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Tetrahedron: *Asymmetry* 18 (2007) 2719–2726

Cinchonine catalyzed diastereo- and enantioselective Michael addition of α-lithiated phosphonates to nitroalkenes

Vishal Rai,[a] Shaikh M. Mobin[b] and Irishi N. N. Namboothiri[a,*]

[a]*Department of Chemistry, Indian Institute of Technology, Bombay, Mumbai 400 076, India*
[b]*National Single Crystal X-ray Diffraction Facility, Indian Institute of Technology, Bombay, Mumbai 400 076, India*

Received 17 October 2007; accepted 2 November 2007

Abstract—Conjugate addition of α-lithiated benzyl- and alkylphosphonates to a variety of aromatic and heteroaromatic nitroalkenes in the presence of 50 mol % of cinchonine–Li catalyst system proceeded in high yields, diastereo- and enantioselectivities in most cases.

1. Introduction

Aminophosphonates are attractive synthetic targets primarily because of their ability to mimic biological processes, particularly, as transition state analogue inhibitors.[1] There are numerous methods, including asymmetric versions, for the synthesis of α-aminophosphonates[2] and their β-analogues.[3] However, only sporadic reports have appeared in the literature for the synthesis of γ-amino phosphonates.[4,5] We envisaged that γ-nitrophosphonate, the isosteric analogue of γ-aminophosphonate, could serve as a key intermediate for GABA (γ-aminobutyric acid) aminotransferase inactivation. We also felt that γ-nitrophosphonates having diverse functionalities in the flexible chain would substantially enhance the scope and potential of small synthetic molecules as enzyme mimics in the biological domain.

Recent developments in the catalytic asymmetric conjugate addition of various nucleophiles to nitroalkenes[6] and our own sustained interest in the chemistry of nitroalkenes[7] encouraged us to employ nitroalkenes for the stereoselective synthesis of γ-nitrophosphonates via the addition of phosphonate stabilized carbanions in the presence of suitable chiral catalysts. To the best of our knowledge, there are no reports in the literature on the asymmetric version, catalytic or otherwise, of the conjugate addition of phosphonates to nitroalkenes.

2. Results and discussion

Our preliminary experiments involving 'interaction-based catalyst optimization (IBCO)', base, solvent and nitroalkene screening for the Michael addition of benzylphosphonate **2a** enabled us to optimize the chemical yield and diastereoselectivity. Thus, the LDA (3 equiv) mediated Michael addition of benzylphosphonate **2a** to *p*-chloronitrostyrene **1a** in the presence of (±)-BINOL (0.5 equiv) in THF provided the Michael adduct **3a** in excellent yield (97%) and diastereoselectivity (88:12). Subsequently, **1a** and **2a** were chosen as model substrates for the enantioselective version of the reaction (Table 1). However, in the presence of (*S*)-(−)-BINOL **L1**, the reaction proceeded with only moderate enantioselectivity (38%, Table 1, entry 1). Compound (−)-DET **L2**, L-proline **L3** and (*R*)-diphenylprolinol **L4** also provided moderate results (Table 1, entries 2–4 and Fig. 1).[8] In this scenario, the success of bifunctional cinchona alkaloids in catalyzing various organic reactions, including Michael addition, in recent years prompted us to screen catalyst **L5** for our reaction.[9,10] Interestingly, although cinchona alkaloids have been used as organocatalysts in various asymmetric reactions,[9] including Michael addition to nitroalkenes,[10] to the best of our knowledge, a Li–alkaloid complex has not been employed as a catalyst.[11]

It is interesting to note that 50 mol % of cinchonine **L5** provided the desired product **3a** in high yield, and diastereo- and enantioselectivities (Table 1, entry 5). At higher catalyst loadings (1–3 equiv), the yield and enantioselectivity remain high, but the diastereoselectivity drops considerably

* Corresponding author. Tel.: +91 22 2576 7196; fax: +91 22 2576 7152; e-mail: irishi@iitb.ac.in

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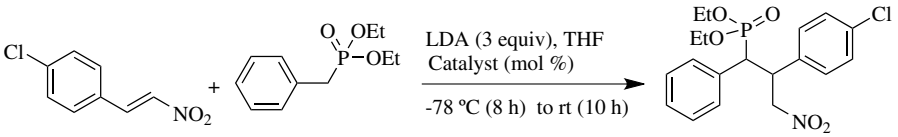
doi:10.1016/j.tetasy.2007.11.001

Table 1. Screening of chiral catalysts for the synthesis of nitrophosphonate **3a**



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

Entry	Catalyst	mol %	Yield[a] (%) of **3a**	dr[b] major/minor	% ee[c] major
1	**L1**	50	94	88:12	38 (*R*,*R*)
2	**L2**	50	30	65:35	16 (*S*,*S*)
3	**L3**	50	41	77:23	78 (*S*,*S*)
4	**L4**	50	80	46:54	37 (*R*,*R*)
5	**L5**	**50**	**81**	**96:04**	**>99 (*R*,*R*)**
6	**L5**	100	91	62:38	>99 (*R*,*R*)
7	**L5**	200	93	64:36	>99 (*R*,*R*)
8	**L5**	300	91	51:49	>99 (*R*,*R*)
9	**L5**	40	79	90:10	94 (*R*,*R*)
10	**L5**	30	81	88:12	92 (*R*,*R*)

[a] Isolated yield after purification by silica gel column chromatography.
[b] Determined by ^{1}H NMR.
[c] Determined by HPLC (Chiralcel OD-H column, 5% IPA in *n*-hexane), the absolute configuration of **3a** was determined by X-ray crystallography (vide infra).

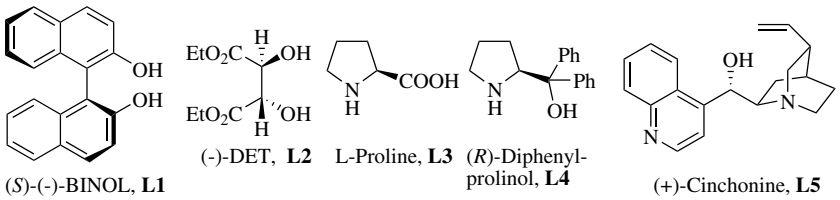


Figure 1. Catalysts screened.

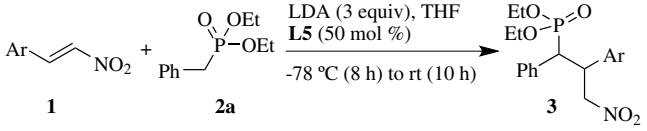
(Table 1, entries 6–8). As the catalyst loading was gradually decreased from 0.5 equiv to 0.4 and 0.3 equiv, the selectivities also decreased (Table 1, entries 9 and 10). Therefore, 50 mol % of the catalyst was used consistently in further reactions (Table 1, entry 5).

