

The Stereoselective Synthesis of Alkenyl- β -lactams by Palladium-Catalyzed [2+2] Carbonylative Cycloaddition

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Allyl halides of different structures, under CO pressure, in the presence of Et₃N, a catalytic amount of Pd(OAc)₂, and triphenylphosphane as ligand, undergo a [2+2] cycloaddition reaction with various imines. The reaction is highly regio- and stereoselective: β -lactams are formed in good yields and

with *trans* diastereoselectivity in both the β -lactam ring and the vinylic moiety. New and important information is suggested regarding the known reaction mechanism.

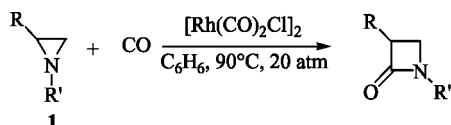
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Introduction

Among the catalyzed carbonylation reactions, the cyclocarbonylation catalyzed by transition metals has recently proved to be an extremely helpful technique for the production of interesting transformations in organic chemistry.^[1–3] In particular, a large number of papers has appeared in which palladium complexes have been used to prepare many new and useful molecules. Particularly interesting seems to be the cyclocarbonylation of unsaturated alcohols,^[4–12] which leads to the formation of lactones.

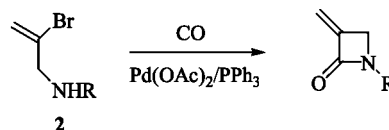
The analogous cyclocarbonylation of unsaturated amines, leading to the formation of lactams, seems to have been studied less in the literature.^[13,14] Of all lactams, the β -lactams^[15–22] are of special biological and pharmaceutical interest, and these compounds have also been obtained by different synthetic pathways, summarized below:

a) Carbonylation of the aziridines **1** in the presence of a catalytic amount of [Rh(CO)₂Cl]₂.^[23–28] The carbonyl insertion is regio- and stereospecific, occurring at the most substituted carbon-nitrogen bond in the aziridine ring, and proceeding with retention of stereochemistry of the substituents linked to the aziridinic carbon atoms (Scheme 1).



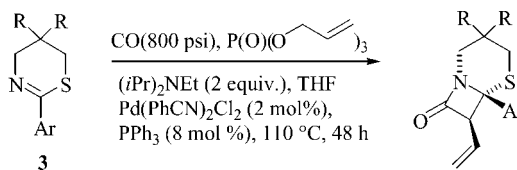
Scheme 1

b) Palladium-catalyzed carbonylation of the aminovinyl bromide **2**. This is a convenient synthesis of vinyl β -lactams^[29–31] (Scheme 2).



Scheme 2

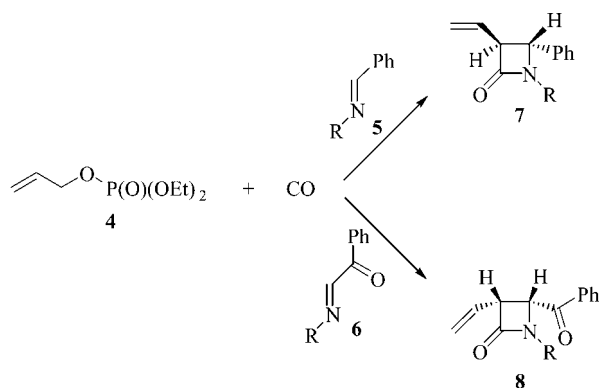
c) Carbonylative coupling and cyclization reaction of the 1,3 thiazines **3** with allyl phosphates, catalyzed by bis(benzonitrile)palladium dichloride.^[32] Several rhodium complexes are also effective catalysts for this process (Scheme 3).



Scheme 3

d) Palladium-catalyzed carbonylation of the allyl phosphate **4** in the presence of imines, under CO pressure.^[33,34] The reaction is stereoselective since the formation of the *trans*-**7** or the *cis*-**8** β -lactam depends on the imine used for the coupling. An imine conjugated **6** with a carbonyl group gives the *cis*- β -lactam, whereas the unconjugated imine **5** gives the *trans* isomer (Scheme 4).

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Scheme 4

No reaction products, or just traces of β -lactams, were reportedly formed when allyl bromide,^[33–37] allylacetate,^[38,39] allyl phenyl ether,^[40] allyl carbonate^[41,42] or allylsulfone^[43] were used under similar reaction conditions. In contrast with these observations, we found that simple allyl halides of various structures react with imines under slightly different reaction conditions, leading to β -lactams in a stereoselective way.

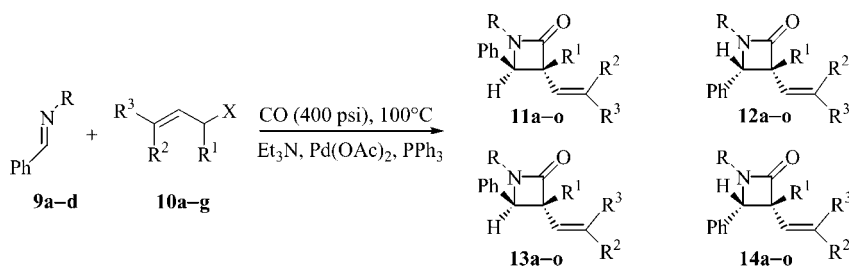
Results and Discussion

Several imines **9a–d**, which were to be used as substrates (Scheme 5), were prepared as reported in the Exp. Sect.

