Electronic Supplementary Material (ESI) for Catalysis Science & Technology.

- Supplementary Information -

Are rate and selectivity correlated in iridium-catalysed hydrogen isotope exchange reactions?

Daria S. Timofeeva, David M. Lindsay,* William J. Kerr,* and David J. Nelson*

WestCHEM Department of Pure and Applied Chemistry, Thomas Graham Building, 295 Cathedral Street, Glasgow, G1 1XL, UK

david.lindsay@strath.ac.uk, w.kerr@strath.ac.uk, david.nelson@strath.ac.uk

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1. General experimental details

General

For the synthetic procedures, standard Schlenk techniques using an inert gas atmosphere (Ar or N_2) were used, unless otherwise stated. Materials obtained from commercial sources (all acetophenones, ethylbenzoate, nitrobenzene, 2-phenylpyridine, 1-phenylpyrazole, 2-phenyloxozoline, 2-phenylbenzothiazole, 4-nitrobenzoate) were used without further purification. All glassware was flame dried and cooled under a stream of nitrogen.

Materials

(1,3-bis-(2,4,6-trimethylphenyl)imidazolium chloride,[S1] phenylthiazoline,[S2] 2-(4-nitrophenyl)-4,5-dihydrothiazole,[S2] and 1-methyl-2-phenylimidazole[S3] were synthesised according to literature procedures. 2-(4-Acetyl)phenyloxazoline and 2-(4-(pyridin-2-yl)phenyl)-4,5-dihydrooxazole were obtained from the reaction between corresponding aryl nitriles and amino alcohols catalysed by [Cu(Cl)(IPr)].[S4] Anhydrous Na[BAr^F_{24}] (BAr^F_{24} = tetrakis[3,5-bis(trifluoromethyl)phenyl]borate)) was obtained following Bergman's synthesis,[S5] followed by recrystallising the crude Na[$BArF_{24}$]·*x*(solvent) prior to drying.[S6] Phosphine/NHC monodentate complex [Ir(COD)(IMes)(PPh_3)][BAr^F_{24}] was synthesised from [IrCl(COD)(IMes)][S7] in a procedure adapted from that published before for preparation of corresponding complexes with BF_4 and OTf counterions.[S8]

Flash column chromatography was carried out using silica gel (230-400 mesh). Thin layer chromatography (TLC) was performed using Merck silica plates coated with fluorescent indicator and visualised by UV light (254 nm).

Analysis

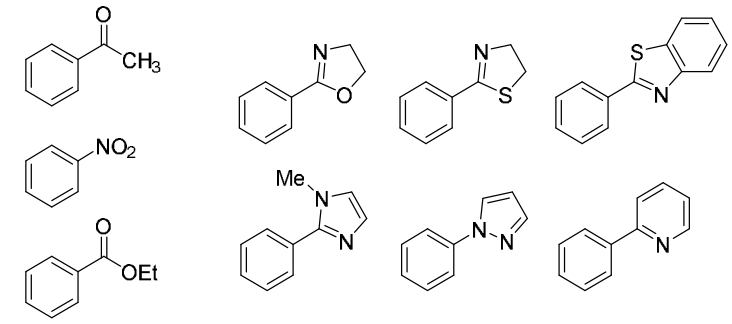
^{1}H (400 MHz) and ^{13}C{^{1}H} (101 MHz) NMR spectra were obtained on a Bruker AV3-400 instrument with a liquid nitrogen Prodigy cryoprobe. The chemical shifts (δ) are reported in ppm relative to the residual protonated solvent for ^{1}H NMR or the solvent signal for ^{13}C{^{1}H} NMR ($CDCl_3$: δ_H 7.26 ppm and δ_C 77.16 ppm).[S9] Coupling constants (*J*) are reported in Hz and refer to $^3J_{H-H}$ couplings, unless otherwise stated. Multiplicities are expressed as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or br (broad signal). If no multiplicity is given for ^{13}C{^{1}H} NMR data, the signal is a singlet. NMR assignments were made using additional 2D NMR experiments where necessary.

LC-MS analyses were carried out using Agilent 6130 with 1200 series LC and UV at 254 nm, with Agilent Poroshell 120 LC column (EC C18 2.7µm x 4.6mm x75mm). LC column conditions were as follows: mobile phase A: water + 5mM ammonium acetate; mobile phase B: acetonitrile + 5mM ammonium acetate; Flow rate: 1.000 mL/min.

Timetable:	Time, min	0	1.48	8.50	13.5	16.5	18.0
	%A	95	95	100	100	95	95
	%B	5	5	0	0	5	5

GC-MS analyses were carried out using an Agilent 7890A gas chromatograph fitted with a ZB-5 MS column (30 m x 0.25 mm I.D. x 0.25 µm) and an Agilent 5975C MSD running in EI mode.

a) For individual kinetics



b) For intramolecular competition kinetics

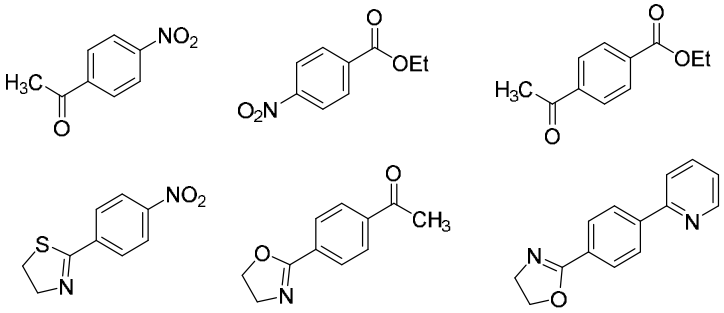
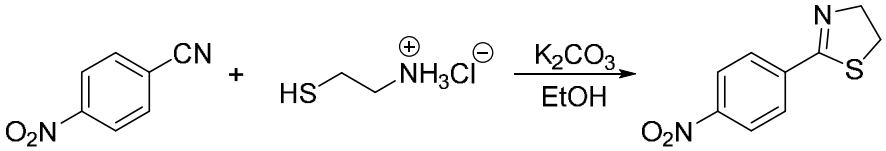


Figure S1. Scope of the substrates used in the study.

2. Synthesis and characterisation

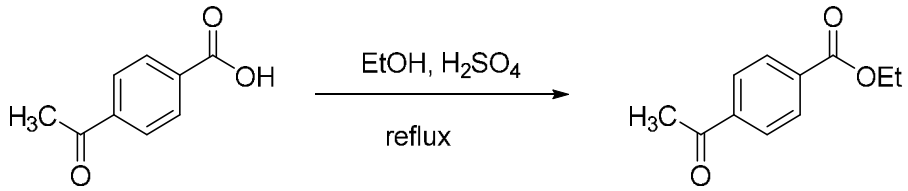
2-(4-nitrophenyl)-4,5-dihydrothiazole[S10]



Potassium carbonate (0.77 g, 5.56 mmol) was added to an ethanol solution (30 ml) of 4-cyanonitrobenzene (0.50 g, 3.37 mmol), and cysteamine hydrochloride (0.57 g, 5.05 mmol) at room temperature. The reaction was then heated at reflux overnight (20 h). The reaction mixture was cooled to room temperature before the ethanol was removed under reduced pressure. The residue was dissolved in ethyl acetate (10 mL) and water (10 mL) was added. The layers were separated and the aqueous layer was then extracted with ethyl acetate (3 × 30 mL). The combined organic layers were dried over $MgSO_4$, filtered, and the solvent was removed under vacuum to give the crude product, which was purified by column chromatography (20 – 50% ethyl acetate in hexane) to afford the title compound as a yellow solid (209 mg, 1.01 mmol, 30 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.28 – 8.22 (m, 2H, Ar-H), 8.03 – 7.94 (m, 2H, Ar-H), 4.51 (t, *J* = 8.5 Hz, 2H, CH_2), 3.49 (t, *J* = 8.5 Hz, 2H, CH_2).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 166.7, 149.4, 138.9, 129.4, 123.8, 65.7, 34.4.
NMR data are consistent with the literature.[S11]

Ethyl 4-acetylbenzoate[S12]

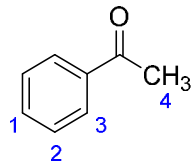


A solution of 4-acetylbenzoic acid (3.0 g, 18.3 mmol) in ethanol (35 mL) was stirred at 0°C in an ice bath. Concentrated H_2SO_4 (0.2 mL, 3.65 mmol) was slowly added and the mixture was heated to 80 °C for 3 h. The the reaction mixture was cooled to room temperature before the ethanol was removed under reduced pressure. The residue was dissolved in ethyl acetate (10 mL) and water (10 mL) was added. The layers were separated and the aqueous layer was then extracted with ethyl acetate (3 × 30 mL). The combined organic layers were dried over MgSO4, filtered, and the solvent was removed under vacuum to give the crude product, which was purified by column chromatography (9% ethyl acetate in hexane) to afford the title compound as a white solid (1.40 g, 7.28 mmol, 38 %).
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.17 – 8.08 (m, 2H, Ar-H), 8.05 – 7.95 (m, 2H, Ar-H), 4.41 (q, *J* = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 2.64 (s, 3H, COC*H*$_3$), 1.41 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ = 197.7, 165.9, 140.3, 134.4, 129.9, 128.3, 61.6, 27.0, 14.4.
NMR data are consistent with the literature.[S12]

Spectral details for unlabeled substrates used in this work:

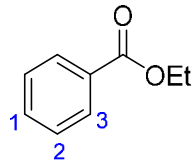
Substrates with single directing groups

Acetophenone



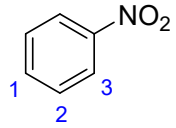
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.99 – 7.93 (m, 2H, H-3), 7.60 – 7.53 (m, 1H, H-1), 7.51 – 7.42 (m, 2H, H-2), 2.61 (s, 3H, H-4).
Incorporation expected at δ 7.99 – 7.93 ppm (H-3)
Determined against integral at δ 2.61 ppm (H-4)

Ethylbenzoate



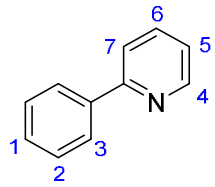
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.08 – 8.02 (m, 2H, H-3), 7.58 – 7.52 (m, 1H, H-1), 7.47 – 7.40 (m, 2H, H-2), 4.38 (q, *J* = 7.1 Hz, 2H, CH_2), 1.40 (t, *J* = 7.1 Hz, 3H, CH_3).
Incorporation expected at δ 8.07 – 8.03 ppm (H-3)
Determined against integral at δ 4.38 ppm (OCH_2CH_3)

Nitrobenzene



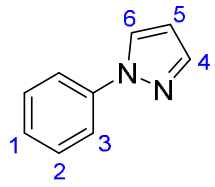
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.26 – 8.20 (m, 2H, H-3), 7.73 – 7.66 (m, 1H, H-1), 7.58 – 7.51 (m, 2H, H-2).
Incorporation expected at δ 8.26 – 8.20 ppm (H-3)
Determined against integral at δ 7.73 – 7.66 ppm (H-1)

2-phenylpyridine



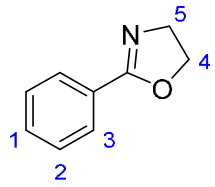
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.73 – 8.67 (m, 1H, H-4), 8.02 – 7.98 (m, 2H, H-3), 7.78 – 7.70 (m, 2H, H-6 and H-7), 7.51 – 7.45 (m, 2H, H-2), 7.45 – 7.39 (m, 1H, H-1), 7.25 – 7.21 (m, 1H, H-5).
Incorporation expected at δ 8.02 – 7.98 ppm (H-3)
Determined against integral at δ 8.73 – 8.67 ppm (H-4) or at δ 7.78 – 7.70 (H-6+H-7) depending on the competition partner.

1-phenylpyrazole



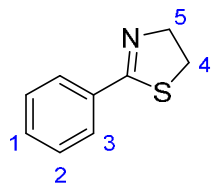
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 (d, *J* = 2.2 Hz, 1H, H-6), 7.75 – 7.68 (m, 3H, H-3 and H-4), 7.48 – 7.43 (m, 2H, H-2), 7.32 – 7.26 (m, 1H, H-1), 6.49 – 6.45 (m, 1H, H-5).
Incorporation expected at δ 7.75 – 7.68 ppm (H-3)
Determined against integral at δ 7.92 ppm (H-6)

2-phenyloxozoline



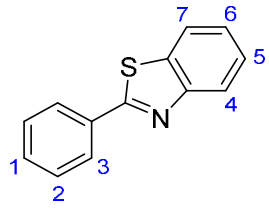
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.97 – 7.93 (m, 2H, H-3), 7.50 – 7.44 (m, 1H, H-1), 7.43 – 7.37 (m, 2H, H-2), 4.43 (t, *J* = 9.5 Hz, 2H, H-4), 4.06 (t, *J* = 9.5 Hz, 2H, H-5).
Incorporation expected at δ 7.97 – 7.93 ppm (H-3)
Determined against integral at δ 4.43 ppm (H-4)

2-phenylthiazoline



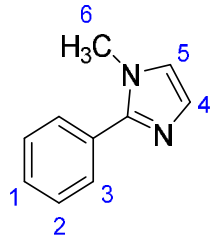
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.86 – 7.81 (m, 2H, H-3), 7.48 – 7.37 (m, 3H, H-1 and H-2), 4.46 (t, *J* = 8.3 Hz, 2H, H-4), 3.41 (t, *J* = 8.3 Hz, 2H, H-5).
Incorporation expected at δ 7.86 – 7.81 ppm (H-3)
Determined against integral at δ 4.46 ppm (H-4)

2-phenylbenzothiazole



^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.14 – 8.06 (m, 3H, H-3 and H-4), 7.91 (d, *J* = 8.0 Hz, 1H, H-7), 7.53 – 7.48 (m, 4H, H-2 and H-5), 7.41-7.37 (m, 1H, H-6).
Incorporation expected at δ 8.14 – 8.06 ppm (H-3)
Incorporation determined against δ 7.91 ppm (H-7)

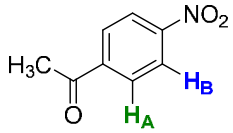
1-methyl-2-phenylimidazole



^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.65 – 7.60 (m, 2H, H-3), 7.47 – 7.34 (m, 3H, H-1 and H-2), 7.12 (d, *J* = 1.2 Hz, 1H, H-5), 6.97 (d, *J* = 1.2 Hz, 1H, H-4), 3.19 (s, 3H, H-6).
Incorporation expected at δ 7.65 – 7.60 ppm (H-3)
Incorporation determined against δ 7.12 ppm (H-5)

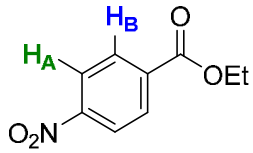
Substrates with multiple directing groups

4-nitroacetophenone



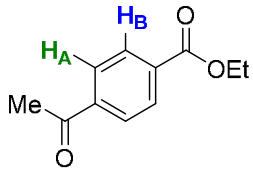
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.33 – 8.30 (m, 2H, H/D_B), 8.13 – 8.09 (m, 2H, H/D_A), 2.68 (s, 3H, CH_3)
Deuteration expected at δ (H_A) = 8.13 – 8.09 ppm and δ (H_B) = 8.33 – 8.30 ppm.
Determined against integral at δ = 2.68 ppm.

ethyl 4-nitrobenzoate



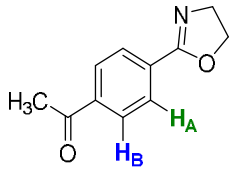
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 – 8.26 (m, 2H, H/D_A), 8.23 – 8.18 (m, 2H, H/D_B), 4.43 (q, *J* = 7.1 Hz, 2H, CH_2), 1.42 (t, *J* = 7.1 Hz, 3H, CH_3).
Deuteration expected at δ (H_A) = 8.30 – 8.26 ppm and δ (H_B) = 8.23 – 8.18 ppm.
Determined against integral at δ = 4.43 ppm.

ethyl 4-acetylbenzoate



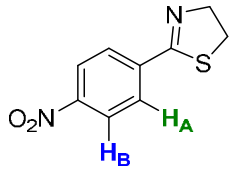
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.17 – 8.08 (m, 2H, Ar-H/D_A), 8.05 – 7.95 (m, 2H, H/D_B), 4.41 (q, *J* = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 2.64 (s, 3H, COC*H*$_3$), 1.41 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$).
Deuteration expected at δ (H_A) = 8.17 – 8.08 ppm and δ (H_B) = 8.05 – 7.95 ppm.
Determined against integral at δ = 4.41 ppm.

2-(4-acetyl)phenyloxazoline



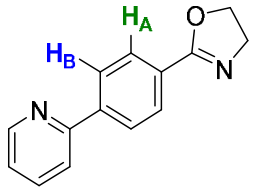
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.06 – 8.01 (m, 2H, H_A), 8.01 – 7.96 (m, 2H, H_B), 4.47 (t, *J* = 9.6 Hz, 3H, CH_2), 4.10 (t, *J* = 9.6 Hz, 2H, CH_2), 2.62 (s, 3H, CH_3).
Deuteration expected at δ (H_A) = 8.06 – 8.01 ppm and δ (H_B) = 8.01 – 7.96 ppm.
Determined against integral at δ = 4.47 ppm.

2-(4-nitrophenyl)-4,5-dihydrothiazole



^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.28 – 8.22 (m, 2H, H_A), 8.03 – 7.94 (m, 2H, H_B), 4.51 (t, *J* = 8.5 Hz, 2H, CH_2), 3.49 (t, *J* = 8.5 Hz, 2H, CH_2).
Deuteration expected at δ (H_A) = 8.28 – 8.22ppm and δ (H_B) =8.03 – 7.94 ppm.
Determined against integral at δ = 4.51 ppm

2-(4-(Pyridin-2-yl)phenyl)-4,5-dihydrooxazole



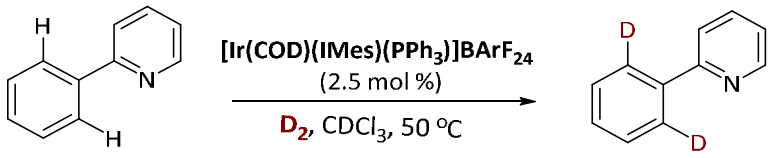
^{1}H NMR (400 MHz, C_6D_6) δ = 8.56 – 8.51 (m, 1H, Ar-H), 8.36 – 8.32 (m, 1H, H_A), 8.17 – 8.11 (m, 2H, H_B), 7.25 – 7.21 (m, 1H, Ar-H), 7.11 – 7.04 (m, 1H, Ar-H), 6.66 – 6.61 (m, 1H, Ar-H), 3.77 – 3.69 (m, 2H, CH_2), 3.67 – 3.59 (m, 2H, CH_2).

Deuteration expected at δ (H_A) = 8.36 – 8.32 ppm and δ (H_B) = 8.17 – 8.11 ppm.

Determined against integral at δ = 3.77 – 3.69 ppm.

3. Kinetic data

3.1. NMR kinetics

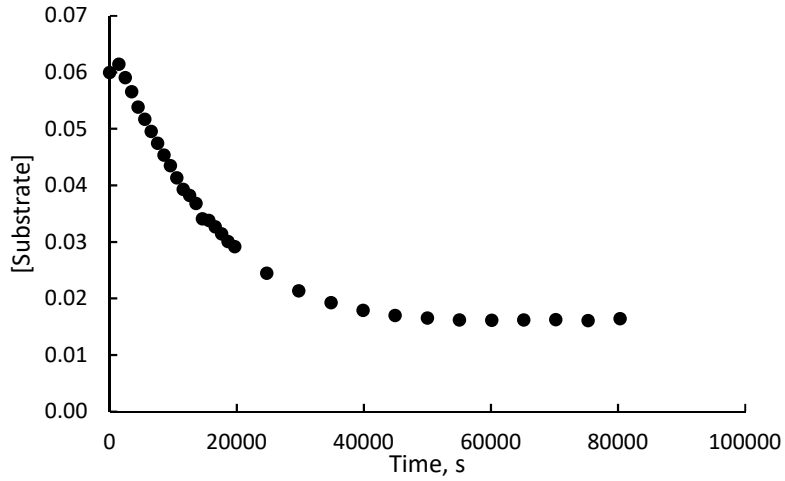


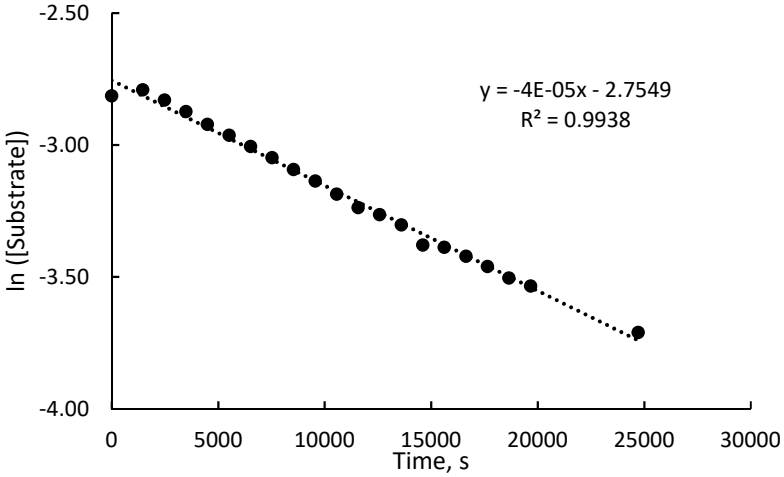
Preparation of Solution 1 (Substrate + catalyst). 2-Phenylpyridine (0.15 mmol, 23.3 mg) and [Ir(COD)(IMes)(PPh_3)][$BAr^F{}_{24}$] (6.5 mg, 0.004 mmol) were added to a 1.00 mL volumetric flask. $CDCl_3$ was then added to the 1 ml mark. The final concentrations were [Substrate]= 0.15 M, [Ir]= 0.004 M.

