Pergamon

Tetrahedron Letters 39 (1998) 5797–5798

TETRAHEDRON LETTERS

Synthesis of Sulfobacin B

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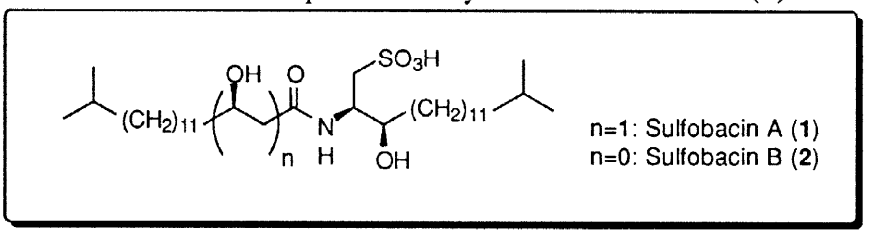
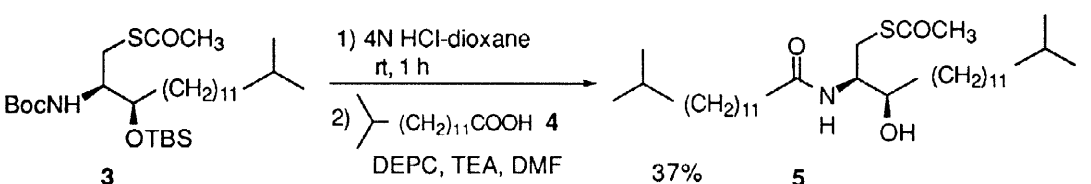
Received 13 May 1998; accepted 5 June 1998

Abstract: Sulfobacin B (**2**), a novel von Willebrand factor (vWF) receptor antagonist isolated from the culture broth of *Chryseobacterium* sp. NR 2993, was efficiently synthesized for the first time.

Sulfobacin B (**2**), a sulfonolipid isolated from the culture broth of *Chryseobacterium* sp. (*Flavobacterium* sp.) NR 2993 as a congener of sulfobacin A (**1**), inhibits the binding of von Willebrand's factor to the GPIb/1X receptors with an IC_{50} of 2.2 μM.[1] In our preceding paper,[2] the first total synthesis of sulfobacin A (**1**) was described. We now wish to report the first synthesis of sulfobacin B (**2**).



