α-Alkylation and Stereochemistry of *cis*- and *trans*-Decahydroquinolines Mediated by the Formamidine and Boc Activating Groups. Synthesis of Pumiliotoxin C†

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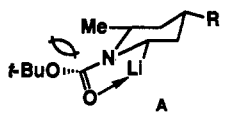
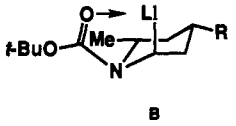
Abstract: *cis*- and *trans*-decahydroquinolines, as their *t*-Boc and formamidine derivatives, have been metalated and alkylated. The former gives mainly axial alkylation whereas the latter gives equatorial alkylation in the *trans* series. For the *cis* series, the *t*-Boc derivative gives essentially pure equatorial alkylation as does the formamidine derivative. Several electron-transfer processes occur simultaneously with the ionic alkylation, and this can be altered by use of pentynylcopper or HMPA. Furthermore, cuprates, when employed, gave good yields of alkylation product via radical pathways, but the stereochemistry suffered. A synthesis of the poison dart frog secretion, pumiliotoxin C, has been accomplished using these alkylation techniques.

We have recently reported[1] the metalation and alkylation of piperidine derivatives containing a formamidine moiety and showed that both the deprotonation step and the alkylation step at C-2 proceed in an equatorial manner. This behavior was similar to that of the *t*-Boc piperidines reported by Beak.[2] However, the latter also showed that the second metalation–alkylation (at the 6-position) led to clean axial substitution whereas with the formamidine piperidine the second alkylation took place again in the equatorial position (Scheme I). Thus, both activating groups act in a complementary fashion, allowing access to either stereoisomer. The rationalization for the dichotomy exhibited by these N-activating groups was attributed to differences in steric parameters (A–C). The *t*-Boc group is larger than the



A



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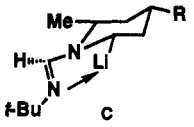
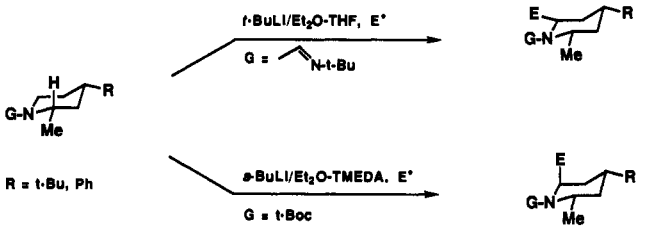


C

formamidine group and causes severe nonbonded interactions as shown in A. However, the formamidine grouping can readily lie in the position shown in C to allow removal of the equatorial proton in the 6-position. The energetically more favorable structure shown in B or a twist-boat form (not shown) would minimize interaction between the *N*-*t*-Boc and the 6-equatorial methyl group, thus allowing axial introduction as shown in Scheme I. The reasons for equatorial deprotonation have also been discussed by Beak[3] and ourselves[4] and rely mainly on the conformation which will allow orthogonality between the developing carbanion and the lone pairs on the activating groups.

We now have examined another system which we felt could be alkylated by formamidine activation; namely decahydroquinoline both as its *cis* and *trans* isomers, **1** and **3**. As a comparison we felt that a study of the corresponding *t*-Boc derivatives **2** and **4** would also be informative and serve to reveal whether there were any differences, as mentioned above. The successful implementation of this alkylation would allow entry into a number of important alkaloids of the dendrobates family,[5] more commonly known as those derived from the poison dart frogs.

Scheme I



Access to the requisite starting materials proved to be straightforward and is outlined in Scheme II. The reported[6] reduction of tetrahydroquinoline (**5**) with rhodium-on-alumina gave a 79% yield of decahydroquinoline (**6**) as a 98:2 mixture favoring the *cis* isomer, whereas the sodium–ethanol reduction[7] of **5** gave a 9:1 mixture favoring the *trans* isomer **7**. Purification of each isomer was accomplished by recrystallization of their picrate salts as described.[7] Both quinolines **6** and **7** were subjected to the formamidine-exchange reaction by heating with *N*,*N*-dimethyl-*N*′-*tert*-butylformamidine[4] to afford the corresponding quinoline formamidines *cis*-**1** and *trans*-**3** in 70–80% yields, respectively. Furthermore, the corresponding *t*-Boc derivatives **2** and **4** were generated from the quinolines **6** and **7** using literature procedures.[2]

Metalation of **3** using *tert*-butyllithium at −20 °C (no metalation occurs below this temperature) followed by introduction of various electrophiles is shown in Table I. Thus, deuteriomethanol gave a 92% yield of exclusively the equatorial 2-D derivative **8a** (89% D-incorporation).

This assignment was readily made by ^{1}H NMR, which exhibited J_{aa} = 12–13 Hz coupling for the 2-H(2.45ppm)–3-H axial protons. Furthermore the equatorial 2-H at 4.45 ppm was virtually absent.

† Dedicated to Professor Ernest L. Eliel on the occasion of his 71st birthday and for his immense contributions to organic stereochemistry.

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(1) Meyers, A. I.; Shawe, T. T. *J. Org. Chem.* **1991**, *56*, 2751.
(2) Beak, P.; Lee, W.-K. *J. Org. Chem.* **1990**, *55*, 2578.
(3) Beak, P.; Lee, W.-K. *J. Org. Chem.* **1993**, *58*, 1109.
(4) Meyers, A. I.; Edwards, P. D.; Reiker, W. F.; Bailey, T. R. *J. Am. Chem. Soc.* **1984**, *106*, 3270.
(5) For an efficient and elegant route to the family of alkaloids, see: Overman, L. E.; Jessup, P. J. *J. Am. Chem. Soc.* **1978**, *100*, 5179 and references cited therein.
(6) Vierhapper, F. W.; Eliel, E. L. *J. Org. Chem.* **1975**, *40*, 2734.
(7) Booth, H.; Bostock, A. H. *J. Chem. Soc., Perkin Trans II* **1972**, 615.
(8) Booth, H.; Griffiths, D. V.; Jozefowicz, M. L. *J. Chem. Soc., Perkin Trans II* **1976**, 751.

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Scheme II

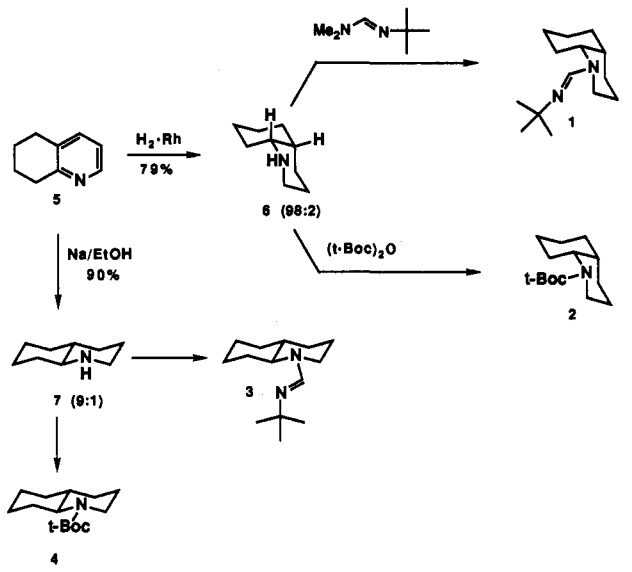
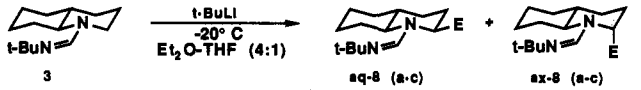


Table I. Monoalkylation of **3** to 2-Substituted Quinolines **8**

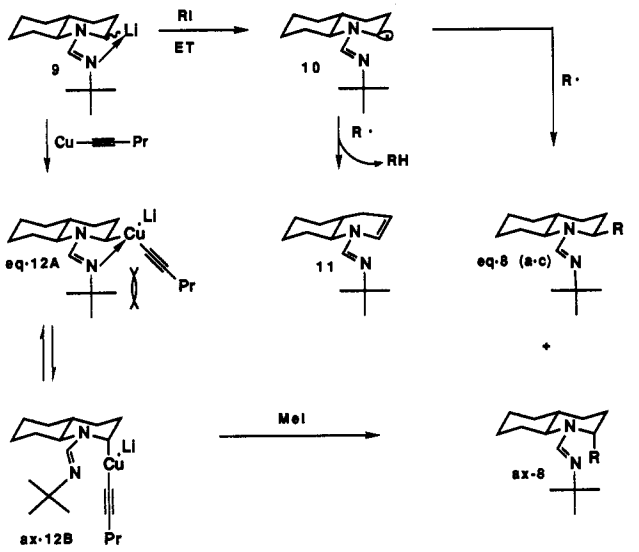


entry	electrophile E^+	alkylation conditions	**8** equat: axial	**8**, yield (%)
a	D^+ (DOMe)	−78 °C	>99:1	**8a**, 92
b	Me_3Si (TMSCl)	−78 °C → −25 °C, 12 h	>99:1	**8b**, 95
c	Me (MeI)	−78 °C → −55 °C, 12 h	85:15	**8c**, 58[a]
d	Me (MeI)	CuC≡C—Pr (−20 °C) −78 °C → −20 °C, 12 h	20:80	**8c**, 62[b,c]
e	Me (MeI)	HMPA (1.5 equiv) −78 °C → −55 °C, 12 h	>95:5	**8c**, 70[d]

[a] Product accompanied by 27% electron-transfer product **11**. [b] The pentynylcopper was added to the lithio formamidine at −20 °C; then the reaction mixture was cooled to −78 °C prior to addition of MeI. [c] Product accompanied by 15% **3** and only 6% **11**. [d] Product accompanied by 8% **3** and 8% **11**.

