Synthesis of Novel D-Secoestrone Isoquinuclidines by an Unpredicted Iminium Ion-Induced 1,5-Hydride Shift

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Unique 9,13-bridged D-secoestrone alkaloids have been synthesized and structurally characterized. Treatment of 3-methoxy-16,17-secoestra-1,3,5(10)-trien-17-al (**6a**) with aniline (**7**) or substituted aniline derivatives **8**–**28** in the presence of different Lewis and Brønsted acids produces the bridged azaestrone derivatives **51**–**67** and the alkenes **68**–**73** in high yields in a domino-type process. The imines **29**–**50** are proposed as intermediates, undergoing 1,5-hydride shifts via the iminium ion salts **75** to give the cations **77**, which, depending on the substitution pattern on the aniline moiety, either afford the bridged compounds through a nucleophilic addition of the formed secondary amine to the benzylic carbocation or give the alkenes through the abstraction of a proton at C-8.

Introduction

One of the current major aims of steroid chemistry is the development of new compounds with useful biological activity. The transformation of external functional groups[1−4] and the functionalization of the sterane skeleton[5−7] are most common for the synthesis of novel derivatives. In addition, ring expansion, resulting in homo derivatives,[8−10] or ring opening, resulting in secosteroids,[11−13] are other possible modifications of the natural framework. Thus, several A- and D-ring-substituted analogues in the estrone series have already been synthesized and examined for their pharmacological effects.[14−16] Although position C-9 in aromatic 19-norsteroids is activated thanks to its benzylic nature, substitution at this carbon is rare. As one example, though, the regio- and stereoselective introduction of an azido group at this position by the application of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone as an oxidant and hydrazoic acid as an azido donor was reported by Guy et al.[17] In addition, C-9 hydroxylation of aromatic steroids by in situ produced dimethyldioxirane,[18,19] ceric ammonium nitrate[20] or chromium trioxide[21] is also known. In contrast to these intermolecular functionalizations, intramolecular reactions that would afford a new ring system have not so far been described, except in our work.

Thus, we have recently reported on a Lewis acid-catalyzed cyclization of arylimines from the normal secoestrone aldehyde **2a** and substituted aniline derivatives to give halogenated D-homosteroids and tetrahydroquinoline derivatives as major products.[22,23] Treatment of **2a** with *p*-bromoaniline, however, also gave, besides **3** and **4**, small amounts of the bridged steroid alkaloid analogue **5** (Scheme 1). Astoundingly, such side reactions can become predominant if the aldehyde **6a**, in which the propenyl side chain of **2a** is hydrogenated, is used as substrate.

Here we describe the regioselective synthesis of some novel and unusual bridged N-heterocyclic estrone derivatives **51**−**67**, through intermediate Lewis acid-induced formation of iminium salts from **6**.[24] The subsequent reaction presumably proceeds through an attack of the iminium ion at the benzylic C−H bond with a 1,5-hydride shift, involving the formation of a tertiary benzylic carbocation and an amine, which then attacks the cation to form a ring. The reactivity scale of Mayr and Ofial indicates that the iminium ion has an electrophilicity similar to that of the *p*-nitrobenzenediazonium ion or the tropylium cation,[25] and it is therefore assumed to be able to cleave a hydride from the activated benzylic position, though such reactions are rather uncommon. The resulting derivatives **51**−**67** contain an isoquinuclidine ring system, a familiar structural moiety in various synthetic pharmacologically active molecules, such as 5-HT_3 antagonists,[26] epibatidine analogues[27] and expectorants.[28] Moreover, isoquinuclidine derivatives are valuable intermediates in alkaloid synthesis.[29]

Results and Discussion

The D-secoestrone (**2a**), easily accessible in four steps from 3-methoxyestrone (**1a**) through a Grob fragmentation

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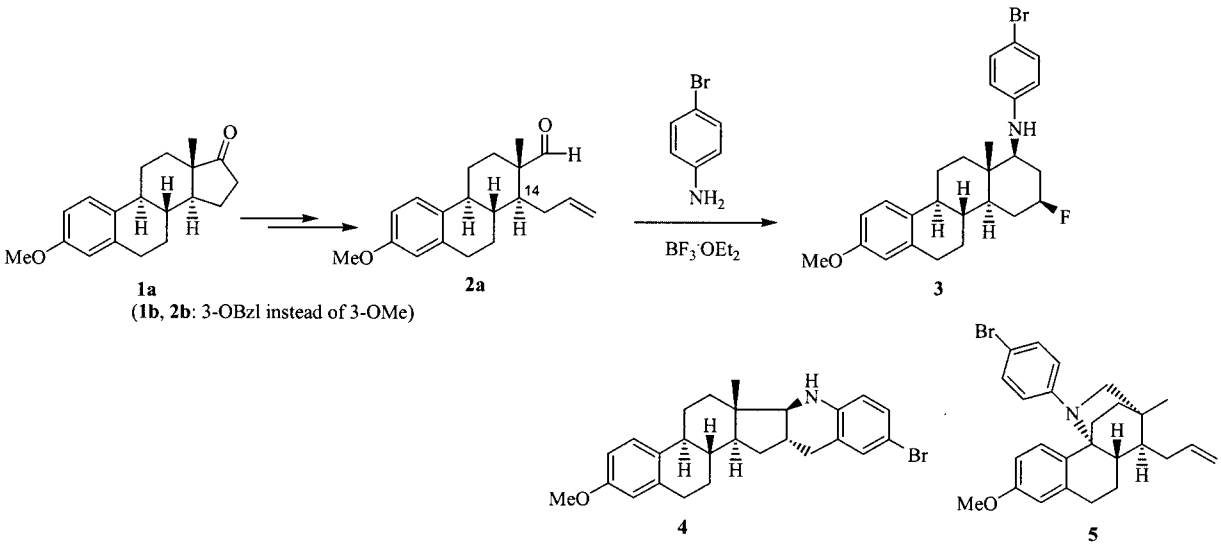


Scheme 1. Reaction of the secoestrone aldehyde **2a** derived from 3-methoxyestrone (**1a**) and *p*-bromoaniline in the presence of BF_3·OEt_2

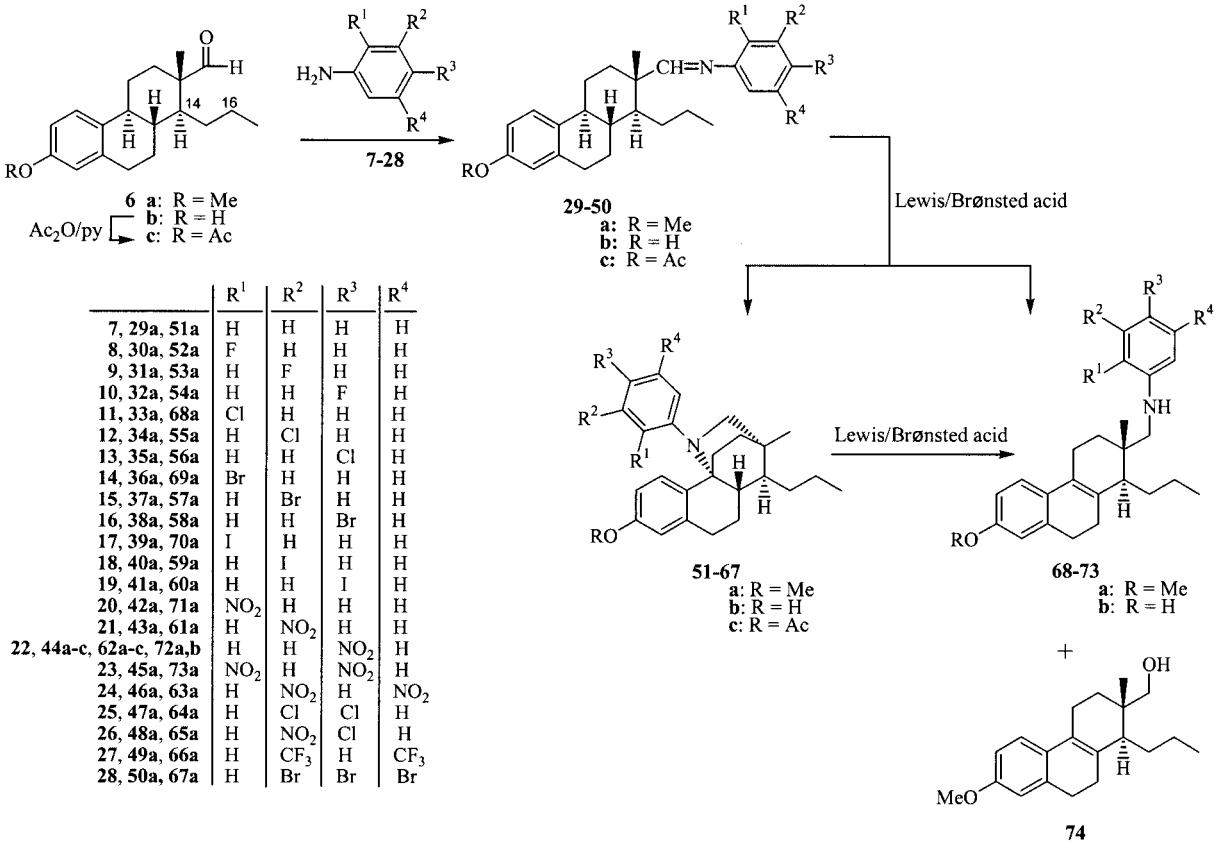
as a key step,[30] was hydrogenated to give the saturated aldehyde **6a** (Scheme 2). Treatment of **6a** with aniline (**7**) or with its mono-, di- and trisubstituted derivatives **8**−**28**, containing electron-withdrawing halo, nitro or halomethyl groups in different positions, produced the imines **29**−**50**, which readily underwent transformation in the presence of BF_3·OEt_2. As expected, the imines proved to be quite unstable, and so purification by column chromatography was difficult, since they are easily converted into the starting materials. The crude imines were therefore used for further transformation through the use of a molar amount of BF_3·OEt_2 to give two kinds of products, depending on the natures and the locations of the substituents on the aniline moiety. More efficiently, though, the transformation could be carried out as an one-pot reaction with the imines formed in situ.

Interestingly, different products were obtained in the reactions involving aniline (**7**) and monosubstituted fluoro- (**8**−**10**), chloro- (**11**−**13**), bromo- (**14**−**16**) and iodoaniline derivatives (**17**−**19**), depending on the substitution pattern. When aniline (**7**) or *meta*- (**9**, **12**, **15** or **18**) or *para*-substituted haloaniline derivatives (**10**, **13**, **16** or **19**) were applied, the isoquinuclidine derivatives (**51a**,[31] **53a**−**60a**) with the unusual molecular framework were obtained nearly exclusively in high yield. Use of aniline derivatives containing an *ortho*-halogen function, on the other hand, resulted in the formation of the unsaturated secondary amines (**68a**−**70a**) in 70−80 % yield, with the exception of the use of *o*-fluoroaniline **8**, which resulted in the formation of the bridged product **52a**. It can be assumed that the steric inhibitory effect of the *ortho* substituent hinders cyclization at position 9 to give the isoquinuclidine derivative. This assumption is also consistent with the reaction of **8**, since the fluorine atom is fairly small, with a size comparable to that of a hydrogen atom. In a similar series, the nitroaniline derivatives **20**−**22** or di- or trisubstituted aniline derivatives **23**−**28** were treated with **6a**. Again, when the functional groups at the aromatic ring were in *meta* and/or *para* positions, the bridged alkaloids **41a**, **42a** and **43a**−**47a** were obtained, while use of the *o*-functionalized aniline derivatives **20** and **23** resulted in the 8,9-unsaturated products **71a** and **73a**. In three cases an additional compound **74** could be isolated, but in a yield of less than 6 %.

In addition to the secoestrone derivative **6a**, we also used the substrates **6b** and **6c**, easily accessible from **1b** by debenzylation ($Pd/C/H_2$) and acetylation, respectively, as the final step. Treatment of either **6b** or **6c** with *p*-nitroaniline (**22**) afforded the imines **44b** and **44c**, containing a hydroxy group and an acetoxy group, respectively, at C-3 of the estrane skeleton. The BF_3·OEt_2-induced transformation of **44b** gave compounds **62b** and **72b** in a ratio of 2:1 within 6 h at room temperature, while such treatment of **44c** merely yielded 16 % of the bridged compound **62c** as the only product after 24 h, together with unchanged starting material. These results indicated that the different substituents at C-3 of the steroid skeleton influenced the reaction rate and the nature of the products.

