Controlled Double-Bond Migration in Palladium-Catalyzed Intramolecular Arylation of Enamidines

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Received May 28, 1996[⊗]

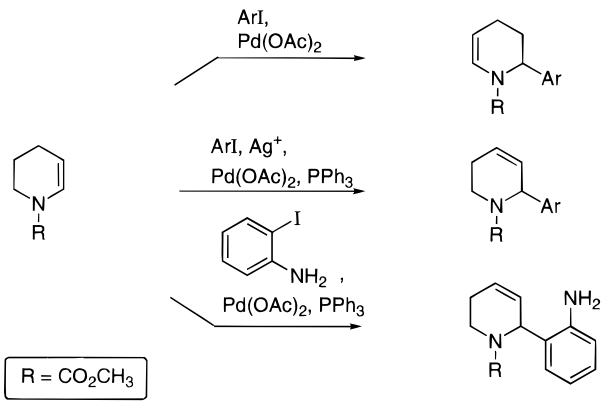
Palladium-catalyzed intramolecular cyclization of *N*-(*N*′-*tert*-butylformimidoyl)-6-[2-(2-iodophenyl)-ethyl]-1,2,3,4-tetrahydropyridine (**1a**) and *N*-(*N*′-*tert*-butylformimidoyl)-6-[3-(2-iodophenyl)propyl]-1,2,3,4-tetrahydropyridine (**1b**) respectively results in formation of spiro compounds 1′-(*N*-*tert*-butylformimidoyl)-3′,4′-dihydrospiro[indan-1,2′(1′*H*)-pyridine] (**4a**), 1′-(*N*-*tert*-butylformimidoyl)-1′,6′-dihydrospiro[indan-1,2′(3′*H*)-pyridine] (**5a**), and 1′-(*N*-*tert*-butylformimidoyl)-5′,6′-dihydrospiro[indan-1,2′(1′*H*)-pyridine] (**6a**) and 1′-(*N*-*tert*-butylformimidoyl)-3,3′,4,4′-tetrahydrospiro[naphthalene-1(2*H*),2′(1′*H*)-pyridine] (**4b**), 1′-(*N*-*tert*-butylformimidoyl)-1′,3,4,6′-tetrahydrospiro[naphthalene-1(2*H*),2′(3′*H*)-pyridine] (**5b**), and 1′-(*N*-*tert*-butylformimidoyl)-3,4,5′,6′-tetrahydrospiro[naphthalene-1(2*H*),2′(1′*H*)-pyridine] (**6b**). The double-bond migration process can be controlled, and any of the three double-bond isomers can be prepared by employing proper ligands. A combination of BINAP and the amidine function was required to obtain the isomers **5a** and **5b** with the double bond in the homoallylic position relative to the aryl group. An electrospray ionization mass spectrometric study was conducted to support suggested reaction intermediates.

Introduction

Palladium-catalyzed arylation of cyclic enol ethers occurs at the α-position with a concomitant migration of the double bond to provide a restored enol ether function on the opposite side of the ring.[1] It was found that cyclic enamides react in a manner similar to cyclic enol ethers and that either of two double-bond isomers could be prepared (Scheme 1).[2]

The α-aryl piperidine fragment is common in many bioactive compounds and molecules with this structural unit are of importance in the search for new, effective analgesics, anticonvulsants and agents against neurodegenerative disorders.[3] Construction of spiro-compounds comprising the α-aryl piperidine fragment[4] using intramolecular Heck arylation methodology for the creation of the tetrasubstituted carbon center was envisioned.[5] This appeared attractive since the double bond, restored after spiro-cyclization, would provide a handle for further selective functionalizations. Cyclization protocols that allow selective synthesis of any of the three double-bond isomers should be of particular value, since such isomers constitute suitable precursors in subsequent structure−activity studies. Therefore, efforts were focused on control of the double-bond migration process. Regioselective palladium-catalyzed β-arylation of enol ethers can be achieved in cases where a palladium-coordinating auxiliary such as an amine[6] is attached to the substrate. Furthermore, arylation of the cyclic

Scheme 1



[⊗] Abstract published in *Advance ACS Abstracts,* September 1, 1996.

(1) For palladium-catalyzed Heck arylation of cyclic enol ethers, see: (a) Andersson, C.-M.; Hallberg, A.; Daves, G. D., Jr. *J. Org. Chem.* **1987**, *52*, 3529−3536. (b) Arai, I.; Daves, G. D., Jr. *J. Org. Chem.* **1979**, *44*, 21−23. (c) Genêt, J. P.; Blart, E.; Savignac, M. *Synlett* **1992**, 715−717. (d) Hillers, S.; Reiser, O. *Synlett* **1995**, 153−154. (e) Hillers, S.; Sartori, S.; Reiser, O. *J. Am. Chem. Soc.* **1996**, *118*, 2087−2088. (f) Larock, R. C.; Gong, W. H.; Baker, B. E. *Tetrahedron Lett.* **1989**, *30*, 2603−2606. (g) Larock, R. C.; Gong, W. H. *J. Org. Chem.* **1990**, *55*, 407−408. For examples of chiral induction in Heck arylation of cyclic enol ethers, see: (h) Hayashi, T.; Kubo, A.; Ozawa, F. *Pure Appl. Chem.* **1992**, *64*, 421−427. (i) Hillers, S.; Reiser, O. *Tetrahedron Lett.* **1993**, *34*, 5265−5268. (j) Loiseleur, O.; Meier, P.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 200−202. (k) Ozawa, F.; Kubo, A.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 1417−1419. (l) Ozawa, F.; Kubo, A.; Hayashi, T. *Tetrahedron Lett.* **1992**, *33*, 1485−1488. (m) Ozawa, F.; Kubo, A.; Matsumoto, Y.; Hayashi, T.; Nishioka, E.; Yanagi, K.; Moriguchi, K.-i. *Organometallics* **1993**, *12*, 4188−4196. (n) Sakamoto, T.; Kondo, Y.; Yamanaka, H. *Tetrahedron Lett.* **1992**, *33*, 6845−6848.

(2) (a) Nilsson, K.; Hallberg, A. *J. Org. Chem.* **1990**, *55*, 2464−2470. For other examples of Heck arylation of cyclic enamides, see: (b) Ozawa, F.; Hayashi, T. *J. Organomet. Chem.* **1992**, *428*, 267−277. See also refs 1e and 1h.

(3) (a) Bigge, C. F. *Biochem. Pharmacol.* **1993**, *45*, 1547−1561. (b) Ornstein, P. L.; Monn, J. A.; Schoepp, D. D. *Drug News Perspec.* **1994**, *7*, 5−12.

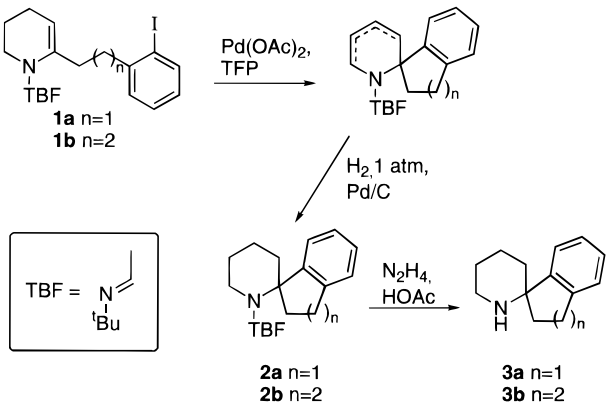
(4) (a) Armour, D. R.; Watson, S. P.; Pegg, N. A.; Heron, N. M.; Middlemiss, D.; Chan, C.; Cholerton, T. J.; Hubbard, T.; Vinader, M. V.; Davies, H. G.; Cocker, J. D.; Bays, D. E.; Ward, P. *Bioorg. Med. Chem. Lett.* **1995**, *5*, 2671−2676. (b) Bahajaj, A. A.; Bailey, P. D.; Moore, M. H.; Morgan, K. M.; Vernon, J. M. *J. Chem. Soc., Chem. Commun.* **1994**, 2511−2512. (c) Reimann, E.; Speckbacher, J. *Arch. Pharm.* (*Weinheim*) **1989**, *322*, 889−892. (d) Watson, S. P.; Knox, G. R.; Heron, N. M. *Tetrahedron Lett.* **1994**, *35*, 9763−9766.

(5) For first examples of the use of Heck arylation for construction of tetrasubstituted carbon centers see: (a) Abelman, M. M.; Oh, T.; Overman, L. E. *J. Org. Chem.* **1987**, *52*, 4130−4133. (b) Grigg, R.; Sridharan, V.; Stevenson, P.; Worakun, T. *J. Chem. Soc., Chem. Commun.* **1986**, 1697−1699. For recent examples including asymmetric induction, see: (c) Kondo, K.; Sodeoka, M.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 4322−4323. (d) Kondo, K.; Sodeoka, M.; Shibasaki, M. *Tetrahedron: Asymmetry* **1995**, 6, 2453−2464. (e) Overman, L. E. *Pure Appl. Chem.* **1994**, *66*, 1423−1430. (f) Takemoto, T.; Sodeoka, M.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1993**, *115*, 8477−8478.

(6) (a) Andersson, C.-M.; Larsson, J.; Hallberg, A. *J. Org. Chem.* **1990**, *55*, 5757−5761. (b) Larhed, M.; Andersson, C.-M.; Hallberg, A. *Tetrahedron* **1994**, *50*, 285−304. See also: (c) Nilsson, K.; Hallberg, A. *J. Org. Chem.* **1992**, *57*, 4015−4017.

S0022-3263(96)00970-X CCC: $12.00

Scheme 2



enamide with *o*-iodoaniline as depicted in Scheme 1 results in suppression of double-bond migration.[2a] We hoped that the nitrogen functionality of amidines, acting either as base[7] or as a ligand to palladium[8] accordingly, might enable an intramolecular regioselective quenching of intermediate palladium π-complexes and thereby conceivably provide double-bond migration control. We herein report that palladium-catalyzed cyclization of two model compounds, **1a** and **1b**, provided proper ligands are employed, allows selective preparation of the double-bond isomers **4a**−**6a** and **4b**−**6b**, respectively.

