Suzuki Reaction of Vinyl Triflates from Six- and Seven-Membered *N*-Alkoxycarbonyl Lactams with Boronic Acids and Esters

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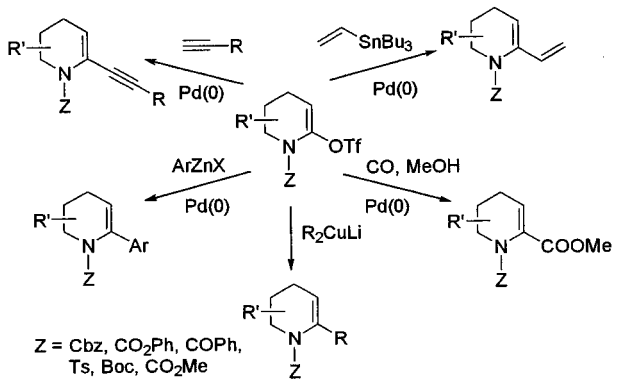
The Pd(0)-catalyzed reaction of vinyl triflates from *N*-alkoxycarbonyl lactams with different boron compounds has been studied. The coupling reaction of alkenylboronates and arylboronic acids with six- and seven-membered lactam-derived *N*-alkoxycarbonyl vinyl triflates was feasible under very mild conditions in THF−water employing $(Ph_3P)_2PdCl_2$ as a catalyst and Na_2CO_3 as a base, which provided in high yields the corresponding 6- or 7-substituted *N*-alkoxycarbonyl-3,4-dihydro-2*H*-pyridines and *N*-alkoxycarbonyl-2,3,4,5-tetrahydroazepines. Allylboronates reacted slower but, with vinyl triflates from *δ*-valerolactam, still gave acceptable yields of the coupling product. Alkylboronic acids required different reaction conditions, in particular the presence of Ag_2O together with a base in anhydrous toluene and $(dppf)PdCl_2$ as a catalyst, affording the corresponding 6-alkyl-*N*-alkoxycarbonyl-3,4-dihydro-2*H*-pyridines in high yields.

Introduction

In recent years there has been a growing interest in the chemistry of lactam-derived vinyl triflates. It has been shown that these compounds can undergo palladium-mediated displacement of the triflate group with nucleophiles such as organotin and organozinc derivatives, as well as methoxycarbonylation reactions.[1] Coupling reactions with organocuprates and organotin compounds[2−4] and Sonogashira-type cross-coupling reactions with monosubstituted acetylenes[5−7] have been described by some authors, too. Most of these reactions have been carried out on vinyl triflates from six-membered lactams (Scheme 1) and on pyrrolidin-2-one-derived triflates. These methodologies have been exploited in the synthesis of naturally occurring compounds such as pipecolic acid,[2] clavepictines A and B,[6] desoxoprosophylline,[8] and lepadin B.[9]

Although the use of organoboron compounds as nucleophiles in Pd-catalyzed cross-coupling reactions with vinyl and aryl triflates is a powerful methodology in organic synthesis,[10] no examples of Suzuki-type reactions

Scheme 1



of lactam-derived vinyl triflates have been yet reported, apart from our recent communication in which we described the reaction of a small number of boron derivatives with a *δ*-valerolactam-derived vinyl triflate.[11] The possibility of forming new C−C bonds by Pd(0)-catalyzed coupling of boronic acids or their esters with vinyl triflates from *N*-alkoxycarbonyl lactams would certainly extend the utility and scope of this reaction in the preparation of heterocyclic compounds. Various methodologies for the preparation of differently substituted boronic acids and esters are indeed known,[10a,12] and moreover, a large number of them are now commercially available. Moreover, unlike many organometallic derivatives, boronic acids and their esters are usually stable to

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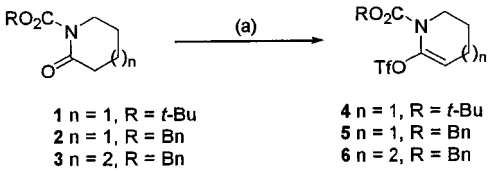
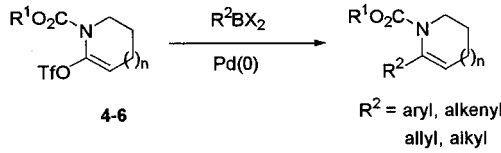
Scheme 2[a]



[a] Key: (a) LiHMDS (1 M in THF), HMPA, $PhNTf_2$, THF, -78 °C to rt, 16 h.

Scheme 3



air and moisture and are of low toxicity and environmental impact. In this paper, we thus wish to report on the Pd(0)-catalyzed reaction of vinyl triflates from six- and seven-membered *N*-alkoxycarbonyl lactams **4**−**6** (Schemes 2 and 3) with aryl-, alkenyl-, allyl-, and alkylboronic acids or their esters and describe, for each case, the best reaction conditions found for the new C−C bond formation.[13]

Results and Discussion

Vinyl triflates **4**−**6** were prepared by treatment of *N*-alkoxycarbonyl lactams **1**−**3** with LiHMDS and *N*-phenyltriflimide, in the presence of HMPA at −78 °C and then being left at room temperature for 16 h (Scheme 2), according to the method reported by Murai.[3,14] *N*-Boc and *N*-Cbz vinyl triflate **4** and **5** were obtained in 75% and 92% yield, respectively, after chromatography. These two compounds are stable at room or higher temperatures and can be stored in the refrigerator for several months. Seven-membered *N*-Cbz vinyl triflate **6** (obtained in 65% yield), in our hands, was more prone to degradation, and during chromatographic purification it gave back a considerable amount (about 25%) of its *N*-Cbz caprolactam precursor **3**. It was also less stable at room temperature than compounds **4** and **5** and had to be stored in the refrigerator to avoid a slow darkening of the neat liquid.

In our study, we initially used *N*-Boc as the electron-withdrawing protecting group. Since it is removable under acid conditions, *N*-Boc can in fact provide possible synthetic alternatives to other protecting groups such as Cbz or Ts in the elaboration toward target heterocycles. We also chose 2-[(*E*)-1-hexenyl]-1,3,2-benzodioxaborole **7**[12a,b] as the boron derivative counterpart, as in the seminal work of Miyaura and Suzuki on the Pd(0)-catalyzed reaction of vinyl triflates with boron compounds.[10b] The reaction of **4** with **7** (Scheme 4) to give 6-[(*E*)-1-hexenyl]-3,4-dihydro-2*H*-piperidine derivative **8** was first attempted under the conditions reported by these authors, i.e., using $(Ph_3P)_4Pd$ catalyst in dioxane at 85 °C

