Supporting Information

Nickel-Catalyzed Selective Reduction of Carboxylic Acids to Aldehydes

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General Considerations

All reactions were performed under an inert atmosphere of nitrogen using purchased dry solvents unless otherwise noted. All commercially available metal salts, organic compounds and dry solvents were used as received from commercial suppliers: Sigma Aldrich, Strem, Combi-Blocks, Enamine, Fluorochem, Alfa Aesar, Acros and ChemBridge. NiCl₂(dme) (98%), NiBr₂(H₂O)₃ (≥98%), 4,4’-di-tert-butyl-2,2’-dipyridyl (dtbbpy, 98%) and diphenylsilane (Ph₂SiH₂, 97%) were purchased from Sigma Aldrich and used as received. Zn (<10 μm) was purchased from Sigma Aldrich and washed with HCl(aq) according to standard procedure.¹ It was either used within two weeks or stored in a glovebox in order to maintain activity over a longer period of time. Dimethyl dicarbonate (DMDC) can decompose over time, and if there is gas evolution upon opening the container, it was subjected to a 5 minutes rotatory evaporation at 40 °C to remove residual CO₂ and MeOH.

NOTE! NiCl₂(dme) and NiBr₂(H₂O)₃ can cause cancer and allergy or asthma symptoms. They are also very toxic to aquatic life with long lasting effects. Please obtain appropriate instructions in handling and disposal of these chemicals.

¹H and ¹³C NMR spectra were recorded on Bruker 400 and 500 MHz spectrometers and chemical shifts are given in parts per million (ppm) relative to residual solvent peaks. Data are presented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant J (Hz) and integration. High resolution mass spectra were obtained using a Waters XEVO qToF instrument. Chromatography was performed using standard techniques on 60Å, 70-230 mesh Merck silica gel. FTIR spectra were recorded on a Bruker Alpha II instrument. Visualization of TLC plates was performed by fluorescence quenching, KMnO₄ stain or 2,4-dinitrophenylhydrazine (2,4-DNPH) stain – specific for aldehyde products.

¹ Yamamura, S.; Toda, M.; Hirata, Y. Org. Synth. 1973, 53, 86. The obtained Zn powder was dried under vacuum at 60 °C with slow stirring by a football-shaped stirbar to grind the powder if necessary.
General procedures for optimization reactions on 0.1 mmol scale (Procedure A)

Zn and DMDC were treated as described in the General Consideration section.  
Preparation of nickel pre-catalyst stock solution: In an oven-dried 4 ml vial, nickel catalyst (0.04 mmol) was stirred vigorously with ligand (0.08 mmol) in 4 ml dry solvent for 10 minutes. If the solution is not fully clear, then it is dispensed as a suspension.  
Reaction set-up: In an oven-dried conical microwave vial (2 ml size) was added carboxylic acid (0.1 mmol) and Zn (0.02 mmol) and the vial was capped. To this was added stock solution of Ni/ligand prepared above (1 ml), base (0.11 mmol) and activator (0.2 mmol) in this order. The mixture was purged with N2 for 15 mins (needle inlet in solution, reaction stirring on plate). Then, silane (0.225 mmol unless specified otherwise) was added via microsyringe, the cap covered in parafilm, and the reaction stirred at 1000 rpm at 40-60 ºC in a pre-heated silicone oil bath. Reaction was cooled down after 16-24 hr as indicated. The cap was then removed. 1 ml CDCl3 was added containing 25 mg 1,1,2,2-tetrachloroethane, 1,2-dibromomethane or 1,3,5-trimethoxybenzene as standard and a reaction aliquot diluted further with CDCl3 and analyzed by 1H NMR (90s relaxation delay) (aldehyde peak integrated vs. standard). Typically, 8 to 16 reactions were screened at once.

General Procedure for isolation of aldehyde products on 1 mmol scale (Procedure B)

Zn and DMDC were treated as described in the General Consideration section.  
Reaction set-up: An oven-dried 50 ml 2- or 3-neck round bottom flask fitted with a condenser was placed under N2. Then, NiCl2(dme) (0.1 mmol, 22 mg) or NiBr2(H2O)3 (0.1 mmol, 27.3 mg) depending on substrate, dtbbpy (0.2 mmol, 53.7 mg) and dry EtOAc (10 ml) were added and stirred vigorously for 10 minutes. Next, carboxylic acid (1 mmol) and Zn (0.2 mmol, 13.1 mg), followed by 2,6-lutidine (1.1 mmol, 127 μL) and DMDC (2 mmol, 215 μL) were added and the mixture stirred for a further 15 minutes. Then, diphenylsilane (2.25 mmol, 418 μL) was added and the reaction placed in an oil bath at 40-80 ºC depending on substrate and stirred at 1000 rpm. It is important to stir at 1000 rpm as at lower stirring speeds the reaction could result in lowered yields. Reaction was cooled down after 16-24 h depending on substrate. The mixture was transferred to a 50 ml round bottom flask with minimal amount of dichloromethane and ~ 1g silica gel was added to the flask. The mixture was concentrated slowly on a rotatory evaporator with a chilled water bath (< 10 ºC) to avoid losing volatile aldehydes, then the silica gel was directly dry-loaded onto a column for chromatography. In most cases, pentane, diethyl ether, MTBE or dichloromethane were used as mobile phase components due to their low boiling point. Desired fractions were concentrated slowly with chilled water bath (< 10 ºC) on a rotatory evaporator to avoid losing volatile aldehyde. Typically, separation can be achieved to purify the aldehyde in pentane/ether, but for low polarity aldehydes, co-elution with silane byproducts is possible and a second column in pentane/DCM mobile phases could be necessary.
For 10 mmol scale reactions, the reaction was carried out in a 250 ml 3-neck flask with a large stir bar (important for aggressive stirring and initiation of the reaction) and performed with increased 0.2 M concentration of carboxylic acid in EtOAc. The reactions were stirred for 48 hr due to slower kinetics. The rest of the procedure remains the same with adjusted quantities of reagents.

**General Procedure for isolation of volatile aldehyde products on 1 mmol scale – isolation via 2,4-dinitrophenylhydrazone derivatives (Procedure C)**

After completion of the reductions, some 1 mmol reactions forming volatile aldehydes were open to air, then H₂O (4 ml), HCl (500 μL, 6 M aq.), then 2,4-dinitrophenylhydrazine (204 mg, 1.03 mmol) were added. Reactions were stirred for an additional hour, upon which full consumption of the aldehyde was confirmed by TLC or crude ¹H NMR. Successful hydrazone formation is accompanied by formation of bright yellow to red precipitates. The slurry was diluted with H₂O (40 mL) and extracted with CH₂Cl₂ (4 x 40 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated on a rotatory evaporator. The resulting solid is purified by column chromatography. Typically, we applied this procedure for the isolation of volatile aldehydes for which we observed substantial loss (>10% of theoretical yield) during isolation following Procedure B. Spectral data for hydrazones provided for major E stereoisomer.
Optimization of Reaction Conditions using Procedure A
Note: Zn used in Tables S1 to S6 was not washed with acid.

Table S1. Initial activator screen – hydrocinnamic acid

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent / Activator</th>
<th>% Aldehyde</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td>MeCN / DCC</td>
<td>0.8</td>
</tr>
<tr>
<td>002</td>
<td>THF / DCC</td>
<td>9.3</td>
</tr>
<tr>
<td>003</td>
<td>MeCN / DIC</td>
<td>0.7</td>
</tr>
<tr>
<td>004</td>
<td>THF / DIC</td>
<td>1.1</td>
</tr>
<tr>
<td>005</td>
<td>MeCN / Piv₂O</td>
<td>35</td>
</tr>
<tr>
<td>006</td>
<td>THF / Piv₂O</td>
<td>38</td>
</tr>
<tr>
<td>007</td>
<td>MeCN / Boc₂O</td>
<td>3.7</td>
</tr>
<tr>
<td>008</td>
<td>THF / Boc₂O</td>
<td>1</td>
</tr>
<tr>
<td>009</td>
<td>MeCN / DMDC</td>
<td>14.8</td>
</tr>
<tr>
<td>010</td>
<td>THF / DMDC</td>
<td>32.8</td>
</tr>
<tr>
<td>011</td>
<td>THF / DMDC (2 eq.)</td>
<td>59.2</td>
</tr>
<tr>
<td>012</td>
<td>THF / DMDC (5 eq.)</td>
<td>40.5</td>
</tr>
<tr>
<td>013</td>
<td>THF / DMDC (2 eq.) @ 40 °C</td>
<td>55.1</td>
</tr>
<tr>
<td>014</td>
<td>THF / DMDC @ room temp.</td>
<td>43.6</td>
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</table>

Table S2. Reductant screen – hydrocinnamic acid

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reductant</th>
<th>% Aldehyde</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td>Mn</td>
<td>19.8</td>
</tr>
<tr>
<td>002</td>
<td>Zn &lt;10 µm</td>
<td>52.4</td>
</tr>
<tr>
<td>003</td>
<td>Zn &lt;150 µm</td>
<td>9.1</td>
</tr>
<tr>
<td>004</td>
<td>Zn &lt;50 nm</td>
<td>39.8</td>
</tr>
<tr>
<td>005</td>
<td>Zn 20-30 mesh</td>
<td>2.9</td>
</tr>
<tr>
<td>006</td>
<td>Tetrakis(dimethylamino)ethylene</td>
<td>8.3</td>
</tr>
</tbody>
</table>
Table S3. Base screen – hydrocinnamic acid

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>% Aldehyde</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td>NMI</td>
<td>0</td>
</tr>
<tr>
<td>002</td>
<td>NEt₃</td>
<td>32.9</td>
</tr>
<tr>
<td><strong>003</strong></td>
<td>2,6-lutidine</td>
<td><strong>75</strong></td>
</tr>
<tr>
<td>004</td>
<td>DIPEA</td>
<td>3</td>
</tr>
<tr>
<td>005</td>
<td>NH₄Cl</td>
<td>14.1</td>
</tr>
<tr>
<td>006</td>
<td>DBU</td>
<td>3.4</td>
</tr>
<tr>
<td>007</td>
<td>TMG</td>
<td>trace</td>
</tr>
<tr>
<td>008</td>
<td>DABCO</td>
<td>3.4</td>
</tr>
</tbody>
</table>