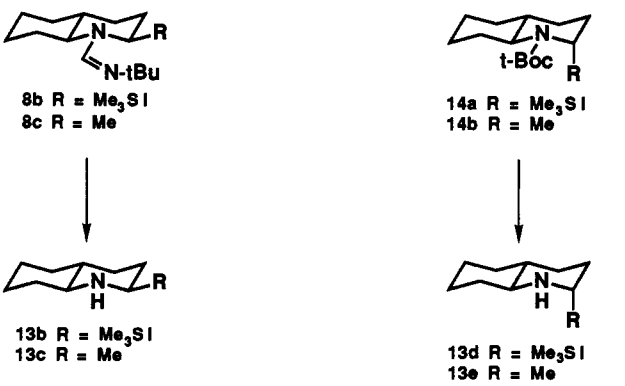
From Table I, it is also seen that when trimethylsilyl chloride was introduced into lithiated **3**, the product **8b** was exclusively obtained, possessing the equatorial TMS group in over 95% yield. This was also shown by NMR to give a J_{aa} = 12.5 Hz for the 2-H (2.10 ppm). Although both of these cases gave exclusive equatorial alkylation, the addition of iodomethane to lithiated **3** (**9**, Scheme III), under these same conditions, produced only 85% equatorial product **8c** along with 15% of the axial isomer of **8c**. Proton multiplets assigned as 2-H_{ax} and 2-H_{eq} were observed at 3.65 ppm (85%) and 4.75 ppm (15%) and suggested, according to previous studies,[1] that the major product still contained the equatorial methyl but now contained a significant amount of axial isomer as well as a 27% yield of the ene–amidine **11** (Scheme III). The latter was shown earlier[4] to arise from an electron-transfer (ET) process when alkyl iodides were utilized as electrophiles. In order to eliminate or minimize the formation of **11**, the use of pentynylcopper was earlier observed to be an effective inhibitor of this process.[4] When 1.5 equiv of pentynylcopper was introduced into the solution of **9** at −20 °C, the amount of ene–amidine **11** was indeed reduced to 6%, but the ratio of equatorial methyl to axial methyl product was now reversed; the axial product **8c** was now favored by 4:1. This is probably due to an intermediate radical.[9] The product was readily confirmed by NMR data which showed the 2-H_{ax} signal, previously the major signal at 3.65 ppm, was now the minor one and the signal at 4.75 ppm (2-H_{eq}) was the major multiplet. Repeating the pentynyl copper experiment wherein the *trans* metalation was allowed to occur at −78 °C did little to alter the

Scheme III



results. As a final experiment to enhance the stereoselectivity of the methylation, HMPA (1.5 equiv) was introduced into the lithio formamidine **9** prior to addition of iodomethane and allowed to react at −78 °C and then warmed to −55 °C (Table I, entry e). In this manner the ratio of equatorial to axial methylation to give **8c** rose to 95–97% accompanied by only a trace of olefinic product **11**. This is the result of a more ionic C–Li bond making the substitution more competitive than the ET process.[4]

Further proof of structure for the equatorial and axial methyl groups in **8c** was obtained by removing the formamidine groups using the hydrazine method reported earlier.[1] This led to the unsubstituted 2-methyldecahydroquinolines **13c** and **13e**, which



were described by Booth[8] and whose stereochemistries were in complete accord with the assignments made herein. The rationalization for the stereochemical results above wherein the copper-mediated alkylations caused a major reversal in methylation (Table I) can be stated by observations based on earlier work from our laboratory.[1]

(9) (a) A recent report by Gawley et al. (*Tetrahedron Lett.* **1991**, *32*, 1941) has shown that SET processes may accompany the polar process in α-aminocarbanions derived from oxazolines, and the present study seems to support this observation. (b) Ashby, E. C.; Coleman, D. *J. Org. Chem.* **1987**, *52*, 4554. (c) In an attempt to assess the degree of radical intermediates in **10A** and **10B**, we treated cuprate **D** with 6-bromohexene and obtained **E** and **F** in a ratio of 1:1, thus strongly indicating considerable radical character in the alkylation step.

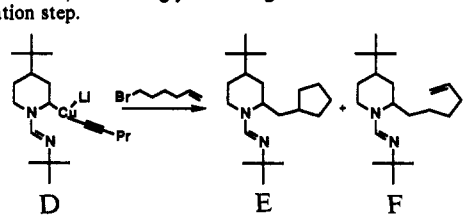
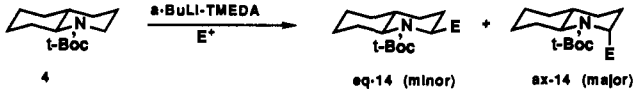


Table II. Alkylation of *N*-*t*-Boc-decahydroquinoline (4)



4 eq-14 (minor) ax-14 (major)

entry	electrophile E^+	14 axial:equat	14, yield (%)
a	D^+ (MeOD)	>95:5	**14a**, 81[a]
b	Me_3Si (TMSCl)	>95:5	**14b**, 84[d]
c	Me (MeI)	>95:5	**14c**, 50[b,d]
d	Me (Me_2SO_4)	>95:5	**14c**, 68[c,d]

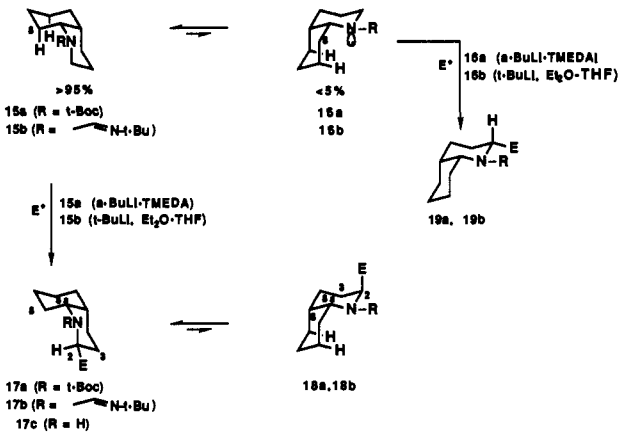
[a] Product contained 92% D. [b] Product accompanied by 15% **4** and 22% electron-transfer product (e.g. **11**, t-Boc in place of formamidine). [c] Product accompanied by 20% **4**. [d] Electrophile added to lithio-**4** at −78 °C and allowed to warm to 25 °C over 12 h.

The lithiated formamidine **9** (Scheme III), when encountering an alkyl halide, undergoes, in addition to an ionic displacement, a competitive electron transfer to form **10**, which may be alkylated from either face to give eq-**8** or ax-**8** and olefinic product **11**.[9] This was observed in our earlier studies[1] and likewise appears to be occurring in the present work. However our earlier studies were not designed to probe stereochemistry when the reactions were mediated by copper compounds, and therefore the reversal in stereochemistry was first observed in the present system. The underlying cause for this reversal is still not clear (Scheme III) but might involve competitive formation of intermediate **10**, produced by single-electron transfer (SET), and the cuprate **12A** or **12B**.[9b,c]

A collateral study was also undertaken to asses the synthetic utility of the *t*-Boc group in the decahydroquinolines, since this activating group has recently been the subject of much activity.[2,10] The *t*-Boc derivatives were prepared and subjected to the metalation conditions described by Beak[2] which were *sec*-butyllithium–TMEDA in ether at −78 °C. Unfortunately we were unable to compare both *t*-Boc and formamidine activating groups under the same conditions because they were mutually incompatible. Thus, use of *tert*-butyllithium in ether–THF, which successfully metalates formamidines, leads to only recovered starting material when *t*-Boc is employed. Conversely, use of *sec*-butyllithium–TMEDA, which is the standard recipe for *t*-Boc metalation, gave only very poor yields (20–25%) of formamidine metalation. When the *trans*-decahydroquinoline containing the *t*-Boc group (**4**) was subjected to metalation (*sec*-butyllithium–TMEDA, ether, −78 °C) followed by introduction of several electrophiles (Table II), the products were consistently found to be the axially substituted derivatives **14** with only a trace of the equatorial isomers being detectable. Thus all the electrophiles shown in Table II entered in an axial fashion. This is again consistent with the earlier results of Beak,[2] since the decahydroquinolines **4** may be envisioned as monosubstituted piperidines with equatorial groups (at the 6-position) already in place.

Thus, the metalation–alkylation sequence described above actually represents the "second alkylation" which is subject to the nonbonded repulsion beween the *t*-Boc and C-8 thereby forcing metalation to occur by removing the axial hydrogen at C-2.[3] The assignment of the axial substituent in **14** was not entirely straightforward. The product obtained from the trimethylsilyl chloride alkylation was at first thought to be the equatorial isomer of **14b** due to a large coupling (J = 13 Hz) for the 2-H at 2.64 ppm. In order to confirm the stereochemical result of the TMS derivative, the *t*-Boc was hydrolyzed (acetyl chloride–MeOH–EtOAc, 0 °C) and the physical properties of the resulting product were compared with those of the product formed from hydrolysis of the formamidine moiety of **8b**. The 2-H of **13d** at 2.51 ppm showed a coupling constant of only 4 Hz while a 12-Hz J value characterized the 2-H of **13b**, which appeared at higher field (2.05 ppm). In view of the iodomethane alkylation of lithiated **4** also furnishing a product whose NMR spectrum was not totally unambiguous, it was again necessary to hydrolyze the *t*-Boc group and compare the properties of that product to those of **13c** and **13e**, obtained from the formamidine study. The result of this comparison confirmed that the axial methyl isomer **13e** was formed when the *t*-Boc derivative **4** was alkylated.

We next examined the metalation–alkylation of the *cis*-decahydroquinoline (**6**) in the form of its formamidine (**1**) and *t*-Boc (**2**) derivatives. The N-alkylation of *cis*-decahydroquinolines has been extensively studied by Booth,[11] who concluded, on the basis of NMR studies, that the preferred conformation of relatively large N-substituted systems was **15** whereas **16** was



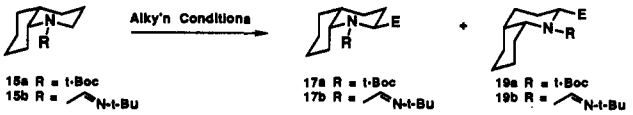
favored with NH or *N*-methyl derivatives. The rational behind this conclusion, which was determined by analysis of low-temperature NMR (^1H, ^{13}C, and ^{19}F), rested with the following. As the size of the N-substituent increases, the nonbonded interaction between it and C-8 in **16** forces ring flipping to **15**, thus alleviating the strain. In light of this finding, we expected that the relatively large formamidine and *t*-Boc derivatives would exist predominately in conformation **15**. That this was indeed the case was readily seen from the proton and carbon spectra of the *t*-Boc and formamidine derivatives, which indicated >95% of one conformer, **15a** and **15b**, respectively. For the *t*-Boc derivative **15a**, metalation–alkylation was performed using *sec*-butyllithium–TMEDA in ether at −78 °C followed by addition of several electrophiles (Table III).

As seen from the table the three electrophiles added to **15a** all gave high (>98%) proportions of equatorial product **17a** (R = D, Me, TMS). When compared to the results of the second alkylation in the piperidine *t*-Boc case (Scheme I), the results appear, *a priori*, to be in conflict. However, the *t*-Boc group in **15a** can readily align itself to bring in the lithium base to remove the equatorial proton. This is mainly because the C-8 substituent occupies an axial position and therefore does not inhibit the *t*-Boc–Li complex **A**. Although **17a** can presumably exist in two conformations (**17a** and **18a**), the latter is unlikely for reasons given above for **16a**, as well as the additional nonbonded interactions created by the axial substituent E. The alkylation of **15a** with iodomethane gave a single detectable product **17a** (E = Me), in which the C-2 proton at 3.90 ppm exhibited an outer line separation of only 27 Hz while J_{Me-H} = 6.6 Hz, leaving a J ($J_{2H3H_{eq}} + J_{2H3H_{ax}}$) of 7 Hz. Thus, it was again necessary to remove the *t*-Boc moiety and compare the ^1H NMR data of the free base to those previously reported by Booth. The result of this comparison confirmed the equatorial methyl isomer **17c** (E = Me). *Thus, once again, the t-Boc group directed the second substitution to the position trans to that of the first substituent.*

(10) (a) Hoppe, D.; Hintze, F.; Tebben, P. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1422 and earlier references cited. (b) Chong, J. M.; Park, S. B. *J. Org. Chem.* **1992**, *57*, 2220. (c) Pearson, W. H.; Lindbeck, A. C. *J. Am. Chem. Soc.* **1991**, *113*, 8546. (d) Iwao, M.; Kuraishi, T. *Heterocycles* **1992**, *34*, 1031.

