Synthesis of a Stereoisomeric Mixture of (±)-PM-Toxin B, a Host-specific Corn Pathotoxin Produced by Phyllosticta maydis

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Received July 19, 1984

A stereoisomeric mixture of (±)-PM-toxin B [6,14,22,30,32-pentahydroxy-8,16,24-trioxotritriacontane] has been synthesized via three steps of Grignard addition and shows virtually the same biological activities as the natural PM-toxin B.

PM-toxin,1) isolated from the corn pathogen, Phyllosticta maydis, selectively damages only corn with Texas-male sterile cytoplasm at 10^-9 to 10^-8 M, but not corn with normal fertile cytoplasm at 10^-5 M. The toxin is a mixture of biogenetically related compounds of apparently equal toxicity. The four major components have been purified and characterized, although the stereochemistry of the hydroxyl functions was not determined.2)

We report here the first synthesis of one of the major components (PM-toxin B) as a mixture of stereoisomers possessing the syn-1,3-hydroxy configuration at C-30 and C-32. Synthetic PM-toxin B has the same specific toxicity toward corn and thus the proposed structure of the natural toxin is confirmed.

Our synthetic outline is shown in Fig. 1. C-C bond formations at C-8, C-16 and C-24 in PM-toxin B were chosen because of their applicability to chiral synthesis by using precursors like β-hydroxyesters which are readily prepared by unsymmetrical reduction of β-ketoesters with baker's yeast. Synthesis of chiral PM-toxin B with a variety of known absolute stereochemistries can not only establish the absolute stereochemistry of the natural toxin, but also may lead to a better understanding of the mode of action for PM-toxins.

Three segments (a, b, c) corresponding to the C1-8, C9-16 and C17-24, and C25-33 units in PM-toxin B were initially synthesized as shown in Scheme 1. The synthesis of segment a (3) started from β-hydroxyoctanoate 1. Etherification3) of 1 with dimethoxymethane and phosphorous pentoxide in chloroform, and the reduction of 2 with diisobutylaluminium hydride in n-hexane (-78°C, 45 min) gave the desired segment a (3) in a 46.9% overall yield.

The synthesis of segments b and c was designed to utilize the convenient monoal-
Alkylation of the dianion of the $\beta$-ketoester and $\beta$-diketone with 1,4-dibromobutane. Condensation of the dianion generated from methyl acetoacetate with 1.5 equiv. of 1,4-dibromobutane (0°C, 10 min) gave the desired $\beta$-ketobromoester 4 in a 52.5% yield. Reduction of 4 with sodium borohydride in methanol (0°C, 30 min) produced the $\beta$-hydroxy bromoester 5, which on reduction with 3 equiv. of diisobutylaluminum hydride in tetrahydrofuran (0°C, 1 hr) gave the $\beta$-dihydroxybromide 6. Acetonization of 6 with 2,2-dimethoxypropane and p-toluenesulfonic acid in dioxane (20°C, 1 hr) afforded the desired segment b (7) in a 63.1% overall yield. Direct conversion of 4 to 6 by reduction with an excess of diisobutylaluminum hydride was unsatisfactory because a considerable amount of 4 invariably remained unreacted.

Alkylation of the dianion of 2,4-pentane-dione to 1,4-dibromobutane (1.5 equiv.) gave the desired $\beta$-diketo-bromide 8, which reacted with sodium borohydride in methanol (10°C, 30 min) to provide a chromatographically separable mixture of the syn and anti isomers (9 and 10) in 10.8% and 37.0% yields, respectively. Acetonization of 9 and 10 gave the desired segment c (11) and its isomer (12), respectively.

The relative configurations of 9 and 10 were determined on the basis of NOE measurements for each benzylideneacetals, 13 and 14 (Fig. 2). Enhancement of both the C-6H and C-8H signals upon irradiation of benzyllic H in 13 (derived from the less polar isomer 9) suggested that C-6H, C-8H and benzyllic H should be syn diaxial. To the contrary, another benzylidene isomer 14 (derived from the more polar isomer 10) consisted of two diasteroisomers, and the expected NOE was observed at either the C-6H or C-8H signal in each isomer. These results show clearly that 13 has the cis configuration and 14A and 14B have trans configuration. The syn stereochemistry for the $\beta$-diol moiety in PM-toxin B was
further elucidated by $^{1}$H- and $^{13}$C-NMR comparisons with the pentaacetate of PM-toxin B, and the diacetates of the 1,3-syn-diol 9 and the anti-diol 10 (Table I). Therefore, the cis-acetonide 11, which was derived from the minor product 9 possessing the same syn stereochemistry as the natural PM-toxin-B, was used as the segment c.