Table S4. Solvent screen – hydrocinnamic acid

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>% Aldehyde</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td>THF</td>
<td>50.4</td>
</tr>
<tr>
<td>002</td>
<td>2-MeTHF</td>
<td>70.5</td>
</tr>
<tr>
<td>003</td>
<td>1,4-Dioxane</td>
<td>53.7</td>
</tr>
<tr>
<td>004</td>
<td>THP</td>
<td>48.6</td>
</tr>
<tr>
<td><strong>005</strong></td>
<td>DME</td>
<td><strong>90.6</strong></td>
</tr>
<tr>
<td>006</td>
<td>CPME</td>
<td>31.8</td>
</tr>
<tr>
<td>007</td>
<td>CHCl₃</td>
<td>0</td>
</tr>
<tr>
<td><strong>008</strong></td>
<td>EtOAc</td>
<td><strong>87.7</strong></td>
</tr>
<tr>
<td>009</td>
<td>DMSO</td>
<td>trace</td>
</tr>
<tr>
<td>010</td>
<td>DMF</td>
<td>2.1</td>
</tr>
<tr>
<td>011</td>
<td>DMAc</td>
<td>trace</td>
</tr>
<tr>
<td>012</td>
<td>Propylene carbonate</td>
<td>7.5</td>
</tr>
</tbody>
</table>
Table S5. Ni source screen – hydrocinnamic acid

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ni source</th>
<th>% Aldehyde</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td>NiCl$_2$(dme)</td>
<td>87.7</td>
</tr>
<tr>
<td>002</td>
<td>NiCl$_2$(H$_2$O)$_6$</td>
<td>54.5</td>
</tr>
<tr>
<td>003</td>
<td>NiBr$_2$(dme)</td>
<td>48.2</td>
</tr>
<tr>
<td>004</td>
<td>NiI$_2$</td>
<td>17.1</td>
</tr>
<tr>
<td>005</td>
<td>Ni(OAc)$_2$(H$_2$O)$_4$</td>
<td>10.5</td>
</tr>
<tr>
<td>006</td>
<td>Ni(acac)$_2$</td>
<td>trace</td>
</tr>
<tr>
<td>007</td>
<td>Ni(hfacac)$_2$</td>
<td>13.6</td>
</tr>
<tr>
<td>008</td>
<td>Ni(ClO$_4$)$_2$</td>
<td>0</td>
</tr>
<tr>
<td>009</td>
<td>NiBr$_2$(H$_2$O)$_3$</td>
<td>93.5</td>
</tr>
<tr>
<td>010</td>
<td>Ni(OTf)$_2$</td>
<td>13.6</td>
</tr>
</tbody>
</table>

Table S6. Ligand screen – hydrocinnamic acid

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ligand</th>
<th>% Aldehyde</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td>bpy</td>
<td>10.3</td>
</tr>
<tr>
<td>002</td>
<td>4,4'-diOMebpy</td>
<td>4.5</td>
</tr>
<tr>
<td>003</td>
<td>phen</td>
<td>7.3</td>
</tr>
<tr>
<td>004</td>
<td>neocuproine</td>
<td>3.4</td>
</tr>
<tr>
<td>005</td>
<td>terpy</td>
<td>3.5</td>
</tr>
<tr>
<td>006</td>
<td>box</td>
<td>0</td>
</tr>
</tbody>
</table>

Table S7. Silane screen – hydrocinnamic acid

<table>
<thead>
<tr>
<th>Entry</th>
<th>Silane</th>
<th>Equivs.</th>
<th>% Aldehyde @ 8 h</th>
<th>% Aldehyde @ 16 h</th>
</tr>
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</table>


Table S8. Additional control reactions – hydrocinnamic acid

<table>
<thead>
<tr>
<th>Entry</th>
<th>Deviation from optimized conditions</th>
<th>% Aldehyde</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td>Ni(COD)$_2$ instead of NiCl$_2$(dme)</td>
<td>44</td>
</tr>
<tr>
<td>002</td>
<td>Ni(COD)$_2$ instead of NiCl$_2$(dme) + 20% ZnCl$_2$</td>
<td>10</td>
</tr>
<tr>
<td>003</td>
<td>no dtbbpy</td>
<td>0</td>
</tr>
<tr>
<td>004</td>
<td>without Ph$_2$SiH$_2$</td>
<td>0</td>
</tr>
<tr>
<td>005</td>
<td>1 equiv. Ph$_2$SiH$_2$</td>
<td>82</td>
</tr>
</tbody>
</table>

Table S9. Pivalic anhydride screen – benzoic acid

\[
\begin{align*}
\text{Entry} & \quad \text{Solvent} & \quad 2,6\text{-Lutidine (equiv.)} & \quad \% \text{ product with 1.1 equiv. Piv}_2\text{O} & \quad \% \text{ product with 3 equiv. Piv}_2\text{O} \\
001 & \quad \text{MeCN} & \quad 0 & \quad 6.6 & \quad 23.5 \\
002 & \quad \text{THF} & \quad 0 & \quad 6.8 & \quad 8.5 \\
003 & \quad \text{DME} & \quad 0 & \quad 18.6 & \quad 21.4 \\
004 & \quad \text{EtOAc} & \quad 0 & \quad 4.5 & \quad 8.4 \\
005 & \quad \text{MeCN} & \quad 1.1 & \quad 4.8 & \quad 25.5 \\
006 & \quad \text{THF} & \quad 1.1 & \quad 2.5 & \quad 3.3 \\
007 & \quad \text{DME} & \quad 1.1 & \quad 0 & \quad 19 \\
008 & \quad \text{EtOAc} & \quad 1.1 & \quad 11.6 & \quad 6.6 \\
\end{align*}
\]

Table S10. DMDC, Ni source and temperature screen – benzoic acid

\[
\begin{align*}
\text{Entry} & \quad \text{Temperature} & \quad \text{[Ni] source} & \quad \% \text{ Zn} & \quad \% \text{ Aldehyde} \\
001 & \quad 40 \ ^\circ \text{C} & \quad \text{NiCl}_2\text{(dme)} & \quad 20 & \quad 18.7 \\
002 & \quad 60 \ ^\circ \text{C} & \quad \text{NiCl}_2\text{(dme)} & \quad 50 & \quad 25.6 \\
003 & \quad \text{NiBr}_2\text{(H}_2\text{O)}_3 & \quad 20 & \quad 49.8 \\
004 & \quad \text{NiBr}_2\text{(H}_2\text{O)}_3 & \quad 50 & \quad 44 \\
005 & \quad 80 \ ^\circ \text{C} & \quad \text{NiCl}_2\text{(dme)} & \quad 20 & \quad 25.8 \\
006 & \quad \text{NiBr}_2\text{(H}_2\text{O)}_3 & \quad 20 & \quad 46.1 \\
007 & \quad \text{NiCl}_2\text{(dme)} & \quad 20 & \quad 19.1 \\
008 & \quad \text{NiBr}_2\text{(H}_2\text{O)}_3 & \quad 20 & \quad 51.1 \\
\end{align*}
\]
Table S11. Silane screen – benzoic acid

![reaction diagram]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Silane</th>
<th>Equivs.</th>
<th>% Aldehyde</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td>PhSiH₃</td>
<td>1.5</td>
<td>35</td>
</tr>
<tr>
<td>002</td>
<td>Ph₂SiH₂</td>
<td>1.5</td>
<td>68</td>
</tr>
<tr>
<td>003</td>
<td>MePhSiH₂</td>
<td>1.5</td>
<td>51.9</td>
</tr>
<tr>
<td>004</td>
<td>HexSiH₃</td>
<td>1.5</td>
<td>61.9</td>
</tr>
<tr>
<td>005</td>
<td>Ph₂SiH₂</td>
<td>2.25</td>
<td>69.5</td>
</tr>
<tr>
<td>006</td>
<td>MePhSiH₂</td>
<td>2.25</td>
<td>56.9</td>
</tr>
<tr>
<td>007</td>
<td>PMHS</td>
<td>100 mg</td>
<td>56</td>
</tr>
</tbody>
</table>

Table S12. Solvent and temperature screen – benzoic acid

![reaction diagram]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Temp.</th>
<th>% Aldehyde</th>
<th>Temp.</th>
<th>% Aldehyde</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td>EtOAc</td>
<td>40 °C</td>
<td>59.8</td>
<td>60 °C</td>
<td>71.3</td>
</tr>
<tr>
<td>002</td>
<td>2-MeTHF</td>
<td>40 °C</td>
<td>51.9</td>
<td>60 °C</td>
<td>62.1</td>
</tr>
<tr>
<td>003</td>
<td>1,4-Dioxane</td>
<td>40 °C</td>
<td>70.3</td>
<td>60 °C</td>
<td>67.0</td>
</tr>
<tr>
<td>004</td>
<td>DME</td>
<td>40 °C</td>
<td>62.1</td>
<td>60 °C</td>
<td>63.8</td>
</tr>
<tr>
<td>005</td>
<td>Toluene</td>
<td>40 °C</td>
<td>41.9</td>
<td>60 °C</td>
<td>42.0</td>
</tr>
<tr>
<td>006</td>
<td>DMSO</td>
<td>40 °C</td>
<td>0</td>
<td>60 °C</td>
<td>0</td>
</tr>
<tr>
<td>007</td>
<td>Et₂O</td>
<td>40 °C</td>
<td>33.0</td>
<td>60 °C</td>
<td>65.6</td>
</tr>
<tr>
<td>008</td>
<td>DCM</td>
<td>40 °C</td>
<td>5.8</td>
<td>60 °C</td>
<td>4.5</td>
</tr>
</tbody>
</table>

Table S13. Base screen – benzoic acid

![reaction diagram]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>% Aldehyde</th>
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</thead>
<tbody>
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<td></td>
<td></td>
</tr>
<tr>
<td>002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>003</td>
<td></td>
<td></td>
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<tr>
<td>004</td>
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<tr>
<td>005</td>
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<td></td>
</tr>
<tr>
<td>006</td>
<td></td>
<td></td>
</tr>
<tr>
<td>007</td>
<td></td>
<td></td>
</tr>
<tr>
<td>008</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table S14. Concentration and Ni loading screen – benzoic acid

