Aryl Radical Endo Cyclization of Enamidines. Selective Preparation of Trans and Cis Fused Octahydrobenzo[*f*]quinolines

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Aryl radicals from *N*-protected 6-[2-(2-halophenyl)ethyl]-1,2,3,4-tetrahydropyridines and 6-[3-(2-halophenyl)propyl]-1,2,3,4-tetrahydropyridines undergo intramolecular cyclization onto the enamide/enamidine double bond by 6-endo and 7-endo closure, respectively. In the 6-endo cyclization the trans/cis ratio of the formed *N*-protected octahydrobenzo[*f*]quinoline can be controlled, and selective synthesis of either the trans or the cis isomer can be achieved with triphenyltin hydride and tris(trimethylsilyl)silicon hydride, respectively. In the 7-endo cyclization to *N*-protected octahydro-1*H*-benzo[3,4]cyclohepta[1,2-*b*]pyridine, the trans fused isomer predominates, although the selectivity is low. The oxidized cyclization products, with a restored enamide/enamidine double bond, are formed at low concentrations of tris(trimethylsilyl)silicon hydride.

Introduction

Radical cyclization of 5-hexenyl and 6-heptenyl radicals occurs normally with a preference for exo cyclization.[1] Functional groups that allow the intermediate radical to be stabilized frequently alter the exo/endo cyclization ratio. Several examples of 5-hexenyl and 6-heptenyl type radical cyclizations onto an enamide or enamine double bond where the regioselectivity of the cyclization is influenced not only by the nitrogen atom but also by a second stabilizing group have been reported.[2] Rigby[3] and Schults[4] have conducted selective 6-endo and 7-endo cyclizations of aryl radicals onto hydroindole and hydroquinoline enamide systems. To our knowledge, all reported alkyl and aryl radical cyclizations onto cyclic enamides and enamines result in the formation of heterocycles comprising the nitrogen atom in the new ring formed (type I, Figure 1).

We herein report a radical endo cyclization where a carbocycle is created (type II) and demonstrate that for the 6-endo cyclization proper selection of reaction conditions allows the isolation in fair yields of either (a) the trans fused product, (b) the cis fused product, or (c) the oxidatively cyclized product. The Heck reaction using the same precursors has been shown to provide the exo cyclized products exclusively.[5]

Results

6-Endo Cyclizations. The results are summarized in Schemes 1 and 2 and in Table 1. In a preparative experiment the trans fused product **5a** was isolated in 61% yield from the aryl iodide **1** (Scheme 1). The reaction

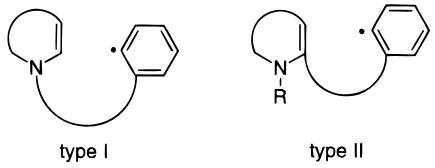

Figure 1.

was conducted in toluene at −20 °C with triphenyltin hydride and with triethylborane as initiator [condition A: $[R_3MH]_0 = 0.03$ M (1.5 equiv), Et_3B[6] (1.0 equiv)]. The amidine **5a** was further converted to the secondary amine

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(1) For selected general reviews and books, see: (a) Curran, D. P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Lonon, 1991; Vol. 4; pp 779−831. (b) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions*; VCH: Weinheim, 1996. (c) Giese, B.; Kopping, B.; Göbel, T.; Dickhaut, J.; Thoma, G.; Kulicke, K. J.; Trach, F. *Org. React.* **1996**, *48*, 301−856. (d) Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237−1286. (e) Motherwell, M. B., Crich, D. In *Best Synthetic Methods, Free Radical Chain Reactions in Organic Synthesis,* Academic Press: London, 1991.

(2) For examples where the nitrogen and the second radical stabilizing group cooperate, see: (a) Colombo, L.; Di Giacomo, M.; Papeo, G.; Carugo, O.; Scolastico, C.; Manzoni, L. *Tetrahedron Lett.* **1994**, *35*, 4031−4034. (b) Colombo, L.; Di Giacomo, M.; Scolastico, C.; Manzoni, L.; Belvisi, L.; Molteni, V. *Tetrahedron Lett.* **1995**, *36*, 625−628. (c) Fang, J.-M.; Chang, H.-T.; Lin, C.-C. *J. Chem. Soc. Chem. Commun.* **1988**, 1385−1388. (d) Fidalgo, J.; Castedo, L.; Domínguez, D. *Tetrahedron Lett.* **1993**, *34*, 7317−7318. (e) Pigeon, P.; Decroix, B. *Tetrahedron Lett.* **1996**, *37*, 7707−7710. (f) Rigby, J. H.; Qabar, M. *J. Am. Chem. Soc.* **1991**, *113*, 8975−8976. (g) Rigby, J. H.; Qabar, M. N. *J. Org. Chem.* **1993**, *58*, 4473−4475. (h) Rodrígues, G.; Cid, M. M.; Saá, C.; Castedo, L.; Domínguez, D. *J. Org. Chem.* **1996**, *61*, 2780−2782. (i) Takano, S.; Suzuki, M.; Ogasawara, K. *Heterocycles* **1990**, *31*, 1151−1156. (j) Takano, S.; Suzuki, M.; Kijima, A.; Ogasawara, K. *Tetrahedron Lett.* **1990**, *31*, 2315−2318. (k) Yang, C.-C.; Fang, J.-M. *J. Chem. Soc., Perkin Trans. 1* **1995**, 879−887. For examples of cyclizations where the directing effect of the nitrogen and the second stabilizing group counteracts, see ref 2b and the following: (l) Beckwith, A. L. J.; Westwood, S. W. *Tetrahedron* **1989**, *45*, 5269−5282. (m) Beckwith, A. L. J.; Joseph, S. P.; Mayadunne, R. T. A. *J. Org. Chem.* **1993**, *58*, 4198−4199. (n) Cladingboel, D. E.; Parsons, P. J. *J. Chem. Soc. Chem. Commun.* **1990**, 1543−1544. (o) Ishibashi, H.; Kawanami, H.; Iriyama, H.; Ikeda, M. *Tetrahedron Lett.* **1995**, *36*, 6733−6734. (p) Ishibashi, H.; Kawanami, H.; Ikeda, M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 817−821. (q) Lee, E.; Li, K. S.; Lim, J. *Tetrahedron Lett.* **1996**, *37*, 1445−1446. (r) Parker, K. A.; Fokas, D. *J. Org. Chem.* **1994**, *59*, 3927−3932. (s) Özlü, Y.; Cladingboel, D. E.; Parsons, P. J. *Tetrahedron* **1994**, *50*, 2183−2206. See also: (t) Glover, S. A.; Warkentin, J. *J. Org. Chem.* **1993**, *58*, 2115−2121. (u) Okano, T.; Sakaida, T.; Eguchi, S. *J. Org. Chem.* **1996**, *61*, 8826−8830.

(3) Rigby, J. H.; Mateo, M. E. *Tetrahedron* **1996**, *52*, 10569−10582.

(4) (a) Schultz, A. G.; Holoboski, M. A.; Smyth, M. S. *J. Am. Chem. Soc.* **1993**, *115*, 7904−7905. (b) Schultz, A. G.; Guzzo, P. R.; Nowak, D. M. *J. Org. Chem.* **1995**, *60*, 8044−8050. (c) Schultz, A. G.; Holoboski, M. A.; Smyth, M. S. *J. Am. Chem. Soc.* **1996**, *118*, 6210−6219.

(5) (a) Ripa, L.; Hallberg, A. *J. Org. Chem.* **1996**, *61*, 7147−7155. (b) Ripa, L.; Hallberg, A. *J. Org. Chem.* **1997**, *62*, 595−602.

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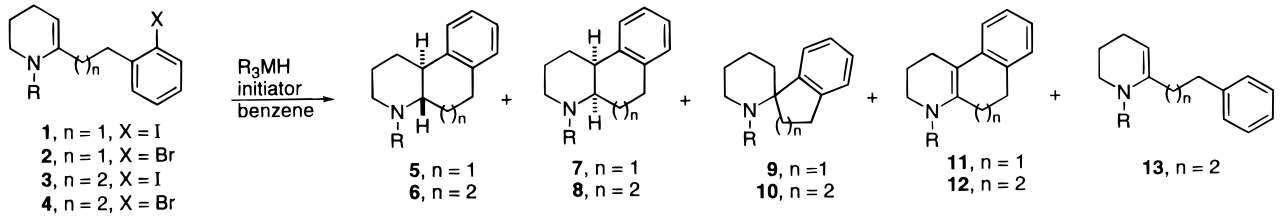
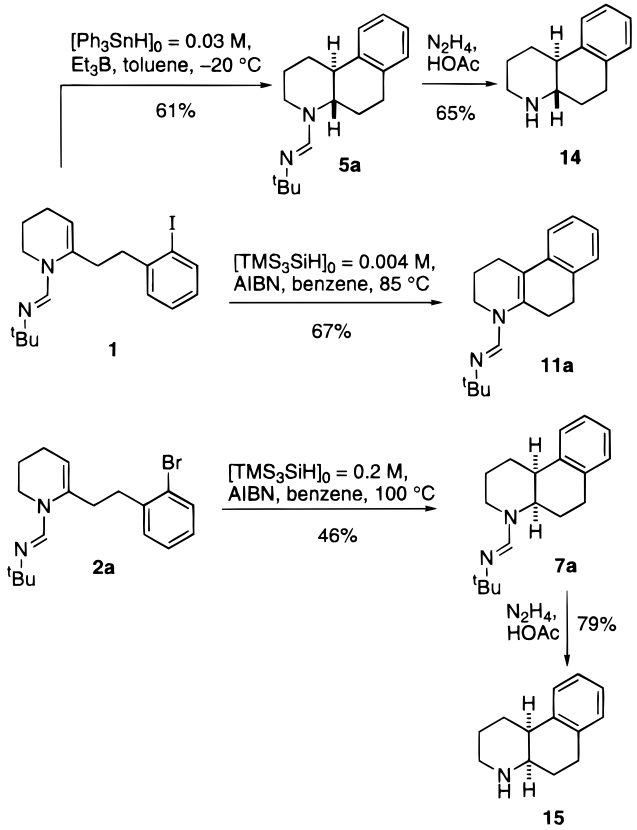
Table 1. Product Distribution in Radical Cyclization Reactions of 1−4



