Nitrogen Assistance in Intramolecular Nickel-Promoted Tandem Cyclization−Quenching Processes

Daniel Solé,[†] Yolanda Cancho,[†] Amadeu Llebaria,[†] Josep M. Moretó,[†] and Antonio Delgado*[,‡]

Departament de Química Orgànica Biològica, C.I.D. (C.S.I.C.), Jordi Girona 18-26, 08034 Barcelona, Spain, and Universitat de Barcelona, Facultat de Farmàcia, Laboratori de Química Farmacèutica, Avgda. Joan XXIII, s/n, 08028 Barcelona, Spain

Received April 12, 1996[⊗]

A diastereoselective and mild cyclization−quenching process based on the treatment of nitrogen-tethered halodienes with stoichiometric $Ni(COD)_2$ is described. The success of this methodology relies on the presence of a distal amino group capable of coordinating with the metal in the transient vinyl or alkylnickel species, thus controlling the diastereoselectivity of the cyclization step and preventing Ni−H β-elimination prior to the quenching. In general, better results are obtained in cyclizations taking place via a 5-exo-trig process, and a diversity of mono- and bicyclic nitrogenated systems are afforded in high yields by the proper choice of starting halodienes and quenching reagents. The presence of 2,2′-bipyridine as a ligand results in an acceleration of the process, and in some cases, higher diastereoselectivities and/or supression of the Ni−H β-elimination are observed.

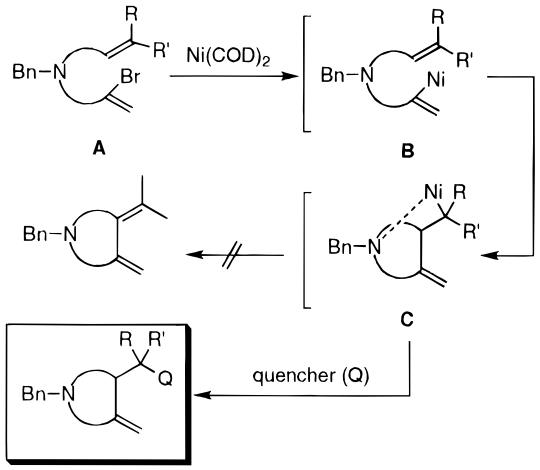
Introduction

The development of synthetic methodologies combining the simultaneous formation of several bonds in a single synthetic sequence (tandem process) represents an attractive and very active field of research.[1,2] During recent years there has been a growing interest in the application of transition metal-promoted processes toward this end and, in particular, to the synthesis of heterocyclic systems.[3,4]

As part of our ongoing research focused on the development of new methodologies leading to functionalized nitrogen heterocycles as precursors of natural products and biologically active agents, we recently reported on a nickel-promoted intramolecular tandem cyclization−capture of amino-tethered vinyl bromides and alkenes,[5] as indicated in Scheme 1.

Treatment of the starting vinyl bromides **A** with a stoichiometric amount of $Ni(COD)_2$ in CH_3CN at room temperature affords a presumed σ-alkylnickel intermediate **C** after oxidative addition and insertion steps. Diastereoselective trapping of **C** with different quencher reagents prior to Ni−H β-elimination can be effectively performed, provided that coordination of the metal with a suitably placed distal nitrogen atom in **C** takes place. This behavior makes this methodology singular and synthetically more efficient than some other related intramolecular cyclization processes, such as the Heck reaction,[6] since examples of capture of a transient σ-alkylpalladium in species where hydride β-elimination is possible are scarce.[7−11]

Scheme 1



In this paper, we present a full account of our results concerning the application of our methodology to the selective synthesis of several functionalized nitrogen-containing mono- and bicyclic systems.

Results and Discussion

Nature of the Substrate. Two types of starting aminodienes have been employed in this study (Figures 1 and 2).

Type I compounds (**1**−**6**) are potential precursors of pyrrolidine derivatives through a 5-exo-trig cyclization mode; by tethering any of the allylic branches of **1a** into a cyclic system (**2**−**6**), formation of a diversity of bicyclic [n + 5] cycloadducts can be envisaged.

On the other side, type II compounds (**7**−**12**) are potential precursors of piperidine derivatives via a 6-exo-trig cyclization mode and of [n + 6]bicyclic systems by analogy to the above series.

* To whom correspondence should be addressed. Tel.: 34-3-4006108. FAX: 34-3-2045904. E-mail: adcqob@cid.csic.es.
† C.I.D. (C.S.I.C.).
‡ Universitat de Barcelona.
⊗ Abstract published in *Advance ACS Abstracts,* August 1, 1996.

(1) Ho, T.-L. *Tandem Organic Reactions*; Wiley Interscience: New York, 1992.
(2) Bunce, R. A. *Tetrahedron* **1995**, *51*, 13103 and references therein.
(3) Grigg, R. *J. Heterocycl. Chem*. **1994**, *31*, 631.
(4) Vanderbaan, J. L.; Vanderheide, T. A. J.; Vanderlouw, J.; Klumpp, G. W. *Synlett* **1995**, 1.
(5) Sole, D.; Cancho, Y.; Llebaria, A.; Moreto, J. M.; Delgado, A. *J. Am. Chem. Soc.* **1994**, *116*, 12133.
(6) Heck, R. F. *Organic Reactions*; John Wiley & Sons: New York, 1982; Vol. 27, p 345.
(7) Trost, B. M. *Acc. Chem. Res.* **1990**, *23*, 34.
(8) Oppolzer, W.; Ruiz Montes, J. *Helv. Chim. Acta* **1993**, *76*, 1266.
(9) Balme, G.; Bouyssi, D. *Tetrahedron* **1994**, *50*, 403.
(10) Stadtmuller, H.; Tucker, C. E.; Vaupel, A.; Knochel, P. *Tetrahedron Lett.* **1993**, *34*, 7911.
(11) Oppolzer, W.; Schroder, F. *Tetrahedron Lett.* **1994**, *35*, 7939.

S0022-3263(96)00677-9 CCC: $12.00

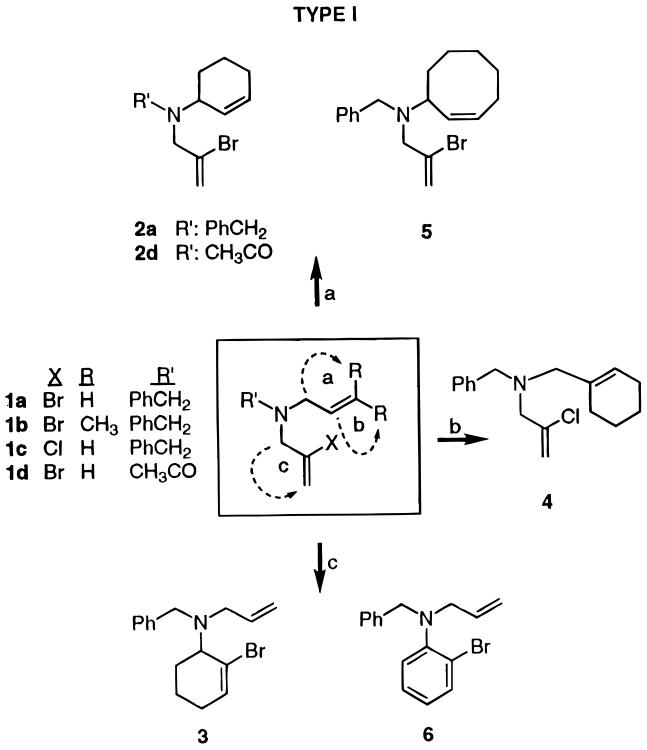


Figure 1.

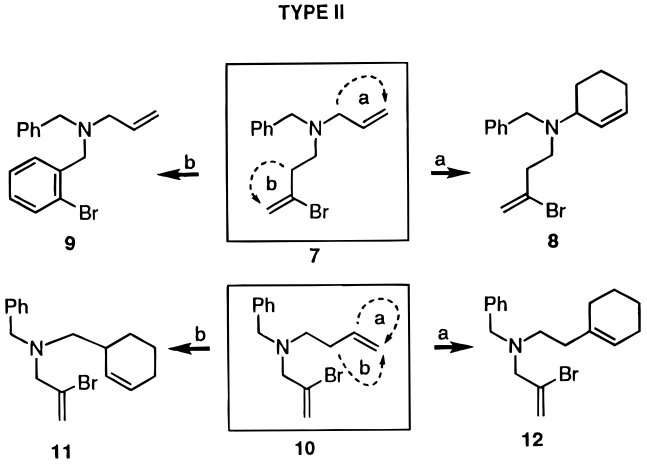


Figure 2.

Concerning the halide, vinyl bromides were generally used in this study as starting materials, although vinyl chlorides behaved similarly (see **1c** and **4**).[12]

Among the several structural factors involved in the final outcome of the process, both the operating cyclization mode (5-exo *vs* 6-exo) of vinylnickel intermediate **B** (see Scheme 1) and the ability of alkylnickel intermediate **C** to develop a stabilizing Ni−N interaction by coordination to the metal by the distal nitrogen atom seem crucial. Thus, Ni−H β-elimination can be hampered by geometrical constraints, and trapping of the intermediate **C** with an appropriate quencher reagent becomes the preferred terminating step. In this context, substrate **1b** was tested as a challenging model. Thus, the corresponding intermediate **C**, arising from **1b** after oxidative addition−insertion, could be effectively trapped, despite having seven hydrogen atoms available for β-elimination (Table 1, entries 7 and 8).

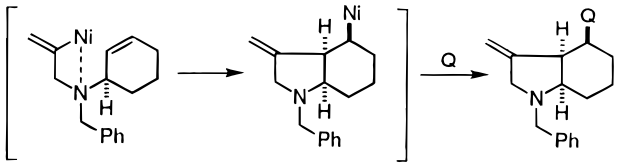
(12) Aryl chlorides did not react under standard conditions.

According to our hypothesis, substrates **1**−**5** represented the better scenario for the present methodology, since they might afford cycloadducts arising from a 5-exo cyclization mode, and the corresponding alkylnickel intermediates **C** would be stabilized through a five-membered Ni−N coordination, as depicted in Figure 3.[13] As expected, good to excellent yields of the corresponding cycloadducts were obtained from substrates **1**−**5**, as indicated in Table 1. Moreover, in the case of **2a**−**4**, the diastereoselectivity was complete and single cycloadducts were obtained in each case. On the other hand, the unavailability of the nitrogen lone pair for coordination as a result of its incorporation into an amide function (**1d** and **2d**, Scheme 2) or delocalization across an aromatic ring (**6**, Table 1, entries 24 and 25) dramatically alters the reaction course affording in all cases the corresponding β-elimination cycloadducts **16**,[14] **23**,[15] **21**,[16] and **22**.[17] (see Scheme 2 and Figure 4).