<table>
<thead>
<tr>
<th>Entry</th>
<th>conc. [M]</th>
<th>% [Ni] source</th>
<th>% Aldehyde</th>
</tr>
</thead>
<tbody>
<tr>
<td>001</td>
<td>0.1</td>
<td>10</td>
<td>61.5</td>
</tr>
<tr>
<td>002</td>
<td>0.05</td>
<td>10</td>
<td>52.5</td>
</tr>
<tr>
<td>003</td>
<td>0.2</td>
<td>10</td>
<td>71.8</td>
</tr>
<tr>
<td>004</td>
<td>0.2</td>
<td>20</td>
<td>79.4</td>
</tr>
<tr>
<td>005</td>
<td>0.2</td>
<td>5</td>
<td>63.3</td>
</tr>
<tr>
<td>006</td>
<td>0.05</td>
<td>20</td>
<td>64.1</td>
</tr>
<tr>
<td>007</td>
<td>0.1</td>
<td>5</td>
<td>55.5</td>
</tr>
<tr>
<td>008</td>
<td>0.1</td>
<td>20</td>
<td>67.7</td>
</tr>
</tbody>
</table>
Table S15. Optimization of the reduction of 1af

0.1 mmol (24 mg)

\[
\begin{array}{c|c|c|c|c|c}
\hline
\text{Entry} & \text{[Ni] source} & \text{Solvent} & \text{Temp. °C} & \text{% Aldehyde} \\
\hline
001 & \text{NiCl}_2\text{(dme)} & \text{EtOAc} & 40 & 25.8 \\
002 & \text{NiBr}_2\text{(H}_2\text{O)}_3 & \text{EtOAc} & 40 & 45 \\
003 & \text{NiCl}_2\text{(dme)} & \text{EtOAc} & 60 & 36.4 \\
004 & \text{NiBr}_2\text{(H}_2\text{O)}_3 & \text{EtOAc} & 60 & 58.3 \\
005 & \text{NiBr}_2\text{(H}_2\text{O)}_3 & \text{1,4-dioxane} & 60 & 73 \\
006 & \text{NiBr}_2\text{(H}_2\text{O)}_3 & \text{THF} & 60 & 44.7 \\
007 & \text{NiBr}_2\text{(H}_2\text{O)}_3 & \text{EtOAc} & 80 & 27.8 \\
\hline
\end{array}
\]

\[\text{10% [Ni] source / 20% dtbbpy / 20% Zn DMDC (2 equiv.), 2,6-lutidine (1.1 equiv.) Ph}_2\text{SiH}_2 \text{(2.25 equiv.) solvent (0.1 M), temp °C, 24 h}\]
Chart S1. Additional substrates tested under the reaction conditions. Green – successful substrates (>65%), orange – low to moderate yields (35-65%), red – unsuccessful substrates (<35%). Yields by \(^1\)H NMR vs. a standard.
Mechanistic Information and Discussion

Monitoring the Anhydride Formation

Procedures A and B for aldehydes formation from carboxylic acids pre-stir all reaction components for 15 minutes prior to silane addition. Therefore, we decided to monitor the formation of various anhydride species after 15 minutes of stirring at room temperature with different reaction components in EtOAc, prior to silane addition. All components were mixed under N₂ with dry solvent and after 15 minutes an aliquot was taken, diluted with CDCl₃ and analyzed by ¹H NMR. Symmetrical anhydride was synthesized according to a known literature procedure as a standard for ¹H NMR.³ Hydrocinnamic acid chemical shifts are known in the literature. The results are in Scheme S2.

Scheme S2. Monitoring the reaction mixture composition after 15 minutes at room temp.

Zn control mixtures: the addition of Zn does not affect the composition of the mixture. See mixture (1) vs (2) and mixture (3) vs (4).

2,6-Lutidine control mixtures: the addition of base has a profound effect on the composition of the mixture. In mixture (2) vs (3) it promotes the formation of mixed anhydride and small quantities of symmetrical anhydride. In mixture (5) vs (6) it promotes formation of both mixed and symmetrical anhydride, with dominant species being the symmetrical anhydride.

**Ni catalyst control mixtures:** the addition of Ni catalyst affects the composition of the mixtures. In mixture (1) vs (5) it promotes formation of small amounts of both anhydrides. In mixture (4) vs (6) formation of symmetrical anhydride is more prevalent than mixed anhydride in the presence of Ni catalyst. Possibly, the Lewis acidic nature of the Ni cat. could be responsible for promoting formation of symmetrical anhydride.

**Mixture (6) resembling the reaction conditions:** in the mixture resembling the reaction conditions most, mixture (6), the dominant species is the symmetrical anhydride. Since the formation of the symmetrical anhydride to mixed anhydride should not be possible under our reaction conditions, we consider the symmetrical anhydride as the active intermediate for the Ni catalysis.

**Time course investigation**

The reduction of hydrocinnamic acid 1a to hydrocinnamaldehyde 1b was monitored by taking aliquots from the reaction mixture containing 1,3,5-trimethoxybenzene as an internal standard and characterization by $^1$H NMR (90 s relaxation delay). Reactions were performed at room temperature (to slow the reaction and observe the induction period) and at 40 °C (representative of the standard reaction conditions). The results are in Scheme S3.

**Scheme S3. Time course at room temperature and 40 °C for reduction of hydrocinnamic acid to hydrocinnamaldehyde**
The reaction at 40 °C proceeds according to standard first order kinetics. However, at room temperature, the reaction is slower and starts after 2 hours. We tentatively attribute this induction period to the initial reduction of the Ni(II) salt by Zn to form catalytically active Ni(0).

**Characterization of silane by-products**

**Dimethoxydiphenylsilane (CAS Registry Number 6843-66-9):** Isolated as a colorless oil from a crude reaction by flash chromatography (0 to 10% MTBE in pentane). Spectral data matches literature.\(^4\) Dimethoxydiphenylsilane was also observed in the crude GCMS trace.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 7.65 – 7.72\) (m, 4H), 7.43 – 7.48 (m, 2H), 7.37 – 7.43 (m, 4H), 3.65 (s, 6H).

\(^13\)C NMR (126 MHz, CDCl\(_3\)) \(\delta 135.0, 132.3, 130.5, 128.1, 51.1\).

GCMS (EI) 244.2 [M], 167.1 [M-C\(_6\)H\(_5\)], 137.1 [M-C\(_7\)H\(_7\)O].

**Diphenylmethoxysilane (CAS Registry Number 40391-85-3):** In \(^1\)H NMR reaction crude, a singlet at 5.37 – 5.40 ppm is observed that grows as the reaction proceeds. We attribute this singlet to the diagnostic hydride in Ph\(_2\)Si(OMe)H which is at 5.41 ppm according to one precedent\(^5\) and 5.36 ppm according to a different precedent.\(^6\) Additionally, GCMS trace of the reaction mixture after completion shows a large peak in the chromatogram that corresponds to the Ph\(_2\)Si(OMe)H byproduct. Fragmentation patterns and mass values are consistent with precedent.\(^6\) For GCMS trace, see below.


Synthesis and Testing of Mixed Anhydride

Methoxycarbonyl 3-phenylpropanoate: a solution of hydrocinnamic acid (2.73 g, 18.2 mmol) and triethylamine (2.21 g, 21.84 mmol) in toluene (100 ml) was cooled to -40 °C and methyl chlorocarbonate (1.892 g, 20.02 mmol) was added dropwise. The reaction mixture was allowed to warm to 0 °C and was stirred for 1 h. Then the reaction was allowed to warm to room temperature and poured into 100 ml water and washed with saturated NaHCO$_3$ and saturated NaCl. The organic phase was dried over MgSO$_4$ and concentrated on the rotatory evaporator to give the mixed anhydride product as a faint yellow liquid (3.64 g, 96% yield).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.31 (t, $J = 7.4$ Hz, 2H), 7.25 – 7.19 (m, 3H), 3.90 (s, 3H), 3.00 (t, $J = 7.7$ Hz, 2H), 2.79 (t, $J = 7.7$ Hz, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 167.2, 149.8, 139.5, 128.8, 128.4, 126.7, 56.0, 36.0, 30.3.

GCMS (EI) 208.0 [M], 180.1 [M-CO], 164.1 [M-CO$_2$], 104.1 [M-C$_3$H$_4$O$_4$].

Methoxycarbonyl 3-phenylpropanoate was next subjected to the reaction conditions described in General Procedure B as in the below scheme: no DMDC was added and 53.5 mg 1,3,5-trimethoxybenzene were added as an internal standard. The reaction resulted in no product after 8 hours and trace amount (<3%) of product after 24 hours by $^1$H NMR.

Testing of Symmetrical Aromatic Acid Anhydrides

Benzoic anhydride is commercially available from Sigma Aldrich. Acid anhydride of 1z was synthesized according to a literature reference with matching spectroscopic data.$^7$ The two anhydrides were subjected to the reaction conditions according to general procedure A (0.1 mmol scale) using NiBr$_2$(H$_2$O)$_3$ and Ph$_2$SiH$_2$ at 60 °C similar to the conditions employed for the corresponding acids 1x and 1z, except without DMDC. Under these conditions, no methoxide anions will be generated from the decomposition of the mixed anhydride intermediate formed.

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with DMDC, which may prevent transmetalation with diphenylsilane. An additional experiment was set up with addition of 1 equiv. of exogeneous NaOMe to attempt to mimic the catalytic reaction conditions more accurately.

![Scheme 2](image)

<table>
<thead>
<tr>
<th>R</th>
<th>Yield of acid reduction (Scheme 2)</th>
<th>Yield of acid anhydride reduction</th>
<th>Yield of acid anhydride reduction with 1 equiv. NaOMe</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>76% (2x)</td>
<td>0%</td>
<td>23.8%</td>
</tr>
<tr>
<td>CF₃</td>
<td>Trace (2z)</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

As can be seen in the results in the table above, anhydrides are inactive substrates, most likely due to lack of methoxide anions to induce transmetalation. When 1 equiv. of NaOMe is added to mimic our catalytic conditions more closely, reduction of acid anhydrides is consistent with the reduction of the parent aromatic acids. Consequently, benzoic anhydride can be obtained in 23.8% yield, whereas the acid anhydride of 1z yields no product. From these experiments it can be tentatively proposed that another aspect of the failure of reduction of 1z and other electron-deficient aromatic acids is that the acid anhydride, *when or if formed*, is also not very reactive within the nickel catalytic cycle.
Spectral Data of Isolated Products

**2,4-Dinitrophenylhydrazone of 3-Phenyl-1-propanal (2a, CAS Registry Number 1237-68-9):** Prepared on 1 mmol scale from hydrocinnamic acid (commercially available) via procedure B using NiCl$_2$(dme) and Ph$_2$SiH$_2$ at 40 °C for 24 h. After completion of the reaction by crude $^1$H NMR, the hydrazone of the aldehyde was formed and isolated using procedure C. The hydrazone product was obtained in 88% yield as an orange solid (eluted with heptane/ethyl acetate 95/5) (276 mg). Characterization data matched those previously reported.$^8$

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 11.04 (s, 1H), 9.14 (d, $J$ = 2.6 Hz, 1H), 8.32 (ddd, $J$ = 9.6, 2.6, 0.6 Hz, 1H), 7.93 (d, $J$ = 9.6 Hz, 1H), 7.58 (t, $J$ = 5 Hz, 1H), 7.38 – 7.33 (m, 2H), 7.28 – 7.25 (m, 3H), 3.00 (t, $J$ = 7.5 Hz, 2H), 2.81 (td, $J$ = 7.5, 5.1 Hz, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 151.2, 145.1, 140.2, 137.9, 129.9, 128.9, 128.7, 128.4, 126.5, 123.5, 116.5, 33.9, 32.4.