We also examined the effects of various Lewis acids, such as $SnCl_4$, Me_2SnCl_2, $AlCl_3$, $TiCl_4$ and trimethylsilyl trifluoromethanesulfonate, and also two Brønsted acids (*p*TsOH and HBF_4·OEt_2), on the reaction between **6a** and *p*-nitroaniline (**22**) under similar conditions. All acid-catalysed transformations of the intermediate imine **44a** seemed to be less chemoselective, and the yield of the desired isoquinuclidine derivative **62a** was much lower than in the reactions with BF_3·OEt_2. In general, all Lewis and Brønsted acids except for BF_3·OEt_2 favoured the formation of the unsaturated compound **72a**; Me_2SnCl_2 allowed only 2 % conversion in 24 h.

The following mechanism is proposed for the described transformation. Reaction between the imines **29**−**50** and the Lewis acid BF_3·OEt_2 results in the iminium ion **75**, which then undergoes a 1,5-hydride shift to give the intermediate tertiary carbocation **77**, containing a secondary



	R^1	R^2	R^3	R^4
7, 29a, 51a	H	H	H	H
8, 30a, 52a	F	H	H	H
9, 31a, 53a	H	F	H	H
10, 32a, 54a	H	H	F	H
11, 33a, 68a	Cl	H	H	H
12, 34a, 55a	H	Cl	H	H
13, 35a, 56a	H	H	Cl	H
14, 36a, 69a	Br	H	H	H
15, 37a, 57a	H	Br	H	H
16, 38a, 58a	H	H	Br	H
17, 39a, 70a	I	H	H	H
18, 40a, 59a	H	I	H	H
19, 41a, 60a	H	H	I	H
20, 42a, 71a	NO_2	H	H	H
21, 43a, 61a	H	NO_2	H	H
22, 44a-c, 62a-c, 72a,b	H	H	NO_2	H
23, 45a, 73a	NO_2	H	NO_2	H
24, 46a, 63a	H	NO_2	H	NO_2
25, 47a, 64a	H	Cl	Cl	H
26, 48a, 65a	H	NO_2	Cl	H
27, 49a, 66a	H	CF_3	H	CF_3
28, 50a, 67a	H	Br	Br	Br

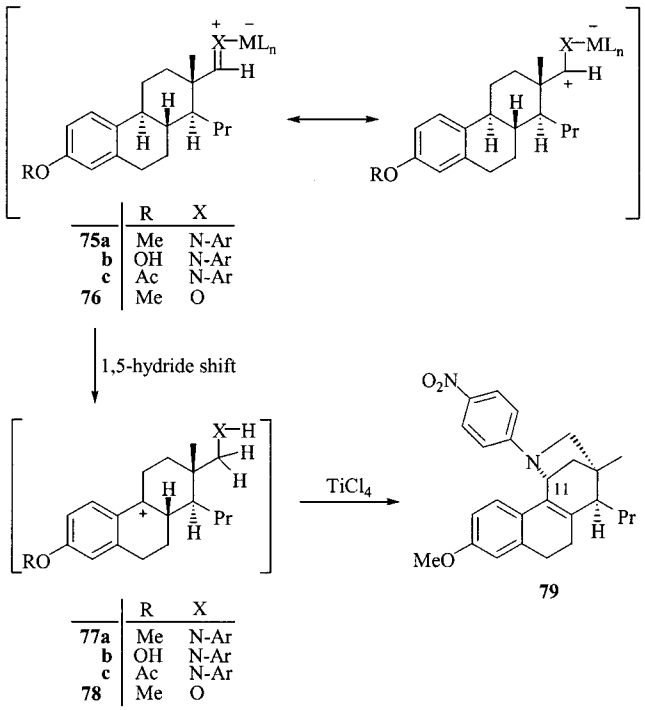
Scheme 2. Reactions of estrone arylimines **29**−**50** derived from secoestrone aldehyde **6** and aniline **7** as well as aniline derivatives **8**−**28** in the presence of different Lewis and Brønsted acids

amine moiety (Scheme 3). This hydride shift occurs only if the aniline derivatives used do not contain an electron-donating group. Thus, treatment of methoxyaniline under the described conditions did not give any of the desired products, the aldehyde **6a** being recovered in 98 % yield after 10 h and aqueous workup. In cases in which the iminium ion is formed from aniline or from an aniline derivative containing an electron-withdrawing group, however, the iminium ion has an oxidative potential high enough to abstract a hydride ion from the benzylic position. No 1,2 or 1,3 shift from the activated benzylic carbon is observed, although these rearrangements require only a low activation energy. The benzylic carbocation can be stabilized either by elimination of a proton to give **68**−**73** or by an intramolecular addition of the intermediately formed secondary amine at position 9 to afford the isoquinuclidines **51**−**67**. The reduced reactivity of **75c** may be explained by the higher dissociation energy of the C−H bond due to the electron-withdrawing characteristics of the 3-acetoxy function. With the electron-donating 3-OH or 3-OMe group, as in **75a** or **75b**, in contrast, formation of the benzylic carbocation is feasible. The formation of the tetrasubstituted double bond in **68**−**73** by deprotonation of the carbocation **77a** is consistent with the higher stability of such an alkene. However, it cannot be excluded that the alkenes **68**−**73** are at least in part formed by elimination of the amino function in **51**−**67**.

Thus, treatment of **62a** with an excess of $BF_3{\cdot}OEt_2$ at room temperature for 24 h furnished **72a** in 85 % yield. A mechanism similar to that depicted for the formation of **51**−**67** and **68**−**73** can also be assumed for the formation of the 8,9-unsaturated alcohol **74**, which was sometimes isolated in low yield. In this case, the Lewis acid coordinates to the oxygen of the carbonyl moiety in **6a** to give the oxonium ion **76**, which is a weaker electrophile than the analogous iminium ion **75a**, but still seems to be able to abstract a hydride from the benzylic carbon. The intermediate carbocation can only undergo an elimination to give **74**; however, this side reaction occurs only to a small extent relative to the reactions of the imines.

The intramolecular 1,5-hydride abstraction by an iminium ion is a rather unusual process and to the best of our knowledge has not been observed previously. However, examples of the opposite reaction can be found, when an iminium ion is produced from an amine and a carbocation.[32,33]

A rather unexpected compound was found in the reaction between **6a** and *p*-nitroaniline (**22**) in the presence of the Lewis acid $TiCl_4$ at room temperature for 24 h. Besides the expected alkene **72a**, a bridged compound was obtained in 65 % yield. This we have assigned structure **79**, for the formation of which an oxidation step must be assumed. Compound **79** could thus be formed either by a hydride abstrac-



	R	X
75a	Me	N-Ar
b	OH	N-Ar
c	Ac	N-Ar
76	Me	O

	R	X
77a	Me	N-Ar
b	OH	N-Ar
c	Ac	N-Ar
78	Me	O

Scheme 3. Proposed mechanism for the formation of the carbocations **77**, **78** and compound **79** in the presence of Lewis acids

tion of **72a** and subsequent addition, or − more probably − by a 1,4-shift of **75a** followed by addition of the amino group and oxidation of the benzylic position.

The structures of the synthesized steroid azacycles **51**−**67** and **79** were determined by NMR spectroscopy, mainly with the aid of X-ray crystal structure analysis of **5**.[31] In the ^{1}H NMR spectra of compounds **51**−**67**, a triplet is observed for 16a-H_3 at δ = 0.94−0.97 ppm with J = 7.0−7.2 Hz, while the corresponding signal in the spectrum of **79** can be identified at δ = 0.87 ppm. The diastereotopic protons of the N−CH_2 group in **51**−**67** resonate about 0.5 ppm apart; the axial one as a double of doublets at δ = 2.9−3.0 ppm, and the equatorial one as a doublet with J = 9.2−10.2 Hz at δ = 3.3−3.5 ppm. For the corresponding protons in **79**, two doublets with J = 10.2 Hz are found at δ = 3.13 and 3.30 ppm. The ^{13}C NMR spectra of **51**−**74** and **79**, obtained by a J-MOD pulse sequence, contain the expected signals. The peaks for the CH_2−N group and the carbon C-9 in **51**−**67** and **79** appear at relatively high chemical shifts, at around δ = 58.0 ppm for C-9 and δ = 63.0 ppm for N−CH_2 in **51**−**67**, and at δ = 54.2 ppm for C-11 and δ = 63.2 ppm for N−CH_2 in **78**. The signals of the double-bonded carbons C-8 and C-9 in **79** can be identified at δ = 137.3 ppm.

Conclusion

In summary, we have developed an efficient route for the synthesis of bridged D-secoestrone azacycles through a Lewis acid-induced cyclization of steroid arylimines. The domino process described is a novel type of transformation accompanied by a 1,5-hydride shift from a benzylic position to an iminium ion, involving the formation of a carbocation, which reacts with the resulting secondary amine. Besides their simplicity and the mild reaction conditions, the cyclizations display high chemo- and regioselectivity.

Experimental Section

General Remarks: All solvents were distilled and dried prior to use. Reagents and materials were obtained from commercial suppliers and were used without further purification. The reactions were monitored by TLC on Kieselgel-G (Merck Si 254 F) layers (0.25 mm thick). The spots were detected by spraying with 5 % phosphomolybdic acid in 50 % aqueous phosphoric acid. The R_f values were determined for spots observed by illumination at 254 and 365 nm. Flash chromatography: silica gel 60, 40−63 μm. All reactions were run under argon. Melting points were determined on a Kofler block and are uncorrected. Specific rotation was measured in $CHCl_3$ (c = 1) at 20 °C with Polamat-A and Perkin−Elmer 241 polarimeters. EI mass spectra were obtained with a Varian MAT 311A spectrometer with ionization energy of 70 eV. ^{1}H NMR spectra were obtained in $CDCl_3$ solution at 300 MHz (Bruker AMX 300), 400 MHz (Bruker AM 400) or 500 MHz (Bruker DRX 500), and the ^{13}C NMR spectra at 75, 100 or 125 MHz with the same instruments. Chemical shifts are reported relative to TMS; J values are given in Hz. ^{13}C NMR spectra are ^{1}H-decoupled. For determination of the multiplicities, the J-MOD pulse sequence was used. Elemental analyses were carried out in the analytical laboratory of the University of Szeged with a Perkin−Elmer model 2400 CHN analyser.

Table 1. Products of the reactions between **6a−c** and the aniline derivatives **7−28** in the presence of $BF_3{\cdot}OEt_2$ and other Lewis or Brønsted acids

Substrates	Lewis acid	Overall yield [%]	Product(s)	Ratio[a]
6a+7	$BF_3{\cdot}OEt_2$	85	**51a**	–
6a+8	$BF_3{\cdot}OEt_2$	72	**52a**	–
6a+9	$BF_3{\cdot}OEt_2$	76	**53a**	–
6a+10	$BF_3{\cdot}OEt_2$	87	**54a** + **74**	82:5
6a+11	$BF_3{\cdot}OEt_2$	70	**68a**	–
6a+12	$BF_3{\cdot}OEt_2$	87	**55a**	–
6a+13	$BF_3{\cdot}OEt_2$	86	**56a**	–
6a+14	$BF_3{\cdot}OEt_2$	69	**69a**	–
6a+15	$BF_3{\cdot}OEt_2$	89	**57a**	–
6a+16	$BF_3{\cdot}OEt_2$	84	**58a**	–
6a+17	$BF_3{\cdot}OEt_2$	78	**70a**	–
6a+18	$BF_3{\cdot}OEt_2$	85	**59a**	–
6a+19	$BF_3{\cdot}OEt_2$	76	**60a+74**	72:4
6a+20	$BF_3{\cdot}OEt_2$	69	**71a**	–
6a+21	$BF_3{\cdot}OEt_2$	82	**61a**	–
6a+22	$BF_3{\cdot}OEt_2$	78	**62a**	–
6a+22	$SnCl_4$	77	**62a+72a**	4:73
6a+22	Me_2SnCl_2	2	**72a**	–
6a+22	$AlCl_3$	72	**62a+72a**	15:57
6a+22	$TiCl_4$	86	**72a+79**	21:65
6a+22	$CF_3SO_2OSiMe_3$	70	**62a+72a**	28:42
6a+22	*p*TsOH	75	**72a**	–
6a+22	$HBF_4{\cdot}OEt_2$	68	**62a+72a**	10:58
6b+22	$BF_3{\cdot}OEt_2$	95	**62b+72b**	63:32
6c+22	$BF_3{\cdot}OEt_2$	16	**62c**	–
6a+23	$BF_3{\cdot}OEt_2$	76	**73a**	–
6a+24	$BF_3{\cdot}OEt_2$	90	**63a**	–
6a+25	$BF_3{\cdot}OEt_2$	82	**64a**	–
6a+26	$BF_3{\cdot}OEt_2$	75	**65a**	–
6a+27	$BF_3{\cdot}OEt_2$	78	**66a**	–
6a+28	$BF_3{\cdot}OEt_2$	84	**67a+74**	78:6

[a] Determined after purification by column chromatography.

