Supporting Information

Experimental Procedures and Characterisation Data for all Products and Substrates

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Palladium-Catalysed Atom-Economical Synthesis of Conjugated Dienals from Terminal Acetylenes and Acrolein

Zoë Hearne and Chao-Jun Li

Department of Chemistry, McGill University, Montréal, Canada.

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1 General Methods

^{1}H, ^{13}C NMR spectra were recorded at ambient temperature on Bruker AVIIIHD 500 (^{1}H 500 MHz, ^{13}C 125 MHz), Bruker AVIIIHD 400 (^{1}H 400 MHz, ^{13}C 100 MHz) and Varian Mercury (^{1}H 400 MHz, ^{13}C 100 MHz) spectrometers at 298 K. ^{1}H spectra are referenced to the resonance from residual $CHCl_3$ at 7.26 ppm, and ^{13}C spectra to the central peak in the signal from $CDCl_3$, at 77.16 ppm.[1] The appearance and multiplicities of ^{1}H NMR resonances are expressed by the abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), qn (quintet), m (multiplet), br (broad), coin (coincidental), app (apparent), arom (aromatic) and combinations thereof for more highly coupled systems. ^{1}H NMR signals are described by chemical shift δ (integration, multiplicity, | J (Hz) |, assignment). ^{13}C NMR signals are described by chemical shift δ

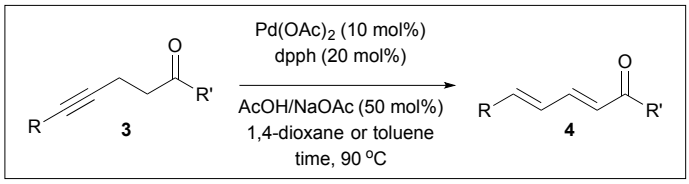
(assignment) and are singlets unless otherwise specified. Assignments are supported by 2D data including ^{1}H-^{1}H COSY and ^{1}H-^{13}C HSQC, and selective 1D experiments including selective TOCSY-1D (^{1}H) and selective NOESY-1D (^{1}H) where appropriate. HRMS was obtained by positive and negative ESI, or positive APCI on a Bruker Maxis Impact QTOF, or a Thermo Scientific Orbitrap Exactive Plus. The results are reported as mass/charge ratios (*m/z*). IR spectra were recorded on a Vertex 70 Bruker Platinum ATR with solid or neat liquid samples.

The melting point was measured using a Gallencamp electronic melting point apparatus. Thin layer chromatography was run on thin layer chromatography (TLC) Silica gel 60 F_{250} glass plates, and then viewed under Ultra-violet light (UV, 254 nm) and/or by developing in potassium permanganate ($KMnO_4$), vanillin or 2,4-dinitrophenylhydrazine (2,4-DNP) dip. Flash column chromatographic product purification was achieved manually by forced-flow chromatography on silica gel (230 – 400 mesh) using the eluent system described for each separation, or by using a Biotage Isolera One automated flash purification system with Biotage Zip® KP-Sil 45 g columns and the eluent system specified. All solvents were obtained in a flame-dried vessel from a PureSolv MD 7 solvent purification system on the day of use, and degassed by bubbling with argon for one hour. Compounds are named according to IUPAC conventions. The number systems presented in the following structures are for the benefit of NMR data and may not reflect the IUPAC nomenclature. Glassware used for the reaction was prepared by washing with aqua regia, rinsing thoroughly with water and acetone, and storing in a drying oven (110 °C) for at least 24 hrs prior to use. All glassware was flame-dried before using in reactions. All reagents were obtained commercially from Sigma-Aldrich and used directly unless otherwise noted.

Diffraction measurements were made on a Bruker D8 APEX2 X-ray diffractometer instrument using graphite-monochromated MoK_α (λ = 0.71073 Å) radiation. The X-ray diffraction data sets were collected using the ω and f scan mode over the 2ϑ range up to 54°. The structures were solved by direct methods implemented in SHELXS and refined using SHELXL.[2] Structure refinement was performed on F^2 using all data. Hydrogen atoms on carbon centres were modelled with appropriate riding-hydrogen models. Hydrogen atoms participating in hydrogen bonds were located from the electron density map whenever data quality was sufficient. Otherwise, they were fixed to appropriate distances and refined from the electron density map. Calculations were performed and the drawings were prepared using the WINGX[3] suite of crystallographic programs. The compound (2*E*,4*E*)-5-(pyridine-3-yl)penta-2,4-dienal (**4h**) crystalizes in space group $P2_1/c$. Structure has been deposited with the Cambridge Structural Database, deposition code CCDC 1527924.

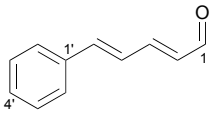
2 Catalytic Isomerisation of 4-Alkynals, 4-Alkynones and 4-Alkynoates

2.1 *General Procedure for the Palladium-Catalyzed Isomerizaton of Alkynes*



To a flame-dried 10 mL microwave vial containing a stir bar was added $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 10 mol%), dpph (18.2 mg, 0.04 mmol, 20 mol%) and NaOAc (8.2 mg, 50 mol%, 0.1 mmol). The vial was sealed with a rubber septa, evacuated under high vacuum (10 minutes), and back-filled with argon; this process was repeated two more times. To this was added 1,4-dioxane or toluene solvent (1 mL), glacial acetic acid (5.7 µL, 50 mol%, 0.1 mmol) and the alkyne substrate (**3**, 0.2 mmol). The microwave vial was clamp-sealed under positive argon pressure with an aluminium cap fitted with a septa and heated to 90 °C until the reaction reached completion, as judged by TLC. The solvent was removed *in vacuo* and the product (**4**) was purified using flash column chromatography.

2.1 *Data for Dienal, Dienone and Dienoate products, **4a – 4o***



(2E,4E)-5-phenylpenta-2,4-dienal [13466-40-5] (**4a**) was synthesised according to general procedure ***2.1*** from 5-phenylpent-4-ynal (**3a**, 31.6 mg, 0.2 mmol) by stirring in 1,4 dioxane solvent for 16 hours. The crude product was purified by flash column chromatography (silica, 15% EtOAC/hexanes) to yield the title compound as an orange solid (28.8 mg, 91%).

Large scale reaction: **4a** was synthesised from **3a** (800.0 mg, 5.1 mmol) by stirring in 1,4-dioxane solvent for 15 hours at 95 °C. The crude product was purified using flash column chromatography (silica, 15% EtOAC/hexanes) to yield the title compound (556.7 mg, 69%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.63 (d, *J* = 8.1 Hz, 1H, C^1(O)H), 7.53 – 7.50 (m, 2H, arom), 7.43 – 7.35 (m, 3H, arom), 7.26 (ddd, *J* = 15.2, 8.2, 2.1 Hz, 1H, C^3-H), 7.05 – 6.97 (m, 2H, C^4-H & C^5-H), 6.28 (dd, *J* = 15.2, 8.1 Hz, 1H, C^2-H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 193.7 (C^1), 152.1 (C^3), 142.6 (C^5), 135.7 (arom), 131.8 (C^2), 129.8 (arom), 129.1 (arom), 127.7 (arom), 126.4 (C^4). Spectral assignments agreed with the literature.[4]

HRESI-MS found 159.08051 [calc. for $C_{11}H_{11}O$ $[M+H]^+$ 159.08044]

IR 2823.56, 2751.62, 1664.23, 1616.82 cm^{-1}

TLC R_f = 0.50 (1:5 EtOAc/hexanes), visible as a bright orange spot with 2,4-DNP dip

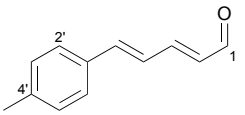
m.p. 37 – 39 °C

(2Z,4E)-5-phenylpenta-2,4-dienal [121077-51-8]

1D ^{1}H TOCSY (400 MHz, $CDCl_3$, irradiation of aldehyde peak at 10.29 ppm, corresponds to the (2*Z*,4*E*)-minor isomer olefinic peaks) δ 10.29 (d, *J* = 7.5 Hz, 1H, C^1(O)H), 7.76 (ddd, *J* = 15.3, 11.8, 1.1 Hz, 1H, C^4-H), 7.09 (ddd, *J* = 11.8, 11.0, 0.8 Hz, 1H, C^3-H), 6.26 (d, *J* = 15.3 Hz, 1H, C^5-H), 5.95 (dd, *J* = 11.0, 7.5 Hz, 1H, C^2-H). Spectral assignments agreed with the literature.[5]

(2E,4Z)-5-phenylpenta-2,4-dienal [121077-50-7]

1D ^{1}H TOCSY (400 MHz, $CDCl_3$, irradiation of aldehyde peak at 9.60 ppm, corresponds to the (2*E*,4*Z*)-minor isomer olefinic peaks) δ 9.60 (d, *J* = 8.0 Hz, 1H, C^1(O)H), 7.61 (ddd, *J* = 15.3, 11.6, 1.1 Hz, 1H, C^3-H), 6.97 (d, *J* = 11.3 Hz, 1H, C^5-H), 6.51 (dd, *J* = 11.6, 11.3 Hz, 1H, C^4-H), 6.29 (dd, *J* = 15.3, 8.0 Hz, 1H, C^2-H).



(2E,4E)-5-(p-tolyl)penta-2,4-dienal [106485-22-7] (**4b**) was synthesised according to general procedure ***2.1*** from 5-(*p*-tolyl)pent-4-ynal (**3b**, 34.4 mg, 0.2 mmol) by stirring in 1,4-dioxane solvent for 16 hours. The crude product was purified by flash column chromatography (silica, 10 – 15% EtOAC/hexanes) to yield the title compound as an orange solid (26.8 mg, 78%).

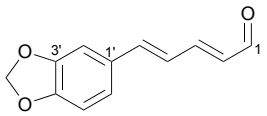
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.61 (d, *J* = 8.0 Hz, 1H, C^1(O)H), 7.40 (d, *J* = 8.0 Hz, 2H, $C^{2'}$-H), 7.26 (dd, *J* = 15.3, 9.3 Hz, 1H, C^3-H), 7.19 (d, *J* = 8.0 Hz, 2H, $C^{3'}$-H), 7.02 – 6.93 (m, 2H, C^4-H & C^5-H), 6.25 (dd, *J* = 15.3, 8.0 Hz, 1H, C^2-H), 2.38 (s, 3H, $C^{4'}$-C**H**$_3$). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.7 (C^1), 152.5 (C^3), 142.7 (C^5), 140.2 ($C^{4'}$), 133.0 ($C^{1'}$), 131.3 (C^2), 129.8 ($C^{3'}$), 127.7 ($C^{2'}$), 125.4 (C^4), 21.6 ($C^{4'}$-**C**H$_3$). Spectral assignments agreed with the literature.[4]

HRAPCI-MS found 173.09639 [calc. for $C_{12}H_{13}O$ $[M+H]^+$ 173.09609]

IR 2922.51, 2847.96, 1654.23, 1615.51 cm^{-1}

TLC R_f = 0.46 (1:5 EtOAc/hexanes), visible as a bright orange spot with 2,4-DNP dip

m.p. 97 – 99 °C



(2E,4E)-5-(benzo[d][1,3]dioxol-5-yl)penta-2,4-dienal [83047-59-0] (**4c**) was synthesised according to general procedure ***2.1*** from 5-(benzo[d][1,3]dioxol-5-yl)pent-4-ynal (**3c**, 40.4 mg, 0.2 mmol) by stirring in 1,4-dioxane solvent for 14 hours. The crude product was purified by flash column chromatography (10 – 30% EtOAc/hexanes) to yield the title compound as an orange solid (24.2 mg, 60%).

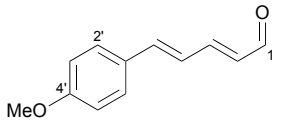
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.60 (d, *J* = 8.0 Hz, 1H, C^1(O)H), 7.24 (dd, *J* = 15.2, 10.7 Hz, 1H, C^3-H) 7.03 (d, *J* = 1.7 Hz, 1H, $C^{2'}$-H), 6.96 (dd, *J* = 8.3, 1.3 Hz, 1H, $C^{6'}$-H), 6.93 (d, *J* = 15.5 Hz, 1H, C^5-H), 6.86 – 6.81 (m, 2H, $C^{5'}$-H & C^4-H), 6.23 (dd, *J* = 15.2, 8.0 Hz, C^2-H), 6.01 (s, 2H, $C^{3'}$-O**C**$_2$O-$C^{4'}$). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.7, 152.5, 149.3, 148.6, 142.3, 131.1, 130.3, 124.6, 123.8, 108.8, 106.2, 101.7.

