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Exploiting the Anders–Gaßner variant on the Wittig reaction: new methodology for the synthesis of 3,3-dimethylacroyl enol esters

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ABSTRACT

A one pot synthesis of the 3,3-dimethylacroyl enol ester function found in the vibsane type diterpenes has been developed based on the Anders–Gaßner variant of the Wittig reaction (AGW reaction). This method uses easily accessible acyloxyalkylidene phosphoranes and a variety of aldehydes.

1. Introduction

The 3,3-dimethylacroyl enol ester function (as highlighted in **5**) is contained only within the vibsane type diterpene natural product family of which 61 examples currently exist.[1–8] Even though the vibsanane type diterpenes are made up of a number of different structure types, for example **1**–**7**, the 3,3-dimethylacroyl enol ester sidechain is maintained nearly throughout the whole family (Fig. 1).

Synthetic methods to construct the 3,3-dimethylacroyl enol ester moiety and vinyl esters in general[9] from aldehydes are mostly limited to variations on anhydride (RCOX)/base (or acid) systems. In comparison, transition metal mediated anti-Markovnikov carboxylic acid addition to triple bonds is about the only alternative.[10–12] The anhydride method is typified by the elegant work of Davies[13] who completed the total synthesis of 5,10-bis-*epi*-vibsanin E **8** (and corresponding *Z* isomer **9**) by treatment of aldehyde **10** with 3,3-dimethylacrylic anhydride (**11**) under basic conditions (Scheme 1).

These methods, however, require a homologated aldehyde [i.e., one alpha (acidic) protoned carbon unit] to install the vinyl ester function, which in many cases, including our own,[14–17] demands an extra synthetic step to accommodate homologation. Taking this into account and the fact that only a handful of synthetic methods are currently available for building such functionality it became apparent that new methodologies are required.

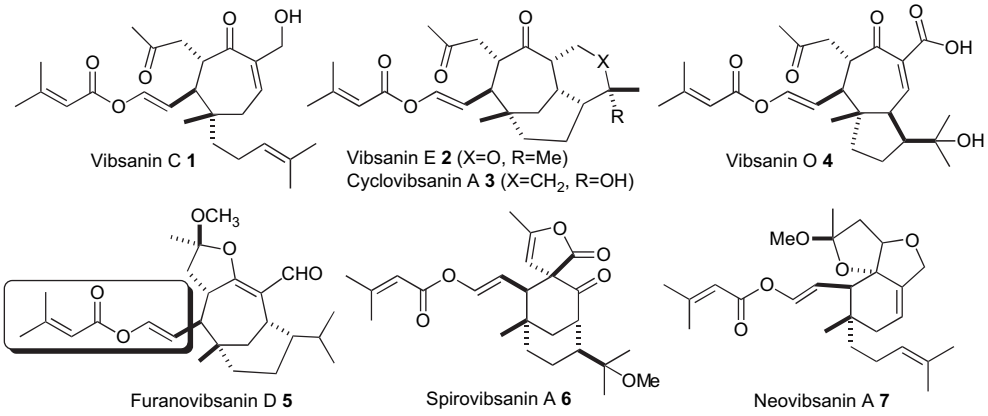

Figure 1. Examples of vibsane type diterpenes containing 3,3-dimethylacroyl enol ester sidechain.

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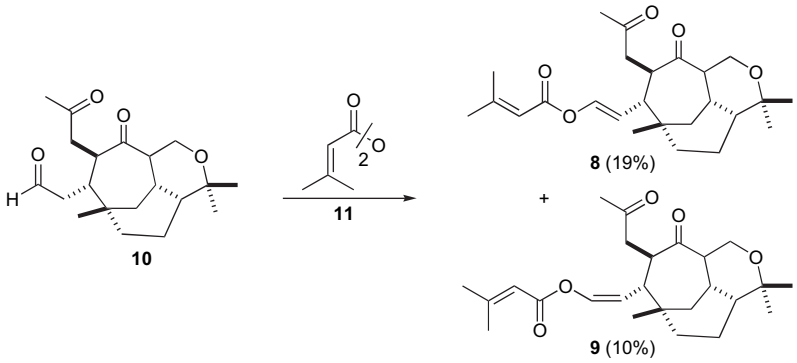
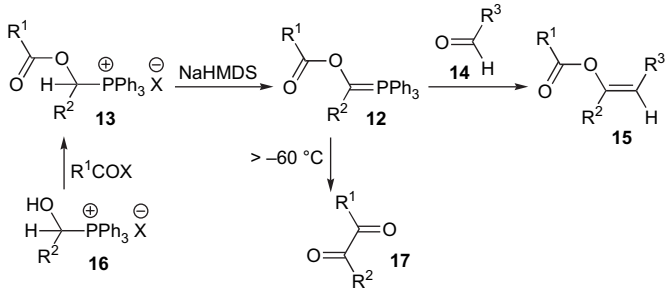


Scheme 1.



Scheme 2.

Considering that the Wittig reaction[18,19] is synonymous throughout organic chemistry as a means of rapidly and mildly constructing carbon–carbon double bonds, including vinyl ethers,[20] we contemplated applying this methodology to create a 3,3-dimethylacroyl enol ester function in a single step. A literature survey, however, revealed the interesting but relatively unknown[21] Anders–Gaßner variant of the Wittig reaction (Scheme 2).[22–28] This reaction is exemplified by the process of an acyloxyalkylidenephosphorane **12** (obtained via the deprotonation of the corresponding phosphonium salt **13**, synthesised from **16**), reacting with an aldehyde (**14**) to afford the vinyl ester **15** (Scheme 2).

