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Alkenylphosphonates: unexpected products from reactions of methyl 2-[(diethoxyphosphoryl)methyl]benzoate under Horner-Wadsworth-Emmons conditions

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General experimental methods

Unless otherwise stated, the following conditions apply. All reactions were performed under argon in oven-dried glassware using dry solvents and standard syringe techniques. Tetrahydrofuran (THF) and diethyl ether were distilled from the sodium salt of the benzophenone ketyl radical anion. Dichloromethane was distilled from CaH₂. *N*-Bromosuccinimide was recrystallised according to Armarego and Perrin.¹ LiHMDS was purchased as a 1.0 molL⁻¹ solution in hexanes. KHMDS was purchased as a 0.5 molL⁻¹ solution in toluene. Benzaldehyde and octanal were dried with molecular sieves under argon for 1 hour prior to their addition to reaction mixtures. All other reagents were of commercial quality and used as received. After workup, partitioned organic layers were dried over magnesium sulfate (MgSO₄).

Reaction progress was monitored using aluminium-backed thin layer chromatography (TLC) plates pre-coated with silica UV254, which were visualised by UV radiation (254 nm) and developed with anisaldehyde dip. Purification of products by flash chromatography was conducted using a column filled with silica gel 60 (220–240 mesh) eluted with the solvent systems indicated. ¹H and ¹³C NMR spectra were recorded on a Varian Unity Inova 500 spectrometer, operating at 500 MHz for ¹H and 125 MHz for ¹³C. All chemical shifts (δ) were referenced to the solvent peaks of CDCl₃ (7.26 ppm for ¹H, 77.0 ppm for ¹³C). Infrared spectra were obtained on a Perkin-Elmer Spectrum One FT-IR spectrometer. High-resolution mass spectrometry was performed on a Waters Q-TOF Premier™ Tandem mass spectrometer.

Methyl 2-(bromomethyl)benzoate (6).² A solution of methyl 2-methylbenzoate (**5**) (1.00 g, 6.66 mmol) and *N*-bromosuccinimide (1.31 g, 7.36 mmol) in CH₂Cl₂ (20 mL) was irradiated with white light (250 W, incandescent bulb) for 30 min, which heated the reaction mixture to reflux. The reaction mixture was then cooled to 0 °C and filtered to remove the solid succinimide before concentrating under reduced pressure to give a pale-yellow oil. This crude residue was purified by flash column chromatography (silica, 1:20 EtOAc/hexanes) to provide the title compound **6** as a colourless oil (1.37 g, 90%). R_f 0.40 (1:10 EtOAc/hexanes). ¹H NMR (500 MHz, CDCl₃) δ 7.97 (dd, *J* = 8.5, 1.2 Hz, 1H), 7.52 – 7.45 (complex m, 2H),

¹ W. L. F. Armarego and D. D. Perrin, *Purification of Laboratory Chemicals*, 4th ed., Butterworth-Heinemann, 2002.

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7.38 (app. td, $J = 7.3$, 2.0 Hz, 1H), 4.96 (s, 2H), 3.95 (s, 3H). The spectral data matched those reported previously.²

Methyl 2-[(diethoxyphosphoryl)methyl]benzoate (4).³ A solution of methyl 2-methylbenzoate (**5**) (2.00 g, 13.3 mmol) and *N*-bromosuccinimide (2.61 g, 14.7 mmol) in CH₂Cl₂ (20 mL) was irradiated with white light (250 W, incandescent bulb) for 30 min, which heated the reaction mixture to reflux. The reaction mixture was then cooled to 0 °C and filtered to remove the solid succinimide before concentrating under reduced pressure to give a pale-yellow oil. This crude methyl 2-(bromomethyl)benzoate (**6**) was stirred with triethyl phosphite (6.91 mL, 39.7 mmol) at 150 °C for 12 h. Distillation to remove the remaining triethyl phosphite provided a yellow oil, which was purified by flash column chromatography (silica, gradient elution 1:2 EtOAc/hexanes to EtOAc) to afford the title compound **4** as a pale-yellow oil (3.38 g, 89%). R_f 0.30 (1:4 EtOAc/hexanes). ¹H NMR (500 MHz, CDCl₃) δ 7.92 (d, $J = 7.8$ Hz, 1H), 7.46 (app. t, $J = 7.5$ Hz, 1H), 7.40 (d, $J = 8.6$ Hz, 1H), 7.32 (app. t, $J = 7.5$ Hz, 1H), 4.00 (quintet, $J = 7.2$ Hz, 4H), 3.91 (s, 3H), 3.81 (d, $J = 22.8$ Hz), 1.22 (t, $J = 7.1$ Hz). The spectral data matched those reported previously.³

***tert*-Butyl 2-methylbenzoate.**⁴ Following a literature procedure,⁵ *tert*-butyl acetate (1.35 mL, 10 mmol) was added rapidly by syringe to a round-bottom flask containing methyl 2-methylbenzoate (**5**) (1.4 mL, 10 mmol). The stirred mixture was treated dropwise with a solution of KO^tBu in THF (1.0 M, 0.10 mL, 0.10 mmol). The resulting solution was stirred under vacuum (*ca.* 70 mmHg), using a cold trap to collect methyl acetate, until the solution stopped bubbling (around 20 – 30 min). A process involving addition of further portions of both *tert*-butyl acetate and KO^tBu and removing the methyl acetate under reduced pressure was repeated five times, until ¹H NMR spectroscopic monitoring indicated a good conversion was achieved. The resulting yellow suspension was partitioned between Et₂O (20 mL) and H₂O (10 mL). The organic fraction was then washed with brine (10 mL) and dried over MgSO₄. The resultant colourless solution was concentrated under reduced pressure, yielding the title compound as a colourless oil (976 mg, 51%) that was used immediately. ¹H NMR (500 MHz, CDCl₃) δ 7.83 (dd, $J = 7.5$, 1.5 Hz, 1H), 7.36 (td, $J = 8.0$, 1.5 Hz, 1H), 7.27 – 7.21 (complex m, 2H), 2.58 (s, 3H), 1.61 (s, 9H). These NMR spectral data matched those reported previously.⁴

***tert*-Butyl 2-(bromomethyl)benzoate.**⁴ A solution of *tert*-butyl 2-methylbenzoate (976 mg, 5.08 mmol) in CH₂Cl₂ (20 mL) under argon at room temperature was treated with *N*-bromosuccinimide (1.05 g, 5.9 mmol) and the resulting pale-yellow solution was irradiated with a white light (250 W, incandescent bulb) for 1 hour, which caused it to reflux. The solution quickly became bright orange and then slowly reverted to a cloudy yellow suspension. The reaction mixture was cooled to 0 °C and filtered to remove solid white

² R. Liu, S. Valiyaveettil, K.-F. Mok, J. J. Vittal and A. K. M. Hoong, *CrystEngComm*, 2002, **4**, 574–9.

³ H. Takahashi, S. Inagaki, N. Yoshii, F. Gao, Y. Nishihara and K. Takagi, *J. Org. Chem.*, 2009, **74**, 2794-7.

⁴ L. Torun, T. W. Robison, J. Krzykawski, D. W. Purkiss and R. A. Bartsch, *Tetrahedron*, 2005, **61**, 8345-50.

⁵ M. G. Stanton and M. R. Gagné, *J. Org. Chem.*, 1997, **62**, 8240-2.

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succinimide, before concentration under reduced pressure to give a yellow oil that contained the title compound, dibrominated by-product and residual succinimide. Flash chromatography (silica, gradient elution 1:49 to 1:4 EtOAc/hexanes) provided the title compound as a pale-yellow oil (1.08 g, 82%). R_f 0.30 (1:30 EtOAc/hexanes). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.89 (d, $J = 7.8$ Hz, 1H), 7.47 – 7.42 (complex m, 2H), 7.36 (td, $J = 7.1$, 0.8 Hz, 1H), 4.93 (s, 2H), 1.64 (s, 9H). These NMR spectral data matched those reported previously.⁴

***tert*-Butyl 2-[(diethoxyphosphoryl)methyl]benzoate (15).** Under argon at room temperature, triethyl phosphite (5.0 mL, 28.7 mmol) was added dropwise to *tert*-butyl 2-(bromomethyl)benzoate (1.08 g, 4.2 mmol) with stirring. The reaction was then heated at reflux (150 °C) for 16 hours to afford a yellow solution. Unreacted triethyl phosphite was removed by distillation to afford a bright yellow, viscous oil. This material was purified by flash chromatography (silica, gradient elution 1:2 EtOAc/hexanes to EtOAc), yielding the title compound **15** as a pale-yellow oil (709 mg, 52%). $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.86 (d, $J = 7.5$ Hz, 1H), 7.44 – 7.38 (complex m, 2H), 7.29 (tt, $J = 7.5$, 2.0 Hz, 1H), 4.00 (m, 4H), 3.80 (d, $J = 23.0$ Hz, 2H), 1.61 (s, 9H), 1.22 (t, $J = 7.0$ Hz, 6H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 166.8 (d, $J = 1.9$ Hz), 132.7 (d, $J = 9.6$ Hz), 132.11 (d, $J = 2.9$ Hz), 132.06 (d, $J = 1.9$ Hz), 131.3 (d, $J = 3.8$ Hz), 130.9 (d, $J = 3.4$ Hz), 126.7 (d, $J = 3.8$ Hz), 81.5, 62.0 (d, $J = 6.6$ Hz), 31.0 (d, $J = 135.5$ Hz), 28.2, 16.3 (d, $J = 5.8$ Hz). IR (neat): 2979, 2932, 1710, 1601, 1578, 1251, 1023 cm^{-1} . HRMS (ESI) calcd. for $\text{C}_{16}\text{H}_{25}\text{O}_5\text{PNa}$ $[\text{M}+\text{Na}]^+$ 351.1337, found 351.1342.