HRAPCI-MS found 203.07023 [calc. for $C_{12}H_{11}O_3$ $[M+H]^+$ 203.07027]

IR 2918.02, 2797.72, 1661.36, 1613.59, 1594.94 cm^{-1}

TLC R_f = 0.33 (1:5 EtOAc/hexanes), visible under UV and as a bright orange spot with 2,4-DNP dip

m.p. 98 – 100 °C



(2E,4E)-5-(4-methoxyphenyl)penta-2,4-dienal [49678-07-1] (**4d**) was synthesised according to general procedure ***2.1*** from 5-(4-methoxyphenyl)pent-4-ynal (**3d**, 37.6 mg, 0.2 mmol) by stirring in 1,4-dioxane solvent for 16 hours. The crude product was purified by flash column chromatography (silica, 10 – 30% EtOAC/hexanes) to yield the title compound as an orange solid (19.4 mg, 52%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.59 (d, *J* = 8.0 Hz, 1H, C^1(O)H), 7.45 (d, *J* = 8.9 Hz, 2H, $C^{2'}$-H), 7.25 (dd, *J* = 15.2, 10.7 Hz, 1H, C^3-H), 6.91 (d, *J* = 8.9 Hz, 2H, $C^{3'}$-H), 6.99 – 6.85 (m, 2H, C^4-H & C^5-H), 6.23 (dd, *J* = 15.2, 8.0 Hz, 1H, C^2-H), 3.84 (s, 3H, $C^{4'}$-OC**H**$_3$). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.7 (C^1), 161.1 ($C^{4'}$), 152.8 (C^3), 142.4 (C^4 or C^5), 130.7 (C^2), 129.3 ($C^{2'}$), 128.6 ($C^{1'}$), 124.2 (C^4 or C^5), 114.6 ($C^{3'}$), 55.5 ($C^{4'}$-O**C**H$_3$). Spectral assignments agreed with the literature.[4]

HRESI-MS found 189.09130 [calc. for $C_{12}H_{13}O_2$ $[M+H]^+$ 189.09101]

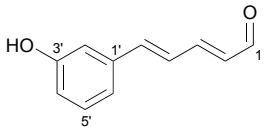
IR 2969.46, 2844.81, 1661.31, 1619.07 cm^{-1}

TLC R_f = 0.29 (1:5 EtOAc/hexanes), visible as a bright orange spot with 2,4-DNP dip

m.p. 72 – 74 °C

(2Z,4E)-5-(4-methoxyphenyl)penta-2,4-dienal [121077-53-0]

1D ^{1}H TOCSY (500 MHz, $CDCl_3$, irradiation of aldehyde peak at 10.25 ppm, corresponds to the (2*Z*,4*E*)-minor isomer olefinic peaks) δ 10.25 (d, *J* = 7.6 Hz, 1H, C^1(O)H), 7.63 (ddd, *J* = 15.3, 11.9, 1.0 Hz, 1H, C^4-H), 7.05 (dd, *J* = 11.9, 11.0 Hz, 1H, C^3-H), 6.86 (d, *J* = 15.3 Hz, 1H, C^5-H), 5.88 (dd, *J* = 11.0, 7.6 Hz, 1H, C^2-H).



(2E,4E)-5-(3-hydroxyphenyl)penta-2,4-dienal [1456621-63-8] (**4e**) was synthesised according to general procedure ***2.1*** from 5-(3-hydroxyphenyl)pent-4-ynal (**3e**, 34.8 mg, 0.2 mmol) by stirring in 1,4-dioxane solvent for 16 hours. The crude product was purified by flash column chromatography (silica, 20 – 30% EtOAC/hexanes) to yield the title compound as a yellow solid (15.3 mg, 44%).

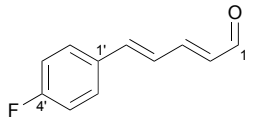
^{1}H NMR (500 MHz, $(CD_3)_2CO$) δ 9.63 (d, *J* = 7.9 Hz, 1H, C^1(O)H), 8.54 (br s, 1H, $C^{3'}$-O**H**), 7.45 (dd, *J* = 15.1 10.0 Hz, 1H, C^3-H), 7.25 – 7.07 (m, 5H), 6.86 (ddd, *J* = 8.1, 2.5, 0.9 Hz, 1H), 6.26 (dd, *J* = 15.1, 7.9 Hz, 1H, C^2-H). **^{13}C NMR** (125 MHz, $(CD_3)_2CO$) δ 194.0 (C^1), 158.9 ($C^{3'}$), 153.0 (C^3), 143.1, 138.5 ($C^{1'}$), 132.8 (C^2), 131.0, 127.7, 120.2, 117.7, 115.0.

HRESI-MS found 173.06006 [calc. for $C_{11}H_9O_2$ $[M-H]^-$ 173.06080]

IR 3201.91, 2961.00, 2848.92, 1645.89, 1616.18, 1574.21 cm^{-1}

TLC R_f = 0.10 (1:5 EtOAc/hexanes), visible with $KMnO_4$ or as a bright orange spot with 2,4-DNP dip

m.p. 160 - 161 °C



(2E,4E)-5-(4-fluorophenyl)penta-2,4-dienal [106485-23-8] (**4f**) was synthesised according to general procedure ***2.1*** from 5-(4-fluorophenyl)pent-4-ynal (**3f**, 35.2 mg, 0.2 mmol) by stirring in 1,4-dioxane solvent for 16 hours. The crude product was purified by flash column chromatography (silica, 15% EtOAC/hexanes) to yield the title compound as an orange solid (22.5 mg, 64%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.62 (d, *J* = 7.9 Hz, 1H, C^1(O)H), 7.50 – 7.48 (m, 2H, $C^{2'}$-H), 7.25 (dd, *J* = 15.2, 10.3 Hz, 1H, C^3-H), 7.10 – 7.06 (m, 2H, $C^{3'}$-H), 7.00 – 6.89 (m, 2H, C^4-H & C^5-H), 6.27 (dd, *J* = 15.2, 7.9 Hz, 1H, C^2-H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.6 (C^1), 163.6 (d, *J* = 249.3 Hz, $C^{4'}$), 151.9 (C^3), 141.1 (C^5), 132.0 (d, *J* = 3.4 Hz, $C^{1'}$), 131.8 (C^2), 129.4 (d, *J* = 8.2 Hz, $C^{3'}$), 126.1 (d, *J* = 2.5 Hz, C^4), 116.2 (d, *J* = 21.8 Hz, $C^{2'}$). Spectral assignments agreed with the literature.[4]

HRAPCI-MS found 177.07132 [calc. for $C_{11}H_{10}OF$ $[M+H]^+$ 177.07102]

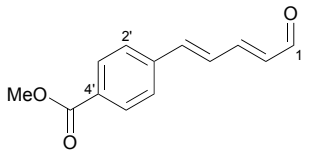
IR 2923.61, 1658.89, 1616.54, 1594.11 cm^{-1}

TLC R_f = 0.35 (1:5 EtOAc/hexanes), visible as a bright orange spot with 2,4-DNP dip

m.p. 76 - 78 °C

(2Z,4E)-5-(4-fluorophenyl)penta-2,4-dienal

1D ^{1}H TOCSY (400 MHz, $CDCl_3$, irradiation of aldehyde peak at 10.23 ppm, corresponds to the (2*Z*,4*E*)-minor isomer olefinic peaks) δ 10.23 (d, *J* = 7.5 Hz, 1H, C^1(O)H), 7.67 (dd, *J* = 15.3, 11.9 Hz, 1H, C^4-H), 7.02 (dd, *J* = 11.9, 11.0 Hz, 1H, C^3-H), 6.86 (d, *J* = 15.3 Hz, 1H, C^5-H), 5.92 (dd, *J* = 11.0, 7.5 Hz, 1H, C^2-H).



Methyl 4-((1E,3E)-5-oxopenta-1,3-dien-1-yl)benzoate (**4g**) was synthesised according to general procedure ***2.1*** from methyl 4-(5-oxopent-1-yn-1-yl)benzoate (**3g**, 43.2 mg, 0.2 mmol) by stirring in 1,4-dioxane solvent for 16 hours. The crude product was purified using flash column chromatography (silica, 15 – 25% EtOAC/hexanes) to yield the title compound as an orange solid (24.7 mg, 57%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.65 (d, 1H, *J* = 7.9 Hz, C^1(O)H), 8.04 (d, 2H, *J* = 8.4 Hz, $C^{3'}$-H), 7.56 (d, 2H, *J* = 8.4 Hz, $C^{2'}$-H), 7.27 (dd, 1H, *J* = 15.2, 10.1 Hz, C^3-H), 7.12 – 7.01 (m, 2H, C^4-H & C^5-H), 6.32 (dd, 1H, *J* = 15.2, 7.9 Hz, C^2-H), 3.93 (s, 3H, $C^{4'}CO_2C\mathbf{H}_3$). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.5 (C^1), 166.6 ($C^{4'}\mathbf{C}O_2CH_3$), 151.1 (C^3), 140.9 (C^5), 139.9 ($C^{1'}$), 132.9 (C^2), 130.9 ($C^{4'}$), 130.3 ($C^{3'}$), 128.6 (C^4), 127.5 ($C^{2'}$), 52.4 ($C^{4'}CO_2\mathbf{C}H_3$).

HRESI-MS found 239.0677 [calc. for $C_{13}H_{12}NaO_3$ $[M+Na]^+$ 239.0679]

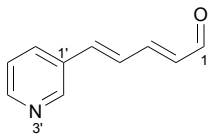
IR 2824.15, 1701.52, 1670.67, 1618.07 cm^{-1}

TLC R_f = 0.15 (1:5 EtOAc/hexanes), visible as a bright orange spot with 2,4-DNP dip

m.p. 91 - 93 °C

Methyl 4-((1Z,3E)-5-oxopenta-1,3-dien-1-yl)benzoate

1D ^{1}H TOCSY (500 MHz, $CDCl_3$, irradiation of aldehyde peak at 10.26 ppm, corresponds to the (1*Z*,3*E*)-minor isomer olefinic peaks) δ 10.26 (d, *J* = 7.3 Hz, 1H, C^1(O)H), 7.83 (ddd, *J* = 15.4, 11.8, 1.0 Hz, 1H, C^4-H), 7.06 (dd, *J* = 11.8, 11.0 Hz, 1H, C^3-H), 6.92 (d, *J* = 15.4 Hz, 1H, C^5-H), 5.99 (dd, *J* = 11.0, 7.3 Hz, 1H, C^2-H).



(2E,4E)-5-(pyridine-3-yl)penta-2,4-dienal [113388-29-7] (**4h**)was synthesised according to general procedure ***2.1*** from 5-(pyridine-3-yl)pent-4-ynal (**3h**, 31.8 mg, 0.2 mmol) by stirring in 1,4-dioxane solvent for 16 hours. The crude product was purified by flash column chromatography (silica, 50 – 100% EtOAc/hexanes) to yield the title compound as pale yellow crystals (13.8 mg, 43%).

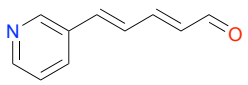
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.64 (d, *J* = 7.8 Hz, 1H, C^1(O)H), 8.71 (br s, 1H, $C^{2'}$-H), 8.56 (br d, *J* = 4.4 Hz, 1H, $C^{4'}$-H), 7.83 (ddd, *J* = 8.0, 1.8, 1.8 Hz, 1H, $C^{6'}$-H), 7.32 (dd, *J* = 8.0 Hz, 4.4 Hz, 1H, $C^{5'}$-H), 7.26 (dd, *J* = 15.2, 9.8 Hz, 1H, C^3-H), 7.06 (dd, *J* = 15.6, 9.8 Hz, 1H, C^4-H), 6.99 (d, *J* = 15.6 Hz, 1H, C^5-H), 6.30 (dd, *J* = 15.2, 7.8 Hz, 1H, C^2-H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.5, 150.9, 150.3, 149.3, 138.2, 133.6, 132.8, 131.5, 128.2, 123.9.

