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Stereoselective Synthesis of (2*E*,4*Z*)-Dienamides Employing (Triphenylphosphoranylidene)ketene

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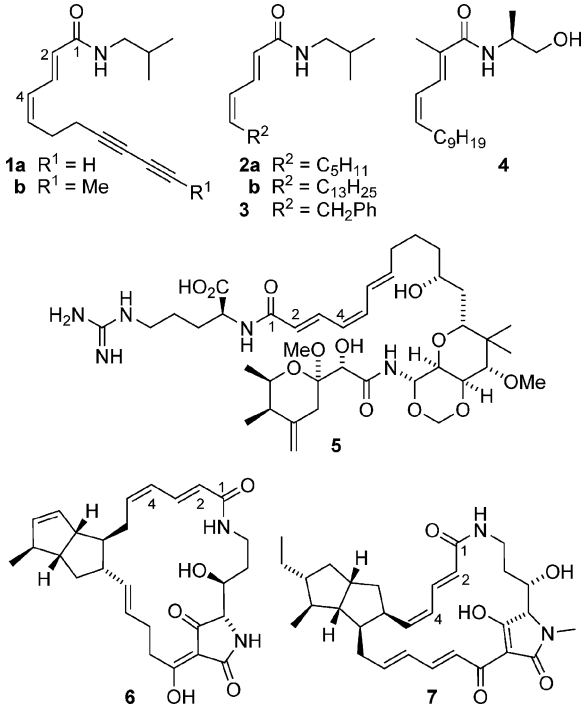
The three-component reaction between ylide Ph_3PCCO, amines and aldehydes is known to afford selectively (*E*)-α,β-unsaturated amides. We applied a variant of this methodology to the preparation of (2*E*,4*Z*)-dienamides **11** utilizing the phosphonium salt formation from ethyl 5-aminopentanoate hydrochloride and Ph_3PCCO followed by deprotonation with DBU and a Wittig olefination of the corresponding ylide with various (*Z*)-α,β-unsaturated aldehydes **10**. The (2*E*,4*Z*)-dienamides **11** were isolated in yields of up to 80 %. The (*Z*)-configuration of the starting aldehydes **10** remained untouched during the reaction.

Introduction

(2*E*,4*Z*)-Dienamides are constituents of a variety of pharmacological relevant natural products such as immunomodulatory, phototoxic antimicrobial and taste active *N*-alkylamides **1a**,**b** from *Echinacea purpurea*,[1–3] *cis*-pellitorine (**2a**) from *Artemisia dracunculus*,[4] pipericine (**2b**) from *Piper nigrum*,[5] mitochondrial complex I inhibiting myxalamide analogues like **4**,[6] cytotoxic (4*Z*)-onnamide A **5** from a marine *Theonella* sponge,[7] cylindramide (**6**) from the marine sponge *Halichondria cylindrata*[8,9] or aburatubolactam A (**7**) produced by a *Streptomyces* species of a marine mollusc[10] as well as non-natural insecticides **3**[11] (Scheme 1).

Synthetic efforts towards these (2*E*,4*Z*)-dienamides relied mainly on Wittig reactions employing amide-derived phosphonium salts or olefination followed by introduction of the amide moiety via acid chloride as the final step.[12,13] Other known synthetic routes involved photoisomerization of the corresponding (2*E*,4*E*)-dienamides[11a] or proceeded via metal exchange starting from *N*-isobutyl-5-telluro-(2*E*,4*Z*)-pentadienamide,[14] or via solid-phase Wittig and Stille reactions of amino acid derivatives.[15]

The *E*,*Z*-dienamide structure in cylindramide **6** was built up by Lindlar reduction of the coupling enyne fragment from the propynyl-substituted pentalene and a hydroxyornithine-derived subunit,[16,17] which is also present in related natural products such as **7**. However, the Lindlar reduction suffered from overreduction of the (*Z*)-configured double bond. Thus, in order to find a more general way to this type of macrocyclic tetramic acid lactams, we developed a procedure allowing the combined preparation of the (2*E*,4*Z*)-diene subunit and the hydroxyornithine-derived



Scheme 1. Some natural products with (2*E*,4*Z*)-dienamide structural motif.

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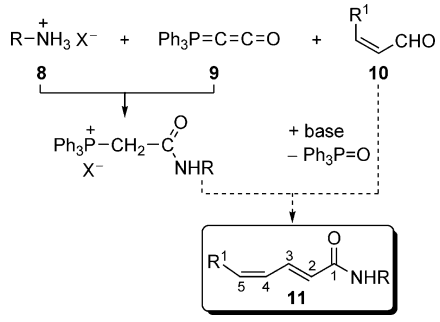
amide function. For this purpose, we intended to use the Bestmann ylide (triphenylphosphoranylidene)ketene[18] ($Ph_3P{=}C{=}C{=}O$, **9**) for preparing (2*E*,4*Z*)-dienamides **11** on the basis of our previous syntheses of (*E*)-α,β-unsaturated amides from aldehydes and amines (Scheme 2).[19,20] The results are reported below.



Scheme 2. Amide formation by intermolecular three-component synthesis.

Results and Discussion

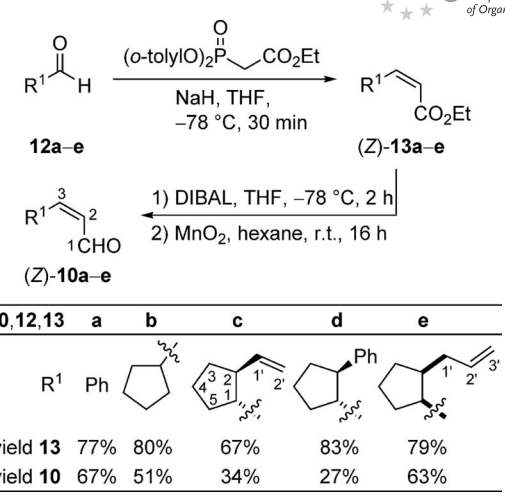
In order to explore the scope and limitations of the envisioned synthetic concept we employed as model compounds the easily available (*Z*)-α,β-unsaturated aldehydes **10a**,**b** as well as the 1,2-difunctionalized cyclopentane derivatives **10c**–**e** (Scheme 3). The starting *trans*-configured cyclopentanecarbaldehydes **12c** and **12d** were prepared in optical purities of 96% *ee* and 80% *ee*, respectively,[21] by conjugate 1,4-addition of Grignard reagents to the chiral α,β-unsaturated aldimine from cyclopentenecarbaldehyde and *tert*-leucine *tert*-butyl ester according to the method by Koga[22] (see Supporting Information). Selective defunctionalization[23,24] of the commercially available Weiss diketone followed by a reaction sequence of Baeyer Villiger oxidation,[25] reduction, ring opening and final DMP oxidation gave the *cis*-configured cyclopentanecarbaldehyde **12e** (see Supporting Information).

Synthesis of (*Z*)-α,β-Unsaturated Aldehydes (*Z*)-10a–e

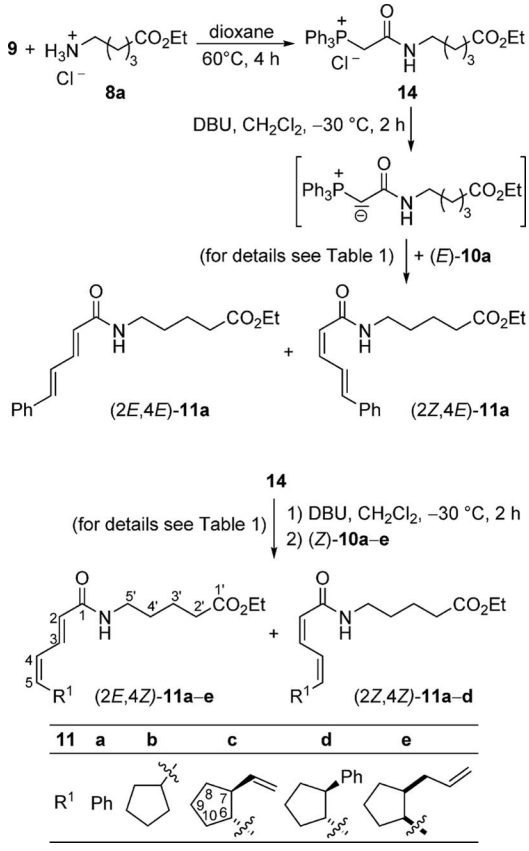
Following a procedure developed by Ando[26] the (*Z*)-acrylates (*Z*)-**13a**, **13b**[27] and **13c**–**e** were obtained in *Z*/*E*-ratios of ca. 70:30 from the corresponding aldehydes **12a**–**e** by Horner–Wadsworth–Emmons olefination employing ethyl (di-*o*-tolylphosphono)acetate (Scheme 3). Subsequent reduction to the respective allyl alcohol with DIBAL in THF at –78 °C, followed by oxidation with MnO_2 in hexane at room temperature gave the target (2*Z*)-alkenals (*Z*)-**10a**,[28] (*Z*)-**10b**,[29] and (*Z*)-**10c**–**e**.