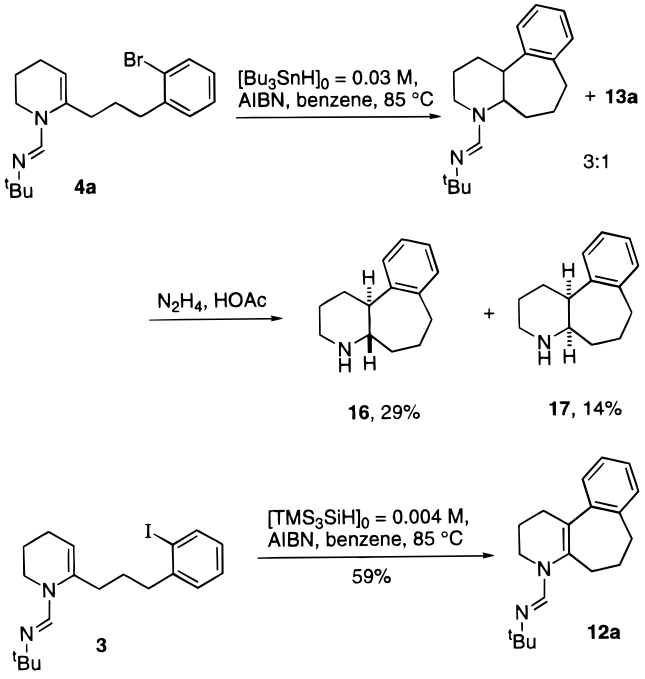
entry		R	R_3MH	cond[a]	temp, °C	cyclization products	ratio of cyclized products[b] trans/cis	endo/exo	red/ox	dehalogenate product	cyclization dehalogenation	% yield
1	**1**	TBF	Ph_3SnH	A[c]	−20	**5a**+**7a**	12:1					84[d]
2	**1**		Ph_3SnH	A	20	**5a**+**7a**	6:1					76[d]
3	**1**		Ph_3SnH	A	85	**5a**+**7a**	5:1					85[d]
4	**1**		Ph_3SnH	B	85	**5a**+**7a**	3:1					74[d]
5	**1**		TMS_3SiH	D	85	**5a**+**7a**+**11a**	1:2		1:15			81[d]
6	**1**		Bu_3SnH	D	85	**5a**+**7a**	3.8:1					77[d]
7	**2a**	TBF	Ph_3SnH	B	85	**5a**+**7a**+**9a**	2.3:1	49:1				85[d]
8	**2a**		Bu_3SnH	B	85	**5a**+**7a**+**9a**	2.4:1	99:1				74[d]
9	**2a**		TMS_3SiH	C	100	**5a**+**7a**+**11a**	1:5.5		12:1			77[d]
10	**2b**	CHO	Ph_3SnH	B	85	**5b**+**7b**+**9b**	3:1	24:1				76[e]
11	**2b**		Bu_3SnH	B	85	**5b**+**7b**+**9b**	9:1	32:1				39[e]
12	**2b**		TMS_3SiH	C	100	**5b**+**7b**+**11b**	1:5		5:1			31[e]
13	**3**	TBF	TMS_3SiH	D	85	**12a**						59[e]
14	**4a**	TBF	Bu_3SnH	B	85	**6a**+**8a**	2:1[f]			**13a**	3:1	99[d]
15	**4a**		Ph_3SnH	B	85	**6a**+**8a**	2:1[f]			**13a**	2:1	82[d]
16	**4a**		TMS_3SiH	C[g]	100	**6a**+**8a**+**12a**	4:1[f]		6.5:1	**13a**	9:1	81[d]
17	**4b**	CHO	Bu_3SnH	B	85	**6b**+**8b**	1:1			**13b**	1.2:1	56[e]

[a] Conditions: A = $[R_3MH]_0$ = 0.03 M (1.5 equiv), Et_3B (1.0 equiv); B = $[R_3MH]_0$ = 0.03 M (1.5 equiv), AIBN (0.1 equiv); C = $[R_3MH]_0$ = 0.2 M (2.0 equiv), AIBN (0.3 equiv); D = $[R_3MH]_0$ = 0.004 (1.2 equiv), AIBN (1.0 equiv). Reactions were run overnight; see ref 41. [b] The isomer ratio was determined by GLC−MS, and the response factors for the isomers were assumed to be identical. When nothing is denoted, the amount was below the detection limit. [c] Toluene was used as solvent. [d] Isolated combined yield after acid/base extraction. [e] Isolated combined yield after chromatography. [f] The **6a**/**8a** ratio was determined by GLC−MS after hydrazinolysis to the secondary amines **16** and **17**. [g] One equivalent of AIBN was used.

Scheme 1



Scheme 2



14 by hydrazinolysis in 65% yield. An inferior trans/cis ratio was encountered after increasing the reaction temperature (cf. entries 1−3). Reactions at the same temperature (85 °C) revealed that triethylborane, as

(6) Triethylborane is known to initiate radical reactions at low temperatures: (a) Nozaki, K.; Oshima, K.; Utimoto, K. *J. Am. Chem. Soc.* **1987**, *109*, 2547−2549. (b) Miura, K.; Ichinose, Y.; Nozaki, K.; Fugami, K.; Oshima, K.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 143−147. See also: (c) Brown, H. C.; Midland, M. M. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 692−700.

compared to azobisisobutyronitrile (AIBN), as initiator provided a better trans/cis ratio (cf. entries 3 and 4). The corresponding aryl bromide **2a** was not suitable as a precursor for the trans product **5a** since **2a** remained intact at the low temperatures required for fair trans/cis selectivity.[7] With AIBN as initiator [condition B: $[R_3MH]_0 = 0.03$ M (1.5 equiv), AIBN (0.1 equiv)] at 85 °C the aryl bromide **2a**, as compared to the aryl iodide **1**, tended to provide more of the cis compound, with a minor amount of the spiro compound **9a** also formed (cf. entries 4 and 7). Substitution of triphenyltin hydride for tributyltin hydride (entry 8) or an alteration of the hydride concentration (0.15 or 0.06 M) had no significant effect on the product ratio. Cyclization of the aryl bromide **2b** (enamide instead of enamidine) employing triphenyltin hydride (condition B) resulted in a similar outcome as with the aryl bromide **2a** (entry 10). However, a combination of **2b** and tributyltin hydride delivered a higher trans/cis ratio (9:1), although the isolated yield was low (entry 11).

The cis fused amidine **7a** could be prepared in 46% yield, after chromatography, by cyclization of **2a** in the presence of tris(trimethylsilyl)silicon hydride[8] [condition C: $[R_3MH]_0 = 0.2$ M (2.0 equiv), AIBN (0.3 equiv)] at 100 °C. Subsequent hydrazinolysis of **7a** gave the secondary amine **15** in 79% yield (Scheme 1). The silicon hydride provided a reversed trans/cis ratio with the cis product predominant. In all experiments performed with tris(trimethylsilyl)silicon hydride, a varying amount of the oxidized[9] product **11a** was obtained, but the formation of this product could be suppressed by using a high concentration[2d] of the silicon hydride (entry 9). A similar product distribution with preference for the cis fused isomer was obtained after cyclization of the enamide **2b** in the presence of tris(trimethylsilyl)silicon hydride, although the yield was low in this case (entry 12).[10]

The preparation of the amidine **11a** was accomplished by refluxing the aryl iodide **1** in the presence of a low concentration of tris(trimethylsilyl)silicon hydride [condition D: $[R_3MH]_0 = 0.004$ M (1.2 equiv), AIBN (1.0 equiv)] and 1 equiv of AIBN. A 67% yield of **11a** was isolated (Scheme 1 and entry 5). No consumption of the starting material was observed in the absence of silicon hydride, and a catalytic amount of tris(trimethylsilyl)silicon hydride (0.1 equiv) caused decomposition of the starting material as deduced from GC−MS. Attempts to improve the yield by either employing a smaller amount of AIBN or by adding tris(trimethylsilyl)silicon hydride and AIBN slowly with a syringe pump met with no success. Furthermore, substitution of the tris(trimethylsilyl)silicon hydride for tributyltin hydride, under otherwise identical conditions, led exclusively to the formation of the trans and cis fused products (cf. entries 5 and 6). The aryl bromide **2a** was not prone to react under the conditions where the corresponding aryl iodide **1** reacted smoothly.