Preparation of Internal Standard (trimethoxybenzene) Solution. Trimethoxybenzene (0.30 mmol) was added to a 3.00 mL volumetric flask. $CDCl_3$ was then added to the 3 ml mark. The final concentrations were [Internal Standard] = 0.10 M.

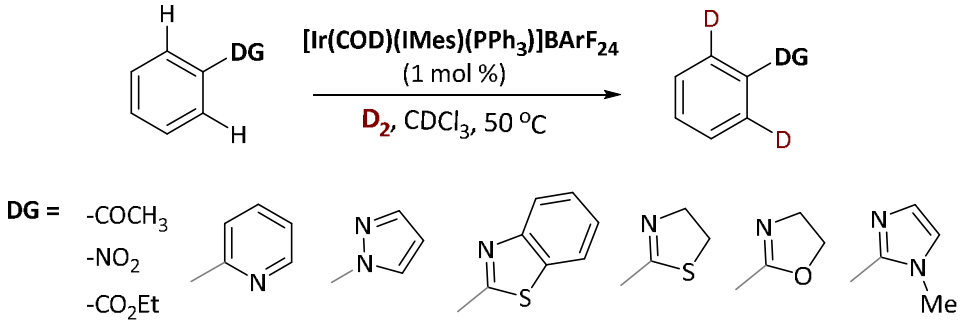
A J. Young NMR tube was charged with 0.20 ml of Solution 1 and 0.3 mL of Internal Standard Solution by syringe ($[substrate]_0$ = 0.06 M). The NMR tube was inserted into the NMR probe, which had been pre-equilibrated to 50 °C, and then after locking and shimming the sample the initial spectrum was acquired. The tube was removed from the magnet, the solution was cooled in an acetone/dry ice bath and the headspace of the tube was evacuated and then refilled with deuterium gas (1 atm) from a balloon. After 3 vacuum/deuterium cycles, the tube was removed from the cooling bath and placed back into the magnet. Automated data acquisition was then started. The kinetics experiment was initiated after reacquiring a lock to $CDCl_3$, but without shimming or tuning. Arrays of ^1H NMR spectra were collected at 600 MHz. Kinetics experiments (arrays of spectra) were implemented using standard Topspin software. Typical experiment: 16 scans per spectrum. The first spectrum was recorded *ca.* 10 min after D_2 was added, with each new spectrum collected in 17 min increments (80 total spectra). The total acquisition time was approximately 22 hours.

The residual proton signal from the site of incorporation (*ortho* to DG) was compared against that of a site where incorporation did not happen and to the peaks of the internal standard. The concentration decay (2-phenylpyridine) over time is shown below for 20 data points each 17 mins and additional 12 data points each 85 mins. The expected linearity of ln [substrate] *vs.* time plots was observed with a gradient of $-k_{obs.}$


0.07
0.06
0.05
0.04
0.03
0.02
0.01
0.00
[Substrate]
0
20000
40000
60000
80000
100000
Time, s


-2.50
-3.00
-3.50
-4.00
ln ([Substrate])
y = -4E-05x - 2.7549
R² = 0.9938
0
5000
10000
15000
20000
25000
30000
Time, s

3.2. General Kinetic Protocol for reaction monitoring by sampling method



Ph-DG (0.50 mmol) and the iridium(I) pre-catalyst (0.005 mmol) were weighed into small vials. The solids were directly transferred to the reaction vial; any liquid substrates were first dissolved in a small amount of $CDCl_3$, the vial was washed with solvent, and the washings were transferred to the reaction vial. The reaction mixture was diluted using 2.5 mL (in total) of $CDCl_3$ ($[Ph\text{-}DG]_0 = 0.20$ mol/L). An aliquot was withdrawn to measure the initial spectrum and the vial was capped.

The solution was cooled in an acetone/dry ice bath and the headspace of the vial was evacuated and then refilled with deuterium gas (1 atm) from the balloon. After 3 vacuum/deuterium cycles, the reaction vial was removed from the cooling bath and placed in an aluminum block or thermostat-controlled water bath that had been preheated to 50 °C and the timer was started. The reaction mixture was then stirred vigorously (860 rpm) at 50 °C for 1-2 mins, allowing for catalyst activation and temperature equilibrium before the first aliquot was taken. The deuterium balloon was left in place for the duration of the reaction to ensure a continuous supply (and an excess) of D_2.

The aliquots (0.04 mL) of reaction mixture were removed at the specified intervals throughout the reaction *via* syringe to an NMR tube and diluted with 0.5 mL of $CDCl_3$.

The concentrations of the Ph-DG substrate (starting material) were determined by ^1H NMR analysis. The residual proton signal from the site of incorporation (*ortho* to DG) was compared against that of a site where incorporation did not happen.

Plots of concentration of unlabeled substrate *vs.* time show clear mono-exponential kinetic behavior. The expected linearity of ln [substrate] *vs.* time plots was observed with a gradient of $-k_{obs}$. All the kinetics with single substrate were run in duplicate and the averaged positive values of this gradient are shown in the manuscript (Table 1).

3.3. Kinetic data from single substrate experiments

Table S1. Rate monitoring for the deuteration of acetophenone (run 1)

Following the General Kinetic Protocol using 60.1 mg of acetophenone, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	300	1.80	0.180	-1.71
2	600	1.63	0.163	-1.81
3	900	1.45	0.145	-1.93
4	1500	1.14	0.114	-2.17
5	2100	0.87	0.087	-2.44
6	2700	0.69	0.069	-2.67
7	3300	0.59	0.059	-2.83
8	3900	0.51	0.051	-2.98
9	6300	0.39	0.039	-3.24
10	9900	0.38	0.038	-3.27
$k_{obs} = 3.88 \times 10^{-4}\ (s^{-1})$				

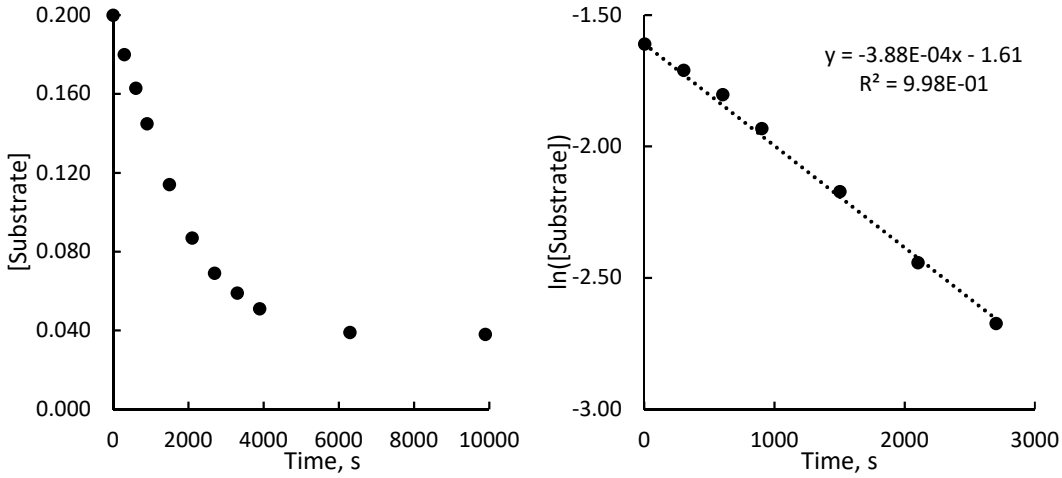


Table S2. Rate monitoring for the deuteration of acetophenone (run 2)

Following the General Kinetic Protocol using 60.1 mg of acetophenone, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	300	1.73	0.173	-1.75
2	600	1.51	0.151	-1.89
3	900	1.32	0.132	-2.02
4	1200	1.16	0.116	-2.15
5	1800	0.98	0.098	-2.32
6	2400	0.82	0.082	-2.50
7	3000	0.73	0.073	-2.62
8	3600	0.64	0.064	-2.75
9	5400	0.56	0.056	-2.88
10	7200	0.54	0.054	-2.92
11	10800	0.50	0.050	-3.00
$k_{obs} = 3.98 \times 10^{-4}\ (s^{-1})$				

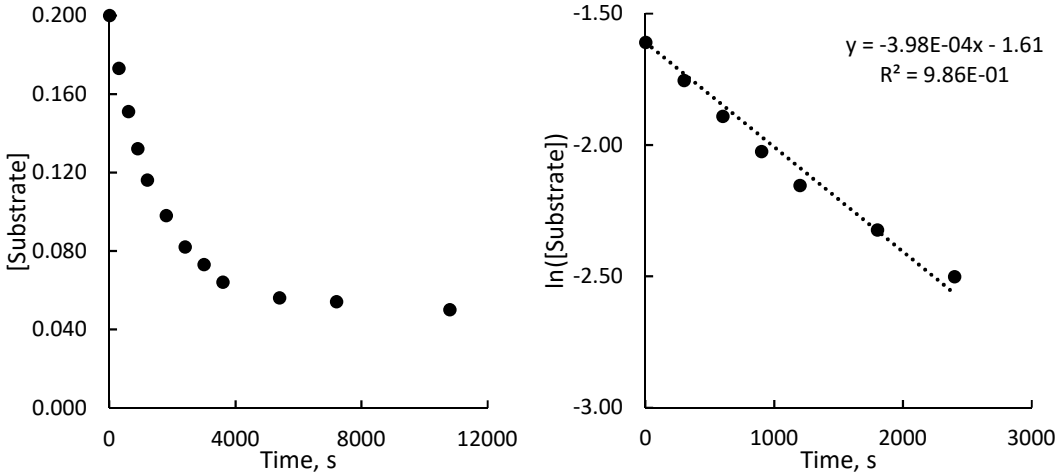
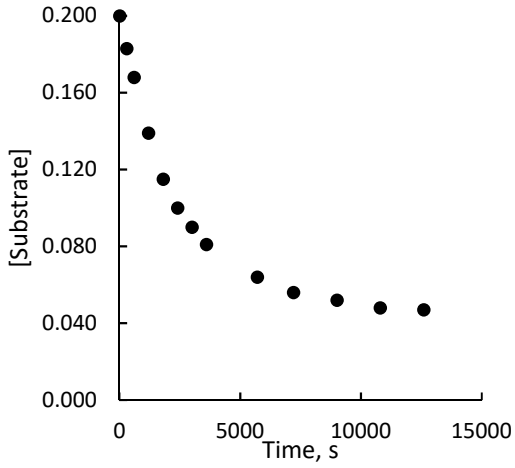


Table S3. Rate monitoring for the deuteration of nitrobenzene (run 1)

Following the General Kinetic Protocol using 61.5 mg of nitrobenzene, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	300	1.83	0.183	-1.70
2	600	1.68	0.168	-1.78
3	1200	1.39	0.139	-1.97
4	1800	1.15	0.115	-2.16
5	2400	1.00	0.100	-2.30
6	3000	0.90	0.090	-2.41
7	3600	0.81	0.081	-2.51
8	5700	0.64	0.064	-2.75
9	7200	0.56	0.056	-2.88
10	9000	0.52	0.052	-2.96
11	10800	0.48	0.048	-3.04
12	12600	0.47	0.047	-3.06
$k_{obs} = 2.70 \times 10^{-4}\ (s^{-1})$				



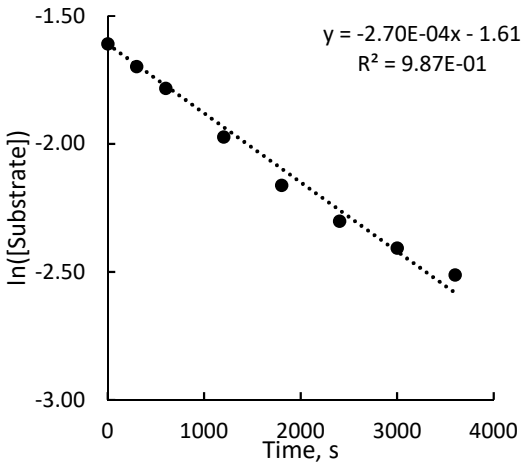
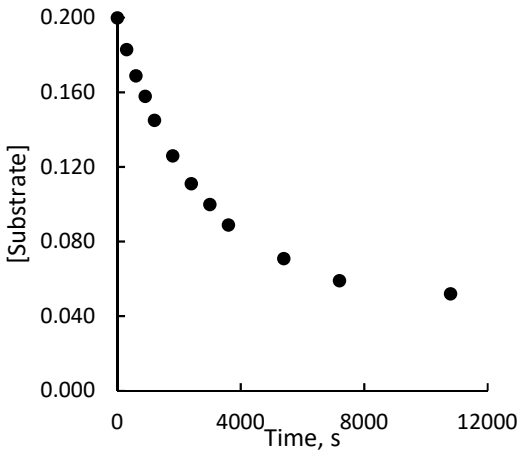


Table S4. Rate monitoring for the deuteration of nitrobenzene (run 2)

Following the General Kinetic Protocol using 61.5 mg of nitrobenzene, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	300	1.83	0.183	-1.70
2	600	1.69	0.169	-1.78
3	900	1.58	0.158	-1.85
4	1200	1.45	0.145	-1.93
5	1800	1.26	0.126	-2.07
6	2400	1.11	0.111	-2.20
7	3000	1.00	0.100	-2.30
8	3600	0.89	0.089	-2.42
9	5400	0.71	0.071	-2.65
10	7200	0.59	0.059	-2.83
11	10800	0.52	0.052	-2.96
$k_{obs} = 2.36 \times 10^{-4}\ (s^{-1})$				



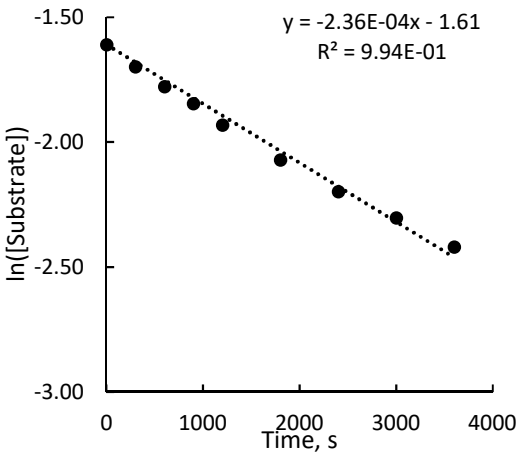
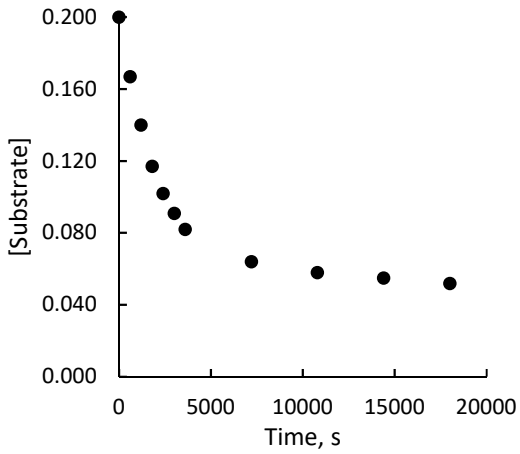


Table S5. Rate monitoring for the deuteration of ethyl benzoate (run 1)

Following the General Kinetic Protocol using 75.1 mg of ethyl benzoate, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	600	1.67	0.167	-1.79
2	1200	1.40	0.140	-1.97
3	1800	1.17	0.117	-2.15
4	2400	1.02	0.102	-2.28
5	3000	0.91	0.091	-2.40
6	3600	0.82	0.082	-2.50
7	7200	0.64	0.064	-2.75
8	10800	0.58	0.058	-2.85
9	14400	0.55	0.055	-2.90
10	18000	0.52	0.052	-2.96
$k_{obs} = 2.65 \times 10^{-4}\ (s^{-1})$				



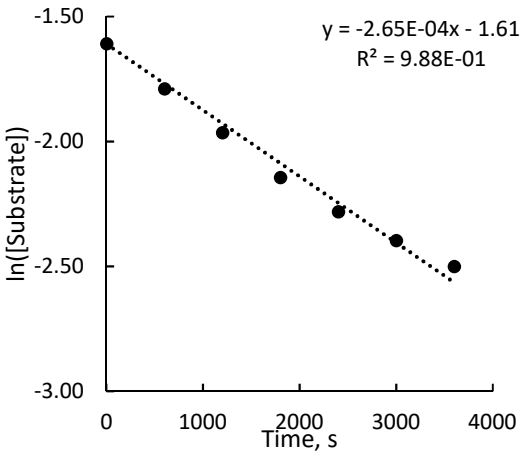


Table S6. Rate monitoring for the deuteration of ethyl benzoate (run 2)

Following the General Kinetic Protocol using 75.1 mg of ethyl benzoate, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	300	1.78	0.178	-1.73
2	600	1.63	0.163	-1.81
3	1200	1.38	0.138	-1.98
4	1800	1.22	0.122	-2.10
5	2400	1.06	0.106	-2.24
6	3000	0.97	0.097	-2.33
7	3600	0.90	0.090	-2.41
8	7200	0.75	0.075	-2.59
9	10800	0.72	0.072	-2.63
$k_{obs} = 2.61 \times 10^{-4}\ (s^{-1})$				

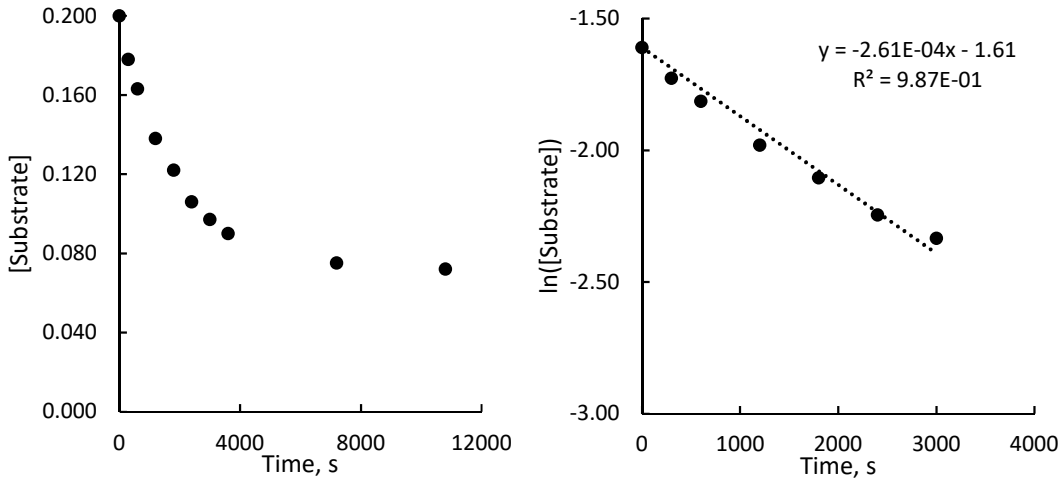
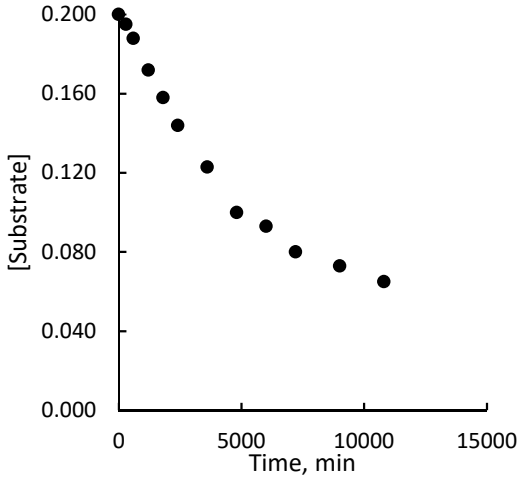