3-Methoxyestra-16,17-seco-1,3,5(10)-trien-17-al (6a): A suspension of **2a** (1.0 g, 3.35 mmol) and Pd/C (420 mg, 10 %) in EtOAc (80 mL) was subjected to 5 bar of H_2 pressure at room temperature for 5 h. The catalyst was then removed by filtration through a short pad of silica gel. After evaporation of the solvent in vacuo, the crude product was purified by column chromatography (silica gel, $CHCl_3$) to give **6a** (0.98 g, 97 %) as a colourless oil. R_f = 0.53 ($CHCl_3$). $[\alpha]_D$ = +92.7 (*c* = 1 in chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 6.9 Hz, 3 H, 16a-H_3), 1.05 (s, 3 H, 18-H_3), 1.24−2.36 (overlapping multiplets, 13 H), 2.86 (m, 2 H, 6-H_2), 3.78 (s, 3 H, 3-OMe), 6.63 (d, *J* = 2.6 Hz, 1 H, 4-H), 6.73 (dd, *J* = 8.6, *J* = 2.6 Hz, 1 H, 2-H), 7.20 (d, *J* = 8.6 Hz, 1 H, 1-H), 9.44 (s, 1 H, formyl-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.0 (C-18), 14.5 (C-16a), 23.7, 25.4, 26.9 (C-7), 30.3 (C-6), 32.7, 32.9, 40.7 (C-8), 43.1 (C-9), 44.3 (C-14), 51.0 (C-13), 55.2 (3-OMe), 111.8 (C-2), 113.5 (C-4), 126.4 (C-1), 131.9 (C-10), 137.8 (C-5), 157.6 (C-3), 206.7 (formyl-C) ppm. MS (70 eV, EI): *m*/*z* (%) = 300 (100) [M^+], 271 (23), 257 (83), 186 (32), 174 (25), 173 (24), 147 (19). $C_{20}H_{28}O_2$ (300.44): calcd. for C 79.96, H 9.39; found C 80.05, H 9.28.

3-Hydroxy16,17-secoestra-1,3,5(10)-trien-17-al (6b): A suspension of **2b** (1.0 g, 2.67 mmol) and Pd/C (420 mg, 10%) in EtOAc (80 mL) was subjected to 5 bar of H_2 pressure at room temperature for 6 h. The catalyst was then removed by filtration through a short pad of silica gel. After evaporation of the solvent in vacuo, the crude product was purified by column chromatography (silica gel, $CHCl_3$) and recrystallized from acetone/PE to give **6b** (0.75 g, 98 %) as white crystals. M.p. 134−135 °C; R_f = 0.42 ($CHCl_3$). $[\alpha]_D$ = +102.9 (*c* = 1 in chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 6.8 Hz, 3 H, 16a-H_3), 1.05 (s, 3 H, 18-H_3), 1.19−2.38 (overlapping multiplets, 13 H), 2.83 (m, 2 H, 6-H_2), 4.90 (s, 1 H, 3-OH), 6.57 (d, *J* = 2.7 Hz, 1 H, 4-H), 6.64 (dd, *J* = 8.5, *J* = 2.7 Hz, 1 H, 2-H), 7.14 (d, *J* = 8.5 Hz, 1 H, 1-H), 9.44 (s, 1 H, formyl-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.4 (C-18), 15.0 (C-16a), 24.1, 25.8, 27.3 (C-7), 30.5 (C-6), 33.1, 33.4, 41.0 (C-8), 43.5 (C-9), 44.7 (C-14), 51.4 (C-13), 113.3 (C-2), 115.4 (C-4), 127.0 (C-1), 132.4 (C-10), 138.5 (C-5), 153.9 (C-3), 207.5 (formyl-C) ppm. MS (70 eV, EI): *m*/*z* (%) = 286 (100) [M^+], 257 (20), 243 (75), 172 (33), 160 (30), 145 (14), 133 (21). $C_{19}H_{26}O_2$ (286.41): calcd. for C 79.68, H 9.15; found C 79.87, H 9.31.

3-Acetoxy-16,17-secoestra-1,3,5(10)-trien-17-al (6c): A solution of **2b** (286 mg, 1.00 mmol) in Ac_2O (3 mL) and pyridine (3 mL) was stirred for 12 h at room temperature. The mixture was then extracted with $CHCl_3$ (10 mL) and washed with water (3 × 10 mL). The organic layer was dried with Na_2SO_4 and the solvents were evaporated in vacuo to give **3c** (312 mg, 95 %) as a colourless oil. R_f = 0.44 (*tert*-butyl methyl ether/$CHCl_3$, 5:95). $[\alpha]_D$ = +80.8 (*c* = 1 in chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 6.8 Hz, 3 H, 16a-H_3), 1.05 (s, 3 H, 18-H_3), 1.20−2.20 (overlapping multiplets, 11 H), 2.28 (s, 3 H, $OCOCH_3$), 2.40 (m, 2 H), 2.87 (m, 2 H, 6-H_2), 6.80 (d, *J* = 2.4 Hz, 1 H, 4-H), 6.86 (dd, *J* = 8.4, *J* = 2.4 Hz, 1 H, 2-H), 7.27 (d, *J* = 8.4 Hz, 1 H, 1-H), 9.44 (s, 1 H, formyl-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.4 (C-18), 14.9 (C-16a), 21.5 ($OCOCH_3$), 24.1, 25.6, 27.1 (C-7), 30.4 (C-6), 33.0, 33.3, 40.7 (C-8), 43.7 (C-9), 44.8 (C-14), 51.3 (C-13), 119.2 (C-2), 121.8 (C-4), 126.9 (C-1), 137.7 and 138.5 (C-5 and C-10), 149.0 (C-3), 170.2 ($OCOCH_3$), 207.1 (formyl-C) ppm. $C_{21}H_{28}O_3$ (328.45): calcd. for C 76.79, H 8.59; found C 76.88, H 8.71.

Typical Procedure: A solution of **6a** (300 mg, 1 mmol), **6b** (286 mg, 1 mmol) or **6c** (328 mg, 1 mmol) and freshly distilled aniline (**7**) or the substituted aniline derivatives **8−28** (1.00 mmol) in CH_2Cl_2 (10 mL) in the presence of molecular sieves (4Å, 150 mg) was stirred under argon at 40 °C for 4 h. The sieves were removed by filtration, and $BF_3{\cdot}OEt_2$ (1 mmol) or some other Lewis or Brønsted acid (1 mmol) was added slowly in two portions at room temperature. After the addition of half of the acid, the mixture was stirred overnight. After the addition of the other half of the acid, the reaction was allowed to proceed until complete conversion (TLC) was achieved. The reaction was then quenched by the addition of ice-cold NaOH (1 N, 30 mL) and the mixture was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine, dried with Na_2SO_4 and concentrated in vacuo, and the crude product was purified by flash chromatography.

Cyclization of 6a with *o*-Fluoroaniline (8): Compound **6a** (300 mg, 1.00 mmol), *o*-fluoroaniline (**8**, 0.10 mL, 1.00 mmol) and $BF_3{\cdot}OEt_2$ (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were allowed to react as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, PE/CH_2Cl_2, 60:40) and recrystallized from acetone to give **52a** (283 mg, 72 %) as yellowish crystals. M.p. 82−84 °C; R_f = 0.51 (PE/CH_2Cl_2, 60:40). $[\alpha]_D$ = +352.2 (*c* = 1 in chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.86 (s, 3 H, 18-H_3), 0.97 (t, *J* = 7.0 Hz, 3 H, 16a-H_3), 1.24−1.92 (overlapping multiplets, 10 H), 2.37 (m, 1 H), 2.70 (m, 1 H), 2.84 (m, 2 H, 6-H_2), 3.02 (dd, *J* = 9.2, *J* = 2.8 Hz, 1 H, N−$CH_{2,ax}$), 3.45 (d, *J* = 9.2 Hz, 1 H, N−$CH_{2,eq}$), 3.66 (s, 3 H, 3-OMe), 6.23 (dd, *J* = 8.7, *J* = 2.5 Hz, 1 H, 2-H), 6.50 (d, *J* = 2.5 Hz, 1 H, 4-H), 6.56 (d, *J* = 8.7 Hz, 1 H, 1-H), 6.70 (t-like m, 1 H, 4′-H), 6.78 (m, 2 H, 3′-H and 6′-H), 6.91 (m, 1 H, 5′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8 (C-16a), 21.7, 23.6 (C-18),

27.2, 28.9, 30.5, 31.7, 33.2 (C-13), 34.2, 48.0 and 48.7 (C-8 and C-14), 55.0 (3-OMe), 57.3 (C-9), 63.0 (N−CH_2), 111.0 (C-2), 112.7 (C-4), 115.6 (J = 22.0 Hz, C-3′), 123.3 and 124.2 (C-4′ and C-6′), 129.2 (C-1), 129.8 (C-5′), 130.4 (C-10), 137.5 (J = 21.0 Hz, C-1′), 139.9 (C-5), 157.9 (C-3), 160.3 (J = 246 Hz, C-2′) ppm. MS (70 eV, EI): m/z (%) = 393 (59) [M^+], 351 (26), 350 (100), 282 (21), 239 (11), 124 (15). $C_{26}H_{32}FNO$ (393.54): calcd. for C 79.35, H 8.21, N 3.56; found C 79.51, H 8.35, N 3.72.

Cyclization of 6a with *m*-Fluoroaniline (9): Compound **6a** (300 mg, 1.00 mmol), *m*-fluoroaniline (**9**, 0.07 mL, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, PE/CH_2Cl_2, 30:70) to give **53a** (299 mg, 76 %) as a colourless oil. R_f = 0.66 (PE/CH_2Cl_2, 30:70). $[\alpha]_D$ = +362.4 (c = 1 in chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.93 (s, 3 H, 18-H_3), 0.94 (t, J = 7.2 Hz, 3 H, 16a-H_3), 1.05−1.88 (overlapping multiplets, 11 H), 2.49 (m, 1 H), 2.84 (m, 2 H, 6-H_2), 2.92 (dd, J = 9.4, J = 2.8 Hz, 1 H, N−$CH_{2,ax}$), 3.43 (d, J = 9.4 Hz, 1 H, N−$CH_{2,eq}$), 3.75 (s, 3 H, 3-OMe), 5.97 (m, 2 H, 2′-H and 6′-H), 6.18 (m, 1 H, 4′-H), 6.57 (dd, J = 8.7, J = 2.5 Hz, 1 H, 2-H), 6.65 (d, J = 2.5 Hz, 1 H, 4-H), 6.74 (m, 1 H, 5′-H), 6.91 (d, J = 8.7 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8 (C-16a), 22.2, 23.5 (C-18), 26.3, 28.4, 30.5, 33.4, 34.4 (C-13), 35.5, 46.5 (C-14), 48.9 (C-8), 55.1 (3-OMe), 58.0 (C-9), 61.8 (N−CH_2), 102.8 (J = 21.4 Hz, C-2′), 103.8 (J = 25.1 Hz, C-4′), 112.2 (C-2), 112.8 (C-6′), 113.5 (C-4), 128.1 (J = 10.1 Hz, C-5′), 129.8 (C-1), 131.2 (C-10), 138.8 (C-5), 150.9 (J = 10.1 Hz, C-1′), 158.5 (C-3), 162.9 (J = 239.5 Hz, C-3′) ppm. MS (70 eV, EI): m/z (%) = 393 (80) [M^+], 350 (100), 282 (26), 269 (18), 225 (10), 124 (28). $C_{26}H_{32}FNO$ (393.54): calcd. for C 79.35, H 8.21, N 3.56; found C 79.22, H 8.37, N 3.75.