7-Endo Cyclizations. Cyclization of **4a** under the conditions A, B, or C furnished either no or low trans/cis selectivity (entries 14−16). With tributyltin hydride under condition B the 7-endo cyclized product was isolated as a mixture of **6a** and **8a** together with the dehalogenated uncyclized product **13a** in a quantitative yield (Scheme 2). Subsequent hydrazinolysis provided the trans and cis fused secondary amines, **16** and **17**, which were isolated in 29% and 14% yield, respectively. Attempts to minimize the dehalogenation by slow addition of tributyltin hydride and AIBN resulted in only minor improvements and with lower yields. A more prevailed dehalogenation was observed with triphenyltin hydride as compared to tributyltin hydride (entry 15), and a combination of triethylborane and aryl iodide **3** (condition A) led to an incomplete conversion and a more predominant formation of **13a**. Tris(trimethylsilyl)silicon hydride as radical chain carrier (condition C) suppressed the formation of **13a** but led to formation of the oxidized product **12a** in a low yield (entry 16). Cyclization of the enamide **4b** under condition B delivered an inferior cyclization/dehalogenation ratio (cf. entries 14 and 17).

Cyclization of enamidine **3** in the presence of tris(trimethylsilyl)silicon hydride at low concentration (condition D) proceeded smoothly and the enamidine **12a** was isolated in 59% yield (Scheme 2 and entry 13).

Attempted 5-Endo Cyclizations. Attempts to cyclize the aryl iodide **21** in a disfavored 5-endo[11] mode, with tributyltin hydride (condition B), led only to the dehalogenated starting material.[12] Lowering the tributyltin hydride concentration by a syringe pump technique or employing tris(trimethylsilyl)silicon hydride resulted in incomplete conversion and no cyclized products.[13]

Determination of the Relative Configuration. The stereochemical assignments of the trans and cis fused cyclization products are based on ^1H and ^{13}C NMR analysis in $CDCl_3$ and in CD_3OD. The *cis*-octahydrobenzo[*f*]quinoline system is reported to exist in two interconvertible conformations,[14] both of which have the angular proton H-4a in a syn-relationship with respect to the nitrogen lone pair. The rigid *trans*-octahydrobenzo[*f*]quinoline system conversely has the angular proton H-4a in an anti position with respect to the nitrogen lone pair. This results in deshielding of the H-4a proton in compound **15** as compared to the H-4a proton in **14**, due to the shielding effect of the nitrogen lone pair.[15] To confirm the stereochemical assignments, compounds **14** and **15** were converted to their *N*-benzylated deriva-

(7) Even at 85 °C the starting material remained intact. See also ref 6b.

(8) Chatgilialoglu, C. *Acc. Chem. Res* **1992**, *25*, 188−194.

(9) Bowman, R. W.; Heaney, H.; Jordan, B. M. *Tetrahedron* **1991**, *47*, 10119−10128. See also refs 2d and 3.

(10) The structure of compound **11b** was confirmed by comparison (GC−MS) with a hydrolyzed (KOH, MeOH/H_2O) sample of **11a**.

(11) For examples of disfavored 5-endo cyclization onto enamides by carbamoylmethyl radicals, see: (a) Goodall, K.; Parsons, A. F. *J. Chem. Soc., Perkin Trans. 1* **1994**, 3257−3259. (b) Ishibashi, H.; Nakamura, N.; Sato, T.; Takeuchi, M.; Ikeda, M. *Tetrahedron Lett.* **1991**, *32*, 1725−1728. (c) Ishibashi, H.; Fuke, Y.; Yamashita, T.; Ikeda, M. *Tetrahedron: Asymmetry* **1996**, *7*, 2531−2538. (d) Sato, T.; Machigashira, N.; Ishibashi, H.; Ikeda, M. *Heterocycles* **1992**, *33*, 139−142. (e) Sato, T.; Nakamura, N.; Ikeda, K.; Okada, M.; Ishibashi, H.; Ikeda, M. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2399−2407. (f) Sato, T.; Chono, N.; Ishibashi, H.; Ikeda, M. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1115−1120. See also ref 4b.

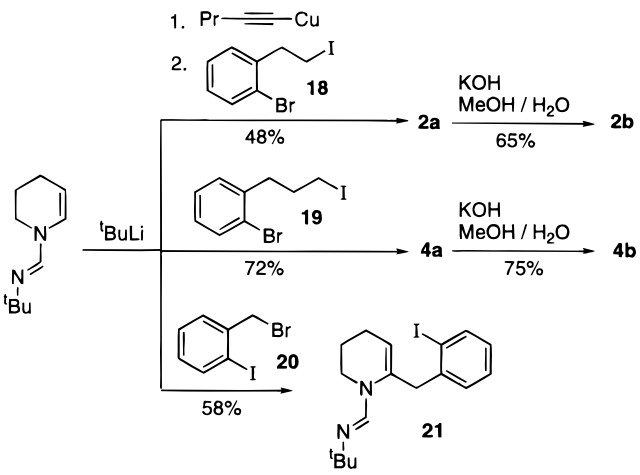
(12) Spectroscopic data was consistent with data described elsewhere: Meyers, A. I.; Edwards, P. D.; Bailey, T. R.; Jagdmann, G. E. J. *J. Org. Chem.* **1985**, *50*, 1019−1026.

(13) Ikeda and co-workers have shown that the cyclization does not occur unless a carbonyl group is incorporated in the new ring formed; see refs 11b and 11d.

(14) (a) Cannon, J. G.; Hatheway, G. J.; Long, J. P.; Sharabi, F. M. *J. Med. Chem.* **1976**, *19*, 987−993. (b) Cannon, J. G.; Suarez-Gutierrez, C.; Lee, T.; Long, J. P.; Costall, B.; Fortune, D. H.; Naylor, R. J. *J. Med. Chem.* **1979**, *22*, 341−347. (c) Cannon, J. G. *Adv. Biosci.* **1979**, *20 (Peipher. Dopaminergic Recept.)*, 87−94.

(15) Rubiralta, M.; Giralt, E.; Diez, A. *Piperidine. Structure, Preparation, Reactivity, and Synthetic Applications of Piperidine and its Derivatives; Studies in Organic Chemistry 43*; Elsevier: Amsterdam, 1991.

Scheme 3



tives.[16] The *N*-benzyl methylene protons of the trans isomer gave rise to a pair of doublets, while the corresponding protons in the cis isomer appeared as a singlet.[17]

For the *trans*- and *cis*-octahydro-1*H*-benzo[3,4]cyclohepta[1,2-*b*]pyridine system, molecular mechanics calculations[18] revealed one low-energy conformation (within 2.6 kcal/mol) for the cis fused ring system **17** having the H-4a proton in a syn relationship to the nitrogen lone pair and five low-energy conformations (within 4.2 kcal/mol) for the trans fused **16** all having the H-4a proton anti with respect to the nitrogen lone pair. This is consistent with the observation that the H-4a proton in compound **16** resonates at a higher field than the corresponding proton in **17**.

Synthesis of Precursors. Compounds **1** and **3** were prepared as described earlier.[5a] In an analogous reaction sequence, the amidines **2a**, **4a,** and **21** were prepared by lithiation and alkylation[19] of *N*-(*N′-tert*-butylformimidoyl)-1,2,3,4-tetrahydropyridine[12] with the corresponding 2-halophenyl alkyl halides in 48%, 72%, and 58% yield, respectively (Scheme 3). Subsequent hydrolysis[5b] of the enamidines **2a** and **4a** afforded the enamides **2b** and **4b** in 65% and 75% yield, respectively.

Discussion

The α-nitrogen radical is derived either from a direct endo cyclization of the aryl radical or alternatively from

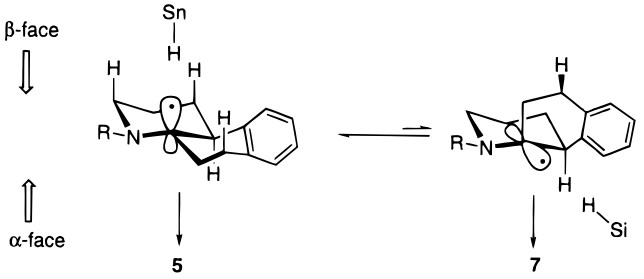


Figure 2.

consecutive exo cyclization and neophyl rearrangement.[20] The ratio of endo/exo cyclization was not affected by the hydride concentration, suggesting that the former process is operating.[21] The trans fused product **5a** should be obtained after an axial hydrogen abstraction by the postcyclization radical[22] (Figure 2) which is anticipated to be slightly pyramidalized.[23] The unpaired electron involved in forming the new bond and the electron pair at the nitrogen atom remain in one plane so that a stabilizing interaction can occur. An axial attack at the stabilized radical is favored,[24] and a *β*-face selective abstraction of hydrogen from the tin hydrides proceeds. However, with the bulkier silicon hydride an approach from the axial direction seems less attractive due to 1,3-steric repulsions, as deduced from an analysis of molecular models. The barrier to inversion is low and an equatorial attack by the silicon hydride at the less hindered α-face appears more favorable,[25] eventually leading to the cis fused product **7a**.