Starting from vinyl bromide **5**, an analogue of **2** with a larger ring as substituent, lower diastereoselectivity was observed under our standard cyclization−quenching conditions, and mixtures of *cis* and *trans* cycloadducts were obtained. Additionally, trapping of the corresponding alkylnickel intermediate **C** arising from **5** with TMSCN afforded mixtures of quenched and β-elimination cycloadducts (Table 1, entry 22). These results can be interpreted on conformational grounds. Thus, the more flexible cyclooctene moiety present in **5** makes the insertion of the vinylnickel intermediate **B-5** with the distal olefin compatible with a final *cis* or *trans* ring fusion. Moreover, the higher conformational freedom of the alkylnickel intermediate **C-5**-*cis* or **C-5**-*trans* might disturb coordination of the metal with the distal nitrogen atom and promote the β-elimination pathway. These problems could be efficiently solved by the use of a nitrogen bidentate ligand such as 2,2′-bipyridine (bpy). Thus, the use of 1:1 $Ni(COD)_2$/bpy complex, followed by quenching with TMSCN, afforded a single *cis*-fused [8 + 5] cycloadduct in 83% yield (Table 1, entry 23). Although the exact role played by bpy in our reaction system is

(13) Coordination in **C-6** is not operating as it is discussed later. For related Ni−heteroatom coordination, see: (a) Ni−N, Tamao, K.; Kobayashi, K.; Ito, Y. *Synlett* **1992**, 539. (b) Ni−P, Didiuk, M. T.; Morken, J. P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1995**, *117*, 7273. (c) Ni−S, Wong, K. T.; Yuan, T. M.; Wang, M. C.; Tung, H. H.; Luh, T. Y. *J. Am. Chem. Soc.* **1994**, *116*, 8920.

(14) Interestingly, in this case the diastereoselectivity was reversed, since a *trans*-fused cycloadduct **16** was obtained (determined by ^{1}H-NMR from the *N*-ethyl derivative arising from $LiAlH_4$ reduction of **16**, see Experimental Section). This change in trend might represent an indirect evidence of the role played by intramolecular Ni−N coordination in a diastereocontrolled insertion in the putative intermediate vinylnickel **B-2a**. For a related example of insertion directed by Ni−N intramolecular coordination, see ref 13a.

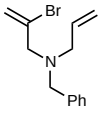
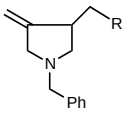
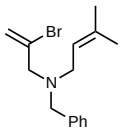
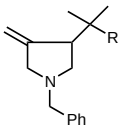
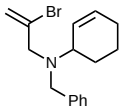
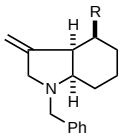
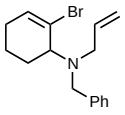
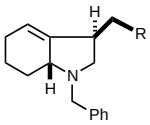
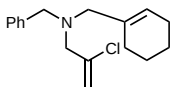
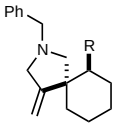
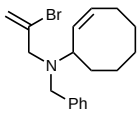
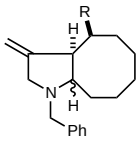
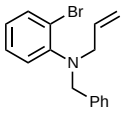
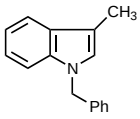


(15) Formation of **23** can be explained by a 5-exo cyclization followed by a cyclopropyl carbinyl rearrangement, Ni−H β-elimination−readdition, and quenching. For related examples, see: Owczarczyk, Z.; Lamaty, F.; Vawter, E. J.; Negishi, E. *J. Am. Chem. Soc.* **1992**, *114*, 10091. Trost, B. M.; Dumas, J. *Tetrahedron Lett.* **1993**, *34*, 19.

(16) Arising from double dond isomerization of the initially formed Heck-type cycloadduct (*N*-benzyl-3-methyleneindoline).

(17) For a related example of formation of indolines in a Ni-promoted oxidative addition−insertion process, see: Rodriguez, J. G.; Canoira, L. *J. Heterocycl. Chem.* **1985**, *22*, 883.

Table 1

entry	substrate	quencher	products[a]	R	yield, %
1		TMSCN		**a**, CN	99
2		CO/MeOH		**b**, $COOCH_3$	70
3		$NaBH_4$/MeOH		**c**, H	45
4		allyl bromide[b]		**d**, $CH_2CH{=}CH_2$	47
5		crotyl bromide[b]		**e**, $CH_2CH{=}CHCH_3$	53[c]
6	**1a**	CH_3COCl	**13a-f**	**f**, $COCH_3$	30
7		CO/MeOH		**g**, $COOCH_3$	61
8		TMSCN		**h**, CN	50
	1b		**13g,h**		
9		TMSCN		**a**, CN	99
10		TMSCN[d]		**a**, CN	57
11		CO/MeOH		**b**, $COOCH_3$	95
12		$NaBH_4$/MeOH		**c**, H	70
13	**2a**	Et_3SiH	**14a-e**	**c**, H	77
14		N_2O		**d**, OH	48[e]
15		O_2		**d**, OH	45[f]
16		$Bu_3SnCH{=}CH_2$		**e**, $CH{=}CH_2$	40[g]
17		CO/MeOH[h]		**b**, $COOCH_3$	85
18		TMSCN		**a**, CN	80
19		CO/MeOH		**b**, $COOCH_3$	57
20		$NaBH_4$/MeOH		**c**, H	75
	3		**17a-c**		
21		TMSCN		CN	84
	4		**18**		
22		TMSCN		CN	44[i,j]
23		TMSCN[d]		CN	83[k]
	5		**19**		
24		TMSCN			48[l,m]
25		TMSCN[d]			40
	6		**21**		

[a] Unambigous assignment carried out by NMR techniques. [b] Method C, see Experimental Section. [c] *E*-isomer. [d] $Ni(COD)_2$/bpy (1:1); Method B, see Experimental Section. [e] **15** (32%) was also obtained (see Figure 4). [f] **15** (45%) was also obtained. [g] **15** (28%) and **25** (10%) were also obtained (see Figure 4). [h] DMF as a solvent. [i] *Cis*/*trans* 9:1. [j] **20** (44%, *cis*/*trans* 9:1) was also obtained (see Figure 4). [k] *Cis* isomer only. [l] 6% recovered starting material. [m] **22** (13%) was also isolated (see Figure 4 and ref 17).

not completely understood, the ability of ligands to modulate the reactivity of organometallic complexes by altering their steric and/or electronic properties is well documented.[18] In the case of **5**, the effect of bpy was beneficial both to induce a total diastereoselectivity during the insertion step and to prevent Ni−H β-elimination. Unfortunately, β-elimination could not be avoided in the case of **6** (entry 25), which seems to indicate that the presence of a coordinating nitrogen lone pair is still required, even when bpy is used as a ligand. Acetamides **1d** and **2d** also failed to give the corresponding cyclization−quenching cycloadducts (Scheme 2). Thus, **1d** afforded a complex mixture from which only the self-coupling adduct **24** could be detected whereas no cyanide incorporation was observed from acetamide **2d**.

Type II substrates were designed as models to test the efficiency of a 6-exo cyclization mode leading to single or fused piperidine derivatives. Unfortunately, treatment of vinyl bromides **7**, **8**, **11**, and **12** under our standard cyclization−quenching conditions was unsuccessful in terms of formation of cycloadducts since only uncyclized vinyl cyanides and coupling adducts could be isolated in low to moderate yields (Table 2, entries 1, 3, 11, and 13).

Nevertheless, 6-exo mode cyclization−quenching from **10** was successful, since the corresponding cycloadducts were isolated in acceptable yields as mixtures of 1,2,5,6-tetrahydropyridines **32** and 3-methylenepiperidines **33**, whose formation can be explained through a common intermediate, **C-10** (Scheme 3). Whereas quenching of **C-10** with the terminating agents leads to the corresponding 3-methylenepiperidines **33a,b**, an alternative termination process triggered by the relatively high

(18) Togni, A.; Venanzi, L. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 497.

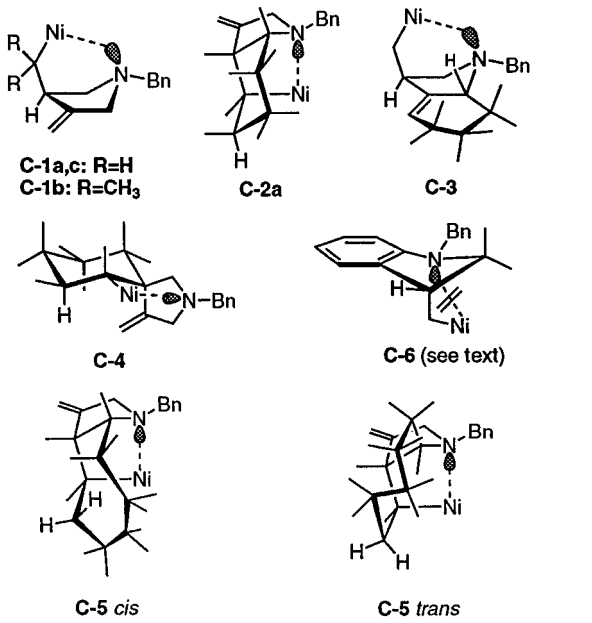


Figure 3.

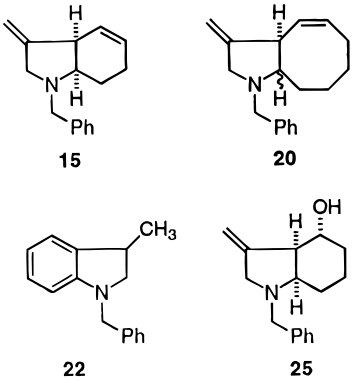
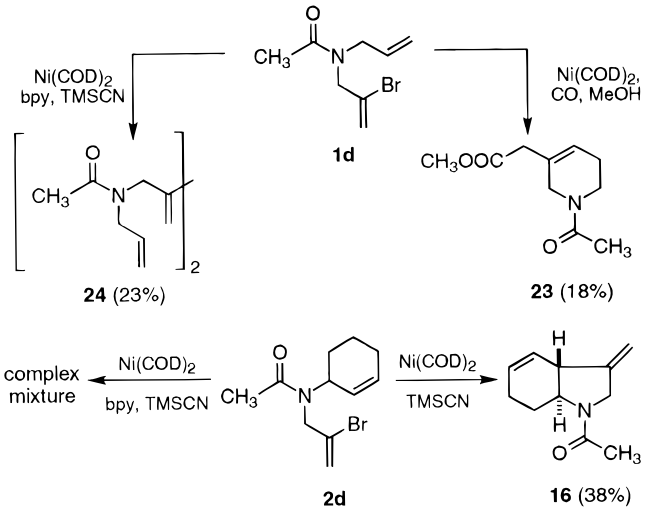


Figure 4.

Scheme 2



energy of the boatlike conformation required for intramolecular Ni−N stabilization in **C-10** can be considered. Thus, Ni−H β-elimination and readdition on the 4-methylene double bond to give a π-allylnickel intermediate **D-10**, followed by reaction with the terminating agent to afford cycloadducts **32a**−**c**, can now become a competitive process.[19]

Moreover, cyclization−quenching with TMSCN from aryl bromide **9** proved efficient although sluggish, since tetrahydroisoquinoline **30** was obtained in 47% yield, together with uncyclized aryl cyanide **31** (25%) and 22% of starting material by quenching after prolonged reaction times (20 min). These results are indicative of a slow oxidative addition−insertion process from **9**, in addition to the formation of a highly stabilized alkylnickel intermediate such as **C-9**, in which coordination of the metal with the distal nitrogen lone pair via a five-membered cyclic system could prevent Ni−H β-elimination (Figure 5).

