Microwave-assisted reactions of allenic esters: [3+2] anellations and allenoate-Claisen rearrangement

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Dedicated to Prof. António Rocha Gonçalves on the occasion of his 70th anniversary

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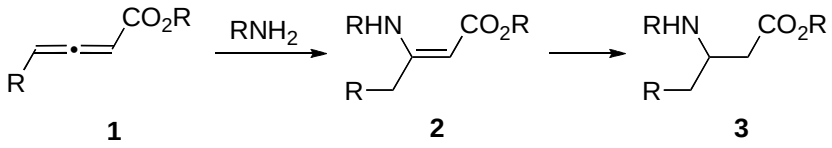
Abstract

The reactivity of allenic esters towards an activated *N*-sulfonylimine and electron-deficient alkenes with a phosphine under microwave irradiation is explored. The methodology is shown to be efficient for the one-step synthesis of 3-pyrrolines and cyclopentenes in a regio- and diastereoselective manner. This formal [3+2] cycloaddition is complete within five minutes. It was also demonstrated that microwave irradiation is the best energy source to carry out the Lewis acid catalyzed allenoate-Claisen rearrangement leading to 3-(pyrrolidin-1-yl)hepta-2,6-dienoates.

Keywords: Microwave-assisted reactions, [3+2] anellation, allenoate-Claisen rearrangement, 3-pyrrolines, cyclopentenes, hepta-2,6-dienoates

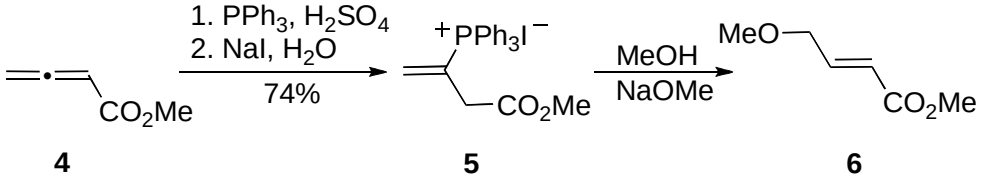
Introduction

Allenes are important and versatile building blocks in organic chemistry.[1-4] The inherent instability associated to the cumulated double bonds has been widely exploited for synthetic purposes. This structural feature makes addition to allenes very favourable, since it involves a relief in strain. We have developed an asymmetric Wittig reaction that allows the synthesis of allenic esters **1** with axial chirality and an approach to chiral β-amino esters **3** involving the stereoselective reduction of β-enamino esters **2** bearing a chiral auxiliary in the ester moiety, obtained from the nucleophilic addition of amines to the chiral 2,3-allenoates (Scheme 1).[5,6] This drove us to explore other aspects of the reactivity of 2,3-butadienoates.



Scheme 1

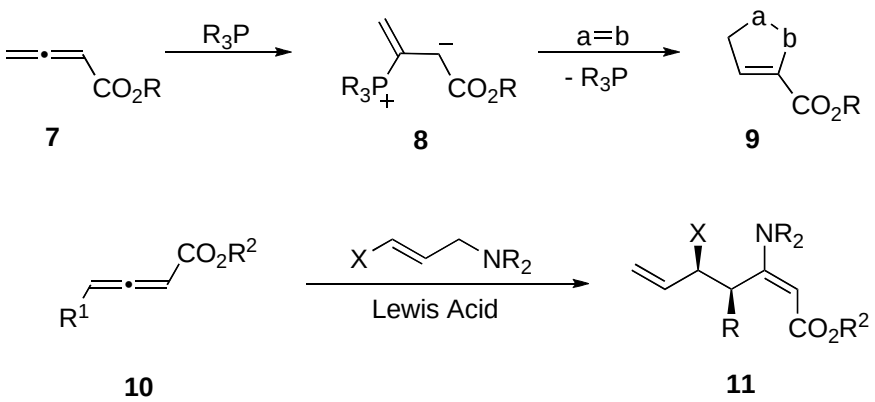
It is known that addition of nucleophiles to electron-deficient allenes occurs at the electrophilic α,β–carbon–carbon double bond to give Michael type adducts.[7] However, reactivity inversion (umpolung) can be achieved. Cristau *et al*. observed that in the presence of phosphines the addition takes place at the β,γ–carbon–carbon double bond.[8] They found that the reaction of methyl 2,3-butadienoate (**4**) with triphenylphosphine followed by the addition of NaI afforded a phosphonium iodide **5**, which allows nucleophilic attack at the γ–carbon leading to the synthesis of 4-substituted-but-2-enoate **6** (Scheme 2).



