Supplementary Materials: Mg-catalyzed Oppenauer Oxidation - Application to the flow synthesis of a natural pheromone

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1. General procedures

General Procedure A

To a solution of alcohol **3** (1 equiv; 0.63 mmol) in deuterated benzene (0.4 mL) was added Mg(O*t*Bu)$_2$ (0.3 equiv). After 5 min at room temperature, 2.0 equiv. of trimethylacetaldehyde were added. The mixture was heated at 80°C for an hour and then cooled to r.t.

General Procedure B

To a solution of alcohol **3** (1 equiv; 0.63 mmol) in toluene (0.4 mL) was added Mg(O*t*Bu)$_2$ (0.3 equiv). After 5 min at room temperature, 2.0 equiv of trimethylacetaldehyde were added. The mixture was heated at 80°C for an hour. The mixture was then cooled to r.t., and brine was added. The aqueous phase was extracted with diethylether, and the combined organic fractions was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (PE/EtOAc).

Flow Procedure

The flow system is composed of a Vapourtec E-series (V-3 perilstatic pumps), a 4.54 mL 1/16" PTFE tubing (0.81mm I.D.) heated at 60°C followed by a 1 mL 1/16" PTFE tubing (0.81mm I.D.) at r.t., was washed with anhydrous THF. Flow rates were set at 329 µL/min for 2-methylpentanal, 1.17 mL/min for *n*BuMgCl (2.04 M in THF) and 1.5 mL/min for HCl (10% in H_2O). 2-methylpentanal and *n*BuMgCl feeds were mixed using a S-Type LFT glass micromixer, at 60°C. Reaction mixture was collected over 8h30. The organic phase was recovered, washed with 200 mL of brine and dried over sodium sulfate. After filtration and concentration under reduced pressure, the desired 1/9 mixture of ferrugineone and ferrugineol was obtained as yellow oil (173g, 91% yield).

2. NMR Data:

Ferrugineol (mixture of 2 diastereoisomers) [152045-16-4]:

^{1}H NMR (300MHz, $CDCl_3$) δ 0.77-1.00 (m, 9H), 1.02 1.73 (m, 11H), 3.36-3.56 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 76.2, 75.3, 38.7, 38.0, 35.7, 34.3, 34.3, 33.2, 28.6, 28.5, 22.9, 22.9, 20.6, 20.5, 15.3, 14.5, 14.5, 14.2, 14.0, 13.6. GC/MS (EI): tr=5.49 min; *m*/*z*=157 (MH+,1%), 114 (2%), 101 (12%), 87 (47%), 69 (100 %), 55 (18%).

Ferrugineone [152203-43-5]: ^{1}H NMR (300MHz, $CDCl_3$) δ 0.93 (d, J = 6.9 Hz, 3H), 0.94 (d, J = 6.9 Hz, 3H), 1.09 (d, J= 6.9 Hz, 3H), 1.21-1.42 (m, 6H), 1.51-1.71 (m, 4H), 2.44-2.49 (m, 2H), 2.51-2.62 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 215.2, 46.2, 41.0, 35.5, 35.3, 25.9, 22.6, 20.2, 16.7, 16.5. GC/MS (EI): tr=5.14 min; *m*/*z*=156 (M+, 3%), 127 (3%), 144 (34%), 85 (100%), 71 (72 %), 57 (88%).

3. NMR study

The ^{1}H NMRs of Ferrugineol and Ferrugineone are reported in respectively Figure S1 and Figure S2.