Scheme 4

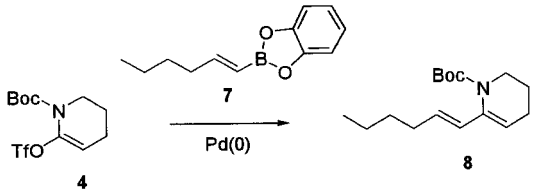


Table 1. Pd(0)-Catalyzed Cross-Coupling Reaction of Vinyl Triflate 4 with Boronate 7

entry	conditions[a]	*T* (°C)	time (h)	yield[b] (%)
1	dioxane, K_3PO_4, 5% $(Ph_3P)_4Pd$	85	5	*c*
2	DMF, Cs_2CO_3, 5% $(Ph_3P)_2PdCl_2$	40	4	*c*
3	DMF/2 M Cs_2CO_3 (aq) (4:1), 5% $(Ph_3P)_2PdCl_2$	40	4	72
4	THF/2 M Na_2CO_3 (aq) (4:1), 5% $(Ph_3P)_2PdCl_2$	20	16	82
		40	6	82
		40	2[d]	82[d]
		80	2	81
5	THF/2 M Na_2CO_3 (aq) (4:1), 5% $(o\text{-}tol_3P)_2PdCl_2$	20	48	16
6	THF/2 M Na_2CO_3 (aq) (4:1), 5% $(dppe)PdCl_2$	40	2	*c*
7	THF/2 M Na_2CO_3 (aq) (4:1), 5% $(dppf)PdCl_2$	40	2	45
8	THF/2 M NaOH (aq) (4:1), 5% $Pd(dba)_2$	40	3	27[e]
9	THF/2 M KF(aq), (3:1), 5% $(Ph_3P)_2PdCl_2$	40	3	76

[a] Reactions carried out with 1.5 equiv of **7** under nitrogen atmosphere; reactions in entries 3−8 were carried out on about 0.3 mmol of **4** in 4 mL of organic solvent with 6.7 equiv of base; the ratio between the volumes of the organic solvent and solution of the base is reported in brackets. [b] Yield of **8** after chromatography. [c] Unreacted **4** was recovered in these cases. [d] Experiment carried out with distilled **7**. [e] Conversion calculated by ^1H NMR analysis of the crude reaction mixture.

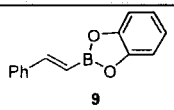
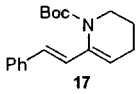
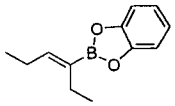
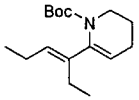
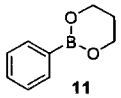
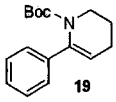
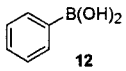
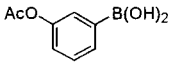
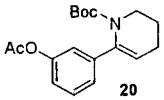
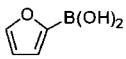
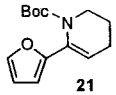
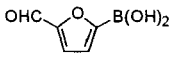
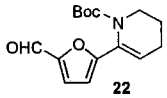
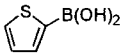
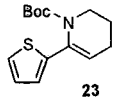
and K_3PO_4 as a base (Table 1, entry 1). However the reaction did not occur at all, and we recovered after 5 h the unreacted starting material **4**. Also by carrying out the reaction in anhydrous DMF, with Cs_2CO_3 as a base, and 5% $(Ph_3P)_2PdCl_2$ as a catalyst (entry 2), we were unable to obtain the coupling product. Instead, the addition of an aqueous base as 2 M Cs_2CO_3 (about 7 equiv) (entry 3) allowed the reaction to occur, affording **8** in 72% yield after 4 h at 40 °C with maintenance of the double-bond geometry. Yields were improved using THF as a solvent: when we used $(Ph_3P)_2PdCl_2$ as a catalyst (5% mol) in a THF−water mixture and in the presence of an excess of Na_2CO_3 (about 7 equiv) as a base (entry 4) the reaction proceeded quite fast at 40 °C, affording **8** after 6 h in 82% yield; the reaction was slightly slower at 20 °C and it reached completion (82% yield) after 16 h, while at 80 °C proceeded fast and was complete (yield 81%) after 2 h. In the above experiments, we used crude 2-[(*E*)-1-hexenyl]-1,3,2-benzodioxaborole **7** obtained from the reaction of 1-hexyne and catecholborane for carrying out the reactions.[12b] However, when we employed distilled **7**, the reaction was much faster and it reached completion after 2 h at 40 °C under the conditions of entry 4.

We also tested $(o\text{-}tol_3P)_2PdCl_2$ and $(dppe)PdCl_2$ as catalysts for the reaction of **4** with **7**. In the first case, the reaction was slower, furnishing **8** in 16% yield after chromatography (the conversion was 35%) after 48 h at room temperature (entry 5). With $(dppe)PdCl_2$ we recovered the unreacted starting material. Better results were obtained by using 5% $(dppf)PdCl_2$ (entry 7), which gave **8** in 45% yield after 2 h at 40 °C (the conversion was 65%). With $Pd(dba)_2$ as a catalyst and 2 M NaOH as a base (entry 8), without phosphine ligands, the conversion was very low after 3 h at 40 °C (27%) (some Pd black precipitated).

(13) We did not extend this study to *N*-alkoxycarbonylpyrrolidin-2-one-derived vinyl triflates since they are highly unstable and of difficult isolation due to rapid decomposition. The corresponding *N*-tosyl-protected compounds are moderately stable only if an alkoxy group is at the α-position to the nitrogen atom (see refs 1a,b and 2).

(14) Comins' reagent *N*-(5-chloro-2-pyridyl)triflimide gives also excellent yields in the preparation of vinyl triflates from lactams (see refs 1a and 2).

Table 2. Pd(0)-Catalyzed Cross-Coupling Reaction of Vinyl Triflate 4 with Boron Derivatives 9−16[a]

entry	boronic acid or ester	time (h)	product	yield (%)[b]
1	 **9**	6	 **17**	76
2	 **10**	6	 **18**	77
3	 **11**	3	 **19**	85
4	 **12**	2	**19**	87
5	 **13**	3	 **20**	88
6	 **14**	2	 **21**	94
7	 **15**	6	 **22**	50[c]
8	 **16**	2	 **23**	91

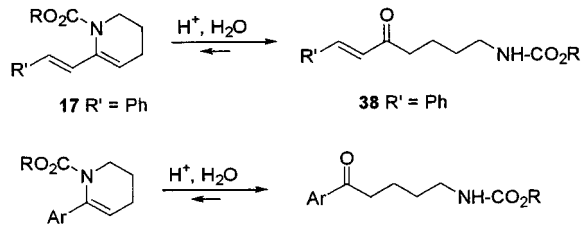
[a] Conditions: THF/2 M Na_2CO_3 (aq) v/v ratio 4:1 (entries 1−3) or 2:1 (entries 4−8), 5% $(Ph_3P)_2PdCl_2$, 40 °C, 1.5 equiv of boron compound, under nitrogen atmosphere. [b] Yield of product after chromatography, with the exception of entry 2 (yield of the crude reaction mixture). [c] Conversion calculated by ^1H NMR analysis of the crude reaction mixture.