Scheme 2

Lu *et al.* explored the reactivity of the intermediates **8** generated from butadienoates and phosphines as the three-carbon synthon in [3+2] anellation reactions (Scheme 3). They reported that reaction with electron-deficient alkenes,[9] and *N*-tosylimines[10] led to the formation of five-membered formal [3+2] cycloadducts **9**. The use of chiral phosphines as catalyst for the formal enantioselective [3+2] cycloaddition of electron-deficient allenes with electron-deficient alkenes and imines has also been reported.[11,12] The reaction of *N*-tosylimines with ethyl 2,3-butadienoate and ethyl penta-2,3-dienoate has been systematically studied in the presence of various nitrogen and phosphine Lewis base promoters.[13] Particular interesting also is the allenoate-Claisen rearrangement allowing the stereoselective synthesis of β-enamino esters **11** comprising 1,2-tertiary-quaternary carbon stereogenic centers from simple butadienoates and allylic amines.[14]

The versatility of 2,3-butadienoate reactivity makes the gathering of new data on these synthetic building blocks a relevant research goal. In this context, the reactivity of allenes towards activated imines and electron-deficient alkenes with phosphine catalysis under microwave irradiation as well as the microwave-assisted allenoate-Claisen rearrangement was explored.



Scheme 3

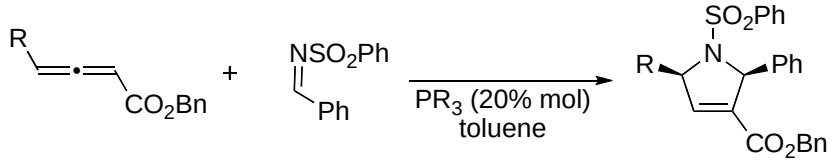
Results and Discussion

3-Pyrrolines are particularly interesting heterocycles since they can be used as intermediates in natural product synthesis[15] and show diverse biological activities.[16] A significant number of synthetic approaches to pyrrolines has been reported.[17] The one-step synthesis of 3-pyrrolines *via* phosphine-catalysed condensation of allenes and imines is an interesting route to this important class of compounds. We carried out the reaction of benzyl 2,3-butadienoate **12a**[18a,14] with *N*-benzylidenebenzenesulfonamide **13**[18b] in the presence of triphenylphosphine at room temperature, which gave the expected 3-pyrroline **14a** in a regioselective fashion and in 69% yield. Compound **14a** was also obtained using conventional thermolysis reaction conditions. Carrying out the reaction at 50 ºC for 1 hour gave product **14a** in 58% yield, at 100 ºC for 1 hour 3-pyrroline **14a** was isolated in 38% yield, and after 2.5 hours at 100 ºC compound **14a** was obtained in significantly lower yield (15%). We observed that under microwave irradiation at 100 ºC for 5 minutes, 3-pyrroline **14a** could be obtained in good yield (64%). Carrying out this microwave-assisted reaction at lower temperature (50 ºC) after 5 minutes the [3+2] cycloadduct was isolated in 35% yield. Irradiation at 150 ºC leads to the degradation of the starting materials without any evidence of the target molecule (Table 1). The results obtained using the optimized conditions for the microwave-assisted [3+2] anellation reaction clearly demonstrate the advantage of using this nonconventional energy source, which allows the reduction of the reaction time to 5 minutes still leading to the desired cycloadduct in good yield.

The reactivity of γ–(*t*-butyl)allenoate **12b**[18a] with *N*-sulfonylimine **13** in the presence of phosphines was also studied (Table 1). A microwave-assisted process using triphenylphosphine as catalyst, did not allow the formation of any product. However, in the presence of tributylphosphine in toluene at room temperature, the *cis*-3-pyrroline **14b** was obtained exclusively in a stereoselective fashion (44% yield). Upon microwave irradiation at 100 ºC for 5 minutes the same diastereoselectivity was observed and the [3+2] cyclized product **14b** obtained in 50% yield. A similar behaviour was also previously observed where more nucleophilic

phosphines such as tributylphosphine instead of triphenylphosphine were required to carry out the reaction of *N*-sulfonylimines with sterically demanding γ–(t-butyl)-allenoates.[19] In contrast with this observation, the reaction of γ–methylallenoate **12c**[18a,14] with *N*-benzylidenebenzenesulfonamide **13** can be carried out in the presence of triphenylphosphine affording the *cis*-3-pyrroline **14c**. Under conventional reaction conditions this heterocycle was obtained in 38% yield, whereas the microwave-assisted reaction led to the same product in 43% yield in a short reaction time.