Cyclization of 6a with *p*-Fluoroaniline (10): Compound **6a** (300 mg, 1.00 mmol), *p*-fluoroaniline (**10**, 0.09 mL, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, PE/CH_2Cl_2, 50:50) to give **54a** (323 mg, 82 %) and **74** (15 mg, 5 %). Compound **54a** was recrystallized from acetone; yellowish crystals; m.p. 146−148 °C; R_f = 0.42 (PE/CH_2Cl_2, 50:50). $[\alpha]_D$ = +406.7 (c = 1 in chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.91 (s, 3 H, 18-H_3), 0.95 (t, J = 7.2 Hz, 3 H, 16a-H_3), 1.18−2.01 (overlapping multiplets, 11 H), 2.50 (m, 1 H), 2.84 (m, 2 H, 6-H_2), 2.90 (dd, J = 9.3, J = 2.9 Hz, 1 H, N−$CH_{2,ax}$), 3.47 (d, J = 9.3 Hz, 1 H, N−$CH_{2,eq}$), 3.73 (s, 3 H, 3-OMe), 6.33 (m, 2 H, 2′-H and 6′-H), 6.43 (dd, J = 8.7, J = 2.3 Hz, 1 H, 2-H), 6.58 (m, 3 H, 4-H, 3′-H and 5′-H), 6.64 (d, J = 8.7 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8 (C-16a), 22.1, 23.6 (C-18), 26.5, 28.8, 30.5, 33.5, 33.6, 34.0 (C-13), 46.8 (C-14), 48.6 (C-8), 55.1 (3-OMe), 57.8 (C-9), 61.9 (N−CH_2), 111.6 (C-2), 113.2 (C-4), 113.9 (2 C, J = 21.6 Hz, C-3′ and C-5′), 121.7 (2 C, J = 7.0 Hz, C-2′ and C-6′), 130.1 (C-1), 131.3 (C-10), 139.0 (C-5), 145.4 (C-1′), 156.3 (J = 236.1 Hz, C-4′), 158.2 (C-3) ppm. MS (70 eV, EI): m/z (%) = 393 (91) [M^+], 350 (100), 282 (20), 269 (14), 124 (16). $C_{26}H_{32}FNO$ (393.54): calcd. for C 79.35, H 8.21, N 3.56; found C 79.17, H 8.29, N 3.68.

Compound 74: A colourless oil; R_f = 0.23 (PE/CH_2Cl_2, 50:50). $[\alpha]_D$ = +23.1 (c = 1 in chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.91 (t, J = 7.1 Hz, 3 H, 16a-H_3), 1.00 (s, 3 H, 18-H_3), 1.26−2.33 (overlapping multiplets, 11 H), 2.68 (m, 2 H, 6-H_2), 2.93 (d, J = 8.5 Hz, 1 H) and 3.07 (d, J = 8.5 Hz, 1 H): O-CH_2, 3.78 (s, 3 H, 3-OMe), 6.66 (d, J = 2.2 Hz, 1 H, 4-H), 6.67 (dd, J = 8.2, J = 2.2 Hz, 1 H, 2-H), 7.05 (d, J = 8.2 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.9 (C-16a), 22.8, 23.2 (C-18), 23.5, 28.0, 29.2 (2 C), 34.0, 37.1, 45.3 (C-14), 55.3 (3-OMe), 77.6 (O−CH_2), 110.8 (C-2), 113.3 (C-4), 122.8 (C-1), 124.5 (C-8), 129.5 (C-10), 135.5 (C-9), 137.4 (C-5), 157.8 (C-3) ppm. MS (70 eV, EI): m/z (%) = 300 (33) [M^+], 282 (29), 254 (100), 228 (34), 139 (23). $C_{20}H_{28}O_2$ (300.44): calcd. for C 79.96, H 9.39; found C 79.85, H 9.47.

Treatment of 3a with *o*-Chloroaniline (11): Compound **6a** (300 mg, 1.00 mmol), *o*-chloroaniline (**11**, 0.10 mL, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, PE/CH_2Cl_2, 55:45) to give **68a** (287 mg, 70 %) as a colourless oil. R_f = 0.73 (PE/CH_2Cl_2, 30:70). $[\alpha]_D$ = +204.2 (c = 1 in chloroform). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, J = 7.1 Hz, 3 H, 16a-H_3), 1.10 (s, 3 H, 18-H_3), 1.32−2.40 (overlapping multiplets, 11 H), 2.74 (m, 2 H, 6-H_2), 3.03 (d, J = 5.4 Hz, 2 H, N−CH_2), 3.79 (s, 3 H, 3-OMe), 4.33 (t-like m, 1 H, N-H), 6.51−6.75 (overlapping multiplets, 4 H, 2-H, 4-H, 4′-H and 6′-H), 7.04 (t-like m, 1 H, 5′-H), 7.12 (d, J = 8.4 Hz, 1 H, 1-H), 7.21 (dd, J = 8.0, J = 1.4 Hz, 1 H, 3′-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.9, (C-16a), 22.6, 23.4, 23.7 (C-18), 28.7, 29.1, 34.2, 36.4 (C-13), 36.5, 46.4 (C-14), 51.0 (N−CH_2), 55.2 (3-OMe), 110.8 and 111.0 (C-2 and C-6′), 113.4 (C-4), 116.4 (C-4′), 118.9 (C-2′), 122.9 (C-5′), 124.6 (C-8), 127.7 (C-1), 128.9 (C-3′), 129.0 (C-9), 134.9 (C-10), 137.3 (C-5), 144.7 (C-1′), 157.9 (C-3) ppm. MS (70 eV, EI): m/z (%) = 411 (26) [M^+], 409 (71), 368 (36), 366 (100), 282 (28), 270 (38), 254 (22), 227 (50), 174 (30), 160 (45), 140 (28). $C_{26}H_{32}ClNO$ (409.99): calcd. for C 76.17, H 7.87, N 3.42; found C 75.98, H 7.95,N 3.62.

Cyclization of 6a with *m*-Chloroaniline (12): Compound **6a** (300 mg, 1.00 mmol), *m*-chloroaniline (**12**, 0.11 mL, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, PE/CH_2Cl_2, 55:45) to give **55a** (357 mg, 87 %) as a colourless oil. R_f = 0.75 (PE/CH_2Cl_2, 30:70). $[\alpha]_D$ = +335.2 (c = 1 in chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.93 (s, 3 H, 18-H_3), 0.94 (t, J = 7.2 Hz, 3 H, 16a-H_3), 1.14−1.93 (overlapping multiplets, 11 H), 2.49 (m, 1 H), 2.85 (m, 2 H, 6-H_2), 2.91 (dd, J = 9.5, J = 2.8 Hz, 1 H, N−$CH_{2,ax}$), 3.44 (d, J = 9.5 Hz, 1 H, N−$CH_{2,eq}$), 3. 75 (s, 3 H, 3-OMe), 6.00 (dd, J = 8.5, J = 2.0 Hz, 1 H. 6′-H), 6.31 (t-like m, 1 H, 2′-H), 6.45 (dd, J = 7.8, J = 0.8 Hz, 1 H, 4′-H), 6.56 (dd, J = 8.7, J = 2.5 Hz, 1 H, 2-H), 6.65 (d, J = 2.5 Hz, 1 H, 4-H), 6.66 (t-like m, 1 H, 5′-H), 6.88 (d, J = 8.7 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8 (C-16a), 22.2, 23.5 (C-18), 26.3, 28.4, 30.5, 33.4, 34.4 (C-13), 35.3, 46.5 (C-14), 48.8 (C-8), 55.2 (3-OMe), 58.1 (C-9), 61.6 (N−CH_2), 112.1 (C-2), 113.6 (C-4), 115.7 and 116.4 and 117.0 (C-2′ and C-4′ and C-6′), 128.2 (C-5′), 129.9 (C-1), 131.1 (C-10), 133.5 (C-3′), 138.9 (C-5), 150.2 (C-1′), 158.6 (C-3) ppm. MS (70 eV, EI): m/z (%) = 411 (30) [M^+], 409 (83), 368 (36), 366 (100), 269 (17), 227 (15). $C_{26}H_{32}ClNO$ (409.99): calcd. for C 76.17, H 7.87, N 3.42; found C 76.05, H 7.76, N 3.25.

Cyclization of 6a with *p*-Chloroaniline (13): Compound **6a** (300 mg, 1.00 mmol), *m*-chloroaniline (**13**, 128 mg, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, PE/CH_2Cl_2, 50:50) and recrystallized from acetone to give **56a** (353 mg, 86 %) as yellowish crystals. M.p. 107−109 °C; R_f = 0.64 (PE/CH_2Cl_2, 20:80). $[\alpha]_D$ = +372.6 (c = 1 in chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.93 (s, 3 H, 18-H_3), 0.94 (t, J = 7.1 Hz, 3 H, 16a-H_3), 1.14−1.91 (overlapping multiplets, 11 H), 2.50 (m, 1 H), 2.84

(m, 2 H, 6-H_2), 2.89 (dd, J = 9.4, J = 2.9 Hz, 1 H, N−$CH_{2,ax}$), 3.45 (d, J = 9.4 Hz, 1 H, N−$CH_{2,eq}$), 3.75 (s, 3 H, 3-OMe), 6.19 (d, J = 9.1 Hz, 2 H, 2′-H and 6′-H), 6.52 (dd, J = 8.7, J = 2.7 Hz, 1 H, 2-H), 6.63 (d, J = 2.7 Hz, 1 H, 4-H), 6.78 (d, J = 9.1 Hz, 2 H, 3′-H and 5′-H), 6.82 (d, J = 8.7 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8 (C-16a), 22.2, 23.5 (C-18), 26.3, 28.5, 30.5, 33.4, 34.3 (C-13), 35.0, 46.5 (C-14), 48.7 (C-8), 55.1 (3-OMe), 57.9 (C-9), 61.6 (N−CH_2), 111.9 (C-2), 113.4 (C-4), 119.1 (2 C, C-2′ and C-6′), 121.7 (C-4′), 127.3 (2 C, C-3′ and C-5′), 129.9 (C-1), 131.2 (C-10), 138.8 (C-5), 147.7 (C-1′), 158.4 (C-3) ppm. MS (70 eV, EI): m/z (%) = 411 (5) [M^+], 409 (14), 366 (15), 272 (23), 270 (34), 266 (36), 227 (100), 225 (56), 149 (22). $C_{26}H_{32}ClNO$ (409.99): calcd. for C 76.17, H 7.87, N 3.42; found C 76.35, H 7.98, N 3.55.

Treatment of 6a with *o*-Bromoaniline (14): Compound **6a** (300 mg, 1.00 mmol), *o*-bromoaniline (**14**, 172 mg, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, PE/CH_2Cl_2, 40:60) to give **69a** (314 mg, 69 %) as a colourless oil. R_f = 0.72 (*tert*-butyl methyl ether/PE, 10:90). $[\alpha]_D$ = +92.7 (c = 1 in chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.92 (t, J = 7.0 Hz, 3 H, 16a-H_3), 1.10 (s, 3 H, 18-H_3), 1.32−2.37 (overlapping multiplets, 11 H), 2.72 (m, 2 H, 6-H_2), 3.02 (d, J = 5.3 Hz, 2 H, N−CH_2), 3.78 (s, 3 H, 3-OMe), 4.34 (t-like m, 1 H, N-H), 6.47 (t-like m, 1 H, 4′-H), 6.50 (d, J = 13.3 Hz, 1 H, 6′-H), 6.70 (m, 2 H, 2-H and 4-H), 7.05 (t-like m, 1 H, 5′-H), 7.10 (d, J = 8.2 Hz, 1 H, 1-H), 7.36 (dd, J = 7.6, J = 0.7 Hz, 1 H, 3′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8, (C-16a), 22.7, 23.4, 23.7 (C-18), 28.8, 29.1, 29.2, 34.3, 36.6 (C-13), 46.6 (C-14), 51.3 (N−CH_2), 55.2 (3-OMe), 109.8 (C-2′), 110.9 (C-6′), 111.3 (C-2), 113.4 (C-4), 117.1 (C-4′), 123.0 (C-5′), 124.7 (C-8), 128.4 (C-1), 129.1 (C-9), 132.2 (C-3′), 134.9 (C-10), 137.4 (C-5), 145.7 (C-1′), 158.0 (C-3) ppm. MS (70 eV, EI): m/z (%) = 455 (23) [M^+], 453 (23), 412 (16), 410 (15), 282 (34), 254 (100), 225 (15), 184 (17). $C_{26}H_{32}BrNO$ (454.44): calcd. for C 68.72, H 7.10, N 3.08; found C 68.92, H 7.25,N 3.26.