Synthesis of (2*E*,4*Z*)-Dienamides 11a–e

Next, we set out to prepare an amide-functionalized phosphonium salt from an amine precursor and Ph_3PCCO[30] (Scheme 4). Because of its structural relationship to the original hydroxyornithine subunit[16] we chose 5-aminopentanoic acid as the amine component, which was treated with $SOCl_2$ in EtOH to give ethyl 5-aminopentanoate hydrochloride **8a**.[31]



Scheme 3. Preparation of (2*Z*)-alkenals (*Z*)-**10a**–**e**. Yields of isolated (*Z*)-isomers after chromatography.



Scheme 4. Preparation of ethyl 5-[*N*-(penta-2,4-dienoyl)amino] pentanoates **11a**–**e**. Atom numbering for assignment of NMR signals.

With hydrochloride **8a** in hand we started our systematic investigation of the olefination reaction using the commercially available (*E*)-cinnamaldehyde (*E*)-**10a**. The reaction

Table 1. Synthesis of 5-substituted ethyl 5-[(penta-2,4-dienoyl)amino]pentanoates **11a–e** under various conditions.[a]

Entry	Enals **10**	Solvent	Method	T [°C]	Time	Yield [%] [c]	Ratio	Products **11**
1	(*E*)-**10a**	THF	one pot	80	20 h	19	80:20	(2*E*,4*E*)-**11a**/(2*Z*,4*E*)-**11a**
2	(*E*)-**10a**	THF	one pot, mw[b]	110	20 min	15	–	(2*E*,4*E*)-**11a**/(2*Z*,4*E*)-**11a**
3	(*E*)-**10a**	THF	one pot, mw[d]	110	20 min	<1	–	(2*E*,4*E*)-**11a**/(2*Z*,4*E*)-**11a**
4	(*E*)-**10a**	toluene/CH_2Cl_2 (9:1)	2 steps, mw	170	20 min	51	74:26	(2*E*,4*E*)-**11a**/(2*Z*,4*E*)-**11a**
5	(*E*)-**10a**	toluene/CH_2Cl_2 (9:1)	2 steps, mw[d]	170	20 min	55	66:34	(2*E*,4*E*)-**11a**/(2*Z*,4*E*)-**11a**
6	(*E*)-**10a**	toluene/CH_2Cl_2 (9:1)	2 steps, mw[d]	170	20 min	39	74:26	(2*E*,4*E*)-**11a**/(2*Z*,4*E*)-**11a**
7	(*Z*)-**10a**	toluene/CH_2Cl_2 (9:1)	2 steps	120	3 d	48	86:14	(2*E*,4*Z*)-**11a**/(2*Z*,4*Z*)-**11a**
8	(*Z*)-**10a**	toluene/CH_2Cl_2 (9:1)	2 steps, mw	160	20 min	63	75:25	(2*E*,4*Z*)-**11a**/(2*Z*,4*Z*)-**11a**
9	(*Z*)-**10b**	toluene/CH_2Cl_2 (9:1)	2 steps	120	3 d	66	77:23	(2*E*,4*Z*)-**11b**/(2*Z*,4*Z*)-**11b**
10	(*Z*)-**10b**	toluene/CH_2Cl_2 (9:1)	2 steps, mw	170	20 min	81	71:29	(2*E*,4*Z*)-**11b**/(2*Z*,4*Z*)-**11b**
11	(*Z*)-**10b**	toluene/CH_2Cl_2 (9:1)	2 steps, mw	190	20 min	44	77:23	(2*E*,4*Z*)-**11b**/(2*Z*,4*Z*)-**11b**
12	(*Z*)-**10c**	toluene/CH_2Cl_2 (9:1)	2 steps, mw	170	20 min	80	80:20	(2*E*,4*Z*)-**11c**/(2*Z*,4*Z*)-**11c**
13	(*Z*)-**10d**	toluene/CH_2Cl_2 (9:1)	2 steps, mw	170	20 min	77	78:22	(2*E*,4*Z*)-**11d**/(2*Z*,4*Z*)-**11d**
14	(*Z*)-**10e**	toluene/CH_2Cl_2 (9:1)	2 steps, mw	170	20 min	58	100:0	(2*E*,4*Z*)-**11e**[e]

[a] See Scheme 4. [b] For microwave (mw) conditions see Experimental. [c] Yields refer to isolated yields, and product ratios were determined from isolated yields after chromatographic separation. [d] With additive LiCl (1 equiv.) (entries 3, 5) or LiBr (1 equiv.) (entry 6). [e] The (2*Z*,4*Z*)-isomer was not detected.

was initially carried out in a one-pot fashion starting from hydrochloride **8a** with Ph_3PCCO (2 equiv.) serving also as the base as shown in Scheme 2. However, a mixture of (2*E*,4*E*)- and (2*Z*,4*E*)-**11a** in only poor yield of 19% was obtained (Table 1, entry 1). The low yield was assumed to arise from incomplete deprotonation of the phosphonium salt **14** by Ph_3PCCO. Therefore, instead of Ph_3PCCO the external base DBU was applied to deprotonate **14**.[19a] In order to exclude an excess of base we performed the reaction in two steps, isolating phosphonium salt **14**, which was prepared from **8a** and Ph_3PCCO in dioxane at 60 °C, prior to deprotonation with DBU and reaction with aldehydes (Scheme 4). Furthermore, due to this modification the solvent THF could be replaced with a mixture of toluene/CH_2Cl_2 (9:1) to improve the solubility of **14** and to allow a high temperature in microwave reactions. Indeed, (2*E*,4*E*)- and (2*Z*,4*E*)-**11a** were isolated in yields of up to 55% by microwave-irradiated two-step reaction (Table 1, entries 4–6). The attempts to enhance the (*E*)-selectivity of the olefination by addition of lithium salts failed. In all cases, the product was obtained with similar (2*E*,4*E*):(2*Z*,4*E*) ratios. Therefore, all further experiments with (*Z*)-aldehydes were carried out without any external additive. The isomers could be separated readily by column chromatography on silica gel and were assigned by the *vicinal* coupling constants of the olefinic 2-H and 3-H signals in ^{1}H NMR spectra, being $J_{2,3}$ = 14.9 Hz (for 2*E*) and $J_{2,3}$ = 11.2 Hz (for 2*Z*). The assignments were further supported by an X-ray crystal structure analysis of compound (2*E*,4*E*)-**11a** (Figure 1).[32]

Next, (*Z*)-cinnamaldehyde (*Z*)-**10a** was treated with phosphonium salt **14** at 120 °C. After 3 d reaction time, the desired (2*E*,4*Z*)-dienamide (2*E*,4*Z*)-**11a** was isolated in 48% yield together with its minor (2*Z*,4*Z*)-isomer (2*Z*,4*Z*)-**11a** in a ratio of 86:14 (entry 7). Again the isomers were separated by simple column chromatography on silica gel, and the ratio was determined from isolated yields. Performing the reaction at 160 °C under microwave irradiation for 20 min further increased the yield to 63%, however, at the expense of the *E*/*Z*-ratio (75:25) (entry 8).