Table S7. Rate monitoring for the deuteration of 2-phenylpyridine (run 1)

Following the General Kinetic Protocol using 77.6 mg of 2-phenylpyridine, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	300	1.95	0.195	-1.63
2	600	1.88	0.188	-1.67
3	1200	1.72	0.172	-1.76
4	1800	1.58	0.158	-1.85
5	2400	1.44	0.144	-1.94
6	3600	1.23	0.123	-2.10
7	4800	1.00	0.100	-2.30
8	6000	0.93	0.093	-2.38
9	7200	0.80	0.080	-2.53
10	9000	0.73	0.073	-2.62
11	10800	0.65	0.065	-2.73
$k_{obs} = 1.32 \times 10^{-4}$ (s^{-1})				



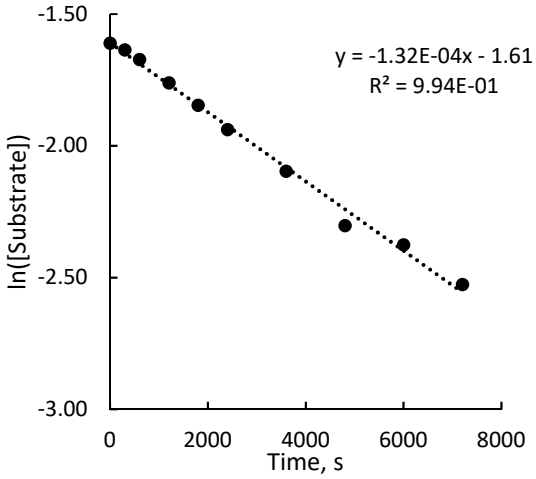
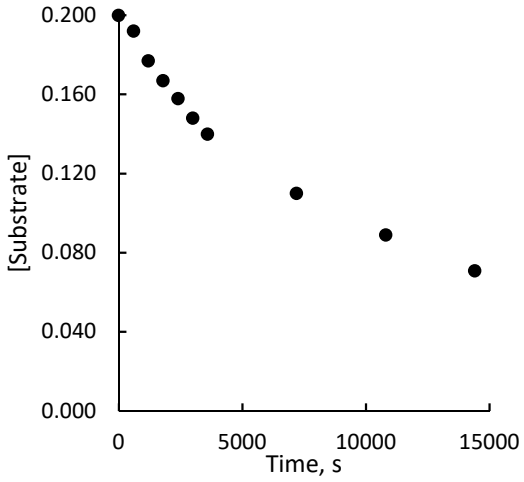


Table S8. Rate monitoring for the deuteration of 2-phenylpyridine (run 2)

Following the General Kinetic Protocol using 77.6 mg of 2-phenylpyridine, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	600	1.92	0.192	-1.65
2	1200	1.77	0.177	-1.73
3	1800	1.67	0.167	-1.79
4	2400	1.58	0.158	-1.85
5	3000	1.48	0.148	-1.91
6	3600	1.40	0.140	-1.97
7	7200	1.10	0.110	-2.21
8	10800	0.89	0.089	-2.42
9	14400	0.71	0.071	-2.65
$k_{obs} = 9.90 \times 10^{-5}\ (s^{-1})$				



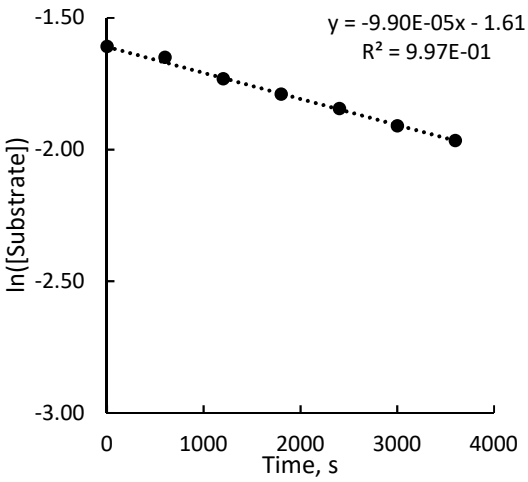
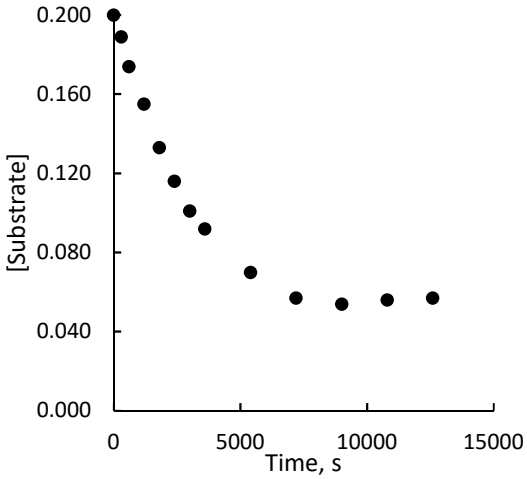


Table S9. Rate monitoring for the deuteration of 2-phenylbenzothiazole (run 1)

Following the General Kinetic Protocol using 105.6 mg of 2-phenylbenzothiazole, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	300	1.89	0.189	-1.67
2	600	1.74	0.174	-1.75
3	1200	1.55	0.155	-1.86
4	1800	1.33	0.133	-2.02
5	2400	1.16	0.116	-2.15
6	3000	1.01	0.101	-2.29
7	3600	0.92	0.092	-2.39
8	5400	0.70	0.070	-2.66
9	7200	0.57	0.057	-2.86
10	9000	0.54	0.054	-2.92
11	10800	0.56	0.056	-2.88
12	12600	0.57	0.057	-2.86
$k_{obs} = 2.24 \times 10^{-4}\ (s^{-1})$				



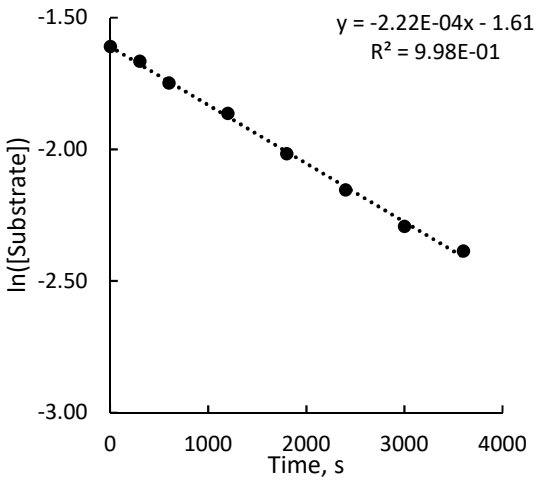


Table S10. Rate monitoring for the deuteration of 2-phenylbenzothiazole (run 2)

Following the General Kinetic Protocol using 105.6 mg of 2-phenylbenzothiazole, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	300	1.88	0.188	-1.67
2	600	1.71	0.171	-1.77
3	900	1.63	0.163	-1.81
4	1200	1.49	0.149	-1.90
5	1800	1.32	0.132	-2.02
6	2400	1.16	0.116	-2.15
7	3000	1.02	0.102	-2.28
8	3600	0.95	0.095	-2.35
9	7200	0.68	0.068	-2.69
10	10800	0.53	0.053	-2.94
11	14400	0.50	0.050	-3.00
$k_{obs} = 2.20 \times 10^{-4}\ (s^{-1})$				

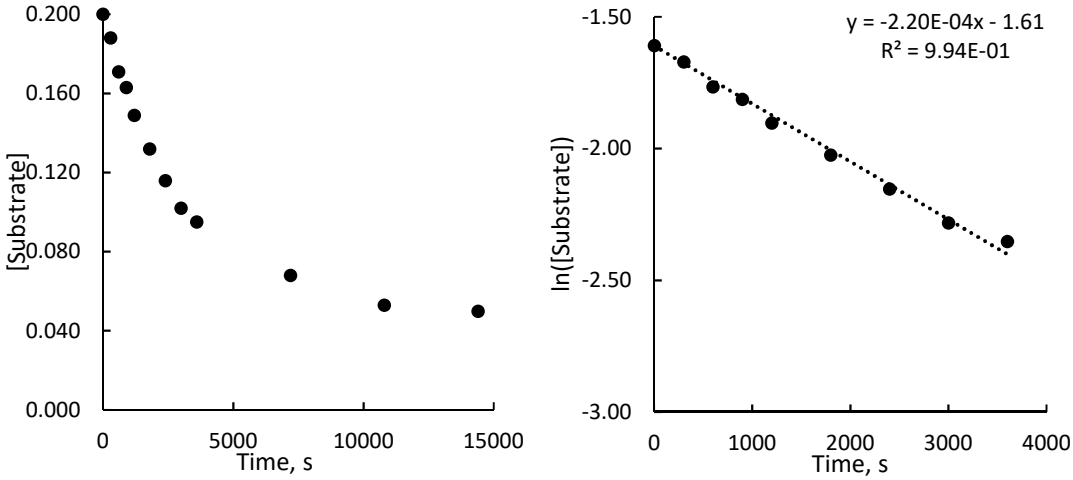
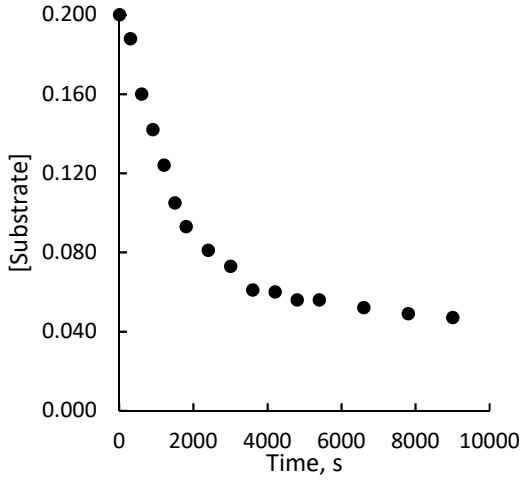


Table S11. Rate monitoring for the deuteration of 1-phenylpyrazole (run 1)

Following the General Kinetic Protocol using 72.1 mg of 1-phenylpyrazole, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	300	1.88	0.188	-1.67
2	600	1.60	0.160	-1.83
3	900	1.42	0.142	-1.95
4	1200	1.24	0.124	-2.09
5	1500	1.05	0.105	-2.25
6	1800	0.93	0.093	-2.38
7	2400	0.81	0.081	-2.51
8	3000	0.73	0.073	-2.62
9	3600	0.61	0.061	-2.80
10	4200	0.60	0.060	-2.81
11	4800	0.56	0.056	-2.88
12	5400	0.56	0.056	-2.88
13	6600	0.52	0.052	-2.96
14	7800	0.49	0.049	-3.02
15	9000	0.47	0.047	-3.06
$k_{obs} = 3.97 \times 10^{-4}\ (s^{-1})$				



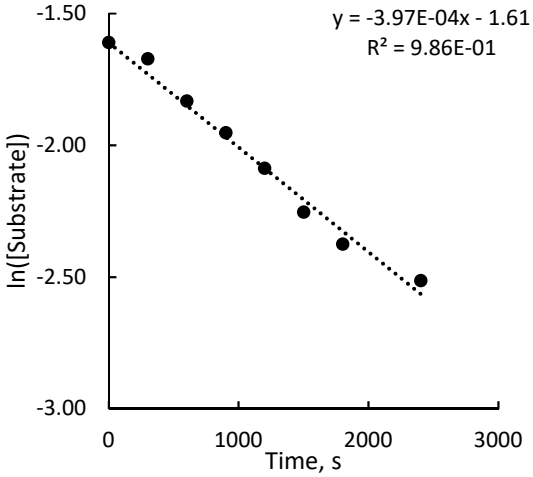
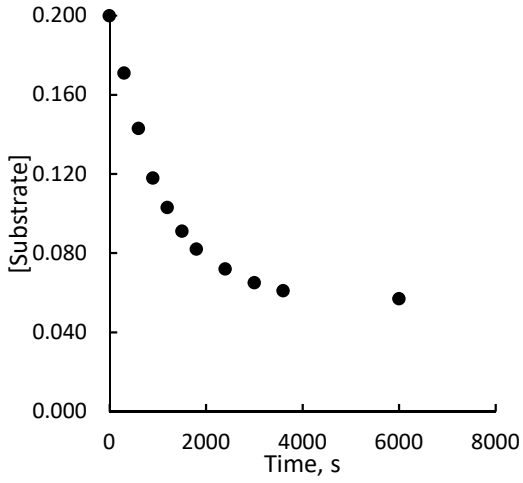


Table S12. Rate monitoring for the deuteration of 1-phenylpyrazole (run 2)

Following the General Kinetic Protocol using 72.1 mg of 1-phenylpyrazole, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	300	1.71	0.171	-1.77
2	600	1.43	0.143	-1.94
3	900	1.18	0.118	-2.14
4	1200	1.03	0.103	-2.27
5	1500	0.91	0.091	-2.40
6	1800	0.82	0.082	-2.50
7	2400	0.72	0.072	-2.63
8	3000	0.65	0.065	-2.73
9	3600	0.61	0.061	-2.80
10	6000	0.57	0.057	-2.86
$k_{obs} = 4.84 \times 10^{-4}$ (s^{-1})				



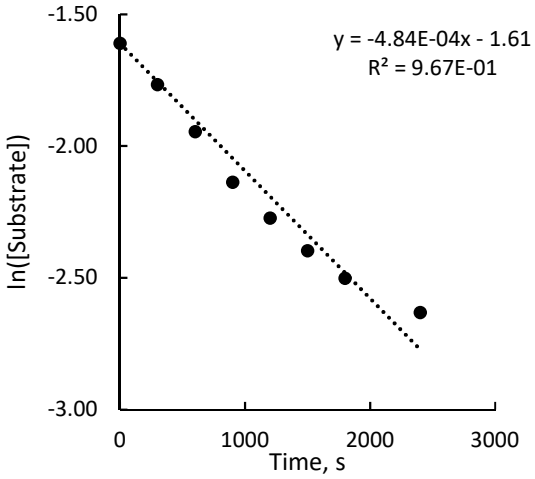


Table S13. Rate monitoring for the deuteration of 2-phenylthiazoline (run 1)

Following the General Kinetic Protocol using 81.6 mg of 2-phenylthiazoline, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	300	1.86	0.186	-1.68
2	1200	1.55	0.155	-1.86
3	1800	1.39	0.139	-1.97
4	2400	1.25	0.125	-2.08
5	3000	1.13	0.113	-2.18
6	3600	1.06	0.106	-2.24
7	7200	0.77	0.077	-2.56
8	10800	0.74	0.074	-2.60
$k_{obs} = 1.96 \times 10^{-4}\ (s^{-1})$				

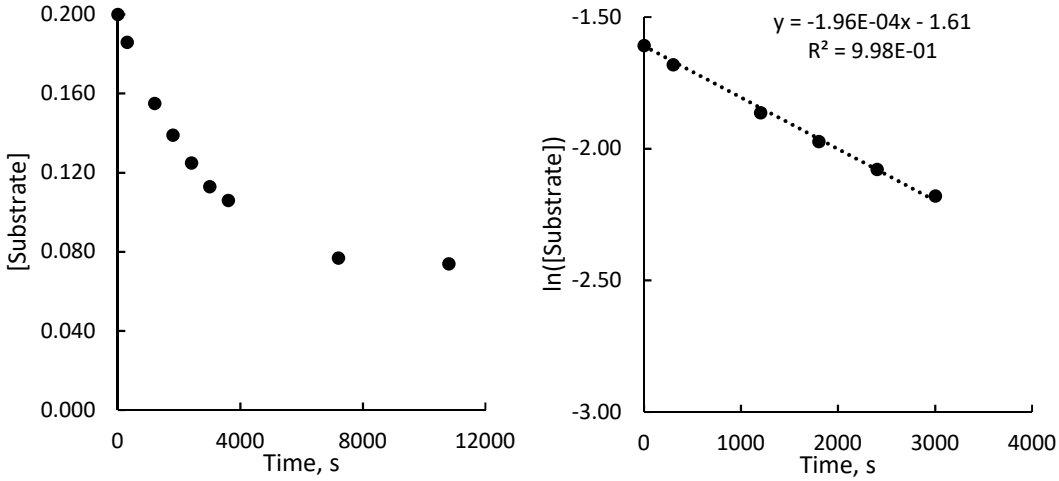


Table S14. Rate monitoring for the deuteration of 2-phenylthiazoline (run 2)

Following the General Kinetic Protocol using 81.6 mg of 2-phenylthiazoline, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	300	1.81	0.181	-1.71
2	600	1.67	0.167	-1.79
3	1200	1.43	0.143	-1.94
4	1800	1.22	0.122	-2.10
5	2400	1.11	0.111	-2.20
6	3000	1.00	0.100	-2.30
7	3600	0.94	0.094	-2.36
8	5400	0.85	0.085	-2.47
9	7200	0.78	0.078	-2.55
$k_{obs} = 2.47 \times 10^{-4}\ (s^{-1})$				

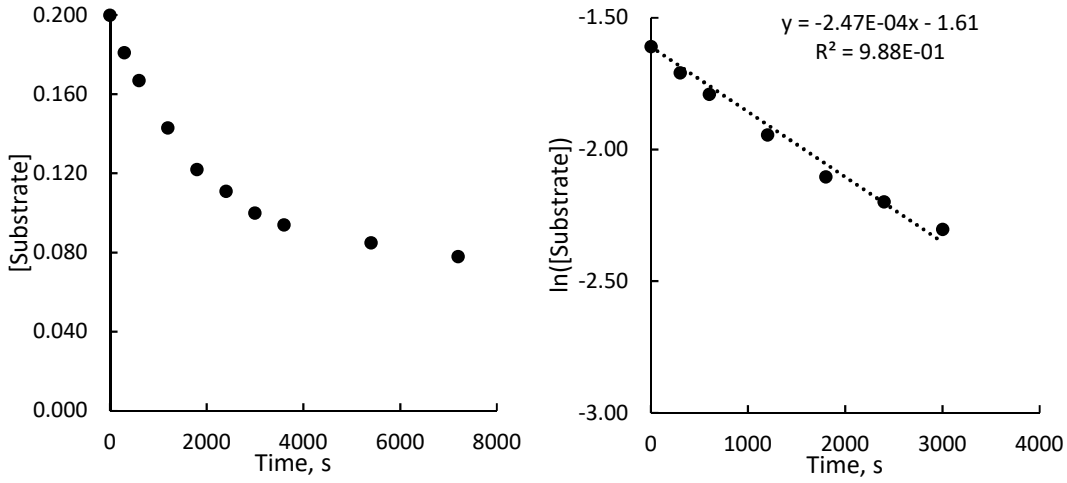


Table S15. Rate monitoring for the deuteration of 2-phenyloxazoline (run 1)

Following the General Kinetic Protocol using 73.6 mg of 2-phenyloxazoline, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	300	1.66	0.166	-1.80
2	600	1.37	0.137	-1.99
3	900	1.06	0.106	-2.24
4	1200	0.87	0.087	-2.44
5	1800	0.64	0.064	-2.75
6	2400	0.56	0.056	-2.88
7	3000	0.51	0.051	-2.98
8	3600	0.50	0.050	-3.00
9	5400	0.49	0.049	-3.02
10	7200	0.48	0.048	-3.04
$k_{obs} = 6.57 \times 10^{-4}\ (s^{-1})$				

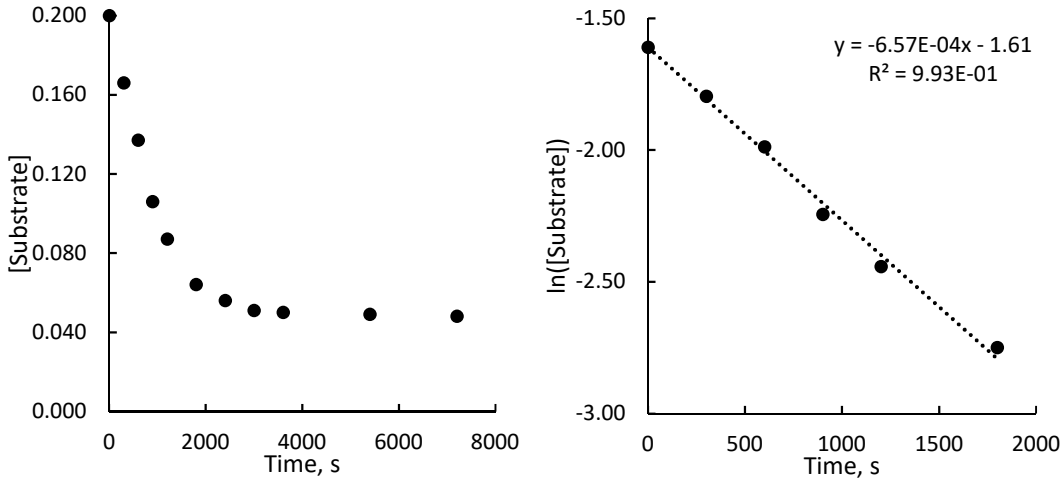


Table S16. Rate monitoring for the deuteration of 2-phenyloxazoline (run 2)