Cyclization of 6a with *m*-Bromoaniline (15): Compound **6a** (300 mg, 1.00 mmol), *m*-bromoaniline (**15**, 0.11 mL, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, PE/CH_2Cl_2, 30:70) to give **57a** (404 mg, 89 %) as a colourless oil. R_f = 0.78 ($CHCl_3$). $[\alpha]_D$ = +309.1 (c = 1 in chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (s, 3 H, 18-H_3), 0.94 (t, J = 7.2 Hz, 3 H, 16a-H_3), 1.12−1.96 (overlapping multiplets, 11 H), 2.50 (m, 1 H), 2.86 (m, 2 H, 6-H_2), 2.89 (dd, J = 9.4, J = 2.8 Hz, 1 H, N−$CH_{2,ax}$), 3.44 (d, J = 9.4 Hz, 1 H, N−$CH_{2,eq}$), 3.76 (s, 3 H, 3-OMe), 6.03 (m, 1 H, 6′-H), 6.46 (m, 1 H, 2′-H), 6.57 (dd, J = 8.7, J = 2.7 Hz, 1 H, 2-H), 6.62 (m, 2 H, 4′-H and 5′-H), 6.66 (d, J = 2.7 Hz, 1 H, 4-H), 6.89 (d, J = 8.7 Hz, 1 H, 1-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8 (C-16a), 22.3, 23.6 (C-18), 26.3, 28.4, 30.5, 33.3, 34.4 (C-13), 35.3, 46.4 (C-14), 48.7 (C-8), 55.2 (3-OMe), 58.1 (C-9), 61.5 (N−CH_2), 112.1 (C-2), 113.5 (C-4), 115.9 (C-2′), 119.2, 119.7 (C-4′ and C-6′), 121.9 (C-3′), 128.4 (C-5′), 129.9 (C-1), 131.0 (C-10), 138.8 (C-5), 150.3 (C-1′), 158.5 (C-3) ppm. MS (70 eV, EI): m/z (%) = 455 (73) [M^+], 453 (74), 412 (100), 410 (99), 269 (26), 225 (17), 184 (20). $C_{26}H_{32}BrNO$ (454.44): calcd. for C 68.72, H 7.10, N 3.08; found C 68.85, H 7.08, N 3.37.

Cyclization of 6a with *p*-Bromoaniline (16): Compound **6a** (300 mg, 1.00 mmol), *p*-bromoaniline (**16**, 172 mg, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, *tert*-butyl methyl ether/PE, 40:60) and recrystallized from PE to give **58a** (382 mg, 84 %) as white crystals. M.p. 127−129 °C; R_f = 0.77 ($CHCl_3$). $[\alpha]_D$ = +307.1 (c = 1 in chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (s, 3 H, 18-H_3), 0.94 (t, J = 7.2 Hz, 3 H, 16a-H_3), 1.13−1.92 (overlapping multiplets, 11 H), 2.48 (m, 1 H), 2.85 (m, 2 H, 6-H_2), 2.88 (dd, J = 9.4, J = 2.8 Hz, 1 H, N−$CH_{2,ax}$), 3.45 (d, J = 9.4 Hz, 1 H, N−$CH_{2,eq}$), 3.76 (s, 3 H, 3-OMe), 6.13 (d, J = 9.0 Hz, 2 H, 2′-H and 6′-H), 6.54 (dd, J = 8.7, J = 2.6 Hz, 1 H, 2-H), 6.64 (d, J = 2.6 Hz, 1 H, 4-H), 6.86 (d, J = 8.7 Hz, 1 H, 1-H), 6.92 (d, J = 9.0 Hz, 2 H, 3′-H and 5′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.9 (C-16a), 22.3, 23.6 (C-18), 26.2, 28.4, 30.5, 33.3, 34.4 (C-13), 35.3, 46.4 (C-14), 48.7 (C-8), 55.1 (3-OMe), 57.9 (C-9), 61.6 (N−CH_2), 108.8 (C-4′), 112.1 (C-2), 113.4 (C-4), 119.1 (2 C, C-2′ and C-6′), 129.9 (C-1), 130.2 (2 C, C-3′ and C-5′), 131.2 (C-10), 138.8 (C-5), 148.0 (C-1′), 158.3 (C-3) ppm. MS (70 eV, EI): m/z (%) = 455 (61) [M^+], 453 (63), 412 (76), 410 (72), 247 (100), 241 (92), 204 (71), 55 (47). $C_{26}H_{32}BrNO$ (454.44): calcd. for C 68.72, H 7.10, N 3.08; found C 68.67, H 7.32, N 3.28.

Reaction of 6a with *o*-Iodoaniline (17): Compound **6a** (300 mg, 1.00 mmol), *o*-iodoaniline (**17**, 219 mg, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, PE/CH_2Cl_2, 55:45) to give **70a** (391 mg, 78 %) as a yellowish oil. R_f = 0.71 (PE/CH_2Cl_2, 30:70). $[\alpha]_D$ = +57.9 (c = 1 in chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.93 (t, J = 7.1 Hz, 3 H, 16a-H_3), 1.12 (s, 3 H, 18-H_3), 1.41−2.42 (overlapping multiplets, 11 H), 2.72 (m, 2 H, 6-H_2), 3.01 (d, J = 5.4 Hz, 2 H, N−CH_2), 3.78 (s, 3 H, 3-OMe), 6.36 (t-like m, 1 H, 4′-H), 6.44 (d, J = 8.0 Hz, 1 H, 6′-H), 6.71 (m, 2 H, 2-H and 4-H), 7.09 (m, 2 H, C-1 and 5′-H), 7.60 (dd, J = 7.7, J = 0.8 Hz, 1 H, 3′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.9 (C-16a), 22.7, 23.5, 23.8 (C-18), 28.8, 29.1, 29.2, 34.3, 36.6 (C-13), 46.6 (C-14), 51.7 (N−CH_2), 55.2 (3-OMe), 85.7 (C-2′), 110.6 and 110.9 (C-2 and C-6′), 113.4 (C-4), 118.0 (C-4′), 123.0 (C-5′), 125.1 (C-8), 128.9 (C-9), 129.4 (C-1), 135.0 (C-10), 137.1 (C-5), 138.8 (C-3′), 147.8 (C-1′), 158.0 (C-3) ppm. MS (70 eV, EI): m/z (%) = 501 (37) [M^+], 458 (20), 282 (36), 254 (100), 232 (22), 225 (15), 106 (8). $C_{26}H_{32}INO$ (501.44): calcd. for C 62.28, H 6.43, N 2.79; found C 62.41, H 6.52, N 2.95.

Cyclization of 6a with *m*-Iodoaniline (18): Compound **6a** (300 mg, 1.00 mmol), *m*-iodoaniline (**18**, 0.12 mL, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, PE/CH_2Cl_2, 20:80) to give **59a** (426 mg, 85 %) as a yellowish oil. R_f = 0.72 (PE/CH_2Cl_2, 20:80). $[\alpha]_D$ = +268.8 (c = 1 in chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (s, 3 H, 18-H_3), 0.94 (t, J = 7.2 Hz, 3 H, 16a-H_3), 1.15−1.92 (overlapping multiplets, 11 H), 2.48 (m, 1 H), 2.84 (m, 2 H, 6-H_2), 2.88 (dd, J = 9.5, J = 2.9 Hz, 1 H, N−$CH_{2,ax}$), 3.42 (d, J = 9.5 Hz, 1 H, N−$CH_{2,eq}$), 3.76 (s, 3 H, 3-OMe), 6.12 (dd, J = 6.6, J = 2.3 Hz, 1 H, 6′-H), 6.49 (t-like m, 1 H, 5′-H), 6.56 (dd, J = 8.7, J = 2.6 Hz, 1 H, 2-H), 6.62 (s, 1 H, 2′-H), 6.66 (d, J = 2.6 Hz, 1 H, 4-H), 6.80 (d-like m, 1 H, 4′-H), 6.87 (d, J = 8.7 Hz, 1 H, 1-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8 (C-16a), 22.2, 23.5 (C-18), 26.3, 28.4, 30.4, 33.3, 34.3 (C-13), 35.1, 46.4 (C-14), 48.7 (C-8), 55.2 (3-OMe), 58.1 (C-9), 61.4 (N−CH_2), 94.1 (C-3′), 112.1 (C-2), 113.6 (C-4), 116.5 (C-6′), 124.3 and 125.4 (C-2′ and C-4′), 128.7 (C-1), 129.9 (C-5′), 131.0 (C-10), 138.8 (C-5), 150.2 (C-1′), 158.6 (C-3) ppm. MS (70 eV, EI): m/z (%) = 501 (99) [M^+], 458 (100), 269 (14), 232 (16). $C_{26}H_{32}INO$ (501.44): calcd. for C 62.28, H 6.43, N 2.79; found C 62.39, H 6.47, N 3.02.

Cyclization of 6a with *p*-Iodoaniline (19): Compound **6a** (300 mg, 1.00 mmol), *p*-iodoaniline (**19**, 219 mg, 1.00 mmol) and $BF_3{\cdot}OEt_2$ (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, PE/CH_2Cl_2, 50:50) to give **60a** (361 mg, 72 %) and **74** (12 mg, 4 %) as a yellowish oil. Compound **60a** was recrystallized from acetone; yellowish crystals; m.p. 102−104 °C; R_f = 0.65 (PE/CH_2Cl_2, 50:50). $[\alpha]_D$ = +340.3 (c = 1 in chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.93 (s, 3 H, 18-H_3), 0.94 (t, J = 7.1 Hz, 3 H, 16a-H_3), 1.10−1.94 (overlapping multiplets, 11 H), 2.49 (m, 1 H), 2.83 (m, 2 H, 6-H_2), 2.88 (dd, J = 9.5, J = 2.8 Hz, 1 H, N−$CH_{2,ax}$), 3.44 (d, J = 9.5 Hz, 1 H, N−$CH_{2,eq}$), 3.76 (s, 3 H, 3-OMe), 6.02 (d, J = 9.0 Hz, 2 H, 2′-H and 6′-H), 6.56 (dd, J = 8.7, J = 2.5 Hz, 1 H, 2-H), 6.63 (d, J = 2.5 Hz, 1 H, 4-H), 6.88 (d, J = 8.7 Hz, 1 H, 1-H), 7.08 (d, J = 9.0 Hz, 2 H, 3′-H and 5′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.7 (C-16a), 22.2, 23.5 (C-18), 26.2, 28.3, 30.4, 33.3, 34.3 (C-13), 35.4, 46.4 (C-14), 48.8 (C-8), 55.1 (3-OMe), 57.9 (C-9), 61.5 (N−CH_2), 77.9 (C-4′), 112.1 (C-2), 113.4 (C-4), 119.4 (2 C, C-2′ and C-6′), 129.8 (C-1), 131.2 (C-10), 136.1 (2 C, C-3′ and C-5′), 138.7 (C-5), 148.7 (C-1′), 158.4 (C-3) ppm. MS (70 eV, EI): m/z (%) = 501 (100) [M^+], 458 (82), 282 (16), 270 (26), 231 (34), 227 (70), 174 (22), 160 (17), 147 (14). $C_{26}H_{32}INO$ (501.44): calcd. for C 62.28, H 6.43, N 2.79; found C 62.51, H 6.38, N 2.87.

Treatment of 6a with *o*-Nitroaniline (20): Compound **6a** (300 mg, 1.00 mmol), *o*-nitroaniline (**20**, 138 mg, 1.00 mmol) and $BF_3{\cdot}OEt_2$ (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, hexanes/$CHCl_3$, 20:80) to give **71a** (290 mg, 69 %) as a yellow oil. R_f = 0.68 ($CHCl_3$). $[\alpha]_D$ = +142.9 (c = 1 in chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, J = 7.0 Hz, 3 H, 16a-H_3), 1.15 (s, 3 H, 18-H_3), 1.34−2.49 (overlapping multiplets, 11 H), 2.73 (m, 2 H, 6-H_2), 3.17 (m, 2 H, N−CH_2), 3.79 (s, 3 H, 3-OMe), 6.57 (t-like m, 1 H, 4′-H), 6.73 (m, 3 H, 2-H, 4-H and 6′-H), 7.11 (d, J = 8.1 Hz, 1 H, 1-H), 7.33 (t-like m, 1 H, 5′-H), 8.15 (dd, J = 8.7, J = 1.4 Hz, 1 H, 3′-H), 8.30 (t-like m, 1 H, N-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.9 (C-16a), 22.6, 23.5, 23.7 (C-18), 28.6, 29.1, 29.3, 34.3, 36.5 (C-13), 46.7 (C-14), 50.4 (N−CH_2), 55.3 (3-OMe), 110.9 (C-2), 113.5 (C-4), 113.8 (C-6′), 114.9 (C-4′), 123.0 (C-1), 124.6 (C-8), 126.9 (C-3′), 128.8 (C-9), 131.7 (C-2′), 134.6 (C-10), 136.2 (C-5′), 137.4 (C-5), 146.3 (C-1′), 158.0 (C-3) ppm. MS (70 eV, EI): m/z (%) = 420 (8) [M^+], 268 (100), 254 (22), 151 (13). $C_{26}H_{32}N_2O_3$ (420.54): calcd. for C 74.26, H 7.67, N 6.66; found C 74.53, H 7.81,N 6.95.