[2+2] Cycloaddition reactions of allyl halides of different structures **10a–l** with the simple imines **9a–d**, under CO pressure, in the presence of Et₃N, triphenylphosphane and a catalytic amount of Pd(OAc)₂, led to β -lactams in good yields and with high diastereoselectivity (Table 1). Slightly different reaction conditions to those reported in the literature, such as the use of Et₃N instead of *i*Pr₂NEt, allyl halides as substrates instead of the less easily accessible allyl phosphates, and a lower pressure of CO, make this methodology much simpler than those reported in the literature.

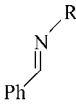
The *trans* relative configuration was found to predominate both in the β -lactam ring and in the C–C double bond of the products. The stereochemistry of the C–C double bond in the products was assigned on the basis of the ³J_{H,H} coupling constants across the double bond. For the β -lactam moiety itself, the stereochemistry was assigned based on of the coupling constants between the protons linked to C-3 and C-4, according to the literature report that for small rings, *J*_{cis} > *J*_{trans}.^[44] The diastereoisomers **11n,11n'** and **11o,11o'** showed *trans*-type coupling constants *J*_{H,H} for the β -lactam ring, similar to those measured for the other compounds. The protons of the R substituent on the nitrogen atom showed a difference in chemical shift (δ) between compounds **11n** and **11n'**, and between **11o** and **11o'**. This suggests two possible configurations of the β -lactamic nitrogen.

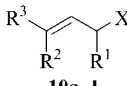
According to the mechanism proposed by Torii^[33] (Scheme 6), the reaction starts by the formation of the π -allyl palladium complex **16**. In the acyl complex **17**, derived from the insertion of CO, the protons alpha to the carbonyl group show appreciable acidity.

Table 1. Cyclocarbonylation of imines **9a–d** with allyl halides **10a–g**

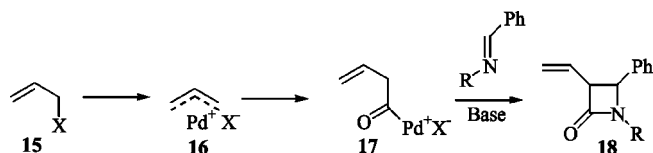
Entry	Imine	Halide	Products (yield, %) ^[a]			
1	9a	10a	11a (84)	12a (5)	—	—
2	9a	10b	11a (81)	12a (6)	—	—
3	9a	10c	11b (81)	12b (15)	—	—
4	9a	10d	11c (58)	12c (traces)	13c (21)	14c (traces)
5	9a	10f	11d (50) ^[b]	—	13d (15) ^[b]	—
6	9a	10g	—	—	13e (6) ^[b]	14e (14) ^[b]
7	9b	10a	11f (85)	—	—	—
8	9b	10c	11g (78)	—	—	—
9	9b	10d	11h (60) ^[b]	12h (traces)	13h (20) ^[b]	14h (traces)
10	9b	10e	11i (98)	—	—	—
11	9b	10f	11l (50) ^[b]	—	13l (15) ^[b]	—
12	9b	10g	—	—	13m (4) ^[b]	14m (11) ^[b]
13	9c	10a	11n (60) + 11n' (32)	—	—	—
14	9d	10a	11o (53) + 11o' (40)	—	—	—

^[a] Isolated yields. ^[b] Inseparable mixture of diastereoisomers (ratio measured by GC and ¹H NMR spectroscopy).

 9a–d				
Imine	R			
9a	Ph			
9b	CH ₂ Ph			
9c	CH(CH ₃)Ph			
9d	CH(Ph)CH ₂ OCH ₃			

 10a–l				
Halide	X	R ¹	R ²	R ³
10a	Br	H	H	H
10b	Cl	H	H	H
10c	Cl	H	CH ₃	CH ₃
10d	Br	H	H	CH ₃
10e	Cl	H	H	Ph
10f	Br	H	H	(CH ₂) ₂ CH ₃
10g	Br	-CH ₂ -CH ₂ -CH ₂ -	H	H
10h	Cl	CH ₃	H	H
10i	Br	CH ₃	H	H
10l	Br	(CH ₂) ₂ CH ₃	H	H

Scheme 5



Scheme 6

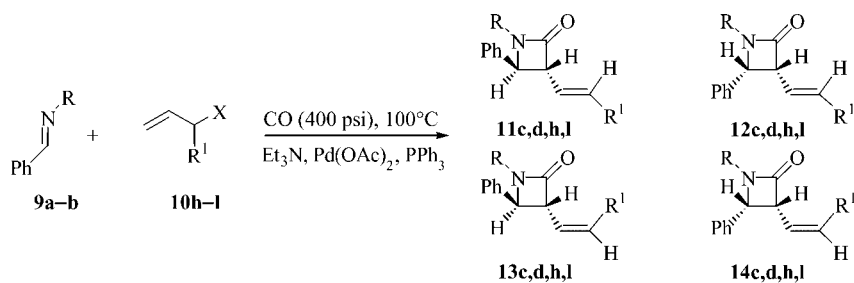
Consequently, deprotonation by Et₃N could lead to the formation of a carbanion, or even a ketene,^[45] which, through an addition reaction with the imine, could form a four-membered ring **18**.

According to previously reported data,^[33,34] as well as the data in Table 1, the CO insertion would always occur between the carbon (C-3) directly attached to the halogen and the palladium (structure **17**). When the halogen is not in the terminal position of the allylic chain, we found, instead, that the insertion occurs at the less hindered carbon atom (C-1) of structure **15**. In particular, when the halo-substrate is 3-chloro-1-butene (**10h**) or 3-bromo-1-butene (**10i**) (R² = R³ = H, R¹ = CH₃), or 3-bromo-1-hexene (**10l**) [R² = R³ = H, R¹ = (CH₂)₂CH₃], carbonylation occurs at the C-1 position, and not at C-3 (Table 2).