Following the General Kinetic Protocol using 73.6 mg of 2-phenyloxazoline, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	300	1.64	0.164	-1.81
2	600	1.43	0.143	-1.94
3	900	1.21	0.121	-2.11
4	1200	1.05	0.105	-2.25
5	1800	0.83	0.083	-2.49
6	2400	0.74	0.074	-2.60
7	3000	0.65	0.065	-2.73
8	3600	0.63	0.063	-2.76
9	5400	0.60	0.060	-2.81
10	7200	0.57	0.057	-2.86
11	10800	0.54	0.054	-2.92
$k_{obs} = 5.16 \times 10^{-4}$ (s^{-1})				

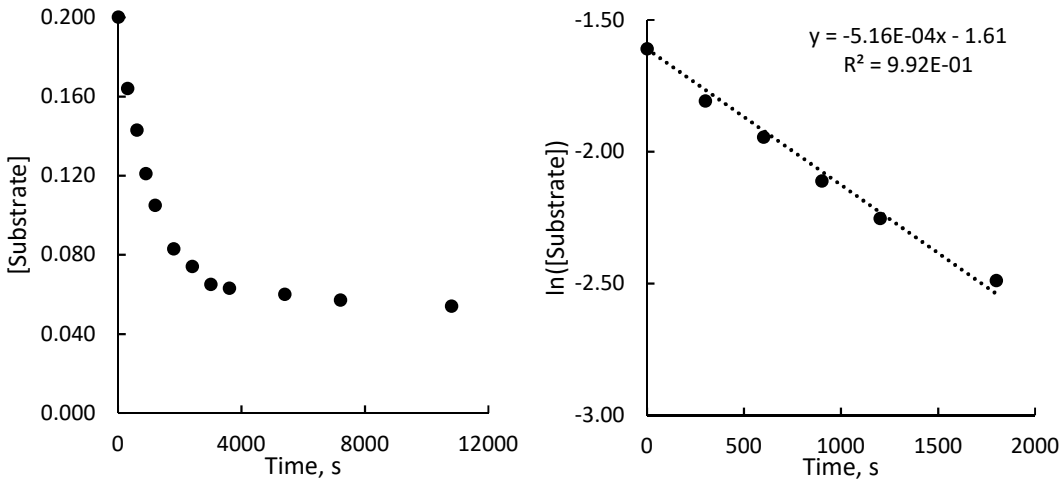
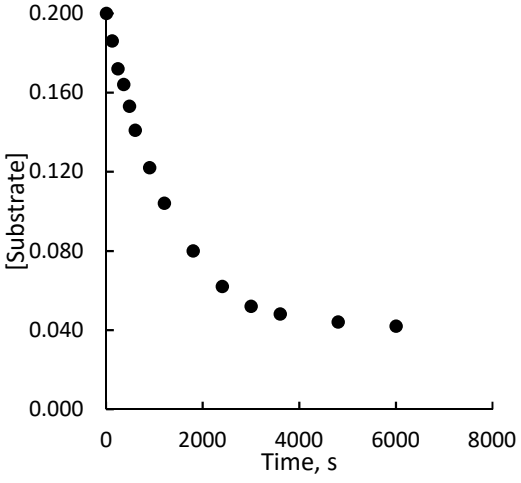


Table S17. Rate monitoring for the deuteration of 1-methyl-2-phenylimidazole (run 1)

Following the General Kinetic Protocol using 79.1 mg of 1-methyl-2-phenylimidazole, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	120	1.86	0.186	-1.68
2	240	1.72	0.172	-1.76
3	360	1.64	0.164	-1.81
4	480	1.53	0.153	-1.88
5	600	1.41	0.141	-1.96
6	900	1.22	0.122	-2.10
7	1200	1.04	0.104	-2.26
8	1800	0.80	0.080	-2.53
9	2400	0.62	0.062	-2.78
10	3000	0.52	0.052	-2.96
11	3600	0.48	0.048	-3.04
12	4800	0.44	0.044	-3.12
13	6000	0.42	0.042	-3.17
$k_{obs} = 5.10 \times 10^{-4}\ (s^{-1})$				



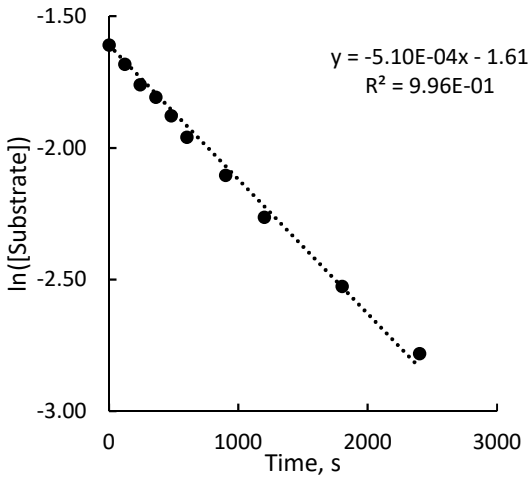
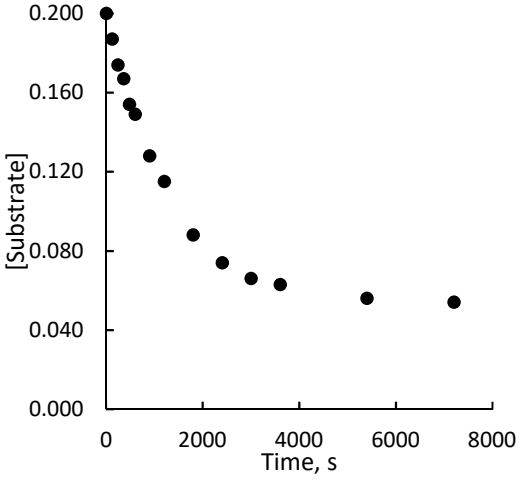


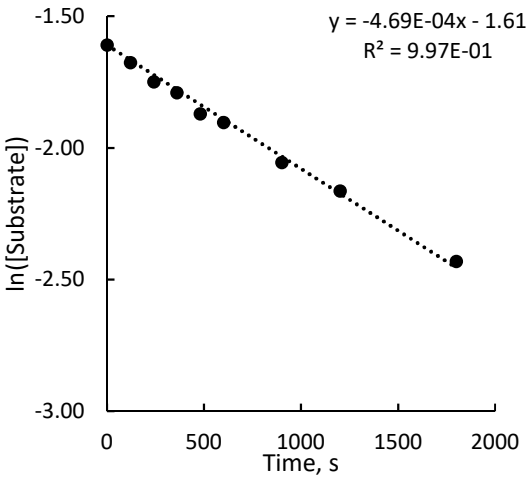
Table S18. Rate monitoring for the deuteration of 1-methyl-2-phenylimidazole (run 2)

Following the General Kinetic Protocol using 79.1 mg of 1-methyl-2-phenylimidazole, 8.7 mg of Ir-catalyst.

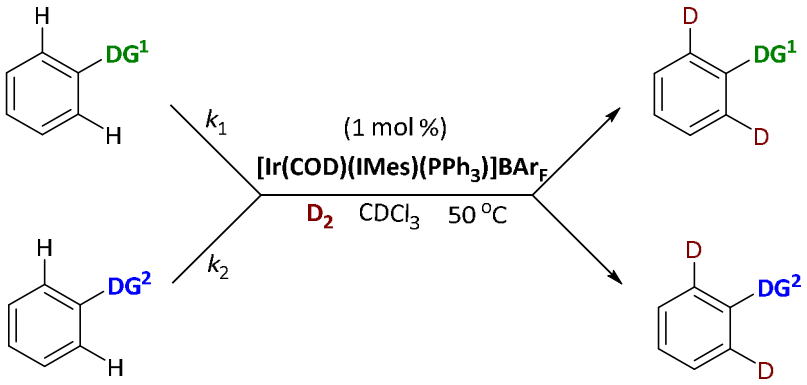
Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	120	1.87	0.187	-1.68
2	240	1.74	0.174	-1.75
3	360	1.67	0.167	-1.79
4	480	1.54	0.154	-1.87
5	600	1.49	0.149	-1.90
6	900	1.28	0.128	-2.06
7	1200	1.15	0.115	-2.16
8	1800	0.88	0.088	-2.43
9	2400	0.74	0.074	-2.60
10	3000	0.66	0.066	-2.72
11	3600	0.63	0.063	-2.76
12	5400	0.56	0.056	-2.88
13	7200	0.54	0.054	-2.92

$$k_{obs} = 4.69 \times 10^{-4}\ (s^{-1})$$





3.4. Kinetic Data from two substrates kinetic experiments (Intermolecular competition)



Following the Standard Kinetics Protocol, the competing isotope labeling of **Ph-DG^1** (0.50 mmol) and **Ph- DG^2** (0.50 mmol) using 1 mol % of the Ir-catalyst (0.005 mmol, 8.7 mg) with respect to both substrates were monitored at 50 °C in $CDCl_3$ by the sampling method and analysed by ^{1}H NMR spectroscopy.

The concentrations of the Ph-DG substrates (starting materials) were determined by ^{1}H NMR analysis. The residual proton signal from the site of incorporation (*ortho* to DG) was compared against that of a site where incorporation did not happen.

The tables and plots below combine the obtained concentration over time data.

Table S19. Rate monitoring for the competing deuteration of acetophenone *vs* nitrobenzene

		acetophenone		nitrobenzene	
Entry	**Time, min**	**integral (H/D)**	**[Ph-DG^1]**	**integral (H/D)**	**[Ph-DG^2]**
0	0	2.00	0.200	2.00	0.200
1	10	1.73	0.173	1.99	0.199
2	20	1.45	0.145	1.89	0.189
3	30	1.26	0.126	1.77	0.177
4	40	1.13	0.113	1.63	0.163
5	50	1.04	0.104	1.50	0.150
6	60	0.98	0.098	1.38	0.138
7	90	0.87	0.087	1.15	0.115
8	120	0.83	0.083	0.98	0.098
9	150	0.78	0.078	0.88	0.088

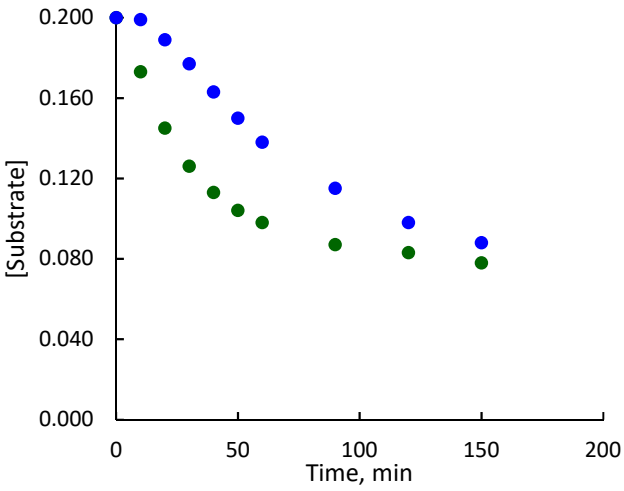


Table S20. Rate monitoring for the competing deuteration of 1-phenylpyrazole *vs* 2-phenylpyridine

		1-phenylpyrazole		2-phenylpyridine	
Entry	**Time, min**	**integral (H/D)**	**[Ph-DG^1]**	**integral (H/D)**	**[Ph-DG^2]**
0	0	2.00	0.200	2.00	0.200
1	10	1.63	0.163	1.83	0.183
2	20	1.45	0.145	1.69	0.169
3	30	1.33	0.133	1.55	0.155
4	40	1.23	0.123	1.43	0.143
5	50	1.19	0.119	1.34	0.134
6	60	1.12	0.112	1.26	0.126
7	90	0.82	0.082	0.87	0.087
8	120	0.69	0.069	0.62	0.062
9	150	0.64	0.064	0.48	0.048

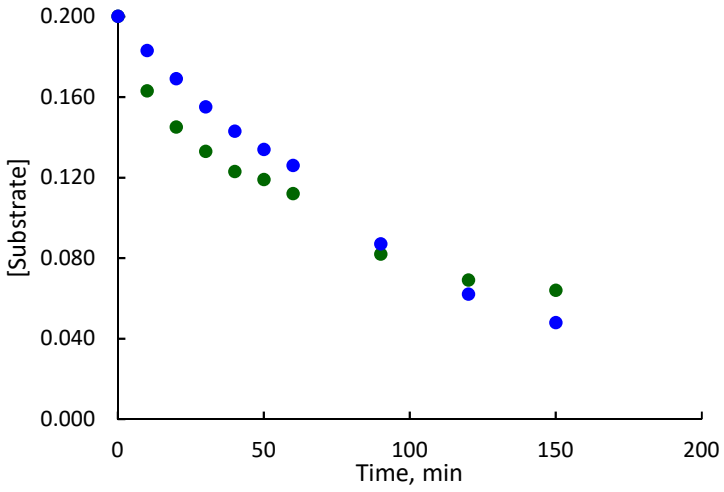
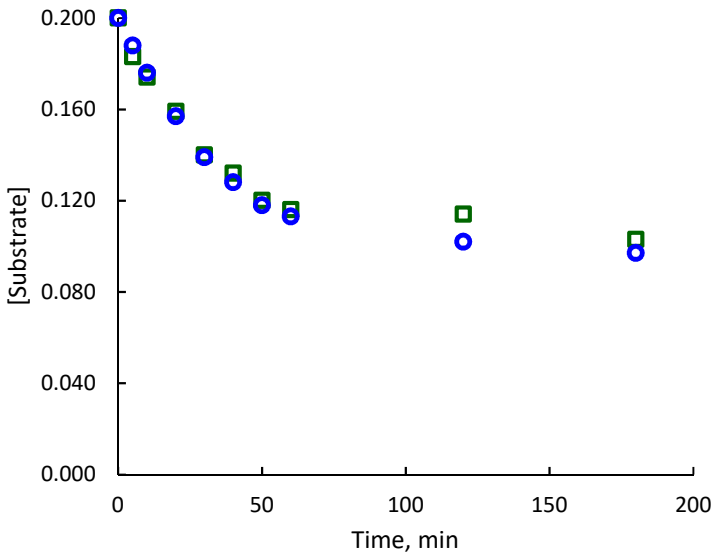


Table S21. Rate monitoring for the competing deuteration of 2-phenyloxazoline *vs* 2-phenylthiazoline

		2-phenyloxazoline		2-phenylthiazoline	
Entry	**Time, min**	**integral (H/D)**	**[Ph-DG^1]**	**integal (H/D)**	**[Ph-DG^2]**
0	0	2.00	0.200	2.00	0.200
1	5	1.83	0.183	1.88	0.188
2	10	1.74	0.174	1.76	0.176
3	20	1.59	0.159	1.57	0.157
4	30	1.40	0.140	1.39	0.139
5	40	1.32	0.132	1.28	0.128
6	50	1.20	0.120	1.18	0.118
7	60	1.16	0.116	1.13	0.113
8	120	1.14	0.114	1.02	0.102
9	180	1.03	0.103	0.97	0.097



(empty circles used as most of the data points overlapped)

Table S22. Rate monitoring for the competing deuteration of 2-phenyloxazoline *vs* 2-phenylpyridine

		2-phenyloxazoline		2-phenylpyridine	
Entry	**Time, min**	**integral (H/D)**	**[Ph-DG^1]**	**integral (H/D)**	**[Ph-DG^2]**
0	0	2.00	0.200	2.00	0.200
1	10	1.71	0.171	1.93	0.193
2	20	1.51	0.151	1.86	0.186
3	30	1.39	0.139	1.77	0.177
4	40	1.3	0.130	1.68	0.168
5	50	1.25	0.125	1.56	0.156
6	60	1.21	0.121	1.5	0.150
7	90	1.17	0.117	1.34	0.134
8	120	1.15	0.115	1.22	0.122
9	150	1.12	0.112	1.18	0.118

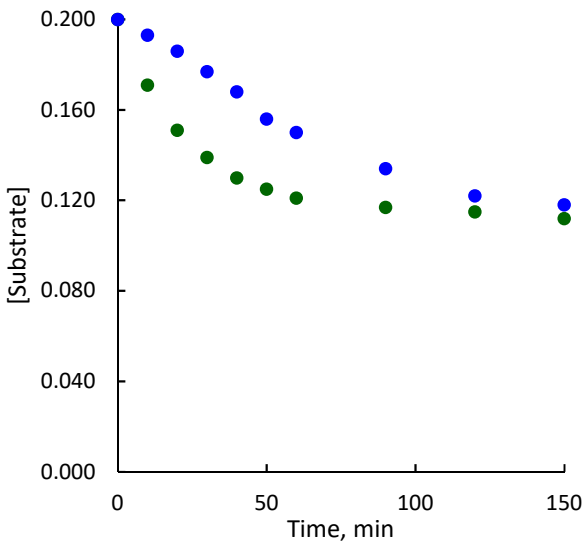


Table S23. Rate monitoring for the competing deuteration of 2-phenyloxazoline *vs* 2-phenylpyridine*

		2-phenyloxazoline		2-phenylpyridine	
Entry	**Time, min**	**integral (H/D)**	**[Ph-DG^1]**	**integral (H/D)**	**[Ph-DG^2]**
0	0	2.00	0.200	2.00	0.200
1	5	1.33	0.133	1.83	0.183
2	10	1.10	0.110	1.77	0.177
3	15	0.94	0.094	1.65	0.165
4	20	0.82	0.082	1.49	0.149
5	30	0.74	0.074	1.28	0.128
6	40	0.67	0.067	1.02	0.102
7	50	0.63	0.063	0.88	0.088
8	60	0.58	0.058	0.73	0.073
9	90	0.57	0.057	0.50	0.050
10	120	0.49	0.049	0.39	0.039
11	150	0.42	0.042	0.30	0.030

*Reaction performed in the 100 mL Schlenk flask (i.e. with higher excess of D_2) showed higher conversion.