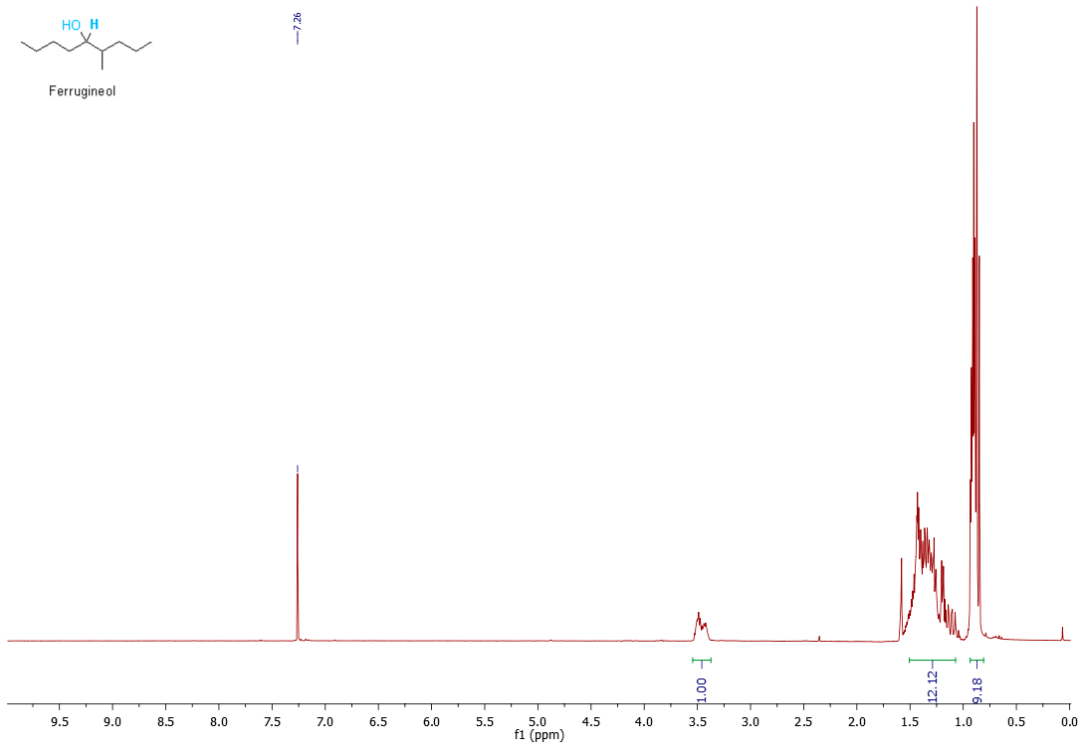

Figure S1. ^{1}H NMR of pure Ferrugineol (**1**).

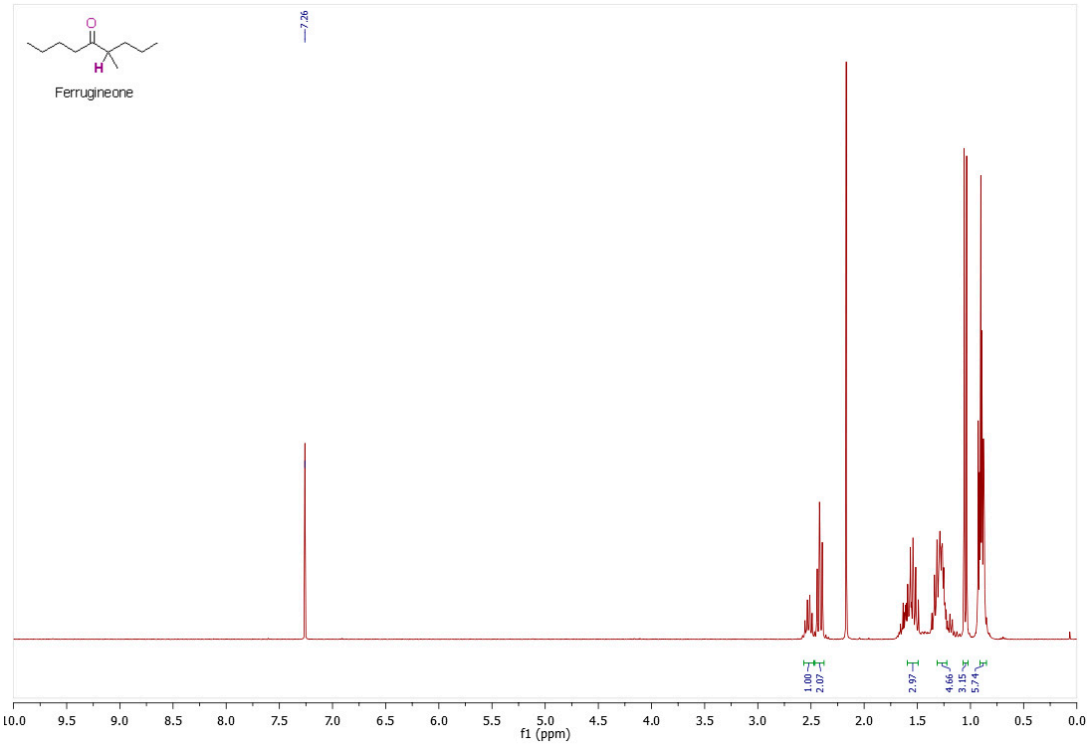

Figure S2. ^{1}H NMR of pure Ferrugineone (**2**).

The ^{1}H NMRs referencing to Table 1 are reported from Figure S3 to Figure S11. Only protons for NMR conversion calculation were integrated for a better understanding.

