DOI: 10.1002/ejoc.200800019

Nitrogen-Containing Tricyclic and Tetracyclic Compounds by Stereoselective Samarium Diiodide Promoted Cyclizations of Quinolyl-Substituted Ketones – A New Access to Azasteroids

Francesca Aulenta,[a,b] Ulrike K. Wefelscheid,[a] Irene Brüdgam,[a][‡] and Hans-Ulrich Reißig*[a]

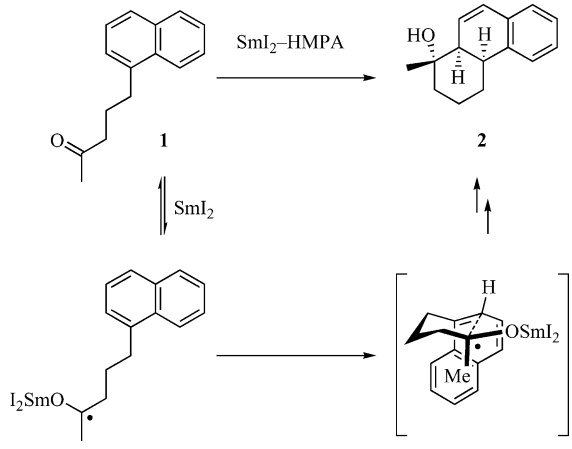
Keywords: Samarium / Electron transfer / Quinolines / Steroids / C–C coupling

In this report, we describe our experiments dealing with samarium diiodide promoted cyclizations of quinolyl-substituted ketones **6**–**12** and also the attempted reductive cyclization of carbazole-containing ketone **13**. These precursors were prepared by Heck-type coupling reactions of the corresponding hetaryl nonaflates with adequately substituted olefins as a key step. The cyclization of compounds **7**–**12** led to nitrogen-containing tri- and tetracyclic compounds **23**–**28** in moderate to good yields and generally proceeded in a highly diastereoselective fashion. The azatetracycles present steroid-like skeletons but with unnatural *cis*–*cis* annulation of rings B, C and D. We also describe the chemical modification of the styrene-type double bond of these products, which provided highly functionalized steroid-type compounds such as **29**, **30** and **32**.

(© Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, Germany, 2008)

Introduction

Heteroatom-containing steroids and in particular azasteroids have proven to be attractive targets in pharmaceutical chemistry. The presence of a nitrogen atom confers to these compounds interesting biological activities,[1] which have encouraged organic chemists to provide not only efficient routes towards the synthesis of known target compounds, but also to generate novel structures that could potentially lead to useful drugs.[2] Our approach towards the synthesis of nitrogen-containing polycyclic structures is based on samarium diiodide promoted cyclizations of hetaryl-substituted ketones. Such methodology has been widely investigated by our group[3] and other authors,[4] and it provides highly functionalized products with very good diastereoselectivities.[5] The cyclizations of γ-aryl and γ-naphthyl ketones such as **1** are promoted by the SmI_2–HMPA complex,[6] which transfers one electron to the carbonyl group to thus generate a samarium ketyl species (Scheme 1). This intermediate attacks the *ortho* position of the aromatic ring, which thereby forms a new six-membered ring. A second electron transfer followed by regioselective protonation affords the final tricyclic compound **2**. The high degree of diastereoselectivity mostly observed could be explained by a six-membered transition structure during the ketyl addition, in which the samariumalkoxy moiety occupies an equatorial position for steric and electronic reasons (Scheme 1).[3a,3f,7]



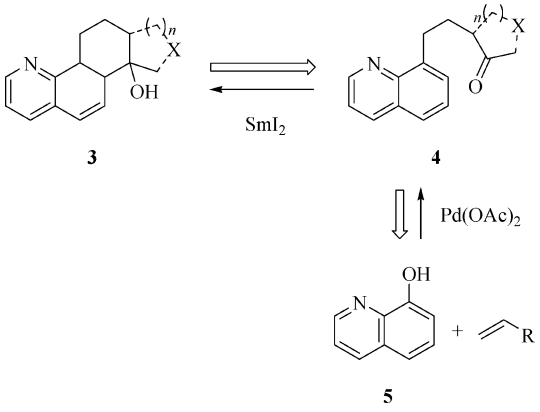
Scheme 1. Proposed mechanism for the samarium diiodide induced diastereoselective cyclization of γ-naphthyl-substituted ketone **1** leading to tricyclic product **2**.

Herein, we report the application of this method to the stereoselective synthesis of nitrogen-containing tricyclic and tetracyclic compounds such as **3** (Scheme 2). Starting materials **4** combine the quinoline moiety with a suitably positioned carbonyl group as a precursor of a samarium ketyl. As a short and potentially flexible synthesis of ketones **4**,

[a] Institut für Chemie und Biochemie, Freie Universität Berlin, Takustr. 3, 14195 Berlin, Germany
Fax: +49-30-83855367
E-mail: hans.reissig@chemie.fu-berlin.de
[b] BASF, GKT/W – B 001, Polymer Research – Biopolymers, 67056 Ludwigshafen, Germany
[‡] Responsible for X-ray crystal structure analysis
Supporting information for this article is available on the WWW under http://www.eurjoc.org or from the author.

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

we envisaged palladium-catalyzed reactions with hydroxyquinoline derivatives such as **5** as precursors. Similarly, we attempted to introduce carbazole derivatives as components in the reductive cyclization process.



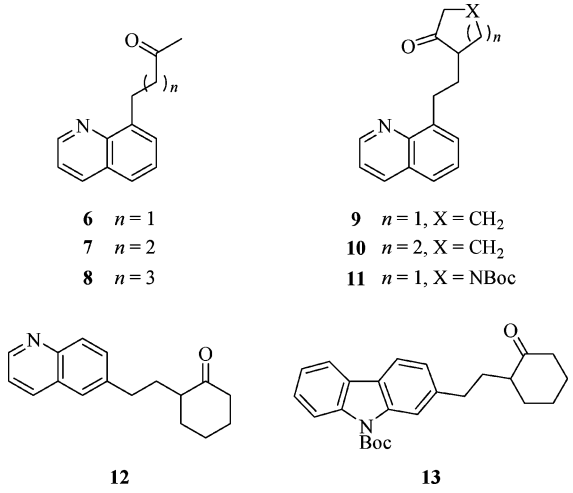
3 **4** **5**

Scheme 2. Retrosynthetic analysis for target compounds **3**.

Results and Discussion

Synthesis of Hetaryl-Substituted Ketones by Heck Couplings

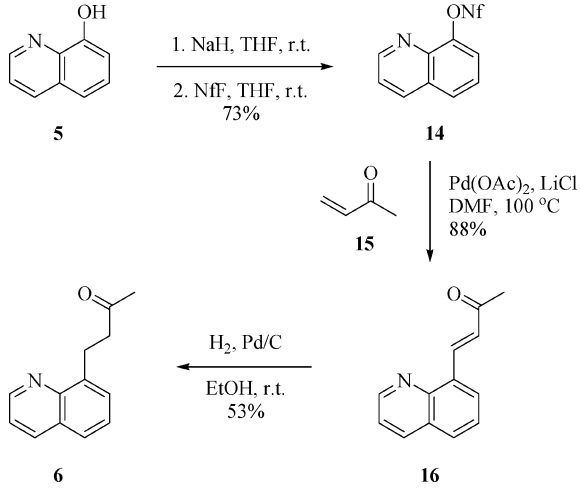
We planned to investigate the cyclizations of γ-hetaryl-substituted ketones **6**–**13** (Scheme 3). Their syntheses were achieved by palladium-promoted arylations (Heck reactions)[8] of quinolyl and carbazolyl nonaflates (nonafluorobutane sulfonates) with a series of adequately substituted olefins.[9] Among the possible hydroxyquinoline and carbazole precursors to be used, we selected 8-hydroxyquinoline, 6-hydroxyquinoline and 2-hydroxy-9*H*-carbazole, because they are stable and commercially available at low cost.



6 $n = 1$
7 $n = 2$
8 $n = 3$
9 $n = 1$, X = CH_2
10 $n = 2$, X = CH_2
11 $n = 1$, X = NBoc
12 **13**

Scheme 3. The β-, γ- and δ-hetaryl-substituted ketones **6**–**13** to be studied in samarium diiodide promoted cyclizations.

As examples, for the preparation of these target compounds we describe the syntheses of ketones **6**, **8** and **10** in detail (see Schemes 4, 5 and 6; for all other precursors see the Supporting Information). The preparation of nonaflate **14** was easily achieved from precursor **5** by a standard method employing sodium hydride as base followed by treatment with nonafluorobutanesulfonyl fluoride (Scheme 4).[10] Although not yet routinely explored in cross-coupling reactions,[11] (het)aryl nonaflates have shown to exhibit several advantages over the corresponding triflates. They are very stable, easily purified by crystallization or column chromatography, and smoothly prepared[12] using the commercially available, non-toxic and cost-effective nonafluorobutanesulfonyl fluoride. The subsequent Heck reaction of quinolyl nonaflate **14** with methyl vinyl ketone **15** was performed in the presence of lithium chloride, triethylamine, and 5 mol-% of palladium diacetate in DMF smoothly affording the expected product **16** in very good yield (Scheme 4), which was reduced to furnish target compound **6**.



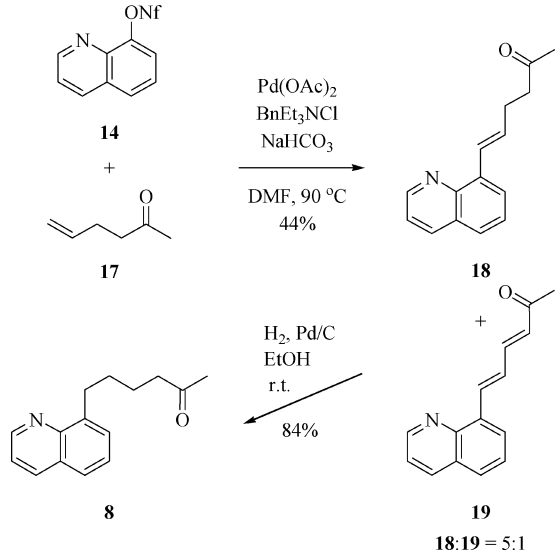
5 **14** **15** **6** **16**

Scheme 4. Synthesis of β-hetaryl ketone **6** via nonaflate **14**.

Coupling of quinolyl nonaflate **14** with olefin **17**, in which the double bond is not activated by a carbonyl group, proved to be more challenging, and ketone **18** was obtained only in moderate yield when modified Jeffery conditions were applied Scheme 5.[13] 1,3-Diene **19** − probably formed by dehydrogenation from **18** − was isolated as a minor component under the reaction conditions applied. This selectivity problem was of no consequence for our purpose, as hydrogenation of the product mixture afforded the desired saturated ketone **8** in good yield.

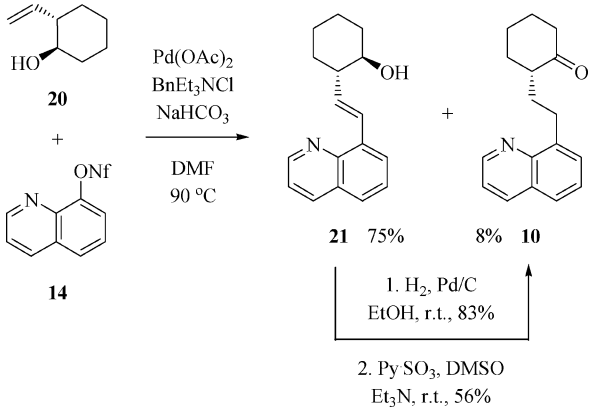
In Scheme 6, we present the synthesis of cyclohexanone derivative **10**. A small amount of this compound was directly formed in the Heck coupling of quinolyl nonaflate **14** with racemic homoallylic alcohol **20**.[14] The major product in this experiment was unsaturated alcohol **21**, which was smoothly transformed into the desired compound **10** by oxidation with the $Py{\cdot}SO_3$ complex in DMSO[15] followed by hydrogenation. The palladium-catalyzed migration of double bonds of allylic and homoallylic alcohols in Heck reactions is well documented in the literature.[16] It is known that the stability of the possible alkene formed governs the outcome of the isomerization reaction. In the case of allylic

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 5. Synthesis of δ-hetaryl ketone **8** starting from nonaflate **14**.