The reactions for coupling each segment, leading to PM-toxin B, were carried out as shown in Scheme 2. The reaction of 3 with the Grignard reagent generated from 7 in tetrahydrofuran (−10 to −5°C, 10 min) produced the alcohol 15 in a 94.0% yield. Oxidation of 15 with pyridinium dichromate in N,N-dimethylformamide (rt, 18 hr) afforded the corresponding ketone 16 (69.6%), which reacted with 4 equiv. of ethanedithiol and boron trifluoride etherate in dichloromethane (tR, 18 hr) to give the dithioacetal 17 (62.8%) with deprotection of the isopropylideneacetal and methoxymethyl ether groups.

Selective tritylation of 17 with 1.0 equiv. of trityl chloride, 4-dimethylaminopyridine and triethylamine in dichloromethane ($t_R$, 4 hr) gave the tribenzyl ether 25 in a 46.5% yield from 23. Finally, debenzylation by hydrogenolysis using an excess of activated palladium black as a catalyst in a mixed solvent (acetic acid-dioxane-water = 4:1:1) at 35°C for 24 hr gave the desired stereoisomeric mixture of (±)-PM-toxin B (37.0% yield), which was identical with natural PM-toxin B by comparison of their FD-MS, 400 MHz $^1$H-NMR and 22.5 MHz $^{13}$C-NMR (Figs. 3 and 4), and behavior with TLC and HPLC. Two shorter chain versions of PM-toxin B, PM-288 (C16) and PM-430 (C24), were also prepared from each protected compound (17 and 21b).

The biological activities of the synthetic...
PM-toxin B and analogs were evaluated using assays of the inhibition of dark CO$_2$ fixation by thin leaf slices and stimulation of NADH oxidation in mitochondria as described previously.$^{10}$ The biological activity of synthetic (±)-PM-toxin B was indistinguishable from that of natural PM-toxin in both assays on susceptible (W64AT) corn (Table II, Fig. 5), providing further evidence that the proposed structure for PM-toxin B$^{1,2}$ is correct. In addition, the fact that the biological activity of the stereoisomeric mixture of synthetic (±)-PM-toxin B is equal to that of natural PM-toxin B suggests that the stereochemistry may not be important for maximum biological activity.

The shorter analogs of PM-toxin B (PM-430 and PM-288) were less active on susceptible corn than PM-toxin B itself. PM-430 was about an order of magnitude less active and PM-288 was about three orders of magnitude less active than PM-toxin B itself.

As with analogs of HMT-toxin examined earlier,$^{10}$ chain length appears to be important
Synthesis of a Stereoismeric Mixture of (±)-PM-Toxin B

![Synthetic and natural PM-Toxin B NMR spectra](image)

**Fig. 4.** 22.5 MHz $^{13}$C-NMR Spectra (PND) of Synthetic and Natural PM-Toxin B in $d_5$-Pyridine.

**Table II.** Effects of Natural and Synthetic PM-Toxin B and Its Shorter Analogs on the Inhibition of Dark CO$_2$ Fixation by Leaf Slices of Susceptible (W64AT) Corn

<table>
<thead>
<tr>
<th>Compound</th>
<th>Concentration (mol/liter)</th>
<th>% Inhibition$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$3 \times 10^{-9}$</td>
<td>$1 \times 10^{-8}$</td>
</tr>
<tr>
<td>PMB (natural)</td>
<td>15</td>
<td>21</td>
</tr>
<tr>
<td>(±)PMB (synthetic)</td>
<td>12</td>
<td>23</td>
</tr>
<tr>
<td>PM 430</td>
<td>4</td>
<td>22</td>
</tr>
<tr>
<td>PM 288</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Averages of two experiments. Control rates of CO$_2$ fixation averaged 17.4 ± 1.8 nmol CO$_2$ slice$^{-1}$ hr$^{-1}$. Standard deviations averaged 4%.

$^b$ Minus indicates rates above control values.

