Received 00th January 20xx,

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Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Phosphorylated cyclopropanes in the synthesis of α-alkylidene-γ-butyrolactones: total synthesis of (±)-savinin, (±)-gadain and (±)-peperomin E.

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Phophorylated cyclopropanes, generated *via* the Rh(II)-catalysed intramolecular cyclopropanation of α-(diethoxyphosphoryl)acetates, have been found to be useful precursors in the synthesis of α-alkylidene-γ-butyrolactones. These cyclopropyl intermediates undergo regioselective reductive ring-opening and subsequent Horner–Wadsworth–Emmons olefination to complete the synthesis. Total syntheses of (±)-savinin and (±)-gadain, as well as the first total synthesis of (±)-peperomin E, are all described using this method.

Introduction

The high natural abundance and varied biological activities of α-alkylidene-γ-butyrolactones has propagated much effort to develop efficient methods for their synthesis.1 With this in mind, we recently introduced a new catalytic approach to convert α-diazo-α-(diethoxyphosphoryl)acetates **1** into α-alkylidene-γ-butyrolactones **4** *via* a telescoped C–H insertion/olefination sequence, using an electrophilic rhodium(II) carbenoid intermediate **2** to perform the key C–H insertion step (Scheme 1A).2a The procedure has since been applied to a range of functionalised compounds (generally with high regioselectivity and diastereoselectivity) and it has also been used in natural product synthesis,2b-d with one of the main advantages of this method being the relative simplicity of the requisite α-diazo-α-(diethoxyphosphoryl)acetate starting materials, which are easily prepared in two steps from simple alcohols.

Herein, we describe an extension of this method, focusing on the reactions of α-diazo-α-(diethoxyphosphoryl)acetates derived from allylic alcohols (Scheme 1B). These starting materials (**5**)are prepared just as easily as those in our earlier work,2a-c but the C–H insertion step is replaced by a rhodium(II)-catalysed cyclopropanation reaction. This results in the formation of phosphorylated cyclopropanes (α-phosphoryl-3-oxabicyclo[3.1.0]hexanones of the form **6**) which may then undergo reductive ring-opening (**6 → 7**) and subsequent Horner–Wadsworth–Emmons olefination to furnish α-alkylidene-γ-butyrolactones **4**.



**Scheme 1.** Previous C–H insertion/olefination sequence to α-alkylidene-γ-butyrolactones (A) compared with our new approach (B) based on the reaction of phosphorylated cyclopropanes.

This alternative route to α-alkylidene-γ-butyrolactones is particularly useful in the case of substrates which do not react well under our original C–H insertion conditions, and is exemplified in this paper by the total syntheses of three natural products, (±)-savinin **8**, (±)-gadain **9** and (±)-peperomin E **10** (Scheme 1, box).3-4 Notably, none these natural products could be formed using the reported C–H insertion procedure,2a-c but all were successfully synthesised using the cyclopropanation methodology described herein.

Results and discussion

This work was initiated during unsuccessful attempts to synthesise isomeric natural products (±)-savinin **8** and (±)-gadain **9**. (–)-Savinin was isolated in 1953 by Hartwell3a and subsequent studies revealed that it possesses cytotoxic,insecticidal and antiviral properties.3b-d (+)-Gadain was isolated later in 1984 and was found to isomerise to (+)-savinin in acidic solution.4 It was originally planned to use our published C–H insertion/olefination method to synthesise each of these compounds. Precedent from our earlier work, as well as additional test reactions performed for this study, both augured well for the success of this approach; unsubstituted homobenzylic substrate **11a** and benzylic methylenedioxy substrate **13** had both already been shown to react well using the original procedure, affording lactones **12a** and **14** respectively, while homobenzylic substrates **11b**–**d** bearing *meta-* and *para*-methoxy substituents **11a** were also compatible, furnishing lactones **12b**–**d**. It therefore appeared logical that the same procedure would be suitable for the synthesis of (±)-savinin **8** and (±)-gadain **9** from closely related diazo precursor **15**, however, to our surprise, no reaction took place when this compound was treated with 2 mol% rhodium(II) octanoate in CH2Cl2 at reflux (our standard C–H insertion conditions), with starting material **15** being the only material recovered from this reaction (Scheme 2).



**Scheme 2.** Telescoped C–H insertion/olefination in the synthesis of compounds **12a**–**d** and **14**; the same procedure was unsuccessful for the synthesis of **16**.

While no reaction products were isolated in the reaction of compound **15**, there was a noticeable and immediate colour change upon addition of the rhodium(II) catalyst (green to dark orange/brown), which is indicative of a change in the rhodium(II) complex, either as a result of ligand coordination to one of the vacant axial coordination sites on the rhodium catalyst or oxidation of Rh(II) to Rh(III).5 No such colour change was observed in the related reactions shown in Scheme 2 (or indeed in any of our previous successful C–H insertion reaction), and it is likely that this outcome is caused by an unwanted intramolecular interaction that is particular to this system. We propose that following diazo decomposition, a complex of the form **18** is produced *via* intramolecular coordination of one of the oxygen atoms of the methylenedioxy motif to rhodium carbenoid **17**, and that this non-productive pathway prevents catalyst turnover (Scheme 3).6

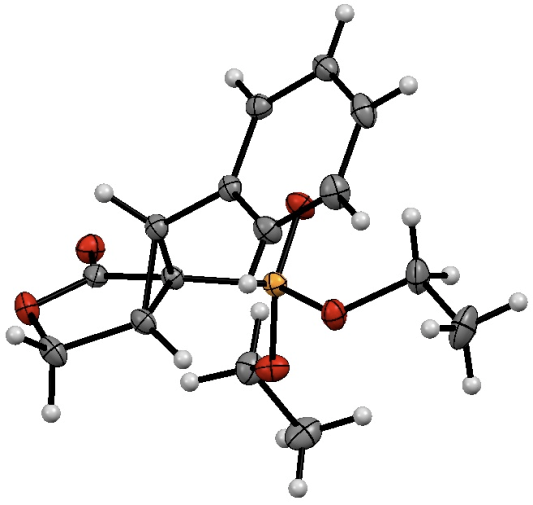


**Scheme 3.** Proposed formation of complex **18** to account for the failure of compound **15** to undergo C–H insertion.

Returning to the synthesis of (±)-savinin **8** and (±)-gadain **9**,it wasat this stage that the use of α-diazo-α-(diethoxyphosphoryl)acetates derived from allyic alcohols were first considered to be viable precursors. Rhodium carbenoids are well known to react with alkenes to form cyclopropanes,7 and it was proposed that the resulting cyclopropanes could undergo reductive ring-opening and subsequent olefination to generate α-methylene-γ-butyrolactones *via* an alternative pathway. It was also thought that the rigidity imparted by the *E-*alkene moiety would minimise unwanted coordination to the intermediate carbenoid, hence the problems associated with the C–H insertion of saturated α-diazo-α-(diethoxyphosphoryl)acetate **15** may be alleviated. As a model system, styrene derivative **19a** was synthesised from cinnamyl alcohol and treated with 2 mol% rhodium(II) octanoate in CH2Cl2 at reflux, mirroring the C–H insertion conditions, and pleasingly this led to the efficient formation of cyclopropane **20a** (Scheme 4). This compound was isolated in 79%yieldas a single diastereoisomer, with its structure and relative configuration confirmed by X-ray crystallography (Figure 1).8 Then, following a brief screen of conditions capable of promoting reductive opening of the cyclopropane,9 it was found that the reaction of compound **24a** with samarium(II) iodide10 in THF at −78 °C led to the formation of lactone **21** in moderate unoptimised yield.11



**Scheme 4.** Cyclopropanation and reductive ring-opening of styrene derivative **19a**.



**Figure 1.** X-ray crystal structure of compound **20a** (CCDC 1465173).

To the best of our knowledge, the synthesis of compound **20a** represents the first reported example of an intramolecular rhodium(II) catalysed cyclopropanation of an α-diazo-α-(dialkoxyphosphoryl)acetate12 and pleasingly, the reaction is also applicable to other allylic alcohol derivatives (Figure 2). The requisite starting materials **19a**–**j** were synthesised in high yields *via* our reported two-step sequence2a-c from known allylic alcohols **22a**–**j**, before each was treated with 2 mol% rhodium(II) octanoate in CH2Cl2 at reflux. A variety of substituted precursors were converted into phosphorylated cyclopropanes **20a**–**j** in moderate to good yields, including substrates derived from unsubstituted allyl alcohol (**19b**), *E-* and *Z*-disubstituted alkenes (**19a**, **19c**–**d**, **19h-j**) and trisubstituted alkenes (**19e**–**g**). It is noteworthy that all of the cyclopropane products were isolated as single diastereoisomers, with the stereochemical outcome being consistent with a concerted cyclopropanation reaction, with the geometry of the alkene precursor being translated into the product. Of particular relevance to the synthesis of natural product targets (±)-savinin **8** and (±)-gadain **9** is the fact that compound **19j** reacted well, delivering cyclopropane **20j** in 73% yield under identical conditions to those that had failed to promote C–H insertion in its saturated analogue **15**.



**Figure 2.** Synthesis of α-phosphoryl-3-oxabicyclo[3.1.0]hexanones **19**–**23a**–**j: a** R1 = H, R2 = Ph; **b** R1 = R2 = H; **c** R1 = *n*-Pr, R2 = H; **d** R1 = H, R2 = CH=CHCH3; **e** R1 = R2 = CH3; **f** R1 = CH3, R2 = CH2CH2CH=C(CH3)2; **g** R1 = Ph, R2 = Ph; **h** R1 = H, R2 = 4-Br-C6H4; **i** R1 = H, R2 = 4-CH3O-C6H4; **j** R1 = H, R2 = 3,4-OCH2O-C6H3. T3P = propyl phosphonic anhydride. *p*-ABSA = 4-acetamidobenzenesulfonyl azide.DBSA = 4-n-dodecylbenzenesulfonyl azide. DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.

With cyclopropane **20j** in hand, the syntheses of (±)-savinin **8** and (±)-gadain **9** was then completed in an additional two steps. First, the treatment of compound **20j** with samarium(II) iodide delivered lactone **16** in 38% (unoptimised) yield, as a single diastereoisomer, which was then heated at reflux in THF with KOBu-*t* and piperonal,13 furnishing a 1.9:1 mixture of α-methylene-γ-butyrolactones (±)-savinin **8**, (±)-gadain **9** in 53% overall yield (Scheme 5). These isomers were partially separable by column chromatography, and the spectral data for both compounds were in full agreement with those published.3-4 Although it was not attempted in this work, the isomerisation of (±)-gadain **9** to (±)-savinin **8** has been described and can be performed if required.4



**Scheme 5.** Syntheses of (±)-savinin **8** and (±)-gadain **9**.

Following the completion of this route, attention switched to a more challenging target, lignan natural product (±)-peperomin E **10**. (+)-Peperomin E was isolated in 1998 by Govindachari and co-workers from *peperomia dindigulensis*,14 a succulent herb, and has been shown to possess a range of biological properties; these include anti-feedant activity,14 cytotoxicity,15a inhibition of malignant lung tumour cells,15b anti-angiogenic activity,15c inhibition of cancer cell lines15d and anti-inflammatory activity.15e To the best of our knowledge, there have been no reported syntheses prior to this publication. It was considered that (+)-peperomin E might be accessible either *via* our previously reported C–H insertion/olefination method or the new cyclopropanation route, and given the similarity of the requisite precursors **24** and **25**,both of these methods were examined (Figure 3).



**Figure 3.** Retrosynthesis of (±)-peperomin E **10**.

The synthesis began with the conversion of commercially available aldehyde **26** into nitrobenzene **27** using concentrated nitric acid, before sequential reduction, diazotisation and iodination afforded iodobenzene derivative **30** in good overall yield. Meanwhile, the same aldehyde precursor **26** wasalso used in a Wittig olefination, furnishing cinnamate **31** in high yield. This alkene was then reacted with iodide **30** in a Heck cross-coupling reaction using conditions reported by Moreno-Mañas and co-workers to form diaryl compound **32** in good yield,16 and subsequent reduction with DIBAL followed by acylation proceeded well, furnishing phosphonate **34**. Finally, diazotisation with DBSA (4-n-dodecylbenzenesulfonyl azide) and LHMDS in the usual way afforded the key cyclopropanation precursor **25**, while performing a standard palladium on carbon hydrogenation prior to diazotisation, also delivered its saturated analogue **24** (Scheme 6).



**Scheme 6.** Synthesis of α-diazo-α-(diethoxyphosphoryl)acetates **40** and **41**.

To investigate the C–H insertion reaction pathway towards peperomin E, α-diazo-α-(diethoxyphosphoryl)acetate **24** was treated with 2 mol% rhodium(II) octanoate in CH2Cl2 at reflux (Scheme 7). Perhaps unsurprisingly, no reaction was observed under these conditions; this outcome is similar to that observed when the analogous reaction was attempted on related compound **15** as described earlier, and we propose that the coordination of one of the oxygen atoms of the methylenedioxy motif of **24** to the rhodium carbenoid (similar to complex **18** in Scheme 3) also takes place in this system, preventing effective catalyst turnover.



**Scheme 7.** Failed C–H insertion reaction of α-diazo-α-(diethoxyphosphoryl)acetate **41**.

Pleasingly, as was the case for the syntheses of (±)-savinin **8** and (±)-gadain **9**, the cyclopropanation reaction of unsaturated analogue **25** was successful. The cyclopropanation of α-diazo-α-(diethoxyphosphoryl)acetate **25** with rhodium(II) octanoate proceeded moderately well, although the isolated yield (35%) was lower than is typical for this transformation. The use of a bulkier rhodium catalyst (rhodium(II) triphenylacetate) led to a modest improvement in the yield for this step. Next, the ring-opening was performed by treating compound **36** with samarium(II) iodide, affording lactone **37** in 55% yield and finally, a facile, high-yielding Horner–Wadsworth–Emmons olefination reaction completed the first reported total synthesis of peperomin E **10**. With the exception of the melting point, all characterisation data recorded for our synthetic material were in accord with those reported in the isolation paper(Scheme 8).14



**Scheme 8.** Total synthesis of peperomin E **10**.

Conclusions

Phosphorylated cyclopropanes formed *via* the rhodium(II) mediated cyclopropanation of allylic α-diazo-α-(diethoxyphosphoryl)acetates have been shown to be useful intermediates en route to α-alkylidene-γ-butyrolactone natural products. Of particular note, the method has been found to proceed well on systems in which the analogous C–H insertion process fails, culminating in the total synthesis of three natural products, (±)-savinin **8**, (±)-gadain **9** and (±)-peperomin E **10**. In this work, we have focused on reductive ring-opening reactions of the key phosphorylated cyclopropane intermediates, but we anticipate that the same compounds will also be amenable to a broader range of transformations; nucleophilic ring-openings, cycloaddition reactions and rearrangement reactions have all been demonstrated on related donor-acceptor cyclopropanes17 and variants of these will be investigated in due course.

Experimental

Except where stated, all reagents were purchased from commercial sources and used without further purification. Except where stated, all experimental procedures were carried out under an atmosphere of argon. Anhydrous CH2Cl2, toluene and DMF were obtained from an Innovative Technology Inc. PureSolv® solvent purification system. Anhydrous THF was obtained by distillation over sodium benzophenone ketyl immediately before use. 1H NMR, 13C NMR and 31P NMR spectra were recorded on a JEOL ECX400 or JEOL ECS400 spectrometer, operating at 400 MHz, 100 MHz and 162 MHz respectively. All spectral data were acquired at 295 K. Chemical shifts (δ) are quoted in parts per million (ppm). The residual solvent peak, δH 7.26 and δC 77.0 for CDCl3 and δH 2.50 and δC 39.5 for DMSO-*d*6. Coupling constants (*J*) are reported in Hertz (Hz) to the nearest 0.1 Hz. The multiplicity abbreviations used are: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). Signal assignment was achieved by analysis of DEPT, COSY, NOESY, HMBC and HSQC experiments where required. Spectra were processed using ‘iNMR’ software which can be obtained free of charge online. Infrared (IR) spectra were recorded on either a ThermoNicolet IR-100 spectrometer with NaCl plates as a thin film dispersed from either CH2Cl2 or CDCl3, or a PerkinElmer UATR Two spectrometer and are reported in wavenumbers (cm−1). Mass-spectra were obtained by the University of York Mass Spectrometry Service, using electrospray ionisation (ESI) on a Bruker Daltonics, Micro-tof spectrometer. Melting points were determined using Gallenkamp apparatus and are uncorrected. Reactions were monitored using thin layer chromatography (TLC), which was carried out on Merck silica gel 60F254 pre-coated aluminium foil sheets and were visualised using UV light (254 nm) and stained with basic aqueous potassium permanganate. Flash column chromatography was carried out using slurry packed Fluka silica gel (SiO2), 35–70 µm, 60 Å, under a light positive pressure, eluting with the specified solvent system. No issues associated with instability or decomposition of the azide reagents or diazo products were observed, with no special handling precautions required.