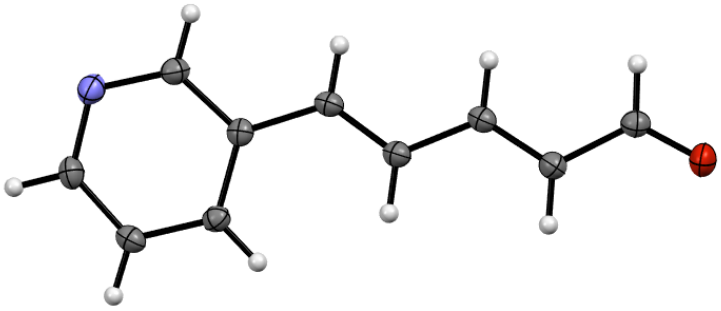
HRESI-MS found 160.0753 [calc. for $C_{10}H_{10}NO$ $[M+H]^+$ 160.0757]

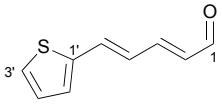
IR 3023.45, 2962.02, 1669.03, 1616.12 cm^{-1}

TLC R_f = 0.41 (EtOAc), visible under UV and as a bright orange spot with 2,4-DNP dip

Crystal and molecular structures of (2*E*,4*E*)-5-(pyridine-3-yl)penta-2,4-dienal (**4h**) were determined by single crystal X-ray diffraction. Diffraction measurements were made on a Bruker D8 APEX2 X-ray diffractometer instrument using graphite-monochromated MoK_α (λ = 0.71073 Å) radiation. The X-ray diffraction data sets were collected using the ω and f scan mode over the 2ϑ range up to 54°. The structures were solved by direct methods implemented in SHELXS and refined using SHELXL.[2] Structure refinement was performed on F^2 using all data. Hydrogen atoms on carbon centres were modelled with appropriate riding-hydrogen models. Hydrogen atoms participating in hydrogen bonds were located from the electron density map whenever data quality was sufficient. Otherwise, they were fixed to appropriate distances and refined from the electron density map. Calculations were performed and the drawings were prepared using the WINGX[3] suite of crystallographic programs. The compound (2*E*,4*E*)-5-(pyridine-3-yl)penta-2,4-dienal (**4h**) crystalizes in space group $P2_1/c$. Structure has been deposited with the Cambridge Structural Database, deposition code CCDC 1527924.







(2E,4E)-5-(thiophen-2-yl)penta-2,4-dienal [62858-67-7] (**4i**) was synthesised according to general procedure ***2.1*** from 5-(thiophen-2-yl)pent-4-ynal (**3i**, 32.8 mg, 0.2 mmol) by stirring in 1,4-dioxane solvent for 16 hours. The crude product was purified by flash column chromatography (15% EtOAc/hexanes) to yield the title compound as an orange oil (13.5 mg, 41%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (d, *J* = 7.9 Hz, 1H, C^{1}(O)H), 7.35 (d, *J* = 5.0 Hz, 1H, $C^{3'}$-H), 7.20 (dd, *J* = 15.2, 11.0 Hz, 1H, C^{3}-H), 7.19 (d, *J* = 3.6 Hz, $C^{5'}$-H), 7.13 (d, *J* = 15.2 Hz, 1H, C^{5}-H), 7.05 (dd, *J* = 5.0, 3.6 Hz, 1H, $C^{4'}$-H), 6.79 (dd, *J* = 15.2, 11.0 Hz, 1H, C^{4}-H), 6.23 (dd, *J* = 15.2, 7.9 Hz, 1H, C^{2}-H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.5, 151.7, 141.2, 134.8, 131.3, 129.6, 128.3, 127.9, 125.7.

HRESI-MS found 187.0187 [calc. for C_9H_8NaOS $[M+Na]^+$ 187.0188]

IR 2815.47, 2728.06, 1667.24, 1601.75 cm^{-1}

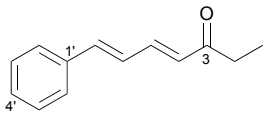
TLC R_f = 0.38 (1:5 EtOAc/hexanes), visible under UV and as a bright orange spot with 2,4-DNP dip

(2E,4Z)-5-(thiophen-2-yl)penta-2,4-dienal

1D ^{1}H TOCSY (400 MHz, $CDCl_3$, irradiation of aldehyde peak at 9.71 ppm, corresponds to the (2*E*,4*Z*)-minor isomer olefinic peaks) δ 9.71 (d, *J* = 7.9 Hz, 1H, C^{1}(O)H), 7.92 (dd, *J* = 15.0, 11.8 Hz, 1H, C^{3}-H), 6.96 (d, *J* = 11.6 Hz, 1H, C^{5}-H), 6.38 (dd, *J* = 11.8, 11.6 Hz, 1H, C^{4}-H), 6.31 (dd, *J* = 15.0, 7.9 Hz, 1H, C^{2}-H).

(2Z,4E)-5-(thiophen-2-yl)penta-2,4-dienal [121742-63-0]

1D ^{1}H TOCSY (400 MHz, $CDCl_3$, irradiation of aldehyde peak at 10.24 ppm, corresponds to the (2*Z*,4*E*)-minor isomer olefinic peaks) δ 10.24 (d, *J* = 7.6 Hz, 1H, C^{1}(O)H), 7.52 (dd, *J* = 15.2, 12.1 Hz, 1H, C^{4}-H), 7.04 (d, *J* = 15.0 Hz, 1H, C^{5}-H), 7.01 (dd, *J* = 12.1, 11.6 Hz, 1H, C^{3}-H), 5.90 (dd, *J* = 11.6, 7.6 Hz, 1H, C^{2}-H). Spectral assignments agreed with the literature.[5]



(4E,6E)-7-phenylhepta-4,6-dien-3-one [75391-05-8] (**4j**) was synthesised according to general procedure ***2.1*** from 7-phenylhept-6-yn-3-one (**3j**, 74.5 mg, 0.4 mmol) by stirring in 1,4-dioxane solvent for 16 hours. The crude product was purified by flash column chromatography (silica, 10 - 15% EtOAC/hexanes) to yield the title compound as a yellow solid (63.3 mg, 85%).

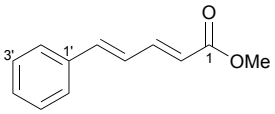
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (br d, *J* = 7.2 Hz, 2H, $C^{2'}$-H), 7.38 – 7.30 (m, 4H, $C^{3'}$-H, $C^{4'}$-H, C^{5}-H), 6.95 (d, *J* = 15.6 Hz, 1H, C^{7}-H), 6.88 (ddd, *J* = 10.4, 15.6, 0.7 Hz, 1H, C^{6}-H), 6.29 (d, *J* = 15.5 Hz, 1H, C^{4}-H), 2.63 (q, 2H, *J* = 7.4 Hz, C^{2}-H_2), 1.15 (t, *J* = 7.4 Hz, 3H, C^{1}-H_2). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.2 (C^{3}), 142.4 (C^{5}), 141.2 (C^{7}), 136.2 ($C^{1'}$), 129.5, 129.3, 129.0, 127.3, 126.9, 34.0 (C^{2}), 8.4 (C^{1}). Spectral assignments agreed with the literature.[6]

HRAPCI-MS found 187.11161 [calc. for $C_{13}H_{15}O$ $[M+H]^+$ 187.11174]

IR 3031.95, 2971.35, 1684.06, 1590.30 cm^{-1}

TLC R_f = 0.49 (1:5 EtOAc/hexanes), visible as a bright orange spot with 2,4-DNP dip

m.p. 51 - 53 °C



Methyl (2E,4E)-5-phenylpenta-2,4-dienoate [24196-39-2] (**4k**) was synthesised according to general procedure ***2.1*** from methyl 5-phenylpent-4-ynoate (**3k**, 37.6 mg, 0.2 mmol) by stirring in 1,4-dioxane solvent for 16 hours. The crude product was purified by flash column chromatography (silica, 10 – 15% EtOAc/hexanes) to yield the title compound as a orange solid (27.0 mg, 72%).

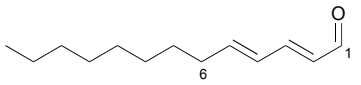
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 – 7.46 (m, 3H, arom & C^{3}-H), 7.46 (coin ddd, *J* = 15.2, 8.9, 1.4 Hz, 1H, C^{3}-H), 7.38 – 7.34 (m, 2H, arom), 7.31 (tt, *J* = 7.3, 1.3 Hz, 1H, $C^{4'}$-H), 6.93 – 6.85 (m, 2H, C^{4}-H & C^{5}-H), 6.0 (d, *J* = 15.2 Hz, 1H, C^{2}-H), 3.78 (s, 3H, C^{1}(O)OC**H**$_3$). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.6, 145.0, 140.7, 136.1, 129.2, 129.0, 127.3, 126.3, 121.0, 51.7. **1D ^{1}H TOCSY** (400 MHz, $CDCl_3$, irradiation of olefinic peak at 6.0 ppm, corresponds to the (2*E*,4*E*)-major isomer olefinic peaks) δ 7.46 (ddd, *J* = 15.2, 8.9, 1.4 Hz, 1H, C^{3}-H), 6.93 – 6.85 (m, 2H, C^{4}-H & C^{5}-H), 6.0 (d, *J* = 15.2 Hz, 1H, C^{2}-H). Spectral assignments agreed with the literature.[7]

HRESI-MS found 211.0734 [calc. for $C_{12}H_{12}O_2Na$ $[M+Na]^+$ 211.0730]

IR 3025.80, 2943.62, 2845.52, 1709.73, 1624.85 cm^{-1}

TLC R_f = 0.64 (1:5 EtOAc/hexanes), visible as a blue spot with vanillin dip (with heat activation)

m.p. 56 - 58 °C



(2E,4E)-Trideca-2,4-dienal [131947-43-8] (**4l**) was synthesised according to general procedure ***2.1*** from tridec-4-ynal (**3l**, 38.9 mg, 0.2 mmol) by stirring in toluene solvent for 2 hours. The crude product was purified by flash column chromatography (silica, 5% EtOAc/hexanes) to yield the title compound as a pale yellow oil (8.6 mg, 22%). The major product is fully characterized below, followed by partial characterisation of minor products.

^{1}H NMR (500 MHz, $CDCl_3$, impurity present in a ratio of 3.3:1 (product:impurity) corresponds to (4*E*,6*E*)-trideca-4,6-dienal, characterized below) δ 9.53 (d, *J* = 8.0 Hz, 1H, C^1(O)H), 7.08 (dd, *J* = 15.3, 9.7 Hz, 1H, C^3-H), 6.34 – 6.24 (m, 2H, C^4-H & C^5-H), 6.07 (dd, *J* = 15.3, 8.0 Hz, 1H, C^2-H), 2.22 (app q, *J* = 6.9 Hz, 2H, C^6-H_2), 1.48 – 1.42 (m, 2H, C^7-H_2), 1.34 – 1.22 (m, 10H, C^8-H_2, C^9-H_2, C^{10}-H_2, C^{11}-H_2, C^{12}-H_2), 0.88 (t, *J* = 6.8 Hz, 3H, C^{13}-H_3). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 194.1 (C^1), 153.1 (C^3), 147.6 (C^4 or C^5), 130.2 (C^2), 128.8 (C^4 or C^5), 33.4 (C^6), 32.0, 29.5, 29.4 (2 peaks, coin), 28.7, 22.8, 14.3 (C^{13}).