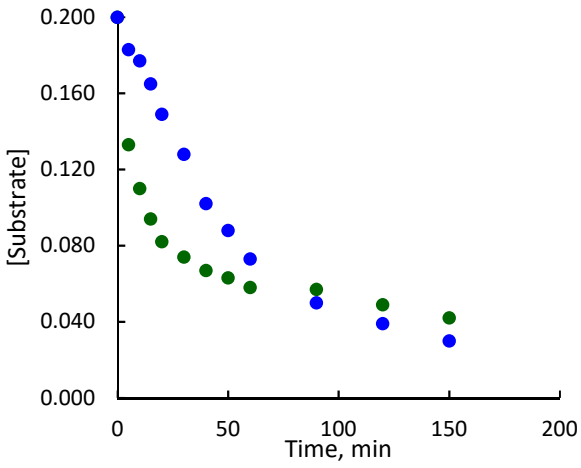


Table S24. Rate monitoring for the competing deuteration of nitrobenzene *vs* ethyl benzoate

		nitrobenzene		ethyl benzoate	
Entry	**Time, min**	**integral (H/D)**	**[Ph-DG^1]**	**integral (H/D)**	**[Ph-DG^2]**
0	0	2.00	0.200	2.00	0.200
1	10	1.85	0.185	1.99	0.199
2	20	1.48	0.148	1.97	0.197
3	30	1.31	0.131	1.94	0.194
4	40	1.18	0.118	1.89	0.189
5	50	1.08	0.108	1.84	0.184
6	60	1.00	0.100	1.81	0.181
7	90	0.83	0.083	1.68	0.168
8	120	0.76	0.076	1.56	0.156
9	180	0.7	0.070	1.36	0.136
10	240	0.68	0.068	1.23	0.123

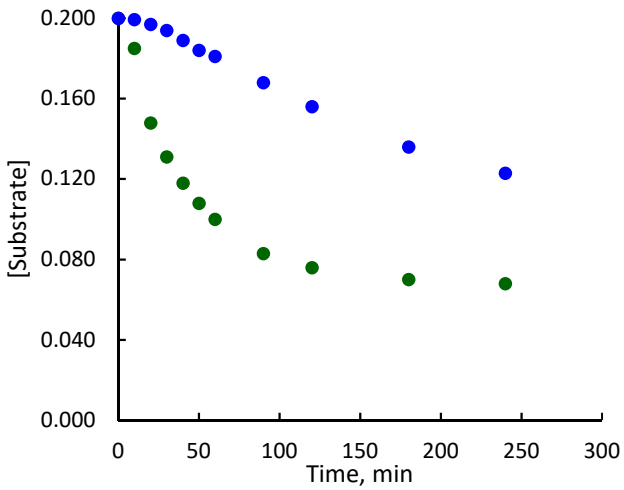


Table S25. Rate monitoring for the competing deuteration of acetophenone *vs* ethyl benzoate

		acetophenone		ethyl benzoate	
Entry	**Time, min**	**integral (H/D)**	**[Ph-DG^1]**	**integral (H/D)**	**[Ph-DG^2]**
0	0	2.00	0.200	2.00	0.200
1	10	1.66	0.166	1.98	0.198
2	20	1.35	0.135	1.98	0.198
3	30	1.14	0.114	1.96	0.196
4	40	0.96	0.096	1.94	0.194
5	50	0.85	0.085	1.92	0.192
6	60	0.77	0.077	1.89	0.189
7	120	0.71	0.071	1.61	0.161
8	180	0.74	0.074	1.35	0.135

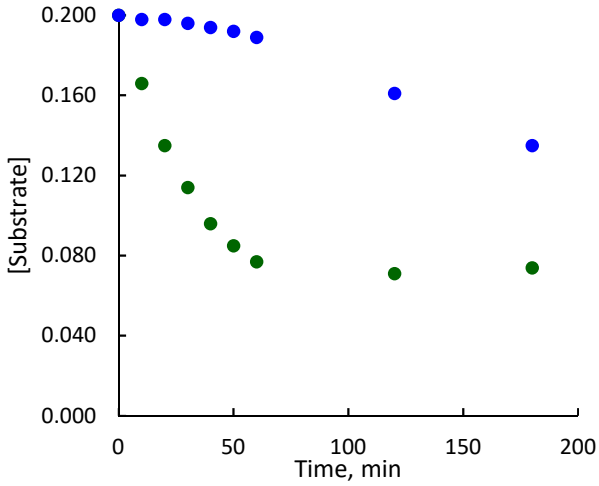


Table S26. Rate monitoring for the competing deuteration of 1-methyl-2-phenylimidazole *vs* 2-phenylpyridine

		1-methyl-2-phenylimidazole		2-phenylpyridine	
Entry	**Time, min**	**integral (H/D)**	**[Ph-DG^1]**	**integral (H/D)**	**[Ph-DG^2]**
0	0	2.00	0.200	2.00	0.200
1	10	1.33	0.133	1.98	0.198
2	20	1.04	0.104	1.88	0.188
3	30	0.88	0.088	1.75	0.175
4	40	0.76	0.076	1.62	0.162
5	50	0.73	0.073	1.49	0.149
6	60	0.70	0.070	1.38	0.138
7	90	0.69	0.069	1.13	0.113
8	120	0.68	0.068	0.98	0.098
9	180	0.59	0.059	0.86	0.086

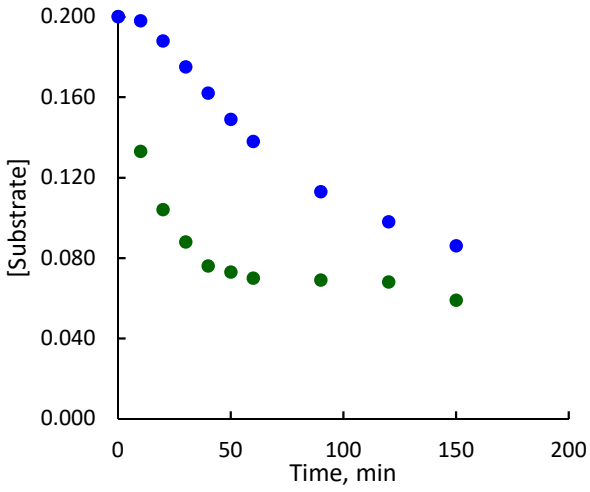


Table S27. Rate monitoring for the competing deuteration of 2-phenyloxazoline *vs* 2-phenylbenzothiazole

		2-phenyloxazoline		2-phenylbenzothiazole	
Entry	**Time, min**	**integral (H/D)**	**[Ph-DG^1]**	**integral (H/D)**	**[Ph-DG^2]**
0	0	2.00	0.200	2.00	0.200
1	10	1.39	0.139	1.97	0.197
2	20	1.10	0.110	1.96	0.196
3	30	0.92	0.092	1.96	0.196
4	40	0.67	0.067	1.98	0.198
5	50	0.58	0.058	1.97	0.197
6	60	0.53	0.053	1.97	0.197
7	90	0.50	0.050	1.96	0.196
8	150	0.50	0.050	1.95	0.195

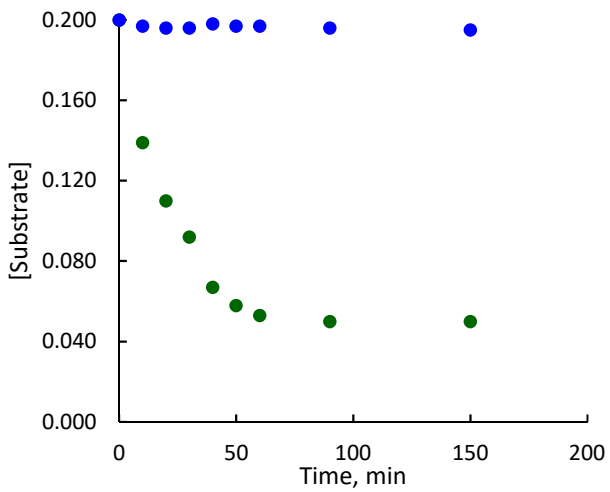


Table S28. Rate monitoring for the competing deuteration of 1-methyl-2-phenylimidazole *vs* acetophenone

		1-methyl-2-phenylimidazole		acetophenone	
Entry	**Time, min**	**integral (H/D)**	**[Ph-DG^1]**	**integral (H/D)**	**[Ph-DG^2]**
0	0	2.00	0.200	2.00	0.200
1	10	1.39	0.139	1.97	0.197
2	20	1.10	0.110	1.96	0.196
3	30	0.92	0.092	1.96	0.196
4	60	0.67	0.067	1.98	0.198
5	90	0.58	0.058	1.97	0.197
6	120	0.53	0.053	1.97	0.197
7	180	0.50	0.050	1.96	0.196

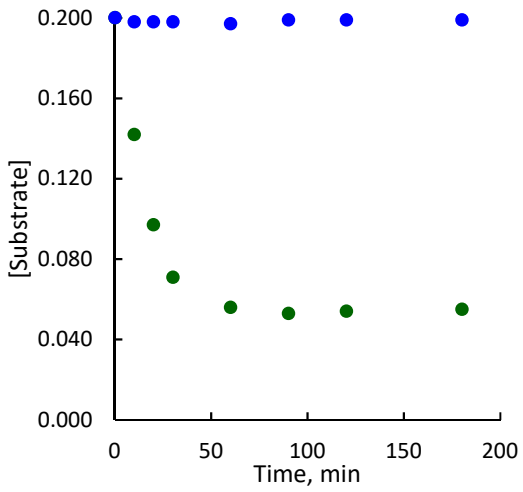


Table S29. Rate monitoring for the competing deuteration of 1-methyl-2-phenylimidazole *vs* 2-phenylbenzothiazole

		1-methyl-2-phenylimidazole		2-phenylbenzothiazole	
Entry	**Time, min**	**integral (H/D)**	**[Ph-DG^1]**	**integral (H/D)**	**[Ph-DG^2]**
0	0	2.00	0.200	2.00	0.200
1	10	1.39	0.139	1.97	0.197
2	20	1.10	0.110	1.96	0.196
3	30	0.92	0.092	1.96	0.196
4	60	0.67	0.067	1.98	0.198
5	90	0.58	0.058	1.97	0.197
6	120	0.53	0.053	1.97	0.197
7	180	0.50	0.050	1.96	0.196
8	240	0.5	0.050	1.95	0.195

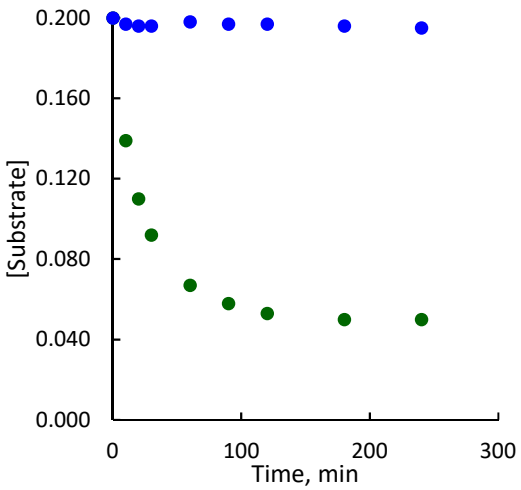


Table S30. Rate monitoring for the competing deuteration of 2-phenylthiazoline *vs* nitrobenzene

		2-phenylthiazoline		nitrobenzene	
Entry	**Time, min**	**integral (H/D)**	**[Ph-DG^1]**	**integral (H/D)**	**[Ph-DG^2]**
0	0	2.00	0.200	2.00	0.200
1	10	1.91	0.191	1.98	0.198
2	20	1.79	0.179	1.96	0.196
3	30	1.63	0.163	1.97	0.197
4	40	1.49	0.149	1.96	0.196
5	50	1.33	0.133	1.96	0.196
6	60	1.22	0.122	1.96	0.196
7	160	0.78	0.078	1.98	0.198
8	260	0.68	0.068	1.96	0.196

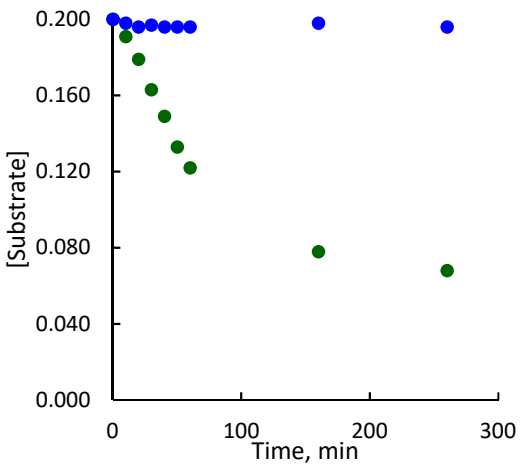
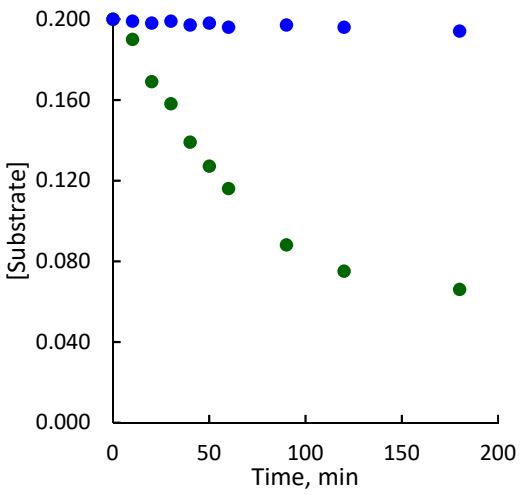
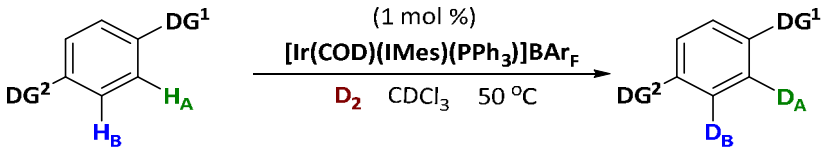


Table S31. Rate monitoring for the competing deuteration of 2-phenypyridine *vs* acetophenone

		2-phenylpyridine		acetophenone	
Entry	**Time, min**	**integral (H/D)**	**[Ph-DG^1]**	**integral (H/D)**	**[Ph-DG^2]**
0	0	2.00	0.200	2.00	0.200
1	10	1.90	0.190	1.99	0.199
2	20	1.69	0.169	1.98	0.198
3	30	1.58	0.158	1.99	0.199
4	40	1.39	0.139	1.97	0.197
5	50	1.27	0.127	1.98	0.198
6	60	1.16	0.116	1.96	0.196
7	90	0.88	0.088	1.97	0.197
8	120	0.75	0.075	1.96	0.196
9	180	0.66	0.066	1.94	0.194



3.5. Kinetic Data for substrates with two directing groups (Intramolecular competition)



Following the Standard Kinetics Protocol, the intramolecular competing isotope labeling of the substrate bearing both directing groups DG^1 and DG^2 (0.50 mmol) using 1 mol % of the Ir-catalyst (0.005 mmol, 8.7 mg) were monitored at 50 °C in $CDCl_3$ by the sampling method and analysed by ^1H NMR spectroscopy.

The residual proton signal from the site of incorporation (*ortho* to DG) was compared against that of a site where incorporation did not happen. The tables and plots below combine the obtained integral change of the protons (H_A and H_B) *ortho* to the directing groups over time.

Table S32. Rate monitoring for the competing deuteration of 4-nitroacetophenone

		integral (H_A and H_B)	
Entry	**Time, min**	**H_A ($COCH_3$)**	**H_B (NO_2)**
0	0	2.00	2.00
1	10	1.52	1.90
2	20	1.31	1.76
3	30	1.15	1.55
4	40	1.07	1.40
5	50	1.01	1.27
6	60	0.97	1.16
7	90	0.44	0.71
8	120	0.27	0.43
9	180	0.21	0.29
10	240	0.15	0.23
11	300	0.11	0.15
12	360	0.10	0.12

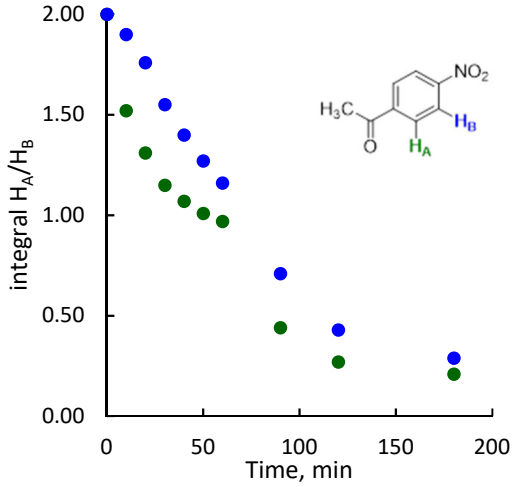


Table S33. Rate monitoring for the competing deuteration of ethyl 4-nitrobenzoate

		integral (H_A and H_B)	
Entry	**Time, min**	**H_A (NO_2)**	**H_B (CO_2Et)**
0	0	2.00	2.00
1	10	1.64	1.80
2	20	1.47	1.63
3	30	1.36	1.51
4	60	1.10	1.19
5	90	0.96	1.03
6	120	0.91	0.93
7	180	0.85	0.88
8	240	0.83	0.85

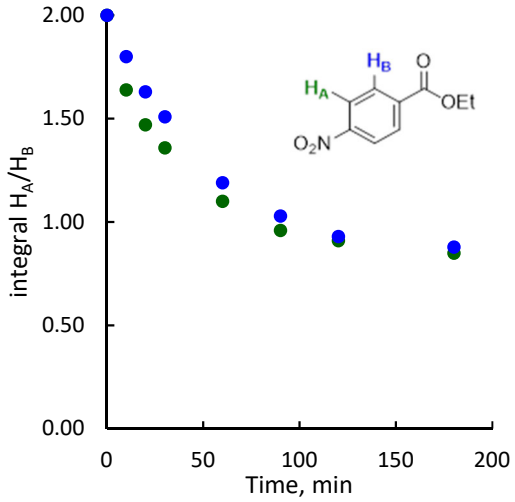


Table S34. Rate monitoring for the competing deuteration of ethyl 4-acetylbenzoate

		integral (H_A and H_B)	
Entry	**Time, min**	**H_A ($COCH_3$)**	**H_B (CO_2Et)**
0	0	2.00	2.00
1	5	1.49	1.97
2	10	1.26	1.91
3	20	1.05	1.62
4	30	0.93	1.38
5	40	0.82	1.20
6	50	0.79	1.03
7	60	0.72	0.92
8	90	0.61	0.67
9	120	0.44	0.51
10	150	0.33	0.38
11	180	0.29	0.31

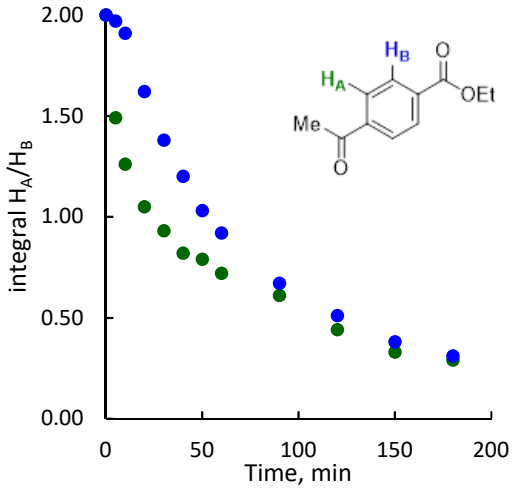


Table S35. Rate monitoring for the competing deuteration of 2-(4-acetyl)phenyloxazoline

		integral (H_A and H_B)	
Entry	**Time, min**	**H_A (oxazoline)**	**H_B ($COCH_3$)**
0	0	2.00	2.00
1	10	1.46	2.00
2	20	1.12	2.00
3	30	0.96	1.99
4	60	0.69	1.98
5	90	0.57	1.98
6	120	0.52	1.99
7	180	0.50	1.98
8	240	0.51	1.98

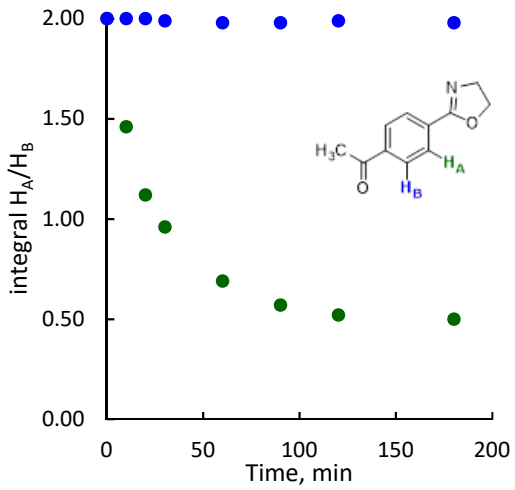


Table S36. Rate monitoring for the competing deuteration of 2-(4-nitrophenyl)-4,5-dihydrothiazole

		integral (H_A and H_B)	
Entry	**Time, min**	**H_A (thiazoline)**	**H_B (NO_2)**
0	0	2.00	2.00
1	5	1.93	2.00
2	10	1.89	1.99
3	20	1.77	1.99
4	30	1.69	1.99
5	40	1.60	1.99
6	50	1.52	1.99
7	60	1.42	1.99
8	90	1.25	1.99
9	120	1.09	1.99
10	180	0.81	1.99
11	240	0.65	1.99
12	300	0.53	1.99
13	360	0.42	1.99

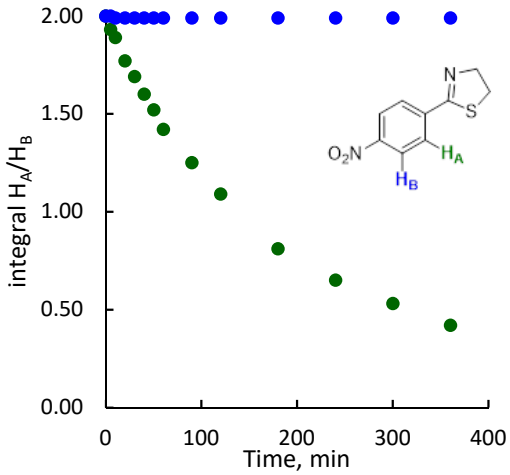
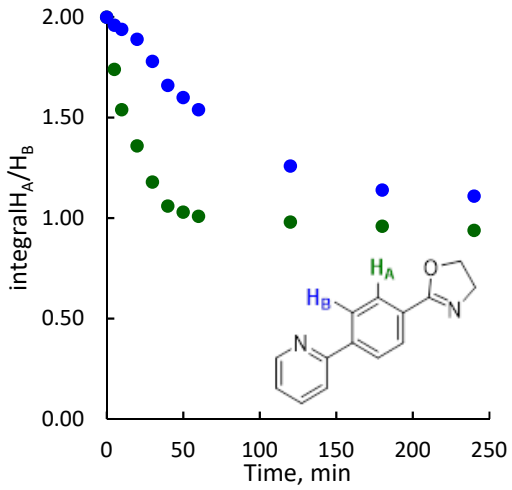