General Procedure for HWE Reactions at 0 or –78 °C

To a stirred solution of phosphonate **4** or **15** in a solvent (THF or Et_2O or toluene, *ca.* 0.1 M concentration) under an atmosphere of argon at the chosen temperature (0 °C or –78 °C) was added, dropwise, a solution of LiHMDS (1 M in hexanes) or KHMDS (0.5 M in toluene). The rapid appearance of an orange colour was taken to mean deprotonation had occurred. The reaction mixture was stirred for 30 minutes and then charged with the aldehyde. The resulting mixture was maintained at the chosen temperature for some time (0.5 – 2 h) and then allowed to warm gradually to room temperature over a number of hours (6 – 16 h). Typically (unless otherwise noted), the reaction was quenched with aqueous HCl (10% v/v) and extracted three times with EtOAc. The combined organic fractions were dried (MgSO_4), filtered and concentrated under reduced pressure to afford the crude reaction mixture as an oil, which was analysed by $^1\text{H NMR}$ spectroscopy to determine the product composition. Silica gel chromatography afforded pure quantities of the products.

HWE Reactions of Phosphonate **4** with Octanal

A. As described in the general procedure, reaction of the phosphonate **4** (103 mg, 0.36 mmol) with LiHMDS solution (360 μL , 0.36 mmol) and octanal (62 μL , 0.40 mmol) in Et_2O at –78 °C for 1 hour, followed by warming to room temperature over 11 hours, provided a 13:81:6 mixture of alkene **8a** : *E*-alkenylphosphonate *E*-**9a** : *Z*-alkenylphosphonate *Z*-**9a** as a pale-yellow oil. The reaction mixture was quenched with saturated aqueous ammonium

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chloride solution and extracted twice with diethyl ether. The combined organic fractions were dried, filtered and concentrated to provide a pale-yellow oil. Purification of this material by flash column chromatography (silica gel, 1:20 EtOAc/hexanes) afforded the alkene **8a** as a colourless oil (6 mg, 7%). Further acidification of the aqueous layer with 10% aqueous HCl solution and extraction with EtOAc provided a pale-yellow oil. Purification of this oil by flash chromatography (silica, 1:15 MeOH/CH₂Cl₂) yielded the *E*-alkenylphosphonate *E-9a* as a colourless oil (78 mg, 57%).

B. As described in the general procedure, reaction of the phosphonate **4** (72 mg, 0.25 mmol) with LiHMDS solution (250 μL, 0.25 mmol) and octanal (43 μL, 0.28 mmol) in toluene at -78 °C for 1 hour, followed by warming to room temperature over 11 hours, provided a 22:78 mixture of alkene **8a** : *E*-alkenylphosphonate *E-9a* as a pale-yellow oil, which also contained unreacted starting materials. Purification of this crude material by flash column chromatography (silica, gradient elution 1:20 EtOAc/hexanes to EtOAc) afforded the alkene **8a** as a colourless oil (8 mg, 12%), recovered benzyl phosphonate **4** as colourless liquid (23 mg, 32%) and *E*-alkenylphosphonate *E-9a* as a colourless oil (47 mg, 49%).

C. As described in the general procedure, reaction of the phosphonate **4** (105 mg, 0.37 mmol) with LiHMDS solution (370 μL, 0.37 mmol) and octanal (63 μL, 0.40 mmol) in THF at -78 °C for 3 hours, followed by warming to room temperature over 13 hours, provided a 79:21 mixture of *E*-alkenylphosphonate *E-9a* : *Z*-alkenylphosphonate *Z-9a* as a pale-yellow oil, which also contained unreacted starting materials but none of the alkene **8a**. Purification of this crude material by flash column chromatography (silica, gradient elution 1:20 EtOAc/hexanes to EtOAc) afforded the *E*-alkenylphosphonate *E-9a* as a colourless oil (100 mg, 71%).

D. As described in the general procedure, reaction of the phosphonate **4** (177 mg, 0.62 mmol) with KHMDS solution (1.36 mL, 0.68 mmol) and octanal (116 μL, 0.74 mmol) in THF at -78 °C for 2 hours, followed by warming to room temperature over 16 hours, provided a 45:55 mixture of alkene **8a** : *E*-alkenylphosphonate *E-9a* as a bright yellow oil, which also contained unreacted starting materials and enal **10**.

E. As described in the general procedure, reaction of the phosphonate **4** (72 mg, 0.25 mmol) with LiHMDS solution (250 μL, 0.25 mmol) and octanal (43 μL, 0.28 mmol) in THF at 0 °C for 1 hour, followed by warming to room temperature over 5 hours, provided a 13:66:21 mixture of alkene **8a** : *E*-alkenylphosphonate *E-9a* : *Z*-alkenylphosphonate *Z-9a* as a pale-yellow oil, which also contained unreacted starting materials.

F. NaOMe (47 mg, 0.87 mmol) was added in one portion to a stirred solution of phosphonate **4** (125 mg, 0.437 mmol) in distilled THF (4 mL) under argon at 0 °C. The resulting suspension was maintained at 0°C for 30 min, whereupon octanal (150 μL, 0.959 mmol) was added dropwise. The reaction was left to warm to room temperature for 3 hours and then heated at reflux for 2 hours, resulting in a pale-yellow suspension. The reaction was cooled to room temperature and then quenched with 10% HCl solution (10 mL) and extracted with

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EtOAc (3 x 10 mL). The pale yellow organic fractions were combined, dried with MgSO₄, filtered and then concentrated under reduced pressure to afford a yellow oil, which contained the *E*-alkenylphosphonate *E*-**9a**, together with enal **10** and recovered phosphonate **4**. None of the alkene **8a** or the *Z*-alkenylphosphonate *Z*-**9a** were observed.

Methyl 2-[(*E*)-non-1-enyl]benzoate (8a**).** *R_f* 0.56 (1:10 EtOAc/hexanes). ¹H NMR (500 MHz, CDCl₃) δ 7.83 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.54 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.43 (td, *J* = 7.6, 1.4 Hz, 1H), 7.25 (td, *J* = 7.6, 1.5 Hz, 1H), 7.12 (d, *J* = 15.7 Hz, 1H), 6.14 (dt, *J* = 15.7, 7.0 Hz, 1H), 3.90 (s, 3H), 2.25 (app. qd, *J* = 7.3, 1.5 Hz, 2H), 1.49 (m, 2H), 1.40 – 1.24 (complex m, 8H), 0.89 (t, *J* = 7.0 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 168.1, 139.7, 134.2, 131.9, 130.2, 128.3, 128.1, 127.2, 126.4, 52.0, 33.2, 31.9, 29.3, 29.21, 29.19, 22.7, 14.1. IR (neat): 2928, 2850, 1723, 1434, 1254, 1121, 1078, 729 cm⁻¹. HRMS (ESI) calcd. for C₁₇H₂₄O₂Na⁺ [M + Na]⁺ 283.1674, found 283.1681.

2-[(*E*)-1-(Diethylphosphono)non-1-enyl]benzoic acid (*E*-9a**).** *R_f* 0.21 (EtOAc). ¹H NMR (300 MHz, CDCl₃) δ 9.26 (broad s, 1H), 7.95 (d, *J* = 7.7 Hz, 1H), 7.48 (tdd, *J* = 7.5, 1.5, 0.7 Hz, 1H), 7.39 (tt, *J* = 7.5, 1.5 Hz, 1H), 7.12 (dt, *J* = 7.5, 1.5 Hz, 1H), 6.72 (dt, *J* = 23.1, 7.3 Hz, 1H), 4.14 (app. quintet, *J* = 7.3 Hz, 2H), 4.09 – 3.97 (complex m, 2H), 1.91 (m, 2H), 1.43 – 1.17 (complex, partially obscured m, 10H), 1.30 (t, *J* = 7.3 Hz, 3H), 1.20 (t, *J* = 7.4 Hz, 3H), 0.82 (t, *J* = 6.8 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 170.0, 148.6 (d, *J* = 8.1 Hz), 135.1 (d, *J* = 10.4 Hz), 132.1, 131.7, 131.0, 130.8, 130.2 (d, *J* = 185.9), 128.0, 62.8 (d, *J* = 6.3 Hz), 62.5 (d, *J* = 6.0), 31.8, 30.0 (d, *J* = 17.7 Hz), 29.3, 29.1, 28.3 (d, *J* = 1.4 Hz), 22.7, 16.4 (d, *J* = 4.4 Hz), 16.3 (d, *J* = 4.3 Hz), 14.1. IR: 3500 – 2500 (br), 2922, 2854, 1716, 1193, 1020 cm⁻¹. HRMS (ESI) calcd. for C₂₀H₃₀O₅P⁻ [M – H]⁻ 381.1831, found 381.1864.

HWE Reactions of Phosphonate **4** with Butyraldehyde

G. As described in the general procedure, reaction of the phosphonate **4** (55 mg, 0.19 mmol) with LiHMDS solution (212 μL, 0.21 mmol) and butanal (19 μL, 0.21 mmol) in Et₂O at –78 °C for 1 hour, followed by warming to room temperature over 11 hours, provided a *ca.* 30:70 mixture of alkene **8b** : *E*-alkenylphosphonate *E*-**9b** as a pale-yellow oil, which also contained trace amounts of unreacted starting materials. Purification of this crude material by flash column chromatography (silica, gradient elution 1:20 EtOAc/hexanes to EtOAc) afforded the alkene **8b** as a colourless oil (8 mg, 21%) and *E*-alkenylphosphonate *E*-**9b** as a colourless oil (19 mg, 31%).

H. As described in the general procedure, reaction of the phosphonate **4** (34 mg, 0.12 mmol) with LiHMDS solution (142 μL, 0.14 mmol) and butanal (13 μL, 0.14 mmol) in toluene at –78 °C for 1 hour, followed by warming to room temperature over 11 hours, provided a *ca.* 35:65 mixture of alkene **8b** : *E*-alkenylphosphonate *E*-**9b** as a pale-yellow oil, which also contained trace amounts of unreacted starting materials. Purification of this crude material by flash column chromatography (silica, gradient elution 1:20 EtOAc/hexanes to EtOAc) afforded the alkene **8b** as a colourless oil (5 mg, 24%), recovered benzyl phosphonate **4** as a

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colourless liquid (6 mg, 18%) and *E*-alkenylphosphonate **E-9b** as a colourless oil (8 mg, 21%).