HRESI-MS found 217.1567 [calc. for $C_{13}H_{22}ONa$ $[M+Na]^+$ 217.1563]

IR 2924.79, 2854.54, 1683.46, 1639.07 cm^{-1}

TLC R_f = 0.58 (1:5 EtOAc/hexanes), visible as a bright orange spot with 2,4-DNP dip

(2E,4E,6E)-trideca-2,4,6-trienal [350696-22-9] (**4m**)

1D ^{1}H TOCSY (400 MHz, $CDCl_3$, irradiation of aldehyde resonance at 9.54 ppm, corresponds to the (2*E*,4*E*,6*E*)-minor product olefinic peaks. Data is identical to that obtained by direct synthesis of **4m** from **3m**, see entry below) δ 9.54 (d, *J* = 8.0 Hz, 1H, C^1(O)H), 7.10 (dd, *J* = 15.1, 11.1 Hz, 1H, C^3-H), 6.64 (dd, *J* = 14.9, 10.5 Hz, 1H, C^5-H), 6.34 (dd, *J* = 14.9, 11.1 Hz, 1H, C^4-H), 6.18 (dd, *J* = 15.2, 10.5 Hz, 1H, C^6-H), 6.12 (dd, *J* = 15.1, 8.0 Hz, 1H, C^2-H), 6.03 (dt, *J* = 15.2, 6.6 Hz, 1H, C^7-H).

HRAPCI-MS found 193.15886 [calc. for $C_{13}H_{21}O$ $[M+H]^+$ 193.15869]

TLC R_f = 0.52 (1:5 EtOAc/hexanes), visible under UV and as a bright orange spot with 2,4-DNP dip

(4E,6E)-trideca-4,6-dienal [1824856-39-4] (**5**)

^{1}H NMR (500 MHz, $CDCl_3$, compound present as impurity in major product spectrum, NMR was partially assigned using ^{1}H-^{1}H COSY and ^{1}H-^{13}C HSQC NMR spectra) δ 9.77 (t, *J* = 1.6 Hz, 1H, C^1(O)H), 6.04 (dd, *J* = 14.4, 10.3 Hz, 1H, C^6-H), 5.98 (dd, *J* = 14.4, 10.3 Hz, 1H, C^5-H), 5.61 (dt, *J* = 14.5, 7.0 Hz, 1H, C^4-H), 5.54 (dt, *J* = 14.5, 7.0 Hz, 1H, C^7-H), 2.55 – 2.51 (m, 2H, C^2-H_2), 2.44 – 2.37 (m, 2H, C^3-H_2), 2.07 – 2.02 (m, 2H, C^8-H_2), 1.34 – 1.22 (m, 8H, C^9-H_2, C^{10}-H_2, C^{11}-H_2, C^{12}-H_2), 0.88 (t, *J* = 6.8 Hz, 3H, C^{13}-H_3). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 134.1 (C^4), 131.9 (C^6), 129.8 (C^5), 129.2 (C^7), 43.5 (C^2), 32.7 (C^8), 31.9, 29.4, 29.0, 25.3, 22.8.

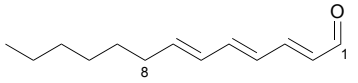
TLC R_f = 0.58 (1:5 EtOAc/hexanes), visible as a bright orange spot with 2,4-DNP dip

(2E,4Z)-Trideca-2,4-dienal [53658-60-9] (**6**)

1D ^{1}H TOCSY (400 MHz, $CDCl_3$, irradiation of aldehyde resonance at 9.55 ppm, corresponds to the (2*E*,4*Z*)-minor isomer olefinic peaks) δ 9.55 (d, *J* = 8.0 Hz, 1H, C^1(O)H), 7.38 (ddd, *J* = 15.4, 11.6, 0.9 Hz, 1H, C^3-H),

6.20 (app t, *J* = 11.6 Hz, 1H, C^4-H), 6.08 (dd, *J* = 15.0, 8.0 Hz, 1H, C^2-H), 5.95 (d, *J* = 10.6 Hz, 1H, C^5-H), 2.27 (m, 2H, C^6-H_2).

TLC R_f = 0.62 (1:5 EtOAc/hexanes), visible as a bright orange spot with 2,4-DNP dip



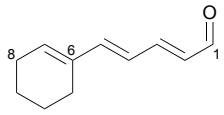
(2E,4E,6E)-trideca-2,4,6-trienal [350696-22-9] (**4m**) was synthesised according to general procedure ***2.1*** from (*E*)-tridec-6-en-4-ynal (**3m**, 38.5 mg, 0.2 mmol) by stirring in toluene solvent for 10 hours. The crude product was purified by flash column chromatography (silica, 5 – 10% EtOAc/hexanes) to yield the title compound as an orange oil (11.2 mg, 29%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.54 (d, *J* = 7.9 Hz, 1H, C^1(O)H), 7.11 (dd, *J* = 15.1, 11.2 Hz, 1H, C^3-H), 6.64 (dd, *J* = 14.9, 10.7 Hz, 1H, C^5-H), 6.34 (dd, *J* = 14.9, 11.2 Hz, 1H, C^4-H), 6.18 (dd, *J* = 15.2, 10.7 Hz, 1H, C^6-H), 6.12 (dd, *J* = 15.1, 7.9 Hz, 1H, C^2-H), 6.03 (dt, *J* = 15.2, 6.9 Hz, 1H, C^7-H), 2.17 (app q, *J* = 7.5 Hz, 2H, C^8-H_2), 1.46 – 1.38 (m, 2H, C^9-H_2), 1.34 – 1.23 (m, 6H, C^{10}-H_2, C^{11}-H_2, C^{12}-H_2), 0.90 – 0.85 (m, 3H, C^{13}-H_3). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 193.7 (C^1), 152.5 (C^3), 143.4 (C^5), 142.9 (C^7), 130.8 (C^2), 129.9 (C^6), 127.9 (C^4), 33.2 (C^8), 31.8 (C^{10} – C^{12}), 29.0 (29.01, C^{10} – C^{12}), 29.0 (28.99, C^9), 22.7 (C^{10} – C^{12}), 14.2 (C^{13}).

HRAPCI-MS found 193.15840 [calc. for $C_{13}H_{21}O$ $[M+H]^+$ 193.15869]

IR 2957.42, 2926.61, 2855.34, 1674.12, 1610.36 cm^{-1}

TLC R_f = 0.52 (1:5 EtOAc/hexanes), visible under UV and as a bright orange spot with 2,4-DNP dip



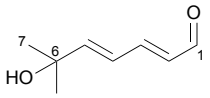
(2E,4E)-5-(cyclohex-1-en-1-yl)penta-2,4-dienal [145299-82-7] (**4n**) was synthesised according to general procedure ***2.1*** from 5-(1-cyclohexen-1-yl)pent-4-ynal (**3n**, 32.4 mg, 0.2 mmol) by stirring in toluene solvent for 9 hours. The crude product was purified by flash column chromatography (silica, 5 – 10% EtOAc/hexanes) to yield the title compound as a yellow oil (24.7 mg, 76%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.53 (d, *J* = 8.0 Hz, 1H, C^1(O)H), 7.14 (dd, *J* = 15.2, 11.0 Hz, 1H, C^3-H), 6.64 (d, *J* = 15.3 Hz, 1H, C^5-H), 6.33 (dd, *J* = 15.3, 11.0 Hz, 1H, C^4-H), 6.13 (dd, *J* = 15.2, 8.0 Hz, 1H, C^2-H), 6.07 (t, *J* = 3.7 Hz, 1H, C^7-H), 2.24 – 2.16 (m, 4H), 1.73 – 1.66 (m, 2H), 1.66 – 1.58 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 193.8, 153.5, 146.7, 137.4, 136.1, 130.5, 123.0, 26.6, 24.4, 22.2 (22.23), 22.2 (22.21).

HRESI-MS found 185.0934 [calc. for $C_{11}H_{14}ONa$ $[M+Na]^+$ 185.0937]

IR 2928.68, 2859.87, 1676.95, 1601.76 cm^{-1}

TLC R_f = 0.43 (1:5 EtOAc/hexanes), visible under UV and as a bright orange spot with 2,4-DNP dip



(2E,4E)-6-hydroxy-4-methylhepta-2,4-dienal (**4o**) was synthesised according to general procedure ***2.1*** from 6-hydroxy-6-methylhept-4-ynal (**3o**, 28.0 mg, 0.2 mmol) by stirring in toluene solvent for 4 hours. The crude product was purified by flash column chromatography (silica, 35 – 45% EtOAc/hexanes) to yield the title compound as an orange solid (16.7 mg, 60%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.54 (d, *J* = 8.0 Hz, 1H, C^1(O)H), 7.10 (dd, *J* = 15.3, 10.9 Hz, 1H, C^3-H), 6.50 (dd, *J* = 15.3, 10.9 Hz, 1H, C^4-H), 6.34 (d, *J* = 15.3 Hz, 1H, C^5-H), 6.15 (dd, *J* = 15.3, 8.0 Hz, 1H, C^2-H), 1.37 (s, 6H, C^7-H_3). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 194.0 (C^1), 152.4 (C^3 or C^5), 152.1 (C^3 or C^5), 131.8 (C^2 or C^4), 124.8 (C^2 or C^4), 71.1 (C^6), 29.6 (C^7).

HRESI-MS found 163.07334 [calc. for $C_8H_{12}O_2Na$ $[M+Na]^+$ 163.07295]

IR 3413.00, 2974.31, 1667.88, 1639.39 cm^{-1}

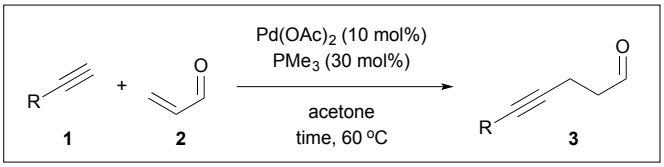
TLC R_f = 0.68 (EtOAc), visible under UV and with $KMnO_4$ dip

(2Z,4E)-6-hydroxy-4-methylhepta-2,4-dienal

1D ^{1}H TOCSY (400 MHz, $CDCl_3$, irradiation of aldehyde peak at 10.23 ppm, corresponds to the (2*Z*,4*E*)-minor isomer olefinic peaks) δ 10.26 (d, *J* = 7.8 Hz, 1H, C^1(O)H), 7.26 (dd, *J* = 14.6, 11.3, 1.0 Hz, 1H, C^4-H), 6.96 (app t, *J* = 11.2 Hz, 1H, C^3-H), 6.26 (d, *J* = 14.6 Hz, 1H, C^5-H), 5.89 (dd, *J* = 11.1, 7.8 Hz, 1H, C^2-H).

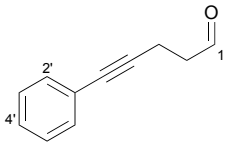
3 Substrate Synthesis

3.1 *General Procedure: Substrate Synthesis by 1,4-addition of Acetylenes to Acrolein,*



4-Alkynals (**3**) were synthesised by a literature procedure.[8] To a flame-dried flask containing a stir-bar was added $Pd(OAc)_2$ (10 mol%). The flask was evacuated under high-vacuum and back-filled with argon. This process was repeated twice before addition of PMe_3 solution (1.0 M in toluene, 30 mol%). The resulting mixture was stirred at 110 °C in an oil bath for 10 minutes until the $Pd(OAc)_2$ had dissolved. The vial was removed from the oil bath, and acetone was added (2 mL per 1 mmol alkyne **1**), followed by a solution of terminal alkyne (**1**, 1 equiv.) and freshly-distilled acrolein (**2**, 3 equiv.). The reaction mixture was stirred at 60 °C in an oil bath until reaction completion, judged by full consumption of alkyne starting material **1** by TLC. The reaction mixture was extracted with ethyl ether (3 x 30 mL), dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by flash column chromatography to give a pure sample of 4-alkynal **3**.