Under the above optimized conditions, that is, 3 equiv of LDA and 50 mol % of cinchonine **L5** in THF at −78 °C, we reacted a variety of aromatic and heteroaromatic nitroalkenes **1b–h** with benzylphosphonate **2a** (Table 2). The reaction of benzylphosphonate **2a** with nitrostyrene **1b** provided the Michael adducts **3b** in high yield (95%), low diastereoselectivity (68:32) and high enantioselectivity (>99%, Table 2, entry 2). The yield was quantitative and the diastereo- and enantioselectivities were moderate for *p*-methoxynitrostyrene **1c** (Table 2, entry 3). Although the yield and selectivities were excellent in the case of aromatic nitroalkene **1d** (Table 2, entry 4), all these factors were moderate for aromatic nitroalkenes possessing strongly electron-donating (NMe_2) or strongly electron-withdrawing (NO_2) groups (entries 5 and 6). As for the reactivity of heteroaromatic nitroalkenes, while **1g** was excellent in terms of yield and selectivities, **1h** reacted with benzyl phosphonate **2a** to afford the Michael adduct **3h** in moderate yield and diastereoselectivity, but with high enantioselectivity (Table 2, entries 7 and 8).

The scope of the reaction was subsequently extended to other benzyl- and alkylphosphonates **2b–f** (Table 3). Thus, the reaction of nitroalkene **1a** with *p*-chlorobenzylphosphonate **2b** provided the desired Michael adduct **3i** in good yield (69%) and excellent diastereo- and enantioselectivities (Table 3, entry 2). Comparable yield and remarkably high selectivities were maintained for the formation of Michael adduct **3k** from **1a** and naphthylphosphonate **2d** as well (Table 3, entry 4). Although low yield and moderate ee were encountered for the formation of Michael adduct **3j** from **1a** and *p*-nitrobenzylphosphonate **2c**, the diastereoselectivity remained high as in other cases (92:8, Table 3, entry 3). Finally, we investigated the reactivity of selected nitroalkenes with alkyl phosphonates **2e–f** (Table 3, entries 5–8). It is interesting to note that nitroalkene **1a** reacted well with methyl phosphonate **2e** and delivered the Michael adduct **3l** in a satisfactory yield and remarkable ee (>99%, Table 3, entry 5). On the other hand, moderate results were obtained when nitrostyrene **1b** and its *p*-methoxy analogue **1c** were reacted with phosphonate **2e** (Table 3, entries 6 and 7). The yield and selectivities were moderate in the case of alkylphosphonate **2f** as well (Table 3, entry 8).

The structure and stereochemistry of **3a** were determined by detailed NMR, including 2D-NOE, analysis. In principle, four stereoisomers, including two diastereomers and their enantiomers as well as their conformational isomers, can be visualized. The coupling between the two vicinal methine protons was in the range of $J = 9.3$–11.3 Hz in compounds **3a–3k** and **3o**, which suggested that their

Table 2. Michael addition of benzylphosphonate **2a** to various nitroalkenes **1a–h**[a]

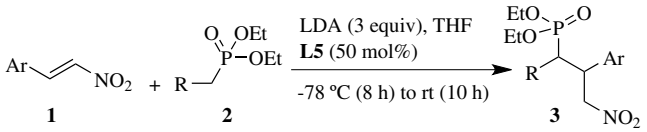


1 2a 3

Entry	1, Ar	3, yield[b] (%)	dr[c]	ee[c] (%) major
1	**1a**, 4-ClPh	**3a**, 81	96:04	>99 (*R*,*R*)
2	**1b**, Ph	**3b**, 95	68:32	>99 (*R*,*R*)
3	**1c**, 4-MeOPh	**3c**, 99	88:12	82 (*R*,*R*)
4	**1d**, Ar[d]	**3d**, 95	100:0	94 (*R*,*R*)
5	**1e**, 4-NMe_2Ph	**3e**, 63	52:48	86 (*R*,*R*)
6	**1f**, 4-NO_2Ph	**3f**, 65	68:32	78 (*R*,*R*)
7	**1g**, 2-Furyl	**3g**, 90	96:04	>99 (*R*,*R*)
8	**1h**, 3-Furyl	**3h**, 60	62:38	98 (*R*,*R*)

[a] The absolute configuration of **3a** was determined by X-ray crystallography (vide infra) and of **3b–h** based on comparison of ^{1}H NMR chemical shifts for the CH_2NO_2 group.
[b] Isolated yield after purification by silica gel column chromatography.
[c] Determined by HPLC (Chiralcel OD-H column, 5–20% IPA in *n*-hexane).
[d] 3,4-OCH_2OPh.

Table 3. Michael addition of phosphonates **2a–f** to various nitroalkenes **1a–c**[a]



1 2 3

Entry	1, Ar	2, R	3, yield[b] (%)	dr[c]	ee[c] (%) major
1	**1a**, 4-ClPh	**2a**, Ph	**3a**, 81	96:04	>99 (*R*,*R*)
2	**1a**, 4-Cl–Ph	**2b**, 4-ClPh	**3i**, 69	100:0	>99 (*R*,*R*)
3	**1a**, 4-Cl–Ph	**2c**, 4-NO_2Ph	**3j**, 45	92:08	80 (*R*,*R*)
4	**1a**, 4-Cl–Ph	**2d**, 2-Naph	**3k**, 74	100:0	>99[d]
5	**1a**, 4-Cl–Ph	**2e**, H	**3l**, 61	—	>99[e]
6	**1b**, Ph	**2e**, H	**3m**, 41	—	68[e]
7	**1c**, 4-MeOPh	**2e**, H	**3n**, 43	—	82[e]
8	**1a**, 4-Cl–Ph	**2f**, *n*-Pr	**3o**, 47	72:28	86 (*R*,*R*)

[a] The absolute configuration of **3a** was determined by X-ray crystallography and of **3i**, **3j** and **3o** based on comparison of ^{1}H NMR chemical shifts for the CH_2NO_2 group.
[b] Isolated yield after purification by silica gel column chromatography.
[c] Determined by HPLC (Chiralcel OD-H column, 5% IPA in *n*-hexane).
[d] (*R*,*S*) or (*S*,*R*).
[e] Absolute configuration was not determined for **3l–3n** (entries 5–7).

relative stereochemistry was *anti*. Additionally, ^{1}H–^{1}H 2D-NOE experiments on **3a** showed strong NOE between the nitromethyl protons and the CH_2 group of diethylphospho nate moiety, thus suggesting that the nitromethyl and phosphonate groups are *syn* to each other. Furthermore, NOE between the nitromethyl protons and the proton α to the phosphonate moiety together with lack of any appreciable NOE between the two vicinal benzylic protons indicated that the stereochemistry is either (1*R*,2*R*)-*syn* or (1*S*,2*S*)-*syn*. This was further unambiguously established by single crystal X-ray analysis (Fig. 2, see also Section 4). Thus, X-ray confirmed the *syn* relationship between the two aryl groups (dihedral angle 45.2°) as well as between the nitromethyl group and the phosphonate moiety (dihedral angle 70°) and the absolute stereochemistry (*R*,*R*). The configuration of **3b–k** and **3o** were assigned by correlating the ^{1}H NMR chemical shifts of the nitromethyl group in these compounds with that of **3a**.

The proposed mechanism envisages that the alkaloid moiety possessing a hydroxyl group (Brønsted acid) and a bridgehead nitrogen (Lewis base) acts as a bidentate ligand and chelates with a lithium coordinated with the carbanion (Scheme 1). The π-interaction between the quinoline moiety and the aromatic ring, if any, in the substrate provides a third point of interaction.[12]

3. Conclusions

A catalytic asymmetric version of the conjugate addition of phosphonate stabilized carbanions to nitroalkenes has been developed for the first time. Under the influence of a cinchonine–Li complex, various benzyl- and alkylphosphonates reacted with a variety of aromatic and hetero aromatic nitroalkenes to afford the adducts in high yields, and diastereo- and enantioselectivities.

