Pergamon

Tetrahedron 56 (2000) 4267–4277

TETRAHEDRON

Competition between Novel 8-*endo-dig* and 6-*trig* Cyclizations of Samarium Ketyls Leading either to Benzannulated Cyclooctene or to Hexahydronaphthalene Derivatives

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Dedicated to Professor Rolf Huisgen on the occasion of his 80th birthday

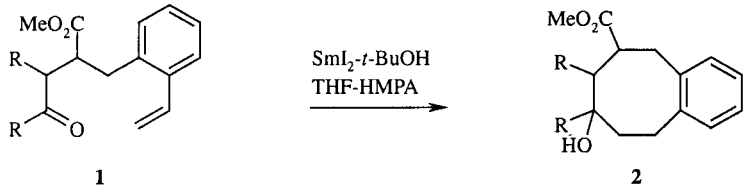
Received 19 April 2000; accepted 28 April 2000

Abstract—Ketoesters **3a**–**3h** with an alkynylaryl substituent were prepared by standard methods starting from siloxycyclopropanes **6a** and **6b**. Their reactions with 2.2 equiv. of samarium diiodide in the presence of hexamethyl phosphoramide either produced benzannulated cyclooctenol derivatives **4b** (or lactone **9**), **4f**, **4g**, and **4h** or hexahydronaphthalene derivatives **5a**, **5c**, and **5d**. The competition between 8-*endo-dig* and 6-*trig* cyclizations strongly depends on the substitution pattern of **3**. Plausible explanations for this competition and of the diastereoselectivity observed are presented in this paper.

Introduction

Metal promoted radical cyclizations are gaining increasing importance for the construction of ring compounds including medium and large ring sizes.[1] Significant progress has been made in recent years by application of samarium diiodide introduced by Kagan et al. as selective one electron transfer reagent.[2] It has been demonstrated that samarium diiodide in the presence of HMPA (hexamethyl phosphoramide) efficiently promotes cyclization of ketones with olefinic units giving not only five- or six-membered rings[3] but also larger rings including cyclooctanol derivatives which may be monocyclic, fused bicyclic or bridged bicyclic systems.[4] We used this surprisingly smooth 8-*endo-trig* cyclization for the conversion of styrene derivatives **1** into compounds **2** with benzannulated cyclooctanol skeletons (Scheme 1).[5] These products are of interest since their transformation into intermediates mimicking the BC rings of taxol derivatives is conceivable.[6] We also tried to extend the cyclizations to alkynyl substituted arenes **3** but found in a preliminary study that the anticipated 8-*endo-dig* reaction **3** to **4** proceeds only in exceptional cases (R^1=H). Most compounds **3** cyclized under attack of the intermediate ketyl on the aromatic ring giving hexahydronaphthalene derivatives **5** (Scheme 2).[7] This 6-*trig* cyclization had not been observed before in samarium chemistry and it should gain considerable synthetic importance due to its efficiency and high diastereoselectivity.[8]

Nevertheless we were still interested in 8-*endo-dig* cyclizations and therefore describe our experiments providing first information about the dependence of the reactions depicted in Scheme 2 on the substitution pattern of precursor **3**.



1 **2**

Scheme 1.

Keywords: samarium(II) iodide; 8-*endo-dig* cyclization; cyclooctenols; hexahydronaphthalenes; Sonogashira reaction; siloxycyclopropanes.
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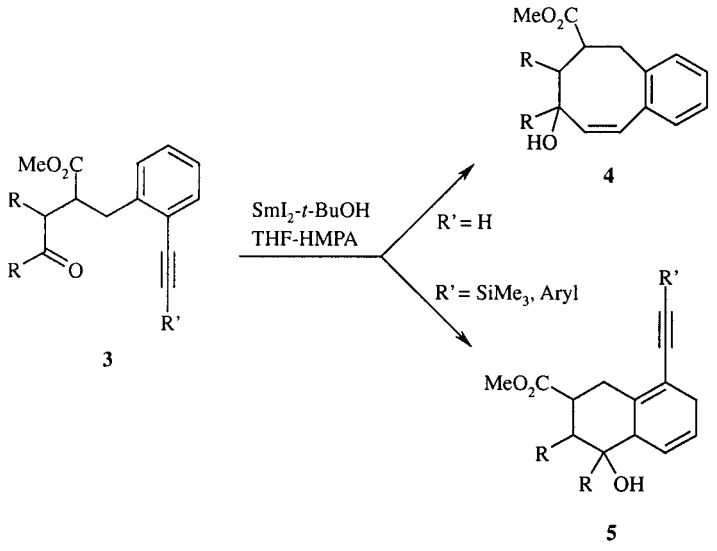
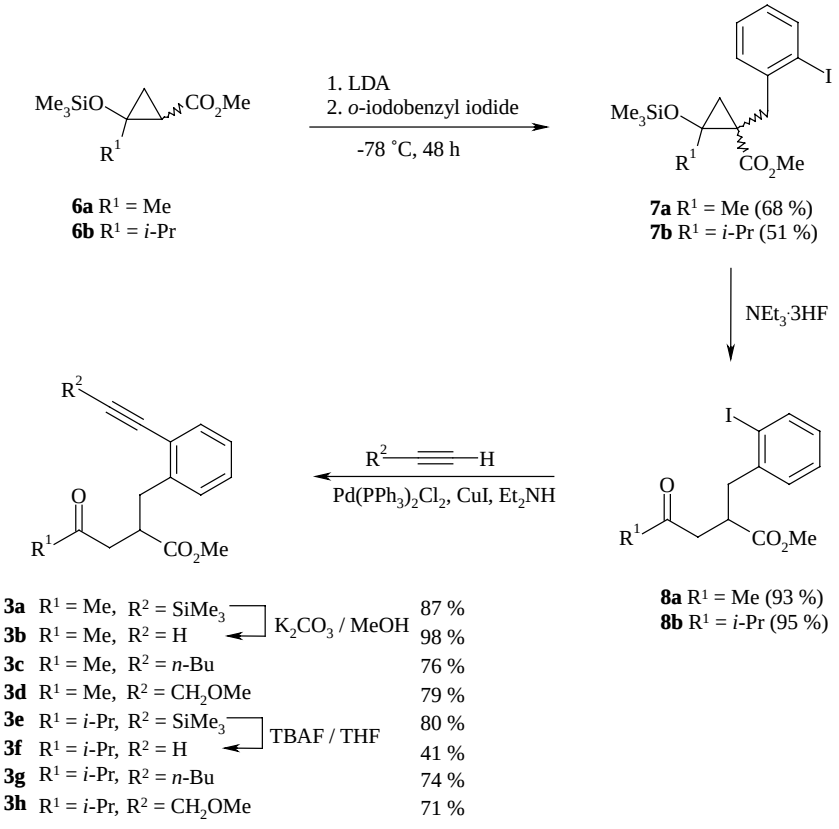


Scheme 2.

Synthesis of Starting Materials

The model substrates **3a**–**3h** for the SmI_2 promoted cyclizations were synthesized as illustrated in Scheme 3. Starting from the known siloxycyclopropanes **6a** and **6b**[9] their deprotonation and alkylation[10] with *o*-iodobenzyl iodide furnished **7a** and **7b**, respectively, and these were ring opened by treatment with triethylamine trishydrofluoride.[11] The two resulting ketoesters **8a** and **8b** with an iodobenzyl substituent were further substituted by Sonogashira reactions.[12] Thus, from **8a** alkynes **3a**–**3d** and from **8b** compounds **3e**–**3h** were smoothly available. The desilylation of **3a** and **3e** was carried out either by treatment with potassium carbonate in methanol or tetrabutylammonium fluoride to form the terminal alkynes **3b** and **3f**.[13] It was found that the potassium carbonate/methanol method resulted in better yields of the desilylated product.