The fact that no cycloadducts were ever isolated from **8**, **11**, and **12** is in agreement with failure of a 6-exo insertion of a vinylnickel intermediate onto a cyclohexene moiety. Steric requirements seem to become very important in this cyclization mode. Finally, the difference in behavior of vinyl bromide **7** in comparison to that of **10** would plausibly arise from the difference in stability and reactivity of both putative alkylnickel intermediates **C-7** and **C-10**. Thus, oxidative addition of **7** was extremely fast, and only untractable mixtures were obtained under standard conditions. However, initial formation of cycloadducts via a 6-exo mode cyclization could not be ruled out, since trace amounts of the desired piperidine **26**, together with the open-chain nitrile **27**, could be detected at short reaction times (see Table 2, entry 1). Taking into account that stabilization of intermediate **C-7** by coordination with the distal nitrogen lone pair would be possible only through a high-energy conformation in which the nickelalkyl moiety should be axial (see Figure 5), Ni−H β-elimination to a very reactive aminodiene can be envisaged as the alternative preferred process.[20]

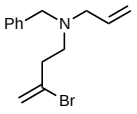
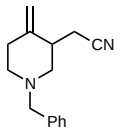
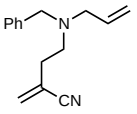
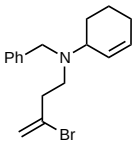
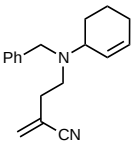
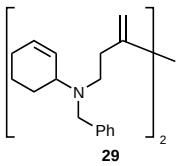
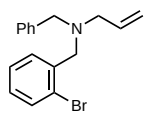
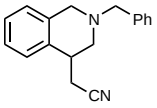
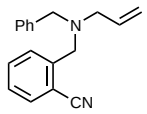
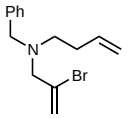
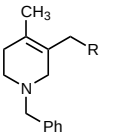
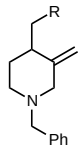
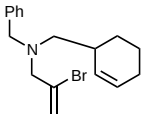
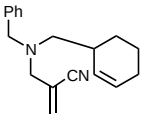
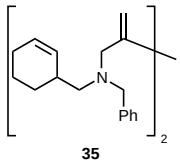
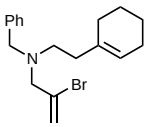
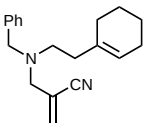
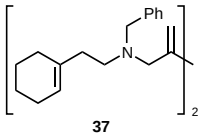
The use of bpy as a ligand in these series was somewhat puzzling. Thus, no improvement was observed from substrates that failed to cyclize under standard conditions (**8**, **11**, and **12**). Surprisingly, in the case of **9**, the presence of bpy was again favorable, presumably by promoting oxidative addition and further insertion of the vinylnickel intermediate, since isoquinoline **30** was now the only isolated compound in 68% yield under otherwise similar reaction conditions. Once again, the effect of bpy showed striking differences between **7** and **10**. Thus, whereas in the case of **10**, complex mixtures were obtained and no cyclization products were detected (entry 10), vinyl bromide **7** afforded the corresponding cycloadduct **26** as the only isolable product, although in modest yield (Table 2, entry 2). This partial success could well be due to a slower Ni−H β-elimination process in this case in comparison with the results obtained in the absence of bpy.

Effect of the Solvent. Preliminary experiments carried out in a low-coordinating solvent such as THF afforded only starting material, together with deposition of metallic Ni(0). This relatively high tendency of Ni(COD)$_2$ to decompose in the reaction mixture was not observed when a stronger coordinating solvent, such as CH_3CN or DMF, was used. In general, CH_3CN proved superior to DMF for this process. Typically, oxidative

(19) This process is well precedented in Heck reactions upon vinyl halides. See, for example: Harris, G. D., Jr.; Herr, R. J.; Weinreb, S. M. *J. Org. Chem.* **1992**, *57*, 2528. In our previous communication (see ref 5), compounds **32** were uncorrectly assigned.

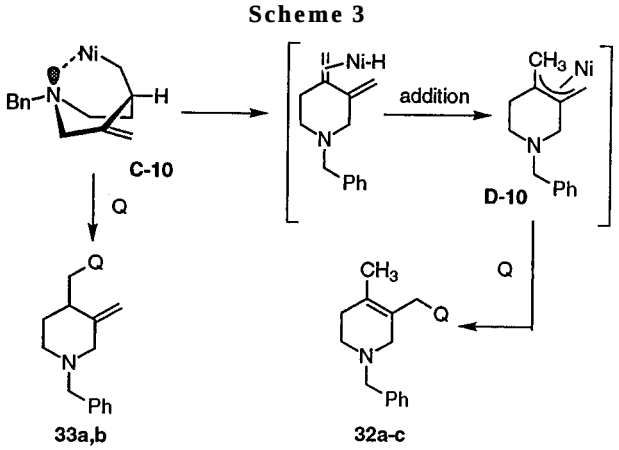
(20) Unlike the results observed from **10**, it seems that, in this case, NiH readdition upon the 3-methylene double bond to generate a π-allylnickel intermediate is slower than competitive collateral reactions leading to decomposition products.

Table 2

entry	substrate	complex	quencher	product[a]	yield, %	product[a]	yield, %
1	 **7**	$Ni(COD)_2$	TMSCN	 **26**	2[b]	 **27**	3[b]
2		$Ni(COD)_2$/bpy	TMSCN		30		
3	 **8**	$Ni(COD)_2$	TMSCN	 **28**	8	 **29**	15
4		$Ni(COD)_2$/bpy	TMSCN				60
5	 **9**	$Ni(COD)_2$	TMSCN	 **30**	47	 **31**	25[c]
6		$Ni(COD)_2$/bpy	TMSCN		68		
7	 **10**	$Ni(COD)_2$	TMSCN	 **32a-c**	**a**, R = CN, 60[d]	 **33a,b**	**a**, R = CN[d]
8		$Ni(COD)_2$	$NaBH_4$/MeOH		**b**, R = $COOCH_3$, 40		
9		$Ni(COD)_2$	CO/MeOH		**c**, R = H, 41[e]		**c**, R = H[e]
10		$Ni(COD)_2$/bpy	TMSCN		f		f
11	 **11**	$Ni(COD)_2$	TMSCN	 **34**	35	 **35**	5[g]
12		$Ni(COD)_2$/bpy	TMSCN				
13	 **12**	$Ni(COD)_2$	TMSCN	 **36**	48	 **37**	24
14		$Ni(COD)_2$/bpy	TMSCN		56		

[a] Unambigous assignment carried out by NMR techniques. [b] After quenching at short reaction times. [c] 22% of recovered starting material. [d] **32a**/**33a** 85:15 unseparable mixture. [e] **32c**/**33c** 75:25 unseparable mixture. [f] Complex mixture. [g] *N*-(2-Cyclohexenylmethyl-)benzylamine (43%) was also isolated.

Scheme 3



additions of starting halides by $Ni(COD)_2$ in CH_3CN took a few minutes and provided homogeneous reaction mixtures. On the contrary, the oxidative addition in DMF was slower, and, although cyclization−quenching cycloadducts could be obtained, yields were generally lower than in CH_3CN due to extensive coupling processes.[21] Similar results were obtained in noncoordinating apolar solvents such as benzene and toluene.

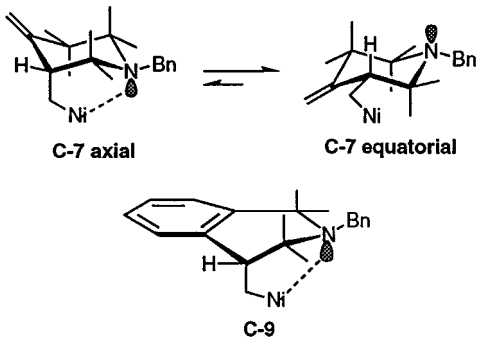


Figure 5.

Terminating Agents. Incorporation of functional groups in a stereoselective way by trapping of the alkylnickel intermediates **C** prior to *β*-elimination expands the versatility of this process from a synthetic standpoint. Among the different terminating reagents used in the present work, those leading to C−C, C−H,

(21) Cyclization−quenching of **2a** represents an exception to this trend (see Table 1, entry 17).

and C−O bond formation have proved successful.[22] Concerning C−C bond formation, CO/MeOH and TMSCN afforded the corresponding methoxycarbonyl and cyano derivatives, respectively, in good to excellent yields. Concerning the cyano group,[23] it is worth noting that quenching with neat TMSCN was superior to KCN/18-crown-6 as described by Grigg[24] for a related Pd-catalyzed intramolecular cyclization−quenching process.[25] Although these results can be explained by the higher solubility of TMSCN relative to the potassium salt in our reaction system, the operation of a trialkylsilyl cyanide−trialkylsilyl isocyanide tautomeric equilibrium to facilitate the halide−cyanide exchange in the coordination sphere of the metal should not be ruled out.[26,27]

Acetyl and vinyl groups can also be introduced, although in modest yields, by quenching with CH_3COCl and $Bu_3SnCH{=}CH_2$, respectively (Table 1, entries 6 and 16). Finally, irradiation with white light is required for the introduction of allyl and crotyl groups (Table 1, entries 4 and 5), an indication that radical intermediates would operate in this coupling process.[28−30] Concerning C−H bond formation, it was achieved in satisfactory yields with excess $NaBH_4$ in MeOH (Table 1, entries 3, 12, and 20) or, alternatively, with neat Et_3SiH (entry 13).

The efficiency of a terminating reagent seems to depend on its rate of coupling with the alkylnickel intermediate **C**. Despite internal stabilization with the distal nitrogen atom, alkylnickel species have a relatively short lifetime, and, if the termination process is slow, β-elimination cycloadducts are isolated. In addition, taking **2a** as a model substrate, we observed that, together with the β-elimination cycloadduct **15**, a small amount of amino alcohol **14d** was also obtained in cases where the terminating agent under examination failed to give any coupling product.[22] Formation of **14d** can be explained by oxidation of the intermediate alkylnickel **C-2a** by adventitious oxygen during the reaction or, more probably, by hydrolysis during the workup process.[31] In an attempt to exploit this observation, we assumed that, by using an oxidant as a terminating reagent, alcohol **14d** could be obtained as a major product. However, the use of O_2 or N_2O[32] afforded only 1:1 mixtures of the expected amino alcohol **14d** and the β-elimination cycloadduct **15**. Further attempts to improve this ratio by using white light irradiation or other oxidizing quenchers, such as H_2O_2 or *t*-BuOOH, as well as H_2O or 50% aqueous NaOH as protic quenchers, were unsuccessful, since β-elimination was still the predominant process. Finally, in all the cases studied in this work, the process showed complete diastereoselectivity, since the functional group arising from the terminating reagent maintains the stereochemistry predicted for the alkylnickel intermediates **C** after a *syn*-olefin insertion.[33]

Conclusions

A diastereoselective and mild cyclization−capture process based on the treatment of nitrogen-tethered halodienes with stoichiometric $Ni(COD)_2$ is described. By choice of a proper terminating reagent, a variety of functional groups can be introduced in the last step of the process. The success of this methodology relies on the presence of a distal amino group able to stabilize, by coordination, a transient alkylnickel intermediate, thus preventing Ni−H β-elimination. In all the substrates examined in this work, cyclization via a 5-exo mode has been shown to be more favorable than that by a 6-exo one. Finally, the results obtained in the presence of bpy as a ligand seem to indicate in some cases a favorable effect on the diastereoselectivity of the process, as in **5**; the supression of the Ni−H β-elimination step, as in **5** and, presumably, also in **7**; and an acceleration of the oxidative addition−insertion step, as in **9**.

Experimental Section

For general experimental procedures, see ref 34. All reactions were conducted under argon atmosphere with rigorous exclusion of oxygen using standard Schlenk techniques. $Ni(COD)_2$ was prepared according to a previously described procedure.[35]

Synthesis of Cycloadducts. Method A. To a solution of $Ni(COD)_2$ (1.5 mmol) in dry CH_3CN (5 mL), at room temperature under argon, was added a solution of the vinyl bromide (1 mmol) and Et_3N (3 mmol) in dry acetonitrile. The reaction mixture, which turned from yellow to red, was stirred at room temperature. When all the starting material was consumed (2.5−30 min, checked by TLC), the quencher (1.5−3.0 mmol) was added via syringe, and the mixture was stirred at room temperature for additional time (0.5−3 h). After filtration through Celite and careful washings with CH_2Cl_2, the mixture was partitioned between CH_2Cl_2 and saturated Na_2CO_3. Drying of the organic phases, followed by filtration and evaporation, afforded the desired cycloadduct.

