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Pyridines and pyridine derivatives from vinyl allenes and imines

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ABSTRACT

The Lewis acid mediated reaction of acyclic vinyl allenes and imines, yielding tetrahydropyridines has been carried out. Only one cycloadduct was observed in each case, and thus, the reaction progressed in all cases with total regio-, face- and *endo*/*exo* selectivities. The cycloadducts were transformed into polysubstituted pyridines, including bipyridines, by catalytic transfer hydrogenation using cyclohexene as hydrogen donor in good yield. The reaction was extended to the aromatization of the bicyclic cycloadducts prepared in previous works from the reaction of semicyclic vinyl allenes and imines, yielding tetrahydropyridines.

1. Introduction

Pyridine derivatives are important compounds due to their properties. Thus, the pyridine moiety forms part of numerous natural and synthetic biologically active compounds.[1] Many of them have found pharmaceutical uses, making the pyridine moiety one of the most studied heterocyclic systems.[2]

The allene functional group has been used in many different reactions, especially in the last years, in which the number of processes involving allenes has grown extraordinarily.[3] The presence of an sp carbon, together with the fact that allenes, due to the presence of a chiral axis, can be prepared in enantiomerically pure form by simple procedures, has made the use of allenes common in many synthetic designs.[4] Vinyl allenes have been used in different reactions, most notably in Diels–Alder cycloadditions,[5] in which the substituents on the non-conjugated double bond, which are orthogonal to the plane of the diene, can exert selectivity on the approach of the dienophile to the dienic part of the molecule.[6]

In previous works, we have found that vinyl allenes can act as dienes in hetero Diels–Alder reactions with both, aldehydes[7] and imines[8] acting as heterodienophiles, in the presence of a Lewis acid. The structural requirements for the reaction imply that the allene must be at least tri-substituted with alkyl or aryl groups. It was found that, when semicyclic vinyl allenes were used, aldehydes gave a mixture of *endo* and *exo* cycloadducts, whereas with imines, only the *endo* isomer was obtained in each case, although in some reactions, products coming from an ene reaction were also obtained.[8] The regio and facial selectivity of the process was complete.

When acyclic vinyl allenes were used with aldehydes as heterodienophiles,[9] again a mixture of cycloadducts was obtained with the *endo* adducts being the major compound isolated. With benzaldehyde as heterodienophile, rearranged products were also obtained under forced reaction conditions.

We also tried the intramolecular version of the reaction, finding that both, aldehydes[10] and imines,[11] reacted to give the expected cycloadducts.

DFT calculations indicated that the cycloaddition reaction with aldehydes is a concerted asynchronous process in both, the intermolecular[7] and the intramolecular[10] processes.

In a previous work of our group, about the intramolecular hetero Diels–Alder reaction of vinyl allenes and *N*-benzyl imines,[11] we tried to deprotect the benzyl group on the cycloadducts by catalytic transfer hydrogenation, using cyclohexene as the hydrogen source and 10% Pd on carbon as the catalyst, following literature reports.[12] However, our attempts resulted in the unexpected aromatization of the nitrogen-containing ring, resulting in the synthesis of an octahydroacridine, a pyridine derivative.

As a continuation of that work, we decided to check whether that was a general result, which would allow us to prepare a variety of pyridine derivatives from the cycloadducts obtained in the hetero Diels–Alder reaction of vinyl allenes and imines.

2. Results and discussion

The preparation of pyridine derivatives (tetrahydroquinolines) could be achieved using the bicyclic cycloadducts prepared in our

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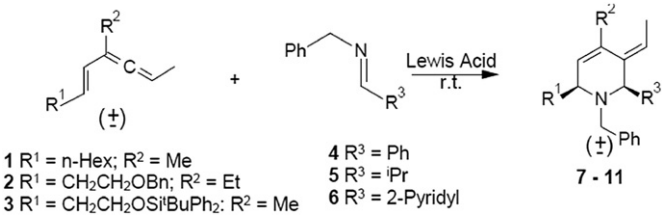
previous work.[8] However, in order to obtain pyridines, we needed monocyclic nitrogen-containing cycloadducts, the result of the reaction of acyclic vinyl allenes and imines, a reaction, which have not been carried out before.

To synthesize those monocyclic cycloadducts, vinyl allenes **1**–**3**, used in our previous study with aldehydes, were chosen. As heterodienophiles we decided to use the benzyl imines of benzaldehyde (**4**), isobutyraldehyde (**5**) and 2-pyridinecarboxaldehyde (**6**). Two Lewis acids, $BF_3{\cdot}OEt_2$ and $AlCl_3$, were used under the same experimental conditions employed in our previous studies, giving the results shown in Table 1.

As observed in Table 1, only one cycloadduct was obtained in each reaction in moderated to good yield. No important difference was observed between the two Lewis acids used. When the substituent at the inner position of the allene (R^2) was a methyl group, a small amount of the compound resulting from an ene reaction was obtained together with the expected cycloadduct (entries 1, 5, and 7, Fig. 1).

