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PAPER

Total synthesis of noricumazole B establishes D-arabinose as glycan unit†

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The total synthesis of noricumazole B, a secondary metabolite from myxobacteria, was achieved. It established the glycan moiety to be D-α-arabinoside.

Introduction

Noricumazole A (**1a**) and the related icumazole A (**2a**) are isolates from the myxobacterium *Sorangium cellulosum* and the structures including all stereogenic centers were established by spectroscopic methods and finally by total synthesis (Fig. 1).[1] Noricumazole A (**1a**) is only one representative of a small family of analogues isolated from myxobacteria. Additionally, we reported on the isolation of noricumazole B (**1b**) and noricumazole C (**1c**) that are glycosylated derivatives at C-11 and C-18, respectively. Likewise, along with icumazole A (**2a**), we also described icumazole B1 (**2b**) and B2 (**2c**).[1] Preliminary biological screening revealed that noricumazole A (**1a**) is the first natural product reported so far that shows a stabilizing effect on the tetrameric architecture of the potassium channel KcsA thereby blocking it (1–4 μM)[1] and that shows anti-HCV activity.[2]

During our studies on the structure elucidation of this new group of secondary metabolites from myxobacteria, we proposed that the glycan moiety in noricumazole B is an α-linked arabinose. This suggestion was based on the following data. The glycosylation site at C-18 was located from correlations in the HMBC spectrum between the anomeric methine C-1′ and the oxymethine C-18. Based on a comparison of ^{1}H and ^{13}C NMR data of **1b** with the literature values, we proposed an α-*arabino*-furanosyl residue.[3] Firstly, the α-*arabino*-furanosyl configuration was assigned from ^{13}C-NMR fingerprint chemical shift values (δ)[1] and secondly from the small coupling constants $J_{1,2}$ = 1.5 Hz and $J_{2,3}$ = 3.7 Hz and a coupling constant of J = 5.9 Hz between H3′ and H4′ which we interpreted to be a *trans* orientation.[4]

These data and rationales can be regarded as a strong indication for the nature of the glycan unit. However, it is definitely not a proof and does not disclose whether the glycan moiety is D- or L-arabinose. Thus, based on our earlier synthetic work[1] which included the preparation of a small compound library derived from noricumazole A,[2] we now report on the total synthesis of noricumazole B (**1b**) and prove that its glycan moiety is α-D-arabinose. The major new issues we had to consider were orthogonal protection of the carbinol groups at C-18 and C-20, the timing of glycosylation and the choice of the glycosyl donor.

Results and discussion

The principal retrosynthetic plan, that is depicted in Scheme 1, relies on our successful total synthesis of noricumazole A (**1a**).[1]

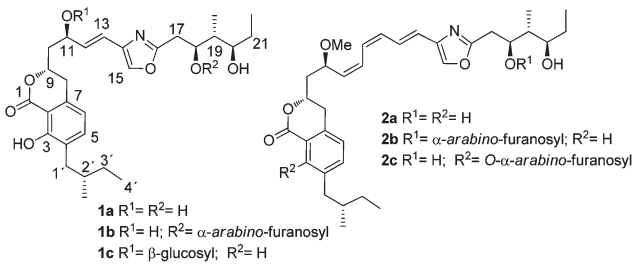
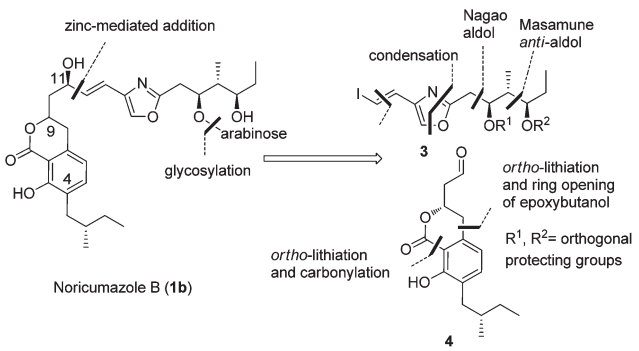


Fig. 1 Noricumazoles A–C (**1a–c**) and icumazoles A–C (**2a–c**) (numbering does not relate to IUPAC; however for clarity reasons the depicted numbering was chosen in this report).



Scheme 1 Retrosynthetic plan.

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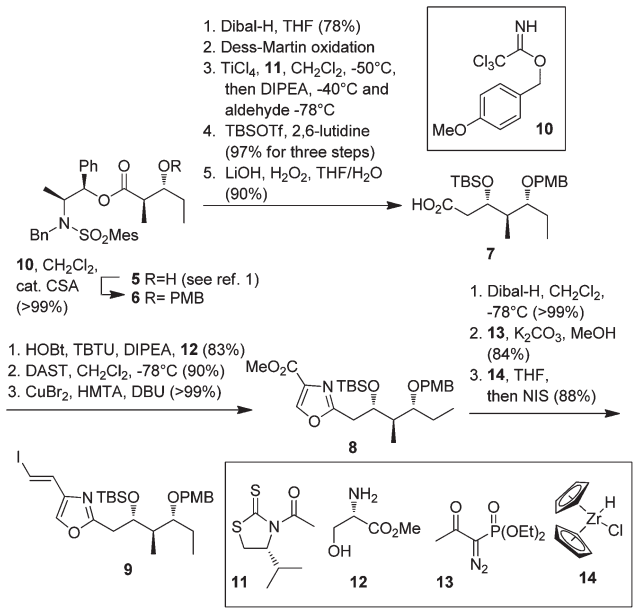
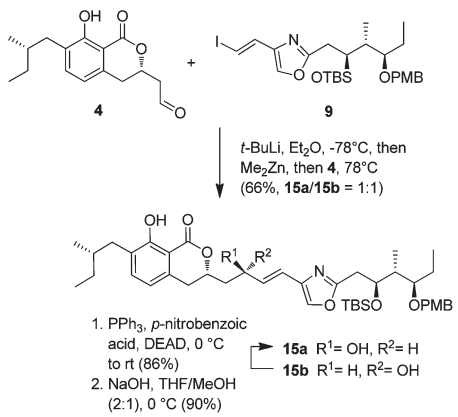


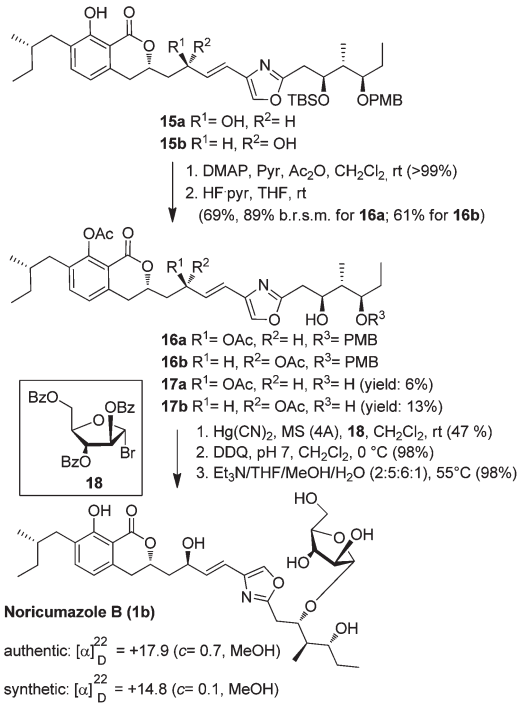
Scheme 2 Synthesis of vinyliodide **9**.



Scheme 3 Coupling of western and eastern fragments **4** and **9** and Mitsunobu inversion.

The synthesis of the eastern fragment started from the published Masamune *anti*-aldol product **5**[5] which was *O*-protected and transformed into the orthogonally protected carboxylate **7** by several standard steps of which the Nagao-aldol reaction[6] was the key step. Coupling with serine-methylester and ring closure gave oxazolidine which was oxidised to oxazole **8** following Barrish and Singh's procedure.[7] Then, the ester was transformed into the homologised vinyliodide **9** by transferring the intermediate aldehyde into the alkyne using the Bestmann–Ohira reagent **13**[8] followed by a hydrozirconation and by *ipso*-iodination.[9]

The western aldehyde **4** was obtained according to our earlier reports[1] so that it could be directly coupled with vinyliodide **9** through vinylzinc addition to aldehyde **4** (Scheme 2). Both epimeric carbinols **15a** and **15b** were formed as a 1 : 1 mixture and were separated by chromatography. Conversion of the undesired coupled product **15b** into the desired compound **15a** was achieved by Mitsunobu inversion[10] followed by ester hydrolysis which led to an increase of the yield from 33% to 59% in favour of the desired carbinol **15a** after coupling (Scheme 3).



Scheme 4 Finalisation of total synthesis.

The free hydroxyl groups in carbinol **15a** were protected as acetates which was followed by desilylation to yield compound **16a**. As a by-product TBS- and PMB-deprotected acetate **17a** was isolated. In order to determine the influence of the stereogenic center at C-11 on the biological activity also the epimer **15b** was deprotected and compared to noricumazole B **1b** (Scheme 4).

Different glycosylation protocols were probed including the use of thioglycosides[11] activated with the reagent systems *N*-iodo succinimide/AgOTf[12] or 1-benzenylsulfinylpiperidine (BSP) and tri-*tert*-butylpyrimidine (TTBP),[13] all of which either gave the desired glycosidation product in low yield or not at all or alternatively led to bis-glycosylation at C-9 as well as at C-11. Obviously, the PMB group is prone to cleavage under these electrophilic activating conditions. Finally, a modification of the Koenigs–Knorr method under Helferich-type conditions[14,15] using commercially available per-*O*-benzylated bromo arabinose **18** was found to be suited to finalise the synthesis of noricumazole B **1b** after global deprotection in a very mild way.[16] Noricumazole B was obtained in 4% overall yield over 19 steps (longest linear sequence) (including Mitsunobu inversion: 21 steps and 6% overall yield).

Conclusions

In summary, the present work discloses the total synthesis of noricumazole B, a secondary metabolite from myxobacterium *Sorangium cellulosum*, thereby establishing the complete structure of noricumazole B whose aglycon is identical to noricumazole A. We demonstrated that the glycan moiety is an α-D-*arabino* furanose.

Experimental

General remarks

^{1}H and ^{13}C NMR spectra were recorded with Bruker DPX-400, AVANCE-400 and DRX-500. The numbering of the protons relates to the numbering chosen in Fig. 1. High resolution mass spectra were obtained with a Micromass LCT *via* loop-mode injection from a Waters (Alliance 2695) HPLC system. Alternatively a Micromass Q-TOF in combination with a Waters Aquity Ultraperformance LC system was employed. Ionization was achieved by ESI or APCI. Modes of ionization, calculated and found mass are given. RP-HPLC was performed on RP-CN with CH_3CN–H_2O gradient elution. CD spectra were obtained using a Jasco J-810 circular dichroism spectropolarimeter. Analytical thin-layer chromatography was performed using precoated silica gel 60 F_{254} plates (Merck, Darmstadt). Flash column chromatography was performed on Merck silica gel (230–400 mesh). Unless otherwise noted, all reactions were carried out under an atmosphere of nitrogen in dry glassware. Commercially available reagents and dry solvents were used as received.

Masamune ester 6. To a solution of alcohol **5**[5] (11.3 g, 21.0 mmol, 1.0 equiv.) in CH_2Cl_2 (250 mL) were sequentially added 4-methoxybenzyl 2,2,2-trichloroacetimidate (13.1 g, 46.5 mmol, 2.2 equiv.) and camphor-10-sulfonic acid (0.9 g, 3.7 mmol, 0.2 equiv.) at room temperature. The reaction mixture was stirred for 16 h at room temperature and terminated by addition of sat. aq. $NaHCO_3$ solution. The mixture was extracted with CH_2Cl_2 and the combined organic extracts were dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (petroleum ether–ethyl acetate = 10 : 1 → 3 : 1) to furnish the PMB-ether **6** as a light yellow oil (19.4 g, 29.6 mmol, quant).

