SUPPORTING INFORMATION

Pd-catalyzed Heck-conjoined amidation and concomitant chemoselective Michael-addition: An efficient tandem approach to highly functionalized tetrahydroquinazolines from o-haloanilines

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X-Ray Crystallographic Studies

Figure I. ORTEP structure of compound 4a

The intensity data for 4a was collected on an Oxford Xcalibur CCD diffractometer equipped with graphite monochromatic Mo-Kα radiation (\(\lambda = 0.71073 \text{ Å}\)) at 293(2) K\(^2\). A multi-scan correction was applied. The structure was solved by the direct methods using SIR-92 and refined by full-matrix least-squares refinement techniques on \(F^3\) using SHELXL97\(^3\). The hydrogen atoms were placed into the calculated positions and included in the last cycles of the refinement. All calculations were done using Wingx software package\(^4\).
**Table I.** Crystallographic data and structure refinement for compounds 4a.

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C₁₇H₁₆N₂O₂S</td>
</tr>
<tr>
<td>Formula weight</td>
<td>312.38</td>
</tr>
<tr>
<td>Temperature</td>
<td>293(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P₂₁/n</td>
</tr>
<tr>
<td>A</td>
<td>9.751(5) Å</td>
</tr>
<tr>
<td>B</td>
<td>18.905(5) Å</td>
</tr>
<tr>
<td>C</td>
<td>16.646(5) Å</td>
</tr>
<tr>
<td>Volume</td>
<td>3066(2) Å³</td>
</tr>
<tr>
<td>Z</td>
<td>8</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.354 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.220 mm⁻¹</td>
</tr>
<tr>
<td>F(000)</td>
<td>1312</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.25 x 0.23 x 0.20 mm³</td>
</tr>
<tr>
<td>Theta range for data collection</td>
<td>2.15 to 24.99°</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-11 ≤ h ≤ 11, -17 ≤ k ≤ 22, -19 ≤ l ≤ 19</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>20532</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>5414 [R(int) = 0.0456]</td>
</tr>
<tr>
<td>Data completeness</td>
<td>100 %</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Multi-scan</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>0.9574 and 0.9471</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>5414 / 0 / 413</td>
</tr>
<tr>
<td>Goodness-of-fit on F²</td>
<td>1.033</td>
</tr>
<tr>
<td>Final R indices [I&gt;2sigma(I)]ᵃᵇ</td>
<td>R₁ = 0.0418, wR₂ = 0.0958</td>
</tr>
<tr>
<td>R indices (all data)</td>
<td>R₁ = 0.0602, wR₂ = 0.1018</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.376 and -0.266 e.Å⁻³</td>
</tr>
</tbody>
</table>

ᵃR = \(\frac{\sum |F_o| - |F_c|}{\sum |F_o|}\) / \(\sum |F_o|\); ᵇR_w = \(\frac{\sum w(F_o^2 - F_c^2)^2}{\sum w(F_o^2)^2}\)^{1/2}
References:

SPECTRA
Methyl 2-(3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4a)
$^{13}$C NMR

Methyl 2-(3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4a)
HRMS

Methyl 2-(3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4a)
Methyl 2-(2-thioxo-3-(m-tolyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4b)
Methyl 2-(2-thioxo-3-\((m\)-tolyl\)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4b)
HRMS

Methyl 2-(2-thioxo-3-(m-tolyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4b)

[Chemical structure image]

+TOF MS: 0.748 to 0.898 min from Sample 1 of 038.wiff

a=4.96358189846040600e-004, t0=-5.66662779057200530e+003 (Turbo Spray)

Max. 315.3 counts.
$^1$H NMR

Methyl 2-(2-thioxo-3-(p-tolyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4c)
$^{13}$C NMR

Methyl 2-(2-thioxo-3-(p-tolyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4c)
HRMS

Methyl 2-(2-thioxo-3-(p-tolyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4c)
Methyl 2-(3-(4-fluorophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4d)
Methyl 2-(3-(4-fluorophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4d)
Methyl 2-(3-(4-fluorophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4d)
$^1$H NMR

Butyl 2-(3-(4-methoxyphenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4e)
$^{13}$C NMR

Butyl 2-(3-(4-methoxyphenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4e)
Butyl 2-(3-(4-methoxyphenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4e)
$^1$H NMR