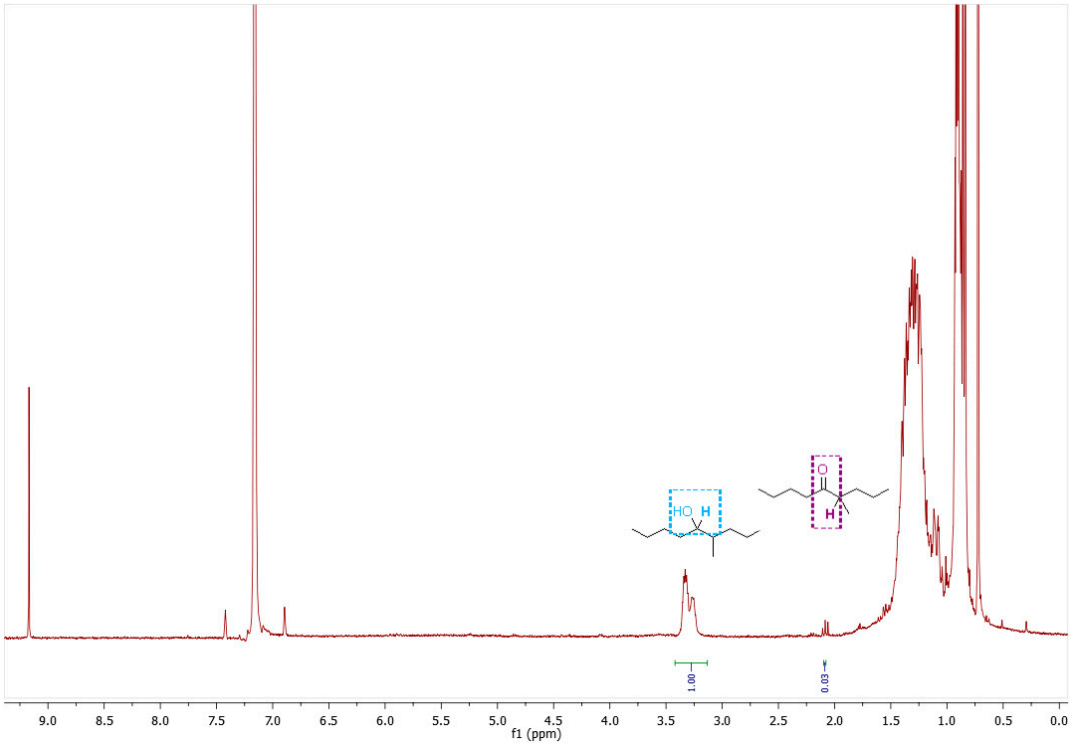

Figure S3. ^{1}H NMR of Table 1 Entry 1. $MgCl_2$ (0.4 equiv), 100°C, 3 hours.

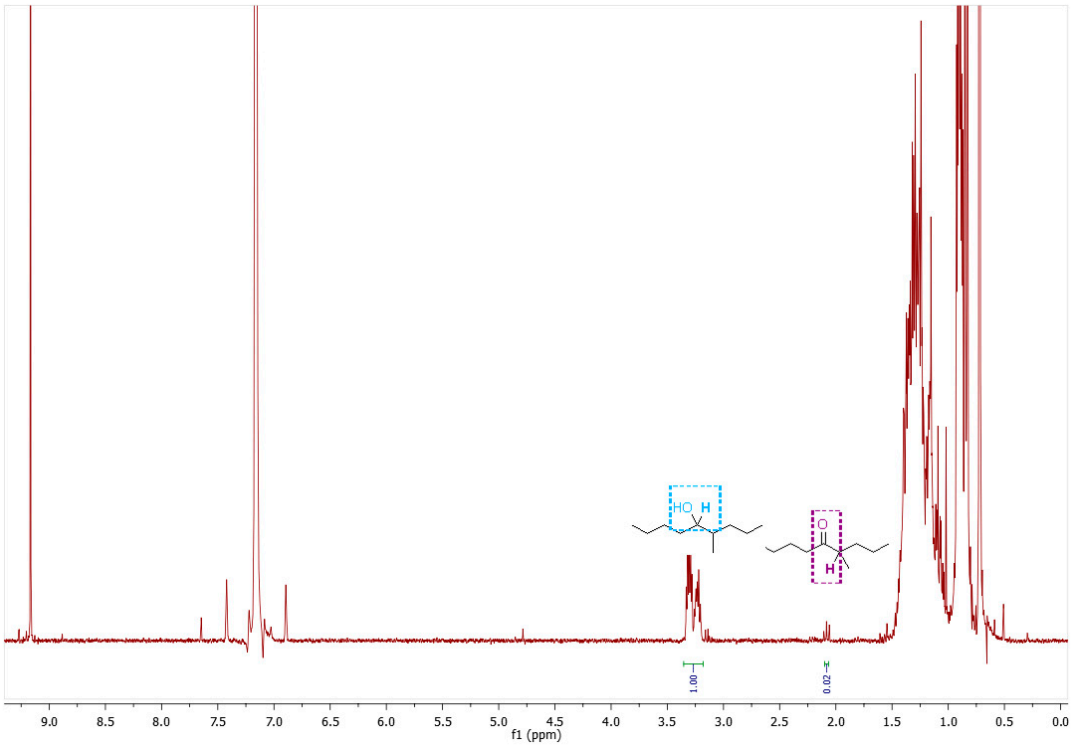

Figure S4. ^{1}H NMR of Table 1 Entry 2. $Mg(OH)_2$ (0.4 equiv), 100°C, 3 hours.