Method B. This method was the same as method A, except that the starting vinyl halide was added to a previously formed complex of $Ni(COD)_2$ (1.5 mmol) and 2,2′-bipyridine (bpy, 1.8 mmol) in dry CH_3CN (5 mL).

Method C. This method was the same as method A, except that, simultaneously with the addition of the quencher, the reaction mixture was irradiated with a 500 W sunlight lamp

(22) The following quenchers were tried with no success using **2a** as a model substrate under cyclization conditions A (see Experimental Section): $CO/BuNH_2$, $TMSN_3$, I_2, TMSI, methyl acrylate, Ph_4BNa, KOAc, $TMSCH{=}CH_2/Bu_4NF$, DMSO, Ni_2O_3, and benzoyl peroxide. Almost invariably, mixtures of the β-elimination cycloadduct **15** and alcohol **14d** were obtained.

(23) For related methods concerning C−CN formation by means of organometallic reagents, see: Torii, S.; Okumoto, H.; Ozaki, H.; Nakayashu, S.; Tadokoro, T.; Kotani, T. *Tetrahedron Lett.* **1992**, *33*, 3499. Oppolzer, W.; Schroder, F. *Tetrahedron Lett.* **1994**, *35*, 7939. Sakakibara, Y.; Enami, H.; Ogawa, H.; Fujimoto, S.; Kato, H.; Kunitake, K.; Sasaki, K.; Sakai, M. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 3137. Sakakibara, Y.; Ido, Y.; Sasaki, K.; Sakai, M.; Uchino, N. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2776. Piers, E.; Fleming, F. F. *Can. J. Chem.* **1993**, *71*, 1867. Ellis, G. P.; Romney-Alexander, T. M. *Chem. Rev.* **1987**, *87*, 779. See also ref 24.

(24) Grigg, R.; Santhakumar, V.; Sridharan, V. *Tetrahedron Lett.* **1993**, *34*, 3163.

(25) Treatment of **2a** with KCN/18-crown-6 in the presence of $Pd(OAc)_2$ under Grigg conditions (ref 24) led to recovery of the starting material.

(26) Seckar, J. A.; Thayer, J. S. *Inorg. Chem.* **1976**, *15*, 501.

(27) (a) Berk, S. C.; Grossman, R. B.; Buchwald, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 4912. (b) Berk, S. C.; Grossman, R. B.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 8593.

(28) Hegedus, L. S.; Thompson, D. H. P. *J. Am. Chem. Soc.* **1985**, *107*, 5663.

(29) Castaño, A. M.; Echavarren, A. M. *Organometallics* **1994**, *13*, 2262.

(30) Johnson, J. R.; Tully, P. S.; Mackenzie, P. B.; Sabat, M. *J. Am. Chem. Soc.* **1991**, *113*, 6172.

(31) Horino, H.; Arai, M.; Inoue, N. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 1683.

(32) Matsunaga, P. T.; Hillhouse, G. L. *J. Am. Chem. Soc.* **1993**, *115*, 2075.

(33) In some experiments using $Bu_3SnCH{=}CH_2$ (Table 1, entry 18), KCN, or KOAc as quencher, a small percentage of amino alcohol **25**, epimeric on the hydroxyl group, was isolated (see Figure 4). This finding would be consistent with an alternative mechanism, probably through the intermediacy of radical species.

(34) Llebaria, A.; Delgado, A.; Camps, F.; Moretó, J. M. *Organometallics* **1993**, *12*, 2825.

(35) Colquhoun, H. M.; Holton, J.; Thompson, D. J.; Twigg, M. V. *New Pathways for Organic Synthesis*; Plenum: New York, 1984; p 389.

while the reaction temperature was kept below 25 °C by means of a circulating cool bath.

***N*-Benzyl-3-(cyanomethyl)-4-methylenepyrrolidine (13a)**. Following method A, starting from 220 mg (0.83 mmol) of **1a**, 460 mg (1.66 mmol) of $Ni(COD)_2$, 0.35 mL (2.48 mmol) of Et_3N in 10 mL of acetonitrile, and 0.25 mL (2 mmol) of TMSCN, 175 mg (99%) of **13a** was obtained after flash chromatography on hexanes/EtOAc 70:30.

^{1}H-NMR (200 MHz): δ 2.54 (2H, d, J = 6.6 Hz), 2.48−2.62 (1H, m), 2.85−3.05 (2H, m), 3.23 (2H, br s), 3.64 (2H, s), 4.98−5.08 (2H, m), 7.20−7.40 (5H, m). ^{13}C-NMR: δ 21.6, 39.1, 58.7, 58.9, 59.8, 107.1, 118.6, 127.0, 128.2, 128.5, 138.3, 148.9. IR: ν 1662, 2246. Anal. Calcd for $C_{14}H_{16}N_2$: C, 79.21; H, 7.60; N, 13.20. Found: C, 79.21; H, 7.62; N, 13.27.

***N*-Benzyl-3-[(methoxycarbonyl)methyl]-4-methylenepyrrolidine (13b)**. Following method A, starting from 261 mg (1.0 mmol) of **1a**, and quenching with CO/MeOH, **13b** was obtained in 70% yield after flash chromatography on hexanes /EtOAc 90:10.

^{1}H-NMR (200 MHz): δ 2.35 (1H, dd, J = 8.8, 6.2 Hz), 2.50 and 2.59 (2H, AB sys, dd, J_{AB} = 15.7 Hz, J_{AX} = 9 Hz , J_{BX} = 5.0 Hz), 2.92−3.19 (3H, m), 3.26 (1H, dm, J = 14.0 Hz), 3.61 (2H, s), 3.67 (3H, s), 4.82−4.88 (1H, m), 4.90−4.95 (1H, m), 7.20−7.40 (5H, m). ^{13}C-NMR (50.3 MHz): δ 38.8, 39.5, 51.9, 59.5, 60.5, 60.6, 105.6, 127.3, 128.6, 129.0, 139.0, 151.5, 173.3. IR: ν 3026, 2786, 1735, 881. Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.45; H, 7.85; N, 5.71.

***N*-Benzyl-4-methyl-3-methylenepyrrolidine (13c)**. Following method A, starting from 250 mg (0.94 mmol) of **1a**, quenching with $NaBH_4$/MeOH afforded **13c** in 45% yield after flash chromatography on hexanes/*t*-BuOMe 90:10.

^{1}H-NMR (200 MHz): δ 1.10 (3H, d, J = 6.6 Hz), 2.06 (1H, dd, J = 8.4, 8.5 Hz), 2.56−2.82 (1H, m), 2.92−3.08 (2H, m), 3.43 (1H, br d, J = 13.6 Hz), 3.55 and 3.64 (2H, AB sys, J = 12.8 Hz), 4.78−4.84 (1H, m), 4.84−4.90 (1H, m), 7.20−7.40 (m, 5 H). ^{13}C-NMR (50.3 MHz): δ 18.1, 38.0, 59.9, 61.1, 62.7, 104.2, 127.3, 128.6, 129.2, 139.3, 154.4. IR: ν 2960, 2783, 1662, 1452, 877. Anal. Calcd for $C_{13}H_{17}N$: C, 83.37; H, 9.15; N, 7.48. Found: C, 83.11; H, 9.22; N, 7.20.

***N*-Benzyl-4-(3-butenyl)-3-methylenepyrrolidine (13d)**. Following method C, starting from 288 mg (1.1 mmol) of **1a,** pyrrolidine **13d** (47%) was obtained after flash chromatography on hexanes/EtOAc 80:20.

^{1}H-NMR (300 MHz): δ 1.30−1.45 (1H, m), 1.58−1.75 (1H, m), 1.9−2.1 (1H, m), 2.07 (1H, t, J = 8.4 Hz), 2.55−2.65 (1H, m), 2.96−3.08 (2H, m), 3.37 (1H, dm, J = 13.2 Hz), 3.47 and 3.55 (2H, AB sys, J = 12.8 Hz), 4.83 (1H, q, J = 2.0 Hz), 4.90 (1H, q, J = 2.0 Hz), 4.82−4.88 (2H, m), 5.62−5.80 (1H, m), 7.2−7.4 (5 H, m). ^{13}C-NMR (50.3 MHz): δ 31.9, 32.9, 42.2, 59.6, 60.3, 60.6, 104.3, 114.6, 126.9, 128,2, 128.7, 138.5, 138.8, 152.6. IR: ν 3077, 3027, 2925, 1662, 1638, 1451, 908, 879. Anal. Calcd for $C_{16}H_{21}N$: C, 84.53; H, 9.31; N, 6.16. Found: C, 84.32; H, 9.33; N, 6.35.

(*E*)-*N*-Benzyl-4-(3-pentenyl)-3-methylenepyrrolidine (13e). Following method C, starting from 269 mg (1.0 mmol) of **1a**, **13e** (53%) was obtained after flash chromatography on hexanes/EtOAc 90:10.

^{1}H-NMR (200 MHz): δ 1.3−1.5 (1H, m), 1.6−1.8 (1H, m), 1.65 (3H, br s), 1.9−2.1 (1H, m), 2.15 (1H, dd, J = 8.4, 8.6 Hz), 2.55−2.75 (1H, m), 2.96−3.08 (2H, m), 3.37 (1H, dm, J = 13.6 Hz), 3.57 and 3.68 (2H, AB sys, J = 12.8 Hz), 4.83 (1H, q, J = 2.2 Hz), 4.90 (1H, q, J = 2.0 Hz), 5.4−5.5 (2H, m), 7.2−7.4 (5H, m). ^{13}C-NMR (50.3 MHz): δ 17.9, 30.8, 33.6, 42.3, 59.6, 60.4, 60.7, 104.1, 125.1, 126.9, 128,2, 128.7, 138.9, 152.8. IR: ν 3025, 2929, 1682, 1662, 1451. Anal. Calcd for $C_{17}H_{23}N$: C, 84.59; H, 9.60; N, 5.80. Found: C, 84.62; H, 9.71; N, 5.75.

***N*-Benzyl-4-(2-oxopropyl)-3-methylenepyrrolidine (13f)**. Following method A, starting from 305 mg (1.1 mmol) of **1a**, ketone **13f** was obtained in 30% yield after flash chromatography on hexanes /EtOAc 70:30 to 20:80.

^{1}H-NMR (200 MHz): δ 2.13 (3H, s), 2.23 (1H, m), 2.57 (1H, dd, J = 17.4, 8.6 Hz), 2.72 (1H, dd, J = 17.4, 4.6 Hz), 3.07 (4H, m), 3.59 (2H, s), 4,79 (1H, m), 4.89 (1H, m), 7.2−7.4 (5H, m). ^{13}C-NMR (50.3 MHz): δ 30.1, 37.9, 48.2, 59.1, 60.2, 60.3, 104.9, 127.1, 128.3, 128.8, 138.7, 151.8, 207.9. IR: ν 1714, 1664, 882. Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.72; H, 8.16; N, 5.91.

***N*-Benzyl-3-[1-(methoxycarbonyl)-1-methylethyl]-4-methylenepyrrolidine (13g)**. Following method A, starting from 294 mg (1.0 mmol) of **1b**, and quenching with CO/MeOH, **13g** was obtained in 61% yield after flash chromatography on hexanes/EtOAc 90:10.