In fact, in these cases, we isolated the same reaction products as were obtained when crotyl bromide (**10d**) or 1-bromo-2-hexene (**10f**) were used to form the intermediate π -allyl palladium complex (Entries 4, 5, 9 and 11, Table 1). The low yield obtained with 3-bromocyclohexene (**10g**) (Entries 6 and 12, Table 1) could be caused by steric effects. The formation of the π -allyl palladium complex, and the subsequent terminal double-bond shift, could not proceed easily for steric reasons, resulting in a considerably lower yield for this reaction.

Conclusion

This protocol can be used to synthesize a large number of new alkenyl- β -lactams stereoselectively. The main advantages of our method, compared to those reported in the literature, are that Et₃N may be used as base, and that simple allyl halides may be used as substrates instead of the less easily accessible allyl phosphates.

Table 2. Cyclocarbonylation of imines **9a–b** with allyl halides **10h–l**

Entry	Imine	Halide	Products (yield, %) ^[a]			
1	9a	10h	11c (60)	12c (traces)	13c (20)	14c (traces)
2	9b	10h	11h (60) ^[b]	12h (traces)	13h (25) ^[b]	14h (traces)
3	9a	10i	11c (55)	12c (traces)	13c (23)	14c (traces)
4	9b	10i	11h (65) ^[b]	12h (traces)	13h (23) ^[b]	14h (traces)
5	9a	10l	11d (52) ^[b]	—	13d (14) ^[b]	—
6	9b	10l	11l (53) ^[b]	—	13l (15) ^[b]	—

^[a] Isolated yields. ^[b] Inseparable mixture of diastereoisomers (ratio measured by GC and ¹H NMR spectroscopy).

Moreover, we have shown a new aspect of the suggested mechanism: the CO insertion can occur on either of the carbon atoms of the intermediate π -allyl palladium complex, depending on the steric environment.

Experimental Section

General Remarks: THF, allyl bromide, allyl chloride, crotyl bromide, 1-chloro-3-methyl-2-butene, cinnamyl chloride, 3-bromocyclohexene, 3-chloro-1-butene, (+/-)- α -methylbenzylamine, aniline, benzaldehyde, triethylamine, palladium(II) acetate, triphenylphosphane and all other chemicals were of commercial grade (Aldrich), and they were used without further purification. Imines were prepared starting from the corresponding carbonyl compounds and amines.^[46] The allylic halides **10f**, **10i** and **10l** were prepared starting from commercially available 1-butene, 2-hexene and 1-hexene, respectively, by bromination with *N*-bromosuccinimide. Petroleum ether refers to the fraction boiling in the range 40–60 °C. ¹H and ¹³C NMR spectra were recorded with a Bruker Avance 400 spectrometer (400.13 MHz and 100.62 MHz, for ¹H and ¹³C, respectively), with CDCl₃ as the solvent (δ = 7.24 ppm for ¹H spectra; δ = 77.0 ppm for ¹³C spectra) with TMS as an internal standard. IR spectra were recorded with a Perkin–Elmer spectrometer Model 283. GC-MS analyses were performed with a Shimadzu–17A gas chromatograph (5% diphenyl/95% dimethylpolysiloxane capillary column, 30 m, 0.25 mm i.d.), equipped with a Shimadzu GCMS–QP5050A mass-selective detector operating at 70 eV (EI). Microanalyses were performed on a Carlo–Erba C,H,N analyser. Melting points were determined using an electrothermal melting point apparatus and are uncorrected. TLC was performed on Merck silica gel plates with F-254 indicator; viewing was by UV light (254 nm). Column chromatography was performed on silica gel (63–200 mm) using petroleum ether/diethyl ether (Et₂O) mixtures as eluents. All reactions involving air-sensitive reagents were performed under nitrogen in oven-dried glassware, using syringe/septum cap techniques.

General Procedure for the Preparation of β -Lactams: 9a–d (1.0 mmol), **10a–l** (1.5 mmol), PPh₃ (0.08 mmol), Pd(AcO)₂ (0.02 mmol), and Et₃N (2 mmol) were dissolved in THF (10 mL), and placed in a 45 mL autoclave. The autoclave was purged, pressurized (400 psi of CO), and then heated to 100 °C for 18 h. The reaction mixture was then cooled to room temperature, and worked up by the addition of water (5 mL) and extraction with Et₂O (3 $\times$ 5 mL). The combined organic layers were dried (Na₂SO₄) and concentrated in vacuo. The crude products were purified by column chromatography (silica gel, petroleum ether/Et₂O, 7:3) to afford the pure β -lactams; yields: 15–98%.

1,4-Diphenyl-3-vinylazetidin-2-one (trans-11a): From allylic halide **10a**, yield 209 mg (84%), solid. M.p. 97.2–99.2 °C (*n*-hexane). ¹H NMR (400.13 MHz, CDCl₃): δ = 3.74 (dd, *J* = 7.8, 2.4 Hz, 1 H), 4.81 (d, *J* = 2.4 Hz, 1 H), 5.35 (dd, *J* = 23.9, 17.2 Hz, 2 H), 6.00–6.10 (m, 1 H), 7.05 (t, *J* = 7.2 Hz, 1 H), 7.16–7.40 (m, 9 H) ppm. ¹³C NMR (100.62 MHz, CDCl₃): δ = 61.2, 64.0, 117.0, 119.9, 123.9, 125.8, 128.6, 129.1, 129.2, 130.5, 137.3, 138.1, 165.3 ppm. GC-MS (70 eV): *m/z* (%) = 249 (5) [M⁺], 181 (30), 180 (33), 130 (100), 129 (64), 115 (26), 77 (50). IR (CHCl₃): $\tilde{\nu}$ = 3050 cm⁻¹, 3020, 3000, 2910, 1740, 1600, 1370. C₁₇H₁₅NO (249.31): calcd. C 81.90, H 6.06, N 5.62; found C 82.10, H 6.10, N 5.55. **cis-12a:** Yield 12 mg (5%), oil. ¹H NMR (400.13 MHz, CDCl₃): δ = 4.29 (dd, *J* = 6.5, 6.4 Hz, 1 H), 5.08–5.12 (m, 1 H), 5.25–5.39 (m, 3 H), 7.06 (t, *J* = 7.3 Hz, 1 H), 7.16–7.34 (m, 9 H) ppm. ¹³C NMR