Similar results were found for (*Z*)-3-cyclopentylacrylaldehyde (*Z*)-**10b** (entries 9–11). At 120 °C a mixture of (2*E*,4*Z*)-**11b** and (2*Z*,4*Z*)-**11b** was isolated in 66% yield with a product ratio of 77:23 in favour of the desired (2*E*,4*Z*)-isomer (entry 9). By using microwave irradiation at 170 °C a further increase to 81% yield was observed, while the (*E*)-selectivity of the olefination slightly decreased (entry 10). An increase of the temperature to 190 °C neither improved the yield nor the (*E*)-selectivity (entry 11).

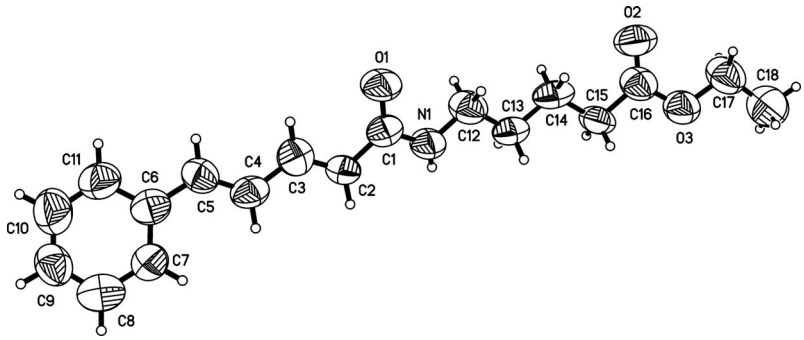


Figure 1. Structure of ethyl 5-{[(2*E*,4*E*)-5-phenylpenta-2,4-dienoyl]amino}pentanoate (2*E*,4*E*)-**11a** in the solid state. Double bond lengths C2=C3 1.31(1) Å and C4=C5 1.31(1) Å.

When 3-(2-vinylcyclopentyl)acrylaldehyde (*Z*)-**10c** and 3-(2-phenylcyclopentyl)acrylaldehyde (*Z*)-**10d** were employed at 170 °C under microwave conditions, the corresponding ethyl [(penta-2,4-dienoyl)amino]pentanoates **11c** and **11d** were isolated in 80% and 77% yield with (2*E*,4*Z*):(2*Z*,4*Z*) ratios of 80:20 and 78:22, respectively (entries 12, 13). Under the same conditions 3-(2-allylcyclopentyl)acrylaldehyde (*Z*)-**10e** reacted cleanly to pentanoate (2*E*,4*Z*)-**11e**. Its isomer (2*Z*,4*Z*)-**11e** could not be detected (entry 14). These results indicate that even substituted enals were suitable starting materials for this olefination reaction.

Despite the harsh reaction conditions the stereochemical integrity of the C=C bond of the starting (*E*)- or (*Z*)-propenals **10** was maintained during the reaction sequence. As already described for the (*E*)-cinnamaldehyde derived products **11a**, this was proved by distinctive *vicinal* coupling constants of the olefinic signals in the ^{1}H NMR spectra as exemplified for (2*E*,4*Z*)-**11b** and (2*Z*,4*Z*)-**11b**. Both isomers can clearly be differentiated by the coupling constants between 2-H and 3-H, which were determined to be $J_{2,3}$ = 14.9 Hz and 11.5 Hz in (2*E*,4*Z*)-**11b** and (2*Z*,4*Z*)-**11b**, respectively, while the coupling constants of the other olefinic 4-H, 5-H, and 6-H protons are comparable.

Conclusions

This study demonstrates the potential of the cumulated phosphorus ylide Ph_3PCCO **9** in the synthesis of (2*E*,4*Z*)-dienamides **11a**–**e** from 5-aminovaleric acid and (*Z*)-α,β-unsaturated aldehydes **10a**–**e**. The three-component reaction was performed in two steps involving formation of phosphonium salt **14** from hydrochloride **8a** and ylide **9** followed by deprotonation of isolated **14** with DBU to give the corresponding acyl ylide and finally its reaction with aldehydes **10**. Noteworthy, (2*E*,4*Z*)-dienamide (2*E*,4*Z*)-**11e** was detected exclusively as product, whereas the *E*,*Z*-selectivity in the reaction of the other propenals **10a**–**d** remained comparable regardless of the conditions, resulting in isomeric ratios of about 80:20 in favour of (2*E*,4*Z*)-**11a**–**d**. However, in all cases, the (*Z*)-configuration of the starting aldehyde **10** was left untouched. This is particularly remarkable because phosphanes are known to catalyze the isomerization of electron-withdrawing (*Z*)-alkenes.[33] The desired (2*E*,4*Z*)-products were easily separated from their minor (2*Z*,4*Z*)-isomers by simple column chromatography with hexanes/EtOAc as eluent.

Experimental Section

Materials and Methods: Melting points were determined on a Büchi SMP 20 and are uncorrected. NMR spectra were recorded on a Bruker Avance 300 and Avance 500 with TMS as an internal standard. TLC: Silica gel 60 F_{254} (Merck). Column chromatography: Kieselgel 60, grain size 40–63 μm (Fluka). IR spectra were recorded on a Bruker Vector 22. Mass spectra were recorded on a Bruker Daltonics micrOTOF_Q. GC-MS: GC HP 5890 series II, HP-5 column (Hewlett–Packard) with helium as carrier gas. Specific rotations were measured on a Perkin–Elmer 241 polarimeter. Microwave: CEM Explorer, 170 °C for 20 min (300 W, isothermic).

General Procedure for the Synthesis of (*Z*)-Acrylates 13: To a suspension of NaH (248 mg, 10.34 mmol) in THF (40 mL) in a flame-dried Schlenk flask at 0 °C was slowly added a solution of ethyl (di-o-tolylphosphono)acetate (3.60 g, 10.34 mmol) in THF (10 mL). After completion of the gas formation, the reaction mixture was cooled to –78 °C, and a solution of the respective aldehyde **12** (9.4 mmol) in THF (10 mL) was added. The reaction mixture was stirred for 1.5 h, warmed to room temperature and after addition of dest. H_2O (50 mL), the layers were separated and the aqueous layer was extracted with Et_2O. The combined organic layers were dried ($MgSO_4$) and concentrated under vacuum. The (*Z*)- and (*E*)-isomers of **13** were separated by chromatography on silica gel with hexanes/EtOAc (10:1) and obtained in all cases in a ratio (*Z*):(*E*) = 70:30.

Ethyl 3-[(1*S*,2*S*)-2-Vinylcyclopentyl]acrylate (13c): Yield 1.22 g (67%). R_f = 0.90 (hexanes/EtOAc, 10:1). $[\alpha]_D^{20}$ = +40.1 (*c* = 1.00, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.1 Hz, 3 H, $CO_2CH_2CH_3$), 1.37 (ddt, *J* = 12.6, 9.7, 8.9 Hz, 1 H, 5-H_a), 1.47–1.56 (m, 1 H, 3-H_a), 1.68–1.79 (m, 2 H, 4-H), 1.92 (ddt, *J* = 12.5, 7.9, 4.5 Hz, 1 H, 3-H_b), 1.99 (ddt, *J* = 12.6, 7.7, 4.8 Hz, 1 H, 5-H_b), 2.12–2.21 (m, 1 H, 2-H), 3.57 (dddd, *J* = 20.1, 9.7, 7.7, 1.0 Hz, 1 H, 1-H), 4.15 (dq, *J* = 7.1, 1.0 Hz, 2 H, $CO_2CH_2CH_3$), 4.89 (ddd, *J* = 10.2, 2.0, 0.9 Hz, 1 H, 2′-H_{cis}), 4.95 (ddd, *J* = 17.1, 2.0, 1.1 Hz, 1 H, 2′-H_{trans}), 5.73 (ddd, *J* = 17.1, 10.2, 7.9 Hz, 1 H, 1′-H), 5.75 (dd, *J* = 11.5, 1.0 Hz, 1 H, CH=C*H*CO_2Et), 6.03 (dd, *J* = 11.5, 10.0 Hz, 1 H, C*H*=CHCO_2Et) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.3 ($CO_2CH_2CH_3$), 23.9 (C-4), 32.6, 32.7 (C-3, C-5), 45.0 (C-1), 52.5 (C-2), 59.8 ($CO_2CH_2CH_3$), 113.7 (C-2′), 119.5 (C-1′), 141.1 (CH*C*HCO$_2$Et), 153.3 (*C*HCHCO$_2$Et), 166.5 (CO_2Et) ppm. FT-IR (ATR): $\tilde{\nu}$ = 2954 (w), 2868 (w), 1719 (vs), 1641 (m), 1418 (w), 1185 (vs), 1031 (m), 908 (m), 821 (m) cm^{-1}. GC-MS (EI): *m*/*z* (%) = 194 (30), 165 (50), 149 (28), 121 (100), 114 (28), 97 (34), 91 (38), 79 (42), 67 (40), 55 (36), 41 (24). HRMS (ESI): calcd. for $C_{12}H_{19}O_2$ [M + H]: 194.1380; found 194.1382.