$[\alpha]_D^{25}$ = +35.0 (*c* 1.0, $CDCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$, $CHCl_3$ = 7.26 ppm) δ 7.35–7.08 (m, 12H, Bn, Mes, Ph), 6.79 (d, *J* = 7.9 Hz, 2H, PMB), 6.74 (d, *J* = 7.9 Hz, 2H, PMB), 5.72 (d, *J* = 4.4 Hz, 1H, OC*H*Ph), 4.69 (d, *J* = 16.0 Hz, 1H, Bn), 4.42 (d, *J* = 11.0 Hz, 1H, PMB), 4.41 (d, *J* = 16.0 Hz, 1H, Bn), 4.38 (d, *J* = 11.0 Hz, 1H, PMB), 3.97 (dddd, *J* = 7.1, 7.1, 7.1, 4.4 Hz, 1H, H-9), 3.77 (s, 3H, PMB), 3.64 (ddd, *J* = 7.5, 6.4, 3.7 Hz, 1H, H-8), 2.75 (quin, *J* = 7.5 Hz, 1H, H-19), 2.46 (s, 6H, Mes), 2.30 (s, 3H, Mes), 1.60 (dddd, *J* = 14.0, 7.3, 7.3, 3.7 Hz, 1H, H-21), 1.48 (dddd, *J* = 14.0, 7.3, 7.3, 6.4 Hz, 1H, H-21′), 1.07 (d, *J* = 7.5 Hz, 3H, H-23), 1.03 (d, *J* = 7.1 Hz, 3H, NCHC*H*$_3$), 0.91 (t, *J* = 7.3 Hz, 3H, H-22) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 77.0 ppm) δ 173.7 (q, C-18), 159.1 (q, PMB), 142.4 (q, Mes), 140.3 (q, Ph), 138.9 (q, Mes), 138.5 (q, Mes), 133.5 (q, Mes), 132.1 (2× t,), 130.5 (q, Bn), 129.4 (2× t, PMB), 129.3 (2× t, Bn), 129.26 (2× t, Mes), 128.3 (t, Ph), 128.2 (t, Ph), 127.9 (2× t, Bn), 127.7 (t, Ph), 127.0 (t, Bn), 125.9 (2× t, Ph), 113.7 (2× t, PMB), 80.6 (t, C-20), 77.9 (t, O*C*HPh), 71.4 (s, PMB), 56.8 (t, N*C*CH$_3$), 55.3 (p, PMB), 48.1 (s, Bn), 42.8 (t, C-19), 29.7 (s, C-21), 22.3 (2× p, Mes), 20.9 (p, Mes), 13.6 (p, C-23), 12.6 (p, NC*C*H$_3$), 8.3 (p, C-22) ppm; HRMS (ESI): *m*/*z*: calculated for $C_{39}H_{47}NO_6SNa$: 680.3022 $[M + Na]^+$, found: 680.3016 $[M + Na]^+$.

(2*S*,3*R*)-3-(4-Methoxybenzyloxy)-2-methylpentan-1-ole (S1). To a solution of PMB-ether **6** (9.7 g, 14.7 mmol, 1.0 equiv.) in THF (100 mL) was added DIBAL-H (1.0 mol L^{-1} in hexane, 44 mL, 44.0 mmol, 3.0 equiv.) at −78 °C. After 1 h, the reaction mixture was warmed up to −20 °C. After 2 h a sat. aq. solution of Rochelle's salt was added and the mixture was stirred for 30 min at room temperature. After extraction with CH_2Cl_2 the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether–ethyl acetate = 5 : 1) furnished alcohol **S1** as a colorless oil (3.2 g, 13.4 mmol, 91%).

$[\alpha]_D^{20}$ = −39.8 (*c* 1.0, $CDCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$, $CHCl_3$ = 7.26 ppm) δ 7.26 (d, *J* = 8.5 Hz, 2H, PMB), 6.88 (d, *J* = 8.5 Hz, 2H, PMB), 4.56 (d, *J* = 10.9 Hz, 1H, PMB), 4.37 (d, *J* = 10.9 Hz, 1H, PMB), 3.80 (s, 3H, PMB), 3.64 (dd, *J* = 10.9, 3.8 Hz, 1H, H-18), 3.55 (dd, *J* = 10.9, 6.9 Hz, 1H, H-18′), 3.35 (ddd, *J* = 6.9, 4.8, 4.8 Hz, 1H, H-20), 2.69 (bs, 1H, O*H*), 1.90 (dsext, *J* = 6.9, 3.8 Hz, 1H, H-19), 1.74 (ddddd, *J* = 14.7, 7.5, 7.5, 7.5, 4.8 Hz, 1H, H-21), 1.60 (ddddd, *J* = 14.7, 7.5, 7.5, 7.5, 4.8 Hz, 1H, H-21′), 0.93 (t, *J* = 7.5 Hz, 3H, H-22), 0.89 (d, *J* = 6.9 Hz, 3H, H-23) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 77.0 ppm) δ 159.2 (q, PMB), 130.3 (q, PMB), 129.4 (2× t, PMB), 113.9 (2× t, PMB), 84.7 (t, C-20), 71.2 (s, PMB), 67.0 (s, C-18), 55.2 (p, PMB), 37.1 (t, C-19), 23.0 (s, C-21), 14.1 (t, C-23), 8.3 (p, C-22); HRMS (ESI): *m*/*z*: calculated for $C_{14}H_{22}O_3Na$: 261.1467 $[M + Na]^+$, found: 261.1471 $[M + Na]^+$.

(2*S*,3*R*)-3-(4-Methoxybenzyloxy)-2-methylpentanal (S2). To a solution of carbinol **S1** (1.6 g, 6.5 mmol, 1.0 equiv.) in CH_2Cl_2 (120 mL) were sequentially added $NaHCO_3$ (2.7 g, 32.5 mmol, 5.0 equiv.) and Dess–Martin periodinane (4.1 g, 9.8 mmol, 1.5 equiv.) at room temperature. After 30 min, the reaction was terminated by addition of a sat. aq. $Na_2S_2O_3$ solution and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The crude aldehyde **S2** was used in the next step without further purification.

(3*S*,4*R*,5*R*)-3-(*tert*-Butyldimethylsilyloxy)-1-[(*R*)-4-isopropyl-2-thioxothiazolidin-3-yl]-5-(4-methoxybenzyloxy)-4-methylheptan-1-one (S3). $TiCl_4$ (1.3 mL, 11.7 mmol, 1.8 equiv.) was added to a solution of 1-[(*R*)-4-isopropyl-2-thioxothiazolidin-3-yl]ethanone (**11**)[6] (2.3 g, 11.1 mmol, 1.7 equiv.) in CH_2Cl_2 (250 mL) at −50 °C. After stirring for 20 min DIPEA (1.9 mL, 11.7 mmol, 1.8 equiv.) was added to the reaction mixture. After stirring for 2 h at −40 °C the reaction mixture was cooled to −78 °C and aldehyde **S2** (1.5 g, 6.5 mmol, 1.0 equiv.) in CH_2Cl_2 (80 mL) was added. After 2 h the reaction was terminated by addition of a sat. aq. NH_4Cl solution and was warmed up to room temperature. The aqueous layer was extracted with CH_2Cl_2 and the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure to furnish the crude product as an orange oil.

This material was dissolved in CH_2Cl_2 (250 mL) and 2,6-lutidine (1.3 mL, 11.4 mmol, 1.8 equiv.) as well as TBSOTf (2.1 mL, 9.1 mmol, 1.4 equiv.) were sequentially added at −78 °C. The mixture was warmed to room temperature and stirred for 3 h. The reaction was terminated by addition of a sat. aq. NH_4Cl solution and extracted with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated under

reduced pressure. Purification by flash chromatography (petroleum ether–ethyl acetate = 15 : 1) yields the TBS-PMB-ether **S3** as a yellow oil (3.5 g, 6.3 mmol, 97%).

$[\alpha]_D^{30}$ = −200.5 (*c* 2.0, $CDCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$, $CHCl_3$ = 7.26 ppm) δ 7.28 (d, *J* = 8.7 Hz, 2H, PMB), 6.85 (d, *J* = 8.7 Hz, 2H, PMB), 5.04 [pt, *J* = 6.6 Hz, 1H, C*H*$(CH_3)_2$], 4.69 (ddd, *J* = 9.2, 3.8, 2.2 Hz, 1H, H-18), 4.46 (d, *J* = 10.9 Hz, 1H, PMB), 4.35 (d, *J* = 10.9 Hz, 1H, PMB), 3.79 (s, 3H, PMB), 3.57 (dd, *J* = 17.1, 9.2 Hz, 1H, H-17), 3.46 (dd, *J* = 11.4, 6.6 Hz, 1H, SCH_2), 3.20 (ddd, *J* = 7.7, 6.6, 3.9 Hz, 1H, H-20), 3.01 (dd, *J* = 11.4, 0.7 Hz, 1H, SCH_2), 2.97 (dd, *J* = 17.1, 2.2 Hz, 1H, H-17′), 2.40 [psext, *J* = 6.6 Hz, 1H, C*H*$(CH_3)_2$], 1.95 (ddq, *J* = 14.6, 6.6, 3.8 Hz, 1H, H-19), 1.70 (ddq, *J* = 14.6, 14.2, 3.9 Hz, 1H, H-21), 1.49 (ddq, *J* = 14.2, 7.7, 7.1 Hz, 1H, H-21′), 1.06 [d, *J* = 6.6 Hz, 3H, CH(CH_3)$_2$], 0.97 [d, *J* = 6.6 Hz, 3H, CH(CH_3)$_2$], 0.93 (t, *J* = 7.1 Hz, 3H, H-22), 0.84 (s, 9H, TBS), 0.82 (d, *J* = 7.2 Hz, 3H, H-23), 0.08 (s, 3H, TBS), 0.02 (s, 3H, TBS) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 77.0 ppm) δ 202.8 (q, *C*S_2), 172.5 (q, N*C*O), 159.0 (q, PMB), 30.9 (q, PMB), 129.4 (2× t, PMB), 113.7 (2× t, PMB), 80.7 (t, C-20), 71.7 (t, N*C*CH), 70.9 (s, PMB), 69.3 (t, C-18), 55.2 (p, PMB), 41.8 (t, C-19), 41.5 (s, C-17), 30.9 [t, *C*H$(CH_3)_2$], 30.8 (s, S*C*H_2), 25.8 (3× p, TBS), 23.1 (s, C-21), 19.2 [p, CH(*C*H_3)$_2$], 18.0 (q, TBS), 17.9 [p, CH(*C*H_3)$_2$], 10.7 (p, C-23), 8.7 (p, C-22), −4.66 (p, TBS), −4.7 (p, TBS) ppm; HRMS (ESI): *m*/*z*: calculated for $C_{28}H_{47}NO_4S_2SiNa$: 576.2614 $[M + Na]^+$, found: 576.2604 $[M + Na]^+$.

(3*S*,4*R*,5*R*)-3-(*tert*-Butyldimethylsilyloxy)-5-(4-methoxybenzyloxy)-4-methylheptanoic acid (7). To a solution of **S3** (198 mg, 0.4 mmol, 1.0 equiv.) in THF–H_2O (4 : 1, 8.3 mL) were sequentially added H_2O_2 (30%, 88 μL, 2.9 mmol, 8.0 equiv.) and 1 N aqueous LiOH (1.4 mL, *c* = 1 mol L^{-1}, 1.4 mmol, 4.0 equiv.) at 0 °C and the reaction mixture was allowed to warm to room temperature. After 3 h, the reaction was terminated by addition of a sat. aq. $Na_2S_2O_3$ solution and H_2O and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether–ethyl acetate = 5 : 1) furnished carboxylic acid **7** as a colorless oil (132 mg, 0.5 mmol, 90%).