General experimental

General procedure A: T3P-mediated esterifications

To a stirred solution of alcohol(8.00 mmol) in toluene (40 mL) under an atmosphere of argon, was added sequentially diethylphosphonoacetic acid (DEPAA) (8.40 mmol, 1.05 eq.), *N*,*N*-diisopropylethylamine (DIPEA) (20.8 mmol, 2.6 eq.) and propylphosphonic anhydride (T3P) (10.4 mmol, 1.3 eq., 50% w/w solution in EtOAc/THF). The solution was stirred at RT for 1–4 h (with progress monitored by TLC analysis), after which time it was diluted with water (50 mL) and extracted with EtOAc (3 × 100 mL) followed by sequential washing of the combined organic extracts with 10% aq. HCl (50 mL), sat. aq. NaHCO3 (50 mL) and brine (50 mL). The organic extract was then dried over MgSO4 and concentrated *in vacuo*, affording the α-(diethoxyphosphoryl)acetate product, which was used without further purification.

General procedure B: Base-mediated diazo transfer (LHMDS or NaH)

To a stirred solution of α-(diethoxyphosphoryl)acetate(5.0 mmol) in THF (25 mL, 5 mL/mmol), cooled to −78 °C under an atmosphere of argon, was added lithium bis(trimethylsilyl)amide (LHMDS) (6.0 mmol, 1.2 eq., 1.0 M solution in THF) or NaH (6.0 mmol, 1.2 eq., 60% dispersion in mineral oil). The solution was allowed to warm to RT and stirred for 10 mins, after which time 4-acetamidobenzenesulfonyl azide (*p*-ABSA) or 4-*n*-dodecylbenzenesulfonyl azide (DBSA) (6.0 mmol, 1.2 eq.) was added to the solution. After stirring for 1 h at RT the mixture was diluted with diethyl ether (100 mL) and water (25 mL) prior to extraction with diethyl ether (3 × 50 mL). The combined organic extracts were washed with sat. aq. NaHCO3 (2 × 25 mL), dried over MgSO4, concentrated *in vacuo* and purified by column chromatography affording the α-diazo(diethoxyphosphoryl)acetate product.

General procedure C: Base-mediated diazo transfer (DBU)

To a stirred solution of α-(diethoxyphosphoryl)acetate(5.0 mmol) and *p*-ABSA or DBSA (7.5 mmol, 1.5 eq.) in CH2Cl2 (50 mL, 10 mL/mmol) cooled to 0 °C under an atmosphere of argon, was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (7.5 mmol, 1.5 eq.) dropwise. The solution was stirred overnight with warming at RT, after which time the mixture was filtered through a pad of Celite and silica. The filtrate was concentrated *in vacuo* then purified by column chromatography affording the α-diazo(diethoxyphosphoryl)acetate product.

General procedure D: **One-pot Rh(II)-catalysed C–H insertion/olefination sequence**

To an oven dried sealable tube containing α-diazo(diethoxyphosphoryl)acetate (0.200 mmol) flushed with argon was added CH2Cl2 (4.0 mL) followed by Rh2(oct)4 (2 mol%). The solution was stirred at 45 °C for 20 h and then concentrated *in vacuo*. The residue was dissolved in THF (4.0 mL) and cooled to 0 °C prior to the addition of KOBu-*t* (1.2 equiv.) which was stirred at 0 °C for 1 h and then cooled to −78 °C. Paraformaldehyde (2.0 equiv.) was added to the solution and stirred for 15 mins at −78 °C and a further 2 h at RT. The solution was quenched with sat. aq. NH4Cl (10 mL) and then diluted with CH2Cl2 (20 mL). The organic layer was separated and the aqueous extracted with EtOAc (2 × 20 mL). The organic extracts were dried over Na2SO4, concentrated *in vacuo* and purified by column chromatography affording the α-methylene-γ-butyrolactone product.

General procedure E: **Rh(II)-catalysed cyclopropanation**

To an oven dried sealable tube containing α-diazo-α-(dialkoxyphosphoryl)acetate (0.200 mmol) flushed with argon was added CH2Cl2 (4.0 mL) followed by Rh2(oct)4 (2 mol%). The solution was stirred at 45 °C for 20 h and then concentrated *in vacuo*. The residue was purified by column chromatography affording the α-phosphoryl-3-oxabicyclo[3.1.0]hexanone product.

Compound Synthesis

**3-(4-Methoxyphenyl)propyl 2-(diethoxyphosphoryl)acetate**. Synthesised using general procedure A with 3-(4-methoxyphenyl)propan-1-ol (831 mg, 5.00 mmol), toluene (25.0 mL), DEPAA (1.03 g, 5.25 mmol), DIPEA (2.26 mL, 13.0 mmol) and T3P (4.14 g, 6.50 mmol, 50% w/w solution in EtOAc) affording the *title compound* as a yellow oil (1.66 g, 96%); Rf 0.09 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2982, 1733, 1612, 1513, 1243, 1177, 1114, 1019, 964, 834, 813, 783; δH (400 MHz, CDCl3) 1.32 (6 H, t, *J* = 7.1), 1.88–1.95 (2 H, m), 2.62 (2 H, t, *J* = 7.6), 2.95 (2 H, d, *J* = 21.6), 3.75 (3 H, s), 4.10–4.19 (6 H, m), 6.80 (2 H, d, *J* = 8.7), 7.07 (2 H, d, *J* = 8.7); δC (100 MHz, CDCl3) 16.2 (d, *J* = 6.4), 30.2, 30.9, 34.2 (d, *J* = 134.1), 55.1, 62.5 (d, *J* = 6.3), 64.7, 113.7, 129.2, 132.9, 157.8, 165.7 (d, *J* = 6.1); δP (162 MHz, CDCl3) 20.4; HRMS (ESI+): Found: 367.1286; C16H25NaO6P (MNa+) Requires 367.1281 (−1.4 ppm error).

**3-(4-Methoxyphenyl)propyl 2-diazo-2-(diethoxyphosphoryl)acetate (**11b). Synthesised using general procedure C with 3-(4-methoxyphenyl)propyl 2-(diethoxyphosphoryl)acetate (1.66 g, 4.82 mmol), DBSA (2.42 mL, 7.23 mmol), DBU (1.08 mL, 7.23 mmol) and CH2Cl2 (48.0 mL). Purification by column chromatography (1:1 hexane:EtOAc) afforded the *title* *compound* **11b** as a pale yellow oil (1.70 g, 95%); Rf 0.57 (1:4 hexane:EtOAc); νmax (thin film)/cm-1 2985, 2128, 1702, 1613, 1513, 1389, 1276, 1246, 1018, 978, 813, 746, 591, 560; δH (400 MHz, CDCl3) 1.36 (6 H, td, *J* = 7.1, *J* = 0.8), 1.91–1.98 (2 H, m), 2.63 (2 H, t, *J* = 7.6), 3.78 (3 H, s), 4.11–4.27 (6 H, m), 6.82 (2 H, d, *J* = 8.7), 7.08 (2 H, d, *J* = 8.7); δC (100 MHz, CDCl3) 16.1 (d, *J* = 7.3), 30.4, 30.9, 54.0 (d, *J* = 226.6), 55.1, 63.5 (d, *J* = 5.9), 64.8, 113.8, 129.2, 132.7, 157.9, 163.3 (d, *J* = 12.3); δP (162 MHz, CDCl3) 10.8; HRMS (ESI+): Found: 393.1196; C16H23N2NaO6P (MNa+) Requires 393.1186 (−2.6 ppm error).

**3-(3-Methoxyphenyl)propyl 2-(diethoxyphosphoryl)acetate**. Starting with known alcohol 3-(3-methoxyphenyl)propan-1-ol (831 mg, 5.00 mmol),18 general procedure A was performed with toluene (25.0 mL), DEPAA (1.03 g, 5.25 mmol), DIPEA (2.26 mL, 13.0 mmol) and T3P (4.14 g, 6.50 mmol, 50% w/w solution in EtOAc) affording the *title compound* as a yellow oil (1.66 g, 96%); Rf 0.09 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2982, 1736, 1601, 1585, 1489, 1392, 1262, 1154, 1117, 1025, 970; δH (400 MHz, CDCl3) 1.33 (6 H, t, *J* = 7.1), 1.92–2.00 (2 H, m), 2.67 (2 H, t, *J* = 7.7), 2.96 (2 H, d, *J* = 21.6), 3.78 (3 H, s), 4.13–4.20 (6 H, m), 6.72–6.77 (3 H, m), 7.16–7.21 (1 H, m); δC (100 MHz, CDCl3) 16.3 (d, *J* = 6.5), 29.9, 31.9, 34.2 (d, *J* = 133.8), 55.0, 62.6 (d, *J* = 6.6), 64.7, 111.2, 114.2, 120.7, 129.3, 142.6, 159.6, 165.8 (d, *J* = 6.1); δP (162 MHz, CDCl3) 20.4; HRMS (ESI+): Found: 367.1272; C16H25NaO6P (MNa+) Requires 367.1281 (2.5 ppm error).

**3-(3-Methoxyphenyl)propyl 2-diazo-2-(diethoxyphosphoryl)acetate (**11c). Synthesised using general procedure C with 3-(3-methoxyphenyl)propyl 2-(diethoxyphosphoryl)acetate(1.66 g, 4.82 mmol), DBSA (2.42 mL, 7.23 mmol), DBU (1.08 mL, 7.23 mmol) and CH2Cl2 (48.0 mL). Purification by column chromatography (1:1 hexane:EtOAc) afforded the *title* *compound* **11c** as a pale yellow oil (1.61 g, 90%); Rf 0.57 (1:4 hexane:EtOAc); νmax (thin film)/cm-1 2983, 2127, 1701, 1602, 1584, 1489, 1455, 1389, 1273, 1015, 976, 780, 745, 590, 559; δH (400 MHz, CDCl3) 1.36 (6 H, td, *J* = 7.1, *J* = 0.7), 1.94–2.01 (2 H, m), 2.67 (2 H, t, *J* = 7.6), 3.78 (3 H, s), 4.11–4.27 (6 H, m), 6.71–6.77 (3 H, m), 7.20 (1 H, app. t, *J* = 7.8); δC (100 MHz, CDCl3) 16.1 (d, *J* = 6.9), 30.0, 31.8, 53.9 (d, *J* = 226.6), 55.0, 63.5 (d, *J* = 6.2), 64.8, 111.1, 114.2, 120.6, 129.3, 142.3, 159.6, 163.3 (d, *J* = 12.1); δP (162 MHz, CDCl3) 10.8; HRMS (ESI+): Found: 393.1177; C16H23N2NaO6P (MNa+) Requires 393.1186 (2.2 ppm error).

**3-(3,4-Dimethoxyphenyl)propyl 2-(diethoxyphosphoryl)acetate.** Synthesised using general procedure A with 3-(3,4-dimethoxyphenyl)propan-1-ol (981 mg, 5.00 mmol), toluene (25.0 mL), DEPAA (1.03 g, 5.25 mmol), DIPEA (2.26 mL, 13.0 mmol) and T3P (4.14 g, 6.50 mmol, 50% w/w solution in EtOAc) affording the *title compound* as a yellow oil (1.87 g, 100%); Rf 0.09 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2936, 1732, 1515, 1465, 1257, 1236, 1157, 1140, 1116, 1019, 965; δH (400 MHz, CDCl3) 1.31 (6 H, td, *J* = 7.1, *J* = 0.4), 1.89–1.96 (2 H, m), 2.62 (2 H, t, *J* = 7.6), 2.95 (2 H, d, *J* = 21.6), 3.82 (3 H, s), 3.84 (3 H, s), 4.11–4.18 (6 H, m), 6.68–6.77 (3 H, m); δC (100 MHz, CDCl3) 16.2 (d, *J* = 6.4), 30.2, 31.4, 34.2 (d, *J* = 134.0), 55.7, 55.8, 62.5 (d, *J* = 6.7), 64.7, 111.1, 111.5, 120.1, 133.5, 147.2, 148.7, 165.7 (d, *J* = 6.4); δP (162 MHz, CDCl3) 20.4; HRMS (ESI+): Found: 397.1392; C17H27NaO7P (MNa+) Requires 397.1387 (−1.4 ppm error).

**3-(3,4-Dimethoxyphenyl)propyl 2-diazo-2-(diethoxyphosphoryl)acetate (11d).** Synthesised using general procedure C with 3-(3,4-dimethoxyphenyl)propyl 2-(diethoxyphosphoryl)acetate **152a** (1.87 g, 5.00 mmol), DBSA (2.42 mL, 7.25 mmol), DBU (1.08 mL, 7.25 mmol) and CH2Cl2 (50.0 mL). Purification by column chromatography (1:1 hexane:EtOAc) afforded the *title* *compound* **152b** as a pale yellow oil (1.97 g, 98%); Rf 0.53 (1:4 hexane:EtOAc); νmax (thin film)/cm-1 2936, 2127, 1701, 1515, 1465, 1274, 1260, 1156, 1015, 976, 799, 731, 589, 558; δH (400 MHz, CDCl3) 1.36 (6 H, td, *J* = 7.1, *J* = 0.8), 1.93–2.00 (2 H, m), 2.64 (2 H, t, *J* = 7.6), 3.85 (3 H, s), 3.87 (3 H, s), 4.12–4.28 (6 H, m), 6.69–6.80 (3 H, m); δC (100 MHz, CDCl3) 16.0 (d, *J* = 7.2), 30.3, 31.3, 53.7 (d, *J* = 229.3), 55.6, 55.7, 63.5 (d, *J* = 6.1), 64.7, 111.1, 111.5, 120.0, 133.2, 147.2, 148.7, 163.2 (d, *J* = 12.5); δP (162 MHz, CDCl3) 10.7; HRMS (ESI+): Found: 423.1275; C17H25N2NaO7P (MNa+) Requires 423.1292 (3.9 ppm error).

**4-(4-Methoxybenzyl)-3-methylenedihydrofuran-2(3*H*)-one (12b).** Synthesised using general procedure D with 3-(4-methoxyphenyl)propyl 2-diazo-2-(diethoxyphosphoryl)acetate **11b** (78 mg, 0.211 mmol), CH2Cl2 (4.2 mL), Rh2(oct)4 (3.3 mg, 4.2 μmol), THF (4.2 mL), KOBu-*t* (28.4 mg, 0.253 mmol) and paraformaldehyde (12.7 mg, 0.422 mmol). Purification by column chromatography (2:1 hexane:EtOAc) afforded the *title compound* **12b** as a colourless oil (20 mg, 43%); Rf 0.53 (2:1 hexane:EtOAc); νmax (thin film)/cm-1 2912, 1760, 1611, 1513, 1301, 1248, 1179, 1114, 1033, 815; δH (400 MHz, CDCl3) 2.75 (1 H, dd, *J* = 13.9, *J* = 8.8), 2.90 (1 H, dd, *J* = 13.9, *J* = 7.0), 3.28–3.36 (1 H, m), 3.80 (3 H, s), 4.05 (1 H, dd, *J* = 9.2, *J* = 5.1), 4.33 (1 H, dd, *J* = 9.2, *J* = 8.1), 5.42 (1 H, d, *J* = 2.3), 6.26 (1 H, d, *J* = 2.6), 6.85 (2 H, d, *J* = 8.6), 7.09 (2 H, d, *J* = 8.6); δC (100 MHz, CDCl3) 39.0, 40.3, 55.2, 70.6, 114.1, 122.7, 129.4, 129.9, 137.6, 158.5, 170.7; HRMS (ESI+): Found: 241.0827; C13H14NaO3 (MNa+) Requires 241.0835 (3.5 ppm error).

**4-(3-Methoxybenzyl)-3-methylenedihydrofuran-2(3*H*)-one (12c).** Synthesised using general procedure D with 3-(3-methoxyphenyl)propyl 2-diazo-2-(diethoxyphosphoryl)acetate **11c** (77 mg, 0.208 mmol), CH2Cl2 (4.2 mL), Rh2(oct)4 (3.2 mg, 4.2 μmol), THF (4.2 mL), KOBu-*t* (28.0 mg, 0.250 mmol) and paraformaldehyde (12.5 mg, 0.416 mmol). Purification by column chromatography (2:1 hexane:EtOAc) afforded the *title* *compound* **12c** as a colourless oil (20 mg, 44%); Rf 0.52 (2:1 hexane:EtOAc); νmax (thin film)/cm-1 2915, 1762, 1601, 1490, 1262, 1154, 1116, 1040; δH (400 MHz, CDCl3) 2.77 (1 H, dd, *J* = 13.8, *J* = 9.0), 2.96 (1 H, dd, *J* = 13.8, *J* = 6.8), 3.33–3.42 (1 H, m), 3.80 (3 H, s), 4.06 (1 H, dd, *J* = 9.2, *J* = 5.2), 4.35 (1 H, dd, *J* = 9.2, *J* = 8.0), 5.47 (1 H, d, *J* = 2.4), 6.28 (1 H, d, *J* = 2.7), 6.71–6.72 (1 H, m), 6.77 (1 H, br. d, *J* = 7.5), 6.79 (1 H, dd, *J* = 8.3, *J* = 2.5), 7.23 (1 H, app. t, *J* = 7.9); δC (100 MHz, CDCl3) 40.0, 40.1, 55.3, 70.7, 112.1, 114.9, 121.3, 122.8, 129.9, 137.7, 139.1, 159.9, 170.8; HRMS (ESI+): Found: 241.0846; C13H14NaO3 (MNa+) Requires 241.0835 (−4.5 ppm error).

