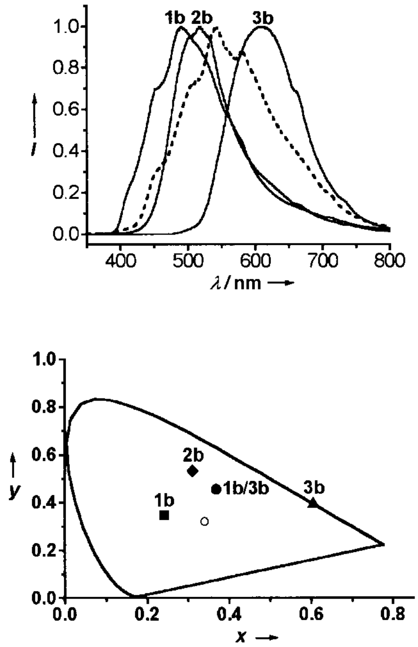

Figure 4. Top: Electroluminescence spectra of diodes (solid lines) that contain an emitting layer of the compounds **1b**, **2b**, and **3b**, and a light-emitting diode that contains two emitting layers made of compound **1b** and compound **3b** (dashed line). Bottom: Chromaticity coordinates of the electroluminescence for **1b**, **2b**, **3b**, and a sample with two emitting layers made of **1b** and **3b**. The open circle in the center represents the panchromatic point (white).

and the lifetime of the device may be improved by simultaneous codeposition of several of these compounds of presumably very similar electro- and photochemical stability. The extent to which the self-organization of the liquid crystalline mesophase can be used, through annealing or similar procedures, to further improve the uniformity of the films and thus the efficiency of these materials, is the subject of forthcoming investigations.

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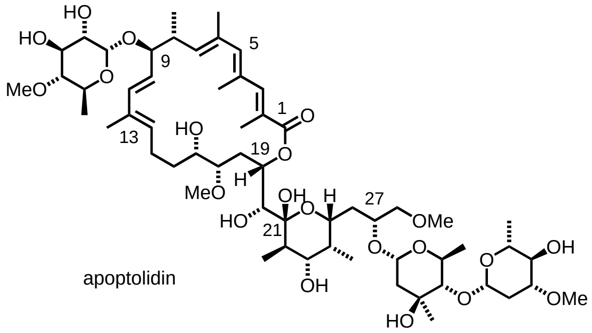
Synthesis of Apoptolidinone[**]

Julia Schuppan, Hermut Wehlan, Sonja Keiper, and Ulrich Koert[*]

Programmed cell death or apoptosis is a basic biological process that regulates, for example, the homeostasis and morphogenesis of organisms.[1] One very promising application of apoptosis control is in tumor therapy.[2] Apoptolidin, a natural product isolated from *Nocardiopsis sp.*, induces apoptosis in rat glia cells transformed with the E1A oncogene ($IC_{50} = 11\ \mathrm{ng\,mL^{-1}}$), but not in untransformed cell lines.[3] Khosla and co-workers identified the mitochondrial F_1F_0 ATP-ase as one possible target to explain the biological action.[4] Apoptolidin is a 20-membered macrolide with a side chain at C19 containing a 6-membered cyclic hemiketal. A disaccharide from D-oleandrose and L-olivomycose is located at C27, while 6-deoxy-4-*O*-methyl-L-glucose is attached at C9. Here we report on the synthesis of apoptolidinone, the aglycon of apoptolidin.[5]



apoptolidin

Our retrosynthetic analysis of apoptolidinone is based on a macrolactonization and a disconnection between C11 and C12

