The Chemistry of Vicinal Tricarbonyls: Total Syntheses of Elastase Inhibitors YM-47141 and YM-47142

by **Harry H. Wasserman***, **Jyun-Hung Chen**, and **Mingde Xia**

Department of Chemistry, Yale University, P.O. Box 208107, New Haven, CT 06520-8107, USA

Dedicated to Professor *Albert Eschenmoser* on the occasion of his 75th birthday

We have completed the total syntheses of elastase inhibitors YM-47141 and YM-47142, the first natural products containing a vicinal tricarbonyl group. The work establishes the configuration at C(4) of the macrocyclic depsipeptide and demonstrates the generality of the phosphoranylidene-ylide activation and protection methodology employed earlier in syntheses of α-keto amides. Key steps involve the coupling of a carboxylic acid with a phosphorane to form a stable ylide intermediate, which contains the highly electrophilic carbonyl group in protected form. The tricarbonyl unit was unmasked at the final stage of the synthesis by oxidative cleavage of the C=P bond.

Introduction. – During extensive studies on the chemistry of 1,2,3-vicinal tricarbonyl systems, we have found that this highly electrophilic unit may serve as a key building block in the synthesis of a variety of bioactive products [1–8]. Interest in this system has been heightened by the findings that potent immunosuppressant natural products such as FK-506 and rapamycin incorporate the vicinal tricarbonyl array in the form of internal hemiketal functions [9][10]. In the course of studies on these products, a number of elegant total syntheses have been reported along with investigations on the formation of substructural units considered to be involved in the biological activity [11][12]¹).

Recently, two novel elastase inhibitors, YM-47141 and YM-47142, isolated from *Flexibacter sp.* Q. 17897, have been shown to incorporate the 1,2,3-vicinal tricarbonyl system in the form of monohydrates. These substances were characterized as the depsipeptides **1a** and **1b** (*Fig.*) by MS and NMR spectroscopic methods, which served to elucidate all stereochemical features except for the configuration at C(4) of the unnatural amino acid 4-amino-6-methyl-2,3-dioxoheptanoic acid (Dah) [13]. In the present work, we report the details of our total syntheses of these macrocycles, the first examples of natural products containing the hydrate of a vicinal tricarbonyl moiety (for a preliminary account, see [14]). Our synthesis shows that the configuration at C(4) corresponds to that of L-leucine.

Results and Discussion. – In developing our synthetic plan, we decided to incorporate the leucine residue encompassing C(4) as the L-isomer, based on analogies to related natural products [15]. We were mindful of the fact that the reactive vicinal

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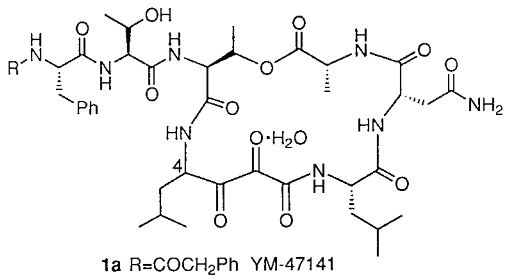
¹) For a recent total synthesis of FK-506 and other references to synthetic work in this field, see [11f].

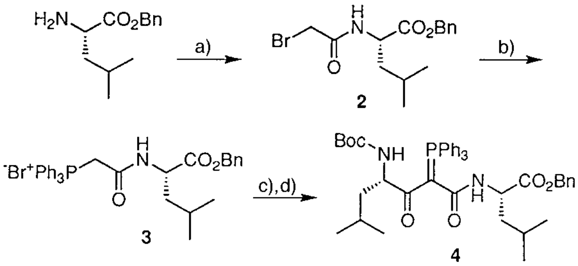


1a R=COCH$_2$Ph YM-47141
1b R=COCH$_2$CH(CH$_3$)$_2$ YM-47142

Figure. *Structures of YM-47141 and YM-47142*

tricarbonyl system is prone to cleavage in both acid and base [16][17], and we, therefore, insulated this sensitive electrophilic unit in the form of the diacyl ylide **4** throughout the synthetic sequence (*Scheme 1*). The relatively robust ylide effectively served to mask the tricarbonyl aggregate during the varied processes of deprotection and coupling. Only at the last stage of the synthesis did we perform the required oxidative cleavage of the C=P bond.

Scheme 1

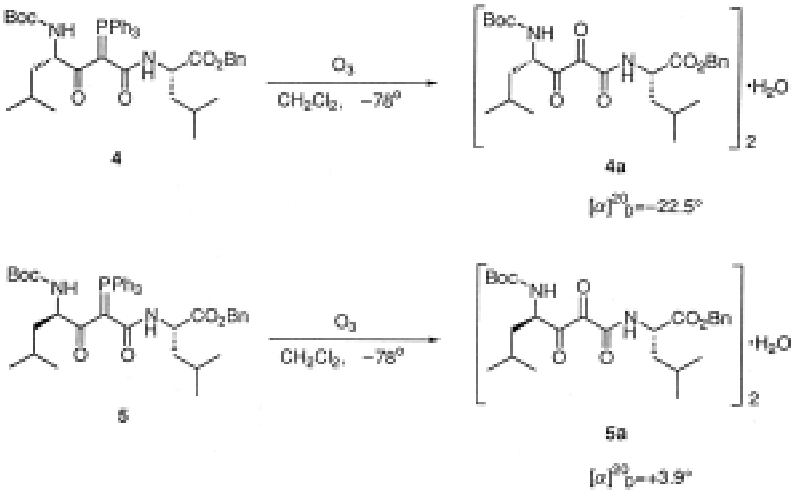


a) BrCH$_2$CO$_2$H, DCC, DMAP (92%). b) PPh$_3$, THF; 97%. c) Et$_3$N, CH$_2$Cl$_2$. d) *N*-Boc-L-Leu-OH, 1,1′-Carbonyldiimidazole (CDI), CH$_2$Cl$_2$; 96% (2 steps).

We began the synthesis by coupling L-leucine benzyl ester with BrCH$_2$CO$_2$H to form **2**, which could readily be converted to the phosphonium salt **3** with PPh$_3$ and then to the corresponding phosphorane with Et$_3$N. The further reaction with *N*-Boc-L-leucine in the presence of 1,1′-carbonyldiimidazole (CDI) took place in excellent yields to form the product **4** containing the two L-leucine residues.

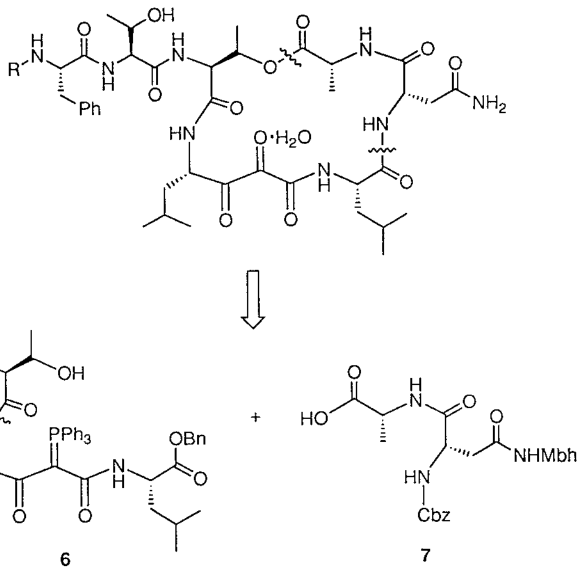
To explore the possibility of epimerization at the C-atom in α-position to the tricarbonyl grouping formed on ozonolysis of **4**, we prepared the stereoisomer **5** containing D-leucine for comparison studies. Ozonolysis of each diacyl phosphorane **4** and **5** gave the corresponding tricarbonyl derivatives isolated as dimer monohydrates **4a** and **5a** (*Scheme 2*). These bis-addition products showed distinctly different rotations, indicating that no scrambling of the configuration at C(α) took place during ozonolysis of the respective ylides (for the L-leucine-L-leucine adduct, $[\alpha]_D^{20} = -22.5$; for the D-leucine-L-leucine adduct, $[\alpha]_D^{20} = +3.9$).