Results

Palladium-Catalyzed Cyclization Reactions. For preparation of the saturated spiro systems **3a** and **3b**, we started from **1a** and **1b**, respectively, and employed tri-2-furylphosphine[9] as ligand. In our initial experiments this ligand, although furnishing an isomer mixture, was found to promote the rate of the cyclization. After 15 h at 80 °C, mixtures of the double-bond isomers **4a**−**6a** and **4b**−**6b** were generated. Hydrogenation of the double bonds was effected under conditions where both the imine bond and the nitrogen−benzylic carbon bond remained intact. Thus, after hydrogenation of the isomer mixtures at 1 atm on Pd/C, **2a** and **2b** were isolated in 69% and 72% yields, respectively. Hydrogenation for a longer reaction time or under higher pressure led to the accumulation of side products.[10] Subsequent hydrazinolysis gave the secondary amines **3a** and **3b** (Scheme 2).

For the preparation of each of the double-bond isomers, careful selection of catalytic systems was required. In preparative experiments the enamidine **4a** was obtained in 54% yield by using palladium acetate and potassium carbonate as base at 100 °C. This reaction, conducted in the absence of phosphine ligand, was sluggish and required 96 h for completion (Scheme 3). Although a fair isomer selectivity was achieved under these conditions, it was observed that substituting potassium carbonate for trialkylamines rendered a higher selectivity for **4a** but unfortunately led to considerable decomposition of the amidines **1a** and **4a** in the reaction medium, and consequently low yields were obtained. Mixtures of trialkylamines and potassium carbonate met with no success, and with proton sponge[11] the starting material **1a** in fact decomposed more quickly than **4a** was created. Cyclization of **1b** (Scheme 4) to form the six-membered ring was even slower than the corresponding cyclization of **1a**. A long reaction time was needed, and a major decomposition of the catalytic system had occurred before satisfactory conversion had been achieved. Triphenylarsine[12] was found to be suitable, providing high isomer selectivity and enabling isolation of **4b** in 44% yield. However employing triphenylarsine as ligand in the cyclization of **1a** did not result in any improvement of the yield of **4a**.

While separation of the enamidines **4** from impurities of **5** and **6** was facile, isolation of either of **5** or **6** from a mixture of **5** and **6** was more troublesome with standard chromatographic procedures. Highly selective protocols were needed therefore for preparation of **5** and **6**, respectively. An initial screening of ligands[13] revealed that BINAP[14] produced a **5a**/**6a** ratio higher than 7 and that this ligand was superior to other bidentate ligands (DPPF, DPPB, DPPP, DPPE, DPPM)[15] and monodentate ligands (PPh_3, P(*o*-tol)$_3$, $AsPh_3$, TFP)[16] tested. For the preparative experiments a procedure developed by Shibasaki[17] was adopted and the palladium acetate was pretreated with cyclohexene in the presence of BINAP with triethylamine as base, which provided an excellent **5a**/**6a** ratio (>50). A 54% yield of **5a** was isolated after a reaction time of 20 h at 80 °C, and transformation of this compound to **7a** was accomplished smoothly by hydrazinolysis (Scheme 3). Cyclization of **1b** under identical conditions furnished **5b**, isolated in 49% yield, which after subsequent hydrazinolysis afforded **7b** (Scheme 4). Low chiral induction (<10% ee) was encountered in cyclizations with (*R*)-BINAP as ligand.[18]

Predominant formation of **6a** and **6b** could be accomplished by using silver[19] or thallium[20] additives with triphenylphosphine as ligand while addition of acetate, previously reported to retard the double-bond migration process in related systems,[21] produced an isomer mixture. Regardless of which silver additive was employed ($AgNO_3$, Ag_2O, Ag_2CO_3, Ag_3PO_4)[22] a **6**/**5** ratio of approxi-

(7) Acidity: pK_a = 10−11. Häfelinger, G.; Kuske, F. K. H. In *The chemistry of amidines and imidates*; Patai, S., Rappoport, Z., Ed.; John Wiley & Sons: 1991; Vol. 2, pp 75−80.

(8) See, for example: Grove, D. M.; van Koten, G.; Ubbels, H. J. C.; Vrieze, K.; Niemann, L. C.; Stam, C. H. *J. Chem. Soc., Dalton Trans.* **1986**, 717−724.

(9) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585−9595.

(10) Meyers, A. I.; Edwards, P. D.; Rieker, W. F.; Bailey, T. R. *J. Am. Chem. Soc.* **1984**, *106*, 3270−3276.

(11) The proton sponge was 1,8-bis(dimethylamino)naphthalene: Alder, R. W.; Bowman, P. S.; Steele, W. R. S.; Winterman, D. R. *Chem. Commun.* **1968**, 723−724.

(12) For use of triphenylarsine in the Heck reaction, see: (a) Zhang, H.-C.; Daves, G. D., Jr. *J. Org. Chem.* **1992**, *57*, 4690−4696. (b) Zhang, H.-C.; Daves, G. D., Jr. *Organometallics* **1993**, *12*, 1499−1500.

(13) Tetrahydropyridine **1a** (0.10 mmol) was added to a mixture of 0.005 mmol of $Pd(OAc)_2$, 0.01 mmol of bidentate ligand or 0.02 mmol of monodentate ligand, 0.20 mmol of triethylamine, and 0.10 mmol of naphthalene (as internal standard). The reaction mixture was heated under Ar in a sealed tube at 80 °C for 12−96 h. The product composition was monitored by GC-MS.

(14) BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl: Noyori, R.; Takaya, H. *Acc. Chem. Res.* **1990**, *23*, 345−350.

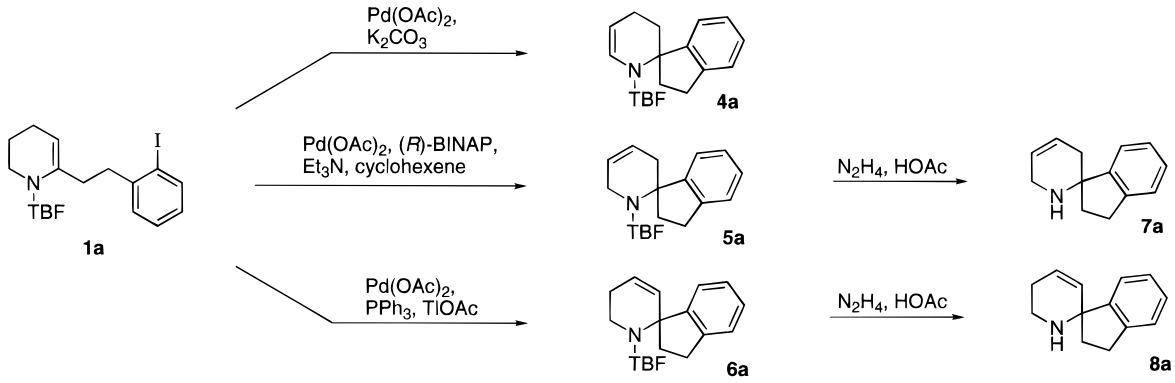
(15) DPPF = 1,1′-bis(diphenylphosphino)ferrocene; DPPB = 1,4-bis(diphenylphosphino)butane; DPPP = 1,3-bis(diphenylphosphino)propane; DPPE = 1,2-bis(diphenylphosphino)ethane; DPPM = bis(diphenylphosphino)methane

(16) PPh_3 = triphenylphosphine, P(*o*-tol)$_3$ = tri-*o*-tolylphosphine, P(*p*-tol)$_3$ = tri-*p*-tolylphosphine, $AsPh_3$ = triphenylarsine, TFP = tri-2-furylphosphine

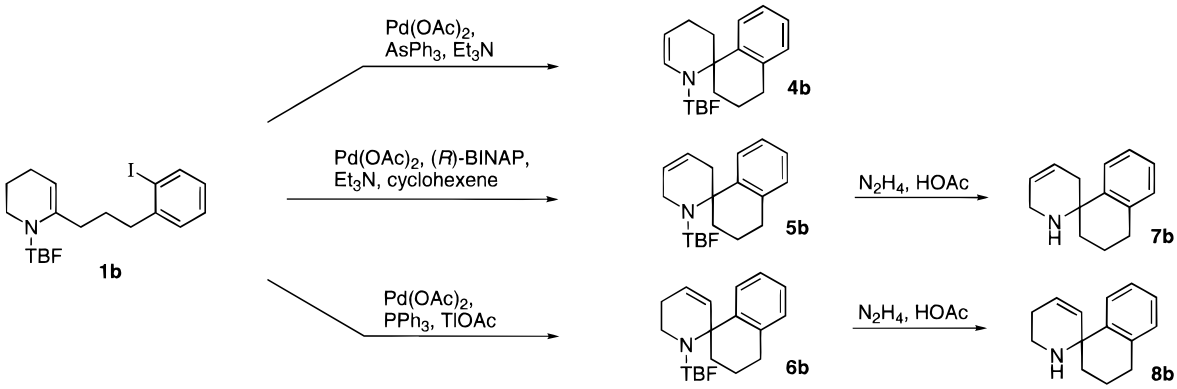
(17) Sato, Y.; Sodoeka, M.; Shibasaki, M. *J. Org. Chem.* **1989**, *54*, 4738−4739.

(18) Dihydospiropyridine **5a** was cleaved with hydrazine, and the resulting secondary amine was analyzed on a chiral GLC-column, heptakis(6-*O*-(*tert*-butyldimethylsilyl)-2,3-di-*O*-methyl-β-cyclodextrin, prepared and developed by Prof. W. A. König. Institut für Organische Chemie, Universität Hamburg, D-201 46 Hamburg, Germany.