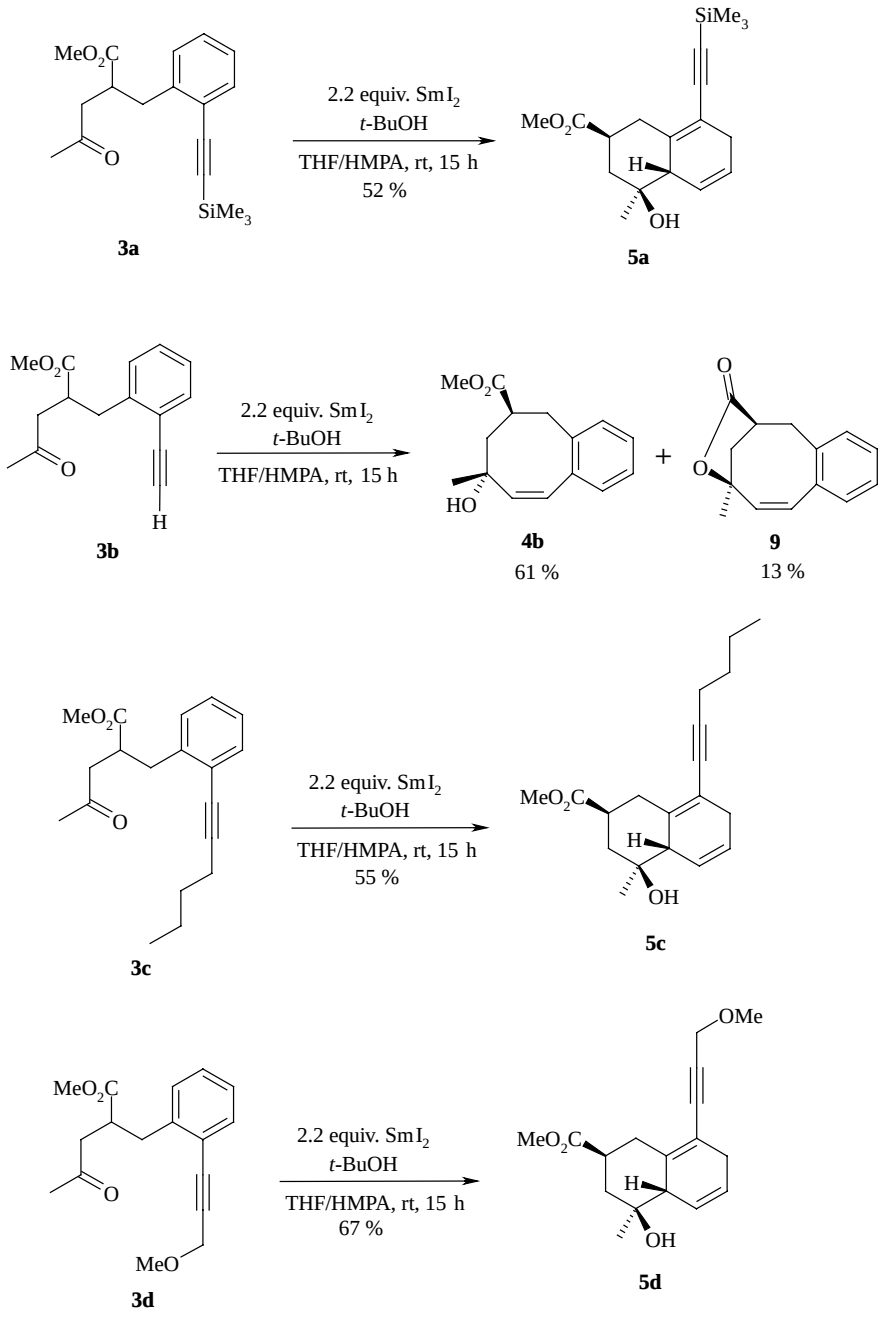
6a R^1 = Me
6b R^1 = *i*-Pr

7a R^1 = Me (68 %)
7b R^1 = *i*-Pr (51 %)

8a R^1 = Me (93 %)
8b R^1 = *i*-Pr (95 %)

3a	R^1 = Me, R^2 = $SiMe_3$	K_2CO_3 / MeOH	87 %
3b	R^1 = Me, R^2 = H		98 %
3c	R^1 = Me, R^2 = *n*-Bu		76 %
3d	R^1 = Me, R^2 = CH_2OMe		79 %
3e	R^1 = *i*-Pr, R^2 = $SiMe_3$	TBAF / THF	80 %
3f	R^1 = *i*-Pr, R^2 = H		41 %
3g	R^1 = *i*-Pr, R^2 = *n*-Bu		74 %
3h	R^1 = *i*-Pr, R^2 = CH_2OMe		71 %

Scheme 3.



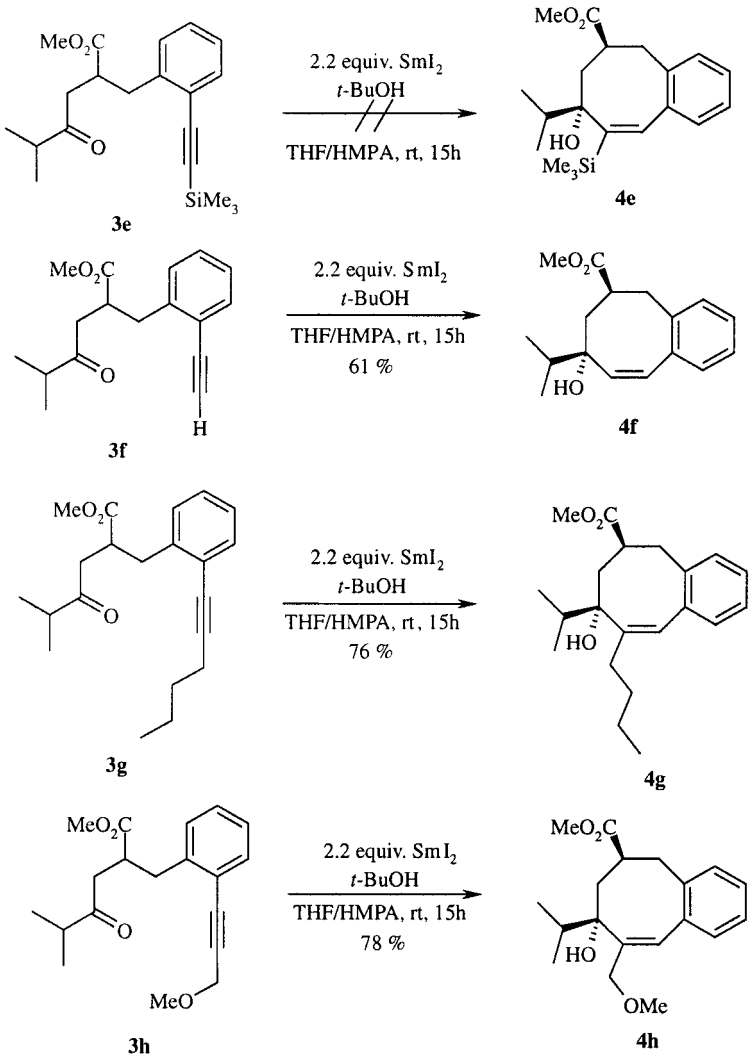
Scheme 4.

SmI_2 Promoted Cyclizations

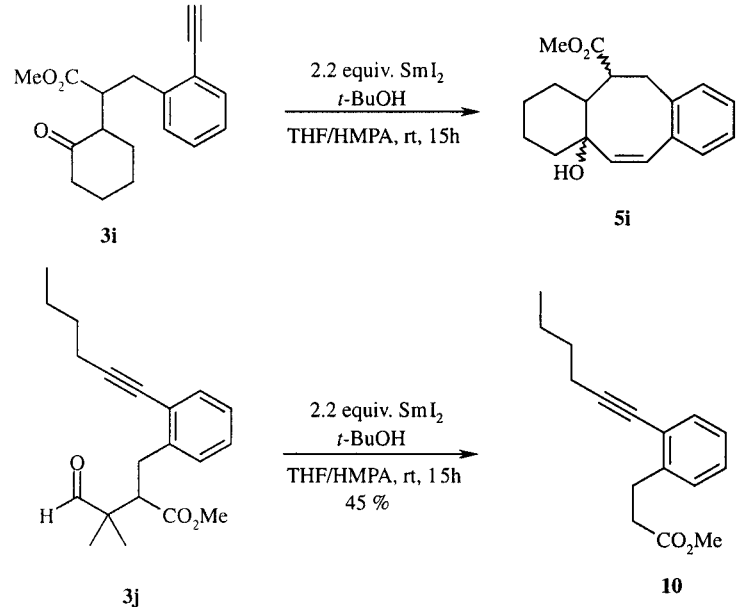
As reported in our preliminary publication, **3a** and 2.2 equiv. of samarium diiodide in the presence of HMPA and *t*-butanol produced hexahydronaphthalene derivatives **5a** in 52% yield as singular diastereomer (Scheme 4).[7] The terminal alkyne moiety of **3b** allowed attack of the ketyl to the triple bond giving a mixture of the expected benzannulated cyclooctenol derivative **4b** (61% yield) and lactone **9** which arises from the diastereomer of **4b**. The two substrates **3c** and **3d** with internal triple bonds behaved similar to **3a** giving again hexahydronaphthalene derivatives **5c** and **5d** by attack on the aryl part.

