Supplementary Material

Convergent synthesis and biological evaluation of 3-[2-(benzylidenehydrazinyl)thiazol-4-yl]-4-hydroxycoumarins

Melody H. Manyeruke,^a Tendamudzimu Tshiwawa,^a Heinrich C.Hoppe,b,c Michelle Isaacs,c Ronnett Seldon,d Digby F. Warner,e Rui W.M. Krause,*^a,c and Perry T. Kaye*^a,c

^aDepartment of Chemistry, ^bDepartment of Biochemistry and Microbiology and ^cCentre for Chemico- and Biomedicinal Research (CCBR), Rhodes University, Makhanda/Grahamstown, 6140, South Africa
^dDrug Discovery and Development Centre (H3-D), Department of Chemistry, University of Cape Town, Rondebosch 7701, South Africa
^eMolecular Mycobacteriology Research Unit, Department of Pathology and Institute of Infectious Disease and Molecular Medicine, University of Cape Town, Cape Town, South Africa

Email: P.Kaye@ru.ac.za, R.Krause@ru.ac.za

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1. **Bioassay and in silico docking protocols and data.**

1.1. **Antimalarial and anti-trypanosomal assays**

To assess antimalarial activity, percentage viability of *Plasmodium falciparum* (3D7 strain) parasites incubated for 48 hours with 20 µM of the test compounds was determined by detecting plasmodium lactate dehydrogenase (pLDH) activity as described previously by Lunga *et al.* (*ChemMedChem* 2018, 13, 1352-1362). For anti-trypanosomal and cytotoxicity evaluation, percentage viability of *Trypanosoma brucei brucei* (427 strain) parasites or HeLa cells incubated with 20 µM of the test compounds for 48 hours was determined using resazurin, as previously described by Veale and Hoppe (*Med. Chem. Commun.* 2018, 9, 2037).

**Table 1.** Anti-bacterial and cytotoxicity data for compounds 14a-c,e,g at a concentration of 50 mg/mL

<table>
<thead>
<tr>
<th>Compd,</th>
<th>E. coli Activity</th>
<th>% growth</th>
<th>S. aureus Activity</th>
<th>% growth a</th>
<th>Cytotoxicity Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>14a</td>
<td>not active</td>
<td>114</td>
<td>active</td>
<td>37-47</td>
<td>not toxic</td>
</tr>
<tr>
<td>14c</td>
<td>not active</td>
<td>97</td>
<td>active</td>
<td>46</td>
<td>toxic</td>
</tr>
<tr>
<td>14d</td>
<td>not active</td>
<td>120</td>
<td>active</td>
<td>31</td>
<td>not toxic</td>
</tr>
<tr>
<td>14e</td>
<td>not active</td>
<td>106</td>
<td>active</td>
<td>43</td>
<td>not toxic</td>
</tr>
<tr>
<td>14g</td>
<td>not active</td>
<td>109</td>
<td>active</td>
<td>50</td>
<td>not toxic</td>
</tr>
</tbody>
</table>

*As % metabolic activity*

2.2. **In silico docking protocols and data.**

In *silico* docking was performed using Schrödinger software (Maestro 11.4, Schrödinger 2017-4). The reported ligands were built in Maestro and prepared for docking using the LigPrep module (Schrodinger, LLC, NY, USA, 2009). The OPLS_2005 force field was selected in LigPrep for the energy minimization of the ligands to generate low-energy ligand isomers. The protein structures were obtained from Protein Data Bank ([http://www.rcsb.org](http://www.rcsb.org)) and prepared for docking using the protein preparation wizard as implemented in Maestro. The receptor grid generations were achieved using “Glide Grid Generation” module and the active site was selected with the radius of 20 Å around the crystal ligand. Glide module (Schrodinger, LLC, NY, USA, 2009) was used for docking protocol using Standard precision (SP) approach. The results obtained were visualized using Maestro interface (Schrödinger Suite, LLC, NY).

**Table 2.** In *silico* binding affinities in Kcal/mol for the ligands 14a-g in selected enzyme receptor sites.
Docking and receptor-site interactions of ligand 14a in the *M.tb* enzyme 4FBW.
Docking and receptor-site interactions of ligand 14b in the T.b.brucei enzyme 4FWN.
2. NMR Spectra.

600 MHz $^1$H NMR spectrum of compound 13g in DMSO-$d_6$.

150 MHz $^{13}$C NMR spectrum of compound 13g in DMSO-$d_6$. 

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600 MHz $^1$H NMR spectrum of compound 14a in DMSO-$d_6$.

150 MHz $^{13}$C NMR spectrum of compound 14a in DMSO-$d_6$. 
600 MHz $^1\text{H}$ NMR spectrum of compound 14b in DMSO-$d_6$.

150 MHz $^{13}\text{C}$ NMR spectrum of compound 14b in DMSO-$d_6$. 
400 MHz $^1$H NMR spectrum of compound 14c in DMSO-$d_6$.

100 MHz $^{13}$C NMR spectrum of compound 14c in DMSO-$d_6$. 
600 MHz $^1$H NMR spectrum of compound 14d in DMSO-$d_6$.

150 MHz $^{13}$C NMR spectrum of compound 14d in DMSO-$d_6$. 
600 MHz COSY NMR spectrum of compound 14d in DMSO-$d_6$.

Partial HSQC NMR spectrum of compound 14d in DMSO-$d_6$. 

Three different carbon signals
HMBC NMR spectrum of compound \textbf{14d} in DMSO-$d_6$. 
600 MHz $^1$H NMR spectrum of compound 14e in DMSO-$d_6$.

150 MHz $^{13}$C NMR spectrum of compound 14e in DMSO-$d_6$. 
600 MHz $^1$H NMR spectrum of compound 14f in DMSO-$d_6$.

150 MHz $^{13}$C NMR spectrum of compound 14f in DMSO-$d_6$. 
600 MHz $^1$H NMR spectrum of compound 14g in DMSO-$d_6$.

150 MHz $^{13}$C NMR spectrum of compound 14g in DMSO-$d_6$. 