

Fast and efficient one step synthesis of dienamides†

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Received 28th January 2009, Accepted 19th March 2009

First published as an Advance Article on the web 16th April 2009

DOI: 10.1039/b901797f

A fast and efficient one-step approach to the synthesis of dienamides is reported. This concise methodology relies on the use of imides as reactive intermediates and allows for the preferential formation of *Z,E*-dienamides in good yields.

Introduction

Dienamides have been long recognised as key reactive intermediates due to their great diversity, synthetic potential and occurrence in nature. Dienamides have been effectively used both as electron rich and electron poor dienes in Diels–Alder reactions.¹ Dienamide based Diels–Alder reactions are regioselective and have also been used recently in asymmetric cycloadditions.²

Acyclic dienamides are also key constituents in a number of biologically active natural products and pharmaceutically relevant units. Examples of these include palmerolide **1**, the lituarines **2**, bacillaene **3**, the retinoidal dienamide **4** and ariakemicins **5** and **6** (Fig. 1).³

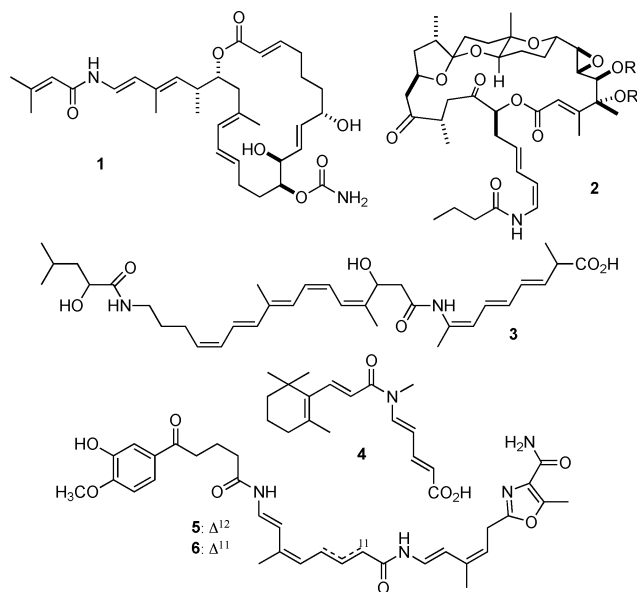


Fig. 1 Dienamide-containing biologically active compounds.

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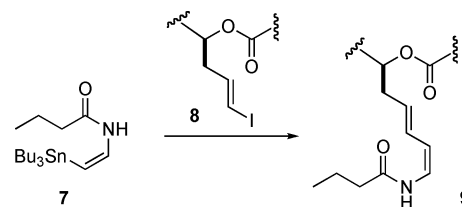
† Electronic supplementary information (ESI) available: Spectral data. CCDC reference number 702660. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b901797f

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Despite their synthetic utility and biological potential, the synthetic routes available for the synthesis of dienamides are limited.⁴ A number of recent approaches to the synthesis of dienamide-containing natural products have relied on the use of the Buchwald palladium–copper catalysed protocol originally developed for the synthesis of enamides.⁵ As demonstrated by Nicolaou and Chen's synthesis of palmerolide **1**, the yields obtained during the actual palladium coupling have proven to be varied and highly dependent on the nature of the coupling partners.⁶

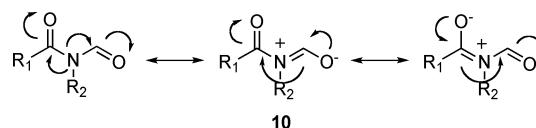
A very interesting approach to the synthesis of *Z,E*-dienamides was recently disclosed by Smith and co-workers as part of their groundbreaking synthesis of lituarine **2**.⁷ Smith's approach to the key *Z,E*-dienamide unit **9** relied on the Stille coupling of a *Z*-stannyl enamide unit **7** with the required *E*-vinyl iodide partner **8** (Scheme 1). Although the coupling was highly successful, the synthesis of the stannyl enamide unit **7** using palladium–copper methodology proved to be very low yielding.



Scheme 1

Results and discussion

In a previous contribution, we reported the use of *N*-formyl imides **10** as *pseudo*-aldehydes.⁸ We have hypothesised that *N*-formyl imides behave as aldehydes due to the presence of the second carbonyl unit, which effectively ties up the nitrogen lone pair (Scheme 2).

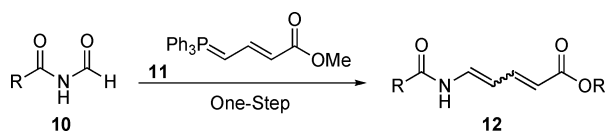


Scheme 2

We would like to report an efficient one step synthesis of dienamide units starting from our previously developed *N*-formyl

imide building blocks. We believe that this approach is an attractive alternative to other methods available currently in terms of the number of steps, yield and overall simplicity.