3.2 *Synthesis and Data of Substrates **3a, 3b, 3d – 3g, 3l, 3n, 3o***



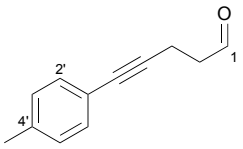
5-phenylpent-4-ynal [70214-59-4] (**3a**) was synthesised according to general procedure ***4.1***, using $Pd(OAc)_2$ (269.4 mg, 1.2 mmol), PMe_3 (3.6 mL, 3.6 mmol), acetone (25 mL), phenylacetylene (**1a**, 1.32 mL, 12 mmol), and acrolein (**2**, 2.4 mL, 36 mmol). The reaction mixture was stirred for 8 hours. The crude product was purified by flash column chromatography (silica, 5 – 10% EtOAc/hexanes) to yield the title compound as a pale yellow oil (1.23 g, 65%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (t, *J* = 0.8 Hz, 1H, C^1(O)H), 9.40 – 9.37 (m, 2H), 7.28 – 7.26 (m, 3H), 2.75 – 2.73 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 200.6, 131.6, 128.2, 127.9, 123.4, 87.8, 81.4, 42.6, 12.7. Spectral assignments agreed with the literature.[8, 9]

HRESI-MS found 159.08027 [calc. for $C_{11}H_{11}O$ $[M+H]^+$ 159.08044]

IR 2914.63, 2830.20, 1724.35 cm^{-1}

TLC R_f = 0.43 (1:5 EtOAc/hexanes), visible as a yellow spot with 2,4-DNP dip



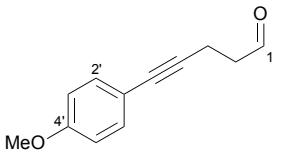
5-(p-tolyl)pent-4-ynal [401901-60-8] (**3b**) was synthesised according to general procedure ***4.1***, using $Pd(OAc)_2$ (44.9 mg, 0.2 mmol), PMe_3 (0.6 mL, 0.6 mmol), acetone (4 mL), 4-ethynyltoluene (**1b**, 254 µL, 2 mmol), and acrolein (**2**, 401 µL, 6 mmol). The reaction was stirred for 4 hours. The crude product was purified by flash column chromatography (silica, 5 – 20% EtOAc/hexanes) to yield the title compound as a yellow oil (170.2 mg, 49%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (br s, 1H, C^1(O)H), 7.28 (d, *J* = 8.0 Hz, 2H, $C^{2'}$-H), 7.09 (d, *J* = 8.0 Hz, 2H, $C^{3'}$-H), 2.77 – 2.70 (m, 4H, C^2-H_2 & C^3-H_2), 2.33 (s, 3H, $C^{5'}$-H_3). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 200.7 (C^1), 138.0 ($C^{4'}$), 131.5 ($C^{2'}$), 129.1 ($C^{3'}$), 120.4 ($C^{1'}$), 87.0 (C^4), 81.6 (C^5), 42.8 (C^2), 21.5 ($C^{5'}$), 12.8 (C^3). Spectral assignments agreed with the literature.[8]

HRESI-MS found 195.07826 [calc. for $C_{12}H_{12}ONa$ $[M+Na]^+$ 195.07804], found 227.10442 [calc. for $C_{13}H_{16}O_2Na$ $[M+MeOH+Na]^+$ 227.10425]

IR 2919.49, 2827.12, 1724.12 cm^{-1}

TLC R_f = 0.43 (1:5 EtOAc/hexanes), visible as a yellow spot with 2,4-DNP dip



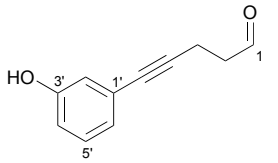
5-(4-methoxyphenyl)pent-4-ynal [873961-36-5] (**3d**) was synthesised according to general procedure ***4.1***, using $Pd(OAc)_2$ (22.5 mg, 0.1 mmol), PMe_3 (0.3 mL, 0.3 mmol), acetone (2 mL), 4-ethynylanisole (**1d**, 130 µL, 1 mmol), and acrolein (**2**, 200 µL, 3 mmol). The reaction was stirred for 5 hours. The crude product was purified by flash column chromatography (silica, 10 – 30% EtOAc/hexanes) to yield the title compound as a yellow oil (110.1 mg, 58%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.83 (br s, 1H, C^1(O)H), 7.31 (d, J = 8.8 Hz, 2H, $C^{2'}$-H), 6.80 (d, J = 8.8 Hz, 2H, $C^{3'}$-H), 3.78 (s, 3H, OMe), 2.75 – 2.70 (m, 4H, C^2-H_2 & C^3-H_2). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 200.7 (C-1), 159.4 (C-4'), 133.0 (C-2'), 115.6 (C-1'), 114.0 (C-3'), 86.2 (C-4), 81.3 (C-5), 55.4 (OMe), 42.8 (C-2), 12.8 (C-3). Spectral assignments agreed with the literature.[8, 10]

HRESI-MS found 211.07299 [calc. for $C_{12}H_{12}O_2Na$ $[M+Na]^+$ 211.07295]

IR 2915.78, 2837.47, 1724.14, 1605.59, 1508.40 cm^{-1}

TLC R_f = 0.35 (1:5 EtOAc/hexanes), visible as a yellow spot with 2,4-DNP dip



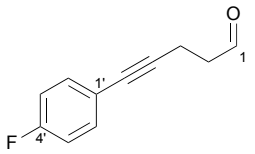
5-(3-hydroxyphenyl)pent-4-ynal [1801972-84-8] (**3e**) was synthesised according to general procedure ***4.1***, using $Pd(OAc)_2$ (22.5 mg, 0.1 mmol), PMe_3 (0.3 mL, 0.3 mmol), acetone (2 mL), 3-hydroxyphenylacetylene (**1d**, 109 µL, 1 mmol), and acrolein (**2**, 200 µL, 3 mmol). The reaction was stirred for 5 hours. The crude product was purified by flash column chromatography (silica, 15 – 25% EtOAc/hexanes) to yield the title compound as a pale yellow oil (82.9 mg, 48%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (t, *J* = 1.2 Hz, 1H, C^1(O)H), 7.14 (dd, *J* = 8.2, 7.7 Hz, 1H, $C^{5'}$-H), 6.95 (ddd, *J* = 7.7, 1.1, 1.1 Hz, 1H, $C^{4'}$-H), 6.85 (dd, *J* = 2.5, 1.1 Hz, 1H, $C^{2'}$-H), 6.77 (ddd, *J* = 8.2 Hz, 2.5, 1.1 Hz, 1H, $C^{6'}$-H), 5.21 (br s, 1H, $C^{3'}$-OH), 2.78 – 2.71 (m, 4H, C^2-H_2 & C^3-H_2). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.2 (C^1), 155.6 ($C^{3'}$), 129.6 ($C^{5'}$), 124.6 ($C^{1'}$), 124.2 ($C^{4'}$), 118.4 ($C^{2'}$), 115.6 ($C^{6'}$), 87.8 (C^4), 81.3 (C^5), 42.7 (C^2), 12.8 (C^3). Spectral assignments agreed with the literature.[8]

HRAPCI-MS found 173.05997 [calc. for $C_{11}H_9O_2$ $[M-H]^-$ 173.06080]

IR 3387.22, 2908.89, 1704.82, 1578.01 cm^{-1}

TLC R_f = 0.13 (1:5 EtOAc/hexanes), visible with $KMnO_4$, or as a yellow spot with 2,4-DNP dip



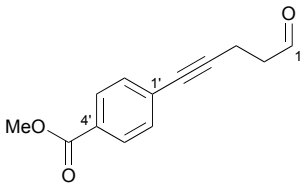
5-(4-fluorophenyl)pent-4-ynal [1801972-86-0] (**3f**) was synthesised according to general procedure ***4.1***, using $Pd(OAc)_2$ (22.5 mg, 0.1 mmol), PMe_3 (0.3 mL, 0.3 mmol), acetone (2 mL), 1-ethynyl-4-fluorobenzene (**1f**, 115 µL, 1 mmol), and acrolein (**2**, 200 µL, 3 mmol). The reaction was stirred for 5 hours. The crude product was purified by flash column chromatography (silica, 5 – 10% EtOAc/hexanes) to yield the title compound as a pale yellow oil (83.0 mg, 47%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (br s, 1H, C^1(O)H), 7.36-7.33 (m, 2H, $C^{2'}$-H), 6.99 – 6.95 (m, 2H, $C^{3'}$-H), 2.77 – 2.70 (m, 4H, C^2-H_2 & C^3-H_2). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 200.4 (C^1), 162.4 (d, *J* = 247.7 Hz, $C^{4'}$), 133.5 (d, *J* = 8.2 Hz, $C^{2'}$), 119.6 (d, *J* = 3.6 Hz, $C^{1'}$), 115.6 (d, *J* = 21.9 Hz, $C^{3'}$), 87.5 (d, *J* = 1.8 Hz, C^4), 80.5 (C^5), 42.7 (C^2), 12.7 (C^3). Spectral assignments agreed with the literature.[8]

HRAPCI-MS found 177.07104 [calc. for $C_{11}H_{10}OF$ $[M+H]^+$ 177.07102], found 209.09722 [calc. for $C_{12}H_{14}O_2F$ $[M+MeOH+H]^+$ 209.09723]

IR 2830.08, 2729.66, 1724.87, 1505.22 cm^{-1}

TLC R_f = 0.33 (1:5 EtOAc/hexanes), visible as a yellow spot with 2,4-DNP dip



Methyl 4-(5-oxopent-1-yn-1-yl)benzoate [1415336-96-7] (**3g**) was synthesised according to general procedure ***4.1***, using $Pd(OAc)_2$ (22.5 mg, 0.1 mmol), PMe_3 (0.3 mL, 0.3 mmol), acetone (2 mL), methyl 4-ethynylbenzoate (**1g**, 160.2 mg, 1 mmol), and acrolein (**2**, 200 µL, 3 mmol). The reaction was stirred for 16 hours. The crude product was purified by flash column chromatography (silica, 10 – 20% EtOAc/hexanes) to yield the title compound as an orange solid (101.9 mg, 47%).

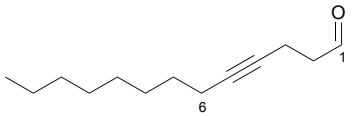
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.85 (br s, 1H, C^1(O)H), 7.95 (d, *J* = 8.4 Hz, 2H, $C^{2'}$-H), 7.43 (d, *J* = 8.4 Hz, 2H, $C^{3'}$-H), 3.90 (s, 3H, $C^{7'}$-H_3), 2.80 – 2.74 (m, 4H, C^2-H_2 & C^3-H_2). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 200.2 (C^1), 166.7 ($C^{5'}$), 131.6 ($C^{3'}$), 129.6 ($C^{2'}$), 129.4 ($C^{1'}$ or $C^{4'}$), 128.3 ($C^{1'}$ or $C^{4'}$), 91.2 (C^4), 81.0 (C^5), 52.3 ($C^{7'}$), 42.6 (C^2), 12.9 (C^3).