Scheme 3



Scheme 4

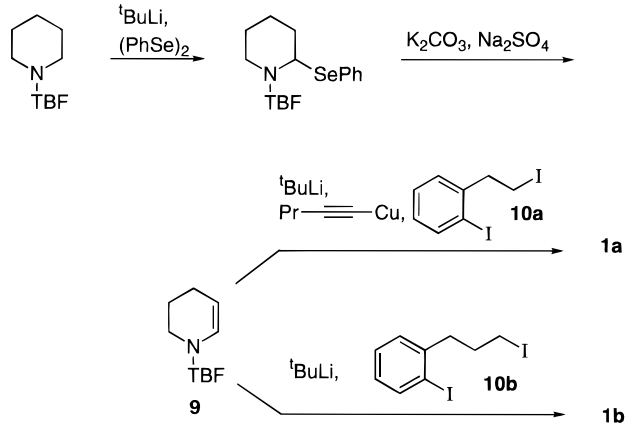


mately 10 was obtained at 40 °C with triethylamine as base and triphenylphosphine as ligand. Thallium acetate effected a higher ratio than thallium carbonate or thallium nitrate and with triphenylphosphine as ligand: thallium acetate resulted in a **6**/**5** selectivity higher than 30. In the preparative runs thallium acetate/triphenylphosphine was used at 80 °C, which delivered **6a** and **6b** in 79% and 52% yields, respectively. The secondary amines **8a** and **8b** were afforded after hydrazinolysis (Scheme 3 and 4).

Addition of silver nitrate to a reaction where (*R*)-BINAP was employed resulted in formation of essentially racemic **5b** and **4b** in a ratio of 2:1 as the major products, while **6b** was now formed in only minor amounts. In contrast to the negligible enantiomeric excess of **5b** (no detectable enantiomeric excess) and **4b** (<15% ee of (*S*)-**4b**), a 68% enantiomeric excess of (*S*)-**6b** was observed.[23]

Starting Materials. For the preparation of the starting materials a procedure based on alkylation of enamidines, developed by Meyers and outlined in Scheme 5, was adopted.[24] The enamidine **9** was obtained after lithiation of *N*-(*N*′-*tert*-butylformimidoyl)piperidine,[10] phenylselenation, and subsequent elimination. Compound **9** was lithiated at −78 °C with *tert*-butyllithium. Pentynylcopper was added thereafter followed by the alkylating agent **10a**, and **1a** was isolated eventually in 54% yield. Conversion to the organocopper compound was necessary, since the alkylation of the lithium reagent was accompanied by a predominant formation of 2-iodostyrene. Compound **1b** was obtained in 71% yield after

Scheme 5



(19) The beneficial effect of silver additives in controlling double-bond isomerization in the Heck reaction was first observed by Overman's group. (a) Abelman, M. M.; Overman, L. E. *J. Am. Chem. Soc.* **1988**, *110*, 2328−2329 and ref 5a. Use of silver for controlling double-bond isomerization in heterocycles. (b) Larock, R. C.; Gong, W. H. *J. Org. Chem.* **1989**, *54*, 2047−2050 and refs 1f,g,n, 2a, and 6c. For the first use of silver salts in the Heck reaction, see: (c) Karabelas, K.; Westerlund, C.; Hallberg, A. *J. Org. Chem.* **1985**, *50*, 3896−3900. Silver salts have also been reported to have a beneficial effect in the asymmetric Heck reaction. (d) Sato, Y.; Sodoeke, M.; Shibasaki, M. *Chem. Lett.* **1990**, 1953−1954. (e) Sato, Y.; Nukui, S.; Sodeoka, M.; Shibasaki, M. *Tetrahedron* **1994**, *50*, 371−382.

(20) Grigg, R.; Loganathan, V.; Santhakumar, V.; Sridharan, V.; Teasdale, A. *Tetrahedron Lett.* **1991**, *32*, 687−690.

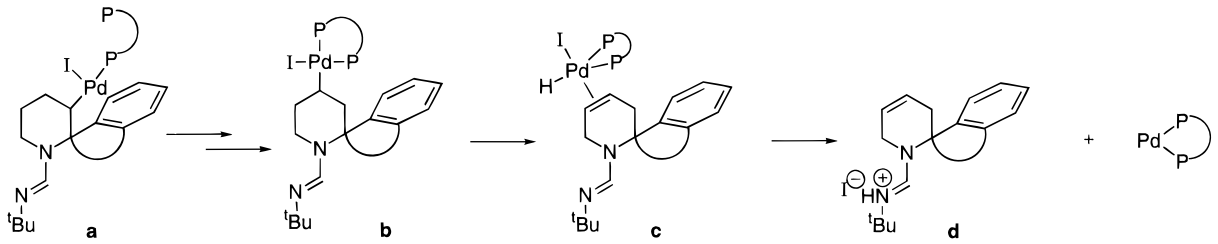
(21) (a) Larock, R. C.; Baker, B. E. *Tetrahedron Lett.* **1988**, *29*, 905−908. (b) Laschat, S.; Narjes, F.; Overman, L. E. *Tetrahedron* **1994**, *50*, 347−358 and ref 1m.

(22) The counter anion of the silver salts has been shown to play a significant role in the asymmetric Heck reaction. Nukui, S.; Sodeoka, M.; Shibasaki, M. *Tetrahedron Lett.* **1993**, *34*, 4965−4968 and refs 19d,e.

(23) The amidines were converted to the corresponding formyl compounds by hydrolysis with KOH in MeOH/water and analyzed with a chiral GLC-column, Heptakis(6-*O*-(*tert*-butyldimethylsilyl))-2,3-di-*O*-methyl-*β*-cyclodextrin, prepared and developed by Prof. W. A. König. Institut für Organische Chemie, Universität Hamburg, D-201 46 Hamburg, Germany.

(24) (a) Meyers, A. I.; Edwards, P. D.; Bailey, T. R.; Jagdmann, G. E. J. *J. Org. Chem.* **1985**, *50*, 1019−1026. See also: (b) Beak, P.; Lee, W. K. *J. Org. Chem.* **1993**, *58*, 1109−1117.

Scheme 6



alkylation of the α-lithiated enamidine **9**. The phenylpropyl iodide **10b** was not prone to undergo elimination, and addition of pentynylcopper therefore was not required in this case. The alkylating agents **10a** and **10b** were synthesized via the mesitylates from the corresponding alcohols.

Initially the palladium-mediated cyclization experiments were conducted with **1a**, contaminated with approximately 5% of the corresponding saturated amidine **11**. This contamination was deleterious for the cyclization and decomposition of **1a** in fact became the predominant reaction. For successful cyclizations therefore it was crucial to start with pure material (>99%). The saturated amidine **11** was derived from an incomplete α-lithiation/phenylselenation of the starting material, *N*-(*N*′-*tert*-butylformimidoyl)piperidine. We took advantage of the higher solubility in methylene chloride of the hydrochloride salt of the α-phenylseleno derivative as compared to the salt of *N*-(*N*′-*tert*-butylformimidoyl)piperidine for an efficient and convenient purification of the former.

Discussion

Prior to the intramolecular arylation of **1a** and **1b**, reduction of Pd(II) to Pd(0)[25] and subsequent oxidative addition[26] occurs. The isomers **4a** and **4b** are afforded thereafter presumably via generation of a π-complex, insertion, and consecutive β-eliminations/readditions[27] of neutral hydridopalladium iodide species. For a satisfactory turnover in the conversion of **1b** to **4b**, triphenylarsine, with the characteristic feature of stabilizing Pd(0) but binding less strongly than triphenylphosphine to Pd(II) species,[28] was employed in order to enhance the reaction rate. Silver and thallium additives used for the preparation of **6a** and **6b** have been suggested to abstract the iodide from the oxidative addition complex,[29] which after π-complex formation and insertion results in a charged σ-complex. The complex is prone to decomplexation after β-elimination,[30] and accordingly the isomers **6a** and **6b** ought to arise from such processes.

To explain the formation of **5a** and **5b**, the formamidine function has to be taken into account since intramolecular cyclizations of enamides did not lead to formation of the corresponding analogues with the double bond in the homoallylic position in relation to the aryl group. The formation of **5** probably proceeds by an initial formation of an oxidative addition complex where the coordination sites are occupied by the amidine nitrogen, the iodo atom, and one of the two phosphines of BINAP.[31] The subsequent generation of the palladium π-complex we assume occurs after displacement of the amidine nitrogen for the double bond (Scheme 6). Insertion leads to a crowded tricoordinated σ-complex (**a**) which is not prone to coordinate the second phosphine of BINAP of steric reasons.[32] After β-hydride elimination and readdition, a new tricoordinated species is created and occupation of the forth coordination site by the second phosphine of BINAP is now sterically allowed (**b**). With BINAP as a cis-coordinating ligand and the nucleophilic iodo atom ligated to the palladium, we assume that the β-elimination creates an unstable pentavalent species (**c**).[33] Amidine-promoted hydrogen abstraction[2a] from this complex and subsequent dissociation or alternatively an olefin−amidine nitrogen ligand exchange could be responsible for liberation of the double-bond isomer **5** (**d**).

The negligible enantiomeric excess observed also after addition of silver ions can be attributed to amidine coordination to the oxidative addition complex. The enantiomeric excess encountered with the minor isomer **6** (68% ee) should arise from dissociation of palladium (*R*)-BINAP complex from the π-complex of the *S*-isomer. This dissociation seems to be promoted by the amidine functionality, since the corresponding enamide results in a very low enantiomeric excess (8% ee) of the corresponding isomer.

The very sluggish reaction encountered in the cyclization of **1a** contaminated with **11**, providing only traces of spiro compounds, we anticipate is attributable to trapping of the catalyst by the amidine functionality of **11**. While no cyclization occurred after using a mixture, consisting of a **1a**/**11** ratio of 3:1, addition of methyl acrylate liberated the catalyst and **1a** then provided the cyclized isomers **4a**, **5a**, and **6a**. Compound **11** had been converted to the arylated methyl acrylate derivative **12**

(25) For olefin as reducing agent, see: (a) Trost, B. M.; Murphy, D. J. *Organometallics* **1985**, *4*, 1143−1145. For amine as reducing agent see: (b) McCrindle, R.; Ferguson, G.; Arsenault, G. J.; McAlees, A. J. *J. Chem. Soc., Chem. Commun.* **1983**, 571−572. For phosphine as reducing agent, see: (c) Amatore, C.; Jutand, A.; M′Barki, M. A. *Organometallics* **1992**, *11*, 3009−3013. (d) Amatore, C.; Carré, E.; Jutand, A.; M′Barki, M. A. *Organometallics* **1995**, *14*, 1818−1826. (e) Mandai, T.; Matsumoto, T.; Tsuji, J. *Tetrahedron Lett.* **1993**, *34*, 2513−2516. (f) Ozawa, F.; Kubo, A.; Hayashi, T. *Chem. Lett.* **1992**, 2177−2180.