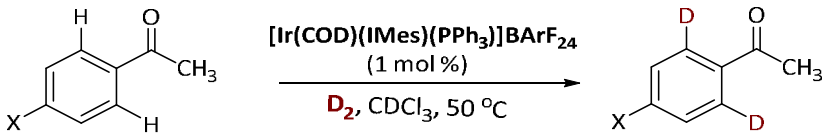
Table S37. Rate monitoring for the competing deuteration of 2-(4-(Pyridin-2-yl)phenyl)-4,5-dihydrooxazole

		integral (H_A and H_B)	
Entry	**Time, min**	**H_A (oxazoline)**	**H_B (pyridine)**
0	0	2.00	2.00
1	5	1.74	1.96
2	10	1.54	1.94
3	20	1.36	1.89
4	30	1.18	1.78
5	40	1.06	1.66
6	50	1.03	1.60
7	60	1.01	1.54
8	120	0.98	1.26
9	180	0.96	1.14
10	240	0.94	1.11



3.6. Hammett plot

Table S38. Rate constants for deuteration of substituted acetophenones and Hammett parameters[S13]



X	k_{obs} (s^{-1})	log (k_X/k_H)	σ_p	σ_p^-	σ_p^+
H	3.93×10^{-4}	0.00	0	0.00	0
OMe	8.06×10^{-4}	0.31	-0.27	-0.26	-0.78
Br	8.52×10^{-4}	0.34	0.23	0.25	0.15
F	8.46×10^{-4}	0.33	0.54	0.65	0.61
CF_3	9.34×10^{-4}	0.38	0.06	-0.03	-0.07
NO_2[a]	2.93×10^{-4}	-0.13	0.78	1.27	0.79
CO_2Et[a]	8.11×10^{-4}	0.31	0.45	0.75	n/a

[a] Approx. k_{obs} calculated from intramolecular kinetics data (see Tables S30 and S32)

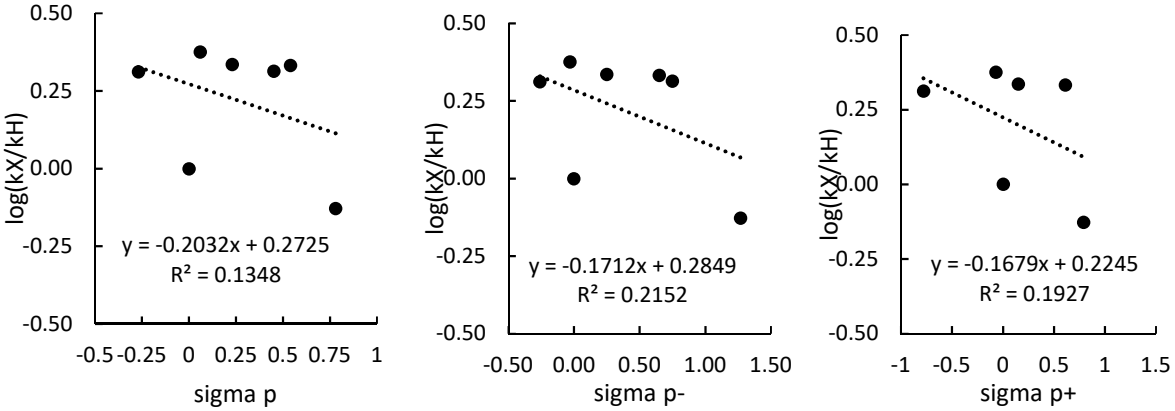
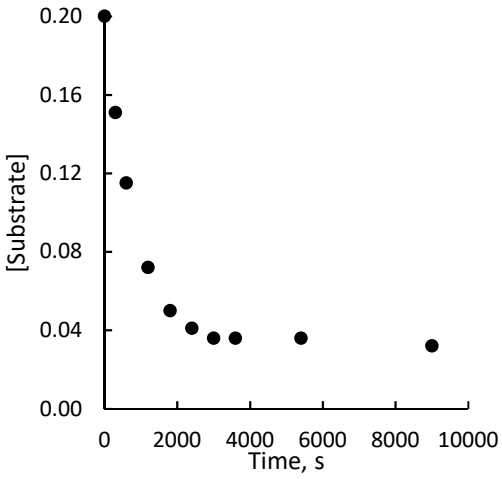


Table S39. Rate monitoring for the deuteration of *p*-methoxy acetophenone

Following the General Kinetic Protocol using 75.1 mg of *p*-methoxy acetophenone, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.20	-1.61
1	300	1.51	0.15	-1.89
2	600	1.15	0.12	-2.16
3	1200	0.72	0.07	-2.63
4	1800	0.50	0.05	-3.00
5	2400	0.41	0.04	-3.19
6	3000	0.36	0.04	-3.32
7	3600	0.36	0.04	-3.32
8	5400	0.36	0.04	-3.32
9	9000	0.32	0.03	-3.44
$k_{obs} = 8.06 \times 10^{-4}\ (s^{-1})$				



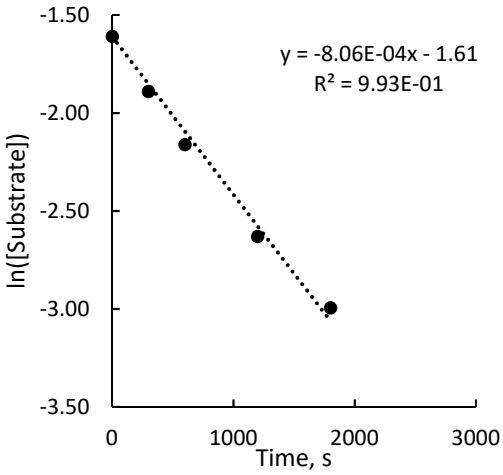
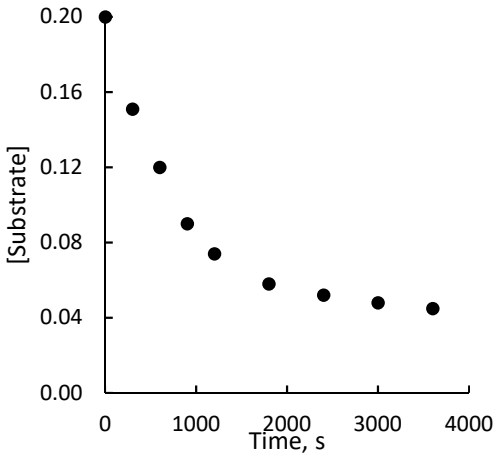


Table S40. Rate monitoring for the deuteration of *p*-bromo acetophenone

Following the General Kinetic Protocol using 99.5 mg of *p*-bromo acetophenone, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.20	-1.61
1	300	1.51	0.15	-1.89
2	600	1.20	0.12	-2.12
3	900	0.90	0.09	-2.41
4	1200	0.74	0.07	-2.60
5	1800	0.58	0.06	-2.85
6	2400	0.52	0.05	-2.96
7	3000	0.48	0.05	-3.04
8	3600	0.45	0.05	-3.10
$k_{obs} = 8.52 \times 10^{-4}\ (s^{-1})$				



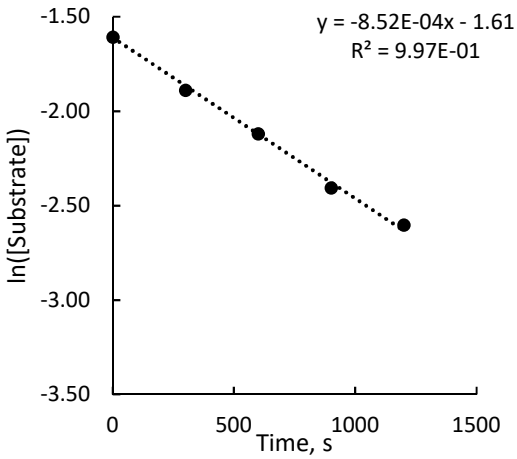
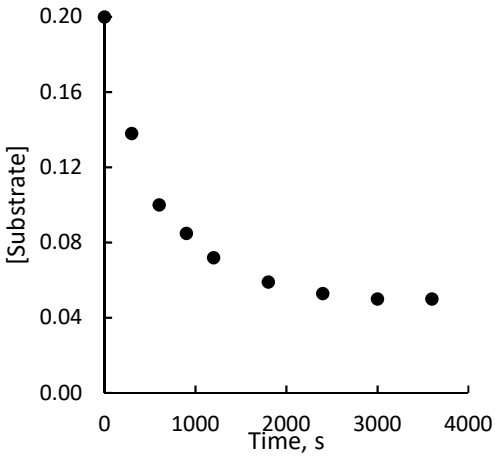


Table S41. Rate monitoring for the deuteration of *p*-fluoro acetophenone

Following the General Kinetic Protocol using 69.1 mg of *p*-fluoro acetophenone, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.20	-1.61
1	300	1.38	0.14	-1.98
2	600	1.00	0.10	-2.30
3	900	0.85	0.09	-2.47
4	1200	0.72	0.07	-2.63
5	1800	0.59	0.06	-2.83
6	2400	0.53	0.05	-2.94
7	3000	0.50	0.05	-3.00
8	3600	0.50	0.05	-3.00
$k_{obs} = 9.34 \times 10^{-4}\ (s^{-1})$				



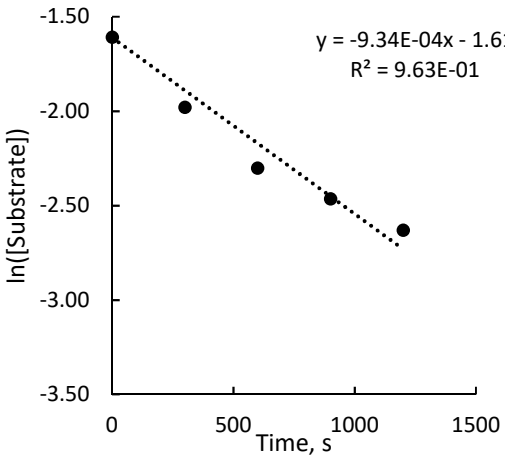
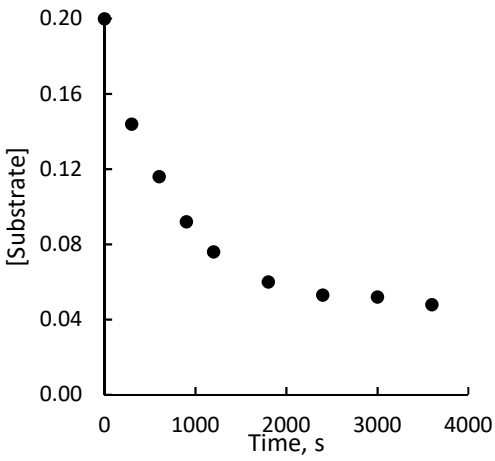


Table S42. Rate monitoring for the deuteration of *p*-trifluoromethyl acetophenone

Following the General Kinetic Protocol using 94.1 mg of *p*-trifluoromethyl acetophenone, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.20	-1.61
1	300	1.44	0.14	-1.94
2	600	1.16	0.12	-2.15
3	900	0.92	0.09	-2.39
4	1200	0.76	0.08	-2.58
5	1800	0.60	0.06	-2.81
6	2400	0.53	0.05	-2.94
7	3000	0.52	0.05	-2.96
8	3600	0.48	0.05	-3.04
$k_{obs} = 8.46 \times 10^{-4}\ (s^{-1})$				



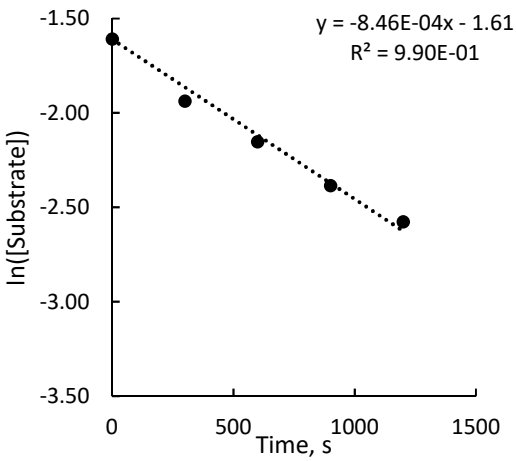


Table S43. Rate monitoring for the deuteration of *p*-nitro acetophenone

(for all data points see Table S30)

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.20	-1.61
1	600	1.52	0.15	-1.88
2	1200	1.31	0.13	-2.03
3	1800	1.15	0.12	-2.16
4	2400	1.07	0.11	-2.23
5	3000	1.01	0.10	-2.29
6	3600	0.97	0.10	-2.33
7	5400	0.44	0.04	-3.12
$k_{obs} = 3.31 \times 10^{-4}\ (s^{-1})$				

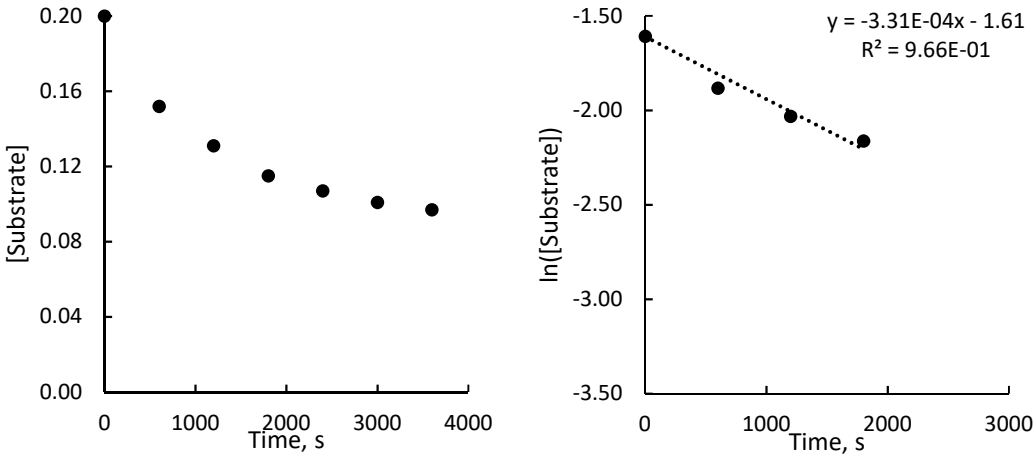
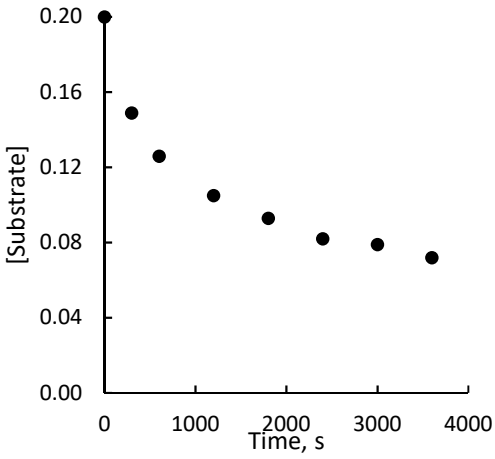
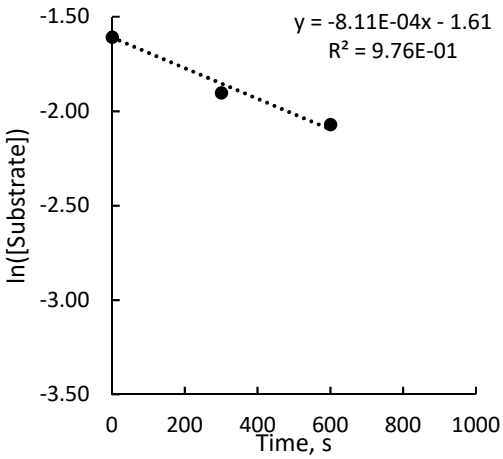


Table S44. Rate monitoring for the deuteration of *p*-CO_2Et acetophenone

(for all data points see Table S30)

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.20	-1.61
1	300	1.49	0.15	-1.90
2	600	1.26	0.13	-2.07
3	1200	1.05	0.11	-2.25
4	1800	0.93	0.09	-2.38
5	2400	0.82	0.08	-2.50
6	3000	0.79	0.08	-2.54
7	3600	0.72	0.07	-2.63
8	5400	0.61	0.06	-2.80
$k_{obs} = 8.11 \times 10^{-4}\ (s^{-1})$				





3.7. Determination of the rate expression using initial rates method.

We have attempted to obtain the rate expression for overall reaction using the initial rate method. The initial rates of the labelling reactions were measured to determine the reaction orders for substrate and catalyst by running the reaction multiple times under general conditions (2.5 mL of $CDCl_3$, 50 °C), and changing the concentration of one component in each case.

The reaction might be broken down into four steps (substrate binding; C-H activation; exchange of D for H; C-D reductive elimination; labelled substrate dissociation) but each of these four steps is formally in equilibrium. If the simplification is made that, at least in the early stages of the reaction, these four steps are irreversible, then one can arrive at a rate expression that is of the form:

$$\text{Rate} = k[IrD_2(IMes)(PPh_3)(solv)_2][\text{substrate}][D_2]$$

If we make a further assumption that pre-catalyst initiation is rapid and irreversible, which seems reasonable given the rapid colour change that is observed as soon as D_2 is introduced, we can obtain:

$$\text{Rate} = k[Ir(COD)(IMes)(PPh_3)][\text{substrate}][D_2]$$

However, initial studies are not consistent with this rate expression, and we are currently unable to reliably and systematically vary $[D_2]$ in these reactions.

Instead, if we express the rate of reaction as each component to an unknown (and not necessarily integer) order, we can obtain:

$$\text{Rate} = k[\text{Ir pre-cat}]^a[\text{substrate}]^b[D_2]^c \qquad \text{(where a, b, and c are the orders in the components)}$$

We observe pseudo-first order behaviour in the reactions, so under these conditions:

$$\text{Rate} = k_{obs}[\text{substrate}]$$

Where it is assumed that:

$$k_{obs} = k[\text{Ir pre-cat}]^a[D_2]^c$$

Therefore, if the reactions are carried out with the same initial concentrations of pre-catalyst, substrate, and deuterium gas, it is reasonable to obtain the approximation:

$$k_{obs}\ (\text{substrate A}) / k_{obs}\ (\text{substrate B}) \approx k\ (\text{substrate A}) / k\ (\text{substrate B})$$

This approximation has been used to examine, empirically, the relative rates of reaction of each substrate and compare these to selectivity data obtained during our previous study.

Table S45. Rate-dependence on catalyst concentration for labelling reaction of acetophenone.

$[Substrate]_0$, M	$[Catalyst]_0$, M	Initial rate, $M^{-1}s^{-1}$	Mol % catalyst
0.2	0.001	8.72×10^{-5}	0.50
0.2	0.0015	9.56×10^{-5}	0.75
0.2	0.002	1.07×10^{-4}	1.00

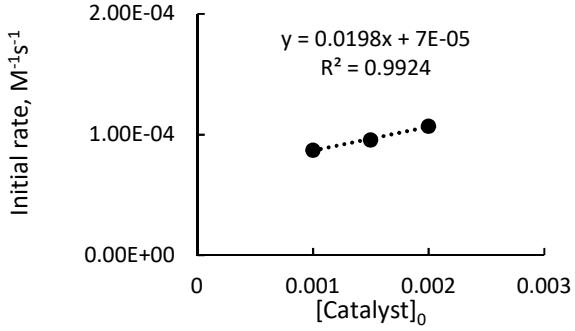


Table S46. Rate monitoring for the deuteration of acetophenone by changing catalyst concentration. Following the General Kinetic Protocol using 60.1 mg of acetophenone (0.2 M).

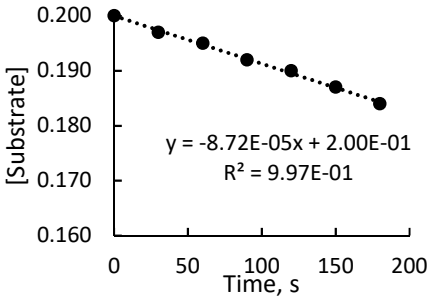
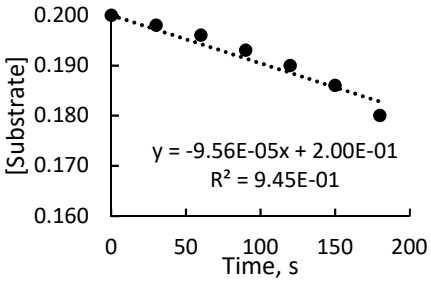
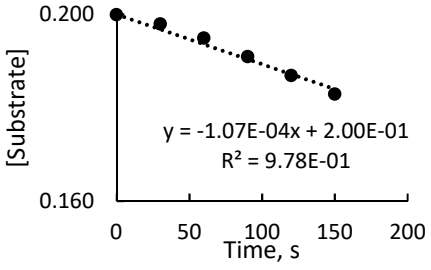
$[Catalyst]_0$	Time, s	Integral (H/D)	[Substrate], M	
0.001 M (4.4 mg)	0	2.00	0.200	
	30	1.97	0.197	
	60	1.95	0.195	
	90	1.92	0.192	
	120	1.90	0.190	
	150	1.87	0.187	
	180	1.84	0.184	
0.0015 M (6.5 mg)	0	2.00	0.200	
	30	1.98	0.198	
	60	1.96	0.196	
	90	1.93	0.193	
	120	1.90	0.190	
	150	1.86	0.186	
	180	1.80	0.180	
0.002 M (8.7 mg)	0	2.00	0.200	
	30	1.98	0.198	
	60	1.95	0.195	
	90	1.91	0.191	
	120	1.87	0.187	
	150	1.83	0.183	

Table S47. Rate-dependence on substrate concentration for labelling reaction of acetophenone.