HRMS (ESI) Calcd. for C$_{15}$H$_{13}$N$_4$O$_4$ ([M-H]$^-$): 313.0937, found: 313.0923.

**2,4-Dinitrophenylhydrazone of 8-bromo-1-octanal (2b):** Prepared on 1 mmol scale from 8-Bromo-octanoic acid (commercially available) via procedure B using NiBr$_2$(H$_2$O)$_3$ and Ph$_2$SiH$_2$ at 60 °C for 16 h. After completion of the reaction by crude $^1$H NMR, the hydrazone of the aldehyde was formed and isolated using procedure C. The hydrazone product was obtained in 87% yield as an orange solid (eluted with heptane/DCM 70/30) (335 mg).

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 11.01 (s, 1H), 9.11 (d, $J$ = 2.1 Hz, 1H), 8.30 (dd, $J$ = 9.6, 2.1 Hz, 1H), 7.92 (d, $J$ = 9.6 Hz, 1H), 7.53 (t, $J$ = 5.3 Hz, 1H), 3.42 (t, $J$ = 6.7 Hz, 2H), 2.47 – 2.40 (m, 2H), 1.87 (p, $J$ = 7 Hz, 2H), 1.63 (p, $J$ = 7.2 Hz, 2H), 1.52 – 1.33 (m, 6H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 152.4, 145.1, 137.8, 130.0, 128.8, 123.6, 116.5, 33.9, 32.7, 32.5, 28.9, 28.5, 28.0, 26.2.

HRMS (ESI) Calcd. for C$_{14}$H$_{18}$BrN$_4$O$_4$ ([M-H]$^-$): 385.0511, found: 385.0481.

IR (ATR, cm$^{-1}$) 3294, 3102, 2928, 1616, 1495, 1330, 1260, 1217, 1077, 599.

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6-oxo-6-phenylhexanal (2c, CAS Registry Number 87258-30-8): Prepared on 1 mmol scale from 5-benzoypentanoic acid (commercially available) via procedure B using NiBr$_2$(H$_2$O)$_3$ and Ph$_2$SiH$_2$ (2.25 equiv.) at 40 °C for 24 h. Obtained in 85% yield as white solid (eluted with pentane/diethyl ether 80/20) (171 mg). Characterization data matched those previously reported.\(^9\)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.79 (s, 1H), 7.95 (d, $J$ = 7.8 Hz, 2H), 7.55 (t, $J$ = 7.5 Hz, 1H), 7.46 (t, $J$ = 7.8 Hz, 2H), 3.01 (t, $J$ = 6.9 Hz, 2H), 2.57 – 2.43 (dt, $J$ = 7.1, 1.0 Hz, 2H), 1.83 – 1.68 (m, 4H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 202.4, 199.9, 137.0, 133.2, 128.8, 128.1, 43.9, 38.3, 23.8, 21.9.


methyl 8-oxooctanoate (2d, CAS Registry Number 3884-92-2): Prepared on 1 mmol scale from Suberic acid monomethyl ester (commercially available) via procedure B using NiCl$_2$(dme) and Ph$_2$SiH$_2$ (2.25 equiv.) at 40 °C for 24 h. Product co-eluted substantially with lutidine during column chromatography (eluted with pentane/MTBE 90/10) and was further subjected to an acid wash as follows: the concentrated desired fractions were diluted with DCM (20 ml) and washed with 15 ml 1M HCl. The aqueous layer was washed two more times with DCM (20 ml). The combined organic layers were dried over Na$_2$SO$_4$, filtered and evaporated to dryness at 10 degrees. Product obtained in 87% yield as colorless oil (150 mg). Characterization data matched those previously reported.\(^10\)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 9.73 (s, 1H), 3.64 (s, 3H), 2.40 (t, $J$ = 7.3 Hz, 2H), 2.28 (t, $J$ = 7.5 Hz, 2H), 1.65 – 1.56 (m, 4H), 1.36 – 1.28 (m, 4H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 202.8, 174.2, 51.6, 43.9, 34.0, 28.9, 28.9, 24.8, 21.9.


9-Cyan-nonanal (2e, CAS No. 18214-19-2): Prepared on 1 mmol scale from 9-cyanopelargonic acid (commercially available) via procedure B using NiCl$_2$(dme) and Ph$_2$SiH$_2$ (2.25 equiv.) at 40

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S20
°C for 24 h. Obtained in 72% yield as colorless oil (eluted with pentane/MTBE 85/15) (120 mg). Characterization data matched those previously reported.\textsuperscript{11}

\textbf{1H NMR} (400 MHz, CDCl\textsubscript{3}) \(\delta\) 9.75 (t, \(J =\) 1.6 Hz, 1H), 2.41 (td, \(J =\) 7.3, 1.5 Hz, 2H), 2.32 (t, \(J =\) 7.1 Hz, 2H), 1.69 – 1.56 (m, 4H), 1.5 – 1.38 (m, 2H), 1.36 – 1.27 (m, 6H).

\textbf{13C NMR} (101 MHz, CDCl\textsubscript{3}) \(\delta\) 202.6, 119.7, 43.7, 28.9, 28.5, 25.3, 21.9, 17.1.

\textbf{HRMS (ESI)} Calcd. for C\textsubscript{10}H\textsubscript{18}NO ([M+H]+): 168.1388, found: 168.1394.

4-Phenoxybutyraldehyde (2f, CAS Registry Number 19790-62-6): Prepared on 1 mmol scale from 5-benzoylpentanoic acid (commercially available) via procedure B using NiBr\textsubscript{2}(H\textsubscript{2}O)\textsubscript{3} and Ph\textsubscript{2}SiH\textsubscript{2} (2.25 equiv.) at 60 °C for 16 h. Obtained in 82% yield as colorless liquid (eluted with pentane/MTBE 95/5 to 90/10) (135 mg). Characterization data matched those previously reported.\textsuperscript{12}

\textbf{1H NMR} (500 MHz, CDCl\textsubscript{3}) \(\delta\) 9.85 (t, \(J =\) 1.2 Hz, 1H), 7.32 – 7.24 (m, 2H), 6.95 (tt, \(J =\) 7.4, 1.0 Hz, 1H), 6.91 – 6.85 (m, 2H), 4.01 (t, \(J =\) 6.0 Hz, 2H), 2.67 (td, \(J =\) 7.0, 1.2 Hz, 2H), 2.21 – 2.05 (m, 2H).

\textbf{13C NMR} (126 MHz, CDCl\textsubscript{3}) \(\delta\) 201.9, 158.8, 129.6, 121.0, 114.6, 66.7, 40.8, 22.2.

\textbf{HRMS (ESI)} Calcd. for C\textsubscript{10}H\textsubscript{13}O\textsubscript{2} ([M+H]+): 165.0916, found: 165.0908.

2,4-Dinitrophenylhydrazone of 3-(2-furyl)propionaldehyde (2g): Prepared on 1 mmol scale from 3-(2-furyl)propanoic acid (commercially available) via procedure B using NiCl\textsubscript{2}(dme) and Ph\textsubscript{2}SiH\textsubscript{2} at 40 °C for 24 h. After completion of the reaction by crude \textbf{1H NMR}, the hydrazone of the aldehyde was formed and isolated using procedure C. The hydrazone product was obtained in 79% yield as an orange solid (eluted with heptane/ethyl acetate 95/5) (241 mg). Characterization data matched those previously reported.\textsuperscript{12}

\textbf{1H NMR} (500 MHz, CDCl\textsubscript{3}) \(\delta\) 11.03 (s, 1H), 9.12 (d, \(J =\) 2.0 Hz, 1H), 8.30 (dd, \(J =\) 9.6, 2.0 Hz, 1H), 7.91 (d, \(J =\) 9.6 Hz, 1H), 7.57 (t, \(J =\) 4.9 Hz, 1H), 7.34 (s, 1H), 6.31 (s, 1H), 6.08 (d, \(J =\) 2.3 Hz, 1H), 3.07 – 2.92 (m, 2H), 2.84 – 2.7 (m, 2H).


\[ ^{13}\text{C NMR} \ (126 \text{ MHz, } \text{CDCl}_3) \ \delta \ 153.9, \ 150.7, \ 145.1, \ 141.4, \ 137.9, \ 130.0, \ 128.9, \ 123.5, \ 116.5, \ 110.3, \ 105.8, \ 31.0, \ 24.8. \]

HRMS (ESI) Calcd. for C_{13}H_{11}N_{4}O_{5} ([M-H]^-): 303.0730, found: 303.0716.

IR (ATR, cm\(^{-1}\)) 3290, 3095, 1618, 1330, 1304, 1261, 741, 599.

2,4-Dinitrophenylhydrazone of 3-(thiophen-2-yl)propanal (2h): Prepared on 1 mmol scale from 3-(thiophen-2-yl)propanoic acid (commercially available) via procedure B using NiCl\(_2\)(dme) and Ph\(_2\)SiH\(_2\) at 40 °C for 24 h. After completion of the reaction by crude \(^1\text{H NMR},\) the hydrazone of the aldehyde was formed and isolated using procedure C. The hydrazone product was obtained in 85% yield as an orange solid (eluted with heptane/ethyl acetate 95/5) (272 mg).