Table 1. [3+2] Anellation reaction of butadienoates with imine **13**



12a R = H
12b R = *t*-Bu
12c R = Me

13

14a R = H
14b R = *t*-Bu
14c R = Me

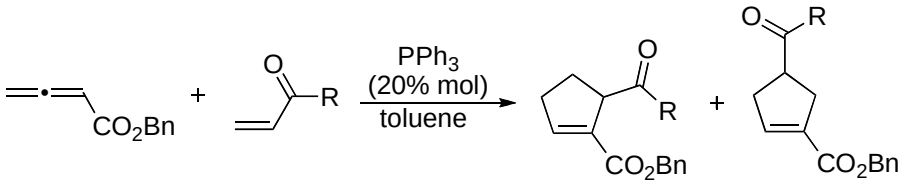
Allene	Phosphine	Reaction conditions	Yield
12a	PPh_3	rt, 1.25 h	69%
12a	PPh_3	50 ºC, 1 h	58%
12a	PPh_3	100 ºC, 1 h	38%
12a	PPh_3	100 ºC, 2.5 h	15%
12a	PPh_3	MW, 100 ºC, 5 min	64%
12a	PPh_3	MW, 50 ºC, 5 min	35%
12b	PBu_3	rt, 18h	44%
12b	PBu_3	MW, 100 ºC, 5 min	50%
12b	PPh_3	MW, 100 ºC, 5 min, then 150 ºC, 15 min	----
12c	PPh_3	rt, 2.5 h	38%
12c	PPh_3	MW, 100 ºC, 5 min	43%

The synthesis of cyclopentenes *via* [3+2] anellation of benzyl 2,3-butadienoate **12a** with electron-deficient alkenes was explored (Table 2). Allene **12a** reacted with methyl vinyl ketone (**15a**, 1 equiv) in the presence of triphenylphosphine in toluene at 70 ºC to produce the regioisomeric cyclopentenes **16** and **17a** in 70% overall yield. The observed regioselectivity is in agreement with the one reported by Lu *et al.*.[9] This reaction could be carried out under microwave irradiation at 50 ºC for 5 minutes giving esters **16** (26%) and **17a** (37%). Performing the microwave-assisted reaction at 70 ºC for 5 minutes gave the same products with a slight improvement in the overall yield (66%).

The triphenylphosphine-catalyzed [3+2] anellation of benzyl 2,3-butadienoate **12a** and acrolein **15b** in toluene at 70 ºC gave regioselectively benzyl 4-formylcyclopent-1-enecarboxylate **17b** in 74% yield.

Unfortunately, under microwave irradiation the cycloadduct **17b** could only be obtained in 24% yield due to the polymerization of the acrolein. Attempts to improve the yield using an excess of acrolein were not successful.

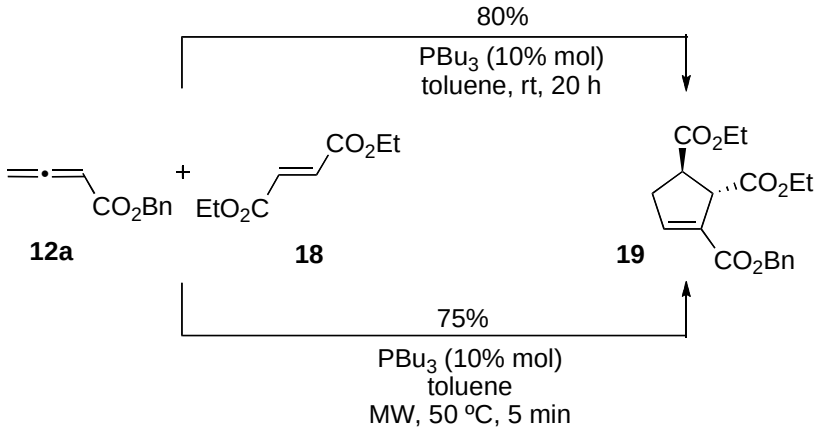
Table 2. [3+2] anellation of allene **12a** with methyl vinyl ketone and acrolein



12a **15a** R = Me **15b** R = H **16** R = Me **17a** R = Me **17b** R = H

Alkene	Reaction conditions	Yield
15a	70 ºC, 1 h	**16** 27%; **17a** 43%
15a	MW, 50 ºC, 5 min	**16** 26%; **17a** 37%
15a	MW, 70 ºC, 5 min	**16** 27%; **17a** 39%
15b	70 ºC, 1 h	--- ; **17b** 74%
15b	MW, 50 ºC, 5 min	--- ; **17b** 18%
15b	MW, 70 ºC, 5 min	--- ; **17b** 24%

Benzyl 2,3-butadienoate **12a** reacted with diethyl fumarate **18** under conventional reaction conditions, using tributylphosphine as catalyst, to give the *trans*-cyclopent-3-ene-1,2,3-tricarboxylate **19** in 80% yield, as a single isomer. Under microwave irradiation at 50 ºC for 5 minutes the same product was isolated in 75% yield (Scheme 4).