Scheme 2



The 3 + 2 Approach. With the elements of leucyl-leucine as our starting material, we first undertook a 3 + 2 approach outlined in *Scheme 3* involving initial addition of a threonine unit to the diacyl ylide **4** in order to form the modified tripeptide **6**. In the next step, we hoped to form a *N,N′*-dicyclohexylcarbodiimide (DCC)-promoted ester link between the OH group of **6** and the COOH group of a doubly protected alanyl-asparagine fragment **7**. The subsequent macrocyclization by formation of a lactam bond between the carboxy group of Leu and the amino group of Asn would furnish the 18-

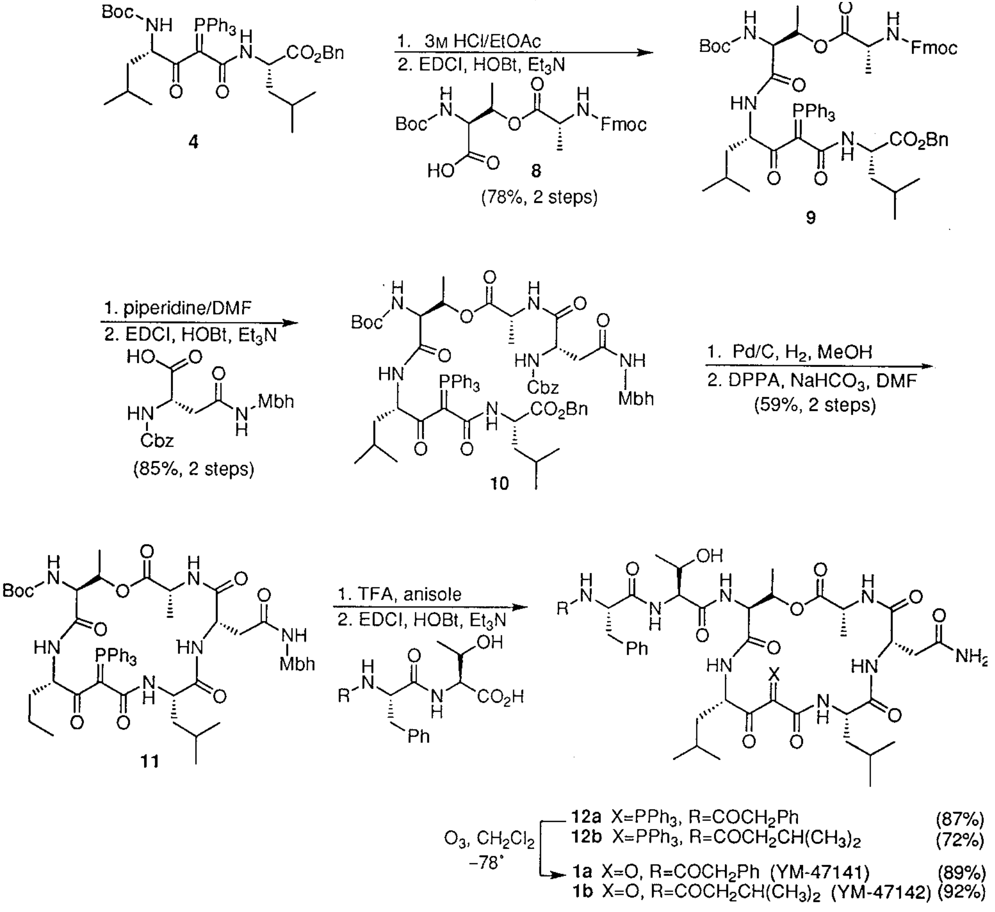
Scheme 3



membered pentadepsipeptide. This approach, however, was not successful at the esterification stage, **6** + **7**, most probably because of steric factors in the reaction with the tripeptide. The only product isolated corresponded to the addition of the COOH group of **7** to DCC.

The 2 + 2 + 1 Approach. We next turned to a 2 + 2 + 1 approach (*Scheme 4*), which would enable us to form the ester link by combining the threonine and alanine units at an early stage, unencumbered by the bulky protected diacyl-ylide fragment **4**. The ester-carboxylic acid **8**, generated in good yield by the coupling of *N*-Boc-L-threonine with *N*-Fmoc-D-alanine was then converted to **9** by reaction (EDCI) with the free amine resulting from HCl removal of the Boc group from **4**. Removal of the Fmoc group of **9** with piperidine was followed by coupling (EDCI) with *N*-Cbz asparagine, the primary

Scheme 4[a])



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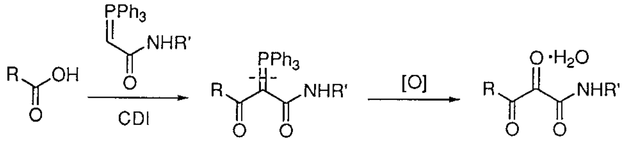
a) Abbreviations: Boc: (*tert*-butoxy)carbonyl, Cbz: (benzyloxy)carbonyl, DPPA: diphenylphosphoryl azide, EDCI: *N*-[3-(dimethylamino)propyl]-*N*′-ethylcarbodiimide, Fmoc: (9*H*-fluoren-9-methoxycarbonyl, HOBt: 1-hydroxybenzotriazole, MbH: 4,4′-dimethoxybenzhydryl, TFA: 2,2,2-trifluoroacetic acid.

amido group of which was protected as the 4,4′-dimethoxybenzhydryl (Mbh) derivative [18]. After Pd/C hydrogenolysis of the Cbz and Bn groups, the differentially protected product **10** containing five amino-acid units was then cyclized to the depsipetide precursor **11** by treatment with DPPA/$NaHCO_3$ in dilute DMF. Installation of each side chain was accomplished by TFA deprotection of both Boc and Mbh groups followed by EDCI coupling with the substituted phenylalanyl-threonine to form **12a** (R = $COCH_2Ph$) or **12b** (R=$COCH_2(CH_3)_2$). The resulting macrocyclic ylides **12a** and **12b** represent precursors that could easily be converted to the desired natural products by oxidative cleavage of the C=P bonds. The final conversion of **12a**,**b** to **1a**,**b** under the mild conditions of ozonolysis (– 78°, 2 min) took place smoothly, forming the natural products in excellent yields (89 and 92%, resp.). The only side product, Ph_3PO, was easily separated by washing with CH_2Cl_2. The ^1H- and ^{13}C-NMR spectra of both synthetic products YM-47141 (**1a**) and YM-47142 (**1b**) were identical in every respect with the corresponding spectra of the natural substances [13]. Since L-leucine was used in the preparation of the Dah fragment, we assign the corresponding L-leucine configuration to the stereogenic center C(4). There was no evidence of any epimerization at this center in our synthetic product.

