Supporting Information

Practical Formal Total Syntheses of the Homocamptothecin Derivative and Anticancer Agent Diflomotecan via Asymmetric Acetate Aldol Additions to Pyridine Ketone Substrates

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<table>
<thead>
<tr>
<th>Compound</th>
<th>H-NMR</th>
<th>C-NMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-methoxy-isonicotinonitrile (20)</td>
<td>S6</td>
<td>S7</td>
</tr>
<tr>
<td>1-(2-methoxy-pyridin-4-yl)-propan-1-one (21)</td>
<td>S8</td>
<td>S9</td>
</tr>
<tr>
<td>4-(2-ethyl-[1,3]dioxan-2-yl)-2-methoxy-pyridine (11)</td>
<td>S10</td>
<td>S11</td>
</tr>
<tr>
<td>4-(2-ethyl-[1,3]dioxan-2-yl)-2-methoxy-pyridine-3-carbaldehyde (12)</td>
<td>S12</td>
<td>S13</td>
</tr>
<tr>
<td>[4-(2-ethyl-[1,3]dioxan-2-yl)-2-methoxy-pyridin-3-yl]-methanol (13)</td>
<td>S14</td>
<td>S15</td>
</tr>
<tr>
<td>3-benzylloxymethyl-4-(2-ethyl-[1,3]dioxan-2-yl)-2-methoxy-pyridine (14)</td>
<td>S16</td>
<td>S17</td>
</tr>
<tr>
<td>1-(3-benzylloxymethyl-2-methoxy-pyridin-4-yl)-propan-1-one (15)</td>
<td>S18</td>
<td>S19</td>
</tr>
</tbody>
</table>
(4R,5S)-3-[(R)-3-(3-benzyloxymethyl-2-methoxy-pyridin-4-yl)-3-hydroxy-pentanoyl]-4,5-diphenyl-oxazolidin-2-one (52)

$^{1}$H-NMR S20

$^{13}$C-NMR S21

(R)-3-(3-benzyloxymethyl-2-methoxy-pyridin-4-yl)-3-hydroxy-pentanoic acid (17)

$^{1}$H-NMR S22

$^{13}$C-NMR S23

(R)-5-ethyl-5-hydroxy-2,5,6,9-tetrahydro-8-oxa-2-aza-benzocycloheptene (7)

$^{1}$H-NMR S24

$^{13}$C-NMR S25

(4R,5S)-3-acetyl-4,5-diphenyl-oxazolidin-2-one (22)

$^{1}$H-NMR S26

$^{13}$C-NMR S27

2-chloro-$N$-isopropyl-isonicotinamide (42)

$^{1}$H-NMR S28

$^{13}$C-NMR S29

N-isopropyl-2-methoxy-isonicotinamide (43)

$^{1}$H-NMR S30

$^{13}$C-NMR S31

3-hydroxy-2-isopropyl-4-methoxy-2,3-dihydro-pyrrolo[3,4-c]pyridin-1-one (44)

$^{1}$H-NMR S32

$^{13}$C-NMR S33
4-methoxy-3H-furo[3,4-c]pyridin-1-one (45)

$^1$H-NMR  
$^{13}$C-NMR  

1-ethyl-4-methoxy-1,3-dihydro-furo[3,4-c]pyridin-1-ol (46)

$^1$H-NMR  
$^{13}$C-NMR  

1-[3-(tert.-butyl-dimethyl-silanyloxymethyl)-2-methoxy-pyridin-4-yl]-propan-1-one (47)

$^1$H-NMR  
$^{13}$C-NMR  

(R)-3- {[3-(tert.-butyl-dimethyl-silanyloxymethyl)-2-methoxy-pyridin-4-yl]-3-hydroxy-pentanoyl}-(R)-4-phenyl-oxazolidin-2-one (48)

$^1$H-NMR  
$^{13}$C-NMR  

(R)-3-hydroxy-3-(3-hydroxymethyl-2-methoxy-pyridin-4-yl)-pentanoic acid (49)

$^1$H-NMR  
$^{13}$C-NMR  

(R)-3-acetyl-4-phenyl-oxazolidin-2-one (39)

$^1$H-NMR  
$^{13}$C-NMR
Experimental

General Methods. Unless otherwise noted, solvents and reagents were used as received from commercial suppliers. All reactions were carried out under argon atmosphere. Thin-layer chromatography (TLC) was performed on silica gel 60 F254 plates, 0.25 mm. Qualitative HPLC was performed with UV detection at a wavelength of 210 nm using Chromolith Performance columns (100 x 4.6 mm) with gradient eluent H₂O/MeCN containing 10% of a phosphate buffer at pH 3.0. ¹H NMR are given in ppm (δ) and coupling constants J are reported in Hz. Peaks in IR spectra are reported in cm⁻¹. Low resolution electron impact mass spectra (EI-MS) were obtained at an ionization voltage of 70 eV. Data are reported in the form of m/z (intensity relative to base = 100). Acetates 24, 25, 28, 29, 30, 32-40 were prepared according to literature procedures. 27, 31 and 38 are commercially available.


Lauf ohne Probe

[Diagramm mit chemischen Strukturformeln und ppm-Werten]
S13
Probenmenge 30.8mg
Labgroup ID petersr3
Contact Person Name Thomas Naber
Contact Person Address 065/712
No title