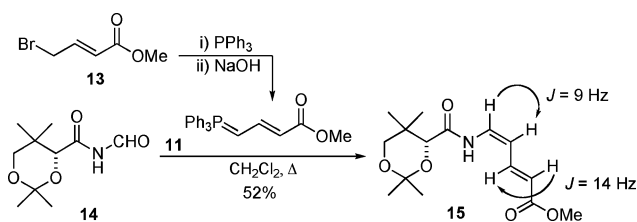
Our one-step approach to the synthesis of dienamides **12** relies on the olefination of *N*-formyl imides through the use of the conjugated ylide **11**.⁹ It was reasoned that the ylide's existing internal double bond geometry would be transposed completely onto the dienamide unit, while the geometry of the double bond generated would be determined by the rate of elimination during the olefination reaction (Scheme 3).



Scheme 3

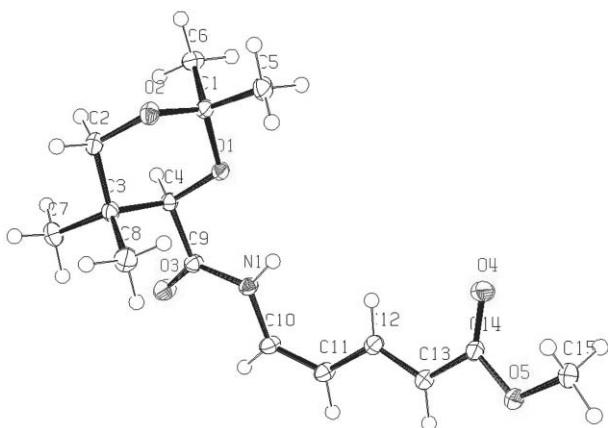
The conjugated phosphorus ylide **11** was synthesised from (*E*)-methyl bromocrotonate **13** in two steps by reaction with triphenylphosphine and deprotonation of the resulting phosphonium salt.

Treatment of the previously generated imide **14** with the conjugated ylide **11** in refluxing dichloromethane afforded the desired dienamide **15** as a single *Z,E* diastereomer in excellent yield. Interestingly, the reaction also proceeded when water was used as a solvent, albeit in a much lower yield (Scheme 4).



Scheme 4

The double bond geometries of the newly generated dienamide **15** were determined unambiguously through ¹H NMR (*J* = 9 Hz and *J* = 14 Hz for the *Z* and *E* double bonds respectively), and crystallographic analysis† (Fig. 2).¹⁰

Fig. 2 Crystal structure of dienamide **15**.

Having successfully generated the desired dienamide unit **15**, the scope and reproducibility of the methodology was explored by applying the same reaction conditions to other imide units (Scheme 5). The imide starting materials were accessed from the corresponding amide starting materials using our previously reported conditions using either acetic formic anhydride (for lactams **16–18**) or *n*-BuLi, *N*-formyl benzotriazole (for amides **14, 19–22**).⁸

Entry	Starting imide	Dienamide	Yield	Ratio (<i>Z,E</i> : <i>E,E</i>)
1)			52 %	(100:0)
2)			56 %	(100:0)
3)			35 %	(10:1)
4)			56 %	(4:1)
5)			97 %	(60:37)
6)			87 %	(3:2)
7)			41 %	(100:0)
8)			42 %	(100:0)

Scheme 5

We are pleased to report that olefination of imides **14, 16–22** with ylide **11** under standard conditions proceeded to generate the desired dienamides **15, 23–29** in good to excellent yields. Interestingly, in all cases, the dienamides obtained exhibited the key *Z,E*-dienamide geometry as either the major or the sole product.

The selectivity of the olefination used to generate the *Z,E*-dienamides is both surprising and unprecedented. Olefination reactions of aldehydes using conjugated ylide **11** have resulted previously in the successful and efficient synthesis of dienes with a marked preference for the generation of *E,E*-dienes.¹¹

The interesting selectivity obtained during the imide olefination could be explained by considering either the geometry of the *N*-formyl group, or by looking at the relative stability

of the intermediate species. The results show that as we move to a larger lactam ring (entries 2 to 4 in Scheme 5) and to aromatic systems (entries 5 and 6), the *E* product increases, which would suggest increased stabilisation of the olefination intermediates. In the aromatic-containing examples, the *E* ratios obtained could be accounted for by invoking an interaction between the aromatic ring and the phenyl rings on the Wittig reagent which could stabilise the olefination intermediate. In the case of the aliphatic ring systems, however, the increase in the *E* ratios observed could not be explained in this fashion. If anything, the larger ring system would have the opposite effect as described by Schlosser and Schaub in their olefination studies.¹² Furthermore, the fact that in the case of the α,β -unsaturated system none of the *E*-olefin is observed adds weight to the view that stabilisation of the olefination intermediates is not taking place.