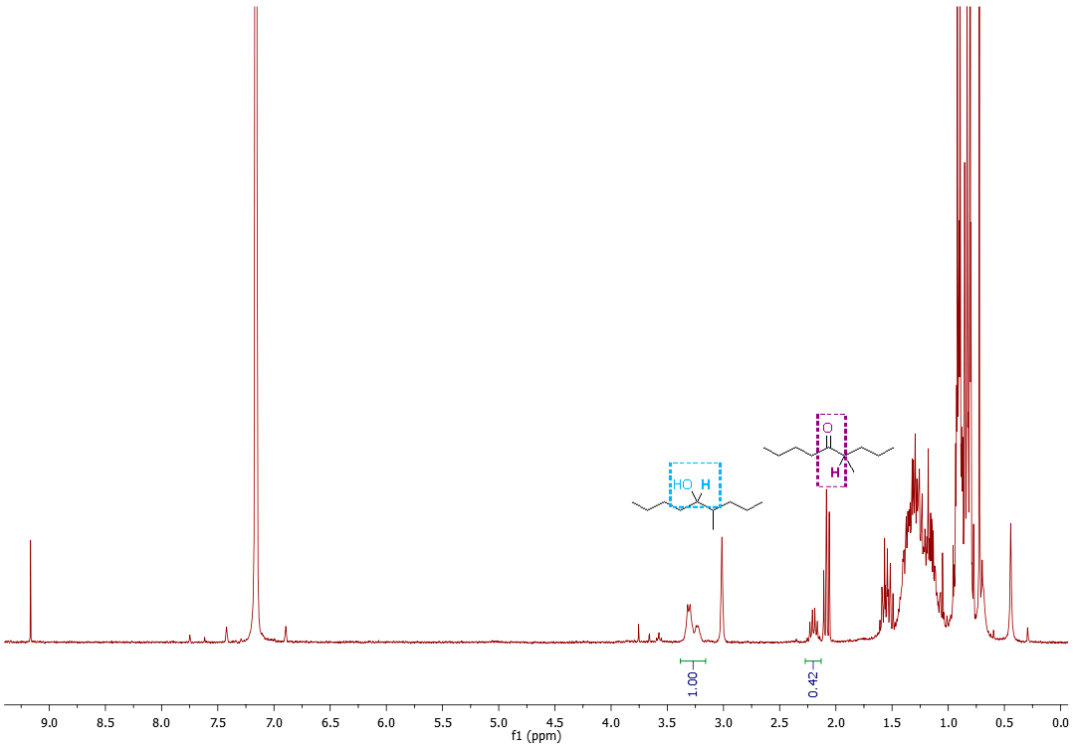

Figure S5. ^{1}H NMR of Table 1 Entry 3. $Mg(OEt)_2$ (0.4 equiv), 100°C, 3 hours.

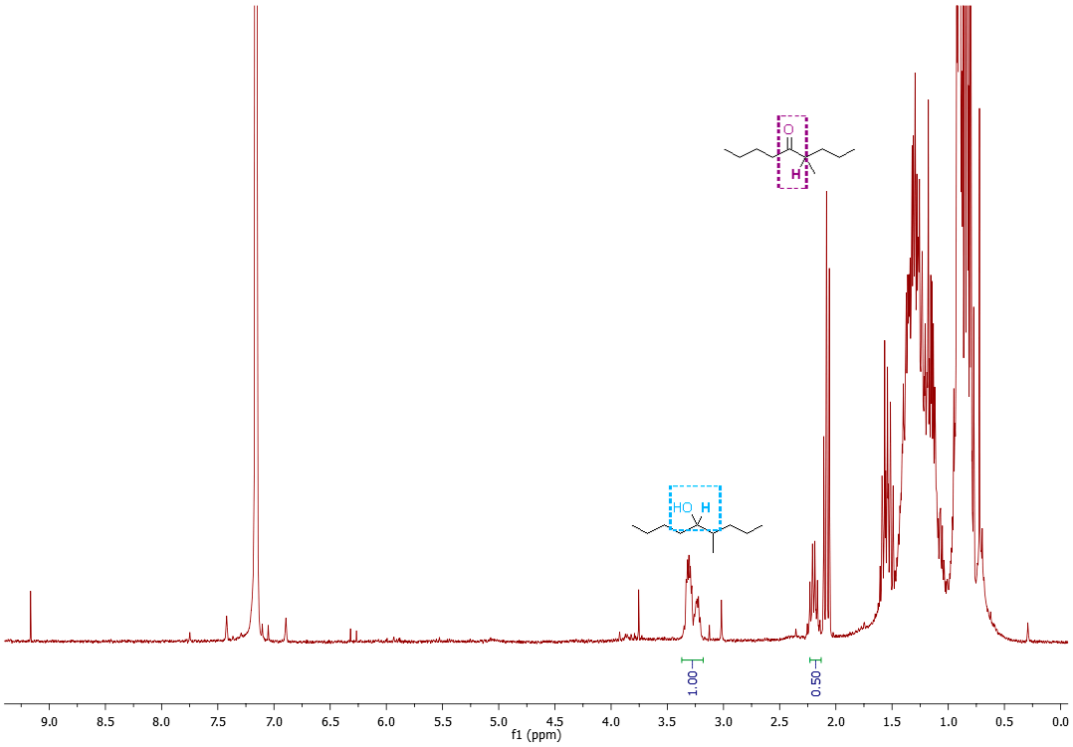

Figure S6. ^{1}H NMR of Table 1 Entry 4. $Mg(OEt)_2$ (0.4 equiv), 100°C, 6 hours.