HRESI-MS found 239.0684 [calc. for $C_{13}H_{12}NaO_3$ $[M+H]^+$ 239.0679], found 271.0952 [calc. for $C_{14}H_{16}NaO_4$ $[M+MeOH + Na]^+$ 271.0941]

IR 2840.06, 2736.71, 1709.53 cm^{-1}

TLC R_f = 0.24 (1:5 EtOAc/hexanes), visible as a yellow spot with 2,4-DNP dip

m.p. 48 - 50 °C



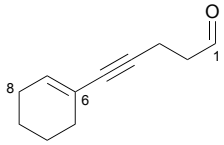
Tridec-4-ynal [335279-03-3] (**3l**) was synthesised according to general procedure ***4.1***, using $Pd(OAc)_2$ (44.9 mg, 0.2 mmol), PMe_3 (0.6 mL, 0.6 mmol), acetone (4 mL), 1-decyne (**1l**, 361 µL, 2 mmol), and acrolein (**2**, 401 µL, 6 mmol). The reaction was stirred for 12 hours. The crude product was purified by flash column chromatography (silica, 10% EtOAc/hexanes) to yield the title compound as a colourless oil (155.2 mg, 40%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.77 (t, *J* = 1.4 Hz, 1H, C^1(O)H), 2.60 (td, *J* = 7.1, 1.4 Hz, 2H, C^2-H_2), 2.46 (tt, *J* = 7.0, 2.3 Hz, 2H, C^6-H_2), 2.10 (tt, *J* = 7.1, 2.3 Hz, 2H, C^3-H_2), 1.44 (tt, *J* = 7.5, 7.0 Hz, 2H, C^7-H_2), 1.36 – 1.20 (m, 10H, C^8-H_2 – C^{12}-H_2), 0.86 (t, *J* = 6.8 Hz, 3H, C^{13}-H_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.2 (C^1), 81.7 (C^4 or C^5), 77.8 (C^4 or C^5), 43.1, 31.9, 29.3, 29.2, 29.0 (29.03), 29.0 (29.96), 22.8, 18.8, 14.2, 12.3. Spectral assignments agreed with the literature.[8]

HRAPCI-MS found 195.17417 [calc. for $C_{13}H_{23}O$ $[M+H]^+$ 195.17434]

IR 2924.86, 2854.81, 1727.38, 1688.58 cm^{-1}

TLC R_f = 0.58 (1:4 EtOAc/hexanes), visible as a navy blue spot with vanillin dip (with heat activation)



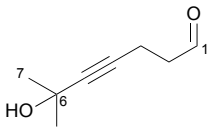
5-(1-cyclohexen-1-yl)pent-4-ynal [873961-38-7] (**3n**) was synthesised according to general procedure ***4.1***, using $Pd(OAc)_2$ (112.3 mg, 0.5 mmol), PMe_3 (1.5 mL, 1.5 mmol), acetone (10 mL), 1-ethynylcyclohexene (**1n**, 588 µL, 5 mmol), and acrolein (**2**, 1.0 mL, 15 mmol). The reaction was stirred for 7 hours. The crude product was purified by flash column chromatography (silica, 5 - 10% EtOAc/hexanes) to yield the title compound as a pale yellow oil (499.8 mg, 62%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.79 (t, *J* = 1.3 Hz, 1H, C^1(O)H), 6.01 – 5.99 (m, 1H, C^7-H), 2.67 – 2.64 (m, 2H, C^2-H_2), 2.62 – 2.59 (m, 2H, C^3-H_2), 2.07 – 2.03 (m, 4H), 1.62 – 1.52 (m, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 200.9 (C^1), 134.2 (C^7), 120.7 (C^6), 84.8 (C^4 or C^5), 83.4 (C^4 or C^5), 42.9 (C^2), 29.5, 25.6, 22.4, 21.6, 12.8 (C^3). Spectral assignments agreed with the literature.[10]

HRESI-MS found 185.0937 [calc. for $C_{11}H_{14}NaO$ $[M+Na]^+$ 185.0937]

IR 2929.13, 2858.37, 1724.33 cm^{-1}

TLC R_f = 0.61 (1:5 EtOAc/hexanes), visible as a navy blue spot with vanillin dip (with heat activation)



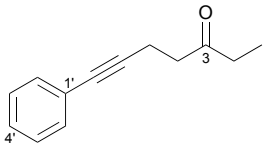
6-hydroxy-6-methylhept-4-ynal [811430-97-4] (**3o**) was synthesised according to general procedure ***4.1***, using $Pd(OAc)_2$ (89.8 mg, 0.4 mmol), PMe_3 (1.2 mL, 1.2 mmol), acetone (8 mL), 2-methylbut-3-yn-2-ol (**1o**, 388 µL, 4 mmol), and acrolein (**2**, 1.0 mL, 15 mmol). The reaction was stirred for 7 hours. The crude product was purified by flash column chromatography (silica, 20 - 50% EtOAc/hexanes) to yield the title compound as a pale yellow oil (274.8 mg, 49%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.77 (t, *J* = 1.2 Hz, 1H, C^1(O)H), 2.64 (td, *J* = 7.3, 1.2 Hz, 2H, C^2-H_2), 2.50 (t, *J* = 7.3 Hz, 2H, C^3-H_2), 1.47 (s, 6H, C^7-H_3). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 200.7 (C^1), 86.2 (C^4 or C^5), or 80.3 (C^4 or C^5), 65.3 (C^6), 42.7 (C^2), 31.7 (C^7), 12.0 (C^3). Spectral assignments agreed with the literature.[8]

HAPCI-MS found 141.09106 [calc. for $C_8H_{13}O_2$ $[M+H]^+$ 141.09101]

IR 3377.65, 2979.40, 2933.58, 1718.76 cm^{-1}

TLC R_f = 0.43 (1:1 EtOAc/hexanes), visible with $KMnO_4$ dip



7-phenylhept-6-yn-3-one [185309-04-0] (**3j**) was synthesised according to a literature procedure.[11] A flame-dried flask with fitted with a stir-bar and charged with $Pd(OAc)_2$ (22.5 mg, 0.1 mmol, 5 mol%). The flask was evacuated under high vacuum, then back-filled with argon. This was repeated two more times. To this was added PMe_3 (1.0 M dissolved in toluene, 0.4 mL, 0.4 mmol, 20 mol%). The flask was stirred at 60 °C in an oil bath for 10 minutes, before addition of acetone (2 mL), and a mixture of phenylacetylene (220 µL, 2 mmol) and ethyl vinyl ketone (396 µL, 4 mmol). The reaction mixture was stirred at 60 °C for 40 hours. The reaction mixture was extracted with ethyl ether (3 x 30 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by flash column chromatography (silica, 15% EtOAc/hexanes) to yield the title compound as an orange oil (283.1 mg, 76%).

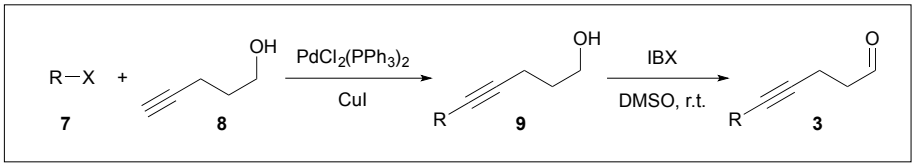
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.35 (m, 2H, arom), 7.28 – 7.24 (m, 3H, arom), 2.74 – 2.64 (m, 4H, C^4-H_2 & C^5-H_2), 2.46 (q, *J* = 7.3 Hz, 2H, C^2-H_2), 1.08 (t, *J* = 7.3 Hz, 3H, C^1-H_3). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 209.4 (C^3), 131.6, 128.3, 127.8, 123.7, 88.8 (C^6), 81.0 (C^7), 41.2 (C^4), 36.1 (C^2), 14.1 (C^5), 7.8 (C^1). Spectral assignments agreed with the literature.[11]

HRAPCI-MS found 187.11168 [calc. for $C_{13}H_{15}O$ $[M+H]^+$ 187.11174]

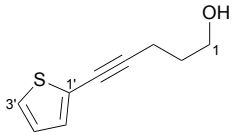
IR 2976.50, 2937.96, 1713.45 cm^{-1}

TLC R_f = 0.49 (1:5 EtOAc/hexanes), visible as a pale yellow spot with 2,4-DNP dip

3.3 *Representative procedure: Substrate Synthesis of **3i***



*3.3.1 Sonogashira Coupling, Synthesis of **9i***



5-(thiophen-2-yl)pent-4-yn-1-ol [124855-50-1] (**9i**) was synthesised according to a modified literature procedure.[12] To a flame-dried flask was added copper iodide (13.9 mg, 0.073 mmol, 5 mol%) and $PdCl_2(PPh_3)_2$ (25.6 mg, 0.037 mmol, 2.5 mol%). The flask was evacuated under high vacuum, and back-filled with argon. This process was repeated two times. To the flask was added 2-iodothiophene (**7i**, 161 µL, 1.46 mmol, 1 equiv.) and triethylamine (7.3 mL). To this was added 4-pentyn-1-ol (**8**, 163 µL, 1.75 mmol, 1.2 equiv.) in a dropwise manner at room temperature. The suspension was stirred at room temperature for 30 minutes, then neutralised by addition of saturated NH_4Cl solution (30 mL). The mixture was transferred to a sepatory funnel and extracted with dichloromethane (3 x 40 mL). The combined organic extracts were washed with water and brine, then dried over $NaSO_4$. Evaporation *in vacuo* returned the crude product. The compound was purified by column chromatography (silica, 10 – 40% EtOAc/hexanes) to return the title compound as an orange oil (110.9 mg, 46%).

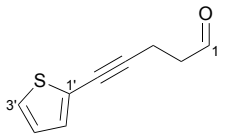
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (dd, *J* = 5.2, 1.0 Hz, 1H, $C^{3'}$-H), 7.11 (br d, *J* = 3.5 Hz, 1H, $C^{5'}$-H), 6.92 (dd, *J* = 5.2, 3.5 Hz, 1H, $C^{4'}$-H), 3.78 (t, *J* = 6.2 Hz, 2H, C^1-**H**$_2$), 2.54 (t, *J* = 7.0 Hz, 2H, C^3-H_2), 2.03 (br s, 1H, C^1-O**H**), 1.84 (app qn, *J* = 6.7 Hz, 2H, C^2-H_2). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 131.2 ($C^{5'}$), 126.9 ($C^{4'}$), 126.2 ($C^{3'}$), 123.9 ($C^{1'}$), 93.6 (C^4 or C^5), 74.3 (C^4 or C^5), 61.7 (C^1), 31.3 (C^2), 16.3 (C^3). Spectral assignments agreed with the literature.[13] The alkyne starting material **8** is present as an inseparable impurity, accounting for 21% of the product mass. This impurity accounts for the peaks in the ^{1}H NMR spectrum at δ 3.74 (t, 2H), 2.31 (td, 2H), 1.97 (t, 1H), 1.77 (tt, 2H), and in the ^{13}C NMR spectrum at δ 84.0, 68.9, 60.9, 31.1 and 14.9.

HRESI-MS found 167.05279 [calc. for $C_9H_{11}OS$ $[M+H]^+$ 167.05251]

IR 3298.07, 2947.44, 2877.44 cm^{-1}

TLC R_f = 0.48 (1:1 EtOAc/hexanes), visible under UV, and with $KMnO_4$ dip

*3.3.2 Oxidation, Synthesis of **3i***



5-(thiophen-2-yl)pent-4-ynal (**3i**) was synthesised according to a modified literature procedure.[12] A solution of 5-(thiophen-2-yl)pent-4-yn-1-ol (**9i**, 109.2 mg, 0.66 mmol, 1 equiv.), 2-iodoxybenzoic acid (IBX, 220.7 mg, 0.78 mmol, 1.2 equiv.) in DMSO (3.3 mL) was stirred at room temperature for 16 hours. The solution was diluted with H_2O (50 mL), and the mixture was extracted with EtOAc (3 x 40 mL). The combined organic extracts were washed with $NaHCO_3$ (3 x 40 mL), H_2O and brine, dried over $NaSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography (silica, 10 – 15%, EtOAc/hexanes) to yield the title compound as an orange oil (63.2 mg, 58%).

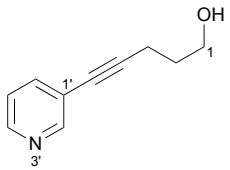
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.83 (s, 1H, C^1(O)H), 7.18 (dd, *J* = 5.2, 1.2 Hz, 1H, $C^{3'}$-H), 7.12 (dd, *J* = 3.6, 1.2 Hz, 1H, $C^{5'}$-H), 6.93 (dd, *J* = 5.2, 3.6 Hz, 1H, $C^{4'}$-H), 2.77 – 2.75 (m, 4H, C^2-H_2 & C^3-H_2). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 200.3 (C^1), 131.5 ($C^{5'}$), 126.9 ($C^{4'}$), 126.5 ($C^{3'}$), 123.5 ($C^{1'}$), 91.9 (C^4 or C^5), 74.7 (C^4 or C^5), 42.5 (C^2), 13.0 (C^3).