Methyl 2-[(*E*)-pent-1-enyl]benzoate (8b).^{6,7} ¹H NMR (300 MHz, CDCl₃) δ 7.83 (d, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.13 (d, *J* = 15.7 Hz, 1H), 6.14 (dt, *J* = 15.6, 6.9 Hz, 1H), 3.89 (s, 3H), 2.23 (app. q, *J* = 7.4 Hz, 2H), 1.52 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H). These NMR data correspond to those reported in the literature.^{6,7}

2-[(*E*)-1-(Diethylphosphono)pent-1-enyl]benzoic acid (E-9b). ¹H NMR (500 MHz, CDCl₃) δ 7.93 (d, *J* = 7.0 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 6.8 – 6.1 (broad s, 1H), 6.70 (dt, *J* = 23.1, 7.3 Hz, 1H), 4.16 (m, 2H), 4.09 – 3.97 (complex m, 2H), 1.89 (m, 2H), 1.44 – 1.16 (partially obscured m, 2H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H), 0.83 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 169.9, 148.3 (d, *J* = 8.1 Hz), 134.4 (d, *J* = 9.5 Hz), 132.5 (d, *J* = 5.0 Hz), 131.2 (d, *J* = 81.2 Hz), 130.8 (d, *J* = 2.0 Hz), 130.6 (d, *J* = 4.6 Hz), 129.3, 128.0 (d, *J* = 2.3 Hz), 63.0 (d, *J* = 6.2 Hz), 62.9 (d, *J* = 6.2 Hz), 31.9 (d, *J* = 17.5 Hz), 21.5 (d, *J* = 1.7 Hz), 16.3 (d, *J* = 6.4 Hz), 16.2 (d, *J* = 6.4 Hz), 13.8. IR (neat): 3418, 2960, 2932, 2872, 1717, 1209, 1138, 1052, 1024, 978 cm⁻¹. HRMS (ESI) calcd. for C₁₆H₂₃O₅PNa⁺ [M + Na]⁺ 349.1181, found 349.1184.

HWE Reaction of Phosphonate 4 with Benzaldehyde

I. As described in the general procedure, reaction of the phosphonate **4** (90 mg, 0.31 mmol) with LiHMDS solution (420 μL, 0.42 mmol) and benzaldehyde (36 μL, 0.35 mmol) in THF at -78 °C for 1.5 hours, followed by warming to room temperature over 13.5 hours, provided a 15:85 mixture of alkene **8c** : *E*-alkenylphosphonate **E-9c** as a pale-yellow oil, which also contained a large amount of unreacted benzaldehyde. Purification of this crude material by flash column chromatography (silica, gradient elution 1:10 EtOAc/hexanes to EtOAc) afforded the alkene **8c** as a colourless oil (8 mg, 11%) and *E*-alkenylphosphonate **E-9c** as a colourless oil (41 mg, 37%). The latter compound (**E-9c**) solidified on standing and was recrystallised from CH₂Cl₂ to afford white prisms.

J. As described in the general procedure, reaction of the phosphonate **4** (107 mg, 0.37 mmol) with LiHMDS solution (410 μL, 0.41 mmol) and benzaldehyde (40 μL, 0.39 mmol) in toluene at -78 °C for 1.5 hours, followed by warming to room temperature over 14 hours, provided a 7:93 mixture of alkene **8c** : *E*-alkenylphosphonate **E-9c** as a pale-yellow oil, which also contained unreacted benzaldehyde and recovered phosphonate **4**.

K. Sodium methoxide was prepared by addition of sodium (5.8 mg, 0.25 mmol) to dry methanol (0.5 mL) and, after dissolution was complete, concentrating the solution under reduced pressure to afford a white solid. To this solid was added a solution of phosphonate **4**

⁶ R. G. F. Giles, V. R. Lee Son and M. V. Sargent, *Aust. J. Chem.*, 1990, **43**, 777-81.

⁷ R. G. F. Giles, I. R. Green and J. A. X. Pestana, *J. Chem. Soc., Perkin Trans. 1*, 1984, 2389-95.

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(60 mg, 0.21 mmol) in THF (2 mL) at 0 °C under an argon atmosphere. After 30 min, benzaldehyde (24 µL, 0.23 mmol) was added and the reaction was maintained at 0 °C for a further 1 h before warming first to room temperature for 1 h and then heating at reflux for 1 h. The reaction was quenched with aqueous HCl solution (10% v/v) and extracted with EtOAc (3 x 10 mL). The combined organic fractions were dried (MgSO₄), filtered and concentrated to a yellow oil, which contained a 29:71 mixture of alkene **8c** : *E*-alkenylphosphonate *E*-**9c**, in addition to large amounts of unreacted benzaldehyde.

Methyl 2-[(*E*)-2-phenylethen-1-yl]benzoate (8c**).**^{8,9} ¹H NMR (500 MHz, CDCl₃) δ 7.99 (d, *J* = 16.1 Hz, 1H), 7.94 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.74 (dd, *J* = 8.0, 0.5 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 2H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.33 (t, *J* = 7.7 Hz, 1H), 7.28 (m, 1H), 7.02 (d, *J* = 16.2 Hz, 1H), 3.93 (s, 3H). These NMR data correspond to those reported in the literature.^{8,9}

2-[(*E*)-1-Diethylphosphono-2-phenylethen-1-yl]benzoic acid (9c**).**¹⁰ m.p. 172 – 175 °C. ¹H NMR (500 MHz, CDCl₃) δ 13 – 10 (broad s, 0.7H), 9.8 – 8.9 (broad s, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.51 (d, *J* = 25.2 Hz, 1H), 7.47 – 7.42 (complex m, 2H), 7.17 (t, *J* = 7.2 Hz, 1H), 7.13 – 7.09 (complex m, 3H), 7.00 (d, *J* = 7.6 Hz, 2H), 4.12 (app. quintet, *J* = 7.1 Hz, 2H), 4.08 – 3.98 (complex m, 2H), 3.6 (broad s, 0.3H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 169.7, 142.0 (d, *J* = 10.1 Hz), 136.2 (d, *J* = 7.2 Hz), 134.8, 134.6, 132.5 (d, *J* = 1.9 Hz), 131.4 (d, *J* = 1.9 Hz), 130.6 (d, *J* = 186.6 Hz), 130.5 (d, *J* = 5.3 Hz), 130.1 (d, *J* = 1.0 Hz), 128.9, 128.2, 128.1 (d, *J* = 2.4 Hz), 63.0 (d, *J* = 6.7 Hz), 62.5 (d, *J* = 5.8 Hz), 16.2 (d, *J* = 6.7 Hz), 16.1 (d, *J* = 6.2 Hz). IR (neat): 3600 – 2400, 2983, 1714, 1617, 1597, 1201, 1017 cm⁻¹. HRMS (ESI) calcd. for C₁₉H₂₀O₅P⁻ [M – H]⁻ 359.1048, found 359.1044.

HWE Reaction of Phosphonate **4** with Pivaldehyde

L. As described in the general procedure, reaction of the phosphonate **4** (83 mg, 0.29 mmol) with LiHMDS solution (320 µL, 0.32 mmol) and pivaldehyde (38 µL, 0.35 mmol) in THF at –78 °C provided, after quenching with saturated aqueous NH₄Cl and extracting three times with EtOAc, a colourless oil that contained the alkene **8d** as the only identifiable product. Purification by flash column chromatography (silica, 1:20 EtOAc/hexanes) yielded the title compound **8d** as a colourless oil (56 mg, 88%).

Methyl 2-[(*E*)-3,3-dimethylbut-1-enyl]benzoate (8d**).** ¹H NMR (300 MHz, CDCl₃) δ 7.85 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.44 (td, *J* = 7.9, 1.3 Hz, 1H), 7.25 (td, *J* = 7.9, 1.3 Hz, 1H), 7.09 (d, *J* = 16.1 Hz, 1H), 6.13 (d, *J* = 16.1 Hz, 1H), 3.90 (s, 3H), 1.14 (s,

⁸ Z. Wang, Q. Ding, X. He and J. Wu, *Org. Biomol. Chem.*, 2009, **7**, 863-5.

⁹ M. Carme Pampín, J. C. Estévez, R. J. Estévez, M. Maestro and L. Castedo, *Tetrahedron*, 2003, **59**, 7231-43.

¹⁰ The chemical shifts of the ¹H and ¹³C signals for compound **9c** were affected by the concentration of the NMR sample.

Supporting information

9H). ^{13}C NMR (125 MHz, CDCl_3) δ 168.1, 144.5, 140.0, 131.9, 130.3, 128.3, 127.2, 126.4, 123.7, 52.0, 33.7, 29.6. IR: 2954, 2866, 1720, 1476, 1434, 1246, 1130, 1078, 735 cm^{-1} . HRMS (ESI) calcd. for $\text{C}_{14}\text{H}_{18}\text{O}_2\text{Na}^+$ $[\text{M} + \text{Na}]^+$ 241.1204, found 241.1203.

Control reaction – treatment of phosphonate **4** with LiHMDS

To a stirred solution of phosphonate **4** (30 mg, 0.10 mmol) in THF at $-78\text{ }^\circ\text{C}$ under an atmosphere of argon was added LiHMDS (0.12 mL, 0.12 mmol). Immediate formation of an orange colour was noted. After 1 h, the reaction was quenched with aqueous HCl (10% v/v, 10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried (MgSO_4), filtered and concentrated to provide a pale-yellow oil (26 mg, 87%), which consisted entirely of recovered starting material **4**, as judged by ^1H NMR spectroscopy.