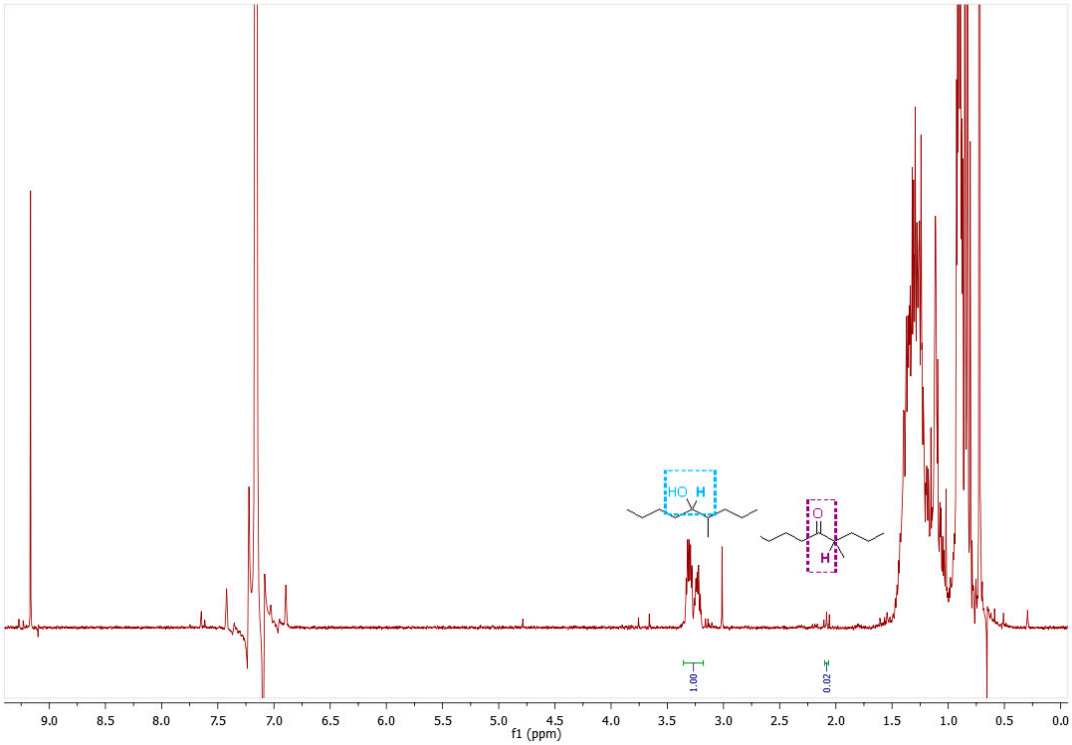

Figure S7. ^{1}H NMR of Table 1 Entry 5. MgO (0.4 equiv), 100°C, 3 hours.

