Electronic supporting information for

"'One-Pot' Hammett Plots: A General Method for the Rapid Acquisition of Relative Rate Data"

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General synthetic procedures

Reagents for syntheses of the ionic liquid precursor, 1-butyl-3-methylimidazolium chloride, were purchased from Sigma-Aldrich and distilled *immediately* before use. Lithium bis(trifluoromethylsulfonyl)imide used in metathesis reactions to give the desired ionic liquid, 1-butyl-3-methylimidazolium bis(trifluoromethanesulfonyl)imide, was purchased from IoLiTec Ionic Liquids Technologies GmbH.

All other reagents used in synthesis were commercially available, purchased from either Sigma Aldrich or Alfa Aesar and used without further purifications. Literature methods were used to synthesise kinetic precursors using starting materials sourced from the mentioned manufacturers.

Organic solvents used in syntheses were either used as received from Ajax Finechem or collected from a Pure Solv MD Solvent Purification System. All organic solvents used in kinetics experiments were either collected from the aforementioned solvent purification system or purified using methods available in the literature.[1] Milli-Q™ water, where mentioned, was collected from a Millipore Milli-Q™ Academic System with a resistivity of 18.2 Ω·cm.

Unless stated otherwise in the text, reduced pressure used in all operations was *ca*. 210 Torr.

Where dry NMR tubes or volumetric equipment were required, drying was achieved by cycling between reduced pressure (< 0.5 Torr) and dry nitrogen three times before the glassware was left under reduced pressure for at least two hours before use. It should be noted that neither the NMR tubes nor the volumetric equipment were subjected to heating.

^{1}H and ^{13}C NMR characterisation was performed on a Bruker DPX 300 MHz spectrometer (^{1}H, 300 MHz; ^{13}C, 75.5 MHz) equipped with an auto-sampler, a Bruker Avance III 400 MHz spectrometer (^{1}H, 400 MHz; ^{13}C, 101 MHz) or a Bruker Avance III 500 MHz spectrometer (^{1}H, 500 MHz; ^{13}C, 126 MHz). All chemical shifts are reported relative to tetramethylsilane. Multiplicities are reported as either singlet (s), doublet (d), triplet (t) or multiplet (m).

1-Butyl-3-methylimidazolium *bis*(trifluoromethylsulfonyl)imide was synthesised from the corresponding chloride[2] according to a modified literature procedure,[3] in which Milli-Q water was used as the medium for salt metathesis instead of dichloromethane.[4] The methoxy benzyl bromide **1a** was prepared from the corresponding alchol, while the bromo derivative **1e** was pre-

pared in a fashion similar to that reported in the literature,[5] where bromination was carried out in acetonitrile by irradiation under sunlight for two days. The carboxymethyl derivative **1f** was prepared from toluic acid *via* methyl toluate through modification of literature procedures,[6,7] with bromination carried out as described for **1e**. The remaining benzyl bromides **1b-d,g** were commercially available as were the acetophenones **3a-d**. Samples of the alcohols **4a-d** were prepared through reduction of the corresponding acetophenones **3a-d** using sodium borohydride (Scheme 2). *tris*(2,4-Pentanedionato)chromium(III) was prepared using a literature method.[8] All compounds prepared had physical and spectral characteristics consistent with those previously reported.

General procedure for kinetic analysis

^{1}H NMR and ^{13}C NMR competition experiments were carried out on a Bruker Avance III 500 spectrometer and a Bruker Avance III 600 MHz spectrometer, respectively. Inversion recover experiments were carried out to determine the longitudinal relaxation times (T_1) for the signals of interest and all analyses of competition experiments used delays such that signal recovery was greater than 99% as determined by inversion recovery experiments.

High-performance liquid chromatography was performed on a Shimadzu Prominence HPLC system using a Restek Pinnacle DB C_{18} column (150 mm x 4.6 mm). All experiments were carried out using an isocratic mobile phase (2:5 acetonitrile:water) at a total flow rate of 0.7 mL·s^{-1} with an injection volume of 20 μL.

Water baths used in the competition experiments were calibrated to ± 0.1 K using a thermocouple fixed in a 5 mm NMR tube containing ethanol.

Competition experiments for the Menschutkin reaction between benzyl bromides and pyridine

Signal resolution in ^{1}H NMR spectroscopy of the signals due to the benzylic protons on either the starting materials **1a-g** or the products **2a-g** was initially tested by stepwise addition of each of the benzyl bromides **1a-g** to acetonitrile-d_3 to determine the feasibility of using ^{1}H NMR spectroscopy (500 MHz) in these experiments. Similarly, signal resolution was determined for the products **2a-g** in the presence of excess pyridine. Considerable signal overlap between benzyl bromides **1a** and **1d** and between benzyl bromides **1c** and **1e** was observed. Substantial signal overlap was also observed between products **2b** and **2c** as well as between products **2d** and **2e**. No substantial signal overlap was observed between all other signals such that confident data deconvolution could be carried out.

Benzyl bromides **1b and 1d-g** (*ca*. 140 μmol) were initially added to a 10 mL volumetric flask followed by the addition of either the ionic liquid, 1-butyl-3-methylimidazolium bis(trifluoromethanesulfonyl)imide or acetonitrile. A portion of the solution (1 mL) containing the benzyl bromides **1b and 1d-g** was set aside. Similarly, benzyl bromide **1c** (*ca*. 130 μmol) was then added to the solution containing benzyl bromides **1b and 1d-g** and a portion of that solution (1 mL) was set aside. Finally, benzyl bromide **1a** (*ca*. 110 μmol) was added to the mixtures containing benzyl bromides **1b-g** and, once again, a portion of the solution (1 mL) was set aside. To a portion of each of the standard solutions (250 μL), acetonitrile-d_3 (250 μL) was added for the determination of the relative ratios of the starting materials using ^{1}H NMR spectroscopy.

The solutions for initiating the competition experiments were prepared by mixing pyridine (*ca*. 190 μmol) with either acetonitrile or the ionic liquid. Each competition experiment was carried out inside a 5 mL NMR tube by mixing an equal volume (250 μL) of the solution containing all seven benzyl bromides **1a-g** and the solution of pyridine (250 μL), in either acetonitrile or [bmim][NCF_3SO_2], prepared as described above and incubated in a water bath calibrated to 300.7 K for 12 hours. ^{1}H NMR spectroscopy was used to determine the distribution of starting materials **1** and products **2** in the reaction mixtures. Integrations for signals where substantial overlapping with other signals exists were calculated from algebraic expressions detailed in Appendix S2 and relative rate constants were calculated as described in the main text and in Appendix S1.

Table S1. Relative ^{1}H NMR integrals determined for the competitive Menschutkin reactions between the benzyl bromides **1a-g** and pyridine carried out in acetonitrile at 300.7 K. Values that are italicised indicate that they were evaluated using algebraic expressions detailed in Appendix S1.

	Relative integration		
Species	**Iteration 1**	**Iteration 2**	**Iteration 3**
Benzyl bromide **1a**	48.9	47.7	54.1
Benzyl bromide **1b**	110.2	100.5	107.9
Benzyl bromide **1c**	128.3	129.8	130.9
Benzyl bromide **1d**	135.4	130.6	128.9
Benzyl bromide **1e**	154.7	147.0	148.7
Benzyl bromide **1f**	159.2	153.5	156.7
Benzyl bromide **1g**	166.6	162.3	165.0
Pyridinium bromide **2a**	152.6	158.6	150.8
Pyridinium bromide **2b**	88.7	101.7	92.5
Pyridinium bromide **2c**	72.9	66.5	68.3
Pyridinium bromide **2d**	59.6	65.3	66.5
Pyridinium bromide **2e**	44.9	52.9	49.7
Pyridinium bromide **2f**	42.7	45.6	43.7
Pyridinium bromide **2g**	35.3	38.0	36.3

Table S2. Relative rate constants determine from the relative integrations shown in Table S1 for the competitive Menschutkin reactions between the benzyl bromides **1a-g** and pyridine carried out in acetonitrile at 300.7 K.

	k / k_H		
Substituent	**Iteration 1**	**Iteration 2**	**Iteration 3**
p-OCH_3 (**1a**)	3.88	3.61	3.20
p-CH_3 (**1b**)	1.62	1.72	1.49
m-CH_3 (**1c**)	1.23	1.02	1.01
H (**1d**)	1.00	1.00	1.00
p-Br (**1e**)	0.70	0.76	0.69
p-CO_2CH_3 (**1f**)	0.65	0.64	0.59
p-NO_2 (**1g**)	0.53	0.52	0.48

Table S3. Relative ^{1}H NMR integrals determined for the competitive Menschutkin reactions between the benzyl bromides **1a-g** and pyridine carried out in [bmim][NCF_3SO_2] at 300.7 K. Values that are italicised indicate that they were evaluated using algebraic expressions detailed in Appendix S1.

	Relative integration		
Species	**Iteration 1**	**Iteration 2**	**Iteration 3**
Benzyl bromide **1a**	*14.3*	*20.7*	*22.5*
Benzyl bromide **1b**	84.7	83.7	83.7
Benzyl bromide **1c**	*140.7*	*135.4*	*142.4*
Benzyl bromide **1d**	*138.3*	*133.0*	*130.4*
Benzyl bromide **1e**	*155.0*	*166.2*	*153.8*
Benzyl bromide **1f**	155.0	156.3	156.6
Benzyl bromide **1g**	169.0	170.8	170.0
Pyridinium bromide **2a**	175.9	173.8	171.2
Pyridinium bromide **2b**	*105.0*	*101.6*	*106.8*
Pyridinium bromide **2c**	*75.4*	*77.6*	*74.2*
Pyridinium bromide **2d**	*51.4*	*57.0*	*59.1*
Pyridinium bromide **2e**	*52.2*	*40.8*	*52.1*
Pyridinium bromide **2f**	44.1	42.9	44.6
Pyridinium bromide **2g**	30.1	27.7	30.0

Table S4. Relative rate constants determine from the relative integrations shown in Table S3 for the competitive Menschutkin reactions between the benzyl bromides **1a-g** and pyridine carried out in [bmim][NCF_3SO_2] at 300.7 K.

	k / k_H		
Substituent	**Iteration 1**	**Iteration 2**	**Iteration 3**
p-OCH_3 (**1a**)	6.99	6.28	6.63
p-CH_3 (**1b**)	2.36	2.23	2.36
m-CH_3 (**1c**)	1.28	1.27	1.19
H (**1d**)	1	1	1
p-Br (**1e**)	0.83	0.62	0.86
p-CO_2CH_3 (**1f**)	0.74	0.68	0.72
p-NO_2 (**1g**)	0.48	0.42	0.47

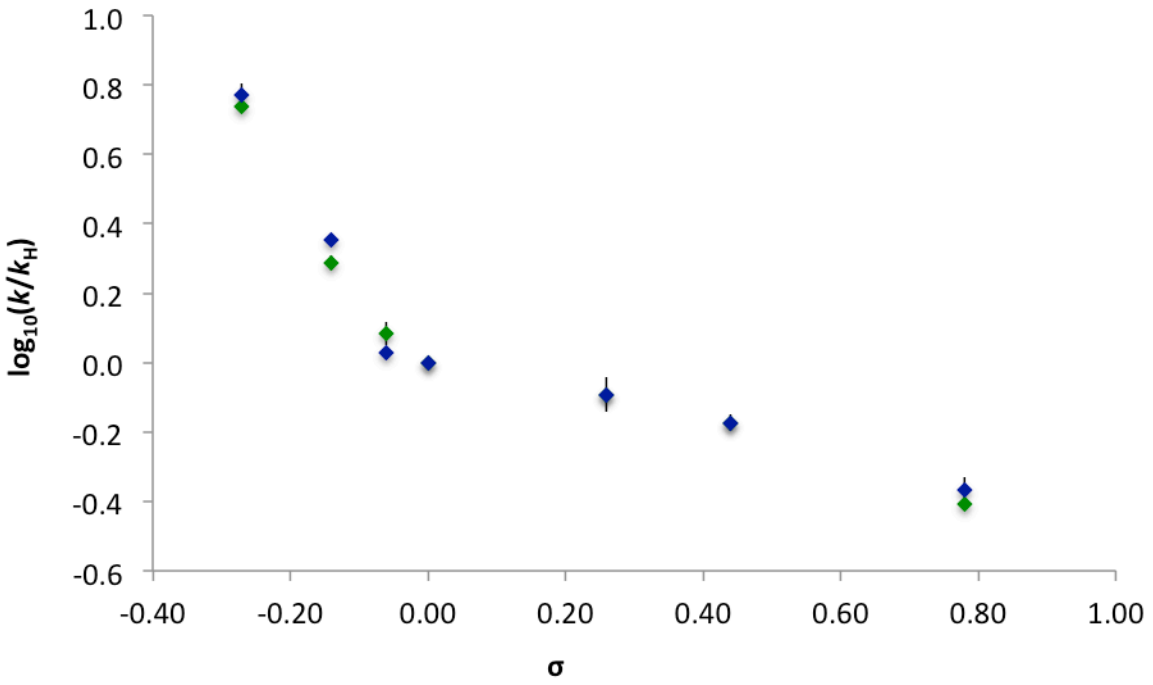

Figure S1. Hammett plots for the reaction between pyridine and benzyl bromides **1a-g** carried out in acetonitrile at 300.7 K constructed from the data described in this work (blue) and previously published results obtained from individual kinetic experiments (green).[9]

NMR Spectra for the competition experiments between benzyl bromide **1a-g** and pyridine

