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

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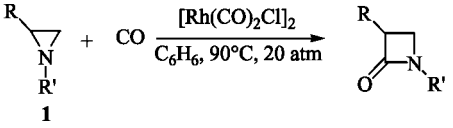
Allyl halides of different structures, under CO pressure, in the presence of Et_3N, a catalytic amount of $Pd(OAc)_2$, and triphenylphosphane as ligand, undergo a [2+2] cycloaddition reaction with various imines. The reaction is highly regio- and stereoselective: β-lactams are formed in good yields and with *trans* diastereoselectivity in both the β-lactam ring and the vinylic moiety. New and important information is suggested regarding the known reaction mechanism.

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.

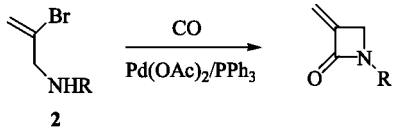
The analogous cyclocarbonylation of unsaturated amines, leading to the formation of lactams, seems to have been studied less in the literature.[13,14] Of all lactams, the β-lactams[15−22] are of special biological and pharmaceutical interest, and these compounds have also been obtained by different synthetic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



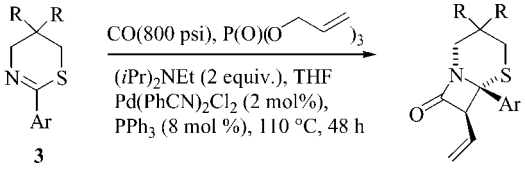
Scheme 1

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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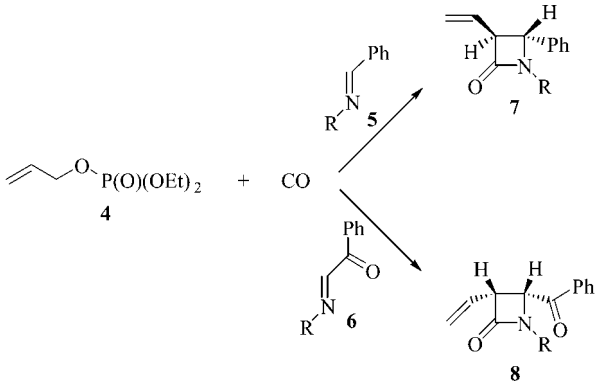


Scheme 4

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.

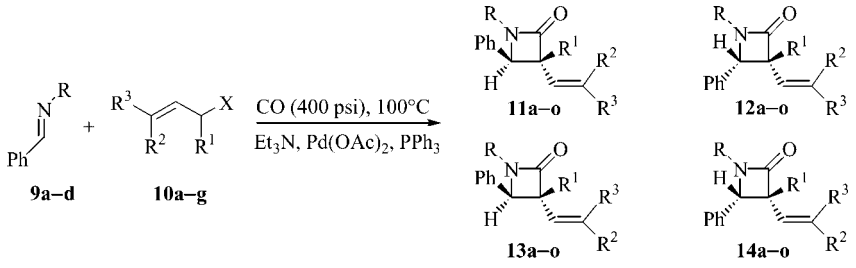
Results and Discussion

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 Et_3N, 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 Et_3N instead of iPr_2NEt, 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.

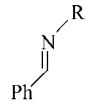
According to the mechanism proposed by Torii[33] (Scheme 6), the reaction starts by the formation of the π-allyl palladium complex **16**. In the acyl complex **17**, derived from the insertion of CO, the protons alpha to the carbonyl group show appreciable acidity.

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



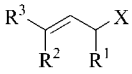
Entry	Imine	Halide	Products (yield, %)[a]			
1	**9a**	**10a**	**11a** (84)	**12a** (5)	–	–
2	**9a**	**10b**	**11a** (81)	**12a** (6)	–	–
3	**9a**	**10c**	**11b** (81)	**12b** (15)	–	–
4	**9a**	**10d**	**11c** (58)	**12c** (traces)	**13c** (21)	**14c** (traces)
5	**9a**	**10f**	**11d** (50)[b]	–	**13d** (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

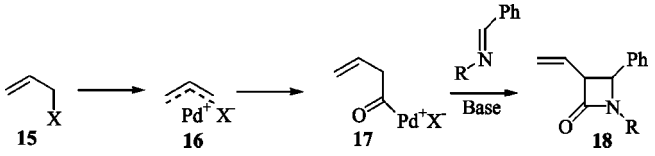
Imine	R
9a	Ph
9b	CH_2Ph
9c	$CH(CH_3)Ph$
9d	$CH(Ph)CH_2OCH_3$



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	$(CH_2)_2CH_3$
10g	Br	$-CH_2-CH_2-CH_2-$		H
10h	Cl	CH_3	H	H
10i	Br	CH_3	H	H
10l	Br	$(CH_2)_2CH_3$	H	H

Scheme 5



Scheme 6

Consequently, deprotonation by Et_3N 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**.