Ethyl 3-[(1*S*,2*R*)-2-Phenylcyclopentyl]acrylate (13d): Yield 1.90 g (83%). R_f = 0.85 (hexanes/EtOAc, 10:1). $[\alpha]_D^{20}$ = +37.2 (*c* = 1.00, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.19 (t, *J* = 7.1 Hz, 3 H, $CO_2CH_2CH_3$), 1.45–1.54 (m, 1 H, 5-H_a), 1.73–1.94 (m, 3 H, 3-H_a, 4-H), 2.11–2.74 (m, 2 H, 3-H_b, 5-H_b), 2.73 (dt, *J* = 10.3, 7.8 Hz, 1 H, 2-H), 3.95–4.04 (m, 1 H, 1-H), 4.02 (q, *J* = 7.1 Hz, 2 H, $CO_2CH_2CH_3$), 5.64 (dd, *J* = 11.5, 0.9 Hz, 1 H, CH=C*H*CO_2Et), 6.07 (dd, *J* = 11.5, 10.0 Hz, 1 H, C*H*=CHCO_2Et), 7.13–7.26 (m, 5 H, Ar) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2 ($CO_2CH_2CH_3$), 24.1 (C-4), 32.9 (C-5), 35.4 (C-3), 45.0 (C-1), 53.9 (C-2), 59.7 ($CO_2CH_2CH_3$), 119.7 (*C*HCHCO$_2$Et), 126.1, 127.4, 128.2, 143.5 (Ar), 152.9 (CH*C*HCO$_2$Et), 166.3 (CO_2Et) ppm. FT-IR (ATR): $\tilde{\nu}$ = 2953 (m), 2870 (w), 1715 (vs), 1644 (m), 1418 (w), 1183 (vs), 1146 (s), 1029 (m), 823 (m), 755 (s), 698 (s) cm^{-1}. MS (ESI): *m*/*z* = 267, 245, 199, 181, 155, 146, 129, 121, 103. HRMS (ESI): calcd. for $C_{16}H_{20}NaO_2$ [M + Na]: 267.1356; found 267.1355.

Ethyl 3-(2-Allylcyclopentyl)acrylate (13e): According to the GP, from **12e** (183 mg, 1.33 mmol), NaH (343 mg, 1.43 mmol), and ethyl (di-o-tolylphosphono)acetate (0.50 g, 1.43 mmol); yield 218 mg (79%). R_f = 0.59 (pentane/Et_2O, 50:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.29 (t, *J* = 7.1 Hz, 3 H, $CO_2CH_2CH_3$), 1.35–1.42 (m, 1 H, 5-H_a), 1.42–1.50 (m, 1 H, 3-H_a), 1.60–1.67 (m, 1 H, 4-H_a), 1.71–1.85 (m, 2 H, 4-H_b, 5-H_b), 1.85–1.95 (m, 2 H, 1′-H_a, 3-H_b), 2.07–2.20 (m, 2 H, 1′-H_b, 1-H), 3.86–3.96 (m, 1 H, 2-H), 4.17 (q, *J* = 7.1 Hz, 2 H, $CO_2CH_2CH_3$), 4.92 (ddd, *J* = 10.1, 2.2, 1.4 Hz, 1 H, 3′-H_{cis}), 4.97 (ddd, *J* = 17.1, 2.2, 1.4 Hz, 1 H, 3′-

H_{trans}), 5.71–5.81 (m, 1 H, 2′-H), 5.77 (dd, J = 11.5, 1.0 Hz, 1 H, CH=C*H*CO_2Et), 6.15 (dd, J = 11.5, 11.5 Hz, 1 H, C*H*=CHCO_2Et) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2 ($CO_2CH_2CH_3$), 23.3 (C-4), 30.4 (C-5), 32.2 (C-3), 35.5 (C-1′), 41.2 (C-2), 43.8 (C-1), 59.7 ($CO_2CH_2CH_3$), 114.9 (C-3′), 119.1 (*C*HCO_2Et), 138.3 (C-2′), 151.8 (*C*HCHCO_2Et), 166.4 (CO_2Et) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3073 (w), 2942 (s), 2868 (m), 1717 (vs), 1640 (m), 1454 (w), 1423 (w), 1382 (w), 1292 (w), 1182 (vs), 1101 (m), 997 (w), 907 (vs), 822 (m), 729 (vs) cm^{-1}. MS (ESI): m/z (%) = 209 (32) [M$^+$ + H], 181 (6), 163 (100), 149 (6), 145 (12), 135 (46), 107 (4). HRMS (ESI): calcd. for $C_{13}H_{20}NaO_2$ [M + Na]: 231.1356; found 231.1354.

General Procedure for the Synthesis of Acrylaldehydes 10: To a solution of the respective **13** (11.9 mmol) in THF (150 mL) at –78 °C was slowly added dropwise a 1 M solution of diisobutylaluminiumhydride in hexane (29.8 mL, 29.8 mmol) and the reaction mixture stirred for 2 h. After addition of a satd. sodium/potassium tartrate solution (100 mL), the reaction mixture was stirred at room temperature for 30 min. The organic layer was separated and washed with brine (200 mL). The aqueous layers were extracted with Et_2O (300 mL). The combined organic layers were dried ($MgSO_4$), the solvent was removed under vacuum and the crude resulted alcohol reacted without further purification.

The alcohol (11.9 mmol) was dissolved in hexane (200 mL) and freshly precipitated MnO_2 (5 g) was added. The suspension was stirred for 16 h, then filtered through Celite (10 g) and the residue washed with Et_2O (200 mL). The combined filtrates were concentrated under vacuum and the crude product chromatographed on silica gel with hexanes/EtOAc (100:1).

3-[(1*S*,2*S*)-2-Vinylcyclopentyl]acrylaldehyde (10c): Yield 607 mg (34%). R_f = 0.85 (hexanes/EtOAc, 10:1). $[\alpha]_D^{20}$ = +107.2 (c = 1.00, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.47–1.64 (m, 2 H, 3-H_a, 5-H_a), 1.75–1.85 (m, 2 H, 4-H), 1.93–2.09 (m, 2 H, 3-H_b, 5-H_b), 2.18–2.31 (m, 1 H, 2-H), 3.09–3.22 (m, 1 H, 1-H), 5.01 (m, 2 H, 2′-H), 5.67 (ddd, J = 17.7, 9.6, 8.1 Hz, 1 H, 1′-H), 5.95 (ddd, J = 11.0, 8.2, 1.0 Hz, 1 H, CH=C*H*CHO), 6.44 (t, J = 11.0 Hz, 1 H, C*H*=CHCHO), 9.96 (dd, J = 8.2, 0.5 Hz, 1 H, CHO) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 24.1 (C-4), 32.5, 33.6 (C-3, C-5), 45.0 (C-1), 52.0 (C-2), 115.5 (C-2′), 130.0 (CH*C*HCHO), 139.7 (C-1′), 156.2 (*C*HCHCHO), 191.5 (CHO) ppm. FT-IR (ATR): $\tilde{\nu}$ = 2955 (m), 2868 (w), 1676 (vs), 1639 (m), 1419 (w), 1172 (m), 995 (m), 911 (s), 761 (s) cm^{-1}. MS (APCI): m/z = 151, 133, 107, 105, 91. HRMS (ESI): calcd. for $C_{10}H_{14}NaO$ [M + Na]: 173.0937; found 173.0934.