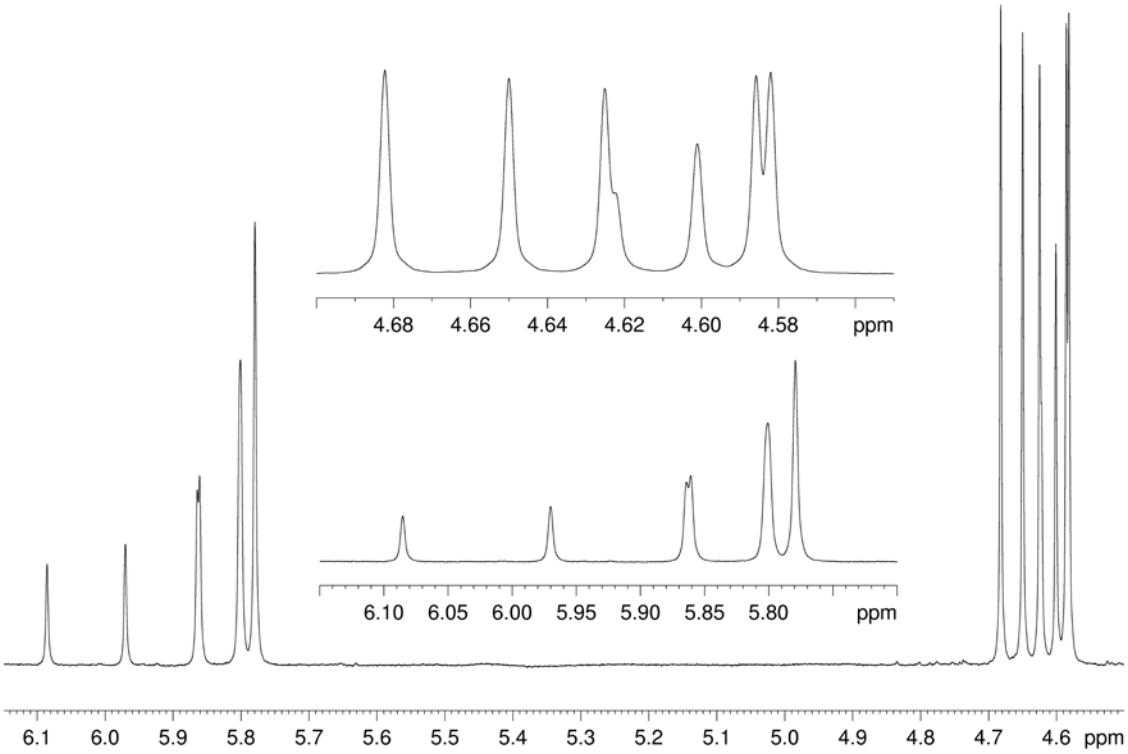

Figure S2. ^{1}H NMR spectrum of the competition experiment corresponding to iteration 1 of the reaction between benzyl bromide 1a-g and pyridine in acetonitrile at 300.7 K.

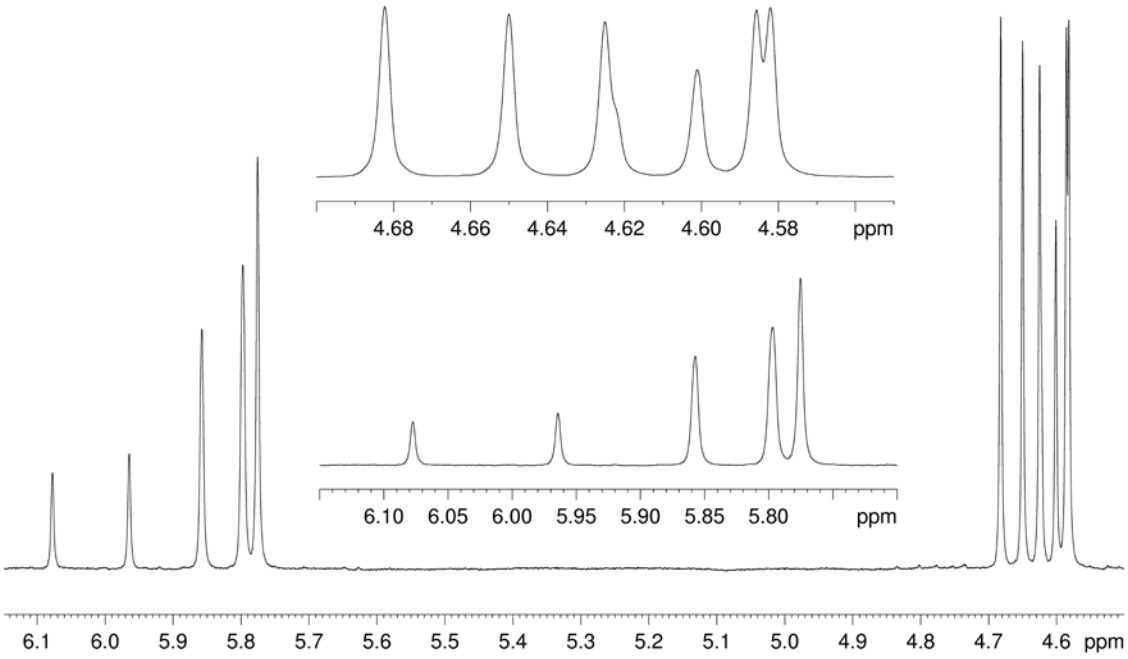

Figure S3. ^{1}H NMR spectrum of the competition experiment corresponding to iteration 2 of the reaction between benzyl bromide 1a-g and pyridine in acetonitrile at 300.7 K.

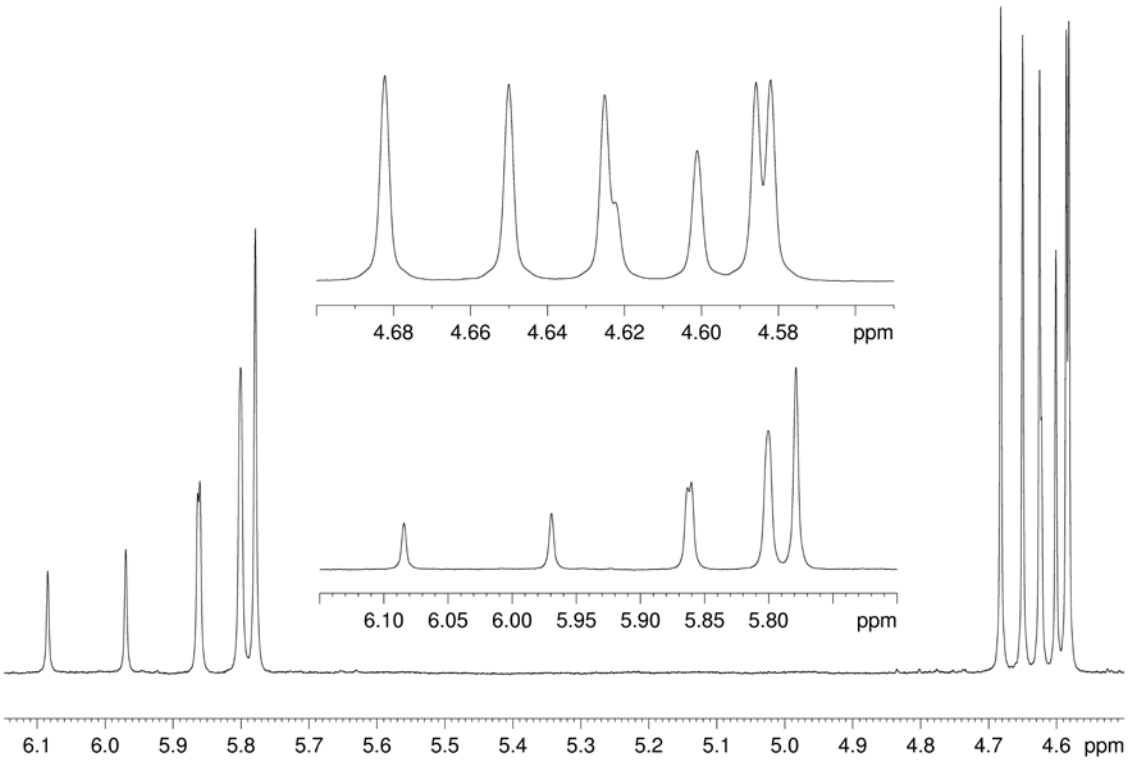

Figure S4. ^{1}H NMR spectrum of the competition experiment corresponding to iteration 3 of the reaction between benzyl bromide 1a-g and pyridine in acetonitrile at 300.7 K.

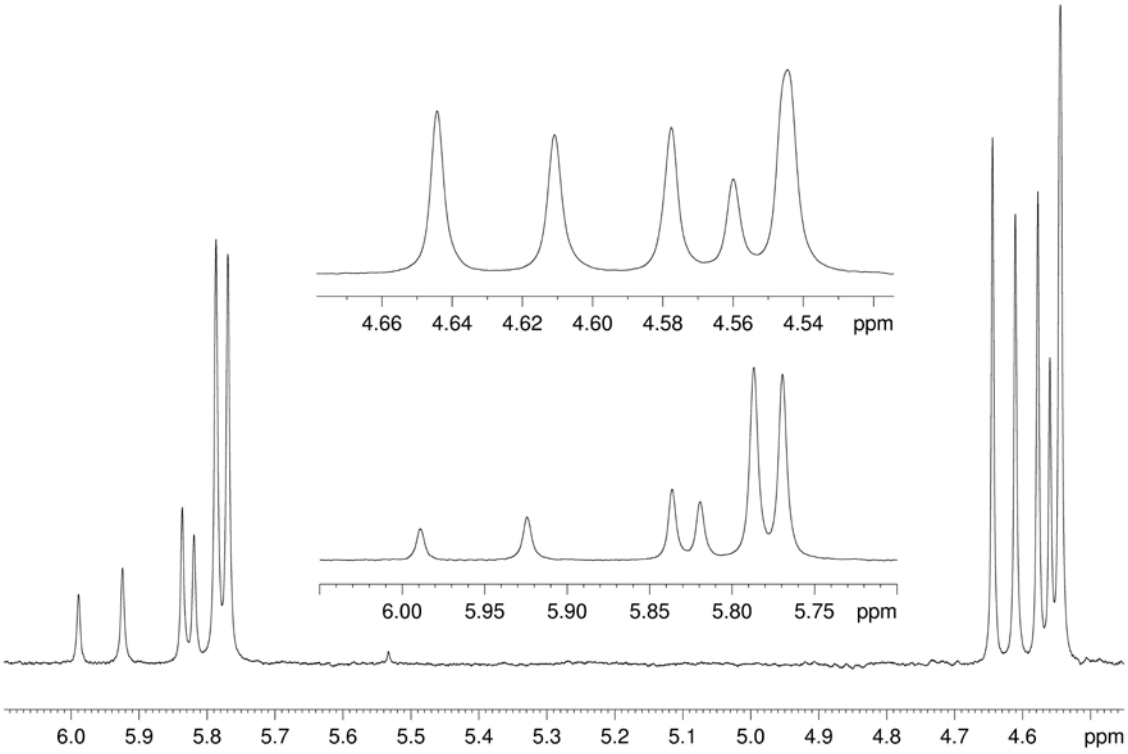

Figure S5. ^{1}H NMR spectrum of the competition experiment corresponding to iteration 1 of the reaction between benzyl bromide 1a-g and pyridine in [bmim][NCF_3SO_2] at 300.7 K.

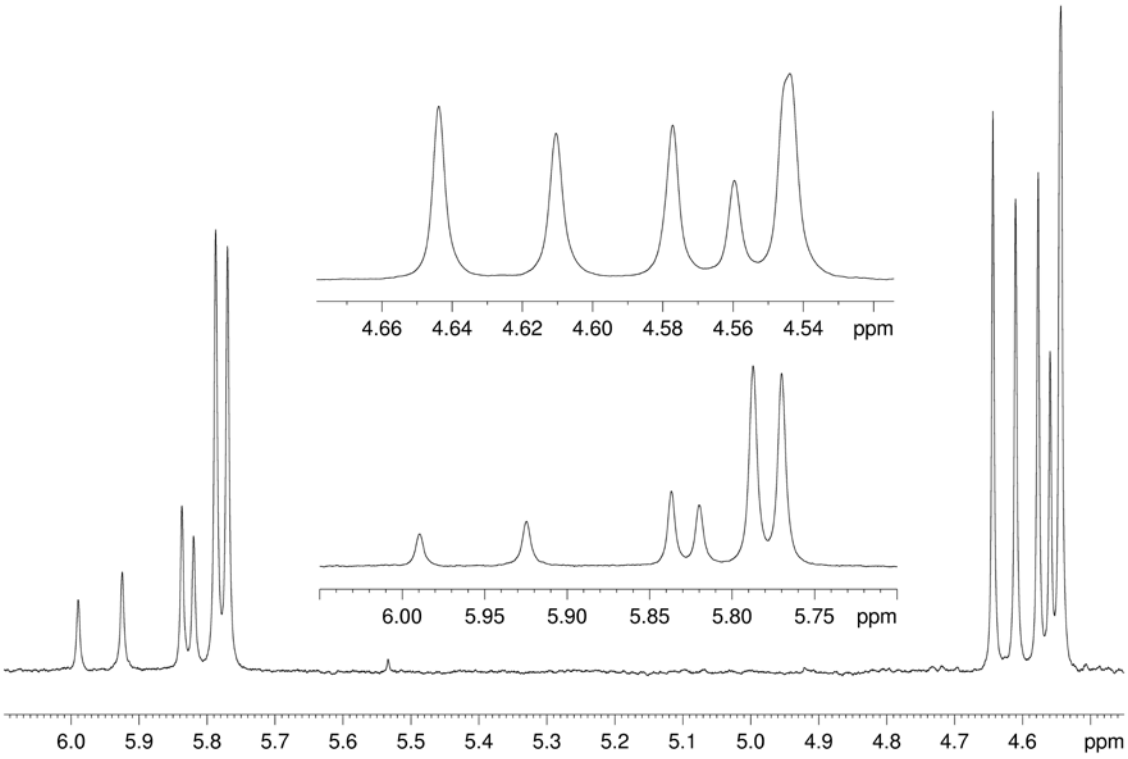

Figure S6. ^{1}H NMR spectrum of the competition experiment corresponding to iteration 2 of the reaction between benzyl bromide 1a-g and pyridine in [bmim][NCF_3SO_2] at 300.7 K.