^{1}H-NMR (300 MHz): δ 1.17 (3H, s), 1.20 (3H, s), 2.41 (1H, dd, J = 9.3, 7.0 Hz), 2.86−2.96 (1H, m), 3.02 (1H, dm), 3.10−3.24 (2H, m), 3.58 (2H, s), 3.66 (3H, s), 4.71−4.74 (1H, m), 4.94−4.96 (1H, m), 7.2−7.4 (5 H, m). ^{13}C-NMR (75.4 MHz): δ 21.5, 23.8, 44.8, 49.0, 51.7, 56.7, 60.5, 60.7, 107.1, 126.9, 128.2, 128.6, 138.8, 148.7, 177.9. IR: ν 1731, 1454. Anal. Calcd for $C_{17}H_{23}NO_2$: C, 73.48; H, 8.34; N, 5.04. Found: C, 73.82; H, 8.46; N, 5.02.

***N*-Benzyl-3-(1-cyano-1-methylethyl)-4-methylenepyrrolidine (13h)**. Following method A, starting from 294 mg (1.0 mmol) of **1b**, **13h** was obtained in 50% yield after flash chromatography on hexanes/EtOAc 80:20.

^{1}H-NMR (200 MHz): δ 1.36 (3H, s), 1.42 (3H, s), 2.59 (1H, dd, J = 9.4, 5.9 Hz), 2.72−2.86 (1H, m), 2.98 (1H, dd, J = 9.2, 7.4 Hz), 3.20 (2H, sa), 3.62 (2H, sa), 5.12−5.18 (1H, m), 5.19−5.24 (1H, m), 7.2−7.4 (5H, m). ^{13}C-NMR (50 MHz): δ 24.1, 25.3, 49.5, 56.9, 60.2, 60.3, 109.7, 124.9, 127.1, 128.3, 128.5, 138.5, 146.7. IR: ν 2236, 1660. Anal. Calcd for $C_{16}H_{20}N_2$: C, 78.48; H, 8.23; N, 11.44. Found: C, 78.66; H, 8.35; N, 11.41.

(3a*RS*,4*SR*,7a*RS*)-*N*-Benzyl-3-methyleneperhydroindole-4-carbonitrile (14a). Following method A, starting from 245 mg (0.8 mmol) of vinyl bromide **2a**, 400 mg (1.45 mmol) of $Ni(COD)_2$, 0.33 mL (2.4 mmol) of Et_3N, in 10 mL of acetonitrile, and 0.5 mL (4 mmol) of TMSCN, 200 mg (99%) of **14a** was obtained after flash chromatography on hexanes/EtOAc 75:25.

^{1}H-NMR (200 MHz): δ 1.15−2.05 (6H, m), 2.54−2.70 (2H, m), 2.74 (1H, dt, J = 14.6, 2.6 Hz), 2.82−2.94 (1H, m), 3.08 and 4.02 (2H, AB sys, J = 13.6 Hz), 3.68 (1H, d, J = 14.6 Hz), 4.89 (1H, dd, J = 3.6, 1.9 Hz), 4.96 (1H, dd, J = 3.6, 2.5 Hz), 7.10−7.40 (5H, m). ^{13}C-NMR (50.3 MHz): δ 16.8, 24.3, 27.7, 31.2, 45.1, 56.9, 58.2, 61.2, 106.7, 122.0, 126.6, 128.0, 128.2, 139.2, 148.2. IR: ν 2235. Anal. Calcd for $C_{17}H_{20}N_2$: C, 80.91; H, 7.99; N, 11.10. Found: C, 80.80; H, 7.98; N, 10.94.

Methyl (3a*RS*,4*SR*,7a*RS*)-*N*-Benzyl-3-methyleneperhydroindole-4-carboxylate (14b). Following method A, starting from 738 mg (2.41 mmol) of vinyl bromide **2a**, 1.25 g (4.55 mmol) of $Ni(COD)_2$, 1 mL (7.23 mmol) of Et_3N in 10 mL of acetonitrile, 0.3 mL (7.19 mmol) of MeOH, and excess CO, 660 mg (95%) of **14b** was obtained after flash chromatography on hexanes/EtOAc 80:20.

^{1}H-NMR (300 MHz): δ 1.02−1.95 (6H, m), 2.63 (1H, dt, J = 12.6, 3.7 Hz), 3.09 (1H, dt, J = 10.4, 5.4 Hz), 3.24 (1H, ddd, J = 14.4, 4.6, 2.2 Hz), 3.44 (1H, br s), 3.52 (1H, ddd, J = 14.4, 4.0, 2.4 Hz), 3.70 (3H, s), 3.66 and 3.78 (2H, AB sys, J = 13.4 Hz), 4.61 (1H, dd, J = 5.2, 2.6 Hz) 4.89 (1H, dd, J = 4.6, 2.2 Hz), 7.09−7.41 (5H, m). ^{13}C-NMR (75.4 MHz): δ 21.7, 22.0, 23.0, 42.2, 44.0, 51.5, 55.8, 56.5, 62.1, 105.3, 126.8, 128.2, 128.4, 139.4, 146.8, 175.0. IR: ν 1731. Anal. Calcd for $C_{18}H_{23}NO_2$: C, 75.76; H, 8.12; N, 4.91. Found: C, 75.68; H, 8.10; N, 4.84.

(3a*RS*,7a*RS*)-*N*-Benzyl-3-methyleneperhydroindole (14c). Following method A, starting from 310 mg (1.01 mmol) of vinyl bromide **2a**, 340 mg (1.24 mmol) of $Ni(COD)_2$, 0.42 mL (3 mmol) of Et_3N in 10 mL of acetonitrile, and 151 mg (4 mmol) of $NaBH_4$ in 3 mL (7.19 mmol) of MeOH, 156 mg (70%) of **14c** was obtained after flash chromatography on hexanes/EtOAc 95:5. Alternatively, using neat Et_3SiH as a quencher (0.4 mL, 2.5 mmol), **14c** was obtained in 77% yield.

^{1}H-NMR (200 MHz): δ 1.10−1.80 (8H, m), 2.47 (1H, bb), 2.65 (1H, dd, J = 9.2, 4.8 Hz), 2.88 (1H, dt, J = 14.4, 2.2 Hz), 3.16 and 3.88 (2H, AB sys, J = 13.4 Hz), 3.40 (1H, dd, J = 14.4, 1.7 Hz), 4.62−4.72 (2H, m), 7.10−7.40 (5H, m). ^{13}C-NMR (50.3 MHz): δ 21.4, 24.2, 24.6, 28.6, 44.1, 57.0, 57.8, 62.4, 102.9, 126.7, 128.2, 128.5, 140.0, 152.2. IR: ν 1452, 1664. Anal. Calcd for $C_{16}H_{21}N$: C, 84.53; H, 9.31; N, 6.16. Found: C, 84.51; H, 9.31; N, 5.87.

(3a*RS*,4*SR*,7a*RS*)-*N*-Benzyl-4-hydroxy-3-methyleneperhydroindole (14d) and (3a*RS*,7a*RS*)-*N*-Benzyl-3-methylene-2,3,3a,6,7,7a-hexahydro-1*H*-indole (15). Following

method A, starting from 290 mg (0.95 mmol) of vinyl bromide **2a**, 430 mg (1.56 mmol) of $Ni(COD)_2$, 0.40 mL (2.84 mmol) of Et_3N in 10 mL of acetonitrile, and excess O_2, 104 mg (45%) of **14d** and 96 mg (45%) of **15** were obtained after flash chromatography on hexanes/EtOAc 75:25 to 80:20. Alternatively, using excess N_2O as a quencher, a mixture of **15** (32%) and **14d** (48%) was obtained.

14d. ^{1}H-NMR (200 MHz): δ 1.20−2.10 (7H, m), 2.26 (1H, dd, J = 9.0, 4.8 Hz), 2.75−2.87 (2H, m), 3.02 and 4.05 (2H, AB sys, J = 13.2 Hz), 3.61 (1H, d, J = 14.4 Hz), 3.68 (1H, ddd, J = 11.1, 9, 4 Hz), 4.82 (1H, br s), 4.97 (1H, br s), 7.20−7.40 (5H, m). ^{13}C-NMR (50.3 MHz): δ 19.6, 25.2, 32.9, 53.8, 57.4, 58.3, 64.0, 70.0, 105.0, 126.8, 128.2, 128.4, 139.6, 149.7. IR: ν 3400, 2931, 1662. Anal. Calcd for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.80; H, 8.67; N, 5.63.

15. ^{1}H-NMR (200 MHz): δ 1.55−2.45 (4H, m), 2.80−3.02 (2H, m), 3.20 (1H, br s), 3.27 and 4.10 (2H, AB sys, J =13.1 Hz), 3.54 (1H, dd, J =13.8, 1.6 Hz), 4.86−4.98 (2H, m), 5.60 (1H, d, J = 10.2 Hz), 5.70−5.84 (1H, m), 7.20−7.45 (5H, m). ^{13}C-NMR (50.3 MHz): δ 20.2, 22.2, 43.5, 57.4, 58.3, 61.6, 105.2, 126.0, 126.7, 128.3, 128.3, 128.7, 139.3, 150.9. IR: ν 1662, 1726. Anal. Calcd for $C_{16}H_{19}N$: C, 85.29; H, 8.99; N, 6.22. Found: C, 85.16; H, 8.99; N, 6.11.

(3a*RS*,4*RS*,7a*RS*)-*N*-Benzyl-3-methylene-4-vinylperhydroindole (14e). Following method A, starting from 320 mg (1.05 mmol) of vinyl bromide **2a**, 380 mg (1.38 mmol) of $Ni(COD)_2$, 0.44 mL (3.15 mmol) of Et_3N in 10 mL of acetonitrile and 0.34 mL (1.16 mmol) of $Bu_3SnCH{=}CH_2$ as a quencher, 96 mg (40%) of **14e**, 75 mg (28%) of **15**, and 24 mg (10%) of alcohol **25** were obtained after flash chromatography with hexanes/EtOAc 95:5 to 80:20.

^{1}H-NMR (200 MHz): δ 1.10−1.90 (6H, m), 2.47 (1H, br s), 2.86−3.02 (2H, m), 3.16 and 3.40 (2H, AB sys, J = 15.6 Hz), 3.50 and 3.85 (2H, AB sys, J = 13.3 Hz), 4.80−5.10 (4H, m), 6.24 (1H, m), 7.10−7.45 (5H, m).^{13}C-NMR (50.3 MHz): δ 20.7, 23.2, 26.8, 41.8, 47.1, 56.7, 58.0, 62.6, 105.5, 113.0, 126.6, 128.1, 128.4, 139.8, 142.4, 149.0. IR: ν 1637, 1662, 1695. Anal. Calcd for $C_{18}H_{23}N$: C, 85.32; H, 9.15; N, 5.53. Found: C, 85.27; H, 9.20; N, 5.52.

(3a*RS*,4*RS*,7a*RS*)-*N*-Benzyl-4-hydroxy-3-methyleneperhydroindole (25). ^{1}H-NMR (200 MHz): δ 1.30−2.10 (6H, m), 2.52 (1H, t, J = 4.4 Hz), 2.68−2.80 (2H, m), 2.98 and 4.12 (2H, AB sys, J = 12.8 Hz), 3.56 (1H, d, J = 14.2 Hz), 3.85 (1H, br s), 4.91 (1H, s), 4.97 (1H, s), 7.20−7.40 (5H, m). ^{13}C-NMR (50.3 MHz): δ 21.4, 24.4, 32.4, 48.9, 57.5, 59.3, 63.5, 70.2, 105.3, 127.2, 128.5, 128.6, 138.3, 148.1. IR: ν 1664, 3355. Anal. Calcd for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.89; H, 8.73; N, 5.78.