(100.62 MHz, CDCl₃): δ = 58.4, 58.8, 117.2, 120.9, 123.9, 127.0, 128.3, 128.7, 128.8, 129.0, 134.7, 137.5, 165.4 ppm. GC-MS (70 eV): *m/z* (%) = 249 (5) [M⁺], 181 (30), 180 (33), 130 (100), 129 (64), 115 (26), 77 (50). IR (film): $\tilde{\nu}$ = 3050 cm⁻¹, 3020, 3000, 2910, 1740, 1600, 1370. (From allylic halide **10b**) **trans-11a:** Yield 202 mg (81%), **cis-12a:** 15 mg (6%).

3-(2-Methylpropenyl)-1,4-diphenylazetidin-2-one, (trans-11b): Yield 224 mg (81%), solid. M.p. 101.0–103.0 °C (*n*-hexane). ¹H NMR (400.13 MHz, CDCl₃): δ = 1.60 (s, 3 H), 1.79 (s, 3 H), 3.88 (dd, *J* = 7.8, 2.4 Hz, 1 H), 4.70 (d, *J* = 2.4 Hz, 1 H), 5.40 (d, *J* = 7.6 Hz, 1 H), 7.05 (t, *J* = 7.2 Hz, 1 H), 7.20–7.37 (m, 9 H) ppm. ¹³C NMR (100.62 MHz, CDCl₃): δ = 18.7, 25.7, 60.3, 62.3, 116.9, 117.1, 123.7, 125.8, 128.3, 128.9, 129.1, 137.7, 137.8, 139.1, 166.9 ppm. GC-MS (70 eV): *m/z* (%) = 277 (1) [M⁺], 180 (17), 158 (72), 143 (100), 128 (20), 115 (10), 77 (32). IR (CHCl₃): $\tilde{\nu}$ = 3030 cm⁻¹, 2970, 2910, 1740, 1600, 1370. C₁₉H₁₉NO (277.37): calcd. C 82.28, H 6.90, N 5.05; found C 82.38, H 7.08, N 5.01. **cis-(12b):** Yield 42 mg (15%), oil. ¹H NMR (400.13 MHz, CDCl₃): δ = 1.53 (s, 3 H), 1.66 (s, 3 H), 4.48 (dd, *J* = 9.0, 6.0 Hz, 1 H), 4.76 (d, *J* = 9.0 Hz, 1 H), 5.25 (d, *J* = 6.0 Hz, 1 H), 7.04 (t, *J* = 7.3 Hz, 1 H), 7.20–7.36 (m, 9 H) ppm. ¹³C NMR (100.62 MHz, CDCl₃): δ = 22.7, 29.7, 54.3, 59.3, 114.6, 117.2, 123.7, 127.0, 128.0, 128.6, 129.0, 135.3, 137.7, 139.1, 167.1 ppm. GC-MS (70 eV): *m/z* (%) = 277 (1) [M⁺], 180 (17), 158 (72), 143 (100), 128 (20), 115 (10), 77 (32). IR (film): $\tilde{\nu}$ = 3030 cm⁻¹, 2970, 2910, 1740, 1600, 1370.

1,4-Diphenyl-3-propenylazetidin-2-one (trans,trans-11c): (From allylic halide **10d**). Yield 153 mg (58%), solid. M.p. 74.0–76.0 °C (*n*-hexane). ¹H NMR (400.13 MHz, CDCl₃): δ = 1.74 (d, *J* = 6.0 Hz, 3 H), 3.66 (dd, *J* = 8.1, 2.3 Hz, 1 H), 4.74 (d, *J* = 2.3 Hz, 1 H), 5.62–5.84 (m, 2 H), 7.01 (t, *J* = 7.5 Hz, 1 H), 7.19–7.50 (m, 9 H) ppm. ¹³C NMR (100.62 MHz, CDCl₃): δ = 18.0, 61.6, 63.4, 116.8, 123.3, 123.7, 125.6, 128.4, 128.9, 129.0, 130.4, 131.2, 137.4, 166.0 ppm. GC-MS (70 eV): *m/z* (%) = 263 (4) [M⁺], 181 (35), 180 (55), 144 (89), 129 (100), 128 (62), 115 (25), 77 (83). IR (CHCl₃): $\tilde{\nu}$ = 3020 cm⁻¹, 2920, 1740, 1600, 1490, 1370. C₁₈H₁₇NO (263.34): calcd. C 82.10, H 6.51, N 5.32; found C 81.86, H 6.42, N 5.15. **trans,cis-13c:** Yield 55 mg (15%), oil. ¹H NMR (400.13 MHz, CDCl₃): δ = 1.59 (dd, *J* = 6.8, 1.1 Hz, 3 H), 3.99 (dd, *J* = 9.0, 2.3 Hz, 1 H), 4.74 (d, *J* = 2.3 Hz, 1 H), 5.62–5.84 (m, 2 H), 7.01 (t, *J* = 7.5 Hz, 1 H), 7.19–7.50 (m, 9 H) ppm. ¹³C NMR (100.62 MHz, CDCl₃): δ = 13.7, 58.9, 61.8, 116.8, 122.5, 123.7, 125.7, 128.3, 128.8, 129.0, 130.4, 131.3, 137.5, 166.0 ppm. GC-MS (70 eV): *m/z* (%) = 263 (2) [M⁺], 180 (18), 144 (64), 129 (100), 115 (10), 77 (34). IR (film): $\tilde{\nu}$ = 3060 cm⁻¹, 3020, 2920, 1740, 1600, 1490, 1370. (From allylic halides **10h** and **10i**) **trans,trans-11c:** 158 mg (60%) and 144 mg (55%), **trans,cis-13c:** 66 mg (25%) and 60 mg (23%) respectively.