From these observations, it would seem likely that the effect of the parent amide on the conformation of the starting *N*-formyl unit is the biggest determinant of the selectivity obtained during the olefination.

We are currently in the process of conducting modelling studies, which we believe will shed light on the factors affecting the selectivities observed during the olefination.

Conclusions

In conclusion, this is a fast, flexible and rapid approach for the synthesis of the *Z,E*-dienamide units and reinforces the potential of *N*-formyl imides as useful synthetic intermediates. The methodology is concise and is amenable to the synthesis of substituted dienamides not readily accessible through other methods. We are in the process of applying this methodology in natural product synthesis.

Experimental

General methods

All reactions were performed in oven-dried glassware under an inert argon atmosphere unless otherwise stated. Tetrahydrofuran (THF), diethyl ether, and dichloromethane (DCM) were purified through a Pure Solv 400–5MD solvent purification system (Innovative Technology, Inc). All reagents were used as received, unless otherwise stated. Solvents were evaporated under reduced pressure at 40 °C using a Buchi Rotavapor.

IR spectra were recorded as thin films on NaCl plates using a JASCO FT/IR410 Fourier Transform spectrometer. Only significant absorptions (ν_{\max}) are reported in wavenumbers (cm^{-1}).

Proton magnetic resonance spectra (^1H NMR) and carbon magnetic resonance spectra (^{13}C NMR) were respectively recorded at 400 MHz and 100 MHz using a Bruker DPX Avance400 instrument. Chemical shifts (δ) are reported in parts per million (ppm) and are referenced to the residual solvent peak. The order of citation in parentheses is (1) number of equivalent nuclei (by integration), (2) multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad, dm = double multiplet), and (3) coupling constant (*J*) quoted in Hertz to the nearest 0.5 Hz.

High resolution mass spectra were recorded on a JEOL JMS-700 spectrometer by electrospray and chemical ionisation mass

spectrometer operating at a resolution of 15000 full widths at half height.

Flash chromatography was performed using silica gel (Apollo Scientific Silica Gel 60, 40–63 micron) as the stationary phase. TLC was performed on aluminium sheets pre-coated with silica (Merck Silica Gel 60 F₂₅₄). The plates were visualised by the quenching of UV fluorescence (λ_{\max} 254 nm) and/or by staining with either anisaldehyde, potassium permanganate, iodine or cerium ammonium molybdate followed by heating.

***N*-Formyl benzotriazole.** A suspension of benzotriazole (50.4 mmol) in dry dichloromethane (90 mL) was cooled to 0 °C in an ice bath, and formic acid (60.4 mmol) and diisopropylcarbodiimide (70.6 mmol) were added sequentially. The reaction mixture was warmed up slowly to room temperature and stirred for 18 h. The resulting white precipitate was removed by filtration, and the filtrate was concentrated under reduced pressure to give a crude white solid. The white solid was triturated in a solution of 30% ethyl acetate in petroleum ether (150 mL) and the remaining white solid was removed by filtration. The filtrate was concentrated under reduced pressure to give 6.22 g (84%) of *N*-formyl benzotriazole as a white solid.

^1H NMR (400 MHz, CDCl_3) δ : 9.80 (1H, s), 8.18 (1H, d, *J* = 8.2 Hz), 8.09 (1H, d, *J* = 8.2 Hz), 7.64 (1H, dt, *J* = 8.1, 0.8 Hz), 7.51 (1H, dt, *J* = 8.2, 0.8 Hz).

Imides **14**, and **19–22** were synthesised using the protocol previously reported by our group.⁸

General conditions for formation of the cyclic lactam-derived imides 16–18. Sodium formate (0.44 mol) was dried under vacuum at 130 °C for 24 hours. The dry sodium formate was suspended in dry diethyl ether (30 mL), and acetyl chloride (1.0 eq.) was added quickly. The resulting solution was then stirred at room temperature under argon overnight. The reaction mixture was treated with the relevant lactam (0.1 eq.) and the solution was stirred at 60 °C overnight. The reaction mixture was cooled down to room temperature and concentrated under reduced pressure to give a white solid which was taken up in dichloromethane (150 mL) and filtered to remove the insoluble salt by-product. The filtrate was washed with water (100 mL) and the aqueous phase was extracted into dichloromethane (50 mL). The combined organic phases were dried over anhydrous sodium sulfate and concentrated under reduced pressure to give a crude brown oil. Purification of the crude oil by column chromatography (silica gel, 20% ethyl acetate/petroleum ether) gave the previously reported imides (**16–18**) as colourless oils.⁸

16. ^1H NMR (400 MHz, CDCl_3) δ : 9.11 (1H, s), 3.75 (2H, t, *J* = 7.2 Hz), 2.62 (2H, t, *J* = 8.1 Hz), 2.15 (2H, qn, *J* = 7.8 Hz). ^{13}C NMR (100 MHz, CDCl_3) δ : 176.9, 160.3, 45.3, 32.1, 17.8.