(26) Aryl iodides are known to react without phosphine ligands: Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146−151.

(27) Heck, R. F. *J. Am. Chem. Soc.* **1971**, *93*, 6896−6901.

(28) Manzer, L. E.; Tolman, C. A. *J. Am. Chem. Soc.* **1975**, *97*, 1955−1956 and ref 9.

(29) Karabelas, K.; Hallberg, A. *J. Org. Chem.* **1988**, *53*, 4909−4914 and ref 20.

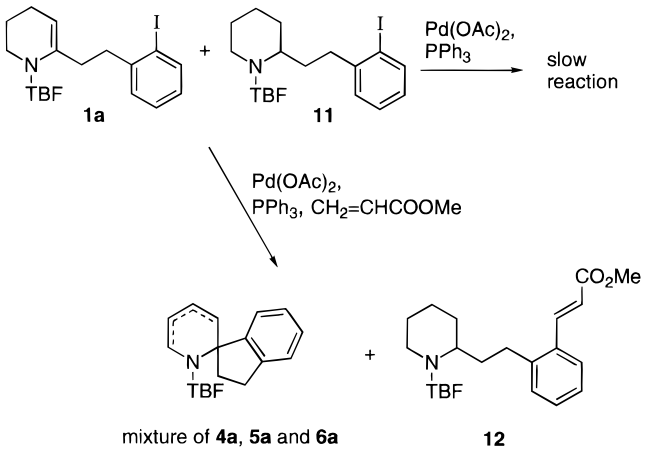
(30) Yamamoto, A. *J. Organomet. Chem.* **1995**, *500*, 337−348.

(31) See ref 19e. Other examples where one of the two phosphine ligands in a bidentate ligand is displaced by the olefin prior to insertion. (a) Cabri, W.; Candiani, I.; DeBernardinis, S.; Francalanci, F.; Penco, S.; Santi, R. *J. Org. Chem.* **1991**, *56*, 5796−5800. (b) Cabri, W.; Candiani, I.; Bedeschi, A.; Penco, S.; Santi, R. *J. Org. Chem.* **1992**, *57*, 1481−1486. (c) Cabri, W.; Candiani, I.; Bedeschi, A.; Santi, R. *J. Org. Chem.* **1992**, *57*, 3558−3563. (d) Hayashi, T.; Konishi, M.; Kobori, Y.; Kumada, M.; Higuchi, T.; Hirotsu, K. *J. Am. Chem. Soc.* **1984**, *106*, 158−163.

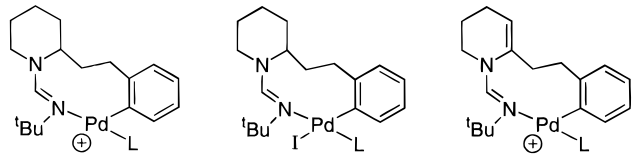
(32) (a) Li, C.-S.; Jou, D.-C.; Cheng, C.-H. *Organometallics* **1993**, *12*, 3945−3954. (b) Portnoy, M.; Ben-David, Y.; Rousso, I.; Milstein, D. *Organometallics* **1994**, *13*, 3465−3479.

(33) Romeo, R.; Alibrandi, G.; Scolaro, L. M. *Inorg. Chem.* **1993**, *32*, 4688−4694.

Scheme 7



(Scheme 7). Recently Canary et al.[34] demonstrated the use of electrospray ionization mass spectrometry (ESI-MS) for the direct observation of catalytic intermediates in a palladium-catalyzed Suzuki reaction. This encouraged us to conduct an electrospray ionization mass spectrometric study, since the reaction of **1a** and **11** in a ratio of 3:1 should provide complexes stable enough for a ESI-MS study. A sample of the reaction mixture after 1 h, prior to addition of methyl acrylate, was quenched in methanol at −78 °C under nitrogen and was injected thereafter into the mass spectrometer. Two strong major palladium-containing peaks were identified at *m*/*z* 639 and 767. The isotope pattern confirmed presence of one palladium atom in each complex. These signals could correspond to the structures **13a** and **14a**, respectively.



13a L = PPh_3
13b L = P(*p*-tol)$_3$

14a L = PPh_3
14b L = P(*p*-tol)$_3$

15 L = PPh_3

Sampling the reaction mixture 10 min after addition of methyl acrylate revealed the absence of the two above peaks. To gain further support for these structures, reactions with tri-*p*-tolylphosphine instead of triphenylphosphine as ligand were conducted, which gave signals at *m*/*z* 681 and 809 corresponding to **13b** and **14b**. These results indicate that compound **11** underwent an oxidative addition in the reaction medium and that one of the phosphine ligands had been displaced by the formamidine nitrogen. The *m*/*z* 639 and 681 signals are attributed to complexes lacking the iodo atom and could be fragments from **14a** and **14b**, respectively, formed in the mass spectrometer.[34a] No corresponding signals derived from the unsaturated **1a** could be assigned in the reaction. However, when starting from pure **1a** a peak at *m*/*z* 637 appeared presumably corresponding to the complex **15**, which again might have been formed in the mass spectrometer from the corresponding iodo complex. In control experiments omitting either the palladium or the starting materials **1a** and **11,** none of the peaks discussed above appear.[35]

Conclusion

In summary, we have demonstrated that spiro compounds comprising the α-aryl piperidine fragment can be constructed by intramolecular cyclization of enamidines. The concomitant double-bond isomerization can be controlled, and any of three double-bond isomers was prepared selectively by employing proper ligands. A combination of BINAP and the amidine function was required to obtain the isomers with the double bond in the homoallylic position to the aryl group. We suggest that this isomer is delivered after quenching of the corresponding pentavalent BINAP hydridopalladium iodide π-complex by the amidine nitrogen either by proton transfer or by amidine-promoted nitrogen−olefin exchange. In the oxidative addition complex, the amidine nitrogen acts as a ligand to palladium as supported by an electrospray ionization mass spectrometric study and no chiral induction is achieved with (*R*)-BINAP.

Experimental Section

General Methods. ^{1}H and ^{13}C NMR spectra were recorded at 270 and 67.8 MHz, respectively. Tetramethylsilane was used as internal standard. Peak assignments of the spiro compounds 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 × 0.20 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 Micro 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. All palladium-catalyzed cyclization reactions were carried out in heavy-walled Pyrex tubes, sealed with a screw cap fitted with a Teflon gasket. Thin layer chromatography (TLC) was carried out on aluminum sheets precoated with silica gel 60 F_{254} (0.2 mm, E. Merck). Column chromatography was performed on silica using kiselgel 60 (0.032−0.065 mm, E. Merck). Preparative thin layer chromatography was carried out on glass sheets precoated with silica gel 60 F_{254} (2.0 mm, E. Merck).

Materials. Triethylamine was distilled from potassium hydroxide prior to use. THF and diethyl ether were distilled from sodium/benzophenone before use. Acetonitrile (CH_3CN) was stored over activated 3 Å molecular sieves and degassed with argon before use. Tri-2-furylphosphine (TFP) (Aldrich), (*R*)-(+)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl ((*R*)-BINAP) (Aldrich), and triphenylarsine ($AsPh_3$) (Acros Chimica) were used as supplied. Triphenylphosphine (PPh_3) (Merck) was recrystallized from 95% ethanol. Compounds **10a** and **10b**[36] were prepared according to a synthetic strategy described elsewhere.[37] 2-Iodobenzyl bromide[38] was synthesized from 2-iodobenzyl alcohol[39] (Aldrich) and used for the preparation of 3-(2′-iodophenyl)propanol.[40] 2-(2′-Iodophenyl)ethanol[41]

(34) (a) Aliprantis, A. O.; Canary, J. W. *J. Am. Chem. Soc.* **1994**, *116*, 6985−6986. See also: (b) Wilson, S. R.; Perez, J.; Pasternak, A. *J. Am. Chem. Soc.* **1993**, *115*, 1994−1997. (c) Wilson, S. R.; Wu, Y. *Organometallics* **1993**, *12*, 1478−1480.

(35) In these experiments the *m*/*z* peak at 579 (see ref 32a) did not contain palladium according to the isotopic distribution.

(36) Meisenheimer, J. *Chem. Ber.* **1928**, *61*, 709−721.

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

(38) Beak, P.; Allen, D. J.; Lee, W. K. *J. Am. Chem. Soc.* **1990**, *112*, 1629−1630.

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

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

(41) Bennett, G. M.; Hafez, M. M. *J. Chem. Soc.* **1941**, 652−659.

is a known compound, and only previously unreported data are given here. *N*-(*N′-tert*-Butylformimidoyl)piperidine was prepared as described elsewhere.[10] Pentynylcopper was prepared from pentyne and CuI.[42] All other reagents were obtained from commercial sources and used as received.

2-(2′-Iodophenyl)ethanol.[41] 2-Iodobenzyl cyanide (34.6 g, 0.142 mol) and 10% aqueous NaOH (103 mL, 0.285 mol) were refluxed overnight. Upon cooling, water (80 mL) was added followed by 50% aqueous H_2SO_4 (80 mL). The reaction mixture was extracted with diethyl ether (4 × 80 mL), and the combined organic layers were washed with water (4 × 70 mL), dried ($MgSO_4$), and concentrated. The crude 2-iodophenylacetic acid, mp 117−118 °C (36.1 g) (mp 118−120 °C[38]), was dissolved in dry THF (140 mL) and cooled to 5 °C, and borane−dimethyl sulfide complex (2 M in THF) (76 mL, 0.152 mol) was added slowly. The reaction mixture was stirred at room temperature overnight, slowly poured into ice-cold methanol (600 mL) with gentle swirling, and allowed to stand for at least 6 h. The clear solution was concentrated, and the crude product was dissolved in diethyl ether (200 mL), washed with saturated $NaHCO_3$ (4 × 50 mL), dried ($MgSO_4$), and concentrated to yield the alcohol (32.7 g, 93%): ^{1}H NMR ($CDCl_3$) δ 7.83 (dd, 1H), 7.32−7.24 (m, 2H), 6.92 (ddd, 1H), 3.85 (t, J = 6.7 Hz, 2H), 3.01 (t, J = 6.7 Hz, 2H), 2.00 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 141.0, 139.7, 130.3, 128.4 (2 C′s), 100.8, 62.2, 43.7; IR (neat) 3600−3100 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 248 (M^+, 81), 217 (100), 121 (79), 91 (76).