Table 1
Hetero Diels–Alder reaction of acyclic vinyl allenes and imines

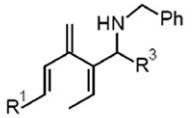


1 R^1 = n-Hex; R^2 = Me
2 R^1 = CH_2CH_2OBn; R^2 = Et
3 R^1 = $CH_2CH_2OSi^tBuPh_2$: R^2 = Me

4 R^3 = Ph
5 R^3 = ^{i}Pr
6 R^3 = 2-Pyridyl

Entry	Vinyl allene	Imine	Lewis acid	*t* (h)	Compounds (%)[a]
1	**1**	**4**	$AlCl_3$	20	**7** (42)[b]
2	**2**	**4**	$BF_3{\cdot}OEt_2$	14	**8** (79)
3	**2**	**4**	$AlCl_3$	24	**8** (79)
4	**2**	**6**	$BF_3{\cdot}OEt_2$	72	**9** (89)
5	**3**	**4**	$BF_3{\cdot}OEt_2$	48	**10** (59)[b]
6	**3**	**5**	$AlCl_3$	24	**11** (36)
7	**3**	**5**	$BF_3{\cdot}OEt_2$	26	**11** (32)[b]

[a] Isolated yield.
[b] Compounds coming from an ene reaction[8] were also isolated (entry 1, **12**, 23%),[14] (entry 5, **13**, 18%),[14] and (entry 7, **14**, 8%).[14]



12 R^1 = n-Hex; R^3 = Ph
13 R^1 = $CH_2CH_2OSi^tBuPh_2$; R^3 = Ph
14 R^1 = $CH_2CH_2OSi^tBuPh_2$; R^3 = ^{i}Pr

Fig. 1. Structure of the minor compounds, coming from ene-reactions, obtained in entries 1, 5, and 7 of Table 1.

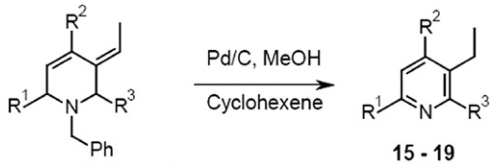
Similar results were obtained in our previous studies with semicyclic vinyl allenes. In those studies, due to the difficulties encountered to assign the relative stereochemistry of the centers adjacent to the nitrogen in the cycloadducts, the stereochemistry was assigned as cis by an X-ray diffraction analysis of one of the compounds obtained.[8] Based on the comparison of the relevant signals on the NMR spectra, the relative stereochemistry of the new cycloadducts was also assigned as cis.

Thus, with acyclic vinyl allenes and imines, the cycloaddition proceeds with total face selectivity, through the less hindered face of the vinyl allene. The regioselectivity and *endo*-selectivity were also complete yielding only one cycloadduct in each case.

Once we had the monocyclic cycloadduct in hand, we decided to check their transformation into pyridines following the same protocol used for the deprotection of the benzyl group in our work on the intramolecular reaction, as indicated in the introduction.[11]

Thus, the tetrahydropyridines obtained as cycloadducts were dissolved in EtOH and refluxed with cyclohexene and Pd/C (10%). After 3–6 h, the corresponding pyridine derivatives were obtained in moderate to good yields as shown in Table 2.

Table 2
Preparation of pyridines from the cycloadducts



7 R^1 = n-Hex; R^2 = Me; R^3 = Ph
8 R^1 = CH_2CH_2OBn; R^2 = Et; R^3 = Ph
9 R^1 = CH_2CH_2OBn; R^2 = Et; R^3 = 2-Pyridyl
10 R^1 = $CH_2CH_2OSi^tBuPh_2$; R^2 = Me; R^3 = Ph
11 R^1 = $CH_2CH_2OSi^tBuPh_2$; R^2 = Me; R^3 = ^{i}Pr

Entry	Cycloadduct	Pyridine (%)[a]
1	**7**	**15** (71)
2	**8**	**16** (62)
3	**9**	**17** (52)
4	**10**	**18** (46)
5	**11**	**19** (45)

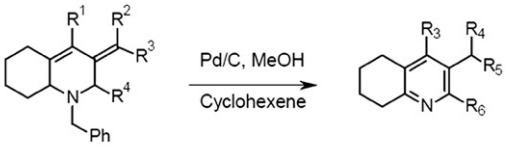
[a] Isolated yield.

All new compounds were identified by complete spectroscopic studies, including 2D NMR experiments.

All cycloadducts, tetrahydropyridines coming from the reaction of acyclic vinyl allenes and imines, reacted in moderate to good yields giving the pyridines as the only isolated compounds.

Once the feasibility of the reaction was confirmed, we decided to expand its scope by subjecting the bicyclic cycloadducts (**20**–**27**), obtained in previous work from semicyclic vinyl allenes and imines,[8] to the same conditions (Table 3).

Table 3
Preparation of tetrahydroquinolines from the bicyclic cycloadducts[8]



20 R^1 = Et; R^2 = Me; R^3 = H; R^4 = Ph
21 R^1 = Et; R^2 = Me; R^3 = H; R^4 = iPr
22 R^1= Me; R^2 = Me; R^3 = H; R^4 = Ph
23 R^1= Me; R^2 = Me; R^3 = H; R^4 = iPr
24 R^1= Me; R^2 = Ph; R^3 = H; R^4 = Ph
25 R^1 = Me; R^2 = Ph; R^3 = H; R^4 = iPr
26 R^1 = Me; R^2 = Me; R^3 = Me; R^4 = Ph
27 R^1 = ^{t}Bu; R^2 = Me; R^3 = H; R^4 = Ph

Entry	Cycloadduct	Pyridine (%)[a]
1	**20**	**28** (69)
2	**21**	**29** (73)
3	**22**	**30** (76)
4	**23**	**31** (83)
5	**24**	**32** (63)
6	**25**	**33** (41)
7	**26**	**34** (66)
8	**27**	—[b]

[a] Isolated yield.
[b] Non aromatic compounds were obtained.