**4-(3,4-Dimethoxybenzyl)-3-methylenedihydrofuran-2(3*H*)-one (12d).** Synthesised using general procedure D with 3-(3,4-dimethoxyphenyl)propyl 2-diazo-2-(diethoxyphosphoryl)acetate **11d** (86 mg, 0.215 mmol), CH2Cl2 (4.3 mL), Rh2(oct)4 (3.4 mg, 4.3 μmol), THF (4.3 mL), KOBu-*t* (29.0 mg, 0.258 mmol) and paraformaldehyde (12.9 mg, 0.430 mmol). Purification by column chromatography (2:1 hexane:EtOAc) afforded the *title compound* **12d** as a colourless oil (20 mg, 37%); Rf 0.26 (2:1 hexane:EtOAc); νmax (thin film)/cm-1 2911, 2836, 1759, 1590, 1515, 1465, 1260, 1157, 1141, 1115, 1026; δH (400 MHz, CDCl3) 2.75 (1 H, dd, *J* = 13.9, *J* = 8.8), 2.90 (1 H, dd, *J* = 13.9, *J* = 7.0), 3.29–3.38 (1 H, m), 3.86 (3 H, s), 3.86 (3 H, s), 4.06 (1 H, dd, *J* = 9.2, *J* = 5.0), 4.34 (1 H, dd, *J* = 9.2, *J* = 8.0), 5.43 (1 H, d, *J* = 2.3), 6.26 (1 H, d, *J* = 2.6), 6.68 (1 H, d, *J* = 2.0), 6.71 (1 H, dd, *J* = 8.1, *J* = 2.0), 6.81 (1 H, d, *J* = 8.1); δC (100 MHz, CDCl3) 39.6, 40.3, 55.8 (2C), 70.5, 111.2, 111.9, 120.9, 122.7, 129.9, 137.5, 147.9, 149.0, 170.7; HRMS (ESI+): Found: 271.0950; C14H16NaO4 (MNa+) Requires 271.0941 (−3.3 ppm error).

**3-(1,3-Benzodioxol-5-yl) 2-(diethoxyphosphoryl)acetate.** To powdered LiAlH4 (1.516 g, 30.5 mmol) under argon was added diethyl ether (120 mL) *via* cannula whilst being cooled to 0 °C. A solution of (*E*)-ethyl 3-(1,3-benzodioxol-5-yl)acrylate (1.68 g, 7.63 mmol) in diethyl ether (20 mL) was added dropwise *via* cannula to the suspension over 5 mins and stirred at 0 °C for 1 h then at RT for 30 mins. The suspension was quenched at 0 °C dropwise with water (1.5 mL) followed by 15% aq. NaOH (1.5 mL) and again with water (4.5 mL) then stirred for 30 mins at RT. The solution was filtered through a pad of Celite and washed with diethyl ether (50 mL). The filtrate was concentrated *in vacuo* affording the allylic alcohol, which was used without further purification.

To a solution of the allylic alcohol in methanol (30 mL) was added palladium on carbon (10% wt. % loading, 100 mg). The flask was evacuated and backfilled 4 times with argon then 4 times with hydrogen. The mixture was stirred at RT for 16 h, after which the mixture was filtered through a pad of Celite and washed with methanol (50 mL). The filtrate was concentrated *in vacuo* to afford the saturated alcohol, which was used without further purification.

Using general procedure A with the saturated alcohol, toluene (40 mL), DEPAA (1.29 mL, 8.01 mmol), DIPEA (3.46 mL, 19.8 mmol) and T3P (6.31 g, 9.92 mmol, 50% w/w solution in EtOAc) afforded the *title compound* as a colourless oil (2.21 g, 81% over 3 steps); Rf 0.28 (1:1 petrol:EtOAc); νmax (thin film)/cm-1 2988, 1735, 1511, 1493, 1450, 1246, 1116, 1024, 970; δH (400 MHz, CDCl3) 1.34 (6 H, td, *J* = 7.1, *J* = 0.5), 1.88–1.96 (2 H, m), 2.62 (2 H, t, *J* = 7.6), 2.97 (2 H, d, *J* = 21.6), 4.11–4.21 (6 H, m), 5.91 (2 H, s), 6.61–6.63 (1 H, m), 6.66–6.67 (1 H, m), 6.72 (1 H, d, *J* = 7.8); δC (100 MHz, CDCl3) 16.3 (d, *J* = 6.2), 30.3, 31.6, 34.3 (d, *J* = 134.2), 62.7 (d, *J* = 6.3), 64.6, 100.8, 108.2, 108.8, 121.2, 134.8, 145.8, 147.6, 165.8 (d, *J* = 6.2); δP (162 MHz, CDCl3) 20.5; HRMS (ESI+): Found: 381.1061; C16H23NaO7P (MNa+) Requires 381.1074 (3.3 ppm error), Found: 359.1245; C16H24O7P (MH+) Requires 359.1254 (2.6 ppm error).

**3-(1,3-Benzodioxol-5-yl)propyl 2-diazo-2-(diethoxyphosphoryl)acetate (15).** Synthesised using general procedure B with 3-(1,3-benzodioxol-5-yl)propyl 2-(diethoxyphosphoryl)acetate (2.09 g, 5.83 mmol), THF (29 mL), LHMDS (7.00 mL, 7.00 mmol, 1.0 M solution in THF) and *p*-ABSA (1.68 g, 7.00 mmol). Purification by column chromatography (2:1 petrol:EtOAc) afforded the *title compound* **15** as a pale yellow oil (1.35 g, 60%); Rf 0.66 (1:1 petrol:EtOAc); νmax (thin film)/cm-1 2984, 2130, 1704, 1504, 1490, 1390, 1280, 1246, 1099, 1020, 978; δH (400 MHz, CDCl3) 1.35 (6 H, td, *J* = 7.1, *J* = 0.7), 1.88–1.95 (2 H, m), 2.60 (2 H, t, *J* = 7.5), 4.10–4.26 (6 H, m), 5.90 (2 H, s), 6.59 (1 H, dd, *J* = 7.9, *J* = 1.7), 6.64 (1 H, d, *J* = 1.7), 6.70 (1 H, d, *J* = 7.9); δC (100 MHz, CDCl3) 16.1 (d, *J* = 6.9), 30.4, 31.5, 53.8 (d, *J* = 228.5), 63.5 (d, *J* = 5.6), 64.6, 100.7, 108.1, 108.7, 121.0, 134.5, 145.8, 147.6, 163.3 (d, *J* = 12.0); δP (162 MHz, CDCl3) 10.8; HRMS (ESI+): Found: 407.0967; C16H21N2NaO7P (MNa+) Requires 407.0979 (2.9 ppm error), Found: 385.1147; C16H22N2O7P (MH+) Requires 385.1159 (3.1 ppm error).

**Cinnamyl 2-(diethoxyphosphoryl)acetate (23a).** Synthesised using general procedure A with cinnamyl alcohol (4.03 g, 30.0 mmol), toluene (150 mL), DEPAA (5.06 mL, 31.5 mmol), DIPEA (13.6 mL, 78.0 mmol) and T3P (24.8 g, 39.0 mmol, 50% w/w solution in EtOAc) affording the *title compound* **23a** as a yellow oil (7.14 g, 76%). No further purification was required; Rf 0.23 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2984, 1737, 1449, 1393, 1264, 1163, 1114, 1050, 1023, 968; δH (400 MHz, CDCl3) 1.33 (6 H, t, *J* = 7.0), 3.01 (2 H, d, *J* = 21.6), 4.13–4.21 (4 H, m), 4.80 (2 H, dd, *J* = 6.5, *J* = 1.2), 6.27 (1 H, dt, *J* = 15.9, *J* = 6.5), 6.68 (1 H, d, *J* = 15.9), 7.24–7.28 (1 H, m), 7.30–7.34 (2 H, m), 7.36–7.39 (2 H, m); δC (100 MHz, CDCl3) 16.3 (d, *J* = 6.2), 34.3 (d, *J* = 134.2), 62.7 (d, *J* = 6.5), 66.0, 122.4, 126.6, 128.1, 128.6, 134.7, 136.0, 165.6 (d, *J* = 6.1); δP (162 MHz, CDCl3) 20.2; HRMS (ESI+): Found: 335.1027; C15H21NaO5P (MNa+) Requires 335.1019 (−2.4 ppm error), Found: 313.1197; C15H22O5P (MH+) Requires 313.1199 (0.7 ppm error).

**Cinnamyl 2-diazo-2-(diethoxyphosphoryl)acetate (19a).** Synthesised using general procedure B with cinnamyl 2-(diethoxyphosphoryl)acetate **23a** (3.12 g, 10.0 mmol), THF (50 mL), LHMDS (12.0 mL, 12.0 mmol, 1.0 M solution in THF) and *p*-ABSA (2.88 g, 12.0 mmol). Purification by column chromatography (2:1 petrol:EtOAc) afforded the *title compound* **19a** as a yellow oil (1.41 g, 42%); Rf 0.50 (1:1 petrol:EtOAc); νmax (thin film)/cm-1 2985, 2128, 1707, 1496, 1449, 1380, 1275, 1214, 1164, 1120, 1020, 975; δH (400 MHz, CDCl3) 1.36 (6 H, t, *J* = 7.1, *J* = 0.8), 4.11–4.29 (4 H, m), 4.86 (2 H, dd, *J* = 6.5, *J* = 1.3), 6.28 (1 H, dt, *J* = 15.9, *J* = 6.5), 6.68 (1 H, d, *J* = 15.9), 7.25–7.40 (5 H, m); δC (100 MHz, CDCl3) 16.1 (d, *J* = 6.9), 53.9 (d, *J* = 227.3), 63.7 (d, *J* = 5.6), 66.0, 122.4, 126.6, 128.2, 128.6, 134.9, 135.9, 163.2 (d, *J* = 11.8); δP (162 MHz, CDCl3) 10.5; HRMS (ESI+): Found: 361.0928; C15H19N2NaO5P (MNa+) Requires 361.0924 (−1.0 ppm error).

**Diethyl ((1*RS*,5*SR*,6*SR*)-2-oxo-6-phenyl-3-oxabicyclo[3.1.0]hexan-1-yl)phosphonate (20a).** To an oven dried 50 mL rbf containing cinnamyl 2-diazo-2-(diethoxyphosphoryl)acetate **19a** (676 mg, 2.00 mmol) flushed with argon was added CH2Cl2 (20 mL) followed by Rh2(oct)4 (31.1 mg, 0.04 mmol). The solution was stirred at 45 °C for 18 h. Concentration *in vacuo* and purification by column chromatography (1:10 hexane:EtOAc) afforded the *title compound* **20a** as a pale yellow solid (490 mg, 79%); Rf 0.15 (1:2 hexane:EtOAc); m.p. 79–81 °C; νmax (thin film)/cm-1 2989, 2909, 1762, 1369, 1251, 1200, 1163, 1098, 1049, 1013, 971; δH (400 MHz, CDCl3) 1.07 (3 H, td, *J* = 7.1, *J* = 0.5), 1.21 (3 H, t, *J* = 7.1), 2.81 (1 H, app. t, *J* = 6.1), 3.30 (1 H, app. dt, *J* = 10.6, *J* = 5.2), 3.80 (2 H, dq, *J* = 8.2, *J* = 7.1), 3.88–4.08 (2 H, m), 4.41 (1 H, dd, *J* = 9.3, *J* = 2.8), 4.51 (1 H, dd, *J* = 9.3, *J* = 4.7), 7.26–7.39 (5 H, m); δC (100 MHz, CDCl3) 16.0 (d, *J* = 6.3), 16.2 (d, *J* = 5.9 28.1, 31.5 (d, *J* = 206.1), 34.9 (d, *J* = 3.0), 62.5 (d, *J* = 6.1), 62.8 (d, *J* = 6.6), 68.0 (d, *J* = 2.4), 128.0, 128.1, 129.4, 131.7 (d, *J* = 4.8), 171.9 (d, *J* = 10.1); δP (162 MHz, CDCl3) 15.3; HRMS (ESI+): Found: 333.0861; C15H19NaO5P (MNa+) Requires 333.0862 (0.4 ppm error), Found: 311.1035; C15H20O5P (MH+) Requires 311.1043 (2.5 ppm error).

**Diethyl ((4*SR*)-4-benzyl-2-oxotetrahydrofuran-3-yl)phosphonate (21).** To a solution of freshly prepared SmI2 (2.00 mL, 0.200 mmol, ~0.1 M in THF) in an oven dried sealable tube at −78 °C under an atmosphere of argon, was added a solution of diethyl ((1*RS*,5*SR*,6*SR*)-2-oxo-6-phenyl-3-oxabicyclo[3.1.0]hexan-1-yl)phosphonate **20a** (31 mg, 0.100 mmol) in THF (0.5 mL). The solution was stirred at −78 °C for 5 mins then quenched with sat. aq. NH4Cl (5 mL) and then allowed to warm at RT. The mixture was diluted with water (5 mL) and extrated with diethyl ether (3 × 10 mL). The combined organic extracts were dried over MgSO4, filtered and concentrated *in vacuo*. Purification by column chromatography (1:2 hexane:EtOAc) afforded the *title compound* **21** as a pale yellow oil (15 mg, 48%); Rf 0.52 (1:4 hexane:EtOAc); νmax (thin film)/cm-1 2983, 2915, 1771, 1497, 1479, 1455, 1381, 1252, 1206, 1160, 1047, 1020, 972, 753, 703; δH (400 MHz, CDCl3) 1.29–1.33 (6 H, m), 2.81 (1 H, dd, *J* = 13.8, *J* = 8.6), 2.83 (1 H, dd, *J* = 23.9, *J* = 4.5), 2.93 (1 H, dd, *J* = 13.8, *J* = 7.1), 3.11–3.24 (1 H, m), 3.99–4.29 (5 H, m), 4.45 (1 H, dd, *J* = 9.1, *J* = 6.9), 7.15–7.18 (2 H, m), 7.23–7.27 (1 H, m), 7.29–7.34 (2 H, m); δC (100 MHz, CDCl3) 16.3 (d, *J* = 6.1), 16.3 (d, *J* = 6.1), 39.3 (d, *J* = 2.6), 39.3 (d, *J* = 10.1), 44.5 (d, *J* = 139.5), 62.9 (d, *J* = 6.8), 63.6 (d, *J* = 6.8), 71.8 (d, *J* = 5.0), 127.0, 128.8, 129.0, 137.2, 171.7 (d, *J* = 3.6); δP (162 MHz, CDCl3) 20.0; HRMS (ESI+): Found: 335.1030; C15H21NaO5P (MNa+) Requires 335.1019 (−3.4 ppm error), Found: 313.1205; C15H22O5P (MH+) Requires 313.1199 (−1.7 ppm error).

**Allyl 2-(diethoxyphosphoryl)acetate (23b).** Synthesised using general procedure A with allyl alcohol (1.16 g, 20.0 mmol), toluene (100 mL), DEPAA (3.38 mL, 21.0 mmol), DIPEA (9.06 mL, 52.0 mmol) and T3P (16.5 g, 26.0 mmol, 50% w/w solution in EtOAc) affording the *title compound* **23b** as an orange oil (4.63 g, 98%). No further purification was required; Rf 0.26 (1:1 petrol:EtOAc); νmax (thin film)/cm-1 2985, 1738, 1394, 1261, 1117, 1050, 1023, 971; δH (400 MHz, CDCl3) 1.32 (6 H, td, *J* = 7.1, *J* = 0.5), 2.98 (2 H, d, *J* = 21.6), 4.12–4.19 (4 H, m), 4.61–4.64 (1 H, m), 5.24 (1 H, app. dq, *J* = 10.4, *J* = 1.3), 5.35 (1 H, app. dq, *J* = 17.2, *J* = 1.5), 5.90 (2 H, ddt, *J* = 17.2, *J* = 10.4, *J* = 5.7); δC (100 MHz, CDCl3) 16.3 (d, *J* = 6.2), 34.2 (d, *J* = 134.3), 62.7 (d, *J* = 6.2), 66.1, 118.7, 131.5, 165.5 (d, *J* = 6.1); δP (162 MHz, CDCl3) 20.1; HRMS (ESI+): Found: 259.0708; C9H17NaO5P (MNa+) Requires 259.0706 (−0.8 ppm error), Found: 237.0890; C9H18O5P (MH+) Requires 237.0886 (−1.6 ppm error).