3-[(1*S*,2*R*)-2-Phenylcyclopentyl]acrylaldehyde (10d): Yield 634 mg (27%). R_f = 0.74 (hexanes/EtOAc, 10:1). $[\alpha]_D^{20}$ = +90.7 (c = 1.00, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.60–1.74 (m, 1 H, 5-H_a), 1.85–1.98 (m, 3 H, 3-H_a, 4-H), 2.14–2.27 (m, 2 H, 3-H_b, 5-H_b), 2.75–2.86 (m, 1 H, 2-H), 3.39–3.48 (m, 1 H, 1-H), 5.83 (ddd, J = 11.0, 8.2, 1.0 Hz, 1 H, CH=C*H*CHO), 6.49 (dd, J = 11.0, 11.0 Hz, 1 H, C*H*=CHCHO), 7.09–7.32 (m, 5 H, Ar), 9.49 (d, J = 8.2 Hz, 1 H, CHO) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 24.6 (C-4), 33.9 (C-5), 34.4 (C-3), 47.5 (C-1), 53.7 (C-2), 126.7, 127.3, 128.6 (Ar), 130.3 (CH*C*HCHO), 155.8 (*C*HCHCHO), 190.9 (CHO) ppm. FT-IR (ATR): $\tilde{\nu}$ = 2953 (m), 2870 (m), 1728 (m), 1684 (vs), 1493 (w), 1451 (w), 1151 (m), 976 (m), 755 (s), 699 (vs) cm^{-1}. MS (APCI): m/z = 201, 199, 183, 155, 145, 141, 129, 117, 91. HRMS (APCI): calcd. for $C_{14}H_{17}O$ [M + H]: 201.1274; found 201.1262.

3-(2-Allylcyclopentyl)acrylaldehyde (10e): According to the GP, from **13e** (218 mg, 1.05 mmol), DIBAL (2.6 mL, 2.6 mmol), and MnO_2 (0.5 g); yield 109 mg (63%). R_f = 0.56 (pentane/Et_2O, 25:1). Z/E ratio >9:1. ^{1}H NMR (500 MHz, acetone): δ = 1.30–1.39 (m, 1 H, 3-H_a), 1.42–1.51 (m, 1 H, 5-H_a), 1.51–1.60 (m, 1 H, 4-H_a), 1.66–1.77 (m, 2 H, 3-H_b, 4-H_b), 1.81–1.90 (m, 2 H, 1′-H_a, 5-H_b), 2.07–2.20 (m, 2 H, 1′-H_b, 1-H), 3.86–3.96 (m, 1 H, 2-H), 4.80 (ddd, J = 11.2, 2.7, 1.4 Hz, 1 H, 3′-H_{cis}), 4.85 (ddd, J = 17.0, 3.8, 1.4 Hz, 1 H, 3′-H_{trans}), 5.61–5.69 (m, 1 H, 2′-H), 5.77 (dd, J = 11.7, 8.0 Hz, 1 H, CH=C*H*CHO), 6.52 (dd, J = 11.7, 11.7 Hz, 1 H C*H*=CHCHO), 9.99 (d, J = 8.0 Hz, 1 H, CHO) ppm. ^{13}C NMR (125 MHz, acetone): δ = 23.8 (C-4), 31.0 (C-5), 33.1 (C-3), 36.1 (C-1′), 41.1 (C-2), 45.1 (C-1), 115.8 (C-3′), 130.4 (CH*C*HCHO), 138.8 (C-2′), 154.7 (*C*HCHCHO), 191.4 (CHO) ppm. FT-IR (ATR): $\tilde{\nu}$ = 2953 (vs), 2869 (m), 1678 (vs), 1640 (m), 1438 (w), 1085 (m), 994 (m), 912 (vs), 772 (s) cm^{-1}. MS (ESI): m/z (%) = 164 (5), 146 (10), 135 (11), 124 (8), 123 (100), 120 (60), 110 (5), 107 (11), 105 (20), 95 (74), 83 (24), 81 (59), 79 (57), 77 (22), 70 (7), 67 (53), 57 (5), 55 (19), 53 (17), 41 (40), 39 (19). HRMS (EI): calcd. for $C_{11}H_{16}O$ [M$^+$]: 164.1201; found 164.1214.

Ethyl 5-({[Chloro(triphenyl)phosphoranyl]acetyl}amino)pentanoate (14): To a solution of **8a** (182 mg, 1 mmol) in dioxane (10 mL) was added Ph_3PCCO (302 mg, 1 mmol) and the cloudy reaction mixture was heated at 60 °C for 4 h. The solvent was removed under vacuum to give **14** (483 mg, 1 mmol, 100%) as a colorless foam. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.24 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 1.37–1.44 (m, 2 H, 4-H), 1.47–1.56 (m, 2 H, 3-H), 2.21 (t, J = 7.4 Hz, 2 H, 2-H), 3.09 (dd, J = 13.2, 6.6 Hz, 2 H, 5-H), 4.09 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 5.06 (d, $J_{P\text{-}H}$ = 14.4 Hz, 2 H, 7-H), 7.58–7.91 (m, 15 H, Ar-H) 9.93 (br., 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.1 (CH_2CH_3), 22.1 (C-3), 28.1 (C-4), 31.9 (d, $J_{P\text{-}C}$ = 55.2 Hz, C-7), 33.6 (C-2), 39.4 (C-5), 60.0 (CH_2CH_3), 118.3 (d, $J_{P\text{-}C}$ = 88.7 Hz, *i*-C), 129.9 (d, $J_{P\text{-}C}$ = 13.0 Hz, *m*-C), 133.9 (d, $J_{P\text{-}C}$ = 10.6 Hz, *o*-C), 134.8 (d, $J_{P\text{-}C}$ = 2.9 Hz, *p*-C), 162.2 (d, $J_{P\text{-}C}$ = 5.0 Hz, C-6), 173.2 (C-1) ppm. ^{31}P NMR ($CDCl_3$, 202 MHz): δ = 22.1 (m) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3056 (w), 2938 (w), 2868 (w), 2362 (w), 2192 (w), 1730 (m), 1666 (s), 1557 (m), 1438 (s), 1163 (m), 1110 (vs), 1096 (s), 910 (s), 790 (vs) cm^{-1}. MS (ESI): m/z = 448, 420, 303, 279, 219, 201, 129, 101. HRMS (ESI): calcd. for $C_{27}H_{31}NO_3P$ 448.2036; found 448.2041.

General Procedure for the Synthesis of (2*E*,4*Z*)-Dienamides 11: To a solution of freshly prepared **14** (483 mg, 1 mmol) in toluene/CH_2Cl_2 (9:1) at –30 °C was added DBU (0.16 mL, 168 mg, 1.1 mmol) and the reaction mixture stirred for 2 h. Then the respective aldehyde **10a**–**d** (0.7 mmol) was added and the reaction mixture was heated at 170 °C for 20 min in a sealed vessel in a microwave oven. After removal of the solvent, the crude product was chromatographed on silica gel with hexanes/EtOAc (2:1) to separate the isomers. **11e** was prepared from **14** (345 mg, 0.71 mmol), DBU (0.11 mL, 120 mg, 0.79 mmol), and **10e** (82 mg, 0.5 mmol).

Ethyl 5-{[(2*E*,4*E*)-5-Phenylpenta-2,4-dienoyl]amino}pentanoate [(2*E*,4*E*)-11a]: Yield 78 mg (57%). R_f = 0.31 (hexanes/EtOAc, 3:1); m.p. 83 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.26 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 1.56–1.64 (m, 2 H, 4′-H), 1.65–1.73 (m, 2 H, 3′-H), 2.35 (t, J = 7.2 Hz, 2 H, 2′-H), 3.37 (td, J = 6.9, 5.8 Hz, 2 H, 5′-H), 4.13 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 5.72 (br., 1 H, N*H*), 5.96 (d, J = 14.9 Hz, 1 H, 2-H), 6.84–6.87 (m, 2 H, 4-H, 5-H), 7.23–7.45 (m, 5 H, Ar), 7.39 (ddd, J = 14.9, 7.6, 2.6 Hz, 1 H, 3-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_2CH_3), 22.1 (C-3′), 29.0 (C-4′), 33.7 (C-2′), 39.2 (C-5′), 60.4 (CH_2CH_3), 123.9 (C-2), 126.3 (C-4), 127.0 (*m*-C), 128.7 (*p*-C), 128.8 (*o*-C), 136.3 (*i*-C), 139.1 (C-5), 140.9 (C-3), 166.0 (C-1), 173.6 (C-1′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3305 (m), 2950 (m), 2866 (w), 1727 (vs), 1643 (s), 1604 (s), 1523 (s), 1486 (w), 1375 (w), 1262 (m), 1164 (m), 1096 (w), 1035 (w), 993 (vs), 983 (s), 836 (m), 689 (s), 623 (s) cm^{-1}. MS (ESI): m/z = 302, 256, 157, 129. HRMS (ESI): calcd. for $C_{18}H_{24}NO_3$ [M + H]: 302.1756; found 302.1753. $C_{18}H_{23}NO_3$ (301.39): calcd. C 71.73, H 7.69, N 4.65; found: C 71.68, H 7.61, N 4.59.