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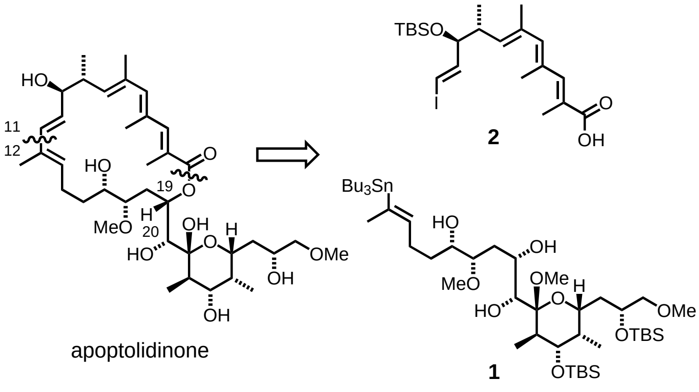
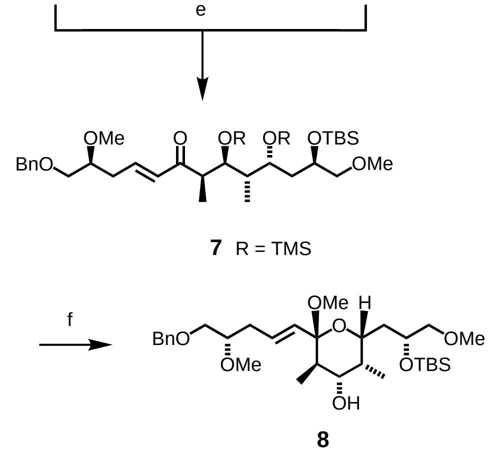
(Cu^I coupling; Scheme 1). This leads to a "southern" half **1** and a "northern" half **2**. No protective group differentiation between the hydroxy functionalities at C19 and C20 was chosen, because a size-selective macrolactonization[6] was expected based on model inspections.



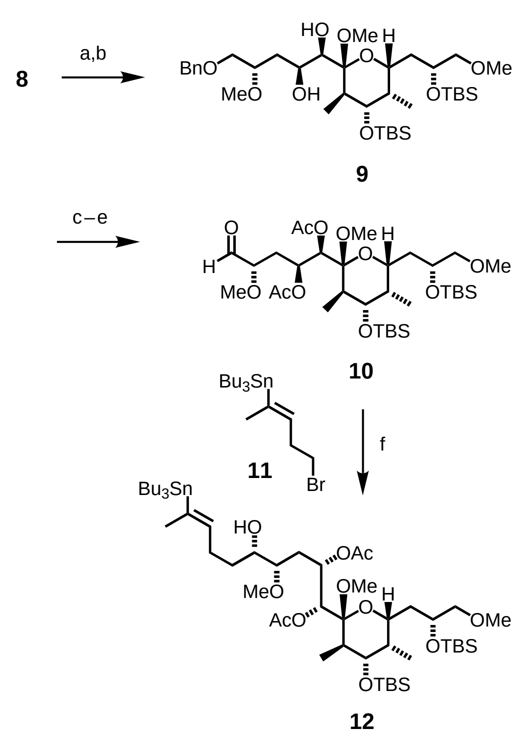
Scheme 1. Retrosynthetic analysis of apoptolidinone. TBS = *tert*-butyldimethylsilyl.

The synthesis of the southern half started with an epoxide opening of compound **3**, the benzyl-protected (*R*)-glycidol[7] (Scheme 2). Subsequent *O*-methylation and removal of the trimethylsilyl group gave the alkyne **4**, which was transformed through hydrozirconation/iodination[8] into the *E*-alkenyl iodide **5** (77 % yield from **3**). Compound **5** was converted by an iodine–lithium exchange into the corresponding organolithium compound, which was allowed to react with Weinreb amide **6**[5a] to yield the ketone **7**. Protodesilylation of the two TMS ether groups in $MeOH/CH_2Cl_2$ and a spontaneous cyclization led to the ketal **8** (87 % yield from **6**).