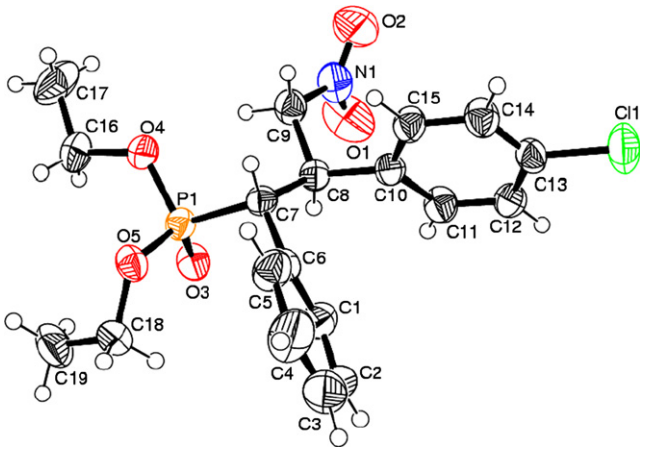
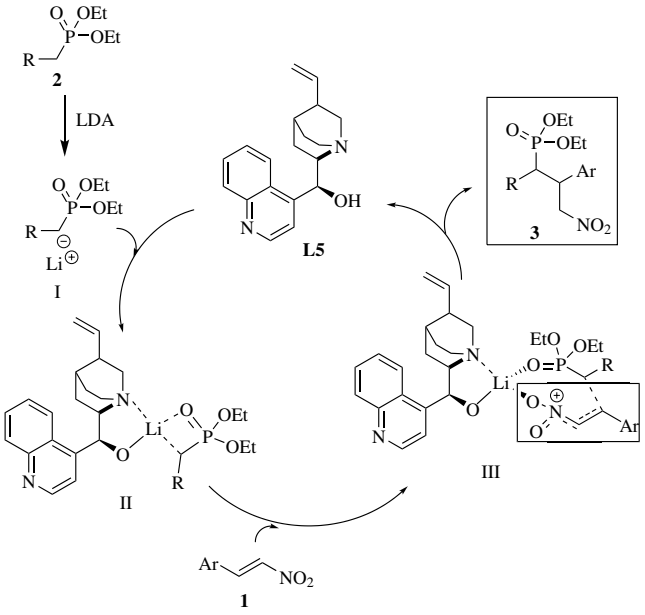


Figure 2. Single crystal X-ray structure of Michael adduct **3a**.

4. Experimental

4.1. General

The melting points were recorded on Thermonik melting point apparatus and are uncorrected. IR spectra were recorded on an Impact 400/Nicolet or Perkin Elmer Spectrum One FT spectrometer. NMR spectra (^{1}H, ^{13}C and ^{31}P) were recorded on an AMX-400 (Varian Mercury Plus OXFORD, broad band, auto switchable and inverse probe) or VXR-300S spectrometer. TMS was the internal standard for ^{1}H and ^{13}C and phosphoric acid was the external standard for ^{31}P. The coupling constants (J values) are given in Hertz. Mass spectra (LR and HR) were recorded at 60–70 eV on a Micromass Q-TOF mass spectrometer under ESI mode. Enantioselectivities were determined with JASCO (PU-2080PLUS pump with UV-2075PLUS detector) HPLC using Chiralcel OD-H column. The Michael adducts were purified by column chromatography on silica gel (60–120 mesh) using a mixture of ethyl acetate and petroleum ether as eluent. Nitroalkenes[13] and phosphonates[14] were prepared following the literature protocols.



Scheme 1. Proposed mechanism of the Michael addition of phosphonate **2** to nitroalkene **1** catalyzed by an Li–cinchonine complex.

4.2. General procedure for the Michael addition of phosphonate 2 to nitroalkene 1 in the presence of an Li–cinchonine L5 complex

A solution of LDA (3 mmol) in THF (3 ml) was prepared by the dropwise addition of *n*-BuLi (3 mmol, 1.6 M solution in hexanes) to diisopropylamine (3 mmol) in THF (3 ml) at 0 °C followed by stirring for 30 min at the same temperature. To this freshly prepared LDA, cooled to −78 °C, was added phosphonate **2** (1 mmol) dropwise. After stirring the reaction mixture for 1 h, cinchonine **L5** in THF (2 ml) was added and the reaction mixture was stirred for an additional 30 min. Subsequently, nitroalkene **1** (1.5 mmol) in THF (1 ml) was added to the reaction mixture and the temperature was maintained at −78 °C for an additional 8 h. The reaction mixture was warmed to ambient temperature and stirring continued for 10 h. The reaction mixture was quenched with saturated aqueous NH_4Cl (2 ml), further saturated with NaCl and extracted with ethyl acetate (3 × 10 ml). The combined organic layers were washed with brine (5 ml), dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography (ethyl acetate/pet ether, 0–50%, gradient elution). The compound was further purified by recrystallization (CH_2Cl_2/pet ether ~10:1).

4.2.1. Diethyl 2-(4-chlorophenyl)-3-nitro-1-phenylpropylphosphonate 3a. Colourless solid; Yield 81% (mixture of diastereomers, crude 96:04, after recrystallization 100:0). Major diastereomer: R_f 0.30 (EtOAc/pet ether 1:1); mp 122–123 °C; IR (film, cm^{-1}) 3055 (m), 2985 (m), 1556 (s), 1494 (m), 1379 (m), 1266 (s), 967 (m), 740 (s); ^{1}H NMR ($CDCl_3$) δ 1.08 (t, $J = 7.3$ Hz, 3H), 1.29 (t, $J = 7.1$ Hz, 3H), 3.34 (dd, $J = 21.0$, 10.8 Hz, 1H), 3.61 (m, 1H), 3.84–3.98 (m, 1H), 4.00–4.16 (m, 2H), 4.18–4.27 (m, 1H), 4.79 (dd, $J = 13.2$, 10.6 Hz, 1H), 5.32 (dd, $J = 13.2$, 4.8 Hz, 1H), 6.93 (d, $J = 8.4$ Hz, 2H), 7.09 (d, $J = 8.4$ Hz, 2H), 7.12–7.22 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 15.9 (d, $J = 6.1$ Hz), 16.1 (d, $J = 6.1$ Hz), 44.9, 47.7 (d, $J = 135.8$ Hz), 62.0 (d, $J = 7.7$ Hz), 63.2 (d, $J = 7.7$ Hz), 79.0, 127.4, 128.3, 128.4, 129.5, 129.6 (d, $J = 7.7$ Hz), 133.1, 133.7 (d, $J = 6.1$ Hz), 135.7 (d, $J = 3.8$ Hz). Multiplicities and J values indicated are only for C–P coupling; ^{31}P NMR ($CDCl_3$) δ 23.36; MS (TOF ES+) *m/e* (rel intensity) 434 (MNa^+, 40), 413 ($[M+2]^+$, 80), 397 (10), 365 (4), 295 (3), 227 (15), 205 (10), 149 (100); HRMS: (MNa^+) calcd for $C_{19}H_{23}NO_5NaPCl$, 434.0900; found, 434.0912. Selected X-ray crystallographic data for **3a**: $C_{19}H_{23}ClNO_5P$, $M = 411.80$, orthorhombic, space group $Pc21b$, $a = 9.4400(7)$ Å, $b = 11.585(2)$ Å, $c = 18.6550(9)$ Å, $\alpha = \beta = \gamma = 90°$; $U = 2040.2(4)$ Å^3, $D_c = 1.341$ Mg/m^3, $Z = 4$, $F(000) = 864$, $\lambda = 0.71073$ Å, $\mu = 0.295$ mm^{-1}, total/unique reflections = 1893/1893 [$R_{int} = 0.0000$], $T = 293(2)$ K, θ range = 2.16–24.98°, Final R indices [$I > 2\sigma(I)$] $R_1 = 0.0416$, $wR_2 = 0.0864$, R indices (all data) $R_1 = 0.1012$, $wR_2 = 0.1005$, Flack x parameter = 0.0557 (0.1302). Crystallographic data (excluding

structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as Supplementary Publication Number CCDC 654262. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