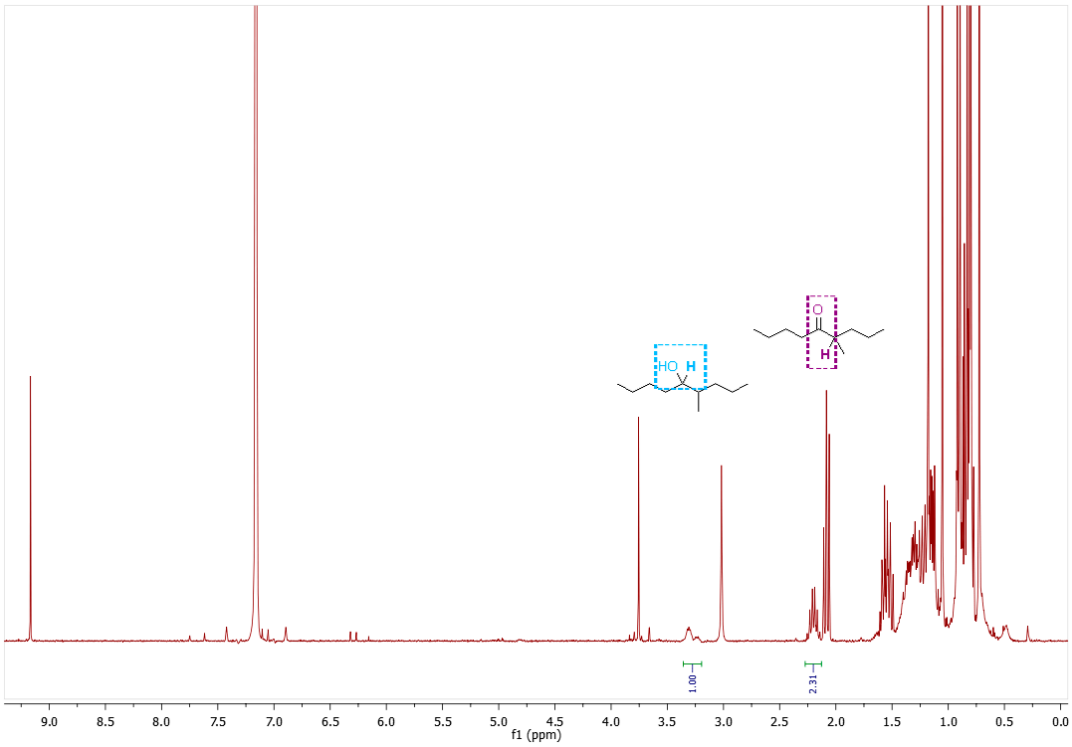

Figure S8. ^{1}H NMR of Table 1 Entry 6. Mg(O*t*Bu)$_2$ (0.3 equiv), 110°C, 1 hour.

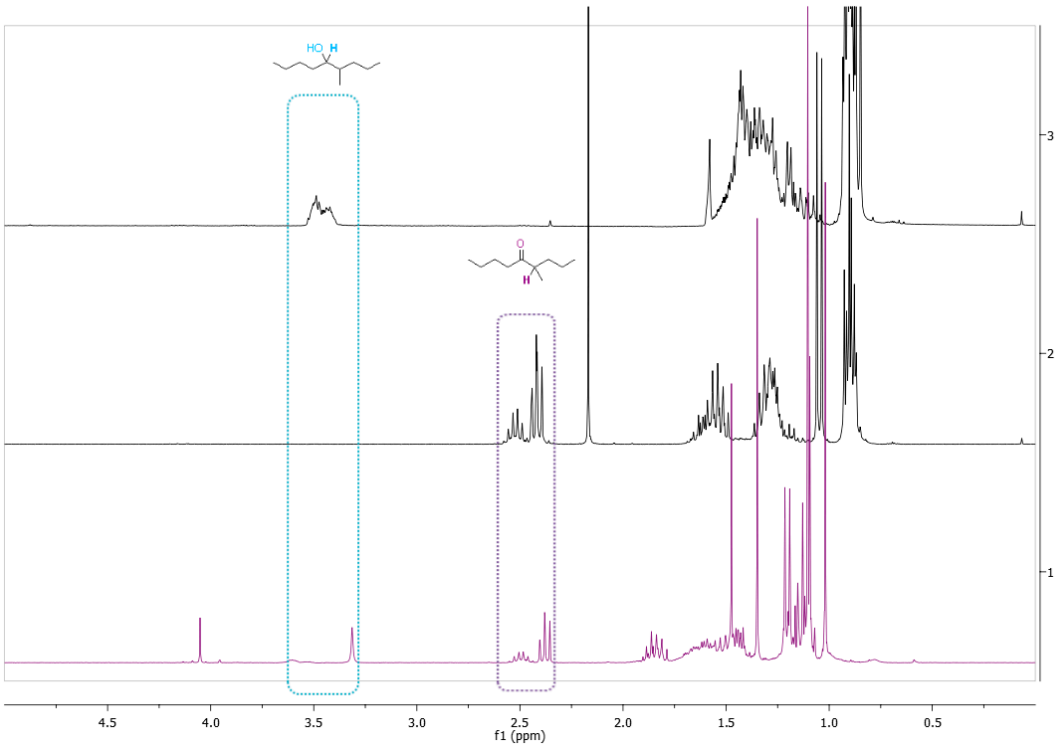

Figure S9. ^{1}H NMR of Table 1 Entry 6 – Zoom from 5 ppm to 0 ppm – Protons attribution.