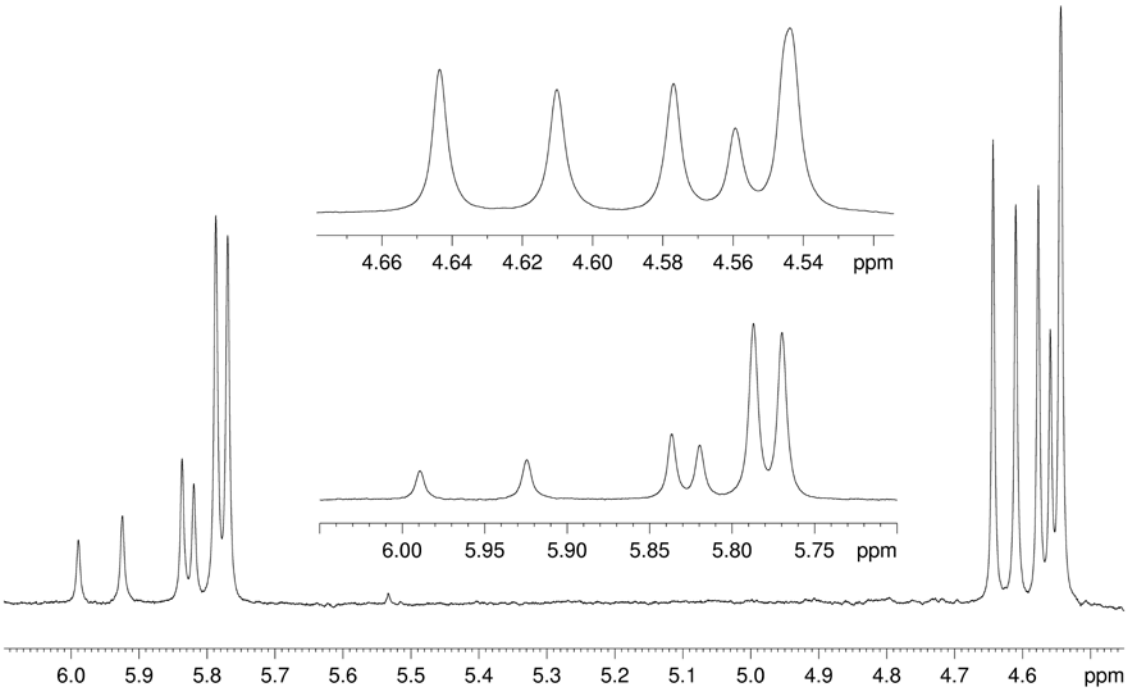

Figure S7. ^{1}H NMR spectrum of the competition experiment corresponding to iteration 3 of the reaction between benzyl bromide 1a-g and pyridine in [bmim][NCF_3SO_2] at 300.7 K.

Binary competition experiments for the sodium borohydride reduction of acetophenones

For each of the binary competition experiments, a pair of acetophenones (either **3a** and **3b**, **3b** and **3c** or **3c** and **3d**; *ca*. 110 μmol each) was dissolved in ethanol (1 mL) followed by the addition of finely crushed sodium borohydride (*ca*. 31 μmol). The reaction mixture was subjected to sonication at 295 K until complete dissolution of sodium borohydride and a portion of the solution (250 μL) was added to a 5 mm NMR tube containing hydrochloric acid (32%, *ca*. 5 mg, 45 μmol) and followed by the addition of chloroform-*d*.

^{1}H NMR spectroscopy was used to analyse each of the competition experiments and the signals due to the methyl protons of the starting materials or the protons at the 2-ethyl position of the products were used to calculate the extent of reaction for each of the pair of acetophenones as described above. Due to partial signal overlap of the doublets of the product pair **3b** and **3c** as well as the pair **3c** and **3d**, only the non-overlapping half of those doublets were used for analysis and scaled accordingly.

Table S5. Relative ^{1}H NMR integrals determined for the binary competition experiments between the acetophenones **3a** and **3b** in ethanol at 295 K.

	Relative integration		
Species	**Iteration 1**	**Iteration 2**	**Iteration 3**
Acetophenone **3a**	414.6	391.1	363.6
Acetophenone **3b**	267.8	238.2	241.0
Alcohol **4a**	119.8	140.9	146.6
Alcohol **4b**	197.8	229.8	248.9

Table S6. Relative ^{1}H NMR integrals determined for the binary competition experiments between the acetophenones **3b** and **3c** in ethanol at 295 K.

	Relative integration		
Species	**Iteration 1**	**Iteration 2**	**Iteration 3**
Acetophenone **3b**	337.6	336.5	384.0
Acetophenone **3c**	194.8	176.9	226.2
Alcohol **4b**	144.7	157.6	122.7
Alcohol **4c**	322.9	329.0	267.1

Table S7. Relative ^{1}H NMR integrals determined for the binary competition experiments between the acetophenones **3c** and **3d** in ethanol at 295 K.

	Relative integration		
Species	**Iteration 1**	**Iteration 2**	**Iteration 3**
Acetophenone **3c**	378.0	352.8	382.5
Acetophenone **3d**	138.2	166.9	157.3
Alcohol **4c**	137.9	126.3	143.6
Alcohol **4d**	345.8	353.9	316.6

Table S8. Relative rate constants determined for the binary competitive sodium borohydride reduction of the acetophenones **3a-d** in ethanol.

	Iteration 1	**Iteration 2**	**Iteration 3**
$k_{\mathbf{3b}} / k_{\mathbf{3a}}$	2.17	2.19	2.09
$k_{\mathbf{3c}} / k_{\mathbf{3b}}$	2.74	2.73	2.81
$k_{\mathbf{3d}} / k_{\mathbf{3c}}$	4.03	3.72	3.46

Competition experiments for the sodium borohydride reduction of acetophenones – ^{1}H NMR spectroscopy case

Signal resolution of the common signal due to the protons on the methyl group of either the starting materials **3a-d** and products **4a-d** were determined by the stepwise addition of the starting materials **64** to a solution containing equal amounts of ethanol and chloroform-*d*. Partial overlap was observed between the signal due to acetophenones **3d** and **3c** but integration could be carried out confidently with the aid of deconvolution.

For each of the competition experiments, a solution of absolute ethanol (2.5 mL) containing the acetophenones **3a-d** (*ca*. 270 μmol each) was prepared and a portion of the solution (250 μL) was placed in a 5 mm NMR tube containing chloroform-*d* (250 μL) for determining the ratios of the starting materials. Finely crushed sodium borohydride (*ca*. 80 μmol) was added to the remaining reaction mixture, which was subjected to sonication at 295 K to facilitate the dissociation of sodium borohydride. After 1 hour, a portion of the solution (250 μL) was added to a 5 mm NMR tube containing excess hydrochloric acid (32% w/w, *ca*. 5 mg, 45 μmol) followed by the addition of chloroform-*d* (250 μL).

Relative amounts of starting materials **3a-d** and products **4a-d** were determined using ^{1}H NMR spectroscopy analysing the signals due to the protons of the common methyl functionality. Relative rate constants were calculated using the known ratios between the starting materials **3a-d** and the final distribution of starting materials **3a-d** normalised against the combined integral of with products **4a-d**.

Table S9. Relative ^{1}H NMR integrals based on the relative amounts of the starting materials **3a-d** before the addition of sodium borohydride.

	Relative integration			
Species	**Iteration 1**	**Iteration 2**	**Iteration 3**	**Iteration 4**
Acetophenone **3a**	254.0	254.7	265.1	258.3
Acetophenone **3b**	236.0	236.5	232.7	261.0
Acetophenone **3c**	245.9	245.7	247.4	238.3
Acetophenone **3d**	264.1	263.1	254.7	242.4

Table S10. Relative ^{1}H NMR integrals determined for the competitive sodium borohydride reduction of the acetophenones **3a-d** in ethanol at 295 K.

	Relative integration			
Species	**Iteration 1**	**Iteration 2**	**Iteration 3**	**Iteration 4**
Acetophenone **3a**	244.3	245.2	252.9	234.5
Acetophenone **3b**	214.8	214.7	218.2	189.7
Acetophenone **3c**	192.6	195.2	204.1	143.2
Acetophenone **3d**	113.7	119.6	122.4	35.0
Sum of alcohol **4a-d**	234.7	225.4	202.3	397.5

Table S11. Relative rate constants determined using ^{1}H NMR spectroscopy for the competitive sodium borohydride reduction of the acetophenones **3a-d** in ethanol at 295 K.

	k / k_H			
Substituent	**Iteration 1**	**Iteration 2**	**Iteration 3**	**Iteration 4**
p-OCH3 (**3a**)	0.16	0.17	0.24	0.19
p-CH_3 (**3b**)	0.39	0.42	0.34	0.63
H (**3c**)	1	1	1	1
p-Br (**3d**)	3.45	3.43	3.81	3.80

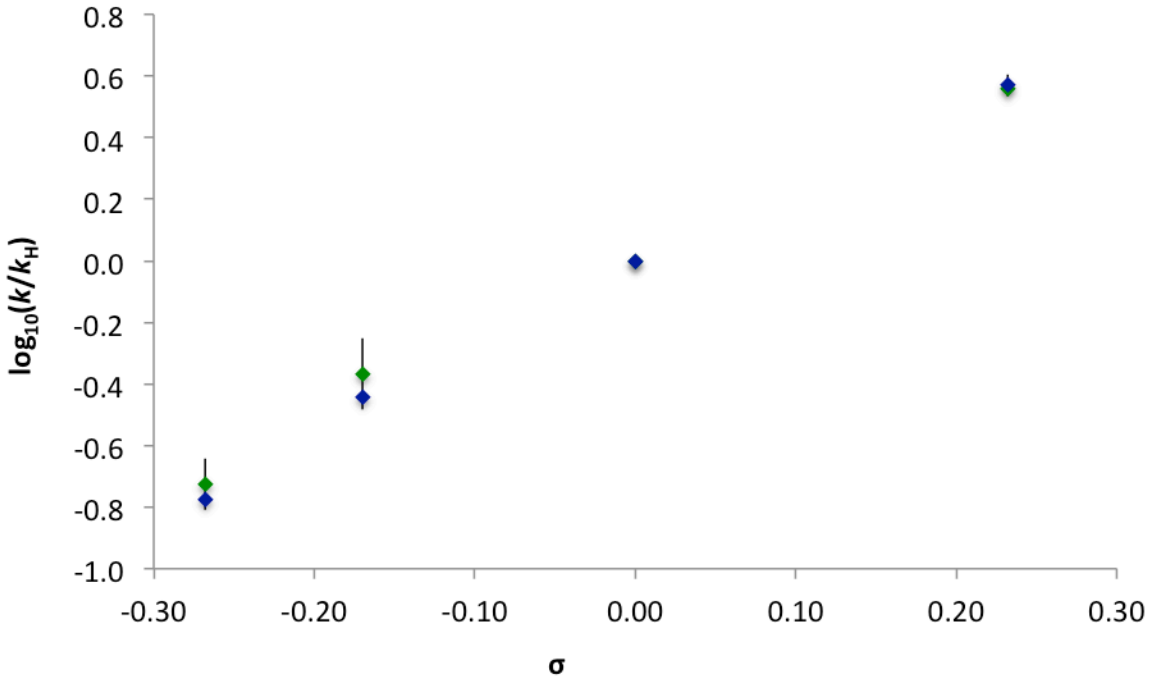

Figure S8. Hammett plots for the competitive sodium borohydride reduction of binary combinations of acetophenones **3a-d** (blue) or all acetophenone **3a-d** simultaneously (green), carried out in ethanol at 295 K and analysed using ^{1}H NMR spectroscopy.

Competition experiments for the sodium borohydride reduction of acetophenones – ^{13}C NMR spectroscopy case

Individual ^{13}C NMR experiments was carried out for each of the starting materials **3a-d** and products **4a-d** in solution containing an equal volume of ethanol and chloroform-*d* and the relaxation reagent, *tris*(2,4-pentanedionate) chromium (*ca*. 14 mg), to aid the identification of signals in subsequent experiments

For each of the competition experiments, a solution of absolute ethanol (2.5 mL) containing the acetophenones **3a-d** (*ca*. 400 μmol each) was prepared and a portion of the solution (250 μL) was placed in a 5 mm NMR tube containing chloroform-*d* (250 μL) for determining the ratios of the starting materials. Finely crushed sodium borohydride (*ca*. 130 μmol) was added to the remaining reaction mixture, which was subjected to sonication at 295 K to facilitate the dissociation of sodium borohydride. After 1 hour, a portion of the solution (250 μL) was added to a 5 mm NMR tube containing excess hydrochloric acid (32% w/w, *ca*. 8 mg, 72 μmol) followed by the addition of chloroform-*d* (250 μL) and the chromium relaxation reagent (*ca*. 14 mg, 40 μmol).