Two possible explanations can be provided which might be responsible for the lack of interest in the AGW reaction by the synthetic community to-date. Firstly, the intermediate acyloxyalkylidene phosphoranes **12** exhibit remarkable instability: above −60 °C an interesting intramolecular rearrangement occurs (accompanied by the elimination of PPh_3) which finally results in the formation of 1,2-diketones **17**.[22–27] Secondly, hitherto the AGW reaction offered limited functional group application, for example, only aryl and heteroaryl groups were demonstrated at R^1 and R^2 (Scheme 2). Irrespective of these two issues, this reaction potentially offers a powerful one-step option to access certain vinyl ester functionalities and as such we embarked on an exploration of a wider range of acceptable functional groups at both R^1 and R^2 with direct application to the vibsane type diterpenes.

2. Results and discussion

The 3,3-dimethylacroyl phosphonium salt **18** was prepared as outlined in Scheme 2 (i.e., **16** to **13**). Unfortunately, attempts to prepare the trifluoroacetyl (i.e., **20**) failed, however, acetyl (i.e., **19**) and pivaloyl (i.e., **21**) were synthesised in acceptable yields (Fig. 2). A range of both aromatic and aliphatic aldehydes were then subjected to **18** in the deprotonated form [(i.e., **12**) Scheme 2], which gratifyingly afforded the desired products (Table 1 and Fig. 3).

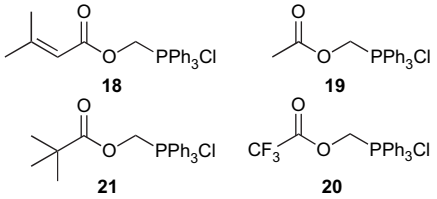


Figure 2.

Although yields are moderate to low they are similar, or even better (see below) to those observed using the base anhydride protocol (i.e., Scheme 1). Ylids resulting from **19** or **21** failed or gave only trace amounts of product, respectively.

In an attempt to increase yields Horner–Wadsworth–Emmons type reagents (i.e., **31** and **32**) were synthesised, however, on treatment with base [$NaN(SiMe_3)_2$] and subsequent reaction with 4-nitrobenzaldehyde only lactone **33** was obtained (Fig. 4). Lactone **33** arises from selective 1,4-deprotonation of the 3,3-dimethylacroyl function followed by an aldol reaction and subsequent lactonisation.

It should be noted for comparative purposes that product **30** (entry 9, Table 1) was synthesised using the traditional method [i.e., 3,3-dimethylacroyl anhydride (**11**), base and the one carbon homologue (**34**)] in 8% yield [*E*/*Z* (1.2:1)], which is a much lower yield to that obtained with the one-step protocol reported herein (Scheme 3).

3. Conclusion

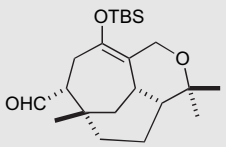
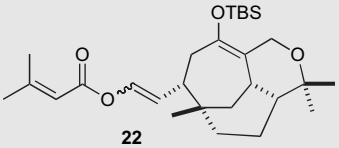
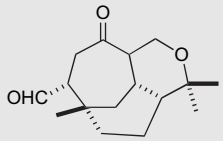
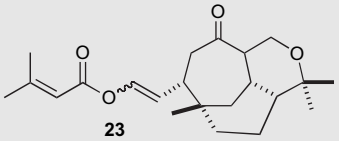
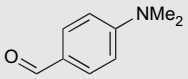
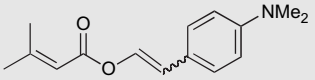
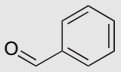
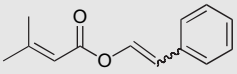
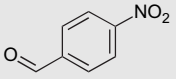
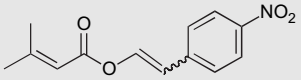
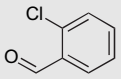
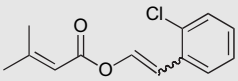
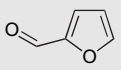
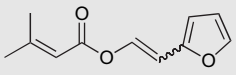
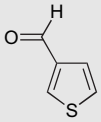
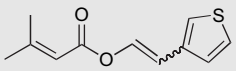
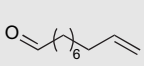
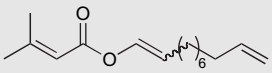
In conclusion, the AGW reaction has been exploited in terms of being extended in scope to adopt 3,3-dimethylacroyl ester functionality. Although yields are moderate to low it should be noted that a unique feature of the current methodology is that construction of an acetylenic or homologated aldehyde moiety is not required, which are the crucial intermediate steps for the other vinyl ester building methodologies and yields of the one-step protocol are higher.