Surprisingly none of the isopropyl ketones **3e**–**3h** furnished the hexahydronaphthalene derivatives (Scheme 5). Whereas the reaction of trimethylsilyl substituted alkyne **3e** did not give any definite product, the three substrates **3f**–**3h** with less shielded alkyne moieties afforded benzannulated cyclooctenol derivatives **4f**–**4h** in good yields. Only one diastereomer was isolated in each of these examples.

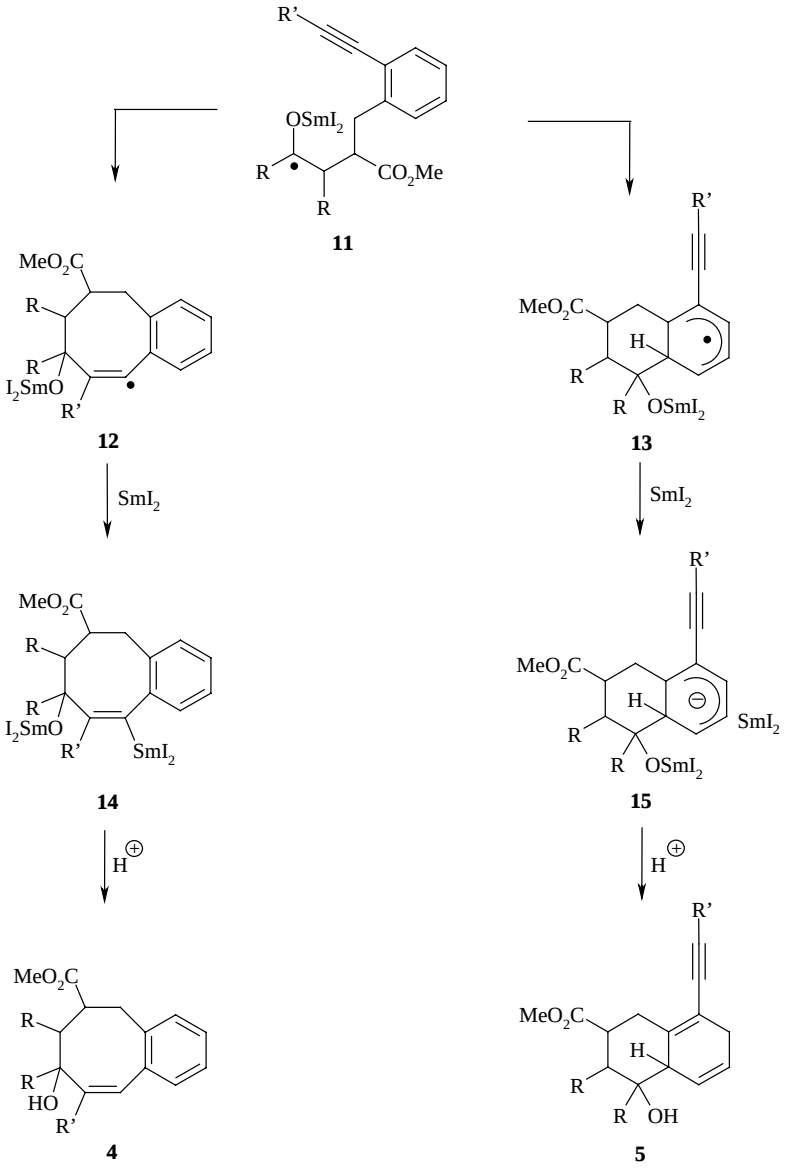
We also investigated substrates **3i** and **3j** which were prepared analogously to the route depicted in Scheme 3. The two diastereomers of **3i** provided an inseparable mixture which apparently contains **5i** but also the starting material (Scheme 6). It will be necessary to separate the diastereomers of **3i** and to study the cyclization in single experiments. By treatment under standard conditions



Scheme 5.



Scheme 6.



Scheme 7.

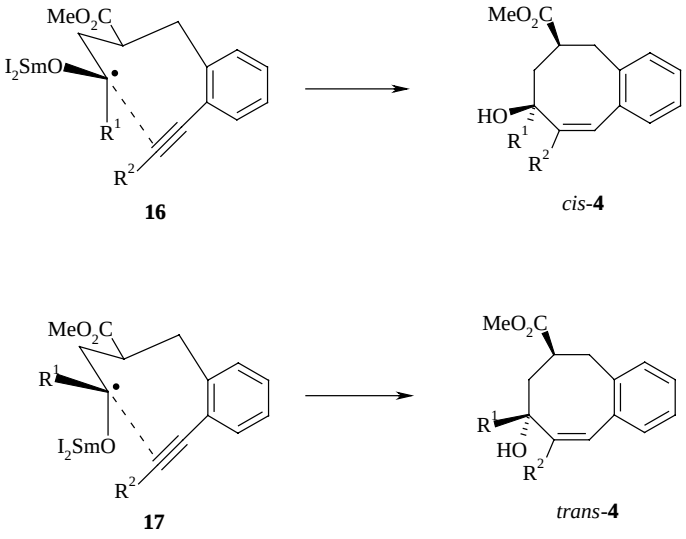
aldehyde **3j** underwent a reductive cleavage and the ester **10** was isolated in moderate yield.[14]

Discussion

The reactions of **3** giving either **4** or **5** start with an electron transfer from samarium diiodide to produce an intermediate ketyl **11** (Scheme 7). The next step is crucial for the selectivity of the sequence. 8-*Endo-dig* cyclization giving the vinyl radical **12** will finally lead to **4**, whereas formation of **5** proceeds via cyclohexadienyl radical **13**. Radicals **12** and **13** are converted into carbanionic species **14** or **15** by a second electron transfer of samarium diiodide before protonation by *t*-butanol furnishes the final products **4** and **5**.

From the examples collected in Schemes 4 and 5 the following conclusions can be drawn: an isopropyl substituted ketyl moiety as derived from ketones **3e**–**3h** is sterically too hindered for an attack of the benzene ring. Hence, an 8-*endo-dig* cyclization occurs in the case that the alkyne moiety is not blocked by a bulky substituent such as a trimethylsilyl group in **3e**. *n*-Butyl or methoxymethyl groups are tolerated as substituent at the alkyne and **4f**–**4h** are formed in good yields. Methyl ketones **3a**–**3d** generally prefer 6-*trig* cyclization to produce hexahydronaphthalene derivatives **5**. Only compound **3b** with a monosubstituted alkyne unit gives the cyclooctenol derivative **4b** and the related lactone **9**. Thus, an unhindered alkyne is required for methyl ketones if the 8-*endo-dig* cyclization should have a chance to compete with the 6-*trig* cyclization.

Another point of concern is the stereoselectivity of these reactions. The configurations of hexahydronaphthalene derivatives **5a**, **5c** and **5d** have been assigned in analogy to an example determined with the help of an X-ray analysis.[15] A plausible explanation for the formation of these compounds was presented in our preliminary communication.[7] The 8-*endo-dig* cyclization leads to one diastereomer in most cases, but ketone **3b** provided a mixture of bicyclic



Scheme 8.

product **4b** and lactone **9**. We could not transform **4b** into **9** and therefore we conclude that these two products should have different relative configurations at the carbon atoms bearing the carboxyl and the oxygen function. Since compounds **4f**–**4h** (Scheme 5) have very similar NMR data they should also have *trans* location of the two functional groups.

How do we explain the high stereoselectivity of the 8-*endo-dig* cyclization? We assume a chair-like folding of the flexible chain with the methoxycarbonyl group occupying an equatorial position.[16] The ketyl unit may be arranged in two variations: the oxygen (with the coordinated samarium ion) in a pseudo-equatorial position and the substituent R^1 in an axial position (**16** in Scheme 8) or in an inverted situation (**17** in Scheme 8). Reactive conformation **16** should provide *cis*-**4** whereas **17** will give *trans*-**4**. Small substituents R^1 and R^2 allow both arrangements as demonstrated by the conversion of **3b** (R^1=Me and R^2=H) into the mixture of **4b** and **9**. A larger substituent R^2 seems to prefer the pseudo-equatorial position as shown by the exclusive formation of *trans*-isomers in the reactions of **3f**, **3g** and **3h**. Of course, this model is speculative and has to be confirmed by further investigations.

Conclusions

We could demonstrate that easily available ketoesters **3** with an alkynylaryl substituent cyclize in the presence of samarium diiodide to produce either benzannulated cyclooctenol derivatives **4** or hexahydronaphthalene derivatives **5**. The competition between both reaction pathways strongly depends on the substitution pattern of **3**. In no example both product types could be isolated. The smooth formation of eight-membered rings is remarkable since not many *endo-dig* cyclizations of samarium ketyls have been reported.[17] To the best of our knowledge, our examples are the first 8-*endo-dig* cyclizations employing Sm(II). The peculiarity of the formation of hexahydronaphthalenes **5** has already been emphasized in our earlier publication.[7] Both reactions will be further investigated to fully explore the scope and limitations and to understand their surprisingly high stereoselectivities.

