Corrigenda

Total Synthesis of Tubulysin U and V

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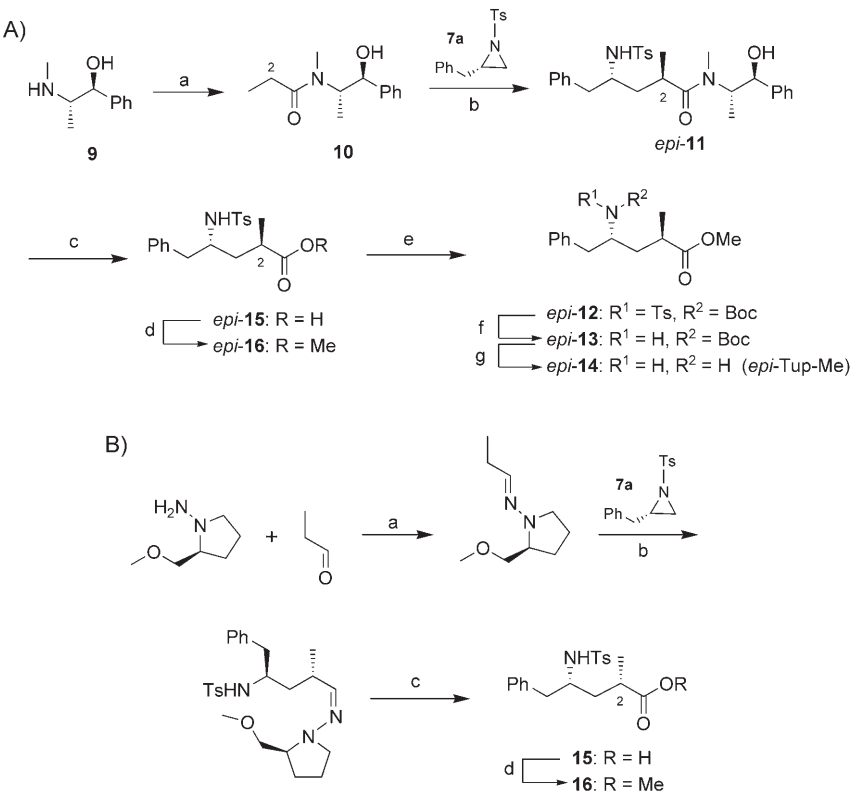
A recent evaluation of the biological activity of the tubulysin U and V diastereomers, shown in the Experimental Section and Supporting Information of our recent Communication, suggest that the wrong diastereomers were selected for data presentation. Re-evaluation of the other diastereomers obtained confirmed that the assignment of the tubuvaline spectra shown in the Supporting Information therein need to be inverted. More importantly, it appears that the synthesis of the first building block, tubuphenylalanine (Tup), shown in Scheme 2 therein and in line with the procedure and assignment reported by Vicario et al.,[1] does not give the diastereomer shown but rather its C2 epimer as the major product (see revised Scheme 2 below, part A). Careful repetitions of the synthesis of Tup using the original unmodified procedure of Vicario et al. or our variation and also using different batches of the auxiliary to exclude mislabeled reagents always led to production of the wrong C2 diastereomers *epi*-**11**–*epi*-**16** as the major components, with only some of the correct diastereomers (**11**–**16**) formed.

To be absolutely sure that the obtained stereochemistry is different from that expected from the report of Vicario et al.,[1] we also synthesized **15** and **16** again through a different pathway, using Enders' SAMP as auxiliary. This approach gave the correct diastereomer of the common intermediate **15** in four steps (Scheme 2 B).[2] In the meantime the syntheses by the groups of Ellman[3] and Zanda[4] also emanated, and comparison of the specific rotation values of **14** and *epi*-**14** with those reported by Zanda



Schema 2. A) Synthesis of the methyl ester of *epi*-tubuphenylalanine (*epi*-Tup) as the major product by the pseudoephedrine route. Reagents and conditions: a) Propionic anhydride, Et_3N, CH_2Cl_2; b) 1. LDA, LiCl, THF, −78 °C; 2. (*S*)-(+)-2-benzyl-1-(toluene-4-sulfonyl)aziridine, THF, −20 °C (Tup is only formed as a minor isomer in step b); c) 4 M H_2SO_4/dioxane, reflux; d) MeOH, conc. HCl, reflux; e) Boc_2O, DMAP, CH_3CN; f) Mg (powder), MeOH, ultrasound; g) 4 N HCl in dioxane. B) Synthesis of Tup derivatives **15** and **16** using Enders' SAMP auxiliary to give the correct diastereomer as the major product. Reagents and conditions: a) neat, 99%; b) 1. LDA, 0 °C; 2. (*S*)-(+)-2-benzyl-1-(toluene-4-sulfonyl)aziridine, THF, −100 °C→RT, 85% major isomer (separated and processed further); c) 1. O_3, acetone, −78 °C; 2. Jones reagent, −78 °C→RT, 55%; d) CH_2N_2, Et_2O/MeOH, 100%. Ts: toluene-4-sulfonyl, Boc: *tert*-butyloxycarbonyl, SAMP: (*S*)-(−)-1-amino-2-methoxymethylpyrrolidine, LDA: lithium diisopropylamide, Jones reagent: chromic acid in acetone.

and co-workers confirmed our findings. It appears that NMR spectroscopy is not ideal to determine the stereochemistry of Tup. Tup and its C2 epimer can display almost identical behavior and spectra, depending considerably on the conditions used. The same is true for the Tuv and Tup diastereomers and the final products, most of which often behave very similarly with respect to NMR spectroscopy and chromatography. Spectra of both Tup epimers and a mixed spectrum are provided in the Supporting Information herein. Vicario et al. used NMR spectroscopy, including nOe studies on a cyclized five-membered ring derivative, for their assignment. Specific rotation and X-ray analyses are more conclusive, but the relevant data were not known at the time of our first synthesis, which was based on analogy and the assignments in reference [1]. More details will be discussed in an upcoming full paper.

Experimental data for the correct diastereomers are hereby provided in the revised Supporting Information. The previously reported diastereomers also have been updated with the corrected names, stereochemical descriptors, and formulas. Finally, in Table 1, column 1, G should read H.

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