**(*Z*)-Hex-2-en-1-yl 2-(diethoxyphosphoryl)acetate (23c).** Synthesised using general procedure A with (*Z*)-hex-2-en-1-ol (2.16 g, 21.6 mmol), toluene (110 mL), DEPAA (3.65 mL, 22.7 mmol), DIPEA (9.78 mL, 56.2 mmol) and T3P (17.8 g, 28.0 mmol, 50% w/w solution in THF) affording the *title compound* **23c** as a yellow oil (1.87 g, 79%). No further purification was required; Rf 0.70 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2963, 2933, 2874, 1738, 1460, 1394, 1267, 1115, 1056, 1026, 971, 842, 782; δH (400 MHz, CDCl3) 0.90 (3 H, t,*J* = 7.4), 1.32–1.44 (8 H, m), 2.05–2.11 (2 H, m), 2.97 (2 H, d, *J* = 21.5), 4.13–4.21 (4 H, m), 4.69 (2 H, dd, *J* = 6.9), 5.54 (1 H, dtt, *J* = 10.9, *J* = 6.9, *J* = 1.4), 5.66 (1 H, dtt, *J* = 10.9, *J* = 7.5, *J* = 1.2); δC (100 MHz, CDCl3) 13.6, 16.3 (d, *J* = 6.2), 22.5, 29.5, 34.3 (d, *J* = 134.3), 61.4, 62.7 (d, *J* = 6.2), 122.8, 135.6, 165.7 (d, *J* = 6.2); δP (162 MHz, CDCl3) 20.3; HRMS (ESI+): Found: 301.1181; C12H23NaO5P (MNa+) Requires 301.1175 (−1.8 ppm error), Found: 279.1361; C12H24O5P (MH+) Requires 279.1356 (−2.0 ppm error).

**(2*E*,4*E*)-Hexa-2,4-dien-1-yl 2-(diethoxyphosphoryl)acetate (23d).** Synthesised using general procedure A with (2*E*,4*E*)-hexa-2,4-dien-1-ol (491 mg, 5.00 mmol), toluene (25.0 mL), DEPAA (1.03 mL, 5.25 mmol), DIPEA (2.26 mL, 13.0 mmol) and T3P (4.14 g, 6.50 mmol, 50% w/w solution in EtOAc) affording the *title compound* **23d** as an orange oil (1.36 g, 98%). No further purification was required; Rf 0.26 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2984, 2934, 1735, 1444, 1393, 1258, 1112, 1020, 965; δH (400 MHz, CDCl3) 1.31 (6 H, t, *J* = 7.1), 1.73 (3 H, d, *J* = 6.7), 2.95 (2 H, d, *J* = 21.5), 4.14 (4 H, app. quin., *J* = 7.5), 4.61 (2 H, d, *J* = 6.7), 5.58 (1 H, dt, *J* = 15.2, *J* = 6.7), 5.73 (1 H, dq, *J* = 15.2, *J* = 6.7), 6.01 (1 H, ddd, *J* = 15.2, *J* = 10.5, *J* = 1.2), 6.24 (1 H, dd, *J* = 15.2, *J* = 10.5); δC (100 MHz, CDCl3) 16.2 (d, *J* = 6.6), 18.1, 34.3 (d, *J* = 134.2), 62.6 (d, *J* = 6.6), 65.9, 122.8, 130.2, 131.6, 135.4, 165.5 (d, *J* = 6.1); δP (162 MHz, CDCl3) 20.2; HRMS (ESI+): Found: 299.1026; C12H21NaO5P (MNa+) Requires 299.1019 (−2.4 ppm error).

**3-Methyl-but-2-en-1-yl 2-(diethoxyphosphoryl)acetate (23e).** Synthesised using general procedure A with 3-methyl-but-2-en-1-ol (431 mg, 5.00 mmol), toluene (25.0 mL), DEPAA (1.03 mL, 5.25 mmol), DIPEA (2.26 mL, 13.0 mmol) and T3P (4.14 g, 6.50 mmol, 50% w/w solution in EtOAc) affording the *title compound* **23e** as a yellow oil (1.25 g, 95%). No further purification was required; Rf 0.24 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2982, 2933, 1734, 1445, 1392, 1264, 1113, 1051, 1029, 968; δH (400 MHz, CDCl3) 1.33 (6 H, t, *J* = 7.1), 1.70 (3 H, s), 1.74 (3 H, s), 2.95 (2 H, d, *J* = 21.5), 4.12–4.19 (4 H, m), 4.62 (2 H, d, *J* = 7.3), 5.31–5.36 (1 H, m); δC (100 MHz, CDCl3) 16.3 (d, *J* = 6.7), 18.0, 25.7, 34.3 (d, *J* = 134.5), 62.4, 62.6 (d, *J* = 6.6), 118.0, 139.7, 165.8 (d, *J* = 6.5); δP (162 MHz, CDCl3) 20.4; HRMS (ESI+): Found: 287.1021; C11H21NaO5P (MNa+) Requires 287.1019 (−0.9 ppm error).

**(*E*)-3,7-Dimethylocta-2,6-dien-1-yl 2-(diethoxyphosphoryl)acetate (23f).** Synthesised using general procedure A with geraniol (771 mg, 5.00 mmol), toluene (25.0 mL), DEPAA (1.03 mL, 5.25 mmol), DIPEA (2.26 mL, 13.0 mmol) and T3P (4.14 g, 6.50 mmol, 50% w/w solution in EtOAc) affording the *title compound* **23f** as an orange oil (1.65 g, 99%). No further purification was required; Rf 0.27 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2980, 2928, 1735, 1444, 1391, 1263, 1112, 1051, 1025, 966; δH (400 MHz, CDCl3) 1.32 (6 H, t, *J* = 7.1), 1.58 (3 H, s), 1.67 (3 H, d, *J* = 0.9), 1.69 (3 H, d, *J* = 0.9), 2.00–2.09 (4 H, m), 2.96 (2 H, d, *J* = 21.5), 4.16 (4 H, app. quin., *J* = 7.4), 4.64 (2 H, d, *J* = 7.2), 5.04–5.08 (1 H, m), 5.31–5.36 (1 H, m); δC (100 MHz, CDCl3) 16.3 (d, *J* = 6.6), 16.4, 17.6, 25.6, 26.2, 34.3 (d, *J* = 134.2), 39.5, 62.4, 62.6 (d, *J* = 6.2), 117.7, 123.6, 131.9, 142.9, 165.8 (d, *J* = 6.1); δP (162 MHz, CDCl3) 20.4; HRMS (ESI+): Found: 355.1644; C16H29NaO5P (MNa+) Requires 355.1645 (0.3 ppm error).

**3,3-Diphenylallyl 2-(diethoxyphosphoryl)acetate (23g).** To a suspension of AgOAc (2.59 g, 15.5 mmol) and Pd(OAc)2 (11.2 mg, 0.05 mmol) in AcOH (15 mL) was added iodobenzene (1.73 mL, 15.5 mmol) and ethyl acrylate (0.54 mL, 5.00 mmol). The mixture was stirred under an atmosphere of argon, at 110 °C for 6 h then allowed cool at RT and diluted with EtOAc (20 mL). The mixture was filtered through a pad of Celite, washed with EtOAc (200 mL) and the filtrate concentrated *in vacuo*. Purification by column chromatography (15:1 hexane:EtOAc) afforded ethyl 3,3-diphenylacrylate as a yellow oil (1.26 g, 100%); Rf 0.26 (15:1 hexane:EtOAc); νmax (thin film)/cm-1 2980, 1722, 1618, 1446, 1369, 1264, 1164, 1038, 771, 697; δH (400 MHz, CDCl3) 1.12 (3 H, t, *J* = 7.1), 4.06 (2 H, q, *J* = 7.1), 6.37 (1 H, s), 7.20–7.24 (2 H, m), 7.29–7.40 (8 H, m); δC (100 MHz, CDCl3) 14.0, 60.0, 117.5, 127.8, 128.1, 128.3, 128.3, 129.1, 129.4, 139.0, 140.8, 156.5, 166.1; MS (ESI+): 275.10 (MNa+), 253.12 (MH+). Obtained data in accord with reported literature.19

To a solution of ethyl 3,3-diphenylacrylate (1.33 g, 5.27 mmol) in THF (19 mL) cooled to −78 °C was added dropwise diisobutylaluminium hydride (DIBAL) (21.1 mL, 21.1 mmol, 1.0 M in hexane) and stirred for 2 h. The solution was quenched with water (15 mL) dropwise and stirred for 30 mins at RT before being filtered through a pad of Celite and silica and washed with diethyl ether (500 mL). The filtrate was concentrated *in vacuo*. Purification by column chromatography (4:1 hexane:EtOAc) afforded 3,3-diphenylprop-2-en-1-ol (886 mg, 80 %) as a white solid; Rf 0.33 (4:1 hexane:EtOAc); m.p. 60–62 °C (lit.20 61–63 °C); νmax (thin film)/cm-1 3325, 3056, 3024, 1598, 1494, 1444, 1074, 1013, 758, 692; δH (400 MHz, CDCl3) 1.50 (1 H, br s), 4.23 (2 H, d, *J* = 6.9), 6.26 (1 H, t, *J* = 6.9), 7.16–7.19 (2 H, m), 7.24–7.40 (8 H, m); δC (100 MHz, CDCl3) 60.7, 127.4, 127.5, 127.6, 127.6, 128.2, 128.2, 129.7, 139.0, 141.8, 144.2; MS (ESI+): 249.07 (MK+), 233.09 (MNa+). Obtained data in accord with reported literature.20,21

The synthesis continued using general procedure A with 3,3-diphenylprop-2-en-1-ol (862 mg, 4.10 mmol), toluene (20.5 mL), DEPAA (0.69 mL, 4.30 mmol), DIPEA (1.86 mL, 10.7 mmol) and T3P (3.40 g, 5.33 mmol, 50% w/w solution in EtOAc) affording the *title compound* **23g** as an orange oil (1.59 g, 100%). No further purification was required; Rf 0.26 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2983, 1736, 1445, 1265, 1113, 1025, 969, 774, 702; δH (400 MHz, CDCl3) 1.33 (6 H, t, *J* = 7.1, *J* = 0.5), 3.00 (2 H, d, *J* = 21.5), 4.13–4.21 (4 H, m), 4.71 (2 H, d, *J* = 7.1), 6.18 (1 H, t, *J* = 7.1), 7.16–7.19 (2 H, m), 7.23–7.40 (8 H, m); δC (100 MHz, CDCl3) 16.3 (d, *J* = 6.3), 34.5 (d, *J* = 134.2), 62.7 (d, *J* = 6.2), 63.7, 121.5, 127.7, 127.9, 127.9, 128.2, 128.3, 129.7, 138.4, 141.4, 147.0, 165.7 (d, *J* = 6.3); δP (162 MHz, CDCl3) 20.2; HRMS (ESI+): Found: 411.1325; C21H25NaO5P (MNa+) Requires 411.1332 (1.8 ppm error).

**(*E*)-3-(4-Bromophenyl)allyl 2-(diethoxyphosphoryl)acetate (23h).** Starting with known alcohol (*E*)-3-(4-bromophenyl)prop-2-en-1-ol (1.58 g, 7.43 mmol),22 general procedure A was performed with toluene (37.2 mL), DEPAA (1.53 g, 7.80 mmol), DIPEA (3.36 mL, 19.3 mmol) and T3P (6.15 g, 9.66 mmol, 50% w/w solution in EtOAc) affording the *title compound* **23h** as an orange oil (2.90 g, 100%). No further purification was required; Rf 0.20 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2982, 1736, 1488, 1402, 1258, 1114, 1049, 1022, 967, 840, 785; δH (400 MHz, CDCl3) 1.32 (6 H, t, *J* = 7.1), 3.01 (2 H, d, *J* = 21.5), 4.13–4.20 (4 H, m), 4.78 (2 H, d, *J* = 6.3), 6.26 (1 H, dt, *J* = 15.9, *J* = 6.3), 6.62 (1 H, d, *J* = 15.9), 7.24 (2 H, d, *J* = 8.5), 7.43 (2 H, d, *J* = 8.5); δC (100 MHz, CDCl3) 16.3 (d, *J* = 6.6), 34.3 (d, *J* = 134.2), 62.7 (d, *J* = 6.7), 65.7, 122.0, 123.3, 128.1, 131.7, 133.2, 135.0, 165.6 (d, *J* = 6.5); δP (162 MHz, CDCl3) 20.1; HRMS (ESI+): Found: 413.0130; C15H2079BrNaO5P (MNa+) Requires 413.0124 (−1.4 ppm error).

**(*E*)-3-(4-Methoxyphenyl)allyl 2-(diethoxyphosphoryl)acetate (23i).** Starting with known alcohol (*E*)-3-(4-methoxyphenyl)prop-2-en-1-ol (1.72 g, 8.34 mmol),23 general procedure A was performed with toluene (41.7 mL), DEPAA (1.72 g, 8.76 mmol), DIPEA (3.78 mL, 21.7 mmol) and T3P (6.90 g, 10.8 mmol, 50% w/w solution in EtOAc) affording the *title compound* **23i** as an orange oil (2.79 g, 98%). No further purification was required; Rf 0.20 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2983, 1733, 1607, 1512, 1247, 1176, 1114, 1023, 966, 841; δH (400 MHz, CDCl3) 1.32 (6 H, t, *J* = 7.1), 3.00 (2 H, d, *J* = 21.5), 3.80 (3 H, s), 4.13–4.20 (4 H, m), 4.77 (2 H, d, *J* = 6.7), 6.14 (1 H, dt, *J* = 15.8, *J* = 6.7), 6.62 (1 H, d, *J* = 15.8), 6.85 (2 H, d, *J* = 8.3), 7.31 (2 H, d, *J* = 8.3); δC (100 MHz, CDCl3) 16.3 (d, *J* = 6.6), 34.3 (d, *J* = 134.2), 55.2, 62.7 (d, *J* = 6.7), 66.3, 114.0, 120.0, 127.8, 128.7, 134.5, 160.0, 165.7 (d, *J* = 6.5); δP (162 MHz, CDCl3) 20.2; HRMS (ESI+): Found: 365.1129; C16H23NaO6P (MNa+) Requires 365.1124 (−1.2 ppm error).

**(*E*)-3-(1,3-Benzodioxol-5-yl)allyl 2-(diethoxyphosphoryl)acetate (23j).** Synthesised using general procedure A with (*E*)-3-(1,3-benzodioxol-5-yl)prop-2-en-1-ol (1.95 g, 10.9 mmol), toluene (55 mL), DEPAA (1.85 mL, 11.5 mmol), DIPEA (4.95 mL, 28.4 mmol) and T3P (9.05 g, 14.2 mmol, 50% w/w solution in EtOAc) affording the *title compound* **23j** as a yellow oil (3.89 g, 100%). No further purification was required; Rf 0.17 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2986, 2908, 1733, 1654, 1607, 1504, 1491, 1446, 1398, 1354, 1248, 1195, 1164, 1021, 965; δH (400 MHz, CDCl3) 1.32 (6 H, t, *J* = 7.1, *J* = 0.4), 2.99 (2 H, d, *J* = 21.5), 4.12–4.20 (4 H, m), 4.75 (2 H, dd, *J* = 6.6, *J* = 1.0), 5.95 (2 H, s), 6.09 (1 H, dt, *J* = 15.8, *J* = 6.6), 6.58 (1 H, d, *J* = 15.8), 6.74 (1 H, d, *J* = 8.0), 6.81 (1 H, dd, *J* = 8.0, *J* = 1.6), 6.91 (1 H, d, *J* = 1.6); δC (100 MHz, CDCl3) 16.3 (d, *J* = 6.2), 34.3 (d, *J* = 134.2), 62.7 (d, *J* = 6.2), 66.1, 101.1, 105.7, 108.3, 120.5, 121.5, 130.4, 134.5, 147.7, 148.0, 165.6 (d, *J* = 6.1); δP (162 MHz, CDCl3) 20.2; HRMS (ESI+): Found: 379.0920; C16H21NaO7P (MNa+) Requires 379.0917 (−0.8 ppm error).

**Allyl 2-diazo-2-(diethoxyphosphoryl)acetate (19b).** Synthesised using general procedure C with 3-(4-methoxyphenyl)propyl 2-(diethoxyphosphoryl)acetate **23b** (2.19 g, 9.27 mmol), DBSA (4.89 g, 13.9 mmol), DBU (2.08 mL, 13.9 mmol) and CH2Cl2 (93.0 mL). Purification by column chromatography (2:1 petrol:EtOAc) affording the *title compound* **19b** as a pale yellow oil (2.02 g, 83%); Rf 0.43 (1:1 petrol:EtOAc); νmax (thin film)/cm-1 2992, 2932, 2129, 1707, 1368, 1276, 1020, 983; δH (400 MHz, CDCl3) 1.33 (6 H, td, *J* = 7.1, *J* = 0.8), 4.09–4.25 (4 H, m), 4.67 (1 H, app. dt, *J* = 5.6, *J* = 1.4), 5.24 (1 H, app. dq, *J* = 10.5, *J* = 1.3), 5.32 (1 H, app. dq, *J* = 17.2, *J* = 1.5), 5.89 (2 H, ddt, *J* = 17.2, *J* = 10.5, *J* = 5.6); δC (100 MHz, CDCl3) 16.1 (d, *J* = 6.9), 53.9 (d, *J* = 226.1), 63.6 (d, *J* = 5.6), 65.9, 118.7, 131.4, 163.1 (d, *J* = 12.0); δP (162 MHz, CDCl3) 10.4; HRMS (ESI+): Found: 285.0603; C9H15N2NaO5P (MNa+) Requires 285.0611 (2.9 ppm error), Found: 263.0792; C9H16N2O5P (MH+) Requires 263.0791 (−0.2 ppm error).