Experimental

General information

All reactions were performed under argon atmosphere in flame dried flasks and the components were added by means of syringes. All solvents were dried by standard procedures. Tetrahydrofuran was freshly distilled from potassium/benzophenone for each of the SmI_2 reactions. Thin layer chromatography (TLC) was carried out on commercial Polygram Sil G/UV_{254} or Alox N/UV_{254} (MACHEREY-NAGEL). Neutral alumina (activity III, Fa. MERCK) or flash silica gel (E. MERCK) were used for column chromatography. IR-spectra were measured on Nicolet 205 FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC 300 or Bruker DRX 500 MHz instruments in $CDCl_3$ solution. The chemical shifts are given relative to the TMS or to the $CDCl_3$ signals (δ_H=7.27, δ_C=77.0). The missing signals of the minor isomer are hidden by signals of the major isomer or they could not be unambiguously identified due to low intensity. HRMS were determined by a Finnigan MAT 711 (8 kV) instrument by direct evaporation method. Melting points (uncorrected) were measured with Büchi (SMP-20) and Gallenkamp (MPD 350). Samarium, hexamethyl phosphoramide, diiodoethane, *t*-butanol, $Pd(PPh_3)_2Cl_2$, diethylamine, copper(I) iodide and copper(II) acetate were commercially available and were used as received. The starting materials **6a**,[9] **6b**,[9] **7a**[18] and **8a**[18] were prepared by literature procedures.

Methyl 1-(2-iodobenzyl)-2-isopropyl-2-trimethylsiloxy-cyclopropanecarboxylate (7b). To a stirred solution of diisopropylamine (1.31 g, 13.0 mmol) in anhydrous THF (25 mL) was added *n*-BuLi (5.54 mL of 2.35 M solution in hexane, 13.0 mmol) dropwise at −78°C and was stirred for 20 min under argon atmosphere. The cyclopropane **6b** (2.50 g, 10.8 mmol) in dry THF (50 mL) was added

dropwise and stirring was continued for 1 h followed by the dropwise addition of a solution of *o*-iodobenzyl iodide (4.65 g, 13.5 mmol) in dry THF (50 mL). The mixture was stirred for additional 48 h at −78°C. The reaction mixture was quenched by saturated aqueous ammonium chloride solution (25 mL) and allowed to warm to room temperature. Water (50 mL) was added and the organic phase was separated. The aqueous layer was extracted with diethyl ether (3×75 mL) and the combined organic extract was washed with water, brine and dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure gave a residue which was purified by column chromatography on neutral alumina using hexane/ethyl acetate mixture (98:2) as eluent to afford a diastereomeric mixture (90:10) of **7b** (2.45 g, 51%) as a colourless oil. IR (Neat): ν=2965–2875 cm^{-1} (C–H), 1725 (CO_2Me). *trans*-Isomer of **7b**: ^1H NMR (300 MHz, $CDCl_3$): δ=7.63 (d, J=7.7 Hz, 1H, Ar), 7.11–7.03 (m, 2H, Ar), 6.72–6.62 (m, 1H, Ar), 3.38 (s, 3H, OCH_3), 3.37 (d, J=18.0 Hz, 1H, CH_2Ar), 2.56 (d, J=18.0 Hz, 1H, CH_2Ar), 1.60 (dd, J=1.4, 6.3 Hz, 1H, 3-H), 1.43 (hept., J=6.9 Hz, 1H, C*H*Me_2), 0.85 (d, J=6.9 Hz, 3H, CH_3), 0.79 (d, J=6.3 Hz, 1H, 3-H), 0.75 (d, J=6.9 Hz, 3H, CH_3), 0.00 (s, 9H, TMS); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=173.8 (s, C=O), 142.7, 139.3, 128.1, 127.5, 127.3, 101.7 (2s, 4d, Ar), 71.0 (s, C-2), 52.1 (q, OCH_3), 40.3 (t, CH_2Ar), 34.4 (s, C-1), 31.9 (d, *C*HMe_2), 25.1 (t, C-3), 19.6, 17.9 (2q, 2CH_3), 1.8 (q, TMS). *cis*-Isomer of **7b**: ^1H NMR (300 MHz, $CDCl_3$): δ=3.40 (s, 3H, OCH_3), 2.36 (d, J=18.0 Hz, 1H, CH_2Ar), 1.76 (d, J=6.3 Hz, 1H, 3-H), 0.95 (d, J=6.9 Hz, 3H, CH_3), 0.89 (d, J=6.9 Hz, 3H, CH_3), 0.01 (s, 9H, TMS); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=171.5 (s, C=O), 142.0, 139.4, 129.2, 128.8, 127.9, 101.0 (2s, 4d, Ar), 69.5 (s, C-2), 51.8 (q, OCH_3), 40.0 (t, CH_2Ar), 37.1 (s, C-1), 33.4 (d, *C*HMe_2), 23.6 (t, C-3), 19.3, 18.0 (2q, 2 CH_3), 1.8 (q, TMS); Calcd for $C_{18}H_{27}IO_3Si$ (446.4): C, 48.43%, H, 6.10%; Found: C, 48.54%, H, 6.16%.

Methyl 2-(2-iodobenzyl)-5-methyl-4-oxopentanoate (8b). To a stirred solution of **7b** (1.40 g, 3.14 mmol) in dry dichloromethane (20 mL) was added triethylamine trishydrofluoride (750 mg, 4.70 mmol) at room temperature under argon atmosphere. The reaction mixture was stirred for 3 h. Water (25 mL) was added, the organic layer was separated and the aqueous layer was extracted with dichloromethane (2×10 mL). The combined organic phase was washed with water, brine and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the crude residue was purified by flash column chromatography on silica gel using hexane/ethyl acetate (9:1) as eluent to afford **8b** (1.11 g, 95%) as a colourless oil. IR (Neat): ν=2970–2875 cm^{-1} (C–H), 1735 (CO_2Me), 1710 (C=O); ^1H NMR (300 MHz, $CDCl_3$): δ=7.83–7.78 (m, 1H, Ar), 7.29–7.13 (m, 2H, Ar), 6.91 (td, J=1.7, 7.6 Hz, 1H, Ar), 3.62 (s, 3H, OCH_3), 3.31–3.20 (m, 1H, 2-H), 3.13 (dd, J=7.1, 13.6 Hz, 1H, CH_2Ar), 2.95 (dd, J=8.2, 13.6 Hz, 1H, CH_2Ar), 2.66–2.50 (m, 2H, 5-H and 3-H), 1.09 (d, J=7.0 Hz, 3H, CH_3), 1.05 (d, J=7.0 Hz, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=212.2 (s, C-4), 174.8 (s, C-1), 141.4, 139.7, 130.1, 128.4, 128.2, 100.7 (2s, 4d, Ar), 51.7 (q, OCH_3), 42.1 (t, CH_2Ar), 41.0 (t, C-3), 40.7 (d, C-2), 40.6 (d, C-5), 18.1, 18.0 (2q, C-6 and C-7); Calcd for $C_{15}H_{19}IO_3$ (374.2): C, 48.14%, H, 5.11%; Found: C, 48.13%, H, 5.39%.

General procedure A, Sonogashira reaction

A 50 mL two necked round bottom flask was charged with the iodo arene (1 equiv.) and diethylamine (approximately 8 mL/mmol) under argon atmosphere at room temperature. The mixture was stirred for 5 min and then cooled to 0°C in an ice bath. $Pd(PPh_3)_2Cl_2$ (0.010–0.017 equiv.) and copper(I) iodide (0.020–0.026 equiv.) were added at once followed by the corresponding alkyne (1.25–1.54 equiv.) and stirring was continued at room temperature. After completion of the reaction (2–6 h, monitored by TLC) the solvent was evaporated under reduced pressure and the residue was dissolved in diethyl ether (10 mL/mmol). Water (10 mL/mmol) was added and the organic phase was separated. The aqueous phase was extracted with ether (3×10 mL/mmol). The combined ether extracts were washed with saturated ammonium chloride solution (10 mL/mmol), dried over anhydrous sodium sulfate, filtered and evaporated to get a residue which was purified by flash column chromatography on silica gel with hexane/ethyl acetate mixture (9:1) as eluent to furnish the corresponding product.