$[\alpha]_D^{23}$ = −22.3 (*c* 1.0, $CDCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$, $CHCl_3$ = 7.26 ppm) δ 7.27 (d, *J* = 8.7 Hz, 2H, PMB), 6.86 (d, *J* = 8.7 Hz, 2H, PMB), 4.48 (d, *J* = 11.1 Hz, 1H, PMB), 4.45 (dt, *J* = 7.9, 4.2 Hz, 1H, H-18), 4.35 (d, *J* = 11.1 Hz, 1H, PMB), 3.79 (s, 3H, PMB), 3.23 (ddd, *J* = 7.5, 4.6, 4.2 Hz, 1H, H-20), 2.46 (dd, *J* = 15.0, 4.2 Hz, 1H, H-17), 2.39 (dd, *J* = 15.0, 7.9 Hz, 1H, H-17′), 1.98 (ddq, *J* = 7.9, 7.3, 4.2 1H, H-19), 1.69 (pdddd, *J* = 14.7, 14.5, 7.3, 4.6 Hz, 1H, H-21), 1.49 (pdddd, *J* = 14.5, 13.2, 7.5, 7.3 Hz, 1H, H-21′), 0.93 (t, *J* = 7.3 Hz, 3H, H-22), 0.87 (s, 9H, TBS), 0.86 (d, *J* = 7.3 Hz, 3H, H-23), 0.06 (s, 3H, TBS), 0.058 (s, 3H, TBS) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 77.0 ppm) δ 177.9 (q, C-16), 159.1 (q, PMB), 130.7 (q, PMB), 129.4 (2× t, PMB), 113.7 (2× t, PMB), 80.2 (t, C-20), 70.7 (s, PMB), 69.8 (t, C-18), 55.2 (p, PMB), 41.3 (t, C-19), 38.4 (s, C-17), 25.8 (3× p, TBS), 22.7 (s, C-21), 18.0 (q, TBS), 10.5 (p, C-23), 8.5 (p, C-22), −4.7 (p, TBS), −4.8 (p, TBS) ppm; HRMS (ESI): *m*/*z*: calculated for $C_{22}H_{37}O_5Si$: 409.2410 $[M - H]^-$, found: 409.2417 $[M - H]^-$.

(*R*)-Methyl-2-[(3*S*,4*R*,5*R*)-3-(*tert*-butyldimethylsilyloxy)-5-(4-methoxybenzyloxy)-4-methylheptanamido]-3-hydroxypropanoate (S4). To a solution of TBTU (103 mg, 0.3 mmol, 1.0 equiv.) and HOBt (49 mg, 0.3 mmol, 1.0 equiv.) in CH_2Cl_2 (2 mL) were sequentially added acid **7** (132 mg, 0.3 mmol, 1.0 equiv.) in CH_2Cl_2 (2 mL) and DIPEA (0.2 mL, 1.0 mmol, 3.0 equiv.). After stirring for 2 h at room temperature L-serine methyl ester (**12**) (60 mg, 0.4 mmol, 1.2 equiv.) was added to the reaction mixture and stirring was continued for 3 days at room temperature. The reaction was terminated by addition of a sat. aq. NH_4Cl solution and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether–ethyl acetate = 3 : 1 → 1 : 1) furnished amide **S4** as a colorless solid (136 mg, 0.3 mmol, 83%).

M.p. = 83–84 °C; $[\alpha]_D^{20}$ = +7.0 (*c* 1.0, $CDCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$, $CHCl_3$ = 7.26 ppm) δ 7.29 (d, *J* = 8.5 Hz, 2H, PMB), 7.11 (d, *J* = 7.3 Hz, 1H, N*H*), 6.86 (d, *J* = 8.5 Hz, 2H, PMB), 4.63 (ddd, *J* = 7.3, 3.9, 3.8 Hz, 1H, H-14), 4.43 (d, *J* = 10.9 Hz, 1H, PMB), 4.41 (d, *J* = 10.9 Hz, 1H, PMB), 4.20 (q, *J* = 5.9 Hz, 1H, H-18), 3.89 (dd, *J* = 11.0, 3.9 Hz, 1H, H-15), 3.81 (dd, *J* = 11.0, 3.8 Hz, 1H, H-15′), 3.79 (s, 3H, PMB), 3.74 (s, 3H, CH_3O), 3.42 (ddd, *J* = 6.9, 6.7, 3.6 Hz, 1H, H-20), 2.55 (dd, *J* = 14.3, 5.9 Hz, 1H, H-17), 2.47 (bs, 1H, O*H*), 2.34 (dd, *J* = 14.3, 5.9 Hz, 1H, H-17′), 2.13 (pdddd, *J* = 12.4, 6.7, 6.7, 5.9 Hz, 1H, H-19), 1.62 (ddddd, *J* = 14.4, 7.7, 7.3, 6.9, 3.6 Hz, 1H, H-21), 1.45 (dquin, *J* = 14.4, 6.8 Hz, 1H, H-21′), 0.92 (t, *J* = 7.7 Hz, 3H, H-22), 0.90 (s, 9H, TBS), 0.85 (d, *J* = 6.8 Hz, 3H, H-23), 0.08 (s, 3H, TBS), 0.07 (s, 3H, TBS) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 77.0 ppm) δ 172.0 (q, C-16), 170.8 (q, C-13), 159.1 (q, PMB), 130.9 (q, PMB), 129.6 (2× t, PMB), 113.7 (2× t, PMB), 80.0 (t, C-20), 71.2 (t, C-18), 70.7 (s, PMB), 63.5 (s, C-15), 55.2 (p, PMB), 54.6 (t, C-14), 52.5 (p, *C*H_3O), 41.4 (s, C-17), 39.9 (t, C-19), 25.8 (3× p, TBS), 22.4 (s, C-21), 18.0 (q, TBS), 11.7 (p, C-23), 8.7 (p, C-22), −4.5 (p, TBS), −4.8 (p, TBS) ppm; HRMS (ESI): *m*/*z*: calculated for $C_{26}H_{46}NO_7Si$: 512.3044 $[M + H]^+$, found: 512.3034 $[M + H]^+$.

(*R*)-Methyl-2-[(2*S*,3*R*,4*R*)-2-(*tert*-butyldimethylsilyloxy)-4-(4-methoxybenzyloxy)-3-methylhexyl]-4,5-dihydrooxazol-4-carboxylate (S5). To a solution of **S4** (1.7 g, 3.2 mmol, 1.0 equiv.) in CH_2Cl_2 (50 mL) was added DAST (0.5 mL, 3.9 mmol, 1.2 equiv.) at −78 °C. After stirring for 2 h at −78 °C K_2CO_3 (807 mg, 5.8 mmol, 1.8 equiv.) and a sat. aq. K_2CO_3 solution were added and the reaction mixture was allowed to warm up to room temperature. After extraction with CH_2Cl_2, the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether–ethyl amine = 4 : 1) furnished oxazolidine **S5** as a colorless oil (1.3 g, 2.7 mmol, 82%).

$[\alpha]_D^{20}$ = +32.1 (*c* 2.0, $CDCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$, $CHCl_3$ = 7.26 ppm) δ 7.28 (d, *J* = 8.6 Hz, 2H, PMB), 6.85 (d, *J* = 8.6 Hz, 2H, PMB), 4.70 (dd, *J* = 11.0, 8.3 Hz, 1H, H-15), 4.49 (dd, *J* = 8.3, 6.0 Hz, 1H, H-15′), 4.44 (d, *J* = 10.7 Hz, 1H, PMB), 4.41 (ddd, *J* = 6.9, 4.4, 2.9 Hz, 1H, H-18), 4.36 (d, *J* = 10.7 Hz, 1H, PMB), 4.34 (dd, *J* = 11.0, 6.0 Hz, 1H, H-14), 3.79 (s, 3H, PMB), 3.75 (s, 3H, CH_3O), 3.23 (ddd, *J* = 7.1, 7.0, 4.9 Hz, 1H, H-20), 2.46 (dd, *J* = 14.5, 6.9 Hz, 1H, H-17), 2.44 (dd, *J* = 14.5, 2.9 Hz, 1H, H-17′), 1.99 (dddd, *J* = 14.3, 7.1, 7.0,

4.4 Hz, 1H, H-19), 1.67 (dddd, J = 14.6, 14.6, 7.1, 4.1 Hz, 1H, H-21), 1.51–1.41 (m, 1H, H-21′), 0.91 (t, J = 7.5 Hz, 3H, H-22), 0.87 (d, J = 7.2 Hz, 3H, H-23), 0.84 (s, 9H, TBS), 0.02 (s, 3H, TBS), −0.00 (s, 3H, TBS) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 77.0 ppm) δ 171.6 (q, C-16), 169.2 (q, C-2), 159.0 (q, PMB), 131.1 (q, PMB), 129.2 (2× t, PMB), 113.7 (2× t, PMB), 80.5 (t, C-20), 70.7 (s, PMB), 69.9 (t, C-18), 68.9 (t, C-14), 68.2 (s, C-15), 55.2 (p, PMB), 52.5 (p, CH_3O), 41.4 (t, C-19), 32.2 (s, C-17), 25.7 (3× p, TBS), 22.9 (s, C-21), 17.9 (q, TBS), 10.1 (p, C-22), 8.7 (p, C-22), −4.6 (p, TBS), −4.9 (p, TBS) ppm; HRMS (ESI): m/z: calculated for $C_{26}H_{44}NO_6Si$: 494.2938 $[M + H]^+$, found: 494.2932 $[M + H]^+$.

Methyl-2-[(2*S*,3*R*,4*R*)-2-(*tert*-butyldimethylsilyloxy)-4-(methoxybenzyloxy)-3-methylhexyl]oxazol-4-carboxylate (8). To a suspension of anhydrous $CuBr_2$ (0.9 g, 4.1 mmol, 4.0 equiv.) in CH_2Cl_2 (15 mL) were added HMTA (0.6 g, 4.1 mmol, 4.0 equiv.) and DBU (0.6 mL, 4.1 mmol, 4.0 equiv.). A solution of **S5** (0.5 g, 1.0 mmol, 1.0 equiv.) in CH_2Cl_2 (15 mL) was added to the suspension and the reaction mixture was stirred for 2 h at room temperature. The organic solvent was removed under reduced pressure and ethyl acetate and a solution of sat. aq. NH_4Cl/30% NH_3 (1 : 1, 100 mL) were sequentially added to the oily residue. The aqueous layer was extracted with ethyl acetate and the combined organic extracts were sequentially washed with a solution of sat. aq. NH_4Cl/30% NH_3 (1 : 1; 3×), 10% citric acid, sat. aq. $NaHCO_3$ and NaCl. The organic extract were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether–ethyl acetate = 5 : 1) furnished oxazole **8** as a colorless oil (0.5 g, 1.0 mmol, quant).

$[\alpha]_D^{24}$ = −18.1 (c 0.4, $CDCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$, $CHCl_3$ = 7.26 ppm) δ 8.14 (s, 1H, H-15), 7.28 (d, J = 8.5 Hz, 2H, PMB), 6.85 (d, J = 8.5 Hz, 2H, PMB), 4.48 (d, J = 11.3 Hz, 1H, PMB), 4.47 (ddd, J = 8.4, 4.7, 3.8 Hz, 1H, H-18), 4.34 (d, J = 11.3 Hz, 1H, PMB), 3.90 (s, 3H, CH_3O), 3.79 (s, 3H, PMB), 3.27 (ddd, J = 7.3, 5.8, 4.2 Hz, 1H, H-20), 2.91 (dd, J = 14.7, 8.4 Hz, 1H, H-17), 2.87 (dd, J = 14.7, 4.7 Hz, 1H, H-17′), 1.98 (pdddd, J = 14.3, 7.3, 7.0, 3.8 Hz, 1H, H-19), 1.71 (pdddd, J = 14.7, 14.7, 7.3, 4.2 Hz, 1H, H-21), 1.44–1.55 (m, 1H, H-21′), 0.92 (t, J = 7.3 Hz, 3H, H-22), 0.91 (d, J = 7.0 Hz, 3H, H-23), 0.78 (s, 9H, TBS), −0.02 (s, 3H, TBS), −0.23 (s, 3H, TBS) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 77.0 ppm) δ 164.6 (q, C-13), 161.8 (q, PMB), 159.0 (q, C-16), 143.6 (t, C-15), 133.2 (q, C-14), 131.0 (q, PMB), 129.2 (2× t, PMB), 113.7 (2× t, PMB), 80.5 (t, C-20), 70.8 (s, PMB), 70.7 (t, C-18), 55.2 (p, CH_3O), 52.0 (p, PMB), 41.5 (t, C-19), 32.1 (s, C-17), 25.6 (3× p, TBS), 22.8 (s, C-21), 17.8 (q, TBS), 10.2 (p, C-23), 8.6 (p, C-22), −4.7 (p, TBS), −5.2 (p, TBS) ppm; HRMS (ESI): m/z: calculated for $C_{26}H_{42}NO_6Si$: 492.2781 $[M + H]^+$, found: 492.2780 $[M + H]^+$.