**(*Z*)-Hex-2-en-1-yl 2-diazo-2-(diethoxyphosphoryl)acetate (19c).** Synthesised using general procedure B with (*Z*)-hex-2-en-1-yl 2-(diethoxyphosphoryl)acetate **23c** (385 mg, 1.38 mmol), THF (50 mL), NaH (66.4 mg, 1.66 mmol, 60% dispersion in mineral oil) and *p*-ABSA (399 mg, 1.66 mmol). Purification by column chromatography (3:1 petrol:EtOAc) afforded the *title compound* **19c** as a yellow oil (315 mg, 75%); Rf 0.52 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2962, 2128, 1709, 1445, 1361, 1279, 1164, 1023, 978; δH (400 MHz, CDCl3) 0.88 (3 H, t, *J* = 7.4), 1.30–1.43 (8 H, m), 2.07 (2 H, qd, *J* = 7.4, *J* = 1.3), 4.09–4.25 (4 H, m), 4.72–4.74 (2 H, m), 5.52 (1 H, dtt, *J* = 10.9, *J* = 6.9, *J* = 1.5), 5.65 (1 H, dtt, *J* = 10.9, *J* = 7.6, *J* = 1.3); δC (100 MHz, CDCl3) 13.5, 16.1 (d, *J* = 6.9), 22.4, 29.4, 53.8 (d, *J* = 227.5), 61.3, 63.6 (d, *J* = 6.0), 122.8, 136.0, 163.3 (d, *J* = 12.3); δP (162 MHz, CDCl3) 10.6; HRMS (ESI+): Found: 327.1087; C12H21N2NaO5P (MNa+) Requires 327.1080 (−2.1 ppm error), Found: 305.1262; C12H22N2O5P (MH+) Requires 305.1261 (−0.5 ppm error).

**(2*E*,4*E*)-Hexa-2,4-dien-1-yl 2-diazo-2-(diethoxyphosphoryl)acetate (19d).** Synthesised using general procedure C with (2*E*,4*E*)-hexa-2,4-dien-1-yl 2-(diethoxyphosphoryl)acetate **23d** (1.36 g, 4.92 mmol), DBSA (2.47 g, 7.38 mmol), DBU (1.10 mL, 7.38 mmol) and CH2Cl2 (49.0 mL). Purification by column chromatography (2:1 hexane:EtOAc) afforded the *title compound* **19d** as a yellow oil (1.54 g, 75%); Rf 0.43 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2985, 2127, 1705, 1445, 1375, 1274, 1113, 1020, 797, 745, 590, 561; δH (400 MHz, CDCl3) 1.34 (6 H, td, *J* = 7.1, *J* = 0.7), 1.75 (3 H, dd, *J* = 6.7, *J* = 1.0), 4.09–4.25 (4 H, m), 4.68 (2 H, d, *J* = 6.7), 5.60 (1 H, dt, *J* = 15.2, *J* = 6.7), 5.75 (1 H, dq, *J* = 15.2, *J* = 6.7), 6.00–6.07 (1 H, m), 6.26 (1 H, dd, *J* = 15.2, *J* = 10.5); δC (100 MHz, CDCl3) 16.1 (d, *J* = 7.1), 18.1, 63.6 (d, *J* = 5.9), 66.0, 122.8, 130.2, 131.8, 135.6, 163.2 (d, *J* = 12.6); δP (162 MHz, CDCl3) 10.6; HRMS (ESI+): Found: 325.0930; C12H19N2NaO5P (MNa+) Requires 325.0924 (−1.9 ppm error).

**3-Methyl-but-2-en-1-yl 2-diazo-2-(diethoxyphosphoryl)acetate (19e).** Synthesised using general procedure C with 3-methyl-but-2-en-1-yl 2-(diethoxyphosphoryl)acetate **23e** (1.24 g, 4.69 mmol), DBSA (2.35 g, 7.04 mmol), DBU (1.05 mL, 7.04 mmol) and CH2Cl2 (47.0 mL). Purification by column chromatography (2:1 hexane:EtOAc) afforded the *title compound* **19e** as a pale yellow oil (1.15 g, 85%); Rf 0.39 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2983, 2933, 2124, 1700, 1445, 1374, 1271, 1110, 1016, 976, 746, 588, 556; δH (400 MHz, CDCl3) 1.34 (6 H, t, *J* = 7.1), 1.70 (3 H, s), 1.74 (3 H, s), 4.09–4.25 (4 H, m), 4.68 (2 H, d, *J* = 7.3), 5.29–5.35 (1 H, m); δC (100 MHz, CDCl3) 16.1 (d, *J* = 7.3), 18.0, 25.7, 62.4, 63.6 (d, *J* = 5.9), 118.0, 139.9, 163.4 (d, *J* = 12.7); δP (162 MHz, CDCl3) 10.7; HRMS (ESI+): Found: 313.0928; C11H19N2NaO5P (MNa+) Requires 313.0924 (−1.4 ppm error).

**(*E*)-3,7-Dimethylocta-2,6-dien-1-yl 2-diazo-2-(diethoxyphosphoryl)acetate (19f).** Synthesised using general procedure C with (*E*)-3,7-dimethylocta-2,6-dien-1-yl 2-(diethoxyphosphoryl)acetate **23f** (1.65 g, 4.96 mmol), *p*-ABSA (1.79 g, 7.45 mmol), DBU (1.11 mL, 7.45 mmol) and CH2Cl2 (50.0 mL). Purification by column chromatography (2:1 hexane:EtOAc) afforded the *title compound* **19f** as a yellow oil (1.12 g, 63%); Rf 0.56 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2981, 2915, 2124, 1701, 1444, 1378, 1273, 1021, 975, 797, 744, 588, 559; δH (400 MHz, CDCl3) 1.32 (6 H, td, *J* = 7.1, *J* = 0.8), 1.56 (3 H, s), 1.64 (3 H, d, *J* = 1.0), 1.68 (3 H, d, *J* = 1.1), 1.98–2.08 (4 H, m), 4.08–4.23 (4 H, m), 4.68 (2 H, d, *J* = 7.2), 5.01–5.05 (1 H, m), 5.28–5.32 (1 H, m); δC (100 MHz, CDCl3) 16.0 (d, *J* = 6.9), 16.4, 17.5, 25.5, 26.1, 39.4, 53.5 (d, *J* = 227.1), 62.3, 63.5 (d, *J* = 5.9), 117.6, 123.5, 131.8, 143.0, 163.3 (d, *J* = 12.6); δP (162 MHz, CDCl3) 10.7; HRMS (ESI+): Found: 381.1549; C16H27N2NaO5P (MNa+) Requires 381.1550 (0.3 ppm error).

**3,3-Diphenylallyl 2-diazo-2-(diethoxyphosphoryl)acetate (19g).** Synthesised using general procedure B with 3,3-diphenylallyl 2-(diethoxyphosphoryl)acetate **23g** (1.59 g, 4.10 mmol), THF (20.5 mL), LHMDS (4.92 mL, 4.92 mmol, 1.0 M solution in THF) and *p*-ABSA (1.18 g, 4.92 mmol). Purification by column chromatography (2:1 hexane:EtOAc) afforded the *title compound* **19g** as a yellow oil (823 g, 48%); Rf 0.52 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2984, 2126, 1703, 1494, 1444, 1377, 1348, 1271, 1214, 1163, 1117, 1099, 1017, 976, 796, 729, 699, 585, 558; δH (400 MHz, CDCl3) 1.35 (6 H, t, *J* = 7.1, *J* = 0.8), 4.12–4.28 (4 H, m), 4.77 (2 H, d, *J* = 7.2), 6.19 (1 H, t, *J* = 7.2), 7.16–7.19 (2 H, m), 7.22–7.39 (8 H, m); δC (100 MHz, CDCl3) 15.9 (d, *J* = 6.9), 53.5 (d, *J* = 227.1), 63.3, 63.4 (d, *J* = 5.7), 121.1, 127.4, 127.7, 127.8, 128.0, 128.1, 129.3, 138.1, 141.0, 147.1, 162.9 (d, *J* = 12.2); δP (162 MHz, CDCl3) 10.5; HRMS (ESI+): Found: 437.1242; C21H23N2NaO5P (MNa+) Requires 437.1237 (−1.1 ppm error).

**(*E*)-3-(4-Bromophenyl)allyl 2-diazo-2-(diethoxyphosphoryl)acetate (19h).** Synthesised using general procedure C with (*E*)-3-(4-bromophenyl)allyl 2-(diethoxyphosphoryl)acetate **23h** (2.90 g, 7.41 mmol), DBSA (3.72 mL, 11.1 mmol), DBU (1.66 mL, 11.1 mmol) and CH2Cl2 (74.1 mL). Purification by column chromatography (2:1 hexane:EtOAc) afforded the *title compound* **19h** as a yellow oil (2.69 g, 87%); Rf 0.42 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2984, 2127, 1705, 1488, 1275, 1020, 975, 798, 744, 590, 560; δH (400 MHz, CDCl3) 1.33–1.37 (6 H, m), 4.12–4.28 (4 H, m), 4.83 (2 H, dd, *J* = 6.4, *J* = 1.3), 6.26 (1 H, dt, *J* = 15.9, *J* = 6.4), 6.61 (1 H, d, *J* = 15.9), 7.24 (2 H, d, *J* = 8.5), 7.44 (2 H, d, *J* = 8.5); δC (100 MHz, CDCl3) 16.3 (d, *J* = 7.2), 63.8 (d, *J* = 6.1), 65.9, 122.2, 123.3, 128.2, 131.9, 133.6, 135.0, 163.3 (d, *J* = 12.6); δP (162 MHz, CDCl3) 10.5; HRMS (ESI+): Found: 439.0019; C15H1879BrN2NaO5P (MNa+) Requires 439.0029 (2.3 ppm error).

**(*E*)-3-(4-Methoxyphenyl)allyl 2-diazo-2-(diethoxyphosphoryl)acetate (19i).** Synthesised using general procedure C with (*E*)-3-(4-methoxyphenyl)allyl 2-(diethoxyphosphoryl)acetate **23i** (2.79 g, 8.15 mmol), DBSA (4.09 mL, 12.2 mmol), DBU (1.82 mL, 12.2 mmol) and CH2Cl2 (81.5 mL). Purification by column chromatography (2:1 hexane:EtOAc) afforded the *title compound* **19i** as a yellow oil (2.26 g, 75%); Rf 0.37 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2985, 2127, 1704, 1607, 1512, 1273, 1250, 1176, 1020, 975; δH (400 MHz, CDCl3) 1.35 (6 H, td, *J* = 7.1, *J* = 0.8), 3.80 (3 H, s), 4.11–4.27 (4 H, m), 4.82 (2 H, dd, *J* = 6.7, *J* = 1.2), 6.14 (1 H, dt, *J* = 15.8, *J* = 6.7), 6.62 (1 H, d, *J* = 15.8), 6.85 (2 H, d, *J* = 8.7), 7.32 (2 H, d, *J* = 8.7); δC (100 MHz, CDCl3) 16.1 (d, *J* = 6.9), 55.2, 63.7 (d, *J* = 6.1), 66.3, 114.0, 120.0, 127.9, 128.6, 134.7, 159.7, 163.2 (d, *J* = 12.8); δP (162 MHz, CDCl3) 10.6; HRMS (ESI+): Found: 391.1032; C16H21N2NaO6P (MNa+) Requires 391.1029 (−0.6 ppm error).

**(*E*)-3-(1,3-Benzodioxol-5-yl)allyl 2-(diethoxyphosphoryl)acetate (19j).** Synthesised using general procedure A with (*E*)-3-(1,3-benzodioxol-5-yl)prop-2-en-1-ol **23j** (1.95 g, 10.9 mmol), toluene (55 mL), DEPAA (1.85 mL, 11.5 mmol), DIPEA (4.95 mL, 28.4 mmol) and T3P (9.05 g, 14.2 mmol, 50% w/w solution in EtOAc) affording the *title compound* **19j** as a yellow oil (3.89 g, 100%). No further purification was required; Rf 0.17 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2986, 2908, 1733, 1654, 1607, 1504, 1491, 1446, 1398, 1354, 1248, 1195, 1164, 1021, 965; δH (400 MHz, CDCl3) 1.32 (6 H, t, *J* = 7.1, *J* = 0.4), 2.99 (2 H, d, *J* = 21.5), 4.12–4.20 (4 H, m), 4.75 (2 H, dd, *J* = 6.6, *J* = 1.0), 5.95 (2 H, s), 6.09 (1 H, dt, *J* = 15.8, *J* = 6.6), 6.58 (1 H, d, *J* = 15.8), 6.74 (1 H, d, *J* = 8.0), 6.81 (1 H, dd, *J* = 8.0, *J* = 1.6), 6.91 (1 H, d, *J* = 1.6); δC (100 MHz, CDCl3) 16.3 (d, *J* = 6.2), 34.3 (d, *J* = 134.2), 62.7 (d, *J* = 6.2), 66.1, 101.1, 105.7, 108.3, 120.5, 121.5, 130.4, 134.5, 147.7, 148.0, 165.6 (d, *J* = 6.1); δP (162 MHz, CDCl3) 20.2; HRMS (ESI+): Found: 379.0920; C16H21NaO7P (MNa+) Requires 379.0917 (−0.8 ppm error).

**Diethyl ((1*RS*,5*SR*)-2-oxo-3-oxabicyclo[3.1.0]hexan-1-yl)phosphonate (20b).** Synthesised using General procedure E with allyl 2-diazo-2-(diethoxyphosphoryl)acetate **19b** (600 mg, 2.29 mmol), CH2Cl2 (17 mL) and Rh2(oct)4 (35.6 mg, 0.046 mmol). Purification by column chromatography (1:20 hexane:EtOAc) afforded the title compound **20b** as a dark yellow oil (417 mg, 78%); Rf 0.30 (1:8 hexane:EtOAc); νmax (thin film)/cm-1 2986, 2920, 2838, 1764, 1376, 1271, 1243, 1015; δH (400 MHz, CDCl3) 1.18–1.22 (1 H, m), 1.27 (3 H, td, *J* = 7.1, *J* = 0.5), 1.29 (3 H, td, *J* = 7.1, *J* = 0.5), 1.76 (1 H, ddd, *J* = 15.2, *J* = 7.8, *J* = 4.7), 2.58–2.65 (1 H, m), 4.07–4.18 (5 H, m), 4.28 (1 H, dd, *J* = 9.5, *J* = 4.7); δC (100 MHz, CDCl3) 16.1 (d, *J* = 6.0), 17.3 (d, *J* = 3.0), 22.5 (d, *J* = 207.0), 24.3 (d, *J* = 1.4), 63.0 (d, *J* = 6.2), 63.0 (d, *J* = 6.2), 67.5 (d, *J* = 2.5), 171.5 (d, *J* = 10.6); δP (162 MHz, CDCl3) 17.9; HRMS (ESI+): Found: 257.0552; C9H15NaO5P (MNa+) Requires 257.0549 (−1.2 ppm error), Found: 235.0737; C9H16O5P (MH+) Requires 235.0730 (−3.0 ppm error).

**Diethyl ((1*RS*,5*SR*,6*SR*)-2-oxo-6-propyl-3-oxabicyclo[3.1.0]hexan-1-yl)phosphonate (20c).** Synthesised using General procedure E with (*Z*)-hex-2-en-1-yl 2-diazo-2-(diethoxyphosphoryl)acetate **19c** (212 mg, 0.697 mmol), CH2Cl2 (7.0 mL) and Rh2(oct)4 (10.8 mg, 13.9 μmol). Purification by column chromatography (1:10 hexane:EtOAc) afforded the *title compound* **20c** as a pale yellow oil (128 mg, 66%); Rf 0.15 (1:2 hexane:EtOAc); νmax (thin film)/cm-1 2963, 2934, 2874, 1764, 1468, 1371, 1254, 1197, 1164, 1130, 1022, 976; δH (400 MHz, CDCl3) 0.97 (3 H, t, *J* = 7.1), 1.29–1.56 (10 H, m), 2.02–2.11 (1 H, m), 2.70 (1 H, dddd, *J* = 11.2, *J* = 8.0, *J* = 5.4, *J* = 0.9), 4.13–4.29 (5 H, m), 4.42 (1 H, dd, *J* = 10.0, *J* = 5.4); δC (100 MHz, CDCl3) 13.7, 16.3 (d, *J* = 6.1), 16.3 (d, *J* = 6.1), 21.9, 24.9, 28.1 (d, *J* = 2.3), 28.1 (d, *J* = 203.3), 29.5 (d, *J* = 2.5), 63.1 (d, *J* = 6.3), 63.2 (d, *J* = 6.2), 64.6 (d, *J* = 3.0), 170.5 (d, *J* = 10.0); δP (162 MHz, CDCl3) 18.8; HRMS (ESI+): Found: 299.1026; C12H21NaO5P (MNa+) Requires 299.1019 (−2.5 ppm error), Found: 277.1212; C12H22O5P (MH+) Requires 277.1199 (−4.5 ppm error).