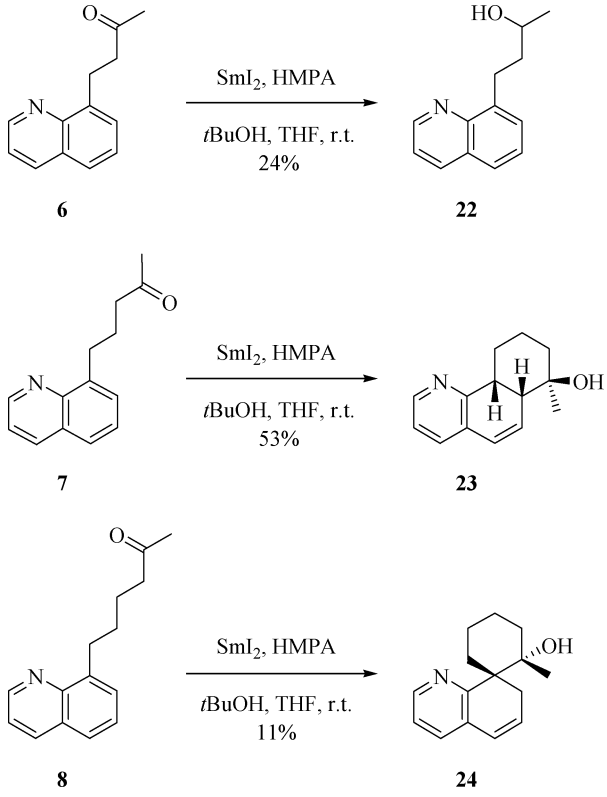
alcohols (especially primary allylic alcohols), the enol is generally the most stable alkene and the corresponding ketone is hence formed upon work up. In the example depicted in Scheme 6, only a small amount of material derived from homoallylic alcohol **20** proceeds through this route to ketone **10**, whereas the major part does not undergo migration of the double bond.



Scheme 6. Synthesis of γ-hetaryl ketone **10** starting from nonaflate **14** and *rac*-**20**.

Samarium Diiodide Induced Cyclizations of Heteroaryl-Substituted Ketones

Studies of the SmI_2–HMPA induced cyclization were performed by employing samarium diiodide (2.5 equiv.) in THF along with a large excess of HMPA (18 equiv.) and *tert*-butanol (2.2 equiv.) as a proton source. This method was previously optimized in our group for other substrates.[3,17] Acyclic ketones were initially employed as model systems, and quinolyl-substituted ketone **6** served as the first substrate. Not unexpectedly,[5j] the possible 5-*trig* cyclization leading to a tricyclic product failed and only secondary alcohol **22** was isolated in 24% yield along with 24% of unconsumed starting material (Scheme 7). Gratifyingly, the 6-*trig* cyclization of ketone **7** afforded the desired tricyclic product **23** as a single diastereomer in 53% yield. As expected, the cyclization occurred exclusively at the 7-position of the quinoline ring and the nitrogen atom of the heterocycle was not attacked. In agreement with previous results,[3f] **23** contains a *cis*-decaline substructure. The relative configuration was proven by two-dimensional NOESY-NMR spectroscopic analysis. This stereochemical result can be rationalized by the transition-structure model discussed in the introduction (Scheme 1), in which the bulky samariumalkoxy moiety adopts an equatorial position. Interestingly, homologous ketone **8** did not lead to the desired tricyclic product containing a seven-membered ring; instead, spiro compound **24** was formed as a single diastereomer, albeit in poor 11% yield. In this experiment, 83% of ketone **8** was recovered, which is indicative of the strong reluctance of this system to undergo reductive cyclization.[18]

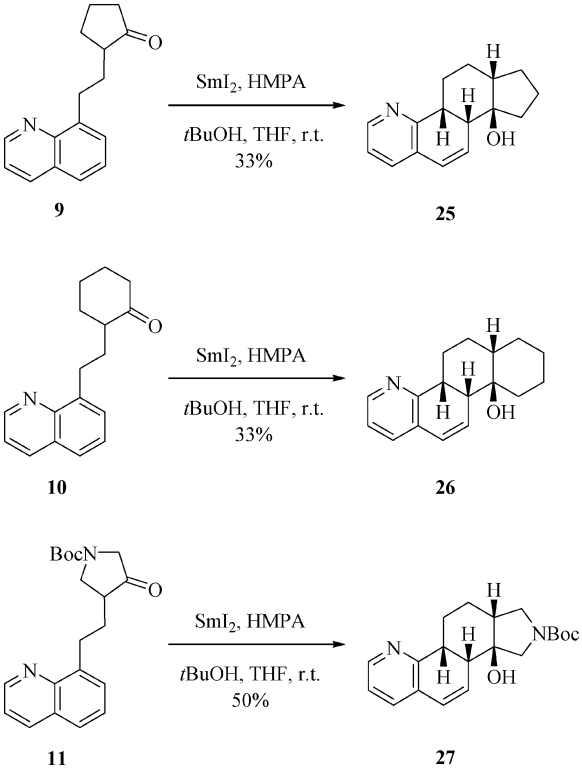


Scheme 7. Samarium diiodide induced reactions of quinolyl-substituted ketones **6**, **7** and **8**.

The successful addition of the ketyl derived from **7** onto the electron-deficient quinoline ring system stereoselectively leading to tricyclic compound **23** prompted us to investigate precursors **9**, **10** and **11** incorporating cyclic ketones. They also bear a three-carbon spacer unit between the carbonyl group and the heterocycle and should generate analogous tetracyclic compounds with steroid-like skeletons (Scheme 8). Actually, ketones **9** and **10** were converted in moderate yields into the corresponding tetracyclic compounds **25** and **26** containing a five- and six-membered "D-

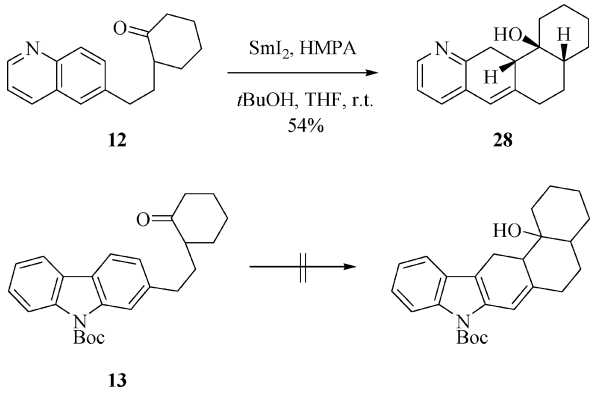
 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

ring", respectively. In both cases, the diastereoselectivity was again excellent and only the "unnatural" *cis–cis* annulated products were isolated. Consistent with this trend, ketone **11** afforded a single "diazasteroid" derivative **27** in 50% yield. NMR spectroscopic analysis of this latter compound, carried out at room temperature, showed two distinct amide rotamers attributable to the presence of the N-Boc group. The presence of rotamers is also visible in the NMR spectra of precursor ketone **11** − a phenomenon typical of amides and carbamate groups.[19]



Scheme 8. Samarium diiodide promoted synthesis of azasteroid derivatives **25** and **26** and that of diazasteroid **27**.

The samarium diiodide induced cyclization smoothly occurred also with precursor **12**, in which the quinoline ring bears the functionalized alkyl chain at C-6. The samarium ketyl attacked the aromatic ring exclusively at C-7 to afford the tetracyclic skeleton **28** as a single diastereomer and in 54% yield (Scheme 9). The observed regioselectivity may be explained by the higher stabilization of the intermediates (radical and anion) by the adjacent pyridine moiety.

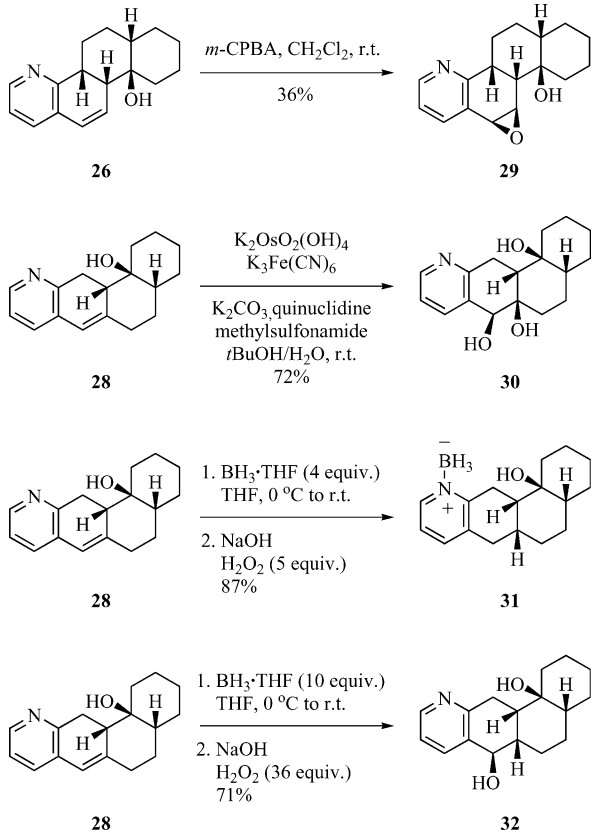


Scheme 9. Samarium diiodide promoted reactions of quinoline derivative **12** and that of carbazole derivative **13**.

Unfortunately, ketone **13** containing a carbazole ring as samarium ketyl acceptors did not undergo the desired cyclization. Instead, only a complex mixture of decomposed material was obtained. We have to conclude that the fairly electron-rich carbazole system is not suitable for these cyclizations, at least when the carbonyl group is connected to C-2. This failure has to be compared to the successful cyclizations employing aniline, pyrrole and indole derivatives studied in our group.[3d,3e,3g,3h]

Typical Subsequent Reactions of Azasteroid Derivatives

The polycyclic compounds obtained under the reductive conditions reported above contain a styrene-type double bond, which provides a suitable handle for subsequent synthetic transformations.[3f,3i,3j] A few typical examples leading to highly functionalized compounds are presented in Scheme 10. They involve the epoxidation of the double bond of compound **26** to afford pentacyclic product **29** by using *meta*-chloroperbenzoic acid, the dihydroxylation of precursor **28** under standard Sharpless conditions[20] to give polycyclic triol **30** and the stereoselective hydroboration of **28** to furnish compound **32**. In the first case, the reaction was low yielding and provided the desired epoxide in only



Scheme 10. Reactions of tetracyclic compounds **26** and **28**.

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

36% yield, possibly as a result of the concurrent oxidation of the pyridine ring to the *N*-oxide. Nevertheless, the reaction occurred in a stereoselective fashion and delivered compound **29** as a single diastereomer. The bowl-like shape of **26** and the steering effect of its hydroxy group contributed to the observed excellent face selectivity. The constitution and relative configuration of **29** were unequivocally assigned by X-ray crystallographic analysis (Figure 1).

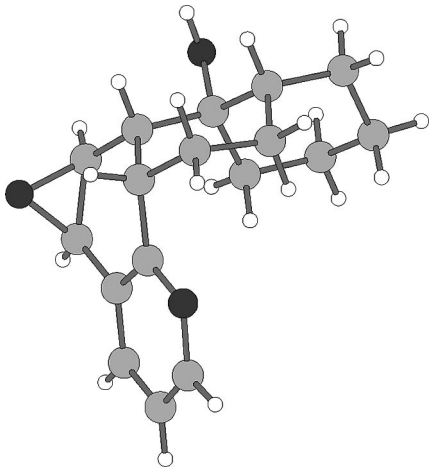


Figure 1. Structure of compound **29**.