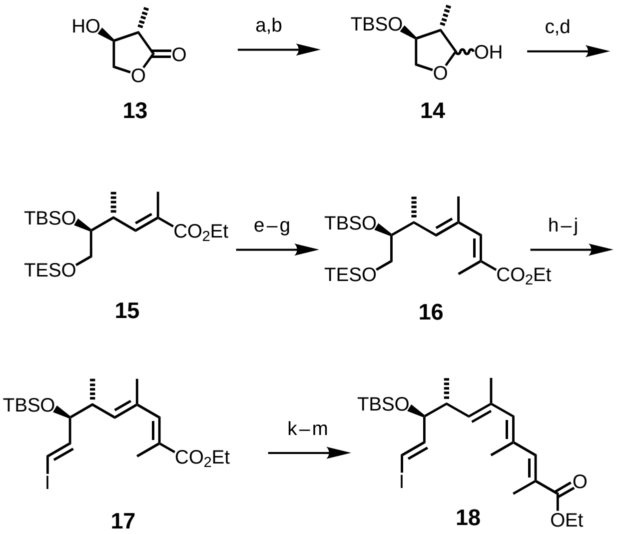
Scheme 2. Synthesis of the southern half, part I. a) $LiCCSiMe_3$, $BF_3 \cdot OEt_2$, THF, −78 °C; b) 3.0 equiv LiHMDS, 7.0 equiv MeI, THF, 0→20 °C; c) Bu_4NF, THF, 0 °C, 88 % (3 steps); d) 2.0 equiv $[Cp_2ZrCl_2]$, 2.0 equiv $LiEt_3BH$, 2.2 equiv NIS, THF, 20 °C, 88 %; e) **5**, *t*BuLi, Et_2O, −78 °C, then **6**; f) PPTS, $MeOH/CH_2Cl_2$ (1:1), 0 °C, 1.5 h, 87 % (2 steps). Bn = benzyl, LiHMDS = lithium hexamethyldisilazide, NIS = *N*-iodosuccinimide, PPTS = pyridinium *p*-toluenesulfonate, TMS = trimethylsilyl.

The hydroxy group at C23 was protected and a subsequent dihydroxylation (*ds* = 6:1) gave the diol **9** (Scheme 3). The stereochemical outcome of this reaction was assigned by comparison of the ^{13}C NMR spectrum with that of a model compound.[5a] Compound **9** was diacetylated and converted into the aldehyde **10** by a standard sequence. Compound **10** was allowed to react with the Grignard reagent prepared from **11**[9] to give the complete diacetylated southern half **12** (*ds* = 93:7, determined by HPLC; chelation control[10]). The compatibility of the organotin and the organomagnesium group is noteworthy.



Scheme 3. Synthesis of the southern half, part II. a) $tBuMe_2SiOTf$, 2,6-lutidine, CH_2Cl_2, −78 °C, 2 h, 98 %; b) $K_2OsO_2(OH)_4$, NMO, $tBuOH/H_2O$, 20 °C, 9 d, 78 %, *ds* = 6:1, chromatographic separation of the diastereomers in the following step; c) Ac_2O, pyridine, DMAP, 40 °C, 3 h, 69 % of the main diastereomer; d) H_2, $Pd(OH)_2/C$, EtOAc, 20 °C, 1 h, 97 %; e) Dess–Martin periodinane, pyridine, CH_2Cl_2, 91 %; f) **11**, Mg, 1,2-dibromoethane, Et_2O, 20 °C, then −78 °C, **10**, 58 %, *ds* = 93:7. DMAP = 4-dimethylaminopyridine, NMO = 4-methyl morpholine *N*-oxide, Tf = triflate = trifluoromethanesulfonyl.

The starting point for the northern half was the *β*-hydroxy lactone **13**,[11] which was protected as its *tert*-butyldimethylsilyl ether and subsequently reduced to the lactol **14** (Scheme 4). The twofold use of an *E*-selective Wittig reaction with commercially available $Ph_3P{=}C(CH_3)COOEt$ led via **15** to the diene **16**. Selective deprotection of the triethylsilyl ether in **16** followed by a Dess–Martin oxidation[12] gave an aldehyde that could be converted by a Takai reaction[13] into the *E*-