4. Experimental

4.1. General

^1H and ^{13}C NMR spectra were recorded on Bruker AV400 (400.13 MHz; 100.62 MHz), AV300 (300.13 MHz; 75.47 MHz) and DRX500 (500.13 MHz; 125.76 MHz) instruments in deuteriochloroform ($CDCl_3$). Coupling constants are given in hertz and chemical shifts are expressed as δ values in parts per million. GC/MS

Table 1
Products **22**–**30** arising from reaction of selected aldehydes **14** with the ylid **12** (R^1=$(CH_3)_2C$=CH, R^2=H; derived from deprotonation of the phosphonium salt **18**)

Entry	Aldehyde	Product	Yield (%)	*E*/*Z* Ratio
1		 **22**	32	2.4:1
2		 **23**	21	3.4:1
3		 **24**	26	1.5:1
4		 **25**	20	1.5:1
5		 **26**	41	1.5:1
6		 **27**	30	10:1
7		 **28**	29	3.5:1
8		 **29**	25	1.7:1
9		 **30**	30	1.3:1

data were recorded on a Shimadzu GC-17A Ver.3, *mass-spectrometer*: MS QP5050A, ionisation at 70 eV, *column*: DB-5ms 30 m×0.25 μm, *carrier-gas*: He, total flow 32.2 mL/min, column flow 1.3 mL/min, *injector temperature*: 250 °C, *standard program*: 2 min at 100 °C, followed by a temperature increase of 16 °C/min and held at 250 °C for 10 min. High resolution electrospray ionisation (HRESIMS) accurate mass measurements were recorded in positive mode on a Bruker MicrOTOF-Q (quadrupole-Time of Flight)

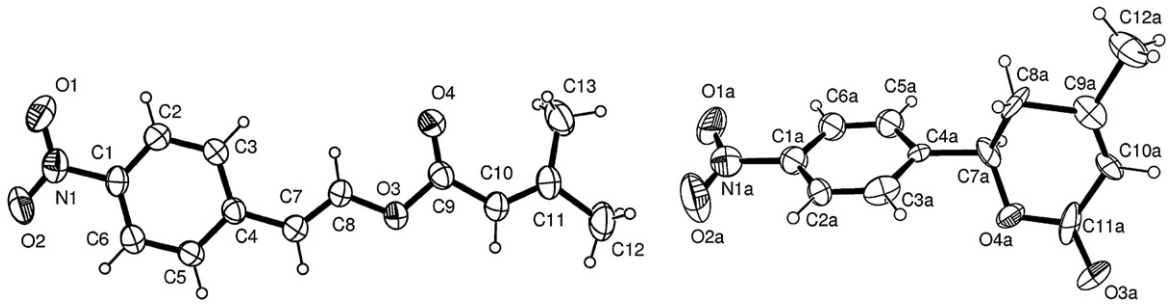


Figure 3. ORTEP diagrams of the molecular structures of **26** and **33**. Displacement ellipsoids are drawn at the 30% probability level.

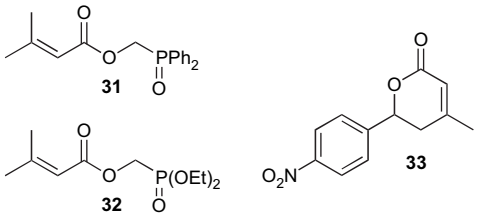
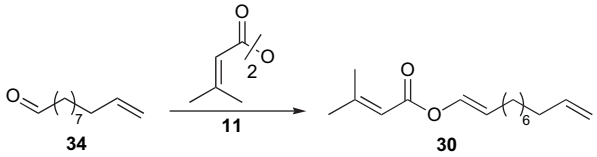


Figure 4.



Scheme 3.

instrument with a Bruker ESI source. Accurate mass measurements were carried out with external calibration using sodium formate as a reference calibrant. Microanalyses were performed by the University of Queensland Microanalytical Service. Column chromatography was undertaken on silica gel (Flash Silica gel 230–400 mesh), with distilled solvents. Anhydrous solvents were prepared according to Perin and Armarego, 'Purification of laboratory solvents', 3rd ed. Tetrahydrofuran was freshly distilled from a sodium/benzophenone still. Melting points were determined on a Fischer Johns melting point apparatus and are uncorrected. Fine chemicals were purchased from the Aldrich Chem. Co.

4.2. X-ray crystallography

Crystallographic data for structures **26** and **33** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-665996 and CCDC-665997 and can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033, or e-mail: deposit@ccdc.cam.ac.uk.

4.3. [(3-Methylbut-2-enoyloxy)methyl]triphenylphosphonium chloride 18

To a solution of (hydroxymethyl)triphenylphosphonium chloride[29] (13.8 g, 42 mmol) in anhydrous dichloromethane (10 mL) under an argon atmosphere was added 3,3-dimethylacroyl chloride (10 g, 85 mmol) dropwise. The mixture was refluxed for 16 h, cooled to room temperature and transferred by pipette to vigorously stirred diethyl ether (50 mL). A white gum formed which was isolated by decanting off the mother liquor and then re-dissolved in dichloromethane (25 mL). The trituration process was repeated with diethylether/dichloromethane until pure by ^{1}H NMR and then the product was placed under high vacuum (0.05 mmHg) for 48 h which afforded ((3-methylbut-2-enoyloxy)methyl)triphenylphosphonium chloride as white powder (15.8 g, 92%). [Note: highly hygroscopic.] ν_{max} (neat) 2913 (br), 1732 (m), 1642 (m), 1437 (s), 1114 (vs), 1073 (vs), 996 (m), 749 (vs), 724 (vs) cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.77–7.86 (9H, m), 7.64–7.72 (6H, m), 6.53 (d, 2H, J=2.8 Hz), 5.53 (1H, sept, J=1.2 Hz), 1.94 (3H, d, J=1.2 Hz), 1.82 (3H, d, J=1.2 Hz); δ_C (100 MHz, $CDCl_3$) 163.6 (d, J=4.6 Hz), 162.0, 135.6 (d, J=3 Hz), 134.2 (d, J=10 Hz), 130.5 (d, J=13 Hz), 115.9 (d, J=86 Hz), 113.2, 55.7 (d, J=65 Hz), 27.5, 20.6. HRMS (ESI): M−Cl$^+$, found 375.1498. $C_{24}H_{24}O_2P$ requires 375.1508.