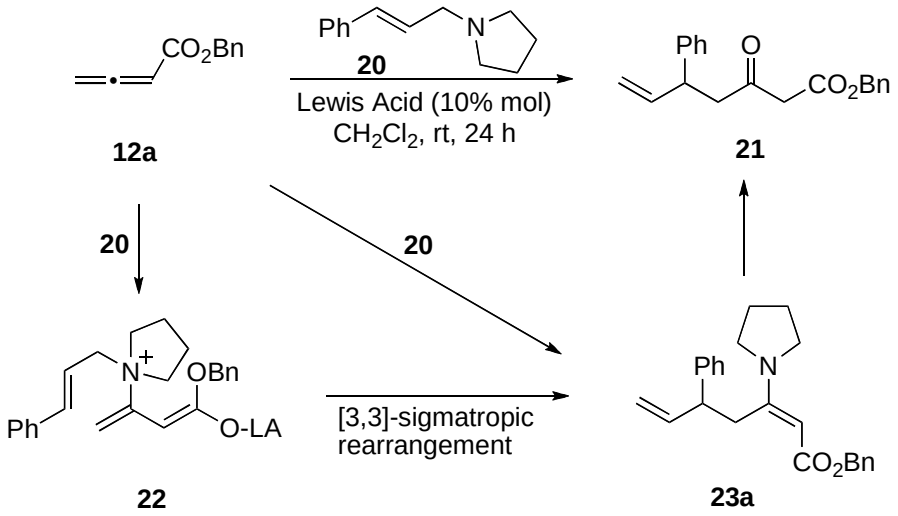


12a 18 19

Scheme 4

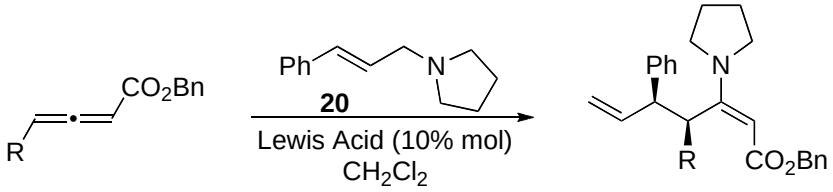
We decided to look into the Lewis acid catalyzed allenoate-Claisen rearrangement and explore the possibility of carrying out the reactions under microwave irradiation in order to determine whether this process could be applied for stereoselective carbon-carbon bond construction. The reaction of allenes **12a** and **12c** with tertiary allylamine 1-cinnamylpyrrolidine[14] (**20**) in the presence of $AlCl_3$ or $Zn(OTf)_2$ was studied.

It was observed that allene **12a** reacts with amine **20** in the presence of either $AlCl_3$ or $Zn(OTf)_2$ giving benzyl 3-oxo-5-phenylhept-6-enoate **21** (64-68% yield) and not the expected β-enamino ester **23a**. The formation of keto ester **21** could be explained by initial generation of zwitterionic allyl-vinylammonium complexes **22**, which participate in a [3,3]-sigmatropic rearrangement, formation of enamine **23a** and subsequent hydrolysis to the corresponding functionalized keto ester **21** (Scheme 5).



Scheme 5

Table 3. Lewis acid-catalyzed allenoate-Claisen rearrangement



12a R = H
12c R = Me

23a R = H
23b R = Me

Entry	Lewis acid	Reaction conditions	Product, Yield	*syn:anti*[a]
1	$AlCl_3$	MW, 100 ºC, 15 min	**23a**, 87%	---
2	$Zn(OTf)_2$	MW, 100 ºC, 15 min	**23a**, 99%	---
3	$AlCl_3$	rt, 24 h	**23b**, 59%	67:33
4	$AlCl_3$	100 ºC, 1 h[b]	**23b**, 61%	70:30
5	$AlCl_3$	MW, 50 ºC, 30 min	**23b**, 72%	75:25
6	$AlCl_3$	MW, 100 ºC, 15 min	**23b**, 91%	76:24
7	$Zn(OTf)_2$	rt, 24 h	**23b**, 64%	70:30
8	$Zn(OTf)_2$	100 ºC, 1 h[b]	**23b**, 64%	70:30
9	$Zn(OTf)_2$	MW, 100 ºC, 15 min	**23b**, 97%	75:25
10	$Zn(OTf)_2$	MW, 100 ºC, 15 min[b]	**23b**, 92%	71:29

[a]Product ratio determined by ^{1}H NMR analysis.
[b]Using toluene as solvent.