![Comparison of PM-Toxin B oxidation](image)

**Fig. 5.** Comparative Effects of Natural and Synthetic PM-Toxin B and Its Shorter Analogs on Oxidation of NADH by Mitochondria of Susceptible (W64AT) Corn.
for the maximum toxicity of PM-toxin analogs. Like the natural PM-toxins, the synthetics are all host-specific. None shows any activity on dark CO₂ fixation or NADH oxidation in resistant (W64AN) corn at 10 µM. Natural and synthetic PM-toxin B and PM-288 were also tested at 100 µM and were still inactive toward resistant corn at these high concentrations.

**EXPERIMENTAL**

NMR spectra were taken on JNM FX-90Q or GX-400 spectrometers. Low-resolution mass spectra (EI-MS) were obtained on a Hitachi RMU-6MG instrument. High-resolution mass spectra (HR-MS) and field-desorption mass spectra (FD-MS) were obtained on a Hitachi M-80 spectrometer. Infrared spectra (IR) were measured on a Shimadzu IR-435 spectrometer with films on NaCl plates or KBr disks.

**Ethyl (±)-3-hydroxyoctanoate-3-methoxymethyl ether 2.** P₂O₅ (ca. 30 g) was added to a stirred solution of 1 (26.7 g, 142 mmol) in dry CHCl₃ (150 ml) and methylal (150 ml) at room temperature. After 10 min., the mixture was decanted and the residue was washed out with EtOAc. The combined solution was washed successively with sat. NaHCO₃ and brine, and dried over MgSO₄. Evaporation of the solvent gave a crude oil of 2 (35.0 g, 63.1%). ¹H-NMR (CDC₁₃): δ 2.44 (t, J = 7 Hz), 2.99 (quint, J = 7 Hz) and 3.48 (t, J = 7 Hz), 3.57 (2H, s), 3.75 (2H, t, J = 7 Hz), 3.79 (2H, m), 4.00 (1H, m). EI-MS: m/z 236 and 234 (M+ + 2-H₂O and M+ - CH₃, 1), 221 and 219 (1), 179 and 177 (20 and 23), 171 (51), 129 (10), 116 (100).

**Methyl (±)-8-bromo-3-oxooctanoate 4.** The diastereomeric product was obtained from methyl acetoacetate (23.2 g, 200 mmol), 60% NaH (8.8 g, 220 mmol) and n-BuLi (133 ml of 1.7 M solution in n-hexane, 212 mmol) in dry THF (400 ml), as previously reported. 1,4-Dibromobutane (65.0 g, 300 mmol) was added in one portion at 0°C. The mixture was stirred at 0°C for 10 min, and conc. HCl (40 ml), water (40 ml) and EtOAc (100 ml) were successively added. The organic phase was separated, washed with brine, dried over MgSO₄, and concentrated in vacuo. The residue was chromatographed on silica gel, eluting with 20% EtOAc in n-hexane to give an oil of 4 (53.0 g, 52.5%). ¹H-NMR (CDCl₃): δ 1.88 (2H, quint, J = 7 Hz), 2.57 (2H, t, J = 7 Hz), 3.40 (2H, t, J = 7 Hz), 3.45 (2H, s), 3.74 (3H, s). EI-MS: m/z 252 and 250 (M+ + 2 and M+, 1), 221 and 219 (1), 179 and 177 (20 and 23), 171 (51), 129 (10), 116 (100).

(±)-8-Bromo-1,3-dihydroxyoctane-1,3-isopropylideneacetel 7 (seg. b). NaBH₄ (2.66 g, 70 mmol) was added to a solution of 4 (53.0 g, 210 mmol) in MeOH (800 ml) at 0°C. Stirring was continued for 1 hr and AcOH (18 ml) was added. The mixture was concentrated at room temperature. The residue was dissolved in EtOAc and the solution was washed with sat. NaHCO₃ and brine, and dried over MgSO₄. Evaporation of the solvent gave a crude oil of 5 (51.5 g). ¹H-NMR (CDCl₃): δ 1.88 (2H, br. quint), 2.36 and 2.56 (each 1H, ABX, J = 16, 7, 4 Hz), 2.90 (1H, d, J = 2H, OH), 3.41 (2H, t, J = 7 Hz), 3.71 (3H, s), 4.00 (1H, m). EI-MS: m/z 236 and 234 (M+ + 2 - H₂O and M+ - CH₃, 5), 103 (100), 74 (30).