The presence of water seems necessary for the reaction to occur. With the aqueous base the trans-metalation process could be accelerated by the OH^- ions that, by quaternization of the boron atom, render the alkenyl group more nucleophilic.[10a] Accordingly, also using 2 M aqueous KF (entry 9), the conversion to product **8** was complete in 3 h at 40 °C (76% yield). In this case, the fluoride ion could have the same role of hydroxide anion in the quaternization of the B atom.[15] The weak basicity and poor nucleophilicity of the fluoride ion could make its use particularly useful in the case of base-sensitive substrate.

The best conditions found in the first set of experiments (Table 1, entry 4) are of general use for alkenylboronates obtained from catecholborane and the corresponding alkynes, as compounds **9**−**10**[12a−b] (Table 2, entries 1 and 2). The reactions, carried out in THF with $(Ph_3P)_2PdCl_2$ and Na_2CO_3 (aq) as a base, were successful in providing the corresponding products **17** and **18** in 76 and 77% yield, respectively (after 6 h at 40 °C the conversion was complete in both cases). Compounds **17** and **18** both maintained the geometry of the double bond.

The introduction of an aryl or heteroaryl group was possible with the same methodology by using arylboronic acids or their esters, such as the commercially available compounds **11**−**16** (Table 2). The reaction of borinane **11** with **4** (entry 3) was complete after 3 h at 40 °C, affording 6-phenyl-substituted *N*-Boc-3,4-dihydro-2*H*-pyridine **19** in 85% yield. The same compound was obtained in 87% yield after 2 h at 40 °C using phenylboronic acid **12** (entry 4). In this case, we increased the volume of the aqueous 2 M Na_2CO_3. All the other boronic acids reacted smoothly with **4** under these conditions, affording coupling products in high yields (entries 5, 6, and 8). The only exception was the electron-poor 3-formylfuran-2-boronic acid **15**, which reacted slowly, furnishing coupling product **22** with a conversion of 50% after 6 h.[16]

Scheme 5

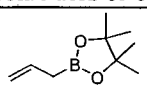
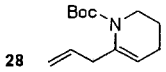
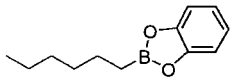
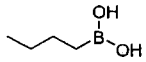
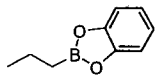
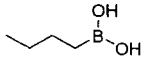
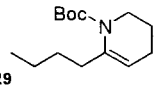


Alkenyl and aryl derivatives **8** and **17**−**23** (also as *N*-Cbz derivatives) are stable under basic or neutral conditions, but they are quite acid sensitive in the

(15) Wright, S. W.; Hageman, D. L.; McClure, L. D. *J. Org. Chem.* **1994**, *59*, 6095−6097.

(16) ^1H NMR data of **22** (from the crude reaction mixture): δ 9.96 (s, 1 H), 7.30 (d, J = 2.2 Hz, 1 H), 6.77 (d, J = 2.2 Hz, 1 H), 5.59 (t, J = 3.9 Hz, 1 H), 3.70 (m, 2 H), 2.34 (m, 2 H), 1.91 (m, 2 H), 1.20 (s, 9 H).

Table 3. Pd(0)-Catalyzed Cross-Coupling Reaction of Vinyl Triflate 4 with Boron Derivatives 24−27

entry	boronic acid or ester	method [a]	T (°C)	time (h)	product	yield (%) [b]
1	 **24**	A	80	3	 **28**	45 [c]
2	 **25**	A	40	6		d
3	 **26**	A	80	3		d
4	 **27**	B	80	7		d
5	 **26**	B	80	9	 **29**	88

[a] Method A: THF/2 M Na_2CO_3 (aq) v/v ratio 4:1 (entries 1−2) or 2:1 (entry 3), 5% $(Ph_3P)_2PdCl_2$, 1.5 equiv of boron compound, under nitrogen atmosphere. Method B: toluene, 3 equiv of K_2CO_3, 2 equiv of Ag_2O, 3% (dppf)$PdCl_2$, 2 equiv of boron compound, under nitrogen atmosphere. [b] Yield of product after chromatography. [c] The conversion was 66% after 3 h. [d] Unreacted **4** was recovered in these cases.

presence of water. They can undergo ring opening to give the corresponding open-chain unsaturated ketones (Scheme 5). Compound **17** was the most acid sensitive and even when left in $CDCl_3$ (not stored over K_2CO_3) underwent ring opening to give **38** in a 6:1 ratio with **17** after 48 h. Therefore, the chromatographic purification of these compounds must be performed using 1‰ Et_3N in the eluant to avoid ring opening.[17] This acid sensitivity is instead lacking in the 6-alkyl and 6-allyl derivatives (see later), since the equilibrium in these cases favors the cyclic compounds.

As expected, alkylboronic acids were worse nucleophiles than alkenyl- and arylboronic acids in the reaction with **4**. The difficulties in Suzuki coupling reactions with these compounds are known.[18] In fact, the conditions found for the reaction of the latter classes of boron derivatives with **4** failed to give coupling products when we used alkylboronates or alkylboronic acids (Table 3 entry 2−3) such as **25**−**26**.[19] Allylboron pinacolate **24** instead reacted with **4**, but the yield of coupling product **28** was only 45% after 3 h at 80 °C. When we carried out the reaction at 40 °C, we recovered the unreacted starting material **4** even after 24 h. Prolonging the reaction time at 80 °C did not considerably improve the conversion, probably due to decomposition of the catalyst.

Because Ag_2O is reported to accelerate the transmetalation process,[20] we tried the conditions reported by Deng for the reaction of cyclopropylboronic acids with acyl chlorides, using 3% (dppf)$PdCl_2$, K_2CO_3, and Ag_2O in anhydrous toluene.[21] The reaction failed to give the coupling product with *n*-propylboronate **27**, while it was successful with *n*-butylboronic acid **26**: after 9 h at 80 °C the coupling product **29** was obtained in 88% yield after chromatography. The formation of a very small amount of *N*-Boc-3,4-dihydro-2*H*-pyridine (less than 8%), derived from β-hydride elimination from the transmetalated complex, was observed in the ^{1}H NMR spectrum of the crude reaction mixture.

The reaction of *N*-Cbz-protected vinyl triflate **5** with one representative of each class of boron derivatives employed in this work was performed under the best conditions previously found in the reactions with **4** (Table 4). We found a slightly higher reactivity compared to the corresponding *N*-Boc derivative although, again, with the allylboronate **24** (entry 3) the conversion was not complete after 3 h at 80 °C (75% versus 66% after 3 h with *N*-Boc derivative **4**). Also, with **26** the reaction occurred only when performed at 80 °C (entry 4) as with *N*-Boc vinyl triflate **4**, affording 6-alkyl derivative **33** in 93% yield (in this case β-H elimination occurred for less than 5%).