HWE Reactions of Phosphonate **15** with Octanal

M. As described in the general procedure, reaction of the phosphonate **15** (140 mg, 0.426 mmol) with LiHMDS solution (0.85 mL, 0.85 mmol) and octanal (147 μL , 0.940 mmol) in THF (4 mL) at $-78\text{ }^\circ\text{C}$ for 30 min, followed by warming to room temperature over 16 hours, provided a 67:33 mixture of alkene **16** : *E*-alkenylphosphonate *E*-**9a** as a yellow oil, which also contained unreacted starting materials. Flash chromatography (silica, gradient elution 1:24 EtOAc/hexanes to EtOAc) provided the alkene **16** as a colourless oil (53 mg, 41%).

N. As described in the general procedure, reaction of the phosphonate **15** (106 mg, 0.323 mmol) with KHMDS solution (1.29 mL, 0.646 mmol) and octanal (111 μL , 0.710 mmol) in THF at $-78\text{ }^\circ\text{C}$ for 1 hour, followed by warming to room temperature over 15 hours, provided a 80:20 mixture of alkene **16** : *E*-alkenylphosphonate *E*-**9a** as an orange-brown oil.

O. NaO^tBu (83 mg, 0.87 mmol) was added in one portion to a stirred solution of phosphonate **15** (142 mg, 0.433 mmol) in distilled THF (4 mL) under argon at $0\text{ }^\circ\text{C}$. The resulting yellow solution was maintained at $0\text{ }^\circ\text{C}$ for 30 min, whereupon octanal (150 μL , 0.959 mmol) was added dropwise. The reaction was left to warm to room temperature for 3 hours and then heated at reflux for 2 hours, resulting in an orange-yellow suspension. The reaction was cooled to room temperature and then quenched with 10 % HCl solution (10 mL) and extracted with EtOAc (3 x 10 mL). The pale yellow organic fractions were combined, dried with MgSO_4 , filtered and then concentrated under reduced pressure to afford a yellow oil, which contained the alkene **16** as the only discernible product. Flash chromatography (silica, 1:24 EtOAc/hexanes) provided the alkene **16** as a colourless oil (41 mg, 31%).

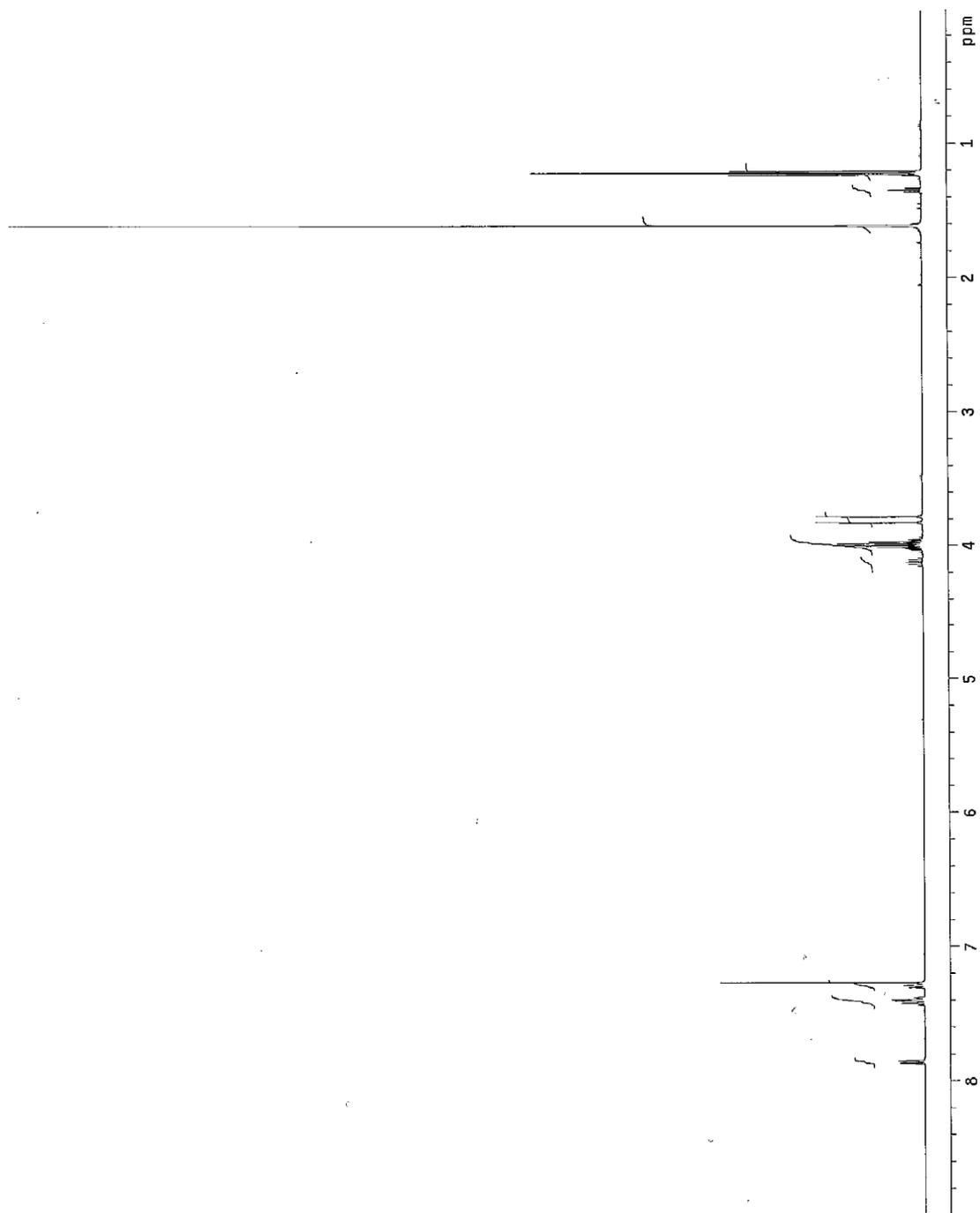
tert-Butyl 2-[(*E*)-non-1-enyl]benzoate (16**).** ^1H NMR (500 MHz, CDCl_3) δ 7.76 (d, $J = 7.8$ Hz, 1H), 7.51 (d, $J = 8.0$ Hz, 1H), 7.40 (dd, $J = 7.8, 7.5$ Hz, 1H), 7.24 (app. t, $J = 7.6$ Hz, 1H), 7.06 (d, $J = 15.6$ Hz, 1H), 6.12 (dt, $J = 15.6, 7.0$ Hz, 1H), 2.25 (dt, $J = 7.6, 7.1$ Hz, 2H), 1.61 (s, 9H), 1.49 (m, 2H), 1.38 – 1.25 (complex m, 8H), 0.89 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 167.3, 138.9, 133.5, 131.2, 130.4, 130.0, 128.5, 127.0, 126.4, 81.3, 33.3, 31.9,

Supporting information

29.4, 29.3, 29.2, 28.3, 22.7, 14.1. IR (neat): 2956, 2925, 2855, 1713, 1644, 1599, 1458, 1251, 1173, 1122 cm^{-1} . HRMS (ESI) calcd. for $\text{C}_{20}\text{H}_{31}\text{O}_2^+$ $[\text{M}+\text{H}]^+$ 303.2324, found 303.2322.

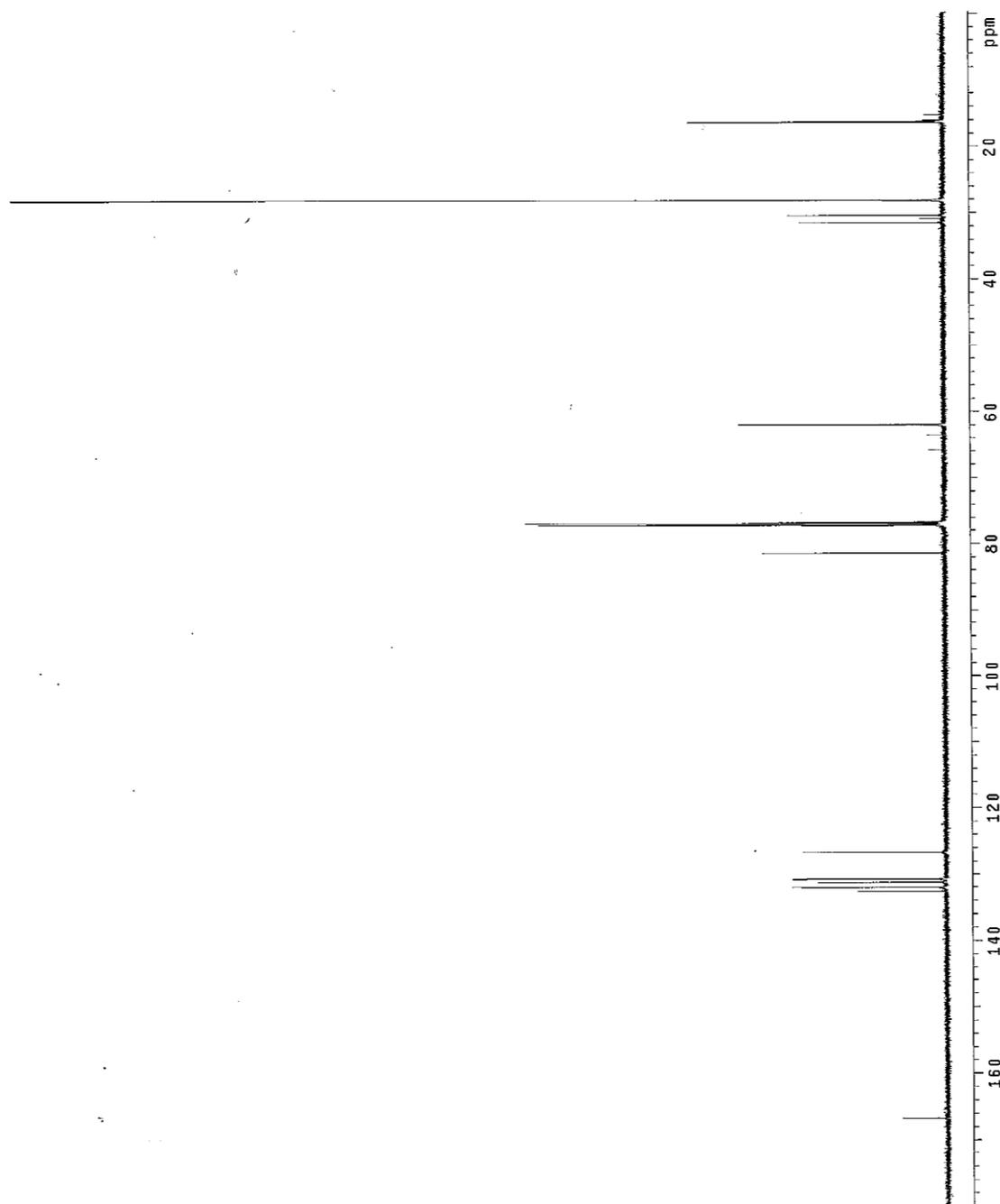
Supporting information

^1H NMR spectrum of *tert*-butyl 2-[(diethoxyphosphoryl)methyl]benzoate (**15**)