However, the (*E*)-5-phenyl-3-(pyrrolidin-1-yl)hepta-2,6-dienoate **23a** could be obtained in high yield carrying out the reaction under microwave irradiation at 100 ºC for 15 minutes (Table 3). Using $AlCl_3$ as Lewis acid compound **23a** was isolated in 87% yield (entry 1) whereas with $Zn(OTf)_2$ hepta-2,6-dienoate **23a** was obtained in 99% yield (entry 2).

Diastereoselective preparation of β-enamino ester **23b** was observed from γ–methylallenoate **12c** and allylic amine **20** in the presence of Lewis acids *via* [3,3]-sigmatropic rearrangement of the corresponding zwitterionic allyl-vinylammonium complexe (Table 3). The reaction catalyzed by $AlCl_3$ using the conventional reaction conditions gave the rearrangement adduct **23b** in 59% yield and 67:33 *syn*:*anti* selectivity (entry 3). The observed diastereoselectivity in the C-C bond formation can be explained by considering that there is a π-facial discrimination in the cumulene addition step leading to selective formation of the *E*-enamino intermediate and the propensity of [3,3]-sigmatropic rearrangements to occur *via* chair-like transition states. The reaction carried out at 100 ºC for 1 hour afforded compound **23b** in similar yield and selectivity (entry 4). Carrying out the microwave irradiation at 50 ºC for 30 minutes an improvement of the yield and stereoselectivity was observed (entry 5) and irradiation at 100 ºC for 15 minutes the desired adduct was obtained in even higher yield (91%) and 76:24 *syn*:*anti* selectivity (entry 6). Using the conventional reaction conditions and $Zn(OTf)_2$ as catalyst, β-enamino ester **23b** was obtained in 64% yield with moderate stereoselectivity (entries 7 and 8). Microwave irradiation at 100 ºC for 15 minutes allowed the synthesis of adduct **23b** in a significant higher yield (entries 9 and 10).

Conclusions

Herein, we have reported that [3+2] anellation reactions of butadienoates with *N*-benzylidenebenzenesulfonamide and electron-deficient alkenes can be carried out under

microwave irradiation. The results disclosed in this paper indicate the success of this approach for the regio- and diastereoselective preparation of 3-pyrrolines and cyclopentenes.

It was also demonstrated that the microwave-assisted reaction of butadienoates with 1-cinnamylpyrrolidine in the presence of Lewis acids afforded efficiently and selectively 3-(pyrrolidin-1-yl)hepta-2,6-dienoates *via* allenoate-Claisen rearrangement.

Experimental Section

General Procedures. ^{1}H NMR spectra were recorded on an instrument operating at 400 MHz. ^{13}C spectra were recorded on an instrument operating at 100 MHz. The solvent was deuteriochloroform except where indicated otherwise. IR spectra were recorded on a Perkin Elmer 1720X FTIR spectrometer. Mass spectra were recorded on a Bruker FTMS APEXIII instrument under electrospray ionization (ESI) or HP 6890 Plus instrument under electron impact (EI). Mps were recorded on a Reichert hot stage and are uncorrected. Flash column chromatography was performed with Merck 9385 silica as the stationary phase.

Synthesis of 3-pyrrolines and cyclopentenes. General procedure

Method A. To a mixture of imine or alkene (1.0 mmol) and PPh_3 or PBu_3 (0.2 mmol) in toluene (1.5 mL) a solution of allene (1.0 mmol) in toluene was added. The mixture was then stirred at room temperature under nitrogen. The reaction was monitored by TLC. After the reaction was completed, the solvent was removed under reduced pressure and the crude product was purified by flash chromatography [ethyl acetate-hexane].

Method B. A suspension of imine **13** or alkene **15** or **18** (0.6 mmol), PPh_3 or PBu_3 (0.12 mmol) and allene **12** (0.6 mmol) in toluene (1 mL) was irradiated in a microwave reactor (CEM Focused Synthesis System, Discover S-Class) for 5 min with the temperature set to 100 ºC for the synthesis of 3-pyrrolines **14**, 70 ºC for cyclopentenes **16** and **17** and 50 ºC for cyclopentene **19**. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography [ethyl acetate-hexane].