17. ^1H NMR (400 MHz, CDCl_3) δ : 9.53 (1H, s), 3.65 (2H, bt, *J* = 4.6 Hz), 2.62 (2H, bt, *J* = 6.9 Hz), 1.88 (4H, appqn, *J* = 3.4 Hz). ^{13}C NMR (100 MHz, CDCl_3) δ : 173.3, 162.9, 41.9, 33.4, 21.8, 20.3.

18. ^1H NMR (400 MHz, CDCl_3) δ : 9.11 (1H, s), 3.75 (2H, m), 2.69–2.72 (2H, m), 1.81–1.83 (4H, m), 1.71–1.72 (2H, m). ^{13}C NMR (100 MHz, CDCl_3) δ : 178.0, 162.1, 39.6, 37.9, 29.3, 28.7, 23.3.

3-Methyl but-2-enamide. A suspension of 3,3-dimethylacrylic acid (19.9 mmol) in dry dichloromethane (50 mL) was cooled to 0 °C in an ice-bath before being treated with a catalytic amount of dimethylformamide (20 µL). Oxalyl chloride (20.9 mmol) was then added dropwise over 2 min and the resulting reaction mixture was stirred at 0 °C for 15 min. The reaction was allowed to warm up to room temperature, and then stirred for a further 90 minutes. Dichloromethane (50 mL), which had been saturated with ammonia gas for 1 h was then cannulated into the reaction. After stirring for an additional 5 min, the reaction mixture was quenched with water (40 mL) and the aqueous phase was extracted with dichloromethane (2 × 30 mL). The combined organic phases were dried over anhydrous sodium sulphate, and concentrated under reduced pressure to give 696 mg (35%) of 3-methyl but-2-enamide as a yellow solid, which could be used without any further purification.

¹H NMR (400 MHz, CDCl₃) δ: 5.56 (1H, sept, *J* = 1.2 Hz), 5.35 (2H, bs), 2.09 (3H, d, *J* = 1.2 Hz), 1.79 (3H, d, *J* = 1.2 Hz). ¹³C NMR (100 MHz, CDCl₃) δ: 168.4, 151.5, 116.6, 26.2, 18.8. *ν*_{max} (neat)/cm⁻¹; 3360, 3292, 3174, 1674, 1610 cm⁻¹.

***N*-Formyl-3-methylbut-2-enamide, 21.** To a 0 °C suspension of vacuum-dried amide (50.4 mmol) in dry tetrahydrofuran (10 mL) was added *n*-butyl lithium (55.5 mmol), and the reaction mixture was stirred at room temperature for 90 min. The reaction mixture was cooled down to 0 °C and a solution of *N*-formyl benzotriazole (60.5 mmol) in dry tetrahydrofuran (10 mL) was added in small amounts. The resulting solution was allowed to warm to room temperature and was stirred overnight. The reaction mixture was diluted with *t*-butyl methyl ether (5 mL), quenched with water (15 mL), and the aqueous phase was extracted with diethyl ether (2 × 10 mL). The combined organic phases were dried over anhydrous sodium sulphate, and concentrated under reduced pressure to give a brown oil. Purification of the crude brown oil by flash column chromatography (silica gel, 15% ethyl acetate in petroleum ether) gave 165 mg (26%) of the desired imide **21** as a yellow solid.

¹H NMR (400 MHz, CDCl₃) δ: 9.09 (1H, d, *J* = 10.1 Hz), 8.65 (1H, bs), 5.60 (1H, s), 2.18 (3H, d, *J* = 1.2 Hz), 1.90 (3H, d, *J* = 1.2 Hz). ¹³C NMR (100 MHz, CDCl₃) δ: 163.4, 160.9, 129.3, 116.0, 27.9, 20.2. *ν*_{max} (neat)/cm⁻¹; 3084, 2933, 1722, 1660, 1633 cm⁻¹.

***N*-Formylbutyramide, 22.** A 0 °C suspension of butyramide (11.5 mmol) in dry tetrahydrofuran (10 mL) was treated with *n*-butyl lithium (12.6 mmol), and the resulting reaction mixture was stirred for 1 h at room temperature. The reaction was cooled down to 0 °C and a solution of *N*-formyl benzotriazole (13.8 mmol) in dry tetrahydrofuran (10 mL) was added dropwise. The resulting solution was allowed to warm to room temperature and stirred overnight. The reaction mixture was diluted with diethyl ether (20 mL), and filtered to remove the precipitate. The filtrate was concentrated under reduced pressure to give a pale yellow oil which was purified by flash column chromatography (silica gel, 20% ethyl acetate/petroleum ether) to give 447 mg (34%) of the desired imide **22** as a colourless oil.