Epoxidation of the double bond of compound **27** was also attempted; however, under the conditions reported above complete decomposition of the starting material was observed. Dihydroxylation of tetracycle **28** occurred smoothly to afford product **30** in good yield (Scheme 10). Again, only a single diastereomer was isolated, as the delivery of the hydroxy groups occurs from the sterically less-hindered convex face of the molecule and *cis* to the bridgehead hydroxy group.[21]

An attempted hydroboration of compound **28** was executed in a first experiment only with a slight excess of hydrogen peroxide (with respect to the borane equivalents) during the oxidative work-up step. As a result, the fairly stable pyridine–borane complex **31** was isolated in high yield (Scheme 10). Apparently, there was insufficient hydrogen peroxide present and hence the carbon–boron bond of the intermediate monoalkylborane species was not oxidized, but just hydrolyzed to give product **31**. Constitution and relative configuration of this unexpected tetracyclic product were again determined by X-ray crystallographic analysis (Figure 2). A second hydroboration/oxidation experiment employing a large excess of hydrogen peroxide finally transformed precursor **28** into the expected hydroxylated product **32** in 71% yield (Scheme 10).[22] The regio- and stereoselectivity of this process were supported by NOE experiments of compound **32** and are in accordance with the expectation.

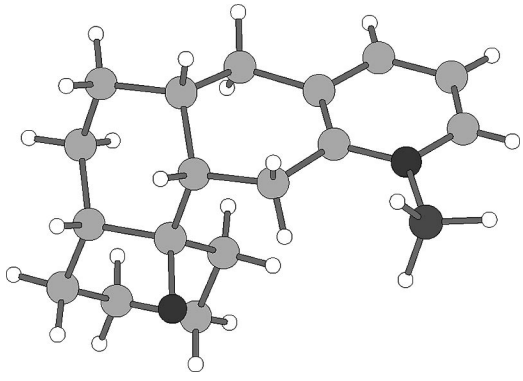


Figure 2. Structure of tetracyclic pyridine–borane complex **31**.

Conclusions

We demonstrated that highly functionalized nitrogen-containing tri- and tetracyclic compounds can be synthesized in a diastereoselective fashion by samarium diiodide induced cyclizations of appropriately substituted γ-hetaryl ketones. The samarium diiodide induced reductive coupling generates *cis–cis* annulated rings and therefore opens the door for molecules with steroid-like frameworks but with "unnatural configuration". Again, the samarium ketyl cyclizations seem to be restricted to the formation of new six-membered rings.[5j] The styrene-type double bond of the resulting products allow a series of smooth addition reactions, which generally occur in a stereoselective fashion due to the shape of the starting materials. The potential biological activity of some of these compounds is at present under examination,[23] and the results obtained will be reported elsewhere. In addition, we demonstrated that a variety of Heck couplings can be performed with hetaryl nonaflates in reasonable efficacy. The corresponding nonaflates employed may also be of value for the introduction of other substituents to the heterocycles by palladium-catalyzed processes.

Experimental Section

General Experimental Procedure: Reactions were generally performed under an atmosphere of argon in flame-dried flasks, and solvents and reagents were added by syringes. 1,2-Diodoethane was dried at 50 °C for 3 h in vacuo. Tetrahydrofuran and diethyl ether were freshly distilled from sodium/benzophenone under an atmosphere of argon. Hexamethylphosphoramide was distilled from calcium hydride (130 °C, 12 mbar) and stored over molecular sieves (4 Å) under an atmosphere of argon. (**Warning:** *HMPA has been identified as a carcinogenic reagent. Appropriate glove protection is required during handling. Reactions and chromatography should be performed in a well-vented hood*). Argon was purged through the solution to eliminate residual oxygen prior to use. Triethylamine and diisopropylamine were distilled from potassium hydroxide and stored over potassium hydroxide under an atmosphere of argon. Dichloromethane was distilled from calcium hydride and stored over molecular sieves (4 Å) under an atmosphere of argon. Ethanol was distilled from magnesium oxide and stored over molecular sieves (4 Å) under an atmosphere of argon. Dry dimethylformamide and dry dimethyl sulfoxide were purchased from Aldrich and used under an atmosphere of argon. Other reagents were purchased and were used as received without further purification unless otherwise stated. Products were purified by flash chromatography on silica

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

gel (230–400 mesh, Merck). Preparative HPLC was carried out on a nucleosil 50–5 column (diameter 16 mm, length 244 mm) and detection was carried out with a Knauer variable UV-detector (λ = 255 nm) and a Knauer refractometer. Unless otherwise stated, yields refer to analytically pure samples. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AC 250 (250 MHz), AC 500 (500 MHz) or Joel Eclipse 500 (500 MHz) instrument. Integrals are in accordance with assignments; coupling constants are given in Hz. IR spectra were measured with an FTIRD spectrometer Nicolet 5 SXC or with a Nexus FTIR spectrometer equipped with a Nicolet Smart DuraSamplIR ATR. MS and HRMS analyses were performed with Finnigan MAT 711 (EI, 80 eV, 8 kV), MAT CH7A (EI, 80 eV, 3 kV) and Varian Ionspec QFT-7 (ESI-FT ICRMS) instruments. Elemental analyses were recorded with "Elemental-Analyzer" (Perkin–Elmer). Melting points were measured with a Reichert apparatus and are uncorrected. Single-crystal X-ray data were collected with a Bruker-XPS diffractometer (CCD area detector, Mo-K_α radiation, λ = 0.71073 A, graphite monochromator), empirical absorption correction by using symmetry-equivalent reflections (SADABS), structure solution and refinement by SHELXS-97 and SHELXL-97 in the WINGX System. The hydrogen atoms were located by difference Fourier syntheses. CCDC-606014 (for **29**) and -606015 (for **31**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Quinolin-8-yl Nonafluorobutane-1-sulfonate (14): To a suspension of sodium hydride (60 wt.-%, 2.48 g, 62.0 mmol) in THF (80 mL) at room temperature was slowly added a solution of 8-hydroxyquinoline (**5**; 5.00 g, 34.4 mmol) in THF (20 mL). The mixture was stirred at room temperature for 20 min. Nonafluorobutanesulfonyl fluoride (18.5 mL, 31.1 g, 103 mmol) was then added, and the mixture was stirred for an additional 4 h. At 0 °C, the mixture was quenched by dropwise addition of distilled water. The product was extracted from the aqueous phase with CH_2Cl_2, and the combined organic layer was washed with brine, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate, 7:1) and subsequent recrystallisation from hexane to furnish **14** as a colourless solid (10.7 g, 73%). M.p. 84 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.39–7.56 (m, 3 H, Ar), 7.75 (d, ^3J = 9.1 Hz, 1 H, Ar), 8.12 (d, ^3J = 8.2 Hz, 1 H, Ar), 8.95 (d, ^3J = 4.6 Hz, 1 H, Ar) ppm. ^{13}C NMR (63 MHz, $CDCl_3$): δ = 121.0, 122.7, 126.0, 128.3 (4 d, Ar), 129.9 (s, Ar), 135.8 (d, Ar), 141.2, 146.5 (2 s, Ar), 151.7 (d, Ar) ppm. IR (KBr): $\tilde{\nu}$ = 3075 (=CH, C–H), 1630, 1600, 1570 (C=C) cm^{-1}. MS (EI, 80 eV, 50 °C): *m/z* (%) = 427 (26) $[M]^+$, 144 (52), 116 (100), 89 (30). HRMS (EI, 80 eV, 50 °C): calcd. for $C_{13}H_6F_9NO_3S$ 426.99246; found 426.99422.

(3*E*)-4-Quinolin-8-ylbut-3-en-2-one (16): A high-pressure tube was loaded with triethylamine (0.43 mL, 3.0 mmol), lithium chloride (0.127 g, 3.00 mmol), compound **14** (0.855 g, 2.00 mmol), palladium(II) acetate (23 mg, 0.10 mmol) and DMF (4 mL). The suspension was stirred at room temperature under an atmosphere of argon for 10 min. A solution of methyl vinyl ketone (**15**) (0.245 mL, 3.00 mmol) in DMF (2 mL) was then added, and the vessel was sealed and heated to 100 °C for 24 h. The mixture was cooled to room temperature, distilled water was added and the two phases were separated. The product was extracted with CH_2Cl_2 (3×10 mL), the combined organic layer was washed with brine (2×10 mL), dried with $MgSO_4$ and the solvent was removed under reduced pressure to afford the crude product, which was purified by column chromatography on silica gel (hexane/ethyl acetate, 3.5:1) to furnish **16** as a colourless solid (0.347 g, 88%). M.p. 86–88 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.51 (s, 3 H, 1-H), 6.94 (d, ^3J = 16.7 Hz, 1 H, 3-H), 7.44 (dd, ^3J = 7.9 Hz, ^3J = 4.3 Hz, 1 H, Ar), 7.54 (t, $^3J \approx 8$ Hz, 1 H, Ar), 7.85 (d, ^3J = 7.9 Hz, 1 H, Ar), 8.00 (d, ^3J = 7.3 Hz, 1 H, Ar), 8.15 (d, ^3J = 8.5 Hz, 1 H, Ar), 8.86 (d, ^3J = 16.7 Hz, 1 H, 4-H), 8.95–8.98 (m, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 26.8 (q, C-1), 121.5 (d, C-3), 126.2, 127.4 (2d, Ar), 128.4 (s, Ar), 129.4, 130.2 (2d, Ar), 133.0 (s, Ar), 136.1 (d, Ar), 139.8 (d, C-4), 146.0 (s, Ar), 150.1 (d, Ar), 199.2 (C-2) ppm. IR (KBr): $\tilde{\nu}$ = 3055, 3025, 2995, 2970, 2920 (=CH, C–H), 1645 (C=O) cm^{-1}. MS (EI, 80 eV, 60 °C): *m/z* (%) = 197 (3) $[M]^+$, 182 (2) $[M - CH_3]^+$, 154 (100) $[M - CH_3CO]^+$. HRMS (EI, 80 eV, 60 °C): calcd. for $C_{13}H_{11}NO$ 197.08406; found 197.08538.