(11) Booth, H.; Griffiths, D. V. *J. Chem. Soc., Perkin Trans II* **1975**, 111.

Table III. Alkylation of *cis*-Decahydroquinolines **15a** and **15b**



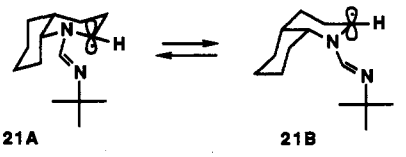
cpd[a]	E^+	alkylation conditions	product	ratio 17:19	yield (%)
15a	MeOD	−78 °C	**17a** (E = D)	>98:2	90[b]
15a	Me_3SiCl	−78 °C → 25 °C, 12 h	**17a** (E = TMS)	>98:2	64
15a	MeI	−78 °C → 25 °C, 12 h	**17a** (E = Me)	>98:2	63[c]
15b	MeOD	−78 °C	**17b** (E = D)	>98:2	87[d]
15b	Me_3SiCl	−78 °C → −55 °C, 12 h	**17b** (E = TMS)	>98:2	84
15b	Me_3SnCl	−78 °C → −55 °C, 12 h	**17b** (E = Me_3Sn)	>98:2	78
15b	MeI	−78 °C → −55 °C, 12 h	**17b** (E = Me)	>98:2	80[e]
15b	MeI	CuC≡CPr (1.5 equiv) −78 °C → −55 °C, 12 h	**17b** (E = Me) **19b**	60:40	70[f]
15b	*n*-PrI	−78 °C → −55 °C, 12 h			*g*
15b	*n*-PrI	CuC≡CPr (1.5 equiv) −78 °C → −55 °C, 12 h			*h*
15b	*n*-PrI	HMPA (1.5 equiv) −78 °C → −55 °C, 12 h			*i*
15b	allyl-Br	CuC≡CPr (1.5 equiv) −78 °C → −55 °C, 12 h	**17b** **19b**	50:50	76[j]
15b	allyl-Br	HMPA (1.5 equiv) −78 °C → −55 °C, 12 h	**17b** **19b**	50:50	50[k]

[a] Metalation conditions: **15a**, *s*-BuLi, TMEDA, ether, −78 °C; **15b**, *t*-BuLi, ether–THF (4:1), −20 °C. [b] 70% D-incorporation. [c] Product accompanied by 6% **15a** and 4% electron-transfer product (e.g. **11**). [d] 93% D-incorporation. [e] Product accompanied by 6% **15b** and 4% electron-transfer product (e.g. **11**). [f] Product accompanied by 10% **15b**. [g] Only starting material **15b** (50%) and electron-transfer product (50%) were obtained. [h] Mixture containing 30% alkylation product, 20% starting material, and 50% electron-transfer product. [i] Mixture containing 12% alkylation product, 25% starting material, and 64% electron-transfer product (e.g. **11**). [j] Product accompanied by 5% electron-transfer product. [k] Product accompanied by 50% electron-transfer product.

For the formamidine derivative **15b**, metalation–alkylation was carried out in the usual manner (*tert*-butyllithium, ether–THF, electrophile) and the results are tabulated in Table III. As seen, introduction of deuterium, trimethylsilyl, and trimethylstannyl groups all proceeded with high stereoselectivity and high yield to **17b**. Likewise, iodomethane gave essentially a single isomer and the stereochemistry was supported by NMR analysis as follows. Irradiation of the methyl doublet at 1.2 ppm resulted in an ill-resolved multiple AB quartet with *J* values of 10.3 and 2.5 Hz. This is quite typical of the axial orientation of the 2-H in **17b**. Furthermore, removal of the formamidine moiety with hydrazine–EtOH–HOAc gave a single product **20** (E = Me), whose NMR data compared quite nicely with the published NMR data for this compound.[8]

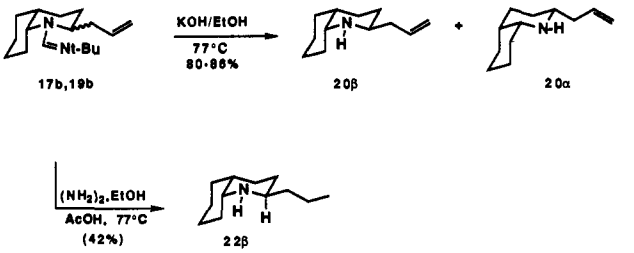
Attempts to introduce the *n*-propyl group into lithiated **15b** to give **17b** (E = *n*-Pr) failed under all conditions (Table III) with the only products being that derived from electron transfer (e.g. **11**) and recovered starting material. Thus, the nucleophilic displacement on alkyl groups larger than methyl (except allylic or benzylic) appeared to be futile, consistent with results for other N-activating systems reported by Gawley[9] and Beak.[2] However, in our earlier report regarding piperidine systems, we observed successful alkylations of a variety of alkyl halides[4] when mediated by copper(I). Even though pentynylcopper was introduced to lithio-**15b**, only poor yields (12–30%) of propylation occurred while significant amounts of ET products were observed, presumably through pathways similar to those shown in Scheme III.

The failure to produce propylated material **17b** (E = Pr) prompted us to re-examine the methylation of **15b** in the presence of pentynylcopper. As seen from Table III, this resulted in a surprisingly poor (60:40) ratio of epimeric methylated products **17b** and **19b**, respectively. These products may result from a conformational equilibrium (**21A**, **21B**) of the radical species



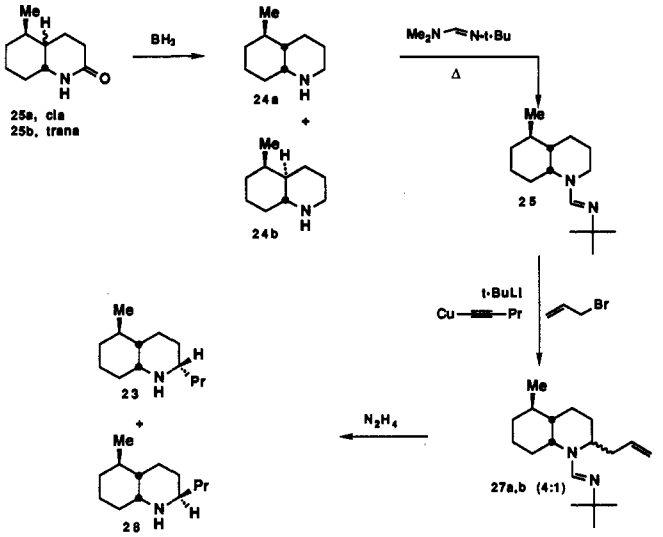
initiated by SET, as suggested earlier in the case of *trans*-decahydroquinoline. It was also necessary to confirm that the other product in the cuprate methylation (**19b**) was actually an epimer of **17b**. Since the NMR spectrum of the 60:40 mixture above was very complex presumably due to the inversion processes taking place, the formamidines were removed and the mixture was separated and compared to both known compounds[8] **17c** (R = H) and **19** (R = H, E = Me), which confirmed that the two products were indeed epimers.

To assess where the boundaries lie for alkylation of **15b**, since iodomethane did alkylate whereas iodopropane did not, we introduced allyl bromide (Table III). In both cases examined (HMPA or pentynylcopper), we were dissappointed to find a lack of stereoselectivity (**17b**:**19b**; 1:1) although reasonable yields of allylated product were obtained. Once again, the use of pentynylcopper to transform the initially formed lithio derivative into a cuprate resulted in a complete lack of stereoselective alkylation. Stereochemical assignment of the mixture from allylation of **15b** was performed after removing the formamidine group in **17b** and **19b** by alkaline hydrolysis to afford both epimers **20**β and **20**α, whose ^{1}H NMR spectra were analyzed in a manner



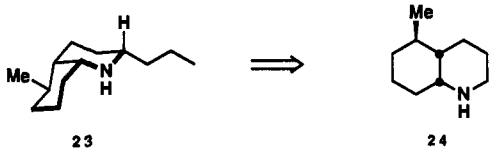
similar to that previously reported by Booth.[11] Interestingly, when the formamidine group was removed using the hydrazine method, the allyl group was simultaneously reduced and a 42% yield of the β-epimer **22** was isolated. This reduction of olefinic

Scheme IV



substituents during the hydrazinolysis has been observed in other related systems and appears to be general.[12]

Finally as an application of the formamidine alkylations, we were drawn to the synthesis of pumiliotoxin C (**23**), a substance that has received considerable attention as a synthetic target in recent years.[5,15,16] It was our intention to simply elaborate the 5β-methyl-*cis*-decahydroquinoline **24** by the metalation–alkylation studies described herein. The route to **24** and the rapid entry into the pumiliotoxin C family is outlined in Scheme IV.



23 **24**

The bicyclic lactam **25** was prepared according to the Diels–Alder strategy described by Overman[5] and was obtained in multigram quantities as a 4:1 mixture of *cis* and *trans* isomers. Borane reduction of the mixture gave an 88% combined yield of decahydroquinoline isomers (75:25) **24a** and **24b**, which were readily separated by chromatography on silica to pure isomers. The stereochemical assignment of each was achieved by NMR analysis of related methylated decahydroquinolines.[8]

The major quinoline isomer (**24a**, 75%) was transformed into the formamidine **26** by thermal exchange with the (dimethylamino)formamidine in 55% yield. Metalation with *tert*-butyllithium followed by introduction of pentynylcopper was then followed by the addition of allyl bromide. In view of the allyl bromide addition to **15b** earlier, wherein no selectivity was observed (Table III), we were expecting similar results with alkylation of **26**. Although we could assess the ratio of products, it was not possible to assign the stereochemistry on **27** although the combined yield was over 80%. This was mainly due to the poorly defined signals of the appropriate protons resulting from the statistical distribution of two equilibrating chair–chair, *cis*-fused, decahydroquinoline ring systems.[5,8,15,16] However, we were able to assess the stereochemical outcome after removal of the formamidine moiety. Thus, when the mixture **27** was treated with hydrazine–ethanol–water, both the formamidine was removed and the propene side chain was reduced cleanly to furnish pumilitoxin C (**23**) and its epimer (**28**). The two epimers (**23** and **28**) were separated by column chromatography to give pure isomers in a 1:4 weight ratio, respectively. The spectral data were in complete accord with the literature data.[5,8,15,16] The latter result therefore indicates that there was some selectivity (4:1) in the allylation step **26** → **27**. This is in contrast to the lack of stereochemical alkylation of **15b** and undoubtedly must be due to the 5-methyl group and its conformational influence on the radical intermediates of type **21A** and **21B**.

(12) Milot, G.; Meyers, A. I. Unpublished results. The authors have now demonstrated in a number of related examples that Cu^{2+} in trace quantities is necessary to effect C=C reduction. Details will be published in the near future.

(13) Castro, C. E.; Stephens, R. D. *J. Org. Chem.* **1963**, *28*, 3313.

(14) We are thankful to Dr. T. T. Shawe of our laboratory for the preparation of **25**.

(15) LeBel, N. A.; Balasubramanian, N. *J. Am. Chem. Soc.* **1989**, *111*, 3363.