4.2.2. Diethyl 3-nitro-1,2-diphenylpropylphosphonate 3b. Colourless solid; Yield 95% (inseparable mixture of diastereomers crude 68:32, after attempted separation by silica gel column chromatography and fractional crystallization ~50:50); R_f 0.30 (EtOAc/pet ether 1:1); mp 117–118 °C; IR (film, cm^{-1}) 3064 (w), 3033 (w), 2983 (w), 2909 (w), 1603 (w), 1554 (s), 1496 (m), 1455 (m), 1380 (m), 1242 (m), 1054 (s), 1026 (s), 968 (s) 701 (s).

Diastereomer 1: ^{1}H NMR ($CDCl_3$) δ 1.09 (t, $J = 7.1$ Hz, 3H), 1.29 (t, $J = 7.3$ Hz, 3H), 3.39 (dd, $J = 21.0$, 10.8 Hz, 1H), 3.62 (m, 1H), 3.95 (m, 1H), 4.10 (m, 2H), 4.23 (dABq, $J = 14.8$, 10.8 Hz, 1H), 4.84 (dd, $J = 12.8$, 10.8 Hz, 1H), 5.34 (dd, $J = 14.8$, 12.8 Hz, 1H), 7.09–7.30 (m, 10H). Multiplicities and J values indicated are both for H–H and P–H coupling; ^{13}C NMR ($CDCl_3$) δ 15.9 (d, $J = 3.0$ Hz), 16.0 (d, $J = 3.0$ Hz), 45.0, 48.5 (d, $J = 140.3$ Hz), 61.3 (d, $J = 7.7$ Hz), 62.9 (d, $J = 6.9$ Hz), 78.7 (d, $J = 14.6$ Hz), 127.9, 128.2, 128.4, 128.5, 129.0, 129.6 (d, $J = 6.9$ Hz), 133.6 (d, $J = 6.1$ Hz), 137.5 (d, $J = 4.0$ Hz). Multiplicities and J values indicated are only for C–P coupling; ^{31}P NMR ($CDCl_3$) δ 23.29.

Diastereomer 2: ^{1}H NMR ($CDCl_3$) δ 0.87 (t, $J = 6.9$ Hz, 3H), 1.00 (t, $J = 7.1$ Hz, 3H), 3.38 (dd, $J = 22.1$, 9.4 Hz, 1H), 3.79 (m, 1H), 3.95 (m, 1H), 4.10 (m, 2H), 4.32 (ABqd, $J = 9.4$, 4.1 Hz, 1H), 4.51 (dd, $J = 12.6$, 9.4 Hz, 1H), 4.64 (dd, $J = 12.6$, 4.1 Hz, 1H), 7.20–7.40 (m, 10H). Multiplicities and J values indicated are both for H–H and P–H coupling; ^{13}C NMR ($CDCl_3$) δ 16.2 (d, $J = 8.1$ Hz), 16.3 (d, $J = 8.1$ Hz), 45.6, 47.9 (d, $J = 135.7$ Hz), 62.0 (d, $J = 6.9$ Hz), 63.3 (d, $J = 7.7$ Hz), 79.3, 127.4 (d, $J = 3.8$ Hz), 127.5, 128.3, 128.4, 128.6, 129.7 (d, $J = 6.9$ Hz), 134.0 (d, $J = 6.8$ Hz), 137.2 (d, $J = 14.4$ Hz). Multiplicities and J values indicated are only for C–P coupling; ^{31}P NMR ($CDCl_3$) δ 23.79.

The peaks for the two diastereomers could be distinguished from NMR of the crude product (ratio 68:32).

MS (TOF ES+) m/e (rel intensity) 400 ([M+Na]$^+$, 45), 378 ([MH$^+$, 100), 331 (5), 204 (5); HRMS: (MH$^+$) calcd for $C_{19}H_{25}NO_5P$, 378.1470; found, 378.1470.

4.2.3. Diethyl 2-(4-methoxyphenyl)-3-nitro-1-phenylpropylphosphonate 3c. Colourless solid; Yield 99% (mixture of diastereomers, crude 88:12, after recrystallization 100:0). Major diastereomer: R_f 0.30 (EtOAc/pet ether 1:1); mp 123–124 °C; IR (film, cm^{-1}) 3055 (w), 2986 (w), 1556 (s), 1514 (m), 1380 (m), 1266 (s), 966 (m), 741 (s); ^{1}H NMR ($CDCl_3$) δ 1.09 (t, $J = 7.0$ Hz, 3H), 1.29 (t, $J = 6.9$ Hz, 3H), 3.35 (dd, $J = 21.0$, 10.8 Hz, 1H), 3.57–3.70 (m, 1H), 3.67 (s, 3H), 3.84–3.98 (m, 1H), 4.00–4.24 (m, 3H), 4.78 (dd, $J = 12.8$, 10.6 Hz, 1H), 5.29 (dd, $J = 12.8$, 4.8 Hz, 1H), 6.63 (d, $J = 8.8$ Hz, 2H), 6.90 (d, $J = 8.8$ Hz, 2H), 7.09–7.19 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 16.1 (d, $J = 6.1$ Hz), 16.3 (d, $J = 6.1$ Hz), 44.9, 48.1 (d, $J = 135.8$ Hz), 55.0, 62.0 (d, $J = 7.6$ Hz), 63.2 (d, $J = 6.9$ Hz), 79.6 (d, $J = 1.5$ Hz), 113.7, 127.3 (d, $J = 2.3$ Hz), 128.3 (d, $J = 2.3$ Hz), 128.9 (d, $J = 14.5$ Hz), 129.2, 129.8 (d, $J = 6.9$ Hz), 134.2 (d, $J = 6.9$ Hz), 158.6. Multiplicities and J values indicated are only for C–P coupling; ^{31}P NMR ($CDCl_3$) δ 23.88; MS (TOF ES+) m/e (relative intensity) 430 (MNa$^+$, 55), 408 (MH$^+$, 100), 361 (30), 158 (11), 141 (20); HRMS: (MH$^+$) calcd for $C_{20}H_{27}NO_6P$, 408.1576; found, 408.1584.