2-[(2*S*,3*R*,4*R*)-2-(*tert*-Butyldimethylsilyloxy)-4-(methoxybenzyloxy)-3-methylhexyl]oxazol-4-carbaldehyde (S6). To a solution of **8** (250 mg, 1.0 mmol, 1.0 equiv.) in CH_2Cl_2 (15 mL) was added Dibal-H (1.2 mol L^{-1} in toluene, 3.0 mL, 3.6 mmol, 6.0 equiv.) at −78 °C within 45 min. After 30 min the reaction was terminated by addition of methanol. A saturated aqueous solution of Rochelle's salt was added and the mixture was stirred at room temperature overnight. After extraction with CH_2Cl_2, the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether–ethyl acetate = 6 : 1 → 1 : 1) furnished aldehyde **S6** as a colorless oil (438 mg, 0.9 mmol, 94%).

$[\alpha]_D^{20}$ = −18.1 (c 1.0, $CDCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$, $CHCl_3$ = 7.26 ppm) δ 9.91 (s, 1H, H-13), 8.15 (s, 1H, H-15), 7.29 (d, J = 8.9 Hz, 2H, PMB), 6.85 (d, J = 8.9 Hz, 2H, PMB), 4.54–4.48 (m, 1H, H-18), 4.51 (d, J = 11.1 Hz, 1H, PMB), 4.35 (d, J = 11.1 Hz, 1H, PMB), 3.79 (s, 3H, PMB), 3.26 (ddd, J = 7.2, 5.5, 4.7 Hz, 1H, H-20), 2.90–2.85 (m, 2H, H-17), 1.99 (pdddd, J = 14.3, 7.2, 7.2, 4.1 Hz, 1H, H-19), 1.78–1.66 (m, 1H, H-21), 1.57–1.48 (m, 1H, H-21′), 0.94 (t, J = 7.3 Hz, 3H, H-22), 0.92 (d, J = 7.2 Hz, 3H, H-23), 0.78 (s, 9H, TBS), −0.01 (s, 3H, TBS), −0.23 (s, 3H, TBS) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 77.0 ppm) δ 184.2 (t, C-13), 165.3 (q, PMB), 159.0 (q, C-16), 143.8 (t, C-15), 140.9 (q, C-14), 130.9 (q, PMB), 129.2 (2× t, PMB), 113.7 (2× t, PMB), 80.4 (t, C-20), 70.8 (s, C-18), 70.7 (s, PMB), 55.2 (p, PMB), 41.4 (t, C-19), 31.9 (s, C-17), 25.6 (3× p, TBS), 22.8 (s, C-21), 17.8 (q, TBS), 10.2 (p, C-23), 8.5 (p, C-22), −4.7 (p, TBS), −5.2 (p, TBS) ppm; HRMS (ESI): m/z: calculated for $C_{25}H_{40}NO_5Si$: 462.2676 $[M + H]^+$, found: 462.2676 $[M + H]^+$.

2-[(2*S*,3*R*,4*R*)-2-(*tert*-Butyldimethylsilyloxy)-4-(4-methoxybenzyloxy)-3-methylhexyl]-4-ethynyloxazole (S7). To a solution of **S6** (438 mg, 0.9 mmol, 1.0 equiv.) in MeOH (10 mL) were sequentially added K_2CO_3 (328 mg, 2.4 mmol, 2.5 equiv.) and the Ohira–Bestmann reagent **13**[8] (456 mg, 2.4 mmol, 1.5 equiv.) at 0 °C. The reaction mixture was allowed to warm to room temperature overnight and was terminated by addition of Et_2O and H_2O. After extraction with Et_2O, the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether–ethyl acetate = 6 : 1) furnished alkine **S7** as a colorless oil (376 mg, 0.8 mmol, 84%).

$[\alpha]_D^{23}$ = −11.2 (c 1.0, $CDCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$, $CHCl_3$ = 7.26 ppm) δ 7.71 (s, 1H, Ar-O*H*), 7.28 (d, J = 8.9 Hz, 2H, PMB), 6.86 (d, J = 8.9 Hz, 2H, PMB), 4.47 (d, J = 11.3 Hz, 1H, PMB), 4.44 (ddd, J = 5.9, 5.9, 4.5 Hz, 1H, H-18), 4.35 (d, J = 11.3 Hz, 1H, PMB), 3.79 (s, 3H, PMB), 3.26 (ddd, J = 7.3, 6.0, 4.3 Hz, 1H, H-20), 3.16 (s, 1H, H-12), 2.84–2.82 (m, 2H, H-17), 1.98 (ddd, J = 7.3, 7.1, 4.5 Hz, 1H, H-19), 1.76–1.66 (m, 1H, H-21), 1.54–1.46 (m, 1H, H-21′), 0.93 (t, J = 8.0 Hz, 3H, H-22), 0.91 (d, J = 7.1 Hz, 3H, H-23), 0.80 (s, 9H), −0.02 (s, 3H), −0.19 (s, 3H) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 77.0 ppm) δ 163.7 (q, C-16), 159.0 (q, PMB), 141.6 (t, C-15), 131.0 (q, PMB), 129.3 (2× t, PMB), 122.8 (q, C-14), 113.7 (2× t, PMB), 80.5 (q, C-13), 80.4 (t, C-20), 74.0 (t, C-12), 70.9 (s, C-18), 70.8 (t, PMB), 55.2 (p, PMB), 41.4 (t, C-19), 32.1 (s, C-17), 25.7 (3× p, TBS), 22.8 (s, C-21), 17.8 (q, TBS), 10.2 (p, C-23), 8.7 (p, C-22), −4.8 (p, TBS), −5.2 (p, TBS) ppm; HRMS (ESI): m/z: calculated for $C_{26}H_{40}NO_4Si$: 458.2727 $[M + H]^+$, found: 458.2724 $[M + H]^+$.

2-{(2*S*,3*R*,4*R*)-2-(*tert*-Butyldimethylsilyloxy)-4-[(4-methoxybenzyl)oxy]-3-methylhexyl}-4-[(*E*)-2-iodovinyl]oxazole (9). To a suspension of Schwartz reagent **14** (433 mg, 1.7 mmol, 2.5 equiv.) in THF (7 mL) was added **S7** (308 mg, 0.7 mmol, 1.0

equiv.) in THF (7 mL) at 0 °C. After 1 h NIS (378 mg, 1.7 mmol, 2.5 equiv.) in THF (8 mL) was added at −78 °C and the reaction mixture was stirred in the dark for 40 min. The reaction was terminated by addition of a sat. aq. $Na_2S_2O_3$ solution and the aqueous layer was extracted with Et_2O. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether–ethyl acetate = 12 : 1) furnished vinyliodide **9** as a colorless oil (348 mg, 0.6 mmol, 88%).

$[\alpha]_D^{23}$ = −12.5 (*c* 1.0, $CDCl_3$); ^{1}H-NMR (400 MHz, C_6D_6, C_6H_6 = 7.16 ppm) δ 7.35 (d, *J* = 8.8 Hz, 2H, PMB), 7.27 (dd, *J* = 14.4, 0.6 Hz, 1H, H-13), 6.93 (dd, *J* = 14.4, 0.4 Hz, 1H, H-12), 6.87 (d, *J* = 8.8 Hz, 2H, PMB), 6.74 (s, 1H, H-15), 4.73 (ddd, *J* = 8.7, 3.8, 3.6 Hz, 1H, H-18), 4.41 (d, *J* = 11.1 Hz, 1H, PMB), 4.22 (d, *J* = 11.1 Hz, 1H, PMB), 3.34 (s, 3H, PMB), 3.04 (ddd, *J* = 7.9, 4.8, 4.3 Hz, 1H, H-20), 2.74 (dd, *J* = 14.6, 8.7 Hz, 1H, H-17), 2.68 (dd, *J* = 14.6, 3.6 Hz, 1H, H-17′), 2.12–2.01 (m, 1H, H-19), 1.59 (pdddd, *J* = 21.9, 7.4, 7.4, 4.3 Hz, 1H, H-21), 1.36 (pdddd, *J* = 21.9, 7.4, 7.4, 4.8 Hz, 1H, H-21′), 0.94 (t, *J* = 7.4 Hz, 3H, H-22), 0.93 (s, 9H, TBS), 0.84 (d, *J* = 7.0 Hz, 3H, H-23), 0.04 (s, 3H, TBS), −0.13 (s, 3H, TBS) ppm; ^{13}C-NMR (100 MHz, C_6D_6, C_6H_6 = 128.0 ppm) δ 164.3 (q, PMB), 159.8 (q, C-16), 140.2 (t, C-13), 134.3 (q, C-14), 133.9 (t, C-15), 131.4 (q, PMB), 129.7 (2× t, PMB), 114.1 (2× t, PMB), 80.4 (t, C-20), 78.3 (t, C-18), 71.4 (t, C-12), 71.1 (s, PMB), 54.8 (p, PMB), 42.0 (t, C-19), 32.0 (s, C-17), 26.0 (3× p, TBS), 22.9 (s, C-21), 18.2 (q, TBS), 10.1 (p, C-23), 8.3 (p, C-22), −4.6 (p, TBS), −5.0 (q, TBS) ppm; HRMS (ESI): *m*/*z*: calculated for $C_{26}H_{40}NO_4ISiNa$: 608.1669 $[M + Na]^+$, found: 608.1674 $[M + Na]^+$.

18-TBS-20-PMB-protected noricumazole A 15a and 11-*epi*-18-TBS-20-PMB-protected noricumazole A 15b. Method A: To a solution of *t*-BuLi (1.7 mol L^{-1} in pentane, 0.8 mL, 1.4 mmol, 4.1 equiv.) in degassed Et_2O (10 mL) was added vinyliodide **9** (388 mg, 0.7 mmol, 2.0 equiv.) in Et_2O (8 mL) at −78 °C under an argon atmosphere. After 1 h, dimethylzinc (1.2 mol L^{-1} in toluene, 0.6 mL, 0.7 mmol, 2.0 equiv.) was added at −78 °C and the reaction mixture was stirred for 15 min. Aldehyde **4** (92 mg, 0.3 mmol, 1.0 equiv.) in Et_2O (8 mL) was added and stirring was continued at −78 °C for 3 h. H_2O and Et_2O were added and the aqueous layer was extracted with Et_2O. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether–ethyl acetate = 15 : 1 → 4 : 1) furnished allylic alcohols **15a** (82 mg, 0.1 mmol, 34%) and 11-*epi*-**15b** (82 mg, 0.1 mmol, 34%) as light yellow oils.

Method B: To a solution of nitrobenzoate **S8** (2 mg, 2.3 μmol, 1.0 equiv.) in THF–MeOH (2 : 1, 0.15 mL) were added NaOH (0.5 mg, 13.6 μmol, 6.0 equiv.) and H_2O (0.1 mL) at 0 °C. The reaction mixture was stirred for 16 h. H_2O was added and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Purification by flash chromatography (PE : EA = 6 : 1) furnished allylic alcohol **15a** as a colorless oil (2 mg, 2.0 μmol, 90%).