Conclusion. – In summary, we have completed the total syntheses of elastase inhibitors YM-47141 (**1a**) and YM-47142 (**1b**), and established the configuration at C(4). This work demonstrates the generality of the phosphoranylidene-ylide activation and protection methodology that we have employed in earlier syntheses of α-keto amides [19–21]. The advantages of this procedure (*Scheme 5*) are the facile coupling of carboxylic acids with phosphoranes to form stable ylide intermediates, which contain the highly electrophilic C=O groups in protected form. The tricarbonyl unit may be easily unmasked at the final stage of the synthesis by oxidative cleavage of the C=P bond to afford the pure product in high yield.

Scheme 5



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Experimental Part

N-*(2-Bromoacetyl)-Leu-OBn* (**2**). A soln. of leucine benzyl ester (15.05 g, 68 mmol) in 400 ml of CH_2Cl_2 was cooled to 0° in an ice-water bath and sequentially treated with $BrCH_2CO_2H$ (10.42 g, 75 mmol), 4-(dimethylamino)pyridine (DMAP; 415 mg, 3.4 mmol) and N,N′-dicyclohexylcarbodiimide (DCC; 14.48 g, 75 mmol). A white precipitate of dicyclohexylurea formed immediately upon the addition of DCC. The mixture was stirred at 0° for 1 h and diluted with Et_2O (500 ml). The white precipitate was removed by filtration. The filtrate was concentrated *in vacuo*. Flash chromatography (FC) (SiO_2; 10 × 30 cm, 1:7 to AcOEt/hexane 1:4) gave the desired product, which was further purified by recrystallization from AcOEt/hexane to provide **2**

(21.43 g, 92%). White needles. M.p. 91.5–92.5°. $[\alpha]_D^{20} = -3.86$ ($c = 10.0$, $CHCl_3$). R_f (SiO_2; AcOEt/hexane 1:4) 0.35. IR (KBr): 3069, 2964, 1742, 1649, 1550, 1189, 1153. ^{1}H-NMR ($CDCl_3$, 500 MHz): 7.40–7.30 (*m*, 5 H); 6.81 (*d*, $J = 7.6$, 1 H); 5.19 (*d*, $J = 12.3$, 1 H); 5.16 (*d*, $J = 12.3$, 1 H); 4.66 (*dt*, $J = 8.5, 5.2$, 1 H); 3.88 (*s*, 2 H); 1.73–1.57 (*m*, 3 H); 0.93 (*d*, $J = 6.3$, 3 H); 0.92 (*d*, $J = 6.3$, 3 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 172.1; 165.2; 135.1; 128.6; 128.5; 128.2; 67.2; 51.5; 41.3; 28.8; 24.8; 22.7; 21.9. HR-MS: 342.0705 ($[M + H]^+$; calc. 342.0705). Anal. calc. for $C_{15}H_{20}BrNO_3$: C 52.64, H 5.89, N 4.09; found: C 52.84, H 5.99, N 4.07.

*{*N*-[2-(Triphenylphosphonium)acetyl]-Leu-OBn} Bromide* (**3**). Compound **2** (10.72 g, 31.3 mmol) was dissolved in THF/Et_2O 1:3 (160 ml), and to this soln., Ph_3P (16.42 g, 62.6 mmol) was added in one portion. After 1 h, the clear mixture began to turn cloudy. The mixture was stirred at 23° and monitored by TLC. After 3 days, the mixture became a thick white suspension, and TLC showed that the compound **2** had been consumed. The white precipitate of the ylide salt **3** was collected by filtration. The filtered white cake was further rinsed with Et_2O (200 ml) and hexane (200 ml) to remove residual Ph_3P. The white precipitate, dried on a vacuum pump, yielded **3** (18.32 g, 97%). M.p. 150–151°. $[\alpha]_D^{20} = -29.72$ ($c = 5.0$, $CHCl_3$). IR (KBr): 3168, 3016, 2955, 1749, 1735, 1667, 1549, 1535, 1439. ^{1}H-NMR ($CDCl_3$, 500 MHz): 9.60 (*d*, $J = 6.6$, 1 H); 7.84–7.56 (*m*, 15 H); 7.33–7.27 (*m*, 5 H); 5.35 (*dd*, $J = 14.3$, J(P,H) = 15.6, 1 H); 5.08 (*d*, $J = 12.5$, 1 H); 5.05 (*dd*, $J = 15.0$, J(P,H) = 15.1, 1 H); 5.04 (*d*, $J = 12.5$, 1 H); 4.26 (*dt*, $J = 10.3, 5.8$, 1 H); 1.85–1.50 (*m*, 3 H); 0.88 (*d*, $J = 6.5$, 3 H); 0.74 (*d*, $J = 6.5$, 3 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 171.3; 162.7 (*d*, J(C,P) = 5.0); 135.8; 134.8; 134.0; 133.9; 130.0 (*d*, J(C,P) = 14.0); 128.1 (*d*, J(C,P) = 64.0); 127.9; 118.4 (*d*, J(C,P) = 88.0, 66.4; 52.3; 39.3; 31.9 (*d*, J(C,P) = 56.0); 24.6; 22.7; 21.4. HR-MS: 524.2355 ($[M - Br]^-$; calc. 524.2355). Anal. calc. for $C_{33}H_{35}BrNO_3P$: C 65.56, H 5.84, N 2.32; found: C 65.37, H 5.82, N 2.33.

N-*((4*S*)-4-{[(*tert-*Butoxy)carbonyl]amino}-6-methyl-3-oxo-2-(triphenylphosphoranylidene)heptanoyl)-Leu-OBn* (**4**). In a 100-ml round-bottomed flask, **3** (7.76 g, 12.8 mmol) was dissolved in 30 ml of CH_2Cl_2 and subsequently treated with 18 ml of Et_3N (129 mmol). The resulting soln. containing the ylide was stirred at 23° under N_2 for 1 h. In another 100-ml round-bottomed flask, a soln. of *N*-Boc-L-Leu-OH (4.45 g, 19.3 mmol) in 30 ml of CH_2Cl_2 was treated with CDI (3.20 g, 19.3 mmol). This soln. was stirred at 23° for 15 min. The above ylide soln. was then transferred into the CDI-activated *N*-Boc-L-Leu-OH soln. through a cannula. The combined mixture was stirred at 23° for an additional 24 h. The mixture was diluted with CH_2Cl_2 (200 ml), washed with H_2O (150 ml), and sat. aq. NaCl soln. (150 ml). The org. phase was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. FC (SiO_2; 8 × 35 cm, Et_2O/hexane 3:1 elution) gave **4** (9.08 g, 96%). White foam: $[\alpha]_D^{20} = -13.85$ ($c = 10.0$, $CHCl_3$). R_f (SiO_2; Et_2O/hexane 3:1) 0.24. IR (KBr): 3431, 3250, 2955, 1743, 1689, 1625, 1523, 1160. ^{1}H-NMR ((D_6)DMSO, 500 MHz): 9.29 (br. *s*, 1 H); 7.60–7.26 (*m*, 20 H); 6.91 (br. *s*, 1 H); 5.09 (*d*, $J = 12.6$, 1 H); 5.05 (*d*, $J = 12.6$, 1 H); 4.90 (br. *s*, 1 H); 4.19 (*ddd*, $J = 10.5, 7.0, 4.5$, 1 H); 1.72–1.69 (*m*, 1 H); 1.68–1.65 (*m*, 1 H); 1.47 (*s*, 9 H); 1.35–1.11 (*m*, 4 H); 0.88 (*d*, $J = 6.5$, 3 H); 0.75 (*d*, $J = 6.5$, 3 H); 0.70 (*d*, $J = 6.5$, 3 H); 0.61 (br. *s*, 3 H). ^{13}C-NMR ((D_6)DMSO, 125 MHz): 188.4; 172.8; 166.2; 156.5; 136.0; 132.7 (*d*, J(C,P) = 10.0); 131.6; 128.4; 128.3; 127.9; 127.6; 126.2 (*d*, J(C,P), = 92.3); 78.2; 73.2 (*d*, J(C,P) = 110.5); 65.6; 51.7; 50.8; 40.6; 40.2; 28.2; 24.3; 24.0; 22.8; 22.7; 22.5; 21.1. HR-MS: 737.3727 ($[M + H]^+$; calc. 737.3720). Anal. calc. for $C_{44}H_{53}N_2O_6P$: C 71.72, H 7.25, N 3.80; found: C 71.75, H 7.27, N 3.86.