Methyl 4-oxo-2-(2-trimethylsilylethynylbenzyl)pentanoate (3a). The reaction was performed as described in general procedure A. Thus, **8a** (173 mg, 0.50 mmol), trimethylsilylacetylene (62.0 mg, 0.60 mmol), $Pd(PPh_3)_2Cl_2$ (4 mg, 0.005 mmol) and copper(I) iodide (2 mg, 0.099 mmol) in diethylamine (4 mL) furnished **3a** (138 mg, 87%) as a pale yellow oil. IR (Neat): ν=3020–2900 cm^{-1} (=C–H, C–H), 2155 (C≡C), 1735 (CO_2Me), 1720 (C=O); ^1H NMR (300 MHz, $CDCl_3$): δ=7.38 (dd, J=1.3, 7.4 Hz, 1H, Ar), 7.20–7.04 (m, 3H, Ar), 3.59 (s, 3H, OCH_3), 3.28–3.18 (m, 1H, 2-H), 3.14 (dd, J=5.9, 13.2 Hz, 1H, C*H*$_2$Ar), 2.82 (dd, J=9.4, 13.2 Hz, 1H, C*H*$_2$Ar), 2.81 (dd, J=9.3, 17.5 Hz, 1H, 3-H), 2.40 (dd, J=3.6, 17.5 Hz, 1H, 3-H), 2.02 (s, 3H, 5-H), 0.20 (s, 9H, TMS); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ=206.3 (s, C-4), 175.1 (s, C-1), 140.9, 132.6, 129.5, 128.6, 126.5, 123.1 (2s, 4d, Ar), 103.3, 98.9 (2s, C≡C), 51.7 (q, OCH_3), 43.9 (t, *C*H$_2$Ar), 41.1 (d, C-2), 36.2 (t, C-3), 29.8 (q, C-5), 0.00 (q, TMS); Calcd for $C_{18}H_{24}O_3Si$ (316.5): C, 68.31%, H, 7.64%; Found: C, 68.19%, H, 7.66%.

Methyl 4-oxo-2-(2-ethynylbenzyl)pentanoate (3b). A flame dried 25 mL round bottom flask was charged with silyl compound **3a** (590 mg, 1.86 mmol) and dry K_2CO_3 (309 mg, 2.24 mmol) in dry methanol (8 mL) under argon atmosphere. The mixture was stirred at room temperature for 2 h (monitored by TLC). The mixture was filtered through a short pad of Celite, washed with diethyl ether and the filtrate was evaporated to dryness to furnish the desilylated product **3b** (420 mg, 98%) as a colourless oil which was used as obtained. IR (Neat): ν=3280 cm^{-1} (≡C–H), 3090–2850 (=C–H, C–H), 2360 (C≡C), 1740 (C=O), 1715 (CO_2Me); ^1H NMR (300 MHz, $CDCl_3$): δ=7.48 (dd, J=1.2, 7.5 Hz, 1H, Ar), 7.30–7.25 (m, 1H, Ar), 7.22–7.14 (m, 2H, Ar), 3.65 (s, 3H, OCH_3), 3.30 (s, 1H, C≡CH), 3.33–3.23 (m, 1H, 2-H), 3.19 (dd, J=6.3, 13.2 Hz, 1H, C*H*$_2$Ar), 2.96 (dd, J=8.7, 13.2 Hz, 1H,

CH_2Ar), 2.89 (dd, J=9.4, 18.0 Hz, 1H, 3-H), 2.47 (dd, J=4.1, 18.0 Hz, 1H, 3-H), 2.10 (s, 3H, 5-H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ=206.4 (s, C-4), 175.0 (s, C-1), 141.1, 133.1, 129.4, 128.9, 126.6, 122.1 (2s, 4d, Ar), 81.9, 81.5 (s, d, C≡CH), 51.7 (q, OCH_3), 44.0 (t, C-3), 41.1 (d, C-2), 35.9 (t, *C*H_2Ar), 29.9 (q, C-5); Calcd for $C_{15}H_6O_3$ (242.3): C, 74.36%, H, 6.65%; Found: C, 73.79%, H, 6.83%.

Methyl 2-(2-hex-1-ynylbenzyl)-4-oxopentanoate (3c). The reaction was performed as described in general procedure A. Thus, **8a** (500 mg, 1.44 mmol), 1-hexyne (148 mg, 1.81 mmol), $Pd(PPh_3)_2Cl_2$ (14 mg, 0.020 mmol) and copper(I) iodide (6 mg, 0.030 mmol) in diethylamine (6 mL) furnished **3c** (330 mg, 76%) as pale yellow liquid. IR (Neat): ν=3065–2870 cm^{-1} (C–H), 2200 (C≡C), 1735 (CO_2Me), 1720 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.38 (dd, J=1.4, 5.5 Hz, 1H, Ar), 7.23–7.08 (m, 3H, Ar), 3.64 (s, 3H, OCH_3), 3.30–3.27 (m, 1H, 2-H), 3.19 (dd, J=5.9, 13.0 Hz, 1H, CH_2Ar), 2.91 (dd, J=7.5, 13.0 Hz, 1H, CH_2Ar), 2.86 (dd, J=9.2, 17.5 Hz, 1H, 3-H), 2.45 (t, J=7.0 Hz, 2H, CH_2), 2.40 (dd, J=4.6, 17.5 Hz, 1H, 3-H), 2.06 (s, 3H, 5-H), 1.60–1.43 (m, 4H, 2 CH_2), 0.95 (t, J=7.2 Hz, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=206.2 (s, C-4), 174.9 (s, C-1), 139.9, 132.1, 129.6, 128.7, 127.9, 123.8 (2s, 4d, Ar), 94.6, 78.5 (2s, C≡C), 51.4 (q, OCH_3), 43.5 (t, C-3), 41.5 (d, C-2), 35.9 (t, CH_2Ar), 30.5 (t, CH_2), 29.6 (q, C-5), 21.8 (t, CH_2), 18.9 (t, CH_2), 13.3 (q, CH_3); Calcd for $C_{19}H_{24}O_3$ (300.4): C, 75.97%, H, 8.05%; Found: C, 76.35%, H, 8.28%.

Methyl 2-[2-(3-methoxyprop-1-ynyl)benzyl]-4-oxopentanoate (3d). The reaction was performed as described in general procedure A. Thus, **8a** (200 mg, 0.580 mmol), propargyl methyl ether (55.0 mg, 0.785 mmol), $Pd(PPh_3)_2Cl_2$ (7 mg, 0.010 mmol) and copper(I) iodide (3 mg, 0.015 mmol) in diethylamine (4 mL) furnished **3d** (132 mg, 79%) as a pale yellow liquid. IR (Neat): ν=2975–2870 cm^{-1} (C–H), 2320 (C≡C), 1735 (CO_2Me), 1720 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.44 (dd, J=1.4, 7.4 Hz, 1H, Ar), 7.26–7.13 (m, 3H, Ar), 4.38 (s, 2H, OCH_2), 3.66 (s, 3H, OCH_3), 3.47 (s, 3H, OCH_3), 3.42–3.39 (m, 1H, 2-H), 3.20 (dd, J=6.0, 13.0 Hz, 1H, CH_2Ar), 2.91 (dd, J=7.6, 13.0 Hz, 1H, CH_2Ar), 2.85 (dd, J=9.4, 18.0 Hz, 1H, 3-H), 2.49 (dd, J=3.9, 18.0 Hz, 1H, 3-H), 2.11 (s, 3H, 5-H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=206.6 (s, C-4), 175.1 (s, C-1), 140.6, 132.7, 129.5, 128.6, 126.7, 122.6 (2s, 4d, Ar), 89.5, 84.5 (2s, C≡C), 60.5 (t, OCH_2), 57.7 (q, OCH_3), 51.9 (q, OCH_3), 43.9 (t, C-3), 41.1 (d, C-2), 36.1 (t, CH_2Ar), 29.9 (q, C-5); Calcd for $C_{17}H_{20}O_4$ (288.3): C, 70.81%, H, 6.99%; Found: C, 71.08%, H, 6.96%.