3-(Pent-1-enyl)-1,4-diphenylazetidin-2-one (inseparable mixture of diastereoisomers, 50:15): (from allylic halide **10f**). Overall yield 190 mg (65%), oil. **trans,trans-11d:** ¹H NMR (400.13 MHz, CDCl₃): δ = 0.91 (t, *J* = 7.4 Hz, 3 H), 1.41 (sext, *J* = 7.4 Hz, 2 H), 2.06 (q, *J* = 7.4 Hz, 2 H), 3.67 (dd, *J* = 8.0, 2.2 Hz, 1 H), 4.74 (d, *J* = 2.2 Hz, 1 H), 5.63 (dd, *J* = 8.0, 15.2 Hz, 1 H), 5.73–5.80 (m, 1 H), 7.02 (t, *J* = 7.2 Hz, 1 H), 7.20–7.38 (m, 9 H) ppm. ¹³C NMR (100.62 MHz, CDCl₃): δ = 13.6, 22.1, 34.6, 61.9, 63.5, 117.0, 122.3, 123.8, 125.8, 128.4, 128.5, 129.0, 129.1, 136.5, 137.6, 166.2 ppm. GC-MS (70 eV): *m/z* (%) = 291 (2) [M⁺], 181(15), (180 (22), 172 (100), 77 (50). **trans,cis-13d:** ¹H NMR (400.13 MHz, CDCl₃): δ = 0.83 (t, *J* = 7.4 Hz, 3 H), 1.33 (sext, *J* = 7.4 Hz, 2 H), 1.96 (q, *J* = 7.4 Hz, 2 H), 3.97 (dd, *J* = 8.0, 2.2 Hz, 1 H), 4.72 (d, *J* = 2.2 Hz, 1 H), 5.63 (dd, *J* = 8.0, 8.0 Hz, 1 H), 5.73–5.80 (m, 1 H), 7.02 (t, *J* = 7.2 Hz, 1 H), 7.20–7.38 (m, 9 H) ppm. ¹³C

NMR (100.62 MHz, CDCl_3): δ = 13.6, 22.6, 29.7, 59.4, 62.1, 116.9, 121.8, 125.8, 127.3, 127.4, 128.6, 129.0, 129.2, 136.3, 137.7, 166.2 ppm. GC-MS (70 eV): m/z (%) = 291 (2) [M^+], 181 (15), 180 (22), 172 (100), 77 (50). IR (film) measured on the mixture: $\tilde{\nu}$ = 3060 cm^{-1} , 3000, 2910, 1740, 1595, 1490, 1370. (From allylic halide **10l**) Overall yield 192 mg (66%), *trans,trans*-**11d** and *trans,cis*-**13d** in a ratio 52:14.

2,3-Diphenyl-2-azaspiro[3.5]non-5-en-1-one (inseparable mixture of diastereoisomers, 6:14): Overall yield 57 mg (20%), oil. *trans*-**13e**: ^1H NMR (400.13 MHz, CDCl_3): δ = 1.50–2.20 (m, 6 H), 4.92 (s, 1 H), 5.83 (d, J = 10.0 Hz, 1 H), 6.06 (dt, J = 10.0, 6.0 Hz, 1 H); 7.15–7.35 (m, 10 H) ppm. ^{13}C NMR (100.62 MHz, CDCl_3): δ = 19.6, 25.1, 29.7, 58.8, 67.0, 117.3, 126.6, 127.6, 128.0, 128.6, 128.7, 128.9, 129.7, 130.1, 134.5, 170.2 ppm. GC-MS (70 eV): m/z (%) = 289 (2) [M^+], 180 (22), 170 (100), 155 (17). *trans*-**14e**: ^1H NMR (400.13 MHz, CDCl_3): δ = 1.50–2.20 (m, 6 H), 4.88 (s, 1 H), 5.19 (d, J = 10.0 Hz, 1 H), 5.77 (dt, J = 10.0, 6.0 Hz, 1 H), 7.15–7.35 (m, 10 H) ppm. ^{13}C NMR (100.62 MHz, CDCl_3): δ = 19.9, 24.6, 30.6, 60.4, 67.8, 117.3, 122.1, 123.7, 126.6, 127.9, 128.7, 129.0, 133.0, 135.5, 137.8, 170.2 ppm. GC-MS (70 eV): m/z (%) = 289 (2) [M^+], 180 (22), 170 (100), 155 (17). IR (film) measured on the mixture: $\tilde{\nu}$ = 3050 cm^{-1} , 3000, 2905, 1735, 1595, 1490, 1370.