As shown in Table 3, the results are similar to those found for the monocyclic cycloadducts, yielding the corresponding tetrahydroquinolines. The only exception was the reaction of compound **27**, which upon the catalytic transfer hydrogenation gave in good yield only the debenzylated compound (**35**),[14] together with a small amount of a partially dehydrogenated product. This result can be due to the difficulties to place the sterically demanding t-butyl group on the molecular plane of a pyridine ring.

This experiment also indicated that the mechanism of the transformation is probably the expected debenzylation followed by the thermal or palladium catalyzed isomerization of the exocyclic double bond and aromatization of the resulting dihydropyridines.

This procedure allows for the preparation of substituted pyridines and tetrahydroquinolines in an easy way starting from vinyl allenes and imines. An interesting application is the synthesis of 2,2′-bipyridines, compounds of great interest as quelating agents among other uses.[13] Using the procedure described in this work (Table 2, entry 3), bipyridine **17** was obtained in two steps in a 46% overall yield, starting from vinyl allene **2** and the imine of 2-pyridinecarboxaldehyde (**6**).

3. Conclusion

In conclusion, we have carried out the Lewis acid-mediated hetero Diels–Alder reaction of acyclic vinyl allenes and imines. The reactions proceed with total facial selectivity, regioselectivity and *endo*/*exo* selectivity giving tetrahydropyridines. The nitrogen-containing cycloadducts can be easily converted into substituted pyridines by catalytic transfer hydrogenation using cyclohexene and Pd/C. This reaction was also extended to the bicyclic cycloadducts (octahydroquinolines) obtained in our previous studies.

4. Experimental section

4.1. General procedures

All the reagents were obtained from commercial sources and used without further purification. Solvents used were purified and dried as needed following standard procedures. The reactions were monitored by thin-layer chromatography (TLC) on silica plated aluminum sheets (Silica gel 60 F_{254}, E. Merck). Flash chromatography was performed on silica gel 60 (0.040–0.063 mm). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker spectrometers at 300–400 MHz and 75–100 MHz, respectively. Chemical shifts are reported on δ scale in parts per million (ppm) with the solvent indicated as the internal reference. The IR spectra were recorded on a BRUKER IFS 66 spectrophotometer. High-resolution mass spectra (HRMS) were recorded on a VG AutoSpec FISONS.

4.2. Typical procedure for the cycloaddition reaction between acyclic vinyl allenes and imines

A solution of the imine (1.5 equiv) and $BF_3{\cdot}Et_2O$ (1.2 equiv) or $AlCl_3$ (1.2 equiv) in dry CH_2Cl_2 (0.1 M) at 0 °C under argon, was stirred for 15 min. Then the vinyl allene (1.0 equiv) was added. The reaction was allowed to reach room temperature and was followed by TLC. Once the vinyl allene was consumed, TEA (2.5 equiv) was added and the reaction was poured over ice-water. The organic phase was extracted with CH_2Cl_2, dried over anhydrous $MgSO_4$, and concentrated. The reaction products were purified by column chromatography using mixtures of hexanes and EtOAc as eluent.

4.2.1. (2R,3E,6S*)-1-Benzyl-3-ethylidene-6-hexyl-4-methyl-2-phenyl-2,6-dihydropyridine (**7**).* Oil; ^{1}H NMR (400 MHz, $CDCl_3$): 7.50–7.08 (m, 10H), 5.35 (s, 1H), 5.26 (c, *J*=7.3 Hz, 1H), 4.10 (s, 1H), 3.82 (d, *J*=12.9 Hz, 1H), 3.66 (d, *J*=12.9 Hz, 1H), 2.94 (br s, 1H), 2.19 (s, 3H), 2.00 (d, *J*=7.3 Hz, 3H), 1.47–1.35 (m, 1H), 1.26–1.18 (m, 2H), 1.13–1.06 (m, 3H), 1.02–0.96 (m, 2H), 0.84 (t, *J*=7.3 Hz, 3H), 0.78–0.75 (m, 1H), 0.68–0.65 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): 144.3 (s), 140.6 (s), 131.4 (s), 130.0 (s), 129.8 (d), 129.3 (d), 128.1 (d), 127.2 (d), 126.8 (d), 126.0 (d), 124.8 (d), 66.7 (d), 62.0 (t), 60.9 (d), 34.9 (t), 31.8 (t), 29.0 (t), 27.0 (t), 23.2 (q), 22.6 (t), 15.2 (q), 14.0 (q); IR (ν_{max}, cm^{-1}): 2900, 1590, 1485,ν 1440. MS (EI) *m*/*z* 373 (M^+, 0.7), 289 (23), 288 (100), 182 (5), 91 (27); HRMS: calcd for $C_{27}H_{35}N$: 373.2769; found: 373.2764.