4.2.4. Diethyl 2-(benzo[*d*][1,3]dioxol-6-yl)-3-nitro-1-phenylpropylphosphonate 3d. Colourless solid; Yield 95% (single diastereomer); R_f 0.30 (EtOAc/pet ether 1:1); mp 145–146 °C; IR (film, cm^{-1}) 2985 (w), 2906 (w), 1554 (s), 1504 (m), 1491 (m), 1445 (m), 1381 (m), 1249 (s), 1040 (s), 967 (m); ^{1}H NMR ($CDCl_3$) δ 1.09 (t, $J = 7.2$ Hz, 3H), 1.29 (t, $J = 7.1$ Hz, 3H), 3.32 (dd, $J = 20.8$, 11.0 Hz, 1H), 3.58–3.64 (m, 1H), 3.83–4.97 (m, 1H), 4.04–4.20 (m, 3H), 4.75 (dd, $J = 12.9$, 11.0 Hz, 1H), 5.30 (dd, $J = 12.9$, 4.6 Hz, 1H), 5.83 (dd, $J = 2.2$, 1.5 Hz, 2H), 6.44 (dd, $J = 7.9$, 1.7 Hz, 2H), 6.50 (d, $J = 1.7$ Hz, 1H), 7.10–7.25 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 16.0 (d, $J = 6.1$ Hz), 16.1 (d, $J = 6.1$ Hz), 45.3, 47.9 (d, $J = 135.0$ Hz), 61.9 (d, $J = 7.7$ Hz), 63.1 (d, $J = 6.1$ Hz), 79.4, 100.9, 107.9, 121.8, 127.2, 128.2 (×2), 129.6 (d, $J = 7.7$ Hz), 130.8 (d, $J = 15.3$ Hz), 134.0 (d, $J = 6.1$ Hz), 146.6, 147.4. Multiplicities and J values indicated are only for C–P coupling; ^{31}P NMR ($CDCl_3$) 23.72; MS (TOF ES+) m/e (rel intensity) 444 (MNa$^+$, 75), 422 (MH$^+$, 100), 375 (12), 159 (5); HRMS: (MH$^+$) calcd for $C_{20}H_{25}NO_7P$, 422.1369; found, 422.1367.

4.2.5. Diethyl 2-(4-(dimethylamino)phenyl)-3-nitro-1-phenylpropylphosphonate 3e. Colourless solid; Yield 63% (mixture of diastereomers in 52:48 ratio, the major isomer was isolated in diastereomerically pure form by repeated recrystallization from CH_2Cl_2/pet ether 10:1). Major diastereomer: R_f 0.30 (EtOAc/pet ether 1:1); mp 140–142 °C; IR (film, cm^{-1}) 2920 (w), 1617 (m), 1548 (s), 1525 (m), 1380 (m), 1354 (m), 1234 (m), 1164 (w), 1046 (m), 1017 (m), 947 (m); ^{1}H NMR ($CDCl_3$) δ 1.09 (t, $J = 7.0$ Hz, 3H), 1.30 (t, $J = 6.9$ Hz, 3H), 2.82 (s, 6H), 3.37 (dd, $J = 21.1$, 10.5 Hz, 1H), 3.54–3.69 (m, 1H), 3.84–3.96 (m, 1H), 3.98–4.18 (m, 3H), 4.77 (dd, $J = 12.7$, 10.5 Hz, 1H), 5.26 (dd, $J = 12.7$, 5.0 Hz, 1H), 6.45 (d, $J = 8.8$ Hz, 2H), 6.83 (d, $J = 8.8$ Hz, 2H), 7.10–7.18 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 16.2 (d, $J = 5.3$ Hz), 16.3 (d, $J = 6.1$ Hz), 40.3, 44.8 (d, $J = 1.6$ Hz), 48.2 (d, $J = 134.3$ Hz), 61.9 (d, $J = 7.6$ Hz), 63.2 (d, $J = 7.6$ Hz), 79.7 (d, $J = 2.3$ Hz), 112.2, 124.3 (d, $J = 14.5$ Hz), 127.2 (d, $J = 3.1$ Hz), 128.3 (d, $J = 2.3$ Hz), 128.8, 129.9 (d, $J = 6.1$ Hz), 134.4 (d, $J = 6.1$ Hz), 149.6. Multiplicities and J values indicated are only for C–P coupling; ^{31}P NMR ($CDCl_3$) δ 24.23; MS (TOF ES+) m/e (rel intensity) 421 (MH$^+$, 100), 374 (11), 360 (7), 236 (16), 149 (20), 134 (30); HRMS: (MH$^+$) calcd for $C_{21}H_{30}N_2O_5P$, 421.1892; found, 421.1900.

4.2.6. Diethyl 3-nitro-2-(4-nitrophenyl)-1-phenylpropylphosphonate 3f. Colourless solid; Yield 65% (mixture of

diastereomers in 68:32 ratio, separated by repeated recrystallization from CH_2Cl_2/hexane 10:1).

Major diastereomer: R_f 0.39 (EtOAc/pet ether 1:1); mp 139–140 °C; IR (film, cm^{-1}) 2991 (m), 2919 (w), 1604 (w), 1552 (s), 1520 (s), 1382 (m), 1345 (s), 1227 (s), 1042 (s), 1015 (s), 965 (s), 944 (m), 754 (m); ^1H NMR ($CDCl_3$) δ 1.08 (t, $J = 7.0$ Hz, 3H), 1.31 (t, $J = 7.2$ Hz, 3H), 3.39 (dd, $J = 20.4$, 11.1 Hz, 1H), 3.56–3.66 (m, 1H), 3.88–3.99 (m, 1H), 4.08–4.17 (m, 2H), 4.33–4.41 (m, 1H), 4.86 (dd, $J = 13.4$, 10.9 Hz, 1H), 5.39 (dd, $J = 13.4$, 4.7 Hz, 1H), 7.10–7.27 (m, 7H), 7.99 (d, $J = 9.0$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 16.2 (d, $J = 6.1$ Hz), 16.4 (d, $J = 6.1$ Hz), 45.4, 47.7 (d, $J = 137.3$ Hz), 62.4 (d, $J = 7.7$ Hz), 63.7 (d, $J = 6.9$ Hz), 78.7, 123.7, 128.0 (d, $J = 2.3$ Hz), 128.8 (d, $J = 1.5$ Hz), 129.4, 129.7 (d, $J = 6.9$ Hz), 133.4 (d, $J = 6.1$ Hz), 145.1 (d, $J = 14.6$ Hz), 147.2. Multiplicities and J values indicated are only for C–P coupling; ^{31}P NMR ($CDCl_3$) δ 22.71. MS (TOF ES+) m/e (relative intensity) 423 (MH^+, 85), 159 (15), 99 (100); HRMS: (MH^+) calcd for $C_{19}H_{24}N_2O_7P$, 423.1321; found, 423.1333.

Minor diastereomer: R_f 0.40 (EtOAc/pet ether 1:1); mp 134–136 °C; IR (film, cm^{-1}) 2990 (m), 2921 (m), 2953 (w), 1604 (w), 1552 (s), 1520 (s), 1382 (m), 1346 (s), 1227 (s), 1213 (m), 1042 (s), 1014 (s), 965 (s), 944 (s), 854 (m), 697 (m), 566 (m); ^1H NMR ($CDCl_3$) δ 0.87 (t, $J = 7.1$ Hz, 3H), 1.03 (t, $J = 7.1$ Hz, 3H), 3.25–3.40 (m, 1H), 3.32 (dd, $J = 21.8$, 9.5 Hz, 1H), 3.61–3.86 (m, 3H), 4.30 (ABqd, $J = 9.5$, 3.9 Hz, 1H), 4.48 (dd, $J = 12.8$, 9.5 Hz, 1H), 4.63 (dd, $J = 12.8$, 3.9 Hz, 1H), 7.19 (d, $J = 8.7$ Hz, 2H), 7.29 (d, $J = 8.7$ Hz, 2H), 7.37 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 16.1 (2 × d, $J = 5.4$ Hz), 44.6, 48.7 (d, $J = 139.5$ Hz), 61.6 (d, $J = 7.7$ Hz), 63.4 (d, $J = 7.7$ Hz), 78.6 (d, $J = 14.6$ Hz), 128.5 (d, $J = 2.3$ Hz), 128.9, 129.4 (d, $J = 1.5$ Hz), 129.7 (d, $J = 6.9$ Hz), 129.9, 133.3 (d, $J = 6.1$ Hz), 134.0, 136.2 (d, $J = 5.4$ Hz). Multiplicities and J values indicated are only for C–P coupling; ^{31}P NMR ($CDCl_3$) δ 22.92. MS (TOF ES+) m/e (relative intensity) 423 (MH^+, 100), 159 (75), 99 (58); HRMS: (MH^+) calcd for $C_{19}H_{24}N_2O_7P$, 423.1321; found, 423.1337.

