0 Hz, 1H), 7.89 (ddd collapsed to dt, J = 7.9, 1.0 Hz, 1H) 8.08 (dd collapsed to dt, J = 1.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 14.2, 16.5 (d, J = 5.0 Hz), 16.6 (d, J = 5.0 Hz), 22.8, 23.6, 23.7, 28.1, 29.3 (d, J = 3.0 Hz), 29.6, 29.6, 32.0, 34.0 (d, J = 4.0 Hz), 36.4, 64.0 (d, J = 7.0 Hz), 64.7 (d, J = 7.0 Hz), 93.2 (d, J = 150.0 Hz), 123.2, 126.8, 130.4, 131.2, 136.3, 138.4, 197.1; ^{31}P NMR (162 MHz, CDCl$_3$) δ 16.2; MS (ES$^+$, Ar) m/z (rel intensity) 559 ([MNa + 3]$^+$, 27), 558 ([MNa + 2]$^+$, 100), 557 ([MNa + 1]$^+$, 28), 556 (MNa$^+$, 100); HRMS (ES$^+$, Ar) calcd for $\mathrm{C_{23}H_{37}NO_6PBrNa}$ (MNa$^+$) 556.1434, found 556.1434; $[\alpha]^{25}_{D}$ = −6.72° (c = 1.00, CHCl$_3$); HPLC Chiralcel OD-H (pet ether/i-PrOH =95/5, flow rate 0.5 mL/min, λ = 230 nm), t_R (major) = 15.3 min, t_R (minor) = 18.3 min; 95% ee.

*Ethyl 8-(3-bromophenyl)-5-(diethoxyphosphoryl)-5-nitro-8-oxooctanoate (**7e**).* Colorless oil; Yield 99 mg, 95%; IR (neat, cm^{-1}) 3062 (m), 2983 (vs), 2939 (vs), 1727 (vs), 1697 (vs), 1548 (vs), 1477 (w), 1445 (w), 1420 (w), 1338 (vw), 1296 (w), 1261 (m), 1184 (m), 1163 (m), 1096 (m), 1047 (s), 1028 (s), 976 (w), 788 (s), 739 (vs), 703 (s), 684 (m), 563 (m); ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.19 (t, J = 7.1 Hz, 3H), 1.29 (t, J = 7.3 Hz, 3H), 1.31 (t, J = 7.3 Hz, 3H), 1.52−1.65 (m, 1H), 1.68−1.82 (m, 1H), 2.12−2.34 (m, 2H), 2.29 (t, J = 7.0 Hz, 2H), 2.42−2.54 (m, 1H), 2.59−2.73 (m, 1H), 3.22 (ABqdd, J = 9.3, 5.9, 3.0 Hz, 2H), 4.07 (q, J = 7.1 Hz, 2H), 4.12−4.27 (m, 4H), 7.28 (t, J = 7.9 Hz, 1H), 7.63 (ddd, J = 7.9, 1.8, 1.0 Hz, 1H), 7.83 (ddd collapsed to dt, J = 7.9, 1.0 Hz, 1H), 8.04 (dd collapsed to t, J = 1.4 Hz, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 14.4, 16.5 (d, J = 5.0 Hz), 16.6 (d, J = 5.0 Hz), 19.2, 19.3, 27.9, 33.7, 34.9, 60.8, 64.2 (d, J = 8.0 Hz), 64.8 (d, J = 6.0 Hz), 92.8 (d, J = 149.0 Hz), 123.2, 126.8, 130.4, 131.3, 136.3, 138.3, 172.7, 196.3; ^{31}P NMR (162 MHz, CDCl$_3$) δ 15.7; MS (ES$^+$, Ar) m/z (rel intensity) 525 ([MH + 3]$^+$, 25), 524 ([MH + 2]$^+$, 100), 523 ([MH + 1]$^+$, 25), 522 (MH$^+$, 100), 478 (40), 477 (36), 476 (40), 475 (30), 431 (20), 429 (20), 301 (31); HRMS (ES$^+$, Ar) calcd for $\mathrm{C_{20}H_{30}NO_8PBr}$ (MH$^+$) 522.0892, found 522.0872; $[\alpha]^{25}_{D}$ = −4.30° (c = 1.00, CHCl$_3$); HPLC Chiralpack IA (pet ether/i-PrOH = 80/20, flow rate 1.0 mL/min, λ = 250 nm), t_R (major) = 10.1 min, t_R (minor) = 8.4 min; 91% ee.