Distribution of signals due to starting materials **3a-d** and products **4a-d**, from which relative rate constants were evaluated, were analysed using the well-resolved ^{13}C NMR signals of either one of the two quaternary carbons in the starting materials.

Table S12. Relative ^{13}C NMR integrals determined for the competitive sodium borohydride reduction of the acetophenones **3a-d** in ethanol at 295 K.

	Relative integration		
Species	**Iteration 1**	**Iteration 2**	**Iteration 3**
Acetophenone **3a**	220.8	233.6	234.5
Acetophenone **3b**	196.5	193.3	184.9
Acetophenone **3c**	148.0	139.7	132.0
Acetophenone **3d**	45.9	34.3	23.1
Alcohol **4a**	14.5	27.6	30.6
Alcohol **4b**	54.1	55.2	54.8
Alcohol **4c**	103.8	106.8	120.7
Alcohol **4d**	206.3	209.5	219.2

Table S13. Relative rate constants determined by means of ^{13}C NMR spectroscopy for the competitive sodium borohydride reduction of the acetophenones **3a-d** in ethanol at 295 K.

	k / k_H		
Substituent	**Iteration 1**	**Iteration 2**	**Iteration 3**
p-OCH_3 (**3a**)	0.12	0.20	0.19
p-CH_3 (**3b**)	1	1	1
H (**3c**)	0.46	0.44	0.40
p-Br (**3d**)	3.20	3.45	3.62

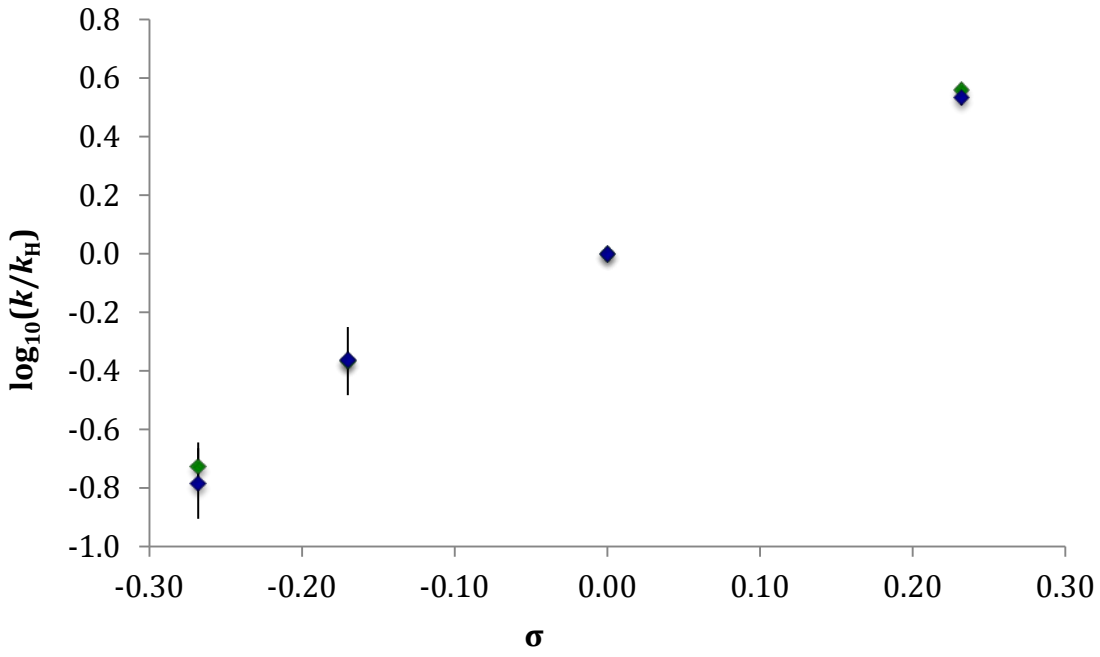

Figure S9. Hammett plots for the competitive sodium borohydride reduction of all acetophenone **3a-d** simultaneously, carried out in ethanol at 295 K, analysed using either ^{1}H NMR spectroscopy (green) or ^{13}C NMR spectroscopy (blue).

NMR Spectra for the competitive sodium borohydride reduction of acetophenones **3a-d**

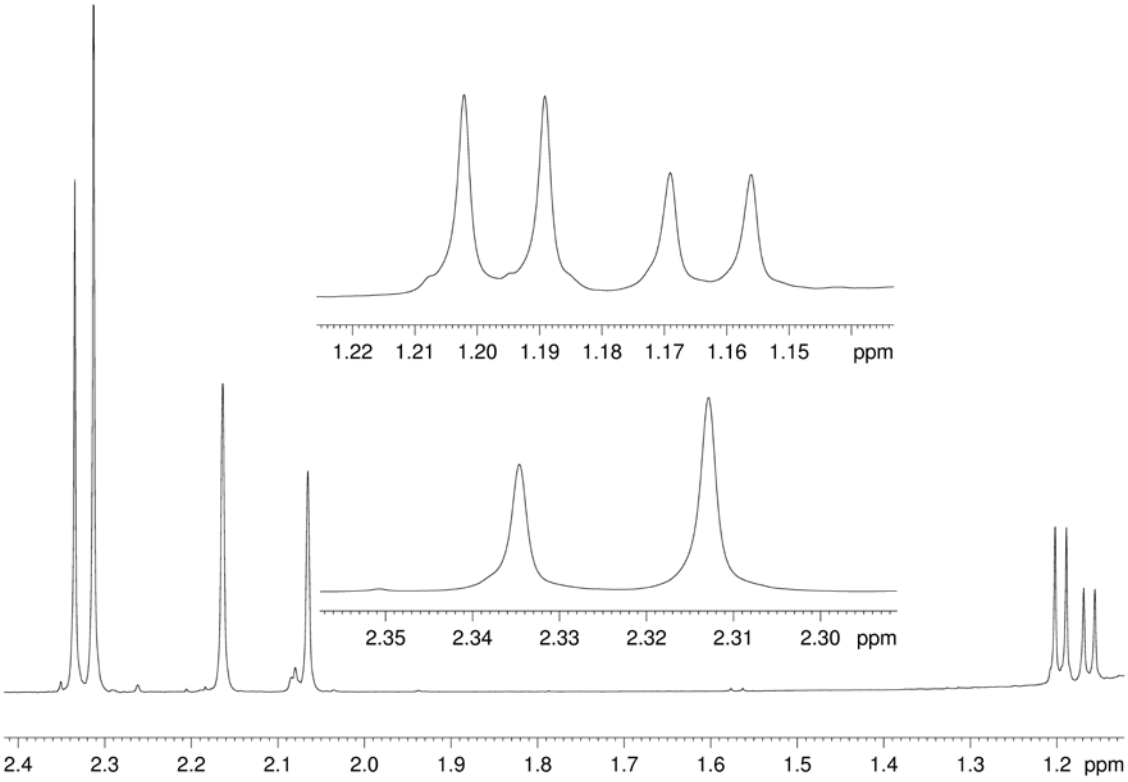

Figure S10. ^{1}H NMR spectrum of the binary competition experiment corresponding to iteration 1 of the sodium borohydride reduction of acetophenones **3a** and **3b**.

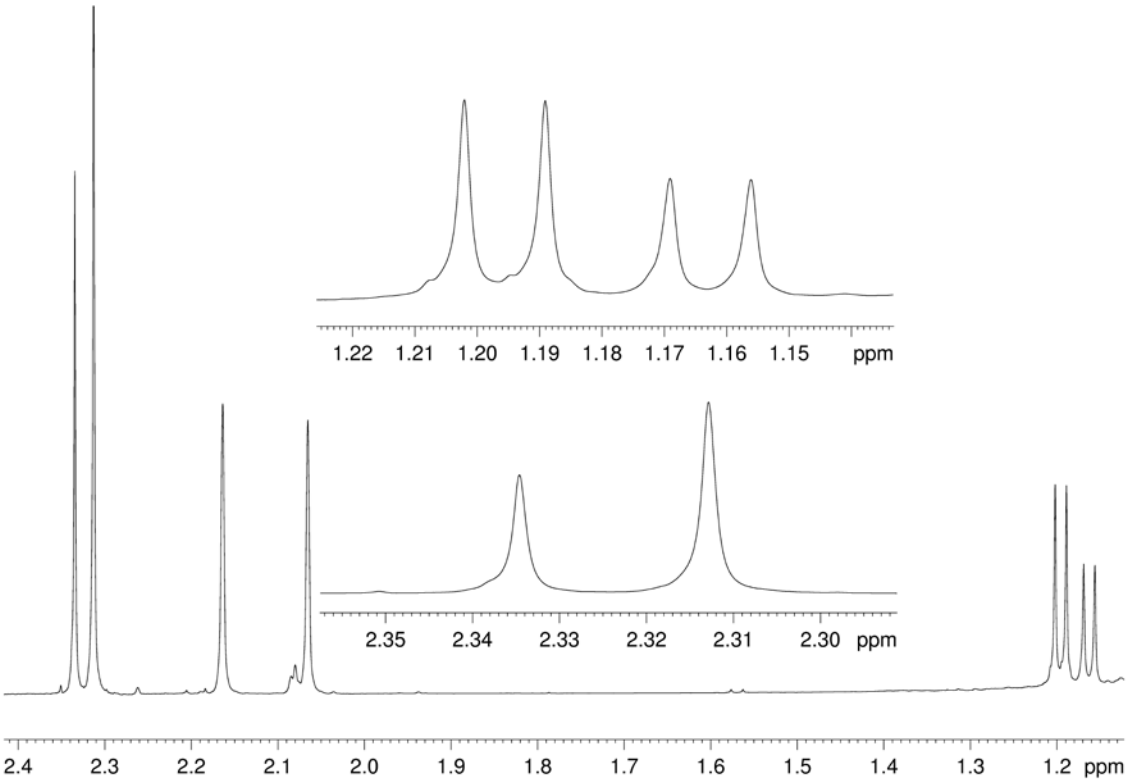

Figure S11. ^{1}H NMR spectrum of the binary competition experiment corresponding to iteration 2 of the sodium borohydride reduction of acetophenones **3a** and **3b**.

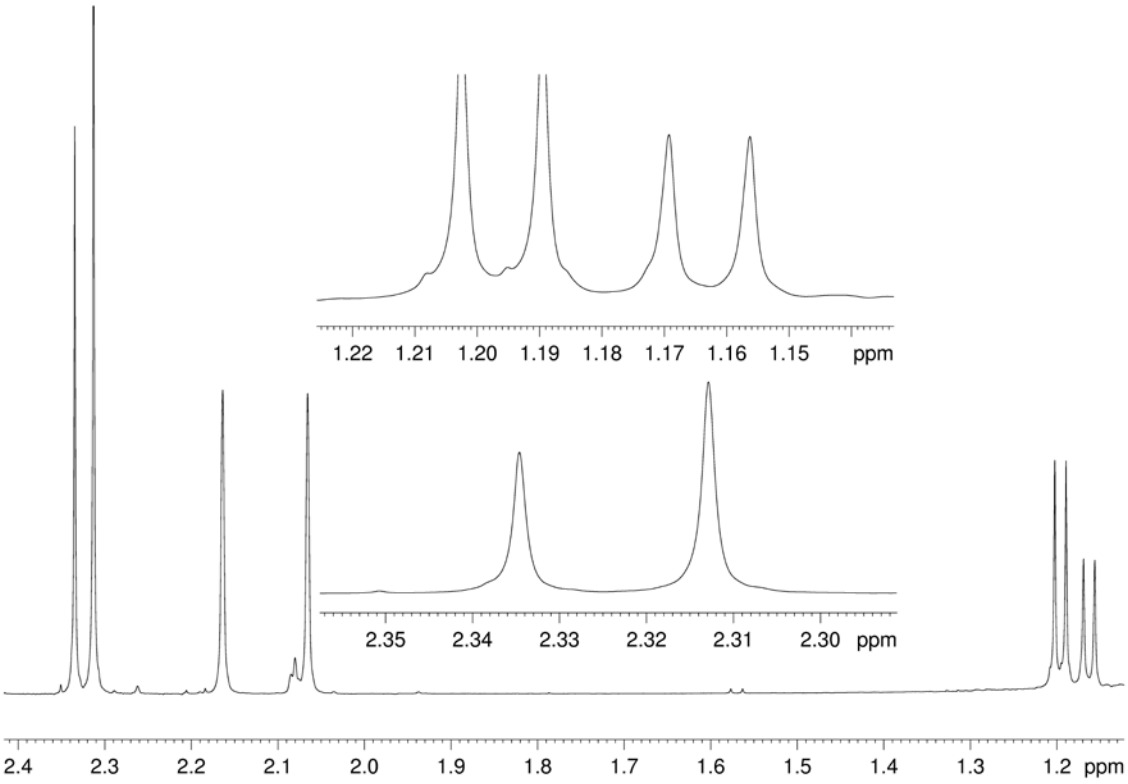

Figure S12. ^{1}H NMR spectrum of the binary competition experiment corresponding to iteration 3 of the sodium borohydride reduction of acetophenones **3a** and **3b**.