4.4. General procedure for preparation of 3,3-dimethylacroyl esters (Table 1)

*2-Chlorostyryl 3-methylbut-2-enoate (**27**).* A suspension of **18** (700 mg, 1.70 mmol) in anhydrous tetrahydrofuran (25 mL) under argon was sonicated for 10 min until a uniform milky dispersion had formed. The mixture was then cooled to −78 °C and a solution of sodium hexamethyldisilazide (1.70 mL, 1.70 mmol, 1 M solution in THF) was added strictly dropwise. The reaction was stirred for 30 min, then a solution of 2-chlorobenzaldehyde (160 mg, 1.13 mmol) in anhydrous tetrahydrofuran (5 mL) was added dropwise and stirred for a further 30 min. The mixture was then poured into saturated ice-cold sodium bicarbonate (10 mL) and extracted with diethyl ether (3×15 mL). The combined organic layer was washed with brine, dried over sodium sulfate and concentrated in vacuo. The residue was purified by flash chromatography (diethyl ether/pet. spirit, 1:25) to give the title compound (**27**) as a colourless oil (80 mg, 30%) [E/Z (10:1)]. R_f (diethyl ether/pet. spirit, 1:20) 0.73; ν_{max} (neat) 1728 (s), 1636 (s), 1438 (m), 1350 (m), 1210 (s), 1122 (vs), 1050 (s), 958 (s), 844 (s), 750 (s) cm^{-1}; δ_H (300 MHz, $CDCl_3$, E isomer only) 7.89 (1H, d, J=12.7 Hz), 7.43–7.49 (1H, m), 7.30–7.37 (1H, m), 7.10–7.23 (2H, m), 6.73 (1H, d, J=12.7 Hz), 5.77 (1H, sept, J=1.2 Hz), 2.22 (3H, d, J=1.2 Hz), 1.96 (3H, d, J=1.2 Hz); δ_C (75 MHz, $CDCl_3$, E isomer only) 163.1, 160.8, 137.8, 132.9, 132.9, 129.7, 128.2, 126.9, 126.5, 114.6, 111.3, 27.7, 20.7; GC/MS (EI): m/z (%) 236 (M$^{+\bullet}$, 2), 190 (0.04), 176 (0.02), 154 (1), 125 (6), 83 (100), 63 (8), 55 (38); HRMS (ESI): MNa$^+$, found 259.0496. $C_{13}H_{13}ClO_2Na^+$ requires 259.0502.

4.4.1. Compound **22**

Colourless oil. Yield 32% [E/Z (2.4:1)]. R_f (EtOAc/pet. spirit, 1:20) 0.41; δ_H (400 MHz, C_6D_6, mixture of cis and trans isomers) 7.56 (1H, d, J=12 Hz), 7.40 (1H, dd, J=6.4, 0.8 Hz), 6.20 (1H, dd, J=12, 11 Hz), 5.70 (1H, sept, J=1.2 Hz), 5.62 (1H, sept, J=1.2 Hz), 5.43 (1H, dd, J=10, 6.4 Hz), 4.87 (1H, br d, J=12 Hz), 4.86 (1H, br d, J=12 Hz), 3.85 (1H, br d, J=12 Hz), 3.82 (1H, br d, J=11.6 Hz), 3.13–3.19 (1H, m), 3.01–3.08 (1H, m), 2.74 (1H, br s), 2.71 (1H, br s), 2.39 (1H, dt, J=14, 3.2 Hz), 2.30 (1H, dt, J=14, 3.2 Hz), 2.23 (1H, dt, J=10.8, 4.0 Hz), 2.04 (3H, d, J=1.2 Hz), 2.03 (3H, d, J=1.2 Hz), 1.86–1.94 (1H, m), 1.69–1.81 (2H, m), 1.37 (3H, d, J=1.6 Hz), 1.36 (3H, d, J=1.6 Hz), 1.25 (3H, s), 1.13 (3H, s), 1.15 (3H, d, J=3.2 Hz), 1.10 (3H, s), 0.93 (18H, s), 0.83 (3H, s), 0.72–1.03 (15H, m), 0.12 (3H, s), 0.06 (3H, s), 0.05 (3H, s), 0.02 (3H, s); δ_C (100 MHz, C_6D_6, mixture of cis and trans isomers) 163.4, 162.9, 159.3, 158.7, 144.3, 144.1, 136.2, 134.3, 116.0, 115.6, 115.5, 115.3, 115.2, 73.6, 73.5, 61.0, 48.6, 47.4, 47.3, 44.9, 41.3, 40.9, 38.0, 37.6, 37.2, 36.9, 36.4, 36.1, 35.0, 34.1, 34.0, 27.8, 27.7, 27.0, 25.9, 23.6, 22.2, 21.7, 20.3, 20.2, 18.3, 18.2, −3.6, −3.9, −4.1; GC/MS (EI): m/z (%) 474 (M$^{+\bullet}$, 3) 459 (0.2), 417 (1), 391 (10), 363 (3), 317 (3), 238 (4), 181 (4), 157 (11), 83 (100), 73 (37), 55 (17).