trans-**1-Benzyl-4-phenyl-3-vinylazetidin-2-one (11f)**: Yield 223 mg (85%), oil. ^1H NMR (400.13 MHz, CDCl_3): δ = 3.64 (dd, J = 7.7, 1.8 Hz, 1 H), 3.76 (d, J = 15.0 Hz, 1 H), 4.19 (d, J = 1.8 Hz, 1 H), 4.83 (d, J = 15.0 Hz, 1 H), 5.23 (dd, J = 23.0, 17.1 Hz, 2 H), 5.86–5.94 (m, 1 H), 7.11 (d, J = 6.5 Hz, 1 H), 7.15–7.35 (m, 9 H) ppm. ^{13}C NMR (100.62 MHz, CDCl_3): δ = 44.1, 60.3, 63.6, 118.7, 126.1, 127.3, 128.0, 128.2, 128.4, 128.7, 130.6, 135.1, 136.8, 167.5 ppm. GC-MS (70 eV): m/z (%) = 263 (1) [M^+], 194 (5), 130 (100), 129 (90), 115 (55), 91 (75). IR (film): $\tilde{\nu}$ = 3060 cm^{-1} , 3020, 2900, 1740, 1490, 1390.

trans-**1-Benzyl-3-(2-methylpropenyl)-4-phenylazetidin-2-one (11g)**: Yield 227 mg (78%), oil. ^1H NMR (400.13 MHz, CDCl_3): δ = 1.51 (d, J = 1.0 Hz, 3 H), 1.72 (s, 3 H), 3.76 (d, J = 15.0 Hz, 1 H), 3.83 (dd, J = 7.9, 2.1 Hz, 1 H), 4.10 (d, J = 2.1 Hz, 1 H), 4.83 (d, J = 15.0 Hz, 1 H), 5.30 (dq, J = 7.9, 1.0 Hz, 1 H), 7.11–7.37 (m, 10 H) ppm. ^{13}C NMR (100.62 MHz, CDCl_3): δ = 18.3, 25.3, 44.1, 59.9, 61.3, 117.1, 126.0, 126.1, 127.3, 128.0, 128.4, 128.6, 135.3, 137.2, 137.8, 169.0 ppm. GC-MS (70 eV): m/z (%) = 291 (0) [M^+], 195 (30), 194 (30), 91 (100). IR (film): $\tilde{\nu}$ = 3060 cm^{-1} , 3030, 2920, 1740, 1600, 1500, 1390.

1-Benzyl-4-phenyl-3-propenylazetidin-2-one (inseparable mixture of diastereoisomers, 60:20): (From allylic halide **10d**). Overall yield 222 mg (80%), oil. *trans,trans*-**11h**: ^1H NMR (400.13 MHz, CDCl_3): δ = 1.70 (d, J = 6.4 Hz, 3 H), 3.60 (dd, J = 8.0, 2.0 Hz, 1 H), 3.77 (d, J = 15.0 Hz, 1 H), 4.14 (d, J = 2.0 Hz, 1 H), 4.85 (d, J = 15.0 Hz, 1 H), 5.53 (dd, J = 16.8, 8.0 Hz, 1 H), 5.70 (dq, J = 16.8, 6.4 Hz, 1 H), 7.13–7.37 (m, 10 H) ppm. *trans,cis*-**13h**: ^1H NMR (400.13 MHz, CDCl_3): δ = 1.55 (d, J = 6.8 Hz, 3 H), 3.77 (d, J = 15.0 Hz, 1 H), 3.93 (dd, J = 8.0, 2.0 Hz, 1 H), 4.12 (d, J = 2.0 Hz, 1 H), 4.85 (d, J = 15.0 Hz, 1 H), 5.53 (dd, J = 8.0, 8.0 Hz, 1 H), 5.70 (dq, J = 8.0, 6.8 Hz, 1 H), 7.13–7.37 (m, 10 H) ppm. ^{13}C NMR, GC-MS and IR data were measured on the mixture. ^{13}C NMR (100.62 MHz, CDCl_3): δ = 13.6, 17.9, 44.3, 44.4, 58.9, 61.1, 61.3, 63.5, 121.7, 122.8, 123.7, 126.38, 126.4, 127.4, 127.6, 128.3, 128.4, 128.41, 128.7, 128.9, 128.91, 129.8, 130.7, 135.4, 135.5, 137.2, 137.3, 138.0, 168.8, 168.9 ppm. GC-MS (70 eV): m/z (%) = 277 (0) [M^+], 196 (7), 144 (68), 129 (100), 91 (43), 65 (20). IR (film): $\tilde{\nu}$ = 3060 cm^{-1} , 3000, 2910, 1740, 1600, 1490, 1380, 1100. (From allylic halide **10h**) Overall yield 235 mg

(85%), *trans,trans*-**11h** and *trans,cis*-**13h** in a ratio 65:25; (from allylic halide **10i**) overall yield 244 mg (88%), *trans,trans*-**11h** and *trans,cis*-**13h** in a ratio 65:25.

trans,trans-**1-Benzyl-4-phenyl-3-styrylazetidin-2-one (11i)**: Yield 332 mg (98%), oil. ^1H NMR (400.13 MHz, CDCl_3): δ = 3.83 (d, J = 15.0 Hz, 1 H), 3.83–3.86 (m, 1 H), 4.27 (d, J = 2.1 Hz, 1 H), 4.90 (d, J = 15.0 Hz, 1 H), 6.26 (dd, J = 15.8, 8.4 Hz, 1 H), 6.58 (d, J = 15.8 Hz, 1 H), 7.20–7.40 (m, 15 H) ppm. ^{13}C NMR (100.62 MHz, CDCl_3): δ = 44.6, 61.3, 63.7, 122.1, 126.4, 126.5, 127.7, 127.8, 128.4, 128.5, 128.6, 128.8, 129.1, 134.1, 135.4, 136.4, 137.1, 168.1 ppm. GC-MS (70 eV): m/z (%) = 339 (0) [M^+], 195 (30), 194 (28), 144 (27), 115 (35), 91 (100). IR (film): $\tilde{\nu}$ = 3060 cm^{-1} , 3020, 2900, 1750, 1600, 1590, 1450, 1350, 730, 690.