Methyl 5-methyl-4-oxo-2-(2-trimethylsilylethynylbenzyl)-hexanoate (3e). The reaction was performed as described in general procedure A. Thus, **8b** (750 mg, 2.00 mmol), trimethylsilylacetylene (250 mg, 2.50 mmol), $Pd(PPh_3)_2Cl_2$ (14 mg, 0.020 mmol) and copper(I) iodide (8 mg, 0.040 mmol) in diethylamine (10 mL) furnished **3e** (550 mg, 80%) as a colourless oil. IR (Neat): ν=3065–2875 cm^{-1} (=C–H, C–H), 2155 (C≡C), 1735 (CO_2Me), 1715 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.38 (dd, J=1.3, 7.5 Hz, 1H, Ar), 7.19–7.04 (m, 3H, Ar), 3.58 (s, 3H, OCH_3), 3.28–3.19 (m, 1H, 2-H), 3.13 (dd, J=6.1, 13.0 Hz, 1H, CH_2Ar), 2.88–2.80 (m, 2H, 3-H, CH_2Ar), 2.48 (sept, J=6.9 Hz, 1H, 5-H), 2.38 (dd, J=3.7, 17.9 Hz, 1H, 3-H), 1.00 (d, J=6.9 Hz, 3H, CH_3), 0.96 (d, J=6.9 Hz, 3H, CH_3), 0.20 (s, 9H, TMS); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=212.4 (s, C-4), 175.2 (s, C-1), 141.1, 132.7, 129.5, 128.6, 126.5, 123.1 (2s, 4d, Ar), 103.4, 98.8 (2s, C≡C), 51.6 (q, OCH_3), 41.0, 40.7 (2d, C-2, C-5), 40.9 (t, C-3), 36.4 (t, *C*H_2Ar), 18.2, 18.0 (2q, CH_3), 0.00 (q, TMS); Calcd for $C_{20}H_{28}O_3Si$ (344.5): C, 69.72%, H, 8.19%; Found: C, 69.82%, H, 8.41%.

Methyl 5-methyl-4-oxo-2-(2-ethynylbenzyl)hexanoate (3f). To a stirred solution of **3e** (500 mg, 1.45 mmol) in anhydrous THF (20 mL) was added tetrabutylammonium fluoride (980 mg, 1.81 mmol, 1 M solution in THF) under argon atmosphere at room temperature and the mixture was stirred for 2 h. Water (10 mL) was added and the organic layer was separated. The aqueous layer was extracted with ether (2×10 mL). The combined organic layer was washed with brine (10 mL) and dried over anhydrous sodium sulfate. Evaporation of the solvent and flash column chromatography on silica gel using hexane/ethyl acetate (5:1) afforded **3f** (160 mg, 41%) as a light pink liquid. IR (Neat): ν=3260 cm^{-1} (≡C–H), 3060–2875 (=C–H, C–H), 2360 (C≡C), 1735 (CO_2Me), 1710 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.48 (dd, J=1.2, 7.4 Hz, 1H, Ar), 7.30–7.25 (m, 1H, Ar), 7.21–7.14 (m, 2H, Ar), 3.63 (s, 3H, OCH_3), 3.29 (s, 1H, ≡CH), 3.34–3.25 (m, 1H, 2-H), 3.18 (dd, J=6.5, 13.3 Hz, 1H, CH_2Ar), 2.97 (dd, J=8.7, 13.3 Hz, 1H, CH_2Ar), 2.93 (dd, J=9.3, 17.9 Hz, 1H, 3-H), 2.55 (sept., J=6.9 Hz, 1H, 5-H), 2.50 (dd, J=4.2, 17.9 Hz, 1H, 3-H), 1.07 (d, J=6.9 Hz, 3H, CH_3), 1.03 (d, J=6.9 Hz, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=212.4 (s, C-4), 175.1 (s, C-1), 141.2, 133.1, 129.4, 128.9, 126.6, 122.2 (2s, 4d, Ar), 82.0, 81.4 (s, d, C≡CH), 51.7 (q, OCH_3), 41.1, 40.7 (2d, C-2, C-5), 41.0 (t, C-3), 36.1 (t, *C*H_2Ar), 18.1, 18.0 (2q, C-6, C-7); Calcd for $C_{17}H_{20}O_3$ (272.4): C, 74.97%, H, 7.50%; Found: C, 75.08%, H, 7.76%.

Methyl 2-(2-hex-1-ynylbenzyl)-5-methyl-4-oxohexanoate (3g). The reaction was performed as described in general procedure A. Thus, **8b** (500 mg, 1.34 mmol), 1-hexyne (139 mg, 1.69 mmol), $Pd(PPh_3)_2Cl_2$ (10 mg, 0.014 mmol) and copper(I) iodide (6 mg, 0.030 mmol) in diethylamine (6 mL) furnished **3g** (328 mg, 74%) as a colourless liquid. IR (Neat): ν=2965–2875 cm^{-1} (C–H), 2360 (C≡C), 1735 (CO_2Me), 1715 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.37 (dd, J=1.3, 7.0 Hz, 1H, Ar), 7.19–7.11 (m, 3H, Ar), 3.65 (s, 3H, OCH_3), 3.35–3.22 (m, 1H, 2-H), 3.17 (dd, J=6.0, 13.1 Hz, 1H, CH_2Ar), 2.93 (dd, J=7.6, 13.1 Hz, 1H, CH_2Ar), 2.88 (dd, J=9.8, 17.9 Hz, 1H, 3-H), 2.54 (m, 2H, 5-H and 3-H), 2.46 (t, J=7.2 Hz, 2H, CH_2), 1.66–1.43 (m, 4H, 2 CH_2), 1.08 (d, J=6.9 Hz, 3H, CH_3), 1.03 (d, J=6.9 Hz, 3H, CH_3), 0.96 (t, J=7.3 Hz, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=212.7 (s, C-4), 175.4 (s, C-1), 141.3, 132.3, 129.3, 127.6, 126.5, 124.0 (2s, 4d, Ar), 94.9, 78.7 (2s, C≡C), 51.7 (q, OCH_3), 40.9 (t, C-3), 40.7 (d, C-2), 40.6 (d, C-5), 36.3 (t, *C*H_2Ar), 30.8 (t, CH_2), 22.1 (t, CH_2), 19.2 (t, CH_2), 18.2 (q, CH_3), 17.9 (q, CH_3), 13.6 (q, CH_3); Calcd for $C_{21}H_{28}O_3$ (328.5): C, 76.79%, H, 8.59%; Found: C, 76.25%, H, 9.41%; HRMS (EI, 80 eV): Calcd for $C_{21}H_{28}O_3$, 328.20385; Found, 328.20413.

Methyl 2-[2-(3-methoxyprop-1-ynyl)benzyl]-4-oxohexanoate (3h). The reaction was performed as described in general procedure A. Thus, **8b** (180 mg, 0.480 mmol), propargyl methyl ether (52 mg, 0.743 mmol), $Pd(PPh_3)_2Cl_2$ (4 mg, 0.005 mmol) and copper(I) iodide (2 mg, 0.009 mmol) in diethylamine (4 mL) furnished **3h** (107 mg, 71%) as a colourless liquid. IR (Neat): ν= 2970–2875 cm^{-1} (C–H), 1735 (CO_2Me), 1712 (C=O); ^1H NMR (300 MHz, $CDCl_3$): δ=7.44 (d, J=6.1 Hz, 1H, Ar), 7.28–7.13 (m, 3H, Ar), 4.38 (s, 2H, OCH_2), 3.63 (s, 3H, OCH_3), 3.47 (s, 3H, OCH_3), 3.41–3.24 (m, 1H, 2-H), 3.20 (dd, J=6.4, 13.2 Hz, 1H, CH_2Ar), 2.91 (dd, J=9.3, 13.2 Hz, 1H, CH_2Ar), 2.88 (dd, J=9.4, 18.0 Hz, 1H, 3-H), 2.56–2.45 (m, 2H, 3-H and 5-H), 1.07 (d, J=6.9 Hz, 3H, CH_3), 1.02 (d, J=6.9 Hz, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=212.4 (s, C-4), 175.1 (s, C-1), 140.6, 132.6, 129.3, 128.5, 126.5, 122.5 (2s, 4d, Ar), 89.4, 84.5 (2s, C≡C), 60.3 (t, OCH_2), 57.6 (q, OCH_3), 51.7 (q, OCH_3), 40.9 (d, C-5), 40.8 (t, CH_2), 40.6 (d, C-2), 36.2 (t, CH_2Ar), 18.1 (q, CH_3), 17.9 (q, CH_3); HRMS (EI, 80 eV): Calcd for $C_{19}H_{24}O_4$, 316.16746; Found, 316.16738.

General procedure B, SmI_2 mediated ketone cyclization

Samarium (2.4 equiv.) was activated in a 50 mL two necked round bottom flask by heating with a hot air gun under argon atmosphere. The flask was cooled to room temperature and freshly distilled THF (5 mL/mmol) was added. Diiodoethane (2.2 equiv.) was added dropwise in THF (15 mL/mmol) under a constant flush of argon. The resultant mixture was stirred for 1 h where it developed a dark bluish green colour. Hexamethyl phosphoramide (18 equiv.) was added in one portion, while the solution turned to deep violet. The mixture was stirred for 5 min and a solution of *t*-butanol (2 equiv.) and the alkynyl ketone (1 equiv.) in THF (20 mL/mmol) was added dropwise over a period of 30 min. After 15 h the reaction was completed (monitored by TLC) and quenched with a saturated aqueous solution of ammonium bicarbonate solution (15 mL/mmol). The organic layer was separated and the aqueous layer was extracted with diethyl ether (3×25 mL). The combined ether extracts were washed with brine (25 mL), water (25 mL), dried over anhydrous sodium sulfate, filtered and evaporated to get a crude residue which was purified by flash column chromatography on silica gel using hexane/ethyl acetate mixture (17:3) as eluent to furnish the corresponding cyclized products.