(3a*RS*,7a*SR*)-*N*-Acetyl-3-methylene-2,3,3a,6,7,7a-hexahydro-1*H*-indole (16). Following method A, starting from 333 mg (1.3 mmol) of vinyl bromide **7**, 650 mg (2.34 mmol) of $Ni(COD)_2$, 0.54 mL (3.9 mmol) of Et_3N, and 0.4 mL (3.254 mmol) of TMSCN, 86 mg (38%) of **16** was obtained after flash chromatography (EtOAc).

^{1}H-NMR: δ 1.50−1.90 (1H, m), 2.00 (1.5H, s, CH_3 rotamer), 2.09 (1.5H, s, CH_3 rotamer), 2.10−2.60 (3H, m), 2.70−3.02 (1H, m), 3.82−4.48 (3H, m), 4.91 (1H, bs), 5.06 (1H, br s), 5.46−5.72 (2H, m). ^{13}C-NMR (50.3 MHz): δ 21.4 and 22.1, 23.1 and 23.4, 25.7 and 26.7, 38.9 and 40.0, 48.9 and 50.9, 53.1 and 55.3, 105.7 and 105.8, 122.6 and 123.9, 124.5 and 124.8, 145.5 and 146.8, 168.5 and 168.8. IR: ν 1643, 1643.

Reduction of the acetamide group with excess $LiAlH_4$ in dry Et_2O (5 mL) gave quantitatively the *N*-ethyl derivative.

(3a*RS*,7a*SR*)-*N*-Ethyl-3,3-methylene-2,3,3a,6,7,7a-hexahydro-1*H*-indole. ^{1}H-NMR (200 MHz): δ 1.09 (3H, t, J = 7.2 Hz), 1.90−2.40 (5H, m), 2.56−2.70 (1H, m), 2.71−2.91 (2H, m), 3.05 and 3.56 (2H, AB sys, J = 14 Hz), 4.80−4.90 (2H, m), 5.60−5.80 (2H, m). ^{13}C-NMR (50.3 MHz): δ 13.3, 24.3, 26.9, 40.7, 47.3, 56.9, 60.5, 103.5, 125.0, 126.1, 151.8.

(3*RS*,7a*RS*)-*N*-Benzyl-3-(cyanomethyl)-2,3,5,6,7,7a-hexahydro-1*H*-indole (17a). Following method A, starting from 305 mg (1 mmol) of vinyl bromide **3**, 450 mg (1.6 mmol) of $Ni(COD)_2$, 0.42 mL (3 mmol) of Et_3N in 10 mL of acetonitrile, and 0.31 mL (2.5 mmol) of TMSCN as a quencher, 204 mg (80%) of **17a** was obtained after flash chromatography on CH_2Cl_2/MeOH 99:1.

^{1}H-NMR (500 MHz): δ 1.08−1.32 (1H, m), 1.38−1.52 (1H, m), 1.76−1.84 (1H, m),1.84 (1H, t, J = 9.2 Hz), 2.00−2.22 (3H, m), 2.33 (2H, d, J = 6.4 Hz), 2.68 (1H, br m), 2.80 (1H, m), 3.21 (1H, dd, J = 9.2, 7.8 Hz), 3.23 and 4.08 (2H, AB sys, J = 12.6 Hz), 5.67 (1H, br s), 7.20−7.40 (5H, m). ^{13}C-NMR (50.3 MHz): δ 19.9, 21.9, 24.9, 27.6, 36.1, 58.0, 58.3, 63.8, 118.5, 121.3, 127.0, 128.1, 128.9, 138.2, 141.3. IR: ν 2246. Anal. Calcd for $C_{17}H_{20}N_2$: C, 80.91; H, 7.99; N, 11.10. Found: C, 80.70; H, 7.94; N, 10.89.

Methyl (3*RS*,7a*RS*)-(*N*-benzyl-2,3,5,6,7,7a-hexahydro-1*H*-indol-3-yl)acetate (17b). Following method A, starting from 275 mg (0.9 mmol) of vinyl bromide **3**, 300 mg (4.55 mmol) of $Ni(COD)_2$, 0.38 mL (2.7 mmol) of Et_3N in 10 mL of acetonitrile, 0.1 mL (2.7 mmol) of MeOH, and excess CO, 146 mg (57%) of **28** was obtained after flash chromatography on hexanes/EtOAc 80:20.

^{1}H-NMR (300 MHz): δ 1.05−1.30 (1H, m), 1.31−1.60 (1H, m), 1.80 (1H, t, J = 9.0 Hz), 1.76−1.94 (1H, m), 1.96−2.18 (3H, m), 2.32 and 2.49 (2H, AB sys, dd, J_{AB} = 15.6, J_{AX} = 8.8 Hz, J_{BX} = 6 Hz), 2.60−2.76 (1H, m), 2.90−3.10 (1H, m), 3.20 and 4.05 (2H, AB sys, J = 12.8 Hz), 3.23 (1H, t, J = 9.4 Hz), 3.64 (3H, s), 5.47 (1H, br s), 7.20−7.40 (5H, m). ^{13}C-NMR (75.4 MHz): δ 20.2, 25.0, 27.8, 36.4, 39.4, 51.4, 58.6, 59.1, 63.9, 119.4, 126.9, 128.1,129.0,138.7, 143.2, 172.8. IR: ν 1739. Anal. Calcd for $C_{18}H_{23}NO_2$: C, 75.76; H, 8.12; N, 4.91. Found: C, 75.78; H, 8.17; N, 4.98.

(3*RS*,7a*RS*)-*N*-Benzyl-3-methyl-2,3,5,6,7,7a-hexahydro-1*H*-indole (17c). Following method A, starting from 314 mg (1.03 mmol) of vinyl bromide **3**, 450 mg (1.6 mmol) of $Ni(COD)_2$, 0.43 mL (3.2 mmol) of Et_3N in 10 mL of acetonitrile, and 156 mg (4.12 mmol) of $NaBH_4$ in 4 mL of MeOH, 175 mg (75%) of **17c** was obtained after flash chromatography with hexanes/EtOAc 90:10.

^{1}H-NMR (300 MHz): δ 1.03 (3H, d, J = 6.8 Hz), 1.06−1.28 (1H, m), 1.34−1.58 (1H, m), 1.68 (1H, t, J = 8.8 Hz), 1.76−1.94 (1H, m), 1.98−2.16 (3H, m), 2.50−2.74 (2H, m), 3.09 (1H, dd, J = 9.0, 7.5 Hz), 3.17 and 4.05 (2H, AB sys, J = 12.8 Hz), 5.42 (1H, br s), 7.20−7.40 (5H, m). ^{13}C-NMR (75.4 MHz): δ 19.3, 20.4, 25.0, 27.8, 34.8, 58.9, 61.2, 64.2, 117.6, 126.8, 128.0, 129.1, 138.9, 146.3. IR: ν 1452, 1494. Anal. Calcd for $C_{16}H_{21}N$: C, 84.53; H, 9.31; N, 6.16. Found: C, 84.47; H, 9.31; N, 6.19.

(5*RS*,6*RS*)-*N*-Benzyl-6-cyano-4-methylene-2-azaspiro-[4.5]decane (18). Starting from 220 mg (0.80 mmol) of vinyl chloride **4**, 246 mg (0.89 mmol) of $Ni(COD)_2$, and 0.15 mL (1.1 mmol) of TMSCN, following method A, 179 mg (0.67 mmol, 83%) of **18** was obtained.

^{1}H-NMR (300 MHz): δ 1.13−1.29 (1H, m), 1.46 (1H, br d, J = 12.3 Hz), 1.60−1.77 (4H, m), 1.86 (1H, dd, J = 13.5, 3.6 Hz), 1.90−1.99 (1H, m), 2.20 and 2.96 (2H, AB sys, d, J_{AB} = 9.2 Hz), 2.98 (1H, AB sys, dt, J_{AB} = 13.8 Hz, J_t = 2.3 Hz), 3.11 (1H, br s), 3.55 (1H, AB sys, br d, J_{AB} = 13.8 Hz), 3.59 and 3.62 (2H, AB sys, J_{AB} = 13.2 Hz), 5.07 (1H, t, J = 2.3 Hz), 5.21 (1H, t, J = 2.3 Hz), 7.24−7.36 (5H, m). ^{13}C-NMR (50.3 MHz): δ 21.5, 22.7, 26.6, 31.8, 35.8, 46.55, 58.79, 59.56, 62.52, 107.6, 121.5, 127.0, 128.3, 138.7, 152.1. IR: ν 2233, 1660. Anal. Calcd for $C_{18}H_{22}N_2$: C, 81.16; H, 8.32; N, 10.52. Found: C, 81.11; H, 8.35; N, 10.48.

(1*RS*,2*SR*,8*RS*)-*N*-Benzyl-11-methylene-9-azabicyclo-[6.3.0]undecan-2-carbonitrile (19-*cis*), (1*RS*,2*SR*,8*SR*)-*N*-Benzyl-11-methylene-9-azabicyclo[6.3.0]undecan-2-carbonitrile (19-*trans*), and *N*-Benzyl-11-methylene-9-azabicyclo[6.3.0]undec-2-ene (20). Following method A, starting from 312 mg (0.93 mmol) of vinyl bromide **5**, 350 mg (1.3 mmol) of $Ni(COD)_2$, 0.39 mL (2.79 mmol) of Et_3N in 10 mL of acetonitrile, and 0.3 mL (2.33 mmol) of TMSCN as a quencher, 105 mg (44%) of a 9:1 *cis*/*trans* mixture of diastereomers **20**, and 114 mg (44%) of a 9:1 mixture of **19**-*cis* and **19**-*trans* were obtained after flash chromatography on hexanes/EtOAc 90:10 to 75:25. Alternatively, following method B, from 351 mg (1.05 mmol) of **5**, 318 mg (1.16 mmol) of $Ni(COD)_2$, 199 mg (1.27 mmol) of bpy, and 0.40 mL (2.9 mmol) of TMSCN, **19**-*cis* was obtained as a single cycloadduct in 83% yield after flash chromatography on hexanes/EtOAc 75:25.

19-*cis*. ^{1}H-NMR (C_6D_6, 300 MHz): δ 1.0−1.1 (1H, m), 1.12−1.42 (7H, m), 1.42−1.58 (1H, m), 1.64−1.76 (1H, m), 2.25−

2.30 (1H, HC_1, m), 2.37−2.46 (1H, HC_2, m), 2.72 (1H, HC_8, dt, J = 4.7, 8.2 Hz), 2.91 (1H, AB sys, J_{AB} = 12.9 Hz), 3.01 (1H, AB sys, dq, J_{AB} = 12.9 Hz, J_q = 2.4 Hz), 3.34 (1H, AB sys, d, J_{AB} = 12.9 Hz), 3.87 (1H, AB sys, J_{AB} = 12.9 Hz), 4.55 (1H, m), 4.79 (1H, m), 7.0−7.3 (5H, m). ^{13}C-NMR (50.3 MHz): δ 22.9, 23.0, 27.5, 27.7, 33.8, 37.4, 47.8, 58.7, 58.8, 66.2, 106.9, 121.3, 127.0, 128.3, 128.8, 139.1, 149.1. IR: ν 2235, 1666. Anal. Calcd for $C_{19}H_{24}N_2$: C, 81.38; H, 8.63; N, 9.99. Found: C, 81.40; H, 8.73; N, 9.94.