15a: $[\alpha]_D^{26}$ = −15.4 (*c* 1.0, $CDCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$, $CHCl_3$ = 7.26 ppm) δ 11.20 (s, 1H, Ar-O*H*), 7.45 (s, 1H, H-15), 7.30 (d, *J* = 8.9 Hz, 2H, PMB), 7.22 (d, *J* = 7.5 Hz, 1H, H-5), 6.85 (d, *J* = 8.9 Hz, 2H, PMB), 6.60 (d, *J* = 7.5 Hz, 1H, H-6), 6.48 (pd, *J* = 2.0 Hz, 2H, H-12, H-13), 4.92 (dddd, *J* = 11.1, 10.0, 3.4, 3.0 Hz, 1H, H-9), 4.70 (dq, *J* = 9.6, 2.8 Hz, 1H, H-11), 4.50 (ddd, *J* = 7.0, 4.6, 4.4 Hz, 1H, H-18), 4.48 (d, *J* = 11.0 Hz, 1H, PMB), 4.36 (d, *J* = 11.0 Hz, 1H, PMB), 3.79 (s, 3H, PMB), 3.25 (ddd, *J* = 7.4, 5.9, 4.0 Hz, 1H, H-20), 2.98 (dd, *J* = 16.4, 11.1 Hz, 1H, H-8), 2.88 (dd, *J* = 16.4, 3.4 Hz, 1H, H-8′), 2.85 (dd, *J* = 7.0, 2.4 Hz, 1H, H-17), 2.82 (dd, *J* = 7.0, 4.6 Hz, 1H, H-17′), 2.64 (dd, *J* = 13.3, 6.1 Hz, 1H, H-24), 2.39 (dd, *J* = 13.3, 8.2 Hz, 1H, H-24′), 2.11 (ddd, *J* = 14.7, 9.6, 3.0 Hz, 1H, H-10), 1.99 (dddd, *J* = 14.5, 7.4, 7.1, 4.4 Hz, 1H, H-19), 1.87 (ddd, *J* = 14.7, 10.9, 2.8 Hz, 1H, H-10′), 1.79–1.68 (m, 1H, H-21, H-25), 1.57–1.45 (m, 1H, H-21), 1.44–1.35 (m, 1H, H-26), 1.20–1.13 (m, 1H, H-26′), 0.94 (t, *J* = 7.5 Hz, 3H, H-22), 0.91 (s, 9H, TBS), 0.89 (t, *J* = 7.5 Hz, 3H, H-27), 0.85 (d, *J* = 7.1 Hz, 3H, H-23), 0.84 (d, *J* = 6.5 Hz, 3H, H-28), −0.03 (s, 3H, TBS), −0.23 (s, 3H, TBS) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 77.0 ppm) δ 170.2 (q, C-1), 164.0 (q, C-3), 160.5 (q, PMB), 159.0 (q, C-16), 137.8 (q, C-7), 137.2 (t, C-15), 136.7 (q, C-14), 134.9 (t, C-5), 133.4 (t, C-12), 131.0 (q, PMB), 129.3 (t, PMB), 128.8 (q, C-4), 118.4 (t, C-13), 117.0 (t, C-6), 113.6 (t, PMB), 107.7 (s, C-2), 80.5 (t, C-20), 76.5 (t, C-9), 70.8 (t, C-18), 70.79 (s, PMB), 69.9 (t, C-11), 55.2 (p, PMB), 42.0 (t, C-19), 41.6 (s, C-10), 36.8 (s, C-24), 34.7 (t, C-25), 33.3 (s, C-8), 32.0 (s, C-17), 29.4 (s, C-26), 25.7 (3× p, TBS), 22.9 (s, C-21), 19.0 (t, C-28), 17.9 (q, TBS), 11.5 (p, C-27), 10.1 (p, C-22), 8.6 (p, C-23), −4.8 (p, TBS), −5.3 (p, TBS) ppm; HRMS (ESI): *m*/*z*: calculated for $C_{42}H_{62}NO_8Si$: 736.4245 $[M + H]^+$, found: 736.4271 $[M + H]^+$.

11-*epi*-**15b**: $[\alpha]_D^{26}$ = +6.2 (*c* 1.0, $CDCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$, $CHCl_3$ = 7.26 ppm) δ 11.17 (s, 1H, Ar-O*H*), 7.46 (s, 1H, H-15), 7.29 (d, *J* = 8.5 Hz, 2H, PMB), 7.21 (d, *J* = 7.5 Hz, 1H, H-5), 6.84 (d, *J* = 8.5 Hz, 2H, PMB), 6.59 (d, *J* = 7.5 Hz, 1H, H-6), 6.49 (d, *J* = 15.7 Hz, 1H, H-13), 6.44 (dd, *J* = 15.7, 5.7 Hz, 1H, H-12), 4.69 (dddd, *J* = 8.6, 7.5, 7.2, 3.6 Hz, 1H, H-9), 4.63 (q, *J* = 5.7 Hz, 1H, H-11), 4.50 (ddd, *J* = 7.8, 4.6, 2.9 Hz, 1H, H-18), 4.47 (d, *J* = 10.9 Hz, 1H, PMB), 4.35 (d, *J* = 10.9 Hz, 1H, PMB), 3.78 (s, 3H, PMB), 3.25 (ddd, *J* = 7.9, 5.8, 4.1 Hz, 1H, H-20), 3.00 (dd, *J* = 16.3, 8.6 Hz, 1H, H-8), 2.91 (dd, *J* = 16.3, 3.6 Hz, 1H, H-8′), 2.88–2.82 (m, 2H, H-17), 2.64 (dd, *J* = 13.3, 6.5 Hz, 1H, H-24), 2.38 (dd, *J* = 13.3, 7.9 Hz, 1H, H-24′), 2.24 (ddd, *J* = 14.2, 7.5, 7.2 Hz, 1H, H-10), 1.97 (ddd, *J* = 14.2, 7.2, 4.5 Hz, 1H, H-10′), 2.04–1.93 (m, 1H, H-19), 1.79–1.66 (m, 1H, H-25), 1.58–1.45 (m, 1H, H-21), 1.44–1.34 (m, 1H, H-21′), 1.24–1.14 (m, 2H, H-26), 0.93 (t, *J* = 7.5 Hz, 3H, H-22), 0.90 (s, 9H, TBS), 0.89 (t, *J* = 7.5 Hz, 3H, H-27), 0.84 (d, *J* = 7.2 Hz, 3H, H-23), 0.83 (d, *J* = 6.5 Hz, 3H, H-28), −0.04 (s, 3H, TBS), −0.24 (s, 3H, TBS) ppm; ^{13}C-NMR (100 MHz, $CDCl_3$, $CDCl_3$ = 77.0 ppm) δ 170.1 (q, C-1), 164.1 (q, C-3), 160.5 (q, PMB), 159.0 (q, C-16), 137.6 (q, C-7), 137.2 (t, C-15), 136.5 (q, C-14), 135.1 (t, C-5), 132.6 (t, C-12), 131.0 (q, PMB), 129.3 (2× t, PMB), 128.9 (q, C-4), 119.5 (t, C-13), 117.1 (t, C-6), 113.6 (3× t, PMB), 107.7 (s, C-2), 80.5 (t, C-20), 77.7 (t, C-9), 70.8 (t, C-18), 70.7 (s, PMB), 69.4 (t, C-11), 55.2 (p, PMB), 41.9 (t, C-19), 41.5 (s, C-10), 36.8 (s, C-24), 34.7 (t, C-25), 33.0 (s, C-8), 32.0 (s, C-17), 29.7 (s, C-26), 25.7 (3× p, TBS), 22.9 (s, C-21), 19.0 (t, C-28), 17.8 (q, TBS), 11.5 (p, C-27), 10.1 (p, C-22), 8.6 (p, C-23), −4.8 (p, TBS), −5.3

(p, TBS) ppm; HRMS (ESI): *m*/*z*: calculated for $C_{42}H_{62}NO_8Si$: 736.4245 $[M + H]^+$, found: 736.4271 $[M + H]^+$.

4-Nitrobenzoate S8. To a solution of 11-*epi*-**15a** (5 mg, 6.8 µmol, 1.0 equiv.) in THF (2 mL) were sequentially added triphenylphosphine (18 mg, 0.1 mmol, 10.0 equiv.), 4-nitrobenzoic acid (11 mg, 0.1 mmol, 10.0 equiv.) and diethyl azodicarboxylate (40% in toluene, 32 µL, 0.1 mmol, 10.0 equiv.) at 0 °C. The reaction temperature was raised to room temperature and the reaction stirred for 30 min. H_2O was added and the aqueous layer was extracted with ethyl acetate. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether : ethyl acetate = 6 : 1 → 4 : 1) furnished nitrobenzoate **S8** as a colorless oil (5 mg, 5.9 µmol, 86%).

$[\alpha]_D^{21}$ = +12.7 (*c* 0.5, MeOH); ^{1}H-NMR (500 MHz, Me_2CO d_6, Me_2CO = 2.05 ppm) δ 11.41 (s, 1H, Ar-O*H*), 8.39 (d, *J* = 8.9 Hz, 2H, CO_2CCH), 8.28 (d, *J* = 8.9 Hz, 2H, NO_2CCH), 7.34 (d, *J* = 7.6 Hz, 1H, H-5), 7.31 (d, *J* = 8.6 Hz, 2H, PMB), 7.24 (s, 1H, H-15), 6.96 (dd, *J* = 15.4, 10.8 Hz, 1H, H-12), 6.84 (d, *J* = 8.6 Hz, 2H, PMB), 6.75 (d, *J* = 7.6 Hz, 1H, H-6), 6.22 (d, *J* = 10.8 Hz, 1H, H-13), 5.97 (ddd, *J* = 15.4, 11.7, 7.4 Hz, 1H, H-11), 4.78 (dddd, *J* = 9.9, 5.7, 5.7, 5.6 Hz, 1H, H-9), 4.71 (ddd, *J* = 9.2, 6.1, 2.8 Hz, 1H, H-18), 4.47 (d, *J* = 11.2 Hz, 1H, PMB), 4.35 (d, *J* = 11.2, 1H, PMB), 3.72 (s, 3H, PMB), 3.33 (ddd, *J* = 11.8, 8.5, 4.5 Hz, 1H, H-20), 3.06–3.01 (m, 2H, H-8), 2.76–2.68 (m, 2H, H-10), 2.75 (dd, *J* = 14.6, 6.1 Hz, 1H, H-17), 2.64 (dd, *J* = 13.2, 6.2 Hz, 1H, H-24), 2.54 (dd, *J* = 14.6, 9.2 Hz, 1H, H-17′), 2.39 (dd, *J* = 13.2, 8.1 Hz, 1H, H-24′), 2.09–2.01 (m, 1H, H-19), 1.86–1.77 (m, 1H, H-21), 1.77–1.69 (m, 1H, H-25), 1.54–1.44 (m, 1H, H-21′), 1.43–1.35 (m, 1H, H-26), 1.22–1.25 (m, 1H, H-26′), 0.92 (s, 9H, TBS), 0.91 (d, *J* = 7.6 Hz, 3H, H-23), 0.89 (t, *J* = 7.1 Hz, 3H, H-27), 0.88 (t, *J* = 8.0 Hz, 3H, H-28), 0.85 (s, 3H, H-22), 0.07 (s, 3H, TBS), 0.05 (s, 3H, TBS) ppm; ^{13}C-NMR (125 MHz, Me_2CO d_6, Me_2CO = 29.84 ppm) δ 171.3 (q, C-1), 164.4 (q, C-16), 161.1 (q, CO_2CCH), 160.0 (q, C-3), 152.0 (q, NO_2C), 147.5 (q, PMB), 138.4 (q, C-7), 138.1 (t, C-5), 135.3 (q, CO_2CCH), 132.0 (2× t, CO_2CCH), 130.4 (t, C-11), 130.2 (2× t, PMB), 130.2 (t, C-12), 130.0 (q, C-14), 128.8 (q, C-4), 124.7 (2× t, NO_2CCH), 119.3 (t, C-13), 118.3 (t, C-6), 114.3 (2× t, PMB), 108.8 (q, C-2), 96.2 (t, C-15), 80.6 (t, C-20), 80.0 (t, C-9), 71.3 (s, PMB), 70.6 (t, C-18), 55.4 (p, PMB), 42.3 (t, C-19), 38.8 (s, C-10), 37.2 (s, C-24), 35.6 (t, C-25), 32.9 (s, C-8), 32.7 (s, C-17), 29.2 (s, C-26), 26.2 (3× p, TBS), 23.1 (s, C-21), 19.2 (q, TBS), 18.6 (p, C-27), 11.7 (p, C-22), 10.1 (p, C-28), 8.3 (p, C-23), −4.37 (p, TBS), −4.4 (p, TBS) ppm; HRMS (ESI): *m*/*z*: calculated for $C_{49}H_{65}N_2O_{11}Si$: 885.4358 $[M + H]^+$, found: 885.4360 $[M + H]^+$.

3,11-Acetate-18-TBS-20-PMB protected 11-*epi*-noricumazole A S9a and 11-epi-S9b. To a solution of alcohol **15a** (27 mg, 36.0 µmol, 1.0 equiv.) in CH_2Cl_2 (7 mL) were added DMAP (0.9 mg, 7.2 µmol, 0.2 equiv.), pyridine (13 µL, 158.4 µmol, 4.4 equiv.) and acidic anhydride (8 µL, 79.2 µmol, 2.2 equiv.) at room temperature. The reaction was terminated after 16 h by addition of H_2O and Et_2O. The aqueous layer was extracted with Et_2O. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether–ethyl acetate = 4 : 1 → 2 : 1) furnished **16a** (25 mg, 29.9 µmol, quant) as a colorless oil.