2-(2′-Iodophenyl)ethyl Mesylate. 2-(2′-Iodophenyl)ethanol[41] (20.4 g, 82 mmol) and triethylamine (17 mL, 123 mmol) were dissolved in CH_2Cl_2 (410 mL). Methanesulfonyl chloride (7.0 mL, 90 mmol) 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 × 200 mL), cold 5 N HCl (2 × 200 mL), saturated aqueous $NaHCO_3$ (2 × 200 mL), and brine (2 × 200 mL), dried ($MgSO_4$), and concentrated to yield 2-(2′-iodophenyl)ethyl mesylate (25.6 g, 96%): ^{1}H NMR ($CDCl_3$) δ 7.84 (d, 1H), 7.38−7.27 (m, 2H), 7.03−6.93 (m, 1H), 4.42 (t, J = 6.9 Hz, 2H), 3.20 (t, J = 6.9 Hz, 2H), 2.89 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 139.7, 138.8, 130.6, 129.0, 128.6, 100.3, 68.6, 40.1, 37.3; IR ($CDCl_3$) 1360, 1175 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 326 (M^+, 9), 230 (100), 217 (32). Anal. Calcd for $C_9H_{11}IO_3S$: C, 33.14; H, 3.40. Found: C, 33.1; H, 3.2.

3-(2′-Iodophenyl)propyl Mesylate. 3-(2′-Iodophenyl)propyl mesylate was synthesized in 96% yield (8.7 g, 26 mmol) from 3-(2′-iodophenyl)propanol[40] (7.0 g, 27 mmol) as described above for the synthesis of 2-(2′-iodophenyl)ethyl mesylate: ^{1}H NMR ($CDCl_3$) δ 7.82 (d, 1H), 7.32−7.21 (m, 2H), 6.94−6.88 (m, 1H), 4.27 (t, J = 6.3 Hz, 2H), 3.03 (s, 3H), 2.89−6.83 (m, 2H), 2.12−2.01 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 142.9, 139.6, 129.6, 128.5, 128.2, 100.3, 68.9, 37.4, 36.5, 29.3.; IR ($CDCl_3$) 1359, 1175 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 340 (M^+, 23), 244 (100), 217 (31), 117 (64). Anal. Calcd for $C_{10}H_{13}IO_3S$: C, 35.31; H, 3.85. Found: C, 35.6; H, 3.8.

2-(2′-Iodophenyl)ethyl Iodide (10a). 2-(2′-Iodophenyl)-ethyl mesylate (31.9 g, 98 mmol) was mixed with NaI (43.8 g, 294 mmol) in acetone (300 mL), and the mixture was refluxed until TLC (SiO_2, pentane) indicated consumption of the starting material. After 3 h water (250 mL) was added and the solution was extracted with diethyl ether (3 × 130 mL). The combined organic layers were washed with water (2 × 130 mL), dried ($MgSO_4$), and concentrated. The product was purified by column chromatography (SiO_2, pentane, R_f 0.49) to yield **10a** (32.4 g, 92%) as a clear oil: ^{1}H NMR ($CDCl_3$) δ 7.82 (d, 1H), 7.33−7.22 (m, 2H), 6.98−6.92 (m, 1H), 3.40−3.23 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 143.2, 139.7, 129.8, 128.7, 128.5, 99.9, 44.9, 3.4.; MS [IP 70 eV; *m*/*z* (% rel int)] 358 (M^+, 23), 231 (100). Anal. Calcd for $C_8H_8I_2$: C, 26.84; H, 2.25. Found: C, 26.9; H, 2.2.

3-(2′-Iodophenyl)propyl Iodide (10b).[36] Compound **10b** was synthesized from 3-(2′-iodophenyl)propyl mesylate (42.5g, 0.12 mol) as described above for the synthesis of **10a**. The product was purified by column chromatography (SiO_2, pentane, R_f 0.40) to yield **10b** (42.0 g, 91%) as a clear oil: ^{1}H NMR ($CDCl_3$) δ 7.81 (d, 1H), 7.30−7.21 (m, 2H), 6.92−6.86 (m, 1H), 3.21 (t, J = 6.9 Hz, 2H), 2.86−2.80 (m, 2H), 2.16−2.06 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 143.0, 139.6, 129.6, 128.4, 128.1, 100.5, 41.2, 33.6, 5.9; MS [IP 70 eV; *m*/*z* (% rel int)] 372 (M^+, 38), 245 (56), 217 (100). Anal. Calcd for $C_9H_{10}I_2$: C, 29.06; H, 2.71. Found: C, 29.2; H, 2.7.

***N*-(*N′-tert*-Butylformimidoyl)-1,2,3,4-tetrahydropyridine (9).**[24a] To a solution of *N*-(*N′-tert*-butylformimidoyl)-piperidine[10] (18.2 g, 108 mmol) in 4:1 diethyl ether/THF (216 mL) was added slowly *t*-BuLi (93 mL, 140 mmol, 1.5 M in hexane) at −78 °C. The yellow solution was stirred at −20 °C until a white solid had precipitated (2 h). The reaction mixture was cooled to −78 °C, diphenyl diselenide (46 g, 150 mmol) was added, and the reaction mixture was stirred at −78 °C for 1 h and then allowed to reach room temperature overnight. The solution was poured into 3 N HCl (1.0 L), washed with diethyl ether (3 × 250 mL), and extracted with CH_2Cl_2 (5 × 200 mL). The combined CH_2Cl_2 layers were washed with 10% aqueous NaOH (2 × 200 mL) and stirred with K_2CO_3 (100 g) and Na_2SO_4 (100 g) under argon for 24 h. The reaction mixture was filtered and concentrated. The residue was taken up in 3 N HCl (500 mL), washed with diethyl ether (3 × 150), made basic with 20% aqueous NaOH (pH 12), extracted with CH_2Cl_2 (5 × 150), dried, and concentrated. The crude product was purified by bulb-to-bulb distillation (0.3 mmHg, oven temperature ≈ 60 °C) to yield *N*-(*N′-tert*-butylformimidoyl)-1,2,3,4-tetrahydropyridine (12.8 g, 71%). Spectroscopic data was consistent with data described elsewhere.[22a]

***N*-(*N′-tert*-Butylformimidoyl)-6-[2-(2-iodophenyl)ethyl]-1,2,3,4-tetrahydropyridine (1a).** To a solution of **9**[24a] (9.1 g, 55 mmol) in 4:1 diethyl ether/THF (55 mL) was added slowly t-BuLi (47 mL, 71 mmol, 1.5 M in hexane) at −78 °C. 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[42] (10 g, 77 mmol) in THF (55 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, **10a** (29 g, 82 mmol) was added, and the reaction mixture was 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 × 100 mL). The combined acidic aqueous layers were extracted with CH_2Cl_2 (5 × 100 mL). The combined CH_2Cl_2 layers were washed with 5% aqueous NaOH (2 × 100 mL) and brine (100 mL), dried over 1:1 K_2CO_3/Na_2SO_4, and concentrated to a yellow oil. The crude product was filtered through a pad of SiO_2 eluting with 10% triethylamine in pentane to yield **1a** (11.9 g, 54%): ^{1}H NMR ($CDCl_3$) δ 7.92 (s, 1H), 7.81 (dd, 1H), 7.27 (app dt, 1H), 7.15 (dd, 1H), 6.89 (app dt, 1H), 4.59 (t, J = 4.0 Hz, 1H), 3.67−3.63 (m, 2H), 2.91−2.85 (m, 2H), 2.55 (app t, 2H), 2.04−1.97 (m, 2H), 1.78−1.69 (m, 2H), 1.21 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 145.4, 143.9, 139.5, 137.6, 129.7, 128.4, 128.0, 103.2, 100.3, 53.7, 42.0, 39.6, 33.5, 31.4, 22.6, 21.8; IR ($CDCl_3$) 1625 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 396 (M^+, 48), 381 (6), 339 (13), 312 (7), 186 (100). Anal. Calcd for $C_{18}H_{25}N_2I$: C, 54.55; H, 6.36; N, 7.07. Found: C,54.3; H, 6.4; N, 7.0.

***N*-(*N′-tert*-Butylformimidoyl)-6-[3-(2-iodophenyl)propyl]-1,2,3,4-tetrahydropyridine (1b).** To a solution of **9**[24a] (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. The yellow solution was stirred at −20 °C until a white solid had precipitated (2 h). The reaction mixture was cooled to −78 °C, **10b** (11.2g, 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 1 N NaOH (2 × 40 mL), dried over 1:1 K_2CO_3/Na_2SO_4, and concentrated to a yellow oil. The crude product was filtered through a pad of SiO_2 eluting with 10% triethylamine in pentane to yield **1b** (5.8 g, 71%): ^{1}H NMR ($CDCl_3$) δ 7.80 (d, 1H), 7.77 (s, 1H), 7.26 (app t, 1H), 7.19 (dd, 1H), 6.88 (app dt, 1H), 4.62 (t, J = 3.9 Hz, 1H), 3.66−3.61 (m, 2H), 2.73 (app t,

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

2H), 2.36 (app t, 2H), 2.06−2.02 (m, 2H), 1.80−1.69 (m, 4H), 1.16 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 145.3, 144.5, 139.4, 137.9, 129.3, 128.2, 127.7, 102.4, 100.5, 53.6, 41.7, 40.2, 32.7, 31.2, 28.4, 22.5, 21.8; IR ($CDCl_3$) 1631 m^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 410 (M^+, 3), 353 (2), 283 (2), 193 (100). Anal. Calcd for $C_{19}H_{27}N_2I$: C, 55.61; H, 6.63; N, 6.83. Found: C, 55.9; H, 6.3; N, 6.6.