DIBAL (520 ml of a 1 m solution in n-hexane, 520 mmol) was added slowly to a cooled solution of 5 (51.5 g) in dry THF (500 ml) at −20°C. The mixture was stirred at −20°C for 1 hr and dilute HCl and Et₂O were added. The organic layer was separated, washed with sat. brine and dried (MgSO₄). Evaporation of the solvent gave a crude oil of 6 (ca. 50 g). ¹H-NMR (CDCl₃): δ 1.88 (2H, br. quint), 2.20 (2H, br. s, OH), 3.41 (2H, t, J = 7 Hz), 3.86 (2H, t, J = 6 Hz), ca. 3.9 (1H, m).

A solution of 6 (ca. 50 g) and p-TsOH (900 mg) in 2,2-dimethoxypropane and dry dioxane (100 ml each) was stirred at 20°C for 1 hr. Powdered NaHCO₃ was added and the solvent was evaporated. The residue was dissolved in EtOAc, and the solution was washed with sat. brine and dried with MgSO₄. Evaporation of the solvent, followed by distillation (85 ~ 90°C/0.2 mmHg) gave an oil of 7 (35.0 g, 63.1%). ¹H-NMR (CDCl₃): δ 1.38 and 1.44 (each 3H, s), 1.88 (2H, br. quint), 2.42 (each 1H, ABX, J = 16, 7, 4 Hz), 2.90 (1H, d, J = 2H, OH), 3.41 (2H, t, J = 7 Hz), 3.86 (2H, t, J = 6 Hz), ca. 3.9 (1H, m).

(±)-1,3-DiBromo-1,3-dihydroxyoctanes 9 and 10. The diastereomeric product was obtained from 2,4-pentanediol (100 mmol) with 1.5 equiv. of 1,4-dibromobutane at 0°C for 5 min. and worked up as described above to give a crude oil of 8 (8.7 g). ¹H-NMR (CDCl₃): δ 2.07 (3H, s), 3.42 (3H, t, J = 7 Hz), ca. 2.3 (2H, m), 5.52 (1H, s), and small peaks due to the ketoform [2.62 (br. t), 3.58 (s)].

The oil of 8 was treated with NaBH₄ (2.54 g, 67 mmol) in MeOH (200 ml) at 10°C for 30 min and worked up as already described. Column chromatography on silica gel with 40% EtOAc in n-hexane gave an oil of 9 (2.58 g).
Similarly, the anti-diacetate was also obtained. Evaporated at room temperature to give the sym-diacetate. A mixture of 9 (10 mg), Ac₂O (1 ml), and dry pyridine was treated at 0°C for 18 hr and the solvent was evaporated. Preparative TLC on silica gel with 5% EtOAc in n-hexane gave an oil of 11 (2.48 g, 85.8%). Similarly, 12 (2.79 g, 84.7%) was also obtained. After purification by chromatography on silica gel with 5% EtOAc in n-hexane, 12 (2.79 g, 84.7%) was also obtained. XH-NMR (CDCl₃): δ 1.18 (3H, d, J = 6 Hz, syn). 

\(+\)-1-Bromo-6,8-dihydroxynonane-6,8-isopropylidenemacetal 11 (seg c) and 12. Acetonization of 9 (2.48 g, 10.4 mM) as above gave an oil of 11 (2.48, 85.8%). After purification by chromatography on silica gel with 5% EtOAc in n-hexane. Similarly, 12 (2.79 g, 84.7%) was also obtained.

11. H-NMR (CDCl₃): δ 1.16 (3H, d, J = 6 Hz), 1.40 and 1.43 (each 3H, s), 3.6~4.2 (2H, m), 3.41 (2H, t, J = 7 Hz). IR νmax cm⁻¹: 3550, 1630, 1450, 1230, 1030. EI-MS: m/z 271 and 269 (M⁺, 100), 205 and 203 (95), 163 and 161 (2), 123 (15), 59 (18).

12. H-NMR (CDCl₃): δ 1.31 (8H, s), 1.35 (6H, s), 3.41 (2H, t, J = 7 Hz), 3.6~4.2 (2H, m). IR νmax cm⁻¹: 1380, 1260, 1200, 1120. EI-MS: m/z 265 and 263 (M⁺ + 2-CH₃ and M⁺-CH₃, 15), 205 and 203 (3), 163 and 161 (2), 123 (15), 59 (18).

anti-Diacetate of 10. H-NMR (CDCl₃): δ 1.22 (3H, d, J = 6 Hz), 2.01 and 2.02 (each 3H, s), 3.40 (2H, t, J = 7 Hz), 4.96 (2H, br. quint). C-NMR (CDCl₃): δ 20.4 (q), 21.0 (q), 21.2 (q), 24.3 (t), 28.0 (t), 32.6 (t), 33.3 (t), 34.1 (t), 40.3 (t), 68.1 (d), 71.1 (d), 170.5 (s)×2. IR νmax cm⁻¹: 1735, 1370, 1240, 1020.