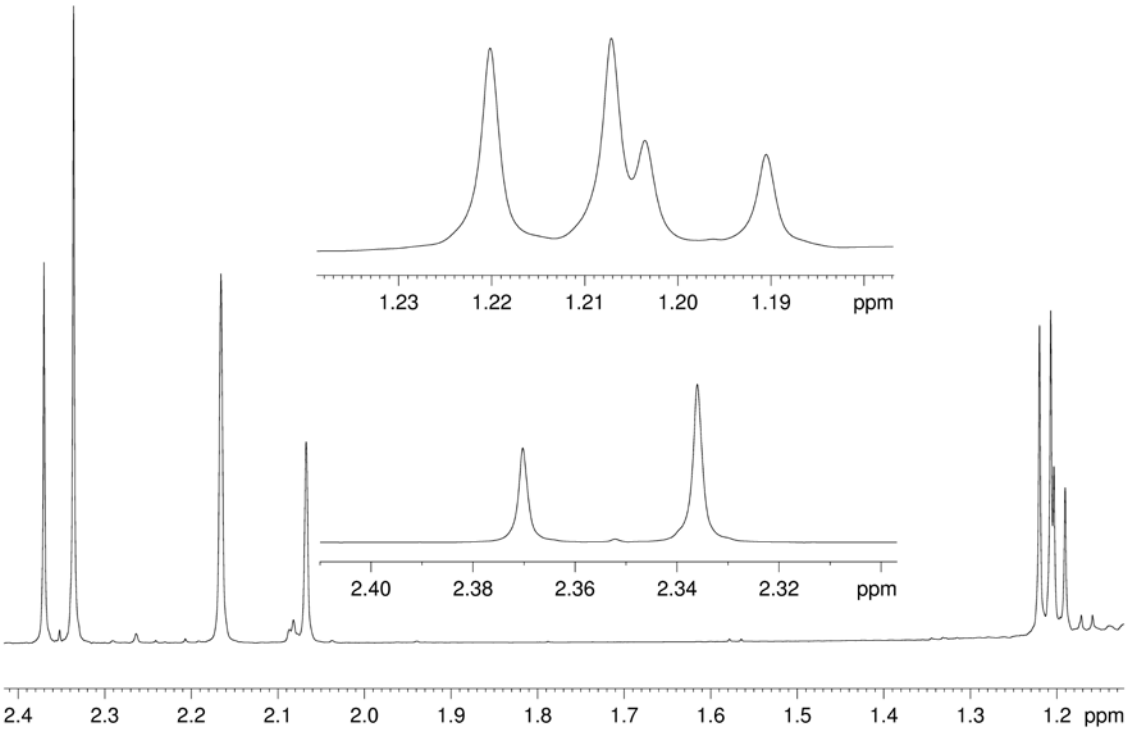

Figure S13. ^{1}H NMR spectrum of the binary competition experiment corresponding to iteration 1 of the sodium borohydride reduction of acetophenones **3b** and **3c**.

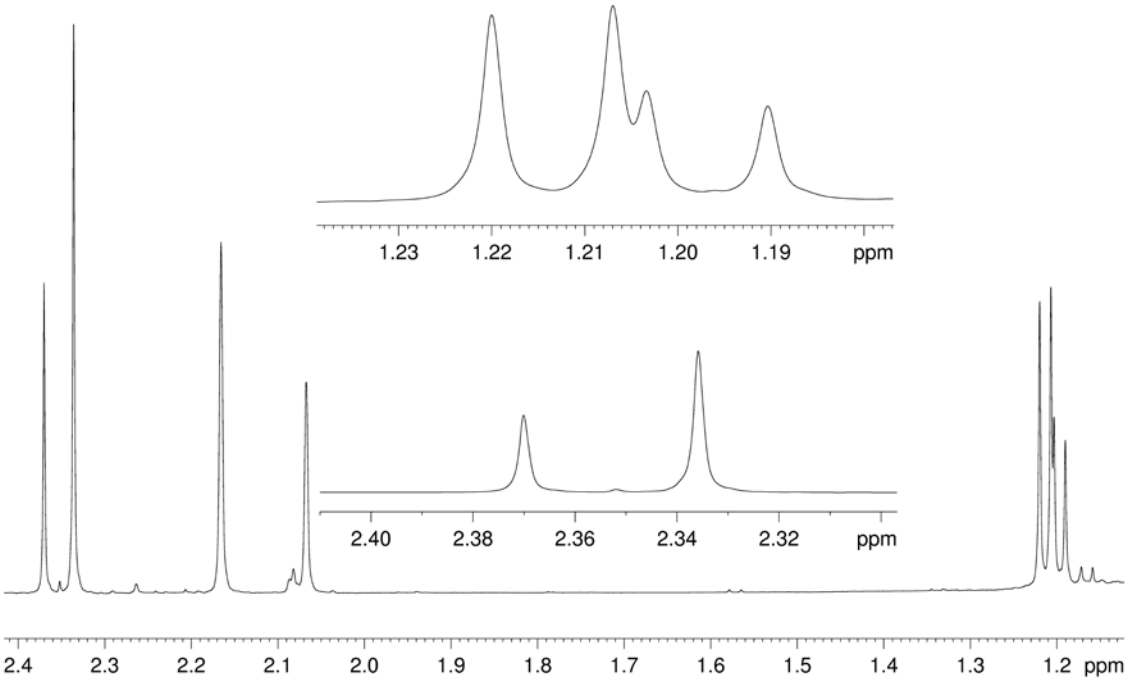

Figure S14. ^{1}H NMR spectrum of the binary competition experiment corresponding to iteration 2 of the sodium borohydride reduction of acetophenones **3b** and **3c**.

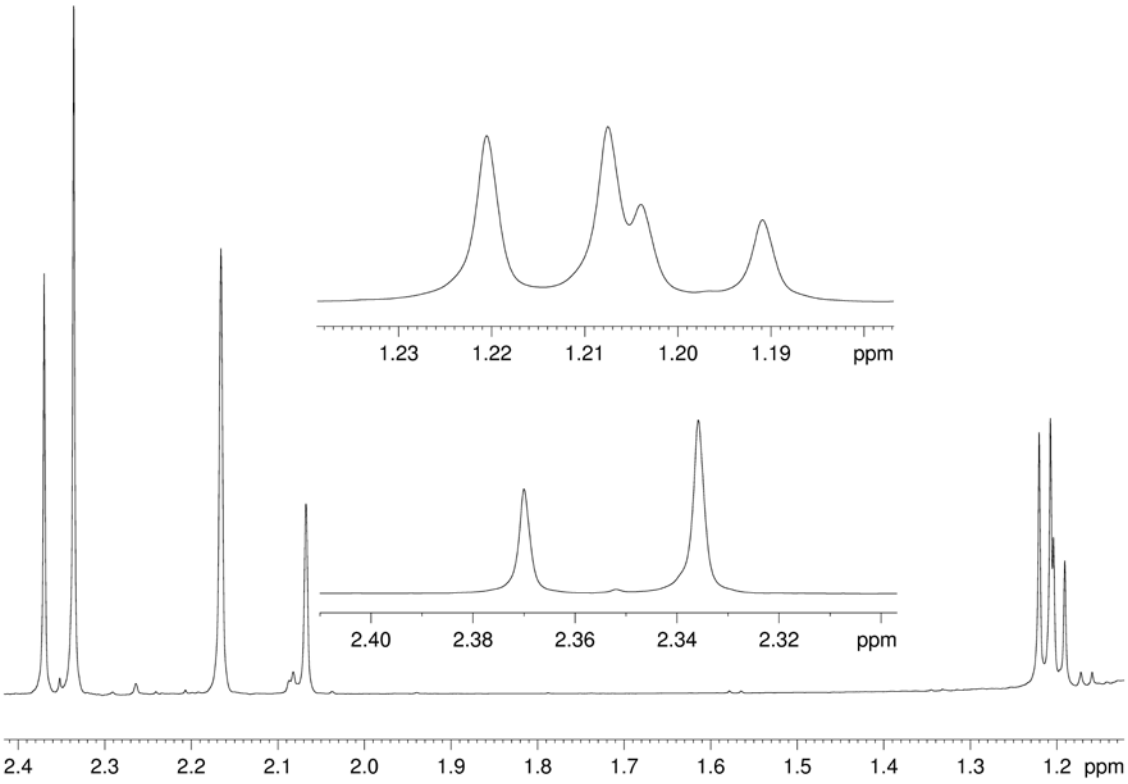

Figure S15. ^{1}H NMR spectrum of the binary competition experiment corresponding to iteration 3 of the sodium borohydride reduction of acetophenones **3b** and **3c**.

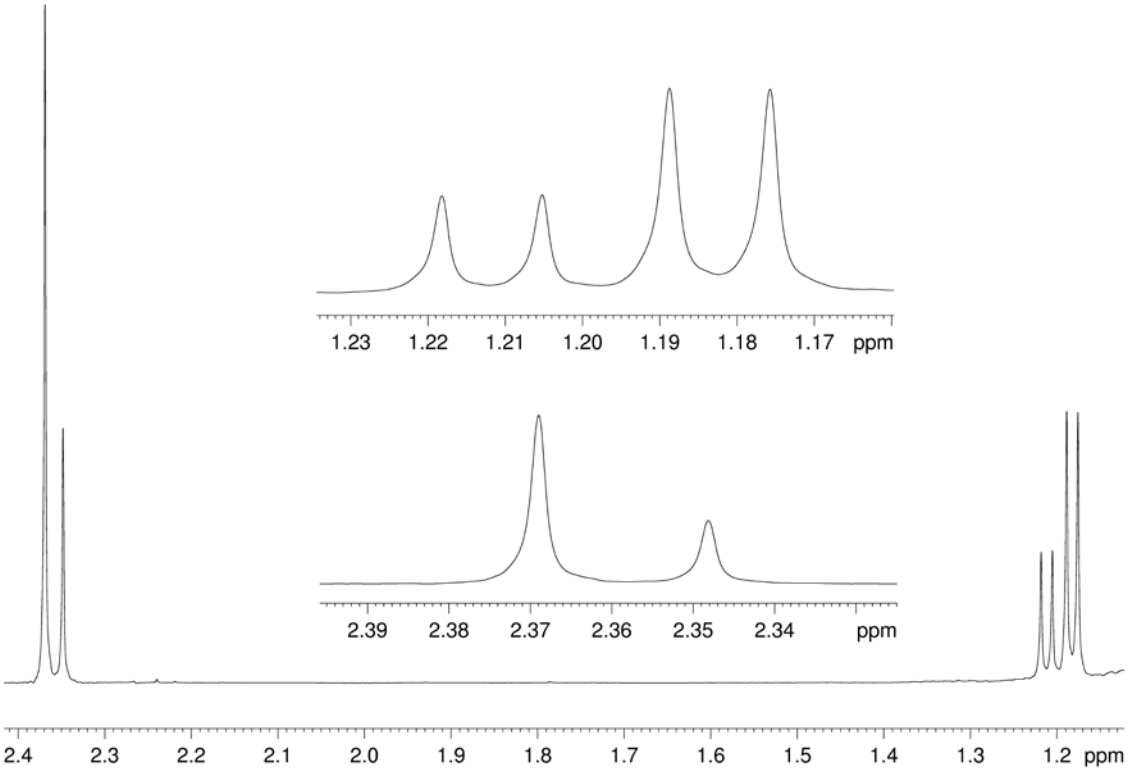

Figure S16. ^{1}H NMR spectrum of the binary competition experiment corresponding to iteration 1 of the sodium borohydride reduction of acetophenones **3c** and **3d**.

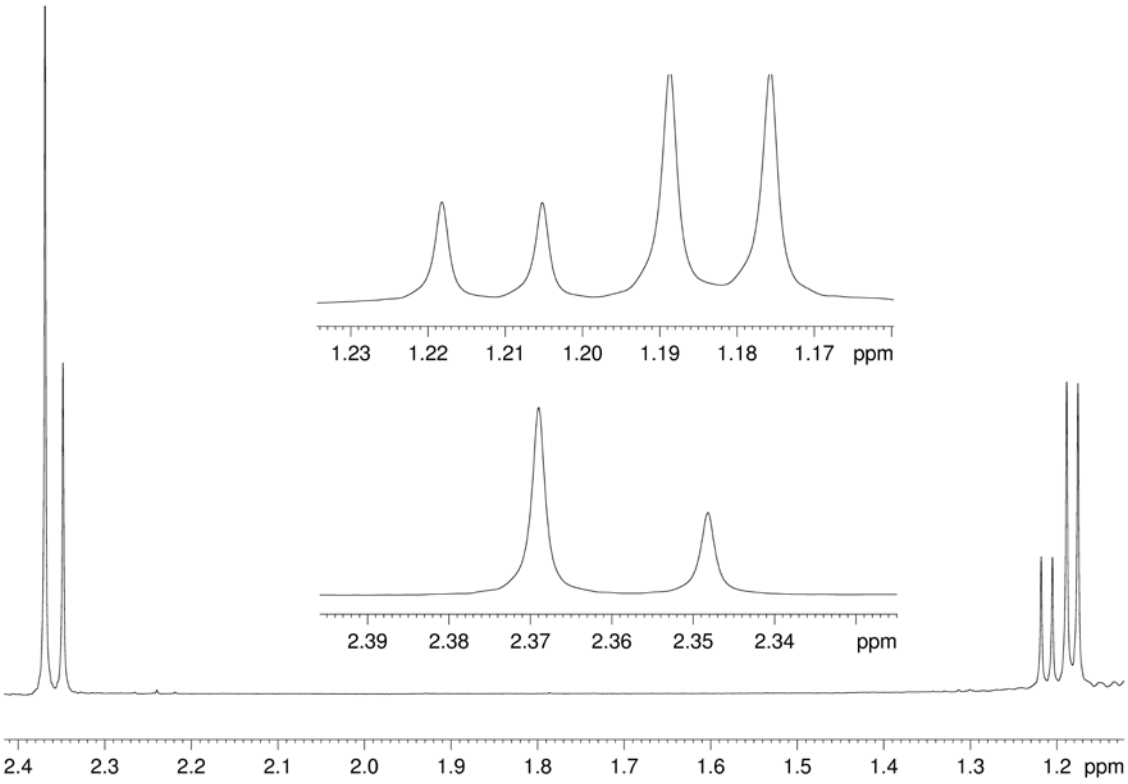

Figure S17. ^{1}H NMR spectrum of the binary competition experiment corresponding to iteration 2 of the sodium borohydride reduction of acetophenones **3c** and **3d**.