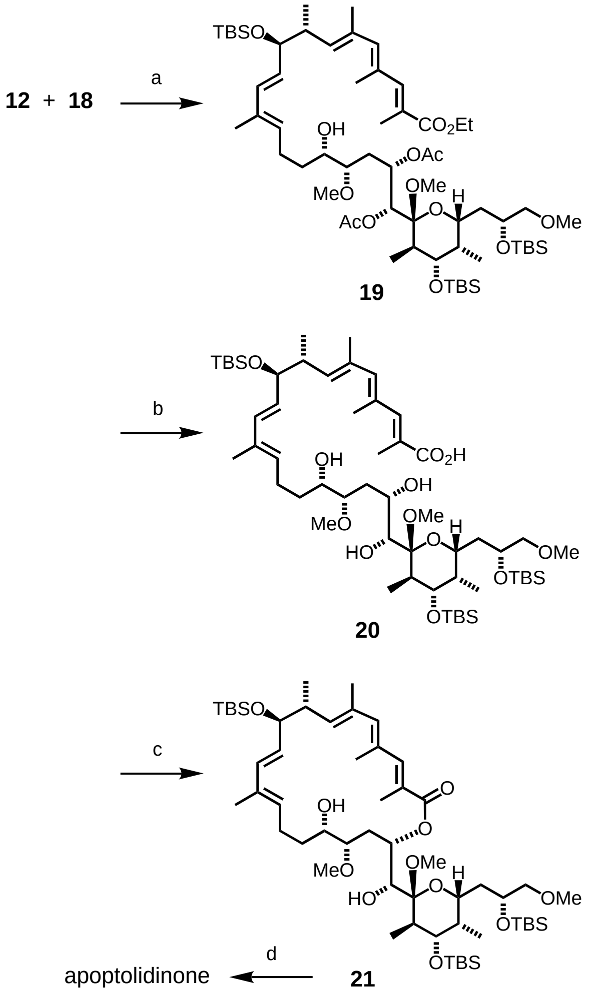
Scheme 4. Synthesis of the northern half. a) tBuMe$_2$SiOTf, 2,6-lutidine, CH$_2$Cl$_2$, 0 °C, 30 min, 90 %; b) DIBAH, CH$_2$Cl$_2$, −78 °C, 15 min, 95 %; c) Ph$_3$P=CCH$_3$CO$_2$Et, toluene, 110 °C, 12 h; d) Et$_3$SiCl, imidazole, CH$_2$Cl$_2$, 0 °C, 82 % (2 steps); e) DIBAH, toluene, −78 °C, 15 min; f) MnO$_2$, CH$_2$Cl$_2$, 40 °C, 30 min; g) Ph$_3$P=CCH$_3$CO$_2$Et, toluene, 110 °C, 86 % (3 steps); h) camphorsulfonic acid, MeOH/CH$_2$Cl$_2$ (1:2) 0 °C, 15 min, 95 %; i) Dess–Martin periodinane, pyridine, CH$_2$Cl$_2$, 20 °C; j) CrCl$_2$, CHI$_3$, cat. hydroquinone, THF, dioxane, 20 °C, 12 h, 69 % (2 steps); k) DIBAH, n-hexane, −78 °C, 1 h, 80 %; l) MnO$_2$, CH$_2$Cl$_2$, 20 °C, 2 h; m) Ph$_3$P=CCH$_3$CO$_2$Et, toluene, 100 °C, 12 h, 60 % (2 steps). DIBAH = diisobutylaluminium hydride, TES = triethylsulfonyl.

alkenyl iodide **17**. After transformation of the ester group into an aldehyde, another Wittig reaction produced the complete northern half ethyl derivative **18**. Compound **18** was found to be light sensitive[14] and all steps beyond **16** were carried out under yellow light.

The final sequence of the synthesis focused on the coupling of the southern and the northern half, as well as on the macrolactonization (Scheme 5). Attempts for a Pd^0-catalyzed Stille coupling[15] between **12** and **18** were disappointing (<30 % yield at prolonged reaction times and 60 °C). In contrast, the use of two equivalents of Cu^I–thiophene carboxylate[16] gave **19** in 80 % yield under very mild conditions (−10 °C, 1 h). Treatment of **19** with LiOH gave the trihydroxycarboxylic acid **20**. The macrolactonization of **20** according to the modified Yamaguchi procedure[17] produced the 20-membered macrolide **21** in 74 % yield (100-mg scale). The ring-size selectivity of this step is remarkable. No 21-membered lactone could be identified. Deprotection of **21** with HF/pyridine gave the target compound apoptolidinone[18] in 2.8 % yield for the longest linear sequence (19 steps).[5a]

The preferred conformation of the 20-membered macrolide is an important aspect of the bioactive conformation of apoptolidin. The analysis of the ROESY NMR spectrum of **21** is summarized in Figure 1. The ROESY crosspeaks that were found support a conformation that is in agreement with the conformation described by Hayakawa and co-workers for apoptolidin.[3a]