4.2.2. (2R,3E,6S*)-1-Benzyl-6-(2-benzyloxyethyl)-4-ethyl-3-ethylidene-2-phenyl-2,6-dihydropyridine (**8**).* Oil; ^{1}H NMR (400 MHz, $CDCl_3$): 7.49–7.11 (m, 15H), 5.44 (br s, 1H), 5.29 (q, *J*=7.3 Hz, 1H), 4.41 (d, *J*=12.0 Hz, 2H), 4.12 (s, 1H), 3.84 (d, *J*=12.9 Hz, 1H), 3.73 (d, *J*=12.9 Hz, 1H), 3.70–3.64 (m, 1H), 3.45 (m, 1H), 3.37 (m, 1H), 2.68–2.64 (m, 1H), 2.57–2.53 (m, 1H), 2.03 (d, *J*=7.3 Hz, 3H), 1.29–1.26 (m, 1H), 1.23 (t, *J*=7.4 Hz, 3H), 1.05–0.99 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 144.1 (s), 140.5 (s), 138.7 (s), 136.2 (s), 130.5 (s), 129.3 (d), 128.2 (d), 128.1 (d), 128.1 (d), 127.6 (d), 127.6 (d), 127.3 (d), 127.2 (d), 126.9 (d), 126.1 (d), 124.6 (d), 72.7 (t), 68.1 (t), 66.4 (d), 61.7 (t), 57.5 (d), 34.8 (t), 28.4 (t),15.2 (q), 13.3 (q); IR (ν_{max}, cm^{-1}): 1485, 1440, 1350. MS (EI) *m*/*z* 437 (M^+, 3.5), 408 (5), 346 (4.5), 303 (25), 302 (100); HRMS: calcd for $C_{31}H_{35}NO$: 437.2718, found: 437.2701.

4.2.3. (2S,3E,6S*)-1-Benzyl-6-(2-benzyloxyethyl)-4-ethyl-3-ethylidene-2-(2-pyridyl)-2,6-dihydropyridine (**9**).* Oil; ^{1}H NMR (400 MHz, $CDCl_3$): 8.46–8.45 (m, 1H), 7.52–7.36 (m, 4H), 7.36–7.24 (m, 8H), 7.03–7.00 (m, 1H), 5.40 (s, 1H), 5.26 (q, *J*=7.2 Hz, 1H), 4.42 (d, *J*=11.9 Hz, 1H), 4.37 (d, *J*=11.9 Hz, 1H), 4.23 (s, 1H), 3.81 (d, *J*=13.3 Hz, 1H), 3.63 (d, *J*=13.3 Hz, 1H), 3.62–3.58 (m, 1H), 3.51–3.46 (m, 1H), 3.31 (br s, 1H), 2.61–2.56 (m, 1H), 2.48–2.42 (m, 1H), 1.95 (d, *J*=7.2 Hz, 3H), 1.39–1.32 (m, 1H), 1.10 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.4 (s), 148.3 (d), 140.1 (s), 138.6 (s), 138.4 (s), 135.1 (d), 132.1 (s), 129.2 (d), 128.4 (d), 128.2 (d), 127.6 (d), 127.4 (d), 126.8 (d), 126.4 (d), 123.6 (d), 123.1 (d), 121.2 (d), 72.7 (t), 69.6 (d), 68.0 (t), 61.2 (t), 56.9 (d), 35.4 (t), 28.1 (t), 15.1 (q), 13.0 (q); MS (EI) *m*/*z* 438 (M^+, 8), 360 (15), 347 (7), 303 (100), 91 (53); HRMS: calcd for $C_{30}H_{34}N_2O$: 438.2671, found: 438.2772.

4.2.4. 2-[(2R,5E,6S*)-1-Benzyl-5-ethylidene-4-methyl-6-phenyl-2,6-dihydropyridine-2-yl]ethoxy-tert-butyl-diphenyl-silane (**10**).* Oil; ^{1}H NMR (400 MHz, $CDCl_3$): 7.68–7.63 (m, 4H), 7.47–7.08 (m, 16H), 5.40 (s, 1H), 5.27 (q, *J*=7.3 Hz, 1H), 4.09 (s, 1H), 3.90–3.79 (m, 3H), 3.61 (m, 1H), 3.46 (br s, 1H), 2.23 (s, 3H), 2.04 (d, *J*=7.3 Hz, 3H), 1.13–1.08 (m, 1H), 1.02 (s, 9H), 0.99–0.95 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 144.7 (s), 141.0 (s), 136.0 (d), 134.6 (s), 131.7 (s), 130.7 (s), 130.4 (d), 129.9 (d), 129.8 (d), 128.6 (d), 128.2 (d), 128.0 (d), 127.7 (d), 127.3 (d), 125.6 (d), 66.1 (d), 62.2 (t), 62.1 (t), 57.9 (d), 38.0 (t), 27.3 (q), 23.6 (q), 19.6 (s), 15.7 (q); IR (ν_{max}, cm^{-1}): 1585, 1450: MS (EI) *m*/*z* 571 (M^+, 8), 422 (6), 289 (27), 288 (100), 199 (24); HRMS: calcd for $C_{39}H_{45}NOSi$: 571.3270; found: 571.3264.

