**Introduction**

Fulicineroside was isolated from the slime mold Fuligo melaena in 2005.[1] It shows inhibitory activity towards Staphylococcus aureus and Bacillus subtilis, while the significant growth inhibition of crown gall tumors suggests in vivo antitumor activity.

Fulicineroside

Structurally unique features are both the highly substituted dibenzofuran core and the rare α,β-unsaturated trisaccharide. β-Linked hexose is unprecedented in natural products.

**Retro-synthetic Analysis**

Our synthetic plan is based on the convergent assembly of three major fragments. Important key steps are a) Julia-Kocienski olefination of sulfone 1 and aldehyde 2 to access the aglycone fulicinerine and a glycosylation for attachment of trisaccharide 3.

**Synthesis of the Dibenzofuran Core**

Bialyl ether 4, an Ullmann product[2] from 5-bromoresorcinol-dimethyl ether and resorcinol, gave the desired dibenzofuran 5 via a carbamate-directed C-H activation along with the minor isomer 6.[2] Anionic Fries rearrangement of 5 with subsequent one-pot methylation to an amide which was reduced to aldehyde 7. Attachment of the C2-side chain was accomplished by addition of the Grignard reagent[3, 4]. The resulting dibenzofuran 9 was transformed into the triolte 10.

**Completion of Fulicinerine**

The attachment of the C6-side chain started with a Stille coupling of triolte 18 and stannane 11. Oxidative PMB-deprotection gave aldehyde 2. A Julia-Kocienski olefination of 2 and sulfone 1 afforded triene 12 with high E-selectivity. After deprotection with HF the resulting allylic alcohol was converted into a 1:1 diastereomeric mixture of epoxides by Sharpless epoxidation. Separation and final deprotection gave the air-sensitive aglycone fulicineroside.

**Synthesis of the Trisaccharide**

The unique α,β,β-linked trisaccharide features a challenging synthetic target. Pd-mediated S_{2}2- reaction of glucose 13 and alcohol 14 gave the β-glycoside 15 selectively.[2] Trisaccharide 16 was obtained by the following six step sequence.

**Synthesis of Fulicineroside**

Prior to the final coupling step CF-OH was TES-protected (18 → 19). The following TMSOTf mediated glycosylation with the trisaccharide 3 gave the α-anomer exclusively. The final deprotection led to fulicineroside (1) which was purified by reversed phase chromatography.

NMR data of synthetic fulicineroside (1) significantly differ from those reported for the natural product which gives rise to a re-evaluation of the natural product structure postulated by Rozanka et al.[1]

**Scheme 1:** Retro-synthetic analysis of fulicineroside

**Scheme 2:** a) Pd(OAc)\textsubscript{2}, AgOAc, PhOH, 89%; b) LDA, Me\textsubscript{3}SiO, KOH, 70%; c) CpZnHCl, 70%; d) Grignard reagent 8, 81%; e) H\textsubscript{2}Pd/C, TFA, 95%; f) DHP, PPTS, 98%; g) LiSi{Ph}O(Tf)\textsubscript{2}, Py, 74% over two steps; h) LITBu, 82%; i) PNTt, NEt\textsubscript{3}, 100%

**Scheme 3:** a) Pd(OAc)\textsubscript{2}, AgOAc, PhOH, 89%; b) LDA, Me\textsubscript{3}SiO, KOH, 70%; c) CpZnHCl, 70%; d) Grignard reagent 8, 81%; e) H\textsubscript{2}Pd/C, TFA, 95%; f) DHP, PPTS, 98%; g) LITBu, 82%; h) PNTt, NEt\textsubscript{3}, 100%

**Scheme 4:** a) ELzN, Pd(OAc)\textsubscript{2}, DTSBIP, 89%; b) K\textsubscript{2}CO\textsubscript{3}, MeOH, 83%; c) Bu\textsubscript{3}P, Py, 96%; d) TBAF, 93%; e) PPh\textsubscript{3}, DIAD, DCH\textsubscript{2}CO\textsubscript{2}H f) MeOH, NEt\textsubscript{3}, 65% over two steps; g) TMSNHNH\textsubscript{2}, NaOAc, 96%

Completion of the trisaccharide 3 was achieved in four steps. Glycosylation between 17 and 16 was followed by tosylation substitution, thioleless deprotection with Raney-Ni and activation as trihalosaccharidate.

**Scheme 5:** a) TMSOTf, 88%; b) Li, 91%; c) Ra-Ni, 86%; d) CC\textsubscript{6}H\textsubscript{5}CN, K\textsubscript{2}CO\textsubscript{3}, 42% (99% brsm).

**Scheme 6:** a) TESOTf, 73%; b) AcOH, 82%; c) TMSOTf, 3, 61%; d) TBAF, e) K\textsubscript{2}CO\textsubscript{3}, MeOH, 61% over two steps.

**Scheme 7:** a) TESOTf, 73%; b) AcOH, 82%; c) TMSOTf, 3, 61%; d) TBAF, e) K\textsubscript{2}CO\textsubscript{3}, MeOH, 61% over two steps.

**Literature**