With the more flexible seven-membered cyclic system, although the selectivities are low, all hydride reagents preferentially attack at the *β*-face. This preference should be attributed to stereoelectronic factors, but no simple explanation is apparent to us, which explains the relatively low trans/cis selectivity encountered.[26] The large amount of dehalogenated product in the cyclization of **4a**, as compared to cyclization of **2**, also at low hydride concentrations, originates mainly from a competing intramolecular 1,5-hydride shift, delivering a stabilized allylic radical.[27] An experiment with tributyltin deuteride clearly demonstrated that the 1,5-hydride shift was the dominating reduction mechanism.

(16) The secondary amines were stirrred with K_2CO_3 (2.6 equiv) and benzyl bromide (1.0 equiv) in acetonitrile under argon.

(17) (a) Cannon, J. G.; Koble-Suarez, C.; Long, J. P.; Ilhan, M.; Bhatnagar, R. K. *J. Pharm. Sci.* **1985**, *74*, 672−675. (b) Cannon, J. G.; Kirschbaum, K. S. *Synthesis* **1993**, 1151−1154. (c) Walsh, D. A.; Smissman, E. E. *J. Org. Chem.* **1974**, *39*, 3705−3708.

(18) The calculations of model compounds **16** an **17** were performed using the MM2* force as implemented in the program Macromodel version 5.5. (a) Still, W. C.; Tempczyk, A.; Hawley, R. C.; Hendrickson, T. *J. Am. Chem. Soc.* **1990**, *112*, 6127−6129. The general born solvent accessible surface area (GB/SA) method for $CHCl_3$ developed by Still was used in the calculations. (b) Mohamadi, F.; Richards, N. G. J.; Guida, W. C.; Liskamp, R.; Lipton, M.; Caufield, C.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comput. Chem.* **1990**, *11*, 440−467. The number of torsion angles allowed to vary simultaneously during each Monte Carlo step ranged from one to four. Conformational searches was conducted by use of the systematic unbound multiple minimum search (SUMM) method in the batchmin program (command SSPMC). (c) Goodman, J. M.; Still, W. C. *J. Comput. Chem.* **1991**, *12*, 1110−1117. 5000-step runs were performed, and those conformations within 50 kJ/mol of the global minimum were kept.

(19) When 2-(2′-bromophenyl)ethyl iodide was used as alkylating agent, the vinyllithium was treated with pentynylcopper prior to alkylation to avoid competing elimination; see ref 5a.

(20) The latter process has recently been discussed as a possible mechanism for endo cyclization of aryl radicals onto enamides; see ref 2p.

(21) (a) Abeywickrema, A. N.; Beckwith, A. L. J.; Gerba, S. *J. Org. Chem.* **1987**, *52*, 4072−4078. (b) Parker, K. A.; Spero, D. M.; Inman, K. C. *Tetrahedron Lett.* **1986**, *27*, 2833−2836.

(22) The α-nitrogen radical may be sufficiently persistent to relax, prior to hydrogen abstraction, to the configurationally more stable chair−chair structure with the aryl group in equatorial position; see ref 2g for an example.

(23) Structural studies of α-aminoalkyl radicals give contradictory results, see: Renaud, P.; Giraud, L. *Synthesis* **1996**, 913−926.

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(25) The trans/cis ratio for the reduction of the bridgehead octahydronaphthalene radical is reported to depend on the size of the hydrogen atom donor, giving more cis fused product with bulkier hydrogen donors. Beckwith, A. L. J.; Gream, G. E.; Struble, D. L. *Aust. J. Chem.* **1972**, *25*, 1081−1105.

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To enforce oxidation, and to provide **11a** and **12a**, we took advantage of the relatively slow hydrogen donor tris(trimethylsilyl)silicon hydride.[28] At a low concentration of this hydride, hydrogen transfer to the postcyclization radical is inefficient and the concomitant oxidation by either single electron transfer[29] followed by proton loss or β-hydrogen atom abstraction[30] predominates.[31]

Conclusion

We have demonstrated that intramolecular radical arylations of cyclic enamidines and enamides can be accomplished to give the endo cyclized products. A selective preparation of either the trans fused product, the cis fused product, or the oxidized compound, the latter with a restored double bond, can be achieved with the enamidine in the 6-endo cyclization.

Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra were recorded at 270 and 67.8 MHz, respectively (400 and 100 MHz for compound **11a**, **16,** and **17**). Spectra were recorded at ambient temperature with $CDCl_3$ as solvent (unless otherwize noted) and tetramethylsilane as internal standard. Peak assignments of the cyclized products were made by ^{13}C−^{13}C and ^{1}H−^{13}C correlation experiments. Coupling constants are given as absolute values. Low-resolution electron-impact MS spectra were measured at an ionization potential of 70 eV. The mass detector was interfaced with a gas chromatograph equipped with a HP-1 (25 m × 0.2 mm) column. Isomers were assumed to have the same response factors. Infrared spectra were recorded on a FTIR spectrophotometer as solutions in $CDCl_3$ unless otherwise noted. Elemental analyses were performed by Mikro Kemi AB, Uppsala, Sweden, or by Analytische Laboratorium, Prof. Dr. H. Malissa and G. Reuter GmbH, Gummersbach, Germany. Melting points were determined in open capillary tubes in a melting point microscope and are uncorrected. Thin-layer chromatography (TLC) was carried out on aluminum sheets precoated with silica gel 60 F_{254} (0.25 mm, Macherey-Nagel). Column chromatography was performed on silica gel S (0.032−0.063 mm, Riedel-de Haën) or silica gel 60 (fine) (0.015−0.040 mm, E. Merck) and centrifugal chromatography was carried out on a Harrison Research Chromatotron (model 7924T) with silica gel 60 PF_{254} containing gypsum (E. Merck) as solid phase. Preparative thin-layer chromatography was carried out on glass sheets precoated with silica gel 60 F_{254} (2.0 mm, E. Merck).

Materials. Benzene was distilled from Na and degassed with argon prior to use. Azobisisobutyronitrile (AIBN), tributyltin hydride (Bu_3SnH), triphenyltin hydride (Ph_3SnH), tributyltin deuteride (Bu_3SnD), and tris(trimethylsilyl)silicon hydride (TMS_3SiH) were used as received. Compounds **18**[32] and **19**[32b,33] were prepared according to a synthetic strategy described elsewhere,[34] and only previously unreported data are given here. 2-Iodobenzyl bromide **20**[32a] was synthesized from 2-iodobenzyl alcohol (Aldrich) as described elsewhere.[35] 2-(2′-Bromophenyl)ethyl mesylate[36] is a known compounds, and only previously unreported data are given here. *N*-(*N*′-*tert*-Butylformimidoyl)-1,2,3,4-tetrahydropyridine was prepared as described previously.[5a,12] Pentynylcopper was prepared from pentyne and CuI.[37] All other reagents were obtained from commercial sources and used as received.

2-(2′-Bromophenyl)ethyl Mesylate.[36] 2-(2′-Bromophenyl)-ethanol[32a,38] (47 g, 0.23 mol) and triethylamine (48 mL, 0.35 mol) were dissolved in CH_2Cl_2 (500 mL). Methanesulfonyl chloride (20 mL, 0.26 mol) was added dropwise at 0 °C under 30 min, and the solution was stirred for 2 h at room temperature. The solution was washed successively with ice−water (2 × 250 mL), cold 5 N HCl (2 × 250 mL), saturated aqueous $NaHCO_3$ (2 × 250 mL), and brine (2 × 250 mL), dried ($MgSO_4$), and concentrated to yield 2-(2′-bromophenyl)ethyl mesylate (61 g, 93%): ^{1}H NMR δ 7.57 (d, 1H), 7.29−7.24 (m, 2H), 7.17−7.11 (m, 1H), 4.45 (t, J = 6.9 Hz, 2H), 3.21 (t, J = 6.9 Hz, 2H), 2.88 (s, 3H); ^{13}C NMR δ 135.5, 133.0, 131.5, 128.9, 127.7, 124.4, 68.4, 37.2, 35.9; IR 1360, 1175 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 280 (M^+ + 2, 1), 278 (M^+, 1), 184 (100), 182 (100), 171 (37), 169 (37).

3-(2′-Bromophenyl)propyl Mesylate. 3-(2′-Bromophenyl)propyl mesylate was synthesized in 97% yield (14 g, 48 mmol) from 3-(2′-bromophenyl)propanol[33,39] (11 g, 49 mmol) as described above for the synthesis of 2-(2′-bromophenyl)ethyl mesylate: ^{1}H NMR δ 7.54 (d, 1H), 7.29−7.22 (m, 2H), 7.14−7.03 (m, 1H), 4.27 (t, J = 6.3 Hz, 2H), 3.03 (s, 3H), 2.88 (t, J = 7.7 Hz, 2H), 2.14−2.06 (m, 2H); ^{13}C NMR δ 139.6, 133.0, 130.6, 128.1, 127.6, 124.3, 69.0, 37.4, 32.1, 29.1; IR 1359, 1176 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 294 (M^+ + 2, 3), 292 (M^+, 3), 198 (57), 196 (57), 117 (100). Anal. Calcd for $C_{10}H_{13}BrO_3S$: C, 40.97; H, 4.47. Found: C, 41.3; H, 4.6.