(5*E*)-6-Quinolin-8-ylhex-5-en-2-one (18) and (3*E*,5*E*)-6-Quinolin-8-ylhexa-3,5-dien-2-one (19): A high-pressure tube was loaded with sodium hydrogencarbonate (0.504 g, 6.00 mmol), triethylbenzylammonium chloride (0.547 g, 2.40 mmol), compound **14** (0.855 g, 2.00 mmol), palladium(II) acetate (45 mg, 0.20 mmol) and DMF (4 mL). The suspension was stirred at room temperature under an atmosphere of argon for 10 min. A solution of 5-hexen-2-one (**17**) (0.925 mL, 8.00 mmol) in DMF (2 mL) was then added, and the vessel was sealed and heated to 90 °C for 48 h. The mixture was cooled to room temperature, distilled water was added and the two phases were separated. The product was extracted with CH_2Cl_2 (3×10 mL), and the combined organic layers were washed with brine (2×10 mL) and dried with $MgSO_4$. The solvent was removed under reduced pressure to leave the crude product, which was purified by column chromatography on silica gel (hexane/ethyl acetate, from 4:1 to 2:1) to afford a 5:1 mixture of **18** and **19** as a colourless solid (0.198 g, 44%). Data for **18** (mixture with **19**): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.16 (s, 3 H, 1-H), 2.32–2.64 (m, 2 H, 4-H), 2.67–2.70 (m, 2 H, 3-H), 6.42 (dt, ^3J = 16.3 Hz, ^3J = 6.7 Hz, 1 H, 5-H), 7.36 (dd, ^3J = 8.1 Hz, ^3J = 4.1 Hz, 1 H, Ar), 7.46 (dd, ^3J = 8.1 Hz, ^3J = 7.1 Hz, 1 H, Ar), 7.66 (dd, ^3J = 8.1 Hz, ^4J = 1.2 Hz, 1 H, Ar), 7.68 (d, ^3J = 16.3 Hz, 1 H, 6-H), 7.82 (dd, ^3J = 7.1 Hz, ^4J = 1.2 Hz, 1 H, Ar), 8.09 (dd, ^3J = 8.1 Hz, ^4J = 1.2 Hz, 1 H, Ar), 8.91 (dd, ^3J = 4.1 Hz, ^4J = 1.2 Hz, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 27.5 (t, C-4), 29.9 (q, C-1), 43.2 (t, C-3), 120.9, 125.3, 126.3, 126.4 (4 d, Ar), 126.8 (d, C-6), 129.1 (s, Ar), 131.1 (d, C-5), 136.2 (d, Ar), 144.4, 145.4 (2s, Ar), 149.3 (d, Ar), 208.2 (C-2) ppm. Data for **19** (mixture with **18**): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.32 (s, 3 H, 1-H), 6.26 (d, ^3J = 15.7 Hz, 1 H, 3-H), 7.15 (ddd, ^3J = 15.7 Hz, ^3J = 10.9 Hz, ^4J = 0.5 Hz, 1 H, 4-H), 7.42 (dd, ^3J = 8.2 Hz, ^3J = 4.1 Hz, 1 H, Ar), 7.44–7.50 (m, 1 H, 5-H), 7.53 (t, $^3J \approx 8$ Hz, 1 H, Ar), 7.77 (dd, ^3J = 7.9 Hz, ^4J = 1.2 Hz, 1 H, Ar), 7.98 (d, ^3J = 7.3 Hz, 1 H, Ar), 8.13 (dd, ^3J = 8.2 Hz, ^4J = 1.7 Hz, 1 H, Ar), 8.29 (d, ^3J = 15.7 Hz, 1 H, 6-H), 8.94 (dd, ^3J = 4.2 Hz, ^4J = 1.7 Hz, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 26.8 (q, C-1), 121.9, 126.2, 126.3, 128.3, 128.4 (5 d, Ar), 129.0 (d, C-4) 131.4 (d, C-3), 134.7 (s, Ar), 137.2 (d, Ar), 137.9 (d, C-6), 145.5 (d, C-5), 145.6, 145.7 (2 s, Ar), 150 (d, Ar), 198.7 (s, C-2) ppm. Data for **18/19**: IR (KBr): $\tilde{\nu}$ = 3045, 3000, 2920, 2850 (=CH, C–H), 1710 (C=O), 1660–1555 (C=C) cm^{-1}. MS (EI, 80 eV, 80 °C): *m/z* (%) = 225 (28) $[M]^+$, 182 (61) $[M - CH_3CO]^+$, 154 (100) $[M - C_4H_7O]^+$, 43 (21) $[CH_3CO]^+$. HRMS (EI, 80 eV, 80 °C): calcd. for $C_{15}H_{15}NO$ 225.11537; found 225.11486.

***trans*-2-[(*E*)-2-Quinolin-8-ylethenyl]cyclohexanol (21) and 2-(2-Quinolin-8-ylethyl)cyclohexanone (10):** A high-pressure tube was loaded with compound **14** (0.855 g, 2.00 mmol), sodium hydrogencarbonate (0.504 g, 6.00 mmol), triethylbenzylammonium chloride (0.547 g, 2.40 mmol), palladium(II) acetate (45 mg, 0.20 mmol) and DMF (4 mL). The suspension was stirred at room temperature under an atmosphere of argon for 10 min. A solution of *trans*-2-vinylcyclohexanol (**20**) (1.01 g, 8.00 mmol) in DMF (2 mL) was then

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

added, and the vessel was sealed and heated to 90 °C for 48 h. The vessel was then cooled to room temperature and distilled water was added. The product was extracted with CH_2Cl_2, the combined organic layer was washed with brine and dried with $MgSO_4$ and the solvent was removed under reduced pressure. Column chromatography on silica gel (hexane/ethyl acetate, from 6:1 to 2:1) yielded **21** as a colourless solid (380 mg, 75%) and **10** as a colourless oil (43 mg, 8%). Data for **21**: M.p. 139–141 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.28–1.36 (m, 4 H, 3-H, 4-H, 6-H), 1.70–1.72 (m, 1 H, 5-H), 1.79–1.81 (m, 1 H, 5-H), 1.90–1.93 (m, 1 H, 3-H), 2.08–2.15 (m, 1 H, 6-H), 2.22 (s, 1 H, OH), 2.25–2.29 (m, 1 H, 2-H), 3.39–3.44 (m, 1 H, 1-H), 6.31 (dd, ^3J = 16.1 Hz, ^3J = 8.8 Hz, 1 H, 1′-H), 7.38 (dd, ^3J = 8.2 Hz, ^3J = 4.2 Hz, 1 H, Ar), 7.48 (t, $^3J \approx$ 7.5 Hz, 1 H, Ar), 7.69 (dd, ^3J = 8.2 Hz, ^4J = 1.2 Hz, 1 H, Ar), 7.80 (d, ^3J = 16.1 Hz, 1 H, 2′-H), 7.87 (dd, ^3J = 7.2 Hz, ^4J = 1.2 Hz, 1 H, Ar), 8.10 (dd, ^3J = 8.2 Hz, ^4J = 1.8 Hz, 1 H, Ar), 8.92 (dd, ^3J = 4.2 Hz, ^4J = 1.8 Hz, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 24.8 (t, C-4), 25.2 (t, C-5), 31.5 (t, C-3), 34.0 (t, C-6) 50.9 (d, C-2), 73.3 (d, C-1), 121.0, 125.5, 126.4, 127.1 (4 d, Ar), 127.9 (d, C-2′), 128.5 (s, Ar), 134.6 (d, C-1′), 135.9 (s, Ar), 136.3 (d, Ar), 145.7 (s, Ar), 149.6 (d, Ar) ppm. IR (KBr): $\tilde{\nu}$ = 3420 (OH), 3045, 3030, 2920, 2845 (=CH, C–H), 1645, 1610, 1595, 1570 (C=C) cm^{-1}. MS (EI, 80 eV, 70 °C): *m*/*z* (%) = 253 (17) [M]$^+$, 225 (7), 154 (100) [M – $C_6H_{11}O$]$^+$. HRMS (EI, 80 eV, 70 °C): calcd. for $C_{17}H_{19}NO$ 253.14667; found 253.14573. Data for **10**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.42–1.45 (m, 1 H, 3-H), 1.57–1.69 (m, 3 H, 1′-H, 4-H, 5-H), 1.79–1.82 (m, 1 H, 5-H), 1.97–1.99 (m, 1 H, 4-H), 2.19–2.29 (m, 3 H, 3-H, 1′-H, 6-H), 2.36–2.41 (m, 2 H, 2-H, 6-H), 3.24–3.29 (m, 2 H, 2′-H), 7.32 (dd, ^3J = 8.2 Hz, ^3J = 4.1 Hz, 1 H, Ar), 7.42 (dd, ^3J = 8.0 Hz, ^3J = 7.1 Hz, 1 H, Ar), 7.55 (d, ^3J = 7.1 Hz, 1 H, Ar), 7.61 (dd, ^3J = 8.0 Hz, ^4J = 1.4 Hz, 1 H, Ar), 8.07 (dd, ^3J = 8.2 Hz, ^4J = 1.8 Hz, 1 H, Ar), 8.87 (dd, ^3J = 4.1 Hz, ^4J = 1.8 Hz, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 24.7 (t, C-5), 28.0 (t, C-4), 28.6 (t, C-2′), 30.2 (t, C-1′), 34.0 (t, C-3), 41.9 (t, C-6), 50.4 (d, C-2), 120.6, 125.8, 126.2 (3 d, Ar), 128.2 (s, Ar), 128.6, 136.2 (2 d, Ar), 140.2, 146.7 (2 s, Ar), 149.1 (d, Ar), 213.4 (s, C-1) ppm. IR (film): $\tilde{\nu}$ = 3060, 3030, 2930, 2860 (=CH, C–H), 1705 (C=O), 1615, 1595, 1575 (C=C) cm^{-1}. $C_{17}H_{19}NO$ (253.3): calcd. C 80.60, H 7.56, N 5.53; found C 80.08, H 7.74, N 4.90.

Typical Hydrogenation Procedure: Hydrogen gas was bubbled through a suspension of Pd/C (10 wt.-%) in EtOH (5 mL/mmol) for 2 h. Then, a solution of the corresponding olefin in EtOH or AcOEt (3 mL/mmol) was added, and the mixture was stirred at room temperature under an atmosphere of hydrogen. Completion of the reaction was followed by TLC analysis (hexane/ethyl acetate, 3:1). The solid residue was filtered off through a pad of silica gel and thoroughly washed with EtOH. The organic solvent was removed under reduced pressure, and the crude product was purified by column chromatography on silica gel.

4-Quinolin-8-ylbutan-2-one (6): Compound **16** (300 mg, 1.52 mmol) and Pd/C (60 mg) afforded, after purification by column chromatography on silica gel (hexane/ethyl acetate, 3:1), **6** as a colourless oil (161 mg, 53%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.11 (s, 3 H, 1-H), 2.94 (t, ^3J = 7.6 Hz, 2 H, 3-H), 3.49 (t, ^3J = 7.6 Hz, 2 H, 4-H), 7.34 (dd, ^3J = 8.2 Hz, ^3J = 4.2 Hz, 1 H, Ar), 7.40 (dd, ^3J = 8.2 Hz, ^3J = 7.0 Hz, 1 H, Ar), 7.55 (d, ^3J = 7.0 Hz, 1 H, Ar), 7.63 (dd, ^3J = 8.2 Hz, ^4J = 1.8 Hz, 1 H, Ar), 8.08 (dd, ^3J = 8.2 Hz, ^4J = 1.8 Hz, 1 H, Ar), 8.88 (dd, ^3J = 4.2 Hz, ^4J = 1.8 Hz, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 26.2 (t, C-4), 29.8 (q, C-1), 44.5 (t, C-3), 120.8, 126.2, 126.3 (3 d, Ar), 128.3 (s, Ar), 129.1, 136.2 (2 d, Ar), 139.6, 146.6 (2 s, Ar), 149.2 (d, Ar), 208.4 (s, C-2) ppm.

6-Quinolin-8-ylhexan-2-one (8): A 5:1 mixture of compounds **18** and **19** (144 mg, 0.647 mmol) and Pd/C (30 mg) afforded, after purification by column chromatography on silica gel (hexane/ethyl acetate from 4:1 to 3:1), **8** as a colourless oil (122 mg, 84%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.63–1.70 (m, 2 H, 4-H),1.72–1.77 (m, 2 H, 5-H), 2.05 (s, 3 H, 1-H), 2.42 (t, ^3J = 7.4 Hz, 2 H, 3-H), 3.24 (t, ^3J = 7.6 Hz 2 H, 6-H), 7.31 (dd, ^3J = 8.2 Hz, ^3J = 4.2 Hz, 1 H, Ar), 7.40 (dd, ^3J = 8.1 Hz, ^3J = 7.0 Hz, 1 H, Ar), 7.49 (dd, ^3J = 7.0 Hz, ^4J = 1.2 Hz, 1 H, Ar), 7.60 (dd, ^3J = 8.1 Hz, ^4J = 1.2 Hz, 1 H, Ar), 8.05 (dd, ^3J = 8.2 Hz, ^4J = 1.8 Hz, 1 H, Ar), 8.87 (dd, ^3J = 4.2 Hz, ^4J = 1.8 Hz, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 23.7 (t, C-4), 29.7 (q, C-1), 29.9 (t, C-5), 31.0 (t, C-6), 43.5 (t, C-3), 120.6, 125.8, 126.1, (3 d, Ar), 128.2 (s, Ar), 128.6, 136.1 (2 d, Ar), 140.7, 146.6 (2 s, Ar), 149.0 (d, Ar), 209.0 (s, CO) ppm. IR (film): $\tilde{\nu}$ = 3080, 3050, 3030, 3005, 2945, 2880, 2860 (=CH, CH), 1710 (C=O), 1615, 1595, 1575 (C=C) cm^{-1}. MS (EI, 80 eV, 60 °C) *m*/*z* (%) = 227 (36) [M]$^+$, 184 (10) [M – CH_3CO]$^+$, 170 (100) [M – C_3H_5O]$^+$, 157 (83) [M – C_4H_7O]$^+$, 142 (8) [M – C_5H_9O]$^+$, 43 (37) [CH_3CO]$^+$. HRMS (EI, 80 eV, 60 °C): calcd. for $C_{15}H_{17}NO$ 227.13101; found 227.13233. $C_{15}H_{17}NO$ (227.3): calcd. C 79.26, H 7.54, N 6.16; found C 78.68, H 7.24, N 5.86.