1,3,11-Trihydroxy-9-oxohexadecan-1,3-isopropylideneacetal-11-methoxymethyl ether 16. A mixture of Mg turnings (1.92 g), 7 (19.1 g, 72 mM) and a crystal of I₂ in dry THF (70 ml) was refluxed under N₂ for 20 min. A solution of 3 (12.2 g, 65 mM) in dry THF (60 ml) was added dropwise at -10°C for 10 min. The mixture was warmed to room temperature during 45 min, and poured into cooled sat. NH₄Cl solution. The mixture was worked up to give a crude oil of 15 (22.83 g). A mixture of 15 (22.83 g) and PDC (46 g, 122 mM) in dry DMF (100 ml) was stirred at room temperature for 18 hr. The mixture was diluted with water (800 ml) and ether. The ether was washed with water and dried over MgSO₄. Evaporation of the solvent and subsequent column chromatography on silica gel with 20% EtOAc in n-hexane gave an oil of 16 (15.8 g, 69.6%). H-NMR (CDCl₃): δ 0.89 (3H, br. t), 1.38 and 1.44 (each 3H, s), 2.44 (2H, t, J = 7 Hz), 2.44 and 2.74 (each 1H, ABX, J = 16, 5, 7 Hz), 3.33 (3H, s), 3.6~4.2 (4H, m), 4.63 (2H, s). IR νmax cm⁻¹: 1712, 1200, 1150, 100, 1040. EI-MS: m/z 357 (M⁺-CH₃, 50), 295 (100). HR-MS Found: M⁺-CH₃ m/z 357.2611; Calc. for C₂₀H₃₇O₅: 357.2639.

1,3,11-Trihydroxy-9-oxohexadecan-9-ethylene-dithioacetal 17. BF₃ etherate (3.37 ml) was added to a solution of 16 (15.8 g, 42.5 mM) and ethanedithiol (16 g, 170 mM) in dry CH₂Cl₂ (180 ml). The solution was stirred at room temperature for 18 hr and 5% NaOH (100 ml) was added. The organic layer was separated, washed with brine and dried over MgSO₄. Evaporation of the solvent yielded the crude product, which was chromatographed on silica gel, eluting with 3% MeOH in CH₂Cl₂, to afford an oil of 17 (9.73 g, 62.8%). H-NMR (CDCl₃): δ 0.89 (3H, br. t), 2.01 (2H, d, J = 5 Hz), 2.40 (2H, br. s, OH), 3.32 (4H, s), 3.42 (1H, d, J = 2 Hz, OH), 3.7~4.1 (4H, m). IR νmax cm⁻¹: 3400, 1640, 1460, 1420, 1050, 1040. EI-MS: m/z 364 (M⁺-CH₃, 10), 301 (8), 249 (45), 219 (95), 119 (100). HR-MS Found: M⁺-CH₃ m/z 364.2146; Calc. for C₁₉H₂₉O₅S₂: 364.2104.

1,3,11-Trihydroxy-9-oxohexadecan-9-ethylendithioacetal-1-trityl ether 18. A mixture of 17 (9.6 g, 26.3 mM), trityl chloride (8.07 g, 29.0 mM), DMAP (161 mg, 1.31 mM) and triethylamine (6.6 ml) in dry CH₂Cl₂ (25 ml) was stirred under N₂ at room temperature for 18 hr. The mixture was diluted with CH₂Cl₂ and the organic phase was washed with sat. NH₄Cl and brine, dried over MgSO₄ and concentrated. The residue was chromatographed on silica gel, eluting with CH₂Cl₂, to afford an oil of 18 (15.46 g, 96.9%). H-NMR
(CDCl$_3$): δ 0.89 (3H, br. t), 2.00 (2H, d, J = 5 Hz), 2.88 (1H, d, J = 2 Hz, OH), 3.30 (4H, s), 3.2 ~ 3.5 (2H, m), 3.44 (1H, d, J = 2 Hz, OH), 3.76 (1H, br. s), 4.00 (1H, br. s), 7.1 ~ 7.6 (15H, m). IR ν$_{\text{max}}$ cm$^{-1}$: 3450, 1595, 1490, 1450, 1220, 1070. EI-MS: m/z 364 (M$^+$ - trityl, 5), 345 (7), 302 (15), 249 (45), 243 (40), 219 (95), 119 (100).