The same series of boron derivatives was used for the reaction with ϵ-caprolactam derived *N*-Cbz vinyl triflate **6** (Table 5). In all cases, decomposition of the starting material to the corresponding lactam **3** occurred in some extent during the reaction, although this was negligible (about 15%) when the reaction was very fast as with boron derivatives **7** and **12** (entries 1 and 2). In fact, with **7** and **12** the reaction was complete just after 15 min at 40 °C, affording compounds **34** and **35** in 56 and 57% yield after chromatography. Unexpectedly, in the reaction carried out under the same conditions and at 40 °C with allylboronate **24** we recovered only *N*-Cbz lactam **3**. The low temperature was not sufficient to promote the reaction, and thus decomposition occurred. Decomposition to lactam **3** was still the main pathway when the reaction was carried out at 80 °C, but in this case we

(17) Ring opening does not occur in the presence of acids under anhydrous conditions. For example, reduction of the double bond in related 6-alkynyl derivatives has been successfully carried out in anhydrous TFA without ring opening (ref 6). Also, we were able to remove the *N*-Boc protection from **19** by treatment with TMSOTf in anhydrous CH_2Cl_2, thus obtaining the corresponding cyclic imine (6-phenyl-2,3,4,5-tetrahydropyridine) in good yield.

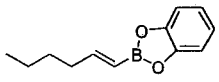
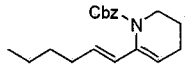
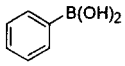
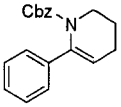
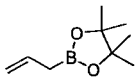
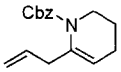
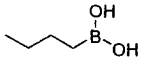
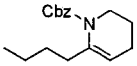
(18) Molander, G. A.; Ito, T. *Org. Lett.* **2001**, *3*, 393−396 and references therein.

(19) Compound **25** was prepared as reported (see ref 12a).

(20) (a) Uenishi, J.; Beau, J.-M.; Armstrong, R. W.; Kishi, Y. *J. Am. Chem. Soc.* **1987**, *109*, 4756−4758. (b) Gillmann, T.; Weeber, T. *Synlett* **1994**, 649−650. (c) Gronowitz, S.; Björk, P.; Malm, J.; Hörnfeldt, A. B. *J. Organomet. Chem.* **1993**, *460*, 127−129.

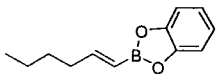
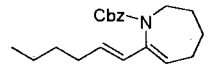
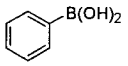
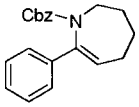
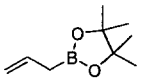
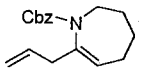
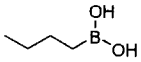
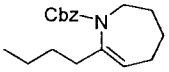
(21) Chen, H.; Deng, M.-Z. *Org. Lett.* **2000**, *2*, 1649−1651.

Table 4. Pd(0)-Catalyzed Cross-Coupling Reaction of Vinyl Triflate 5 with Selected Boron Derivatives

entry	boronic acid or ester	method [a]	T (°C)	time (h)	product	yield (%) [b]
1	 **7**	A	40	1.5	 **30**	86
2	 **12**	A	40	2	 **31**	84
3	 **24**	A	80	3	 **32**	65 [c]
4	 **26**	B	80	8	 **33**	93

[a] Method A: THF/2 M Na_2CO_3 (aq) v/v ratio 4:1 (entries 1 and 3) or 2:1 (entry 2), 5% $(Ph_3P)_2PdCl_2$, 1.5 equiv of boron compound, under nitrogen atmosphere. Method B: toluene, 3 equiv of K_2CO_3, 2 equiv of Ag_2O, 3% (dppf)$PdCl_2$, 2 equiv of boron compound, under nitrogen atmosphere. [b] Yield of product after chromatography with the exception of entry 2 (yield of the crude reaction mixture). [c] The conversion was 75% after 3 h.

Table 5. Pd(0)-Catalyzed Cross-Coupling Reaction of Vinyl Triflate 6 with Selected Boron Derivatives

entry	boronic acid or ester	method [a]	T (°C)	time (h)	product	yield (%) [b]
1	 **7**	A	40	0.25	 **34**	56
2	 **12**	A	40	0.25	 **35**	57
3	 **24**	A	80	4	 **36**	27 [c]
4	 **26**	B	80	7	 **37**	22

[a] Method A: THF/2 M Na_2CO_3 (aq) v/v ratio 4:1 (entries 1 and 3) or 2:1 (entry 2), 5% $(Ph_3P)_2PdCl_2$, 1.5 equiv of boron compound, under nitrogen atmosphere. Method B: toluene, 3 equiv of K_2CO_3, 2 equiv of Ag_2O, 3% (dppf)$PdCl_2$, 2 equiv of boron compound, under nitrogen atmosphere. [b] Yield of product after chromatography. [c] Conversion calculated by ^1H NMR analysis of the crude reaction mixture.

observed a 27% conversion to **36**.[22] Analogously, the reaction did not proceed well under Deng's conditions (method B) and we obtained, after 7 h at 80 °C, again mainly decomposition to **3** and coupling product **37** in 22% yield after chromatography. From these results, it appears that the triflates from a seven-membered ring, although more reactive, are more susceptible to decomposition when the reaction is slow[23] and only those boron reagents that react quickly with **6** appear useful for the C−C bond formation.

Conclusion

In conclusion, we have shown that the Suzuki reaction is suitable for introducing aryl, alkenyl, allyl, and alkyl groups on piperidine and azepine rings by coupling with the corresponding *N*-alkoxycarbonyl vinyl triflates. The coupling reaction of alkenylboronates and arylboronic acids with six- and seven-membered lactam-derived *N*-alkoxycarbonyl vinyl triflates is feasible under very mild conditions in THF−water, employing $(Ph_3P)_2PdCl_2$ as a catalyst, which provides in high yields the corresponding 6- or 7-substituted *N*-alkoxycarbonyl-3,4-dihydro-2*H*-pyridines and *N*-alkoxycarbonyl-2,3,4,5-tetrahydroazepines. Allylboronates react slower under those conditions but, with vinyl triflates from δ-valerolactam, still give acceptable yields of the coupling product. Alkylboronic acids require different reaction conditions, in particular the presence of Ag_2O together with a base in anhydrous toluene and (dppf)$PdCl_2$ as catalyst. Under these conditions, vinyl triflates **4** and **5** react smoothly to give the corresponding 6-alkyl-3,4-dihydro-2*H*-piperidines in high yields. The application of this methodology to the synthesis of heterocyclic compounds is currently investigated in our laboratory.