***trans*-2-(2-Quinolin-8-ylethyl)cyclohexanol:** Compound **21** (0.516 g, 2.04 mmol) and Pd/C (103 mg) afforded, after purification by column chromatography on silica gel (hexane/ethyl acetate, 3:1), the product as colourless oil (430 mg, 83%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.09–1.40 (m, 4 H, 4-H, 5-H), 1.61–1.90 (m, 6 H, 1′-H, 3-H, 6-H), 2.01–2.06 (m, 1 H, 2-H), 3.08 (ddd, ^2J = 12.6 Hz, ^3J = 11.0 Hz, ^3J = 5.8 Hz, 1 H, 2′-H), 3.38 (ddd, ^2J = 12.6 Hz, ^3J = 10.8 Hz, ^3J = 5.4 Hz, 1 H, 2′-H), 3.51–3.59 (m, 1 H, 1-H), 5.66 (br. s, 1 H, OH), 7.33 (dd, ^3J = 8.1 Hz, ^3J = 4.1 Hz, 1 H, Ar), 7.38 (t, $^3J \approx$ 7.5 Hz, 1 H, Ar), 7.49 (d, ^3J = 6.3 Hz, 1 H, Ar), 7.60 (d, ^3J = 8.2 Hz, 1 H, Ar), 8.09 (dd, ^3J = 8.1 Hz, ^4J = 1.8 Hz, 1 H, Ar), 8.84 (dd, ^3J = 4.1 Hz, ^4J = 1.8 Hz, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 25.1, 28.0, 28.4, 31.1 34.6, 34.6 (6 t, C-3, C-4, C-5, C-6, C-1′, C-2′), 45.0 (d, C-2), 74.5 (d, C-1), 120.6, 125.8, 126.2, 128.4, 128.8 (5 d, Ar), 136.8, 141.4, 146.0 (3 s, Ar), 148.8 (d, Ar) ppm. IR (film): $\tilde{\nu}$ = 3375 (OH), 3060, 3030, 3040, 2925, 2855 (=CH, C–H), 1615, 1595, 1575 (C=C) cm^{-1}. MS (EI, 80 eV, 80 °C): *m*/*z* (%) = 255 (43) [M]$^+$, 237 (11) [M – H_2O]$^+$, 156 (69) [$C_{11}H_{10}N$]$^+$, 143 (100). HRMS (EI, 80 eV, 80 °C): calcd. for $C_{17}H_{21}NO$ 255.16231; found 255.16352.

2-(2-Quinolin-8-ylethyl)cyclohexanone (10): A solution of *trans*-2-(2-quinolin-8-ylethyl)cyclohexanol (800 mg, 3.14 mmol) and triethylamine (0.80 mL, 6.0 mmol) in DMSO (30 mL) was cooled to 0 °C and Py·SO_3 complex (848 mg, 5.33 mmol) was then added. The mixture was stirred for 20 min at this temperature and then warmed to room temperature and stirred for another 2 h. The mixture was quenched with distilled water, and the product was extracted with CH_2Cl_2. The combined organic phase was washed with brine, dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate, 3:1) to yield **10** as a colourless oil (447 mg, 56%). For analytical data see above.

General Procedure for SmI_2 Induced Coupling Reactions: Samarium (2.6–3.0 equiv.) and 1,2-diiodoethane (2.4–2.7 equiv.) were suspended in THF (25 mL/2.20 mmol SmI_2) under an atmosphere of argon and stirred at room temperature until the colour of the suspension turned to dark blue (approximately 2 h). The flask was evacuated, purged with argon and HMPA (18 equiv.) was added. The hetaryl-substituted ketone (1 equiv.) and *t*BuOH (2.2 equiv.) were dissolved in THF (15 mL/mmol of ketone) and argon was purged through for 10 min. The solution was then added to the

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

deep-violet solution of SmI_2 in THF–HMPA. The reaction was stirred for 16 h at room temperature and then quenched by the addition of a saturated solution of sodium hydrogencarbonate (15 mL). The aqueous phase was extracted with Et_2O (3 × 20 mL), and the combined organic layers were washed with distilled water (1×) and brine (2×), dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure to give the crude product.

4-Quinolin-8-ylbutan-2-ol (22): Compound **6** (110 mg, 0.552 mmol), samarium (0.226 g, 1.50 mmol), 1,2-diiodoethane (0.386 g, 1.38 mmol), HMPA (1.76 mL, 9.90 mmol) and *t*BuOH (0.11 mL, 1.2 mmol) afforded, after purification by column chromatography on silica gel (hexane/ethyl acetate from 3:1 to 1:1), **22** as a brownish oil (27 mg, 24%). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.12 (d, ^3J = 5.6 Hz, 3 H, 1-H), 1.75–1.95 (m, 2 H, 3-H), 2.97–3.03 (m, 1 H, 4-H), 3.37–3.44 (m, 1 H, 4-H), 3.70–3.82 (m, 1 H, 2-H), 5.49 (br. s, 1 H, OH), 7.41 (dd, ^3J = 8.5 Hz, ^3J = 4.3 Hz, 1 H, Ar), 7.50 (t, ^3J ≈ 7.5 Hz, 1 H, Ar), 7.60 (d, ^3J = 7.3 Hz, 1 H, Ar), 7.69 (dd, ^3J = 7.9 Hz, ^4J = 1.2 Hz, 1 H, Ar), 8.17 (dd, ^3J = 8.5 Hz, ^4J = 1.8 Hz, 1 H, Ar), 8.88 (d, ^3J = 4.3 Hz, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 22.7 (q, C-1), 27.0 (t, C-4), 41.2 (t, C-3), 64.6 (d, C-2), 121.0, 126.2, 126.7 (3 d, Ar), 128.2 (s, Ar), 130.1, 137.0 (2 d, Ar), 140.7, 146.8 (2 s, Ar), 149.3 (d, Ar) ppm. IR (film): $\tilde{\nu}$ = 3360 (OH), 3085, 3060, 3045, 3005, 2965, 2925, 2870 (=CH, C–H), 1615, 1595, 1580 (C=C) cm^{-1}. MS (EI, 80 eV, 50 °C) *m*/*z* (%) = 201 (19) $[M]^+$, 200 (5) $[M - H]^+$, 186 (13) $[M - CH_3]^+$, 156 (100) $[M - C_2H_5O]^+$. HRMS (EI, 80 eV, 50 °C): calcd. for $C_{13}H_{15}NO$ 201.11537; found 201.11644.

***rac*-(6a*R*,10a*R*)-7-Methyl-6a,7,8,9,10,10a-hexahydrobenzo[*h*]-quinolin-7-ol (23):** Compound **7** (0.087 g, 0.41 mmol), samarium (0.168 g, 1.12 mmol), 1,2-diiodoethane (0.288 g, 1.03 mmol), HMPA (1.31 mL, 7.38 mmol) and *t*BuOH (0.08 mL, 0.9 mmol) afforded, after purification by column chromatography on silica gel (hexane/ethyl acetate from 4:1 to 1:1), **23** as a brownish oil (47 mg, 53%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.34 (s, 3 H, CH_3), 1.40–1.55, 1.60–1.63, 1.80–1.84 (3 m, 4 H, 1 H, 1 H, 8-H, 9-H, 10-H), 2.64 (m_c, 1 H, 6a-H), 2.97 (br. s, 1 H, OH), 3.45–3.48 (m, 1 H, 10a-H), 5.78 (dd, ^3J = 9.8 Hz, ^3J = 1.2 Hz, 1 H, 6-H), 6.38 (dd, ^3J = 9.8 Hz, ^3J = 3.2 Hz, 1 H, 5-H), 7.02 (dd, ^3J = 7.5 Hz, ^3J = 4.3 Hz, 1 H, Ar), 7.25 (dd, ^3J = 7.5 Hz, ^4J = 1.6 Hz, 1 H, Ar), 8.27 (d, ^3J = 4.3 Hz, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 19.8, 25.5 (2 t, C-9, C-10), 28.6 (q, CH_3), 35.2 (t, C-8), 39.0 (d, C-10a), 46.7 (d, C-6a), 70.5 (s, C-7), 121.7 (d, Ar), 126.3 (d, C-5), 128.1 (s, Ar), 129.8 (d, C-6), 132.8, 147.1 (2 d, Ar), 160.7 (s, Ar) ppm. IR (film): $\tilde{\nu}$ = 3360 (OH), 3040, 2930, 2855 (=CH, C–H), 1630, 1580, 1565 (C=C) cm^{-1}. MS (EI, 80 eV, 50 °C) *m*/*z* (%) = 215 (3) $[M]^+$, 214 (2) $[M - H]^+$, 130 (100) $[M - C_5H_9O]^+$. HRMS (EI, 80 eV, 50 °C): calcd. for $C_{14}H_{17}NO$ 215.13101; found 215.13099.

***rac*-(1*R*,2*S*)-2-Methyl-7′*H*-spiro[cyclohexane-1,8′-quinolin]-2-ol (24):** Compound **8** (0.095 g, 0.42 mmol), samarium (0.171 g, 1.14 mmol), 1,2-diiodoethane (0.293 g, 1.04 mmol), HMPA (1.33 mL, 7.52 mmol) and *t*BuOH (0.08 mL, 0.9 mmol) afforded, after purification by column chromatography on silica gel (hexane/ethyl acetate, 3.5:1), **24** as a brownish oil (11 mg, 11%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.38, 1.53–1.61, 1.78, 2.01–2.16, 2.43 (m_c, 1 H; m, 4 H; td, J = 13.8 Hz, ^3J = 4.1 Hz, 1 H; m, 1 H; td, J = 12.8 Hz, ^3J = 4.9 Hz, 1 H; 3-H, 4-H, 5-H, 6-H), 3.40 (m_c, 2 H, 7′-H), 5.92 (dt, ^3J = 10.5 Hz, ^3J = 3.6 Hz, 1 H, 6′-H), 6.24 (dt, ^3J = 10.5 Hz, ^3J = 2.0 Hz, 1 H, 5′-H), 7.12 (dd, ^3J = 7.7 Hz, ^3J = 4.8 Hz, 1 H, Ar), 7.46 (ddt, ^3J = 7.7 Hz, ^4J = 1.6 Hz, ^4J = 0.8 Hz, 1 H, Ar), 7.65 (s, 1 H, OH), 8.37 (ddt, ^3J = 4.8 Hz, ^4J = 1.6 Hz, ^4J = 0.8 Hz, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.0, 21.1 (2 t, C-4, C-5), 27.6 (q, CH_3), 29.8 (t, C-7′), 34.8, 35.6 (2 t, C-3, C-6), 46.4 (s, C-1), 73.9 (s, C-2), 121.2 (d, Ar), 122.7 (d, C-6′), 130.5 (s, Ar), 131.7 (d, C-5′), 136.7, 145.5 (2 d, Ar), 161.3 (s, Ar) ppm. IR (film): $\tilde{\nu}$ = 3250 (OH), 3045, 2930, 2860 (=CH, C–H), 1670, 1615, 1590, 1575 (C=C) cm^{-1}. MS (EI, 80 eV, 30 °C) *m*/*z* (%) = 229 (60) $[M]^+$, 228 (60) $[M - H]^+$, 214 (2) $[M - CH_3]^+$, 144 (100) $[M - C_5H_8O]^+$, 130 (43) $[M - C_6H_{11}O]^+$. HRMS (EI, 80 eV, 30 °C): calcd. for $C_{15}H_{19}NO$ 229.14667; found 229.14588.