**Diethyl ((1*RS*,5*SR*,6*RS*)-2-oxo-6-((*E*)-prop-1-en-1-yl)-3-oxabicyclo[3.1.0]hexan-1-yl)phosphonate (20d).** Synthesised using General procedure E with (2*E*,4*E*)-hexa-2,4-dien-1-yl 2-diazo-2-(diethoxyphosphoryl)acetate **19d** (68.6 mg, 0.250 mmol), CH2Cl2 (5.0 mL) and Rh2(oct)4 (4.0 mg, 5.0 μmol). Purification by column chromatography (1:10 hexane:EtOAc) afforded the *title compound* **20d** as a pale yellow oil (33 mg, 48%); Rf 0.34 (EtOAc); νmax (thin film)/cm-1 2983, 1767, 1370, 1276, 1246, 1157, 1025, 971, 590; δH (400 MHz, CDCl3) 1.32 (3 H, t, *J* = 7.1), 1.33 (3 H, t, *J* = 7.1), 1.72 (3 H, dd, *J* = 6.5, *J* = 1.6), 2.17 (1 H, ddd, *J* = 9.4, *J* = 6.0, *J* = 5.3), 2.73 (1 H, app. dt, *J* = 10.3, *J* = 5.0), 4.14–4.22 (4 H, m), 4.27 (1 H, dd, *J* = 9.4, *J* = 3.0), 4.34 (1 H, dd, *J* = 9.4, *J* = 4.6), 5.60 (1 H, ddq, *J* = 15.3, *J* = 9.4, *J* = 1.6), 5.80 (1 H, dq, *J* = 15.3, *J* = 6.5); δC (100 MHz, CDCl3) 16.2, 16.3, 17.9, 29.5 (d, *J* = 202.7), 30.3, 34.6 (d, *J* = 2.8), 62.8 (d, *J* = 6.5), 63.1 (d, *J* = 6.4), 67.7 (d, *J* = 2.9), 124.3 (d, *J* = 4.8), 130.8, 171.7 (d, *J* = 9.1); δP (162 MHz, CDCl3) 16.5; HRMS (ESI+): Found: 297.0866; C12H19NaO5P (MNa+) Requires 297.0862 (−1.1 ppm error), Found: 275.1044; C12H20O5P (MH+) Requires 275.1043 (−0.3 ppm error).

**Diethyl ((1*SR*,5*SR*)-6,6-dimethyl-2-oxo-3-oxabicyclo[3.1.0]hexan-1-yl)phosphonate (20e).** Synthesised using General procedure E with 3-methyl-but-2-en-1-yl 2-diazo-2-(diethoxyphosphoryl)acetate **19e** (74.0 mg, 0.255 mmol), CH2Cl2 (5.1 mL) and Rh2(oct)4 (4.0 mg, 5.1 μmol). Purification by column chromatography (1:10 hexane:EtOAc) afforded the *title compound* **20e** as a pale yellow oil (39 mg, 58%); Rf 0.27 (EtOAc); νmax (thin film)/cm-1 2985, 1764, 1389, 1364, 1260, 1181, 1052, 1025, 995, 971, 591; δH (400 MHz, CDCl3) 1.24 (3 H, s), 1.32 (3 H, t, *J* = 7.1), 1.35 (3 H, t, *J* = 7.1), 1.50 (3 H, s), 2.58 (1 H, dd, *J* = 12.2, *J* = 5.3), 4.12–4.27 (5 H, m), 4.38 (1 H, dd, *J* = 10.0, *J* = 5.3); δC (100 MHz, CDCl3) 16.3 (d, *J* = 6.2), 16.3 (d, *J* = 6.8), 16.5, 21.6 (d, *J* = 4.8), 30.0 (d, *J* = 2.8), 33.9 (d, *J* = 197.6), 36.3 (d, *J* = 3.8), 62.6 (d, *J* = 6.5), 62.9 (d, *J* = 6.8), 65.2 (d, *J* = 2.9), 171.4 (d, *J* = 9.8); δP (162 MHz, CDCl3) 18.6; HRMS (ESI+): Found: 285.0865; C11H19NaO5P (MNa+) Requires 285.0862 (−1.1 ppm error), Found: 263.1043; C11H20O5P (MH+) Requires 263.1043 (−0.2 ppm error).

**Diethyl ((1*SR*,5*SR*,6*RS*)-6-methyl-6-(4-methylpent-3-en-1-yl)-2-oxo-3-oxabicyclo[3.1.0]hexan-1-yl)phosphonate (20f).** Synthesised using General procedure E with (*E*)-3,7-dimethylocta-2,6-dien-1-yl 2-diazo-2-(diethoxyphosphoryl)acetate **19f** (71.7 mg, 0.200 mmol), CH2Cl2 (4.0 mL) and Rh2(oct)4 (3.1 mg, 4.0 μmol). Purification by column chromatography (2:1 → 1:1 hexane:EtOAc) afforded the *title compound* **20f** as a pale yellow oil (42 mg, 64%); Rf 0.20 (1:1 hexane:EtOAc); νmax (thin film)/cm-1 2977, 2912, 1764, 1445, 1391, 1366, 1255, 1172, 1051, 1023, 993, 970, 597; δH (400 MHz, CDCl3) 1.24 (3 H, d, *J* = 0.6), 1.33 (3 H, t, *J* = 7.1), 1.36 (3 H, t, *J* = 7.1), 1.60 (3 H, s), 1.65 (3 H, d, *J* = 0.5), 1.76–1.93 (2 H, m), 2.03–2.12 (1 H, m), 2.17–2.26 (1 H, m), 2.59 (1 H, ddd, *J* = 12.5, *J* = 5.3, *J* = 0.5), 4.11–4.29 (5 H, m), 4.40 (1 H, dd, *J* = 10.0, *J* = 5.3), 5.05–5.10 (1 H, m); δC (100 MHz, CDCl3) 13.4, 16.3, 16.3, 17.6, 25.3, 25.6, 33.8 (d, *J* = 1.9), 34.2 (d, *J* = 198.2), 34.4 (d, *J* = 4.2), 35.7 (d, *J* = 3.6), 62.6 (d, *J* = 6.6), 63.0 (d, *J* = 6.6), 65.2 (d, *J* = 2.1), 123.2, 132.2, 171.4 (d, *J* = 9.6); δP (162 MHz, CDCl3) 18.8; HRMS (ESI+): Found: 353.1493; C16H27NaO5P (MNa+) Requires 353.1488 (−1.2 ppm error), Found: 331.1668; C16H28O5P (MH+) Requires 331.1669 (0.1 ppm error).

**Diethyl ((1*SR*,5*SR*)-2-oxo-6,6-diphenyl-3-oxabicyclo[3.1.0]hexan-1-yl)phosphonate (20g).** Synthesised using General procedure E with 3,3-diphenylallyl 2-diazo-2-(diethoxyphosphoryl)acetate **19g** (78 mg, 0.188 mmol), CH2Cl2 (3.8 mL) and Rh2(oct)4 (2.9 mg, 3.8 μmol). Purification by column chromatography (1:10 hexane:EtOAc) afforded the *title compound* **20g** as a pale yellow oil (38 mg, 51%); Rf 0.18 (1:2 hexane:EtOAc); νmax (thin film)/cm-1 2982, 2908, 1761, 1600, 1495, 1474, 1449, 1388, 1365, 1252, 1221, 1195, 1162, 1071, 1054, 1019, 973, 710; δH (400 MHz, CDCl3) 1.11 (3 H, t, *J* = 7.1), 1.22 (3 H, t, *J* = 7.1), 3.53 (1 H, dd, *J* = 12.3, *J* = 5.3), 3.68 (1 H, ddq, *J* = 10.2, *J* = 9.5, *J* = 7.1), 3.89–3.99 (1 H, m), 4.04–4.13 (2 H, m), 4.27 (1 H, ddd, *J* = 9.9, *J* = 2.8, *J* = 0.7), 4.54 (1 H, dd, *J* = 9.9, *J* = 5.3), 7.16–7.34 (6 H, m), 7.42–7.50 (4 H, m); δC (100 MHz, CDCl3) 16.2 (d, *J* = 6.1), 16.2 (d, *J* = 6.3), 33.7 (d, *J* = 3.2), 37.3 (d, *J* = 203.9), 46.5 (d, *J* = 2.5), 62.4 (d, *J* = 6.2), 63.4 (d, *J* = 6.5), 65.4 (d, *J* = 2.5), 127.6, 128.0, 128.4, 128.6, 129.1, 129.3, 136.5, 138.7 (d, *J* = 4.6), 171.3 (d, *J* = 10.4); δP (162 MHz, CDCl3) 16.1; HRMS (ESI+): Found: 409.1172; C21H23NaO5P (MNa+) Requires 409.1175 (0.9 ppm error), Found: 387.1352; C21H24O5P (MH+) Requires 387.1356 (0.9 ppm error).

**Diethyl ((1*RS*,5*SR*,6*SR*)-6-(4-bromophenyl)-2-oxo-3-oxabicyclo[3.1.0]hexan-1-yl)phosphonate (20h).** Synthesised using General procedure E with (*E*)-3-(4-bromophenyl)allyl 2-diazo-2-(diethoxyphosphoryl)acetate **19h** (97 mg, 0.250 mmol), CH2Cl2 (5.0 mL) and Rh2(oct)4 (4.0 mg, 5.0 μmol). Purification by column chromatography (EtOAc) afforded the *title compound* **20h** as a pale yellow oil (72 mg, 74%); Rf 0.32 (EtOAc); νmax (thin film)/cm-1 2982, 1768, 1492, 1369, 1252, 1053, 1019, 974, 810, 590; δH (400 MHz, CDCl3) 1.09 (3 H, t, *J* = 7.1), 1.21 (3 H, t, *J* = 7.1), 2.71 (1 H, app. t, *J* = 6.0), 3.24 (1 H, app. dt, *J* = 10.7, *J* = 5.2), 3.81–4.08 (4 H, m), 4.38 (1 H, dd, *J* = 9.4, *J* = 2.8), 4.48 (1 H, dd, *J* = 9.4, *J* = 4.8), 7.22 (2 H, d, *J* = 8.5), 7.43 (2 H, d, *J* = 8.5); δC (100 MHz, CDCl3) 16.0 (d, *J* = 6.6), 16.1 (d, *J* = 6.0), 28.1, 31.4 (d, *J* = 205.8), 34.0 (d, *J* = 3.7), 62.6 (d, *J* = 6.6), 62.9 (d, *J* = 6.8), 67.8 (d, *J* = 3.1), 122.0, 130.9 (d, *J* = 5.7), 131.0, 131.1, 171.5 (d, *J* = 10.2); δP (162 MHz, CDCl3) 15.0; HRMS (ESI+): Found: 410.9970; C15H1879BrNaO5P (MNa+) Requires 410.9967 (−0.6 ppm error), Found: 389.0154; C15H1979BrO5P (MH+) Requires 389.0148 (−1.5 ppm error).

**Diethyl ((1*RS*,5*SR*,6*SR*)-6-(4-methoxyphenyl)-2-oxo-3-oxabicyclo[3.1.0]hexan-1-yl)phosphonate (20i).** Synthesised using General procedure E with (*E*)-3-(4-methoxyphenyl)allyl 2-diazo-2-(diethoxyphosphoryl)acetate **19i** (85 mg, 0.250 mmol), CH2Cl2 (5.0 mL) and Rh2(oct)4 (4.0 mg, 5.0 μmol). Purification by column chromatography (EtOAc) afforded the *title compound* **20i** as a pale yellow oil (45 mg, 53%); Rf 0.23 (EtOAc); νmax (thin film)/cm-1 2982, 1764, 1613, 1518, 1370, 1294, 1249, 1182, 1052, 1020, 983, 820; δH (400 MHz, CDCl3) 1.09 (3 H, td, *J* = 7.1, *J* = 0.4), 1.20 (3 H, t, *J* = 7.1), 2.73 (1 H, app. t, *J* = 6.1), 3.24 (1 H, app. dt, *J* = 10.6, *J* = 5.2), 3.76 (3 H, s), 3.77–4.06 (4 H, m), 4.36 (1 H, dd, *J* = 9.3, *J* = 2.8), 4.46 (1 H, dd, *J* = 9.3, *J* = 4.7), 6.83 (2 H, d, *J* = 8.8), 7.26 (2 H, d, *J* = 8.8); δC (100 MHz, CDCl3) 16.1 (d, *J* = 6.6), 16.2 (d, *J* = 6.0), 28.3, 31.6 (d, *J* = 206.2), 34.6 (d, *J* = 3.2), 55.2, 62.5 (d, *J* = 6.6), 62.8 (d, *J* = 6.8), 68.0 (d, *J* = 3.0), 113.4, 123.5 (d, *J* = 5.6), 130.5, 159.3, 171.9 (d, *J* = 10.2); δP (162 MHz, CDCl3) 15.5; HRMS (ESI+): Found: 363.0960; C16H21NaO6P (MNa+) Requires 363.0968 (2.1 ppm error), Found: 341.1140; C16H22O6P (MH+) Requires 341.1149 (2.6 ppm error).

**Diethyl ((1*RS*,5*SR*,6*SR*)-6-(1,3-benzodioxol-5-yl)-2-oxo-3-oxabicyclo[3.1.0]hexan-1-yl)phosphonate (20j).** Synthesised using General procedure E with (*E*)-3-(1,3-benzodioxol-5-yl)allyl 2-diazo-2-(diethoxyphosphoryl)acetate **19j** (68 mg, 0.178 mmol), CH2Cl2 (3.6 mL) and Rh2(oct)4 (2.8 mg, 3.6 μmol). Purification by column chromatography (1:10 hexane:EtOAc) afforded the *title compound* **29j** as a pale yellow solid (46 mg, 73%); Rf 0.17 (1:2 hexane:EtOAc); m.p. 96–99 °C; νmax (thin film)/cm-1 2980, 2910, 1754, 1500, 1489, 1447, 1395, 1371, 1311, 1233, 1214, 1180, 1098, 1014, 832, 807, 585; δH (400 MHz, CDCl3) 1.15 (3 H, t, *J* = 7.1), 1.24 (3 H, t, *J* = 7.1), 2.74 (1 H, app. t, *J* = 6.1), 3.21 (1 H, app. dt, *J* = 10.7, *J* = 5.2), 3.89–4.12 (4 H, m), 4.38 (1 H, dd, *J* = 9.3, *J* = 2.8), 4.48 (1 H, dd, *J* = 9.3, *J* = 4.7), 5.94 (2 H, s), 6.75 (1 H, d, *J* = 7.9), 6.81–6.84 (2 H, m); δC (100 MHz, CDCl3) 16.1 (d, *J* = 6.5), 16.3 (d, *J* = 6.0), 28.4, 31.5 (d, *J* = 205.7), 34.9 (d, *J* = 3.0), 62.6 (d, *J* = 6.1), 62.9 (d, *J* = 6.6), 68.0 (d, *J* = 2.4), 101.2, 107.9, 109.8, 123.0, 125.3 (d, *J* = 5.1), 147.4, 147.4, 171.8 (d, *J* = 10.2); δP (162 MHz, CDCl3) 15.4; HRMS (ESI+): Found: 377.0750; C16H19NaO7P (MNa+) Requires 377.0761 (2.8 ppm error), Found: 355.0925; C16H20O7P (MH+) Requires 355.0941 (4.4 ppm error).

**Diethyl ((3*RS*,4*SR*)-4-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-oxotetrahydrofuran-3-yl)phosphonate (16).** To a solution of freshly prepared SmI2 (4.00 mL, 0.400 mmol, ~0.1 M in THF) in an oven dried sealable tube at −78 °C under an atmosphere of argon, was added a solution of diethyl ((1*RS*,5*SR*,6*SR*)-6-(1,3-benzodioxol-5-yl)-2-oxo-3-oxabicyclo[3.1.0]hexan-1-yl)phosphonate **20j** (70.9 mg, 0.200 mmol) in THF (1.0 mL). The solution was stirred at −78 °C for 30 mins then quenched with sat. aq. NH4Cl (1.70 mL) and then allowed to warm at RT. The mixture was diluted with water (10 mL) and extracted with diethyl ether (3 × 20 mL). The combined organic extracts were dried over MgSO4, filtered and concentrated *in vacuo*. Purification by column chromatography (1:4 hexane:EtOAc) afforded the *title compound* **16** as a yellow oil (27 mg, 38%); Rf 0.55 (EtOAc); νmax (thin film)/cm-1 2983, 2910, 1768, 1503, 1490, 1443, 1245, 1196, 1149, 1018, 971, 809, 549; δH (400 MHz, CDCl3) 1.33 (6 H, t, *J* = 7.1), 2.69–2.87 (3 H, m), 3.04–3.16 (1 H, m), 4.04–4.22 (5 H, m), 4.44 (1 H, dd, *J* = 9.1, *J* = 6.9), 5.94 (2 H, s), 6.60 (1 H, dd, *J* = 7.9, *J* = 1.4), 6.65 (1 H, d, *J* = 1.4), 6.74 (1 H, d, *J* = 7.9); δC (100 MHz, CDCl3) 16.3 (app. t, *J* = 6.4), 39.0 (d, *J* = 10.0), 39.3 (d, *J* = 3.0), 44.5 (d, *J* = 139.9), 62.9 (d, *J* = 7.3), 63.7 (d, *J* = 7.0), 71.7 (d, *J* = 5.3), 101.1, 108.4, 109.1, 122.2, 130.8, 146.6, 148.0, 171.7 (d, *J* = 3.8); δP (162 MHz, CDCl3) 20.1; HRMS (ESI+): Found: 379.0923; C16H21NaO7P (MNa+) Requires 379.0917 (−1.6 ppm error), Found: 357.1100; C16H22O7P (MH+) Requires 357.1098 (−0.8 ppm error).