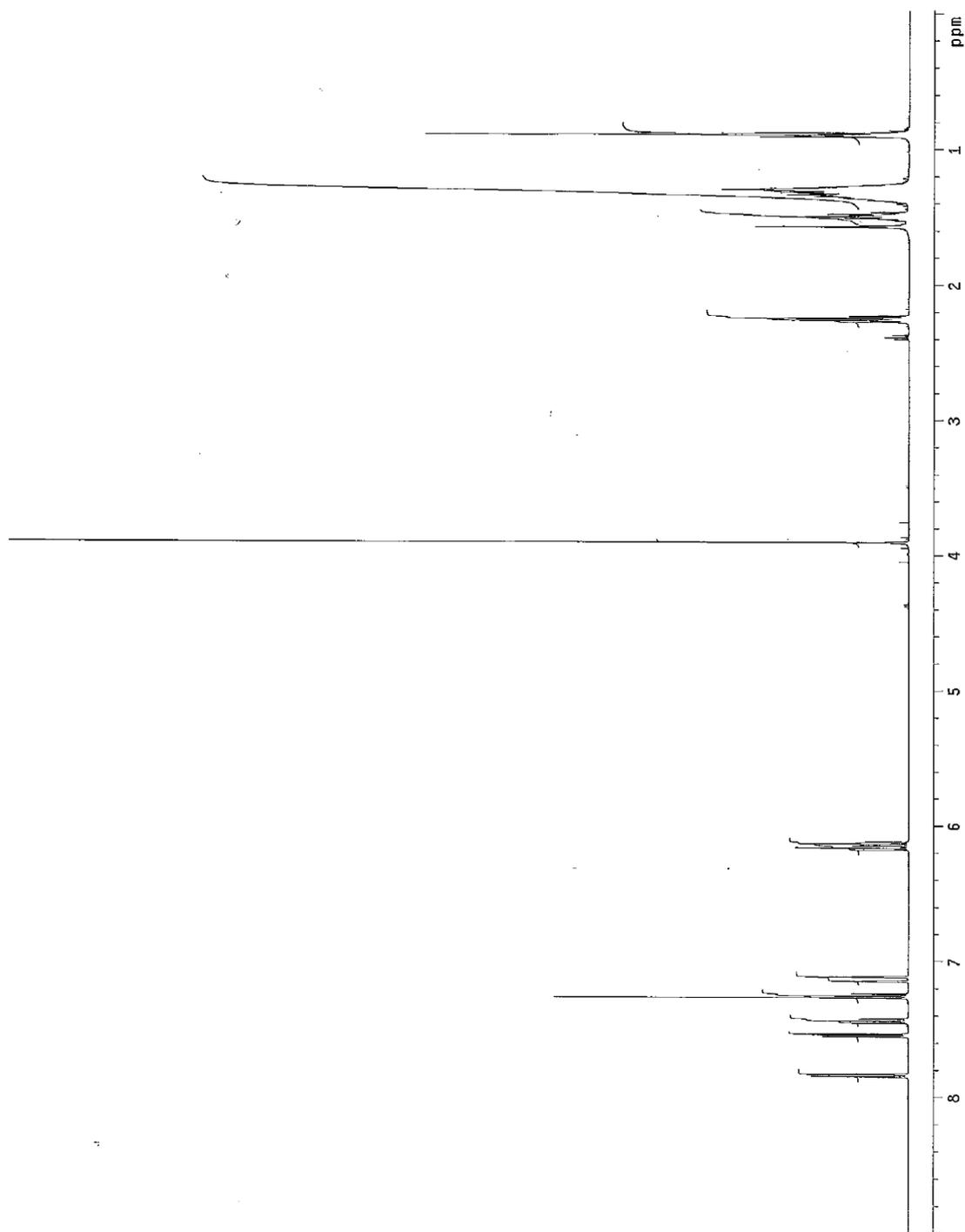
Supporting information

^{13}C NMR spectrum of *tert*-butyl 2-[(diethoxyphosphoryl)methyl]benzoate (**15**)



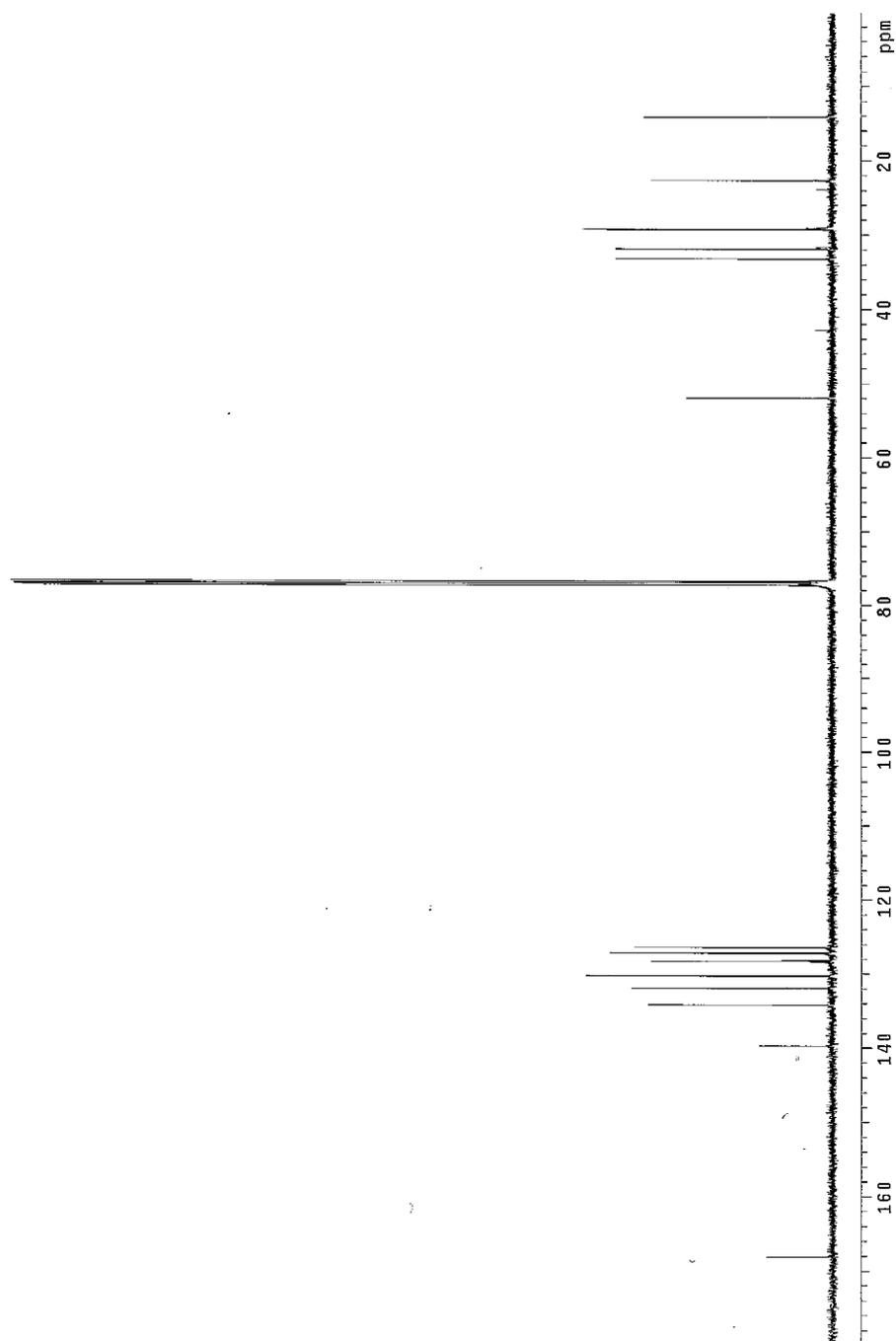
Supporting information

^1H NMR spectrum of methyl 2-[(*E*)-non-1-enyl]benzoate (**8a**)