(16) Polniaszek, R. P.; Dillard, L. W. *J. Org. Chem.* **1992**, *57*, 4103.

Experimental Section

Solvents used in these experiments were prepared by refluxing over the appropriate drying agent with storage over molecular sieves (3 Å) under a blanket of argon. Methylene chloride and triethylamine were distilled under argon from calcium hydride. Diethyl ether and tetrahydrofuran were distilled under an atmosphere of argon from sodium–benzophenone ketyl. Chromatographic solvents were redistilled prior to use. Aldrich Grade 951 silica gel refers to Catalog No. 34,333-1 silica catalyst support. Metalation–alkylations were routinely carried out under a positive pressure of argon that had been passed through a calcium sulfate drying tube and a deoxygenation column consisting of a BASF copper-based catalyst operating at 200–220 °C and stirred by means of a Teflon-coated magnetic stirring bar, unless otherwise noted. Pentynylcopper was prepared as described by Castro.[13]

***trans*-Decahydroquinoline (7).** The title compound **7** was prepared according the literature procedure:[7] mp 48 °C (lit. 48 °C); IR (film) 3271, 2919, 2848, 2790, 1443, 1331, 1296, 1231, 1125, 984 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) δ 0.93–1.76 (m, 13H), 2.04–2.12 (m, 1H), 2.60–2.69 (ddd, 1H, J = 2.9, 11.9, 11.9 Hz), 3.02–3.07 (app d, 1H, J = 2.0, 11.8 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 25.42, 26.08, 27.09, 32.26, 32.44, 33.81, 43.12, 47.17, 61.92.

***N*-(*N'-tert*-Butylformimidoyl)-*trans*-decahydroquinoline (3).** *trans*-Decahydroquinoline (**7**) (1.0 g, 7.1 mmol), *N,N*-dimethyl-*N'-tert*-butylformamidine[4] (4.6 g, 36.0 mmol), and a catalytic amount of ammonium sulfate (100 mg) in 20 mL of dry xylene were heated to reflux for 48 h. The solvent was removed under reduced pressure and the residue purified by flash chromatography on silica gel (Aldrich Grade 951) deactivated with 5% triethylamine in hexanes and eluted with the same solvent mixture. Further purification was accomplished by vacuum distillation (Kugelrohr 150 °C, 0.1 mmHg) to yield 1.27 g (79%) of **3** as a clear, colorless oil: IR (film) 2921, 2855, 1626, 1447, 1354, 1251, 1212, 1191, 931 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) δ 1.00–1.72 (m, 20H), 1.86–1.91 (app dd, 1H, J = 9.4 Hz), 2.03–2.07 (app dd, 1H, J = 3.1, 12.0 Hz), 2.39–2.48 (ddd, 1H, J = 4.29, 12.8, 12.8 Hz), 2.55–2.63 (m, 1H), 4.42–4.46 (app d, 1H, J = 12.8 Hz), 7.61 (s, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 24.71, 25.58, 25.87, 29.53, 31.36, 32.89, 32.92, 42.79, 44.31, 53.17, 63.48 147.00. Anal. Calcd for $C_{14}H_{26}N_2$: C, 75.60; H, 11.79; N, 12.60. Found: C, 75.48; H, 11.75; N, 12.47.

***cis*-Decahydroquinoline[6] (6).** A solution of freshly distilled 2,3-cyclohexenopyridine (Aldrich) (15.3 g, 114.5 mmol) in 30 mL of acetic acid containing 1.5 g of rhodium (5% on alumina) was hydrogenated under 40 psi of hydrogen at 55 °C for a period of 3 days. The catalyst was removed by filtration through Celite, and the acidic solution was basified (40% sodium hydroxide solution) and extracted several times with hexanes. The combined portions were dried over K_2CO_3, filtered, and concentrated under reduced pressure. Distillation of the residue (bp 77 °C, 10 mmHg (lit.[6] 80–83 °C, 13 mmHg)) gave 11.0 g (70%) of a 97.6% (GC assay) pure *cis* product as a colorless oil: IR (film) 3275, 2920, 2853, 2787, 1441, 1358, 1302, 1136, 1103, 1064, 965, 843, 766, 632 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) δ 1.10–1.80 (m, 13H), 2.61–2.69 (ddd, 1H, J = 3.7, 12.0, 12.0 Hz), 2.83–2.84 (app d, 1H, J = 3.4 Hz), 3.00–3.06 (app d, 1H, J = 12.1 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 21.40 (broad), 22.60 (broad), 25.46 (broad), 26.28 (broad), 27.14 (broad), 29.72 (broad), 31.82 (broad), 32.29 (broad), 32.48 (broad), 35.67, 46.69 (broad), 54.95.

***N*-(*N'-tert*-Butylformimidoyl)-*cis*-decahydroquinoline (1).** *cis*-Decahydroquinoline (**6**) (4.5 g, 31.2 mmoL), *N,N*-dimethyl-*N'-tert*-butylformamidine (6.0 g, 46.9 mmol), and a catalytic amount of ammonium

sulfate (500 mg) in 100 mL of dry xylene were heated to reflux for 48 h. The solvent was removed under reduced pressure and the product purified by flash chromatography on silica gel (Aldrich Grade 951) deactivated with 5% triethylamine in hexanes and eluted with the same solvent mixture. Further purification was accomplished by vacuum distillation (Kugelrohr 150 °C, 0.1 mmHg) to yield 5.3 g (76%) of **1** as a clear, colorless oil: IR (film) 2923, 2851, 1641, 1466, 1446, 1405, 1348, 1261, 1210, 1194, 1148, 1128, 1112, 989, 841 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) δ 1.15 (s, 9H), 1.25–1.89 (m, 13H), 2.72–2.80 (app t, 1H, J = 12.6 Hz), 3.47 (app s (broad), 1H), 3.67 (app d (broad), 1H), 7.32 (s, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 20.39, 24.29, 24.88, 25.50, 25.60, 31.36, 31.43, 35.37, 39.79 (broad), 52.79, 56.99 (broad), 151.00. Anal. Calcd for $C_{14}H_{26}N_2$: C, 75.60; H, 11.79; N, 12.60. Found: C, 75.46; H, 11.73; N, 12.54.

***N*-((*tert*-Butoxy)carbonyl)-*trans*-decahydroquinoline (4).** A solution of *trans*-decahydroisoquinoline (**7**) (1.0 g, 7.1 mmol), triethylamine (2.0 mL, 15 mmol), and DMAP (180 mg) in 20 mL of CH_2Cl_2 was treated with a solution of di-*tert*-butyl dicarbonate (1.8 mL, 8.6 mmol). The mixture was diluted with 15 mL of water and extracted with CH_2Cl_2 (2 × 10 mL). The combined extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The desired material was isolated by column chromatography on silica gel (Aldrich, Grade 951) eluted with 5% ethyl acetate in hexanes. Further purification was accomplished by vacuum distillation (Kugelrohr 150 °C, 0.1 mmHg) to yield 1.5 g (89%) of 4 as a clear, colorless oil: IR (film) 2926, 2856, 1691, 1478, 1449, 1407, 1363, 1279, 1246, 1146, 1083, 987, 770 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) δ 0.90–1.90 (m, 12H), 1.45 (s, 9H), 2.08 (m, 1H), 2.97–3.06 (ddd, 1H, J = 3.1, 10.6, 10.6 Hz), 3.12–3.22 (ddd, 1H, J = 5.0, 10.6, 10.6 Hz), 3.57–3.64 (ddd, 1H, J = 2.8, 6.5, 10.6 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 22.96 (t), 25.62 (t), 26.15 (t), 27.33 (t), 28.50 (q), 31.54 (t), 33.18 (t), 38.23 (d), 39.12 (t), 61.86 (d), 78.84 (s), 155.46 (s). Anal. Calcd for $C_{14}H_{25}NO_2$: C, 70.23; H, 10.53; N, 5.85. Found: C, 70.16; H, 10.50; N, 5.81.

***N*-((*tert*-Butoxy)carbonyl)-*cis*-decahydroquinoline (2).** A solution of *cis*-decahydroquinoline (**6**) (1.5 g, 10.7 mmol), triethylamine (3.0 mL, 21.4 mmol), and DMAP (130 mg) in 20 mL of CH_2Cl_2 was treated with a solution of di-*tert*-butyl dicarbonate (3.0 mL, 13.0 mmol). Workup and purification as described for **4** gave 2.4 g (95%) of **2** as a clear, colorless oil: IR (film) 2829, 2862, 1693, 1470, 1447, 1410, 1364, 1312, 1269, 1251, 1181, 1147, 1128, 1088, 1043, 993 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) δ 1.23–1.86 (m, 13H), 1.45 (s, 9H), 2.69–2.78 (ddd, 1H, J = 2.0, 12.3, 12.3 Hz), 3.82–3.95 (dm, 1H, J = 2.2, 12.2 Hz), 4.00–4.12 (app dt, 1H, J = 4.6, 12.4 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 20.30 (t), 23.80 (t), 23.92 (t), 25.71 (t), 27.83 (t), 28.45 (q), 31.43 (t), 34.99 (d), 38.79 (t), 52.91 (d), 78.88 (s), 154.96 (s). Anal. Calcd for $C_{14}H_{25}NO_2$: C, 70.23; H, 10.53; N, 5.85. Found: C, 70.35; H, 10.46; N, 5.90.

***N*-(*N'*-*tert*-Butylformimidoyl)-2β-deuterio-*trans*-decahydroquinoline (8a).** A solution of formimidoyl **3** (109 mg, 0.45 mmol) in a mixture of ether (1.0 mL) and THF (0.25 mL), cooled at –78 °C with an acetone–dry ice bath, was treated with a 1.7 M solution of *tert*-butyllithium in pentanes (0.40 mL, 0.67 mmol, 1.5 equiv). This resulted in the formation of a yellow precipitate that dissolved when the temperature was raised to –20 °C. During 2.5 h at –20 °C, a white precipitate again formed. The lithio derivative was quenched at –78 °C by the direct addition of deuteriomethanol (Aldrich 99.5%, 0.10 mL, 2.20 mmol, 10 equiv), and the reaction mixture was stirred at this temperature for 1 h.

The reaction mixture was quenched with 1 mL of a 4:1 mixture of saturated sodium chloride solution and water, made basic (2 N) by the addition of solid NaOH, and then transferred into 10 mL of hexanes in a separatory funnel. The organic layer contained a copious precipitate that was digested by the addition of 3 mL of basic brine and vigorous shaking. The organic layer was washed with an additional 3 mL of basic brine, and the aqueous layer was back-extracted with 10 mL of hexanes. The combined organic layers were dried on Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the crude mixture by column chromatography on silica gel deactivated with 5% triethylamine in hexanes and eluted with the same solvent mixture provided 100 mg (92%) of **8a** as a colorless oil: IR (film) 2915, 2843, 1628, 1446, 1353, 1296, 1275, 1213, 1187 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) δ 0.87–1.72 (m 19H), 1.86–1.92 (m, 1H), 2.04–2.08 (dd, 1H, J = 3.1, 11.8 Hz), 2.40–2.45 (app dd, 1H, J = 3.5, 10 Hz), 2.55–2.67 (m, 1H), 4.45 (dm, 0.1H), 7.60 (s, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 24.61, 25.58, 25.87, 29.52, 31.36, 32.89, 42.79, 44.32 (t, J = 23.5 Hz), 53.13, 63.43, 147.00.