N-*((4*R*)-4-{[(*tert-*Butoxy)carbonyl]amino}-6-methyl-3-oxo-2-(triphenylphosphoranylidene)heptanoyl)-Leu-OBn* (**5**). The ylide salt **3** (2.95 g, 4.88 mmol) was dissolved in 15 ml of CH_2Cl_2 and then treated with Et_3N (6.8 ml, 48.8 mmol). The mixture was stirred under N_2 for 1 h. In another flask, Boc-D-Leu-OH (1.75 g, 7.56 mmol) was dissolved in 10 ml of CH_2Cl_2 and was treated with CDI (1.25 g, 7.56 mmol). The ylide was then added to CDI-activated Boc-D-Leu-OH soln. The resulting mixture was stirred for 24 h and then was washed with H_2O. The org. layer was dried (Na_2SO_4). After the solvent was evaporated *in vacuo*, the residue was purified by FC (AcOEt/$CHCl_3$ 1:3) to give 3.2 g (89%) of **5**. White foam. $[\alpha]_D^{20} = -22.33$ ($c = 7.0$, $CHCl_3$). IR (KBr): 3435, 3274, 2959, 1743, 1687, 1625, 1512. ^{1}H-NMR ($CDCl_3$, 300 MHz): 8.71 (br. *s*, 1 H); 7.70–7.29 (*m*, 20 H); 7.09 (*d*, $J = 7.3$, 1 H); 5.16 (*m*, 1 H); 5.09 (*d*, $J = 12.7$, 1 H); 5.03 (*d*, $J = 12.7$, 1 H); 4.41 (*m*, 1 H); 1.69 (*m*, 2 H); 1.55 (*m*, 2 H); 1.49 (*s*, 9 H); 1.34 (*m*, 2 H); 0.93 (*d*, $J = 6.4$, 3 H); 0.89 (*d*, $J = 5.9$, 3 H); 0.79 (*d*, $J = 5.7$, 3 H); 0.65 (br. *s*, 3 H). ^{13}C-NMR ($CDCl_3$, 75 Hz): 188.9; 173.8; 167.5; 156.8; 136.3; 133.3 (*d*, J(C,P) = 10.0); 131.5; 128.5; 128.4; 127.9; 127.7; 126.3 (*d*, J(C,P) = 93.6); 78.9; 73.9 (*d*, J(C,P) = 107.6); 66.1, 51.9; 50.9; 41.0; 40.6; 28.4; 25.1; 24.6; 23.2; 22.7; 22.0; 21.5. HR-MS: 737.3727 ($[M + H]^+$; calc. 737.3719). Anal. calc. for $C_{44}H_{53}N_2O_6P$: C 71.72, H 7.25, N 3.80; found: C 71.50, H 7.24, N 3.88.

Ozonolysis of Ylide **4**. The ylide **4** (0.51 g, 0.69 mmol) was dissolved in 20 ml of CH_2Cl_2, ozonized at −78° for 7 min, and the soln. was then purged with N_2 for 10 min. After the solvent was evaporated *in vacuo*, the residue was purified by FC (AcOEt/hexanes 1:2) to give 0.27 g (79%) of dimer monohydrate **4a**. $[\alpha]_D^{20} = -22.5$ ($c = 5.0$, $CHCl_3$). IR (KBr): 3370, 2965, 1752, 1675, 1545. ^{1}H-NMR ((D_6)DMSO, 300 MHz): 7.92 (*d*, $J = 8.3$, 1 H); 7.82 (*s*, 1 H); 7.34 (*m*, 10 H); 7.12 (*d*, $J = 6.7$, 2 H); 6.90 (*d*, $J = 8.5$, 1 H); 6.64 (*s*, 1 H); 5.10 (*s*, 4 H); 4.73

(*m*, 1 H); 4.34 (*m*, 3 H); 1.58 (*m*, 12 H); 1.33 (*s*, 18 H); 0.82 (*m*, 24 H). HR-MS: 1021.5366 ($[M+\mathrm{Na}]^+$; calc. 1021.5361).

Ozonolysis of Ylide **5**. The ylide **5** (0.28 g, 0.38 mmol) in 10 ml of CH_2Cl_2 was ozonized at −78° for 3 min, and the soln. was then purged with N_2 for 5 min. After the solvent was evaporated *in vacuo*, the residue was purified by FC (AcOEt/hexanes 1:2) to give 0.14 g (71%) of dimer monohydrate **5a**. $[\alpha]_D^{20} = +3.9$ ($c = 5.0$, $CHCl_3$). ^1H-NMR ($CDCl_3$, 300 MHz): 7.37–7.10 (*m*, 14 H); 5.97 (*s*, 1 H); 5.84 (*s*, 1 H); 5.18 (*m*, 4 H); 4.63 (*m*, 4 H); 1.65 (*m*, 12 H); 0.92 (*s*, 18 H); 0.87 (*m*, 24 H). IR (KBr): 3423, 3021, 2975, 1733, 1702, 1687, 1496. HR-MS: 1021.5365 ($[M+\mathrm{Na}]^+$; calc. 1021.5361).