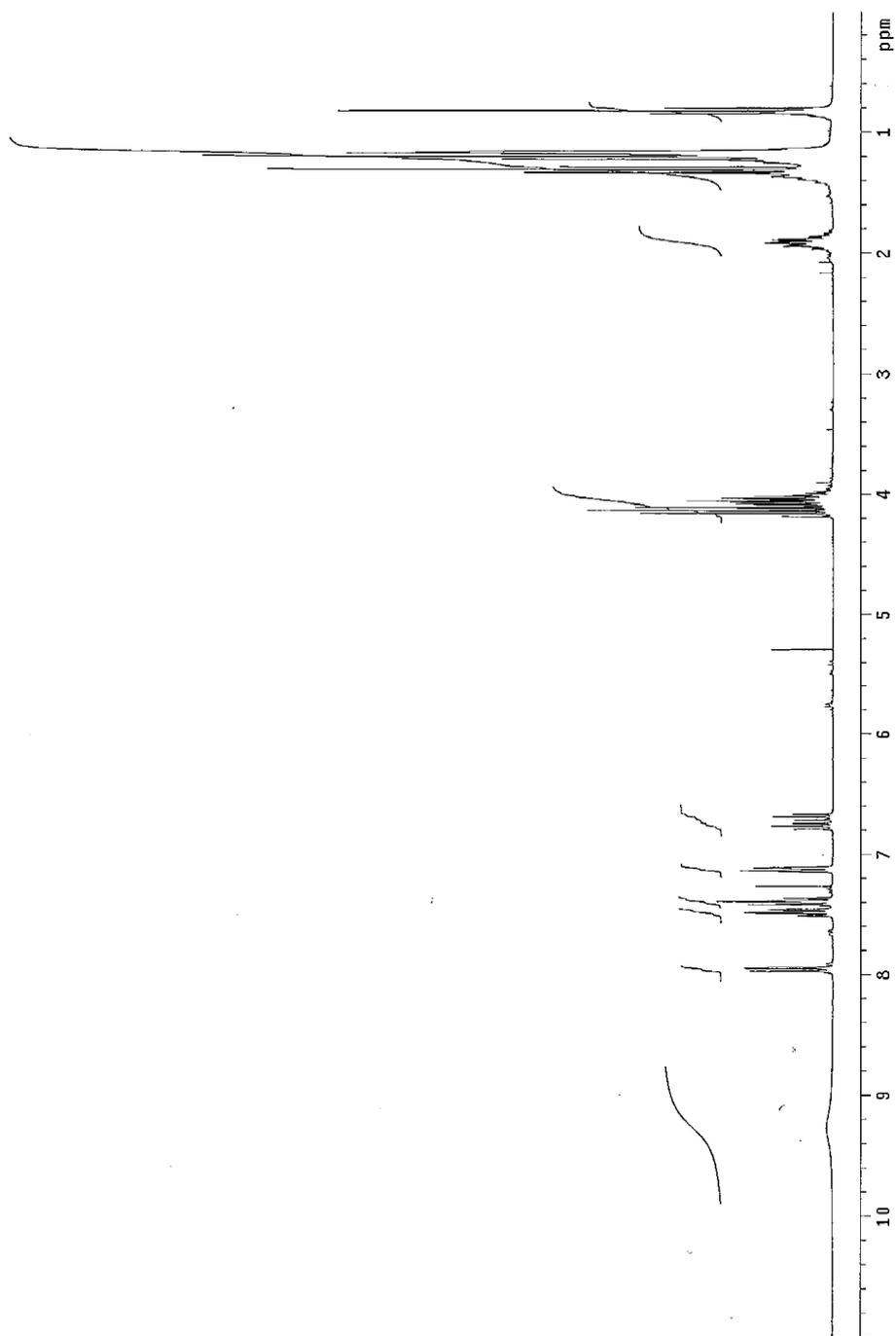
Supporting information

^{13}C NMR spectrum of methyl 2-[(*E*)-non-1-enyl]benzoate (**8a**)



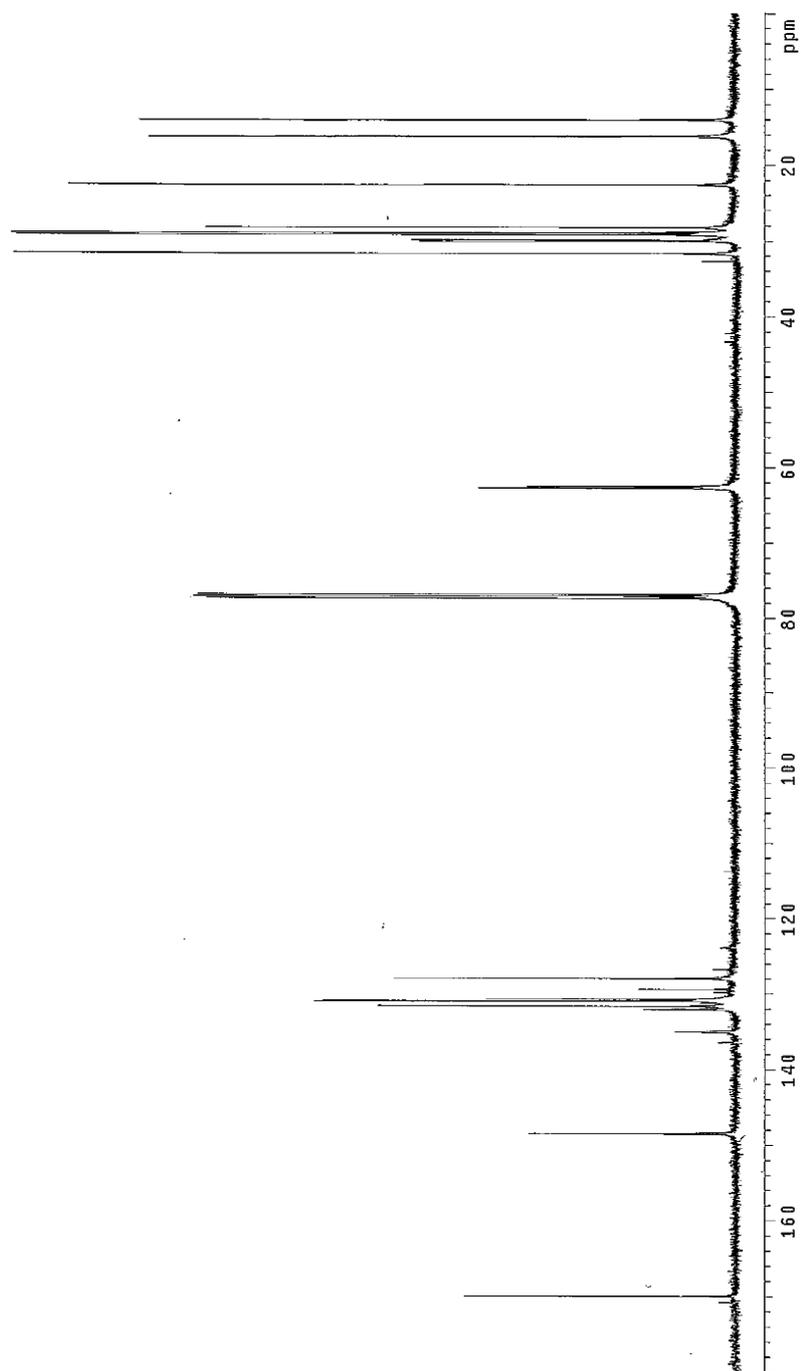
Supporting information

^1H NMR spectrum of 2-[(*E*)-1-(diethylphosphono)non-1-enyl]benzoic acid (*E*-9a)



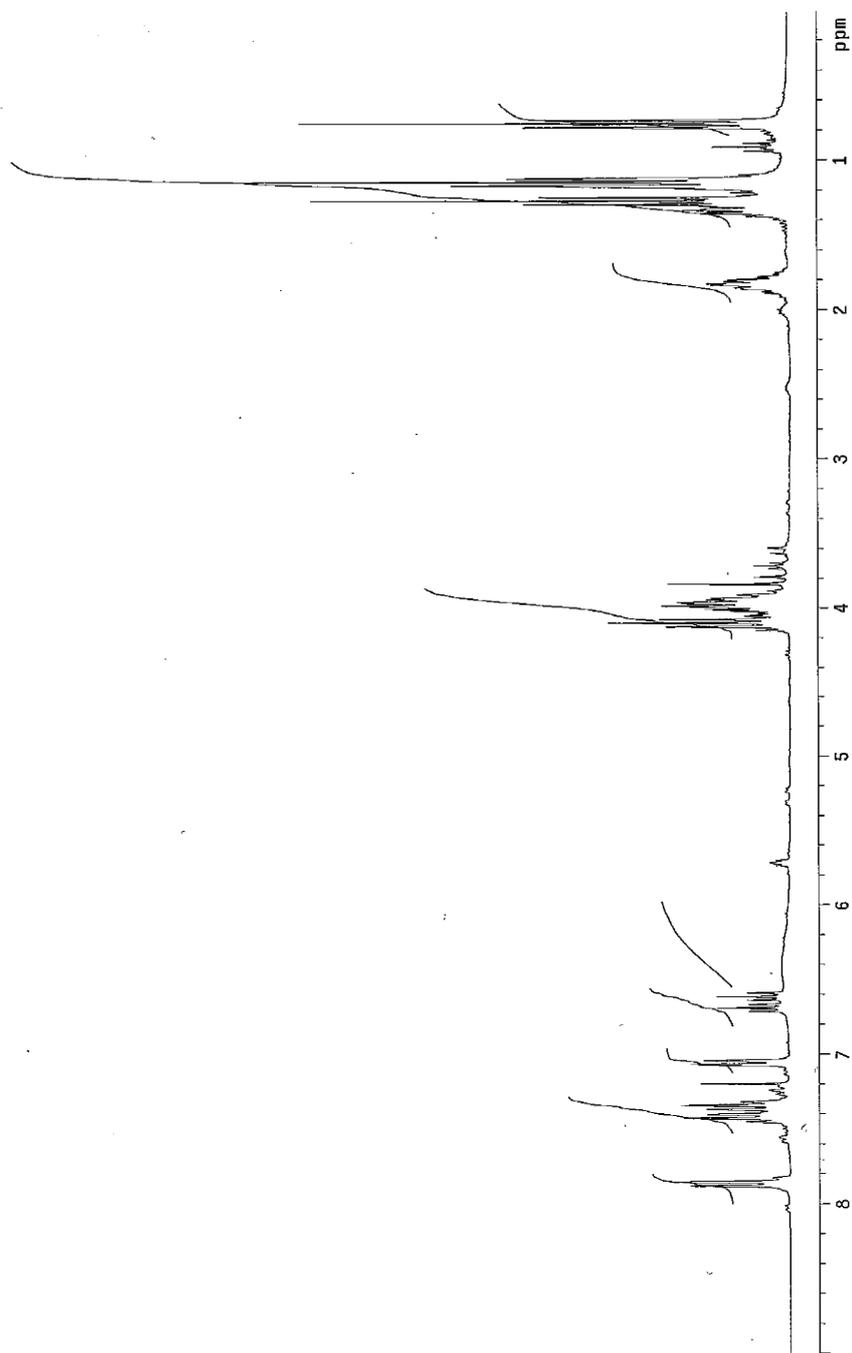
Supporting information

^{13}C NMR spectrum of 2-[(*E*)-1-(diethylphosphono)non-1-enyl]benzoic acid (*E*-**9a**)