2-(2′-Bromophenyl)ethyl Iodide (18).[32] 2-(2-Bromophenyl)ethyl mesylate[36] (5.9 g, 20 mmol) was mixed with NaI (13 g, 85 mmol) in acetone (80 mL), and the mixture was refluxed until TLC indicated full conversion of the starting material. After 2 h water (200 mL) was added and the solution was extracted with diethyl ether (3 × 100 mL). The combined organic layers were washed with water (2 × 50 mL), dried ($MgSO_4$), and concentrated. The product was purified by column chromatography (SiO_2, pentane, R_f 0.44) to yield **18** (6.35 g, 99%) as a clear oil. Spectroscopic data were consistent with data described elsewhere.[32b] ^{13}C NMR δ 139.8, 133.0, 130.7, 128.6, 127.6, 124.0, 40.5, 3.2.

3-(2′-Bromophenyl)propyl Iodide (19). Compound **19** was synthesized from 3-(2′-bromophenyl)propyl mesylate (14 g, 48 mmol) as described above for the synthesis of **18**. The product was purified by column chromatography (SiO_2, pentane, R_f 0.39) to yield **19** (14 g, 87%). Spectroscopic data were consistient with data described elsewere.[33]

***N*-(*N*′-*tert*-Butylformimidoyl)-6-[2-(2-bromophenyl)-ethyl]-1,2,3,4-tetrahydropyridine (2a).** To a solution of *N*-(*N*′-*tert*-butylformimidoyl)-1,2,3,4-tetrahydropyridine[5a,12] (5.5 g, 33 mmol) in 4:1 diethyl ether/THF (33 mL) was added slowly *t*-BuLi (29 mL, 43 mmol, 1.5 M in hexane) at −78 °C under argon. The yellow solution was stirred at −20 °C until a white solid had precipitated (2 h). The reaction mixture was cooled to −50 °C, pentynylcopper[37] (6.0 g, 46 mmol) in THF (33 mL) was added, and the reaction mixture was allowed to stir at −20 °C for 1 h. The reaction mixture was cooled to −78 °C, compound **18** (15 g, 49 mmol) was added, and the mixture was

(27) Such a 1,5-hydride shift occurs readily to an aryl radical especially when a stabilized radical is formed. (a) Cohen, T.; McMullen, C. H.; Smith, K. *J. Am. Chem. Soc.* **1968**, *90*, 6866−6867. (b) Snieckus, V.; Cuevas, J.-C.; Sloan, C. P.; Liu, H.; Curran, D. P. *J. Am. Chem. Soc.* **1990**, *112*, 896−898. See also refs 2l and 4b,c.

(28) Tris(trimethylsilyl)silicon hydride is about 13 times slower than triphenyltin hydride at donating a hydrogen atom to an alkyl radical. Newcomb, M. *Tetrahedron* **1993**, *49*, 1151−1176.

(29) Radicals located α to a nitrogen atom are sensitive to oxidation, see: Curran, D. P. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Ed.; Pergamon: Oxford, 1991; Vol. 4; p 726.

(30) Bogen, S.; Malacria, M. *J. Am. Chem. Soc.* **1996**, *118*, 3992−3993.

(31) Oxidation products has been observed in cyclization reactions of enamides mediated with tributyltin hydride; see refs 2d and 3. A pseudo $S_{RN}1$ mechanism has been suggested for similar processes; see ref 9.

(32) (a) Beak, P.; Allen, D. J.; Lee, W. K. *J. Am. Chem. Soc.* **1990**, *112*, 1629−1630. (b) Wender, P. A.; White, A. W. *J. Am. Chem. Soc.* **1988**, *110*, 2218−2223.

(33) Beak, P.; Allen, D. J. *J. Am. Chem. Soc.* **1992**, *114*, 3420−3425.

(34) Ciulfolini, M. A.; Qi, H.-B.; Browne, M. E. *J. Org. Chem.* **1988**, *53*, 4149−4151.

(35) L′abbé, G.; Leurs, S.; Sannen, I.; Dehaen, W. *Tetrahedron* **1993**, *49*, 4439−4446.

(36) Bickelhaupt, F.; Stach, K.; Thiel, M. *Chem. Ber.* **1965**, *98*, 685−704.

(37) Stephens, R. D.; Castro, C. E. *J. Org. Chem.* **1963**, *28*, 3313−3315.

(38) Gilman, H.; Marrs, O. L. *J. Org. Chem.* **1965**, *30*, 325−328.

(39) Beeby, M. H.; Mann, F. G. *J. Chem. Soc.* **1951**, 411−415.

thereafter stirred at −20 °C overnight. The reaction mixture was filtered, diluted with more diethyl ether, washed several times with aqueous NH_3 (until the aqueous layer no longer was colored blue), and extracted with 3 N HCl (5 × 60 mL). The combined acidic aqueous layers were extracted with CH_2Cl_2 (5 × 60 mL). The combined CH_2Cl_2 layers were washed with 5% aqueous NaOH (2 × 60 mL) and brine (60 mL), dried over K_2CO_3/Na_2SO_4 1:1, and concentrated to a yellow oil. The crude product was filtered through a pad of SiO_2 eluting with 10% triethylamine in pentane[40] to yield **2a** (5.6 g, 48%): ^{1}H NMR δ 7.94 (s, 1H), 7.53 (dd, 1H), 7.24−7.14 (m, 2H), 7.10−7.04 (m, 1H), 4.59 (t, J = 4.0 Hz, 1H), 3.67−3.63 (m, 2H), 2.94−2.85 (m, 2H), 2.56 (app t, 2H), 2.05−1.96 (m, 2H), 1.80−1.69 (m, 2H), 1.22 (s, 9H); ^{13}C NMR δ 145.4, 140.5, 137.7, 132.7, 130.6, 127.8, 127.4, 124.2, 103.1, 53.6, 41.9, 35.2, 33.3, 31.3, 22.5, 21.7; IR 1626 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 350 (M^+ + 2, 17), 348 (M^+, 17), 186 (100). Anal. Calcd for $C_{18}H_{25}BrN_2$: C, 61.89; H, 7.21; N, 8.02. Found: C, 61.8; H, 7.2; N, 8.0

***N*-(*N′-tert*-Butylformimidoyl)-6-[3-(2-bromophenyl)propyl]-1,2,3,4-tetrahydropyridine (4a).** To a solution of *N*-(*N′-tert*-butylformimidoyl)-1,2,3,4-tetrahydropyridine[5a,12] (3.3 g, 20 mmol) in 4:1 diethyl ether/THF (40 mL) was added slowly *t*-BuLi (19 mL, 26 mmol, 1.4 M in hexane) at −78 °C under argon. The yellow solution was stirred at −20 °C until a white solid had precipitated (2 h). The reaction mixture was cooled to −78 °C, compound **19** (9.8 g, 30 mmol) was added, and the reaction mixture was stirred at −20 °C overnight. The reaction mixture was poured into 3 N HCl (150 mL), washed with diethyl ether (3 × 50 mL), and extracted with CH_2Cl_2 (5 × 50 mL). The combined CH_2Cl_2 layers were washed with 1N NaOH (2 × 40 mL), dried over K_2CO_3/Na_2SO_4 1:1, and concentrated to a yellow oil. The crude product was filtered through a pad of SiO_2 eluting with 10% triethylamine in pentane[40] to yield **4a** (5.3 g, 72%): ^{1}H NMR δ 7.76 (s, 1H), 7.52 (dd, 1H), 7.23−7.18 (m, 2H), 7.08−7.02 (m, 1H), 4.62 (t, J = 4.0 Hz, 1H), 3.65−3.61 (m, 2H), 2.78−2.72 (m, 2H), 2.34 (t, J = 7.6 Hz, 2H), 2.05−2.01 (m, 2H), 1.83−1.71 (m, 4H), 1.15 (s, 9H); ^{13}C NMR δ 145.4, 141.2, 138.0, 132.8, 130.3, 127.6, 127.4, 124.4, 102.4, 53.6, 41.8, 35.6, 32.8, 31.2, 28.2, 22.5, 21.8. IR 1625 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 364 (M^+ + 2, 11), 362 (M^+, 11), 193 (100), 97 (97). Anal. Calcd for $C_{19}H_{27}BrN_2$: C, 62.81; H, 7.49; N, 7.71. Found: C, 63.1; H, 7.6; N, 7.6.

***N*-(*N′-tert*-Butylformimidoyl)-6-[(2-iodophenyl)methyl]-1,2,3,4-tetrahydropyridin (21).** Compound **21** was synthesized from *N*-(*N′-tert*-butylformimidoyl)-1,2,3,4-tetrahydropyridine[5a,12] (0.78 g, 4.7 mmol) and 2-iodobenzylbromide (2.1 g, 7.0 mmol) as described above for the synthesis of **3a**. The crude product was filtered through a pad of SiO_2 eluting with 10% triethylamine in pentane[40] to yield **21** (1.1 g, 58%): ^{1}H NMR δ 7.83 (dd, 1H), 7.37 (s, 1H), 7.31−7.19 (m, 2H), 6.94−6.88 (m, 1H), 4.69 (t, J = 3.8 Hz, 1H), 3.72−3.63 (m, AB-spectra, 2H), 2.18−2.12 (m, 2H), 1.89−1.81 (m, 2H), 0.95 (s, 9H); ^{13}C NMR δ 146.3, 140.6, 139.3, 135.8, 128.8, 128.6, 128.3, 105.2, 100.7, 53.5, 45.2, 41.6, 39.6, 31.0, 22.7, 21.6. IR 1633 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 382 (M^+, 75), 179 (85), 172 (100). Anal. Calcd for $C_{17}H_{23}IN_2$: C, 53.41; H, 6.06; N, 7.32. Found: C, 53.8; H, 6.3; N, 6.9.