Cyclization of 6a with *m*-Nitroaniline (21): Compound **6a** (300 mg, 1.00 mmol), *m*-nitroaniline (**21**, 138 mg, 1.00 mmol) and $BF_3{\cdot}OEt_2$ (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, $CHCl_3$) to give **61a** (345 mg, 82 %) as a yellow oil. R_f = 0.57 ($CHCl_3$). $[\alpha]_D$ = +374.0 (c = 1 in chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, J = 7.2 Hz, 3 H, 16a-H_3), 0.98 (s, 3 H, 18-H_3), 1.12−1.99 (overlapping multiplets, 11 H), 2.51 (m, 1 H), 2.89 (m, 2 H, 6-H_2), 2.95 (dd, J = 9.5, J = 2.8 Hz, 1 H, N−$CH_{2,ax}$), 3.52 (d, J = 9.5 Hz, 1 H, N−$CH_{2,eq}$), 3.77 (s, 3 H, 3-OMe), 6.36 (dd-like m, 1 H, 6′-H), 6.57 (dd, J = 8.7, J = 2.5 Hz, 1 H, 2-H), 6.71 (d, J = 2.5 Hz, 1 H, 4-H), 6.87 (t-like m, 1 H, 5′-H), 6.90 (d, J = 8.7 Hz, 1 H, 1-H), 7.16 (t-like m, 1 H, 2′-H), 7.29 (dd-like m, 1 H, 4′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8 (C-16a), 22.3, 23.5 (C-18), 26.3, 28.2, 30.4, 33.3, 34.5 (C-13), 35.7, 46.4 (C-14), 48.6 (C-8), 55.2 (3-OMe), 58.4 (C-9), 61.6 (N−CH_2), 110.4 and 110.8 (C-2′ and C-4′), 112.6 (C-2), 113.7 (C-4), 122.3 (C-6′), 127.7 (C-5′), 129.6 (C-1), 130.4 (C-10), 138.9 (C-5), 148.3 (C-1′), 149.7 (C-3′), 158.7 (C-3) ppm. MS (70 eV, EI): m/z (%) = 420 (100) [M^+], 377 (44), 282 (26), 269 (34), 254 (29), 225 (24), 151 (19), 147 (16). $C_{26}H_{32}N_2O_3$ (420.54): calcd. for C 74.26, H 7.67, N 6.66; found C 74.42, H 7.52, N 6.92.

Cyclization of 6a with *p*-Nitroaniline (22) in the Presence of $BF_3{\cdot}OEt_2$: Compound **6a** (300 mg, 1.00 mmol), *p*-nitroaniline (**22**, 138 mg, 1.00 mmol) and $BF_3{\cdot}OEt_2$ (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, *tert*-butyl methyl ether/PE, 20:80) to give **62a** (328 mg, 78 %) as a yellow oil. R_f = 0.50 ($CHCl_3$). $[\alpha]_D$ = +610.4 (c = 1 in chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, J = 7.2 Hz, 3 H, 16a-H_3), 0.99 (s, 3 H, 18-H_3), 1.10−2.00 (overlapping multiplets, 11 H), 2.53 (m, 1 H), 2.88 (m, 2 H, 6-H_2), 3.01 (dd, J = 10.2, J = 2.6 Hz, 1 H, N−$CH_{2,ax}$), 3.52 (d, J = 10.2 Hz, 1 H, N−$CH_{2,eq}$), 3.80 (s, 3 H, 3-OMe), 6.13 (d, J = 9.5 Hz, 2 H, 2′-H and 6′-H), 6.64 (dd, J = 8.7, J = 2.6 Hz, 1 H, 2-H), 6.70 (d, J = 2.6 Hz, 1 H, 4-H), 7.01 (d, J = 8.7 Hz, 1 H, 1-H), 7.72 (d, J = 9.5 Hz, 2 H, 3′-H and 5′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8 (C-16a), 22.3, 23.4 (C-18), 26.0, 27.8, 30.4, 33.1, 34.5 (C-13), 36.4, 46.1 (C-14), 48.7 (C-8), 55.2 (3-OMe), 59.3 (C-9), 62.1 (N−CH_2), 112.7 (C-2), 113.6 (2 C, C-2′ and C-6′), 113.9 (C-4), 124.6 (2 C, C-3′ and C-5′), 129.3 (C-1), 130.4 (C-10), 136.3 (C-4′), 138.6 (C-5), 154.4 (C-1′), 158.9 (C-3) ppm. MS (70 eV, EI): m/z (%) = 420 (70) [M^+], 377 (100), 282 (14), 269 (16), 225 (11), 174 (10). $C_{26}H_{32}N_2O_3$ (420.54): calcd. for C 74.26, H 7.67, N 6.66; found C 74.30, H 7.45, N 6.88.

Treatment of 6a with *p*-Nitroaniline (22) in the Presence of $SnCl_4$: Compound **6a** (300 mg, 1.00 mmol), *p*-nitroaniline (**22**, 138 mg, 1.00 mmol) and $SnCl_4$ (99.95 %, 0.12 mL, 1.00 mmol) were treated as described in the Typical Procedure for 24 h. The crude product was purified by column chromatography (silica gel, *tert*-butyl methyl ether/PE, 20:80) to give **62a** (17 mg, 4 %) and **72a** (307 mg, 73 %). **Compound 72a:** Yellow oil; R_f = 0.16 (*tert*-butyl methyl ether/PE, 20:80). $[\alpha]_D$ = −70.9 (c = 1 in chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.90 (t, J = 7.2 Hz, 3 H, 16a-H_3), 1.06 (s, 3 H, 18-H_3), 1.32−2.47 (overlapping multiplets, 11 H), 2.74 (m, 2 H, 6-H_2), 3.08 (m, 2 H, N−CH_2), 3.78 (s, 3 H, 3-OMe), 4.48 (t-like m, 1 H, N-H), 6.46 (d, J = 9.2 Hz, 2 H, 2′-H and 6′-H), 6.68 (d, J = 2.7 Hz, 1 H, 4-H), 6.72 (dd, J = 8.1, J = 2.7 Hz, 1 H, 2-H), 7.10 (d, J = 8.1 Hz, 1 H, 1-H), 8.00 (d, J = 9.2 Hz, 2 H, 3′-H and 5′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.9 (C-16a), 22.5, 23.4, 23.6 (C-18), 28.6, 29.1, 29.2, 34.2, 36.7 (C-13), 46.3 (C-14), 50.7 (N−CH_2), 55.3 (3-OMe), 110.9 (3C, C-2, C-2′ and C-6′), 113.5 (C-4), 123.0 (C-1), 126.4 (2 C, C-3′ and C-5′), 124.7 (C-8), 128.7 (C-9), 134.5 (C-10), 137.3 (C-5), 137.6 (C-4′), 154.1 (C-1′), 158.1 (C-3) ppm. MS (70 eV, EI): m/z (%) = 420 (23) [M^+], 282 (15), 269 (18), 254 (80), 225 (13), 151 (14), 119 (23), 105 (46), 91 (32), 57 (100), 43 (82). $C_{26}H_{32}N_2O_3$ (420.54): calcd. for C 74.26, H 7.67, N 6.66; found C 74.35, H 7.82, N 6.58.

Treatment of 6a with *p*-Nitroaniline (22) in the Presence of Me_2SnCl_2: Compound **6a** (300 mg, 1.00 mmol), *p*-nitroaniline (**22**, 138 mg, 1.00 mmol) and Me_2SnCl_4 (220 mg, 1.00 mmol) were treated as described in the Typical Procedure for 24 h. The crude product was purified by column chromatography (silica gel, *tert*-butyl methyl ether/PE, 20:80) to give only **72a** (8 mg, 2 %), together with starting material.

Treatment of 6a with *p*-Nitroaniline (22) in the Presence of $AlCl_3$: Compound **3a** (300 mg, 1.00 mmol), *p*-nitroaniline (**22**, 138 mg,

1.00 mmol) and $AlCl_3$ (133 mg, 1.00 mmol) were treated as described in the Typical Procedure for 24 h. The crude product was purified by column chromatography (silica gel, *tert*-butyl methyl ether/PE, 20:80) to give **62a** (63 mg, 15 %) and **72a** (239 mg, 57 %).

Treatment of 6a with *p*-Nitroaniline (22) in the Presence of $TiCl_4$: Compound **6a** (300 mg, 1.00 mmol), *p*-nitroaniline (**22**, 138 mg, 1.00 mmol) and $TiCl_4$ (0.11 mL, 1.00 mmol) were treated as described in the Typical Procedure for 24 h. The crude product was purified by column chromatography (silica gel, *tert*-butyl methyl ether/PE, 20:80) to give **72a** (88 mg, 21 %) and **79** (272 mg, 65 %). **Compound 79:** Yellow oil; R_f = 0.39 (*tert*-butyl methyl ether/PE, 20:80). $[\alpha]_D$ = +50.0 (c = 1 in chloroform). ^{1}H NMR (300 MHz, $CDCl_3$): 0.87 (t, J = 7.2 Hz, 3 H, 16a-H_3), 1.32 (s, 3 H, 18-H_3), 1.45−2.31 (overlapping multiplets, 9 H), 2.55 (m, 2 H, 6-H_2), 3.13 (d, J = 10.2 Hz, 1 H) and 3.30 (d, J = 10.2 Hz, 1 H): N−CH_2, 3.79 (s, 3 H, 3-OMe), 5.02 (d, J = 4.8 Hz, 1 H, 11-H), 6.31 (d, J = 9.5 Hz, 2 H, 2′-H and 6′-H), 6.66 (d, J = 2.6 Hz, 1 H, 4-H), 6.80 (dd, J = 8.4, J = 2.6 Hz, 1 H, 2-H), 7.37 (d, J = 8.4 Hz, 1 H, 1-H), 7.89 (d, J = 9.5 Hz, 2 H, 3′-H and 5′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8 (C-16a), 21.4, 23.1 (C-18), 27.4, 28.9, 32.2, 39.1, 41.9, 53.2 (C-14), 54.2 (C-11), 55.2 (3-OMe), 63.2 (N−CH_2), 110.4 (2 C, C-2′ and C-6′), 111.1 (C-2), 114.0 (C-4), 122.0 (C-1), 126.3 (2 C, C-3′ and C-5′), 127.2 (C-10), 131.7 and 135.8 and 135.9 and 137.3 (C-5, C-8, C-9 and C-4′), 150.2 (C-1′), 158.3 (C-3) ppm. MS (70 eV, EI): *m*/*z* (%) = 418 (70) [M^+], 281 (21), 267 (89), 225 (100), 210 (23), 152 (67), 44 (21). $C_{26}H_{30}N_2O_3$ (418.53): calcd. for C 74.61, H 7.22, N 6.69; found C 74.78, H 7.15, N 7.05.

Treatment of 6a with *p*-Nitroaniline (22) in the Presence of Trimethylsilyl Trifluoromethanesulfonate: Compound **6a** (300 mg, 1.00 mmol), *p*-nitroaniline (**22**, 138 mg, 1.00 mmol) and $CF_3SO_2OSiMe_3$ (0.18 mL, 1.00 mmol) were treated as described in the Typical Procedure for 24 h. The crude product was purified by column chromatography (silica gel, *tert*-butyl methyl ether/PE, 20:80) to give **62a** (118 mg, 28 %) and **72a** (177 mg, 42 %).

Treatment of 6a with *p*-Nitroaniline (22) in the Presence of *p*-Toluenesulfonic Acid Monohydrate: Compound **6a** (300 mg, 1.00 mmol), *p*-nitroaniline (**22**, 138 mg, 1.00 mmol) and *p*TsOH (190 mg, 1.00 mmol) were treated as described in the Typical Procedure for 24 h. The crude product was purified by column chromatography (silica gel, *tert*-butyl methyl ether/PE, 20:80) to give only **72a** (315 mg, 75 %).

Treatment of 6a with *p*-Nitroaniline (22) in the Presence of HBF_4·OEt_2: Compound **6a** (300 mg, 1.00 mmol), *p*-nitroaniline (**22**, 138 mg, 1.00 mmol) and HBF_4·OEt_2 (85 %, 0.18 mL, 1.00 mmol) were treated as described in the Typical Procedure for 24 h. The crude product was purified by column chromatography (silica gel, *tert*-butyl methyl ether/PE, 20:80) to give **62a** (42 mg, 10 %) and **72a** (244 mg, 58 %).