The synthesis of the apoptolidin aglycon described here provides, for the first time, synthetic access to this molecular



Scheme 5. Coupling of **12** and **18** and completion of the synthesis. a) Cu^I–thiophene-2-carboxylate, N-methylpyrrolidinone, −10 °C, 1 h, 80 %; b) LiOH, THF/MeOH/H$_2$O (2:1:1), 25→40 °C, 40 h, 87 %; c) 2,4,6-trichlorobenzoyl chloride, Et$_3$N, THF, 18 h, 25 °C, then DMAP, toluene, 80 °C, 6 h, 74 %; d) HF/pyridine, THF, 0→25 °C, 24 h, 55 %.

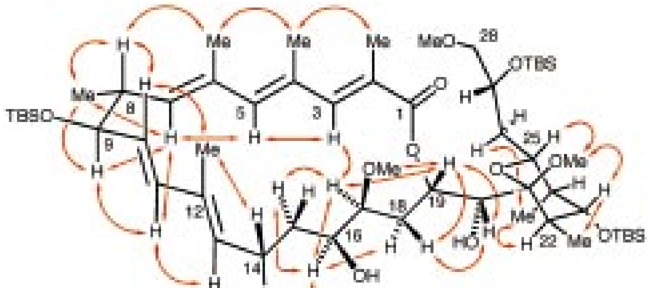


Figure 1. Conformation of **21** in C$_6$D$_6$, as determined from selected ROESY NMR spectroscopic data. ROESY cross signals are indicated with double-ended arrows.

framework with a very promising antitumor bioactivity. It forms the basis for the attachment of the sugar residues at C9 and C27. Our convergent strategy allows access to synthetic derivatives of the natural product, which will be of interest for further pharmacological developments.

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[18] Analytical data (R_f and $[\alpha]_D$ values, IR, ^{1}H and ^{13}C NMR, and HR mass spectra) of **12**, **18**, **20**, **21**, and apoptolidinone are available in the Supporting Information.

Carbon Nanofilaments in Heterogeneous Catalysis: An Industrial Application for New Carbon Materials?[**]

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Nicolas Keller, Vladimir V. Roddatis, and
Robert Schlögl[*]

The direct dehydrogenation of ethylbenzene to styrene is one of the ten most important industrial processes. In this process a potassium-promoted iron catalyst is used at temperatures between 870 and 930 K.[1] However, this method is thermodynamically limited and, because of the required excess of steam, very energy consuming.[2, 3] The oxidative dehydrogenation (ODH) of ethylbenzene could be a promising alternative in which the hydrogen generated is directly oxidized making the overall process exothermic.

Mechanistic studies of the dehydrogenation of ethylbenzene on single-crystal model surfaces provide fundamental information about the role of the active K–Fe phase.[4–7] This surface is evidently well suited to generate a graphitic carbon deposit. Therefore, it is possible that these carbon deposits are actually the catalytically active phase.

Transition metal oxides[8] and phosphates[9, 10] as well as polymers[11] have been described as active and selective catalysts for the ODH of ethylbenzene. The carbon deposits[12] detected on such catalysts again point to an active role of carbon in this reaction. Accordingly, catalytic activity in the ODH was demonstrated for activated charcoals,[13, 14] their commercialization however, is impossible because of their low oxidation resistance.[15] Graphite, on the other hand, exhibits activity in the ODH of methanol.[16] Thus, graphitic carbon materials, that is, nanofilaments with high surface area, are promising candidates for dehydrogenation catalysts in the presence of oxygen.

We have tested the catalytic properties of lamp soot, graphite, and nanofilaments for the ODH of ethylbenzene to styrene. Figure 1 displays the catalytic properties of the investigated carbon materials with time on stream *t*. The higher activity of nanofilaments relative to soot and graphite is evident. While the catalytic activity of soot decreases during the induction period because of burn-off, that of graphite and the nanofilaments increases with time. This behavior can be correlated with the stability toward combustion. Nanofilaments show a higher activity, selectivity, and yield relative to graphite. The catalytic properties of the three investigated carbon materials after 7 h operation are given in Table 1. Again the superiority of the nanofilaments over graphite is evident. Although the specific activity of nanofilaments is somewhat lower, they exhibit comparable selectivity and

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