***N*-(*N′*-*tert*-Butylformimidoyl)-2-[2-(2-iodophenyl)ethyl]-piperidine (11).** Compound **11** was synthesized from *N*-(*N′*-*tert*-butylformimidoyl)piperidine[10] (0.6 g, 3.4 mmol) and **10a** (1.6 g, 6.2 mmol) as described above for the synthesis of **1a.** The product was purified by bulb-to-bulb distillation (0.2 mmHg, oven temperature ≈ 115 °C) to yield **11** (0.5 g, 34%) as a white solid, mp 50−52 °C: ^{1}H NMR ($CDCl_3$) δ 7.80 (d, 1H), 7.36 (s, 1H), 7.29−7.21 (m, 2H), 6.90−6.84 (m, 1H), 3.76−3.69 (m, 2H), 2.98 (dt, J = 12.7 and 3.0 Hz, 1H), 2.68−2.62 (m, 2H), 2.08−1.93 (m, 1H), 1.75−1.59 (m, 6H), 1.44−1.40 (m, 1H), 1.17 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 150.9, 144.8, 139.4, 129.3, 128.4, 127.7, 100.4, 53.9, 52.8, 40.8, 38.2, 31.4, 30.7, 28.9, 25.3, 20.1. IR ($CDCl_3$) 1633 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 398 (M^+, 39), 383 (80), 314 (33), 168 (100). Anal. Calcd for $C_{18}H_{27}N_2I$: C, 54.28; H, 6.83; N, 7.03. Found: C, 54.5; H, 6.9; N, 7.0.

1′-(*N*-*tert*-Butylformimidoyl)-3′,4′-dihydrospiro[indan-1,2′(1′*H*)-pyridine] (4a). $Pd(OAc)_2$ (5.6 mg, 0.025 mmol) and K_2CO_3 (138 mg, 1.0 mmol) were mixed in CH_3CN (25 mL) under a stream of argon. **1a** (198 mg, 0.50 mmol) was added to the mixture. The reaction mixture was stirred and heated at 100 °C for 168 h. After cooling, the black mixture was poured into saturated aqueous $NaHCO_3$ (60 mL) and extracted with diethyl ether (3 × 40 mL), the combined ether layers were extracted with 3 N HCl (3 × 40 mL), and the combined acidic aqueous layers were extracted with CH_2Cl_2 (5 × 30 mL). The combined CH_2Cl_2 layers were washed with 1 N NaOH, dried K_2CO_3, and concentrated. Purification by preparative TLC (SiO_2, eluting with 10% triethylamine in pentane, R_f 0.55) gave **4a** (72.8 mg 54%) as an oil: ^{1}H NMR ($CDCl_3$) δ 7.31−7.16 (m, 5H, Ar-H, H-6′), 6.99 (s, 1H, NC*H*═N), 4.98−4.89 (m, 1H, H-5′), 3.04−2.82 (m, 2H, H-3), 2.37−2.18 (m, 2H, H-4′), 2.12 (app t, 2H, H-2), 2.19−2.00 (m, 1H, H-3′), 1.80−1.72 (m, 1H, H-3′), 0.96 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 145.5 (N*C*H═N), 145.4, 143.5 (C-8, C-9), 128.2, 127.1, 125.3, 125.0, 123.7 (C-4, C-5, C-6, C-7, C-6′), 102.8 (C-5′), 67.8 (C-1), 53.5 (*C*(CH$_3$)$_3$), 37.5 (C-2), 33.9 (C-3′), 30.9 (C(*C*H$_3$)$_3$), 29.4 (C-3), 20.2 (C-4′); IR ($CDCl_3$) 1625 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 268 (M^+, 50), 185 (35), 168 (37), 139 (49). Anal. Calcd for $C_{18}H_{24}N_2$: C, 80.55; H, 9.01; N,10.43. Found: C, 80.3; H, 9.1; N, 10.3.

1′-(*N*-*tert*-Butylformimidoyl)-3,3′,4,4′-tetrahydrospiro-[naphthalene-1(2*H*),2′(1′*H*)-pyridine] (4b). $Pd(OAc)_2$ (9.0 mg, 0.040 mmol) and $AsPh_3$ (49 mg, 0.16 mmol) were mixed in CH_3CN (25 mL) under a stream of argon. Triethylamine (101 mg, 1.0 mmol) and **1b** (205 mg, 0.50 mmol) were added to the mixture. The reaction mixture was stirred and heated at 80 °C for 38 h. Workup as described for **4a** and preparative TLC (SiO_2, eluting with 10% triethylamine in isohexane, R_f 0.45) gave **4b** (62 mg, 44%): ^{1}H NMR ($CDCl_3$) δ 7.29−7.09 (m, 5H, Ar-H, H-6′), 7.04 (s, 1H, NC*H*═N), 4.93−4.86 (m, 1H, H-5′), 2.86−2.73 (m, 2H, H-4), 2.15−1.68 (m, 8H, H-2, H-3, H-3′, H-4′), 0.95 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 147.0 (N*C*H═N), 139.8, 137.8 (C-9, C-10), 129.1, 127.7, 126.9, 126.4, 125.1 (C-5, C-6, C-7, C-8, C-6′), 102.0 (C-5′), 57.8 (C-1), 53.4 (*C*(CH$_3$)$_3$), 36.3, 32.6, 19.6, 19.0 (C-2, C-3, C-3′, C-4′), 30.9 (C(*C*H$_3$)$_3$), 30.1 (C-4); IR ($CDCl_3$) 1634 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 282 (M^+, 93), 225 (16), 210 (14), 199 (65), 182 (100), 170 (89), 139 (66), 129 (91). Anal. Calcd for $C_{19}H_{26}N_2$: C, 80.80; H, 9.28; N, 9.92. Found: C, 80.7; H, 9.1; N, 9.9.

1′-(*N*-*tert*-Butylformimidoyl)-1′,6′-dihydrospiro[indan-1,2′(3′*H*)-pyridine] (5a). $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), (*R*)-BINAP (62 mg, 0.10 mmol), triethylamine (101 mg, 1.0 mmol), and cyclohexene (8.2 mg, 0.10 mmol) were mixed under argon in CH_3CN (15 mL) and heated at 60 °C for 3 h. **1a** (198 mg, 0.50 mmol) was added, and the reaction mixture was heated at 80 °C for 20 h. Workup as described for **4a** gave a mixture of **5a** and **4a** (103 mg). Preparative TLC (SiO_2, eluting with 10% triethylamine in pentane, R_f 0.50) gave **5a** (72 mg, 54%) as an oil: ^{1}H NMR ($CDCl_3$) δ 7.30−7.26 (m, 4H, Ar-H), 7.21 (s, 1H, NC*H*═N), 5.87−5.80 (m, AB-spectra, 2H, H-4′, H-5′), 4.26−4.16 (m, 1H, H-6′), 3.64−3.55 (m, 1H, H-6′), 2.86 (app t, 2H, H-3), 2.70−2.61 (m, 1H, H-3′), 2.16−2.04 (m, 1H, H-3′), 2.07 (app t, 2H, H-2), 0.95 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 149.5 (N*C*H═N), 144.6, 143.8 (C-8, C-9), 128.2, 126.9, 125.1, 124.4 (2 C′s), 123.0 (C-4, C-5, C-6, C-7, C-4′, C-5′), 67.6 (C-1), 53.5 (*C*(CH$_3$)$_3$), 43.3 (C-6′), 37.9 (C-3′), 35.7 (C-2), 31.0 (C(*C*H$_3$)$_3$), 29.5 (C-3); IR ($CDCl_3$) 1623 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 268 (M^+, 77), 211 (18), 169 (71), 167 (100), 115 (75). Anal. Calcd for $C_{18}H_{24}N_2$: C, 80.55; H, 9.01; N, 10.44. Found: C, 80.4; H, 8.9; N, 10.4.

1′-(*N*-*tert*-Butylformimidoyl)-1′,3,4,6′-tetrahydrospiro-[naphthalene-1(2*H*),2′(3′*H*)-pyridine] (5b). Compound **5b** was synthesized from **1b** (205 mg, 0.50 mmol), $Pd(OAc)_2$ (11.2 mg, 0.050 mmol), (*R*)-BINAP (62 mg, 0.10 mmol), triethylamine (101 mg, 1.0 mmol), and cyclohexene (8.2 mg, 0.10 mmol) as described above for the synthesis of **5a**. Preparative TLC (SiO_2, eluting with 10% triethylamine in isohexane, R_f 0.40) gave **5b** (70 mg, 49%): ^{1}H NMR ($CDCl_3$) δ 7.43 (dd, 1H, Ar-H), 7.23−7.11 (m, 4H, Ar-H, NC*H*═N), 5.92−5.78 (m, AB-spectra, 2H, H-4′, H-5′), 4.22 (app d, 1H, H-6′), 3.56 (app d, 1H, H-6′), 2.83−2.71 (m, 3H, H-4, H-3′), 2.30−2.18 (m, 1H, H-3′), 1.92−1.57 (m, 4H, H-2, H-3), 0.87 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 151.7 (N*C*H═N), 139.4, 138.6 (C-9, C-10), 129.1, 128.6, 127.1, 126.5 (C-5, C-6, C-7, C-8), 123.7, 122.8 (C-4′, C-5′), 57.7 (C-1), 53.5 (*C*(CH$_3$)$_3$), 43.0 (C-6′), 39.5 (C-3′), 32.4 (C-2), 31.0 (C(*C*H$_3$)$_3$), 30.4 (C-4), 19.6 (C-3); IR ($CDCl_3$) 1622 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 282 (M^+, 100), 225 (21), 208 (13), 198 (16), 181 (50), 167 (42). Anal. Calcd for $C_{19}H_{26}N_2 \cdot {}^1/_4H_2O$: C, 79.53; H, 9.31; N, 9.76. Found: C, 79.7; H, 9.1; N, 9.5.

