Improved synthesis of the PAR-1 thrombin receptor antagonist RWJ-58259

Ángel M. Valdivielso, M. Teresa García-López, and Rosario Herranz*

Instituto de Química Médica (CSIC), Juan de la Cierva 3, 28006 Madrid, Spain
E-mail: rosario@iqm.csic.es

Supporting Information

Contents:

Comparative HPLC-EMS of crude reaction mixtures of urea 6 obtained by the patented methodology and by our optimized procedure ..................................................  S2
HPLC-EMS of isolated ureas 6 and 7 ........................................................................ S3
1H NMR spectra of ureas 6 and 7 ...........................................................................  S4
Comparative HPLC-EMS of the crude reaction mixtures of urea 6 obtained by the patented methodology and by our optimized procedure

### Patented synthesis of 6 (crude reaction mixture)

<table>
<thead>
<tr>
<th>compd</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>area (%)</td>
<td>42.24</td>
<td>5.96</td>
<td>9.90</td>
</tr>
</tbody>
</table>

### Improved synthesis of 6 (crude reaction mixture)

<table>
<thead>
<tr>
<th>compd</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>area (%)</td>
<td>1.28</td>
<td>13.14</td>
<td>58.69</td>
</tr>
</tbody>
</table>
HPLC-EMS of isolated ureas 6 and 7

Urea 6

6 (95.38%, [M+1]^+: 891.77)

Urea 7

7 (95.07%, [M+1]^+: 791.72)
$^1$H NMR spectra of ureas 6 and 7

Urea 6
(400 MHz, DMSO-d$_6$)

Urea 7
(400 MHz, DMSO-d$_6$)