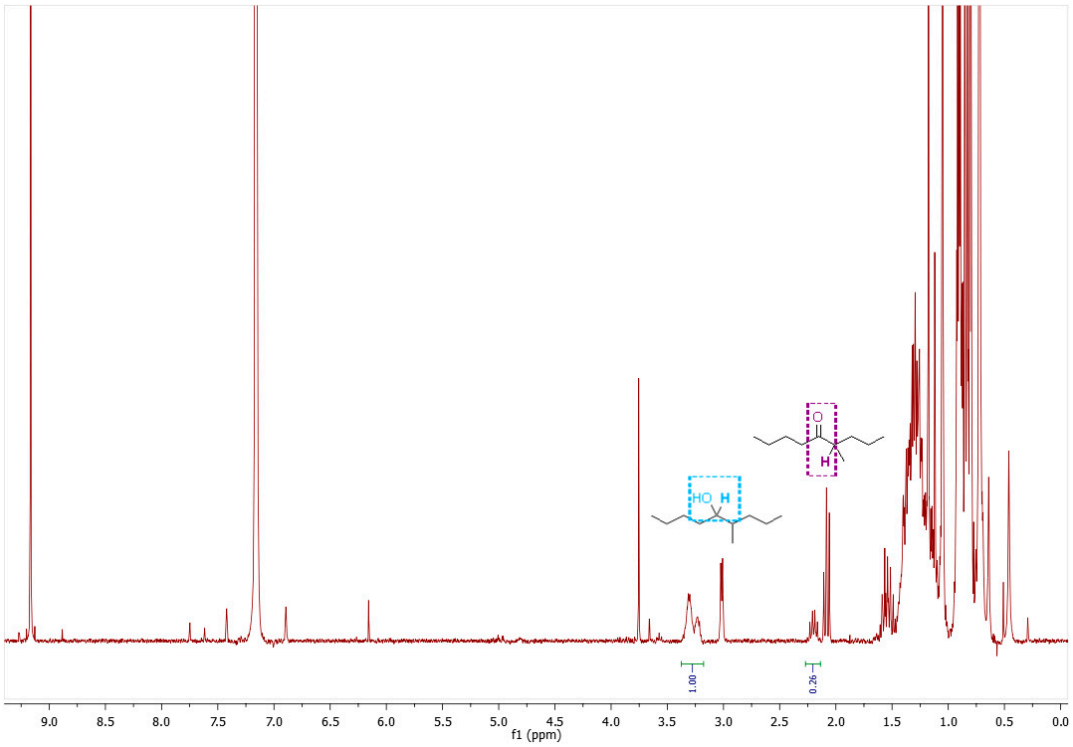

Figure S10. ^{1}H NMR of Table 1 Entry 7. Mg(O*t*Bu)$_2$ (0.3 equiv), 60°C, 1 hour.

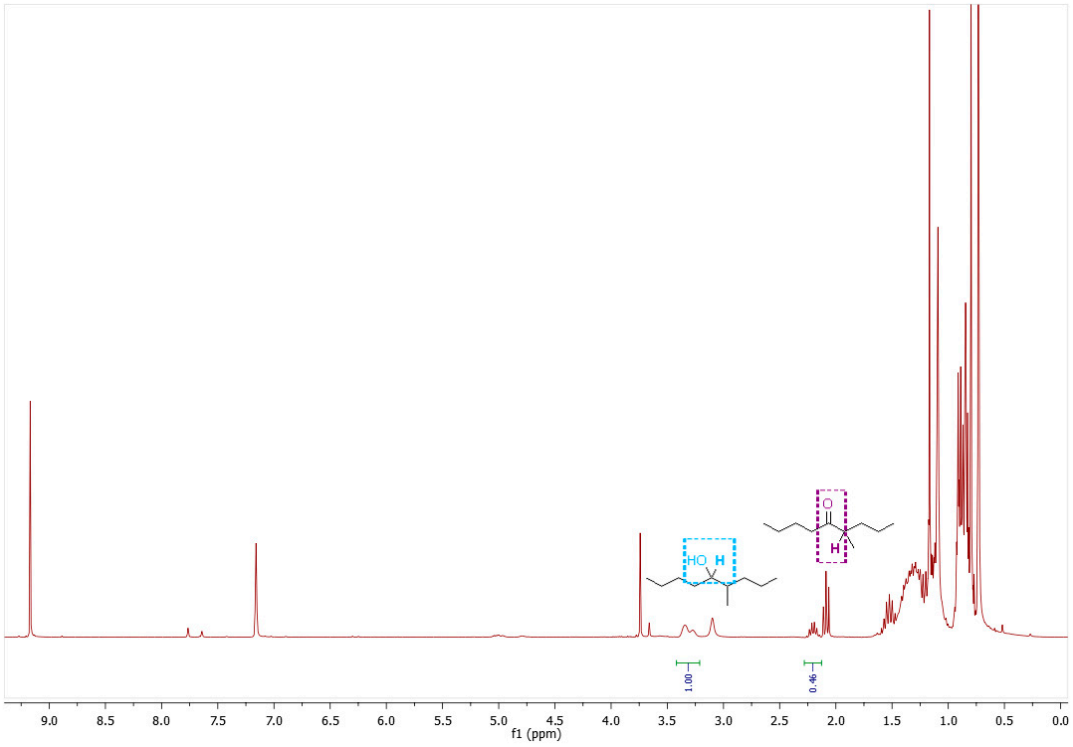

Figure S11. ^{1}H NMR of Table 1 Entry 8. Mg(O*t*Bu)$_2$ (0.3 equiv), 60°C, 3 hours.

The ^{1}H NMRs of reactions to get **(4j)** and **(4l)** from Figure 1 of the paper are reported on Figure S12 and Figure S13 to show how the NMR conversion was calculated on others reactions than ferrugineol/ferrugineone.