Treatment of 6b with *p*-Nitroaniline (22) in the Presence of BF_3·OEt_2: Compound **6b** (286 mg, 1.00 mmol), *p*-nitroaniline (**22**, 138 mg, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, *tert*-butyl methyl ether/PE, 40:60) to give **62b** (256 mg, 63 %) and **72b** (130 mg, 32 %). Compound **62b** was recrystallized from acetone/PE; yellow crystals; m.p. 179−181 °C; R_f = 0.50 (*tert*-butyl methyl ether/PE, 40:60). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, J = 7.2 Hz, 3 H, 16a-H_3), 0.99 (s, 3 H, 18-H_3), 1.05−1.99 (overlapping multiplets, 11 H), 2.51 (m, 1 H), 2.86 (m, 2 H, 6-H_2), 3.01 (dd, J = 10.2, J = 2.8 Hz, 1 H, N−$CH_{2,ax}$), 3.51 (d, J = 10.2 Hz, 1 H, N−$CH_{2,eq}$), 4.97 (s, 1 H, 3-OH), 6.14 (d, J = 9.6 Hz, 2 H, 2′-H and 6′-H), 6.56 (dd, J = 8.5, J = 2.7 Hz, 1 H, 2-H), 6.67 (d, J = 2.7 Hz, 1 H, 4-H), 6.97 (d, J = 8.5 Hz, 1 H, 1-H), 7.73 (d, J = 9.6 Hz, 2 H, 3′-H and 5′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.2 (C-16a), 22.7, 23.8 (C-18), 26.3, 28.2, 30.6, 33.5, 34.9 (C-13), 36.8, 46.4 (C-14), 49.0 (C-8), 59.6 (C-9), 62.5 (N−CH_2), 114.1 (2 C, C-2′ and C-6′), 114.5 (C-2), 116.0 (C-4), 125.0 (2 C, C-3′ and C-5′), 130.0 (C-1), 130.9 (C-10), 136.6 (C-4′), 139.3 (C-5), 154.8 and 155.4 (C-1′ and C-3) ppm. MS (70 eV, EI): *m*/*z* (%) = 406 (70) [M^+], 363 (100), 286 (52), 243 (50), 159 (46), 133 (46). $C_{25}H_{30}N_2O_3$ (406.52): calcd. for C 73.86, H 7.44, N 6.89; found C 73.70, H 7.55, N 7.08.

Compound 72b: Yellow oil; R_f = 0.29 (*tert*-butyl methyl ether/PE, 40:60). $[\alpha]_D$ = −55.3 (c = 1 in chloroform). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, J = 7.2 Hz, 3 H, 16a-H_3), 1.07 (s, 3 H, 18-H_3), 1.10−2.50 (overlapping multiplets, 11 H), 2.72 (m, 2 H, 6-H_2), 3.11 (m, 2 H, N−CH_2), 4.50 (t like m, 1 H, N-H), 4.91 (s, 1 H, 3-OH), 6.47 (d, J = 9.2 Hz, 2 H, 2′-H and 6′-H), 6.64 (d, J = 2.7 Hz, 1 H, 4-H), 6.67 (dd, J = 8.1, J = 2.7 Hz, 1 H, 2-H), 7.06 (d, J = 8.1 Hz, 1 H, 1-H), 8.02 (d, J = 9.2 Hz, 2 H, 3′-H and 5′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.3 (C-16a), 22.9, 23.8, 24.0 (C-18), 29.1, 29.3, 29.5, 34.6, 37.1 (C-13), 46.7 (C-14), 51.2 (N−CH_2), 111.3 (2 C, C-2′ and C-6′), 113.1 (C-2), 115.0 (C-4), 123.6 (C-1), 126.9 (2 C, C-3′ and C-5′), 125.1 (C-8), 129.2 (C-9), 134.9 (C-10), 138.0 (2 C, C-4′ and C-5), 154.5 (2 C, C-1′ and C-3) ppm. MS (70 eV, EI): *m*/*z* (%) = 406 (18) [M^+], 268 (24), 240 (100), 211 (22), 151 (26), 105 (14). $C_{25}H_{30}N_2O_3$ (406.52): calcd. for C 73.86, H 7.44, N 6.89; found C 74.03, H 7.31, N 6.72.

Cyclization of 6c with *p*-Nitroaniline (22) in the Presence of BF_3·OEt_2: Compound **6c** (328 mg, 1.00 mmol), *p*-nitroaniline (**22**, 138 mg, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, *tert*-butyl methyl ether/PE, 25:75) to give **62c** (72 mg, 16 %) as a yellow oil. R_f = 0.29 ($CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, J = 7.2 Hz, 3 H, 16a-H_3), 1.00 (s, 3 H, 18-H_3), 1.09−2.01 (overlapping multiplets, 11 H), 2.28 (s, 3 H, OC-OCH_3), 2.50 (m, 1 H), 2.90 (m, 2 H, 6-H_2), 3.03 (dd, J = 10.1, J = 2.8 Hz, 1 H, N−$CH_{2,ax}$), 3.54 (d, J = 10.1 Hz, 1 H, N−$CH_{2,eq}$), 6.12 (d, J = 9.6 Hz, 2 H, 2′-H and 6′-H), 6.81 (dd, J = 8.6, J = 2.5 Hz, 1 H, 2-H), 6.95 (d, J = 2.5 Hz, 1 H, 4-H), 7.11 (d, J = 8.6 Hz, 1 H, 1-H), 7.74 (d, J = 9.6 Hz, 2 H, 3′-H and 5′-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.2 (C-16a), 21.5 (OCO*CH*$_3$), 22.7, 23.7 (C-18), 26.1, 28.2, 30.6, 33.5, 35.0 (C-13), 36.7, 46.4 (C-14), 48.9 (C-8), 59.6 (C-9), 62.5 (N−CH_2), 114.2 (2 C, C-2′ and C-6′), 120.2 (C-2), 122.6 (C-4), 124.9 (2 C, C-3′ and C-5′), 129.8 (C-1), 136.1 and 137.0 (C-4′ and C-10), 139.2 (C-5), 150.4 (C-3), 154.5 (C-1′), 170.2 (O*C*OCH$_3$). $C_{27}H_{32}N_2O_4$ (448.55): calcd. for C 72.30, H 7.19, N 6.25; found C 72.05, H 7.28, N 6.05.

Treatment of 6a with 2,4-Dinitroaniline (23): Compound **6a** (300 mg, 1.00 mmol), 2,4-dinitroaniline (**23**, 183 mg, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, *tert*-butyl methyl ether/PE, 15:85) to give **73a** (354 mg, 76 %) as an orange oil. R_f = 0.55 (PE/CH_2Cl_2, 20:80). $[\alpha]_D$ = +27.7 (c = 1 in chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.94 (t, J = 7.0 Hz, 3 H, 16a-H_3), 1.17 (s, 3 H, 18-H_3), 1.32−2.51 (overlapping multiplets, 11 H), 2.74 (m, 2 H, 6-H_2), 3.28 (m, 2 H, N−CH_2), 3.79 (s, 3 H, 3-OMe), 6.71 (m, 2 H, 2-H and 4-H), 6.83 (d, J = 9.6 Hz, 1 H, 6′-H), 7.10 (d, J = 8.1 Hz, 1 H, 1-H), 8.16 (dd, J = 9.6, J =

2.6 Hz, 1 H, 5′-H), 8.78 (t-like m, 1 H, N-H), 9.10 (d, J = 2.6 Hz, 1 H, 3′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8 (C-16a), 22.5, 23.4, 23.7 (C-18), 28.5, 29.1, 29.3, 34.3, 36.6 (C-13), 46.7 (C-14), 51.0 (N−CH_2), 55.3 (3-OMe), 111.0 (C-2), 113.6 (C-4), 114.0 (C-4′), 123.0 (C-1), 124.4 (C-3′), 124.8 (C-8), 128.5 (C-9), 130.3 (C-5′), 134.1 (2 C, C-10 and C-4′), 135.8 (C-2′), 137.3 (C-5), 148.9 (C-1′), 158.3 (C-3) ppm. MS (70 eV, EI): *m/z* (%) = 465 (22) [M^+], 268 (100), 254 (13), 226 (30). $C_{26}H_{31}N_3O_5$ (465.54): calcd. for C 67.08, H 6.71, N 9.03; found C 66.91, H 6.85, N 8.93.

Cyclization of 6a with 3,5-Dinitroaniline (24): Compound **6a** (300 mg, 1.00 mmol), 3,5-dinitroaniline (**24**, 183 mg, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, PE/CH_2Cl_2, 30:40) to give **63a** (419 mg, 90 %) as an orange oil. R_f = 0.56 (PE/CH_2Cl_2, 30:70). [α]$_D$ = +507.1 (c = 1 in chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.96 (t, J = 7.2 Hz, 3 H, 16a-H_3), 1.03 (s, 3 H, 18-H_3), 1.15−2.08 (overlapping multiplets, 11 H), 2.53 (m, 1 H), 2.94 (m, 2 H, 6-H_2), 2.99 (dd, J = 9.7, J = 2.7 Hz, 1 H, N−$CH_{2,ax}$), 3.53 (d, J = 9.7 Hz, 1 H, N−$CH_{2,eq}$), 3.79 (s, 3 H, 3-OMe), 6.62 (dd, J = 8.7, J = 2.6 Hz, 1 H, 2-H), 6.80 (d, J = 2.6 Hz, 1 H, 4-H), 6.96 (d, J = 8.7 Hz, 1 H, 1-H), 7.25 (d-like m, 2 H, 2′-H and 6′-H), 8.02 (d-like m, 1 H, 4′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8 (C-16a), 22.2, 23.3 (C-18), 26.5, 27.9, 30.3, 33.2, 34.6 (C-13), 35.8, 46.4 (C-14), 48.5 (C-8), 55.4 (3-OMe), 59.3 (C-9), 62.0 (N−CH_2), 104.6 (C-4′), 113.6 (C-2), 114.2 (3C, C-4, C-2′ and C-6′), 129.0 (C-10), 129.1 (C-1), 139.0 (C-5), 148.1 (2 C, C-3′ and C-5′), 150.1 (C-1′), 159.5 (C-3) ppm. MS (70 eV, EI): *m/z* (%) = 465 (88) [M^+], 422 (100), 269 (14). $C_{26}H_{31}N_3O_5$ (465.54): calcd. for C 67.08, H 6.71, N 9.03; found C 67.15, H 6.62, N 9.21.

Cyclization of 6a with 3,4-Dichloroaniline (25): Compound **6a** (300 mg, 1.00 mmol), 3,4-dichloroaniline (**25**, 162 mg, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, *tert*-butyl methyl ether/PE, 10:90) to give **64a** (364 mg, 82 %) as a colourless oil. R_f = 0.81 (PE/CH_2Cl_2, 30:70). [α]$_D$ = +352.6 (c = 1 in chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.94 (t, J = 7.2 Hz, 3 H, 16a-H_3), 0.95 (s, 3 H, 18-H_3), 1.13−1.95 (overlapping multiplets, 11 H), 2.49 (m, 1 H), 2.85 (m, 2 H, 6-H_2), 2.86 (dd, J = 9.4, J = 2.9 Hz, 1 H, N−$CH_{2,ax}$), 3.40 (d, J = 9.4 Hz, 1 H, N−$CH_{2,eq}$), 3.77 (s, 3 H, 3-OMe), 5.92 (dd, J = 9.1, J = 2.9 Hz, 1 H, 6′-H), 6.39 (d, J = 2.9 Hz, 1 H, 2′-H), 6.58 (dd, J = 8.7, J = 2.7 Hz, 1 H, 2-H), 6.66 (d, J = 2.7 Hz, 1 H, 4-H), 6.78 (d, J = 9.1 Hz, 1 H, 5′-H), 6.88 (d, J = 8.7 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8 (C-16a), 22.2, 23.5 (C-18), 26.3, 28.3, 30.4, 33.3, 34.4 (C-13), 35.3, 46.4 (C-14), 48.7 (C-8), 55.2 (3-OMe), 58.2 (C-9), 61.6 (N−CH_2), 112.3 (C-2), 113.7 (C-4), 116.8 and 118.0 (C-2′ and C-6′), 119.0 (C-4′), 128.5 (C-1), 129.8 (C-5′), 130.7 (C-10), 131.2 (C-3′), 138.9 (C-5), 148.6 (C-1′), 158.7 (C-3) ppm. MS (70 eV, EI): *m/z* (%) = 445 (48) [M^+], 443 (73), 400 (100), 282 (83), 269 (56), 239 (24), 225 (28), 174 (35), 161 (67), 147 (39). $C_{26}H_{31}Cl_2NO$ (444.44): calcd. for C 70.26, H 7.03, N 3.15; found C 70.42, H 6.98, N 3.45.