\(^1\text{H NMR} \ (500 \text{ MHz, } \text{CDCl}_3) \ \delta \ 11.07 \ (s, 1\text{H}), \ 9.15 \ (d, J = 2.6 \text{ Hz, } 1\text{H}), \ 8.34 \ (dd, J = 9.6, 0.6 \text{ Hz, } 1\text{H}), \ 7.96 \ (d, J = 9.6 \text{ Hz, } 1\text{H}), \ 7.60 \ (t, J = 4.8 \text{ Hz, } 1\text{H}), \ 7.20 \ (dd, J = 5.1, 1.2 \text{ Hz, } 1\text{H}), \ 6.98 \ (dd, J = 5.1, 3.4 \text{ Hz, } 1\text{H}), \ 6.95 – 6.86 \ (m, 1\text{H}), \ 3.24 \ (t, J = 7.5 \text{ Hz, } 2\text{H}), \ 2.86 \ (dt, J = 7.5, 4.9 \text{ Hz, } 2\text{H}).\]

\[^{13}\text{C NMR} \ (126 \text{ MHz, } \text{CDCl}_3) \ \delta \ 150.4, \ 149.2, \ 145.1, \ 142.9, \ 137.9, \ 130.0, \ 127.0, \ 124.9, \ 123.8, \ 123.5, \ 116.6, \ 34.2, \ 26.5.\]

HRMS (ESI) Calcd. for C_{13}H_{11}N_{4}O_{5} ([M-H]^-): 319.0501, found: 319.0492.

IR (ATR, cm\(^{-1}\)) 3290, 3093, 1617, 1494, 1331, 1304, 1260, 1215, 710.

N-[3-(1H-indol-3-yl)propylideneamino]-2,4-dinitro-aniline (2i): Prepared on 1 mmol scale from 3-indolepropionic acid (commercially available) via procedure B using NiCl\(_2\)(dme) and Ph\(_2\)SiH\(_2\) (2.25 equiv.) at 40 °C for 24 h. After completion of the reaction by crude \(^1\text{H NMR},\) the hydrazone of the aldehyde was formed and isolated using procedure C. The hydrazone product was obtained in 88% yield as an orange solid (eluted with heptane/ethyl acetate 90/10 to 70/30) (312 mg).

\(^1\text{H NMR} \ (500 \text{ MHz, } \text{DMSO-d}_6) \ \delta \ 11.36 \ (s, 1\text{H}), \ 10.85 \ (s, 1\text{H} – \text{ minor isomer}), \ 10.81 \ (s, 1\text{H}), \ 8.88 – 8.80 \ (m, 1\text{H}), \ 8.40 – 8.27 \ (m, 1\text{H}), \ 8.10 \ (t, J = 5.1 \text{ Hz, } 1\text{H}), \ 7.89 – 7.81 \ (m, 1\text{H}), \ 7.62 –
7.53 (m, 1H), 7.36 – 7.30 (m, 1H), 7.22 -7.15 (m, 1H), 7.07 (t, J = 7.4 Hz, 1H), 6.99 (t, J = 7.4 Hz, 1H), 2.99 (t, J = 7.3 Hz, 2H), 2.81 – 2.71 (m, 2H);

$^1$H NMR (126 MHz, DMSO-d$_6$) δ 154.9, 144.8, 136.4, 136.3, 129.7, 128.7, 127.0, 123.1, 122.6, 120.9, 118.3, 118.2, 116.4, 113.2, 111.4, 32.9, 21.6;

HRMS (ESI) Calcd. for C$_{17}$H$_{14}$N$_5$O$_4$ ([M-H]$: 352.1046, found: 352.1063.

IR (ATR, cm$^{-1}$) 3408, 3316, 1586, 1499, 1327, 1049, 723, 534.

(3-acetyl-2,2-dimethylcyclobutyl)acetaldehyde (2j, CAS Registry Number 2704-78-1): Prepared on 1 mmol scale from cis-Pinonic acid (commercially available) via procedure B using NiCl$_2$(dme) and Ph$_2$SiH$_2$ (2.25 equiv.) at 40 °C for 24 h. Product co-eluted substantially with lutidine during column chromatography (eluted with diethyl ether/pentane 20/80) and was further subjected to an acid wash as follows: the concentrated desired fractions were diluted with DCM (40 ml) and washed with 25 ml 1M HCl. The aqueous layer was washed two more times with DCM (40 ml). The combined organic layers were dried over MgSO$_4$, filtered and evaporated to dryness at 10 degrees. Product obtained in 79% yield as colorless oil (133 mg). Characterization data matched those previously reported.$^{13}$

$^1$H NMR (500 MHz, CDCl$_3$) δ 9.72 (s, 1H), 2.91 (dd, J = 9.9, 7.9 Hz, 1H), 2.52 – 2.36 (m, 3H), 2.03 (s, 3H), 2.02 – 1.88 (m, 2H), 1.32 (s, 3H), 0.83 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 207.5, 201.5, 54.5, 45.2, 43.4, 35.9, 30.5, 22.9, 17.8.

HRMS (ESI) Calcd. for C$_{10}$H$_{17}$O$_2$ ([M+H]$^+$): 169.1229, found: 169.1221.

$^{3}$α-hydroxy-5β-cholanal-(24) (2k, CAS Registry Number 21555-85-1): Prepared on 1 mmol scale from lithocholic acid (commercially available) via procedure B using NiCl$_2$(dme) and PhSiH$_3$ (1.5 equiv.) at 60 °C for 16 h. Obtained in 73% yield as white solid (eluted with pentane/MTBE 80/20) (263.5 mg). Characterization data matched those previously reported.$^{14}$

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$^{14}$ Maione, A. M.; Romerio, A. Synthesis 1984, 11, 955.
\textbf{1H NMR} (500 MHz, CDCl$_3$) $\delta$ 9.75 (t, $J = 1.9$ Hz, 1H), 3.66 – 3.57 (m, 1H), 2.48 – 2.40 (m, 1H), 2.39 – 2.28 (m, 1H), 1.95 (dt, $J = 12.2$, 2.8 Hz, 1H), 1.89 – 1.72 (m, 5H), 1.70 – 1.60 (m, 2H), 1.60 – 1.54 (m, 1H), 1.53 – 1.46 (m, 1H), 1.46 – 0.92 (m, 17H), 0.92 – 0.88 (m, 6H), 0.63 (s, 3H).

\textbf{13C NMR} (126 MHz, CDCl$_3$) $\delta$ 203.4, 71.9, 56.6, 56.1, 42.9, 42.2, 41.1, 40.6, 40.3 (2C), 36.6, 36.0, 35.5, 34.7, 30.7, 28.4, 28.1, 27.3, 26.5, 24.3, 23.5, 20.9, 18.5, 12.2.

\textbf{HRMS (ESI)} Calcd. for C$_{24}$H$_{41}$O$_2$ ([M+H]$^+$): 361.3107, found: 361.3123.

3-formylmethyl-2-(cis-2-n-pentenyl)-1-cyclopentanone (2l, CAS Registry Number 56987-99-6): Prepared on 1 mmol scale from jasmonic acid (commercially available, 85% purity) via procedure B using NiCl$_2$(dme) and Ph$_2$SiH$_2$ (2.25 equiv.) at 40 °C for 24 h. Obtained in 72% yield as colorless oil (eluted with pentane/MTBE 90/10) (139.7 mg). Characterization data matched those previously reported.\textsuperscript{15}

\textbf{1H NMR} (500 MHz, CDCl$_3$) $\delta$ 9.75 (t, $J = 1.5$ Hz, 1H), 5.44 – 5.35 (m, 1H), 5.23 – 5.12 (m, 1H), 2.83 – 2.71 (m, 1H), 2.46 – 2.38 (m, 1H), 2.37 – 2.18 (m, 5H), 2.12 – 2.02 (m, 1H), 2.01 – 1.93 (m, 2H), 1.86 – 1.78 (m, 1H), 1.44 – 1.33 (m, 1H), 0.88 (t, $J = 7.5$ Hz, 3H).

\textbf{13C NMR} (126 MHz, CDCl$_3$) $\delta$ 218.7, 201.1, 134.3, 125.1, 54.1, 48.9, 37.9, 35.9, 27.6, 25.7, 20.8, 14.2.

\textbf{HRMS (ESI)} Calcd. for C$_{12}$H$_{19}$O$_2$ ([M+H]$^+$): 195.1385, found: 195.1380.

\textbf{N-(2,4-dinitrophenyl)-N’-(2-ethylhexylidene)hydrazine} (2m, CAS Registry Number 14086-22-7): Prepared on 1 mmol scale from 2-ethylhexanoic acid (commercially available) via procedure B using NiCl$_2$(dme) and Ph$_2$SiH$_2$ (2.25 equiv.) at 60 °C for 16 h. After completion of the reaction by crude \textbf{1H NMR}, the hydrazone of the aldehyde was formed and isolated using procedure C. The hydrazone product was obtained in 82% yield as an orange solid (eluted with heptane/ethyl acetate 97/3) (252 mg). Characterization data matched those previously reported.\textsuperscript{16}


\textsuperscript{16} Košmrlj, J.; Weigel, L. O.; Evans, D. A.; Downey, C. W.; Wu, J. J. Am. Chem. Soc. 2003, 125, 3208.
**1H NMR** (500 MHz, CDCl₃) δ 11.33 (s, 1H – minor isomer), 11.00 (s, 1H), 9.12 (d, J = 2.6 Hz, 1H), 8.30 (d, J = 9.6, 2.6 Hz, 1H), 7.93 (d, J = 9.6 Hz, 1H), 7.34 (d, J = 6.9 Hz, 1H), 2.64 – 2.54 (m, 1H, minor isomer), 2.39 – 2.30 (m, 1H), 1.66 – 1.45 (m, 4H), 1.39 – 1.27 (m, 4H), 0.95 (t, J = 7.4 Hz, 3H), 0.91 (t, J = 6.9 Hz, 3H).

**13C NMR** (126 MHz, CDCl₃) δ 156.6, 145.3, 137.9, 130.1, 128.9, 123.7, 116.7, 44.2, 32.2, 29.5, 25.8, 22.9, 14.1, 11.8.


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**trans-2-phenylcyclopropanecarbaldehyde (2n, CAS Registry Number 34271-31-3):** Prepared on 1 mmol scale from trans-2-Phenylcyclopropane-1-carboxylic acid (commercially available) via procedure B using NiCl₂(dme) and Ph₂SiH₂ (2.25 equiv.) at 60 °C for 16 h. Obtained in 79% yield as white solid (eluted with pentane/MTBE 98/2 to 95/5) (115 mg). Characterization data matched those previously reported.¹⁷

**1H NMR** (500 MHz, CDCl₃) δ 9.33 (d, J = 4.5 Hz, 1H), 7.30 (t, J = 7.5 Hz, 2H), 7.23 (t, J = 7.2 Hz, 1H), 7.12 (d, J = 7.7 Hz, 2H), 2.67 – 2.60 (m, 1H), 2.18 (dq, J = 8.9, 4.5 Hz, 1H), 1.74 (dt, J = 9.6, 5.0 Hz, 1H), 1.53 (dd, J = 12.8, 7.5 Hz, 1H).