***rac*-(4b*R*,6a*S*,9a*R*,9b*R*)-4b,5,6,6a,7,8,9,9b-Octahydro-9a*H*-indeno-[4,5-*h*]quinolin-9a-ol (25):** Compound **9** (0.90 g, 0.38 mmol), samarium (0.154 g, 1.02 mmol), 1,2-diiodoethane (0.264 g, 0.937 mmol), HMPA (1.2 mL, 6.8 mmol) and *t*BuOH (0.07 mL, 0.8 mmol) afforded, after purification by column chromatography on silica gel (hexane/ethyl acetate, 4:1), **25** as a colourless oil (30 mg, 33%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.13–1.25 (m, 2 H, 6-H, 9-H), 1.27–1.37 (m, 3 H, 7-H, 9-H, OH), 1.39–1.43 (m, 1 H, 8-H), 1.57–1.62 (m, 3 H, 5-H, 6-H, 8-H), 1.72–1.79 (m, 1 H, 6a-H), 1.98 (ddt, ^2J = 12.9 Hz, ^3J = 11.0 Hz, ^3J ≈ 6.5 Hz, 1 H, 7-H), 2.78–2.81 (m, 2 H, 5-H, 9b-H), 3.35 (quint., J ≈ 4 Hz, 1 H, 4b-H), 6.30 (dd, ^3J = 9.8 Hz, ^3J = 5.6 Hz, 1 H, 10-H), 6.47 (dd, ^3J = 9.8 Hz, ^4J = 1.0 Hz, 1 H, 11-H), 7.03 (ddd, ^3J = 7.5 Hz, ^3J = 5.0 Hz, ^4J = 1.0 Hz, 1 H, Ar), 7.23 (dd, ^3J = 7.5 Hz, ^4J = 1.6 Hz, 1 H, Ar), 8.34 (dd, ^3J = 5.0 Hz, ^4J = 1.6 Hz, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 19.7, 23.4, 27.3, 29.2, 32.7 (5 t, C-5, C-6, C-7, C-8, C-9), 39.4 (d, C-4b), 44.7 (d, C-9b), 47.8 (d, C-6a), 84.3 (s, C-9a), 121.3 (d, Ar), 126.7 (d, C-11), 129.6 (s, Ar), 132.0 (d, Ar), 132.2 (d, C-10), 147.1 (d, Ar), 157.7 (s, Ar) ppm. IR (film): $\tilde{\nu}$ = 3390 (OH), 3040, 2950, 2925, 2870 (=CH, C–H), 1665, 1635, 1580, 1560 (C=C) cm^{-1}. MS (EI, 80 eV, 40 °C): *m*/*z* (%) = 241 (3) $[M]^+$, 142 (3) $[M - C_6H_{11}O]^+$, 130 (100) $[C_9H_8N]^+$. HRMS (EI, 80 eV, 40 °C): calcd. for $C_{16}H_{19}NO$ 241.14667; found 241.14733.

***rac*-(4b*R*,6a*S*,10a*R*,10b*R*)-4b,6,6a,7,8,9,10,10b-Octahydronaphtho-[1,2-*h*]quinolin-10a(5*H*)-ol (26):** Compound **10** (0.342 g, 1.35 mmol), samarium (0.602 g, 4.00 mmol), 1,2-diiodoethane (1.02 g, 3.65 mmol), HMPA (4.31 mL, 24.3 mmol) and *t*BuOH (0.26 mL, 3.0 mmol) afforded, after purification by column chromatography on silica gel (hexane/ethyl acetate, 4:1) and preparative HPLC (hexane/2-propanol, 95:5), **26** as a colourless oil (115 mg, 33%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.74 (td, J ≈ 13.5 Hz, ^3J = 4.1 Hz, 1 H, 10-H), 1.14–1.31 (m, 7 H, 7-H, 8-H, 9-H, 10-H, OH), 1.40–1.44 (m, 1 H, 6-H), 1.53–1.60 (m, 1 H, 6a-H), 1.62 (ddd, ^2J = 13.2 Hz, ^3J = 5.3 Hz, ^3J = 3.4 Hz, 1 H, 5-H), 1.73 (qd, J ≈ 13 Hz, ^3J = 3.4 Hz, 1 H, 6-H), 1.86 (tt, J ≈ 13.5 Hz, ^3J ≈ 4.5 Hz, 1 H, 7-H), 2.55 (dd, ^3J = 7.7 Hz, ^3J = 6.1 Hz, 1 H, 10b-H), 2.94 (dq, ^2J = 13.2 Hz, ^3J ≈ 2 Hz, 1 H, 5-H), 3.31 (t, ^3J ≈ 6.5 Hz, 1 H, 4b-H), 6.22 (dd, ^3J = 9.8 Hz, ^3J = 6.1 Hz, 1 H, 11-H), 6.53 (d, ^3J = 9.8 Hz, 1 H, 12-H), 7.01 (ddd, ^3J = 7.5 Hz, ^3J = 4.9 Hz, ^4J = 1.0 Hz, 1 H, Ar), 7.20 (dd, ^3J = 7.5 Hz, ^4J = 1.6 Hz, 1 H, Ar), 8.34 (dd, ^3J = 4.9 Hz, ^4J = 1.6 Hz, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.2, 21.3, 24.0, 25.3, 27.0, 27.3 (6 t, C-5, C-6, C-7, C-8, C-9, C-10), 39.8 (d, C-4b), 43.8 (d, C-6a), 48.4 (d, C-10b), 74.0 (s, C-10a), 121.1 (d, Ar), 128.0 (d, C-12), 130.0 (s, Ar), 131.4 (d, C-11), 132.0, 146.9 (2 d, Ar), 157.9 (s, Ar) ppm. IR (film): $\tilde{\nu}$ = 3400 (OH), 3040, 2930, 2860 (=CH, C–H), 1635, 1615, 1595, 1580, 1560 (C=C) cm^{-1}. MS (EI, 80 eV, 70 °C): *m*/*z* (%) = 255 (9) $[M]^+$, 130 (100). HRMS (EI, 80 eV, 70 °C): calcd. for $C_{17}H_{21}NO$ 255.16231; found 255.16165.

***rac-tert*-Butyl (3a*S*,3b*R*,9b*R*,11a*R*)-3a-Hydroxy-1,3,3a,3b,9b,10,-11,11a-octahydro-2*H*-isoindolo[4,5-*h*]quinoline-2-carboxylate (27):** Compound **11** (60 mg, 0.18 mmol), samarium (0.079 g, 0.53 mmol), 1,2-diiodoethane (0.122 g, 0.433 mmol), HMPA (0.56 mL, 3.2 mmol) and *t*BuOH (0.03 mL, 0.4 mmol) afforded, af-

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

ter purification by column chromatography on silica gel (hexane/ethyl acetate from 3:1 to ethyl acetate 100%) and repeated washing of the solid with cold Et_2O, **27** as a colourless solid (30 mg, 50%).[24] M.p. 201–205 °C. ^{1}H NMR (500 MHz, CD_3OD): δ = 1.20–1.25 (m, 2 H, 11-H), 1.30 (s, 4 H, *t*Bu), 1.38 (s, 5 H, *t*Bu), 1.63 (m_c, 1 H, 10-H), 1.72 (m_c, 1 H, 10-H), 2.03 (m_c, 1 H, 11a-H), 2.70–2.81 (m, 2 H, 3-H, OH), 2.85 (m_c, 1 H, 3b-H), 3.08–3.10 (m, 2 H, 1-H, 3-H), 3.38 (m_c, 1 H, 9b-H), 3.56 (m_c, 1 H, 1-H), 6.28 (m_c, 1 H, 4-H), 6.59 (m_c, 1 H, 5-H), 7.19 (m_c, 1 H, Ar), 7.44 (m_c, 1 H, Ar), 8.29 (m_c, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, CD_3OD): δ = 23.5, 23.6, 26.4, 26.6 (4 t, C-10, C-11), 28.6, 28.7 (2 q, *t*Bu), 40.4, 44.9, 46.1, 46.8 (4 d, C-3b, C-9b, C-11a), 51.5, 52.0, 54.0, 54.6 (4 t, C-1, C-3), 80.6, 80.7, 80.8 (3 q, *t*Bu, C-3a), 123.29, 123.32, 128.01, 128.04 (4 d, Ar, C-5), 131.16, 131.24 (2 s, Ar), 131.8, 131.9, 134.4, 134.6 (4 d, C-4, Ar), 148.1 (d, Ar), 156.7, 156.8, 158.2, 158.3 (4 s, C=O, Ar) ppm. IR (KBr): $\tilde{\nu}$ = 3345 (OH), 3050, 2985, 2935, 2885 (=CH, C–H), 1665, 1655 (C=O), 1565 (C=C) cm^{-1}. MS (EI, 80 eV, 120 °C): *m*/*z* (%) = 342 (26) $[M]^+$, 286 (7) $[M - C_4H_8]^+$, 130 (100) $[C_9H_8N]^+$, 57 (91) $[C_4H_9]^+$. HRMS (EI, 80 eV, 120 °C): calcd. for $C_{20}H_{26}N_2O_3$ 342.19434; found 342.19544.

***rac*-(4a*R*,12a*S*,12b*S*)-2,3,4,4a,5,6,12,12a-Octahydronaphtho[2,1-*g*]-quinolin-12b(1*H*)-ol (28):** Compound **12** (0.300 g, 1.19 mmol), samarium (0.464 g, 3.09 mmol), 1,2-diiodoethane (0.835 g, 2.96 mmol), HMPA (3.2 mL, 21 mmol) and *t*BuOH (0.22 mL, 2.6 mmol) afforded, after purification by column chromatography on silica gel (hexane/ethyl acetate, 3:1) and repeated washing of the solid with cold Et_2O, **28** as a colourless solid (125 mg, 54%). M.p. 193–195 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.23–1.44 (m, 7 H, 1-H, 2-H, 3-H, 4-H), 1.62–1.68 (m, 1 H, 5-H), 1.69–1.75 (m, 2 H, 4a-H, 5-H), 1.95 (dddd, ^2J = 14.5 Hz, ^3J = 14.5 Hz, ^3J = 3.9 Hz, ^3J = 3.9 Hz, 1 H, 4-H), 2.06 (br. s, 1 H, OH), 2.25 (ddd, ^2J = 11.6 Hz, ^3J = 11.6 Hz, ^3J = 5.2 Hz, 1 H, 6-H), 2.40 (m_c, 1 H, 6-H), 2.57 (br. d, ^3J = 11.1 Hz, 1 H, 12a-H), 3.16 (dd, ^2J = 18.1 Hz, ^3J = 11.1 Hz, 1 H, 12-H), 3.40 (dd, ^2J = 18.1 Hz, ^3J = 1.8 Hz, 1 H, 12-H), 6.11 (s, 1 H, 7-H), 6.97 (ddd, ^3J = 7.5 Hz, ^3J = 5.0 Hz, ^5J = 0.6 Hz, 1 H, Ar), 7.13 (dd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1 H, Ar), 8.20 (dd, ^3J = 5.0 Hz, ^4J = 1.5 Hz, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 19.9, 21.1, 25.7, 27.0, 29.1, 29.9, 35.1 (7 t, C-1, C-2, C-3, C-4, C-5, C-6, C-12), 43.6 (d, C-4a), 49.9 (d, C-12a), 76.0 (s, C-12b), 119.3 (d, C-7), 121.4 (d, Ar), 128.8 (s, Ar), 131.7 (d, Ar), 143.0 (s, C-6a), 146.5 (d, Ar), 155.2 (s, Ar) ppm. IR (KBr): $\tilde{\nu}$ = 3310 (OH), 3070, 3045, 3010, 2920, 2910, 2860, 2850 (=CH, C–H), 1660, 1570 (C=C) cm^{-1}. $C_{17}H_{21}NO$ (255.4): calcd. C 79.96, H 8.29, N 5.49; found C 79.83, H 7.94, N 5.80.