Benzyl 2-phenyl-1-(phenylsulfonyl)-2,5-dihydro-1*H*-pyrrole-3-carboxylate (14a). Compound **14a** was obtained as an oil. Yield: **Method A** 69% and **Method B** 64%. ν_{max}(film)/cm^{-1} 1720, 1641, 1165, 1346. δ_H 4.38 (1H, ddd, J = 1.9 Hz, J = 5.8 Hz and J = 17.0 Hz), 4.55 (1H, dt, J_1 = 2.4 Hz and J_2 = 17.0 Hz), 4.93 (1H, d, J = 12.4 Hz), 5.03 (1H, d, J = 12.4 Hz), 5.77-5.80 (1H, m), 6.84-6.86 (1H, m), 7.02-7.05 (2H, m Ar-H), 7.17-7.33 (10H, m, Ar-H), 7.46-7.49 (3H, m, Ar-H). δ_C 54.9, 66.5, 68.9, 126.9, 127.9, 128.1, 128.2, 128.4, 128.5, 128.8, 132.4, 135.1, 135.6, 136.2, 138.6, 139.0, 161.5. *m/z* (CI) 420 (93%, $MH^{+\bullet}$), 364 (51), 328 (59), 278 (97), 252 (100), 188 (42), 143 (86). HRMS (CI) *m/z* 420.1270 ($C_{24}H_{22}NO_4S$ [M^+], 420.1269).

Benzyl 5-tert-butyl-2-phenyl-1-(phenylsulfonyl)-2,5-dihydro-1*H*-pyrrole-3-carboxylate (14b). Compound **14b** was obtained as a white solid, mp 105.3-106.4 ºC (from AcOEt/Hexane). Yield: **Method A** 44% and **Method B** 50%. ν_{max}(KBr)/cm^{-1} 2958, 1733, 1650. δ_H 0.79 (9H, s),

4.39 (1H, bs), 5.09 (2H, s), 5.92 (1H, bs), 6.78 (1H, bs), 7.09-7.11 (2H, m, Ar-H), 7.26-7.31 (6H, m, Ar-H), 7.38-7.42 (4H, m, Ar-H), 7.51-7.54 (1H, m, Ar-H), 7.79-7.81 (2H, m, Ar-H). δ_C 27.9, 35.9, 66.5, 68.4, 77.9, 127.7, 127.9, 128.0, 128.1, 128.2, 128.3, 128.5, 128.9, 133.0, 133.9, 135.3, 136.9, 139.4, 141.9, 162.4. *m/z* (ESI) 476 (100, $MH^{+\bullet}$), 419 (58), 319 (62), 229 (46). HRMS (ESI) *m/z* 476.18901 ($C_{28}H_{30}NO_4S$ [MH^+], 476.18955).

Benzyl 5-methyl-2-phenyl-1-(phenylsulfonyl)-2,5-dihydro-1*H*-pyrrole-3-carboxylate (14c). Compound **14c** was obtained as an oil. Yield: **Method A** 38% and **Method B** 43%. ν_{max}(film)/cm^{-1} 1720, 1659, 1328, 1163. δ_H 1.22 (3H, d, *J* = 6.8 Hz), 4.07-4.12 (1H, m), 5.12 (2H, s), 5.85 (1H, d, *J* = 15.6 Hz), 6.67 (1H, dd, *J* = 5.6 Hz and *J* = 15.6 Hz), 7.18-7.52 (13H, m, Ar-H), 7.78-7.85 (2H, m, Ar-H). δ_C 21.6, 50.3, 66.4. 121.2, 127.1, 127.2, 128.3, 128.6, 129.0, 129.2, 132.7, 132.8, 135.7, 140.6, 147.9, 150.4, 165.6. *m/z* (ESI) 434 (11%, $MH^{+\bullet}$), 368 (100), 346 (39), 248 (16). HRMS (ESI) *m/z* 434.14206 ($C_{25}H_{24}NO_4S$ [MH^+], 434.14260).