4.4.2. Compound **23**

Colourless oil. Yield 21% [E/Z (3.4:1)]. R_f (EtOAc/pet. spirit, 1:10) 0.33; δ_H (400 MHz, C_6D_6, mixture of cis and trans isomers) 7.49 (1H, d, J=12 Hz), 7.38 (1H, dd, J=6.4, 0.8 Hz), 5.76 (1H, dd, J=12, 11 Hz), 5.67 (1H, sept, J=1.2 Hz), 5.66 (1H, sept, J=1.2 Hz), 4.96 (1H, dd, J=11, 6.4 Hz), 4.35 (1H, d, J=12 Hz), 3.32 (1H, dd, J=12, 4 Hz), 3.27 (1H, dd, J=12, 3.6 Hz), 2.98–3.05 (1H, m), 2.56 (1H, dd, J=12, 6 Hz), 2.48 (1H, dd, J=12, 6.8 Hz), 2.32 (1H, dd, J=13, 6 Hz), 2.21 (1H, dd, J=12, 4.8 Hz), 2.06 (3H, d, J=1.6 Hz), 2.04 (3H, d, J=1.6 Hz), 2.01–2.10 (3H, m), 1.93–2.00 (2H, m), 1.62–1.80 (6H, m), 1.55–1.59 (1H, m), 1.381 (3H, s), 1.378 (3H, s), 1.14–1.29 (4H, m), 1.10 (3H, s), 1.06 (6H, s), 1.05 (3H, s), 1.00 (3H, s), 0.77 (3H, s), 0.56–0.76 (4H, m); δ_C (100 MHz, C_6D_6, mixture of cis and trans isomers) 209.8, 209.6, 163.4, 162.9, 159.6, 159.2, 135.9, 134.2, 115.4, 115.2, 115.0, 114.0, 72.8, 72.7, 60.1, 59.7, 50.9, 50.7, 48.0, 47.4, 43.7, 43.5, 43.4, 43.3, 42.4, 39.9, 35.8, 35.1, 34.9, 34.8, 30.4, 30.3, 28.1, 27.0, 23.5, 23.3, 21.5, 21.0, 20.3;

GC/MS (EI): *m*/*z* (%) 360 ($M^{+\bullet}$,0.1), 345 (0.1), 277 (1), 260 (1), 135 (1), 83 (100), 55 (19); HRMS (ESI): MNa^+, found 383.2203. $C_{22}H_{32}NaO_4$ requires 383.2198.

4.4.3. 4-(Dimethylamino)styryl 3-methylbut-2-enoate **24**

Grey powder, mp 55–60 °C. Yield 26% [*E*/*Z* (1.5:1)]. R_f (diethyl ether/pet. spirit, 1:20) 0.28; δ_H (400 MHz, C_6D_6, cis isomer) 7.65–7.72 (2H, m), 7.59 (1H, d, *J*=6.6 Hz), 6.58–6.63 (2H, m), 5.76 (1H, sept, *J*=1.2 Hz), 5.59 (1H, d, *J*=6.6 Hz), 2.5 (6H, s), 2.06 (3H, d, *J*=1.2 Hz), 1.39 (3H, d, *J*=1.2 Hz); δ_H (400 MHz, C_6D_6, trans isomer) 8.27 (1H, d, *J*=12.8 Hz), 7.15–7.20 (2H, m), 6.56 (1H, d, *J*=12.8 Hz), 6.43–6.48 (2H, m), 5.70 (1H, sept, *J*=1.2 Hz), 2.47 (6H, s), 2.08 (3H, d, *J*=1.2 Hz), 1.4 (3H, d, *J*=1.2 Hz); δ_C (100 MHz, C_6D_6, mixture of cis and trans isomers) 163.4, 162.8, 159.4, 158.9, 150.1, 149.8, 134.1, 131.7, 130.7, 127.5, 123.8, 123.1, 115.5, 115.5, 115.4, 113.0, 112.5, 112.2, 40.1, 40.0, 27.1, 27.0, 20.3, 20.3; GC/MS (EI): *m*/*z* (%) 245 ($M^{+\bullet}$, 6), 187 (0.6), 163 (33), 134 (47), 118 (21), 83 (91), 55 (100), 51 (26); HRMS (ESI): MNa^+, found 246.1475. $C_{15}H_{20}NO_2$ requires 246.1494.