4.2.7. Diethyl 2-(furan-2-yl)-3-nitro-1-phenylpropylphosphonate 3g. Brown liquid; Yield 90% (inseparable mixture of diastereomers in 96:04 ratio, part of the major diastereomer was removed during attempted purification, that is, removal of unreacted benzyl phosphonate and probably an unexpected change at the configurationally labile C–P carbon changed the original ratio of 96:04 to 60:40, see ^1H NMR); R_f 0.30 (EtOAc/pet ether 1:1); IR (film, cm^{-1}) 2984 (m), 2910 (w), 1556 (s), 1497 (w), 1455 (w), 1378 (m), 1244 (m), 1053 (s), 1024 (s), 970 (s).

Major diastereomer: ^1H NMR ($CDCl_3$) δ 1.09 (t, $J = 7.2$ Hz, 3H), 1.28 (t, $J = 7.0$ Hz, 3H), 3.51 (dd, $J = 20.5$, 10.2 Hz, 1H), 3.90 (m, 2H), 4.07 (m, 2H), 4.33 (ABqd, $J = 10.2$, 4.8 Hz, 1H), 4.86 (dd, $J = 13.2$, 10.2 Hz, 1H), 5.20 (dd, $J = 13.2$, 4.8 Hz, 1H), 5.89 (d, $J = 3.3$ Hz, 1H), 6.06 (dd, $J = 3.3$, 1.6 Hz, 1H), 7.19 (d, $J = 1.6$ Hz, 1H), 7.15–7.40 (m, 5H). Multiplicities and J values indicated are both for H–H and P–H coupling; ^{31}P NMR ($CDCl_3$) δ 23.23.

Minor diastereomer: ^1H NMR ($CDCl_3$) δ 0.93 (t, $J = 6.9$ Hz, 3H), 1.19 (t, $J = 7.0$ Hz, 3H), 3.43 (m, 1H), 3.57 (dd, $J = 22.0$, 8.8 Hz, 1H), 3.66 (m, 1H), 3.75 (m, 2H), 4.45 (ABqd, $J = 8.8$, 3.6 Hz, 1H), 4.50 (dd, $J = 11.7$, 8.8 Hz, 1H), 4.58 (dd, $J = 11.7$, 3.6 Hz, 1H), 6.23 (d, $J = 3.3$ Hz, 1H), 6.29 (dd, $J = 3.3$, 1.6 Hz, 1H), 7.40 (d, $J = 1.6$ Hz, 1H), 7.20–7.40 (m, 5H). Multiplicities and J values indicated are both for H–H and P–H coupling; ^{31}P NMR ($CDCl_3$) δ 22.97.

^{13}C NMR ($CDCl_3$, mixture of diastereomers) δ 15.9 (d, $J = 6.1$ Hz), 16.0 (2 × d, $J = 5.3$ Hz), 16.2 (d, $J = 5.4$ Hz), 38.8, 39.7, 45.3 (d, $J = 16.8$ Hz), 46.7 (d, $J = 19.8$ Hz), 61.6 (d, $J = 7.6$ Hz), 62.1 (d, $J = 7.6$ Hz), 63.1 (d, $J = 7.6$ Hz), 63.2 (d, $J = 7.6$ Hz), 76.5 (d, $J = 13.7$ Hz), 76.8, 109.0, 109.1, 110.0, 110.4, 127.5, 128.2, 128.3, 129.0, 129.3, 129.4, 133.1 (d, $J = 5.3$ Hz), 133.8 (d, $J = 6.8$ Hz), 142.0, 142.3, 149.6 (d, $J = 15.2$ Hz), 149.9 (d, $J = 6.1$ Hz). Multiplicities and J values indicated are only for C–P coupling. MS (TOF ES+) m/e (relative intensity) 390 (MNa^+, 5), 368 (MH^+, 100), 321 (28); HRMS: (MH^+) calcd for $C_{17}H_{23}NO_6P$, 368.1263; found, 368.1258.

4.2.8. Diethyl 2-(furan-3-yl)-3-nitro-1-phenylpropylphosphonate 3h. Colourless solid; Yield 60% (inseparable mixture of diastereomers in 62:38 ratio); R_f 0.30 (EtOAc/pet ether 1:1); mp 92–93 °C; IR (film, cm^{-1}) 2982 (s), 2020 (s), 1547 (s), 1446 (m), 1383 (m), 1231 (s), 1040 (s), 963 (s), 795 (m), 557 (m); ^1H NMR ($CDCl_3$) δ 0.92 (t, $J = 7.0$ Hz, 3H), 1.08 (t, $J = 7.2$ Hz, 3H), 1.18 (t, $J = 7.0$ Hz, 3H), 1.29 (t, $J = 7.0$ Hz, 3H), 3.32 (dd, $J = 21.1$, 10.3 Hz, 1H), 3.34 (dd, $J = 22.0$, 8.4 Hz, 1H), 3.40–3.50 (m, 1H), 3.58–3.69 (m, 1H), 3.76–4.29 (m, 8H), 4.33 (ABq, $J = 10.3$ Hz, 1H), 4.68 (dd, $J = 12.7$, 5.0 Hz, 1H), 4.71 (ABq, $J = 10.3$ Hz, 1H), 5.15 (dd, $J = 13.0$, 5.0 Hz, 1H), 6.12 (t, $J = 0.9$ Hz, 1H), 6.25 (t, $J = 0.9$ Hz, 1H), 7.00–7.02 (unresolved m, 1H), 7.16–7.26 (m, 6H), 7.32–7.40 (m, 7H). Multiplicities and J values indicated are both for H–H and P–H coupling; ^{13}C NMR ($CDCl_3$) δ 15.8 (d, $J = 8.1$ Hz), 15.9 (d, $J = 8.1$ Hz), 16.0 (d, $J = 8.1$ Hz), 16.1 (d, $J = 8.1$ Hz), 36.0, 36.5, 46.5 (d, $J = 55.4$ Hz), 48.3 (d, $J = 59.2$ Hz), 61.3 (d, $J = 7.6$ Hz), 61.9 (d, $J = 6.8$ Hz), 62.9 (d, $J = 7.6$ Hz), 63.1 (d, $J = 6.8$ Hz), 78.2 (d, $J = 12.9$ Hz), 78.6 (d, $J = 3.0$ Hz), 108.7, 109.2, 121.1 (d, $J = 15.2$ Hz), 121.5 (d, $J = 6.8$ Hz), 127.5 (d, $J = 2.3$ Hz), 128.0, 128.3, 128.9, 129.4, 129.6 (d, $J = 2.3$ Hz), 129.7, 133.4 (d, $J = 5.3$ Hz), 134.0 (d, $J = 6.9$ Hz), 140.8, 142.9, 143.0, Multiplicities and J values indicated are only for C–P coupling; ^{31}P NMR ($CDCl_3$) δ 23.43 (minor) 23.46 (major). MS (TOF ES+) m/e (relative intensity) 390 (MNa^+, 5), 368 ([MH^+, 18), 321 (4), 158 (22), 156 (35), 141 (45); HRMS: (MH^+) calcd for $C_{17}H_{23}NO_6P$, 368.1263; found, 368.1274.