N-*Boc-Thr[*N-*Fmoc-*D-*Ala]-OBn* (*Benzyl Ester of* **8**). A suspension of *N*-Fmoc-D-Ala-OH (10.34 g, 33.2 mmol) in 200 ml of CH_2Cl_2 was added to CDI (5.49 g, 33.2 mmol) in two portions. The resulting mixture immediately turned clear, and CO_2 vigorously effervesced. After 15 min, a soln. of *N*-Boc-Thr-OBn (25.45 g, 82.3 mmol) in 200 ml of CH_2Cl_2 was added through a cannula. The mixture was stirred at 23° for 20 h under N_2 and then was put through a short silica gel column (8 × 12 cm) directly and rinsed with 1.5 l of 40% AcOEt/hexane. The fractions containing the product and unreacted *N*-Boc-Thr-OBn were concentrated. The residue was purified by FC (SiO_2; 8 × 20 cm, AcOEt/hexane 1:6 to 1:4) to give the benzyl ester of **8** (15.973 g, 80%) along with recovered *N*-Boc-Thr-OBn (16.56 g). The product was further purified to yield white needles by recrystallization from Et_2O/hexane mixture. M.p. 125.5°–126.5°. $[\alpha]_D^{20} = +14.65$ ($c = 11.0$, $CHCl_3$): R_f (AcOEt/hexane 1:2) 0.53. IR (KBr): 3396, 3339, 2797, 1750, 1714, 1513, 1216, 1165. ^1H-NMR ((D_6)DMSO, 500 MHz): 7.88 (*d*, $J = 7.6$, 2 H); 7.73–7.68 (*m*, 3 H); 7.44–7.32 (*m*, 9 H); 7.25 (*d*, $J = 9.2$, 1 H); 5.24 (*dq*, $J = 6.5$, 3.2, 1 H); 5.10 (*d*, $J = 12.5$, 1 H); 5.06 (*d*, $J = 12.5$, 1 H); 4.39 (*dd*, $J = 9.2$, 3.2, 1 H); 4.29 (*d*, $J = 6.8$, 2 H); 4.21 (*t*, $J = 6.8$, 1 H); 4.03 (*dq*, $J = 7.5$, 7.2, 1 H); 1.37 (*s*, 9 H); 1.18 (*d*, $J = 7.5$, 3 H); 1.16 (*d*, $J = 6.5$, 3 H). ^{13}C-NMR ((D_6)DMSO, 125 MHz): 171.9; 169.6; 155.9; 155.8; 143.8; 143.7; 140.7; 135.6; 128.3; 128.1; 127.8; 127.6; 127.0; 125.2; 120.1; 78.6; 70.2; 66.4; 65.6; 57.0; 49.4; 46.6; 28.1; 16.9; 16.4. HR-MS: 603.2705 ($[M+\mathrm{H}]^+$, calc. 603.2706). Anal. calc. for $C_{34}H_{38}N_2O_8$: C 67.76, H 6.35, N 4.65; found: C 67.78, H 6.33, N 4.61.

N-*Boc-Thr-[*N-*Fmoc-*D-*Ala]-{*N-*[(4*S*)-4-amino-6-methyl-3-oxo-2-(triphenylphosphoranylidene)heptanoyl]-Leu}-OBn* (**9**). A soln. of benzyl ester of **8** (4.63 g, 7.7 mmol) in 80 ml of CH_2Cl_2 was treated with 10% Pd−C (460 mg), and the resulting black suspension was stirred at 23° under H_2 (balloon) for 14 h. The catalyst was removed by filtration through a short pad of *Celite* and rinsed with an additional 300 ml of CH_2Cl_2. The filtrate was concentrated to give crude acid **8**, which was used directly in the next reaction without further purification.

In another 100-ml round-bottomed flask, 5.83 g of **4** (7.91 mmol) was treated with 15 ml of 3M HCl/AcOEt. The mixture was stirred at 23° for 30 min. AcOEt and excess HCl was removed *in vacuo*. The residual HCl was further removed by adding Et_2O (30 ml) to the HCl salt, followed by its removal *in vacuo*. After this procedure was repeated twice, the HCl salt thus obtained was used in the following reaction immediately without further purification.

A soln. of acid **8** and the above HCl salt in 60 ml of CH_2Cl_2 was cooled to 0° and sequentially treated with HOBt (1.03 g, 7.6 mmol), Et_3N (1.54 g, 15.2 mmol), and EDCI (1.46 g, 7.6 mmol). The mixture was stirred at 0° for 2 h, slowly warmed to 23° and stirred for an additional 20 h. The mixture was poured into H_2O (150 ml) and extracted with AcOEt (3 × 200 ml). The combined org. phases were washed with sat. aq. NaCl soln. (200 ml), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. FC (SiO_2; 8 × 18 cm, 40–60% AcOEt/hexane gradient elution) of the crude product afforded **9** (6.81 g, 78%). White foam. $[\alpha]_D^{20} = -1.38$ ($c = 10.0$, $CHCl_3$). IR (KBr): 3270, 3061, 2956, 1722, 1659, 1515, 1163. ^1H-NMR ((D_6)DMSO, 500 MHz): 9.06 (br. *s*, 1 H); 8.11 (br. *s*, 1 H); 7.88 (*d*, $J = 7.5$, 2 H); 7.78–7.69 (*m*, 3 H); 7.59–7.27 (*m*, 24 H); 6.95 (*d*, $J = 9.1$, 1 H); 5.15–4.98 (*m*, 4 H); 4.32–4.21 (*m*, 5 H); 4.04 (*t*, $J = 7.2$, 1 H); 1.59–1.41 (*m*, 4 H); 1.36 (*s*, 9 H); 1.26 (*d*, $J = 7.1$, 3 H); 1.23–1.20 (*m*, 2 H); 1.12 (*d*, $J = 5.4$, 3 H); 0.85 (*d*, $J = 6.4$, 3 H); 0.71 (*d*, $J = 5.9$, 3 H); 0.62 (*d*, $J = 6.1$, 3 H); 0.58 (br. *s*, 3 H). ^{13}C-NMR ((D_6)DMSO, 125 MHz): 186.6; 172.7; 172.3; 172.2; 169.6; 168.7; 166.0; 155.9; 155.2; 143.8; 143.7; 140.7; 135.9; 132.8 (*d*, J(C,P) = 9.5); 131.6; 128.3; 127.9; 127.8; 127.6; 127.2; 125.9 (*d*, J(C,P) = 92.1); 125.2; 120.1; 78.4; 74.0 (*d*, J(C,P) = 105.5); 71.2; 65.7; 65.6; 57.7; 51.4; 50.7; 49.4; 46.6; 40.9; 40.7; 28.1; 24.2; 23.8; 22.9; 22.7; 22.2; 22.0; 21.3; 16.9. HR-MS: 1131.5248 ($[M+\mathrm{H}]^+$; calc. 1131.5248). Anal. calc. for $C_{66}H_{75}N_4O_{11}P$: C 70.07, H 6.68, N 4.95: found: C 69.87, H 6.88, N 4.93.

N-*Boc-Thr-{[*N^α*-Cbz-*N^γ*-(4,4′-dimethoxylbenzhydryl)-Asn]-*D-*Ala}-{*N-*[(4*S*)-4-amino-6-methyl-3-oxo-2-(triphenylphosphoranylidene)heptanoyl]-Leu}-OBn* (**10**). A soln. of **9** (4.24 g, 3.75 mmol) in 80 ml of DMF was treated with 20 ml of piperidine. The resulting mixture was stirred at 23° for 1 h under N_2. The mixture was poured onto 200 ml of H_2O and extracted with AcOEt (3 × 200 ml). The combined org. layers were washed with 200 ml of sat. aq. NaCl soln., dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was chromatographed (SiO_2; 6 × 20 cm) by first eluting with AcOEt followed by 10% Et_3N/AcOEt elution to yield free amine as an off-white foam, which was used immediately in the next reaction.