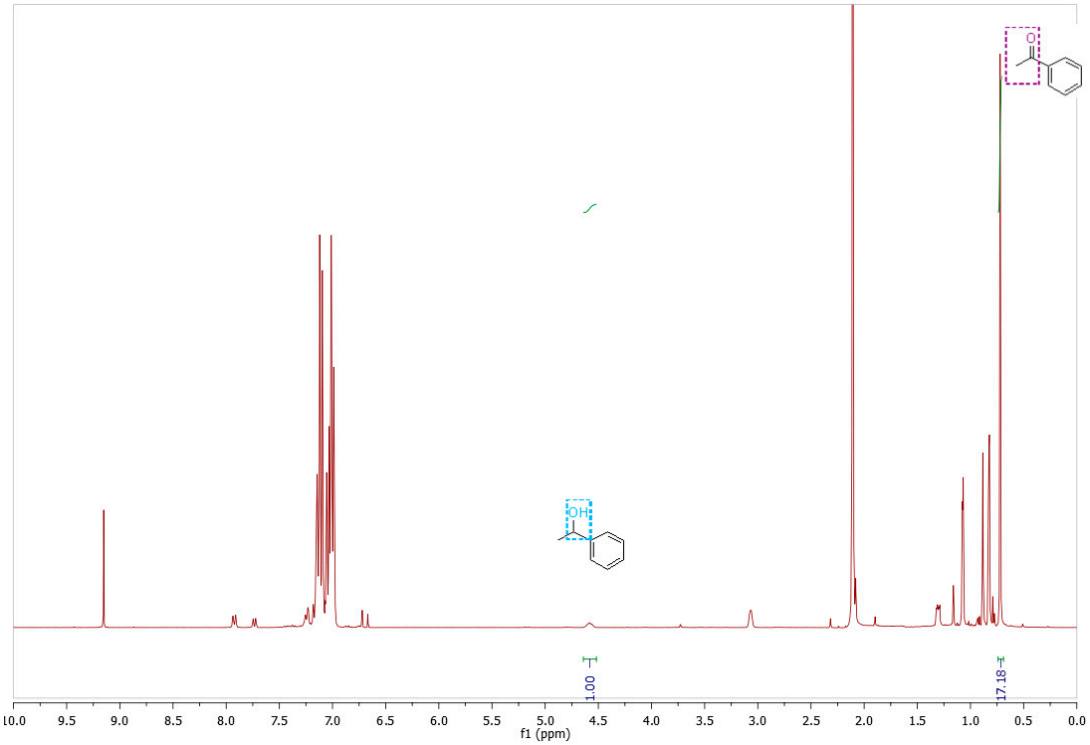

Figure S12. ^{1}H NMR of **(4j).** Mg(O*t*Bu)$_2$ (0.3 equiv), 60°C, 1 hour.

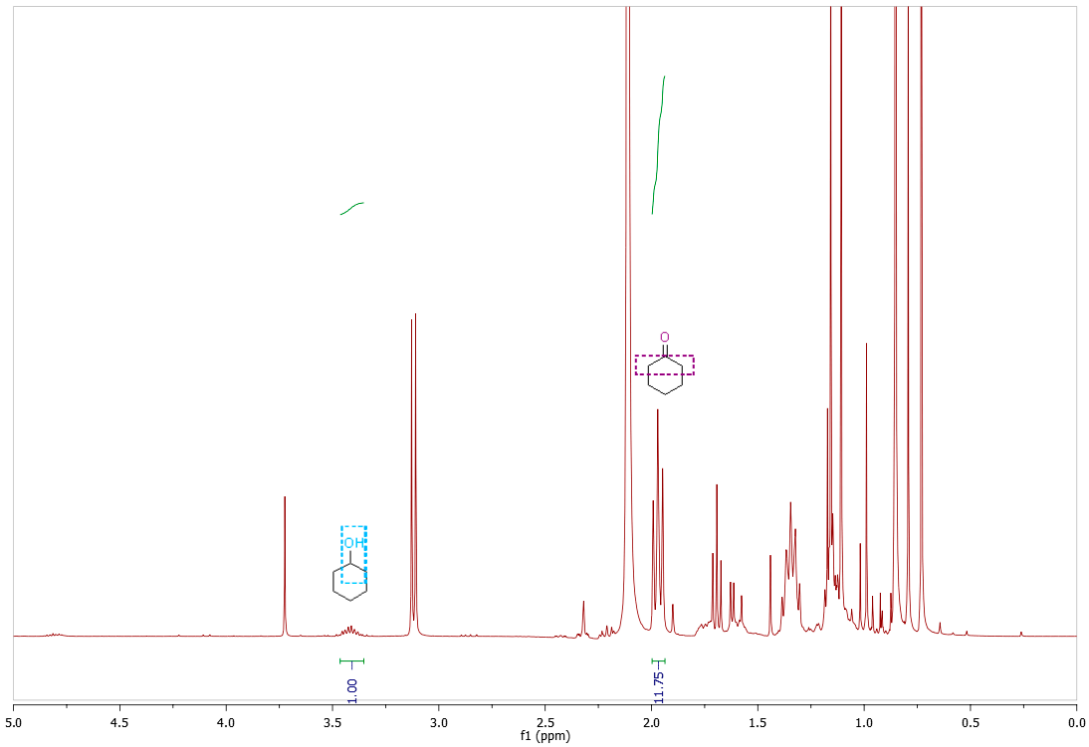

Figure S13. ^{1}H NMR of **(4l).** Mg(O*t*Bu)$_2$ (0.3 equiv), 60°C, 1 hour.