1′-(*N*-*tert*-Butylformimidoyl)-5′,6′-dihydrospiro[indan-1,2′(1′*H*)-pyridine] (6a). $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), PPh_3 (26 mg, 0.10 mmol), and TlOAc (145 mg, 0.55 mmol) were mixed in CH_3CN (25 mL) under a stream of argon. Triethylamine (101 mg, 1.0 mmol) and **1a** (198 mg, 0.50 mmol) were added to the mixture. The reaction mixture was stirred and heated at 80 °C for 17 h. Workup as described for **4a** and filtering through a pad of SiO_2 eluting with 10% triethylamine in pentane gave **6a** (106 mg, 79%) as an oil which solidified upon standing, mp 41−44 °C: ^{1}H NMR ($CDCl_3$) δ 7.28−7.17 (m, 4H, Ar-H), 6.99 (s, 1H, NC*H*═N), 5.90 (ddd, J = 9.9, 5.7, and 2.1 Hz, 1H, H-4′), 5.55 (ddd, J = 9.9, 2.2, and 1.0 Hz, 1H, H-3′), 4.32 (ddd, J = 12.9, 5.4, and 1.5 Hz, 1H, H-6′), 3.00−2.81 (m, 3H, H-3, H-6′), 2.46−2.29 (m, 1H, H-5′), 2.28−2.16 (m, 2H, H-2), 2.16−2.02 (m, 1H, H-5′), 0.96 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) δ 149.9 (N*C*H═N), 145.3, 143.9 (C-8, C-9), 132.8 (C-3′), 128.3, 127.1, 124.8, 124.7 (C-4, C-5, C-6, C-7), 124.3 (C-4′), 69.3 (C-1), 53.1 (*C*(CH$_3$)$_3$), 38.1 (C-2), 37.6 (C-6′), 31.1 (C(CH$_3$)$_3$), 30.0 (C-3), 24.6 (C-5′); IR ($CDCl_3$) 1629 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 268 (M^+, 100), 253 (12), 211 (11), 184 (23), 168 (25), 113 (40), 57 (79). Anal. Calcd for $C_{18}H_{24}N_2$: C, 80.55; H, 9.01; N, 10.43. Found: C, 80.5; H, 9.1; N, 10.0.

1′-(*N*-*tert*-Butylformimidoyl)-3,4,5′,6′-tetrahydrospiro-[naphthalene-1(2*H*),2′(1′*H*)-pyridine] (6b). Compound **6b** was synthesized from **1b** (205 mg, 0.50 mmol), $Pd(OAc)_2$ (9.0 mg, 0.040 mmol), PPh_3 (42 mg, 0.16 mmol), TlOAc (145 mg, 0.55 mmol), and triethylamine (101 mg, 1.0 mmol) as described above for the synthesis of **6a**. Preparative TLC (SiO_2, eluting with 10% triethylamine in isohexane, R_f 0.40) gave **6b** (74 mg, 52%) as a light yellow solid, mp 69−71 °C: ^{1}H NMR ($CDCl_3$) δ 7.31−7.26 (m, 1H), 7.19−7.08 (m, 3H), 7.06 (s, 1H), 5.90−5.87 (m, 1H), 5.60 (ddd, J = 10.0, 2.7, and 1.1 Hz, 1H), 4.40 (app dd, 1H), 2.98 (ddd, J = 13.1, 11.3, and 4.1 Hz, 1H), 2.82−2.76 (m, 2H), 2.48−2.35 (m, 1H), 2.13−2.02 (m, 2H), 1.94−1.66 (m, 3H), 0.94 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 151.6, 138.5, 137.9, 135.0, 129.3, 128.8, 127.1, 126.4, 123.5, 59.1, 52.9, 35.8, 34.4, 31.1, 29.7, 24.7, 19.0; IR ($CDCl_3$) 1626 cm^{-1}; MS [IP 70 eV; *m*/*z* (% rel int)] 282 (M^+, 100), 267 (29), 225 (23), 210 (23), 182 (29), 170 (43). Anal. Calcd for $C_{19}H_{26}N_2$: C, 80.81; H, 9.28; N, 9.91. Found: C, 80.7; H, 9.2; N, 9.8.

(*E*)-Methyl 3-(2-{2-[*N*-(*N′*-*tert*-Butylformimidoyl)-2-piperidyl]ethyl}phenyl)propenoate (12). $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), PPh_3 (11 mg, 0.04 mmol), triethylamine (41 mg, 0.4 mmol), and **11** (80 mg, 0.2 mmol) were mixed in CH_3CN

(2 mL) under a stream of argon and stirred for 5 min before methyl acrylate (35 mg, 0.4 mmol) was added to the mixture. The reaction mixture was stirred and heated at 80 °C for 22 h. Workup as described for **4a** and filtering through a pad of SiO_2 eluting with 10% triethylamine in 8:1 pentane/EtOAc gave **12** (61 mg, 85%) as an oil: ^{1}H NMR ($CDCl_3$) δ 7.99 (d, J = 15.8 Hz, 1H), 7.58−7.53 (m, 1H), 7.33 (s, 1H), 7.31−7.19 (m, 3H), 6.37 (d, J = 15.8, 1H), 3.81 (s, 3H), 3.74−3.54 (m, 2H), 2.99−2.86 (m, 1H), 2.78−2.64 (m, 2H), 2.05−1.93 (m, 1H), 1.71−1.60 (m, 6H), 1.52−1.36 (m, 1H), 1.16 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 167.3, 150.9, 142.2, 142.0, 132.8, 130.1, 130.0, 126.6, 126.5, 119.1, 53.5, 52.8, 51.7, 41.0, 31.9, 31.3, 30.5, 28.8, 25.3, 20.0; IR ($CDCl_3$) 1711, 1627 cm^{-1}; MS [IP 70 eV; m/z (% rel int)] 356 (M^+, 31), 341 (77), 297 (56), 168 (82), 111 (69), 84 (100). Anal. Calcd for $C_{22}H_{32}N_2O_2$: C, 74.12; H, 9.05; N, 7.86. Found: C, 74.0; H, 8.9; N, 7.8.

1′-(*N*-*tert*-Butylformimidoyl)spiro[indan-1,2′-piperidine] (2a). $Pd(OAc)_2$ (5.6 mg, 0.025 mmol) and TFP (24 mg, 0.10 mmol) were mixed in CH_3CN (25 mL) under a stream of argon. Triethylamine (101 mg, 1.0 mmol) and **1a** (198 mg, 0.50 mmol) were added to the mixture. The reaction mixture was stirred and heated at 80 °C for 19 h. Workup as described for **4a** and filtering through a pad of SiO_2 eluting with 10% triethylamine in pentane gave a mixture of **4a**, **5a**, and **6a** (106 mg, 79%). The product mixture (50 mg, 0.19 mmol) and 10% Pd/C (20 mg, 0.019 mmol) were mixed in absolute ethanol (5 mL) and stirred under H_2 (1 atm) for 16 h.[43] The mixture was filtered through Celite and concentrated. The residue was dissolved in 5 mL of diethyl ether, washed with 10% NaOH (2 × 1 mL), dried (K_2CO_3), and concentrated to yield **2a** (44 mg, 88%, two steps 70%): ^{1}H NMR ($CDCl_3$) δ 7.31−7.24 (m, 4H, Ar-H), 7.09 (s, 1H, NC*H*=N), 4.14−4.09 (m, 1H, H-6′), 2.84 (t, J = 7.23 Hz, 2H, H-3), 2.70−2.61 (m, 1H, H-6′), 2.25−2.15 (m, 1H, H-2), 2.05−1.98 (m, 1H, H-2), 1.84−1.57 (m, 6H, H-3′, H-4′, H-5′), 0.93 (s, 9H, C(C*H*$_3$)$_3$); ^{13}C NMR ($CDCl_3$) δ 151.2 (N*C*H=N), 146.3, 143.2 (C-8, C-9), 128.0, 126.8, 124.9, 124.0 (C-4, C-5, C-6, C-7), 69.7 (C-1), 53.3 (*C*(CH$_3$)$_3$), 41.5 (C-6′), 37.9, 24.9, 21.6 (C-3′, C-4′, C-5′), 33.7 (C-2), 31.1 (C(*C*H$_3$)$_3$), 29.7 (C-3); IR ($CDCl_3$) 1628 cm^{-1}; MS [IP 70 eV; m/z (% rel int)] 270 (M^+, 93), 255 (13), 198 (27), 172 (48), 128 (100), 115 (91). Anal. Calcd for $C_{18}H_{26}N_2$: C, 79.95; H, 9.69; N, 10.35. Found: C, 79.9; H, 9.6; N, 10.3.

1′-(*N*-*tert*-Butylformimidoyl)-3,4-dihydrospiro[naphthalene-1(2*H*),2′-piperidine] (2b). Compound **2b** was prepared from **1b** (205 mg, 0.50 mmol), $Pd(OAc)_2$ (9.0 mg, 0.040 mmol), TFP (37 mg, 0.16 mmol), and triethylamine (101 mg, 1.0 mmol) as described above for the synthesis of **2a** to give a mixture of **4b**, **5b** and **6b**, (111 mg, 79%) that was hydrogenated as described above to yield **2b** (101 mg, 91%, two steps 72%) as a white solid mp 51−54 °C: ^{1}H NMR ($CDCl_3$) δ 7.52 (dd, 1H, Ar-H), 7.22−7.06 (m, 4H, Ar-H, NC*H*=N), 4.05−4.01 (m, 1H, H-6′), 2.82−2.73 (m, 3H, H-4, H-6′), 2.15−2.07 (m, 1H, H-2), 1.85−1.64 (m, 9H, H-2, H-3, H-3′, H-4′, H-5′), 0.93 (s, 9H, C(C*H*$_3$)$_3$); ^{13}C NMR ($CDCl_3$) δ 152.8 (N*C*H=N), 141.3, 137.9 (C-9, C-10), 128.8, 128.1, 126.5, 126.2 (C-5, C-6, C-7, C-8), 59.0 (C-1), 53.2 (*C*(CH$_3$)$_3$), 40.0 (C-6′), 39.6, 24.9, 19.7 (C-3′, C-4′, C-5′), 31.1 (C(*C*H$_3$)$_3$), 30.5 (C-2), 30.2 (C-4), 20.3 (C-3); IR ($CDCl_3$) 1626 cm^{-1}; MS [IP 70 eV; m/z (% rel int)] 284 (M^+, 100), 269 (23), 227 (35), 212 (30), 128 (57). Anal. Calcd for $C_{19}H_{28}N_2$: C, 80.23; H, 9.92; N, 9.84. Found: C, 80.2; H, 9.9; N, 9.7.