***rac*-(1a*S*,5b*R*,7a*S*,11a*R*,11b*S*,11c*R*)-5b,6,7,7a,8,9,10,11,11b,11c-Decahydronaphtho[1,2-*h*]oxireno[*f*]quinolin-11a(1a*H*)-ol (29):** To a solution of compound **26** (60 mg, 0.23 mmol) in CH_2Cl_2 (5 mL) at 0 °C was slowly added *m*-chloroperbenzoic acid (44 mg, 0.26 mmol), and the mixture was stirred at room temperature for 16 h. An aqueous solution of NaOH (10%, 1 mL) was added, and the two phases were separated. The product was extracted from the aqueous layer with CH_2Cl_2 (3 × 3 mL), the combined organic layer was washed with brine (3 × 3 mL), dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure to leave the crude product, which was purified by column chromatography on silica gel (hexane/ethyl acetate, 3:1) to afford **29** as a colourless solid (23 mg, 36%). M.p. 170–175 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.66 (td, J = 13.8 Hz, ^3J = 4.5 Hz, 1 H, 11-H), 1.10–1.43 (m, 7 H, 7-H, 8-H, 9-H, 10-H, 11-H), 1.48–1.69 (m, 4 H, 6-H, 7-H, 7a-H, OH), 1.88 (tt, $J \approx$ 13.5 Hz, $^3J \approx$ 4.5 Hz, 1 H, 8-H), 2.63 (dd, ^3J = 7.0 Hz, ^3J = 2.5 Hz, 1 H, 11b-H), 3.00 (dq, ^2J = 13.1 Hz, $^3J \approx$ 2.5 Hz, 1 H, 6-H), 3.17 (br. t, $^3J \approx$ 5.5 Hz, 1 H, 5b-H), 3.85 (dd, ^3J = 3.9 Hz, ^5J = 1.0 Hz, 1 H, 1a-H), 4.00 (ddd, ^3J = 3.9 Hz, ^3J = 2.5 Hz, ^4J = 0.6 Hz, 1 H, 11c-H), 7.12 (ddd, ^3J = 7.6 Hz, ^3J = 4.9 Hz, ^5J = 1.0 Hz, 1 H, Ar), 7.63 (dd, ^3J = 7.6 Hz, ^4J = 1.7 Hz, 1 H, Ar), 8.53 (dd, ^3J = 4.9 Hz, ^4J = 1.7 Hz, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.0, 21.2, 24.2, 25.2, 27.0, 28.6 (6 t, C-6, C-7, C-8, C-9, C-10, C-11), 35.2 (d, C-5b), 44.8 (d, C-7a), 46.2 (d, C-11b), 53.4 (d, C-1a), 55.1 (d, C-11), 73.8 (s, C-11a), 120.9 (d, Ar), 128.8 (s, Ar), 136.4, 148.8 (2 d, Ar), 157.7 (s, Ar) ppm. IR (KBr): $\tilde{\nu}$ = 3490 (OH), 3065, 3045, 3005, 2945, 2930, 2850 (=CH, C–H), 1595, 1575 (C=C) cm^{-1}. $C_{17}H_{21}NO_2$ (271.4): calcd. C 75.25, H 7.80, N 5.16; found C 75.61, H 7.58, N 5.03.

***rac*-(4a*R*,6a*R*,7*S*,12a*R*,12b*S*)-2,3,4,4a,5,6,12,12a-Octahydronaphtho[2,1-*g*]quinoline-6a,7,12b(1*H*,7*H*)-triol (30):** To a solution of compound **28** (70 mg, 0.27 mmol) in *t*BuOH (1.35 mL) was added distilled water (1.35 mL), potassium carbonate (112 mg, 0.810 mmol), quinuclidine (5 mg, 0.04 mmol), methylsulfonamide (26 mg, 0.27 mmol), potassium osmate(VI) dihydrate (2.5 mg, 0.0068 mmol) and potassium hexacyanoferrate(III) (267 mg, 0.810 mmol), and the mixture was stirred vigorously overnight. Then, saturated solution of $NaHSO_3$ (3 mL) was added, and the reaction mixture was stirred for 1 h. The aqueous phase was separated and extracted with CH_2Cl_2 (3 × 5 mL). The organic phase was dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (ethyl acetate/MeOH, 1:0 to 7:3) to afford **30** as a colourless solid (56 mg, 72%). M.p. 210–215 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.91 (td, $J \approx$ 13 Hz, ^3J = 3.1 Hz, 1 H, 1-H), 1.02 (br. d, $^3J \approx$ 13 Hz, 1 H, 1-H), 1.14 (td, $J \approx$ 13 Hz, ^3J = 3.8 Hz, 1 H, 6-H), 1.15–1.28, 1.37–1.45, 1.63–1.70 (3 m, 2 H, 3 H, 3 H, 2-H, 3-H, 4-H, 5-H, 4a-H), 2.16 (m_c, 1 H, 4-H), 2.44 (dt, J = 13.0 Hz, ^3J = 2.3 Hz, 1 H, 6-H), 2.62 (d, ^3J = 9.2 Hz, 1 H, 12a-H), 2.63 (br. s, 1 H, OH), 3.28 (br. s, 1 H, OH), 3.49–3.58 (m, 2 H, 12-H), 4.64 (s, 1 H, 7-H), 4.90 (br. s, 1 H, OH), 7.11 (dd, ^3J = 7.8 Hz, ^3J = 4.8 Hz, 1 H, Ar), 7.91 (dd, ^3J = 7.8 Hz, ^4J = 1.4 Hz, 1 H, Ar), 8.19 (dd, ^3J = 4.8 Hz, ^4J = 1.4 Hz, 1 H, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.5, 21.7, 25.6, 26.8, 27.3, 30.1, 36.8 (7 t, C-1, C-2, C-3, C-4, C-5, C-6, C-12), 44.0 (d, C-4a), 54.7 (d, C-12a), 68.9 (d, C-7), 71.3, 74.6 (2 s, C-6a, C-12b), 121.9 (d, Ar), 134.6 (s, Ar), 137.9 (d, Ar), 146.8 (d, Ar), 156.2 (s, Ar) ppm. IR (KBr): $\tilde{\nu}$ = 3465, 3415, 3175 (OH), 3065, 3010, 2935, 2865, 2850 (=CH, C–H), 1585 (C=C) cm^{-1}. $C_{17}H_{23}NO_3$ (289.4): calcd. C 70.56, H 8.01, N 4.84; found C 70.06, H 7.77, N 5.01.

***rac*-(4a*R*,6a*R*,12a*S*,12b*S*)-2,3,4,4a,5,6,6a,7,12,12a-Decahydronaphtho[2,1-*g*]quinolin-12b(1*H*)-ol-borane Complex (31):** To a solution of compound **28** (60 mg, 0.23 mmol) in THF (3 mL) was added BH_3·THF (ca. 1 M sol. in THF, 0.94 mL, 0.94 mmol, 4.1 equiv.) dropwise. The mixture was stirred at 0 °C for 2 h and then 2 h at room temperature. Then, an aqueous solution of NaOH (2.5 M, 1.22 mL, 3.06 mmol, 13 equiv.) and H_2O_2 (30 wt.-%, 0.115 mL, 1.13 mmol, 4.9 equiv.) were added with cooling, and the mixture was stirred for another 2 h at room temperature. The two phases were separated, and the product was extracted from the aqueous layer with ethyl acetate (3 × 5 mL). The combined organic layer was washed with brine (3 × 3 mL), dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate, 7:1) to afford **31** as a colourless solid (54 mg, 87%). M.p. 135–140 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.98 (br. d, ^3J = 13.4 Hz, 1 H, 1-H), 1.17 (td, J = 13.4 Hz, ^3J = 4.1 Hz, 1 H, 1-H), 1.26–1.50 (m, 6 H, 2-H, 3-H, 4-H, 5-H), 1.58* (m_c, 1 H, 4a-H), 1.60* (br. s, 1 H, OH), 1.64–1.70 (m, 1 H, 6-H), 1.75–1.85 (m, 2 H, 5-H, 6-H), 1.93 (tt, $J \approx$ 13 Hz, $^3J \approx$ 4.5 Hz, 1 H, 4-H), 2.14 (ddd, ^3J = 7.8 Hz, ^3J = 6.1 Hz, ^3J = 1.1 Hz, 1 H, 12a-H), 2.30–2.35 (m, 1 H, 6a-H), 2.55 (br. s, 3 H, BH_3), 2.75 (dd, ^2J = 17.9 Hz, ^3J

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

= 7.9 Hz, 1 H, 7-H), 2.90 (dd, ^2J = 20.0 Hz, ^3J = 7.8 Hz, 1 H, 12-H), 2.95 (dd, ^2J = 17.9 Hz, ^3J = 12.2 Hz, 1 H, 7-H), 3.86 (d, ^2J = 20.0 Hz, 1 H, 12-H), 7.16 (dd, ^3J = 7.5 Hz, ^3J = 5.9 Hz, 1 H, Ar), 7.58 (d, ^3J = 7.5 Hz, 1 H, Ar), 8.62 (d, ^3J = 5.9 Hz, 1 H, Ar) ppm. *Overlapping signals. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.9, 21.8, 24.5, 27.9, 28.9, 29.8, 30.3, 31.1, 31.2 (8 t, d, C-1, C-2, C-3, C-4, C-5, C-6, C-7, C-12, C-6a), 44.4, 45.2 (2 d, C-4a, C-12a), 73.3 (s, C-12b), 121.4 (d, Ar), 134.7 (s, Ar), 139.9, 147.0 (2 d, Ar), 156.6 (s, Ar) ppm. IR (KBr): $\tilde{\nu}$ = 3485 (OH), 3100, 3055, 3035, 2960, 2930, 2860 (=CH, C–H), 2370, 2315, 2275 (B–H), 1605, 1585 (C=C) cm^{-1}. MS (EI, 80 eV, 100 °C): *m*/*z* (%) = 271 (14) $[M]^+$, 270 (61), 269 (31), 268 (46), 257 (53), 240 (100), 214 (25), 142 (25), 132 (87), 130 (47), 118 (27), 73 (24), 69 (27), 60 (37), 57 (33), 55 (45), 43 (59), 41 (45), 29 (27), 28 (24). HRMS (EI, 80 eV, 100 °C): calcd. for $C_{17}H_{24}{}^{11}BNO$ 269.19509; found 269.19522. HRMS (EI, 80 eV, 100 °C): calcd. for $C_{17}H_{23}NO$ 257.17796; found 257.17775. $C_{17}H_{26}BNO$ (271.2): calcd. C 75.29, H 9.66, N 5.16; found C 75.26, H 9.62, N 5.16.

***rac*-(4a*R*,6a*S*,7*R*,12a*S*,12b*S*)-2,3,4,4a,5,6,6a,7,12,12a-Decahydronaphtho[2,1-*g*]quinoline-7,12b(1*H*)-diol (32):** To a solution of compound **28** (10.5 mg, 0.041 mmol) in THF (1 mL) was added BH_3·THF (ca. 1 M sol. in THF, 0.41 mL, 0.41 mmol, 10 equiv.) at 0 °C. The mixture was stirred at 0 °C for 1.5 h and then 2 h at room temperature. An aqueous solution of NaOH (2.5 M, 0.62 mL, 1.56 mmol, 38 equiv.) and H_2O_2 (30 wt.-%, 0.15 mL, 1.48 mmol, 36 equiv.) were added with cooling. The mixture was stirred for 2 h at room temperature and diluted with Et_2O (15 mL). The two phases were separated, and the product was extracted from the aqueous layer with Et_2O (1 × 15 mL). The combined organic layer was dried with Na_2SO_4 and filtered, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate, 1:2) to afford **32** as a colourless solid (8.0 mg, 71%). M.p. 220–224 °C.[22] ^{1}H NMR (500 MHz, CD_3OD): δ = 0.91, 1.07, 1.25–1.69 (br. d, $^2J \approx$ 12 Hz, 1 H; td, $J \approx$ 13 Hz, ^3J = 4.4 Hz, 1 H; m, 8 H; 1-H, 2-H, 3-H, 4-H, 5-H, 6-H, 4a-H), 1.90 (q d, J = 13.2 Hz, ^3J = 3.0 Hz, 1 H, 5-H), 1.97–2.07 (m, 1 H, 4-H), 2.08–2.15 (m, 1 H, 6a-H), 2.18 (dq, ^2J = 12.9 Hz, $^3J \approx$ 2 Hz 1 H, 6-H), 2.25 (t, $^3J \approx$ 6.5 Hz, 1 H, 12a-H), 2.50 (br. s, 2 H, OH), 2.94 (dd, ^2J = 19.9 Hz, ^3J = 7.7 Hz, 1 H, 12-H), 3.88 (d, ^2J = 19.9 Hz, 1 H, 12-H), 4.80 (d, ^3J = 10.9 Hz, 1 H, 7-H), 7.40 (dd,^3J = 7.8 Hz, ^3J = 5.7 Hz, 1 H, Ar), 8.20 (d, ^3J = 7.8 Hz, 1 H, Ar), 8.68 (d, ^3J = 5.7 Hz, 1 H, Ar) ppm. ^{13}C NMR (126 MHz, CD_3OD): δ = 21.6, 22.7, 25.6, 27.4, 28.8, 29.4, 31.1 (7 t, C-1, C-2, C-3, C-4, C-5, C-6, C-12), 41.9, 45.5, 47.2 (3 d, C-4a, C-6a, C-12a), 67.5 (d, C-7), 74.4 (s, C-12b), 123.2 (d, Ar), 139.7 (s, Ar), 141.2, 149.0 (2 d, Ar), 157.5 (s, Ar) ppm. IR (ATR): $\tilde{\nu}$ = 3350 (OH), 3010, 2920, 2860 (=CH, C–H), 1585 (C=C) cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{23}NO_2{\cdot}H^+$ 274.1807; found 274.1792.

