Application of Carbohydrate-Templated Asymmetric Diels–Alder Reaction to the Syntheses of ent-Penicillones A and B

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Supporting Information

ABSTRACT: Total syntheses of ent-penicillones A (ent-1) and B (ent-2) from 3,5-dimethylcatechol (3) were accomplished in 10 and 9 synthetic steps, respectively. A carbohydrate-templated asymmetric intramolecular Diels–Alder reaction of a masked o-benzoquinone (MOB) 9 and an aqueous acid-catalyzed intramolecular aldol reaction are the key synthetic steps. In addition, the absolute configurations of the bicyclo[2.2.2]oct-5-en-2-one core obtained from the per-O-benzylated α-D-glucopyranosyl as a carbohydrate template in the intramolecular Diels–Alder reaction of MOBs were revised.

Penicillones A (1) and B (2), possessing a novel tricyclo[5.3.1.03,8]undecane skeleton (Figure 1), were isolated from a fungus Penicillium terrestre obtained from marine sediments of Jiaozhou Bay, Qingdao.1 Penicillone A (1) shows cytotoxicity against P-388 and A-549 cancer cell lines, while penicillone B (2) was inactive against P-388. The absolute configuration of (−)-2 has been determined by Mosher’s ester analysis. A comparison of CD absorptions of (+)-1 and (−)-2 suggested that these two compounds have the same absolute configuration. Therefore, the absolute configurations of (+)-1 and (−)-2 were concluded to be 1R,3S,7R,8S,9S,11R and 1R,3S,4R,7R,8S,9S,11R, respectively.

Masked o-benzoquinones (MOBs) have been demonstrated as valuable intermediates in organic synthesis.2 We have accomplished several natural product syntheses employing MOB intermediates,3,4 including (+)-penicillones A and B.5 Recently, Hung reported a three-step synthesis of optically pure bicyclo[2.2.2]oct-5-en-2-one via carbohydrate-templated asymmetric intramolecular Diels–Alder reactions of MOBs.6 Thus, we decided to use this strategy to synthesize optically pure penicillones A and B. The synthesis of optically pure 1 and 2 started from 3,5-dimethylcatechol (3).7 Better diastereoselectivity has been observed when using per-O-benzylated β-D-glucopyranosyl as the carbohydrate template in the oxidative coupling of phenol with allyl alcohols.8 Thus, installation of the carbohydrate template in catechol 3 was first carried out via coupling 2,3,4,6-tetra-O-benzyl-D-glucopyranosyl (4) with 3 using a Mitsunobu-type glycosylation.9 Unfortunately, this reaction gave four regio- and stereoisomers in low yield (Scheme 1). We turned our attention to using D-glucopyranose trichloroacetimidate (5) in the O-glycosylation under Lewis acidic conditions.10 Although the yield increased to 74%, the regio- and stereoselectivity were...
still poor. We noted that, in certain cases, the stereochemical outcome of the glycosylation reaction was affected by the type of protecting group employed at the 2-position in the glycosyl donor. A participating group, typically one containing a carboxyl group, can result in the predominant formation of a β-glycosylation. Thus, α-glucopyranose derivative 6 was used in the O-glycosylation. However, neighboring group participation was not observed in this glycosylation, and the stereoselectivity still was not improved. To our delight, a solution was found by treating catechol 3 with α-glucopyranose derivative 7 under basic conditions to give a single β-form product 8. The exclusive β-form product was obtained via an S_N2 replacement of the less hindered hydroxyl group in 3 with chloride. The stereochemistry of the acetal moiety in 8 was assigned using its proton coupling constant.

With phenol 8 in hand, the next step was the asymmetric intramolecular Diels–Alder reaction of the masked α-benzoquinone, which was generated from phenol 8 and diacetoxyiodobenzene (DAIB) in the presence of trans-crotyl alcohol (Table 1). The reaction was first carried out at −30°C for 6 h to form MOB 9 before the reaction mixture was heated under reflux for 20 h. The intramolecular Diels–Alder reaction of 9 proceeded smoothly at reflux to generate desired tricyclic β,γ-enediones 10 and 11 in 58% total yield and a 2:1 ratio (entry 1). Compounds 10 and 11 were easily separated by silica-gel chromatography. Better diastereoselectivity was observed when the oxidation was carried out at −50°C (entry 2). However, an attempt to improve the diastereoselectivity using an even lower temperature (−78 °C) was unsuccessful (entry 3). We reasoned that the poor selectivity in this reaction was attributed to the poor solubility of DAIB in CH$_2$Cl$_2$ at −78 °C and the oxidation not proceeding very well at this temperature. When the reaction mixture was heated to reflux, the oxidation and cyclization occurred simultaneously, giving a 1:1 mixture of the products. The best diastereoselectivity was observed when the oxidation was carried out at −78 °C and then warmed up slowly to −50 °C (entry 4). The absolute configurations of the bicyclo[2.2.2]oct-5-en-2-one cores in 10 and 11 were assigned by comparing their specific rotations with similar structures of known compounds. Accordingly, a negative specific rotation indicated an absolute configuration of 1S,3R,6S,7S,10S in the bicyclo[2.2.2]oct-5-en-2-one core, while a positive specific rotation indicated an absolute configuration of 1R,3S,6R,7R,10R. Therefore, the synthesis of natural penicillones was started from 11.

To complete the total synthesis, ketone 11 was first reduced with samarium diiodide in THF in the presence of MeOH to furnish alcohol 12 in 90% yield (Scheme 2). Compound 12 could then be converted to penicillones according to a literature procedure. Thus, stereocontrolled installation of the C-5 hydroxyl group was achieved via sequential epoxidation, epoxide ring-opening, and saponification. The next stage was a two-carbon homologation of the C-8 hydroxymethyl side chain, accomplished by oxidizing the primary and secondary alcohols to an aldehyde and ketone, respectively, simultaneously with IBX and then treating with (1,3-dioxolan-2-yl)methyltriphenylphosphonium bromide and t-BuOK to give unsaturated dioxolane intermediate 15 as an E/Z-mixture (E/Z = 1:8). Replacing t-BuOK with n-BuLi as a base in the Wittig reaction was unsuccessful. Hydrogenation of the unsaturated dioxolane 15 over 5% Rh on alumina afforded aldol precursor 16. Finally, aqueous acid-catalyzed hydrolysis and an aldol reaction were carried out in refluxing THF with 2 M H$_2$SO$_4$ to generate the desired product, penicillone B (2) as an only epimer. The reason for the formation of a single endo-epimer is presumably due to the 1,3-diaxial interaction present in the exo-epimer. Oxidation of penicillone B (2) with IBX furnished penicillone A (1). Spectra for these products were fully consistent with the literature data and our synthesized racemic penicillones. However, the specific rotation of synthetic penicillone B ([α]$_D^{20}$ +12.6 (c 0.2, MeOH)) was found to have the opposite sign to that of the natural product ([α]$_D^{20}$ −13.7 (c 0.2, MeOH)) (Scheme 3). Moreover, the specific rotation of synthetic penicillone A ([α]$_D^{25}$ −140.5 (c

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**Table 1. DAIB-Oxidized Intramolecular [4 + 2] Cycloaddition of Phenol 8 with trans-Crotyl Alcohol**

<table>
<thead>
<tr>
<th>entry</th>
<th>DAIB (equiv)</th>
<th>temp (°C)</th>
<th>time (h)</th>
<th>yield (%)</th>
<th>10:11</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>−30</td>
<td>6</td>
<td>58</td>
<td>2:1</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>−50</td>
<td>20</td>
<td>60</td>
<td>2.3:1</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>−78</td>
<td>20</td>
<td>39</td>
<td>1:1</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>−78 to −50</td>
<td>20</td>
<td>53</td>
<td>3.3:1</td>
</tr>
</tbody>
</table>

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**Scheme 2. Final Steps of the Total Synthesis of Penicillones A (1) and B (2)**

![Scheme 2. Final Steps of the Total Synthesis of Penicillones A (1) and B (2)](image-url)
configuration of 19 was confirmed by single-crystal X-ray diffraction analysis (Figure 2). Hydrolysis of the ketal moiety in 19 and 20 under acidic aqueous conditions afforded hemiketals 21 and 22. We then compared the optical rotations of 21 and 22 with the literature data and found their values to be quite different from those reported (Table 2). The specific rotation of synthetic 21 ([α]D28 +454.9 (c 1.5, CHCl3)) was found to have the opposite sign and different magnitude compared to that reported ([α]D 28 −287.5 (c 1.3, CHCl3)). The same pattern was also found for 22 ([α]D29 +453.9 (c 0.8, CHCl3)) compared to its reported value ([α]D28 +257.2 (c 0.5, CHCl3)). Due to these differences in optical rotation values between the synthetic and reported compounds, we believed that the absolute configurations of tricyclic cores in 10 and 11 were opposite to each other. Therefore, the absolute configurations of 10 and 11 in the bicyclo[2.2.2]oct-5-en-2-one cores should be 1R,3S,6R,7R,10R and 1S,3R,6S,7S,10S, respectively. The structures of 10 and 11 in Table 1 are revised-10 and revised-11, respectively, as shown in Table 3. Furthermore, since the structure of 11 has been revised to revised-11, other structures in Scheme 2 should also be revised to their enantiomers and shown in Scheme 4.

Table 3. Revised Structures of DAIB-Oxidized Intramolecular [4 + 2] Cycloaddition of Phenol 8 with trans-Crotyl Alcohol

<table>
<thead>
<tr>
<th>entry</th>
<th>DAIB (equiv)</th>
<th>temp (°C)</th>
<th>time (h)</th>
<th>yield (%)</th>
</tr>
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<td>−50</td>
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<td>3</td>
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<td>−78</td>
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</tr>
<tr>
<td>4</td>
<td>10</td>
<td>−78 to −50</td>
<td>20</td>
<td>53</td>
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</table>

The diastereoselectivity of oxidative coupling of phenol 8 with trans-crotyl alcohol is proposed from examination of the possible reactive conformations of the oxocarbenium intermediate that is presumably formed during the formation of the ketal with trans-crotyl alcohol (Figure 3). The conformation 23 not only has a higher steric hindrance between the phenyl ring and cationized cyclohexadienone but also possesses a stronger dipole–dipole interaction between the carbonyl group and the C1′−O bond in the pyranosyl ring. These effects presumably result in a preference for conformer 24 which can be attacked by trans-crotyl alcohol from the α-face.

## CONCLUSION

In summary, we accomplished the total synthesis of ent-penicillones A (ent-1) and B (ent-2) from 3,5-dimethylcatechol.
(3) in 10 and 9 synthetic steps, respectively, using a carbohydrate-templated MOB strategy. We also revised the absolute configurations of the bicyclo[2.2.2]oct-5-en-2-one core obtained from per-O-benzylated α-d-glucopyranosyl as the carbohydrate template in the intramolecular Diels–Alder reaction of MOBs.

**EXPERIMENTAL SECTION**

**General Information.** Unless stated otherwise, reagents were obtained from commercial sources and used without further purification. All reactions were performed under a nitrogen atmosphere in anhydrous solvents, which were dried prior to use following standard procedures. Reactions were monitored by thin-layer chromatography on 0.25 mm E. Merck silica gel plates (60F-254) using 7% ethanolic phosphomolybdic acid as the developing agent. Standard column chromatography was conducted using 70–230 mesh silica gel from E. Merck. Flash column chromatography was performed using 230–400 mesh silica gel from E. Merck. IR spectra were recorded as films on NaCl plates. 1H NMR spectra were obtained in CDCl3 unless otherwise noted at 400 or 600 MHz. 13C NMR spectra were obtained at 100 or 150 MHz. Chemical shifts were reported in δ (ppm) using solvent resonance as the internal reference. High resolution mass spectra (HRMS) were obtained on a TOF MS instrument with an EI or ESI source.

3,5-Dimethyl-2-hydroxyphenyl-2,3,4,6-tetra-O-benzyl-β-D-glucopyranoside (8). A mixture of NaH (0.16 g, 4.02 mmol, 60% in w/w oil) and 3 (0.37 g, 2.68 mmol) in DMF (27 mL) was stirred at 0 °C for 10 min. A solution of 7 (1.00 g, 1.79 mmol) in DMF (9 mL) was added to the reaction mixture. After stirring at room temperature for 12 h, the mixture was quenched with saturated aqueous NH4Cl and extracted with EtOAc. The combined extracts were washed with brine, dried over MgSO4, filtered, and concentrated. The crude product was purified by silica-gel chromatography (hexane/EtOAc/CH2Cl2 = 8:1:2) to give 8 (0.61 g, 52%) as a colorless oil. [α]D20 31.0 (c 1.0, CHCl3); IR (neat) ν 3452, 3043, 2935, 2879, 1644, 1496, 1454, 1359, 1310, 1070, 736 cm⁻¹; 1H NMR (400 MHz, CDCl3) δ 7.30–7.15 (m, 18H), 7.10–7.05 (m, 2H), 6.65 (s, 1H), 6.65 (s, 1H), 6.59 (bs, 1H), 4.92 (d, J = 10.8 Hz, 1H), 4.85 (d, J = 11.0 Hz, 1H), 4.81 (d, J = 11.0 Hz, 1H), 4.77 (d, J = 11.0 Hz, 1H), 4.74 (d, J = 10.8 Hz, 1H), 4.63 (d, J = 7.2 Hz, 1H), 4.49 (d, J = 12.0 Hz, 1H), 4.49 (d, J = 10.8 Hz, 1H), 4.44 (d, J = 12.0 Hz, 1H), 3.65–3.57 (m, 5H), 3.38 (m, 1H), 2.13 (s, 3H), 2.09 (s, 3H); 13C NMR (150 MHz, CDCl3) δ 144.6 (C), 144.3 (C), 138.4 (C), 137.94 (C), 137.92 (C), 137.8 (C), 128.7 (C), 128.5–127.4 (CH × 20), 125.6 (C), 118.9 (CH), 116.9 (CH), 105.3 (CH), 84.7 (CH), 81.6 (CH), 77.5 (CH), 75.6 (CH), 75.3 (CH2), 75.0 (CH2), 73.5 (CH), 68.5 (CH2), 20.5 (CH2), 15.8 (CH3); HRMS (ESI, M + Na)+ calc for C46H50O8Na 753.3498, found 753.3496.

(15,35,6R,7R,10R)-3-(2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosyl)-1,8,10-trimethyl-4-oxatricyclo[4.3.1.03,7]dec-8-ene-2-one (revised-10) and (18R36,65,73,105)-3-(2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosyl)-1,8,10-trimethyl-4-oxatricyclo[4.3.1.03,7]dec-8-ene-2-one (revised-11). To a mixture of 8 (0.58 g, 0.88 mmol) and trans-crotyl alcohol (58 mL) and in CH2Cl2 (12 mL) was added PhI(OAc)2 (0.85 g, 2.64 mmol) at −30 °C. After being stirred at −30 °C for 6 h, the reaction mixture was heated to reflux for 16 h. The solution was cooled to room temperature, and the reaction mixture was quenched with saturated aqueous NaHCO3 and extracted with EtOAc. The combined extracts were washed with brine, dried over MgSO4, filtered, and concentrated. The crude product was purified by flash silica-gel chromatography (hexane/EtOAc/CH2Cl2 = 8:1:2) to give revised-10 (247 mg, 39%) and revised-11 (124 mg, 19%). Revised-10: [α]D20 = −260 (c 2.0, CHCl3); IR (neat) ν 3065, 3030, 2868, 2174, 1947, 1454, 1360, 994, 738, 698 cm⁻¹; 1H NMR (600 MHz, CDCl3) δ 7.39–7.34 (m, 2H), 7.26–7.15 (m, 16H), 7.07–7.05 (m, 2H), 5.30 (s, 1H), 5.15 (d, J = 10.8 Hz, 1H), 4.91 (d, J = 10.9 Hz, 1H), 4.91 (d, J = 7.8 Hz, 1H), 4.73 (d, J = 10.8 Hz, 1H), 4.67 (d, J = 10.8 Hz, 1H), 4.66 (d, J = 10.8 Hz, 1H), 4.43 (d, J = 10.8 Hz, 1H), 4.41 (d, J = 10.8 Hz, 1H), 4.38 (d, J = 10.8 Hz, 1H), 4.05 dd, J = 7.8, 3.2 Hz, 1H), 3.81 (m, 2H), 3.74 (d, J = 8.1 Hz, 1H), 3.74–3.58 (m, 2H), 3.52–3.38 (m, 4H), 3.09 (dd, J = 4.2, 1.8 Hz, 1H), 1.88 (m, 1H), 1.81 (s, 1H), 1.71 (q, J = 7.1 Hz, 1H), 1.16 (s, 3H), 0.84 (d, J = 7.1 Hz, 3H); 13C NMR (150 MHz, CDCl3) δ 138.6 (C), 138.0 (C), 137.8 (C), 129.2–127.5 (CH × 20), 124.5 (CH), 100.1 (CH), 96.5 (CH), 84.4 (CH), 80.9 (CH), 77.5 (CH), 75.7 (CH), 75.3 (CH2), 74.8 (CH), 74.5 (CH2), 74.2 (CH2), 73.4 (CH2), 69.4 (CH2), 50.3 (C), 48.6 (CH4), 45.4 (CH2), 42.0 (CH2), 16.5 (CH2), 15.2 (CH2), 14.2 (CH2); HRMS (ESI, M + Na)+ calc for C22H26O5Na 360.1761, found 360.1762.

(11424)

**Note**
THF, 31 mL, 3.1 mmol) at room temperature under an Ar atmosphere. After the mixture was stirred for 20 min, the solvent was evaporated. The residue was dissolved in water and 2 M HCl and extracted with EtOAc. The combined extracts were washed successively with saturated aqueous NaHCO₃, saturated aqueous Na₂SO₃, and brine, dried over Na₂SO₄, filtered, and concentrated. The crude product was purified by flash silica-gel chromatography (hexane/EtOAc = 1:1) to give ent-12 (134 mg, 90%) as a white solid. Analytically pure ent-12 was obtained by crystallization from Et₂O/hexane: mp 100–101 °C; [α]D25 +269.4° (c 1.8, CHCl₃); IR (ν) ν = 3414, 3029, 2966, 2921, 2817, 1717, 1651, 1455, 1379, 1166, 1090, 1047, 999, 872 cm⁻¹; 1H NMR (600 MHz, CDCl₃) δ 5.92 (s, 1H), 5.75 (d, J = 10.8, 8.5 Hz, 1H), 5.59 (dd, δ = 10.8, 7.2 Hz, 1H), 5.54 (d, δ = 7.2 Hz, 1H), 4.00–3.87 (m, 4H), 3.12 (m, 1H), 2.78 (dd, δ = 19.7, 2.7 Hz, 1H), 2.76 (brs, 1H), 2.55 (dd, δ = 19.7, 3.4, 1.8 Hz, 1H), 2.24 (m, 1H), 1.71 (m, 1H), 1.18 (s, 3H), 1.08 (s, 3H), 0.89 (d, δ = 6.8 Hz, 3H); 13C NMR (150 MHz, CDCl₃) δ 211.3 (C), 206.8 (C), 137.0 (CH), 129.4 (CH₂), 98.7 (CH₂), 76.2 (C), 65.6 (C), 65.0 (CH₂ × 2), 43.8 (CH₃), 43.3 (CH), 37.9 (CH), 36.1 (CH₂), 23.0 (CH₃), 15.4 (CH₃), 9.1 (CH₃); MS (EI, 70 eV) m/z (% base peak) 294 (M⁺, 1), 266 (20), 223 (10), 204 (2), 179 (5), 161 (5), 149 (4), 121 (1), 99 (8), 83 (100), 73 (22); HRMS (EI) calc for C₂₅H₂₅O₃ (M⁺ = 382) 266.1518, found 266.1515.

**ent-Penicillin B (ent-2).** A mixture of ent-16 (34 mg, 72%) and 5% Rh/Al₂O₃ (47 mg) in EtOAc (1 mL) was stirred under a hydrogen balloon at room temperature for 1 h. Filtration and concentration in vacuo gave a residue, which was purified by flash silica-gel column chromatography (hexane/EtOAc = 2:3) to give ent-16 (34 mg, 72%) as a white solid. Analytically pure ent-16 was obtained by crystallization from CH₂Cl₂/hexane: mp 93–94 °C; [α]D25 +20.5° (c 1.5, CHCl₃); IR (ν) ν = 3435, 2935, 2879, 2736, 1714, 1455, 1413, 1142, 1025, 935 cm⁻¹; 1H NMR (600 MHz, CDCl₃) δ 4.86 (dd, δ = 4.5, 4.4 Hz, 1H), 3.82–3.95 (m, 9H), 2.72 (dd, δ = 19.7, 2.7 Hz, 1H), 2.68 (brs, 1H), 2.51 (dd, δ = 19.7, 3.3, 1.9 Hz, 1H), 2.22 (m, 1H), 1.98 (m, 1H), 1.77–1.44 (m, 5H), 1.19 (s, 3H), 1.05 (s, 3H), 0.89 (d, δ = 6.8 Hz, 3H); 13C NMR (150 MHz, CDCl₃) δ 211.8 (C), 207.3 (C), 140.4 (CH), 75.7 (C), 66.2 (C), 64.9 (CH × 2), 43.8, 40.6 (CH), 38.8 (CH), 36.0 (CH₂), 31.9 (CH₂), 26.8 (CH₃), 23.5 (CH₃), 16.3 (CH₃), 9.3 (CH₃); MS (EI, 70 eV) m/z (% base peak) 296 (M⁺, 1), 268 (22), 225 (45), 206 (4), 191 (3), 163 (91), 135 (52), 123 (15), 107 (9), 99 (16), 83 (13), 73 (100); HRMS (EI) calc for C₁₄H₂₀O₄ (M⁺ = 28) 268.1675, found 268.1678.

**ent-Penicillin A (ent-1).** A mixture of ent-2 (20 mg, 0.08 mmol) and IBX (44 mg, 0.16 mmol) in DMSO (0.55 mL) was stirred at room temperature for 18 h. The reaction mixture was quenched with water and extracted with EtOAc. The combined extracts were washed with brine, dried over Na₂SO₄, filtered, and concentrated. The crude product was purified by flash silica-gel chromatography (CH₂Cl₂/MeOH = 3:1) to give ent-1 (34 mg, 60%) as a white solid. Analytically pure ent-1 was obtained by crystallization from acetone: mp 192–193 °C; [α]D25 +12.6° (c 1.3, MeOH); IR (ν) ν = 3520, 3318, 2956, 2921, 1733, 1694, 1458, 1411, 1261, 1161, 1093, 1053, 1028, 951, 915 cm⁻¹; 1H NMR (600 MHz, acetone-d₆) δ 4.75 (brs, 1H), 3.72 (m, 1H), 3.56 (d, δ = 9.7 Hz, 1H), 2.79 (m, 1H), 2.35 (m, 1H), 2.04 (m, 1H), 1.83 (m, 1H), 1.73 (m, 1H), 1.65 (dq, δ = 7.1, 3.9 Hz, 1H), 1.58 (t, δ = 3.7, 3.9 Hz, 1H), 1.31 (m, 1H), 1.27 (s, 3H), 0.99 (d, δ = 7.1 Hz, 3H), 0.98 (s, 3H); 13C NMR (150 MHz, acetone-d₆) δ 215.0 (C), 201.3 (C), 196.6 (CH₂), 75.1 (C), 65.6 (C), 52.7 (CH₂), 37.6 (CH), 37.1 (CH₂), 34.6 (CH₂), 22.9 (CH₃), 17.1 (CH₂), 9.1 (CH₃); MS (EI, 70 eV) m/z (% base peak) 252 (M⁺, 26), 224 (89), 209 (30), 191 (22), 178 (10), 163 (50), 149 (77), 135 (38), 128 (45), 121 (100), 78 (28), 83 (9); HRMS (EI) calc for C₁₄H₁₆O₄ 252.1362, found 252.1366.

**ent-Penicillin C (ent-3).** A mixture of ent-12 (20 mg, 0.08 mmol) and IBX (44 mg, 0.16 mmol) in DMSO (0.55 mL) was stirred at room temperature for 18 h. The reaction mixture was quenched with water and extracted with EtOAc. The combined extracts were washed with brine, dried over Na₂SO₄, filtered, and concentrated. The crude product was purified by flash silica-gel chromatography (hexane/EtOAc = 1:1) to give ent-12 (16 mg, 80%) as a white solid. Analytically pure ent-12 was obtained by crystallization from acetone: mp 190–191
**X-ray crystallographic data for 19**: copies of $^1$H and $^{13}$C NMR for compounds ent-1–2, 8, revised-10–11, and ent-12–16; copies of $^{13}$C NMR for compounds 19–22 (PDF)

Crystallographic data for 19 (CIF)

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**REFERENCES**