***N*-Formyl-6-[3-(2-bromophenyl)propyl]-1,2,3,4-tetrahydropyridine (4b).** A solution of **4a** (80 mg, 0.22 mmol) and KOH (85 mg, 1.5 mmol) in MeOH (1.8 mL) and water (0.70 mL) was heated at 60 °C under argon until TLC indicated complete consumption of the enamidine (3 h). Upon cooling, the solvent was removed under reduced pressure and the residue was dissolved in CH_2Cl_2 (3 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (3 × 1 mL) and brine (2 mL), dried (K_2CO_3), and concentrated. Purification by column chromatography [SiO_2 (fine), pentane/EtOAc 3:1, R_f 0.33] gave **4b** (51 mg, 75%). The ^{1}H NMR spectra show the existence of two rotamers in an approximately 98:2 ratio. Shift values are given only for the major isomer. ^{1}H NMR δ 8.51 (s, 1H), 7.53 (app d, 1H), 7.26−7.13 (m, 2H), 7.06 (m, 1H), 4.3 (t, J = 3.5 Hz, 1H), 3.68−3.64 (m, 2H), 2.76 (app t, 2H), 2.44 (app t, 2H), 2.13−2.07 (m, 2H), 1.88−1.73 (m, 4H); ^{13}C NMR δ 159.9, 140.7, 135.4, 132.8, 130.2, 127.7, 127.4, 124.3, 108.8, 39.4, 35.4, 32.0, 27.4, 22.5, 21.4; IR 1647 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 309 (M^+ + 2, 13), 307 (M^+, 13), 228 (8), 125 (53), 97 (100). Anal. Calcd for $C_{15}H_{18}BrNO$: C, 58.45; H, 5.89; N, 4.54. Found: C, 58.6; H, 6.0; N, 4.5.

***N*-Formyl-6-[2-(2-bromophenyl)ethyl]-1,2,3,4-tetrahydropyridine (2b).** Compound **2b** was synthesized from **2a** (1.5 g, 4.2 mmol) as described above for the synthesis of **4b**. Purification by column chromatography (SiO_2, pentane/EtOAc 3:1, R_f 0.24) gave **2b** (0.80 g, 65%). The ^{1}H NMR spectra show the existence of two rotamers in an approximately 98:2 ratio. Shift values are given only for the major isomer. ^{1}H NMR δ 8.69 (s, 1H), 7.54 (app d, 1H), 7.27−7.11 (m, 3H), 4.89 (t, J = 3.8 Hz, 1H), 3.70−3.65 (m, 2H), 2.94 (app t, 2H), 2.66 (app t, 2H), 2.07−2.03 (m, 2H), 1.81−1.73 (m, 2H); ^{13}C NMR δ 159.0, 139.8, 135.1, 132.8, 130.4, 128.0, 127.5, 124.1, 109.4, 39.4, 34.6, 32.7, 22.5, 21.3; IR 1650 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 294 (3), 292 (3), 214 (100), 186 (54). Anal. Calcd for $C_{14}H_{16}BrNO$: C, 57.16; H, 5.48; N, 4.76. Found: C, 57.1 H, 5.6; N, 4.6.

***trans*- and *cis*-4-Formyl-1,2,3,4,4a,5,6,10b-octahydrobenzo[*f*]quinoline (5b and 7b).** Compound **2b** (0.20 g, 0.67 mmol) was dissolved in degassed benzene (33 mL), AIBN (33 mg, 0.2 mmol) and Bu_3SnH (0.29 g, 1.0 mmol) were added, and the solution was refluxed overnight.[41] After cooling, the solvent was evaporated and the residue was dissolved in diethyl ether (15 mL) and stirred with 1 N KF (10 mL) for 2 h. The mixture was filtered and the aqueous layer was extracted with diethyl ether (5 mL). The combined organic layers were dried (K_2CO_3) and concentrated, and the resulting oil was washed with isohexane (3 × 1 mL) to yield the crude product. The mixture was filtered through a short pad of SiO_2 and the cis and trans isomers were isolated with centrifugal chromatography (EtOAc/isohexane 9:1) to yield **5b** (46 mg, 32%) and **7b** (4 mg, 3%). Compound **5b:** ^{1}H NMR δ 8.29 (s, 1H, C*H*O), 7.32−7.07 (m, 4H, Ar−H), 4.75−4.66 (m, 1H, H-3), 3.22 (ddd, J = 12.3, 10.3, and 2.3 Hz, 1H, H-4a), 3.12−2.88 (m, 2H, H-6), 2.68−2.56 (m, 2H, H-1, H-10b), 2.54 (ddd, J = 12.9, 12.9, and 3.2, 1H, H-3), 2.42−2.31 (m, 1H, H-5), 2.16−1.98 (m, 1H, H-5), 1.96−1.84 (m, 1H, H-2), 1.80−1.58 (m, 1H, H-2), 1.55−1.36 (m, 1H, H-1); ^{13}C NMR δ 158.5 (*C*HO), 137.3, 134.6 (C-6a, C-10a), 128.9, 126.5, 126.3, 126.0 (C-7, C-8, C-9, C-10), 60.7 (C-4a), 44.6 (C-10b), 41.8 (C-3), 30.5 (C-1), 29.6 (C-6), 25.8 (C-5), 25.6 (C-2); IR 1642 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 215 (M^+, 58), 170 (62), 144 (89), 129 (100). Compound **7b:** The ^{1}H NMR spectra show the existence of two rotamers in an approximately 1:1 ratio. ^{1}H NMR δ 8.18 and 8.11 (s, 1H, C*H*O), 7.22−7.03 (m, 4H, Ar−H), 4.81 and 3.89 (ddd, J = 13.0, 5.2, and 3.5 Hz, 1H, H-4a), 4.42−4.31 and 3.52−3.41 (m, 1H, H-3), 3.26−3.13 and 2.79−2.66 (m, 1H, H-3), 3.11−2.79 (m, 3H, H-6, H-10b), 2.50−2.30 and 2.30−2.11 (m, 1H, H-5), 2.07−1.93 (m, 1H, H-1), 1.88−1.40 (m, 4H, H-1, H-2, H-5); ^{13}C NMR δ 161.3 and 161.2 (*C*HO), 139.6, 139.5, 134.7, 134.2 (C-6a, C-10a), 129.0, 128.8, 126.3, 126.2, 126.1, 125.9 (two pairs of signals are overlapping) (C-7, C-8, C-9, C-10), 54.8, 47.6 (C-4a), 42.4, 35.9 (C-3), 39.9, 38.3 (C-10b), 31.2, 31.1 (C-1), 29.0 (C-6), 26.4, 25.1 (C-2), 23.4, 21.4 (C-5); IR 1658 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 215 (M^+, 100), 170 (17), 144 (18), 129 (60). For comparison, compounds **5b** and **7b** were converted (MeLi, THF, 0 °C)[5b] to **14** and **15**, respectively.

***trans*- and *cis*-1-Formyl-2,3,4,4a,5,6,7,11b-octahydro-1*H*-benzo[3,4]cyclohepta[1,2-*b*]pyridine (6b and 8b).** Compounds **6b** and **8b** was synthesized from **4b** (0.15 g, 0.50 mmol), AIBN (24 mg, 0.15 mmol), and Bu_3SnH (0.22 g, 0.75 mmol) in degassed benzene (25 mL) as described above for the synthesis of **5b** and **7b**. The mixture was filtered through a short pad of SiO_2 and the cis and trans isomers were isolated with centrifugal chromatography (EtOAc/isohexane 7:3) to yield **6b** (12 mg, 11%) and **8b** (7 mg, 6%), together with a mixed

(40) The amidines were purified essentially according to a procedure developed by Meyers; see ref 12.