**13C NMR** (126 MHz, CDCl₃) δ 199.8, 139.1, 128.8, 127.0, 126.4, 33.9, 26.7, 16.6.


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**tert-butyl 6-formyl-2-azaspiro[3.3]heptane-2-carboxylate (2o):** Prepared on 1 mmol scale from 2-[(tert-butoxy)carbonyl]-2-azaspiro[3.3]heptane-6-carboxylic acid (commercially available) via procedure B using NiCl₂(dme) and Ph₂SiH₂ (2.25 equiv.) at 40 °C for 24 h. Obtained in 70% yield as white solid (eluted with pentane/MTBE 70/30) (158 mg).

**1H NMR** (500 MHz, CDCl₃) δ 9.71 (d, J = 1.5 Hz, 1H), 3.94 (s, 2H), 3.82 (s, 2H), 3.15 – 3.00 (m, 1H), 2.51 – 2.27 (m, 4H), 1.42 (s, 9H);

**13C NMR** (126 MHz, CDCl₃) δ 201.5, 156.1, 79.5, 61.5 (broad), 39.9, 35.8, 34.7, 32.9, 28.3.

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HRMS (ESI) Calcd. for C_{12}H_{20}O_{3} ([M+H]^+): 226.1440, found: 226.1442.

IR (ATR, cm^{-1}) 2977, 2935, 1710, 1682, 1395, 1364, 1163, 1103, 771.

**indan-2-carbaldehyde (2p, CAS Registry Number 37414-44-1):** Prepared on 1 mmol scale from indan-2-carboxylic acid (commercially available) via procedure B using NiCl_{2}(dme) and Ph_{2}SiH_{2} (2.25 equiv.) at 60 °C for 16 h. Obtained in 81% yield as colorless oil (eluted with pentane/diethyl ether 95/5) (118 mg). Characterization data matched those previously reported.\(^{18}\)

\(^{1}\)H NMR (500 MHz, CDCl_{3}) δ 9.78 (s, 1H), 7.25 – 7.21 (m, 2H), 7.20 – 7.14 (m, 2H), 3.35 – 3.24 (m, 3H), 3.24 – 3.15 (m, 2H).

\(^{13}\)C NMR (126 MHz, CDCl_{3}) δ 202.9, 141.2, 126.9, 124.8, 50.8, 33.1.

HRMS (ESI) Calcd. for C_{10}H_{11}O ([M+H]^+): 147.0810, found: 147.0818.

**tert-butyl 3-formylpyrrolidine-1-carboxylate (2q, CAS Registry Number 59379-02-1):** Prepared on 1 mmol scale from 1-(tert-butoxycarbonyl)pyrrolidine-3-carboxylic acid (commercially available) via procedure B using NiCl_{2}(dme) and PhSi_{2}H_{2} at 40 °C for 24 h. Obtained in 71% yield as colorless oil (eluted with pentane/diethyl ether 80/20 to 70/30) (141 mg). Characterization data matched those previously reported.\(^{19}\)

\(^{1}\)H NMR (500 MHz, CDCl_{3}) δ 9.67 (d, J = 1.6 Hz, 1H), 3.76 – 3.59 (m, 1H), 3.55 – 3.43 (m, 1H), 3.42 – 3.26 (m, 2H), 3.05 – 2.95 (m, 1H), 2.24 – 2.00 (m, 2H), 1.44 (s, 9H).

\(^{13}\)C NMR (126 MHz, CDCl_{3}) δ 200.7, 200.6, 154.3, 79.6, 50.5, 49.6, 45.0, 44.7, 28.4, 25.8, 25.3 (rotamers present).

HRMS (ESI) Calcd. for C_{10}H_{18}NO_{3} ([M+H]^+): 200.1287, found: 200.1298.

**tert-butyl 4-formylpiperidine-1-carboxylate (2r, CAS Registry Number 137076-22-3):** Prepared on 1 mmol scale from N-[(tert-butoxy)carbonyl]piperidine-4-carboxylic acid (commercially available) via procedure B using NiCl_{2}(dme) and Ph_{2}SiH_{2} (2.25 equiv.) at 40 °C


for 24 h. Obtained in 78% yield as colorless oil (eluted with pentane/Et₂O 80/20) (166 mg). Characterization data matched those previously reported.²⁰

¹H NMR (500 MHz, CDCl₃) δ 9.65 (s, 1H), 4.05 – 3.90 (m, 2H), 2.93 (t, J = 11 Hz, 2H), 2.42 (tt, J = 10.6, 3.9 Hz, 1H), 1.94 – 1.85 (m, 2H), 1.59 – 1.50 (m, 2H), 1.48 (s, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 203.0, 154.7, 79.7, 48.0, 42.8 (broad), 28.4, 25.2.


cyclododecylcarboxaldehyde 2,4-dinitro-phenylhydrazone (2s, CAS Registry Number 21519-52-8): Prepared on 1 mmol scale from cyclododecanecarboxylic acid (commercially available) via procedure B using NiCl₂(dme) and Ph₂SiH₂ (2.25 equiv.) at 60 °C for 16 h. After completion of the reaction by crude ¹H NMR, the hydrazone of the aldehyde was formed and isolated using procedure C. The hydrazone product was obtained in 75% yield as an orange solid (eluted with heptane/ethyl acetate 97/3) (252 mg).

¹H NMR (400 MHz, CDCl₃) δ 10.98 (s, 1H), 9.12 (d, J = 2.7 Hz, 1H), 8.30 (ddd, J = 9.6, 2.7, 0.5 Hz, 1H), 7.93 (d, J = 9.6 Hz, 1H), 7.43 (d, J = 5.8 Hz, 1H), 2.65 – 2.57 (m, 1H), 1.7 – 1.6 (m, 2H), 1.58 – 1.49 (m, 2H), 1.49 – 1.31 (m, 18H).

¹³C NMR (100 MHz, CDCl₃) δ 157.0, 145.4, 137.8, 130.1, 128.9, 123.7, 116.8, 37.8, 27.5, 23.9, 23.8, 23.7, 23.5, 22.4.


IR (ATR, cm⁻¹) 3286, 2928, 1614, 1514, 1328, 621.

tert-butyl 3-formyl-3-methylpiperidine-1-carboxylate (2t, CAS Registry Number 406212-49-5): Prepared on 1 mmol scale from 1-(tert-butoxycarbonyl)-3-methylpiperidine-3-carboxylic

acid (commercially available) via procedure B using NiCl₂(dme) and Ph₂SiH₂ (2.25 equiv.) at 75 °C for 16 h. Obtained in 90% yield as colorless oil (eluted with DCM) (204 mg).

**1H NMR** (500 MHz, CDCl₃) δ 9.55 (s, 1H), 4.30 – 3.77 (m, 1H), 3.76 – 3.57 (m, 1H), 3.23 – 2.81 (m, 2H), 2.12 – 1.96 (m, 1H), 1.64 – 1.53 (m, 2H), 1.51 (s, 10H), 1.43 – 1.31 (m, 1H), 1.03 (s, 3H).

**13C NMR** (126 MHz, CDCl₃) δ 204.8, 154.6, 79.9, 49.9 (broad), 49.3 (broad), 46.7, 44.3 (broad), 43.4 (broad), 33.6, 31.0, 28.4, 21.9 (broad), 19.4 (broad).

**HRMS (ESI)** Calcd. for C₁₂H₂₂NO₃ ([M+H]+): 228.1600, found: 228.1605.

**IR (ATR, cm⁻¹)** 2974, 2933, 1727, 1687, 1421, 1276, 1156.

1-Adamantane-carbaldehyde 2,4-dinitro-phenylhydrazone (2u, CAS Registry Number 18220-81-0): Prepared on 1 mmol scale from 1-Adamantanecarboxylic acid (commercially available) via procedure B using NiCl₂(dme) and Ph₂SiH₂ (2.25 equiv.) at 60 °C for 16 h. After completion of the reaction by crude ¹H NMR, the hydrazone of the aldehyde was formed and isolated using procedure C. The hydrazone product was obtained in 88% yield as an orange solid (eluted with heptane/ethyl acetate 97/3) (252 mg).

**1H NMR** (500 MHz, CDCl₃) δ 10.87 (s, 1H), 9.05 (d, J = 2.6 Hz, 1H), 8.26 – 8.17 (m, 1H), 7.85 (d, J = 9.6 Hz, 1H), 7.21 (s, 1H), 2.02 (s, 3H), 1.79 – 1.70 (m, 9H), 1.70 – 1.62 (m, 3H).

**13C NMR** (126 MHz, CDCl₃) δ 158.6, 144.3, 136.6, 128.9, 127.7, 122.5, 115.6, 38.8, 36.5, 35.5, 26.8.


**IR (ATR, cm⁻¹)** 3280, 3103, 2901, 2849, 1613, 1583, 1502, 1305, 1255, 1069, 906, 728, 620.

Glycyrrhetinaldehyde (2v, CAS Registry Number 50627-79-7): Prepared on 1 mmol scale from 18β-Glycyrrhetinic acid (commercially available) via procedure B using NiCl₂(dme) and Ph₂SiH₂ (2.25 equiv.) at 80 °C for 24 h. Reaction used tetrahydrofuran instead of ethyl acetate
as solvent. Obtained in 90% yield as white solid (eluted with pentane/MTBE 70/30 to 40/60) (407 mg). Characterization data matched those previously reported.\textsuperscript{21}

\[ ^{1}H \text{ NMR} \ (500 \text{ MHz, CDCl}_3) \delta 9.42 \ (s, 1H), 5.66 \ (s, 1H), 3.22 \ (dd, J = 11.7, 4.6 \text{ Hz}, 1H), 2.80 \ (dt, J = 13.5, 3.6 \text{ Hz}, 1H), 2.34 \ (s, 1H), 2.09 – 1.97 \ (m, 2H), 1.92 – 1.76 \ (m, 3H), 1.76 – 1.51 \ (m, 6H), 1.51 – 1.34 \ (m, 7H), 1.27 \ (dd, J = 14.4, 4.4 \text{ Hz}, 1H), 1.22 – 1.16 \ (m, 1H), 1.15 – 1.09 \ (m, 6H), 1.05 – 0.93 \ (m, 8H), 0.84 – 0.76 \ (m, 6H), 0.70 \ (dd, J = 11.9, 2.0 \text{ Hz}, 1H). \]

\[ ^{13}C \text{ NMR} \ (126 \text{ MHz, CDCl}_3) \delta 205.8, 200.2, 168.7, 128.8, 78.9, 62.0, 55.1, 47.8, 47.0, 45.6, 43.4, 39.3, 39.3, 38.5, 37.2, 32.9, 32.1, 28.7, 28.5, 28.2, 27.4, 26.6, 26.3, 24.2, 23.8, 18.8, 17.6, 16.5, 15.7. \]