4.2.5. 2-[(2S,5E,6R*)-1-Benzyl-5-ethylidene-6-isopropyl-4-methyl-2,6-dihydropyridin-2-yl]ethoxy-tert-butyl-diphenyl-silane (**11**).* Oil; ^{1}H NMR (400 MHz, $CDCl_3$): 7.71–7.68 (m, 4H), 7.46–7.22 (m, 11H), 5.45 (s, 1H), 5.04 (q, *J*=7.2 Hz, 1H), 4.01 (m, 1H), 3.88 (m, 1H), 3.65 (AB system, *J*=13.0 Hz, 2H), 3.35 (br s, 1H), 2.21 (d, *J*=10.5 Hz, 1H), 2.06 (s, 3H), 1.89 (d, *J*=7.2 Hz, 3H), 1.84–1.57 (m, 2H), 1.06 (s, 9H), 1.02–0.90 (m, 1H), 0.80 (d, *J*=6.5 Hz, 3H), 0.60 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 141.2 (s), 136.1 (d), 134.5 (s), 134.1 (s), 130.8 (s), 129.9 (d), 129.8 (d), 129.1 (d), 128.3 (d), 128.0 (d), 127.0 (d), 122.2 (d), 72.0 (d), 62.4 (t), 57.6 (d), 40.4 (t), 29.4 (d), 27.3 (q), 3.1 (q), 21.7 (q), 20.7 (q), 19.6 (s), 15.3 (q); IR (ν_{max}, cm^{-1}): 2900, 1585, 1450; MS

(EI) *m/z* 537 (M^+, 0.9), 494 (100), 254 (18), 199 (42), 91 (34); HRMS: calcd for $C_{36}H_{47}NOSi$: 537.3427; found: 537.3484.

*4.2.6. (±)-(E,2Z)-N-Benzyl-2-ethylidene-3-methylene-1-phenyl-undec-4-en-1-amine (**12**).* Oil; ^1H NMR (400 MHz, $CDCl_3$): 7.39–7.24 (m, 10H), 5.99 (d, *J*=15.5 Hz, 1H), 5.79 (q, *J*=6.7 Hz, 1H), 5.47 (dt, *J*=7.7, 15.5 Hz, 1H), 5.07 (s, 1H), 4.57 (s, 1H), 4.28 (s, 1H), 3.76 (AB system, *J*=13.4 Hz, 2H), 2.02–1.99 (m, 3H), 1.59 (d, *J*=6.7 Hz, 3H), 1.36–1.29 (m, 8H), 0.95 (t, *J*=6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 145.4 (s), 142.4 (s), 141.7 (s), 140.7 (s), 133.1 (d), 130.5 (d), 128.3 (d), 128.1 (d), 128.0 (d), 126.8 (d), 126.8 (d), 122.5 (d), 115.5 (t), 67.2 (d), 51.9 (t), 32.6 (t), 31.7 (t), 29.3 (t), 28.9 (t), 22.6 (t), 14.5 (q), 14.1 (q); IR (ν_{max}, cm^{-1}): 2900, 1585, 1485, 1445.

*4.2.7. (±)-(E,2Z)-N-Benzyl-7-[tert-butyl(diphenyl)silyl]oxy-2-ethylidene-3-methylene-1-phenyl-hept-4-en-1-amine (**13**).* Oil; ^1H NMR (400 MHz, $CDCl_3$): 7.74–7.15 (m, 20H), 6.03 (d, *J*=15.5 Hz, 1H), 5.81 (q, *J*=6.7 Hz, 1H), 5.46 (dt, *J*=7.8 Hz, *J*=15.5 Hz, 1H), 5.10 (s, 1H), 4.61 (s, 1H), 4.27 (s, 1H), 3.75 (AB system, *J*=13.2 Hz, 2H), 3.60 (t, *J*=6.8 Hz, 2H), 2.29 (q, *J*=6.8 Hz, 2H), 1,82 (br s, 1H), 1.59 (d, *J*=6.7 Hz, 3H), 1.11 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): 145.7 (s), 142.7 (s), 142.0 (s), 141.1 (s), 136.0 (d), 134.5 (s), 132.9 (d), 130.0 (d), 129.2 (d), 128.7 (d), 128.5 (d), 128.4 (d), 128.1 (d), 127.3 (d), 127.2 (d), 123.1 (d), 116.7 (t), 67.5 (d), 64.0 (t), 52.2 (t), 36.4 (t), 27.3 (q), 19.7 (s), 14.9 (q); IR (ν_{max}, cm^{-1}): 2900, 1585, 1450. MS (EI) *m/z* 571 (M^+, 68), 494 (34), 302 (21), 199 (71), 196 (77), 91 (100); HRMS: calcd for $C_{39}H_{45}NOSi$: 571.3270, found: 571.3264.