19-*trans*. ^{1}H-NMR (200 MHz): δ 1.20−2.20 (10H, m), 2.55 (1H, br s), 2.84−3.08 (2H, m), 2.90 and 3.35 (2H, AB sys, J = 14 Hz, 10-H), 3.28 and 4.53 (2H, AB sys, J = 12.9 Hz), 4.80 (1H, br s), 4.86 (1H, br s), 7.20−7.40 (5H, m). ^{13}C-NMR (50.3 MHz): δ 24.8, 25.0, 25.2, 26.2, 36.2, 36.7, 46.0, 58.5, 60.0, 71.2, 105.2, 122.6, 127.1, 128.3, 128.8, 138.7, 150.7. Anal. Calcd for $C_{19}H_{24}N_2$: C, 81.38; H, 8.63; N, 9.99. Found: C, 81.48; H, 8.60; N, 9.87.

20 (major isomer). ^{13}C-NMR (50.3 MHz): δ 23.8, 24.5, 32.1, 34.4, 47.2, 58.5, 59.1, 70.7, 104.2, 126.9, 128.2, 128.9, 129.5, 130.4, 139.2, 152.7.

20 (minor isomer). ^{13}C-NMR (50.3 MHz): δ 24.3, 25.1, 27.4, 28.6, 51.1, 58.2, 59.0, 71.2, 103.0, 126.9, 128.2, 128.9, 129.2, 130.0, 138.8, 150.4.

***N*-Benzyl-3-methylindole (21) and *N*-Benzyl-3-methyl-2,3-dihydro-1*H*-indole (22)**. Starting from 302 mg (1.0 mmol) of bromoaniline **6**, 325 mg (1.2 mmol) of $Ni(COD)_2$, and 0.15 mL (1.1 mmol) of TMSCN, following method A, 18 mg (0.06 mmol, 6%) of starting bromide **6**, 106 mg (0.48 mmol, 48%) of **21**,[36] and 29 mg (0.13 mmol, 13%) of **22**[36] were obtained.

21. ^{1}H-NMR (200 MHz): δ 2.35 (3H, s), 5.28 (2H, s), 6.91 (1H, s), 7.08−7.36 (8H, m), 7.6 (1H, d, J = 6 Hz). ^{13}C-NMR (50.3 MHz): δ 9.6, 49.8, 109.4, 110.9, 118.8, 119.0, 121.6, 125.8, 126.8, 127.5, 128.7, 128.9, 136.7, 137.9. IR: ν 2917, 1465, 1328.

22. ^{1}H NMR (200 MHz): δ 1.30 (3H, d, J = 6.8 Hz), 2.84 (1H, t, J = 8.4 Hz), 3.20−3.40 (1H, m), 3.51 (1H, t, J = 8.4 Hz), 4.10 and 4.38 (2H, AB sys, J = 15 Hz), 6.50 (1H, d, J = 6.9 Hz), 6.70 (1H, t, J = 7.5 Hz), 7.02−7.12 (2H, m), 7.22−7.42 (5H, m). ^{13}C-NMR (50.3 MHz): δ 18.6, 35.2, 53.4, 61.6, 106.9, 117.7, 123.2, 127.1, 127.4, 127.9, 128.9, 135.0, 138.5, 152.1. IR: ν 2958, 1604, 1486, 1251.

***N*-Acetyl-3-[(methoxycarbonyl)methyl]-1,2,5,6-tetrahydropyridine (23)**. Following method A, from 290 mg (1.03 mmol) of amide **1d** and CO/MeOH as a quencher, **23** (52 mg, 0.18 mmol, 18%) was obtained after flash chromatography on elution with hexanes/EtOAc 60:40.

^{1}H-NMR (200 MHz): δ 2.08 (3H, s), 2.04−2.26 (2H, m), 2.99 (2H, br s), 3.46 (1H, t, J = 8.4 Hz), 3.61 (1H, t, J = 8.4 Hz), 3.65 and 3.67 (3H, s, amide rotamers), 3.92 (1H, br s), 4.01 (1H, br s), 5.6 and 5.8 (1H, br s, amide rotamers). ^{13}C-NMR (50.3 MHz) (two amide rotamers): δ 21.8 and 22.3, 25.0 and 25.9, 38.1 and 40.4, 40.7 and 43.1, 44.5 and 48.2, 52.0 and 52.3, 123.8 and 126.0, 128.1 and 129.6, 169.5 and 169.7, 171.7 and 171.8. IR: ν 2945, 1650, 1419.

***N,N′*-Diacetyl-*N,N′*-diallyl-3,4-dimethylene-1,6-hexanediamine (24).** Following method B, cyclization and quenching with TMSCN from 296 mg (1.36 mmol) of **1d** afforded 86 mg (0.31 mmol, 23%) of **24** after flash chromatography on elution with 50% hexanes/EtOAc.

^{1}H-NMR (300 MHz):[37] δ 2.03−2.04 (3H, d), 2.11−2.12 (3H, d), 3.81−3.83 (2H, m), 3.92−3.97 (2H, m), 4.02−4.05 (2H, m), 4.21−4.23 (2H, m), 4.95−5.01 (2H, m), 5.05−5.24 (4H, m), 5.28−5.32 (2H, m), 5.66−5.84 (2H, m). ^{13}C-NMR (75.4 MHz): [37] 21.0, 21.33, 21.39, 47.32, 47.39, 48.20, 48.30, 49.63, 49.64, 111.3, 112.3, 113.4, 114.2, 116.6, 116.8, 117.2, 117.4, 132.2, 132.3, 132.9, 133.0, 139.8, 140.7, 170.7, 171.1. IR: ν 3076, 2978, 1650, 1471, 1434, 1415, 1249. MS: m/z 276, 233, 134, 122, 94, 70.

***N*-Benzyl-4-methylene-3-(cyanomethyl)piperidine (26) and *N*-Allyl-*N*-benzyl-3-cyano-3-butenylamine (27)**. According to method B, cyclization−quenching from 182 mg (0.65 mmol) of amine **7,** 198 mg (0.72 mmol) of $Ni(COD)_2$, 135 mg (0.86 mmol) of bpy, and 0.16 mL (1.2 mmol) of TMSCN afforded 45 mg (0.20 mmol, 30%) of **26** after chromatography with hexanes/*t*-BuOMe 4:1. Employing method A, **26** (2%) and open-chain nitrile **27** (3%) were the only isolated products.

26. ^{1}H NMR (300 MHz): δ 2.1−2.7 (9H, m), 3.43 and 3.46 (2H, AB sys, J_{AB} = 13.2 Hz), 4.71 (1H, s), 4.77 (1H, s), 7.2−7.4 (5H, m). ^{13}C-NMR (75.4 MHz): δ 19.7, 32.4, 54.5, 58.1, 62.3, 109.7, 118.7, 127.1, 128.2, 128.7, 138.1, 145.3. IR: ν 3027, 2938, 2244, 1650, 1494. Anal. Calcd for $C_{15}H_{18}N_2$: C, 79.61; H, 8.02; N, 12.38. Found: C, 79.71; H, 8.06; N, 12.25.

27. ^{1}H-NMR (200 MHz): δ 2.34−2.44 (2H, m), 2.63−2.75 (2H, m), 3.11 (2H, br d, J = 6.6 Hz), 3.60 (2H), 5.11−5.25 (2H, m), 5.67 (1H, br s), 5.76−6.00 (1H, m), 5.85 (1H, br s), 7.20−7.40 (5H, m). ^{13}C-NMR (50.3 MHz): δ 32.6, 51.3, 56.8, 58.1, 117.7, 121.6, 127.0, 128.1, 128.8, 131.2, 135.3, 139.0. IR: ν 2223, 1642, 1621. HRMS: m/z [M^+] calcd for $C_{15}H_{18}N_2$ 226.1471, obsd 226.1466.

***N*-Benzyl-*N*-(2-cyclohexenyl)-3-cyano-3-butenylamine (28) and *N,N′*-Dibenzyl-*N,N′*-bis(2-cyclohexenyl)-3,4-dimethylenehexane-1,6-diamine (29)**. Following method A, starting from 357 mg (1.1 mmol) of vinyl bromide **8**, 342 mg (1.35 mmol) of $Ni(COD)_2$, 0.40 mL (3.1 mmol) of Et_3N in 18 mL of acetonitrile, and 0.25 mL (1.8 mmol) of TMSCN, 23 mg (0.09 mmol, 8%) of **28** and 29 mg (0.06 mmol, 15%) of **29** were obtained after flash chromatography with hexanes/EtOAc 95:5. Employing method B, diene **29** (60%) was the only isolated product.

28. ^{1}H-NMR (200 MHz): δ 1.40−1.65 (2H, m), 1.60−1.90 (2H, m), 1.90−2.05 (2H, m); 2.38 (2H, t, J = 6.3 Hz), 2.6−2.8 (2H, m), 3.34 (1H, br s), 3.57 and 3.76 (2H, AB sys, J_{AB} = 14.3 Hz), 5.50−5.90 (4H, m), 7.20−7.35 (5H, m). ^{13}C-NMR (75.4 MHz): δ 21.8, 23.8, 25.2, 34.5, 48.8, 54.8, 56.8, 121.7, 126.7, 128.0, 128.1, 128.4, 130.2, 130.4, 131.1, 140.6. IR: ν 2223, 1453.

29. ^{1}H-NMR (300 MHz): δ 1.22−1.55 (4H, m), 1.76−1.90 (4H, m), 1.96 (4H, m), 2.24−2.40 (4H, m), 2.48−2.64 (4H, m), 3.36 (2H, br s), 3.52−3.77 (4H, AB sys, δ_A = 3.55, δ_B = 3.72, J_{AB} = 14.1 Hz), 4.83 (2H, s), 4.96 (2H, s), 5.67 (2H, br d, J = 10.2 Hz), 5.76−5.84 (2H, m), 7.20−7.40 (10H, m). ^{13}C-NMR (75.4 MHz): δ 21.0, 23.9, 25.3, 34.3, 50.4, 54.7, 56.6, 112.6, 126.5, 128.1, 128.4, 129.7, 130.9, 141.4, 145.6. IR: ν 1593, 1492, 1451. Anal. Calcd for $C_{34}H_{44}N_2$: C, 84.95; H, 9.23; N, 5.83. Found: C, 84.80; H, 9.48; N, 5.73

***N*-Benzyl-4-(cyanomethyl)-1,2,3,4-tetrahydroisoquinoline (30) and 2-[(*N*-Allyl-*N*-benzylamino)methyl]benzonitrile (31)**. According to method A, 194 mg (0.61 mmol) of aryl bromide **9**, 186 mg (0.67 mmol) of $Ni(COD)_2$, and 0.25 mL (1.8 mmol) of TMSCN gave 75 mg (0.29 mmol, 47%) of **30**, 40 mg (0.15 mmol, 25%) of **31**, and 41 mg (0.13 mmol, 22%) of recovered starting material **9** after column chromatography with hexanes/*t*-BuOMe 6:1. When **9** was subjected to method B conditions, **30** was the only isolated product in 68% yield.