$[Substrate]_0$, M	$[Catalyst]_0$, M	Initial rate, $M^{-1}s^{-1}$	Mol % catalyst
0.10	0.002	1.30×10^{-4}	2.00
0.15	0.002	1.25×10^{-4}	1.33
0.20	0.002	1.07×10^{-4}	1.00
0.25	0.002	8.93×10^{-5}	0.80

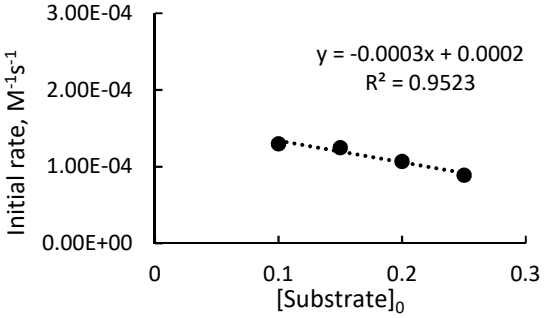


Table S48. Rate monitoring for the deuteration of acetophenone by changing catalyst concentration. Following the General Kinetic Protocol using 8.7 mg of catalyst (0.002M).

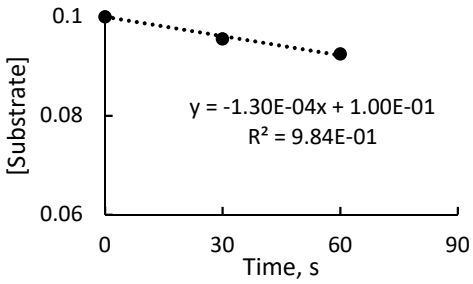
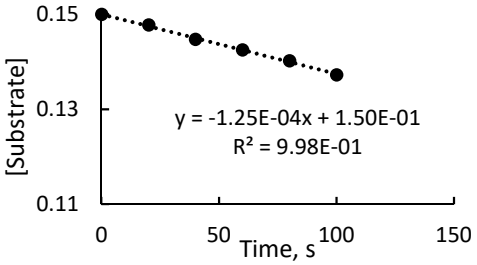
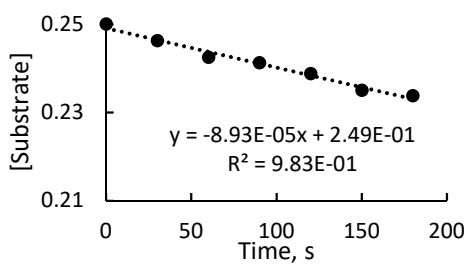
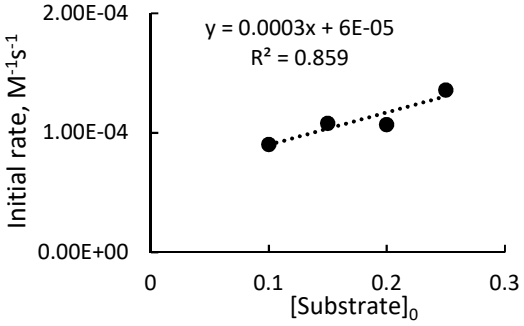
$[substrate]_0$	Time, s	Integral (H/D)	[Substrate], M	
0.10 M (30 mg)	0	2.00	0.100	
	30	1.89	0.095	
	60	1.82	0.091	
0.15 M (45 mg)	0	2.00	0.150	
	20	1.97	0.148	
	40	1.93	0.145	
	60	1.90	0.143	
	80	1.87	0.140	
	100	1.83	0.137	
0.20 M	See Table S46			
0.25 M (75 mg)	0	2.00	0.250	
	30	1.97	0.246	
	60	1.94	0.243	
	90	1.93	0.241	
	120	1.91	0.239	
	150	1.88	0.235	
	180	1.87	0.234	

Table S49. Rate-dependence on substrate and catalyst concentration for labelling reaction of acetophenone.

$[Substrate]_0$, M	$[Catalyst]_0$, M	Initial rate, $M^{-1}s^{-1}$	Mol % catalyst
0.10	0.0010	9.05×10^{-5}	1.0
0.15	0.0015	1.08×10^{-4}	1.0
0.20	0.0020	1.07×10^{-4}	1.0
0.25	0.0025	1.36×10^{-5}	1.0



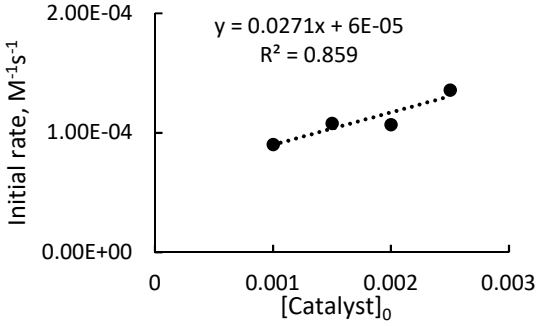


Table S50. Rate monitoring for the deuteration of acetophenone by changing substrate and catalyst concentration, keeping the ratio catalyst/substrate constant.

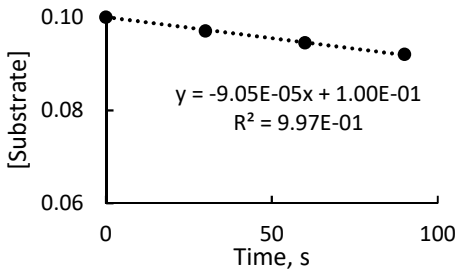
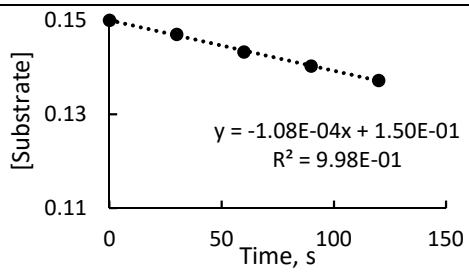
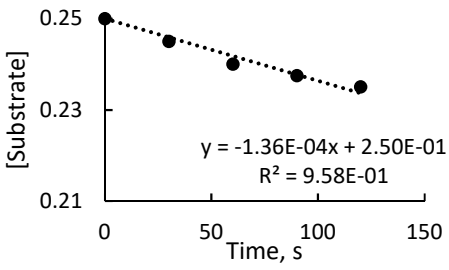
	Time, s	Integral (H/D)	[Substrate], M	
$[substrate]_0$ 0.10 M $[Catalyst]_0$ 0.001 M	0	2.00	0.100	
	30	1.94	0.097	
	60	1.89	0.095	
	90	1.84	0.092	
$[substrate]_0$ 0.15 M $[Catalyst]_0$ 0.0015 M	0	2.00	0.150	
	30	1.96	0.147	
	60	1.91	0.143	
	90	1.87	0.140	
	120	1.83	0.137	
$[substrate]_0$ 0.20 M $[Catalyst]_0$ 0.002 M	See Table S46			
$[substrate]_0$ 0.25 M $[Catalyst]_0$ 0.0025 M	0	2.00	0.250	
	30	1.96	0.245	
	60	1.92	0.240	
	90	1.90	0.238	
	120	1.88	0.235	

Table S51. Rate-dependence on catalyst concentration for labelling reaction of 2-phenylpyridine.

$[Substrate]_0$, M	$[Catalyst]_0$, M	Initial rate, $M^{-1}s^{-1}$	Mol % catalyst
0.2	0.0015	1.10×10^{-5}	0.75
0.2	0.0020	1.27×10^{-5}	1.00
0.2	0.0025	1.55×10^{-5}	1.25

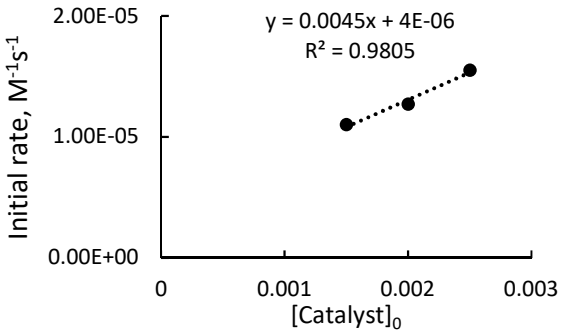


Table S52. Rate monitoring for the deuteration of 2-phenylpyridine by changing catalyst concentration.

Following the General Kinetic Protocol using 77.6 mg of 2-phenylpyridine (0.2 M).

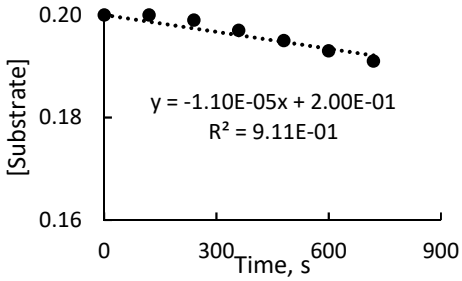
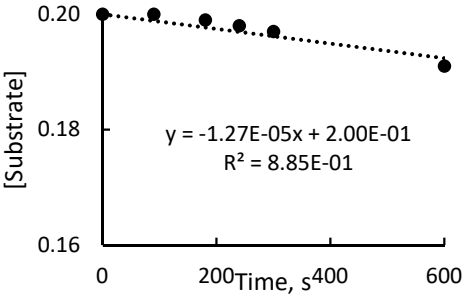
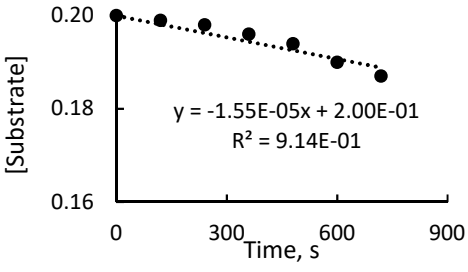
$[Catalyst]_0$	Time, s	Integral (H/D)	[Substrate], M	
0.0015 M (6.5 mg)	0	2.00	0.200	
	120	2.00	0.200	
	240	1.99	0.199	
	360	1.97	0.197	
	480	1.95	0.195	
	600	1.93	0.193	
	720	1.91	0.191	
0.002 M (8.7 mg)	0	2.00	0.200	
	90	2.00	0.200	
	180	1.99	0.199	
	240	1.98	0.198	
	300	1.97	0.197	
	600	1.91	0.191	
0.0025 M (10.8 mg)	0	2	0.2	
	120	1.99	0.199	
	240	1.98	0.198	
	360	1.96	0.196	
	480	1.94	0.194	
	600	1.9	0.19	
	720	1.87	0.187	

Table S53. Rate-dependence on catalyst concentration for labelling reaction of 2-phenylpyridine.

$[Substrate]_0$, M	$[Catalyst]_0$, M	Initial rate, $M^{-1}s^{-1}$	Mol % catalyst
0.10	0.0010	1.24×10^{-5}	1.00
0.20	0.0020	1.27×10^{-5}	1.00
0.25	0.0025	1.37×10^{-5}	1.00

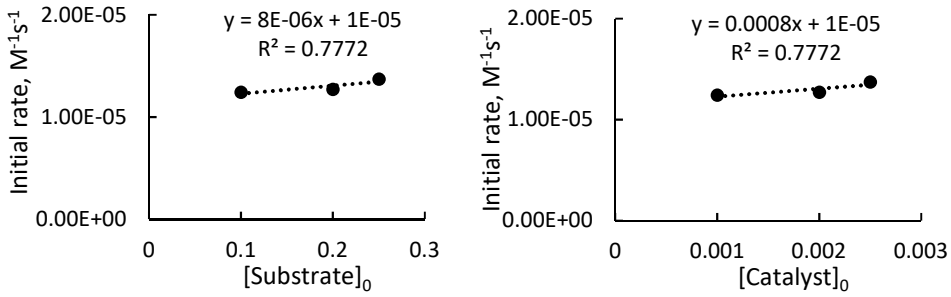
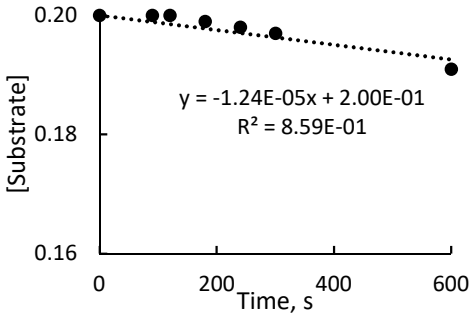
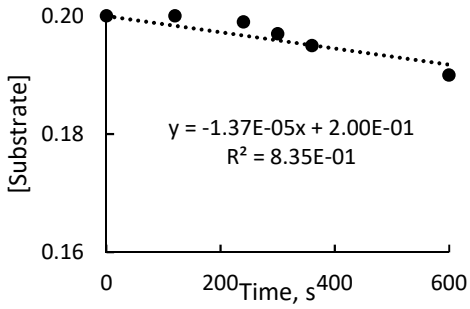


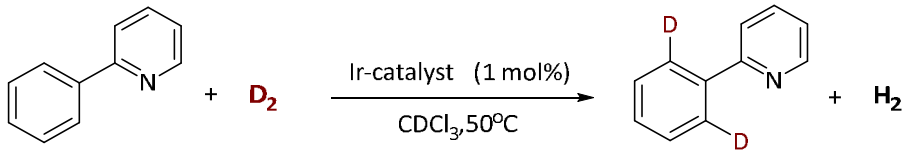
Table S54. Rate monitoring for the deuteration of 2-phenylpyridine by changing substrate and catalyst concentration, keeping the ratio catalyst/substrate constant.

$[Catalyst]_0$	Time, s	Integral (H/D)	[Substrate], M	
$[substrate]_0$ 0.10 M $[Catalyst]_0$ 0.001 M	0	2.00	0.200	
	120	2.00	0.200	
	180	1.99	0.199	
	240	1.98	0.198	
	300	1.97	0.197	
	600	1.91	0.191	
$[substrate]_0$ 0.20 M $[Catalyst]_0$ 0.002 M	See Table S52			
$[substrate]_0$ 0.25 M $[Catalyst]_0$ 0.0025 M	0	2.00	0.200	
	120	2.00	0.200	
	240	1.99	0.199	
	300	1.97	0.197	
	360	1.95	0.195	
	600	1.9	0.190	

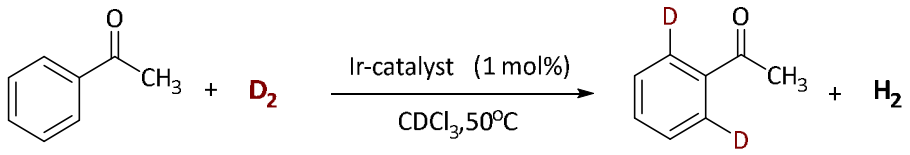
3.8. Additional control experiments

Rate-dependence on the reaction surface area

HIE reactions were performed in different reaction vessels: NMR tube (online monitoring), Microwave vial (sampling) and 100mL Schlenk flask (sampling) for 2-phenylpyridine and acetophenone.



Reaction vessel	Surface area, mm^2	k_{obs}	k_{rel}
J. Young NMR tube	12.5	4.00×10^{-5}	0.34
Microwave vial	615	1.16×10^{-4}	1
Schlenk flask	1100	1.47×10^{-4}	1.27



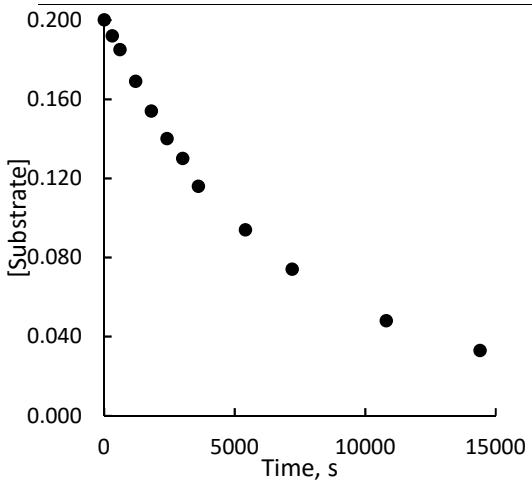
Reaction vessel	Surface area, mm^2	k_{obs}	k_{rel}
Microwave vial	615	3.93×10^{-4}	1
Schlenk flask	1100	1.51×10^{-3}	3.84

Table S55. Rate monitoring for the deuteration of 2-phenylpyridine in Schlenk flask (run 1)

Following the General Kinetic Protocol using 77.6 mg of 2-phenylpyridine, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	300	1.92	0.192	-1.65
2	600	1.85	0.185	-1.69
3	1200	1.69	0.169	-1.78
4	1800	1.54	0.154	-1.87
5	2400	1.40	0.140	-1.97
6	3000	1.30	0.130	-2.04
7	3600	1.16	0.116	-2.15
8	5400	0.94	0.094	-2.36
9	7200	0.74	0.074	-2.60
10	10800	0.48	0.048	-3.04
11	14400	0.33	0.033	-3.41

$k_{obs} = 1.41 \times 10^{-4}\ (s^{-1})$



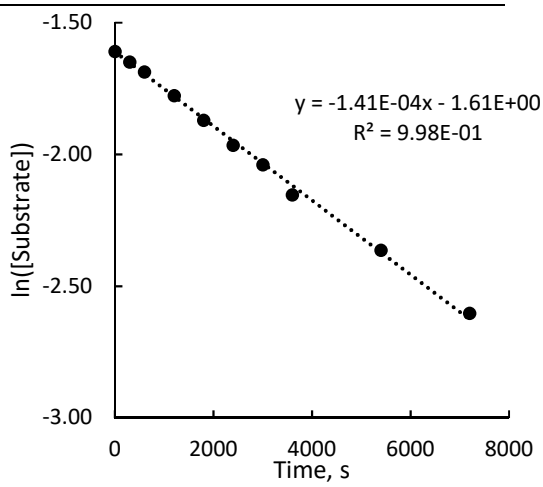
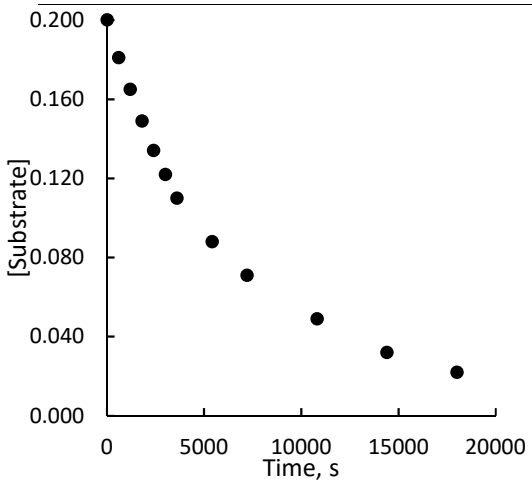


Table S56. Rate monitoring for the deuteration of 2-phenylpyridine in Schlenk flask (run 2)

Following the General Kinetic Protocol using 77.6 mg of 2-phenylpyridine, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	600	1.81	0.181	-1.71
2	1200	1.65	0.165	-1.80
3	1800	1.49	0.149	-1.90
4	2400	1.34	0.134	-2.01
5	3000	1.22	0.122	-2.10
6	3600	1.10	0.110	-2.21
7	5400	0.88	0.088	-2.43
8	7200	0.71	0.071	-2.65
9	10800	0.49	0.049	-3.02
10	14400	0.32	0.032	-3.44
11	18000	0.22	0.022	-3.82

$k_{obs} = 1.52 \times 10^{-4}\ (s^{-1})$



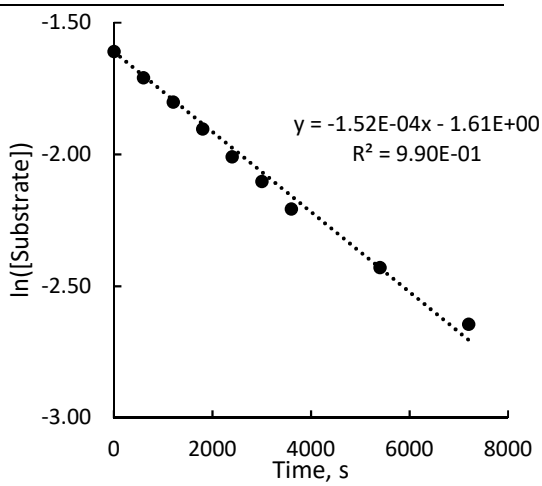


Table S57. Rate monitoring for the deuteration of acetophenone in Schlenk flask (run 1)