(41) The reaction times were not optimized.

fraction of cis and trans isomers (20 mg) and the dehalogenated starting material **13b** (30 mg). The ^{1}H NMR spectra show the existence of two rotamers in an approximately 2:3 ratio for **6b** and 1:1 ratio for **8b**. Compound **6b**: ^{1}H NMR δ 8.02 and 7.99 (s, 1H, C*H*O), 7.24−7.07 (m, 4H, Ar−H), 4.25−4.12 (m, 0.4H, H-3), 3.93−3.80 and 3.22−3.09 (m, 1H, H-4a), 3.52−3.30 (m, 1.2H, H-3), 3.08−2.84 (m, 2.2H, H-3, H-7, H-11b), 2.82−2.68 (m, 1.2H, H-7), 2.26−1.42 (m, 8H, H-1, H-2, H-5, H-6); ^{13}C NMR δ 161.6 and 161.0 (*C*HO), 142.7, 142.2, 141.9, 141.8 (C-7a, C-11a), 129.0, 128.8, 126.6, 126.4, 126.3, 124.5, 124.3 (two peaks overlaps, C-8, C-9, C-10, C-11), 59.9 and 54.6 (C-4a), 42.2 and 41.4 (C-11b), 37.9 and 32.5 (C-3), 37.3 and 34.9 (C-1),35.0 and 34.4 (C-7), 26.5 and 26.2 (C-5), 23.2 and 22.8 (C-2), 22.8 and 21.2 (C-6); IR 1668 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 229 (M$^+$, 100), 184 (43), 143 (62), 129 (70), 115 (55). Compound **8b**: ^{1}H NMR δ 8.13 and 8.02 (s, 1H, C*H*O), 7.26−7.01 (m, 4H, Ar−H), 4.70 and 3.79 (ddd, J = 12.6, 4.1 and 4.1 Hz, 1H, H-4a), 4.33 (m, 0.5H, H-3α) 3.44−3.38 (m, AB-spectra, 1H, H-3β, H-3α) 3.05−2.67 (m, 2.5H, H-3β, H-11b, H-7), 2.65−2.46 (m, 0.5H, H-5), 2.42−2.18 (m, 1.5H), 2.14−1.95 (m, 1H), 1.94−1.76 (m, 2H), 1.75−1.40 (m, 4H); ^{13}C NMR δ 160.8, 160.4 (*C*HO), 142.1 (br), 141.3, 141.0 (C-7a, C-11a), 131.6, 131.4, 130.4, 130.3, 127.0, 126.8, 126.6, 126.5 (C-8, C-9, C-10, C-11), 57.4, 50.1 (C-4a), 52.8, 51.1 (C-11b), 41.7, 35.2 (C-3), 36.7, 36.3 (C-7), 32.2, 30.1, 27.3, 26.7 (br), 25.91, 25.87, 25.8; IR 1656 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 229 (M$^+$, 100), 184 (28), 143 (52), 129 (60), 115 (45). For comparison compounds **6b** and **8b** were converted (MeLi, THF, 0 °C)[5b] to **16** and **17**, respectively.

***trans*-4-(*N*-*tert*-Butylformimidoyl)-1,2,3,4,4a,5,6,10b-octahydrobenzo[*f*]quinoline (5a).** Compound **1** (0.20 g, 0.50 mmol) and Ph_3SnH (0.26 g, 0.70 mmol) were dissolved in toluene (25 mL) and cooled to −20 °C, air was bubbled through the solution for 2 min, Et_3B (0.50 mL, 1 M in hexane, 0.50 mmol) was added, and the solution was stirred at −20 °C overnight.[41] The solvent was evaporated and the resulting residue was partitioned between 3 N HCl (25 mL) and EtOAc (15 mL) until all the white foam was dissolved. The aqueous layer was washed with EtOAc (2 × 15 mL) and the combined organic layers were extracted with 3 N HCl (15 mL). The combined acidic aqueous layers were extracted with CH_2Cl_2 (4 × 20 mL) and the combined CH_2Cl_2 layers were washed with 1 N NaOH (2 × 20 mL), dried (K_2CO_3), and concentrated to yield the crude product (0.13 g). The crude product was purified on preparative TLC (SiO_2, 10% triethylamine in isohexane,[40] R_f 0.28) to yield **5a** as an oil (83 mg, 61%): ^{1}H NMR δ 7.62 (s, 1H, NC*H*═N), 7.30−7.03 (m, 4H, Ar−H), 4.58−4.46 (m, 1H, H-3), 3.07 (ddd, J = 12.2, 10.3, and 2.5 Hz, 1H, H-4a), 3.08−2.88 (m, 2H, H-6), 2.67−2.25 (m, 3H, H-1, H-3, H-10b), 2.32−2.21 (m, 1H, H-5), 2.12−1.88 (m, 1H, H-5), 1.83−1.67 (m, 2H, H-2), 1.52−1.32 (m, 1H, H-1) 1.17 (s, 9H, C(C*H*$_3$)$_3$); ^{13}C NMR δ 146.4, (N═*C*H), 138.5, 135.2 (C-6a, C-10a), 128.7, 126.0 (3C's) (C-7, C-8, C-9, C-10), 61.7 (C-4a), 53.3 (*C*(CH$_3$)$_3$), 44.6 (C-3), 43.6 (C-10b), 31.3 (C(*C*H$_3$)$_3$), 30.9 (C-1), 29.9 (C-6), 26.4 (C-5), 24.5 (C-2); IR 1622 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 270 (M$^+$, 100), 255 (58), 213 (54), 198 (22), 186 (36). Anal. Calcd for $C_{18}H_{26}N_2$: C, 79.95; H, 9.69; N, 10.36. Found: C, 79.8 H, 9.6; N, 10.2.

***cis*-4-(*N*-*tert*-Butylformimidoyl)-1,2,3,4,4a,5,6,10b-octahydrobenzo[*f*]quinoline (7a).** Compound **2a** (0.35 g, 1.0 mmol) was dissolved in degassed benzene (10 mL), AIBN (49 mg, 0.30 mmol) and TMS_3SiH (0.50 g, 2.0 mmol) were added, and the solution was heated in a sealed Pyrex tube at 100 °C overnight.[41] Workup as described for compound **5a** and purification on preparative TLC (SiO_2, 10% triethylamine in isohexane,[40] R_f 0.42) gave **7a** as an oil (0.13 g, 46%): ^{1}H NMR δ 7.40 (s, 1H, NC*H*═N), 7.24−7.06 (m, 4H, Ar−H), 3.92 (app br d, 1H, H-4a), 3.81 (app br d, 1H, H-3), 3.05−2.78 (m, 4H, H-3, H-6, H-10b), 2.30−2.14 (m, 1H, H-5), 2.06−1.85 (m, 1H, H-1), 1.78−1.56 (m, 4H, H-1, H-2, H-5), 1.17 (s, 9H, C(C*H*$_3$)$_3$); ^{13}C NMR δ 150.6, (N═*C*H), 140.7, 134.9 (C-6a, C-10a), 129.0, 128.6, 125.9, 125.7 (C-7, C-8, C-9, C-10), 54.6 (br, C-4a), 52.9 (*C*(CH$_3$)$_3$), 40.2 (C-3), 39.2 (C-10b), 31.4 (C-1), 31.3 (C(*C*H$_3$)$_3$), 29.2 (C-6), 25.4 (C-2), 21.6 (C-5); IR 1631 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 270 (M$^+$, 100), 255 (49), 213 (61), 198 (57) 186 (33). Anal. Calcd for $C_{18}H_{26}N_2$: C, 79.95; H, 9.69; N, 10.36. Found: C, 79.8; H, 9.7; N, 10.3.

***trans*-1,2,3,4,4a,5,6,10b-Octahydrobenzo[*f*]quinoline (14).**[17a] Compound **5a** (51 mg, 0.2 mmol) was mixed with hydrazine monohydrate (76 mg, 1.5 mmol) and acetic acid (34 mg, 0.57 mmol) in EtOH (2.8 mL) and the mixture warmed at 60 °C until TLC indicated full conversion of the amidine. After 6 h the reaction mixture was allowed to cool, concentrated, taken up in 1 N NaOH (5 mL), and extracted with CH_2Cl_2 (5 × 2 mL). The combined organic layers were dried (K_2CO_3) and concentrated. The crude product was purified by column chromatography (SiO_2, 10% triethylamine in isohexane/EtOAc 1:1) to yield **14** as a white solid (23 mg, 65%), mp 88−89 °C. For elemental analyses, the secondary amine was converted to the HCl salt, mp 277−278 °C: ^{1}H NMR (CD_3OD) δ 7.25−7.21 (m, 1H, Ar−H), 7.12−7.00 (m, 3H, Ar−H), 3.12−3.03 (m, 1H, H-3), 3.02 (m, 2H, H-6), 2.68 (ddd, J = 12.2, 12.2 and 3.2 Hz, 1H, H-3), 2.59−2.48 (m, 1H, H-1), 2.47−2.33 (m, 2H, H-4a, H-10b), 1.97−1.59 (m, 4H, H-2, H-5), 1.33−1.15 (m, 1H, H-1); ^{13}C NMR (CD_3OD) δ 140.4, 137.9 (C-6a, C-10a), 130.5, 127.73, 127.67, 127.1 (C-7, C-8, C-9, C-10), 61.2 (C-4a), 48.2 (C-3), 44.8-(C-10b), 31.9 (C-5), 31.3 (C-1), 30.7 (C-6), 28.3 (C-2); MS [IP 70 eV; *m*/*z* (% rel int)] 187 (M$^+$, 100), 186 (42). Anal. Calcd for $C_{13}H_{17}N$·HCl: C, 69.79; H, 8.11; N, 6.26. Found: C, 69.9; H, 8.0; N, 6.2.