*4.2.8. (±)-(E,4Z)-N-Benzyl-9-[tert-butyl(diphenyl)silyl]oxy-4-ethylidene-2-methyl-5-methylene-non-6-en-3-amine (**14**).* Oil; ^1H NMR (400 MHz, $CDCl_3$): 7.68–7.66 (m, 4H), 7.44–7.22 (m, 11H), 6.09 (d, *J*=15.6 Hz, 1H), 5.71 (dt, *J*=7.8 Hz, *J*=15.6 Hz, 1H), 5.60 (q, *J*=6.7 Hz, 1H), 5.16 (s, 1H), 4.75 (s, 1H), 3.80–3.58 (AB system, *J*=13.2 Hz, 2H), 3.69 (t, *J*=6.5 Hz, 2H), 2.86 (d, *J*=4.5 Hz, 1H), 2.34 (q, *J*=6.6 Hz, 2H), 1.79 (m, 1H), 1.62 (d, *J*=6.7 Hz, 3H), 1.60 (br s, 1H), 1.05 (s, 9H), 0.93 (d, *J*=6.7 Hz, 3H), 0.84 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 146.0 (s), 141.2 (s), 138.8 (s), 135.5 (d), 133.9 (s), 133.0 (d), 129.4 (d), 128.6 (d), 128.1 (d), 127.5 (d), 126.5 (d), 122.2 (d),115.5 (t), 68.6 (d), 63.4 (t), 51.5 (t), 35.9 (t), 29.7 (d), 26.7 (q), 21.0 (q), 19.1 (s), 16.7 (q), 14.5 (q); IR (ν_{max}, cm^{-1}): 2900, 1715, 1585, 1450; MS (EI) *m/z* 537 (M^+, 41), 495 (64), 494 (87), 480 ($M^+-{}^t$Bu, 12), 199 (100); HRMS: calcd for $C_{36}H_{47}NOSi$: 537.3427, found: 537.3456.

4.3. Typical procedure for the dehydrogenation reaction

To a solution of the cycloadduct in methanol (0.045 M) and cyclohexene (0.25 M), was added 10% Pd/C (50% in weight). The mixture was refluxed for 3–6 h. After cooling, the reaction was filtered, washed with methanol and concentrated. The crude mixture was purified by column chromatography using mixtures of hexanes and EtOAc as eluent.

*4.3.1. 3-Ethyl-6-hexyl-4-methyl-2-phenyl-pyridine (**15**).* Oil; ^1H NMR (300 MHz, $CDCl_3$): 7.42–7.26 (m, 5H), 6.95 (s, 1H), 2.75 (t, *J*=7.8 Hz, 2H), 2.57 (q, *J*=7.5 Hz, 2H), 2.37 (s, 3H), 1.77–1.67 (m, 2H), 1.41–1.32 (m, 6H), 1.03 (t, *J*=7.5 Hz, 3H), 0.91–0.87 (t, *J*=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 158.8 (s), 158.5 (s), 145.9 (s), 141.8 (s), 132.8 (s), 128.7 (d), 128.0 (d), 127.3 (d), 123.3 (d), 38.1 (t), 31.8 (t), 30.2 (t), 29.2 (t), 22.6 (t), 22.1 (t), 19.2 (q), 14.3 (q), 14.1 (q); IR (ν_{max}, cm^{-1}): 2900, 1585, 1540, 1450; MS (EI) *m/z* 282 (M^++1, 100), 211 (4), 154 (16); HRMS: calcd for $C_{20}H_{27}N$: 281.2143, found: 281.2049.

*4.3.2. 6-(2-Benzyloxyethyl)-3,4-diethyl-2-phenyl-pyridine (**16**).* Oil; ^1H NMR (400 MHz, $CDCl_3$): 7.42–7.26 (m, 10H), 7.08 (s, 1H), 4.55 (s, 2H), 3.89 (t, *J*=6.7 Hz, 2H), 3.12 (t, *J*=6.7 Hz, 2H), 2.71 (q, *J*=7.5 Hz, 2H), 2.60 (q, *J*=7.5 Hz, 2H), 1.30 (t, *J*=7.5 Hz, 3H), 1.02 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 159.3 (s), 156.0 (s), 152.1 (s), 142.2 (s), 139.0 (s), 133.1 (s), 129.1 (d), 128.7 (d), 128.5 (d), 28.0 (d), 127.9 (d), 122.7 (d), 73.3 (t), 70.4 (t), 38.8 (t), 25.5 (t), 21.9 (t), 15.1 (q), 3.1 (q); IR (ν_{max}, cm^{-1}): 2900, 1585, 1445, 1445; MS (EI) *m/z* 346 (M^++1, 93), 307 (25), 254 (15), 154 (100); HRMS: calcd for $C_{24}H_{27}NO$: 345.2092, found: 345.2146.

*4.3.3. 6-(2-Benzyloxyethyl)-3,4-diethyl-2-(2-pyridyl)pyridine (**17**).* Oil; ^1H NMR (400 MHz, $CDCl_3$): 8.66 (br s, 1H), 7.80–7.76 (m, 1H), 7.57–7.55 (m, 1H), 7.32–7.25 (m, 6H), 7.13 (s, 1H), 4.53 (s, 2H), 3.87 (t, *J*=6.7 Hz, 2H), 3.14 (t, *J*=6.7 Hz, 2H), 2.77–2.69 (m, 4H), 1.27 (t, *J*=7.5 Hz, 3H), 1.01 (t, *J*=7.5 Hz, 3H), ^{13}C NMR (75 MHz, $CDCl_3$): 159.2 (s), 156.1 (s), 155.4 (s), 152.9 (s), 148.5 (d), 138.5 (s), 136.5 (d), 133.9 (s), 128.3 (d), 127.6 (d), 127.5 (d), 124.4 (d), 123.4 (d), 122.6 (d), 72.9 (t), 69.9 (t), 38.0 (t), 25.1 (t), 20.9 (t), 15.0 (q), 14.6 (q); MS (EI) *m/z* 346 (M^+, 82), 331 (56), 303 (59), 255 (49), 91 (100); HRMS: calcd for $C_{23}H_{26}N2O$: 346.2045, found: 346.2053.