A soln. of the above free amine and N^{α}-Cbz-N^{γ}-Mbh-Asn-OH (1.84 g, 3.74 mmol) in 40 ml of DMF was sequentially treated with Et_3N (1.04 ml, 7.48 mmol), HOBt (0.51 g, 3.74 mmol), and EDCI (0.72 g, 3.74 mmol). The mixture was stirred at 0° for 2 h under N_2, and allowed to warm to 23° and stirred for additional 16 h. The mixture was poured onto 200 ml of H_2O and extracted with AcOEt (3 × 250 ml). The combined org. layers were washed with sat. aq. NaCl soln. (300 ml), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. FC (SiO_2; 8 × 20 cm, 50–70% AcOEt/hexane) of the crude product afforded **10** (4.40 g, 85%). White foam. $[\alpha]_D^{20} = -2.9$ ($c = 20$, $CHCl_3$). R_f 0.35 (SiO_2; AcOEt/hexane 2 : 1). IR (KBr): 3300, 3070, 2958, 1742, 1717, 1659, 1518, 1250, 1182. ^1H-NMR ((D_6)DMSO, 500 MHz): 9.08 (br. *s*, 1 H); 8.59 (*d*, $J = 8.4$, 1 H); 8.20 (*m*, 2 H); 7.57–7.30 (*m*, 26 H); 7.16 (*dd*, $J = 8.4$, 3.3, 4 H); 6.95 (*d*, $J = 8.9$, 1 H); 6.85 (*d*, $J = 8.4$, 2 H); 6.82 (*d*, $J = 8.4$, 2 H); 6.00 (*d*, $J = 8.4$, 1 H); 5.05 (*m*, 6 H); 4.48 (*m*, 1 H); 4.34 (*m*, 1 H); 4.27 (*m*, 1 H); 4.22 (*t*, $J = 7.1$, 1 H); 3.70 (*s*, 3 H); 3.68 (*s*, 3 H); 2.58 (*m*, 2 H); 1.55 (*m*, 1 H); 1.47 (*m*, 1 H); 1.38 (*s*, 9 H); 1.23–1.15 (*m*, 10 H); 0.86 (*d*, $J = 6.1$, 3 H); 0.72 (*d*, $J = 5.1$, 3 H); 0.65 (*d*, $J = 5.2$, 3 H); 0.61 (br. *s*, 3 H). ^{13}C-NMR ((D_6)DMSO, 125 MHz): 186.7; 172.7; 171.7; 171.0; 168.1; 158.1; 158.0; 155.7; 155.2; 136.9; 135.9; 134.9; 134.7; 132.8 (*d*, J(C,P) = 9.6); 131.7; 128.6; 128.4; 128.3; 127.9; 127.8; 127.7; 127.6; 125.9 (*d*, J(C,P) = 92.4); 113.6; 113.5; 78.4; 73.7 (*d*, J(C,P) = 104.0); 71.2; 65.7; 65.5; 57.6; 55.0; 54.9; 51.6; 50.7; 47.8; 40.6; 37.9; 28.1; 24.2; 23.8; 22.9; 22.7; 22.2; 21.3; 17.0; 16.8. HR-MS: 1383.6328 ($[M + H]^+$; calc. 1383.6358).

N-*Boc-Thr-{*N*-[(4*S*)-4-amino-3-oxo-2-(triphenylphosphoranylidene)heptanoyl]-Leu}-[*N^{γ}*-(4,4′-dimethoxylbenzhydryl)-Asn]-*D*-Ala (Threonine Hydroxy) Lactone* (**11**). A soln. of **10** (3.50 g, 2.53 mmol) in 50 ml of MeOH was treated with 10% Pd–C (400 mg), and the resulting black suspension was stirred at 23° under H_2 (1 atm) for 24 h. The catalyst was removed by filtration through *Celite*, and the filtrate was concentrated *in vacuo* to give the crude amino acid, which was used directly in the next reaction without further purification.

A soln. of the above product and $NaHCO_3$ (217 mg, 2.58 mmol) in 500 ml of degassed DMF was cooled to 0° and treated with diphenylphosphoryl azide (DPPA) (2.30 ml, 10.7 mmol). The mixture was stirred at 0° for 72 h. The mixture was concentrated *in vacuo*, and the residue was diluted with 250 ml of AcOEt. The org. phase was washed with H_2O (150 ml) and sat. aq. NaCl soln. (150 ml), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. FC (SiO_2; 5 × 20 cm, AcOEt/hexane 3 : 1 to 4 : 1) afforded **11** (1.70 g, 59%). White powder. $[\alpha]_D^{20} = +48.0$ ($c = 10.0$, $CHCl_3$). R_f (AcOEt/hexane 4 : 1) 0.28. IR (KBr): 3428, 3059, 2955, 1672, 1510, 1248, 1175. ^1H-NMR ($CDCl_3$, 500 MHz): 7.89–7.78 (*m*, 7 H); 7.52–7.36 (*m*, 10 H); 7.02 (*m*, 1 H); 6.98 (*d*, $J = 8.3$, 2 H); 6.89 (*d*, $J = 8.3$, 2 H); 6.75 (*m*, 4 H); 6.41 (*d*, $J = 7.0$, 1 H); 6.12 (*m*, 1 H); 5.67 (*d*, $J = 8.2$, 1 H); 5.61 (*d*, $J = 8.3$, 1 H); 5.38 (*m*, 1 H); 4.71 (*m*, 1 H); 4.62 (*m*, 1 H); 4.15 (*m*, 1 H); 4.10 (*d*, $J = 8.1$, 1 H); 3.97 (*m*, 1 H); 3.73 (*s*, 6 H); 3.04 (*dd*, $J = 14.9$, 3.8, 1 H); 2.32 (*m*, 1 H); 1.58 (*m*, 1 H); 1.41 (*s*, 9 H); 1.38–1.09 (*m*, 8 H); 0.95 (*d*, $J = 6.2$, 3 H); 0.88 (*m*, 6 H); 0.72 (*d*, $J = 6.2$, 3 H); 0.68 (*d*, $J = 6.2$, 3 H). ^{13}C-NMR ($CDCl_3$, 125 MHz): 196.6; 172.9; 170.7; 169.6; 167.6; 158.6; 158.5; 155.7; 134.3; 133.8 (*d*, J(C,P) = 9.9); 135.5; 132.1; 128.9 (*d*, J(C,P) = 12.6); 128.6; 128.3; 125.9 (*d*, J(C,P) = 91.8); 113.8; 113.5; 79.4; 71.6; 71.5 (*d*, $J = 101.5$); 57.2; 55.1; 54.8; 53.9; 53.3; 49.6; 47.4; 44.6; 40.1; 35.9; 28.2; 25.2; 24.7; 23.2; 22.8; 22.6; 20.9; 18.8; 16.2. HR-MS: 1141.5402 ($[M + H]^+$; calc. 1141.5415).

N-*[*N*-(Phenylacetyl)-Phe-Thr]-Thr-{*N*-[(4*S*)-4-amino-3-oxo-2-(triphenylphosphoranylidene)heptanoyl]-Leu}-Asn-*D*-Ala (Threonine Hydroxy) Lactone* (**12a**, YM-47141 precursor). A mixture of **11** (245 mg, 0.215 mmol) and anisole (0.5 ml) was treated with TFA (5 ml). The resulting mixture was stirred at 23° for 3 h. The volatiles were removed *in vacuo*. The residue was triturated with Et_2O (10 ml) and collected by filtration to give a white powder, which was used directly in the following reaction without further purification.