**(*RS*,*E*)-4-(benzo[*d*][1,3]dioxol-5-ylmethyl)-3-(benzo[*d*][1,3]dioxol-5-ylmethylene)dihydrofuran-2(3*H*)-one ((±)-savinin) (8) and (*RS*,*Z*)-4-(benzo[*d*][1,3]dioxol-5-ylmethyl)-3-(benzo[*d*][1,3]dioxol-5-ylmethylene)dihydrofuran-2(3*H*)-one ((±)-gadain) (9).** To a solution of diethyl ((3*RS*,4*SR*)-4-(benzo[*d*][1,3]dioxol-5-ylmethyl)-2-oxotetrahydrofuran-3-yl)phosphonate **16** (59 mg, 0.166 mmol) in THF (3.3 mL) at 0 °C was added KOBu-*t* (27.9 mg, 0.248 mmol). The solution was stirred at 0 °C for 60 mins, after which, piperonal (49.8 mg, 0.332 mmol) was added to the solution, which was refluxed for 2 h. After cooling at RT, the solution was quenched with sat. aq. NH4Cl (10 mL). The organic layer was separated and the aqueous extracted with EtOAc (2 × 10 mL). The organic extracts were dried over MgSO4, filtered and concentrated *in vacuo*. Purification by column chromatography (5:1 hexane:EtOAc → 3:1 hexane:EtOAc) afforded the title compounds as mixture (**8**:**9** 1.9:1) (31 mg, 53%). Small quantities of each compound were isolated separately for characterisation purposes.

Data for savinin, **8**; White solid; Rf 0.20 (4:1 hexane:EtOAc); m.p. 127–129 °C (lit.3a 146.4–148.4 °C); νmax (thin film)/cm-1 2908, 1744, 1646, 1503, 1490, 1447, 1341, 1250, 1214, 1180, 1037, 927, 810; δH (400 MHz, CDCl3) 2.59 (1 H, dd, *J* = 14.2, *J* = 10.1), 2.99 (1 H, dd, *J* = 14.2, *J* = 4.5), 3.71–3.77 (1 H, m), 4.22–4.29 (2 H, m), 5.93 (1 H, d, *J* = 1.4), 5.94 (1 H, d, *J* = 1.4), 6.05 (2 H, s), 6.64 (1 H, dd, *J* = 7.8, *J* = 1.6), 6.67 (1 H, d, *J* = 1.6), 6.74 (1 H, d, *J* = 7.8), 6.88 (1 H, d, *J* = 8.1), 7.05 (1 H, d, *J* = 1.7), 7.08 (1 H, dd, *J* = 8.1, *J* = 1.7), 7.50 (1 H, d, *J* = 1.9); δC (100 MHz, CDCl3) 37.5, 39.9, 69.5, 101.0, 101.7, 108.5, 108.6, 108.8, 109.2, 122.2, 125.8, 126.1, 128.2, 131.5, 137.5, 146.5, 147.9, 148.3, 149.2, 172.6; HRMS (ESI+): Found: 375.0833; C20H16NaO6 (MNa+) Requires 375.0839 (1.5 ppm error), Found: 353.1019; C20H17O6 (MH+) Requires 353.1020 (0.3 ppm error). Obtained data in accord with reported literature.3a,3b

Data for gadain, **9**; White solid; Rf 0.26 (4:1 hexane:EtOAc); m.p. 136–139 °C (lit.4b 145 °C); νmax (thin film)/cm-1 2906, 1741, 1634, 1600, 1503, 1488, 1446, 1246, 1171, 1083, 1037, 928, 810; δH (400 MHz, CDCl3) 2.78 (1 H, dd, *J* = 13.8, *J* = 8.9), 2.91 (1 H, dd, *J* = 13.8, *J* = 6.9), 3.29 (1 H, app. dtdd, *J* = 8.9, *J* = 7.1, *J* = 3.8, *J* = 1.7),4.10 (1 H, dd, *J* = 9.1, *J* = 3.8), 4.32 (1 H, dd, *J* = 9.1, *J* = 7.3), 5.95 (1 H, d, *J* = 1.4), 5.96 (1 H, d, *J* = 1.4), 6.00 (2 H, s), 6.59 (1 H, d, *J* = 1.7), 6.62 (1 H, dd, *J* = 7.9, *J* = 1.7), 6.69 (1 H, d, *J* = 1.7), 6.76 (1 H, d, *J* = 7.9), 6.79 (1 H, d, *J* = 8.1), 7.15 (1 H, dd, *J* = 8.1, *J* = 1.7), 7.74 (1 H, d, *J* = 1.7); δC (100 MHz, CDCl3) 40.7, 44.2, 69.8, 101.0, 101.4, 107.9, 108.4, 109.3, 110.7, 122.3, 125.2, 126.9, 127.9, 131.4, 140.4, 146.5, 147.6, 147.9, 149.0, 169.3; HRMS (ESI+): Found: 375.0843; C20H16NaO6 (MNa+) Requires 375.0839 (−1.2 ppm error), Found: 353.1027; C20H17O6 (MH+) Requires 353.1020 (−2.0 ppm error). Obtained data in accord with reported literature.3c

**4-Methoxy-6-nitrobenzo[*d*][1,3]dioxole (27).** Prepared according to a modified literature procedure:5 To a flask containing stirred concentrated nitric acid (70% solution, 100 mL) cooled to 0 °C was added 5-methoxypiperonal **26** (10.81 g, 60.0 mmol) portionwise over 2 h. After a further 1 h the yellow mixture was poured onto ice water (1 L) to precipitate a pale yellow solid, which was collected by suction filitration and washed with water (3 × 100 mL). Purification by column chromatography (7:1 hexane:EtOAc) afforded the title compound **27** as a pale yellow solid (6.92 g, 59%); Rf 0.45 (4:1 hexane:EtOAc); m.p. 130–132 °C (lit.24 145–146 °C); νmax (thin film)/cm-1 3109, 1645, 1521, 1491, 1451, 1435, 1347, 1316, 1218, 1198, 1112, 1090, 970, 918, 861, 770, 742; δH (400 MHz, DMSO-*d*6) 3.93 (3 H, s), 6.24 (2 H, s), 7.53 (1 H, d, *J* = 2.2), 7.62 (1 H, d, *J* = 2.2); δH (400 MHz, CDCl3) 3.96 (3 H, s), 6.14 (2 H, s), 7.42 (1 H, d, *J* = 2.1), 7.56 (1 H, d, *J* = 2.1); δC (100 MHz, CDCl3) 56.8, 99.0, 103.3, 104.9, 141.1, 142.8, 142.9, 148.7; HRMS (ESI+): Found: 220.0218; C8H7NNaO5 (MNa+) Requires 220.0216 (–0.6 ppm error). NMR data in accord with reported literature.25

**7-Methoxybenzo[*d*][1,3]dioxol-5-amine (28).** To a suspension of 4-methoxy-6-nitrobenzo[*d*][1,3]dioxole **27** (6.86 g, 34.8 mmol) in MeOH (174 mL) under an atmosphere of argon, was added ammonium formate (11.0 g, 174.0 mmol) and palladium on carbon (10% wt. % loading, 1.74 g). The solution was stirred for 16 h then filtered through a pad of Celite and washed with MeOH (100 mL). The filtrate was concentrated *in vacuo*. The residue was diluted with brine (250 mL) and extracted with EtOAc (2 × 250 mL). The combined organic extracts were dried over MgSO4, filtered and concentrated *in vacuo*. Purification by column chromatography (1:1 hexane:EtOAc) afforded the title compound **28** as an off-white solid (5.41 g, 93%); Rf 0.45 (1:1 hexane:EtOAc); m.p. 75–76 °C (lit.26 85–86 °C); νmax (thin film)/cm-1 3397, 3312, 3210, 2886, 1640, 1508, 1459, 1183, 1144, 1087, 1037, 958, 924, 802, 703, 618; δH (400 MHz, DMSO-d6) 3.71 (3 H, s), 4.83 (2 H, br. s), 5.75 (2 H, s), 5.82 (1 H, d, *J* = 2.0), 5.86 (1 H, d, *J* = 2.0); δH (400 MHz, CDCl3) 3.49 (2 H, br. s), 3.84 (3 H, s), 5.85 (2 H, s), 5.86 (1 H, d, *J* = 2.0), 5.96 (1 H, d, *J* = 2.0); δC (100 MHz, CDCl3) 56.4, 91.0, 94.3, 100.8, 128.0, 142.1, 143.9, 149.3; HRMS (ESI+): Found: 169.0657; C8H10NO3 (MNa+) Requires 168.0655 (−0.8 ppm error).

**7-Methoxybenzo[*d*][1,3]dioxole-5-diazonium tetrafluoroborate (29).** Procedure developed from literature precedent:26 To a solution of 7-methoxybenzo[*d*][1,3]dioxol-5-amine **28** (5.22 g, 31.2 mmol) in ethanol (10.3 mL), cooled to 0 °C was added an aqueous solution of HBF4 (50% w/, 11.0 g, 62.5 mmol) followed by *tert*-butyl nitrite (7.43 mL, 62.5 mmol) dropwise. The solution was stirred for 1 h after which diethyl ether (50 mL) was added, forming a precipitate. The solution was filtered and the solid washed with diethyl ether (3 × 100 mL). The solid was dried *in vacuo*, affording the *title compound* **29** as a yellow solid (7.57 g, 91%). No further purification was required. Rf 0.00 (1:1 hexane:EtOAc); m.p. decomposes at 126 °C; νmax (thin film)/cm-1 3119, 2257, 1624, 1587, 1495, 1454, 1442, 1308, 1240, 1223, 1114, 1072, 1023, 962, 854, 522; δH (400 MHz, DMSO-*d*6) 3.94 (3 H, s), 6.45 (2 H, s), 7.95 (1 H, d, *J* = 2.0), 8.29 (1 H, d, *J* = 2.0); δC (100 MHz, DMSO-*d*6) 57.5, 104.1, 105.9, 106.5, 116.2, 143.2, 148.0, 148.9; HRMS (ESI+): Found: 179.0447; C8H7N2O3 (MNa+) Requires 179.0451 (2.1 ppm error).

**6-Iodo-4-methoxybenzo[*d*][1,3]dioxole (30).** To a solution of KI (10.4 g, 62.5 mmol) in water (187 mL) and acetone (125 mL) was added 7-methoxybenzo[*d*][1,3]dioxole-5-diazonium tetrafluoroborate **29** (7.57 g, 28.3 mmol) over 15 mins. The mixture was stirred for 1 h and the acetone removed *in vacuo*. The residue was extracted with diethyl ether (3 × 250 mL). The combined organic extracts were washed with sat. aq. Na2S2O3 (250 mL) then water (250 mL) then dried over MgSO4, filtered and concentrated *in vacuo*. Purification by column chromatography (8:1 hexane:EtOAc) afforded the title compound **30** as white crystals (4.78 g, 61%); Rf 0.63 (4:1 hexane:EtOAc); m.p. 55–58 °C (lit.28 71–72 °C); νmax (thin film)/cm-1 3098, 2939, 2893, 2775, 1623, 1483, 1443, 1414, 1288, 1230, 1175, 1097, 1031, 966, 928, 811, 764, 709, 564; δH (400 MHz, CDCl3) 3.85 (3 H, s), 5.94 (2 H, s), 6.81–6.82 (2 H, m); δC (100 MHz, CDCl3) 56.6, 82.0, 101.7, 111.6, 116.8, 135.7, 144.4, 149.4; HRMS (ESI+): Found: 277.9441; C8H7IO3 (MNa+) Requires 277.9434 (−2.3 ppm error).

**(*E*)-Ethyl 3-(7-methoxybenzo[*d*][1,3]dioxol-5-yl)acrylate (31).** To a solution of 5-methoxypiperonal **26** (5.17 g, 28.7 mmol) in THF (86 mL) was added (carbethoxymethylene)triphenylphosphorane (12.0 g, 34.4 mmol) and refluxed for 16 h. Concentration *in vacuo* and purification by column chromatography (4:1 hexane:EtOAc) afforded the title compound **31** as a crystalline white solid (6.78 g, 95%); Rf 0.46 (4:1 hexane:EtOAc); m.p. 65–68 °C (lit.29 76 °C); νmax (thin film)/cm-1 2996, 2975, 2908, 1702, 1622, 1593, 1511, 1431, 1324, 1281, 1171, 1137, 1093, 1038, 996, 925, 846, 819, 594, 477; δH (400 MHz, CDCl3) 1.31 (3 H, t, *J* = 7.1), 3.90 (3 H, s), 4.23 (2 H, q, *J* = 7.1), 5.99 (2 H, s), 6.25 (1 H, d, *J* = 15.9), 6.68 (1 H, d, *J* = 1.4), 6.72 (1 H, d, *J* = 1.4), 7.54 (1 H, d, *J* = 15.9); δC (100 MHz, CDCl3) 14.3, 56.5, 60.4, 101.2, 101.9, 109.0, 116.6, 129.2, 137.2, 143.6, 144.2, 149.2, 167.0; HRMS (ESI+): Found: 273.0731; C13H14NaO5 (MNa+) Requires 273.0733 (0.8 ppm error).

**Ethyl 3,3-bis(7-methoxybenzo[*d*][1,3]dioxol-5-yl)acrylate (32).** Procedure developed from literature precedent:16 To an oven dried sealable tube was added (*E*)-ethyl 3-(7-methoxybenzo[*d*][1,3]dioxol-5-yl)acrylate **31** (500 mg, 2.00 mmol), 6-iodo-4-methoxybenzo[*d*][1,3]dioxole **30** (834 mg, 3.00 mmol), tetra-*n*-butylammonium bromide (709 mg, 2.20 mmol), NaHCO3 (420 mg, 5.00 mmol), Pd(OAc)2 (44.9 mg, 0.20 mmol) and DMF (5 mL). The tube was sealed and flushed with argon then heated at 120 °C for 16 h. The mixture was cooled at RT, diluted with water (50 mL) and extracted with diethyl ether (3 × 50 mL). The combined organic extracts were washed with brine (50 mL), dried over MgSO4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (4:1 hexane:EtOAc) affording the *title compound* **32** as an orange oil that later crystallised (695 mg, 87%); Rf 0.22 (4:1 hexane:EtOAc); m.p. 72–76 °C; νmax (thin film)/cm-1 2976, 2939, 2900, 1715, 1627, 1600, 1506, 1426, 1377, 1290, 1222, 1171, 1112, 1083, 1044, 968, 929, 844, 730; δH (400 MHz, CDCl3) 1.16 (3 H, t, *J* = 7.1), 3.84 (6 H, app. s), 4.07 (2 H, q, *J* = 7.1), 5.97 (2 H, s), 5.99 (2 H, s), 6.18 (1 H, s), 6.36 (1 H, d, *J* = 1.3), 6.38 (1 H, d, *J* = 1.3), 6.48 (1 H, d, *J* = 1.5), 6.51 (1 H, d, *J* = 1.5); δC (100 MHz, CDCl3) 14.0, 56.5, 56.7, 59.9, 101.5, 101.8, 102.2, 103.8, 108.7, 109.0, 116.2, 132.9, 132.9, 135.3, 135.4, 136.5, 143.1, 143.1, 148.3, 148.8, 155.5, 165.9; HRMS (ESI+): Found: 423.1048; C21H20NaO8 (MNa+) Requires 423.1050 (0.5 ppm error), Found: 401.1220; C21H21O8 (MH+) Requires 401.1231 (2.8 ppm error).

**3,3-Bis(7-methoxybenzo[*d*][1,3]dioxol-5-yl)prop-2-en-1-ol (33).** To a solution of ethyl 3,3-bis(7-methoxybenzo[*d*][1,3]dioxol-5-yl)acrylate **32** (1.32 g, 3.30 mmol) in THF (16 mL) cooled to −78 °C was added dropwise DIBAL (6.60 mL, 6.60 mmol, 1.0 M in hexane) and stirred for 2 h. The solution was quenched with water (15 mL) dropwise and stirred for 30 mins at RT before being filtered through a pad of Celite and washed with diethyl ether (500 mL). The filtrate was concentrated *in vacuo*. Purification by column chromatography (4:1 hexane:EtOAc) afforded the *title compound* **33** as a yellow gum (1.08 g, 91%); Rf 0.31 (4:1 hexane:EtOAc); νmax (thin film)/cm-1 3360br, 2889, 1626, 1505, 1447, 1424, 1376, 1191, 1153, 1085, 1042, 967, 928, 844, 728; δH (400 MHz, CDCl3) 2.15 (1 H, br. s), 3.80 (3 H, s), 3.82 (3 H, s), 4.16 (2 H, d, *J* = 6.8), 5.91 (2 H, s), 5.95 (2 H, s), 6.04 (1 H, t, *J* = 6.8), 6.31 (1 H, d, *J* = 1.4), 6.31 (1 H, d, *J* = 1.4), 6.41 (1 H, d, *J* = 1.5), 6.42 (1 H, d, *J* = 1.5); δC (100 MHz, CDCl3) 56.4, 56.5, 60.4, 101.4 (2C), 101.8, 103.8, 107.5, 109.1, 126.5, 133.1, 134.5, 134.8, 136.5, 142.9, 143.1, 143.2, 148.4, 148.5; HRMS (ESI+): Found: 381.0938; C19H18NaO7 (MNa+) Requires 381.0945 (1.7 ppm error).