*4.3.4. tert-Butyl-[2-(5-ethyl-4-methyl-6-phenyl-2-pyridyl)ethoxy]-diphenyl-silane (**18**).* Oil; ^1H NMR (400 MHz, $CDCl_3$): 7.62–7.59 (m, 4H), 7.43–7.32 (m, 11H), 7.05 (s, 1H), 4.05 (t, *J*=6.3 Hz, 2H), 3.04 (t, *J*=6.3 Hz, 2H), 2.60 (q, *J*=7.5 Hz, 2H), 2.36 (s, 3H), 1.05 (t, *J*=7.4 Hz, 3H), 1.02 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): 158.6 (s), 155.7 (s), 145.7 (s), 141.7 (s), 135.6 (d), 133.9 (s), 133.3 (s), 129.5 (d), 128.8 (d), 128.0 (d), 127.5 (d), 127.4 (d), 125.1 (d), 63.8 (t), 41.0 (t), 26.8 (q), 22.1 (t), 19.2 (q), 19.2 (s), 14.3 (q); IR (ν_{max}, cm^{-1}): 2900, 1590, 1450, 1460, MS (EI) *m/z* 480 (M^++1, 97), 460 (18), 422 (43), 307 (100), 289 (36); HRMS: calcd for $C_{32}H_{37}NOSi$: 479.2644, found: 479.2711.

*4.3.5. tert-Butyl-[2-(5-ethyl-6-isopropyl-4-methyl-2-pyridyl)ethoxy]-diphenyl-silane (**19**).* Oil; ^1H NMR (400 MHz, $CDCl_3$): 7.62–7.60 (m, 4H), 7.42–7.33 (m, 6H), 6.79 (br s, 1H), 4.03 (t, *J*=6.6 Hz, 2H), 3.28 (m, 1H), 2.97 (br s, 2H), 2.66 (q, *J*=7.5 Hz, 2H), 2.26 (s, 3H), 1.29–1.23 (m, 6H), 1.13 (t, *J*=7.5 Hz, 3H), 1.02 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): 163.9 (s), 158.8 (s), 144.8 (s), 136.0 (d), 134.5 (s), 132.0 (s), 129.8 (d), 127.9 (d), 123.5 (s), 64.4 (t), 41.6 (t), 31.0 (d), 27.2 (q), 23.1 (q), 21.3 (t), 19.6 (s), 15.0 (q); IR (ν_{max}, cm^{-1}): 2900, 1590, 1450, 1460. MS (EI) *m/z* 446 (M^++1, 100), 388 (74), 368 (40); HRMS: calcd for $C_{29}H_{39}NOSi$: 445.2801, found 445.2706.

*4.3.6. 3,4-Diethyl-2-phenyl-5,6,7,8-tetrahydroquinoline (**28**).* Oil; ^1H NMR (300 MHz, $CDCl_3$): 7.43–7.31 (m, 5H), 2.93 (br s, 2H), 2.79 (br s, 2H), 2.70 (q, *J*=7.5 Hz, 2H), 2.58 (q, *J*=7.5 Hz, 2H), 1.88 (m, 4H), 1.18 (t, *J*=7.5 Hz, 3H), 1.00 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 156.7 (s), 153.8 (s), 149.7 (s), 142.1 (s), 132.1 (s), 129.1 (s), 128.7 (d), 128.0 (d), 127.2 (d), 33.2 (t), 25.7 (t), 23.1 (t), 22.9 (t), 21.8 (t), 21.4 (t), 15.6 (q), 13.8 (q); IR (ν_{max}, cm^{-1}): 2900, 1700, 1550, 1440, 1400. MS (FAB) *m/z* 266 (M^++1, 100), 154 (11); HRMS: calcd for $C_{19}H_{23}N$: 265.1830, found: 265.1907.

*4.3.7. 3,4-Diethyl-2-isopropyl-5,6,7,8-tetrahydroquinoline (**29**).* Oil; ^1H NMR (400 MHz, $CDCl_3$): 3.25 (m, 1H), 2.88 (br s, 2H), 2.71–2.57 (m, 6H), 1.82 (br s, 4H), 1.27 (d, *J*=6.7 Hz, 6H), 1.16 (t, *J*=7.5 Hz, 3H), 1.13 (t, *J*=7.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 161.8 (s), 154.2 (s), 149.1 (s), 131.1 (s), 128.9 (s), 33.6 (t), 30.9 (d), 26.0 (t), 23.7 (t), 23.4 (t), 23.2 (q), 21.9 (t), 21.2 (t), 16.2 (q), 14.2 (q); IR (ν_{max}, cm^{-1}): 2900, 1555, 1450, 1400; MS (FAB) *m/z* 232 (M^++1, 72), 231 (12), 154 (100), 136 (55); HRMS: calcd for $C_{16}H_{25}N$: 231.1987, found: 231.2079.