4.4.4. Styryl 3-methylbut-2-enoate **25**

Colourless oil. Yield 20% [*E*/*Z* (1.5:1)]. R_f (diethyl ether/pet. spirit, 1:20) 0.44; ν_{max} (neat) 1730 (s), 1642 (s), 1440 (m), 1217 (s), 1122 (vs), 1073 (s), 932 (m), 844 (m), 692 (m) cm^{-1}; δ_H (400 MHz, C_6D_6, mixture of cis and trans isomers) 8.40 (1H, d, *J*=12.9 Hz), 7.57 (1H, d, *J*=7.3 Hz), 7.16–7.23 (2H, m), 6.95–7.10 (6H, m), 6.41 (1H, d, *J*=12.9 Hz), 5.65 (1H, sept, *J*=1.3 Hz), 5.63 (1H, sept, *J*=1.2 Hz), 5.47 (1H, d, *J*=7.3 Hz), 2.05 (3H, d, *J*=1.2 Hz), 2.02 (3H, d, *J*=1.3 Hz), 1.38 (3H, d, *J*=1.2 Hz), 1.33 (3H, d, *J*=1.3 Hz); δ_C (100 MHz, C_6D_6, mixture of cis and trans isomers) 163.0, 162.5, 160.4, 159.9, 136.8, 135.2, 135.0, 134.4, 129.6, 128.9, 128.6, 128.1, 127.9, 127.2, 126.5, 115.0, 111.6, 27.0, 26.9, 20.3, 20.3; GC/MS (EI): *m*/*z* (%) 202 ($M^{+\bullet}$, 0.1), 187 (0.03), 177 (0.03), 156 (0.1), 120 (1), 102 (0.5), 91 (7), 83 (100), 55 (33); HRMS (ESI): MNa^+, found 225.0886. $C_{13}H_{14}NaO_2$ requires 225.0891.

4.4.5. 4-Nitrostyryl 3-methylbut-2-enoate **26**

Pale yellow solid, mp 79–82 °C. Yield 41% [*E*/*Z* (1.5:1)]. [Found: C, 63.33; H, 5.36; N, 5.63. $C_{13}H_{13}NO_4$ requires C, 63.15; H, 5.30; N 5.67%.] R_f (diethyl ether/pet. spirit, 1:20) 0.35; ν_{max} (neat) 1735 (s), 1633 (s), 1597 (s), 1517 (s), 1342 (vs), 1214 (s), 1121 (vs), 1050 (m), 952 (s), 925 (vs), 861 (vs), 747 (s), 688 (s) cm^{-1}; δ_H (300 MHz, C_6D_6, trans isomer) 8.13–8.19 (2H, m), 8.08 (1H, d, *J*=12.9 Hz), 7.42–7.47 (2H, m), 6.40 (1H, d, *J*=12.9 Hz), 5.75–5.78 (1H, m), 2.24 (3H, d, *J*=1.3 Hz), 1.98 (3H, d, *J*=1.3 Hz,); δ_H (300 MHz, $CDCl_3$, cis isomer) 8.16–8.21 (2H, m), 7.70–7.75 (2H, m), 7.3 (1H, d, *J*=7.3 Hz), 5.85–5.87 (1H, m), 5.74 (1H, d, *J*=7.3 Hz), 2.26 (3H, d, *J*=1.3 Hz), 2.02 (3H, d, *J*=1.3 Hz); δ_C (125 MHz, C_6D_6, mixture of cis and trans isomers) 162.6, 162.2, 161.8, 161.7, 146.9, 146.6, 141.2, 140.9, 139.6, 137.0, 129.5, 126.3, 124.0, 123.7, 114.5, 114.3, 112.9, 109.3, 27.1, 27.1, 20.5, 20.5; GC/MS (EI): *m*/*z* (%) 247 ($M^{+\bullet}$, 1), 217 (0.2), 204 (0.03), 171 (0.03), 118 (4), 89 (20), 83 (100), 55 (65); HRMS (ESI): MNa^+, found 270.0737. $C_{13}H_{13}NNaO_4$ requires 270.0742.

4.4.6. 2-(Furan-2-yl)vinyl 3-methylbut-2-enoate **28**

Colourless oil. Yield 29% [*E*/*Z* (3.5:1)]. δ_H (400 MHz, C_6D_6, trans isomer) 8.36 (1H, d, *J*=12.7 Hz), 6.92–6.93 (1H, m), 6.22 (1H, d, *J*=12.6 Hz), 6.01 (1H, dd, *J*=3.3, 1.9 Hz), 5.87–5.88 (1H, m), 5.58 (1H, sept, *J*=1.3 Hz), 1.99 (3H, d, *J*=1.3 Hz), 1.35 (3H, d, *J*=1.3 Hz); δ_H (400 MHz, C_6D_6, cis isomer) 7.40–7.42 (1H, d, *J*=7.1 Hz), 7.07–7.08 (1H, m), 6.70–6.71 (1H, m), 6.20 (1H, ddd, *J*=3.4, 1.8, 0.6 Hz), 5.64 (1H, sept, *J*=1.3 Hz), 5.62–5.64 (1H, m), 2.01 (3H, d, *J*=1.3 Hz), 1.36 (3H, d, *J*=1.3 Hz); δ_C (100 MHz, C_6D_6, mixture of cis and trans isomers) 162.7, 162.2, 160.6, 160.0, 150.3, 141.8, 141.4, 136.4, 132.9, 114.9, 114.8, 111.8, 111.3, 110.4, 107.8, 104.4, 101.7, 27.3, 27.0, 20.3, 20.3; GC/MS (EI): *m*/*z* (%) 208 ($M^{+\bullet}$, 2), 180 (0.04), 166 (0.1), 149 (0.02), 108 (1), 83 (100), 55 (30).