¹H NMR (400 MHz, CDCl₃) δ: 9.15 (1H, s), 2.40 (2H, t, *J* = 7.3 Hz), 1.70–1.80 (2H, m), 1.03 (3H, t, *J* = 7.3 Hz). ¹³C NMR (100 MHz, CDCl₃) δ: 173.8, 163.6, 33.4, 17.8, 13.6. *ν*_{max} (neat)/cm⁻¹; 2968.5, 1745.6, 1689.7 cm⁻¹.

(*E*)-(4-Methoxy-4-oxobut-2-enyl)triphenylphosphonium bromide. A suspension of triphenylphosphine (43.0 mmol) in dry toluene (50 mL) was treated with methyl 4-bromocrotonate (42.0 mmol) and the resulting mixture was stirred at room temperature for 4 hours. The resulting precipitate was removed by filtration and the filtrate was concentrated under vacuum to give 11.4 g (62%) of the desired triphenylphosphonium bromide as a white solid which was taken directly onto the next step without any purification.

Methyl (2*E*)-4-(triphenylphosphoranylidene)but-2-enoate, 11. The crude phosphonium bromide (26.0 mmol) was taken up in water (200 mL), and stirred until homogenous (12 hours). A solution of 1M aq. sodium hydroxide (100 mL) was then added dropwise, which caused a yellow precipitate to form immediately. The reaction mixture was extracted with dichloromethane (3 × 200 mL) and the combined organic phases were dried over anhydrous sodium sulphate, and concentrated under reduced pressure to give 6.89 g (74%) of the desired ylide **11** as an orange solid. The crude orange solid was ground using a pestle and mortar, and dried under high vacuum overnight. The fine powder obtained could be used in the subsequent steps without any further purification.

General procedure for the synthesis of dienamides 15, and 23–29. A suspension of the relevant imide (1.0 eq.) (**14**, **16–22**) in dry dichloromethane was treated with ylide **11** (3.0 eq) and the resulting suspension was refluxed overnight. The reaction mixture was concentrated under reduced pressure to give a crude brown oil, which upon purification by flash column chromatography (silica gel, 10% ethyl acetate, 1% triethylamine/petroleum ether) afforded the desired dienamide products (**15**, **23–29**).

(2*E*,4*Z*)-Methyl 5-((*R*)-2,2,5,5-tetramethyl-1,3-dioxane-4-carboxamido)penta-2,4-dienoate, 15. Dienamide **15** was prepared using the general procedure, starting from a solution of imide (**20** mg, 0.93 mmol) in dichloromethane (15 mL) and using ylide **11** (1.0 g, 2.78 mmol). Purification by flash column chromatography (silica gel, 10% ethyl acetate, 1% triethylamine/petroleum ether) afforded 145 mg of dienamide **15** (52%) as a single *Z,E*-isomer.

¹H NMR (400 MHz, CDCl₃) δ: 8.73 (1H, bd, *J* = 11.9 Hz), 7.46 (1H, dd, *J* = 14.5, 12.6 Hz), 7.03 (1H, dd, *J* = 11.5, 9.4 Hz), 5.93 (1H, dd, *J* = 14.9 Hz), 5.58 (1H, dd, *J* = 11.7, 9.3 Hz), 4.24 (1H, s), 3.80 (3H, s), 3.75 (1H, d, *J* = 12.4 Hz), 3.36 (1H, d, *J* = 12.4 Hz), 1.60 (3H, s), 1.50 (3H, s), 1.10 (3H, s), 1.06 (3H, s). ¹³C NMR (CDCl₃) δ: 167.5, 167.1, 136.3, 126.7, 119.6, 107.7, 99.6, 76.7, 71.3, 51.7, 33.4, 29.4, 22.0, 18.9, 18.7. *ν*_{max} (neat)/cm⁻¹; 2962.8, 1699.3, 1660.8, 1626.0 cm⁻¹. HRMS(EI) found [M]⁺ 297.1572, C₁₅H₂₃O₅N requires 297.1576. [α]_D +3.84 (c = 1.0, CHCl₃).

(2*E*,4*Z*)-Methyl 5-(2-oxopyrrolidin-1-yl)penta-2,4-dienoate, 23. Dienamide **23** was prepared using the general procedure, starting from a solution of imide **16** (100 mg, 0.88 mmol) in dichloromethane (10 mL) and using ylide **11** (955 mg, 2.65 mmol). Purification by flash column chromatography (silica gel, 10% ethyl acetate, 1% triethylamine/petroleum ether) afforded 94 mg of dienamide **23** (55%) as a single *Z,E*-isomer.