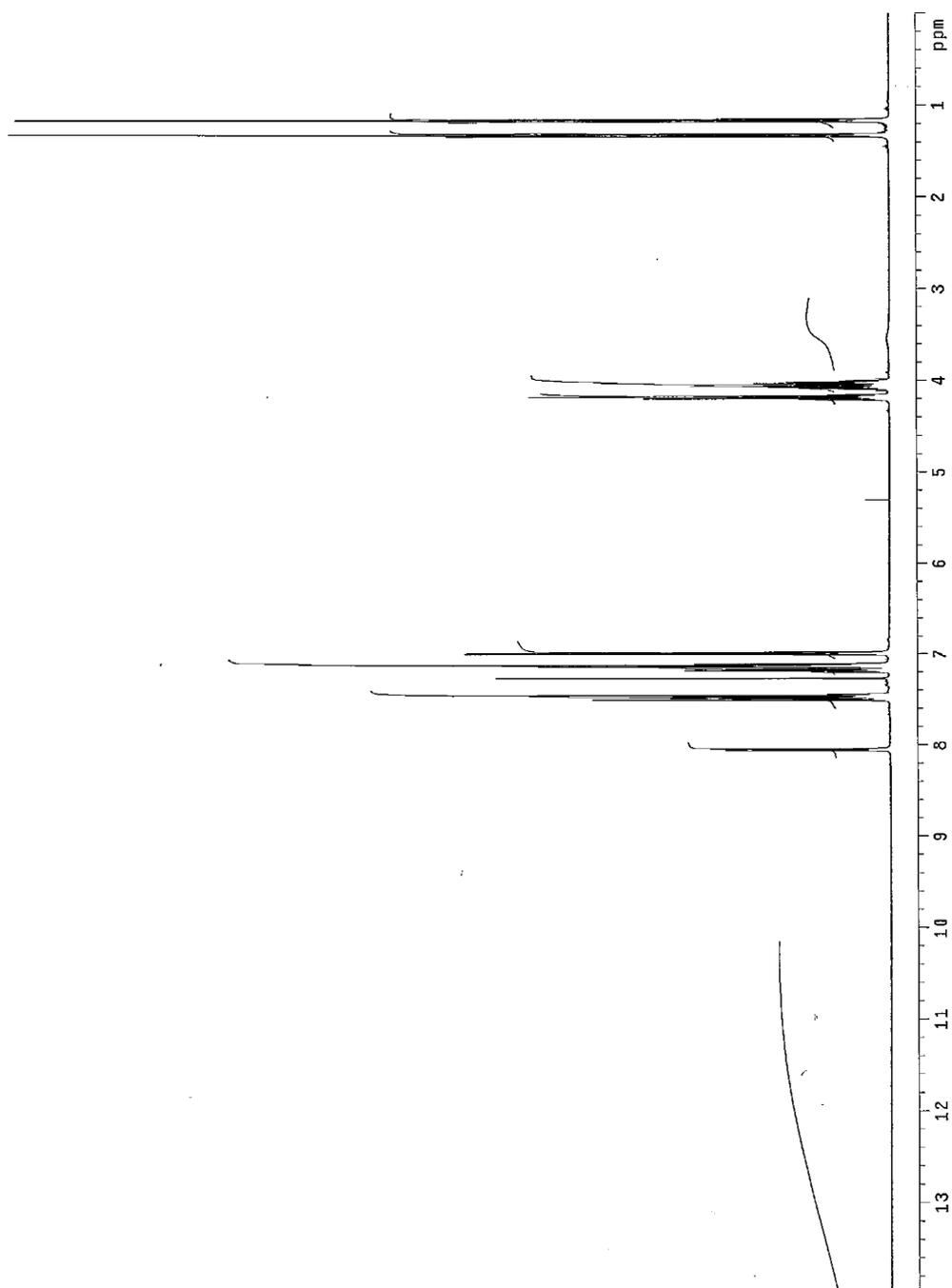
Supporting information

^1H NMR spectrum of 2-[(*E*)-1-(diethylphosphono)pent-1-enyl]benzoic acid (*E*-**9b**)



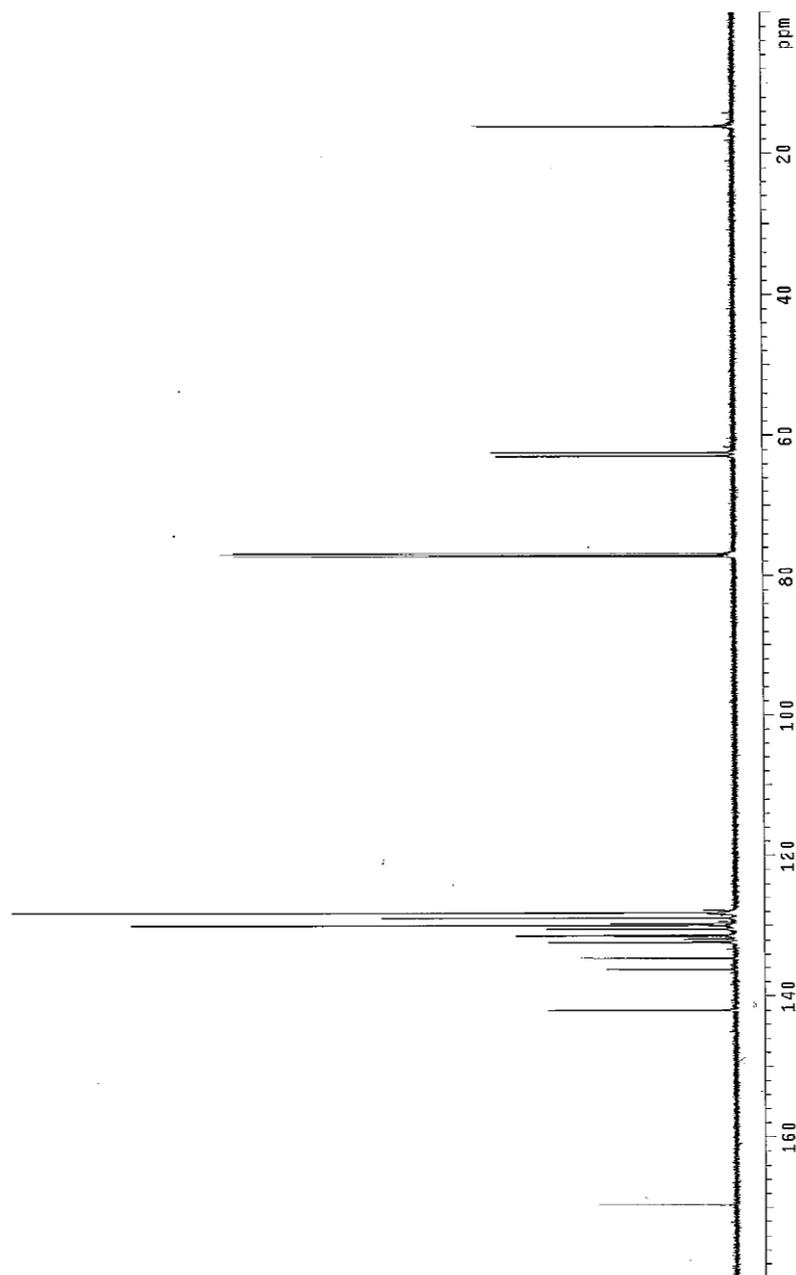
Supporting information

^1H NMR spectrum of 2-[(*E*)-1-diethylphosphono-2-phenylethen-1-yl]benzoic acid (*E*-**9c**)