Methyl 4-hydroxy-4-methyl-8-trimethylsilylethynyl-1,2,3,4,4a,7-hexahydronaphthalene-2-carboxylate (5a). The reaction was performed as described in general procedure B. Thus, **3a** (210 mg, 0.66 mmol), samarium (240 mg, 1.59 mmol), diiodoethane (420 mg, 1.45 mmol), HMPA (2.14 g, 11.9 mmol) and *t*-BuOH (98 mg, 1.32 mmol) in THF (35 mL) gave **5a** (110 mg, 52%) as a colourless oil. IR (Neat): ν=3430 cm^{-1} (br, OH), 3025–2825 (C–H), 2140 (C≡C), 1720 (C=O); ^1H NMR (300 MHz, $CDCl_3$): δ=5.62 (s, 2H, 5-H, 6-H), 3.51 (s, 3H, OCH_3), 3.11 (ddd, J=1.7, 4.0, 13.5 Hz, 1H, 1-H), 2.61–2.53 (m, 3H, 7-H, 4a-H), 2.28 (tt, J=3.9, 13.5 Hz, 1H, 1-H), 1.91–1.78 (m, 2H, 2-H, OH), 1.64–1.55 (m, 2H, 3-H), 0.84 (s, 3H, CH_3), 0.00 (s, 9H, TMS); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.8 (s, C=O), 140.6 (s, C-8a), 125.0, 122.7 (2d, C-5, C-6), 113.9 (s, C-8), 104.2, 97.4 (2s, C≡C), 74.2 (s, C-4), 51.8 (q, OCH_3), 49.1 (d, C-2), 43.8 (t, C-7), 40.3 (d, C-4a), 34.4, 31.0 (2t, C-1, C-3), 22.2 (q, CH_3), 0.00 (q, TMS); Calcd for $C_{18}H_{26}O_3Si$ (318.5): C, 67.88%, H, 8.23%; Found: C, 67.73%, H, 8.21%.

Methyl 8-hydroxy-8-methyl-5,6,7,8-tetrahydrobenzocyclooctene-6-carboxylate (4b) and 11-methyl-12-oxatricyclo[9.2.1.0^{3,8}]tetradeca-3,5,7,9-tetraen-13-one (9). The reaction was performed as described in general procedure B. Thus, **3b** (246 mg, 1.00 mmol), samarium (361 mg, 2.40 mmol), diiodoethane (620 mg, 2.20 mmol), HMPA (3.22 g, 18.0 mmol) and *t*-BuOH (148 mg, 2.00 mmol) in THF (40 mL) gave **4b** (146 mg, 61%) and **9** (27 mg, 13%) as colourless liquids. **4b**: IR (Neat) ν=3450 cm^{-1} (OH), 3060–2880 (C–H), 1730 (C=O); ^1H NMR (300 MHz, $CDCl_3$): δ=7.23–7.11 (m, 4H, Ar), 6.31 (d, J=12.6 Hz, 1H, 9-H), 5.71 (dd, J=1.2, 12.6 Hz, 1H, 10-H), 3.71 (s, 3H, OCH_3), 3.11 (bs, 3H, 5-H and 6-H), 1.84 (d, J=13.2 Hz, 1H, 7-H), 1.68–1.54 (m, 2H, 7-H and OH), 1.34 (s, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=175.5 (s, CO), 137.6, 137.1, 135.8, 129.7, 128.9, 127.4, 126.3, 125.4 (2s, 6d, Ar, C-9, C-10), 71.8 (s, C-8), 51.6 (q, OCH_3), 40.8 (d, C-6), 36.3 (t, C-5), 33.1 (t, C-7), 20.3 (q, CH_3); Calcd for $C_{15}H_{18}O_3$ (246.3): C, 73.15%, H, 7.36%; Found: C, 72.69%, H, 7.38%. **9**: IR (Neat): ν=3010–2875 cm^{-1} (C–H), 1770 (C=O), 1630 (C=C); ^1H NMR (300 MHz, $CDCl_3$): δ=7.29–7.26 (m, 3H, Ar), 7.18–7.15 (m, 1H, Ar), 6.52 (d, J=12.6 Hz, 1H, 10-H), 5.86 (dd, J=1.6, 12.6 Hz, 1H, 9-H), 3.25 (dd, J=9.6, 13.3 Hz, 1H, CH_2Ar), 2.95 (dt, J=6.5, 9.5 Hz, 1H, 1-H), 2.76 (dd, J=9.5, 13.3 Hz, 1H, CH_2Ar), 1.95 (d, J=13.4 Hz, 1H, 14-H), 1.79–1.72 (m, 2H, OH and 14-H), 1.53 (s, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=178.2 (s, C=O), 137.0, 136.2, 132.5, 129.3, 129.2, 128.3, 126.8 (2s, 5d, Ar, C-9 and C-10), 84.1 (s, C-11), 40.6 (d, C-1), 34.9 (t, C-2), 33.5 (t, C-14), 28.7 (q, CH_3); Calcd for $C_{14}H_{14}O_2$ (214.3): C, 78.48%, H, 6.59%; Found: C, 77.66%, H, 6.71%; HRMS (EI, 80 eV): Calcd for $C_{14}H_{14}O_2$, 214.09938; Found, 214.09730.

Methyl 8-(hex-1-ynyl)-4-hydroxy-4-methyl-1,2,3,4,4a,7-hexahydronaphthalene-2-carboxylate (5c). The reaction was performed as described in general procedure B. Thus, **3c** (100 mg, 0.330 mmol), samarium (120 mg, 0.800 mmol), diiodoethane (206 mg, 0.730 mmol), HMPA (1.10 g, 5.90 mmol) and *t*-BuOH (49 mg, 0.66 mmol) in THF (25 mL) gave **5c** (55 mg, 55%) as a colourless syrupy liquid. IR (Neat): ν=3450 cm^{-1} (bs, OH), 3035–2865 (C–H), 2210 (C≡C),1740 (C=O); ^1H NMR (300 MHz, $CDCl_3$): δ=5.82 (s, 2H, 5-H and 6-H), 3.71 (s, 3H, OCH_3), 3.31 (ddd, J=1.8, 4.0, 13.0 Hz, 1H, 1-H), 2.76 (bs, 3H, 7-H and 4a-H), 2.45 (tt, J=3.9, 13.0 Hz, 1H, 1-H), 2.34 (t, J=6.8 Hz, 2H, CH_2), 2.10–1.74 (m, 4H, 2 CH_2), 1.04 (s, 3H, CH_3), 0.92 (t, J=7.2 Hz, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.9 (s, C=O), 137.4 (s, C-8a), 125.1 (d, C-5), 122.9 (d, C-6), 114.1 (s, C-8), 93.5, 79.4 (2s, C≡C), 74.1 (s, C-4), 51.8 (q, OCH_3), 48.9 (d, C-2), 43.8 (t, C-7), 40.4 (d, C-4a), 34.1 (t, C-1), 31.5 (t, C-3), 30.9 (t, CH_2), 22.1 (q, CH_3), 21.9 (t, CH_2), 19.1 (t, CH_2), 13.5 (q, CH_3); Calcd for $C_{19}H_{26}O_3$ (302.4): C, 75.46%, H, 8.67%; Found: C, 75.46%, H, 8.31%.

Methyl 4-hydroxy-8-(3-methoxyprop-1-ynyl)-4-methyl-1,2,3,4,4a,7-hexahydronaphthalene-2-carboxylate (5d). The reaction was performed as described in general procedure B. Thus, **3d** (100 mg, 0.346 mmol), samarium (125 mg, 0.830 mmol), diiodoethane (220 mg, 0.780 mmol), HMPA (1.13 g, 6.30 mmol) and *t*-BuOH (52 mg, 0.70 mmol) in THF (40 mL) gave **5d** (68 mg, 67%) as a colourless liquid. IR (Neat): ν=3445 cm^{-1} (bs, OH), 2975–2825 (C–H), 2220 (C≡C), 1735 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.84 (s, 2H, 5-H and 6-H), 4.25 (s, 2H, OCH_2), 3.71 (s, 3H, OCH_3), 3.41 (s, 3H, OCH_3), 3.32 (ddd, *J*=2.4, 4.1, 13.5 Hz, 1H, 1-H), 2.80 (bs, 3H, 7-H and 4a-H), 2.46 (tt, *J*=3.9, 13.5 Hz, 1H, 1-H), 2.11–1.68 (m, 4H, 2-H, 3-H and OH), 1.05 (s, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=174.7 (s, C=O), 139.8 (s, C-8a), 125.0 (d, C-5), 122.8 (d, C-6), 113.3 (s, C-8), 88.1, 85.2 (2s, C≡C), 74.1 (s, C-4), 60.5 (t, OCH_2), 57.5 (q, OCH_3), 51.9 (q, OCH_3), 49.0 (d, C-2), 43.8 (t, C-7), 40.4 (d, C-4a), 34.3 (t, C-1), 31.2 (t, C-3), 22.1 (q, CH_3); Calcd for $C_{17}H_{22}O_4$ (290.4): C, 70.32%, H, 7.64%; Found: C, 70.08%, H, 7.21%; HRMS (EI, 80 eV): Calcd for $C_{17}H_{22}O_4$, 290.15181; Found, 290.15119.