A soln. of the above salt in 5 ml of CH_2Cl_2 was sequentially treated with *N*-(phenylacetyl)-Phe-Thr-OH (165 mg, 0.43 mmol), HOBt (58 mg, 0.43 mmol), Et_3N (109 mg, 1.07 mmol), and EDCI (82.4 mg, 0.43 mmol). The resulting mixture was stirred at 23° for 36 h. The soln. was then diluted with CH_2Cl_2 (30 ml) and washed with H_2O (15 ml) and sat. aq. NaCl soln. (15 ml). The org. layer was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was purified on a chromatotron plate (coated with 6-mm thickness silica-gel-gypsum, 10% EtOH/$CHCl_3$ eluent) to yield **12a** (222 mg, 87%). White powder. $[\alpha]_D^{20} = -40.1$ ($c = 4.0$, $CHCl_3$). R_f (SiO_2; 10% MeOH/$CHCl_3$) 0.4. IR (KBr): 3308, 3061, 3032, 2955, 1743, 1662, 1522. ^1H-NMR ((D_6)DMSO, 500 MHz): 9.39 (br. *s*, 1 H); 8.31 (*m*, 3 H); 7.80–7.03 (*m*, 25 H); 6.85 (br. *s*, 1 H); 5.64 (br. *s*, 1 H); 5.59 (*m*, 1 H); 5.44 (*m*, 1 H); 5.15 (*d*, $J = 4.1$, 1 H); 4.73 (*m*, 2 H); 4.46–4.40 (*m*, 3 H); 4.25 (*m*, 1 H); 4.10 (*m*, 1 H); 4.02 (*m*, 1 H); 3.91 (*m*, 1 H); 3.40 (*d*, $J = 14.0$, 1 H); 3.33 (*d*, $J = 14.0$, 1 H); 3.13 (*d*, $J = 12.0$, 1 H); 2.78 (*m*, 2 H); 2.55 (*dd*, $J = 15.6$, 4.6, 1 H); 2.44 (*dd*, $J = 15.3$, 6.4, 1 H); 1.47 (*m*, 3 H); 1.35 (*d*, $J = 6.7$, 3 H); 1.27 (*m*, 1 H); 1.18 (*m*, 4 H); 1.04 (*d*, $J = 5.7$, 3 H); 1.01 (*m*, 2 H); 0.83 (*m*, 5 H); 0.67 (*d*, $J = 5.7$, 3 H); 0.64 (*d*, $J = 5.7$, 3 H). ^{13}C-NMR ((D_6)DMSO, 125 MHz): 192.7; 172.7; 172.0; 171.8; 170.3; 170.0; 169.9; 169.7; 168.2; 166.5; 138.0; 136.2; 133.5; 133.4 (*d*, J(C,P) = 9.2); 132.1; 129.4; 128.9; 128.8; 128.0; 127.9; 126.1; 125.8 (*d*, J(C,P) = 87.8); 79.2; 71.8; 70.9 (*d*, J(C,P) = 104.0); 66.3; 57.9; 54.9; 53.9; 52.6; 49.5; 47.6; 43.4; 42.1; 40.2; 37.6; 35.6; 24.4; 23.9; 23.3; 22.8; 22.4; 21.9; 19.2; 18.2; 16.6. HR-MS: 1181.5472 ($[M + H]^+$; calc. 1181.5477).

YM-47141 (**1a**). A soln. of **12a** (0.20 g, 0.17 mmol) in 10 ml of CH_2Cl_2 was ozonized at $-78°$ for 2 min. The light-blue mixture was purged with O_2 and N_2 for 3 and 5 min, respectively, to remove excess O_3. During ozonolysis, the product precipitated out of the reaction soln. Filtration and washing the residue with CH_2Cl_2 provided 0.14 g (89%) of *YM-47141* (**1a**) as a white powder identical in all respects to a sample of natural material. $[\alpha]_D^{20} = -8.6$ ($c = 0.3$, MeCN) (lit.: $[\alpha]_D^{25} = -10.1$ ($c = 0.2$, CH_3CN). IR (KBr): 3400, 3067, 2960, 1737, 1662, 1528. ^1H-NMR ((D_6)DMSO, 500 MHz): 8.49 (*d*, *J* = 8.8, 1 H); 8.38 (*d*, *J* = 8.3, 1 H); 8.11 (*d*, *J* = 7.3, 1 H); 7.99 (*d*, *J* = 7.8, 1 H); 7.90 (*d*, *J* = 6.8, 1 H); 7.57 (*d*, *J* = 9.3, 1 H); 7.54 (*s*, 1 H); 7.35 (*s*, 1 H); 7.33 (*s*, 1 H); 7.30 (*m*, 2 H); 7.21 (*m*, 2 H); 7.16 (*m*, 4 H); 7.02 (*m*, 2 H); 6.98 (*d*, *J* = 9.8, 1 H); 6.95 (*s*, 1 H); 5.42 (*m*, 1 H); 5.10 (*d*, *J* = 4.9, 1 H); 5.00 (*m*, 1 H); 4.69 (*m*, 1 H); 4.64 (*dd*, *J* = 9.3, 2.4, 1 H); 4.46 (*m*, 1 H); 4.41 (*m*, 1 H); 4.36 (*dd*, *J* = 8.8, 2.9, 1 H); 4.13 (*m*, 1 H); 4.02 (*m*, 1 H); 3.35 (*d*, *J* = 13.7, 1 H); 3.30 (*d*, *J* = 13.7, 1 H); 3.10 (*dd*, *J* = 13.7, 2.4, 1 H); 2.75 (*dd*, *J* = 13.7, 11.2, 1 H); 2.60 (*dd*, *J* = 15.6, 3.4, 1 H); 2.38 (*dd*, *J* = 15.6, 10.2, 1 H); 2.16 (*m*, 1 H); 1.61 (*m*, 2 H); 1.54 (*m*, 1 H); 1.43 (*m*, 1 H); 1.31 (*m*, 1 H); 1.13 (*d*, *J* = 6.3, 3 H); 1.03 (*d*, *J* = 6.3, 3 H); 1.00 (*d*, *J* = 6.8, 3 H); 0.89 (*d*, *J* = 6.3, 3 H); 0.87 (*d*, *J* = 6.4, 3 H); 0.85 (*d*, *J* = 6.3, 3 H); 0.81 (*d*, *J* = 6.4, 3 H). ^{13}C-NMR ((D_6)DMSO, 125 MHz): 206.3; 172.2; 170.9; 170.6; 170.5; 170.4; 170.1; 170.0; 167.6; 138.1; 136.3; 129.5; 129.0; 128.1; 127.9; 126.2; 94.7; 71.9; 66.3; 57.9; 54.6; 54.1; 53.7; 53.3; 50.4; 46.7; 42.1; 38.6; 37.8; 36.8; 24.9; 24.1; 23.6; 22.7; 22.0; 20.7; 20.0; 16.5; 16.1. HR-MS: 975.4435 ($[M + Na]^+$; calc. 975.4440).