Butyl 2-(3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4f)
$^{13}$C NMR

Butyl 2-(3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4f)
Butyl 2-(3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4f)
Butyl 2-(3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-D-4-yl)acetate (4f')
**^1H NMR**

*tert*-Butyl 2-(3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4g)
**\(^{13}\)C NMR**

*tert*-Butyl 2-(3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4g)
tert-butyl 2-(3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4g)
$^1$H NMR

Methyl 2-(6-methyl-3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4h)
Methyl 2-(6-methyl-3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4h)
Methyl 2-(6-methyl-3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4h)
$^1$H NMR

Butyl 2-(3-(2,4-dichlorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4i)
$^{13}$C NMR

Butyl 2-(3-(2,4-dichlorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4i)
HRMS

Butyl 2-(3-(2,4-dichlorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4i)
$^1$H NMR

Ethyl 2-((3-(4-fluorophenyl))-6-methyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4j)
Ethyl 2-(3-(4-fluorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4j)
HRMS

Ethyl 2-(3-(4-fluorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4j)

+TOF MS: 0.432 to 1.797 min from Sample 1 (TuneSampleID) of r70wiff.wiff

\[ a=3.90185123223385200e-004, t0=-6.01277179989931290e+000 \] (Turbo Spray)

Max. 793.0 counts.

0 50 100 150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900 950 1000

m/z, Da

358.1150

0 50 100 150 200 250 300 350 400 450 500 550 600 650 700 750

Intensity, counts

100 150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900 950 1000

m/z, Da

358.1150
$^1$H NMR

tert-Butyl 2-(6-methyl-3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4k)
tert-Butyl 2-(6-methyl-3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4k)
HRMS

tert-butyl 2-(6-methyl-3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4k)


$^1$H NMR

tert-Butyl 2-(6-methyl-3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4l)
tert-Butyl 2-(6-methyl-3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4l)
**tert-Butyl 2-(6-methyl-3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4l)**

HRMS

+TOF MS: 1.081 to 1.214 min from Sample 1 of r196.wiff

a=3.59142292061445240e-004, t0=-6.01277179989930400e+000 (Turbo Spray)

Max. 995.3 counts.

![Mass Spectrogram](chart.png)

- m/z, Da
- Intensity, counts
$^1$H NMR

Butyl 2-(6-chloro-2-thioxo-3-(o-tolyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4m)
**$^{13}$C NMR**

Butyl 2-(6-chloro-2-thioxo-3-(o-tolyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4m)
Butyl 2-(6-chloro-2-thioxo-3-(o-tolyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4m)
Butyl 2-(6-chloro-2-thioxo-3-(m-tolyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4n)
Butyl 2-(6-chloro-2-thioxo-3-(m-tolyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4n)
Butyl 2-(6-chloro-2-thioxo-3-\((m\)-tolyl\)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4n)
$^1$H NMR

Butyl 2-(6-chloro-2-thioxo-3-(p-tolyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4o)
\(^{13}\text{C NMR}\)

Butyl 2-(6-chloro-2-thioxo-3-(\(\rho\)-tolyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4o)
Butyl 2-(6-chloro-2-thioxo-3-(p-toly)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4o)
$^1$H NMR

Butyl 2-(6-chloro-3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4p)
Butyl 2-(6-chloro-3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4p)

$^{13}$C NMR
HRMS

Butyl 2-(6-chloro-3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate
(4p)
Methyl 2-(3-(4-nitrophenyl)-2-thioxo-6-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4q)
Methyl 2-(3-(4-nitrophenyl)-2-thioxo-6-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4q)
Methyl 2-(3-(4-nitrophenyl)-2-thioxo-6-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4q)
Butyl 2-(6-chloro-8-fluoro-3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4r)
Butyl 2-(6-chloro-8-fluoro-3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4r)
Butyl 2-(6-chloro-8-fluoro-3-phenyl-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4r)

HRMS
$^1$H NMR

Butyl 2-(6-chloro-8-fluoro-3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4s)
Butyl 2-(6-chloro-8-fluoro-3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4s)
Butyl 2-(6-chloro-8-fluoro-3-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4s)
Butyl 2-(6-chloro-3-(2,4-dichlorophenyl)-8-fluoro-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4t)
\[^{13}\text{C} \text{NMR}\n\]