¹H NMR (400 MHz, CDCl₃) δ: 7.65 (1H, appt, *J* = 13.6 Hz), 6.85 (1H, d, *J* = 9.9 Hz), 5.76 (1H, d, *J* = 14.9 Hz), 5.46 (1H, dd, *J* = 12.3, 10.6 Hz), 3.93 (2H, t, *J* = 7.1 Hz), 3.68 (3H, s), 2.42

(2H, t, $J = 8.1$ Hz), 2.11 (2H, qn, $J = 7.5$ Hz). ^{13}C NMR (100 MHz, CDCl_3) δ : 174.8, 167.7, 138.9, 128.0, 119.8, 107.5, 51.6, 48.8, 29.8, 18.2. ν_{max} (neat)/ cm^{-1} : 1749, 1699, 1614 cm^{-1} . HRMS(EI) found $[\text{M}]^+$ 195.0898, $\text{C}_{10}\text{H}_{13}\text{O}_3\text{N}$ requires 195.0895.

(2*E*,4*Z*)-Methyl 5-(2-oxopiperidin-1-yl)penta-2,4-dienoate, 24*Z*, *E*, and (2*E*,4*E*)-Methyl 5-(2-oxopiperidin-1-yl)penta-2,4-dienoate, 24*E*,*E*. Dienamides 24*Z*,*E* and 24*E*,*E* were prepared using the general procedure, starting from a solution of imide **17** (200 mg, 1.57 mmol) in dichloromethane (15 mL) and using ylide **11** (1.70 g, 4.72 mmol). Purification by flash column chromatography (silica gel, 10% ethyl acetate, 1% triethylamine/petroleum ether) afforded 114 mg of dienamides 24*Z*,*E* and 24*E*,*E* (35%) as a 10:1 mixture of inseparable isomers.

24*Z*,*E* ^1H NMR (400 MHz, CDCl_3) δ = 7.56 (1H, appt, $J = 13.4$ Hz), 7.04 (1H, d, $J = 9.8$ Hz), 5.74 (1H, d, $J = 14.9$ Hz), 5.54 (1H, dd, $J = 12.1$, 10.6 Hz), 3.73 (2H, $J = 5.6$ Hz), 3.70 (3H, s), 2.48 (2H, t, $J = 5.8$ Hz), 1.75–1.85 (4H, m). ^{13}C NMR (100 MHz, CDCl_3) δ = 169.9, 167.6, 139.2, 133.0, 120.7, 111.3, 51.6, 50.8, 32.6, 23.3, 20.8.

24*E*,*E* ^1H NMR (400 MHz, CDCl_3) characteristic peaks δ = 7.87 (1H, d, $J = 14.5$ Hz), 7.32 (1H, dd, $J = 15.6$, 10.8 Hz). ^{13}C NMR (100 MHz, CDCl_3) δ = 168.9, 167.6, 144.5, 136.6, 117.7, 108.4, 51.4, 45.4, 33.0, 22.4, 20.3. ν_{max} (neat)/ cm^{-1} : 1707, 1660, 1614 cm^{-1} . HRMS(EI) found $[\text{M}]^+$ 209.1057, $\text{C}_{11}\text{H}_{15}\text{O}_3\text{N}$ requires 209.1052.

(2*E*,4*Z*)-Methyl 5-(2-oxoazepan-1-yl)penta-2,4-dienoate, 25*Z*, *E*, and (2*E*,4*E*)-Methyl 5-(2-oxoazepan-1-yl)penta-2,4-dienoate, 25*E*,*E*. Dienamides 25*Z*,*E* and 25*E*,*E* were prepared using the general procedure, starting from a solution of imide **18** (200 mg, 1.42 mmol) in dichloromethane (15 mL) and using ylide **11** (1.53 g, 4.25 mmol). Purification by flash column chromatography (silica gel, 10% ethyl acetate, 1% triethylamine/petroleum ether) afforded 176 mg of dienamide 25*Z*,*E* and 25*E*,*E* (56%) as a 4:1 mixture.

25*Z*,*E* ^1H NMR (400 MHz, CDCl_3) δ = 7.40 (1H, ddd, $J = 15.1$, 12.1, 1.0 Hz), 6.85 (1H, d, $J = 9.1$ Hz), 5.79 (1H, d, $J = 15.1$ Hz), 5.58 (1H, ddd, $J = 12.1$, 9.0, 0.7 Hz), 3.68 (3H, s), 3.66–3.69 (2H, m), 2.57–2.62 (2H, m), 1.77–1.80 (2H, m), 1.70–1.75 (4H, m). ^{13}C NMR (100 MHz, CDCl_3) δ = 176.0, 167.4, 138.5, 135.4, 120.7, 113.2, 51.7, 37.3, 37.1, 29.6, 28.8, 23.4.