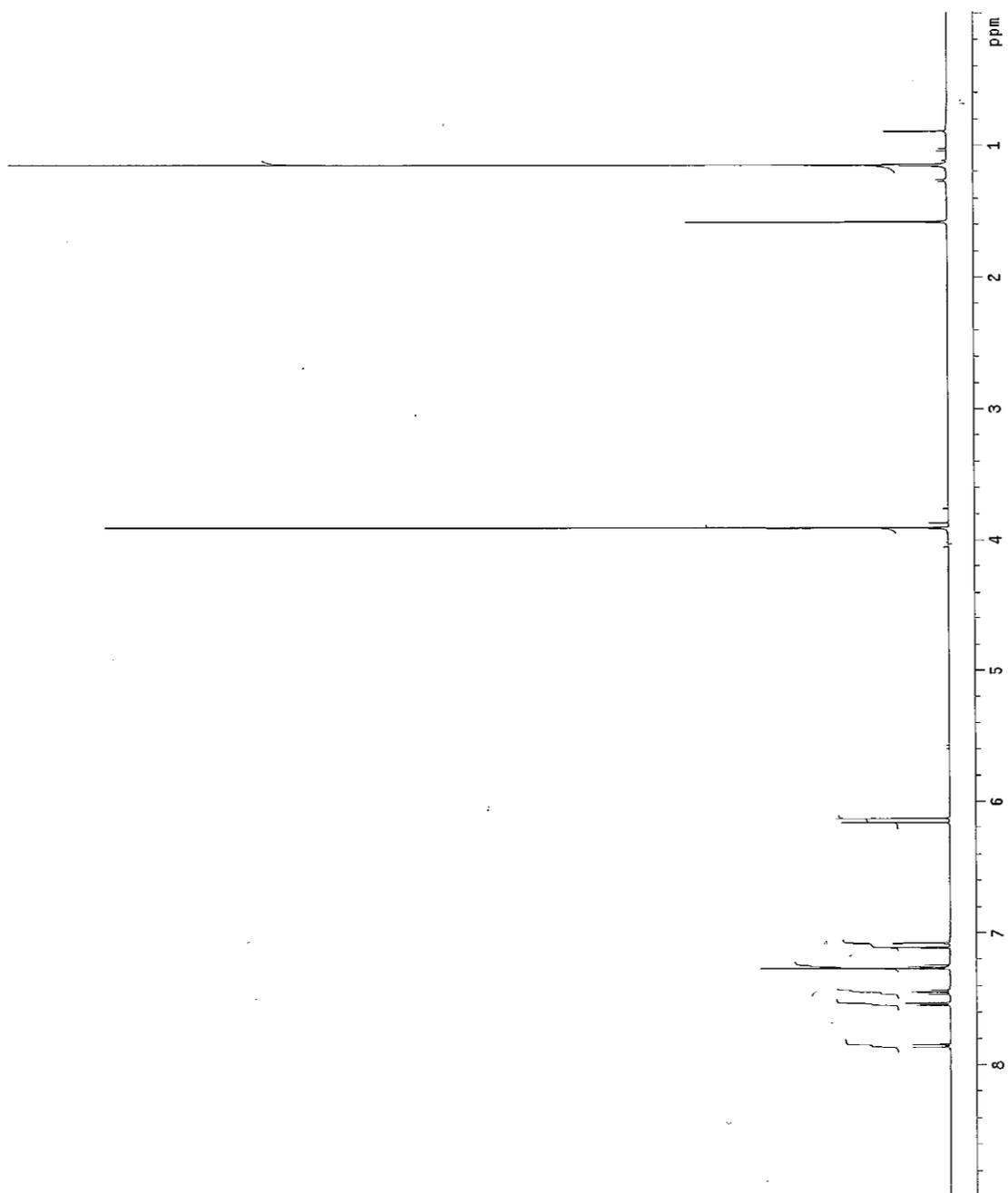
Supporting information

^{13}C NMR spectrum of 2-[(*E*)-1-diethylphosphono-2-phenylethen-1-yl]benzoic acid (*E*-9c)



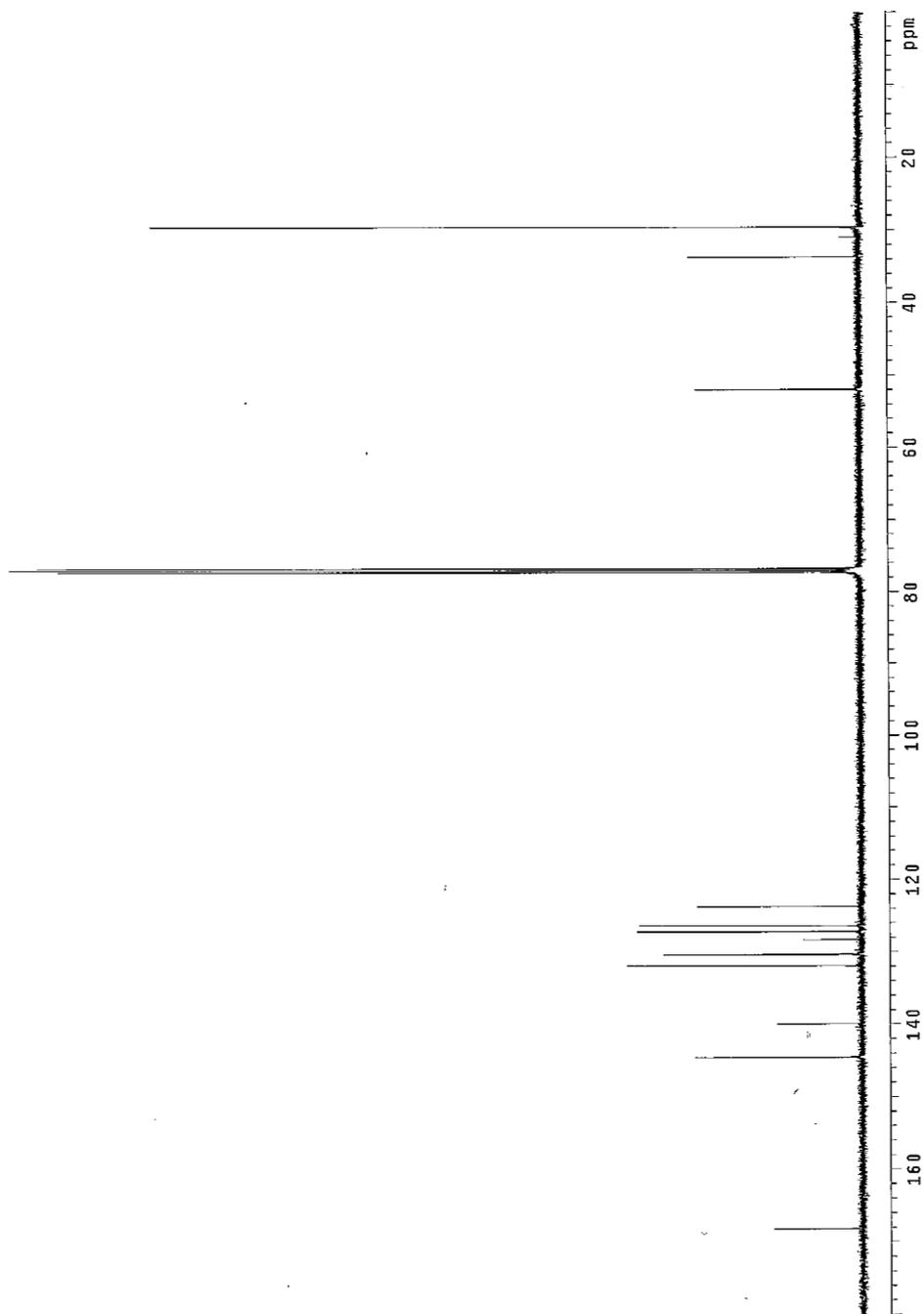
Supporting information

^1H NMR spectrum of methyl 2-[(*E*)-3,3-dimethylbut-1-enyl]benzoate (**8d**)



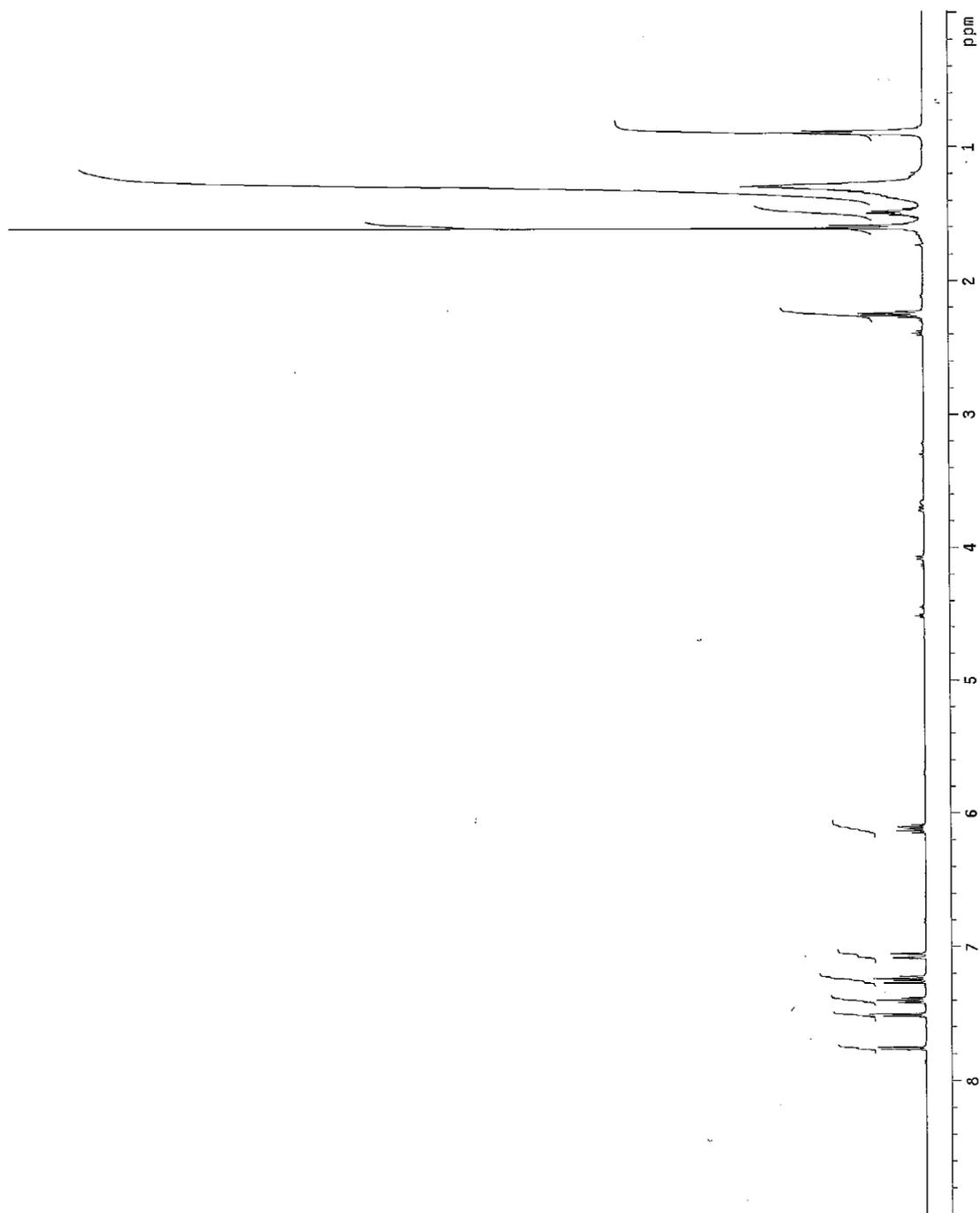
Supporting information

^{13}C NMR spectrum of methyl 2-[(*E*)-3,3-dimethylbut-1-enyl]benzoate (**8d**)



Supporting information

^1H NMR spectrum of *tert*-butyl 2-[(*E*)-non-1-enyl]benzoate (**16**)



Supporting information

^{13}C NMR spectrum of *tert*-butyl 2-[(*E*)-non-1-enyl]benzoate (**16**)