1-Benzyl-3-(pent-1-enyl)-4-phenylazetidin-2-one (inseparable mixture of diastereoisomers, 50:15): (From allylic halide **10f**). Overall yield 229 mg (75%), mixture of solid. M.p. 60–63 °C (*n*-hexane). *trans,trans*-**11l**: ^1H NMR (400.13 MHz, CDCl_3): δ = 0.87 (t, J = 7.3 Hz, 3 H), 1.37 (sext, J = 7.3 Hz, 2 H), 2.00 (q, J = 7.3 Hz, 2 H), 3.61 (dd, J = 8.0, 1.6 Hz, 1 H), 3.76 (d, J = 15.0 Hz, 1 H), 4.14 (d, J = 1.6 Hz, 1 H), 4.86 (d, J = 15.0 Hz, 1 H), 5.50 (dd, J = 16.0, 8.0 Hz, 1 H), 5.66–5.70 (m, 1 H), 7.13 (d, J = 6.5 Hz, 2 H), 7.22 (d, J = 6.5 Hz, 2 H), 7.27–7.37 (m, 6 H) ppm. ^{13}C NMR (100.62 MHz, CDCl_3): δ = 13.5, 22.0, 34.5, 44.3, 61.2, 63.4, 122.5, 126.3, 127.5, 128.26, 128.3, 128.31, 128.6, 128.8, 135.6, 137.3, 168.7 ppm. GC-MS (70 eV): m/z (%) = 305 (1) [M^+], 196 (10), 172 (62), 143 (45), 129 (100), 115 (17), 91 (59). *trans,cis*-**13l**: ^1H NMR (400.13 MHz, CDCl_3): δ = 0.77 (t, J = 7.3 Hz, 3 H), 1.33 (sext, J = 7.3 Hz, 2 H), 1.90 (q, J = 7.3 Hz, 2 H), 3.77 (d, J = 15.0 Hz, 1 H), 3.90 (dd, J = 8.0, 1.6 Hz, 1 H), 4.14 (d, J = 1.6 Hz, 1 H), 4.84 (d, J = 15.0 Hz, 1 H), 5.50 (dd, J = 8.0, 8.0 Hz, 1 H), 5.66–5.70 (m, 1 H), 7.13 (d, J = 6.5 Hz, 2 H), 7.22 (d, J = 6.5 Hz, 2 H), 7.27–7.37 (m, 6 H) ppm. ^{13}C NMR (100.62 MHz, CDCl_3): δ = 13.5, 22.4, 29.8, 44.4, 59.3, 61.4, 122.0, 126.3, 127.5, 128.2, 128.3, 128.4, 128.6, 128.9, 135.5, 137.3, 168.7 ppm. GC-MS (70 eV): m/z (%) = 305 (1) [M^+], 196 (10), 172 (62), 143 (45), 129 (100), 115 (17), 91 (59). IR (film) measured on the mixture: $\tilde{\nu}$ = 3060 cm^{-1} , 3000, 2910, 1740, 1600, 1490, 1380, 1110. $\text{C}_{21}\text{H}_{23}\text{NO}$ (305.42) measured on the mixture: calcd. C 82.58, H 7.59, N 4.59; found C 82.10, H 7.72, N 4.50. (From allylic halide **10l**). Overall yield 207 mg (68%), *trans,trans*-**11l** and *trans,cis*-**13l** in a ratio 53:15.

2-Benzyl-3-phenyl-2-azaspiro[3.5]non-5-en-1-one (inseparable mixture of diastereoisomers, 4:11): Overall yield 45 mg (15%), oil. *trans*-**13m**: ^1H NMR (400.13 MHz, CDCl_3): δ = 1.50–2.10 (m, 6 H), 3.90 (d, J = 14.8 Hz, 1 H), 4.28 (s, 1 H), 4.96 (d, J = 14.8 Hz, 1 H), 5.67 (d, J = 10.2 Hz, 1 H), 5.96 (dt, J = 10.2, 6.3 Hz, 1 H), 7.15–7.39 (m, 10 H). *cis*-**14m**: ^1H NMR (400.13 MHz, CDCl_3): δ = 1.50–2.10 (m, 6 H), 3.88 (d, J = 14.8 Hz, 1 H), 4.22 (s, 1 H), 5.00 (d, J = 14.8 Hz, 1 H), 5.23 (d, J = 10.2 Hz, 1 H), 5.71 (dt, J = 10.2, 6.3 Hz, 1 H), 7.15–7.39 (m, 10 H) ppm. ^{13}C NMR, GC-MS and IR data were measured on the mixture. ^{13}C NMR (100.62 MHz, CDCl_3): δ = 19.1, 19.9, 24.4, 24.6, 24.7, 30.0, 44.1, 44.3, 60.9, 61.2, 65.8, 67.3, 122.4, 125.7, 126.9, 127.2, 127.6, 127.7, 127.8, 128.1, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 132.1, 132.5, 135.6, 135.8, 136.0, 138.1, 172.6, 172.8 ppm. GC-MS (70 eV): m/z (%) = 303 (2) [M^+], 196 (7), 170 (100), 155 (17), 144 (17), 142 (17), 141 (16), 115 (10), 108 (22), 91 (67). IR (film): $\tilde{\nu}$ = 3060 cm^{-1} , 3020, 2900, 1740, 1490, 1450.