25*E*,*E* ^1H NMR (400 MHz, CDCl_3) δ = 7.66 (1H, d, $J = 14.5$ Hz), 7.32 (1H, ddd, $J = 15.0$, 11.1, 0.8 Hz), 5.71 (1H, d, $J = 14.9$ Hz), 5.70 (1H, appt, $J = 12.0$ Hz), 3.66 (3H, s), 3.66–3.69 (2H, m), 2.57–2.62 (2H, m), 1.77–1.80 (2H, m), 1.70–1.75 (4H, m). ^{13}C NMR (100 MHz, CDCl_3) δ = 174.5, 167.7, 144.8, 136.7, 117.0, 107.7, 51.4, 45.3, 37.0, 29.3, 27.4, 23.5. ν_{max} (neat)/ cm^{-1} : 1708, 1662, 1653, 1624 cm^{-1} . HRMS(CI) found $[\text{M} + \text{H}]^+$ 224.1284, $\text{C}_{12}\text{H}_{18}\text{O}_3\text{N}$ requires 224.1287.

(2*E*,4*Z*)-Methyl 5-benzamidopenta-2,4-dienoate, 26*Z*,*E*, and (2*E*,4*E*)-Methyl 5-benzamidopenta-2,4-dienoate, 26*E*,*E*. Dienamides 26*Z*,*E* and 26*E*,*E* were prepared using the general procedure, starting from a solution of imide **19** (100 mg, 0.67 mmol) in dichloromethane (10 mL) and using ylide **11** (725 mg, 2.01 mmol). Purification by flash column chromatography (silica gel, 10% ethyl acetate, 1% triethylamine/petroleum ether) afforded 92.5 mg of the *Z*,*E*-dienamide 26*Z*,*E* (60%) and 57.1 mg of the *E*,*E*-dienamide 26*E*,*E* (37%) as separable clear oils.

26*Z*,*E* ^1H NMR (400 MHz, CDCl_3) δ : 8.33 (1H, bd, $J = 8.6$ Hz), 7.89–7.90 (2H, m), 7.61–7.67 (4H, m), 7.30 (1H, dd, $J = 10.9$, 9.6 Hz), 5.97 (1H, d, $J = 14.9$ Hz), 5.66 (1H, dd, $J = 12.3$, 9.0 Hz), 3.73 (3H, s). ^{13}C NMR (100 MHz, CDCl_3) δ : 167.7, 164.4, 136.6, 132.9, 132.7, 128.9, 128.6, 127.4, 119.4, 107.6, 51.7. ν_{max} (neat)/ cm^{-1} : 3308.0, 1683.9, 1666.5, 1626.0, 1602.9 cm^{-1} . HRMS(EI) found $[\text{M}]^+$ 231.0899, $\text{C}_{13}\text{H}_{13}\text{O}_3\text{N}$ requires 231.0895.

26*E*,*E* ^1H NMR (400 MHz, CDCl_3) δ : 7.99 (1H, bd, $J = 12.3$ Hz), 7.85–7.87 (2H, m), 7.51–7.64 (4H, m), 7.41 (1H, dd, $J = 15.2$, 11.4 Hz), 6.12 (1H, dd, $J = 14.1$, 11.9 Hz), 5.86 (1H, d, $J = 15.2$ Hz), 3.78 (3H, s, CH_3). ^{13}C NMR (100 MHz, CDCl_3) δ : 166.6, 163.5, 142.5, 132.1, 131.6, 127.8, 126.3, 116.9, 110.2, 50.5. ν_{max} (neat)/ cm^{-1} : 3304.1, 1670.4, 1622.2, 1608.7, 1583.6 cm^{-1} . HRMS(EI) found $[\text{M}]^+$ 231.0897, $\text{C}_{13}\text{H}_{13}\text{O}_3\text{N}$ requires 231.0895.

(2*E*,4*Z*)-Methyl 5-(picolinamido)penta-2,4-dienoate, 27*Z*,*E*, and (2*E*,4*E*)-Methyl 5-(picolinamido)penta-2,4-dienoate, 27*E*,*E*. Dienamides 27*Z*,*E* and 27*E*,*E* were prepared using the general procedure, starting from a solution of imide **20** (100 mg, 0.66 mmol) in dichloromethane (10 mL) and using ylide **11** (720 mg, 1.99 mmol). Purification by flash column chromatography (silica gel, 10% ethyl acetate, 1% triethylamine/petroleum ether) afforded 132 mg (87%) of the *Z*,*E*-dienamide 27*Z*,*E* and *E*,*E*-dienamide 27*E*,*E* as an inseparable (3:2) mixture of isomers, and as a clear oil.