(22) ^1H NMR data of **36** (from the crude reaction mixture): δ 7.42−7.27 (m, 5 H), 5.85−5.60 (m, 1 H), 5.43 (t, J = 5.5 Hz, 1 H), 5.14 (s, 2 H), 5.00−4.85 (m, 2 H), 3.56 (m, 2 H), 2.92 (d, J = 7.3 Hz, 2 H), 2.23 (m, 2 H), 2.13 (m, 2 H), 1.57−1.44 (m, 4 H).

(23) If the trans-metalation process is slow, either the high temperature or the presence of water cause progressive degradation of the starting material during the course of the reaction.

Experimental Section

All solvents were degassed before use. Chromatographic separations were performed under pressure on silica gel using flash-column techniques; R_f values refer to TLC carried out on 25-mm silica gel plates (Merck F254), with the same eluant indicated for the column chromatography. ^{1}H and ^{13}C NMR spectra were recorded at 200 and 50.33 MHz, respectively. Boron derivatives **11**−**16**, **24**, **26**, and **27** are commercially available.

6-Trifluoromethanesulfonyloxy-3,4-dihydro-2*H*-pyridine-1-carboxylic Acid *tert*-Butyl Ester (4). To a solution of **1** (1.0 g, 5.02 mmol) in anhydrous THF (30 mL), cooled to −78 °C, was added a 1 M solution of LiHMDS in THF (6.25 mL, 6.25 mmol) over 35 min, and the mixture was stirred for 70 min. Distilled HMPA (1.75 mL, 10.04 mmol) was added, the solution was stirred for an additional 15 min, and then a solution of $PhNTf_2$ (2.23 g, 6.25 mmol) in anhydrous THF (5 mL) was added and the mixture allowed to warm to room temperature and left to react for 15 h. Water (50 mL) was added, and the organic products were extracted with diethyl ether (3 × 40 mL), washed with 10% aqueous NaOH, and dried over anhydrous K_2CO_3. The crude product was purified by flash chromatography (CH_2Cl_2−petroleum ether 1:2, R_f 0.27) affording compound **4** (1.24 g, 75%) as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 5.27 (t, J = 4.0 Hz, 1 H), 3.58 (m, 2 H), 2.24 (m, 2 H), 1.74 (m, 2 H), 1.47 (s, 9 H).

6-Trifluoromethanesulfonyloxy-3,4-dihydro-2*H*-pyridine-1-carboxylic Acid Benzyl Ester (5). A solution of **2** (2.61 g, 11.2 mmol) in anhydrous THF (60 mL) was cooled to −78 °C, a 1 M solution of LiHMDS in THF (14 mL, 14.0 mmol) was added over 30 min, and the mixture was stirred for 70 min. Distilled HMPA (3.92 mL, 22.5 mmol) was added, the solution was stirred for an additional 15 min, and then a solution of $PhNTf_2$ (5.0 g, 14.0 mmol) in anhydrous THF (12 mL) was added and the mixture allowed to warm to room temperature and left to react for 15 h. Water (100 mL) was added, and the organic products were extracted with diethyl ether (3 × 60 mL), washed with 10% aqueous NaOH, and dried over anhydrous K_2CO_3. The crude mixture was purified by flash chromatography (EtOAc−petroleum ether 1:5, R_f 0.41) yielding pure compound **4** (3.76 g, 92%) as a yellowish oil: ^{1}H NMR ($CDCl_3$) δ 7.34 (m, 5 H), 5.32 (t, J = 4.0 Hz, 1 H), 5.19 (s, 2 H), 3.66 (m, 2 H), 2.25 (m, 2 H), 1.76 (m, 2 H).

7-Trifluoromethanesulfonyloxy-2,3,4,5-tetrahydroazepine-1-carboxylic Acid Benzyl Ester (6). Compound **6** was prepared according to the procedure reported for **5** starting from **3** (2.2 g, 8.9 mmol). Pure **6** (2.19 g, 65%) was obtained as a yellow oil after a rapid purification by chromatography on silica gel using a more polar eluant (EtOAc−petroleum ether 1:2, R_f 0.76): ^{1}H NMR ($CDCl_3$) δ 7.33 (m, 5 H), 5.69 (t, J = 7.0 Hz, 1 H), 5.19 (s, 2 H), 3.58 (m, 2 H), 2.13 (m, 2 H), 1.73 (m, 2 H), 1.55 (m, 2 H).

6-[(*E*)-Hex-1-enyl]-3,4-dihydro-2*H*-pyridine-1-carboxylic Acid *tert*-Butyl Ester (8). To a solution of **4** (93 mg, 0.28 mmol) in THF (4 mL) were added, under a nitrogen atmosphere, $(Ph_3P)_2PdCl_2$ (10 mg, 14 μmol), distilled **7** (85 mg, 0.42 mmol), and a 2 M aqueous Na_2CO_3 solution (1 mL). The mixture continued stirring for 2 h at 40 °C. Water (10 mL) was then added and the mixture extracted with diethyl ether and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded a brown oil that was purified by chromatography (CH_2Cl_2−petroleum ether 1:2, 1‰ Et_3N, R_f 0.15) to give **8** (61 mg, 82%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 5.85 (d, J = 15.6 Hz, 1 H), 5.67 (m, 1 H), 5.19 (t, J = 3.8 Hz, 1 H), 3.50 (t, J = 5.2 Hz, 2 H), 2.09 (m, 4 H), 1.75 (m, 2 H), 1.41 (s, 9 H), 1.29 (m, 4 H), 0.86 (t, J = 6.6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 147.5 (s), 138.5 (s), 128.4 (d), 127.8 (d), 112.9 (d), 80.3 (s), 44.4 (t), 32.2 (t), 31.5 (t), 28.3 (q, 3 C), 23.5 (t), 23.4 (t), 22.4 (t), 14.0 (q); MS m/z 265 (M^+, 0.2), 166 (8), 165 (2), 57 (100). Anal. Calcd for $C_{16}H_{27}NO_2$: C, 72.41; H, 10.25; N, 5.28. Found: C, 72.11; H, 10.43; N, 5.01.

6-[(*E*)-Styryl]-3,4-dihydro-2*H*-pyridine-1-carboxylic Acid *tert*-Butyl Ester (17). Compound **17** was prepared as reported for **8** starting from **4** (80 mg, 0.24 mmol) and **9** (80 mg, 0.36 mmol), but heating at 40 °C for 6 h. Pure **17** (52 mg, 76%) was obtained after purification by chromatography (CH_2Cl_2−petroleum ether 1:2, Et_3N 1‰, R_f 0.14) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.40−7.13 (m, 5 H), 6.55 (AB system, J = 16 Hz, 2 H), 5.43 (t, J = 3.8 Hz, 1 H), 3.57 (m, 2 H), 2.22 (m, 2 H), 1.79 (m, 2 H), 1.37 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 138.5 (s), 137.4 (s), 128.5 (d, 2 C), 127.9 (s), 127.7 (d), 127.1 (d), 126.3 (d), 126.2 (d, 2 C), 115.7 (d), 80.5 (s), 44.4 (t), 28.3 (q, 3 C), 23.7 (t), 23.4 (t); MS m/z 285 (M^+, 1), 186 (26), 103 (40), 57 (100). Anal. Calcd for $C_{18}H_{23}NO_2$: C, 75.76; H, 8.12; N, 4.91. Found: C, 75.61; H, 8.46; N, 4.77.