Benzyl 5-acetylcyclopent-1-enecarboxylate (16) and benzyl 4-acetylcyclopent-1-enecarboxylate (17a). Yield: **Method A 16** (27%) and **17a** (43%); **Method B 16** (27%) and **17a** (39%). Workup by flash chromatography [hexane–ethyl acetate] gave the following (in order of elution): (i) *Benzyl 5-acetylcyclopent-1-enecarboxylate* 16 was obtained as an oil. ν_{max}(film)/cm^{-1} 1712, 1629, 1268. δ_H 1.96-2.05 (1H, m), 2.19 (3H, s), 2.25-2.32 (1H, m), 2.53-2.65 (2H, m), 3.90-3.94 (1H, m), 5.13 (1H, d, *J* = 12.4 Hz), 5.20 (1H, d, *J* = 12.4 Hz), 7.02 (1H, s), 7.26-7.34 (5H, m, Ar-H). δ_C 27.8, 29.0, 32.7, 56.5, 66.3, 128.1, 128.2, 128.5, 135.5, 135.9, 147.4, 164.1, 209.6. MS (EI) *m/z* 244 (M^+, 1%), 184 (80), 91 (100); HRMS (EI) *m/z* 244.1100 ($C_{15}H_{16}O_3$ [M^+], 244.1099). (ii) *Benzyl 4-acetylcyclopent-1-enecarboxylate* 17a was obtained as an oil. ν_{max}(film)/cm^{-1} 1711, 1635, 1266. δ_H 2.19 (3H, s), 2.81-2.84 (1H, m), 2.84-2.90 (3H, m), 3.32-3.38 (1H, m), 5.18 (2H, s), 6.72-6.74 (1H, m), 7.26-7.37 (5H, m, Ar-H). δ_C 28.4, 34.0, 35.0, 49.6, 66.1, 128.1, 128.2, 128.5, 134.2, 136.0, 142.1, 164.3, 208.4. *m/z* (EI) 244 (1%, $MH^{+\bullet}$), 184 (12), 91 (100). HRMS (EI) *m/z* 244.1102 ($C_{15}H_{16}O_3$ [M^+], 244.1099).

Benzyl 4-formylcyclopent-1-enecarboxylate (17b). Compound **17b** was obtained as an oil. Yield: **Method A** 74% and **Method B** 24%. ν_{max}(film)/cm^{-1} 1713, 1635, 1264. δ_H 2.73-2.76 (1H, m), 2.87-2.96 (3H, m), 3.16-3.22 (1H, m), 5.16 (2H, s), 6.75 (1H, s), 7.26-7.37 (5H, m, Ar-H), 9.67 (1H, s, C*H*O). δ_C 31.7, 33.1, 48.6, 66.2, 128.1, 128.2, 128.6, 134.6, 135.9, 141.9, 164.2, 201.5. *m/z* (EI) 230 (1%, $MH^{+\bullet}$), 124 (10), 91 (100), 65 (17). HRMS (EI) *m/z* 230.0942 ($C_{14}H_{14}O_3$ [M^+], 230.0943).

3-Benzyl 1,2-diethyl cyclopent-3-ene-1,2,3-tricarboxylate (19). Compound **19** was obtained as an oil. Yield: **Method A** 80% and **Method B** 75%. ν_{max}(film)/cm^{-1} 1732, 1638, 1268. δ_H 1.19 (3H, t, *J* = 7.2 Hz), 1.27 (3H, t, *J* = 7.2 Hz), 2.82-2.97 (m, 2H), 3.39 (1H, dt, *J* = 6.4 Hz and *J* = 12.8 Hz), 4.05-4.21 (5H, m), 5.13 (d, 1H, *J* = 12.4 Hz), 5.22 (d, 1H, *J* = 12.4 Hz), 6.89-6.91 (1H, m), 7.30-7.36 (5H, m, Ar-H). δ_C 14.0, 14.2, 35.9, 47.0, 52.9, 61.2, 62.3, 66.4, 128.1, 128.2, 128.5, 133.8, 135.7, 144.6, 163.3, 173.2. *m/z* (EI) 346 (3%, $MH^{+\bullet}$), 300 (26), 240 (27), 166 (45), 91 (100). HRMS (EI) *m/z* 346.1424 ($C_{19}H_{22}O_6$ [M^+], 346.1416).

Synthesis of benzyl 3-oxo-5-phenylhept-6-enoate (21). The cinnamyl pyrrolidine **20** (215 mg, 1.15 mmol) and allenic ester **12a** (101 mg, 0.58 mmol) in dichloromethane (3 mL) were added sequentially to a round bottom flask containing $AlCl_3$ (7.6 mg, 0.058 mmol). The reaction mixture was stirred at room temperature under nitrogen for 24 h. The crude product was purified by flash chromatography [ethyl acetate-hexane (1:5)] giving compound **21** as an oil (68%). ν_{max}(film)/cm^{-1} 1743, 1717, 1401, 699. δ_H 2.89 (1H, dd, *J* = 6.8 Hz and *J* = 16.8 Hz), 2.96 (1H, dd, *J* = 7.6 Hz and *J* = 16.8 Hz), 3.35 (1H, d, *J* = 15.6 Hz), 3.40 (1H, d, *J* = 15.6 Hz), 3.87-3.93 (1H, m), 4.97-5.04 (2H, m), 5.12 (2H, s), 5.87-5.96 (1H, m), 7.14-7.20 (4H, m, Ar-H), 7.28-7.35 (6H, m, Ar-H). δ_C 44.1, 48.2, 49.8, 67.1, 114.9, 126.7, 127.6, 128.4, 128.4, 128.6, 128.6, 135.3, 140.1, 142.4, 166.7, 200.6. *m/z* (EI) 308 (0.1%, MH$^{+\bullet}$), 217 (46), 157 (83), 129 (46), 117 (78%), 115 (73), 91 (100), 77 (31). HRMS (EI) *m/z* 308.1410 ($C_{20}H_{20}O_3$ [M$^+$], 308.1412).