*4.3.8. 3-Ethyl-4-methyl-2-phenyl-5,6,7,8-tetrahydroquinoline (**30**).* Oil; ^1H NMR (400 MHz, $CDCl_3$): 7.40–7.37 (m, 5H), 2.93 (br s, 2H), 2.69 (br s, 2H), 2.57 (q, *J*=7.5 Hz, 2H), 2.23 (s, 3H), 1.88–1.85 (m, 4H), 1.03 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 156.5 (s), 153.8 (s), 144.8 (s), 142.5 (s), 133.1 (s), 130.3 (s), 129.1 (d), 128.4 (d), 127.7 (d), 36.6 (t), 27.1 (t), 23.5 (t), 23.3 (t), 23.0 (t), 15.1 (q), 15.0 (q);

IR (ν_{max}, cm^{-1}): 2900, 2500, 1560, 1440, 1410; MS (FAB) *m/z* 252 (M^++1, 100), 154 (6); HRMS: calcd for $C_{18}H_{21}N$: 251.1674, found: 251.1660.

*4.3.9. 3-Ethyl-2-isopropyl-4-methyl-5,6,7,8-tetrahydroquinoline (**31**).* Oil; ^1H NMR (300 MHz, $CDCl_3$): 3.26 (m, 1H), 2.88 (br s, 2H), 2.72–2.61 (m, 4H), 2.16 (s, 3H), 1.85–1.80 (m, 4H), 1.28 (d, *J*=6.7 Hz, 6H), 1.13 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 160.6 (s), 153.3 (s), 131.3 (s), 127.9 (s), 33.1 (t), 30.6 (d), 26.6 (t), 23.2 (t), 22.9 (t), 22.7 (q), 21.3 (t), 14.7 (q), 14.3 (q); IR (ν_{max}, cm^{-1}): 2900, 1550, 1440, 1400. MS (FAB) *m/z* 218 (M^++1, 100), 217 (M^+, 22), 154 (49), 137 (37); HRMS: calcd for $C_{15}H_{23}N$: 217.1830, found: 217.1928.

*4.3.10. 3-Benzyl-4-methyl-2-phenyl-5,6,7,8-tetrahydroquinoline (**32**).* White solid; mp: 150–152 °C; ^1H NMR (400 MHz, $CDCl_3$): 7.38–6.99 (m, 10H), 4.0 (s, 2H), 3.01 (br s, 2H), 2.70 (br s, 2H), 2.06 (s, 3H), 1.91–1.89 (br s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): 156.8 (s), 154.6 (s), 145.9 (s), 141.5 (s), 140.6 (s), 130.0 (s), 128.7 (d), 128.4 (d), 128.0 (d), 127.9 (d), 127.4 (d), 125.7 (d), 35.6 (t), 33.3 (t), 26.6 (t), 23.0 (t), 22.8 (t), 15.3 (q).

*4.3.11. 3-Benzyl-2-isopropyl-4-methyl-5,6,7,8-tetrahydroquinoline (**33**).* Oil; ^1H NMR (400 MHz, $CDCl_3$): 7.28–7.18 (m, 3H), 7.04–7.02 (m, 2H), 4.10 (s, 2H), 3.19 (m, 1H), 2.94 (br s, 2H), 2.64 (br s, 2H), 2.06 (s, 3H), 1.86 (br s, 4H), 1.21 (d, *J*=6.7 Hz, 6H), ^{13}C NMR (100 MHz, $CDCl_3$): 162.0 (s), 154.7 (s), 145.3 (s), 140.5 (s), 128.8 (d), 128.6 (s), 128.3 (d), 127.7 (s), 126.3 (d), 34.1 (t), 33.7 (t), 31.6 (d), 27.0 (t), 26.3 (t), 23.3 (t), 22.8 (q), 15.5 (q).

*4.3.12. 3-Isopropyl-4-methyl-2-phenyl-5,6,7,8-tetrahydroquinoline (**34**).* White solid; mp: 90–93 °C; ^1H NMR (300 MHz, $CDCl_3$): 7.43–7.31 (m, 5H), 3.26 (m, 1H); 2.96 (br s, 2H), 2.68 (br s, 2H), 2.34 (s, 3H), 1.87 (br s, 4H), 1.26 (d, *J*=7.3 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): 156.4 (s), 153.1 (s), 145.0 (s), 143.0 (s), 136.1 (s), 130.8 (s), 128.6 (d), 128.2 (d), 127.1 (d), 33.1 (t), 29.8 (d), 26.5 (t), 23.1 (t), 22.8 (t), 21.6 (q), 16.3 (q); IR (ν_{max}, cm^{-1}): 2950, 1550, 1435; MS (EI) *m/z* 265 (M^+, 46), 264 (100), 250 (24), 235 (8); HRMS: calcd for $C_{19}H_{23}N$: 265.1830, found: 265.1769.

4.3.13. (2S,8aR*,E)-4-tert-Butyl-3-ethylidene-2-phenyl-1,2,3,5,6,7,8,8a-octahydroquinoline (**35**).* Oil; ^1H NMR (300 MHz, $CDCl_3$): 7.90–7.88 (m, 2H), 7.41–7.30 (m, 3H), 5.46 (br s, 1H), 2.96–2.86 (m, 1H), 2.32 (m, 2H), 2.03–1.48 (m, 6H), 1.80 (d, *J*=7.0 Hz, 3H), 1.36 (s, 9H); MS (EI) *m/z* 293 (M^+, 60), 292 (100), 278 (30), 267 (51), 236 (88), HRMS: calcd for $C_{21}H_{27}N$: 293.2143, found: 293.2113.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2012.09.057.

References and notes

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14. See Experimental section for analytical data and Supplementary data for copies of spectra.