HRAPCI-MS found 165.03705 [calc. for C_9H_9OS $[M+H]^+$ 165.03686], found 197.06328 [calc. for $C_{10}H_{13}O_2S$ $[M+MeOH]^+$ 197.06308]

IR cm^{-1} 3105.83, 2905.24, 2828.27, 2727.71, 1720.66 cm^{-1}

TLC R_f = 0.46 (1:5, EtOAc/hexanes), visible under UV, and as a yellow spot with 2,4-DNP dip

3.4 *Synthesis and data of substrates **3h, 3k, 3l, 3m***



5-(pyridine-3-yl)pent-4-yn-1-ol [138745-76-3] (**9h**) was synthesised according to representative procedure ***4.3.1***, using copper iodide (13.9 mg, 0.073 mmol, 5 mol%), $PdCl_2(PPh_3)_2$ (25.6 mg, 0.037 mmol, 2.5 mol%), 3-iodopyridine (**7h**, 300.0 mg, 1.46 mmol, 1 equiv.) and triethylamine (7.3 mL). To this was added 4-pentyn-1-ol (**8**, 163 µL, 1.75 mmol, 1.2 equiv.). After addition of the reagents the mixture was heated to 90 °C for 30 minutes before neutralisation and work-up. The crude reaction mixture was purified by flash column chromatography (silica, 20 – 50% EtOAc/hexanes) to yield the title compound as a yellow oil (158.9 mg, 68%).

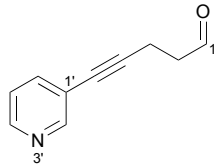
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.58 (s, 1H, $C^{2'}$-H), 8.44 (br d, *J* = 4.9 Hz, 1H, $C^{4'}$-H), 7.64 (dt, *J* = 7.9, 1.9 Hz, 1H, $C^{6'}$-H), 7.19 (dd, *J* = 7.9, 4.9 Hz, 1H, $C^{5'}$-H), 3.79 (t, *J* = 6.2 Hz, 2H, C^1-**H_2**), 3.04 (br s, 1H, C^1-O**H**), 2.53 (t, *J* = 7.0 Hz, 2H, C^3-H_2), 1.84 (tt, *J* = 7.0, 6.2 Hz, 2H, C^2-H_2). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 152.1 ($C^{2'}$), 147.8 ($C^{4'}$),

138.7 ($C^{6'}$), 123.1 ($C^{5'}$), 121.2 ($C^{1'}$), 93.5 (C^4 or C^5), 77.6 (C^4 or C^5), 61.2 (C^1), 31.4 (C^2), 16.0 (C^3). Spectral assignments agreed with the literature.[12, 13]

HRESI-MS found 162.09177 [calc. for $C_{10}H_{12}ON$ $[M+H]^+$ 162.09134]

IR 3306.26, 2945.42, 2869.35 cm^{-1}

TLC R_f = 0.38 (EtOAc), visible under UV, and with $KMnO_4$ dip



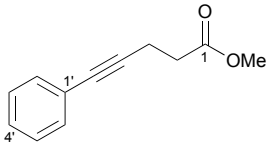
5-(pyridin-3-yl)pent-4-ynal [1422747-52-1] (**3h**) was synthesised according to representative procedure ***4.3.2***, using 5-(pyridine-3-yl)pent-4-yn-1-ol (**9h**, 156 mg, 0.97 mmol, 1 equiv.), IBX (325.4 mg, 1.16 mmol, 1.2 equiv.) and DMSO (5 mL). The crude product was purified using flash column chromatography (silica, 25 – 45% EtOAc/hexanes) to yield the title compound as an orange oil (71.1 mg, 46%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (t, *J* = 1.0 Hz, 1H, C^1(O)H), 8.60 (br s, 1H, $C^{2'}$-H), 8.48 (dd, *J* = 4.9, 1.7 Hz, 1H, $C^{4'}$-H), 7.65 (ddd, *J* = 7.9, 2.0, 1.7 Hz, 1H, $C^{6'}$-H), 7.21 (ddd, *J* = 7.9, 4.9, 0.9, 1H, $C^{5'}$-H), 2.80 – 2.72 (m, 4H, C^2-H_2 & C^3-H_2). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 200.1 (C^1), 152.3 ($C^{2'}$), 148.2 ($C^{4'}$), 138.7 ($C^{6'}$), 123.1 ($C^{5'}$), 120.7 ($C^{1'}$), 91.6 (C^4), 78.2 (C^5), 42.5 (C^2), 12.7 (C^3).

HRESI-MS found 160.07603 [calc. for $C_{10}H_{10}ON$ $[M+H]^+$ 160.07569]

IR 2908.37, 2830.75, 2729.74, 1722.34 cm^{-1}

TLC R_f = 0.10 (1:5 EtOAc/hexanes), visible under UV, and as a yellow spot with 2,4-DNP dip



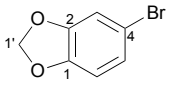
Methyl 5-phenylpent-4-ynoate [30780-51-9] (**3k**) was synthesised according to representative procedure ***4.3.1***, using methyl pent-4-ynoate (210.7 mg, 1.88 mmol, 1.2 equiv.), iodobenzene (**7k**, 172 µL, 1.54 mmol, 1 equiv.), copper iodide (29.7 mg, 0.16 mmol, 10 mol%), $PdCl_2(PPh_3)_2$ (54.8 mg, 0.078 mmol, 5 mol%) and triethylamine (10 mL). The product was purified by flash column chromatography (silica, 10 – 15% EtOAc/hexanes) to yield the title compound as a yellow oil (135.2 mg, 47%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.38 (m, 2H, arom), 7.29 – 7.27 (m, 3H, arom), 3.72 (s, 3H, C^1(O)OC**H**$_3$), 2.74 (t, *J* = 7.6 Hz, 2H, C^2-H_2), 2.64 (t, *J* = 7.6, 2H, C^3-H_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5 (C^1), 131.7 (arom), 128.3 (arom), 127.9 (arom), 123.6 (arom), 88.1 (C^4 or C^5), 81.3 (C^4 or C^5), 52.0 (C^1(O)O**C**H$_3$), 33.6 (C^2), 15.5 (C^3). Spectral assignments agreed with the literature.[11]

HRESI-MS found 211.0727 [calc. for $C_{12}H_{12}NaO_2$ $[M+Na]^+$ 211.0730]

IR 2952.11, 1735.87 cm^{-1}

TLC R_f = 0.40 (1:5 EtOAc/hexanes), visible under UV, and as an orange spot with vanillin dip (with heat activation)



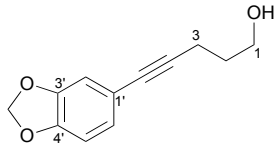
5-bromobenzo[d][1,3]dioxole [2635-13-4] (**7c**) was synthesised according to a literature procedure.[14] N-bromosuccinamide (540 mg, 3 mmol, 1 equiv.), $AuCl_3$ (4.5 mg, 0.015 mmol, 0.5 mol%), benzo[*d*][1,3]dioxole (344 µL, 3 mmol, 1 equiv.) and DCE (5 mL) were added to a flame-dried, 20 mL flask. The reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was then concentrated *in vacuo* and purified by flash column chromatography (silica, 5% EtOAc/hexanes) to yield the title compound as a pale yellow oil (377.5 mg, 63%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.95 (s, 1H, C^3-H), 6.94 (dd, *J* = 9.0, 2.0 Hz, 1H, C^5-H), 6.68 (d, *J* = 9.0 Hz, 1H, C^6-H). 5.96 (s, 2H, $C^{1'}$-H_2). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 148.7 (C^2), 147.1 (C^1), 124.4 (C^5), 113.1 (C^4), 112.4 (C^3), 109.6 (C^6), 101.7 ($C^{1'}$). Spectral assignments agreed with the literature.[14]

HRAPCI-MS found 199.9471 [calc. for $C_7H_5BrO_2$ $[M\text{-}e]^+$ 199.9467]. Measured isotopic pattern (199.95 (97%), 200.95 (19%), 201.95 (100%), 202.95 (22%)) consistent with predicted isotopic ratio

IR 2893.61, 1499.82, 1468.96 cm^{-1}

TLC R_f = 0.71 (1:5, EtOAc/hexanes), visible under UV



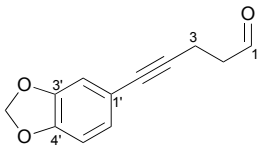
5-(benzo)[d][1,3]dioxol-5-yl)pent-4-yn-1-ol [1122011-56-6] (**9c**) was synthesised according to a modified literature procedure.[15] A solution of 5-bromobenzo[d][1,3]dioxole (**7c**, 250.0 mg, 1.24 mmol, 1 equiv.) in freshly distilled n-butylamine (5 mL) was prepared. To this was added 4-pentyn-1-ol (**8**, 139 µL, 1.49 mmol, 1.2 equiv.), copper iodide (23.6 mg, 0.12 mmol, 10 mol%) and $PdCl_2(PPh_3)_2$ (43.5 mg, 0.062 mmol, 5 mol%). The resulting solution was heated at reflux for 16 hours. The reaction was cooled to room temperature, diluted with water (50 mL) and extracted with Et_2O (3 x 40 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography (silica, 50% EtOAc/hexanes) to yield an orange oil (125.3 mg, 49%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89 (dd, *J* = 8.0, 1.6 Hz, 1H, $C^{6'}$-H), 6.83 (d, *J* = 1.6 Hz, 1H, $C^{2'}$-H), 6.70 (d, *J* = 8.0 Hz, 1H, $C^{5'}$-H), 5.93 (s, 2H, $C^{3'}$-OC**H**$_2$O-$C^{4'}$), 3.78 (t, *J* = 6.2 Hz, 2H, C^1-**H**$_2$), 2.49 (t, *J* = 7.0 Hz, 2H, C^3-H_2), 1.96 (br s, 1H, C^1-O**H**), 1.82 (tt, *J* = 7.0, 6.2 Hz, 2H, C^2-H_2). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.4 (147.43, $C^{3'}$ or $C^{4'}$), 147.4 (147.38, $C^{3'}$ or $C^{4'}$), 126.0 (arom), 117.1 (arom), 111.7 (arom), 108.4 (arom), 101.3 ($C^{3'}$-O**C**H_2O-$C^{4'}$), 87.6 (C^4 or C^5), 80.9 (C^4 or C^5), 61.8 (C^1), 31.5 (C^2), 16.0 (C^3). Spectral assignments agreed with the literature.[15]

HRAPCI-MS found 205.08599 [calc. for $C_{12}H_{13}O_3$ $[M+H]^+$ 205.08592]

IR 3390.67, 2931.61, 2898.43, 1734.38 cm^{-1}

TLC R_f = 0.40 (1:1, EtOAc/hexanes), visible under UV and with $KMnO_4$ dip



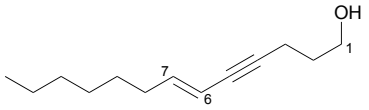
5-(benzo[d][1,3]dioxol-5-yl)pent-4-ynal [114092-52-3] (**3c**) was synthesised according to representative procedure ***4.3.2***, using 5-(benzo)[*d*][1,3]dioxol-5-yl)pent-4-yn-1-ol (**9c**, 125.3 mg, 0.61 mmol, 1 equiv.), IBX (207.2 mg, 0.74 mmol, 1.2 equiv.) and DMSO (3 mL). The crude product was purified by flash column chromatography (silica, 20 – 25% EtOAc/hexanes) to yield the title compound as yellow crystals (98.5 mg, 78%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.83 (t, *J* = 1.0 Hz, 1H, C^1(O)H), 6.89 (dd, *J* = 8.1, 1.6 Hz, 1H, $C^{6'}$-H), 6.82 (d, *J* = 1.6 Hz, 1H, $C^{2'}$-H), 6.71 (d, *J* = 8.0 Hz, 1H, $C^{5'}$-H), 5.94 (s, 2H, $C^{3'}$-OC**H**$_2$O-$C^{4'}$), 2.76 – 2.68 (m, 4H, C^3-H_2 & C^2-H_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.6 (C^1), 147.6 ($C^{3'}$ or $C^{4'}$), 147.4 ($C^{3'}$ or $C^{4'}$), 126.1 (arom), 116.7 (arom), 111.7 (arom), 108.4 (arom), 101.3 ($C^{3'}$-O**C**H_2O-$C^{4'}$), 86.1 (C^4 or C^5), 81.3 (C^4 or C^5), 42.8 (C^2), 12.8 (C^3).