Compound (2*Z*,4*E*)-11a: Yield 38 mg (18%). R_f = 0.38 (hexanes/EtOAc, 3:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 1.57–1.64 (m, 2 H, 4′-H), 1.65–1.73 (m, 2 H, 3′-H), 2.34 (t, J = 7.2 Hz, 2 H, 2′-H), 3.35 (td, J = 6.9, 5.8 Hz, 2 H, 5′-H), 4.13 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 5.61 (ddd, J = 11.2, 1.1, 0.8 Hz, 1 H, 2-H), 5.72 (br., 1 H, N*H*), 6.57 (td, J = 11.2, 0.9 Hz, 1 H, 3-H), 6.73 (d, J = 15.8 Hz, 1 H, 5-H), 7.25–7.34 (m, 3 H, Ar), 7.50–7.54 (m, 2 H, Ar), 8.30 (ddd, J = 15.8, 11.2, 1.1 Hz, 1 H, 4-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_2CH_3), 22.1 (C-3′), 29.0 (C-4′), 33.8 (C-2′), 39.0 (C-5′), 60.4 (CH_2CH_3), 120.1 (C-2), 125.3 (C-4), 127.4 (*m*-C), 128.6 (*p*-C), 128.7 (*o*-C), 136.6 (*i*-C), 139.7 (C-5), 141.4 (C-3), 166.4 (C-1), 173.6 (C-1′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3249 (m), 2934 (m), 2868 (w), 2182 (w), 1730 (vs), 1649 (s), 1615 (s), 1538 (s), 1449 (m), 1371 (m), 1242 (s), 1170 (vs), 1100 (m), 1029 (m), 1001 (m), 966 (m), 747 (m), 692 (s) cm^{-1}. MS (ESI): *m*/*z* = 302, 157, 145, 129, 115. HRMS (ESI): calcd. for $C_{18}H_{24}NO_3$ [M + H]: 302.1756; found 302.1758.

Compound (2*E*,4*Z*)-11a: Yield 99 mg (47%). R_f = 0.34 (hexanes/EtOAc, 3:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 1.50–1.74 (m, 4 H, 3′-H, 4′-H), 2.33 (t, J = 7.2 Hz, 2 H, 2′-H), 3.34 (td, J = 6.8, 5.8 Hz, 2 H, 5′-H), 4.13 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 5.70 (br., 1 H, N*H*), 5.99 (dt, J = 14.9, 0.9 Hz, 1 H, 2-H), 6.32 (td, J = 11.6, 0.9 Hz, 1 H, 4-H), 6.72–6.77 (m, 1 H, 5-H), 7.26–7.45 (m, 5 H, Ar), 7.72 (ddd, J = 14.9, 11.6, 0.9 Hz, 1 H, 3-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_2CH_3), 22.1 (C-3′), 29.0 (C-4′), 33.8 (C-2′), 39.1 (C-5′), 60.4 (CH_2CH_3), 126.4 (C-2), 127.5 (C-4), 127.9, 128.5, 129.2 (Ar), 136.5 (Ar), 136.5, 136.6 (C-3, C-5), 166.1 (C-1), 173.6 (C-1′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3281 (m), 2935 (m), 2869 (w), 2175 (m), 1730 (vs), 1650 (s), 1614 (s), 1540 (s), 1486 (w), 1273 (m), 1177 (s), 1100 (w), 1029 (w), 997 (m), 869 (m), 696 (s) cm^{-1}. MS (ESI): *m*/*z* = 324, 302, 279, 157, 145, 129, 115. HRMS (ESI): calcd. for $C_{18}H_{23}NO_3Na$ [M + Na]: 324.1570; found 324.1562.

Compound (2*Z*,4*Z*)-11a: Yield 34 mg (16%). R_f = 0.37 (hexanes/EtOAc, 3:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 1.56–1.63 (m, 2 H, 4′-H), 1.66–1.73 (m, 2 H, 3′-H), 2.34 (t, J = 7.2 Hz, 2 H, 2′-H), 3.37 (td, J = 6.9, 5.8 Hz, 2 H, 5′-H), 4.13 (q, J = 7.1 Hz, 2 H, CH_2CH_3), 5.72 (br., 1 H, N*H*), 5.69 (dt, J = 11.5, 1.3 Hz, 1 H, 2-H), 6.87 (td, J = 11.5, 1.3 Hz, 1 H, 3-H), 6.79–6.82 (m, 1 H, 5-H), 7.57 (td, J = 11.5, 1.3 Hz, 1 H, 4-H), 7.24–7.37 (m, 5 H, Ar) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.3 (CH_2CH_3), 22.2 (C-3′), 29.1 (C-4′), 33.9 (C-2′), 38.8 (C-5′), 60.4 (CH_2CH_3), 122.5 (C-2), 126.0 (C-4), 127.7 (*m*-C), 128.3 (*p*-C), 129.4 (*o*-C), 136.2 (C-5), 136.5 (C-3), 136.6 (*i*-C), 166.3 (C-1), 173.6 (C-1′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3296 (m), 2934 (m), 2869 (w), 1730 (vs), 1638 (s), 1532 (s), 1436 (w), 1371 (w), 1243 (m), 1164 (s), 1096 (m), 1028 (m), 813 (m), 697 (s) cm^{-1}. MS (ESI): *m*/*z* = 324, 302, 157, 145, 129, 115. HRMS (ESI): calcd. for $C_{18}H_{23}NO_3Na$ [M + Na]: 324.1570; found 324.1564.

Ethyl 5-{[(2*E*,4*Z*)-5-Cyclopentylpenta-2,4-dienoyl]amino}pentanoate [(2*E*,4*Z*)-11b]: Yield 120 mg (58%). R_f = 0.42 (hexanes/EtOAc, 2:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.22–1.29 (m, 2 H, 7-H_a, 10-H_a), 1.25 (t, J = 7.1 Hz, 3 H, CH_3CH_2O), 1.54–1.72 (m, 8 H, 3′-H, 4′-H, 8-H, 9-H), 1.77–1.88 (m, 2 H, 7-H_b, 10-H_b), 2.33 (t, J = 7.2 Hz, 2 H, 2′-H), 2.98–3.01 (m, 1 H, 6-H), 3.35 (td, J = 6.9, 5.8 Hz, 2 H, 5′-H), 4.13 (q, J = 7.1 Hz, 2 H, CH_3CH_2O), 5.69 (ddt, J = 10.7, 9.8, 1.0 Hz, 1 H, 5-H), 5.75–5.80 (m, 1 H, N*H*), 5.82 (dd, J = 14.9, 0.9 Hz, 1 H, 2-H), 6.00 (ddt, J = 11.6, 10.7, 0.9 Hz, 1 H, 4-H), 7.57 (ddd, J = 14.9, 11.6, 1.0 Hz, 1 H, 3-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_3CH_2O), 22.1 (C-3′), 25.5 (C-8, C-9), 29.0 (C-4′), 33.7 (C-2′), 33.8 (C-7, C-10), 39.0 (C-6), 39.1 (C-5′), 60.4 (CH_3CH_2O), 123.4 (C-5), 124.9 (C-2), 136.4 (C-4), 145.5 (C-3), 166.4 (C-1), 173.6 (C-1′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3270 (w), 2944 (s), 2868 (s), 1730 (vs), 1650 (s), 1542 (s), 1447 (w), 1324 (w), 1163 (vs), 1096 (s), 1029 (s), 981 (s), 724 (w) cm^{-1}. MS (ESI): *m*/*z* = 294, 149, 131, 121, 100. HRMS (ESI): calcd. for $C_{17}H_{28}NO_3$ [M + H]: 294.2064; found 294.2065.