4-Phenyl-1-(1-phenyl-ethyl)-3-vinylazetidin-2-one (trans-11n): Yield 166 mg (60%), oil. ^1H NMR (400.13 MHz, CDCl_3): δ = 1.80 (d, J = 7.1 Hz, 3 H), 3.59 (dd, J = 7.7, 1.9 Hz, 1 H), 4.13 (d, J =

1.9 Hz, 1 H), 4.28 (q, $J = 7.1$ Hz, 1 H), 5.24 (dd, $J = 17.7$, 10.3 Hz, 2 H), 5.87–5.96 (m, 1 H), 7.16–7.32 (m, 10 H) ppm. ^{13}C NMR (100.62 MHz, CDCl_3): $\delta = 20.1$, 54.6, 60.5, 63.1, 118.9, 126.5, 126.7, 127.4, 128.3, 128.5, 128.8, 131.0, 137.6, 141.3, 168.0 ppm. GC-MS (70 eV): m/z (%) = 264 (0) [M^+], 130 (100), 129 (50), 115 (20), 105 (22), 77 (21). IR (film): $\tilde{\nu} = 3060\text{ cm}^{-1}$, 2980, 1735, 1450. **trans-11n'**: Yield 89 mg (32%), oil. ^1H NMR (400.13 MHz, CDCl_3): $\delta = 1.31$ (d, $J = 7.2$ Hz, 3 H), 3.62 (dd, $J = 7.6$, 2.2 Hz, 1 H), 4.05 (d, $J = 2.2$ Hz, 1 H), 5.06 (q, $J = 7.2$ Hz, 1 H), 5.15–5.26 (m, 2 H), 5.77–5.86 (m, 1 H), 7.20–7.33 (m, 10 H) ppm. ^{13}C NMR (100.62 MHz, CDCl_3): $\delta = 18.6$, 52.0, 60.7, 63.2, 119.0, 126.7, 127.2, 127.7, 128.5, 128.6, 128.7, 130.7, 138.9, 139.8, 168.2 ppm. GC-MS (70 eV): m/z (%) = 264 (0) [M^+], 130 (100), 129 (50), 115 (20), 105 (22), 77 (21). IR (film): $\tilde{\nu} = 3060\text{ cm}^{-1}$, 2980, 1735, 1450.

1-(2-Methoxy-1-phenylethyl)-4-phenyl-3-vinylazetidin-2-one (trans-11o): Yield 160 mg (52%), solid. M.p. 97.2–99.2 °C (*n*-hexane). ^1H NMR (400.13 MHz, CDCl_3): $\delta = 3.40$ (s, 3 H), 3.61 (dd, $J = 7.9$, 2.0 Hz, 1 H), 3.69 (dd, $J = 6.9$, 2.4 Hz, 1 H), 4.22 (d, $J = 2.0$ Hz, 1 H), 4.28–4.33 (m, 2 H), 5.25 (dd, $J = 19.0$, 10.4 Hz, 2 H), 5.90–5.98 (m, 1 H), 7.19–7.36 (m, 10 H) ppm. ^{13}C NMR (100.62 MHz, CDCl_3): $\delta = 58.7$, 59.0, 60.4, 63.4, 73.0, 119.0, 126.6, 127.4, 127.8, 128.3, 128.6, 128.7, 131.0, 137.5, 137.6, 168.1 ppm. GC-MS (70 eV): m/z (%) = 307 (0) [M^+], 262 (10), 240 (21), 194 (27), 130 (100), 129 (81), 115 (50), 91 (28). IR (CHCl_3): $\tilde{\nu} = 3060\text{ cm}^{-1}$, 3030, 2920, 2850, 1600, 1520, 1490, 1430, 1340, 1310, 1110, 960, 760, 730, 690. $\text{C}_{20}\text{H}_{21}\text{NO}_2$ (307.39): calcd. C 78.14, H 6.89, N 4.55; found C 78.10, H 7.02, N 4.50. **trans-11o'**: Yield 123 mg (40%), oil. ^1H NMR (400.13 MHz, CDCl_3): $\delta = 3.25$ (s, 3 H), 3.43 (dd, $J = 9.3$, 5.4 Hz, 1 H), 3.60 (dd, $J = 8.0$, 2.0 Hz, 1 H), 3.75 (t, $J = 9.3$ Hz, 1 H), 4.24 (d, $J = 2.0$ Hz, 1 H), 4.81 (dd, $J = 9.3$, 5.4 Hz, 1 H), 5.18–5.23 (m, 2 H), 5.83–5.97 (m, 1 H), 7.22–7.34 (m, 10 H) ppm. ^{13}C NMR (100.62 MHz, CDCl_3): $\delta = 57.8$, 58.5, 62.3, 63.2, 72.0, 119.0, 126.6, 126.8, 127.8, 127.9, 128.3, 128.6, 130.9, 136.7, 138.6, 168.7 ppm. GC-MS (70 eV): m/z (%) = 307 (0) [M^+], 262 (10), 240 (21), 194 (27), 130 (100), 129 (81), 115 (50), 91 (28). IR (film): $\tilde{\nu} = 3060\text{ cm}^{-1}$, 3030, 2920, 2850, 1600, 1520, 1490, 1430, 1340, 1310, 1110, 960, 760, 730, 690.

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