4.4.7. 2-(Thiophen-3-yl)vinyl 3-methylbut-2-enoate **29**

Colourless oil. Yield 25% [*E*/*Z* (1.7:1)]. R_f (diethyl ether/pet. spirit, 1:20) 0.39; ν_{max} (neat) 1721 (s), 1691 (m), 1642 (s), 1350 (m), 1219 (s), 1127 (vs), 1074 (s), 844 (s), 640 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$, trans isomer) 7.83 (1H, dd, *J*=12.8, 0.3 Hz), 7.27 (1H, ddd, *J*=5.1, 2.9, 0.6 Hz), 7.14 (1H, ddd, *J*=5.1, 1.3, 0.4 Hz), 7.08–7.09 (1H, m), 6.39 (1H, ddd, *J*=12.7, 1.1, 0.6 Hz), 5.73–5.75 (1H, m), 2.21 (3H, d, *J*=1.3 Hz), 1.94 (3H, d, *J*=1.3 Hz); δ_C (100 MHz, $CDCl_3$, trans isomer) 163.2, 160.2, 136.3, 135.9, 126.2, 124.7, 121.3, 114.7, 109.4, 27.6, 20.6; δ_H (400 MHz, $CDCl_3$, cis isomer) 7.46–7.47 (1H, m), 7.37 (1H, dd, *J*=5.0, 1.2 Hz), 7.33 (1H, dd, *J*=7.0, 0.3 Hz), 7.27 (1H, ddd, *J*=5.1, 3.0, 0.5 Hz), 5.87–5.89 (1H, m), 5.81 (1H, ddd, *J*=7.0, 0.9, 0.5 Hz), 2.27 (3H, d, *J*=1.3 Hz), 2.01 (3H, d, *J*=1.3 Hz); δ_C (100 MHz, $CDCl_3$, cis isomer) 162.62, 160.9, 135.2, 133.0, 128.5, 125.0, 123.8, 114.6, 106.0, 27.6, 0.6; GC/MS (EI): *m*/*z* (%) 208 ($M^{+\bullet}$, 4), 177 (0.03), 147 (0.1), 125 (0.3), 97 (11), 83 (100), 55 (40); HRMS (ESI): MNa^+, found 231.0450. $C_{11}H_{12}NaO_2S$ requires 231.0456.

4.4.8. Undeca-1,10-dienyl 3-methylbut-2-enoate **30**

Colourless oil. Yield 30% [*E*/*Z* (1.3:1)]. R_f (diethyl ether/pet. spirit, 1:20) 0.31; ν_{max} (neat) 1776 (m), 1717 (m), 1635 (m), 1443 (m), 1379 (m), 1205 (m), 1092 (m), 1022 (vs), 940 (s), 896 (m), 841 (m) cm^{-1}; δ_H (400 MHz, $CDCl_3$, trans isomer) 7.10 (1H, dt, *J*=12.4, 1.5 Hz), 5.79 (1H, ddt, *J*=16.9, 10.2, 6.7 Hz), 5.66–5.68 (1H, m), 5.38 (1H, dt, *J*=12.3, 7.6 Hz), 4.94–5.00 (2H, m), 4.89–4.92 (1H, m), 2.17 (3H, d, *J*=1.3 Hz), 1.95–2.05 (4H, m), 1.90 (3H, d, *J*=1.3 Hz), 1.23–1.39 (10H, m); δ_H (400 MHz, $CDCl_3$, cis isomer) 7.05 (1H, dt, *J*=6.4, 1.5 Hz), 5.79 (1H, ddt, *J*=16.9, 10.2, 6.7 Hz), 5.71–5.73 (1H, m), 4.83 (1H, td, *J*=7.5, 6.5 Hz), 2.18 (3H, m), 2.09–2.15 (2H, m), 1.95–2.05 (2H, m), 1.92 (3H, m), 1.23–1.39 (10H, m); δ_C (100 MHz, $CDCl_3$, mixture of cis and trans isomers) 163.6, 163.5, 159.0, 159.0, 139.2, 135.2, 133.8, 115.2, 115.1, 114.5, 114.1, 114.1, 113.8, 33.8, 29.6, 29.3, 29.2, 29.2, 29.1, 29.1, 29.0, 29.0, 28.9, 28.9, 27.5, 27.4, 24.5, 20.5, 20.4; GC/MS (EI): *m*/*z* (%) 250 ($M^{+\bullet}$, 0.1), 235 (0.01), 222 (0.2), 207 (0.02), 83 (100), 67 (6), 55 (54), 41 (33); HRMS (EI): M^+, found 250.1931. $C_{16}H_{26}O_2$ requires 250.1933.