6-[(*E*)-(1-Ethyl-but-1-enyl)-3,4-dihydro-2*H*-pyridine-1-carboxylic Acid *tert*-Butyl Ester (18). Compound **18** was prepared as reported for **8** starting from **4** (52 mg, 0.16 mmol) and **10** (48 mg, 0.24 mmol), but heating at 40 °C for 6 h. Compound **18** (33 mg, 77%) was obtained after usual workup as a sufficiently pure oil: ^{1}H NMR ($CDCl_3$) δ 5.37 (t, J = 7.0 Hz, 1 H), 5.12 (t, J = 3.7 Hz, 1 H), 3.51 (m, 2 H), 2.36−1.98 (m, 6 H), 1.76 (m, 2 H), 1.38 (s, 9 H), 0.96 (t, J = 7.7 Hz, 3 H), 0.85 (t, J = 7.3 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 141.0 (s), 126.9 (s), 126.1 (d), 113.1 (d), 112.1 (s), 80.2 (s), 44.3 (t), 28.3 (q, 3 C), 23.8 (t), 23.4 (t), 21.4 (t), 21.0 (t), 14.3 (q), 13.3 (q); MS m/z 265 (M^+, 0.5), 164 (70), 57 (100). Anal. Calcd for $C_{16}H_{27}NO_2$: C, 72.41; H, 10.25; N, 5.28. Found: C, 72.13; H, 10.03; N, 4.98.

6-Phenyl-3,4-dihydro-2*H*-pyridine-1-carboxylic Acid *tert*-Butyl Ester (19). To a solution of **4** (70 mg, 0.21 mmol) in THF (4 mL) were added, under a nitrogen atmosphere, $(Ph_3P)_2PdCl_2$ (7.5 mg, 10.5 μmol), phenylboronic acid **12** (122 mg, 0.32 mmol), and a 2 M aqueous Na_2CO_3 solution (2 mL). The mixture continued stirring for 2 h at 40 °C. Water (10 mL) was then added and the mixture extracted with diethyl ether and dried over anhydrous sodium sulfate. Chromatography (CH_2Cl_2−petroleum ether 1:2, Et_3N 1‰, R_f 0.15) afforded **19** (47 mg, 87%) as an oil: ^{1}H NMR ($CDCl_3$) δ 7.26 (m, 5 H), 5.31 (t, J = 3.7 Hz, 1 H), 3.71 (m, 2 H), 2.26 (dt, J = 7.0, 3.7 Hz, 2 H), 1.87 (m, 2 H), 1.06 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 140.8 (s), 131.9 (s), 128.7 (s), 127.8 (d, 2 C), 126.7 (d), 125.2 (d, 2 C), 115.0 (d), 80.3 (s), 44.4 (t), 27.7 (q, 3 C), 23.7 (t), 23.6 (t); MS m/z 259 (M^+, 10), 159 (51), 158 (86), 84 (83), 57 (83). Anal. Calcd for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16; N, 5.40. Found: C, 73.92; H, 8.34; N, 5.09.

6-(3-Acetoxyphenyl)-3,4-dihydro-2*H*-pyridine-1-carboxylic Acid *tert*-Butyl Ester (20). Compound **20** was prepared according to the procedure reported for **19** starting from **4** (103 mg, 0.31 mmol) and **13** (76 mg, 0.47 mmol). Pure **20** (86 mg, 88%) was obtained after chromatography (CH_2Cl_2−petroleum ether 1:2, Et_3N 1‰, R_f 0.4) as an oil: ^{1}H NMR ($CDCl_3$) δ 7.80 (m, 2 H), 7.50−7.26 (m, 2 H), 5.35 (t, J = 3.7 Hz, 1 H), 3.69 (m, 2 H), 2.55 (s, 3 H), 2.25 (m, 2 H), 1.84 (m, 2 H), 1.02 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 197.9 (s), 153.6 (s), 141.3 (s), 139.3 (s), 136.8 (s), 129.8 (d), 128.1 (d), 126.6 (d), 125.1 (d), 116.0 (d), 80.4 (s), 44.4 (t), 27.7 (q, 3 C), 26.6 (q), 23.7 (t), 23.4 (t); MS m/z 301 (M^+-15, 1), 201 (40), 57 (100). Anal. Calcd for $C_{18}H_{23}NO_4$: C, 68.12; H, 7.30; N, 4.41. Found: C, 68.00; H, 6.98; N, 4.33.

6-Furan-2-yl-3,4-dihydro-2*H*-pyridine-1-carboxylic Acid *tert*-Butyl Ester (21). Compound **21** was prepared according to the procedure reported for **19** starting from **4** (50 mg, 0.15 mmol) and **14** (25 mg, 0.23 mmol). Pure **21** (35 mg, 94%) was obtained after chromatography (CH_2Cl_2−petroleum ether 1:2, Et_3N 1‰, R_f 0.38) as an oil: ^{1}H NMR ($CDCl_3$) δ 7.31 (br s, 1 H), 6.33 (m, 1 H), 6.20 (d, J = 3.3 Hz, 1 H), 5.50 (t, J = 3.8 Hz, 1 H), 3.64 (m, 2 H), 2.24 (m, 2 H), 1.83 (m, 2 H), 1.24 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 152.8 (s), 141.6 (s), 140.2 (d), 131.4 (s), 114.3 (d), 110.8 (d), 104.7 (d), 80.4 (s), 44.1 (t), 27.8 (q, 3 C), 23.5 (t), 23.2 (t); MS m/z 249 (M^+, 8), 183 (11), 149 (34), 84 (100). Anal. Calcd for $C_{14}H_{19}NO_3$: C, 67.45; H, 7.68; N, 5.62. Found: C, 67.32; H, 7.74; N, 5.42.

6-Thiophen-2-yl-3,4-dihydro-2*H*-pyridine-1-carboxylic Acid *tert*-Butyl Ester (23). Compound **23** was prepared according to the procedure reported for **19** starting from **4** (50 mg, 0.15 mmol) and **16** (29 mg, 0.23 mmol). Pure **23** (36 mg, 91%) was obtained after chromatography (CH_2Cl_2−petroleum ether 1:2, Et_3N 1‰, R_f 0.43) as an oil: ^{1}H NMR ($CDCl_3$) δ 7.10 (dd, J = 4.4, 2.2 Hz, 1 H), 6.92 (m, 2 H), 5.44 (t, J = 3.8 Hz, 1

H), 3.65 (m, 2 H), 2.24 (m, 2 H), 1.83 (m, 2 H), 1.19 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 144.5 (s), 134.3 (s), 131.9 (s), 126.5 (d), 122.9 (d), 122.3 (d), 115.2 (d), 80.6 (s), 44.6 (t), 27.8 (q, 3 C), 23.6 (t), 23.4 (t); MS *m*/*z* 265 (M^+, 6), 165 (22), 84 (100). Anal. Calcd for $C_{14}H_{19}NO_2S$: C, 63.36; H, 7.22; N, 5.28. Found: C, 63.08; H, 7.44; N, 4.97.