**3,3-Bis(7-methoxybenzo[*d*][1,3]dioxol-5-yl)allyl 2-(diethoxyphosphoryl)acetate (34).** Synthesised using general procedure A with 3,3-bis(7-methoxybenzo[*d*][1,3]dioxol-5-yl)prop-2-en-1-ol **33** (973 mg, 2.72 mmol), toluene (13.6 mL), DEPAA (559 mg, 2.85 mmol), DIPEA (1.23 mL, 7.07 mmol) and T3P (2.25 g, 3.54 mmol, 50% w/w solution in THF) affording the *title compound* **34** as a yellow oil (1.45 g, 99%); Rf 0.26 (1:2 hexane:EtOAc); νmax (thin film)/cm-1 2984, 2936, 2902, 1733, 1626, 1507, 1426, 1262, 1160, 1107, 1042, 1020, 965, 929, 839, 728; δH (400 MHz, CDCl3) 1.29 (6 H, td, *J* = 7.1, *J* = 0.4), 2.95 (2 H, d, *J* = 21.5), 3.81 (3 H, s), 3.83 (3 H, s), 4.09–4.17 (4 H, m), 4.65 (2 H, d, *J* = 7.2), 5.91 (2 H, s), 5.96 (2 H, s), 5.98 (1 H, t, *J* = 7.2), 6.31 (1 H, d, *J* = 1.4), 6.33 (1 H, d, *J* = 1.4), 6.39 (1 H, d, *J* = 1.6), 6.41 (1 H, d, *J* = 1.6); δC (100 MHz, CDCl3) 16.2 (d, *J* = 6.6), 34.2 (d, *J* = 134.2), 56.5, 56.5, 62.6 (d, *J* = 6.5), 63.6, 101.4 (2C), 101.9, 103.8, 107.7, 109.2, 120.5, 132.5, 134.8, 135.2, 136.0, 143.0, 143.2, 146.2, 148.6, 148.6, 165.5 (d, *J* = 6.5); δP (162 MHz, CDCl3) 20.2; HRMS (ESI+): Found: 559.1348; C25H29NaO11P (MNa+) Requires 559.1340 (−1.5 ppm error).

**3,3-Bis(7-methoxybenzo[*d*][1,3]dioxol-5-yl)propyl 2-diazo-2-(diethoxyphosphoryl)acetate (24).** To a solution of 3,3-bis(7-methoxybenzo[*d*][1,3]dioxol-5-yl)allyl 2-(diethoxyphosphoryl)acetate **34** (457 mg, 0.852 mmol)in methanol (4.26 mL) was added palladium on carbon (10% wt. % loading, 17 mg). The flask was purged 4 times with argon then 4 times with hydrogen. The mixture was stirred at RT for 16 h. The mixture was filtered through a pad of Celite and washed with methanol (50 mL) and the filtrate concentrated *in vacuo*. Purification by column chromatography (1:2 hexane:EtOAc) afforded 3,3-bis(7-methoxybenzo[*d*][1,3]dioxol-5-yl)propyl 2-(diethoxyphosphoryl)acetate as a yellow oil (280 mg, 61%); Rf 0.21 (1:2 hexane:EtOAc); νmax (thin film)/cm-1 2982, 2940, 2905, 1733, 1632, 1507, 1449, 1430, 1266, 1193, 1128, 1091, 1019, 964, 929, 834; δH (400 MHz, CDCl3) 1.30 (6 H, t, *J* = 7.1), 2.24 (2 H, app. q, *J* = 7.2), 2.94 (2 H, d, *J* = 21.6), 3.85 (6 H, s), 3.87 (1 H, t, *J* = 7.9), 4.05 (2 H, t, *J* = 6.5), 4.14 (4 H, dq, *J* = 8.3, *J* = 7.1), 5.88 (4 H, s), 6.37 (2 H, d, *J* = 1.4), 6.38 (2 H, d, *J* = 1.4); δC (100 MHz, CDCl3) 16.2 (d, *J* = 6.1), 34.2 (d, *J* = 133.6), 34.2, 46.9, 56.6, 62.6 (d, *J* = 6.4), 63.6, 101.2, 101.4, 107.3, 133.6, 138.3, 143.3, 148.9, 165.5 (d, *J* = 5.9); δP (162 MHz, CDCl3) 20.4; HRMS (ESI+): Found: 561.1503; C25H31NaO11P (MNa+) Requires 561.1496 (−1.1 ppm error).

The synthesis continued using general procedure B with 3,3-bis(7-methoxybenzo[*d*][1,3]dioxol-5-yl)propyl 2-(diethoxyphosphoryl)acetate(278 mg, 0.516 mmol), THF (2.58 mL), LHMDS (0.620 mL, 0.620 mmol, 1.0 M solution in THF) and DBSA (0.21 mL, 0.620 mmol). Purification by column chromatography (1:2 hexane:EtOAc) afforded the *title* *compound* **24** as a yellow oil (147 mg, 51%); Rf 0.70 (1:4 hexane:EtOAc); νmax (thin film)/cm-1 2982, 2941, 2906, 2129, 1704, 1633, 1508, 1451, 1431, 1369, 1279, 1194, 1131, 1092, 1041, 1019, 977; δH (400 MHz, CDCl3) 1.36 (6 H, td, *J* = 7.1, *J* = 0.7), 2.27 (2 H, app. q, *J* = 7.2), 3.85 (1 H, t, *J* = 7.8), 3.87 (6 H, s), 4.11–4.27 (6 H, m), 5.92 (4 H, s), 6.37 (2 H, d, *J* = 1.4), 6.39 (2 H, d, *J* = 1.4); δC (100 MHz, CDCl3) 16.2 (d, *J* = 6.8), 34.5, 47.2, 53.7 (d, *J* = 231.7), 56.8, 63.6 (d, *J* = 5.7), 63.9, 101.5, 101.5, 107.4, 133.8, 138.3, 143.4, 149.1, 163.2 (d, *J* = 11.8); δP (162 MHz, CDCl3) 10.7; HRMS (ESI+): Found: 587.1406; C25H29N2NaO11P (MNa+) Requires 587.1401 (−0.8 ppm error).

**3,3-Bis(7-methoxybenzo[*d*][1,3]dioxol-5-yl)allyl 2-diazo-2-(diethoxyphosphoryl)acetate (25).** Synthesised using general procedure B with 3,3-bis(7-methoxybenzo[*d*][1,3]dioxol-5-yl)allyl 2-(diethoxyphosphoryl)acetate **34** (996 mg, 1.86 mmol), THF (9.30 mL), LHMDS (2.23 mL, 2.23 mmol, 1.0 M solution in THF) and DBSA (0.75 mL, 2.23 mmol). Purification by column chromatography (1:1 hexane:EtOAc) afforded the *title* *compound* **25** as a yellow oil (665 mg, 63%); Rf 0.27 (1:2 hexane:EtOAc); νmax (thin film)/cm-1 2984, 2943, 2905, 2129, 1703, 1627, 1507, 1427, 1275, 1162, 1108, 1094, 1044, 1020, 970, 932; δH (400 MHz, CDCl3) 1.34 (6 H, td, *J* = 7.1, *J* = 0.6), 3.84 (3 H, s), 3.86 (3 H, s), 4.08–4.27 (4 H, m), 4.74 (2 H, d, *J* = 7.2), 5.95 (2 H, s), 5.99 (2 H, s), 6.01 (1 H, t, *J* = 7.2), 6.34–6.35 (2 H, m), 6.42 (1 H, d, *J* = 1.6), 6.43 (1 H, d, *J* = 1.6); δC (100 MHz, CDCl3) 16.1 (2 C, d, *J* = 6.9), 53.6 (d, *J* = 228.1), 56.6, 56.7, 63.6–63.7 (3C, m), 101.6 (2 C), 102.1, 103.9, 107.9, 109.2, 120.3, 132.5, 135.0, 135.4, 136.0, 143.1, 143.4, 146.9, 148.7, 148.8, 163.3 (d, *J* = 12.7); δP (162 MHz, CDCl3) 10.6; HRMS (ESI+): Found: 585.1240; C25H27N2NaO11P (MNa+) Requires 585.1245 (0.7 ppm error).

**Diethyl ((1*SR*,5*SR*)-6,6-bis(7-methoxybenzo[*d*][1,3]dioxol-5-yl)-2-oxo-3-oxabicyclo[3.1.0]hexan-1-yl)phosphonate (36). S**ynthesised using General procedure E with 3,3-bis(7-methoxybenzo[*d*][1,3]dioxol-5-yl)allyl 2-diazo-2-(diethoxyphosphoryl)acetate **25** (368 mg, 0.654 mmol), CH2Cl2 (13.1 mL) and rhodium(II) triphenylacetate dimer as complex with DCM (Rh2(tpa)4) (18.8 mg, 13.1 μmol). Purification by column chromatography (1:4 hexane:EtOAc → EtOAc) afforded the *title compound* **36** as an off-white solid (153 mg, 44%); Rf 0.24 (1:4 hexane:EtOAc); m.p. 81–84 °C; νmax (thin film)/cm-1 2926, 1758, 1632, 1507, 1429, 1364, 1240, 1192, 1155, 1093, 1042, 1015, 968, 929, 728; δH (400 MHz, CDCl3) 1.14 (3 H, t, *J* = 7.1), 1.27 (3 H, t, *J* = 7.1), 3.36 (1 H, dd, *J* = 12.5, *J* = 4.8), 3.69–3.81 (1 H, m), 3.88 (3 H, s), 3.89 (3 H, s), 3.91–4.01 (1 H, m), 4.06–4.23 (2 H, m), 4.28 (1 H, dd, *J* = 9.9, *J* = 2.2), 4.50 (1 H, dd, *J* = 9.9, *J* = 5.3), 5.89–5.93 (4 H, m), 6.51 (1 H, br. s), 6.60–6.61 (2 H, m), 6.72 (1 H, d, *J* = 1.6); δC (100 MHz, CDCl3) 16.2 (d, *J* = 6.1), 16.3 (d, *J* = 6.5), 34.5 (d, *J* = 4.0), 37.8 (d, *J* = 203.9), 46.4 (d, *J* = 2.8), 56.7, 56.7, 62.3 (d, *J* = 6.5), 63.5 (d, *J* = 6.9), 65.5 (d, *J* = 3.5), 101.5, 101.6, 102.4, 102.9, 108.1, 109.3, 130.6 (d, *J* = 1.8), 133.2 (d, *J* = 5.5), 134.6, 135.0, 143.1, 143.9, 148.7, 149.2, 171.2 (d, *J* = 10.5); δP (162 MHz, CDCl3) 16.2; HRMS (ESI+): Found: 557.1169; C25H27NaO11P (MNa+) Requires 557.1183 (2.5 ppm error), Found: 535.1362; C25H28O11P (MH+) Requires 535.1364 (0.2 ppm error).

**Diethyl ((3*RS*,4*SR*)-4-(bis(7-methoxybenzo[*d*][1,3]dioxol-5-yl)methyl)-2-oxotetrahydrofuran-3-yl)phosphonate (37).** To an oven dried sealable tube containing SmI2 (10.6 mL, 1.06 mmol, ~0.1 M solution in THF) under an atmosphere of argon, atmosphere and cooled to −78 °C was added dropwise a solution of diethyl ((1*SR*,5*SR*)-6,6-bis(7-methoxybenzo[*d*][1,3]dioxol-5-yl)-2-oxo-3-oxabicyclo[3.1.0]hexan-1-yl)phosphonate **36** (142 mg, 0.266 mmol) in THF (2.66 mL). The mixture was stirred at −78 °C for 10 mins then quenched by addition of sat. aq. NH4Cl (5 mL) and allowed to warm at RT. The biphasic mixture was extracted with EtOAc (3 × 25 mL) and the combined organic extracts dried over MgSO4, filtered and concentrated *in vacuo*. Purification by column chromatography (1:2 hexane:EtOAc) afforded the *title compound* **37** as a white solid (78 mg, 55%); Rf 0.44 (1:2 hexane:EtOAc); m.p. 59–62 °C; νmax (thin film)/cm-1 2981, 2909, 1770, 1633, 1508, 1451, 1433, 1370, 1316, 1248, 1197, 1156, 1132, 1091, 1042, 1021, 968, 731; δH (400 MHz, CDCl3) 1.31 (3 H, t, *J* = 7.1), 1.31 (3 H, t, *J* = 7.1), 2.84 (1 H, d, *J* = 24.5), 3.44–3.53 (1 H, m), 3.61 (1 H, d, *J* = 12.4), 3.88 (3 H, s), 3.90 (3 H, s), 3.99–4.21 (5 H, m), 4.49 (1 H, dd, *J* = 9.4, *J* = 6.0), 5.90–5.92 (4 H, m), 6.37 (1 H, d, *J* = 1.4), 6.41 (1 H, d, *J* = 1.4), 6.45 (1 H, d, *J* = 1.3), 6.46 (1 H, d, *J* = 1.3); δC (100 MHz, CDCl3) 16.1 (d, *J* = 6.5), 16.2 (d, *J* = 6.2), 42.1 (d, *J* = 2.6), 44.8 (d, *J* = 133.0), 54.2 (d, *J* = 13.9), 56.7, 56.8, 63.1 (d, *J* = 7.0), 63.7 (d, *J* = 7.1), 70.6, 101.2, 101.4, 101.5, 101.9, 107.6, 107.9, 134.2, 134.3, 135.3, 136.2 (d, *J* = 1.8), 143.6, 143.6, 149.2, 149.4, 171.7 (d, *J* = 5.4); δP (162 MHz, CDCl3) 19.7; HRMS (ESI+): Found: 559.1329; C25H29NaO11P (MNa+) Requires 559.1340 (1.8 ppm error).

**(±)-Peperomin E (10). T**o a solution of diethyl ((3*RS*,4*SR*)-4-(bis(7-methoxybenzo[*d*][1,3]dioxol-5-yl)methyl)-2-oxotetrahydrofuran-3-yl)phosphonate **37** (66 mg, 0.123 mmol) in THF (2.5 mL) cooled to 0 °C under an argon atmosphere was added KOBu-*t* (16.6 mg, 0.148 mmol). The solution was stirred for 30 mins after which paraformaldehyde (18.5 mg, 0.615 mmol) was added in one portion. The mixture was stirred for 30 mins at 0°C then 1 h at RT then quenched by addition of sat. aq. NH4Cl (5 mL). The mixture was extracted with EtOAc (3 × 25 mL) and the combined organic extracts dried over MgSO4, filtered and concentrated *in vacuo*. Purification by column chromatography (2:1 hexane:EtOAc) afforded the title compound **10** as a white crystalline solid (44 mg, 87%); Rf 0.68 (1:1 hexane:EtOAc); m.p. 56–59 °C (lit.14 140 °C); νmax (thin film)/cm-1 2903, 1760, 1633, 1508, 1451, 1432, 1363, 1315, 1195, 1130, 1092, 1042, 927, 730; δH (400 MHz, CDCl3) 3.66 (1 H, d, *J* = 11.6), 3.75 (1 H, app. dddt, *J* = 11.6, *J* = 7.7, *J* = 4.4, *J* = 2.2), 3.88 (3 H, s), 3.89 (3 H, s), 3.98 (1 H, dd, *J* = 9.5, *J* = 4.4), 4.32 (1 H, dd, *J* = 9.5, *J* = 7.7), 4.93 (1 H, d, *J* = 2.0), 5.93–5.95 (4 H, m), 6.14 (1 H, d, *J* = 2.3), 6.36 (1 H, d, *J* = 1.5), 6.38 (1 H, d, *J* = 1.5), 6.45 (1 H, d, *J* = 1.5), 6.46 (1 H, d, *J* = 1.5); δC (100 MHz, CDCl3) 42.4, 55.3, 56.8, 56.9, 69.7, 101.1, 101.5 (2C), 101.5, 107.9, 108.3, 124.9, 134.2, 134.3, 135.8, 136.0, 136.1, 143.4, 143.6, 149.2, 149.5, 170.7; HRMS (ESI+): Found: 435.1050; C22H20NaO8 (MNa+) Requires 435.1050 (0.1 ppm error). Obtained data in accord with reported literature, with the exception of the melting point.14

Acknowledgements

The authors wish to thank the Elsevier Foundation (M. G. L.), the University of York and the Leverhulme Trust (for an Early Career Fellowship, ECF-2015-013, W. P. U.) for funding, Dr. Adrian C. Whitwood (University of York) for X-ray crystallography and Euticals for kindly providing T3P.

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