S9a: $[\alpha]_D^{24}$ = −22.4 (*c* 1.0, MeOH); ^{1}H-NMR (400 MHz, Me_2CO d_6, Me_2CO = 2.05 ppm) δ 7.80 (s, 1H, H-15), 7.49 (d, *J* = 7.8 Hz, 1H, H-5), 7.37 (d, *J* = 8.8 Hz, 2H, PMB), 7.19 (d, *J* = 7.8 Hz, 1H, H-6), 6.88 (d, *J* = 8.8 Hz, 2H, PMB), 6.59 (dd, *J* = 15.5, 0.8 Hz, 1H, H-13), 6.40 (ddd, *J* = 15.5, 7.2, 0.5 Hz, 1H, H-12), 5.67 (dq, *J* = 7.2, 0.8 Hz, 1H, H-11), 4.68 (ddd, *J* = 9.2, 4.5, 3.0 Hz, 1H, H-9), 4.57–4.53 (m, 1H, H-18), 4.51 (d, *J* = 11.0 Hz, 1H, PMB), 4.39 (d, *J* = 11.0 Hz, 1H, PMB), 3.78 (s, 3H, PMB), 3.34 (ddd, *J* = 8.2, 5.2, 4.0 Hz, 1H, H-20), 3.12 (dd, *J* = 16.1, 3.0 Hz, 1H, H-17), 3.04 (dd, *J* = 16.1, 10.1 Hz, 1H, H-17′), 2.87 (dd, *J* = 15.0, 3.0 Hz, 1H, H-8), 2.73 (dd, *J* = 15.0, 9.2 Hz, 1H, H-8′), 2.58 (dd, *J* = 13.3, 5.9 Hz, 1H, H-24), 2.33 (dd, *J* = 13.3, 8.7 Hz, 1H, H-24′), 2.32–2.27 (m, 1H, H-10), 2.29 (s, 3H, Ac), 2.10 (ddd, *J* = 13.9, 7.2, 4.5 Hz, 1H, H-10′), 2.06 (s, 3H, Ac), 1.98 (ddd, *J* = 6.6, 4.0, 1.9 Hz, 1H, H-19), 1.82 (pdddd, *J* = 14.6, 7.3, 7.3, 4.3 Hz, 1H, H-21), 1.69–1.59 (m, 1H, H-25), 1.50 (pdddd, *J* = 14.6, 7.3, 7.3, 5.2 Hz, 1H, H-21′), 1.41–1.32 (m, 1H, H-26), 1.26–1.14 (m, 1H, H-26′), 0.93 (d, *J* = 6.6 Hz, 3H, H-23), 0.91 (t, *J* = 7.3 Hz, 3H, H-22), 0.90 (t, *J* = 7.4 Hz, 3H, H-27), 0.83 (d, *J* = 6.7 Hz, 3H, H-28), 0.75 (s, 9H, TBS), −0.03 (s, 3H, TBS), −0.25 (s, 3H, TBS) ppm; ^{13}C-NMR (100 MHz, Me_2CO d_6, Me_2CO = 29.84 ppm) δ 170.3 (2× q, Ac), 169.5 (q, C-1), 164.5 (q, C-16), 160.1 (q, PMB), 150.9 (q, C-3), 140.1 (q, C-7), 139.1 (q, C-14), 136.8 (t, C-15), 136.7 (t, C-5), 135.3 (q, C-4), 132.1 (q, PMB), 130.2 (2× t, PMB), 129.5 (t, C-12), 125.6 (t, C-6), 121.8 (t, C-13), 118.6 (q, C-2), 114.4 (2× t, PMB), 81.1 (t, C-20), 75.3 (t, C-18), 71.9 (t, C-9), 71.5 (s, PMB), 70.7 (t, C-11), 55.5 (p, PMB), 42.5 (t, C-19), 40.4 (s, C-10), 37.7 (s, C-24), 36.3 (t, C-25), 34.1 (s, C-17), 32.2 (s, C-8), under Me_2CO-Signal (s, C-26), 26.2 (3× p, TBS), 23.4 (s, C-21), 21.1 (p, Ac), 21.07 (p, Ac), 19.3 (t, C-28), 18.5 (q, TBS), 11.8 (p, C-27), 10.2 (p, C-23), 8.5 (p, C-22), −4.5 (p, TBS), −4.9 (p, TBS) ppm; HRMS (ESI): *m*/*z*: calculated for $C_{46}H_{66}NO_{10}Si$: 820.4456 $[M + H]^+$, found: 820.4437 $[M + H]^+$.

11-*epi*-**S9b**: yield: quant., 0.1 mmol; $[\alpha]_D^{25}$ = −12.6 (*c* 0.9, MeOH); ^{1}H-NMR (400 MHz, Me_2CO d_6, Me_2CO = 2.05 ppm) δ 7.80 (s, 1H, H-15), 7.49 (d, *J* = 7.8 Hz, 1H, H-5), 7.37 (d, *J* = 8.8 Hz, 2H, PMB), 7.19 (d, *J* = 7.8 Hz, 1H, H-6), 6.88 (d, *J* = 8.8 Hz, 2H, PMB), 6.59 (dd, *J* = 15.5, 0.8 Hz, 1H, H-13), 6.40 (ddd, *J* = 15.5, 7.2, 0.5 Hz, 1H, H-12), 5.67 (dq, *J* = 7.2, 0.8 Hz, 1H, H-11), 4.68 (ddd, *J* = 9.2, 4.5, 3.0 Hz, 1H, H-9), 4.57–4.53 (m, 1H, H-18), 4.51 (d, *J* = 11.0 Hz, 1H, PMB), 4.39 (d, *J* = 11.0 Hz, 1H, PMB), 3.78 (s, 3H, PMB), 3.34 (ddd, *J* = 8.2, 5.2, 4.0 Hz, 1H, H-20), 3.12 (dd, *J* = 16.1, 3.0 Hz, 1H, H-17), 3.04 (dd, *J* = 16.1, 10.1 Hz, 1H, H-17′), 2.87 (dd, *J* = 15.0, 3.0 Hz, 1H, H-8), 2.73 (dd, *J* = 15.0, 9.2 Hz, 1H, H-8′), 2.58 (dd, *J* = 13.3, 5.9 Hz, 1H, H-24), 2.33 (dd, *J* = 13.3, 8.7 Hz, 1H, H-24′), 2.32–2.27 (m, 1H, H-10), 2.29 (s, 3H, Ac), 2.10 (ddd, *J* = 13.9, 7.2, 4.5 Hz, 1H, H-10′), 2.06 (s, 3H, Ac), 1.98 (ddd, *J* = 6.6, 4.0, 1.9 Hz, 1H, H-19), 1.82 (pdddd, *J* = 14.6, 7.3, 7.3, 4.3 Hz, 1H, H-21), 1.69–1.59 (m, 1H, H-25), 1.50 (pdddd, *J* = 14.6, 7.3, 7.3, 5.2 Hz, 1H, H-21′), 1.41–1.32 (m, 1H, H-26), 1.26–1.14 (m, 1H, H-26′), 0.93 (d, *J* = 6.6 Hz, 3H, H-23), 0.91 (t, *J* = 7.3 Hz, 3H, H-22), 0.90 (t, *J* = 7.4 Hz, 3H, H-27), 0.83 (d, *J* = 6.7 Hz, 3H, H-28), 0.75 (s, 9H, TBS), −0.03 (s, 3H, TBS), −0.25 (s, 3H, TBS) ppm; ^{13}C-NMR (125 MHz, MeOH d_4,

MeOH d_3 = 49.0 ppm) δ 171.9 (2× q, Ac), 165.8 (2× q, C-1, C-3), 160.7 (2× q, C-16, PMB), 140.7 (q, C-14), 139.0 (q, C-7), 137.73 (t, C-12), 137.7 (2× t, C-5, C-15), 132.1 (2× t, PMB), 130.8 (1× q, 1× s, PMB, C-4), 129.1 (t, C-15), 126.1 (q, C-2), 123.0 (2× t, C-6, C-13), 114.7 (2× t, PMB), 81.6 (t, C-20), 77.1 (t, C-18), 72.6 (t, C-9), 72.1 (t, C-11), 71.9 (s, PMB), 55.7 (p, PMB), 42.8 (t, C-19), 40.2 (s, C-10), 38.1 (s, C-24), 36.8 (t, C-25), 34.3 (s, C-8), 32.2 (s, C-17), 30.5 (s, C-26), 26.2 (3× p, TBS), 23.6 (s, C-21), 21.14 (p, Ac), 21.1 (p, Ac), 19.4 (t, C-28), 18.7 (q, TBS), 11.9 (p, C-27), 10.1 (p, C-22), 8.4 (p, C-23), −4.4 (p, TBS), −5.0 (p, TBS) ppm; HRMS (ESI): *m*/*z*: calculated for $C_{46}H_{66}NO_{10}Si$: 820.4456 $[M + H]^+$, found: 820.4437 $[M + H]^+$.

3,11-Acetate-PMB protected noricumazole A 16a and 11-epi-16b. To a solution of protected noricumazole A **S9a** (14 mg, 17.3 µmol, 1.0 equiv.) in THF (7 mL) was added hydrofluoric acid in pyridine (70%, as HF 30%, 0.7 mL) *via* a syringe pump over 14 h at room temperature. The reaction was terminated by addition of sat. aq. $NaHCO_3$ solution and the aqueous layer was extracted with ethyl acetate. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was taken up in MeOH and H_2O (1 : 1) and purified by RP-HPLC (MeOH–H_2O, gradient elution). Compound **16a** (8 mg, 11.9 µmol, 69%, 89% b.r.s.m.) was obtained as a colorless oil. As a side product acetate-protected **17a** was obtained.

16a: $[\alpha]_D^{20}$ = −27.1 (*c* 0.8, MeOH); ^{1}H-NMR (500 MHz, MeOH d_4, MeOH d_3 = 3.31 ppm) δ 7.78 (s, 1H, H-15), 7.49 (d, *J* = 7.9 Hz, 1H, H-5), 7.28 (d, *J* = 8.9 Hz, 2H, PMB), 7.19 (d, *J* = 7.9 Hz, 1H, H-6), 6.86 (d, *J* = 8.9 Hz, 2H, PMB), 6.54 (dd, *J* = 15.6, 0.3 Hz, 1H, H-13), 6.33 (dd, *J* = 15.6, 6.7 Hz, 1H, H-12), 5.65 (dq, *J* = 6.7, 0.5 Hz, 1H, H-11), 4.64 (dddd, *J* = 10.4, 5.8, 5.8, 4.2 Hz, 1H, H-9), 4.43 (d, *J* = 11.3 Hz, 1H, PMB), 4.40 (d, *J* = 11.3 Hz, 1H, PMB), 4.17 (ddd, *J* = 9.4, 6.6, 3.2 Hz, 1H, H-18), 3.77 (s, 3H, PMB), 3.49 (ddd, *J* = 7.2, 6.6, 3.6 Hz, 1H, H-20), 3.05 (dd, *J* = 14.6, 4.2 Hz, 1H, H-8), 3.01 (dd, *J* = 16.6, 10.4 Hz, 1H, H-8′), 2.94 (dd, *J* = 15.2, 3.2 Hz, 1H, H-17), 2.77 (dd, *J* = 15.2, 9.4 Hz, 1H, H-17′), 2.59 (dd, *J* = 13.3, 6.1 Hz, 1H, H-24), 2.38–2.31 (m, 1H, H-24′), 2.31 (s, 3H, Ac), 2.14 (dd, *J* = 6.7, 5.8 Hz, 2H, H-10), 2.06 (s, 3H, Ac), 2.02 (sext, *J* = 6.6 Hz, 1H, H-19), 1.70 (pdddd, *J* = 7.2, 7.2, 6.6, 3.6 Hz, 1H, H-21), 1.64–1.58 (m, 1H, H-25), 1.47 (sext, *J* = 7.2 Hz, 1H, H-21′), 1.41–1.30 (m, 1H, H-26), 1.30–1.17 (m, 1H, H-26′), 0.94 (t, *J* = 7.2 Hz, 3H, H-27), 0.91 (t, *J* = 8.7 Hz, 3H, H-22), 0.90 (d, *J* = 7.9 Hz, 3H, H-23), 0.85 (d, *J* = 6.6 Hz, 3H, H-28) ppm; ^{13}C-NMR (125 MHz, MeOH d_4, MeOH d_3 = 49.0 ppm) δ 172.1 (2× q, Ac), 171.2 (q, C-1), 165.7 (q, C-16), 160.8 (q, PMB), 149.7 (q, C-3), 140.6 (q, C-7), 139.0 (q, C-14), 137.8 (t, C-15), 137.7 (t, C-5), 135.5 (q, C-4), 132.1 (q, PMB), 130.8 (2× t, PMB), 129.8 (t, C-12), 126.1 (t, C-6), 122.0 (t, C-13), 118.6 (q, C-2), 114.7 (2× t, PMB), 82.1 (t, C-20), 76.3 (t, C-9), 72.0 (s, PMB), 71.7 (t, C-11), 71.6 (t, C-18), 55.7 (p, PMB), 42.1 (t, C-19), 40.5 (s, C-10), 38.1 (s, C-24), 36.9 (t, C-25), 34.3 (s, C-8), 33.8 (s, C-17), 30.5 (s, C-26), 23.1 (s, C-21), 21.1 (p, Ac), 21.0 (p, Ac), 19.4 (t, C-28), 11.9 (p, C-27), 10.8 (p, C-23), 9.6 (p, C-22) ppm; HRMS (ESI): *m*/*z*: calculated for $C_{40}H_{52}NO_{10}$: 706.3591 $[M + H]^+$, found: 706.3591 $[M + H]^+$.