N-*[*N-*(Isopropylacetyl)-Phe-Thr]-{*N-*[(4*S*)-4-amino-6-methyl-3-oxo-2-(triphenylphosphoranylidene)heptanoyl]-Leu}-Asn-*D-*Ala] (Threonine Hydroxy) Lactone* (**12b**, YM-47142 precursor). A mixture of **11** (0.49 g, 0.43 mmol) and anisole (1 ml) was treated with TFA (8 ml). The resulting soln. was stirred for 2 h at r.t. and then was evaporated *in vacuo*. The residue was washed with Et_2O (15 × 2 ml) to give a white powder, which was used directly in the following reaction without further purification.

A soln. of the above salt in 10 ml of CH_2Cl_2 was treated with *N*-(isopropylacetyl)-Phe-Thr-OH (0.30 g, 0.86 mmol), HOBt (0.12 g, 0.89 mmol), Et_3N (0.30 ml, 2.15 mmol), and EDCI (0.16 g, 0.84 mmol). The resulting mixture was stirred for 40 h at r.t. and then was diluted with CH_2Cl_2 (20 ml), and washed with H_2O (20 × 2 ml) and brine (20 ml). The org. layer was dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified on a chromatotron (EtOH/$CHCl_3$ 1:9) to give 0.35 g (72%) of **12b**. White powder. $[\alpha]_D^{20} = -32.4$ ($c = 5.0$, $CHCl_3$). IR (KBr): 3289, 3016, 2952, 1661, 1519. ^1H-NMR ((D_6)DMSO, 500 MHz): 9.38 (br. *s*, 1 H); 8.14 (*d*, *J* = 8.3, 1 H); 8.02 (*d*, *J* = 7.8, 1 H); 7.78–7.14 (*m*, 23 H); 6.82 (br. *s*, 1 H); 5.67 (*m*, 1 H); 5.49 (*m*, 1 H); 5.41 (*m*, 1 H); 5.13 (*d*, *J* = 3.9, 1 H); 5.02 (*m*, 1 H); 4.67 (*m*, 2 H); 4.42 (*m*, 3 H); 4.09 (*m*, 1 H); 3.93 (*m*, 1 H); 3.08 (*d*, *J* = 13.2, 1 H); 2.72 (*m*, 2 H); 2.54 (*m*, 1 H); 2.40 (*m*, 1 H); 1.85 (*m*, 2 H); 1.79 (*m*, 1 H); 1.44 (*m*, 3 H); 1.32 (*d*, *J* = 6.3, 3 H); 1.16 (*m*, 6 H); 1.03 (*d*, *J* = 5.4, 3 H); 1.00 (*m*, 1 H); 0.93 (*m*, 1 H); 0.80 (*m*, 6 H); 0.71 (*d*, *J* = 6.3, 3 H); 0.65 (*d*, *J* = 5.9, 3 H); 0.63 (*d*, *J* = 6.3, 3 H). ^{13}C-NMR ((D_6)DMSO, 125 MHz): 192.5; 172.6; 172.1; 171.4; 170.2; 169.9; 169.8; 169.6; 168.2; 166.4; 138.2; 133.4 (*d*, *J*(C,P) = 9.4); 132.0; 129.2; 128.8; 127.8; 126.0; 125.7 (*d*, *J*(C,P) = 81.0); 71.7; 70.9 (*d*, *J*(C,P) = 106.1); 66.2; 57.7; 54.9; 53.6; 52.5; 52.2; 49.5; 47.6; 44.5; 39.9; 38.9; 37.3; 35.6; 25.4; 24.4; 23.8; 23.3; 22.8; 22.2; 22.1; 22.0; 20.8; 19.1; 18.1; 16.5. HR-MS: 1147.5641 ($[M + H]^+$; calc. 1147.5633).

YM-47142 (**1b**). A soln. of **12b** (0.30 g, 0.26 mmol) in 10 ml of CH_2Cl_2 was ozonized at $-78°$ for 2 min and then was purged with N_2. During ozonolysis, the product precipitated out of the reaction soln. Filtration and washing the residue with CH_2Cl_2 provided 0.22 g (92%) of **1b** as a white powder identical to the authentic natural product. $[\alpha]_D^{20} = -2.0$ ($c = 0.2$, MeCN) (lit.: $[\alpha]_D^{25} = -1.8$ ($c = 0.5$, MeCN)). IR (KBr): 3299, 2959, 1651, 1532. ^1H-NMR ((D_6)DMSO, 500 MHz): 8.35 (*d*, *J* = 8.8, 1 H); 8.10 (*d*, *J* = 7.8, 1 H); 8.07 (*d*, *J* = 8.3, 1 H); 7.99 (*d*, *J* = 8.3, 1 H); 7.90 (*d*, *J* = 6.8, 1 H); 7.57 (*d*, *J* = 8.8, 1 H); 7.53 (*s*, 1 H); 7.35 (*s*, 1 H); 7.32 (*m*, 2 H); 7.30 (*s*, 1 H); 7.21 (*m*, 2 H); 7.13 (*m*, 1 H); 6.98 (*d*, *J* = 9.3, 1 H); 6.94 (*s*, 1 H); 5.41 (*m*, 1 H); 5.09 (*d*, *J* = 4.9, 1 H); 5.00 (*m*, 1 H); 4.69 (*m*, 1 H); 4.62 (*dd*, *J* = 8.8, 2.0, 1 H); 4.46 (*m*, 1 H); 4.41 (*m*, 1 H); 4.35 (*dd*, *J* = 8.3, 2.9, 1 H); 4.14 (*m*, 1 H); 4.02 (*m*, 1 H); 3.06 (*dd*, *J* = 13.2, 2.4, 1 H); 2.71 (*dd*, *J* = 13.2, 11.7, 1 H); 2.60 (*dd*, *J* = 15.6, 3.4, 1 H); 2.38 (*dd*, *J* = 15.6, 10.2, 1 H); 2.15 (*m*, 1 H); 1.85 (*m*, 2 H); 1.80 (*m*, 1 H); 1.60 (*m*, 1 H); 1.59 (*m*, 1 H); 1.53 (*m*, 1 H); 1.44 (*m*, 1 H); 1.30 (*m*, 1 H); 1.13 (*d*, *J* = 6.3, 3 H); 1.03 (*d*, *J* = 5.9, 3 H); 1.00 (*d*, *J* = 7.3, 3 H); 0.88 (*d*, *J* = 6.8, 3 H); 0.86 (*d*, *J* = 6.8, 3 H); 0.85 (*d*, *J* = 6.8, 3 H); 0.81 (*d*, *J* = 6.3, 3 H); 0.71 (*d*, *J* = 6.4, 3 H); 0.62 (*d*, *J* = 6.8, 3 H). ^{13}C-NMR ((D_6)DMSO, 125 MHz): 206.4; 172.5; 172.4; 171.7; 171.1; 170.7; 170.6; 170.5; 170.2; 167.6; 138.4; 129.5; 128.1; 126.3; 94.7; 72.0; 66.4; 57.9; 54.7; 54.0; 53.8; 53.4; 50.5; 46.8; 44.6; 40.0; 38.7; 37.6; 36.8; 25.7; 25.0; 24.2; 23.7; 22.8; 22.3; 22.2; 22.0; 20.8; 19.7; 16.6; 16.2. HR-MS: 919.4779 ($[M + H]^+$; calc. 919.4776).

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