30. ^{1}H-NMR (300 MHz): δ 2.68 (1H, AB sys, dd, J_{AB} = 12.0 Hz, J_d = 3.3 Hz), 2.70 (1H, AB sys, dd, J_{AB} = 16.8 Hz, J_d= 6.5 Hz), 2.87 (1H, AB sys, d, J_{AB} = 16.8 Hz, J_d = 9.0 Hz), 2.99 (1H, AB sys, dm, J_{AB} = 12.0 Hz), 3.16 (1H, m), 3.55 and 3.85 (2H, AB sys, J_{AB} = 15.1 Hz), 3.69 and 3.73 (2H, AB sys, J = 13.2 Hz), 7.00−7.03 (1H, m), 7.15−7.40 (8H, m). ^{13}C-NMR (75.4 MHz): δ 24.2 36.3, 53.9, 56.0, 62.6, 119.1, 126.6, 126.7, 127.0, 127.3, 128.4, 128.4, 128.9, 134.9, 135.0, 137.9. IR: ν 3060, 2921, 2245, 1652, 1494. Anal. Calcd for $C_{18}H_{18}N_2$: C, 82.41; H, 6.91; N, 10.68. Found: C, 82.44; H, 6.87; N, 10.65.

31. ^{1}H-NMR (200 MHz): δ 3.10 (2H, br d, J = 6.3 Hz), 3.62 (2H, s), 3.80 (2H, s), 5.16−5.28 (2H, m), 5.88−6.02 (1H, m), 7.22−7.42 (6H, m), 7.50−7.72 (3H, m).^{13}C-NMR (75.4 MHz): δ 55.8, 56.6, 58.0, 112.4, 117.9, 117.9, 127.0, 127.3, 128.2, 128.7, 129.6, 132.6, 132.8, 135.2, 139.0, 144.0. IR: ν 3062, 3028, 2223, 1641, 1598. Anal. Calcd for $C_{18}H_{18}N_2$: C, 82.41; H, 6.91; N, 10.68. Found: C, 82.38; H, 7.16; N, 10.28.

***N*-Benzyl-3-(cyanomethyl)-4-methyl-1,2,5,6-tetrahydropyridine (32a) and *N*-Benzyl-4-(cyanomethyl)-3-methylenepiperidine (33a).** Following method A, starting from 395 mg (1.4 mmol) of **10**, a mixture of **32a** and **33a** (85:15 from ^{1}HNMR, 60% combined yield) was obtained after quenching

(36) Kiguchi, T.; Kuninobu, N.; Takahashi, Y.; Yoshida, Y.; Naito, T.; Ninomiya, I. *Synthesis* **1989**, 778.

(37) Mixture of rotameric species due to the amide groups.

with TMSCN and flash chromatography on hexanes/EtOAc 70:30. Repeated attempts to separate these compounds were not successful.

Selected data for **32a** (signals taken from the mixture of **32a** and **33a**). ^{1}H-NMR (200 MHz): δ 1.61 (3H, s), 2.03 (2H, sa), 2.46 (2H, t, J = 5,9 Hz), 2.92 (4H, sa), 3.51 (2H, br s), 7.01−7.4 (5H, m). ^{13}C-NMR (50.3 MHz): δ 18.3, 19.1, 32.0, 49.3, 55.5, 62.3, 117.2, 117.5, 127.0, 128.1, 129.0, 131.1, 138.0. IR (mixture of **32a** and **33b**): ν 3020, 2912, 2245 , 1450, 1452.

Selected data for **33a** (signals taken from the mixture of **32a** and **33a**). ^{1}H NMR (200 MHz): δ 4.83 (s, 1 H, CH_2=C), 4.60 (s, 1 H, CH_2=C). ^{13}C NMR (50.3 MHz): δ 20.2, 31.4, 37.5, 52.0, 59.7, 109.0, 117.2, 144.1

***N*-Benzyl-4-methyl-3-[(methoxycarbonyl)methyl]-1,2,5,6-tetrahydropyridine (32b)**. Following method A, starting from 423 mg (1.5 mmol) of **10**, using CO/MeOH as a quencher, **32b** (40%)was isolated after flash chromatography on hexanes/EtOAc 75:25.

^{1}H-NMR (200 MHz): δ 1.67 (3 H, s), 2.10 (2 H, sa), 2.52 (2 H, t, J = 5.8 Hz), 2.9−3.1 (4 H, m), 3.55 (2 H, s), 3.65 (3H, s), 7.1−7.40 (5 H, m).^{13}C-NMR (50.3 MHz): δ 18.6, 32.1, 36.8, 49.7, 51.7, 56.8, 62.6, 121.5, 127.0, 128.1, 129.2, 129.5, 138.1, 172.0. IR: ν 2948, 2812, 1737, 1434. HRMS: m/z [M$^+$] calcd for $C_{18}H_{21}NO_2$ 259.1572, obsd 259.1563.

***N*-Benzyl-3,4-dimethyl-1,2,5,6-tetrahydropyridine (32c) and *N*-Benzyl-4-methyl-3-methylenepiperidine (33c).** Following method A, starting from 427 mg of **10**, a mixture of **32c** and **33c** (41%) was obtained after quenching with $NaBH_4$ and flash chromatography with hexanes/EtOAc 90:10. Repeated attempts to separate these compounds were not successful.

Selected data for **32c** (signals taken from the mixture of **32c** and **33c**). ^{1}H-NMR (200 MHz): δ 1.49 (3H, s, CH_3), 1.56 (3H, s), 1.99 (2H, br s), 2.44 (2H, t, J = 5.6 Hz), 2.77 (s, 2 H), 3.49 (2 H, s), 7.1−7.4 (5 H, m).^{13}C-NMR (50.3 MHz): δ 16.6, 18.3, 32.1, 50.3, 58.2, 63.0, 124.0, 124.5, 127.0, 128.2, 129.2 , 138.5.

Selected data for **33c** (signals taken from the mixture of **32c** and **33c**). ^{1}H-NMR (200 MHz): δ 1.02 (3H, d, J = 6.4 Hz), 4.65 (1H, s), 4.75 (1H, s). ^{13}C-NMR (50.3 MHz): δ 17.7, 34.6, 35.6, 53.4, 60.8, 107.0, 149.0. IR (mixture of **32c** and **33c**): ν 2910, 2796, 1652, 1454.

***N*-Benzyl-*N*-[(2-cyclohexenyl)methyl]-2-cyano-2-propenylamine (34) and *N*,*N*′-Dibenzyl-*N*,*N*′-bis[(2-cyclohexenyl)methyl]-2,3-dimethylenebutane-1,4-diamine (35)**. Following method A, starting from 326 mg (1.0 mmol) of vinyl bromide **11**, 423 mg (1.5 mmol) of $Ni(COD)_2$, 0.43 mL (3.2 mmol) of Et_3N in 20 mL of acetonitrile, and 0.25 mL (1.8 mmol) of TMSCN, 91 mg (0.35 mmol, 35%) of **34** was obtained after flash chromatography with hexanes/EtOAc 90:10. Employing method B for the cyclization, diene **35** (5%) and *N*-(2-cyclohexenylmethyl)benzylamine (43%) were the only isolated products.

34. ^{1}H NMR (200 MHz): δ 1.20−2.10 (6H, m), 2.36 (3H, br s), 3.12 and 3.25 (2H, AB sys, J = 14.5 Hz), 3.55 and 3.70 (2H, AB sys, J = 13.8 Hz), 5.52−5.56 (2H, m), 5.89 (1H, s), 5.96 (1H, s), 7.20−7.50 (5H, m). ^{13}C-NMR (50.3 MHz): δ 21.0, 25.4, 27.2, 33.3, 57.0, 58.2, 59.1, 118.3, 122.1, 127.1, 128.1, 128.3, 128.7, 129.5, 131.7, 138.5. IR: ν 2223.

35. ^{1}H NMR (200 MHz): δ 1.02−2.00 (12H, m), 2.00−2.40 (6H, m), 3.07 and 3.20 (4H, AB sys, J = 13.7 Hz), 3.30−3.60 (4H, m), 5.19 (2H, s), 5.24 (2H, s), 5.50−5.70 (4H, m), 7.10−7.45 (10H, m).^{13}C NMR (50.3 MHz): δ 21.0, 25.5, 27.4, 33.1, 58.8, 58.9, 59.5, 115.2, 126.6, 127.3, 127.9, 129.0, 130.4, 139.8, 146.0. IR: ν 1450, 1494. Anal. Calcd for $C_{34}H_{44}N_2$: C, 84.95; H, 9.23; N, 5.83. Found: C, 84.94; H, 9.33; N, 5.85.

***N*-Benzyl-*N*-[2-(1-cyclohexenyl)ethyl]-2-cyano-2-propenylamine (36) and *N*,*N*′-dibenzyl-*N*,*N*′-bis[2-(1-cyclohexenyl)ethyl]-2,3-dimethylenebutane-1,4-diamine (37)**. Following method A, starting from 370 mg (1.1 mmol) of vinyl bromide **12**, 331 mg (1.3 mmol) of $Ni(COD)_2$, 0.40 mL (3.1 mmol) of Et_3N in 22 mL of acetonitrile, and 0.25 mL (1.8 mmol) of TMSCN, 125 mg (0.53 mmol, 48%) of **36** and 68 mg (0.14 mmol, 24%) of **37** were obtained after flash chromatography with hexanes/EtOAc 90:10. Employing method B for the cyclization, **36** (56%) was isolated.

36. ^{1}H-NMR (300 MHz): δ 1.44−1.65 (4H, m), 1.85 (2H, br m), 1.96 (2H, br m), 2.13 (2H, br t, J = 7.2 Hz), 2.57 (2H, dd, J = 6.0, 7.8 Hz), 3.20 (2H, s), 3.62 (2H, s), 5.40 (1H, br m), 5.92 (1H, br q, J = 0.9 Hz), 5.96 (1H, br q, J = 0.9 Hz), 7.20−7.40 (5H, m). ^{13}C-NMR (75.4 MHz): δ 22.4, 22.9, 25.2, 29.0, 35.4, 51.8, 56.4, 57.7, 118.4, 122.1, 122.5, 127.1, 128.3, 128.7, 131.6, 135.5, 138.8. IR: ν 2927, 2223, 1623, 1600. Anal. Calcd for $C_{19}H_{24}N_2$: C, 81.38; H, 8.63; N, 9.99. Found: C, 81.60; H, 8.51; N, 10.15.

37. ^{1}H-NMR (300 MHz): δ 1.44−1.65 (4H, m), 1.80 (2H, br m), 1.94 (2H, br m), 2.06 (2H, br t, J = 7.0 Hz), 2.57 (2H, dd, J = 5.4, 8.1 Hz), 3.19 (2H, s), 3.48 (2H, s), 5.18 (1H, s), 5.29 (1H, d, J = 2.1 Hz), 5.33 (1H, br s), 7.20−7.40 (5H, m). ^{13}C-NMR (75.4 MHz): δ 22.4, 23.0, 25.3, 28.4, 34.9, 52.1, 58.0, 58.3, 114.94, 121.7, 126.6, 128.0, 128.9, 136.3, 140.1, 146.0. IR: ν 2927, 2223, 1664, 1595. Anal. Calcd for $C_{36}H_{48}N_2$: C, 84.99; H, 9.51; N, 5.50. Found: C, 85.11; H, 9.71; N, 5.71

Acknowledgment. Financial support from CICYT and Comissionat per a Universitats i Recerca, Generalitat de Catalunya (Projects QFN 95-4718, GRQ 93-8016, and GRQ 94-1035), is gratefully acknowledged. Y.C. also thanks CIRIT (Generalitat de Catalunya) for a predoctoral fellowship.

Supporting Information Available: Experimental procedures, spectroscopic data for starting compounds **1**−**12**, and stereochemical assignment for **17c**, **18**, and **19** (17 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO960677Y