Spiro[indan-1,2′-piperidine] (3a). **2a** (60 mg, 0.22 mmol) was mixed with hydrazine monohydrate (88 mg, 1.62 mmol) and acetic acid (40 mg, 0.66 mmol) in EtOH (3.0 mL) and warmed at 50 °C until TLC indicated consumption of the amidine. 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 filtered through a pad of SiO_2 eluting with 10% triethylamine in pentane to yield **3a** (35 mg, 82%). For elemental analyses the amine was converted to the HCl salt, mp 227 °C dec: ^{1}H NMR (free amine, $CDCl_3$) δ 7.39−7.31 (m, 1H, Ar-H), 7.21−7.18 (m, 3H, Ar-H), 3.02−2.78 (m, 4H, H-3, H-6′), 2.39−2.30 (m, 1H, H-2), 2.09−1.98 (m, 1H, H-2), 1.81−1.58 (m, 7H, H-3′, H-4′, H-5′, NH); ^{13}C NMR (free amine, $CDCl_3$) δ 150.2, 142.6 (C-8, C-9), 127.5, 126.5, 124.6, 123.2 (C-4, C-5, C-6, C-7), 65.8 (C-1), 43.1, 29.5 (C-3, C-6′), 35.9, 35.8, 26.1, 22.2 (C-2, C-3′, C-4′, C-5′); MS [IP 70 eV; m/z (% rel int)] (free amine) 187 (M^+, 50), 158 (100), 145 (99), 130 (60), 115 (67). Anal. Calcd for $C_{13}H_{17}N$·HCl: C, 69.79; H, 8.11; N, 6.26. Found: C, 69.7; H, 8.2; N, 6.2.

3,4-Dihydrospiro[naphthalene-1(2*H*),2′-piperidine] (3b). Compound **3b** was synthesized from **2b** (62 mg, 0.22 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 to yield **3b** (38 mg, 86%). For elemental analyses the amine was converted to the HCl salt, mp 263 °C dec: ^{1}H NMR (free amine, $CDCl_3$) δ 7.73 (dd, 1H, Ar-H), 7.22−6.87 (m, 3H, Ar-H), 3.07−2.68 (m, 4H, H-4, H-6′), 2.24-2.15 (m, 1H, H-2), 1.90−1.57 (m, 9H, H-2, H-3, H-3′, H-4′, H-5′), 1.40 (br s, 1H, NH); ^{13}C NMR (free amine, $CDCl_3$) δ 144.9, 137.0 (C-9, C-10), 128.6, 127.4, 126.2, 126.0 (C-5, C-6, C-7, C-8), 53.9 (C-1), 41.2 (C-6′), 37.4, 26.2, 20.8 (C-3′, C-4′, C-5′), 30.4 (2 C′s, C-2, C-4), 19.7 (C-3); MS [IP 70 eV; m/z (% rel int)] (free amine) 201 (M^+, 63), 186 (11), 172 (100), 158 (84), 144 (28). Anal. Calcd for $C_{14}H_{19}N$·HCl: C, 70.72; H, 8.48; N, 5.89. Found: C, 70.9; H, 8.4; N, 5.9.

1′,6′-Dihydrospiro[indan-1,2′(3′*H*)-pyridine] (7a). Compound **7a** was synthesized from **5a** (30 mg, 0.11 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 to yield **7a** (19 mg, 92%). For elemental analyses the amine was converted to the HCl salt, mp 214 °C dec: ^{1}H NMR (free amine, $CDCl_3$) δ 7.37−7.34 (m, 1H, Ar-H), 7.25−7.17 (m, 3H, Ar-H), 5.89−5.85 (m, 2H, AB-spectra, H-4′, H-5′), 3.59−3.36 (m, 2H, H-6′), 3.04−2.81 (m, 2H, H-3), 2.36−2.15 (m, 3H, H-2, H-3′), 2.08−1.97 (m, 1H, H-2), 1.68 (br s, 1H, NH); ^{13}C NMR (free amine, $CDCl_3$) δ 148.6, 142.9 (C-8, C-9), 127.5, 126.4, 126.1, 125.1, 124.7, 123.1 (C-4, C-5, C-6, C-7, C-4′, C-5′), 63.1 (C-1), 42.5 (C-6′), 38.5 (C-3′), 35.9 (C-2), 29.4 (C-3); MS [IP 70 eV; m/z (% rel int)] (free amine) 185 (M^+, 70), 184 (100), 170 (66), 156 (27), 130 (85), 115 (50). Anal. Calcd for $C_{13}H_{15}N$·HCl: C, 70.42; H, 7.27; N, 6.32. Found: C, 70.2; H, 7.1; N, 6.3.

1′,3,4,6′-Tetrahydrospiro[naphthalene-1(2*H*),2′(3′*H*)-pyridine] (7b). Compound **7b** was synthesized from **5b** (43 mg, 0.15 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 to yield **7b** (26 mg, 86%). For elemental analyses the amine was converted to the HCl salt, mp 269 °C dec: ^{1}H NMR ($CDCl_3$) δ 7.58 (dd, 1H, Ar-H), 7.21−7.05 (m, 3H, Ar-H), 5.84−5.81 (m, AB-spectra, 2H, H-4′, H-5′), 3.59−3.33 (m, 2H, H-6′), 2.81 (app t, 2H, H-4), 2.53−2.45 (m, 1H, H-3′), 2.20−2.05 (m, 2H, H-2, H-3′), 1.91−1.70 (m, 3H, H-2, H-3), 1.53 (br s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 143.4, 137.0 (C-9, C-10), 128.7, 127.2, 126.4, 126.1 (C-5, C-6, C-7, C-8), 125.3, 125.2 (C-4′, C-5′), 52.1 (C-1), 41.8 (C-6′), 37.7 (C-3′), 32.4 (C-2), 30.3 (C-4), 19.6 (C-3); MS [IP 70 eV; m/z (% rel int)] 199 (M^+, 67), 198 (73), 184 (46), 170 (100), 117 (86). Anal. Calcd for $C_{14}H_{17}N$·HCl: C, 71.33; H, 7.70; N, 5.94. Found: C, 71.3; H, 7.8; N, 5.6.

5′,6′-Dihydrospiro[indan-1,2′(1′*H*)-pyridine] (8a). Compound **8a** was synthesized from **6a** (40 mg, 0.15 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 to yield **8a** (23 mg, 82%). For elemental analyses the amine was converted to the HCl salt, mp 176−177 °C: ^{1}H NMR (free amine, $CDCl_3$) δ 7.27−7.18 (m, 4H, Ar-H), 5.97 (dt, J = 10.2 and 3.8 Hz, 1H, H-4′), 5.67 (dt, J = 10.2 and 2.1 Hz, 1H, H-3′), 3.16−2.80 (m, 4H, H-3, H-6′), 2.22−2.08 (m, 4H, H-2, H-5′), 1.60 (br s, 1H, NH); ^{13}C NMR (free amine, $CDCl_3$) δ 148.4, 143.5 (C-8, C-9), 133.2, 127.7, 126.2, 125.9, 125.0, 123.8 (C-4, C-5, C-6, C-7, C-3′, C-4′), 65.3 (C-1), 40.3, 39.8 (C-5′, C-6′), 29.8, 25.5 (C-2, C-3); MS [IP 70 eV; m/z (% rel int)] (free amine) 185 (M^+, 82), 184 (83), 170 (43), 156

(43) Hydrogenation with platinum oxide in acetic acid at 55 psi was almost as effective, providing an alternative procedure, delivering less undesired products.

(100), 141 (33), 128 (69), 115 (73). Anal. Calcd for $C_{13}H_{15}N\cdot$HCl: C, 70.42; H, 7.27; N, 6.32. Found: C, 70.2; H, 7.3; N, 6.3.

3,4,5′,6′-Tetrahydrospiro[naphthalene-1(2*H*),2′(1′*H*)-pyridine] (8b). Compound **8b** was synthesized from **6b** (68 mg, 0.24 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 to yield **8b** (43 mg, 90%). For elemental analyses the amine was converted to the HCl salt, mp 238−239 °C: ^{1}H NMR (free amine, $CDCl_3$) δ 7.44−7.40 (m, 1H, Ar-H), 7.16−7.07 (m, 3H, Ar-H), 5.96 (dt, J = 10.2 and 3.9 Hz, 1H, H-4′), 5.60 (dt, J = 10.2 and 1.9 Hz, 1H, H-3′), 2.98 (dd, J = 6.9 and 5.2 Hz, 2H, H-6′), 2.83−2.77 (m, 2H, H-4), 2.21−1.65 (m, 6H, H-2, H-3, H-5′), 1.55 (br s, 1H, NH); ^{13}C NMR (free amine, $CDCl_3$) δ 141.6, 136.6 (C-9, C-10), 135.4 (C-3′), 129.2, 128.5, 126.7, 125.6 (C-5, C-6, C-7, C-8), 125.2 (C-4′), 54.3 (C-1), 38.6, 29.6 (C-4, C-6′), 34.8, 25.7, 18.4 (C-2, C-3, C-5′); MS [IP 70 eV; m/z (% rel int)] 199 (M^+, 45), 184 (13), 170 (100). Anal. Calcd for $C_{14}H_{17}N\cdot HCl\cdot{}^1/_4H_2O$: C, 70.00; H, 7.76; N, 5.83. Found: C, 70.3; H, 7.6; N, 5.9.

Acknowledgment. The authors are grateful to the Swedish Natural Science Research Council for financial support and to Mats Berglund and Magnus Jörntén-Karlsson (Astra Draco AB, Lund, Sweden) for the electrospray ionization mass spectrometry data.

Supporting Information Available: Experimental section for ESI-MS experiments and observed ESI-MS spectra and isotopic distributions for peaks mentioned (8 pages). This material is contained in the libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO960970Y