6-Allyl-3,4-dihydro-2*H*-pyridine-1-carboxylic Acid *tert*-Butyl Ester (28). Compound **28** was prepared as reported for **8** starting from **4** (106 mg, 0.32 mmol) and **24** (90 μL, 0.48 mmol) but heating at 80 °C for 3 h. Pure **28** (34 mg, 45%) was obtained after purification by chromatography (CH_2Cl_2−MeOH 20:1, 1‰ Et_3N, R_f 0.3): ^{1}H NMR ($CDCl_3$) δ 5.84−5.67 (m, 1 H), 5.03 (dd, J = 9.9, 1.8 Hz, 1 H), 4.96 (m, 2 H), 3.50 (m, 2 H), 3.18 (dd, J = 6.6, 1.5 Hz, 2 H), 2.04 (m, 2 H), 1.73 (m, 2 H), 1.41 (s, 9 H); ^{13}C NMR ($CDCl_3$): δ 152.2 (s), 140.1 (s), 136.0 (d), 115.8 (t), 112.6 (d), 80.4 (s), 44.9 (t), 39.5 (t), 28.4 (q, 3 C), 23.4 (t), 23.1 (t); MS *m*/*z* 122 (M^+-101, 36), 57 (100). Anal. Calcd for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48; N, 6.27. Found: C, 70.04; H, 9.22; N, 6.12.

6-Butyl-3,4-dihydro-2*H*-pyridine-1-carboxylic Acid *tert*-Butyl Ester (29). To a solution of **4** (110 mg, 0.33 mmol) in anhydrous toluene (2 mL) were added, under a nitrogen atmosphere, (dppf)$PdCl_2$ (7 mg, 9.9 μmol), **26** (67 mg, 0.66 mmol), Ag_2O (152 mg, 0.66 mmol), and finely triturated K_2CO_3 (137 mg, 0.99 mmol). The mixture continued stirring for 9 h at 80 °C. Diethyl ether (10 mL) was then added, Ag_2O filtered out, and the filtrate washed with water and dried over anhydrous sodium sulfate. After evaporation of the solvent, the crude mixture was purified by chromatography (EtOAc−petroleum ether 1:15, R_f 0.56) to give **29** (69 mg, 88%) as an oil: ^{1}H NMR ($CDCl_3$) δ 4.92 (t, J = 3.6 Hz, 1 H), 3.48 (m, 2 H), 2.44 (t, J = 7.4 Hz, 2 H), 2.04 (m, 2 H), 1.78−1.70 (m, 2 H), 1.46 (s, 9 H), 1.37−1.19 (m, 4 H), 0.86 (t, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$): δ 140.1 (s), 128.2 (s), 111.9 (d), 80.2 (s), 44.9 (t), 35.1 (t), 29.9 (t), 28.4 (q, 3 C), 23.6 (t), 23.1 (t), 22.3 (t), 14.1 (q); MS *m*/*z* 239 (M^+, 6), 141 (60), 97 (100). Anal. Calcd for $C_{14}H_{25}NO_2$: C, 70.25; H, 10.53; N, 5.85. Found: C, 70.51; H, 10.37; N, 5.72.

6-[(*E*)-Hex-1-enyl]-3,4-dihydro-2*H*-pyridine-1-carboxylic Acid Benzyl Ester (30). Compound **30** was prepared as reported for **8** starting from **5** (365 mg, 1.00 mmol) and **7** (303 mg, 1.50 mmol), but heating 1.5 h at 40 °C. Pure **30** (257 mg, 86%) was obtained after purification by chromatography (EtOAc−petroleum ether 1:5, 1‰ Et_3N, R_f 0.56) as an oil: ^{1}H NMR ($CDCl_3$) δ 7.37−7.29 (m, 5 H), 5.90 (d, J = 15.7 Hz, 1 H), 5.74−5.60 (m, 1 H), 5.27 (t, J = 4.0 Hz, 1 H), 5.14 (s, 2 H), 3.60 (m, 2 H), 2.15 (m, 2 H), 2.02 (m, 2 H), 1.80 (m, 2 H), 1.28 (m, 4 H), 0.86 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 154.8 (s), 138.2 (s), 136.2 (s), 128.6 (d), 128.4 (d), 128.2 (d, 2 C), 127.8 (d, 2 C), 127.7 (d), 113.8 (d), 67.3 (t), 44.8 (t), 32.0 (t), 31.3 (t), 23.3 (t), 23.1 (t), 22.2 (t), 13.9 (q); MS *m*/*z* 299 (M^+, 2), 91 (100). Anal. Calcd for $C_{19}H_{25}NO_2$: C, 76.22; H, 8.42; N, 4.68. Found: C, 76.04; H, 8.19; N, 4.51.

6-Phenyl-3,4-dihydro-2*H*-pyridine-1-carboxylic Acid Benzyl Ester (31). Compound **31** was prepared according to the procedure reported for **19**, starting from **5** (180 mg, 0.50 mmol) and **12** (91 mg, 0.75 mmol). Compound **31** (123 mg, 84%) was obtained after usual workup in sufficiently pure form as an oil: ^{1}H NMR ($CDCl_3$) δ 7.29−7.18 (m, 8 H), 6.79 (m, 2 H), 5.43 (t, J = 4.0 Hz, 1 H), 4.93 (s, 2 H), 3.79 (m, 2 H), 2.28 (m, 2 H), 1.89 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 154.9 (s), 139.8 (s), 132.0 (s), 131.8 (s), 128.0 (d, 2 C), 127.9 (d, 2 C), 127.5 (d), 127.4 (d, 2 C), 127.0 (d), 125.0 (d, 2 C), 116.3 (d), 67.4 (t), 45.1 (t), 23.5 (t, 2 C); MS *m*/*z* 293 (M^+, 4), 91 (100). Anal. Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53; N, 4.77. Found: C, 77.82; H, 6.54; N, 4.68.