3,11-Di(benzyl)oxy-1-hydroxy-9-oxohexadecane-9-ethylenedithioacetal 20. A mixture of 18 (15.34 g, 25.2 mmol) and 60% NaH (4.04 g, 100 mmol) in dry THF (100 ml) was stirred at room temperature for 1.5 hr under N$_2$, and then Bu$_4$N (270 mg, 1 mmol) and benzyl bromide (17.2 g, 100 mmol) were added. The mixture was stirred for 2 days and diluted with EtOAc, and the organic layer was washed with sat. NH$_4$Cl and brine, dried over MgSO$_4$, and evaporated to afford a crude oil of 19. This crude oil was dissolved in MeOH-CHCl$_3$ (1:1, 150 ml) and stirred with P-TsOH (430 mg, 2.52 mmol) at 20°C for 2.5 hr. Powdered NaHCO$_3$ was added, the solvent was removed and the residue was dissolved in EtOAc. The organic phase was washed with brine and dried with MgSO$_4$, followed by column chromatography on silica gel with 20% EtOAc in n-hexane gave a pale yellow oil of 20 (5.45 g, 39.9%).

3,11-Di(benzyl)oxy-9-oxohexadecanal-9-ethylenedithioacetal 21. A solution of 20 (10.43 g, 19.2 mmol) in dry pyridine (100 ml) was added to a slurry of CrO$_3$ (9.6 g, 96 mmol) in dry pyridine (500 ml). The mixture was stirred at room temperature for 18 hr. Ether (430 ml) was added, the mixture filtered, and the residue washed out with ether. The ether extract was washed with dilute HCl, 5% NaOH and sat. brine, and dried (MgSO$_4$). Evaporation of the solvent, followed by chromatography on silica gel with 20% EtOAc in n-hexane gave an oil of 21 (5.26 g, 50.5%).

3,11-Di(benzyl)oxy-9-oxohexadecan-9-ethylenedithioacet 21. A solution of 20 (10.43 g, 19.2 mmol) in dry pyridine (100 ml) was added to a slurry of CrO$_3$ (9.6 g, 96 mmol) in dry pyridine (500 ml). The mixture was stirred at room temperature for 18 hr. Ether (430 ml) was added, the mixture filtered, and the residue washed out with ether. The ether extract was washed with dilute HCl, 5% NaOH and sat. brine, and dried (MgSO$_4$).

Evaporation of the solvent, followed by chromatography on silica gel with 20% EtOAc in n-hexane gave an oil of 21 (5.26 g, 50.5%).

$^1$H-NMR (CDCl$_3$): δ 0.89 (3H, br. t), 1.38 and 1.43 (each 3H, s), 2.42 (2H, t, J = 7 Hz), 2.46 and 2.72 (each 1H, ABX, J = 16, 7, 5 Hz), 2.08 and 2.32 (each 1H, ABX, J = 15, 7, 4 Hz), 2.4 and 2.72 (each 1H, ABX, J = 11 Hz), 4.44 and 4.60 (each 1H, ABQ, J = 11 Hz). IR ν$_{\text{max}}$ cm$^{-1}$: 1710, 1495, 1455, 1380 1370, 1200, 1100, 1065. EI-MS: m/z 726 (M$^+$, 0.1), 712 (M$^+$-CH$_3$, 2), 603 (25), 549 (30), 453 (60), 355 (75), 309 (40), 203 (100), 191 (100). HR-MS Found: M$^+$ m/z 726.4387; Calc. for C$_{43}$H$_{66}$O$_5$S$_2$: 726.4348.

$^1$H-NMR (CDCl$_3$): δ 0.89 (3H, br. t), 1.96 ~ 2.46 (4H, m), 3.26 (8H, s), 3.62 (2H, m), 3.90 (2H, m), 4.50 (4H, m), 7.2 ~ 7.5 (10H, m). FD-MS: m/z 762 (M$^+$, 100).