***cis*-1,2,3,4,4a,5,6,10b-Octahydrobenzo[*f*]quinoline (15).**[17a] Compound **15** was synthesized from **7a** (71 mg, 0.27 mmol) as described above for the synthesis of **14**. The crude product was purified by column chromatography (SiO_2, 10% triethylamine in isohexane/EtOAc 1:1) to yield **15** as a white solid (40 mg, 79%), mp 66−68 °C. For elemental analyses the amine was converted to the HCl salt, mp 262−263 °C: ^{1}H NMR (CD_3OD) δ 7.14−7.03 (m, 4H, Ar−H), 3.18 (ddd, J = 10.1, 4.6 and 3.2 Hz, 1H, H-4a), 2.98−2.67 (m, 5H, H-3, H-6, H-10b), 2.30−2.13 (m, 1H, H-5), 1.89−1.79 (m, 2H, H-1), 1.78−1.66 (m, 1H, H-5), 1.64−1.52 (m, 2H, H-2); ^{13}C NMR (CD_3OD) δ 142.0, 137.4 (C-6a, C-10a), 130.6, 130.2, 127.73, 127.66 (C-7, C-8, C-9, C-10), 54.6 (C-4a), 43.0, 40.9 (C-3, C-10b), 31.7 (C-1), 30.1 (C-6), 27.0 (C-2), 26.0 (C-5); MS [IP 70 eV; *m*/*z* (% rel int)] 187 (M$^+$, 100), 186 (41). Anal. Calcd for $C_{13}H_{17}N$·HCl: C, 69.79; H, 8.11; N, 6.26. Found: C, 69.9; H, 8.0; N, 6.2.

***trans*- and *cis*-2,3,4,4a,5,6,7,11b-Octahydro-1*H*-benzo-[3,4]cyclohepta[1,2-*b*]pyridine (16** and **17).** Compound **4a** (0.36 g, 1.0 mmol) was dissolved in degassed benzene (50 mL), AIBN (16.4 mg, 0.1 mmol) and Bu_3SnH (0.44 g, 1.5 mmol) were added, and the solution was refluxed overnight.[41] After cooling, the solvent was evaporated and the resulting residue was partitioned between 3 N HCl (50 mL) and diethyl ether (3 × 25 mL). The combined organic layers were extracted with 3 N HCl (25 mL) and the combined acidic aqueous layers were thereafter extracted with CH_2Cl_2 (4 × 25 mL). The combined CH_2Cl_2 layers were washed with 1 N NaOH (2 × 25 mL), dried (K_2CO_3), and concentrated to yield the crude product (0.30 g), as a mixture of **6a** and **8a**, and the dehalogenated starting material **13a**. The crude product was mixed with hydrazine monohydrate (0.40 g, 8.0 mmol) and acetic acid (0.18 g, 3.0 mmol) in EtOH (11 mL) and warmed at 60 °C until TLC indicated full conversion of the amidine. After 4 h the reaction mixture was allowed to cool and concentrated. The resulting residue was taken up in 3 N HCl (15 mL), washed with EtOAc (2 × 5 mL), made basic with 1 N NaOH, and extracted with CH_2Cl_2 (6 × 8 mL). The combined organic layers were dried (K_2CO_3) and concentrated. The trans and cis isomers were separated by column chromatography (SiO_2, 10% triethylamine in isohexane/EtOAc 1:1) to yield **16** (58 mg, 29%) and **17** (29 mg, 14%) as low-melting solids. Compound **16**: For elemental analyses the amine was converted to the HCl salt, mp 241−242 °C: ^{1}H NMR (CD_3OD) δ 7.22−7.05 (m, 4H, Ar−H), 3.17−3.08 (m, 1H, H-3), 3.09−3.01 (m, 1H, H-7), 2.82−2.65 (m, 3H, H-3, H-7, H-11b), 2.41 (ddd, J = 9.7, 4.8, and 4.8 Hz, 1H, H-4a), 2.11−1.83 (m, 4H, H-2, H-5, H-6), 1.77−1.54 (m, 3H, H-1, H-2, H-6), 1.50−1.41 (m, 1H, H-1); ^{13}C NMR (CD_3OD) δ 142.4, 142.3 (C-7a, C-11a), 129.9, 127.4 (2 C's), 125.8 (C-8, C-9, C-10, C-11), 61.4 (C-4a), 47.7 (C-3), 45.1 (C-11b), 34.6 (C-1), 33.8 (C-7), 30.3 (C-5), 27.5 (C-2), 22.5 (C-6); MS [IP

70 eV; *m*/*z* (% rel int)] 201 (M^+, 100), 186 (18), 158 (39). Anal. Calcd for $C_{14}H_{19}N \cdot HCl \cdot {}^1/_4H_2O$: C, 69.40; H, 8.53; N, 5.78. Found: C, 69.6; H, 8.3; N, 5.8. Compound **17**: For elemental analyses the amine was converted to the HCl salt, mp 250−252 °C: ^{1}H NMR (CD_3OD) δ 7.23 (app d, 1H, Ar−H), 7.16−7.04 (m, 3H, Ar−H), 3.13 (ddd, J = 11.3, 3.7 and 3.6 Hz, 1H, H-4a), 3.16−3.05 (m, 2H, H-3, H-11b), 2.84 (ddd, J = 14.8, 10.5, and 3.0 Hz, 1H, H-7), 2.81−2.75 (m, 2H, H-3, H-7), 2.32−2.23 (m, 2H, H-1, H-5), 2.08−2.00 (m, 1H, H-6), 1.91−1.81 (m, 2H, H-1, H-2) 1.79−1.71 (m, 1H, H-2), 1.69−1.52 (m, 1H, H-5), 1.50−1.42 (m, 1H, H-6); ^{13}C NMR (CD_3OD) δ 143.4, 143.2 (C-7a, C-11a), 131.5, 131.0, 127.5, 127.4 (C-8, C-9, C-10, C-11), 56.4 (C-4a), 50.9 (br, C-11b), 41.1 (C-3), 36.7 (C-7), 31.9 (C-1), 27.7 (C-2), 27.1 (C-6), 26.7 (C-5); MS [IP 70 eV; *m*/*z* (% rel int)] 201 (M^+, 100), 186 (17), 158 (36). Anal. Calcd for $C_{14}H_{19}N \cdot HCl$: C, 70.72; H, 8.48; N, 5.89. Found: C, 70.5; H, 8.3; N, 5.8.

4-(*N*-*tert*-Butylformimidoyl)-1,2,3,4,5,6-hexahydrobenzo[*f*]quinoline (11a). Compound **1** (120 mg, 0.30 mmol) was dissolved in degassed benzene (90 mL), AIBN (49 mg, 0.3 mmol) and TMS_3SiH (90 mg, 0.36 mmol) were added, and the solution was refluxed overnight.[39] Workup as described above for the synthesis of **5a** and filtration through a pad of SiO_2 eluting with 10% triethylamine in isohexane[40] gave **11a** (54 mg, 67%). ^{1}H NMR δ 8.02 (s, 1H, NC*H*═N), 7.20−7.17 (ddd, 1H, Ar−H), 7.13−7.06 (m, 2H, Ar−H), 7.04−6.98 (ddd, 1H, Ar−H), 3.71 (m, 2H, H-3), 2.86 (app t, 2H, H-6), 2.58−2.52 (m, 2H, H-5), 2.47−2.41 (m, 2H, H-1), 2.00−1.93 (m, 2H, H-2), 1.21 (s, 9H, C(CH_3)$_3$); ^{13}C NMR δ 144.5, (N═*C*H), 136.8, 135.8, 132.0, 109.2 (C-4a, C-6a, C-10a, C-10b), 126.5, 126.4, 124.1, 120.8 (C-7, C-8, C-9, C-10), 54.0 (*C*(CH$_3$)$_3$), 42.2 (C-3), 31.1 (C(*C*H$_3$)$_3$), 28.3 (C-6), 24.7 (C-5), 23.1 (C-1), 21.6 (C-2); IR 1614 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 268 (M^+, 26), 211 (10), 185 (100). Anal. Calcd for $C_{18}H_{24}N_2 \cdot {}^1/_4H_2O$: C, 79.22; H, 9.05; N, 10.26. Found: C, 79.4 H, 8.9; N, 10.0.

4-(*N*-*tert*-Butylformimidoyl)-2,3,4,5,6,7-hexahydro-1*H*-benzo[3,4]cyclohepta[1,2-*b*]pyridine (12a). Compound **3** (120 mg, 0.30 mmol) was dissolved in degassed benzene (90 mL), AIBN (49 mg, 0.3 mmol) and TMS_3SiH (90 mg, 0.36 mmol) were added, and the solution was refluxed overnight.[41] Workup as described above for the synthesis of **5a** and filtration through a pad of SiO_2 eluting with 10% triethylamine in isohexane[40] gave **12a** (50 mg, 59%). ^{1}H NMR δ 7.92 (s, 1H, NC*H*═N), 7.29−7.07 (m, 4H, Ar−H), 3.79−3.73 (m, 2H, H-3), 2.60 (app t, 2H, H-7), 2.45 (app t, 2H, H-2), 2.23−2.07 (m, 4H, H-5, H-6), 1.98−1.86 (m, 2H, H-1), 1.22 (s, 9H, C(CH_3)$_3$); ^{13}C NMR δ 145.5, (N═*C*H), 142.8, 139.8, 136.5, 113.0 (C-4a, C-7a, C-11a, C-11b), 128.6, 126.4, 126.1, 125.5 (C-8, C-9, C-10, C-11), 53.8 (*C*(CH$_3$)$_3$), 42.4 (C-3), 33.8, 26.7 (C-5, C-6), 32.3 (C-7), 31.2 (C(*C*H$_3$)$_3$), 26.9 (C-2), 22.3 (C-1); IR 1615 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 282 (M^+, 49), 199 (100). Anal. Calcd for $C_{19}H_{26}N_2 \cdot {}^1/_2H_2O$: C, 78.30; H, 9.34; N, 9.61. Found: C, 78.1; H, 9.0; N, 9.6.

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