***N*-(*N'*-*tert*-Butylformimidoyl)-2β-(trimethylsilyl)-*trans*-decahydroquinoline (8b).** Using the same metalation procedure described above, a solution of formimidoyl **3** (106 mg, 0.48 mmol) in a mixture of ether (1.0 mL) and THF (0.25 mL) was treated with a 1.7 M solution of *tert*-butyllithium in pentanes (0.40 mL, 0.67 mmol, 1.5 equiv), followed by the addition at –78 °C of chlorotrimethylsilane (0.16 mL, 1.3 mmol, 3 equiv). The solution was stirred overnight at –20 °C, followed by workup as described previously. Purification of the crude mixture by column chromatography on silica gel deactivated with 5% triethylamine in hexanes and eluted with the same solvent mixture provided 133 mg (95%) of **8b** as a colorless oil: IR (film) 2953, 2922, 2850, 1640, 1445, 1353, 1235, 1204, 1158, 1143, 856, 830 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) δ 0.04 (s, 9H), 0.84–2.00 (m, 22H), 2.10–2.15 (dd, 1H, J = 1.8, 12.1 Hz), 2.65–2.73 (ddd, 1H, J = 3.0, 9.3, 12.3 Hz), 7.36 (s, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ –0.65, 24.19, 25.99, 26.58, 30.76, 31.30, 33.70, 35.62, 43.10, 53.69, 53.91, 67.29, 145.45. Anal. Calcd for $C_{17}H_{34}N_2Si$: C, 69.30; H, 11.64; N, 9.51. Found: C, 69.42; H, 11.68; N, 9.49.

***N*-(*N'*-*tert*-Butylformimidoyl)-2β-methyl-*trans*-decahydroquinoline (8c).** A solution of **3** (100 mg, 0.45 mmol) in a mixture of ether (1.0 mL) and THF (0.25 mL) was treated with a 1.7 M solution of *tert*-butyllithium in pentanes (0.40 mL, 0.67 mmol, 1.5 equiv) as described for **8a**, followed by the addition at –78 °C of HMPA (0.12 mL, 0.67 mmol) and then of a solution of purified iodomethane (0.17 mL, 2.70 mmol, 6 equiv) in 1 mL of diethyl ether. The reaction mixture was stirred overnight at –55 °C. Workup as described previously provided 103 mg (103%) of a pale-yellow oil that was determined by integration of formamidine protons in the proton NMR to consist of 84% desired product, 8% recovered starting material, and 8% a substance assumed to be the single-electron reduction product (**11**). Purification of the crude mixture by column chromatography on silica gel deactivated with 1% triethylamine in hexanes and eluted with the same solvent mixture provided 73 mg (70%) of **8c** as a pale-yellow oil: IR (film) 2953, 2921, 2855, 1637, 1447, 1403, 1370, 1349, 1289, 1207, 1191 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) δ 1.13 (s, 9H), 1.29–1.31 (d, 3H, J = 6.6 Hz), 1.32–1.88 (m, 12H), 2.19–2.22 (d, 1H, J = 9.4 Hz), 2.77–2.85 (dt, 1H, J = 3.5, 10.6 Hz), 3.19–3.70 (m, 1H, J_{2H3H} = 12.28 Hz), 7.49 (s, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 22.97, 25.69, 26.03, 28.59, 29.55, 31.10, 32.47, 33.70, 39.00, 50.84, 53.27, 62.32, 148.66. Anal. Calcd for $C_{15}H_{28}N_2$: C, 76.19; H, 11.95; N, 11.86. Found: C, 76.23; H, 11.99; N, 11.80.

***N*-(*N'*-*tert*-Butylformimidoyl)-2α-methyl-*trans*-decahydroquinoline (ax-8, R = Me).** Using the same metalation procedure described above, a solution of formimidoyl **3** (113 mg, 0.51 mmol) in a mixture of ether (2.0 mL) and THF (0.5 mL) was treated with a 1.7 M solution of *tert*-butyllithium in pentanes (0.40 mL, 0.67 mmol, 1.5 equiv), followed by the addition at –20 °C of pentynylcopper (78 mg, 0.67 mmol). The mixture was stirred for 1 h and then cooled at –20 °C and treated with a solution of purified iodomethane (0.17 mL, 2.70 mmol) in 1 mL of diethyl ether. The reaction mixture was stirred overnight at –20 °C. Workup as described previously provided 116 mg (97%) of a pale-yellow oil that was determined by integration of formamidine protons in the proton NMR to consist of 79% desired product, 15% recovered starting material, and 6% a substance assumed to be the single-electron reduction product (**11**). Purification of the crude mixture by column chromatography on silica gel deactivated with 1% triethylamine in hexanes and eluted with the same solvent mixture provided 75 mg (62%) of **ax-8** (R = Me) as a pale-yellow oil: IR (film) 2956, 2924, 2851, 1624, 1457, 1446, 1357, 1326, 1279, 1242, 1216, 1184, 1195, 1169, 1132 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) δ 1.03–1.10 (d, 3H, J = 6.95 Hz), 1.13 (s, 9H), 1.20–2.20 (m, 13H), 2.79–2.86 (m, 1H), 4.70–4.78 (m, 1H, J_{2H3H} = 5.28 Hz), 7.57 (s, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 14.23, 25.57, 25.68, 25.95, 27.55, 29.13, 29.77, 31.09, 31.37, 32.88, 43.09, 44.53, 53.28, 56.78, 146.45.

2β-Methyl-*trans*-decahydroquinoline (13e). The crude mixture of **8c** obtained from above (400 mg, 1.7 mmol) was dissolved in 15 mL of 95% ethanol and treated with 0.66 mL (21.2 mmol) of hydrazine hydrate and 0.45 mL (8.0 mmol) of acetic acid. The solution was brought to reflux and was stirred for 24 h under argon. The cooled reaction mixture was concentrated under reduced pressure, and the residue was basified by adding a saturated aqueous potassium carbonate solution (5 mL) and extracted with ether (3 × 5 mL). The combined organic phases were dried over potassium carbonate, filtered, and concentrated under reduced pressure. The crude product was chromatographed on silica gel deactivated with a mixture of 5:4:1 ethyl acetate–hexanes–triethylamine and eluted with the same solvent mixture. There was obtained 104 mg

(40%) of 2β-methyldecahydroquinoline:[8] IR (film) 3276, 2922, 2858, 2788, 1654, 1447, 1375, 1335, 1299, 1241, 1179, 1140, 1124, 778, 743 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.90–1.4 (m, 7H), 1.06 (d, 3H, J = 6.3 Hz), 1.45–1.70 (m, 7H), 2.11–2.18 (m, 1H), 2.60–2.72 (m, 1H, J_{2H3H} = 13.8 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 22.78 (q), 25.27 (t), 26.02 (t), 32.06 (t), 32.22 (t), 33.62 (t), 34.74 (t), 42.18 (d), 52.26 (d), 61.71 (d); ^{13}C NMR (C_6D_6, 300 MHz, C_6D_6 = 128.00 ppm) δ 23.25, 25.78, 26.70, 32.53, 32.95, 34.18, 35.39, 42.67, 52.63, 62.24.

2α-Methyl-*trans*-decahydroquinoline (13e). By the same procedure employed above, ax-**8** (R = Me) (301 mg, 1.3 mmol) gave 100 mg (50%) of **13e** as a pale-yellow oil:[8] IR (film) 3268, 2921, 2852, 1447, 1372, 1343, 1240, 1158, 1138, 1014, 781, 738 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.90–1.90 (m, 14H), 1.15 (d, 3H, J = 6.9 Hz), 2.40 (m, 1H), 3.26 (m, 1H, J_{2H3H} = 4.0 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 18.51 (q), 25.54 (t), 26.20 (t), 26.66 (t), 31.19 (t), 32.38 (t), 34.19 (t), 43.80 (d), 47.49 (d), 53.87 (d).

N-((*tert*-Butoxy)carbonyl)-2α-deuterio-*trans*-decahydroquinoline (14a). A solution of **4** (143 mg, 0.60 mmol) in ether (2.0 mL) was treated with TMEDA (181 μL, 1.2 mmol) followed by a 1.25 M solution of *sec*-BuLi in cyclohexane (0.7 mL, 0.9 mmol). The mixture was stirred for 6 h and treated with deuteriomethanol (0.10 mL, 2.2 mmol) and then slowly warmed to room temperature and diluted with 2 mL of a saturated aqueous solution of sodium chloride. The mixture was extracted with ether (3 × 5 mL), and the combined extracts were dried over K_2CO_3 and concentrated under reduced pressure. The residue was purified by filtration on a short plug of silica gel (hexanes/EtOAc (95:5)) to yield 120 mg (84%) of **14a** (92% D-incorporation) as a colorless oil: IR (film) 2926, 2856, 1692, 1450, 1408, 1364, 1310, 1289, 1250, 1179, 1146, 999 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 7.24 ppm) δ 0.80–1.90 (m, 12H), 1.46 (s, 9H), 2.10 (m, 1H), 3.00 (ddd, 1H, J = 3.2, 10.6 Hz), 3.15 (dd, 1H, J = 4.4, 10.6 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 22.78 (t), 25.56 (t), 26.10 (t), 27.21 (t), 28.44 (q), 31.49 (t), 33.13 (t), 38.17 (d), 38.73 (t, J = 21.3 Hz), 61.75 (d), 78.77 (s), 155.39 (s).

N-((*tert*-Butoxy)carbonyl)-2α-(trimethylsilyl)-*trans*-decahydroquinoline (14b). Using the same metalation procedure described above, a solution of **4** (200 mg, 0.83 mmol) in ether (2.5 mL) was treated with TMEDA (345 μL, 2.25 mmol) followed by a 1.24 M solution of *sec*-BuLi in cyclohexane (1.0 mL, 1.24 mmol) and then with chlorotrimethylsilane (200 μL, 0.60 mmol). The residue obtained following the workup described above was chromatographed on silica gel (hexanes/EtOAc (95:5)) to yield 218 mg (84%) of **14b** as a colorless solid: mp 74–75 °C; IR (film) 2931, 2856, 1693, 1449, 1416, 1365, 1284, 1245, 1165, 1120, 990, 897, 852 cm^{-1}; ^{1}H NMR (C_6D_6, 300 MHz) δ 0.34 (s, 9H), 0.82–1.84 (m, 12H), 1.40 (s, 9H), 2.05 (m, 1H), 2.60–2.66 (dd, 1H, J = 5.0, 12.5 Hz), 3.04–3.13 (ddd, 1H, J = 3.2, 10.8 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ –0.45 (q), 24.50 (t), 26.11 (t), 26.22 (t), 28.04 (t), 28.50 (q), 31.72 (t), 33.23 (t), 38.62 (d), 42.50 (d), 63.13 (d), 78.51 (s), 155.97 (s). Anal. Calcd for $C_{17}H_{33}NO_2Si$: C, 65.52; H, 10.68; N, 4.49. Found: C, 65.71; H, 10.72; N, 4.40.