4.2.9. Diethyl 1,2-bis(4-chlorophenyl)-3-nitropropylphosphonate 3i. Colourless solid; Yield 69% (single diastereomer); R_f 0.32 (EtOAc/pet ether 1:1); mp 175–176 °C; IR (film, cm^{-1}) 2985 (m), 2922 (m), 1550 (s), 1492 (m), 1379 (m), 1235 (s), 1164 (m), 1092 (m), 1044 (s), 1014 (s), 937 (s), 745 (m), 569 (s); ^1H NMR ($CDCl_3$) δ 1.14 (t, $J = 7.0$ Hz, 3H), 1.30 (t, $J = 7.0$ Hz, 3H), 3.34 (dd, $J = 21.1$, 10.7 Hz, 1H), 3.64–3.75 (m, 1H), 3.90–4.00 (m, 1H), 4.02–4.21 (m,

3H), 4.77 (dd, $J = 12.8$, 10.5 Hz, 1H), 5.31 (dd, $J = 12.8$, 4.9 Hz, 1H), 6.92 (d, $J = 8.6$ Hz, 2H), 7.05 (dd, $J = 8.6$, 1.8 Hz, 2H), 7.11 (d, $J = 8.6$ Hz, 2H), 7.15 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 16.1 (d, $J = 5.3$ Hz), 16.2 (d, $J = 6.1$ Hz), 44.8, 47.1 (d, $J = 35.7$ Hz), 62.2 (d, $J = 7.6$ Hz), 63.4 (d, $J = 6.9$ Hz), 78.9, 128.6 (d, $J = 1.6$ Hz), 128.7, 129.4, 130.8 (d, $J = 6.1$ Hz), 132.4 (d, $J = 6.8$ Hz), 133.4 (d, $J = 3.0$ Hz), 133.5, 135.4 (d, $J = 15.2$ Hz). Multiplicities indicated are only for C–P coupling; ^{31}P NMR ($CDCl_3$) δ 22.72; MS (TOF ES+) *m/e* (relative intensity) 446 (MH^+, 5), 158 (7), 141 (40), 124 (100); HRMS: (MH^+) calcd for $C_{19}H_{23}NO_5PCl_2$, 446.0690; found, 446.0691.

4.2.10. Diethyl 2-(4-chlorophenyl)-3-nitro-1-(4-nitrophenyl) propylphosphonate 3j. Colourless solid; Yield 45% (mixture of diastereomers in 92:08 ratio, the major isomer was isolated in pure form by repeated recrystallization from CH_2Cl_2/pet ether 10:1); R_f 0.38 (EtOAc/pet ether 1:1); mp 162–163 °C; IR (film, cm^{-1}) 2985 (m), 1600 (m), 1521 (s), 1348 (vs), 1247 (s), 1026 (vs), 969 (s), 861 (m); ^{1}H NMR ($CDCl_3$) δ 1.19 (t, $J = 7.1$ Hz, 3H), 1.31 (t, $J = 7.1$ Hz, 3H), 3.55 (dd, $J = 21.0$, 11.3 Hz, 1H), 3.79–3.85 (m, 1H), 3.99–4.23 (m, 4H), 4.81 (dd, $J = 13.2$, 10.4 Hz, 1H), 5.37 (dd, $J = 13.2$, 4.5 Hz, 1H), 6.94 (d, $J = 8.5$ Hz, 2H), 7.12 (d, $J = 8.5$ Hz, 2H), 7.30 (d, $J = 8.6$ Hz, 2H), 8.38 (d, $J = 8.6$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 16.4 (2 × d, $J = 6.1$ Hz), 44.9, 47.9 (d, $J = 136.5$ Hz), 62.9, 63.8, 79.1, 123.8, 129.2, 129.5, 130.6, 130.7, 134.1, 135.1, 147.2 (Multiplicities and J values indicated are only for C–P coupling); ^{31}P NMR ($CDCl_3$) δ 21.53; MS (TOF ES+) *m/e* (relative intensity) 457 ([MH^+, 100), 439 (10), 411 (5), 339 (5); HRMS: (M^+) calcd for $C_{19}H_{23}N_2O_7PCl$, 457.0931; found, 457.0933.

4.2.11. Diethyl 2-(4-chlorophenyl)-1-(naphthalen-2-yl)-3-nitropropylphosphonate 3k. Colourless solid; Yield 74% (single diastereomer); R_f 0.39 (EtOAc/pet ether 1:1); mp 179–180 °C; IR (film, cm^{-1}) 2928 (m), 2853 (w), 1556 (s), 1494 (w), 1379 (w), 1247 (m), 1095 (m), 1027 (s), 971 (w), 913 (m), 742 (s); ^{1}H NMR ($CDCl_3$) δ 0.81 (t, $J = 7.2$ Hz, 3H), 1.05 (t, $J = 6.8$ Hz, 3H), 3.30 (m, 1H), 3.50 (dd, $J = 22.0$, 9.3 Hz, 1H), 3.70 (m, 2H), 3.86 (m, 1H), 4.40 (ABqd, $J = 9.3$, 3.7 Hz, 1H), 4.51 (dd, $J = 12.0$, 9.3 Hz, 1H), 4.64 (dd, $J = 12.0$, 3.7 Hz, 1H), 7.26–7.31 (m, 5H), 7.48–7.50 (m, 1H), 7.52–7.55 (m, 2H), 7.82 (m, 3H). Multiplicities and J values indicated are both for H–H and P–H coupling; ^{13}C NMR ($CDCl_3$) δ 16.0 (2 × d, $J = 5.3$ Hz), 44.5, 48.7 (d, $J = 139.5$ Hz), 61.5 (d, $J = 6.9$ Hz), 63.3 (d, $J = 6.8$ Hz), 78.5 (d, $J = 13.7$ Hz), 126.6, 126.8, 127.7, 127.9, 128.8, 129.1, 129.8, 130.6, 130.7, 132.9, 133.3, 133.9, 135.98, 136.03; ^{31}P NMR ($CDCl_3$) δ 22.82. MS (TOF ES+) *m/e* (relative intensity) 464 (MH^+, 100), 297 (9), 214 (4), 158 (6), 99 (10), 85 (12); HRMS: calcd for $C_{23}H_{26}NO_5PCl$, 462.1237; found, 462.1247.