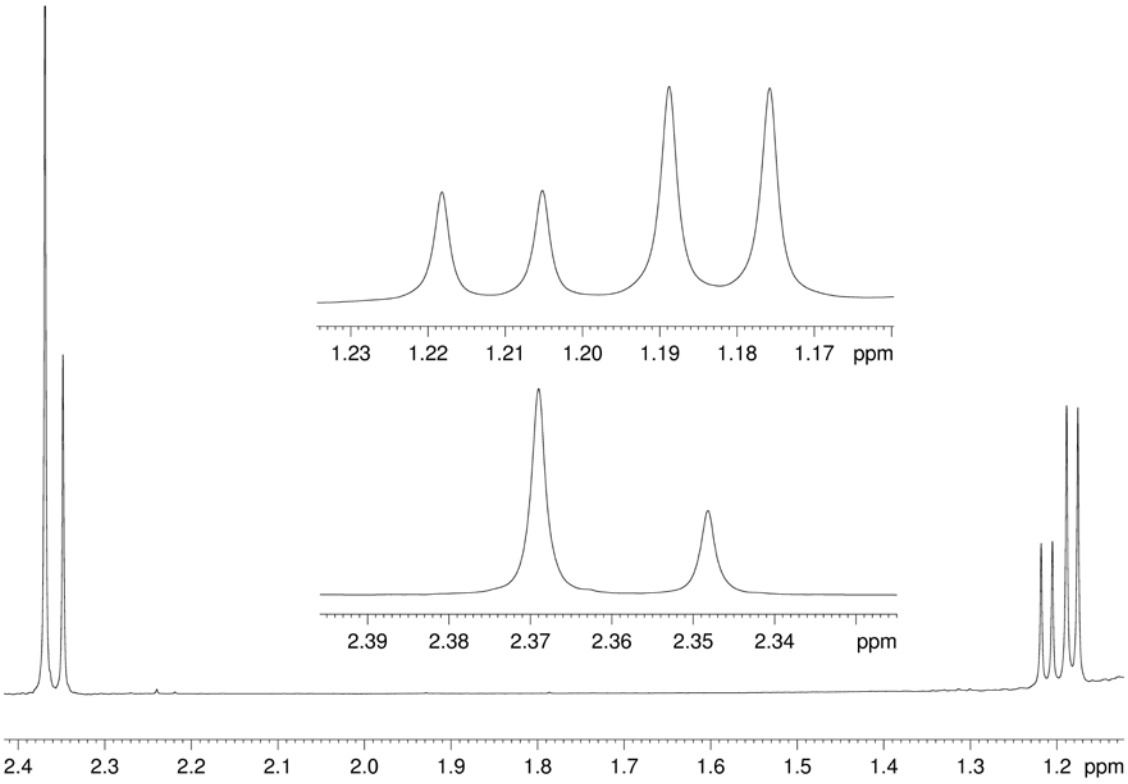

Figure S18. ^{1}H NMR spectrum of the binary competition experiment corresponding to iteration 3 of the sodium borohydride reduction of acetophenones **3c** and **3d**.

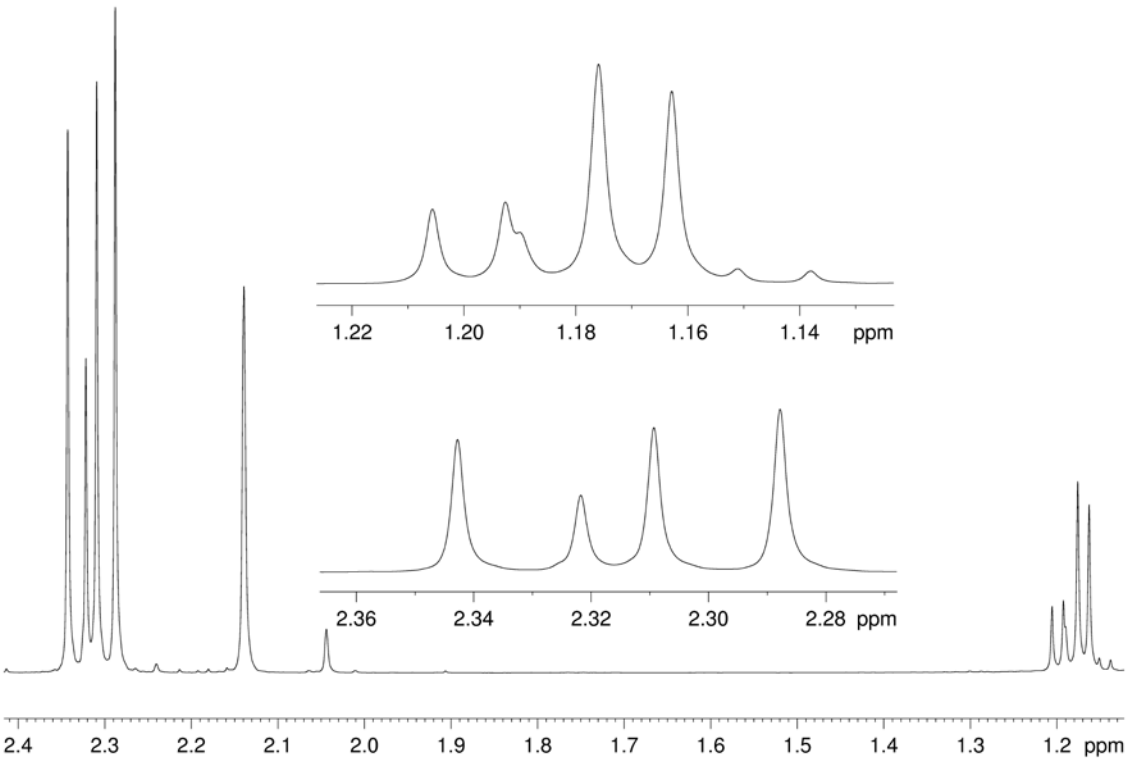

Figure S19. ^{1}H NMR spectrum of the experiment corresponding to iteration 1 of the competitive sodium borohydride reduction of acetophenones **3a-d**.

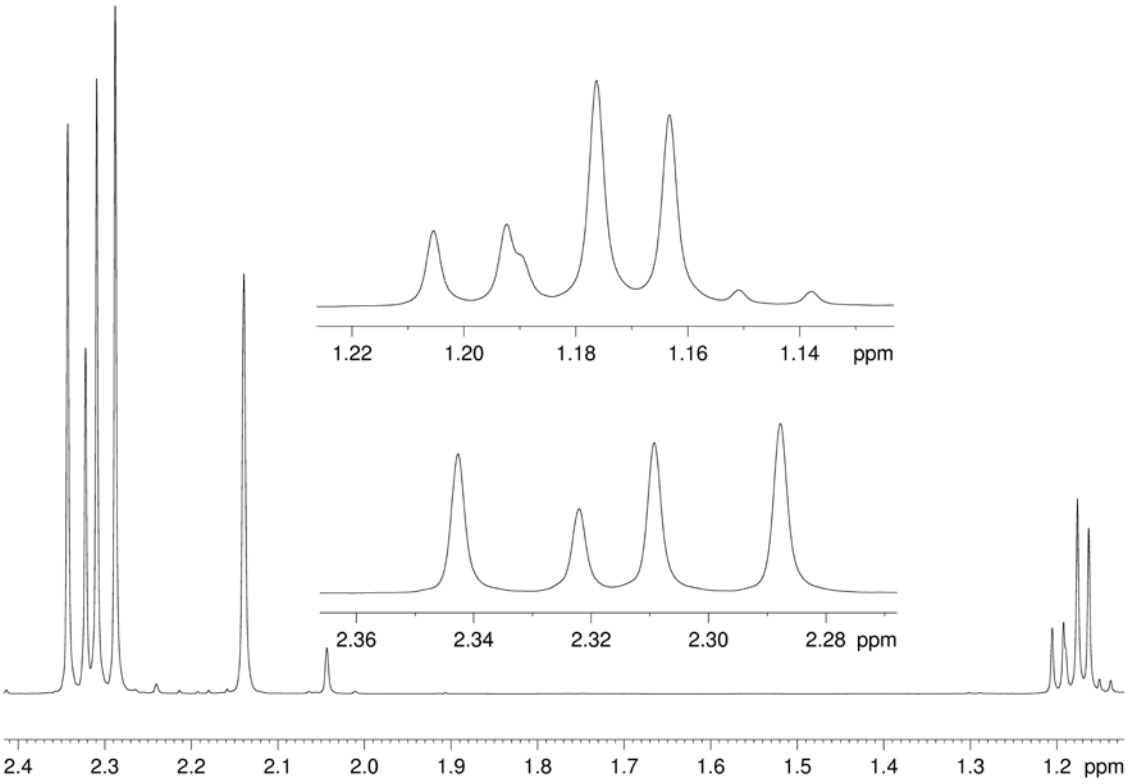

Figure S20. ^{1}H NMR spectrum of the experiment corresponding to iteration 2 of the competitive sodium borohydride reduction of acetophenones **3a-d**.

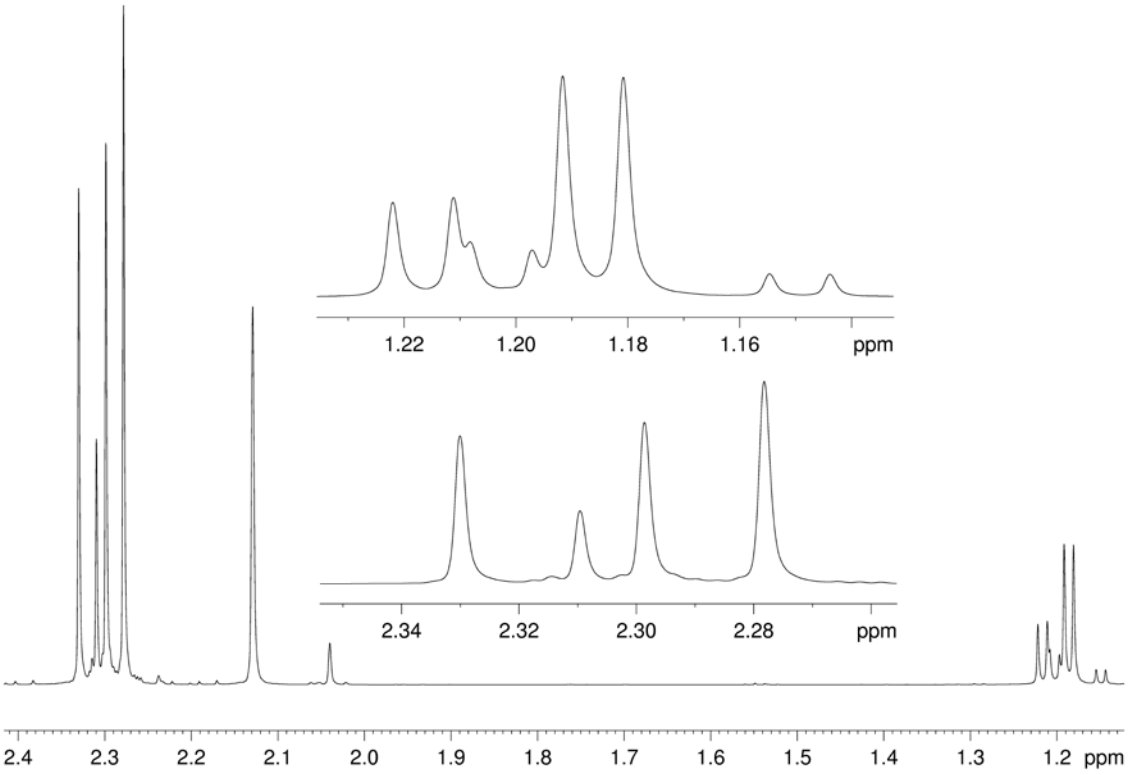

Figure S21. ^{1}H NMR spectrum of the experiment corresponding to iteration 3 of the competitive sodium borohydride reduction of acetophenones **3a-d**.