4.5. (Diphenylphosphoryl)methyl 3-methylbut-2-enoate 31

To a solution of dicyclohexylcarbodiimide (1.7 g, 8.14 mmol), 3,3-dimethylacrylic acid (814 mg, 8.14 mmol) and (diphenylphosphoryl)methanol[30] (1.73 g, 7.40 mmol), in dichloromethane (20 mL) at 0 °C was added 4-dimethylaminopyridine (100 mg, 0.81 mmol) and the reaction mixture was stirred for 2 h. The reaction was warmed to room temperature overnight, filtered through a plug of Celite, concentrated in vacuo and purified by flash chromatography (EtOAc/DCM, 1:1) affording (diphenylphosphoryl)methyl 3-methylbut-2-enoate (**31**) (606 mg, 26%) as colourless needles, mp 85–88 °C. R_f (EtOAc/dichloromethane, 1:1) 0.71; ν_{max} (neat) 2970 (br), 1747 (m), 1725 (s), 1650 (m), 1438 (s), 1186 (vs), 1132 (vs), 1077 (vs), 848 (s), 718 (vs), 693 (vs) cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.72–7.82 (4H, m), 7.40–7.60 (6H, m), 5.61 (1H, sept, *J*=1.3 Hz), 4.85 (2H, d, *J*=5.3 Hz), 2.05 (3H, d, *J*=1.3 Hz), 1.84 (3H, d, *J*=1.3 Hz); δ_C (125 MHz, $CDCl_3$) 165.2 (d, *J*=7.8 Hz), 159.3, 132.3–132.4 (m), 131.2–131.5 (m), 130.3 (d, *J*=101.8 Hz), 128.5–128.9 (m), 114.6, 59.9 (d, *J*=86.8 Hz), 27.4, 20.3; HRMS (ESI): MNa^+, found 337.0964. $C_{18}H_{19}NaO_3P$ requires 337.0970.

4.6. (Diethoxyphosphoryl)methyl 3-methylbut-2-enoate 32

(Diethoxyphosphoryl)methyl 3-methylbut-2-enoate (**32**) (58%, colourless oil) was synthesised from diethyl hydroxymethylphosphonate[31] following the analogous procedure for that of **31**. R_f (dichloromethane) 0.43; ν_{max} (neat) 2984 (br), 1724 (m), 1650 (m), 1221 (m), 1140 (s), 1019 (vs), 962 (s), 845 (m) cm^{-1}; δ_H (300 MHz, $CDCl_3$) 5.72 (1H, sept, *J*=1.3 Hz), 4.36 (2H, d, *J*=8.6 Hz), 4.15 (4H, dq, *J*=8.0, 7.1 Hz), 2.15 (3H, d, *J*=1.3 Hz), 1.89 (3H, d, *J*=1.3 Hz), 1.31 (6H, dt, *J*=7.0, 0.4 Hz); δ_C (75 MHz, $CDCl_3$) 164.9 (d, *J*=8.6 Hz); 158.6, 114.4,

62.4 (d, J=6.2 Hz), 55.5 (d, J=169 Hz), 27.2, 20.1, 16.1 (d, J=5.8 Hz); HRMS (ESI): MH^+, found 251.1043. $C_{10}H_{20}O_5P$ requires 251.1048.

4.7. 4-Methyl-6-(4-nitrophenyl)-5,6-dihydro-2*H*-pyran-2-one 33

To a solution of (diphenylphosphoryl)methyl 3-methylbut-2-enoate (**31**) (880 mg, 2.82 mmol) in anhydrous tetrahydrofuran (25 mL) at −78 °C was added a solution of sodium hexamethyldisilazide (2.96 mL, 2.96 mmol, 1 M solution in THF) strictly dropwise. The reaction was stirred for 30 min, then a solution of 4-nitrobenzaldehyde (430 mg, 2.82 mmol) in anhydrous tetrahydrofuran (5 mL) was added dropwise and stirred for a further 30 min. The mixture was then poured onto saturated ice-cold sodium bicarbonate (10 mL) and extracted with diethyl ether (3×15 mL). The combined organic layer was washed with brine, dried over sodium sulfate and concentrated in vacuo. The residue was purified by flash chromatography (dichloromethane) to give the title compound **33** (280 mg, 45%) as pale yellow needles (mp 112–114 °C). 4-Methyl-6-(4-nitrophenyl)-5,6-dihydro-2*H*-pyran-2-one **33** was also obtained in 36% yield from reaction with **32**. [Found C, 61.73; H, 4.77; N, 5.88. $C_{12}H_{11}NO_4$ requires C, 61.80; H, 4.75; N 6.01%.] R_f (EtOAc/pet. spirit, 1:1) 0.54; ν_{max} (neat) 1711 (vs), 1602 (m), 1511 (vs), 1347 (vs), 1234 (vs), 1083 (s), 1048 (s), 851 (s), 748 (s), 694 (s) cm^{-1}; δ_H (300 MHz, $CDCl_3$) 8.17–8.22 (2H, m), 7.54–7.59 (2H, m), 5.87–5.90 (1H, m), 5.50 (1H, dd. J=11.1, 5.0 Hz), 2.46–2.65 (2H, m), 2.01–2.02 (3H, m); δ_C (75 MHz, $CDCl_3$) 163.8, 156.8, 147.7, 145.6, 126.7, 123.8, 116.6, 77.1, 36.5, 22.8; GC/MS (EI): m/z (%) 233 ($M^{+\bullet}$, 0.1), 217 (0.1), 208 (0.02), 203 (0.1), 150 (2), 115 (3), 82 (100), 77 (11), 54 (25); HRMS (ESI): MNa^+, found 256.0580. $C_{12}H_{11}NNaO_4$ requires 256.0586.

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Supplementary data

Copies of ^1H and ^{13}C NMR spectra. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.04.068.

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