4.2.12. Diethyl 2-(4-chlorophenyl)-3-nitropropylphosphonate 3l. Light red liquid; Yield 61%; R_f 0.25 (EtOAc/pet ether 1:1); IR (film, cm^{-1}) 2984 (m), 2929 (m), 1555 (s), 1294 (m), 1379 (m), 1235 (s), 1028 (s), 966 (s), 830 (m); ^{1}H NMR ($CDCl_3$) δ 1.26 (td, $J = 7.1$, 1.0 Hz, 6H), 2.13 (dd, $J = 7.2$, 6.0 Hz, 1H), 2.17 (dd, $J = 7.3$, 5.3 Hz, 1H), 3.80–4.20 (m, 5H), 4.60 (dd, $J = 12.8$, 9.0 Hz, 1H), 4.89 (dd, $J = 12.8$, 6.0 Hz, 1H), 7.19 (d, $J = 8.4$ Hz, 2H), 7.32 (d, $J = 8.4$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 16.3, δ 16.4, 30.2 (d, $J = 141.7$ Hz), 38.3 (d, $J = 2.6$ Hz), 62.0 (d, $J = 6.9$ Hz), 62.1 (d, $J = 6.9$ Hz), 79.8 (d, $J = 10.4$ Hz), 128.8, 129.2, 134.0, 137.5 (d, $J = 10.1$ Hz). Multiplicities and J values indicated are only for C–P coupling; ^{31}P NMR ($CDCl_3$) δ 24.93; MS (TOF ES+) *m/e* (relative intensity) 358 (MNa^+, 50), 336 ([MH^+, 100), 125 (5), 97 (10); HRMS: (MH^+) calcd for $C_{13}H_{20}NO_5PCl$, 336.0768; found, 336.0759.

4.2.13. Diethyl 3-nitro-2-phenylpropylphosphonate 3m. Light red liquid; Yield 41%; R_f 0.28 (EtOAc/pet ether 1:1); IR (film, cm^{-1}) 2984 (m), 2930 (m), 1555 (s), 1380 (m), 1236 (s), 1028 (s), 965 (m), 788 (m), 763 (m), 701 (m); ^{1}H NMR ($CDCl_3$) δ 1.22 (td, $J = 7.0$, 1.7 Hz, 6H), 2.19 (dd, $J = 7.6$, 3.5 Hz, 1H), 2.23 (dd, $J = 7.3$, 3.1 Hz, 1H), 3.80–4.10 (m, 5H), 4.63 (dd, $J = 12.7$, 8.9 Hz, 1H), 4.87 (dd, $J = 12.7$, 6.1 Hz, 1H), 7.20–7.30 (m, 5H); ^{13}C NMR ($CDCl_3$) 16.0 (d, $J = 3.1$ Hz), 16.1 (d, $J = 3.1$ Hz), 29.3 (d, $J = 11.5$ Hz), 38.6 (d, $J = 2.3$ Hz), 61.8 (d, $J = 6.1$ Hz), 62.0 (d, $J = 6.9$ Hz), 79.9 (d, $J = 3.1$ Hz), 127.2, 127.9, 128.8, 138.8 (d, $J = 9.2$ Hz), Multiplicities and J values indicated are only for C–P coupling; ^{31}P NMR ($CDCl_3$) δ 25.47; MS (TOF ES+) *m/e* (relative intensity) 302 ([MH^+, 100), 256 (5), 228 (5), 153 (5), 125 (18); HRMS: (MH^+) calcd for $C_{13}H_{21}NO_5P$, 302.1157; found, 302.1155.

4.2.14. Diethyl 2-(4-methoxyphenyl)-3-nitropropylphosphonate 3n. Light red liquid; Yield 43%; R_f 0.15 (EtOAc/pet ether 1:1); IR (film, cm^{-1}) 3055 (m), 2986 (m), 1612 (m), 1555 (s), 1515 (s), 1442 (w), 1379 (m), 1266 (s), 1030 (s), 966 (m), 896 (m), 832 (m), 742 (s); ^{1}H NMR ($CDCl_3$) δ 1.23 (t, $J = 7.1$ Hz, 6H), 2.12 (dd, $J = 7.3$, 4.4 Hz, 1H), 2.17 (dd, $J = 7.3$, 3.8 Hz, 1H), 3.76 (s, 3H), 3.90–4.10 (m, 5H), 4.56 (dd, $J = 12.5$, 8.9 Hz, 1H), 4.83 (dd, $J = 12.5$, 6.1 Hz, 1H), δ 6.84 (d, $J = 8.7$ Hz, 2H), δ 7.13 (d, $J = 8.7$ Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 16.1 (d, $J = 3.1$ Hz), 16.2 (d, $J = 3.1$ Hz), 29.6 (d, $J = 140.3$ Hz), 38.0 (d, $J = 2.3$ Hz), 55.1, 61.7 (d, $J = 6.9$ Hz), 61.8 (d, $J = 6.8$ Hz); 80.2 (d, $J = 10.7$ Hz), 114.2, 128.3, 130.8 (d, $J = 10.0$ Hz), 159.1. Multiplicities and J values indicated are only for C–P coupling; ^{31}P NMR ($CDCl_3$) δ 25.55; MS (TOF ES+) *m/e* (relative intensity) 332 (MH^+, 100), 285 (80), 271 (10), 158 (4), 99 (7), 73 (43); HRMS: (MH^+) calcd for $C_{14}H_{23}NO_6P$, 332.1263; found, 332.1257.

4.2.15. Diethyl 2-(4-chlorophenyl)-1-nitrohexan-3-ylphosphonate 3o. Light red liquid; Yield 47% (mixture of diastereomers in 72:28 ratio, the major isomer was isolated in pure form via silica gel column chromatography); R_f 0.30 (EtOAc/pet ether 1:1); IR (film, cm^{-1}) 2963 (m), 2932 (m), 2974 (w), 1555 (s), 1494 (m), 1379 (m), 1236 (s), 1053 (s), 1026 (s), 963 (s); ^{1}H NMR ($CDCl_3$) δ 0.86 (t, $J = 6.8$ Hz, 3H), 1.17 (t, $J = 7.0$ Hz, 3H), 1.32 (t, $J = 7.2$, 3H), 1.38–1.50 (m, 2H), 1.52–1.64 (m, 1H), 2.10 (dddd, $J = 21.7$, 9.9, 5.9, 3.8 Hz, 1H), 3.92–4.04 (m, 4H), 4.06–4.16 (m, 2H), 4.96 (dd, $J = 13.3$, 9.7 Hz, 1H), 5.17 (dd, $J = 13.3$, 5.9 Hz, 1H), δ 7.29 (m, 4H). Multiplicities and J values indicated are both for H–H and P–H coupling; ^{13}C NMR ($CDCl_3$) δ 13.9, 16.3 (d, $J = 6.1$ Hz), 16.6 (d,

$J = 5.4$ Hz), 21.2 (d, $J = 7.7$ Hz), 28.2 (d, $J = 3.8$ Hz), 40.5 (d, $J = 138.8$ Hz), 42.1, 61.8 (d, $J = 6.9$ Hz), 62.3 (d, $J = 6.1$ Hz), 76.9, 128.9 (d, $J = 13.0$ Hz), 129.9, 133.8, 135.8 (d, $J = 8.4$ Hz). Multiplicities and J values indicated are only for C–P coupling; ^{31}P NMR ($CDCl_3$) δ 27.82. MS (TOF ES+) *m/e* (relative intensity) 400 (MNa^+, 55), 378 (M^+, 100), 331 (35), 275 (60), 179 (95), 151 (55); HRMS: calcd for $C_{16}H_{25}NO_5PClNa$, 400.1057; found, 400.1068.

Acknowledgements

The authors thank DST, India, for financial assistance. V.R. thanks CSIR, India for a research fellowship.

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