*Diethyl 6-(3-bromophenyl)-3-nitro-6-oxo-1-phenylhexan-3-ylphosphonate (**7f**).* Colorless oil; Yield 100 mg, 98%; IR (neat, cm^{-1}) 3063 (w), 3027 (w), 2982 (s), 2934 (m), 2870 (w), 1691 (vs), 1548 (vs), 1497 (w), 1442 (m), 1421 (m), 1393 (w), 1338 (w), 1257 (vs), 1209 (s), 1163 (w), 1096 (w), 1044 (vs), 974 (s), 791 (m), 756 (s), 738 (s), 701 (s); ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.29 (t, J = 7.1 Hz, 3H), 1.32 (t, J = 7.1 Hz, 3H), 2.32−2.45 (m, 1H), 2.46−2.64 (m, 3H), 2.65−2.79 (m, 2H), 3.22 (ABqdd, J = 18.0, 10.4, 5.0 Hz, 2H), 4.12−4.30 (m, 4H), 7.12 (dd, J = 7.7, 1.3 Hz, 2H), 7.16 (dt, J = 7.7, 1.3 Hz, 1H), 7.23 (t, J = 7.7 Hz, 2H), 7.28 (t, J = 7.9 Hz, 1H), 7.62

(ddd, J = 7.9, 1.8, 1.0 Hz, 1H), 7.82 (ddd, J = 7.9, 1.8, 1.0 Hz, 1H), 8.01 (dd collapsed to t, J = 1.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.5 (d, J = 6.0 Hz), 16.6 (d, J = 5.0 Hz), 28.6, 30.3 (d, J = 6.0 Hz), 33.9 (d, J = 4.0 Hz), 38.3, 64.1 (d, J = 7.0 Hz), 64.9 (d, J = 7.0 Hz), 93.0 (d, J = 150.0 Hz), 123.3, 126.7, 126.8, 128.6, 128.9, 130.4, 131.2, 136.4, 138.3, 140.1, 196.8; ^{31}P NMR (162 MHz, $CDCl_3$) δ 15.7; MS (ES$^+$, Ar) m/z (rel intensity) 515 ([MH + 3]$^+$, 25), 514 ([MH + 2]$^+$, 85), 513 ([MH + 1]$^+$, 20), 512 (MH$^+$, 100), 468 (18), 467 (61), 466 (20), 465 (66), 377 (13), 375 (14), 329 (15), 327 (19); HRMS (ES$^+$, Ar) calcd for $C_{22}H_{28}NO_6PBr$ (MH$^+$) 512.0838, found 512.0831; $[\alpha]^{25}_{D}$ = −7.58° (c = 1.00, $CHCl_3$); HPLC Chiralcel OD-H (pet ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 230 nm), t_R (major) = 37.6 min, t_R (minor) = 47.8 min; 98% ee.

*(R)-Diisopropyl 2-nitro-5-(4-nitrophenyl)-5-oxopentan-2-ylphosphonate (**13**).* Yellow oil; Yield 35 mg, 42%; IR (neat, cm^{-1}) 2983 (m), 2941 (w), 1696 (m), 1603 (w), 1546 (s), 1531 (s), 1463 (w), 1454 (w), 1386 (w), 1376 (w), 1347 (s), 1320 (w), 1255 (m), 1208 (w), 1179 (w), 1143 (w), 1103 (m), 996 (vs), 856 (m), 740 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34−1.41 (m, 12H), 1.84 (d, J = 14.2 Hz, 3H), 2.58 (dtd, J = 15.1, 10.2, 5.1 Hz, 1H), 2.78 (dtd, J = 15.1, 10.2, 5.1 Hz, 1H), 3.15, 3.25 (ABqdd, J = 17.8, 10.2, 5.1 Hz, 2H), 4.75−4.92 (m, 2H), 8.10 (d, J = 8.9 Hz, 2H), 8.31 (d, J = 8.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 23.7 (d, J = 6.0 Hz), 23.8 (d, J = 6.0 Hz), 24.3 (d, J = 3.0 Hz), 24.4 (d, J = 3.0 Hz), 30.1, 34.0 (d, J = 7.0 Hz), 73.5 (d, J = 7.0 Hz), 73.9 (d, J = 7.0 Hz), 89.4 (d, J = 150.0 Hz), 124.1, 129.3, 140.9, 150.7, 196.5; ^{31}P NMR (162 MHz, $CDCl_3$) δ 14.14; MS (ES$^+$, Ar) m/z (rel intensity) 441 ([MNa + 2]$^+$, 4), 440 ([MNa + 1]$^+$, 18), 439 (MNa$^+$, 100), 417 (4), 397 (13); HRMS (ES$^+$, Ar) calcd for $C_{17}H_{25}N_2O_8PNa$ (MNa$^+$, 100) 439.1241, found 439.1246; $[\alpha]^{25}_{D}$ = −5.38° (c = 1.00, $CHCl_3$); HPLC Chiralpack IC (pet ether/i-PrOH = 70/30, flow rate 1.0 mL/min, λ = 230 nm), t_R (major) = 22.3 min, t_R (minor) = 30.6 min; 74% ee.