N-((*tert*-Butoxy)carbonyl)-2α-methyl-*trans*-decahydroquinoline (14c). Using the same metalation procedure described above, a solution of 4 (179 mg, 0.75 mmol) in ether (2.0 mL) was treated with TMEDA (210 μL, 1.40 mmol) followed by a 1.25 M solution of *sec*-BuLi in cyclohexane (0.90 mL, 1.12 mmol) and then with dimethyl sulfate (140 μL, 1.50 mmol). Workup as described above gave 129 mg (68%) of **14c** as a colorless oil: IR (film) 2973, 2925, 2855, 1702, 1678, 1453, 1423, 1364, 1336, 1228, 1237, 1178, 1136, 1084, 1008 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.00–2.10 (m, 12H), 1.15–1.18 (d, 3H, J = 7.0 Hz), 1.45 (s, 9H), 2.26 (m, 1H), 2.79–2.87 (ddd, 1H, J = 3.5, 10.0 Hz), 4.39–4.49 (m, 1H, J = 1.2, 5.0, 7.0 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 16.56 (q), 25.82 (t), 26.81 (t), 27.32 (t), 28.50 (t), 29.72 (t), 31.73 (t), 33.77 (t), 40.66 (d), 49.81 (d), 57.53 (d), 78.90 (s), 156.21 (s). Anal. Calcd for $C_{15}H_{27}NO_2$: C, 71.10; H, 10.74; N, 5.53. Found: C, 70.99; H, 10.68; N, 5.51.

N-(N'-*tert*-Butylformimidoyl)-2β-deuterio-*cis*-decahydroquinoline (17b, E = D). Using the same metalation procedure described for **8a**, a solution of **15b** (100 mg, 0.45 mmol) in a mixture of ether (1.0 mL) and tetrahydrofuran (0.5 mL) was treated with a 1.7 M solution of *tert*-butyllithium in pentanes (0.40 mL, 0.67 mmol, 1.5 equiv) followed by addition at –78 °C of deuteriomethanol (0.17 mL, 4.20 mmol). The solution was stirred for 1 h at –78 °C, quenched with 1 mL of a 4:1 mixture of saturated sodium chloride solution and water, made basic (2 N) by the addition of solid NaOH, and then transferred into 10 mL of hexanes in a separatory funnel. The organic layer contained a copious precipitate that was digested by the addition of 3 mL of basic brine and vigorous shaking. The organic layer was washed with an additional 3 mL of basic brine, and the aqueous layer was back-extracted with 10 mL of hexanes. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the residual oil by chromatography on silica gel deactivated with 5% triethylamine in hexanes and eluted with the same solvent mixture provided 87 mg (87%) of **17b** (E = D) as a colorless oil. Proton NMR analysis showed the presence of 7% undeuterated material by integration of the equatorial protons (1-H) and axial (1-H) protons: IR (film) 2953, 2921, 2855, 1643, 1458, 1441, 1403, 1376, 1349, 1278, 1196, 1169, 1131, 1065, 1029, 951, 826 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) δ 1.14 (s, 9H), 1.25–1.89 (m, 13H), 2.73–2.76 (d, 1H, J = 11.7 Hz), 3.44 (s (broad), 1H), 3.46 (s (broad), 0.07H), 7.32 (s, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 20.35, 24.25, 24.80, 25.35, 25.57, 31.32, 31.40, 35.34, 39.69 (broad, CH*D*), 52.74, 56.96 (broad), 150.92.

N-(N'-*tert*-Butylformimidoyl)-2β-trimethylsilyl-*cis*-decahydroquinoline (17b, E = Me_3Si). Using the same metalation procedure described above, a solution of **15b** (222 mg, 1.0 mmol) in a mixture of ether (2.0 mL) and tetrahydrofuran (0.5 mL) was treated with a 1.8 M solution of *tert*-butyllithium in pentanes (850 μL, 1.5 mmol, 1.5 equiv), followed by the addition at –78 °C of chlorotrimethylsilane (400 μL, 3.0 mmol, 3 equiv). The solution was stirred overnight at –20 °C and was followed by workup as described above. Purification of the crude mixture by column chromatography on silica gel deactivated with 5% triethylamine in hexanes and eluted with the same solvent mixture provided 240 mg (84%) of **17b** (E = Me_3Si) as a colorless oil: IR (film) 2921, 2855, 1637, 1456, 1407, 1376, 1354, 1245, 1234, 1201, 1142, 1120, 1033, 831 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) δ 0.09 (s, 9H), 1.13 (s, 9H), 1.15–1.85 (m, 13H), 2.56–2.60 (app d, 1H, J = 12.4 Hz), 4.00 (app d (broad), 1H, J = 10.7 Hz), 7.39 (s, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ –0.89, 20.69, 23.87, 25.72, 26.64, 27.38, 31.40, 31.53, 34.30, 44.33, 53.06, 54.23 (broad), 150,32. Anal. Calcd for $C_{17}H_{34}N_2Si$: C, 69.30; H, 11.64; N, 9.51. Found: C, 69.40; H, 11.56; N, 9.45.

N-(N'-*tert*-Butylformimidoyl)-2β-(trimethylstaannyl)-*cis*-decahydroquinoline (17b, E = Me_3Sn). Using the same metalation procedure described above, a solution of **15b** (200 mg, 0.9 mmol) in a mixture of ether (2.0 mL) and tetrahydrofuran (0.5 mL) was treated with a 1.7 M solution of *tert*-butyllithium in pentanes (0.8 mL, 1.3 mmol, 1.5 equiv), followed by the addition at –78 °C of chlorotrimethylstannane (400 μL, 3.0 mmol, 3 equiv). The solution was stirred overnight at –20 °C, followed by workup as described above. Purification of the residual oil by column chromatography on silica gel deactivated with 5% triethylamine in hexanes and eluted with the same solvent mixture provided 270 mg (78%) of **17b** (E = Me_3Sn) as a colorless oil: IR (film) 2953, 2923, 2861, 1631, 1461, 1405, 1379, 1353, 1271, 1210, 1143, 764 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ –0.02 (t, 9H, J_{MeSn} = 26.0 Hz), 1.08 (s, 9H), 1.13–2.02 (m, H), 2.54–2.59 (m, 1H, J_{2H3H} = 2.4, 13.0 Hz, J_{2HSN} = 13.0 Hz), 3.08–3.14 (dt, 1H, J = 3.9, 12.2 Hz), 7.30 (s, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ –4.14, 20.37, 25.39, 25.82, 27.43, 29.51, 31.49, 31.64, 36.31, 38.93, 52.82, 61.88, 152.43. Anal. Calcd for $C_{17}H_{34}N_2Sn$: C, 53.00; H, 8.90; N, 7.27. Found: C, 53.07; H, 8.95; N, 7.23.

N-(N'-*tert*-Butylformimidoyl)-2β-methyl-*cis*-decahydroquinoline (17b, E = Me). Using the same metalation procedure described above, a solution of **15b** (1.0 g, 4.5 mmol) in a mixture of ether (8.0 mL) and THF (2.0 mL) was treated with a 1.7 M solution of *tert*-butyllithium in pentanes (4.0 mL, 6.7 mmol, 1.5 equiv), followed by addition at –78 °C of a solution of purified iodomethane (1.0 mL, 20.0 mmol, 6 equiv) in 2.0 mL of diethyl ether. Immediate thickening and cloudiness of the mixture was observed, and the reaction mixture was stirred overnight at –78 °C. Workup as described above and purification of the crude mixture by column chromatography on silica gel deactivated with 2% triethylamine in hexanes and eluted with the same solvent mixture provided 840 mg (80%) of **17b** (E = Me) as a pale-yellow oil: IR (film) 2956, 2924, 2851, 1629, 1462, 1446, 1388, 1362, 1347, 1331, 1279, 1205, 1163, 1142, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) δ 1.13 (s, 9H), 1.22–1.24 (d, 3H, J = 6.5 Hz), 1.29–2.00 (m, 13H), 3.30–3.47 (m (broad), 1H, J_{2a3a} = 10.3 Hz, J_{2a3e} = 2.4 Hz), 4.20–4.30 (dt (broad), 1H, J = 4.7, 10.0 Hz), 7.57 (s, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 19.63, 21.19, 22.82, 24.52, 25.17, 30.61, 31.33, 34.32, 35.00, 47.39, 51.81, 53.17, 147.44. Anal. Calcd for $C_{15}H_{28}N_2$: C, 76.19; H, 11.95; N, 11.86. Found: C, 75.97; H, 11.96; N, 11.77.

Mixture of 17b (R = Me) and 19b (R = Me) Using Pentynylcopper. A solution of **15b** (500 mg, 2.25 mmol) in a mixture of ether (4.0 mL) and THF (1.0 mL) was treated with a 1.6 M solution of *tert*-butyllithium in pentanes (2.10 mL, 3.37 mmol, 1.5 equiv). To the suspension of the

lithio compound was added solid pentynylcopper[13] (440 mg, 3.37 mmol). The resulting yellow suspension was stirred at −20 °C for 1 h followed by the addition at −78 °C of a solution of purified iodomethane (371 μL, 6.00 mmol, 3 equiv) in 1 mL of diethyl ether. The reaction mixture was stirred overnight at −20 °C, quenched with 1 mL of a 4:1 mixture of saturated sodium chloride solution and water, and made basic (2 N) by the addition of solid NaOH. After dilution with hexanes (10 mL), the mixture was filtered through Celite and volatiles were removed in vacuo. Purification of the crude mixture by column chromatography on silica gel deactivated with 2% triethylamine in hexanes and eluted with the same solvent mixture provided 370 mg (70%) of **17b**:**19b** (60:40) as a pale-yellow oil: IR (film) (mixture) 2953, 2927, 2855, 1633, 1463, 1447, 1403, 1354, 1283, 1206, 1174, 1136, 1109, 1076, 1043, 956, 945, 929, 847, 749 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) (mixture) δ 1.13 (s, 9H), 1.14–1.15 (s, 9H overlapping a d, 3H), 1.22–1.24 (d, 3H, J = 6.5 Hz), 1.29–2.00 (m, 13H), 3.30–3.60 (two overlapping m (broad), 2H), 4.00 (s (broad), 1H), 4.29 (dt, 1H, J = 4.7, 10.0 Hz), 7.57 (s, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) (mixture) δ 19.50, 20.24, 20.66, 20.84, 21.11, 22.51, 22.71, 24.43, 25.07, 25.99, 29.48, 30.42, 31.23, 31.75, 34.24, 34.92, 35.94, 46.19, 47.30, 51.71, 52.75, 53.06, 56.45, 147.24, 149.95. Anal. Calcd for $C_{15}H_{28}N_2$: C, 76.19; H, 11.95; N, 11.86. Found: C, 76.24; H, 11.90; N, 11.76.