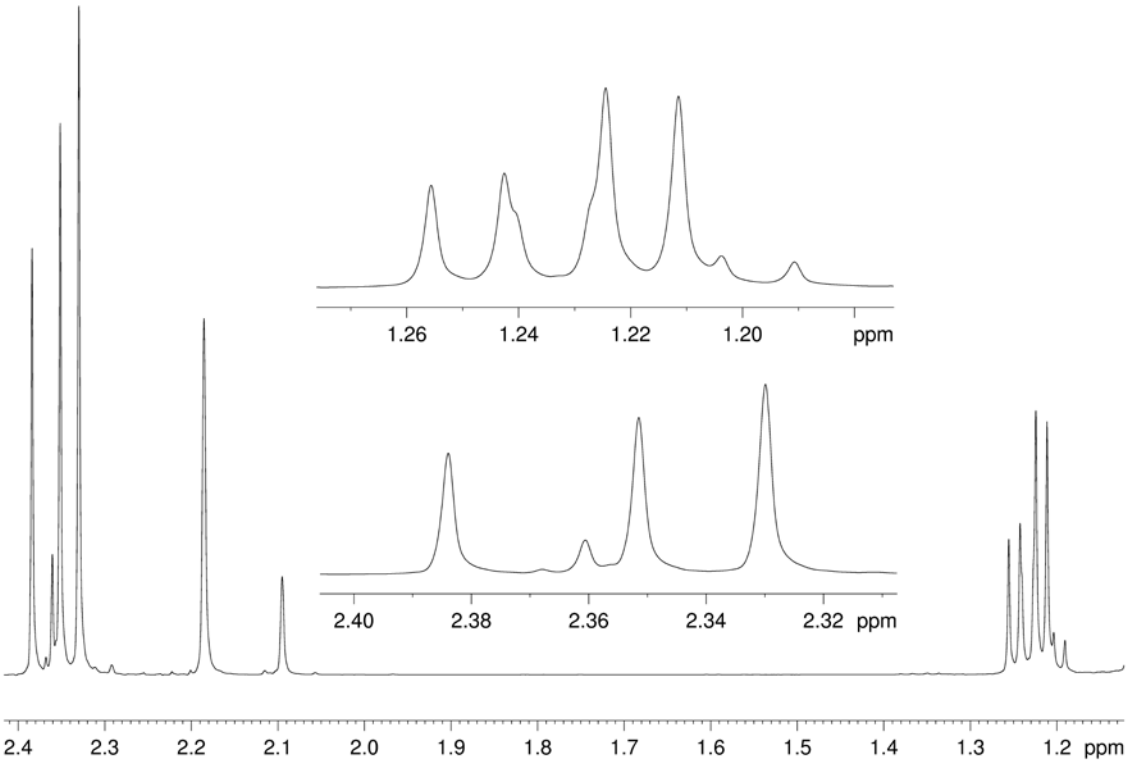

Figure S22. ^{1}H NMR spectrum of the experiment corresponding to iteration 4 of the competitive sodium borohydride reduction of acetophenones **3a-d**.

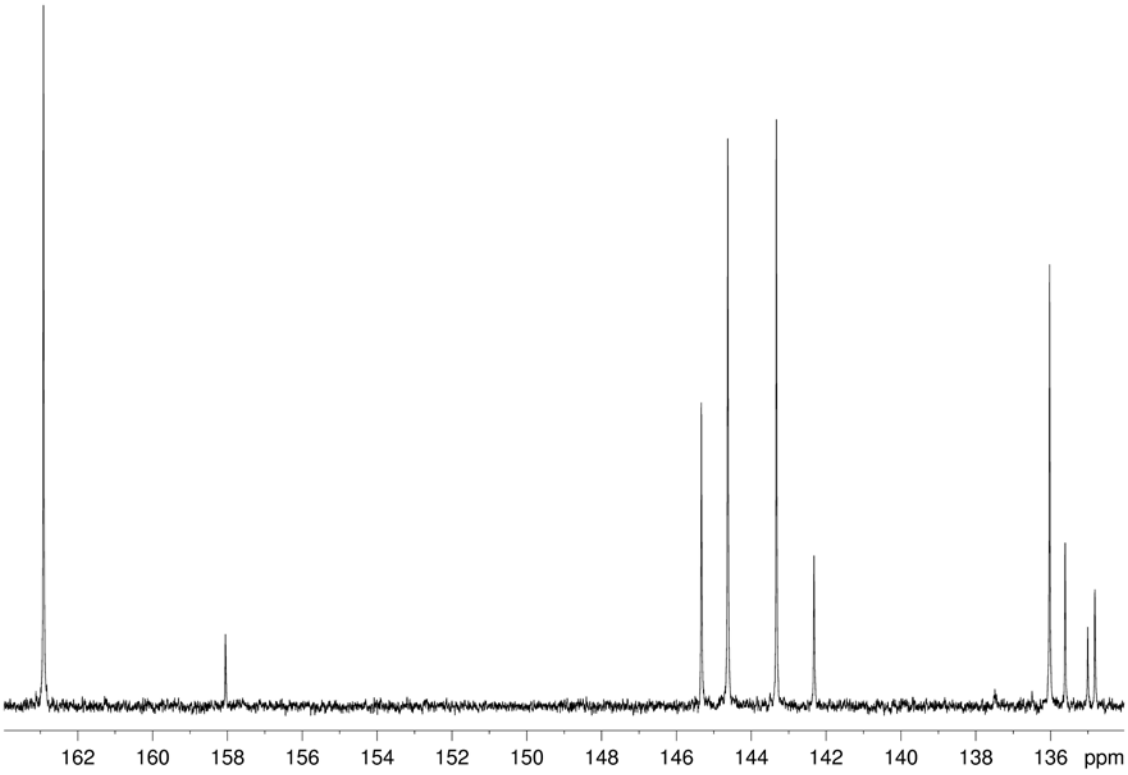

Figure S23. ^{13}C NMR spectrum of the experiment corresponding to iteration 1 of the competitive sodium borohydride reduction of acetophenones **3a-d**.

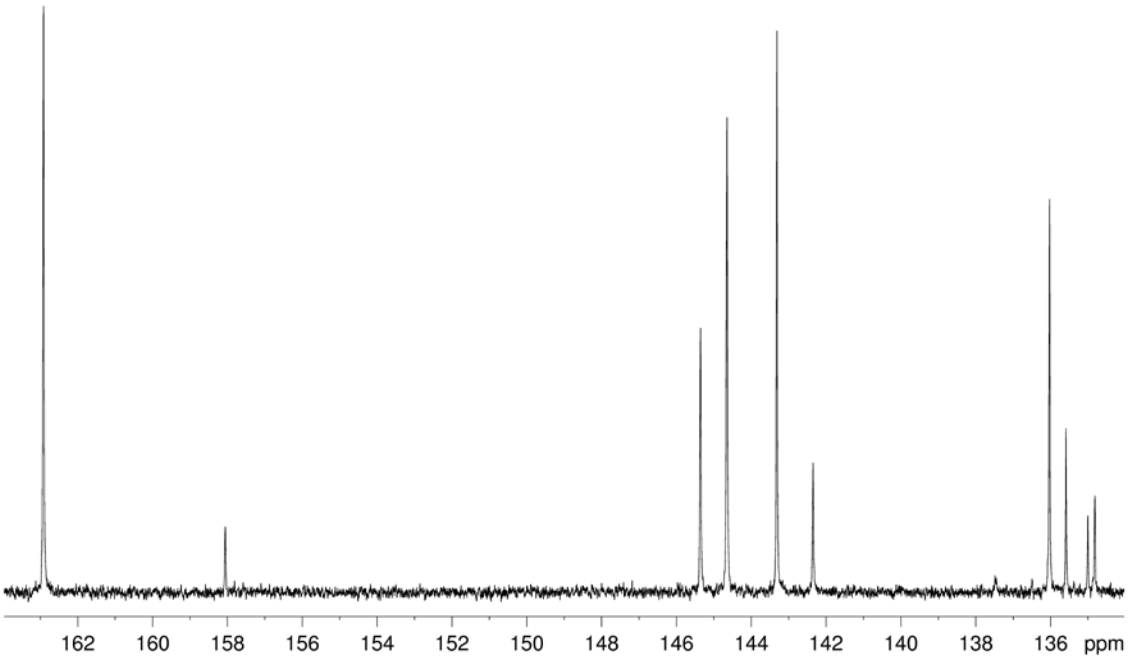

Figure S24. ^{13}C NMR spectrum of the experiment corresponding to iteration 2 of the competitive sodium borohydride reduction of acetophenones **3a-d**.

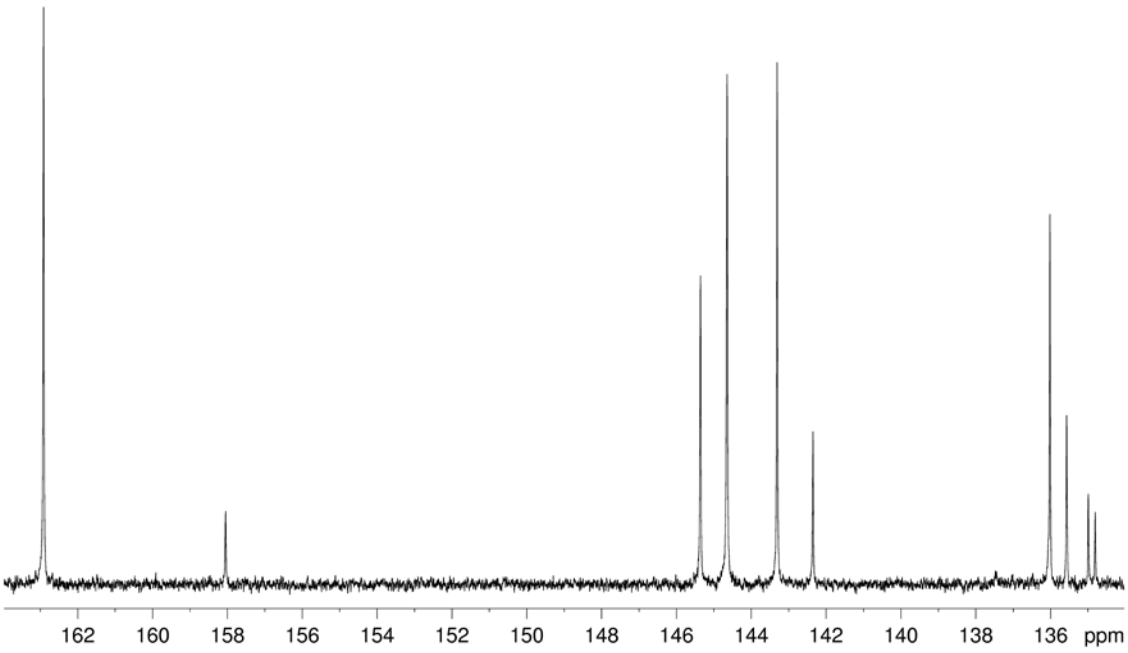

Figure S25. ^{13}C NMR spectrum of the experiment corresponding to iteration 3 of the competitive sodium borohydride reduction of acetophenones **3a-d**.

Competition experiments for the sodium borohydride reduction of acetophenones – reverse-phase HPLC case

For each competition experiment, the reaction mixture was prepared by firstly dissolving the acetophenones **3a-d** (*ca*. 300 μmol each) in absolutely ethanol (2.0 mL) followed by the addition of sodium borohydride (*ca*. 110 μmol), which was then subjected to sonication at 295 K to facilitate the dissociation of sodium borohydride. After 1 hour, hydrochloric acid (32% w/w, *ca*. 60 mg, 526 μmol) was added, followed by the addition of a solution of sodium bicarbonate (*ca*. 18 mg, 214 μmol) in Milli-Q™ water (200 μL) to neutralise excess hydrochloric acid. The mixture, which contains suspended sodium chloride and sodium bicarbonate, was filtered with additional absolutely ethanol and made up to the desired volume with additional absolute ethanol (10 mL). A drop of the solution was mixed a few drops of water and tested neutral using indicator paper.

Each of the ethanolic solutions was further diluted by a factor of 10 into acetonitrile-water (2:5) before reverse-phase HPLC analysis. Optimal elution conditions were determined as reported in the general procedures. Standards for the construction of calibration curves as well as mixed standards for assessing matrix effects were prepared by serial dilution of an ethanolic stock solution (*ca*. 10 mg·mL^{-1}) to give the desired concentrations shown in Table S14 to Table S30. Note that deviation from linearity was observed in the calibration curves related to alcohol **4a-c** such that a second-order polynomial fitting procedure was required. The final concentrations of each species in each competition experiment, calculated as detailed in Appendix S3, are presented in Table S31.

Table S14. Reverse-phase HPLC data for the construction of calibration curve for 4-methoxyacetophenone (**3a**) at 271 nm.

Concentration / 10^{-5} mol·L^{-1}	**Absorbance / L·mol^{-1}**
133	31137197
93.1	23585786
66.5	17396873
26.6	7192506
13.3	3512730
2.66	710722

Table S15. Reverse-phase HPLC data for the construction of calibration curve for 4-methoxyacetophenone (**3a**) at 235 nm.

Concentration / 10^{-5} mol·L^{-1}	**Absorbance / L·mol^{-1}**
133	3131975
93.1	2211294
66.5	1598700
26.6	659929
13.3	323753
2.66	66021

Table S16. Reverse-phase HPLC data for the construction of calibration curve for 4-methoxyacetophenone (**3a**) at 220 nm.

Concentration / 10^{-5} mol·L^{-1}	**Absorbance / L·mol^{-1}**
133	18383812
93.1	14313938
66.5	10857904
26.6	4646804
13.3	2287173
2.66	465138

Table S17. Reverse-phase HPLC data for the construction of calibration curve for 4-methylacetophenone (**3b**) at 251 nm.

Concentration / 10^{-5} mol·L^{-1}	**Absorbance / L·mol^{-1}**
148	33593354
104	24246259
74.0	17234966
29.6	7133485
14.8	3455340
2.96	692275

Table S18. Reverse-phase HPLC data for the construction of calibration curve for acetophenone (**3c**) at 235 nm.

Concentration / 10^{-5} mol·L^{-1}	**Absorbance / L·mol^{-1}**
166	26685361
116	18978812
83.2	13587535
33.3	5505478
16.6	2711041
3.33	541861

Table S19. Reverse-phase HPLC data for the construction of calibration curve for acetophenone (**3c**) at 220 nm.

Concentration / 10^{-5} mol·L^{-1}	**Absorbance / L·mol^{-1}**
166	6269543
116	4481947
83.2	3229166
33.3	1338614
16.6	668441
3.33	135352

Table S20. Reverse-phase HPLC data for the construction of calibration curve for 4-bromoacetophenone (**3d**) at 207 nm.