Synthetic Applications of Nitrophosphonates 3b. *p-Tolyl 4-(diethoxyphosphoryl)-4-nitropentanoate (**8**).*[19] TFA (2.7 mmol, 200 μL) was added to a stirred solution of m-chloroperbenzoic acid (55−75%, 4 mmol, 1.0 g) in dichloromethane (3 mL) at rt and the stirring was continued for 6 h. A solution of **3b** (0.5 mmol, 179 mg) in dichloromethane (1 mL) was added to the reaction mixture and stirring was continued for another 14 h at rt. The reaction mixture was diluted with ether (15 mL), washed with a 1 N NaOH solution (10 mL), brine (10 mL) and dried over anhyd sodium sulfate. The organic layer was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography using EtOAc−pet ether (35%) as eluent to afford the ester **8**. Light yellow oil; Yield 63 mg, 93%; $[\alpha]^{25}_{D}$ = 2.77° (c = 1.00, $CHCl_3$); HPLC Chiralpack IA (pet ether/i-PrOH = 98/2, flow rate 1 mL/min, λ = 216 nm), t_R (major) = 38.5 min, t_R (minor) = 41.9 min; 95% ee.

*4-(Diethoxyphosphoryl)-4-nitropentanoic acid (**9**).* To a solution of **8** (149 mg, 0.40 mmol) in THF (5.0 mL) and H_2O (3.0 mL) was added $LiOH\cdot H_2O$ (33 mg, 0.80 mmol) and the mixture was stirred at room temperature for 30 min. The mixture was acidified with 1 N HCl and extracted with Et_2O (3 × 15 mL). The combined extract was dried over anhyd sodium sulfate. The organic layer was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography using EtOAc−pet ether (90%) as eluent to afford the acid **9**. Colorless oil; Yield 95 mg, 84%; IR (neat, cm^{-1}) 3459 (br w), 2990 (m), 1733 (s), 1549 (s), 1446 (w), 1390 (w), 1337 (w), 1243 (m), 1021 (vs), 980 (m), 860 (w), 740 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (t, J = 7.0 Hz, 3H), 1.32 (t, J = 7.0 Hz, 3H), 1.75 (d, J = 14.6 Hz, 3H), 2.29−2.50 (m, 3H), 2.53−2.73 (m, 1H), 4.13−4.26 (m, 4H), 9.92 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3 (d, J = 1.0 Hz), 16.4 (d, J = 1.0 Hz), 19.7, 28.5 (d, J = 9.0 Hz), 30.6, 64.8 (d, J = 7.0 Hz), 65.0 (d, J = 7.0 Hz), 89.0 (d, J = 151.0 Hz), 175.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ 16.4; MS (ES$^+$, Ar) m/z (rel intensity) 307 ([MNa + 1]$^+$, 10), 306 (MNa$^+$, 100), 284 (19), 266 (31), 242 (8), 234 (12); HRMS (ES$^+$, Ar) calcd for $C_9H_{18}NO_7PNa$ (MNa$^+$) 306.0713, found 306.0713; $[\alpha]^{25}_{D}$ = −1.38° (c = 1.00, $CHCl_3$).