2β-Methyl-*cis*-decahydroquinoline (17c) and 2α-Methyl-*cis*-decahydroquinoline (19, R = H, E = Me). The purified mixture (60:40) of products obtained above (370 mg, 1.35 mmol) was dissolved in 15 mL of 95% ethanol and treated with 0.66 mL (21.2 mmol) of hydrazine hydrate and 0.45 mL (8.0 mmol) of acetic acid. The solution was brought to reflux and was stirred for 24 h under argon. The cooled reaction mixture was concentrated under reduced pressure and the residue diluted with 5 mL of a 1 N aqueous NaOH solution. The amines were then extracted with ether (3 × 5 mL). The combined organic phases were dried over potassium carbonate, filtered, and concentrated under reduced pressure. The crude mixture of products was chromatographed on silica gel deactivated with 10% triethylamine and eluted first with the same solvent mixture and then with a mixture composed of triethylamine–EtOAc–hexanes, 1:5:4. There were obtained 84 mg of 2α-methyl-*cis*-decahydroquinoline (**19**) (E = Me)[11] and 63 mg of 2β-methyl-*cis*-decahydroquinoline (**17c**)[11] (88% combined yield) as pale-yellow oils. **2α-Methyl-*cis*-decahydroquinoline (19)**: IR (film) 3286, 2924, 2851, 1444, 1376, 1316, 1133, 1086, 1008, 774, 741, 668, 649 cm^{-1}; ^{1}H NMR (C_6D_6, 300 MHz) δ 0.5 (s, 1H), 0.96 (d, 3H, J = 6.1 Hz), 1.08–1.54 (m, 10H), 1.64–1.79 (m, 2H), 1.93–2.06 (dq, 1H, J = 3.4, 12.6 Hz), 2.42–2.53 (m, 1H, J_{2H3H} = 13.4 Hz), 2.70–2.73 (dd, 1H, J = 2.9, 5.8 Hz); ^{13}C NMR (C_6D_6, 300 MHz, C_6D_6 = 128.00 ppm) δ 20.89 (t), 23.37 (q), 25.64 (t), 27.39 (t), 30.03 (t), 31.53 (t), 33.85 (t), 35.78 (d), 53.67 (d), 55.58 (d). **2β-Methyl-*cis*-decahydroquinoline (17c)**: IR (film) 3269, 2963, 2855, 1446, 1375, 1145, 935 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) δ 0.99 (d, 3H, J = 6.2 Hz), 1.02–2.00 (m, 14H), 2.80–2.95 (m, 2H); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 20.79 (t), 23.01 (q), 24.56 (t), 25.75 (t), 27.20 (t), 31.09 (t), 34.94 (t), 35.44 (d), 44.60 (d), 54.68 (d).

2α- and 2β-Allyldecahydroquinoline–Formamidines 17b and 19b (E = allyl). A solution of **15b** (500 mg, 2.25 mmol) in a mixture of ether (4.0 mL) and THF (1.0 mL) was treated with a 1.6 M solution of *tert*-butyllithium in pentanes (2.1 mL, 3.4 mmol, 1.5 equiv) and then with solid pentynylcopper[13] (440 mg, 3.4 mmol) at −20 °C followed by the addition at −20 °C of a solution of purified allyl bromide (518 μL, 6.0 mmol) in 1 mL of diethyl ether. The mixture was stirred overnight at −20 °C and worked-up as described above. Purification of the crude mixture by column chromatography on silica gel deactivated with 2% triethylamine in hexanes and eluted with the same solvent mixture provided 450 mg (76%) of the mixture of **17b** and **19b** (E = allyl) as a pale-yellow oil: IR (film) (mixture) 2928, 2850, 1636, 1463, 1442, 1402, 1352, 1286, 1197, 1163, 1041, 985, 908 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) (mixture) δ 1.12 (s, 9H), 1.12–2.10 (m, 14H), 2.10–2.60 (m, 2H), 3.50–3.60 (m, 2H), 3.80 (s (broad), 1H), 4.15–4.19 (dt, 1H, J = 4.8, 10.4 Hz), 4.96–5.09 (m, 2H), 5.70–5.85 (m, 1H), 7.53 (s, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) (mixture) δ 20.81, 21.59, 24.14, 24.38, 24.53, 25.85, 27.43, 28.68, 29.85, 30.15, 31.15, 31.24, 31.34, 31.67, 33.94, 35.83, 36.87, 39.23, 51.05, 51.97, 52.58, 53.06, 116.04, 116.44, 135.68, 137.16, 147.69, 149.96. Anal. Calcd for $C_{17}H_{30}N_2$: C, 77.80; H, 11.52; N, 10.67. Found: C, 77.72; H, 11.48; N, 10.62.

2β-Propenyl-*cis*-decahydroquinoline (20β) and 2α-Propenyl-*cis*-decahydroquinoline (20α). To a solution of *N*-(*N'*-*tert*-butylformimidoyl)-2β- and 2α-allyl-*cis*-decahydroquinoline (**17b–19b**) in a mixture of MeOH–H_2O (2:1) (15 mL) was added solid KOH (1.7 g). The solution was heated at reflux for 24 h. The cooled mixture was extracted several times with hexanes. The combined extracts were dried over sodium sulfate and concentrated. The crude mixture of products was chromatographed on silica gel deactivated with 10% triethylamine and eluted first with the same solvent mixture and then with a mixture composed of triethylamine–ethyl acetate–hexanes, 1:5:4. There were obtained 117 mg of 2α-allyl-*cis*-decahydroquinoline (**20α**) and 100 mg of 2β-allyl-*cis*-decahydroquinoline (**20β**) (80% combined yield) as pale-yellow oils. **2α-Allyl-*cis*-decahydroquinoline (20α)**: IR (film) 3291, 3075, 2925, 2851, 2796, 2722, 1440, 1324, 1305, 1126, 1076, 992, 914, 775, 746, 648 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.9–1.9 (m, 14H), 2.10–2.20 (m, 2H), 2.50–2.60 (m, 1H, J = 2.6, 10.8 Hz), 2.85 (app d, 1H, J = 2.2 Hz), 5.01–5.12 (m, 2H), 5.72–5.86 (m, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 20.45 (t), 25.18 (t), 26.63 (t), 27.48 (t), 30.90 (t), 33.07 (t), 35.33 (d), 41.71 (t), 55.13 (d), 57.24 (d), 116.68 (t), 135.91 (d). **2β-Allyl-*cis*-decahydroquinoline (20β)**: IR (film) 3291, 3075, 2923, 2858, 1654, 1640, 1475, 1355, 1304, 1140, 993, 912 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) δ 0.90–2.20 (m, 16H), 2.75–2.80 (m, 1H, J = 10 Hz), 2.90–2.96 (dt, 1H, J = 4.3, 11.2 Hz), 5.00–5.12 (m, 2H), 5.68–5.81 (m, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 20.83 (t), 24.51 (t), 25.53 (t), 27.29 (t), 30.96 (t), 32.63 (t), 35.45 (d), 41.58 (t), 48.45 (d), 54.44 (d), 116.86 (t), 135.79 (d).

2β-Propyl-*cis*-decahydroquinoline (22β). The purified mixture of products obtained above (**17b–19b**) (407 mg, 2.25 mmol) was dissolved in 15 mL of 95% ethanol and treated with 1.0 mL of hydrazine hydrate and 0.7 mL of acetic acid. The solution was brought to reflux and was stirred for 24 h under argon. The cooled reaction mixture was concentrated under reduced pressure, and the residue was basified by adding a saturated aqueous potassium carbonate solution (5 mL) and extracted with ether (3 × 5 mL). The combined organic phases were dried over potassium carbonate, filtered, and concentrated under reduced pressure. The crude mixture of products was chromatographed on silica gel deactivated with a 5:4:1 mixture of ethyl acetate–hexanes–Et_3N and eluted with the same solvent mixture. There was obtained 200 mg (42%) of 2β-propyl-*cis*-decahydroquinoline (**22**) as a pale-yellow oil: IR (film) 3279, 2923, 2855, 1455, 1326, 1142, 1074, 948, 721 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.90 (t, 3H, J = 7.0 Hz), 1.00–2.00 (m, 18 H), 2.68–2.75 (m, 1H, $J_{1/2heigh}$ = 23 Hz), 2.88–2.95 (dt, 1H, J = 4.2, 11.69 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 14.09 (q), 19.06 (t), 20.84 (t), 24.52 (t), 25.60 (t), 27.29 (t), 31.01 (t), 32.87 (t), 35.75 (d), 39.38 (t), 48.73 (d), 54.46 (d). Anal. Calcd for $C_{17}H_{31}NO_2$ (*t*-Boc derivative): C, 72.55; H, 11.10; N, 4.97. Found: C, 72.57; H, 11.10; N, 4.99.

***N*-((*tert*-Butoxy)carbonyl)-2β-deuterio-*cis*-decahydroquinoline (17a), E = D).** A solution of **15a** (119 mg, 0.50 mmol) in ether (2.0 mL) was treated at −78 °C with TMEDA (166 μL, 1.10 mmol) followed by a 1.24 M solution of *sec*-BuLi in cyclohexane (500 μL, 0.60 mmol). The mixture was stirred for 6 h, treated with deuteriomethanol (0.10 mL, 2.2 mmol), and then slowly warmed to room temperature and diluted with 2 mL of a saturated aqueous solution of sodium chloride. The mixture was extracted with ether (3 × 5 mL), and the combined extracts were dried over K_2CO_3 and concentrated under reduced pressure. The residue was purified by filtration on a short plug of silica gel (hexanes–EtOAc (95:5)) to yield 108 mg (90%) of **17a** (E = D) (70% D-incorporation) as a colorless oil: IR (film) 2928, 2862, 1691, 1407, 1364, 1304, 1287, 1253, 1176, 1140, 1123 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, Me_4Si = 0.00 ppm) δ 1.10–1.90 (m, 13H), 1.39 (s, 9H), 2.65 (d, 1H, J = 12.3 Hz), 4.00 (s (broad), 1H); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 20.26 (t), 23.85 (two C overlapping, t), 25.67 (t), 28.25 (t), 28.40 (q), 31.39 (t), 34.95 (d), 38.55 (d (broad)), 52.34 (d (broad)), 78.87 (s), 154.92 (s).

***N*-((*tert*-Butoxy)carbonyl)-2β-(trimethylsilyl)-*cis*-decahydroquinoline (17a, E = Me_3Si).** Using the same metalation procedure described above, a solution of **15a** (119 mg, 0.50 mmol) in ether (2.0 mL) was treated with TMEDA (200 μL, 1.38 mmol) followed by a 1.24 M solution of *sec*-BuLi in cyclohexane (0.60 mL, 0.75 mmol) and then with chlorotrimethylsilane (135 μL, 1.06 mmol). The residue obtained following the workup described above was chromatographed on silica gel (hexanes–EtOAc (95:5)) to yield 102 mg (64%) of product **17a** (E = Me_3Si) as a white solid: mp 72–73 °C; IR (film) 2973, 2926, 2864, 1688, 1417, 1365, 1286, 1246, 1163, 1107, 1024, 984, 970, 851 cm^{-1}; ^{1}H NMR (C_6D_6, 300 MHz) δ 0.04 (s, 9H), 1.19–1.76 (m, 13H), 1.43 (s, 9H), 2.36 (d, 1H, J = 12.4 Hz), 3.95–4.02 (dt, 1H, J = 4.2, 12.3 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ −0.08 (q), 20.39 (t), 25.08 (t), 25.99 (t), 27.20 (t), 28.47 (q), 31.58 (t), 35.26 (d), 42.76 (d), 55.18 (d), 78.67 (s), 155.38 (s). Anal. Calcd for $C_{17}H_{33}NO_2Si$: C, 65.52; H, 10.68; N, 4.49. Found: C, 65.59; H, 10.66; N, 4.40.