$^1$H-NMR (CDCl$_3$): δ 0.89 (3H, br. t), 2.08 and 2.32 (each 2H, ABX, J = 15, 7, 4 Hz), 2.6 (2H, m), 3.26 (8H, s), 3.56 (2H, m), 3.86 (1H, m), 4.51 (6H, m). IR ν$_{\text{max}}$ cm$^{-1}$: 1705, 1495, 1455, 1380 1370, 1200, 1100, 1065. EI-MS: m/z 852 (M$^+$, 1), 759 (10), 745 (15), 655 (45), 647 (30), 339 (100), 303 (30). HR-MS Found: M$^+$ m/z 852.4350; Calc. for C$_{49}$H$_{72}$O$_4$S$_4$: 852.4310.

$^1$H-NMR (CDCl$_3$): δ 0.89 (3H, br. t), 2.08 and 2.32 (each 2H, ABX, J = 15, 7, 4 Hz), 2.36 (8H, s), 3.4 ~ 3.9 (5H, m), 4.44 and 4.56 (each 2H, ABQ, J = 11 Hz), 4.44 and 4.60 (each 1H, ABQ, J = 11 Hz), 3.15 and 5.5 (15H, m). IR ν$_{\text{max}}$ cm$^{-1}$: 3430, 1600, 1495, 1350, 1090, 1060. EI-MS: m/z 852 (M$^+$, 1), 759 (10), 745 (15), 655 (45), 647 (30), 339 (100), 303 (30). HR-MS Found: M$^+$ m/z 852.4350; Calc. for C$_{49}$H$_{72}$O$_4$S$_4$: 852.4310.

$^1$H-NMR (CDCl$_3$): δ 0.89 (3H, br. t), 2.08 and 2.32 (each 2H, ABX, J = 15, 7, 4 Hz), 2.6 (2H, m), 3.26 (8H, s), 3.56 (2H, m), 3.86 (1H, m), 4.51 (6H, m). IR ν$_{\text{max}}$ cm$^{-1}$: 2700, 1720, 1495, 1455, 1350, 1090, 1060. FD-MS: m/z 850
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6,14,22-Tri(benzyl)oxy-30,32-dihydroxy-8,16,24-trioxotritriacontane 25. A mixture of 23 (820 mg, 0.78 mm) in ACOH (35 ml) water (15 ml), and THF (20 ml) was stirred at 50°C for 5 hr. The solvent was evaporated at room temperature to give an oil of 24 (780 mg, 97.7%). A solution of 24 (760 mg, 0.76 mm), HgCl₂ (1.14 g) and HgO (350 mg) in CH₂CN (25 ml) and water (1.5 ml) was stirred at 25°C for 4 hr under N₂. The mixture was filtered and the filtrate was diluted with water and CHCl₃. The organic phase was separated, washed with sat. NH₄Cl solution and dried (MgSO₄). Evaporation of the solvent, followed by column chromatography on silica gel with 2% i-PrOH in CH₂Cl₂ afforded an oil of 25 (430 mg, 64.9%).

24. ¹H-NMR (CDCl₃): δ 0.89 (3H, br. t), 1.19 (3H, d, J = 6 Hz), 3.26 (8H, s), 3.6-3.9 (5H, m), 4.49 (6H, m). IR ν^cm⁻¹: 3400, 1709, 1410, 1495, 1455, 1380, 1110, 1065. FD-MS: m/z 1048 (M⁺, 100).

25. ¹H-NMR (CDCl₃): δ 0.88 (3H, br. t), 1.19 (3H, d, J = 6 Hz), 2.41 (6H, t, J = 6 Hz), 2.41 and 2.74 (each 3H, ABX, J = 16, 7, 5 Hz), 2.96 (2H, br. s, OH), 3.92 (5H, m), 4.48 (6H, m). IR ν^cm⁻¹: 3400, 1719, 1495, 1455, 1380, 1110, 1065. FD-MS: m/z 1008 (M⁺, 100).

6,14,22,30,32-Pentahydroxy-8,16,24-trioxotritriacontane (PM-toxin B). A mixture of 25 (50 mg) and activated Pd black (200 mg) in MeOH–dioxane–water (4: 1: 1, 35 ml) was treated with 1 atom/cm² of H₂ at 35°C for 24 hr. The mixture was filtered and the filtrate concentrated. Preparative TLC afforded an oil of PM-430 (25 mg, 64.9%).

REFERENCES