11-*epi*-**16b**: yield: 61%, 16.7 µmol; $[\alpha]_D^{25}$ = −12.6 (*c* 0.9, MeOH); ^{1}H-NMR (500 MHz, MeOH d_4, MeOH d_3 = 3.31 ppm) δ 7.79 (s, 1H, H-15), 7.48 (d, *J* = 7.8 Hz, 1H, H-5), 7.27 (d, *J* = 8.7 Hz, 2H, PMB), 7.19 (d, *J* = 7.8 Hz, 1H, H-6), 6.85 (d, *J* = 8.7 Hz, 2H, PMB), 6.56 (d, *J* = 15.7 Hz, 1H, H-13), 6.32 (dd, *J* = 15.7, 7.2 Hz, 1H, H-12), 5.66 (ddd, *J* = 7.2, 7.0, 6.7 Hz, 1H, H-11), 4.57 (ddd, *J* = 14.9, 8.1, 3.9 Hz, 1H, H-9), 4.42 (d, *J* = 11.0 Hz, 1H, PMB), 4.39 (d, *J* = 11.0 Hz, 1H, PMB), 4.15 (ddd, *J* = 9.5, 6.6, 3.2 Hz, 1H, H-18), 3.76 (s, 3H, PMB), 3.48 (ddd, *J* = 6.6, 6.1, 3.4 Hz, 1H, H-20), 3.08 (dd, *J* = 16.1, 3.9 Hz, 1H, H-8), 3.00 (dd, *J* = 16.1, 8.1 Hz, 1H, H-8′), 2.92 (dd, *J* = 15.1, 3.2 Hz, 1H, H-17), 2.76 (dd, *J* = 15.1, 9.5 Hz, 1H, H-17′), 2.58 (dd, *J* = 13.4, 6.4 Hz, 1H, H-24), 2.37–2.30 (m, 1H, H-24′), 2.31 (s, 3H, Ac), 2.28 (ddd, *J* = 14.3, 8.1, 6.7 Hz, 1H, H-10), 2.07 (s, 3H, Ac), 2.02 (ddd, *J* = 14.3, 7.0, 3.9 Hz, 1H, H-10′), 2.01 (sext, *J* = 6.6 Hz, 1H, H-19), 1.68 (pdddd, *J* = 14.0, 7.5, 7.5, 3.4 Hz, 1H, H-21), 1.61 (oct, *J* = 6.4 Hz, 1H, H-25), 1.45 (sext, *J* = 7.3 Hz, 1H, H-26), 1.36 (pddd, *J* = 14.0, 7.5, 6.1 Hz, 1H, H-21′), 1.24–1.14 (m, 1H, H-26′), 0.93 (t, *J* = 7.3 Hz, 3H, H-27), 0.91 (t, *J* = 7.5 Hz, 3H, H-22), 0.90 (d, *J* = 6.6 Hz, 3H, H-23), 0.84 (d, *J* = 6.4 Hz, 3H, H-28) ppm; ^{13}C-NMR (125 MHz, MeOH d_4, MeOH d_3 = 49.0 ppm) δ 172.0 (2× q, Ac), 171.1 (q, C-1), 165.7 (q, C-16), 160.8 (q, PMB), 150.0 (q, C-3), 140.1 (q, C-14), 138.9 (t, C-15), 137.9 (t, C-15), 137.8 (q, C-7), 136.0 (q, C-4), 132.0 (q, PMB), 130.8 (2× t, PMB), 129.2 (t, C-12), 126.1 (t, C-6), 122.8 (t, C-13), 118.4 (q, C-2), 114.6 (2× t, PMB), 82.0 (t, C-20), 77.2 (t, C-9), 72.5 (t, C-11), 71.9 (s, PMB), 71.5 (t, C-18), 55.6 (p, PMB), 42.1 (t, C-19), 40.2 (s, C-10), 38.1 (s, C-24), 36.9 (t, C-25), 34.2 (s, C-8), 33.7 (s, C-17), 30.5 (s, C-26), 23.1 (s, C-21), 21.14 (p, Ac), 21.1 (p, Ac), 19.4 (t, C-28), 11.9 (p, C-27), 10.7 (p, C-22), 9.6 (p, C-23) ppm; HRMS (ESI): *m*/*z*: calculated for $C_{40}H_{52}NO_{10}$: 706.3591 $[M + H]^+$, found: 706.3591 $[M + H]^+$.

3,11-Diacetyl protected noricumazole A 17a and 11-epi-17b. 17a: yield: 6%, 1.0 µmol; $[\alpha]_D^{24}$ = −12.5 (*c* 0.9, MeOH); ^{1}H-NMR (500 MHz, MeOH d_4, MeOH d_3 = 3.31 ppm) δ 7.79 (s, 1H, H-15), 7.49 (d, *J* = 7.8 Hz, 1H, H-5), 7.21 (d, *J* = 7.8 Hz, 1H, H-6), 6.54 (dd, *J* = 15.8, 0.6 Hz, 1H, H-13), 6.32 (dd, *J* = 15.8, 6.5 Hz, 1H, H-12), 5.65 (q, *J* = 6.5 Hz, 1H, H-11), 4.69–4.63 (m, 1H, H-9), 4.18 (ddd, *J* = 9.5, 6.7, 3.3 Hz, 1H, H-18), 3.54 (ddd, *J* = 9.0, 6.7, 2.6 Hz, 1H, H-20), 3.09–3.05 (m, 1H, H-8), 3.00 (dd, *J* = 16.4, 3.9 Hz, 1H, H-8′), 3.00 (dd, *J* = 15.1, 3.3 Hz, 1H, H-17), 2.81 (dd, *J* = 15.1, 9.5 Hz, 1H, H-17′), 2.59 (dd, *J* = 13.4, 6.1 Hz, 1H, H-24), 2.41–2.32 (m, 1H, H-24′), 2.32 (s, 3H, Ac), 2.15 (pt, *J* = 6.5 Hz, 2H, H-10), 2.07 (s, 3H, Ac), 1.77 (sext, *J* = 6.7 Hz, 1H, H-19), 1.69–1.58 (m, 2H, H-21, H-25), 1.45–1.33 (m, 2H, H-21′, H-26), 1.25–1.17 (sext, *J* = 7.2 Hz, 1H, H-26′), 0.98 (t, *J* = 7.4 Hz, 3H, H-27), 0.92 (t, *J* = 7.5 Hz, 3H, H-22), 0.91 (d, *J* = 7.0 Hz, 3H, H-23), 0.85 (d, *J* = 6.6 Hz, 3H, H-28) ppm; ^{13}C-NMR (125 MHz, MeOH d_4, MeOH d_3 = 49.0 ppm) δ 172.1 (2× q, Ac), 171.2 (q, C-1), 165.9 (q, C-16), 149.6 (q, C-3), 140.7 (q, C-7), 138.9 (t, C-5), 137.8 (t, C-15), 130.7 (q, C-14), 129.8 (t, C-12), 126.1 (t, C-6), 122.0 (t, C-13), 118.5 (q, C-4), 114.8 (q, C-2), 76.3 (t, C-9), 75.4 (t, C-20), 72.3 (t, C-18), 71.6 (t, C-11), 45.6 (t, C-19), 40.5 (s, C-10), 38.1 (s, C-24), 36.9 (t, C-25), 34.3 (s, C-8), 33.7 (s, C-17), 30.5 (s, C-26), 27.2 (s, C-21), 21.1 (p, Ac), 21.0 (p, Ac), 19.4 (t, C-28), 11.9 (p, C-23), 11.3 (p, C-22), 10.4

(p, C-27) ppm; HRMS (ESI): *m/z*: calculated for $C_{32}H_{44}NO_9$: 586.3016 $[M + H]^+$, found: 586.3002 $[M + H]^+$.

11-*epi*-**17b**: yield: 13%, 3.6 µmol; $[\alpha]_D^{25} = -12.6$ (*c* 0.9, MeOH); ^{1}H-NMR (500 MHz, MeOH d_4, MeOH d_3 = 3.31 ppm) δ 7.78 (s, 1H, H-15), 7.49 (d, *J* = 7.8 Hz, 1H, H-5), 7.19 (d, *J* = 7.8 Hz, 1H, H-6), 6.55 (dd, *J* = 15.6, 0.2 Hz, 1H, H-13), 6.31 (dd, *J* = 15.6, 7.1 Hz, 1H, H-12), 5.66 (ddd, *J* = 7.1, 6.9, 6.9 Hz, 1H, H-11), 4.58 (ddd, *J* = 7.1, 6.9, 6.9 Hz, 1H, H-9), 4.17 (dddd, *J* = 10.5, 8.1, 3.9, 3.6 Hz, 1H, H-18), 3.53 (ddd, *J* = 8.9, 6.6, 2.7 Hz, 1H, H-20), 3.06 (dd, *J* = 16.0, 3.6 Hz, 1H, H-8), 3.04 (dd, *J* = 16.0, 3.9 Hz, 1H, H-8′), 3.00 (dd, *J* = 15.0, 3.2 Hz, 1H, H-17), 2.80 (dd, *J* = 15.0, 9.6 Hz, 1H, H-17′), 2.58 (dd, *J* = 13.4, 6.1 Hz, 1H, H-24), 2.34–2.31 (m, 1H, H-24′), 2.31 (s, 3H, Ac), 2.28 (ddd, *J* = 14.4, 8.1, 6.9 Hz, 1H, H-10), 2.11–2.06 (m, 1H, H-10′), 2.08 (s, 3H, Ac), 1.76 (sext, *J* = 6.6 Hz, 1H, H-19), 1.67–1.57 (m, 2H, H-21, H-25), 1.43–1.33 (m, 2H, H-21′, H-26), 1.27–1.15 (m, 1H, H-26′), 0.97 (t, *J* = 7.4 Hz, 3H, H-27), 0.91 (t, *J* = 7.5 Hz, 3H, H-22), 0.89 (d, *J* = 6.6 Hz, 3H, H-23), 0.84 (d, *J* = 6.6 Hz, 3H, H-28) ppm; ^{13}C-NMR (125 MHz, MeOH d_4, MeOH d_3 = 49.0 ppm) δ 172.0 (2× q, Ac), 171.1 (q, C-1), 165.9 (q, C-16), 151.9 (q, C-3), 138.8 (t, C-15), 137.9 (t, C-5), 137.8 (q, C-7), 130.7 (q, C-14), 129.2 (2× t, C-6, C-12), 126.1 (t, C-4), 122.7 (t, C-13), 114.8 (q, C-2), 77.2 (t, C-9), 75.4 (t, C-20), 72.5 (t, C-11), 72.3 (t, C-18), 45.6 (t, C-19), 40.2 (s, C-10), 38.1 (s, C-24), 36.9 (t, C-25), 34.7 (t, C-25), 34.2 (s, C-8), 33.7 (s, C-17), 30.5 (s, C-26), 27.2 (s, C-21), 21.1 (p, Ac), 21.08 (p, Ac), 19.4 (t, C-28), 11.9 (p, C-23), 11.3 (p, C-22), 10.4 (p, C-27) ppm; HRMS (ESI): *m/z*: calculated for $C_{32}H_{44}NO_9$: 586.3016 $[M + H]^+$, found: 586.3002 $[M + H]^+$.