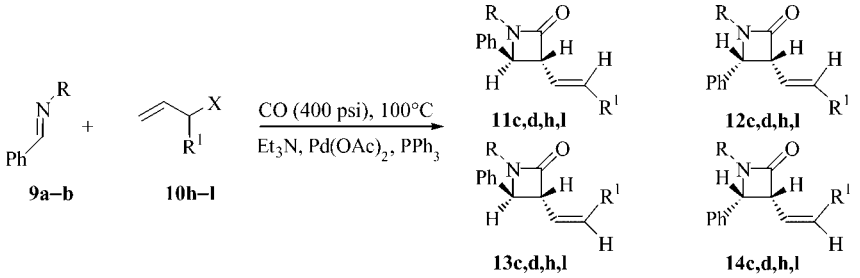
According to previously reported data,[33,34] as well as the data in Table 1, the CO insertion would always occur between the carbon (C-3) directly attached to the halogen and the palladium (structure **17**). When the halogen is not in the terminal position of the allylic chain, we found, instead, that 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**) ($R^2 = R^3 = H$, $R^1 = CH_3$), or 3-bromo-1-hexene (**10l**) [$R^2 = R^3 = H$, $R^1 = (CH_2)_2CH_3$], 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 Et_3N 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. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker Avance 400 spectrometer (400.13 MHz and 100.62 MHz, for ^{1}H and ^{13}C, respectively), with $CDCl_3$ as the solvent (δ = 7.24 ppm for ^{1}H spectra; δ = 77.0 ppm for ^{13}C 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 (Et_2O) 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), PPh_3 (0.08 mmol), $Pd(AcO)_2$ (0.02 mmol), and Et_3N (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 Et_2O (3 × 5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The crude products were purified by column chromatography (silica gel, petroleum ether/Et_2O, 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). ^{1}H NMR (400.13 MHz, $CDCl_3$): 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. ^{13}C NMR (100.62 MHz, $CDCl_3$): 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 ($CHCl_3$): ṽ = 3050 cm^{-1}, 3020, 3000, 2910, 1740, 1600, 1370. $C_{17}H_{15}NO$ (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. ^{1}H NMR (400.13 MHz, $CDCl_3$): 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. ^{13}C NMR (100.62 MHz, $CDCl_3$): 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): ṽ = 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). ^{1}H NMR (400.13 MHz, $CDCl_3$): 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. ^{13}C NMR (100.62 MHz, $CDCl_3$): 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 ($CHCl_3$): ṽ = 3030 cm^{-1}, 2970, 2910, 1740, 1600, 1370. $C_{19}H_{19}NO$ (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. ^{1}H NMR (400.13 MHz, $CDCl_3$): 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. ^{13}C NMR (100.62 MHz, $CDCl_3$): 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): ṽ = 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). ^{1}H NMR (400.13 MHz, $CDCl_3$): 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. ^{13}C NMR (100.62 MHz, $CDCl_3$): 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 ($CHCl_3$): ṽ = 3020 cm^{-1}, 2920, 1740, 1600, 1490, 1370. $C_{18}H_{17}NO$ (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. ^{1}H NMR (400.13 MHz, $CDCl_3$): 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. ^{13}C NMR (100.62 MHz, $CDCl_3$): 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): ṽ = 3060 cm^{-1}, 3020, 2920, 1740, 1600, 1490, 1370. (From allylic halides **10h** and **10i**) Yield ***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:** ^{1}H NMR (400.13 MHz, $CDCl_3$): 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. ^{13}C NMR (100.62 MHz, $CDCl_3$): 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:** ^{1}H NMR (400.13 MHz, $CDCl_3$): 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. ^{13}C

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. $C_{21}H_{23}NO$ (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 = 1.5 0−2.10 (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, $CDCl_3$): δ = 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 cm^{-1}, 2980, 1735, 1450. ***trans*-11n′:** Yield 89 mg (32%), oil. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 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, $CDCl_3$): δ = 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 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). ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 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, $CDCl_3$): δ = 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 cm^{-1}, 3030, 2920, 2850, 1600, 1520, 1490, 1430, 1340, 1310, 1110, 960, 760, 730, 690. $C_{20}H_{21}NO_2$ (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. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 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, $CDCl_3$): δ = 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 cm^{-1}, 3030, 2920, 2850, 1600, 1520, 1490, 1430, 1340, 1310, 1110, 960, 760, 730, 690.

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