27*Z*,*E* ^1H NMR (400 MHz, CDCl_3) δ : 10.27 (1H, bd, $J = 11.5$ Hz), 7.82–7.86 (2H, m), 7.65 (1H, dd, $J = 12.2$, 14.9 Hz), 7.39–7.47 (2H, m), 7.14 (1H, dd, $J = 11.7$, 9.1 Hz), 5.88 (1H, d, $J = 14.9$ Hz), 5.59 (1H, dd, $J = 8.9$, 12.2 Hz), 3.73 (3H, s). ^{13}C NMR (100 MHz, CDCl_3) δ = 167.6, 161.3, 148.4, 148.3, 137.7, 136.7, 127.6, 127.1, 122.8, 119.5, 108.3, 51.6.

27*E*,*E* ^1H NMR (400 MHz, CDCl_3) δ : 9.88 (1H, bd, $J = 10.4$ Hz), 8.52–8.60 (2H, m), 8.15 (2H, m), 7.39–7.47 (1H, dd, $J = 15.2$, 11.3 Hz), 7.33 (1H, dd, $J = 13.2$, 11.0 Hz), 6.11 (1H, dd, $J = 13.3$, 11.3 Hz), 5.78 (1H, d, $J = 15.2$ Hz), 3.68 (3H, s). ν_{max} (neat)/ cm^{-1} : 3362, 1705, 1627, 1618 cm^{-1} . HRMS(EI) found $[\text{M}]^+$ 232.0850, $\text{C}_{12}\text{H}_{12}\text{O}_3\text{N}_2$ requires 232.0848.

(2*E*,4*Z*)-Methyl 5-(3-methylbut-2-enamido)penta-2,4-dienoate, 28. Dienamide **28** was prepared using the general procedure, starting from a solution of imide **21** (165 mg, 1.29 mmol) in dichloromethane (10 mL) and using ylide **11** (1.40 g, 3.89 mmol). Purification by flash column chromatography (silica gel, 10% ethyl acetate, 1% triethylamine/petroleum ether) afforded 110 mg of dienamide **28** (41%) as a single *Z*,*E*-isomer.

^1H NMR (400 MHz, CDCl_3) δ : 7.71 (1H, bd, $J = 11.6$ Hz), 7.47 (1H, ddd, $J = 14.9$, 12.2, 0.9 Hz), 7.06 (1H, dd, $J = 11.8$, 9.0 Hz), 5.78 (1H, d, $J = 14.9$ Hz), 5.63 (1H, bs), 5.42 (1H, dd, $J = 12.2$, 9.0 Hz), 3.68 (3H, s), 2.16 (3H, d, $J = 0.8$ Hz), 1.85 (3H, d, $J = 1.2$ Hz). ^{13}C NMR (100 MHz, CDCl_3) δ : 168.0, 163.3, 137.2, 129.0, 125.9, 118.3, 117.1, 105.9, 51.8, 27.9, 20.5. ν_{max} (neat)/ cm^{-1} : 3010, 1730, 1701, 1658, 1639, 1624 cm^{-1} . HRMS(CI) found $[\text{M} + \text{H}]^+$ 210.1128, $\text{C}_{11}\text{H}_{16}\text{O}_3\text{N}$ requires 210.1130.

(2*E*,4*Z*)-Methyl 5-butyramidopenta-2,4-dienoate, 29. Dienamide **29** was prepared using the general procedure, starting from a solution of imide **22** (100 mg, 0.87 mmol) in dichloromethane (10 mL) and using ylide **11** (940 mg, 2.60 mmol). Purification by flash column chromatography (silica gel, 10% ethyl acetate, 1% triethylamine/petroleum ether) afforded 72.4 mg of dienamide **29** (42%) as a single *Z*,*E*-isomer.

^1H NMR (400 MHz, CDCl_3) δ : 8.36 (1H, bd, $J = 11.2$ Hz) 7.54 (1H, dd, $J = 14.8, 12.1$ Hz), 6.99 (1H, dd, $J = 11.8, 9.0$ Hz), 5.80 (1H, d, $J = 14.9$ Hz), 5.42 (1H, d, $J = 12.2, 9.0$ Hz), 3.70 (3H, s), 2.25 (2H, t, $J = 7.3$ Hz), 1.60–1.71 (2H, m), 0.92 (3H, t, $J = 7.4$ Hz). ^{13}C NMR (100 MHz, CDCl_3) $\delta = 170.9, 168.0, 137.6, 128.7, 118.4, 106.3, 51.1, 38.4, 18.8, 13.7$. ν_{max} (neat)/ cm^{-1} : 2987, 1707, 1629 cm^{-1} . HRMS(CI) found $[\text{M} + \text{H}]^+$ 198.1128, $\text{C}_{10}\text{H}_{16}\text{O}_3\text{N}$ requires 198.1130.

Acknowledgements

We would like to thank AstraZeneca and the University of Glasgow for postgraduate funding (J.E.M) The authors also thank Dr. Ian Sword and the University of Glasgow for funding. We would like to thank Rigaku for the loan of an R-Axis RAPID image plate diffractometer, and Oxford Cryosystems for the loan of a low temperature device.

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