N-((*tert*-Butoxy)carbonyl)-2β-methyl-*cis*-decahydroquinoline (17a, E = Me). Using the same metalation procedure described above, a solution of **15a** (119 mg, 0.50 mmol) in ether (2.0 mL) was treated with TMEDA (200 μL, 1.38 mmol) followed by a 1.24 M solution of *sec*-BuLi in cyclohexane (0.60 mL, 0.75 mmol) and then with purified methyl iodide (160 μL, 2.25 mmol). Workup as described above gave 80 mg (63%) of product **17a** (E = Me) as a colorless: IR (film) 2930, 2867, 1688, 1470, 1396, 1372, 1322, 1248, 1176, 1132, 1098, 1069, 1005, 880, 773 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.24–1.99 (m, 12H), 1.20 (d, 3H, *J* = 6.6 Hz), 1.46 (s, 9H), 2.26 (m, 1H), 3.68–3.75 (dt, 1H, *J* = 4.5, 11.4 Hz), 3.88–3.97 (m, 1H, *J* = 3.0, 5.0, 6.6 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz, $CDCl_3$ = 77.00 ppm) δ 17.88 (t), 19.95 (t), 21.45 (q), 25.09 (t), 26.13 (t), 28.53 (q), 29.49 (t), 30.05 (d), 30.46 (t), 46.27 (d), 54.25 (d), 78.66 (s), 155.0 (s). Anal. Calcd for $C_{15}H_{27}NO_2$: C, 71.10; H, 10.74; N, 5.53. Found: C, 70.98; H, 10.69; N, 5.50.

5-Methyl-*cis*-decahydroquinoline (24a) and 5-Methyl-*trans*-decahydroquinoline (24b). To a solution of a mixture of lactams **25a–25b**[5] (540 mg, 3.22 mmol) in 10 mL of THF was added a 2 M solution of BH_3·SMe_2 (3.5 mL, 7.00 mmol). The solution was heated to reflux for 6 h, cooled, and quenched with a few drops of MeOH. Volatiles were removed in vacuo, and the residue was treated with a 3 N aqueous HCl solution (5 mL). The mixture was stirred vigorously for 3 h, basified (1 N aqueous NaOH), and extracted with ether. Chromatography of the residue (430 mg) (88%) (4:1 mixture as determined by GC) on silica gel deactivated with 5% Et_3N in hexanes and eluted with the same solvent mixture gave 260 mg of **24a** and 100 mg of **24b** (73% combined yield) as colorless oils. **5β-Methyl-*cis*-decahydroquinoline (24a)**: IR (film) 3282, 2929, 2860, 2792, 1442, 1375, 1359, 1311, 1180, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.78 (d, 3H, *J* = 6.6 Hz), 0.80–1.70 (m, 10H), 1.75–1.90 (m, 2H), 2.60 (dt, 1H, *J* = 2.9, 11.7 Hz), 2.75 (ill-resolved dd, 1H, *J* = 2.9, 5.9 Hz), 3.05 (dm, 1H, *J* = 11.5 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 19.82 (q), 21.11 (t), 21.52 (t), 26.99 (t), 27.71 (d), 33.03 (t), 35.33 (t), 42.65 (d), 47.66 (t), 55.60 (d). **5β-Methyl-*trans*-decahydroquinoline (24b)**: IR (film) 3269, 2920, 2853, 2794, 2736, 1667, 1445, 1375, 1326, 1244, 1132, 1066, 969, 880, 828 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.78 (d, 3H, *J* = 6.1 Hz), 0.60–1.70 (m, 11H), 1.90 (ill-resolved dm, 1H, *J* = 13.0 Hz), 2.07 (m, 1H), 2.54 (dt, 1H, *J* = 2.8, 12.0 Hz), 2.91–2.99 (dm, 1H, *J* = 11.8 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 18.92 (q), 24.68 (t), 27.18 (t), 28.86 (t), 34.05 (t), 35.55 (t), 36.20 (d), 47.00 (t), 49.06 (d), 61.31 (d).

N-(*N'-tert*-Butylformimidoyl)-5β-methyl-*cis*-decahydroquinoline (26). A solution of the secondary amine **24a** (260 mg, 1.69 mmol) and *N,N'*-dimethyl-*tert*-butylformamidine (1.1 g, 8.50 mmol) in 15 mL of dry xylene was refluxed for 48 h in the presence of a catalytic amount of ammonium sulfate (80 mg). Volatiles were removed in vacuo, and the residue was distilled at 200 °C (0.5 mmHg) to afford 222 mg (55%) of **26** as a colorless oil: IR (film) 2960, 2930, 2862, 1642, 1462, 1410, 1378, 1355, 1259, 1210, 1192, 1155, 1120 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.05 (d, 3H, *J* = 7.3 Hz), 1.15 (s, 9H), 1.16–1.9 (m, 12H), 1.73–1.81 (dt, 1H, *J* = 3.6 Hz), 3.55 (m (broad), 1H), 3.7 (d (broad), 1H, *J* = 13.9 Hz), 7.9 (s, 1H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 19.01 (q), 19.99 (t), 24.88 (t), 25.17 (t), 26.53 (t), 31.31 (q), 33.85 (d), 39.58 (t (broad)), 41.54 (d), 52.76 (s), 53.88 (d), 151.02 (d). Anal. Calcd for $C_{15}H_{28}N_2$: C, 76.21; H, 11.93; N, 11.85. Found: C, 75.95; H, 11.89; N, 11.89.

Mixture of *N*-(*N'-tert*-Butylformimidoyl)-2α-propenyl-5-methyl-*cis*-decahydroquinoline (27a) and *N*-(*N'-tert*-Butylformimidoyl)-2β-propenyl-5-methyl-*cis*-decahydroquinoline (27b). A solution of **26** (165 mg, 0.69 mmol) in a mixture of ether (2.0 mL) and THF (0.5 mL) was treated at −78 °C with a 1.4 M solution of *tert*-butyllithium in pentanes (0.75 mL, 1.05 mmol, 1.5 equiv). The mixture was brought to −20 °C over a period of 1 h and stirred at that temperature for 2 h. Solid pentynylcopper (136 mg, 1.05 mmol) was added (under argon), and the yellow suspension was stirred for 1 h. Purified allyl bromide (170 μL, 2.00 mmol) was injected, and the reaction mixture was stirred overnight at −20 °C and subjected to the standard isolation procedure. Purification of the crude mixture by column chromatography on silica gel deactivated with 2% triethylamine in hexanes and eluted with the same solvent mixture provided 155 mg (81%) of the 4:1 mixture of **27a** and **27b** as a pale-yellow oil. Further purification was achieved by bulb to bulb distillation (200 °C, 0.5 mmHg): IR (film) (mixture) 3073, 2932, 2866, 1633, 1458, 1441, 1376, 1354, 1294, 1267, 1207, 1196, 1163, 989, 913 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) (mixture) δ {0.90–0.93 (d, *J* = 6.9 Hz), 0.94–0.96 (d, *J* = 7.3 Hz), 3H}, {1.34 (s), 1.35 (s), 9H}, 1.00–1.80 (m, H), {2.10 (m), 2.20 (m), 1H}, 2.50 (m, 1H), 3.97 (m, large, 1H), 4.17 (m, large, 1H), 5.10 (m, 2H), 5.85 (m, 1H), {7.37 (s), 7.68 (s), 1H}; ^{13}C NMR ($CDCl_3$, 300 MHz) (mixture) δ 19.23 (q), 19.42 (q), 20.29 (t), 20.62 (t), 22.58 (t), 23.49 (t), 25.72 (t (broad)), 26.69 (t), 26.85 (t), 27.29 (t (broad)), 29.51 (t (broad)), 31.21 (d (broad)), 31.27 (q), 31.36 (q), 31.61 (d, overlapping a broad t), 34.45 (d), 35.31 (t), 39.00 (d (broad)), 41.86 (d), 42.11 (d), 50.04 (d), 50.39 (d), 52.79 (s), 53.14 (s), 115.96 (t), 116.08 (t), 136.57 (d), 137.55 (d), 147.94 (d), 150.05 (d). Anal. Calcd for $C_{18}H_{32}N_2$ (mixture): C, 78.20; H, 11.66; N, 10.13. Found: C, 78.28; H, 11.64; N, 10.07.

Preparation of Pumiliotoxin C (23) and 2-*epi*-Pumiliotoxin C (28). By the same procedure employed in the transformation of 2-propenyl-*cis*-decahydroquinoline (**17b**) to 2-propyl-*cis*-decahydroquinoline (**22**), the mixture of **27a** and **27b** (116 mg, 0.42 mmol) was heated at reflux in EtOH (15 mL) in the presence of hydrazine monohydrate (1.0 mL) and acetic acid (0.7 mL) for 48 h. The reaction mixture was worked-up as described previously, and the residue was chromatographed on silica gel deactivated with 5% Et_3N in hexanes and eluted with the same solvent. There were obtained 13 mg of pumiliotoxin C (**23**) and 51 mg of 2-*epi*-pumiliotoxin C (**28**) (80% combined yield). **Pumiliotoxin C (free base)**: IR (film) 2926, 2863, 2796, 1448, 1376, 1312, 1123, 1094, 1078, 755, 650 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.82–0.84 (d, 3H, *J* = 6.6 Hz), 0.87–1.70 (m, 17H), 1.80–2.00 (overlapping m, 2H), 2.49–2.55 (large m, 1H, $J_{1/2\text{height width}}$ = 19.6 Hz, C_2H), 2.83–2.85 (m, 1H, $J_{1/2\text{height width}}$ = 8.4 Hz, $C_{8a}H$); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 14.33 (q), 19.17 (t), 19.93 (q), 21.28 (t), 27.10 (t), 27.40 (overlapping d and t), 33.49 (t), 35.96 (t), 39.80 (t), 42.62 (d), 55.98 (d), 57.74 (d). **2-*epi*-Pumiliotoxin C**: IR (film) 3280, 2926, 2869, 1463, 1376, 1360, 1303, 1206, 1131, 1079, 971, 943, 865, 742, 720 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86–0.92 (m, 3H), 0.97–1.00 (d, 3H, *J* = 7.2 Hz), 1.01–1.89 (m, 17H), 2.75–2.81 (m, 1H, C_2H), 3.07–3.13 (dt, 1H, *J* = 4.3, 10.5 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 14.16 (q), 19.24 (t), 19.32 (q), 20.47 (t), 25.26 (t (broad)), 28.47 (t (broad)), 31.54 (t (broad)), 32.50 (d (broad)), 38.51 (t (broad)), 41.97 (d), 49.43 (d), 49.92 (d).

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