HRMS (ESI) Calcd. for C\(_{30}\)H\(_{47}\)O\(_{3}\) ([M+H]+): 455.3525, found: 455.3528.

\[ \text{5-(2,5-dimethylphenoxy)-2,2-dimethylpentanal (2w, CAS Registry Number 39938-97-1):} \]

Prepared on 1 mmol scale from Gemfibrozil (commercially available) via procedure B using NiCl\(_2\)(dme) and Ph\(_2\)SiH\(_2\) (2.25 equiv.) at 60 °C for 16 h. Obtained in 84% yield as slight yellow oil (eluted with pentane/MTBE 96/4 then one more column with DCM/pentane 95/5 to 0/100) (196 mg). Characterization data matched those previously reported.\textsuperscript{22}

\[ ^{1}H \text{ NMR} \ (500 \text{ MHz, CDCl}_3) \delta 9.50 \ (s, 1H), 7.01 \ (d, J = 7.4 \text{ Hz}, 1H), 6.67 \ (d, J = 7.4 \text{ Hz}, 1H), 6.61 \ (s, 1H), 3.93 \ (t, J = 5.6 \text{ Hz}, 2H), 2.31 \ (s, 3H), 2.18 \ (s, 3H), 1.78 – 1.64 \ (m, 4H), 1.11 \ (s, 6H). \]

\[ ^{13}C \text{ NMR} \ (126 \text{ MHz, CDCl}_3) \delta 206.2, 157.0, 136.6, 130.5, 123.7, 120.9, 112.1, 67.9, 45.7, 33.8, 24.6, 21.5, 21.5, 15.9. \]


\[ \text{Benzaldehyde (2x, CAS Registry Number 100-52-7):} \]

Prepared on 1 mmol scale from benzoic acid (commercially available) via procedure B using NiBr\(_2\)(H\(_2\)O)\(_3\) and PhSi\(_2\)H\(_2\) (2.25 equiv.) at 60 °C for 24 h. Obtained in 76% NMR yield with dibromomethane as standard (added after the reaction was completed).
4-methoxy-benzaldehyde (2y, CAS Registry Number 123-11-5): Prepared on 1 mmol scale from 4-methoxy-benzoic acid (commercially available) via procedure B using NiBr₂(H₂O)₃ and PhSi₂H₂ (2.25 equiv.) at 60 °C for 24 h. Obtained in 87% NMR yield with dibromomethane as standard (added after the reaction was completed).

2-naphthylbenzaldehyde (2z, CAS Registry Number 66-99-9): Prepared on 1 mmol scale from 2-naphthoic acid (commercially available) via procedure B using NiBr₂(H₂O)₃ and PhSi₂H₂ (2.25 equiv.) at 60 °C for 24 h. Obtained in 71% NMR yield with dibromomethane as standard (added after the reaction was completed).

4-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-butyraldehyde (2ab, CAS Registry Number 3598-60-5): Prepared on 1 mmol scale from 4-phthalimidobutyric acid (commercially available) via procedure B using NiBr₂(H₂O)₃ and PhSi₂H₂ (2.25 equiv.) at 60 °C for 16 h. Obtained in 86% yield as white solid (eluted with MTBE/pentane 20/80) (187 mg). Characterization data matched those previously reported.²³

This reaction was also set up on 10 mmol scale according to the scale-up part of procedure B using NiBr₂(H₂O)₃ and PhSi₂H₂ (2.25 equiv.) at 60 °C for 48 h. The aldehyde product was similarly obtained as a white solid in 73% yield (1.585 g).

¹H NMR (500 MHz, CDCl₃) δ 9.77 (s, 1H), 7.85 (dd, J = 5.4, 3.1 Hz, 2H), 7.72 (dd, J = 5.4, 3.1 Hz, 2H), 3.75 (t, J = 6.8 Hz, 2H), 2.54 (t, J = 7.3 Hz, 2H), 2.02 (p, J = 7.0 Hz, 2H).

¹³C NMR (126 MHz, CDCl₃) δ 201.0, 168.5, 134.2, 132.1, 123.4, 41.2, 37.3, 21.3.


trans-4-(4-chlorophenyl)cyclohexanecarbaldehyde (2ac, CAS Registry Number 1228658-09-0): Prepared on 1 mmol scale from trans-4-(4-chlorophenyl)cyclohexane-1-carboxylic acid (commercially available) via procedure B using NiCl₂(dme) and Ph₂SiH₂ (2.25 equiv.) at 40 °C for 24 h. Obtained in 87% yield as white solid (eluted with pentane/DCM 80/20 then one more

column with pentane/MTBE 97/3) (194 mg). Characterization data matched those previously reported.

This reaction was also set up on 10 mmol scale according to the scale-up part of procedure B using NiCl2(dme) and Ph2SiH2 (2.25 equiv.) at 40 °C for 48 h. The aldehyde product was similarly obtained as a white solid in 79% yield (1.75 g).

**1H NMR** (500 MHz, CDCl3) δ 9.68 (d, J = 1.2 Hz, 1H), 7.29 – 7.25 (m, 2H), 7.16 – 7.12 (m, 2H), 2.53 – 2.40 (m, 1H), 2.34 – 2.21 (m, 1H), 2.17 – 2.11 (m, 2H), 2.04 – 1.99 (m, 2H), 1.54 – 1.37 (m, 4H);

**13C NMR** (126 MHz, CDCl3) δ 204.4, 145.2, 131.9, 128.7, 128.2, 49.9, 43.3, 33.1, 26.4.

**HRMS (ESI)** Calcd. for C13H14ClO ([M-H]–): 221.0733, found: 221.0737.

Tetrahydro-2H-thiopyran-4-carbaldehyde 1,1-dioxide (2ad, CAS Registry Number 494210-61-6): Prepared on 1 mmol scale from tetrahydro-2H-thiopyran-4-carboxylic acid 1,1-dioxide (commercially available) via procedure B using NiBr2(H2O)3 and Ph2SiH2 (2.25 equiv.) at 60 °C for 16 h. Obtained in 73% yield as white solid (eluted with pentane/MTBE 20/80 to 0/100) (119 mg). Characterization data matched those previously reported.

**1H NMR** (500 MHz, CDCl3) δ 9.69 (s, 1H), 3.12 – 3.05 (m, 2H), 3.04 – 2.97 (m, 2H), 2.59 – 2.49 (m, 1H), 2.48 – 2.38 (m, 2H), 2.37 – 2.25 (m, 2H).

**13C NMR** (126 MHz, CDCl3) δ 200.6, 49.8, 45.9, 23.7.

**HRMS (ESI)** Calcd. for C6H9O3S ([M-H]–): 161.0272, found: 161.0290.

4-phenylbicyclo[2.2.2]octane-1-carboxaldehyde (2ae, CAS Registry Number 94994-29-3): Prepared on 1 mmol scale from tetrahydro-2H-thiopyran-4-carboxylic acid 1,1-dioxide (commercially available) via procedure B using NiCl2(dme) and Ph2SiH2 (2.25 equiv.) at 40 °C for 24 h. Obtained in 83% yield as white solid (eluted with pentane/MTBE 99/1 to 97/3) (177.4 mg). Characterization data matched those previously reported.


\(^1\text{H NMR}\) (500 MHz, CDCl\(_3\)) \(\delta\) 9.55 (s, 1H), 7.39 – 7.30 (m, 4H), 7.26 – 7.19 (m, 1H), 1.97 – 1.90 (m, 6H), 1.85 – 1.78 (m, 6H).

\(^{13}\text{C NMR}\) (126 MHz, CDCl\(_3\)) \(\delta\) 206.3, 149.0, 128.4, 126.0, 125.6, 44.1, 35.7, 31.4, 26.2.

HRMS (ESI) Product did not ionize well using ESI. GCMS (EI) data is included below.

GCMS (EI) 214.2 [M], 185.2 [M-CHO], 129.1 [M-C\(_5\)H\(_9\)O], 91.1 [M-C\(_8\)H\(_{11}\)O].

\(\text{trans-3-chloro-4-(2-formylcyclopropyl)benzamide (2af)}\): Prepared on 1 mmol scale from \(\text{trans-2-(4-carbamoyl-2-chlorophenyl)cyclopropane-1-carboxylic acid}\) via procedure B using NiBr\(_2\)(H\(_2\)O)\(_3\) and Ph\(_2\)SiH\(_2\) (2.25 equiv.) at 60 °C for 16 h. \(\text{1,4-Dioxane was used as a solvent instead of ethyl acetate for this substrate}\). Obtained in 72% yield as white solid (eluted with heptane/ethyl acetate 40/60 to 0/100) (160 mg).
**1H NMR** (500 MHz, CDCl$_3$) δ 9.36 (d, $J = 4.4$ Hz, 1H), 7.78 (d, $J = 1.8$ Hz, 1H), 7.58 (dd, $J = 8.0$, 1.8 Hz, 1H), 7.04 (d, $J = 8.1$ Hz, 1H), 5.89 (d, $J = 124.5$ Hz, 2H), 2.81 (ddd, $J = 9.1$, 6.9, 4.4 Hz, 1H), 2.08 – 2.00 (m, 1H), 1.74 (dt, $J = 9.1$, 5.2 Hz, 1H), 1.51 (ddd, $J = 8.3$, 6.9, 5.1 Hz, 1H).

**13C NMR** (126 MHz, CDCl$_3$) δ 199.2, 167.4, 140.7, 136.0, 133.3, 128.5, 125.9, 32.3, 24.3, 15.2.

**HRMS (ESI)** Calcd. for C$_{11}$H$_{11}$ClNO$_2$ ([M+H]$^+$): 224.0478, found: 224.0463.

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**1-deutero-3-phenylpropionaldehyde (4a, CAS Registry Number 29372-37-0):** Prepared on 1 mmol scale from hydrocinnamic acid (commercially available) via procedure B using NiCl$_2$(dme) and Ph$_2$SiD$_2$ (2.25 equiv.) at 40 °C for 24 h. Obtained in 87% yield as colorless oil (eluted with pentane/MTBE 99/1 to 95/5) (117 mg). Characterization data matched those previously reported.$^{27}$

**1H NMR** (500 MHz, CDCl$_3$) δ 7.33 – 7.27 (m, 2H), 7.24 – 7.18 (m, 3H), 2.97 (t, $J = 7.6$ Hz, 2H), 2.78 (t, $J = 7.6$ Hz, 2H).