Aglycon S10. A solution of acceptor **16a** (8 mg, 11.9 µmol, 1.0 equiv.) in CH_2Cl_2 (2.3 mL) was added to activated molecular sieves (powder, 4 Å) under an atmosphere of argon. $Hg(CN)_2$ (7 mg, 26.1 µmol, 2.2 equiv.) was added to the suspension at room temperature. After stirring for 45 min glycosyl donor **18** (45 mg, 85.6 µmol, 7.2 equiv.) in CH_2Cl_2 (1.5 mL) which was codistilled before with benzene was added. After 2.25 h the reaction was quenched by addition of MeOH. The reaction mixture was filtered over Celite® and the organic layer washed with a sat. aq. KBr solution and water. The organic extract was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was taken up in MeOH and H_2O (1 : 1) and purified by RP-HPLC (MeOH–H_2O, gradient elution). Aglycon **S10** (6 mg, 5.2 µmol, 47%) was obtained as a colorless oil.

$[\alpha]_D^{22} = -10.3$ (*c* 0.5, MeOH); ^{1}H-NMR (500 MHz, MeOH d_4, MeOH d_3 = 3.31 ppm) δ 8.08–8.02 (m, 2 H, Bz), 7.98–7.91 (m, 4 H, Bz), 7.69 (s, 1H, H-15), 7.67–7.59 (m, 2H, Bz), 7.46–7.45 (m, 5H, Bz), 7.44 (d, *J* = 7.8 Hz, 1H, H-5), 7.28–7.20 (m, 2H, Bz), 7.19 (d, *J* = 8.7 Hz, 2H, PMB), 7.15 (d, *J* = 7.8 Hz, 1H, H-6), 6.78 (d, *J* = 8.7 Hz, 2H, PMB), 6.32 (d, *J* = 15.8 Hz, 1H, H-13), 6.26 (dd, *J* = 15.8, 6.4 Hz, 1H, H-12), 5.60–5.50 (m, 1H, H-11), 5.41 (pd, *J* = 4.7 Hz, 1H, H-4′), 5.39 (ps, 1H, H-2′), 5.17 (ps, 1H, H-1′), 4.69 (dd, *J* = 11.9, 3.4 Hz, 1H, H-5′), 4.61 (d, *J* = 11.1 Hz, 1H, PMB), 4.59 (dd, *J* = 11.9, 5.1 Hz, 1H, H-5″), 4.58–4.56 (m, 1H, H-9), 4.47 (d, *J* = 11.1 Hz, 1H, PMB), 4.48 (dd, *J* = 8.3, 4.7 Hz, 1H, H-3′), 4.41–4.36 (m, 1H, H-18), 3.71 (s, 3H, PMB), 3.47–3.42 (m, 1H, H-20), 3.00 (dd, *J* = 15.8, 4.0 Hz, 1H, H-17), 2.98–2.93 (m, 2H, H-8), 2.89 (dd, *J* = 15.8, 10.8 Hz, 1H, H-17′), 2.56 (dd, *J* = 13.5, 6.1 Hz, 1H, H-24), 2.29 (dd, *J* = 13.5, 8.4 Hz, 1H, H-24′), 2.28–2.24 (m, 1H, H-19), 2.03 (ddd, *J* = 14.7, 9.0, 4.1 Hz, 1H, H-10), 1.91 (ddd, *J* = 14.7, 6.8, 3.5 Hz, 1H, H-10′), 1.73 (ddd, *J* = 14.5, 7.1, 3.7 Hz, 1H, H-21), 1.63–1.55 (m, 1H, H-25), 1.46–1.37 (m, 1H, H-21′), 1.45 (sext, *J* = 7.0 Hz, 1H, H-26), 1.18 (sext, *J* = 7.0 Hz, 1H, H-26′), 0.98 (t, *J* = 7.0 Hz, 3H, H-22), 0.91 (t, *J* = 7.1 Hz, 3H, H-27), 0.90 (d, *J* = 7.0 Hz, 3H, H-23), 0.82 (d, *J* = 6.6 Hz, 3H, H-28) ppm; ^{13}C-NMR (125 MHz, MeOH d_4, MeOH d_3 = 49.0 ppm) δ 172.0 (2× q, Ac), 171.2 (q, C-1), 167.6 (q, Bz), 167.1 (q, Bz), 166.5 (q, Bz), 164.7 (q, C-16), 160.7 (q, PMB), 149.0 (q, C-3), 140.6 (t, C-7), 139.1 (t, C-15), 137.8 (q, C-5), 134.9 (q, C-14), 130.91 (q, PMB), 130.9 (3× t, Bz), 130.89 (2× t, PMB), 130.8 (2× t, Bz), 129.9 (2× t, Bz), 129.86 (t, C-12), 129.8 (q, C-4), 129.77 (3× t, Bz), 128.9 (t, C-5), 127.0 (t, C-6), 121.8 (t, C-13), 118.5 (q, C-2), 114.7 (2× t, PMB), 107.4 (t, C-1′), 83.3 (t, C-4′), 83.1 (t, C-2′), 81.2 (t, C-20), 79.2 (t, C-3′), 79.1 (t, C-18), 76.1 (t, C-9), 71.6 (s, PMB), 71.4 (t, C-11), 65.0 (s, C-5′), 55.6 (p, PMB), 40.5 (t, C-19), 40.2 (s, C-10), 38.1 (s, C-24), 36.8 (t, C-25), 34.3 (s, C-8), 31.1 (s, C-17), 30.5 (s, C-26), 23.2 (s, C-21), 21.1 (p, Ac), 21.0 (p, Ac), 19.4 (t, C-28), 11.9 (p, C-22), 10.9 (p, C-23), 19.7 (p, C-27) ppm; HRMS (ESI): *m/z*: calculated for $C_{66}H_{72}NO_{17}$: 1150.4800 $[M + H]^+$, found: 1150.4789 $[M + H]^+$.

Aglycon (-PMB) S11. To a solution of aglycon **S10** (3 mg, 2.9 µmol, 1.0 equiv.) in CH_2Cl_2 (1.5 mL) were added phosphate buffer (0.3 mL) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (1 mg, 5.7 µmol, 2.0 equiv.) in CH_2Cl_2 (0.7 mL) at room temperature. After stirring for 1.5 h the reaction was quenched by addition of a sat. aq. $NaHCO_3$ solution and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was taken up in MeOH and H_2O (1 : 1) and purified by RP-HPLC (MeOH–H_2O, gradient elution). Compound **S11** (3 mg, 2.8 µmol, 98%) was obtained as a colorless oil.

$[\alpha]_D^{22} = -21.8$ (*c* 0.3, MeOH); ^{1}H-NMR (500 MHz, MeOH d_4, MeOH d_3 = 3.31 ppm) δ 8.08–8.03 (m, 2H, Bz), 7.98–7.92 (m, 4H, Bz), 7.70 (s, 1H, H-15), 7.68–7.63 (m, 2H, Bz), 7.54–7.49 (m, 2H, Bz), 7.98–7.95 (m, 1H, Bz), 7.44 (d, *J* = 7.9 Hz, 1H, H-5), 7.30–7.25 (m, 2H, Bz), 7.16 (d, *J* = 7.9 Hz, 1H, H-6), 6.33 (d, *J* = 15.6 Hz, 1H, H-13), 6.24 (dd, *J* = 15.6, 6.3 Hz, 1H, H-12), 5.55–5.48 (m, 1H, H-11), 5.45 (pdd, *J* = 4.6, 1.2 Hz, 1H, H-4′), 5.35 (ps, 1H, H-2′), 5.15 (ps, 1H, H-1′), 4.74 (dd, *J* = 11.7, 4.6 Hz, 1H, H-5′), 4.63 (dd, *J* = 11.7, 4.6 Hz, 1H, H-5″), 4.57 (dd, *J* = 9.2, 4.6 Hz, 1H, H-3′), 4.55–4.59 (m, 2H, H-9, H-18), 3.50–3.47 (m, 1H, H-20), 3.09–2.99 (m, 2H, H-8), 2.97 (dd, *J* = 16.6, 3.9 Hz, 1H, H-17), 2.92 (dd, *J* = 16.6, 10.6 Hz, 1H, H-17′), 2.57 (dd, *J* = 13.5, 6.3 Hz, 1H, H-24), 2.36–2.31 (m, 1H, H-24′), 2.31 (s, 3H, Ac), 2.14–2.09 (m, 1H, H-19), 2.03–1.94 (m, 2H, H-10), 2.00 (s, 3H, Ac), 1.69–1.63 (m, 1H, H-21), 1.62–1.54 (m, 1H, H-25), 1.46–1.39 (m, 1H, H-21′), 1.31–1.25 (m, 1H, H-26), 1.19–1.13 (m, 1H, H-26′), 1.03 (d, *J* = 6.8 Hz, 3H, H-23), 1.00 (t, *J* = 7.3 Hz, 3H, H-22), 0.92 (t, *J* = 7.3 Hz, 3H, H-27), 0.83 (d, *J* = 6.5 Hz, 3H, H-28) ppm; ^{13}C-NMR (125 MHz, MeOH d_4, MeOH d_3 = 49.0 ppm) δ 172.0 (2× q, Ac), 171.2 (q, C-1), 167.6 (q, Bz), 167.1 (q, Bz), 166.5 (q, Bz), 165.1 (q, C-16), 150.0 (q, C-3), 140.6 (q, C-14), 139.0 (q, C-7), 137.8 (t, C-5), 134.8 (t, C-12), 134.4 (t, C-15), 130.9 (6× t, Bz), 130.6 (4× t, Bz), 129.9 (2× t, Bz), 129.8 (2× t,

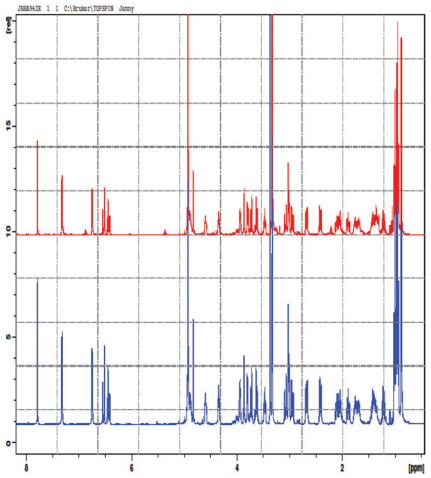


Fig. 2 ^{1}H-NMR spectra of authentic (blue; bottom) and synthetic (red; top) noricumazole B (**1b**).

Bz), 129.6 (4× t, Bz), 127.1 (q, C-2), 126.1 (t, C-6), 121.8 (t, C-13), 118.6 (q, C-4), 107.7 (t, C-1′), 83.4 (t, C-2′), 82.9 (t, C-3′), 79.2 (t, C-4′), 79.1 (t, C-18), 76.2 (t, C-9), 74.9 (t, C-20), 71.4 (t, C-11), 64.9 (s, C-5′), 44.4 (t, C-19), 40.2 (s, C-10), 38.1 (s, C-24), 36.8 (t, C-25), 34.2 (s, C-17), 30.5 (s, C-26), 30.4 (s, C-8), 27.8 (s, C-21), 21.0 (2× p, Ac), 19.4 (t, C-28), 11.9 (p, C-23), 11.0 (p, C-22), 10.5 (p, C-27) ppm; HRMS (ESI): *m*/*z*: calculated for $C_{58}H_{64}NO_{16}$: 1030.4225 $[M + H]^+$, found: 1030.4240 $[M + H]^+$.

Noricumazole B (1b). A solution of aglycon **S11** (2 mg, 1.5 µmol, 1.0 equiv.) in MeOH–THF–H_2O–Et_3N (1.4 mL, 6 : 5 : 1 : 2) was stirred at 55 °C. After stirring for 2 days the solvent of the reaction mixture was removed and the residue directly taken up in MeOH and H_2O (1 : 1) and purified by RP-HPLC (MeOH–H_2O, gradient elution). Noricumazole B (**1b**) (1 mg, 1.4 µmol, 98%) was obtained as a colorless oil.

Synthetic noricumazole B: $[\alpha]_D^{22}$ = +14.8 (*c* 0.1, MeOH); authentic noricumazole B[1]: $[\alpha]_D^{20}$ = +13.3 (*c* 0.86 in MeOH); HRMS (ESI): *m*/*z*: calculated for $C_{33}H_{48}NO_{11}$: 634.3227 $[M + H]^+$, found: 634.3228 $[M + H]^+$. For NMR-spectra and data see Fig. 2 and refer to ref. 1.

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