Supporting Information (see also the footnote on the first page of this article): Synthesis and analytical data for compounds **7**, **9**, **11**, **12** and **13** and their precursors.

Acknowledgments

Support of this work by the Deutsche Forschungsgemeinschaft, the European Community (Marie Curie fellowship for F. A.), the Fonds der Chemischen Industrie and the Bayer Schering Pharma AG is most gratefully acknowledged. We thank Dr. R. Zimmer for his help during preparation of this manuscript.

[1] a) R. W. Chesnut, N. N. Durham, R. A. Brown, E. A. Mawdsley, K. D. Berlin, *Steroids* **1976**, *27*, 525–541; b) R. E. Dolle, H. S. Allaudeen, L. I. Kruse, *J. Med. Chem.* **1990**, *33*, 877–880; c) C. Lange, N. Holzhey, B. Schönecker, R. Beckert, U. Möllmann, H.-M. Dahse, *Bioorg. Med. Chem.* **2004**, *12*, 3357–3362.

[2] For selected examples, see: a) F. Cachoux, M. Ibrahim-Ouali, M. Santelli, *Tetrahedron Lett.* **2001**, *42*, 843–845; b) K. Oumzil, M. Ibrahim-Ouali, M. Santelli, *Synlett* **2005**, 1695–1698; c) H. W. Sünnemann, A. Hofmeister, J. Magull, A. de Meijere, *Chem. Eur. J.* **2006**, *12*, 8336–8344; d) A. Jacob von Wangelin, H. Neumann, D. Gordes, S. Huber, C. Wendler, S. Klaus, D. Strubing, A. Spannenberg, H. J. Jiao, L. El Firdoussi, K. Thurow, N. Stoll, M. Beller, *Synthesis* **2005**, 2029–2038.

[3] a) C. U. Dinesh, H.-U. Reißig, *Angew. Chem.* **1999**, *111*, 874–876; *Angew. Chem. Int. Ed.* **1999**, *38*, 789–791; b) E. Nandanan, C. U. Dinesh, H.-U. Reißig, *Tetrahedron* **2000**, *56*, 4267–4277; c) M. Berndt, H.-U. Reißig, *Synlett* **2001**, 1290–1291; d) S. Gross, H.-U. Reißig, *Synlett* **2002**, 2027–2030; e) S. Gross, H.-U. Reißig, *Org. Lett.* **2003**, *5*, 4305–4307; f) M. Berndt, I. Hlobilová, H.-U. Reißig, *Org. Lett.* **2004**, *6*, 957–960; g) V. Blot, H.-U. Reißig, *Eur. J. Org. Chem.* **2006**, 4989–4992; h) V. Blot, H.-U. Reißig, *Synlett* **2006**, 2763–2766; i) F. Aulenta, M. Berndt, I. Brüdgam, H. Hartl, S. Sörgel, H.-U. Reißig, *Chem. Eur. J.* **2007**, *13*, 6047–6062; j) U. K. Wefelscheid, H.-U. Reißig, *Adv. Synth. Catal.* **2008**, 350, 65–69.

[4] For related aryl carbonyl couplings, see: a) H. Ohno, S. Maeda, M. Okumura, R. Wakayama, T. Tanaka, *Chem. Commun.* **2002**, 316–317; b) H. Ohno, R. Wakayama, S. Maeda, H. Iwasaki, M. Okumura, C. Iwata, H. Mikamiyama, T. Tanaka, *J. Org. Chem.* **2003**, *68*, 5909–5916; c) H. Ohno, M. Okumura, S. Maeda, H. Iwasaki, R. Wakayama, T. Tanaka, *J. Org. Chem.* **2003**, *68*, 7722–7732; d) C.-W. Kuo, J.-M. Fang, *Synth. Commun.* **2001**, *31*, 877–892; e) J.-S. Shiue, M.-H. Lin, J.-M. Fang, *J. Org. Chem.* **1997**, *62*, 4643–4649; f) H.-G. Schmalz, S. Siegel, J. W. Bats, *Angew. Chem.* **1995**, *107*, 2597–2599; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2383–2385.

[5] Selected reviews dealing with samarium-promoted reactions: a) G. A. Molander, C. R. Harris, *Chem. Rev.* **1996**, *96*, 307–338; b) F. A. Khan, R. Zimmer, *J. Prakt. Chem.* **1997**, *339*, 101–104; c) G. A. Molander, C. R. Harris, *Tetrahedron* **1998**, *54*, 3321–3354; d) A. Krief, A.-M. Laval, *Chem. Rev.* **1999**, *99*, 745–777; e) H. B. Kagan, J. L. Namy in *Topics in Organometallic Chemistry Vol. 2: Lanthanides – Chemistry and Use in Organic Synthesis* (Ed.: S. Kobayashi), Springer, Berlin, **1999**, pp. 155–198; f) P. G. Steel, *J. Chem. Soc. Perkin Trans. 1* **2001**, 2727–2751; g) A. Hölemann, *Synlett* **2001**, 1497–1498; h) B. K. Banik, *Eur. J. Org. Chem.* **2002**, 2431–2444; i) H. B. Kagan, *Tetrahedron* **2003**, *59*, 10351–10372; j) M. Berndt, S. Gross, A. Hölemann, H.-U. Reißig, *Synlett* **2004**, 422–438; k) D. J. Edmonds, D. Johnston, D.-J. Procter, *Chem. Rev.* **2004**, *104*, 3371–3404; l) J. M. Concellón, H. Rodriguez-Solla, *Chem. Soc. Rev.* **2004**, *33*, 599–609.

[6] The use of HMPA as an additive raises the reducing ability of SmI_2 and it is required for many ketyl-coupling reactions, see: a) E. Prasad, R. A. Flowers II, *J. Am. Chem. Soc.* **2002**, *124*, 6895–6899; b) J. Inanaga, M. Ishikawa, M. Yamaguchi, *Chem. Lett.* **1987**, 1485–1486.

[7] a) D. C. Spellmeyer, K. N. Houk, *J. Org. Chem.* **1987**, *52*, 959–974; b) A. L. J. Beckwith, *Tetrahedron* **1981**, *37*, 3073–3100.

[8] a) T. Mizoroki, K. Mori, A. Ozaki, *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581–581; b) R. F. Heck, J. P. Nolley Jr., *J. Org. Chem.* **1972**, *37*, 2320–2322; c) Selected Reviews: I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009–3066; d) G. T. Crisp, *Chem. Soc. Rev.* **1998**, *27*, 345–390; e) A. de Meijere, F. E. Meyer, *Angew. Chem.* **1994**, *106*, 2473–2506; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2379–2411; for a scope of reaction conditions, see: f) S. Bräse, A. de Meijere, "Cross-Coupling of Organyl Halides with Alkenes: The Heck Reaction" in *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: A. de Meijere, F. Diederich), Wiley-VCH, Weinheim, **1998**, ch. 3; g) R. F. Heck, *Comprehensive Organic Synthesis* (Ed.: B. M. Trost), Pergamon, New York, **1991**, vol. 4, ch. 4.3.

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

[9] F. Aulenta, H.-U. Reißig, *Synlett* **2006**, 2993–2996.
[10] For a previous synthesis of nonaflate **14**, see: A. G. Martinez, A. H. Fernandez, R. M. Alvarez, *Synthesis* **1984**, 481–485.
[11] a) G. P. Roth, C. E. Fuller, *J. Org. Chem.* **1991**, *56*, 3493–3496; b) M. Rottländer, P. Knochel, *J. Org. Chem.* **1998**, *63*, 203–208; c) S. E. Denmark, R. F. Sweis, *Org. Lett.* **2002**, *4*, 3771–3774; d) O. Flögel, J. Dash, I. Brüdgam, H. Hartl, H.-U. Reißig, *Chem. Eur. J.* **2004**, *10*, 4283–4290; e) A. Gavryushin, C. Kofink, G. Manolikakes, P. Knochel, *Org. Lett.* **2005**, *7*, 4871–4874; f) R. E. Tundel, K. W. Anderson, S. L. Buchwald, *J. Org. Chem.* **2006**, *71*, 430–433; g) J. Dash, T. Lechel, H.-U. Reißig, *Org. Lett.* **2007**, *9*, 5541–5544.
[12] L. R. Subramanian, H. Bentz, M. Hanack, *Synthesis* **1973**, 293–294.
[13] A. Padwa, A. Zanka, J. M. Harris, *Tetrahedron* **2003**, *59*, 4939–4944.
[14] For the synthesis of **20** see: D. Tobia, B. Rickborn, *J. Org. Chem.* **1989**, *54*, 777–782.
[15] J. R. Parikh, W. v. E. Doering, *J. Am. Chem. Soc.* **1967**, *89*, 5505–5507.
[16] For example: a) T. Jeffery, *J. Chem. Soc., Chem. Commun.* **1984**, 1287–1289; b) T. Jeffery, *Tetrahedron Lett.* **1985**, *26*, 2667–2670; c) S.-K. Kang, K.-Y. Jung, C.-H. Park, E.-Y. Namkoong, T.-H. Kim, *Tetrahedron Lett.* **1995**, *36*, 6287–6290; d) E. C. Taylor, Y. Wang, *Heterocycles* **1998**, *48*, 1537–1553; e) A. F. Littke, G. C. Fu, *J. Am. Chem. Soc.* **2001**, *123*, 6989–7000; see also ref.[13]
[17] F. Aulenta, A. Hölemann, H.-U. Reißig, *Eur. J. Org. Chem.* **2006**, 1733–1739.
[18] For other samarium diiodide mediated spirocyclizations of aryl ketones, see refs.[4a,4b]
[19] D. Marcovici-Mizrahi, H. E. Gottlieb, V. Marks, A. Nudelman, *J. Org. Chem.* **1996**, *61*, 8402–8406.
[20] H. C. Kolb, M. S. VanNieuwenhze, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483–2547.
[21] For a review dealing with directed dihydroxylation reactions see: T. J. Donohoe, *Synlett* **2002**, 1223–1232.
[22] Remarkably, compound **32** slowly isomerized by standing in deuterated methanol into an isomer with very similar spectroscopic data. The structure of this compound and the mechanism of its formation could not unambiguously be established so far. Experiments dealing with this observation are in progress.
[23] Compound **27** showed a high affinity towards the estrogenic receptor at 1 μM concentration: I. Ott, R. Gust, Institut für Pharmazie der Freien Universität Berlin, unpublished results.
[24] Two distinct rotamers were visible in the NMR spectroscopic analysis performed at room temperature.

Received: January 7, 2008
Published Online: March 10, 2008

 © 2008 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim