Supporting Information

A Relay Ring-Closing Metathesis/Diels-Alder Approach to Sugar-Derived Pluramycin- Hybrids

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1. Scheme S1: Preparation of known aldehyde 15 from D-glucose:

Following the literature procedure, aldehyde 15 was prepared in 4-step sequences from commercially available D-glucose starting material.

2. Scheme S2: Synthesis of diene 41 from alcohol 25:

The β-isomer of diene (41) was synthesized in an overall 6 steps from the minor isomer of alkynol (25) in a similar synthetic procedure as employed for the α-isomer of 25.
3. Table 1: Optimizing Conditions for Selective Reduction of Ketone S9:
The reduction of the crude product of alkynone S9 was attempted under various conditions with the aim of obtaining a single isomer. It was discovered that all of the selective reduction outcomes occurred through a non-chelated Felkin-Anh transition state. Among the various options, diisobutylaluminium hydride (DIBAL-H), a sterically hindered electrophilic hydride donor, was found to produce predominantly a single isomer, as illustrated in (Table S1, Entry 4).

![Chemical structure of S9 and S26]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction conditions</th>
<th>d.r.</th>
<th>Yield(^b) of 26</th>
</tr>
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<tr>
<td>1.</td>
<td>LAH, THF, 0 °C to RT, 4 h</td>
<td>1.2:1</td>
<td>50%</td>
</tr>
<tr>
<td>2.</td>
<td>LAH, THF, -78 °C to RT, 6 h</td>
<td>3:1</td>
<td>60%</td>
</tr>
<tr>
<td>3.</td>
<td>LAH, CeCl₃, MeOH, THF, -78 °C to RT, 12 h</td>
<td>4:1</td>
<td>72%</td>
</tr>
<tr>
<td>4.</td>
<td>DIBAL-H, Et₂O, -78 °C to RT, 8 h</td>
<td>20:1</td>
<td>85%</td>
</tr>
</tbody>
</table>

\(^a\)Ratio were calculated with a crude mixture of \(^1\)HNMR analysis. \(^b\)Isolated yield of major isomer 26

Experimental procedure:
An oven-dried, two-neck round bottom flask was evacuated under vacuum and charged with a solution of ketone S9 (100 mg, 0.22 mmol, 1.0 eq) in dry Et₂O (10 mL) under N₂ atmosphere. The reaction temperature was brought to -78 °C, and 1 M solution of DIBAL-H in toluene (0.33 mmol, 1.5 eq) was added slowly at the same temperature. The reaction mixture was stirred for 8 h. The reaction mixture was then extracted twice with ethyl acetate (2×10 mL). The combined organic layers were dried over Na₂SO₄ and concentrated in vacuo. The crude product was purified by column chromatography using silica gel (100-200 mesh) chromatography using hexane-ethyl acetate (4:1) as the solvent system to afford the corresponding alcohol 26 (86 mg, 85%) as a colourless liquid.

4. Reference:

5. $^1$H, $^{13}$C and 2D NMR Spectral Data

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 Hz, CDCl$_3$)
$1^3$C NMR (100 Hz, CDCl$_3$)

$1^1$H NMR (400 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (125 Hz, CDCl$_3$)
$^{1}H$ NMR (400 MHz, CDCl$_3$)

$^{13}C$ NMR (100 Hz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)

26
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
**1H NMR (500 MHz, CDCl₃)**

**13C NMR (125 MHz, CDCl₃)**
$^{1}H$ NMR (400 MHz, CDCl$_3$)

$^{13}C$ NMR (100 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
$\text{H NMR (500 MHz, CDCl}_3\text{)}$

$\text{^13C NMR (125 MHz, CDCl}_3\text{)}$
S5

$^{1}H$ NMR (400 MHz, CDCl$_3$)

$^{13}C$ NMR (100 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (100 MHz, CDCl$_3$)
\[ \text{S8} \]

$^1\text{H NMR (500 MHz, CDCl}_3\text{)}$

\[ \text{S8} \]

$^1\text{C NMR (125 MHz, CDCl}_3\text{)}$
1H-1H COSY NMR of Minor Diastereomer 41 (500 MHz, CDCl$_3$)
1H-1H NOESY NMR of Minor Diastereomer 41 (500 MHz, CDCl₃)
135-DEPT NMR (100 MHz, CDCl₃)
HRMS Mass Data for the crude Reaction Mixture of intermediate 34
HRMS Mass Data for the crude Reaction Mixture of intermediate 44

+ Scan (rt: 0.282-1.243 min)  Peak 1 from + TIC Scan

Count vs. Mass-to-Charge (m/z)

Compound Details

<table>
<thead>
<tr>
<th>Cmp. 1: C37 H36 O9</th>
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<tr>
<td><strong>Formula</strong></td>
</tr>
<tr>
<td><strong>m/z</strong></td>
</tr>
<tr>
<td><strong>Observed M/z</strong></td>
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<tr>
<td><strong>Difference Da</strong></td>
</tr>
<tr>
<td><strong>Difference PPM</strong></td>
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<tr>
<td><strong>Score</strong></td>
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Compound Spectra (Zoomed)

Target: C37 H36 O9 (6.215s) + FBF Spectrum (rt: 0.182-0.382 min) 664-207 ATAA D48.14.131 Substrat

Counts vs. Mass-to-Charge (m/z)