Compound (2*Z*,4*Z*)-11b: Yield 46 mg (22%). R_f = 0.47 (hexanes/EtOAc, 2:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.21–1.34 (m, 2 H, 7-H_a, 10-H_a), 1.26 (t, J = 7.1 Hz, 3 H, CH_3CH_2O), 1.54–1.73 (m, 8 H, 3′-H, 4′-H, 8-H, 9-H), 1.78–1.86 (m, 2 H, 7-H_b, 10-H_b), 2.33 (t, J = 7.3 Hz, 2 H, 2′-H), 2.90–3.41 (m, 1 H, 6-H), 3.31 (td, J = 6.9, 5.7 Hz, 2 H, 5′-H), 4.13 (q, J = 7.1 Hz, 2 H, CH_3CH_2O), 5.56 (dt, J = 11.5, 1.4 Hz, 1 H, 2-H), 5.59–5.68 (m, 1 H, N*H*), 5.72 (ddt, J = 11.0, 9.7, 1.4 Hz, 1 H, 5-H), 6.78 (td, J = 11.5, 1.4 Hz, 1 H, 3-H), 7.17–7.22 (m, 1 H, 4-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_3CH_2O), 22.1 (C-3′), 25.5 (C-8, C-9), 29.0 (C-4′), 33.7 (C-2′), 33.8 (C-7, C-10), 38.1 (C-6), 38.6 (C-5′), 60.4 (CH_3CH_2O), 120.2 (C-2), 122.9 (C-5), 135.5 (C-3), 145.1 (C-4), 166.6 (C-1), 173.6 (C-1′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3293 (w), 2949 (s), 2867 (s), 1732 (vs), 1645 (s), 1535 (s), 1447 (m), 1372 (m), 1243 (s), 1162 (vs), 1096 (m), 1030 (m), 710 (w) cm^{-1}. MS (ESI): *m*/*z* = 316, 294, 149, 131, 121, 93. HRMS (ESI): calcd. for $C_{17}H_{28}NO_3$ [M + H]: 294.2064; found 294.2043.

Ethyl 5-({(2*E*,4*Z*)-5-[(1*S*,2*S*)-2-Vinylcyclopentyl]penta-2,4-dienoyl}amino)pentanoate [(2*E*,4*Z*)-11c]: Yield 145 mg (65%). R_f = 0.52 (hexanes/EtOAc, 1:1). $[\alpha]_D^{20}$ = +94.1 (c = 1.00, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.1 Hz, 3 H, CH_3CH_2O), 1.35–1.54 (m, 2 H, 8-H_a, 10-H_a), 1.54–1.61 (m, 2 H, 4′-H), 1.64–1.73 (m, 4 H, 3′-H, 9-H), 1.87–1.95 (m, 2 H, 8-H_b, 10-H_b), 2.13–2.20 (m, 1 H, 7-H), 2.33 (t, J = 7.2 Hz, 2 H, 2′-H), 2.79 (dddd, J = 19.9, 10.0, 7.7, 0.9 Hz, 1 H, 6-H), 3.34 (tdd, J = 6.8, 5.9, 1.0 Hz, 2 H, 5′-H), 4.13 (q, J = 7.1 Hz, 2 H, CH_3CH_2O), 4.90 (ddd, J = 10.2, 2.0, 0.9 Hz, 1 H, *cis*-CH_2=), 4.93 (ddd, J = 17.1, 2.0, 1.1 Hz, 1 H, *trans*-CH_2=), 5.59–5.64 (m, 1 H, 5-H), 5.69 (ddd, J = 17.1, 10.2, 7.8 Hz, 1 H, CH=), 5.80 (dt, J = 14.8, 0.8 Hz, 1 H, 2-H), 6.09 (ddt, J = 11.6, 10.7, 0.9 Hz, 1 H, 4-H), 7.49 (ddd, J = 14.8, 11.6, 1.1 Hz, 1 H, 3-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_3CH_2O), 22.1, 23.8 (C-3′, C-9), 29.0 (C-4′), 32.3 (C-8), 33.4 (C-10), 33.7 (C-2′), 39.1 (C-5′), 45.4 (C-6), 51.9 (C-12), 60.4 (CH_3CH_2O), 114.1 (CH_2=), 123.8 (C-2), 126.4 (C-4), 136.5 (C-3), 141.0 (CH=), 143.5 (C-5), 166.4 (C-1), 173.6 (C-1′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3273 (w), 2941 (m), 2867 (m), 1733 (vs), 1652 (s), 1619 (s), 1542 (s), 1447 (w), 1321 (m), 1272 (m), 1163 (vs), 1097 (s), 1030 (m), 992 (s), 908 (m), 867 (m), 668 (m) cm^{-1}. MS (ESI): *m*/*z* = 320, 175, 157, 147, 133, 119, 105, 91. HRMS (ESI): calcd. for $C_{19}H_{29}NO_3Na$ [M + Na]: 342.2040; found 342.2037.

Compound (2*Z*,4*Z*)-11c: Yield 34 mg (15%). R_f = 0.60 (hexanes/EtOAc, 1:1). $[\alpha]_D^{20}$ = +37.2 (c = 1.00, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.1 Hz, 3 H, CH_3CH_2O), 1.38–1.75 (m, 8 H, 3′-H, 4′-H, 8-H_a, 9-H, 10-H_a), 1.82–1.99 (m, 2 H, 8-H_b, 10-H_b), 2.11–2.25 (m, 1 H, 7-H), 2.33 (t, J = 7.1 Hz, 2 H, 2′-H), 2.61–2.76 (m, 1 H, 6-H), 3.31 (td, J = 6.8, 5.8 Hz, 2 H, 5′-H), 4.12 (q, J = 7.1 Hz, 2 H, CH_3CH_2O), 4.90 (ddd, J = 10.3, 1.9, 1.0 Hz, 1 H, *cis*-CH_2=), 4.96 (ddd, J = 17.2, 1.9, 1.1 Hz, 1 H, *trans*-CH_2=), 5.55 (dt, J = 11.7, 1.1 Hz, 1 H, 2-H), 5.58–5.78 (m, 3 H, CH=, 5-H, N*H*), 6.69 (td, J = 11.7, 1.2 Hz, 1 H, 3-H), 7.27 (ddt, J = 11.7, 10.9, 1.1 Hz, 1 H, 4-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_3CH_2O), 22.2, 23.9 (C-3′, C-9), 29.1 (C-4′), 32.2 (C-8), 33.4 (C-10), 33.8 (C-2′), 38.9 (C-5′), 44.6 (C-6), 51.6 (C-7), 60.4 (CH_3CH_2O), 114.1 (CH_2=), 120.7 (C-2), 124.3 (C-4), 135.6 (C-3), 141.0 (CH=), 143.1 (C-5), 166.4 (C-1), 173.5 (C-1′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3294 (w), 2937 (m), 2868 (m), 1732 (vs), 1640 (s), 1535 (s), 1446 (w), 1372 (m), 1241 (s), 1162 (vs), 1096 (s), 1030 (m), 996

(m), 908 (m), 798 (m), 710 (w), 669 (w) cm^{-1}. MS (ESI): *m*/*z* = 320, 175, 157, 147, 133, 119, 105, 91. HRMS (ESI): calcd. for $C_{19}H_{30}NO_3$ [M + H]: 320.2220; found 320.2211.