6-Allyl-3,4-dihydro-2*H*-pyridine-1-carboxylic Acid Benzyl Ester (32). Compound **32** was prepared as reported for **8** starting from **5** (92 mg, 0.25 mmol) and **24** (70 μL, 0.37 mmol), but heating for 3 h at 80 °C. Pure **32** (42 mg, 65%) was obtained after purification by chromatography (EtOAc−petroleum ether 1:4, R_f 0.68) as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 7.34 (m, 5 H), 5.85−5.65 (m, 1 H), 5.14 (s, 2 H), 5.16−4.93 (m, 3 H), 3.59 (m, 2 H), 3.21 (d, J = 5.5 Hz, 2 H), 2.06 (m, 2 H), 1.76 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 154.2 (s), 136.4 (s), 135.9 (d), 129.4 (s), 128.4 (d, 2 C), 128.0 (d, 3 C), 115.9 (t), 113.2 (d), 67.3 (t), 45.2 (t), 39.2 (t), 29.7 (t), 23.0 (t); MS *m*/*z* 257 (M^+, 2), 91 (100). Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44. Found: C, 74.77; H, 7.22; N, 5.38.

6-Butyl-3,4-dihydro-2*H*-pyridine-1-carboxylic Acid Benzyl Ester (33). Compound **33** was prepared as reported for **29** starting from **5** (180 mg, 0.49 mmol) and **26** (101 mg, 0.98 mmol), heating 8 h at 80 °C. Pure **33** (124 mg, 93%) was obtained after chromatography (EtOAc−petroleum ether 1:4, R_f 0.6): ^{1}H NMR ($CDCl_3$) δ 7.33 (m, 5 H), 5.13 (s, 2 H), 4.96 (t, J = 3.6 Hz, 1 H), 3.56 (m, 2 H), 2.44 (t, J = 7.0 Hz, 2 H), 2.02 (m, 2 H), 1.75 (m, 2 H), 1.24 (m, 4 H), 0.82 (t, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 154.1 (s), 139.8 (s), 136.3 (s), 128.3 (d, 2 C), 128.0 (d, 2 C), 127.9 (d), 112.4 (d), 67.2 (t), 45.1 (t), 34.7 (t), 29.9 (t), 23.4 (t), 22.8 (t), 22.2 (t), 13.9 (q); MS *m*/*z* 182 (M^+ − 91, 2), 91 (100). Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.45; H, 8.18; N, 5.01.

7-[(*E*)-Hex-1-enyl]-2,3,4,5-tetrahydroazepine-1-carboxylic Acid Benzyl Ester (34). Compound **34** was prepared as reported for **8** starting from **6** (80 mg, 0.21 mmol) and **7** (63 mg, 0.32 mmol), but heating for 15 min at 40 °C. Pure **34** (37 mg, 56%) was obtained after purification by chromatography (EtOAc−petroleum ether 1:4, 1‰ Et_3N, R_f 0.75) as an oil: ^{1}H NMR ($CDCl_3$) δ 7.34 (m, 5 H), 6.02−5.86 (m, 1 H), 5.72−5.41 (m, 1 H), 5.21−5.00 (m, 1 H), 5.15 (s, 2 H), 3.70 (m, 2 H), 2.02 (m, 2 H), 1.74 (m, 4 H), 1.34−1.15 (m, 6 H), 0.87 (t, J = 6.6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 152.2 (s), 133.5 (s), 130.1 (s), 129.7 (d), 128.4 (d, 2 C), 127.7 (d, 2 C), 122.3 (d), 112.1 (d), 67.8 (t), 47.7 (t), 35.7 (t), 35.2 (t), 30.5 (t), 30.3 (t), 25.5 (t), 22.2 (t), 13.9 (q); MS *m*/*z* 313 (M^+, 2), 178 (10), 91 (100). Anal. Calcd for $C_{20}H_{27}NO_2$: C, 76.64; H, 8.68; N, 4.47. Found: C, 76.51; H, 8.79; N, 4.48.

7-Phenyl-2,3,4,5-tetrahydroazepine-1-carboxylic Acid Benzyl Ester (35). Compound **35** was prepared according to the procedure reported for **19**, starting from **6** (80 mg, 0.21 mmol) and **12** (38 mg, 0.32 mmol), but heating for 15 min at 40 °C. Pure **35** (37 mg, 57%) was obtained after chromatography (EtOAc−petroleum ether 1:4, 1‰ Et_3N, R_f 0.56) as a white solid: mp 82−83 °C; ^{1}H NMR ($CDCl_3$) (3:1 mixture of rotamers) δ 7.60−7.25 (m, 6 H), 7.11 (m, 2 H), 6.68 (dd, J = 8.1, 2.2 Hz, 2 H), 6.03 (t, J = 6.6 Hz, 1 H), 4.92 (br s, 1 H), 3.80−3.40 (br s, 2 H), 2.28 (m, 2 H), 1.86 (m, 2 H), 1.56 (m, 2 H) (major rotamer), 6.10 (t, J = 6.6 Hz, 1 H) and 5.14 (s, 2 H) (minor rotamer); ^{13}C NMR ($CDCl_3$) δ 143.6 (s), 138.4 (s), 128.6 (s), 128.3 (d, 2 C), 127.9 (d, 2 C), 127.4 (d), 127.3 (d), 127.1 (s), 127.0 (d, 2 C), 124.6 (d, 2 C), 123.9 (d), 66.9 (t), 48.5 (t), 29.7 (t), 27.3 (t), 24.1 (t); MS *m*/*z* 307 (M^+, 14), 172 (36), 91 (100). Anal. Calcd for $C_{20}H_{21}NO_2$: C, 78.15; H, 6.89; N, 4.56. Found: C, 78.10; H, 6.76; N, 4.51.

7-Butyl-2,3,4,5-tetrahydroazepine-1-carboxylic Acid Benzyl Ester (37). Compound **37** was prepared as reported for **29** starting from **6** (93 mg, 0.25 mmol) and **26** (40 mg, 0.38 mmol), heating 7 h at 80 °C. Pure **37** (15 mg, 22%) was obtained after chromatography (EtOAc−petroleum ether 1:4, R_f 0.95) as an oil: ^{1}H NMR ($CDCl_3$) (1.5:1 mixture of rotamers) δ 7.35−7.06 (m, 5 H), 5.40 (t, J = 6.2 Hz, 1 H), 5.16 (s, 2 H), 3.70 (m, 2 H), 2.35−2.04 (m, 4 H), 1.86−1.17 (m, 8 H), 0.85 (m, 3 H) (major rotamer), 5.51 (t, J = 6.5 Hz, 1 H), 5.14 (s, 2 H), and 3.78 (m, 2 H) (minor rotamer), ^{13}C NMR ($CDCl_3$) δ 153.6 (s), 136.4 (s), 130.1 (s), 129.1 (d), 128.4 (d, 2 C), 127.8 (d, 2 C), 115.8 (d), 66.8 (t), 47.7 (t), 37.9 (t), 28.1 (t), 26.7 (t), 25.1 (t), 24.6 (t), 22.4 (t), 13.9 (q); MS *m*/*z* 287 (M^+, 1), 91 (100). Anal. Calcd for $C_{18}H_{25}NO_2$: C, 75.22; H, 8.77; N, 4.87. Found: C, 75.12; H, 8.99; N, 4.52.

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