*Diethyl 5-(hydroxyamino)-2-nitro-5-oxopentan-2-ylphosphonate (**12**).* To a solution of **8** (149 mg, 0.40 mmol) in EtOH-DCM (7:3, 7.0 mL) was added $HONH_2\cdot HCl$ (112 mg, 1.62 mmol, 4 equiv) and pyridine (131 μL, 1.62 mmol) at rt and the mixture was stirred at rt for 12 h. The mixture was concentrated in vacuo, and the residue was purified by silica gel column chromatography using EtOAc−MeOH (5%) as eluent to afford the hydroxamic acid **12**. Reddish oil; Yield 150 mg, 94%; IR (neat, cm^{-1}) 3226 (br vs), 2987 (s), 2929 (s), 1664 (s), 1550 (s), 1445 (m), 1389 (m), 1336 (m), 1243 (s), 1163 (m), 1092 (m), 1048 (s), 1024 (s), 980 (m), 912 (s), 861 (m), 795 (w), 735 (s), 647 (w), 587 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (t, J = 7.0 Hz, 3H), 1.38 (t, J = 7.0 Hz, 3H), 1.80 (d, J = 14.4 Hz, 3H), 2.19−2.38 (m, 2H), 2.39−2.54 (m, 1H), 2.58−2.72 (m, 1H), 4.17−4.32 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.3 (d, J = 5.0 Hz), 16.3 (d, J = 6.3 Hz), 19.8, 27.1 (d, J = 8.8 Hz), 31.1, 64.6 (d, J = 7.5 Hz), 65.0 (d, J = 7.5 Hz), 89.8 (d, J = 152.2 Hz), 169.4; ^{31}P NMR (202 MHz, $CDCl_3$) δ 16.4; MS (ES$^+$, Ar) m/z (rel intensity) 322 ([MNa + 1]$^+$, 10), 321 (MNa$^+$, 100); HRMS (ES$^+$, Ar) calcd for $C_9H_{19}N_2O_7PNa$ (MNa$^+$) 321.0822, found 321.0826; $[\alpha]^{25}_{D}$ = −4.64° (c = 0.56, $CHCl_3$).

*Diethyl 5-(benzylamino)-2-nitro-5-oxopentan-2-ylphosphonate (**11**).* To a solution of ester **8** (205 mg, 0.55 mmol) in THF (5 mL) was added benzylamine (120 μL, 1.10 mmol) and the mixture was refluxed for 24 h. The mixture was concentrated in vacuo, and the residue was dissolved in EtOAc (15 mL), the organic layer was washed with 1 N HCl (2 × 5 mL), dried over anhyd sodium sulfate and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography using EtOAc−Pet ether (50−90%) as eluent to afford the amide **11**. Colorless oil; Yield 168 mg, 82%; IR (neat, cm^{-1}) 3431 (br vs), 3302 (br vs), 2988 (w), 2923 (w), 1654 (s), 1546 (vs), 1454 (w), 1389 (w), 1336 (w), 1245 (s), 1162 (w), 1020 (vs), 977 (w), 860 (w), 751 (w), 701 (w); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (t, J = 7.1 Hz, 6H), 1.78 (d, J = 14.3 Hz, 3H), 2.22−2.39 (m, 2H), 2.45−2.59 (m, 1H), 2.62−2.76 (m, 1H), 4.15−4.27 (m, 4H), 4.41 (d, J = 5.4 Hz, 2H), 6.03 (t, J = 5.4 Hz, 1H), 7.23−7.30 (m, 3H), 7.30−7.36 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.4 (d, J = 6.0 Hz), 16.5 (d, J = 6.0 Hz), 20.1, 30.5 (d, J = 9.0 Hz), 31.5, 43.8, 64.4 (d, J = 7.0 Hz), 64.5 (d, J = 8.0 Hz), 89.6 (d, J = 152.2 Hz), 127.6, 127.9, 128.8, 138.2, 170.9; ^{31}P NMR (202 MHz, $CDCl_3$) δ 16.4; MS (ES$^+$, Ar) m/z (rel intensity) 396 ([MNa + 1]$^+$, 13), 395 (MNa$^+$, 100), 373 (45), 367 (13), 350 (26), 328 (19); HRMS (ES$^+$, Ar) calcd for $C_{16}H_{25}N_2O_6PNa$ (MNa$^+$) 395.1342, found 395.1344; $[\alpha]^{25}_{D}$ = −5.68° (c = 1.00, $CHCl_3$); HPLC Chiralcel AD-H (pet ether/i-PrOH = 95/5, flow rate 0.5 mL/min, λ = 204 nm), t_R (major) = 20.3 min, t_R (minor) = 26.0 min; 95% ee.