Butyl 2-[(6-chloro-3-(2,4-dichlorophenyl)-8-fluoro-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4t)
Butyl 2-(6-chloro-3-(2,4-dichlorophenyl)-8-fluoro-2-thioxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4t)
$^1$H NMR

(E)-Methyl 3-(2-(3-(4-nitrophenyl)ureido)phenyl)acrylate

(5a')
\(^{13}\text{C} \text{ NMR}\)

(E)-Methyl 3-(2-(3-(4-nitrophenyl)ureido)phenyl)acrylate

\((5a')\)
(E)-Methyl 3-(2-(3-(4-nitrophenyl)ureido)phenyl)acrylate

(5a')

Max. 1068.2 counts.
\(^{13}\)C NMR

\((E)-\text{Butyl}\ 3-(2-(3-(2\text{-chlorophenyl})\text{ureido})\text{phenyl})\text{acrylate (5b')}\)
HRMS

(E)-Butyl 3-(2-(3-(2-chlorophenyl)ureido)phenyl)acrylate (5b')

Max. 8.1e4 counts.
$^1$H NMR

$(E)$-Methyl 3-(2-(3-(2-fluorophenyl)ureido)-5-methylphenyl)acrylate

$(5c')$
$^{13}$C NMR

(E)-Methyl 3-(2-(3-(2-fluorophenyl)ureido)-5-methylphenyl)acrylate

(5c')
HRMS

(E)-Methyl 3-(2-(3-(2-fluorophenyl)ureido)-5-methylphenyl)acrylate

(5c')

Max. 9.6e4 counts.

m/z, Da

Intensity, counts

328.1223

851.8313
Methyl 2-(3-(4-nitrophenoxy)-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5a)
Methyl 2-(3-(4-nitrophenyl)-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5a)

$^{13}$C NMR
Methyl 2-(3-(4-nitrophenyl)-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5a)

HRMS

[Chemical Structure Image]

Max. 1068.2 counts.

100 150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900 950 1000
m/z, Da

341.1015

m/z Da
Methyl 2-(3-(4-chlorophenyl)-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5b)

$^1$H NMR
Methyl 2-(3-(4-chlorophenyl)-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5b)
Methyl 2-(3-(4-chlorophenyl)-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5b)
\(^1\text{H NMR}\)

Methyl 2-\((3-(2\text{-chlorophenyl})-2\text{-oxo-1,2,3,4-tetrahydroquinazolin-4-yl})\)acetate (5c)
Methyl 2-(3-(2-chlorophenyl)-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5c)
HRMS

Methyl 2-(3-(2-chlorophenyl)-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5c)

![HRMS spectrum](image-url)

- m/z: 303.0772
- 100 150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900 950 1000
- 0 20 40 60 80 100 120 140 160 180 200 220 240 260 280 300 320 340 360
- Max. 363.4 counts.
Methyl 2-(3-(2-fluorophenyl)-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5d)
$^{13}$C NMR

Methyl 2-(3-(2-fluorophenyl)-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5d)
HRMS

Methyl 2-(3-(2-fluorophenyl)-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5d)

![HRMS Chart]

TOF MS: 3.396 to 4.995 m/z from Sample 1 of 3 wff

314.1029

Max. 474.8 counts.
Methyl 2-(2-oxo-3-(p-tolyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5e)
Methyl 2-(2-oxo-3-(p-tolyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5e)
Methyl 2-(2-oxo-3-(p-tolyl)-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5e)
$^1$H NMR

Methyl 2-(3-(4-fluorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5f)
Methyl 2-(3-(4-fluorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5f)
Methyl 2-((3-(4-fluorophenyl))-6-methyl-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (5f)

HRMS

TOF MS: 0.415 to 0.482 min from Sample 1 (TuneSampleID) of r62, wiff
a=3.73483892037463840e-004, t0=-6.01277179989930310e+000 (Turbo Spray)
Max. 9.64e4 counts.

93
\(^1\)H NMR

\[(E)-\text{Methyl 3-(2-aminophenyl)acrylate (6)}\]
$^{13}$C NMR

(\textit{E})-Methyl 3-(2-aminophenyl)acrylate (6)
HRMS

(\(E\))-Methyl 3-(2-aminophenyl)acrylate (6)