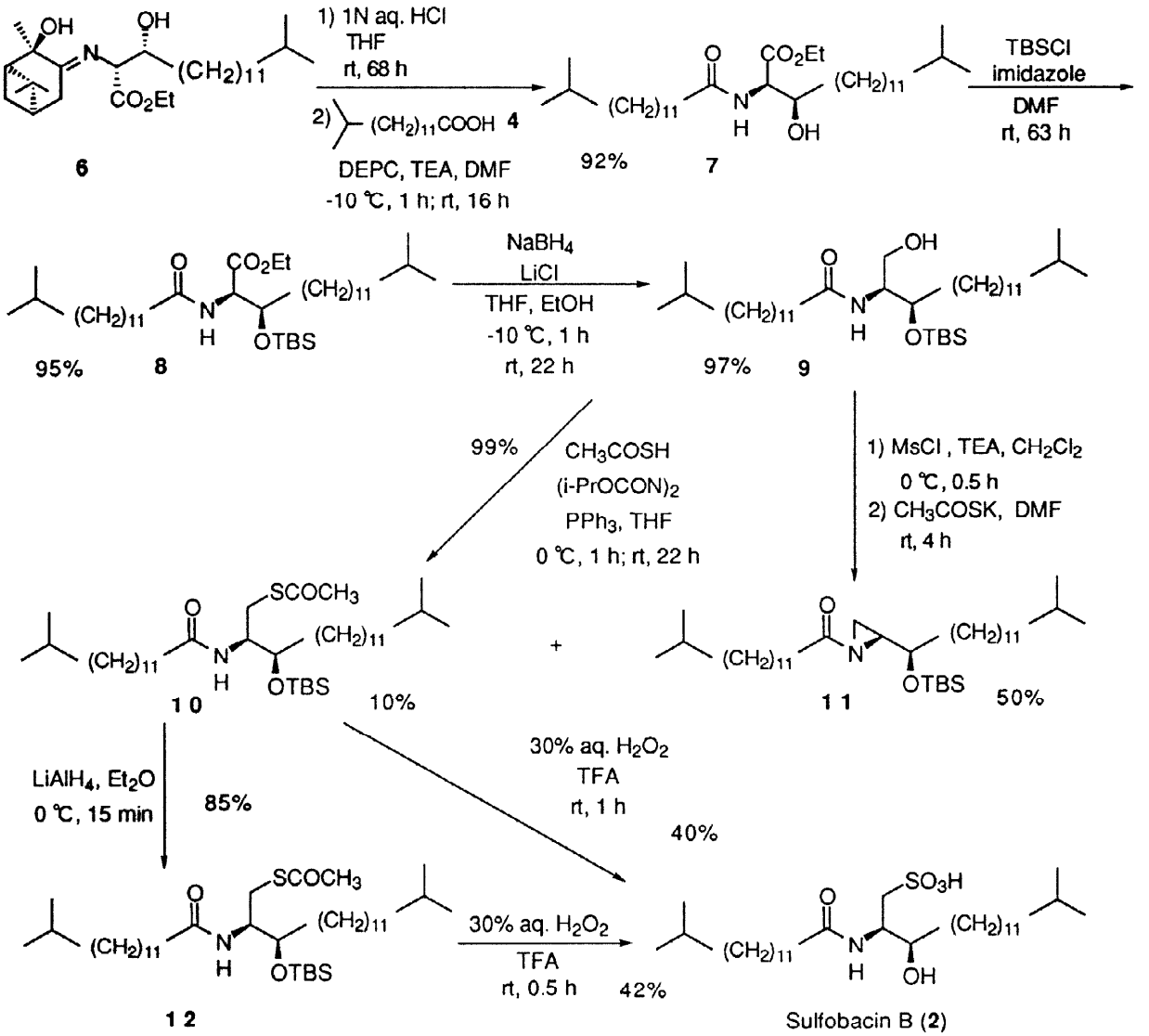
The synthesis route used for sulfobacin A (**1**) was applied to the synthesis of sulfobacin B (**2**). The attempted coupling of the thioacetate **3**,[2] after deprotection, with the carboxylic acid **4**[2] afforded the acylated product **5** in only 37% yield. This unsatisfactory result led us to try another route.



Scheme 1

After removal of the chiral auxiliary, the aldol adduct **6**[2] was smoothly condensed with the carboxylic acid **4**[2] using diethyl phosphorocyanidate (DEPC, $(C_2H_5O)_2P(O)CN$)[3] to give the amide **7**. Treatment of **7** with *tert*-butyldimethylsilyl(TBS) chloride followed by the reduction with $NaBH_4$-LiCl gave the primary alcohol **9**. Replacement of the hydroxy group with the *O*-mesyl one, followed by treatment with potassium thioacetate afforded the desired thioacetate **10** in only 10% yield together with the aziridine **11** in 50 % yield. However, the Mitsunobu reaction[4] of the alcohol **9** with thioacetic acid smoothly proceeded to give the thioacetate **10** in 99% yield. The thioacetate **10** was subjected to either the pertrifluoroacetic acid oxidation or the reduction followed by treatment with pertrifluoroacetic acid to give sulfobacin B (**2**). The synthetic sulfobacin B (**2**) ($[\alpha]_D^{18}$ -18.7° (c 0.14, MeOH) was indistinguishable from the natural one[1] based on $[\alpha]_D^{24}$ -19° (c 0.14, MeOH), IR, ^1H NMR spectra and TLC. Thus, we have completed the first total synthesis of sulfobacin B (**2**) using an alternative method to that for the synthesis of sulfobacin A (**1**).[1]

0040-4039/98/$19.00
PII: S0040-4039(98)01178-2



Scheme 2

Acknowledgments: We are grateful to Dr. T. Kamiyama (Nippon Roche Research Center) for the gift of natural sulfobacin B (**2**). This research was supported in part by a Grant-in-Aid from the Ministry of Education, Science, Sports and Culture, Japan.

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