*Diethyl 2-amino-5-(benzylamino)-5-oxopentan-2-ylphosphonate (**10**).* Activated Zn (440 mg, 6.71 mmol) was added to a solution of **10** (100 mg, 0.27 mmol, 95% ee) in EtOH (5 mL) and 2 N HCl (2 mL) at 0 °C. The reaction mixture was stirred for 2 h at rt. Then the crude residue was filtered through Celite and concentrated under reduced pressure. The resulting residue was dissolved in EtOAc (15 mL), the organic layer was washed with water (2 × 5 mL) and dried over anhyd sodium sulfate. The solvent was evaporated under reduced pressure to afford **10**. Colorless oil; Yield 89 mg, 96%; IR (neat, cm^{-1}) 3290 (br s), 3066 (w), 2981 (m), 2933 (w), 1651 (vs), 1552 (m), 1497 (w), 1455 (m), 1391 (w), 1223 (vs), 1163 (w), 1129 (w), 1026 (vs), 964 (vs), 791 (w), 753 (m), 701 (m); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25 (d, J = 15.9 Hz, 3H), 1.30 (t, J = 7.1 Hz, 6H), 1.92−2.08 (m, 2H), 2.20 (brs, 2H), 2.38, 2.46 (ABqdd, J = 15.0, 9.6, 6.5 Hz, 2H), 4.06−4.16 (m, 4H), 4.39 (d, J = 5.0 Hz, 2H), 6.50 (t, J = 5.0 Hz, 1H), 7.21−7.26 (m, 3H), 7.27−7.32 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.6, 16.6, 22.1, 30.4 (d, J = 7.5 Hz), 32.8 (d, J = 5.0 Hz), 43.6, 51.7 (d, J = 148.4 Hz), 62.7 (d, J = 7.5 Hz), 62.8 (d, J = 7.5 Hz), 127.4, 127.8, 128.7, 138.5, 173.0; ^{31}P NMR (202 MHz, $CDCl_3$) δ 30.4; MS (ES$^+$, Ar) m/z (rel intensity) 366 ([MNa + 1]$^+$, 18), 365 (MNa$^+$, 100), 343 (13); HRMS (ES$^+$, Ar) calcd for $C_{16}H_{27}N_2O_4PNa$ (MNa$^+$) 365.1601, found 365.1600; $[\alpha]^{25}_{D}$ = 1.80° (c = 1.00, MeOH); HPLC Lux Amylose-2 (pet ether/i-PrOH = 80/20, flow rate 0.5 mL/min, λ = 204 nm), t_R (major) = 46.6 min, t_R (minor) = 34.3 min; 95% ee.

*(R)-2-Nitro-5-(4-nitrophenyl)-5-oxopentan-2-ylphosphonic acid (**14**).* A solution of nitrophosphonate **3f** (100 mg, 0.26 mmol) in 8 N HCl (10 mL) was refluxed for 6 h. The reaction mixture was washed

with EtOAc (3 × 15 mL), the combined organic layer was dried over anhyd sodium sulfate. Evaporation of organic layer under reduced pressure afforded the phosphonic acid **13**. Gray solid; Yield 65 mg, 75%; mp 150−152 °C; IR (film, cm^{-1}) 3577 (m), 3110 (m), 3077 (w), 2913 (w), 2868 (w), 1697 (vs), 1602 (m), 1532 (vs), 1465 (w), 1444 (w), 1409 (m), 1388 (m), 1347 (vs), 1321 (s), 1207 (vs), 1110 (w), 1085 (w), 1011 (vs), 990 (vs), 940 (vs), 857 (vs), 832 (m), 784 (w), 736 (s), 685 (m); ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.72 (d, J = 13.4 Hz, 3H), 2.30−2.40 (m, 1H), 2.76 (dtd, J = 14.7, 10.6, 4.6 Hz, 1H), 2.99 (ddd, J = 18.1, 10.6, 4.6 Hz, 1H), 3.34 (ddd, J = 18.1, 10.6, 4.6 Hz, 1H), 8.19 (d, J = 8.9 Hz, 2H), 8.32 (d, J = 8.9 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 18.8, 29.0, 33.4 (d, J = 8.8 Hz), 89.5 (d, J = 133.8 Hz), 123.8, 129.4, 141.0, 150.0, 197.8; ^{31}P NMR (162 MHz, DMSO-d_6) δ 12.12; MS (ES$^+$, Ar) m/z (rel intensity) 334 ([MH + 1]$^+$, 14), 333 (MH$^+$, 100), 315 (13), 308 (9); HRMS (ES$^+$, Ar) calcd for $C_{11}H_{14}N_2O_8P$ (MH$^+$) 333.0482, found 333.0484; $[\alpha]^{25}_{D}$ = +8.73° (c = 0.33, DMSO).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of NMR spectra and HPLC for all the new/relevant compounds as well as CIF for representative compounds **3n** and **4a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

This paper is dedicated to Prof. S. M. Khopkar on account of his pioneering contributions to analytical chemistry.

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