Concentration / 10^{-5} mol·L^{-1}	**Absorbance / L·mol^{-1}**
100	21247416
70.2	15236201
50.2	10971056
20.1	4447163
10.0	2313168
2.01	441967

Table S21. Reverse-phase HPLC data for the construction of calibration curve for 1-(4-methoxyphenyl)-ethanol (**4a**) at 197 nm.

Concentration / 10^{-5} mol·L^{-1}	**Absorbance / L·mol^{-1}**
132	46470237
92.2	36825047
65.9	28416935
26.4	12321197
13.2	6265088
2.64	1257686

Table S22. Reverse-phase HPLC data for the construction of calibration curve for 1-(4-methylphenyl)-ethanol (**4b**) at 220 nm.

Concentration / 10^{-5} mol·L^{-1}	**Absorbance / L·mol^{-1}**
147	12408893
103	9791710
73.6	7271535
29.5	3089577
14.7	1544508
2.95	308949

Table S23. Reverse-phase HPLC data for the construction of calibration curve for 1-phenylethanol (**4c**) at 198 nm.

Concentration / 10^{-5} mol·L^{-1}	**Absorbance / L·mol^{-1}**
140	18261622
98.3	14448237
70.2	11109072
28.1	4783958
14.0	2441598
2.81	495077

Table S24. Reverse-phase HPLC data for the construction of calibration curve for 1-(4-bromophenyl)-ethanol (**4d**) at 218 nm.

Concentration / 10^{-5} mol·L^{-1}	**Absorbance / L·mol^{-1}**
98.6	15228608
69.0	10945513
49.3	7879877
19.7	3169096
9.86	1582123
1.97	314966

Table S25. Concentrations for each of the starting materials **3a-d** and products **4a-d** used in the low-concentration mixed standard in reverse-phase HPLC experiments for the assessment of matrix effects.

Species	**Concentration / 10^{-5} mol·L^{-1}**
Acetophenone **3a**	13.3
Acetophenone **3b**	14.8
Acetophenone **3c**	16.6
Acetophenone **3d**	10.0
Alcohol **4a**	13.2
Alcohol **4b**	14.7
Alcohol **4c**	14.0
Alcohol **4d**	9.86

Table S26. Data obtained for the low-concentration mixed standard in reverse-phase HPLC experiments for the assessment of matrix effects.

Species	Wavelength / nm	Absorbance / $L \cdot mol^{-1}$
Acetophenone **3a**	271	3919156
Acetophenones **3a** + **3c**	235	2802761
Acetophenone **3b**	251	3572534
Acetophenone **3d**	207	2250015
Alcohol **4a**	197	6367062
Alcohol **4b**	220	1545643
Alcohol **4c**	198	2589073
Alcohol **4d**	218	1594539

Table S27. Concentrations for each of the starting materials **3a-d** and products **4a-d** used in the medium-concentration mixed standard in reverse-phase HPLC experiments for the assessment of matrix effects.

Species	Concentration / 10^{-5} $mol \cdot L^{-1}$
Acetophenone **3a**	66.5
Acetophenone **3b**	74.0
Acetophenone **3c**	83.2
Acetophenone **3d**	50.2
Alcohol **4a**	65.9
Alcohol **4b**	73.6
Alcohol **4c**	70.2
Alcohol **4d**	49.3

Table S28. Data obtained for the medium-concentration mixed standard in reverse-phase HPLC experiments for the assessment of matrix effects.

Species	Wavelength / nm	Absorbance / $L \cdot mol^{-1}$
Acetophenone **3a**	271	19281569
Acetophenones **3a** + **3c**	235	13884743
Acetophenone **3b**	251	17651997
Acetophenone **3d**	207	11111957
Alcohol **4a**	197	28703437
Alcohol **4b**	220	6673104
Alcohol **4c**	198	11675428
Alcohol **4d**	218	7927818

Table S29. Concentrations for each of the starting materials **3a-d** and products **4a-d** used in the high-concentration mixed standard in reverse-phase HPLC experiments for the assessment of matrix effects.

Species	Concentration / 10^{-5} $mol \cdot L^{-1}$
Acetophenone **3a**	133
Acetophenone **3b**	148
Acetophenone **3c**	166
Acetophenone **3d**	100
Alcohol **4a**	132
Alcohol **4b**	147
Alcohol **4c**	140
Alcohol **4d**	98.6

Table S30. Data obtained for the high-concentration mixed standard in reverse-phase HPLC experiments for the assessment of matrix effects.

Species	Wavelength / nm	Absorbance / $L \cdot mol^{-1}$
Acetophenone **3a**	271	34998514
Acetophenones **3a** + **3c**	235	27556691
Acetophenone **3b**	251	33793977
Acetophenone **3d**	207	21432646
Alcohol **4a**	197	46770934
Alcohol **4b**	220	30185657
Alcohol **4c**	198	18974122
Alcohol **4d**	218	15346562

Table S31. Concentrations obtained from reverse-phase HPLC experiments for the competitive sodium borohydride reduction of acetophenones **3a-d** in ethanol at 295 K.

	Concentration / 10^{-5} $mol \cdot L^{-1}$			
Species	**Iteration 1**	**Iteration 2**	**Iteration 3**	**Iteration 4**
Acetophenone **3a**	58.1	49.5	50.5	50.4
Acetophenone **3b**	58.7	43.9	50.9	51.3
Acetophenone **3c**	50.4	28.2	34.3	36.2
Acetophenone **3d**	18.6	7.51	13.7	18.9
Alcohol **4a**	4.63	6.59	4.84	3.86
Alcohol **4b**	3.83	7.38	4.87	2.88
Alcohol **4c**	24.7	23.3	17.3	12.1
Alcohol **4d**	47.9	51.1	45.5	41.4

References

1. W. L. F. Armarego and C. L. L. Chai, *Purification of Laboratory Chemicals*; 6th ed.; Butterworth-Heinemann: Oxford, United Kingdom, 2009.

2. S. Steines, P. Wasserscheid and B. Drießen-Hölscher, *J. Prakt. Chem.*, 2000, **342**, 348.

3. L. Cammarata, S. G. Kazarian, P. A. Salter and T. Welton, *Phys. Chem. Chem. Phys.*, 2001, **3**, 5192.

4. K. K. Mayer, S. Prior and W. Wiegrebe, *Monatsh. Chem.*, 1986, **117**, 511.

5. X.-K. Jiang, G.-Z. Ji and D. Z.-R. Wang, *J. Fluor. Chem.*, 1996, **79**, 173.

6. W. Franek, *Monatsh. Chem.*, 1996, **127**, 895.

7. S. H. Reich, M. A. M. Fuhry, D. Nguyen, M. J. Pino, K. M. Welsh, S. Webber, C. A. Janson, S. R. Jordan and D. A. Matthews, *J. Med. Chem.*, 1992, **35**, 847.

8. W. C. Fernelius, J. E. Blanch, B. E. Bryant, K. Terada, R. S. Drago and J. K. Stille, *Inorg. Synth.*, 1957, **5**, 130.

9. H. M. Yau, A. G. Howe, J. M. Hook, A. K. Croft and J. B. Harper, *Org. Biomol. Chem.*, **2009**, *7*, 3572.

Appendix S1. Derivation of the equation used for calculating relative rate information

For the reaction between *n* and *i* competing reactants s_1, s_2, … s_i, the rate equation related to a given species *i* is:

$$\frac{\mathrm{d}s_i}{\mathrm{dt}} = k_i s_i \left[n_{\mathrm{t=0}} - (s_{1,\mathrm{t=0}} - s_1) - (s_{2,\mathrm{t=0}} - s_2) \ldots + (s_{i,\mathrm{t=0}} - s_i)\right]$$

And its partially integrated form can be expressed as:

$$\ln\left(\frac{s_i}{s_{i,\mathrm{t=0}}}\right) = k_i \int \left[n_{\mathrm{t=0}} - (s_{1,\mathrm{t=0}} - s_1) - (s_{2,\mathrm{t=0}} - s_2) \ldots + (s_{i,\mathrm{t=0}} - s_i)\right] \mathrm{dt}$$

Solving the equation simultaneously for two competing species *x* and *y*, the following expression can be obtained for the calculation of relative rate information based on the amount of starting materials left.

$$\frac{\ln\left(\frac{s_x}{s_{x,\mathrm{t=0}}}\right)}{\ln\left(\frac{s_y}{s_{y,\mathrm{t=0}}}\right)} = \frac{k_x}{k_y}$$

Appendix S2. Details for the calculations of relative rate information using data obtained from NMR spectroscopy

The following nomenclature will be used in the following derivations:

$$X^{(\prime)}{}_{\sigma,n}$$

Where X = N for the integration of a bromide before pyridine was added, S for an integration related to a bromide starting material after a competition experiment and P for an integration related to a pyridinium bromide product after a competition experiment; σ is the relevant substituent; n is the number of bromides initially present. An un-primed term corresponds to the absolute integration of a species where as a primed term correspond to a normalised integration. Additionally, the terms related to integrations that could not be experimentally separated form one another are always given together as:

$$(\overline{X}'_{\sigma_1,n} + \overline{X}'_{\sigma_2,n})$$

For signals in the starting material mixture containing all seven starting materials that are unresolved due to overlap with the signal of another species, its normalised integration can be calculated as follows:

$$N'_{R,7} = \frac{N'_{R,5}}{m}\left(\sum_{m}\frac{N'_{\sigma_m,7}}{N'_{\sigma_m,5}}\right)$$

Where m (≥ 1) is the number of pairs of starting material and product that are both well-resolved in the NMR spectrum.

For the two starting materials that are not initially present in the mixture containing only five starting materials with well-resolved signals, their normalised integrations are given by:

$$N'_R = (\overline{N}'_R + \overline{N}'_\sigma) - N'_\sigma$$

For any well-resolved signal the following expressions can be used to calculate its normalised integration:

$$N'_{R,7} = \frac{N_{R,7}}{\sum N_{\sigma,7}}$$

$$S'_{R,7} = \frac{S_{R,7}}{\sum S_{\sigma,7} + \sum P_{\sigma,7}}$$

And

$$P'_{R,7} = \frac{P_{R,7}}{\sum S_{\sigma,7} + \sum P_{\sigma,7}}$$

If the only one of the signals of a starting material and its related product is unresolved, the following expressions can be used to calculate the relevant normalised integration of interest:

$$S'_{R,7} = N'_{R,7} - S'_{R,7}$$

And

$$P'_{R,7} = N'_{R,7} - S'_{R,7}$$

The normalised integrations for all other species with both signals due to the starting material and its related product unresolved, the normalised integration of interest can be calculated as:

$$S'_{R_1} = \left(\bar{S}'_{R_1} + \bar{S}'_{R_2}\right) - S'_{R_2}$$

Or

$$P'_{R_1} = \left(\bar{P}'_{R_1} + \bar{P}'_{R_2}\right) - P'_{R_2}$$

Appendix S3. Details for the calculation of relative rate information using data obtained from reverse-phase HPLC

The nomenclature used in the following derivation is given by:

$$X^{(\circ)}{}_{\sigma,\lambda}$$

Where X = S and s for the integration and concentration, respectively, of an acetophenone starting material, P and p for the integration and concentration, respectively, of an aryl ethyl alcohol product; σ is the substituent in question; λ is the operating wavelength. The superscript ° indicates whether or not matrix effect is accounted for using calibration curves obtained from mixed standards consisting of all starting materials and products. When two signals cannot be resolved due to overlap, the sum of their integrations are expressed as:

$$\left(\overline{X}^{\circ}{}_{\sigma_1,\lambda} + \overline{X}^{\circ}{}_{\sigma_2,\lambda}\right)$$

The concentration of a given well-resolved starting material or product is calculated using calibration curves obtained from mixed standards such that matrix effects are accounted for:

$$s_{\sigma,\lambda} = \frac{S^{\circ}{}_{\sigma,\lambda} - b^{\circ}{}_{\sigma,\lambda}}{\varepsilon^{\circ}{}_{\sigma,\lambda}}$$

Or

$$p_{\sigma,\lambda} = \frac{P^{\circ}{}_{\sigma,\lambda} - b^{\circ}{}_{\sigma,\lambda}}{\varepsilon^{\circ}{}_{\sigma,\lambda}}$$

Where ε° and b° are the slope and intercept of the relevant calibration curve.

In cases where the signals due to two species, σ_1 and σ_2, overlap at one wavelength, λ_1, and one of them, say, σ_2, is only observable at another wavelength, λ_2; the integration of σ_1 can be calculated by the following expression:

$$X_{\sigma_1,\lambda_1} = \left(\overline{X}^{\circ}{}_{\sigma_1,\lambda_1} + \overline{X}^{\circ}{}_{\sigma_2,\lambda_1}\right) - X_{\sigma_2,\lambda_1}\left(\frac{X^{\circ}{}_{\sigma_2,\lambda_2}}{X_{\sigma_2,\lambda_2}}\right)$$

Which can be used to construct a calibration curve that takes into account matrix effect for the overlapping species, σ_1, and subsequently used in concentration analyses:

$$x_{\sigma_1,\lambda_1} = \frac{\left[\left(\overline{X}^{\circ}_{\sigma_1,\lambda_1} + \overline{X}^{\circ}_{\sigma_2,\lambda_1}\right) - X_{\sigma_2,\lambda_1}\left(\frac{X^{\circ}_{\sigma_2,\lambda_2}}{X_{\sigma_2,\lambda_2}}\right)\right] - b^{\circ}_{\sigma_1,\lambda_1}}{\varepsilon^{\circ}_{\sigma_1,\lambda_1}}$$