Cyclization of 6a with 4-Chloro-3-nitroaniline (26): Compound **6a** (300 mg, 1.00 mmol), 4-chloro-3-nitroaniline (**26**, 173 mg, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, PE/CH_2Cl_2, 55:45) and recrystallized from acetone to give **65a** (341 mg, 75 %) as yellow crystals. M.p. 110−112 °C; R_f = 0.35 (PE/CH_2Cl_2, 55:45). [α]$_D$ = +415.2 (c = 1 in chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.94 (t, J = 7.2 Hz, 3 H, 16a-H_3), 0.96 (s, 3 H, 18-H_3), 1.08−1.98 (overlapping multiplets, 11 H), 2.50 (m, 1 H), 2.86 (m, 2 H, 6-H_2), 2.87 (dd, J = 9.5, J = 2.7 Hz, 1 H, N−$CH_{2,ax}$), 3.43 (d, J = 9.5 Hz, 1 H, N−$CH_{2,eq}$), 3.78 (s, 3 H, 3-OMe), 6.18 (dd, J = 9.1, J = 3.0 Hz, 1 H, 6′-H), 6.61 (dd, J = 8.7, J = 2.5 Hz, 1 H, 2-H), 6.69 (m, 2 H, 4-H and 2′-H), 6.85 (d, J = 9.1 Hz, 1 H, 5′-H), 6.92 (d, J = 8.7 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8 (C-16a), 22.2, 23.4 (C-18), 26.3, 28.1, 30.4, 33.2, 34.4 (C-13), 35.7, 46.3 (C-14), 48.6 (C-8), 55.2 (3-OMe), 58.6 (C-9), 61.6 (N−CH_2), 112.0 (C-2′), 112.3 (C-4′), 112.8 (C-2), 113.9 (C-4), 120.5 (C-6′), 129.6 and 130.0 (C-1 and C-5′), 130.7 (C-10), 138.9 (C-5), 147.8 (C-1′), 148.2 (C-3′), 159.0 (C-3) ppm. MS (70 eV, EI): *m/z* (%) = 456 (35) [M^+], 454 (100), 411 (66), 282 (14), 269 (15). $C_{26}H_{31}ClN_2O_3$ (454.99): calcd. for C 68.63, H 6.87, N 6.16; found C 68.81, H 7.02, N 6.25.

Cyclization of 6a with 3,5-Bis(trifluoromethyl)aniline (27): Compound **6a** (300 mg, 1.00 mmol), 3,5-bis(trifluoromethyl)aniline (**27**, 0.13 mL, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, PE/CH_2Cl_2, 50:50) to give **66a** (399 mg, 78 %) as a colourless oil. R_f = 0.58 (PE/CH_2Cl_2, 70:30). [α]$_D$ = +326.7 (c = 1 in chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.96 (t, J = 7.2 Hz, 3 H, 16a-H_3), 0.99 (s, 3 H, 18-H_3), 1.15−2.00 (overlapping multiplets, 11 H), 2.52 (m, 1 H), 2.89 (m, 2 H, 6-H_2), 2.93 (dd, J = 9.4, J = 2.7 Hz, 1 H, N−$CH_{2,ax}$), 3.50 (d, J = 9.4 Hz, 1 H, N−$CH_{2,eq}$), 3.77 (s, 3 H, 3-OMe), 6.54 (s, 2 H, 2′-H and 6′-H), 6.60 (dd, J = 8.7, J = 2.5 Hz, 1 H, 2-H), 6.72 (d, J = 2.5 Hz, 1 H, 4-H), 6.90 (d, J = 8.7 Hz, 1 H, 1-H), 6.92 (s, 1 H, 4′-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8 (C-16a), 22.3, 23.5 (C-18), 26.4, 28.4, 30.4, 33.3, 34.5 (C-13), 35.6, 46.4 (C-14), 48.7 (C-8), 55.3 (3-OMe), 58.7 (C-9), 61.4 (N−CH_2), 108.8 (C-4′), 112.2 (C-2), 114.1 (C-4), 115.3 (2 C, C-2′ and C-6′), 123.7 (q, 2 C, J = 271 Hz, 2 CF_3), 129.6 (C-1), 130.3 (2 C, C-3′ and C-5′), 130.9 (C-10), 138.9 (C-5), 149.4 (C-1′), 159.3 (C-3) ppm. MS (70 eV, EI): *m/z* (%) = 511 (81) [M^+], 468 (100), 400 (11), 282 (12), 269 (12). $C_{28}H_{31}F_6NO$ (511.54): calcd. for C 65.74, H 6.11, N 2.74; found C 65.52, H 6.27, N 2.50.

Cyclization of 6a with 3,4,5-Tribromoaniline (28): Compound **6a** (300 mg, 1.00 mmol), 3,4,5-tribromoaniline (**28**, 330 mg, 1.00 mmol) and BF_3·OEt_2 (a 48 % solution in diethyl ether, 0.29 mL, 1.00 mmol) were treated as described in the Typical Procedure. The crude product was purified by column chromatography (silica gel, PE/CH_2Cl_2, 50:50) to give **67a** (514 mg, 84 %) and **74** (18 mg, 6 %). **Compound 67a:** Colourless oil; R_f = 0.83 (PE/CH_2Cl_2, 50:50). [α]$_D$ = +228.1 (c = 1 in chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.94 (t, J = 7.1 Hz, 3 H, 16a-H_3), 0.95 (s, 3 H, 18-H_3), 1.11−1.93 (overlapping multiplets, 11 H), 2.49 (m, 1 H), 2.83 (dd, J = 9.5, J = 2.7 Hz, 1 H, N−$CH_{2,ax}$), 2.85 (m, 2 H, 6-H_2), 3.33 (d, J = 9.5 Hz, 1 H, N−$CH_{2,eq}$), 3.79 (s, 3 H, 3-OMe), 6.35 (s, 2 H, 2′-H and 6′-H), 6.65 (dd, J = 8.7, J = 2.5 Hz, 1 H, 2-H), 6.70 (d, J = 2.5 Hz, 1 H, 4-H), 6.93 (d, J = 8.7 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8 (C-16a), 22.2, 23.5 (C-18), 26.4, 28.1, 30.4, 33.3, 34.4 (C-13), 35.3, 46.4 (C-14), 48.6 (C-8), 55.4 (3-OMe), 58.6 (C-9), 61.5 (N−CH_2), 111.6 (C-4′), 112.6 (C-2), 114.1 (C-4), 120.1 (2 C, C-2′ and C-6′), 124.2 (2 C, C-3′ and C-5′), 129.7 (C-1), 130.0 (C-10), 138.9 (C-5), 149.1 (C-1′), 159.1 (C-3) ppm. MS (70 eV, EI): *m/z* (%) = 613 (98) [M^+], 611 (100), 568 (74), 533 (36), 490 (34), 488 (17), 282 (36), 269 (31), 225 (14). $C_{26}H_{30}Br_3NO$ (612.23): calcd. for C 51.01, H 4.94, N 2.29; found C 49.92, H 5.03, N 2.41.

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[1] V. Gandon, P. Bertus, J. Szymoniak, *Eur. J. Org. Chem.* **2000**, *22*, 3713−3720.
[2] M. Adamczyk, Y-Y. Chen, P. G. Mattingly, *Tetrahedron Lett.* **2001**, *42*, 4285−4288.
[3] M. Gonschior, M. Kötteritzsch, M. Rost, B. Schönecker, *Tetrahedron: Asymmetry* **2000**, *11*, 2159−2182.
[4] V. K. Yadav, K. G. Babu, M. Mittal, *Tetrahedron* **2001**, *57*, 7047−7052.
[5] N. K. Dunlap, M. R. Sabol, D. S. Watt, *Tetrahedron Lett.* **1984**, *25*, 5839−5842.
[6] M. Vujcic, R. M. Jankov, *Steroids* **1990**, *55*, 17−21.
[7] R. P. Boivin, V. Luu-The, R. Lachance, F. Labrie, D. Poirier, *J. Med. Chem.* **2000**, *43*, 4465− 4478.
[8] N. L. Wendler, D. Taub, R. W. Walker, *Tetrahedron* **1960**, *11*, 163−170.
[9] L. E. Contreras, J. M. Evans, D. de Marcano, L. Marqez, M. Molina, L. Tempestini, *J. Org. Chem.* **1974**, *39*, 1550−1554.
[10] J. B. Jones, P. Price, *Tetrahedron* **1973**, *29*, 1941−1947.
[11] K. M. Penov Gaši, S. M. Stanković, J. J. Csanádi, E. A. Djurendić, M. N. Sakač, L. Medić Mijačević, O. N. Arcson, S. Z. Stojanović, S. Andrić, D. Molnar Gabor, R. Kovačević, *Steroids* **2001**, *66*, 645−653.
[12] P. A. Procopiou, S. M. Lynn, A. D. Roberts, *Tetrahedron* **1999**, *55*, 3649−3656.
[13] I. L. Reich, H. Lardy, Y. Wei, P. Marwah, N. Kneer, D. R. Powell, H. J. Reich, *Steroids* **1998**, *63*, 542−553.
[14] P. C. Bulman Page, F. Hussain, J. L. M. P. Morgan, B. K. Park, *Tetrahedron* **1990**, *46*, 2059− 2068.
[15] H. Künzer, M. Thiel, *Tetrahedron Lett.* **1988**, *29*, 3223−3226.
[16] B. Schönecker, C. Lange, M. Kötteritzsch, W. Günther, J. Weston, E. Anders, H. Görls, *J. Org. Chem.* **2000**, *65*, 5487−5497.
[17] A. Guy, J. Doussot, M. Lemaire, *Synthesis* **1991**, 460−462.
[18] S. Schwarz, M. Schumacher, S. Ring, A. Nanninga, G. Weber, I. Thieme, B. Undeutsch, W. Elger, *Steroids* **1999**, *64*, 460−471.
[19] P. Bovicelli, P. Lupattelli, E. Mincione, T. Prencipe, R. Curci, *J. Org. Chem.* **1992**, *57*, 2182− 2184.
[20] R. Tedesco, J. A. Katzenellenbogen, E. Napolitano, *Bioorg. Med. Chem. Lett.* **1997**, *7*, 2919− 2924.
[21] R. C. Cambie, V. F. Carlisle, C. J. Le Quesne, T. D. R. Manning, *J. Chem. Soc. (C)* **1969**, 1234−1240.
[22] J. Wölfling, É. Frank, G. Schneider, L. F. Tietze, *Eur. J. Org. Chem.* **1999**, 3013−3020.
[23] J. Wölfling, É. Frank, G. Schneider, M. T. Bes, L. F. Tietze, *Synlett* **1998**, 1205−1206.
[24] Part of this work has already been published as a communication: J. Wölfling, É. Frank, G. Schneider, L. F. Tietze, *Angew. Chem.* **1999**, *111*, 151−152; *Angew. Chem. Int. Ed.* **1999**, *38*, 200− 201.
[25] H. Mayr, A. R. Ofial, *Tetrahedron Lett.* **1997**, *38*, 3503−3506.
[26] I. Iriepa, F. J. Villasante, E. Gálvez, L. Labeaga, A. Innerarity, A. Orjales, *Bioorg. Med. Chem. Lett.* **2002**, *12*, 189−192.
[27] G. R. Krow, O. H. Cheung, Z. Hu, Q. Huang, J. Hutchinson, N. Liu, K. T. Nguyen, S. Ulrich, J. Yuan, Y. Xiao, D. M. Wypij, F. Zuo, P. J. Carroll, *Tetrahedron* **1999**, *55*, 7747−7756.
[28] M. Yokota, E. Takizawa, Y. Ohkura, C. Fukai, T. Tomiyama, *Eur. J. Med. Chem.* **1997**, *32*, 377−384.
[29] D. C. dos Santos, R. P. de Freitas Gil, L. Gil, C. Marazano, *Tetrahedron Lett.* **2001**, *42*, 6109− 6111.
[30] G. Schneider, S. Bottka, L. Hackler, J. Wölfling, P. Sohár, *Liebigs Ann. Chem.* **1989**, 263−267.
[31] Crystallographic data (excluding structure factors) for **5** have been deposited with the Cambridge Crystallographic Data Centre, as supplementary publication no. CCDC-102885. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033; E-mail: deposit@ccdc.cam.ac.uk).
[32] C. H. Heathcock, M. M. Hansen, R. B. Ruggeri, J. C. Kath, *J. Org. Chem.* **1992**, *57*, 2544−2553.
[33] S. Laschat, *Liebigs Ann./Recueil* **1997**, 1−11.

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