HRESI-MS found 225.0519 [calc. for $C_{12}H_{10}NaO_3$ $[M+Na]^+$ 225.0522]

IR 2907.82, 2845.71, 1715.89 cm^{-1}

TLC R_f = 0.66 (1:1, EtOAc/hexanes), visible under UV and as a yellow spot with 2,4-DNP dip



(E)-tridec-6-en-4-yn-1-ol (**9m**) was synthesised according to a modified literature procedure.[16] Copper iodide (38.1 mg, 0.20 mmol, 10 mol%) and $Pd(PPh_3)_2Cl_2$ (22.5 mg, 0.10 mmol, 5 mol%) were added to a flame-dried schlenk flask. The flask was evacuated under high vacuum and back-filled with argon before adding pent-4-yn-1-ol (**8**, 186 µL, 2.0 mmol, 1 equiv.), (*E*)-1-iodooct-1-ene (**7m**, 381 µL, 2.4 mmol, 1.2 equiv.), NEt_3 (5 mL) and THF (5 mL). The resulting mixture was degassed using three freeze-pump-thaw cycles. The reaction was heated to 80 °C for 2 hours. The reaction was quenched with saturated NH_4Cl solution(10 mL) and extracted with DCM (3 x 40 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography (silica, 15 – 20% EtOAc/hexanes) to yield the title compound as a yellow oil (253.9 mg, 1.31 mmol, 65%).

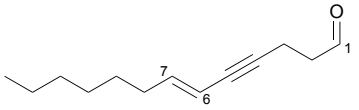
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.04 (dt, *J* = 15.8, 7.1 Hz, 1H, C^7-H), 5.42 (dt, *J* = 15.8, 1.8 Hz, 1H, C^6-H), 3.74 (t, *J* = 6.1 Hz, 2H, C^1-**H**$_2$), 2.40 (td, *J* = 6.9, 1.8 Hz, 2H, C^3-H_2), 2.09 – 2.03 (m, 2H, C^8-H_2), 1.76 (tt, *J* = 6.8, 6.2 Hz, 2H, C^2-H_2), 1.70 (br s, 1H, C^1-O**H**), 1.37 – 1.23 (m, 2H, C^9-H_2 – C^{12}-H_2), 0.87 (t, *J* = 6.8 Hz, 3H, C^{13}-H_2). **^{13}C**

NMR (125 MHz, $CDCl_3$) δ 144.0 (C^7), 109.6 (C^6), 87.6 (C^4 or C^5), 80.0 (C^4 or C^5), 62.0 (C^1), 33.1, 31.8, 31.5, 28.9, 22.7, 16.1, 14.2 + obscured peak.

HRESI-MS found 195.17423 [calc. for $C_{13}H_{23}O$ $[M+H]^+$ 195.17434]

IR 3329.94, 2924.91, 2855.18 cm^{-1}

TLC R_f = 0.62 (1:1, EtOAc/hexanes), visible under UV and with $KMnO_4$ dip



(E)-tridec-6-en-4-ynal (**3m**) was synthesised according to representative procedure ***4.3.2***, using (*E*)-tridec-6-en-4-yn-1-ol (**9m**, 253.9 mg, 1.31 mmol, 1 equiv.), IBX (439.6 mg, 1.57 mmol, 1.2 equiv.) and DMSO (10 mL). The product, a yellow oil, was sufficiently clean without further purification (226.6 mg, 1.18 mmol, 90%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.79 (t, *J* = 1.2 Hz, 1H, C^1(O)H), 6.05 (dt, *J* = 15.8, 7.1 Hz, 1H, C^7-H), 5.41 (dt, *J* = 15.8, 2.0 Hz, 1H, C^6-H), 2.68 – 2.65 (m, 2H, C^2-H_2 or C^3-H_2), 2.62 – 2.59 (m, 2H, C^2-H_2 or C^3-H_2), 2.08 – 2.04 (m, 2H, C^8-H_2), 1.38 – 1.23 (m, 8H, C^9-H_2 – C^{12}-H_2), 0.87 (t, *J* = 6.8 Hz, 3H, C^{13}-H_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.8 (C^1), 144.5 (C^7), 109.4 (C^6), 86.0 (C^4 OR C^5), 80.3 (C^4 OR C^5), 42.8, 33.1, 31.8, 28.9 (28.90), 28.9 (28.85), 22.7, 14.2, 12.8.

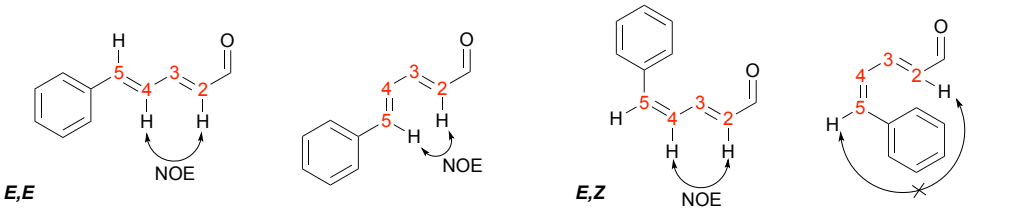
HRESI-MS found 215.1405 [calc. for $C_{13}H_{20}NaO$ $[M+Na]^+$ 215.1406], found 247.1670 [calc. for $C_{14}H_{24}NaO_2$ [M+MeOH+Na]+ 247.1669]

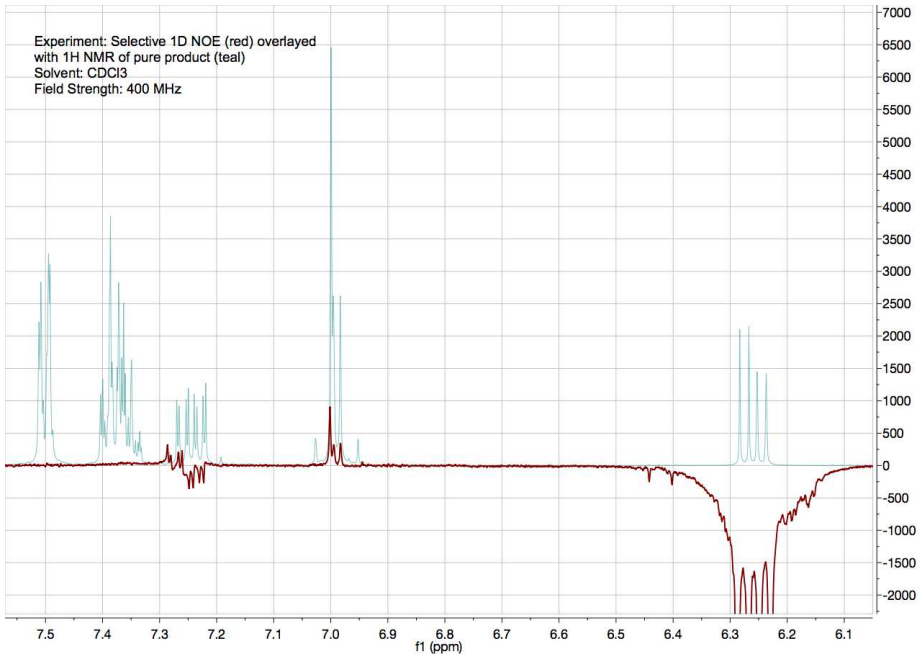
IR 2925.36, 2855.21, 1726.47 cm^{-1}

TLC R_f = 0.53 (1:5, EtOAc/hexanes), visible under UV and as a yellow spot with 2,4-DNP dip

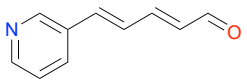
4 Stereochemical Assignments

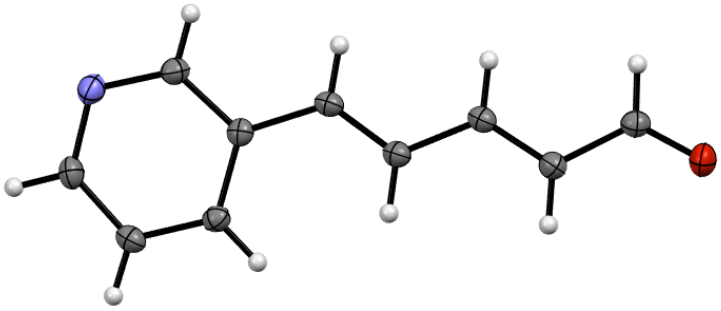
1D-selective NOE experiments were conducted on (2*E*,4*E*)-5-phenylpenta-2,4-dienal, to moderate success. The trans stereochemistry of the bond comprising C^2 and C^3 is evident due to a coupling constant of 15.1 Hz. However, the stereochemistry of the bond comprising C^4 and C^5 is difficult to ascertain because the proton resonances are deceptively simple. It was reasoned that if the resonance for proton H^2 was saturated, and an NOE was observed between H^2 and H^5 – the only way such a through-space interaction could exist was if the stereochemistry is trans-trans as predicted. The peaks corresponding to the position of proton H^3 in the 1D-selective NOE experiment have a dispersive quality (positive and negative regions), this is rationalised by the occurrence of zero-quantum coherence due to strong *J*-coupling with the saturated peak.





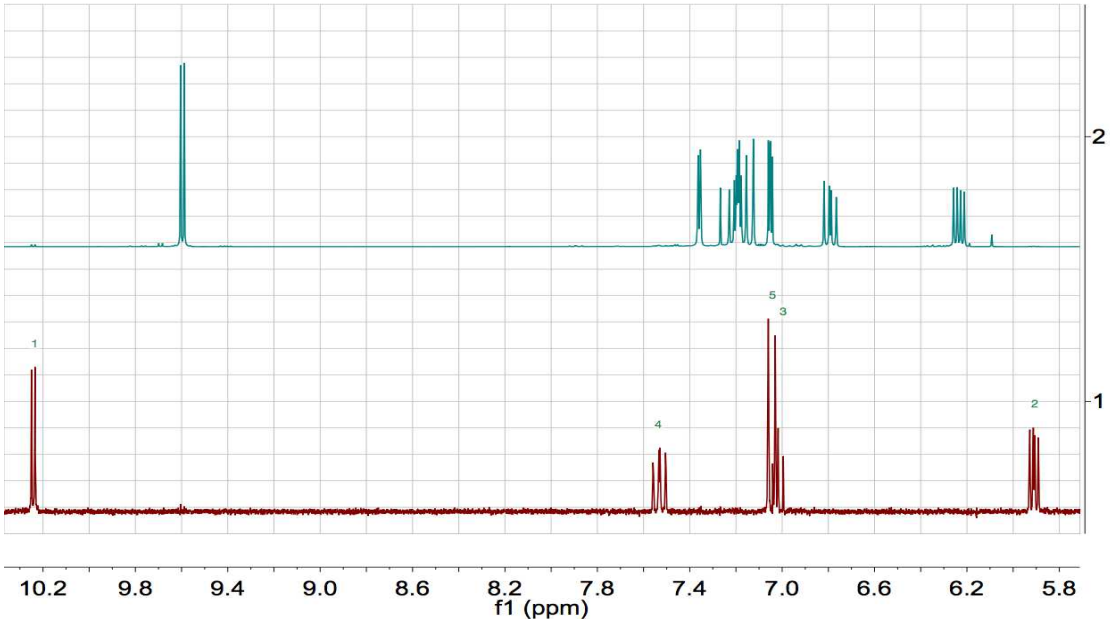
A more definitive stereochemical assignment was achieved by crystallising the product (2*E*,4*E*)-5-(pyridine-3-yl)penta-2,4-dienal (**4h**), and solving the single crystal X-ray structure. Assignments for all other reaction products were made by analogy.





Stereochemical assignments of the minor isomers for each product were made by analysing the coupling constants in the alkenic region. To enhance and identify these minor peaks in the crude ^{1}H NMR spectra 1D-selective TOCSY NMR was utilised. Irradiation of the aldehyde peaks of the minor isomers revealed spectra representing the aldehyde-diene spin system.

A representative example is shown below for *(2E,4E)-5-(thiophen-2-yl)penta-2,4-dienal* (**4i**). The top spectrum (teal coloured) represents the ^{1}H NMR spectrum of the purified major (*E*,*E*)-isomer.



Selective saturation of the resonance at 10.24 using a 1D selective ^{1}H-TOCSY pulse sequence elucidates the spectrum corresponding to the minor (*Z*,*E*)-isomer (bottom spectrum, maroon coloured). The product was characterised by analysing the coupling constants of the olefinic resonances.

5 References

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