**13C NMR** (126 MHz, CDCl$_3$) δ 201.4 (t, $J = 26.4$ Hz), 140.5, 128.7, 128.4, 126.4, 45.2 (t, $J = 3.9$ Hz), 28.2.

**HRMS (ESI)** Calcd. for C$_9$H$_8$DO ([M-H]$^-)$: 134.0715, found: 134.0738.

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**1-deutero-trans-4-(4-chlorophenyl)cyclohexanecarbaldehyde (4ac):** Prepared on 1 mmol scale from trans-4-(4-chlorophenyl)cyclohexane-1-carboxylic acid (commercially available) via procedure B using NiCl$_2$(dme) and Ph$_2$SiD$_2$ (2.25 equiv.) at 40 °C for 24 h. Obtained in 83% yield as white solid (purified in a similar manner to 2c) (185.2 mg). Characterization data matched the proteo version 2ac of the compound except for the missing aldehyde deuterium in the $^1$H NMR, the C–D coupling with the aldehyde and enolate carbon in the $^{13}$C NMR and one more mass unit in HRMS.

**1H NMR** (400 MHz, CDCl$_3$) δ 7.31 – 7.21 (m, 2H), 7.17 – 7.08 (m, 2H), 2.53 – 2.40 (m, 1H), 2.34 – 2.21 (m, 1H), 2.16 – 2.06 (m, 2H), 2.05 – 1.95 (m, 2H), 1.55 – 1.32 (m, 4H).

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\[^{13}\text{C}\ \text{NMR}\ (101\ \text{MHz},\ \text{CDCl}_3)\ \delta\ 204.0\ (t,\ J = 26.1\ \text{Hz}),\ 145.2,\ 131.8,\ 128.6,\ 128.2,\ 49.7\ (t,\ J = 3.3\ \text{Hz}),\ 43.3,\ 33.0,\ 26.3.\]

\textbf{HRMS (ESI)}\ \text{Calcd. for C}_{13}\text{H}_{13}\text{ClDO} ([M-H]^{-}): 222.0795,\ \text{found: 222.0795.}

1-deutero-5-(2,5-dimethylphenoxy)-2,2-dimethylpentanal (4w): Prepared on 1 mmol scale from Gemfibrozil (commercially available) via procedure B using NiCl\textsubscript{2}(dme) and Ph\textsubscript{2}SiD\textsubscript{2} (2.25 equiv.) at 60 °C for 16 h. Obtained in 86% yield as colorless oil (purified in a similar manner to 2c) (202 mg). Characterization data matched the proteo version of the compound 2w except for the missing aldehyde deuterium in the \[^1\text{H}\ \text{NMR},\ the\ C–D\ coupling\ with\ the\ aldehyde\ and\ enolate\ carbon\ in\ the\ \[^{13}\text{C}\ \text{NMR}\ and\ one\ more\ mass\ unit\ in\ HRMS.\]

\[^1\text{H}\ \text{NMR}\ (500\ \text{MHz},\ \text{CDCl}_3)\ \delta\ 7.02\ (d,\ J = 7.5\ \text{Hz},\ 1\text{H}),\ 6.68\ (d,\ J = 7.5\ \text{Hz},\ 1\text{H}),\ 6.62\ (s,\ 1\text{H}),\ 3.94\ (t,\ J = 5.8\ \text{Hz},\ 2\text{H}),\ 2.32\ (s,\ 3\text{H}),\ 2.19\ (s,\ 3\text{H}),\ 1.79 – 1.66\ (m,\ 4\text{H}),\ 1.12\ (s,\ 6\text{H}).\]

\[^{13}\text{C}\ \text{NMR}\ (126\ \text{MHz},\ \text{CDCl}_3)\ \delta\ 205.9\ (t,\ J = 25.9\ \text{Hz}),\ 157.0,\ 136.6,\ 130.4,\ 123.7,\ 120.9,\ 112.1,\ 67.9,\ 45.5\ (t,\ J = 3.2\ \text{Hz}),\ 33.7,\ 24.6,\ 21.5,\ 21.4,\ 15.9.\]

\textbf{HRMS (ESI)}\ \text{Calcd. for C}_{15}\text{H}_{22}\text{DO} ([M+H]\textsuperscript{+}): 236.1760,\ \text{found: 236.1762.}

4-(3-phenylpropyl)morpholine (5a, CAS Registry Number 25262-57-1): Prepared on 1 mmol scale from hydrocinnamic acid (commercially available) via procedure B using NiCl\textsubscript{2}(dme) and Ph\textsubscript{2}SiH\textsubscript{2} (2.25 equiv.) at 40 °C for 24 h. The crude reaction mixture was used directly in the subsequent step after being cooled to room temperature.

To the crude aldehyde formation reaction mixture was added morpholine (2 equiv.) and AcOH (1 equiv.) and the reaction stirred for one hour. Then sodium triacetoxyborohydride (3 equiv.) was added and the reaction stirred overnight. The reaction was worked up with 50 ml sat. NaHCO\textsubscript{3} solution diluted by a factor of 2. Then 20 ml of 2N HCl was added. The aqueous layer was the basified with NaOH to pH 9 and then extracted 3x with 50 ml DCM. The organic layer was washed with brine, dried over MgSO\textsubscript{4} and concentrated in vacuo. The crude was purified by column chromatography (MTBE in pentane 0 to 50%) to furnish the amine product in 80% yield as slightly yellow (164 mg). Characterization data matched those previously reported.\textsuperscript{28}

Procedure was unoptimized.

$^{1}$H NMR (500 MHz, CDCl$_3$) δ 7.31 – 7.24 (m, 2H), 7.21 – 7.15 (m, 3H), 3.79 – 3.62 (m, 4H), 2.68 – 2.61 (m, 2H), 2.51 – 2.39 (m, 4H), 2.39 – 2.34 (m, 2H), 1.83 (p, $J = 7.7$ Hz, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 142.2, 128.5, 128.5, 125.9, 67.1, 58.5, 53.8, 33.7, 28.4.

HRMS (ESI) Calcd. for C$_{13}$H$_{20}$NO ([M+H]$^+$): 206.1545, found: 206.1538.

2-(benzylamino)-4-phenylbutanenitrile (5b, CAS Registry Number 919789-43-8): Prepared on 1 mmol scale from hydrocinnamic acid (commercially available) via procedure B using NiCl$_2$(dme) and Ph$_2$SiH$_2$ (2.25 equiv.) at 40 °C for 24 h. The crude reaction mixture was used directly in the subsequent step after being cooled to room temperature.

Benzylamine (1 equiv.) was added and the mixture was stirred for one hour. Then TMSCN (1 equiv.) was added and the reaction turned orange. The mixture was stirred for 16 h at room temperature, at which point it was pale-pink. To the mixture was added ~ 0.5g silica gel and the mixture was directly dry loaded for column chromatography. Product was obtained as pale yellow oil in 59% yield (148 mg) after elution with MTBE/pentane 0/100 to 10/90). Characterization data matched those previously reported.$^{29}$ Procedure was unoptimized.

$^{1}$H NMR (500 MHz, CDCl$_3$) δ 7.30 – 7.34 (m, 4H), 7.33 – 7.28 (m, 3H), 7.25 – 7.21 (m, 1H), 7.21 – 7.16 (m, 2H), 4.08 (d, $J = 12.8$ Hz, 1H), 3.82 (d, $J = 12.8$ Hz, 1H), 3.49 (t, $J = 7.2$ Hz, 1H), 2.93 – 2.81 (m, 2H), 2.15 – 2.08 (m, 2H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ 140.1, 138.4, 128.8, 128.7, 128.6, 127.8, 126.6, 120.2, 51.8, 49.1, 35.2, 31.9.

HRMS (ESI) Calcd. for C$_{17}$H$_{19}$N$_2$ ([M+H]$^+$): 251.1548, found: 251.1546.

1,3-diphenylpropan-1-ol (5c, CAS Registry Number 14097-24-6): Prepared on 1 mmol scale from hydrocinnamic acid (commercially available) via procedure B using NiCl$_2$(dme) and Ph$_2$SiH$_2$ (2.25 equiv.) at 40 °C for 24 h. For this one-pot reaction, the reduction was set-up in THF instead of EtOAc. The crude reaction mixture was used directly in the subsequent step after being cooled to room temperature.

The crude aldehyde reaction mixture was cooled to 0 °C, then PhMgBr (1 equiv. added as 1M THF solution) was added dropwise. The reaction was allowed to warm to room temperature and

stirred for 16 hours. The mixture was cooled to 0 °C and 2 ml of water was added dropwise. The mixture was concentrated on rotatory evaporator, then diluted with 50 ml DCM. The DCM was washed with sat. NaHCO₃ aq. solution, then brine. The DCM was then dried over MgSO₄ and concentrated in vacuo. The product was obtained in 63% yield (134 mg) as a colorless oil after column chromatography (MTBE/pentane 0/100 to 10/90). Characterization data matched those previously reported.³⁰ Procedure was unoptimized.

**H NMR** (500 MHz, CDCl₃) δ 7.41 – 7.33 (m, 4H), 7.33 – 7.27 (m, 3H), 7.24 – 7.16 (m, 3H), 4.70 (dd, J = 7.8, 5.4 Hz, 1H), 2.84 – 2.73 (m, 1H), 2.73 – 2.64 (m, 1H), 2.20 – 2.10 (m, 1H), 2.10 – 2.00 (m, 1H), 1.86 (s, 1H).

**C NMR** (126 MHz, CDCl₃) δ 144.7, 141.9, 128.7, 128.6, 128.5, 127.8, 126.1, 126.0, 74.0, 40.6, 32.2.

**HRMS (ESI)** Calcd. for C₁₅H₁₅O ([M-H]⁺): 211.1123, found: 211.1136.

hydrazone of 1a
Hydrazone of 2g
hydrazone of 2h

S44
hydrazone of 2i
hydrazone of 2m

Me
N
H
Me

Me
N
H
Me

S49
hydrazone of 2s

hydrazone of 2s
hydrazone of 2u

S57