Methyl 8-hydroxy-8-isopropyl-5,6,7,8-tetrahydrobenzocyclooctene-6-carboxylate (4f). The reaction was performed as described in general procedure B. Thus, **3f** (100 mg, 0.370 mmol), samarium (132 mg, 0.880 mmol), diiodoethane (230 mg, 0.814 mmol), HMPA (1.19 g, 6.66 mmol) and *t*-BuOH (55 mg, 0.74 mmol) in THF (20 mL) gave **3f** (62 mg, 61%) as a colourless liquid. IR (Neat): ν=3500 cm^{-1} (br, OH), 3075–2875 (C–H), 1715 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.23–7.12 (m, 4H, Ar), 6.47 (d, *J*=12.6 Hz, 1H, 9-H), 5.61 (d, *J*=12.6 Hz, 1H, 10-H), 3.70 (s, 3H, OCH_3), 3.12 (bs, 3H, 5-H and 6-H), 1.71 (sept., *J*=6.9 Hz, 1H, C*H*Me_2), 1.66–1.44 (m, 3H, OH and 7-H), 0.87 (d, *J*=6.9 Hz, 3H, CH_3), 0.85 (d, *J*=6.9 Hz, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=175.8 (s, C=O), 137.4, 135.6, 135.1, 129.8, 128.3, 127.9, 127.3, 126.4 (2s, 6d, Ar, C-9, C-10), 76.0 (s, C-8), 51.4 (q, OCH_3), 41.5, 40.2 (2d, C-6, *C*HMe_2), 33.4, 31.1 (2t, C-5, C-7), 17.3 (q, CH_3), 16.5 (q, CH_3); Calcd for $C_{17}H_{22}O_3$ (274.4): C, 74.42%, H, 8.08%; Found: C, 74.41%, H, 8.00%.

Methyl 9-butyl-8-hydroxy-8-isopropyl-5,6,7,8-tetrahydrobenzocyclooctene-6-carboxylate (4g). The reaction was performed as described in general procedure B. Thus, **3g** (100 mg, 0.310 mmol), samarium (110 mg, 0.730 mmol), diiodoethane (192 mg, 0.680 mmol), HMPA (1.00 g, 5.60 mmol) and *t*-BuOH (46 mg, 0.62 mmol) in THF (20 mL) gave **4g** (78 mg, 76%) as a colourless crystalline solid. Mp: 96–99°C; IR (KBr): ν=3505 cm^{-1} (OH), 3055–2840 (C–H), 1720 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.26–7.09 (m, 4H, Ar), 6.36 (s, 1H, 10-H), 3.69 (s, 3H, OCH_3), 3.10–3.06 (m, 3H, 5-H and 6-H), 2.38–2.28 (m, 1H, 7-H), 2.19–2.04 (m, 1H, 7-H), 2.01 (sept., *J*=7.0 Hz, 1H, C*H*Me_2), 1.69–1.34 (m, 7H, OH, 3 CH_2), 0.95 (t, *J*=7.2 Hz, 3H, CH_3), 0.91 (d, *J*=7.0 Hz, 3H, CH_3), 0.70 (d, *J*=7.0 Hz, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=176.1 (s, C=O), 146.2, 139.4, 135.1, 129.1, 128.1, 126.5, 126.2, 125.4 (3s, 5d, Ar, C-9, C-10), 79.1 (s, C-8), 51.6 (q, OCH_3), 38.9 (d, C-6), 37.2 (d, *C*HMe_2), 34.6 (t, C-5), 33.4 (t, C-7), 30.8 (t, CH_2), 29.4 (t, CH_2), 23.0 (t, CH_2), 17.8 (q, CH_3), 15.9 (q, CH_3), 14.1 (q, CH_3); Calcd for $C_{21}H_{30}O_3$ (330.5): C, 76.33%, H, 9.15%; Found: C, 76.25%, H, 9.41%.

Methyl 8-hydroxy-8-isopropyl-9-methoxymethyl-5,6,7,8-tetrahydrobenzocyclooctene-6-carboxylate (4h). The reaction was performed as described in general procedure B. Thus, **3h** (90 mg, 0.290 mmol), samarium (103 mg, 0.680 mmol), diiodoethane (181 mg, 0.640 mmol), HMPA (935 mg, 5.22 mmol) and *t*-BuOH (43 mg, 0.58 mmol) in THF (20 mL) gave **4h** (72 mg, 78%) as a colourless liquid. IR (Neat): ν=3480 cm^{-1} (bs, OH), 3060–2820 (C–H), 1735 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.19–7.08 (m, 4H, Ar), 6.57 (s, 1H, 10-H), 4.58 (d, *J*=11.0 Hz, 1H, OCH_2), 3.88 (d, *J*=11.0 Hz, 1H, OCH_2), 3.68 (s, 3H, OCH_3), 3.42 (s, 3H, OCH_3), 3.32–3.07 (m, 3H, 5-H, 6-H), 2.01 (sept., *J*=6.9 Hz, 1H, C*H*Me_2), 1.78–1.22 (m, 3H, OH, 7-H), 0.97 (d, *J*=6.7 Hz, 3H, CH_3), 0.68 (d, *J*=6.7 Hz, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=176.1 (s, C=O), 140.3, 137.6, 130.5, 129.3, 127.8, 127.2, 126.5, 126.2 (3s, 5d, Ar, C-9, C-10), 78.5 (s, C-8), 78.1 (t, OCH_2), 58.1 (q, OCH_3), 51.5 (q, OCH_3), 38.9 (d, C-6), 37.6 (d, *C*HMe_2), 32.9 (t, C-5), 28.3 (t, C-7), 17.7 (q, CH_3), 16.1 (q, CH_3); Calcd for $C_{19}H_{26}O_4$ (318.4): C, 71.67%, H, 8.23%; Found: C, 71.63%, H, 8.12%.

Methyl 3-(2-hex-1-ynylphenyl)propionate (10). The reaction was performed as described in the general procedure B. Thus, **3j** (140 mg, 0.450 mmol), samarium (161 mg, 1.07 mmol), diiodoethane (279 mg, 0.990 mmol), HMPA (1.45 g, 8.10 mmol) and *t*-BuOH (67 mg, 0.90 mmol) in THF (25 mL) gave **10** (64 mg, 45%) as a colourless liquid. IR (Neat): ν=2975–2840 cm^{-1} (C–H), 2205 (C≡C), 1740 (CO_2Me); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.37 (d, *J*=7.2 Hz, 1H, Ar), 7.19–7.12 (m, 3H, Ar), 3.67 (s, 3H, OCH_3), 3.08 (t, *J*=7.6 Hz, 2H, CH_2), 2.66 (t, *J*=7.6 Hz, 2H, CH_2), 2.44 (t, *J*=7.6 Hz, 2H, CH_2), 1.62–1.44 (m, 4H, 2 CH_2), 0.95 (t, *J*=7.2 Hz, 3H, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=173.5 (s, C=O), 142.1, 132.2, 128.6, 127.7, 126.2, 123.5 (2s, 4d, Ar), 94.6, 78.7 (2s, C≡C), 51.5 (q, OCH_3), 34.5 (t, CH_2), 30.8 (t, CH_2), 29.9 (t, CH_2), 21.9 (t, CH_2), 19.2 (t, CH_2), 13.6 (q, CH_3).

Acknowledgements

E. N. and C. U. D. thank the Alexander-von-Humboldt foundation for research fellowships. Support by the Volkswagen-Stiftung and the Fonds der Chemischen Industrie is most gratefully acknowledged. We thank Dr R. Zimmer (Freie Universität Berlin) for helpful discussions and Dr M. Gruner (Technische Universität Dresden) for NMR spectra measurements and their interpretations.

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