Synthesis of β-enamino esters 23. General procedure

Method A. The cinnamyl pyrrolidine **20** (215 mg, 1.15 mmol) and allenic ester **12a** or **12c** (109 mg, 0.58 mmol) in dichloromethane (3 mL) were added sequentially to a round bottom flask containing the corresponding catalyst (0.058 mmol). The reaction mixture was stirred at room temperature under nitrogen for 24 h. The solvent was removed under reduced pressure and the product was purified by flash column chromatography [ethyl acetate-hexane (1:5)].

Method B. A suspension of cinnamyl pyrrolidine **20** (215 mg, 1.15 mmol), allenic ester **12a** or **12c** (0.58 mmol) and catalyst (0.058 mmol) in dichloromethane (3 mL) was irradiated in a microwave reactor (CEM Focused Synthesis System, Discover S-Class) with the temperature set to 100 ºC for 15 min. The solvent was removed under reduced pressure and the product was purified by flash column chromatography [ethyl acetate-hexane (1:5)].

(*E*)-Benzyl 5-phenyl-3-(pyrrolidin-1-yl)hepta-2,6-dienoate (23a).[12] Compound **23a** was obtained as an oil. Yield using $Zn(OTf)_2$: method B (99%). ν_{max}(film)/cm^{-1} 3130, 1678, 1563, 1450, 1402, 1345, 1130, 1057, 1028. δ_H 1.61 (1H, s), 1.72 (3H, brs), 2.83-3.08 (5H, brm), 3.64-3.75 (2H, m), 4.57 (1H, s), 5.09-5.19 (4H, m), 6.16 (1H, m), 7.27-7.40 (10H, m, Ar-H); MS (EI) *m/z* 361 (36%, MH$^{+\bullet}$), 270 (85), 226 (72), 91 (100). δ_C 24.9, 36.0, 48.0, 48.7, 64.1, 83.6, 114.6, 126.3, 127.4, 127.8, 128.1, 128.2, 128.3, 137.8, 140.1, 143.3, 161.7, 168.1.

(*E*)-Benzyl 4-methyl-5-phenyl-3-(pyrrolidin-1-yl)hepta-2,6-dienoate (23b).[12] Compound **23b** was obtained as an oil. Yield using $Zn(OTf)_2$: method A (64%, 70:30 *syn*:*anti*) and method B (97%, 75:25 *syn*:*anti*). *Syn*, *E* isomer: ν_{max}(film)/cm^{-1} 3136, 1675, 1559, 1400, 1126. δ_H 1.00 (3H, d, *J* = 7.2 Hz), 1.86 – 1.89 (4H, m), 3.39-3.42 (4H, m), 4,59 (1H, s), 4.84 (1H, d, *J* = 2 Hz), 4.88 (1H, d, *J* = 9.6 Hz), 5.13 (1H, d, *J* = 4 Hz), 5.15 (1H, d, *J* = 3.6 Hz), 5.44 (1H, dq, *J* = 7.2 Hz, *J* = 14.4 Hz), 6.06 (1H, ddd, *J* = 9.6 Hz, *J* = 9.2 Hz, *J* = 16.8 Hz), 7.30-7.41 (10H, m, Ar-H). δ_C 14.7, 16.0, 25.1, 25.3, 36.7, 43.0, 49.5, 50.7, 51.1, 54.8, 64.4, 64.5, 83.9, 85.7, 113.7, 115.4, 126.4, 127.5, 127.9, 128.1, 128.4, 128.6, 128.7, 137.8, 140.9, 141.3, 143.3, 143.5, 165.3, 166.7, 167.1, 168.9. *m/z* (EI) 375 (31%, MH$^{+\bullet}$), 284 (100), 240 (59), 91 (78).

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