Ethyl 5-({(2*E*,4*Z*)-5-[(1*S*,2*R*)-2-Phenylcyclopentyl]penta-2,4-dienoyl}-amino)pentanoate [(2*E*,4*Z*)-11d]: Yield 155 mg (60%). R_f = 0.45 (hexanes/EtOAc, 1:1). $[\alpha]_D^{20}$ = +8.6 (*c* = 1.00, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.23 (t, *J* = 7.1 Hz, 3 H, CH_3CH_2O), 1.47–1.60 (m, 3 H, 4′-H, 10-H_a), 1.62–1.70 (m, 2 H, 3′-H), 1.76–1.92 (m, 3 H, 8-H_a, 9-H), 2.02–2.10 (m, 1 H, 10-H_b), 2.12–2.20 (m, 1 H, 8-H_b), 2.33 (t, *J* = 7.2 Hz, 2 H, 2′-H), 2.73 (td, *J* = 10.0, 7.9 Hz, 1 H, 7-H), 3.10–3.13 (m, 1 H, 6-H), 3.23–3.31 (m, 2 H, 5′-H), 4.13 (q, *J* = 7.1 Hz, 2 H, CH_3CH_2O), 5.51 (br., 1 H, N*H*), 5.64–5.71 (m, 2 H, 2-H, 5-H), 5.97 (dddd, *J* = 11.6, 10.6, 0.9, 0.9 Hz, 1 H, 4-H), 7.11–7.15 (m, 1 H, 3-H), 7.17–7.21 (m, 1 H, *p*-H), 7.23–7.28 (m, 4 H, *o*-H, *m*-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_3CH_2O), 22.1 (C-3′), 24.3 (C-8), 29.0 (C-4′), 33.8 (C-2′), 33.9 (C-7), 34.8 (C-9), 39.1 (C-5′), 47.2 (C-6), 53.5 (C-10), 60.4 (CH_3CH_2O), 123.9 (C-2), 126.1 (*p*-C), 126.7 (C-3), 128.3 (*o*-C), 128.5 (*m*-C), 135.7 (C-4), 143.0 (C-5), 143.7 (*i*-C), 166.3 (C-1), 173.6 (C-1′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3278 (w), 2941 (m), 2861 (m), 1731 (vs), 1652 (s), 1620 (s), 1542 (s), 1452 (m), 1372 (w), 1163 (vs), 1097 (m), 1030 (m), 992 (m), 960 (w), 905 (m), 868 (m), 699 (vs) cm^{-1}. MS (ESI): *m*/*z* = 370, 255, 197, 183, 169, 141, 117, 105. HRMS (ESI): calcd. for $C_{23}H_{31}NNaO_3$ [M + Na]: 392.2196; found 392.2190.

Compound (2*Z*,4*Z*)-11d: Yield 44 mg (17%). R_f = 0.56 (hexanes/EtOAc, 1:1). $[\alpha]_D^{20}$ = –0.5 (*c* = 1.00, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 1.23 (t, *J* = 7.3 Hz, 3 H, CH_3CH_2O), 1.49–1.58 (m, 3 H, 4′-H, 10-H_a), 1.59–1.67 (m, 2 H, 3′-H), 1.79–1.89 (m, 3 H, 8-H_a, 9-H), 1.98–2.08 (m, 1 H, 10-H_b), 2.11–2.21 (m, 1 H, 8-H_b), 2.33 (t, *J* = 7.3 Hz, 2 H, 2′-H), 2.73 (td, *J* = 9.8, 7.6 Hz, 1 H, 7-H), 3.01–3.12 (m, 1 H, 6-H), 3.19–3.28 (m, 2 H, 5′-H), 4.13 (q, *J* = 7.3 Hz, 2 H, CH_3CH_2O), 5.34 (dt, *J* = 11.3, 1.3 Hz, 1 H, 2-H), 5.50 (br., 1 H, N*H*), 5.70 (ddt, *J* = 11.1, 9.8, 1.3 Hz, 1 H, 5-H), 6.30 (td, *J* = 11.3, 1.3 Hz, 1 H, 3-H), 7.12–7.21 (m, 4 H, 4-H, *o*-H, *p*-H), 7.21–7.27 (m, 2 H, *m*-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2 (CH_3CH_2O), 22.1 (C-3′), 24.6 (C-8), 29.0 (C-4′), 33.8 (C-2′), 33.9 (C-7), 34.6 (C-9), 38.8 (C-5′), 46.8 (C-6), 53.5 (C-10), 60.4 (CH_3CH_2O), 120.4 (C-2), 124.4 (C-4), 126.0 (*p*-C), 127.4 (*o*-C), 128.3 (*m*-C), 135.3 (C-3), 141.3 (C-5), 142.7 (*i*-C), 166.5 (C-1), 173.5 (C-1′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3295 (w), 2947 (m), 2868 (m), 1730 (vs), 1632 (s), 1531 (s), 1452 (m), 1368 (w), 1166 (vs), 1095 (m), 1032 (m), 939 (m), 897 (m), 750 (m), 700 (vs) cm^{-1}. MS (ESI): *m*/*z* = 370, 255, 197, 183, 169, 141, 117, 105. HRMS (ESI): calcd. for $C_{23}H_{31}NNaO_3$ [M + Na]: 392.2196; found 392.2190.

Ethyl 5-({(2*E*,4*Z*)-5-[2-Allylcyclopentyl]penta-2,4-dienoyl}amino)-pentanoate [(2*E*,4*Z*)-11e]: Yield 96 mg (58%). R_f = 0.36 (hexanes/EtOAc, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.1 Hz, 3 H, $CO_2CH_2CH_3$), 1.31–1.40 (m, 1 H, 8-H_a), 1.40–1.49 (m, 1 H, 10-H_a), 1.54–1.64 (m, 3 H, 4′-H, 9-H_a), 1.64–1.71 (m, 2 H, 3′-H), 1.70–1.89 (m, 4 H, =CHC$H_a$$H_b$, 8-$H_b$, 9-$H_b$, 10-$H_b$), 1.99–2.05 (m, 1 H, 7-H), 2.06–2.13 (m, 1 H, =CHC$H_a$$H_b$), 2.33 (t, *J* = 7.2 Hz, 2 H, 2′-H), 3.15–3.28 (m, 1 H, 6-H), 3.35 (td, *J* = 6.7, 5.7 Hz, 2 H, 5′-H), 4.12 (q, *J* = 7.1 Hz, 2 H, $CO_2CH_2CH_3$), 4.92 (ddt, *J* = 10.2, 2.4, 1.1 Hz, 1 H, *cis*-CH_2=), 4.95 (ddt, *J* = 17.0, 2.4, 1.3 Hz, 1 H, *trans*-CH_2=), 5.68–5.77 (m, 2 H, C*H*=CH_2, 5-H), 5.86 (dt, *J* = 14.9, 0.8 Hz, 1 H, 2-H), 5.96–6.00 (m, 1 H, N*H*), 6.09 (ddt, *J* = 11.7, 10.7, 0.9 Hz, 1 H, 4-H), 7.57 (ddd, *J* = 14.9, 11.7, 1.2 Hz, 1 H, 3-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2 ($CO_2CH_2CH_3$), 22.1 (C-3′), 23.2 (C-9), 29.0 (C-4′), 30.4 (C-8), 32.5 (C-10), 33.8 (C-2′), 35.5 (CHCH_2), 39.1 (C-5′), 41.1 (C-6), 44.0 (C-7), 60.4 ($CO_2CH_2CH_3$), 115.1 (CH_2=), 124.0 (C-2), 126.1 (C-4), 136.0 (C-3), 138.2 (CH=), 141.5 (C-5), 166.4 (C-1), 173.6 (C-1′) ppm. FT-IR (ATR): $\tilde{\nu}$ = 3279 (w), 2942 (m), 2869 (m), 1733 (vs), 1652 (s), 1618 (s), 1542 (s), 1442 (m), 1372 (m), 1326 (m), 1273 (s), 1163 (vs), 1097 (m), 1031 (m), 993 (s), 962 (m), 910 (m), 869 (m), 786 (w), 732 (w), 674 (w) cm^{-1}. MS (ESI): *m*/*z* (%) = 334 (47) [M^+ + H], 189 (28), 171 (30), 161 (100), 133 (19). HRMS (ESI): calcd. for $C_{20}H_{31}NNaO_3$ [M + Na]: 356.2196; found 356.2202.

Supporting Information (see also the footnote on the first page of this article): Detailed procedures, ^1H and ^{13}C NMR spectra, analytical data of precursors. GC separations of the enantiomers of derivatives **12c**,**d**.

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