Following the General Kinetic Protocol using 60.1 mg of acetophenone, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	120	1.82	0.182	-1.70
2	240	1.51	0.151	-1.89
3	360	1.23	0.123	-2.10
4	480	1.02	0.102	-2.28
5	600	0.82	0.082	-2.50
6	900	0.52	0.052	-2.96
7	1200	0.37	0.037	-3.30
8	1800	0.18	0.018	-4.02
9	2400	0.14	0.014	-4.27
10	3600	0.12	0.012	-4.42
11	7200	0.11	0.011	-4.51

$k_{obs} = 1.43 \times 10^{-3}\ (s^{-1})$

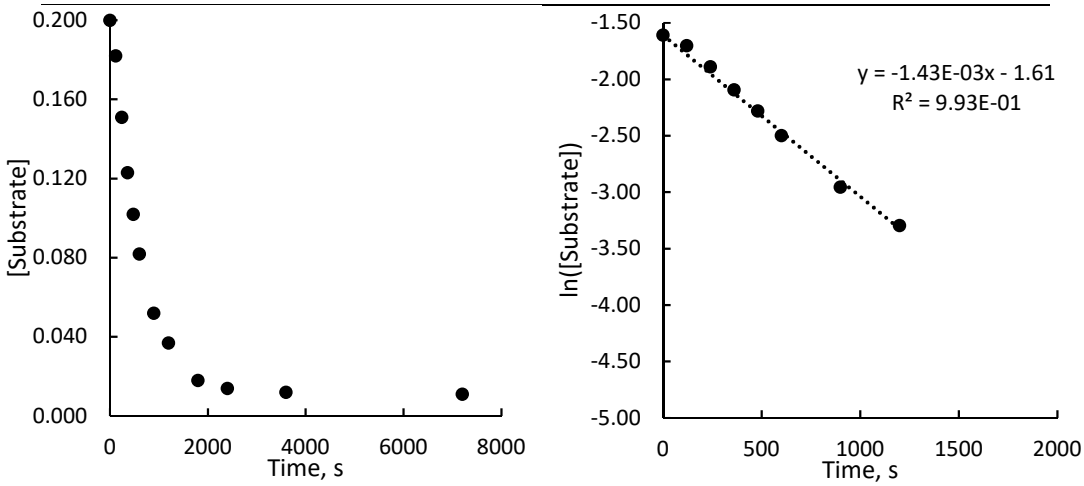
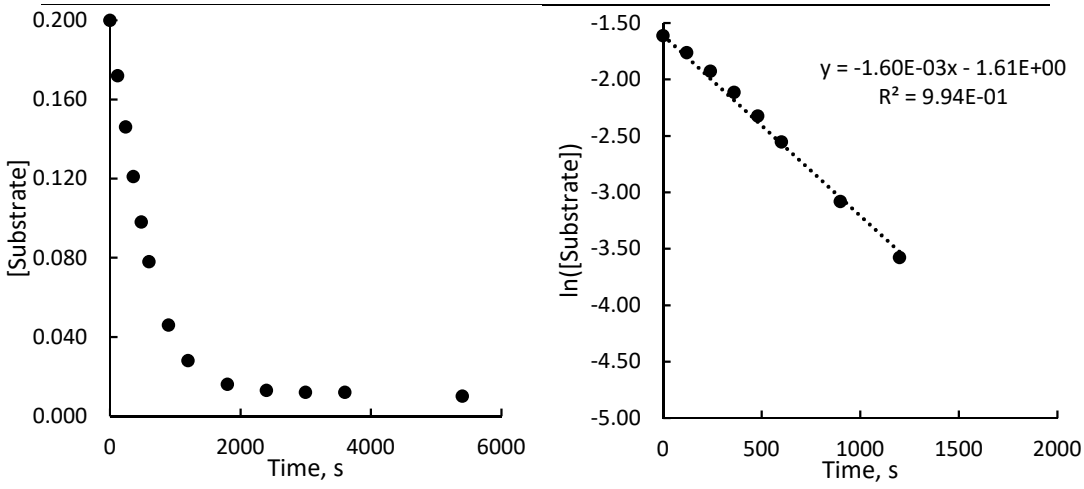


Table S58. Rate monitoring for the deuteration of acetophenone in Schlenk flask (run 2)

Following the General Kinetic Protocol using 60.1 mg of acetophenone, 8.7 mg of Ir-catalyst.

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	120	1.72	0.172	-1.76
2	240	1.46	0.146	-1.92
3	360	1.21	0.121	-2.11
4	480	0.98	0.098	-2.32
5	600	0.78	0.078	-2.55
6	900	0.46	0.046	-3.08
7	1200	0.28	0.028	-3.58
8	1800	0.16	0.016	-4.14
9	2400	0.13	0.013	-4.34
10	3000	0.12	0.012	-4.42
11	3600	0.12	0.012	-4.42

$k_{obs} = 1.60 \times 10^{-4}\ (s^{-1})$



Rate monitoring of HIE reaction with D_2 solution

The hydrogen isotope exchange reaction of acetophenone was performed using a solution of deuterium gas in $CDCl_3$. The observed rate of the reaction did not show a significant difference.

Procedure: Deuterium gas (from a balloon) was bubbled through the solution of acetophenone (0.50 mmol, 60.1 mg) in 2 mL of $CDCl_3$ for 30 min. The headspace of the vial was flushed with nitrogen for 5 minutes to remove the remaining D_2. The iridium(I) pre-catalyst (0.005 mmol, 8.7 mg) was dissolved in 0.5 mL of $CDCl_3$ and added to the reaction mixture, the reaction vessel was placed in a thermostat-controlled water bath that had been preheated to 50 °C, and the timer was started. The aliquots (0.04 mL) of reaction mixture were removed at the specified intervals throughout the reaction *via* syringe to an NMR tube and diluted with 0.5 mL of $CDCl_3$. The concentrations of the Ph-DG substrate (starting material) were determined by ^1H NMR analysis.

Table S59. Rate monitoring for the deuteration of acetophenone with D_2 solution (run 1)

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	120	1.87	0.187	-1.68
2	240	1.78	0.178	-1.73
3	480	1.59	0.159	-1.84
4	900	1.36	0.136	-2.00
5	1800	1.02	0.102	-2.28
6	3600	0.75	0.075	-2.59
7	5400	0.66	0.066	-2.72

$k_{obs} = 3.91 \times 10^{-4}\ (s^{-1})$

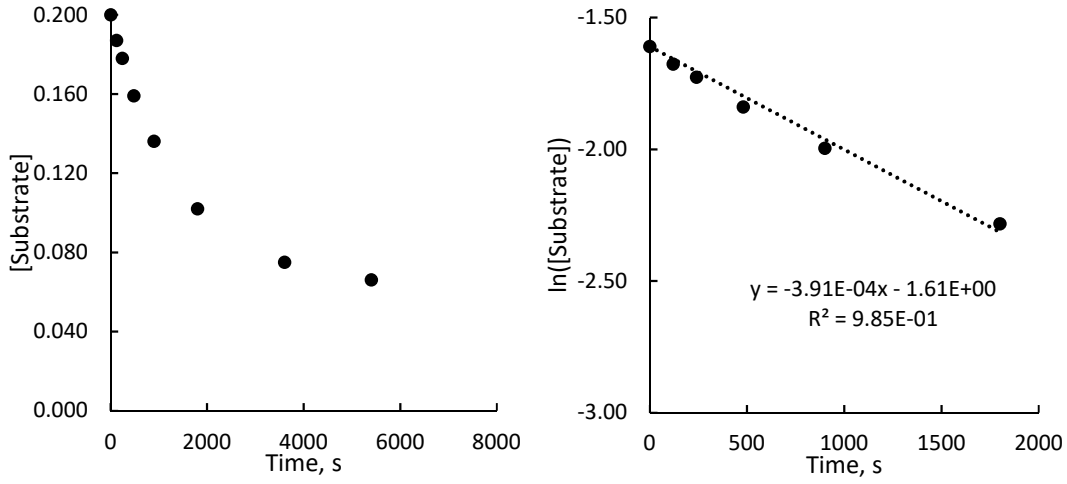
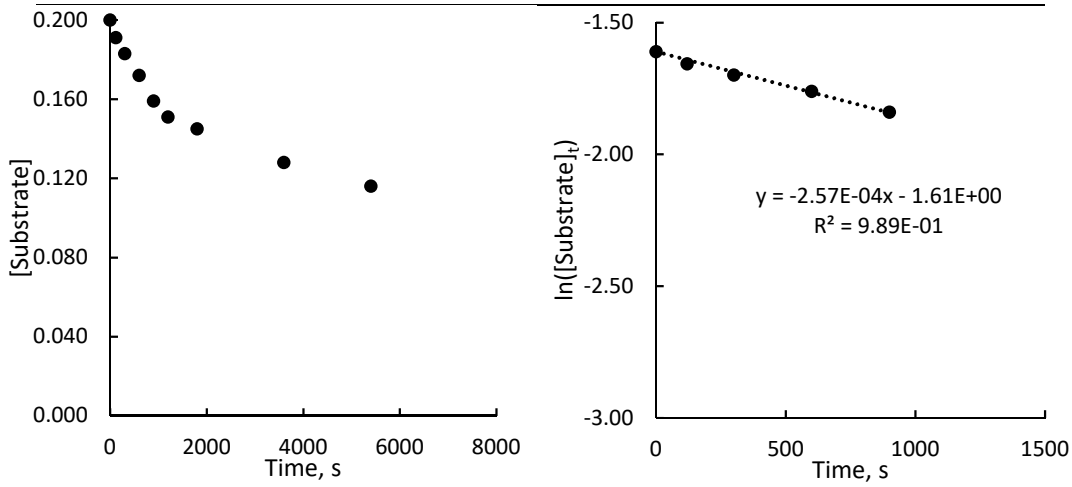


Table S60. Rate monitoring for the deuteration of acetophenone with D_2 solution (run 2)

Entry	Time, s	Integral (H/D)	[Substrate], M	ln [Substrate]
0	0	2.00	0.200	-1.61
1	120	1.91	0.191	-1.66
2	300	1.83	0.183	-1.70
3	600	1.72	0.172	-1.76
4	900	1.59	0.159	-1.84
5	1200	1.51	0.151	-1.89
6	1800	1.45	0.145	-1.93
7	3600	1.28	0.128	-2.06
8	5400	1.16	0.116	-2.15

$k_{obs} = 2.57 \times 10^{-4}\ (s^{-1})$



3.9. Mass spectrometry analysis for d_0, d_1, d_2 distribution over time.

The distribution of d_0, d_1, and d_2 isotopologues in the products was determined by a liquid chromatography-mass spectrometry (LC-MS) for 2-phenylpyridine and gas chromatography-mass spectrometry (GC-MS) for acetophenone by analysing the aliquots taken from the HIE reactions performed in the Schlenk flask (see previous Section Table S56 for 2-phenylpyridine and Table S58 for acetophenone).

For GC-MS: the aliquots taken for the NMR analysis of the reaction were diluted with $CHCl_3$ prior to the analysis. For LC-MS: the solvent was removed in vacuum and the residue was dissolved in an acetonitrile/water mixture.

The distribution of d_0, d_1, and d_2 substrates was determined from the corresponding normalised relative abundances at peaks of [M] (d_0), [M+1] (d_1), [M+2] (d_2) for GC-MS and at peaks [M+H] (d_0), [M+1+H] (d_1), [M+2+H] (d_2) for LC-MS analysis.

The observed relative isotopic abundances were corrected with regard to the amount of ^{13}C isotope (1.1 % natural abundance). The normalised abundances were obtained by dividing those relative numbers by the total abundance.

The overall level of deuterium incorporation in each substrate was determined according to Equation 1, using the relative peak abundances (d_0, d_1, or d_2) for each substrate:

$$\%\ Deuteration\ (\text{mass spectrometry}) = (0.5 \times d_1\ ) + d_2 \quad (1)$$

The values were in fairly good agreement with those obtained from ^1H NMR spectra (calculated using Equation 2).

$$\%\ Deuteration\ (\text{NMR}) = 100 - [\left(\frac{residual\ integral}{number\ of\ labelling\ sites}\right) \times\ 100] \quad (2)$$

The levels of deuterium incorporation derived from both methods are in good agreement.

Table S61. The extent of deuterium labelling and the distribution of d_0, d_1, and d_2 in acetophenone as determined by GC-MS analysis.

Observed relative abundances							
		m/z	**Ph(H_2)DG**	**2 min**	**4 min**	**6 min**	**8 min**
M	d_0	120	100.0	100.0	100.0	74.5	48.7
M+1	d_1	121	8.8	38.4	81.1	100.0	100.0
M+2	d_2	122	0.6	5.0	17.4	34.4	58.3
			10 min	**15 min**	**20 min**	**30 min**	**Ph(D_2)DG**
M	d_0	120	31.7	7.0	2.5	1.0	0.0
M+1	d_1	121	100.0	60.0	36.9	22.8	6.6
M+2	d_2	122	76.0	100.0	100.0	100.0	100.0

Relative abundances corrected for natural abundance of isotopes												
		m/z	**Ph(H_2)DG**	**2 min**	**4 min**	**6 min**	**8 min**	**10 min**	**15 min**	**20 min**	**30 min**	**Ph(D_2)DG**
M	d_0	120	100.0	100.0	100.0	74.5	48.7	31.7	7.0	2.5	1.0	0.0
M+1	d_1	121	0.0	29.6	72.3	93.4	95.7	97.2	59.4	36.7	22.7	6.6
M+2	d_2	122	0.0	1.8	10.5	25.7	49.6	67.2	94.7	96.8	98.0	99.4
Total abundance			100	131.4	182.7	193.6	194.0	196.1	161.1	135.9	121.7	106.1
Normalised relative abundances												
	%	m/z	**Ph(H_2)DG**	**2 min**	**4 min**	**6 min**	**8 min**	**10 min**	**15 min**	**20 min**	**30 min**	**Ph(D_2)DG**
	d_0	120	100.0	76.1	54.7	38.5	25.1	16.1	4.3	1.8	0.8	0.0
	d_1	121	0.0	22.6	39.6	48.3	49.3	49.6	36.9	27.0	18.6	6.3
	d_2	122	0.0	1.3	5.7	13.3	25.5	34.3	58.8	71.2	80.5	93.7
Level of deuterium incorporation												
			Ph(H_2)DG	**2 min**	**4 min**	**6 min**	**8 min**	**10 min**	**15 min**	**20 min**	**30 min**	**Ph(D_2)DG**
%D by GC-MS			0	13	25	37	50	59	77	85	90	97
%D by NMR			0	14	27	39.5	51	61	77	86	92	96.5

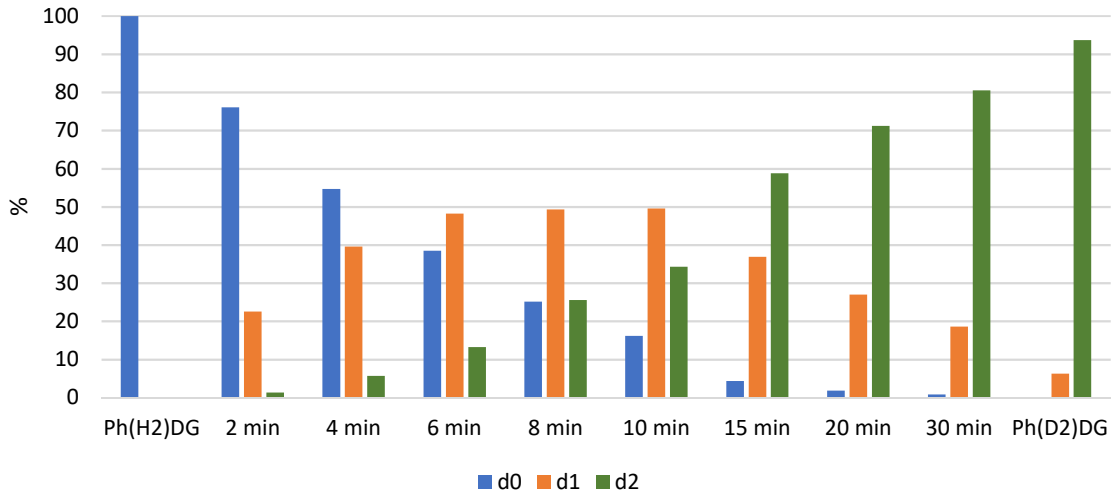


Figure S2. The distribution of d_0, d_1, and d_2 during acetophenone labelling as determined by GC-MS analysis**.**

Table S62. The extent of deuterium labelling and the distribution of d_0, d_1, and d_2 in 2-phenylpyridine as determined by LC-MS analysis.

Observed relative abundances							
		m/z	**Ph(H_2)DG**	**10 min**	**30 min**	**60 min**	**90 min**
(M+H)	d_0	156	100.0	100.0	100.0	74.5	80.5
(M+H)+1	d_1	157	13.3	15.5	22.6	100.0	32.8
(M+H)+2	d_2	158	0.9	9.5	32.4	34.4	100.0
			120 min	**180 min**	**240 min**	**Ph(D_2)DG**	
(M+H)	d_0	156	53.2	44.1	27.2	1.6	
(M+H)+1	d_1	157	31.2	32.7	33.2	6.2	
(M+H)+2	d_2	158	100.0	100.0	100.0	100.0	

Relative abundances corrected for natural abundance of isotopes											
		m/z	**Ph(H_2)DG**	**10 min**	**30 min**	**60 min**	**90 min**	**120 min**	**180 min**	**240 min**	**Ph(D_2)DG**
(M+H)	d_0	156	100.0	100.0	100.0	100.0	80.5	53.2	44.1	27.2	1.6
(M+H)+1	d_1	157	0.0	2.2	9.3	20.4	22.1	24.1	26.8	29.6	6.0
(M+H)+2	d_2	158	0.0	8.3	30.3	77.5	96.3	96.3	96.0	95.8	99.2
Total abundance			100	110.5	139.6	197.9	198.9	173.6	167.0	152.6	106.8
Normalised relative abundances											
	%	m/z	**Ph(H_2)DG**	**10 min**	**30 min**	**60 min**	**90 min**	**120 min**	**180 min**	**240 min**	**Ph(D_2)DG**
(M+H)	d_0	156	100.0	90.5	71.7	50.5	40.5	30.6	26.4	17.8	1.5
(M+H)+1	d_1	157	0.0	2.0	6.7	10.3	11.1	13.9	16.1	19.4	5.6
(M+H)+2	d_2	158	0.0	7.5	21.7	39.2	48.4	55.5	57.5	62.8	92.9
Level of deuterium incorporation											
			Ph(H_2)DG	**10 min**	**30 min**	**60 min**	**90 min**	**120 min**	**180 min**	**240 min**	**Ph(D_2)DG**
%D by GC-MS			0	9	25	44	54	62	66	72	96
%D by NMR			0	10	26	45	56	65	76	84	97

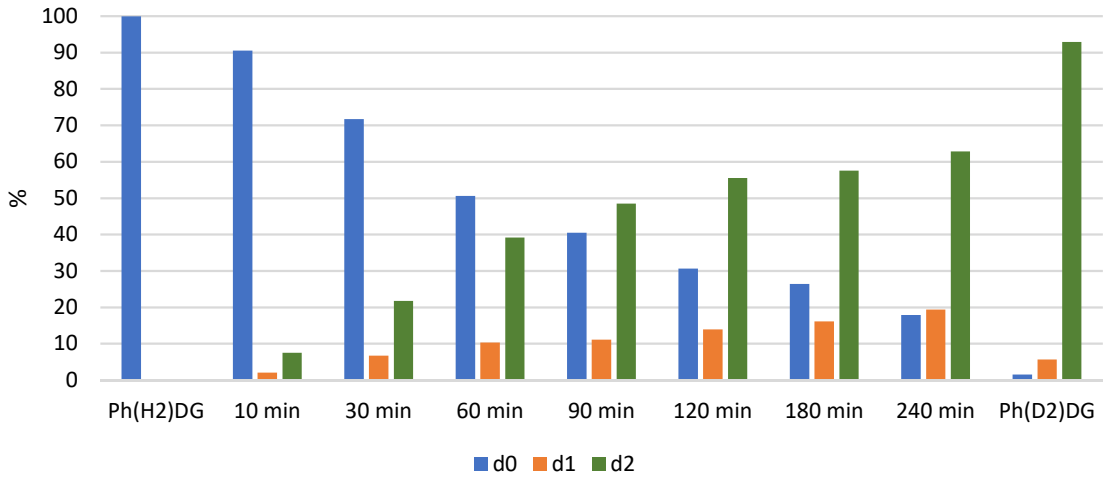


Figure S3. The distribution of d_0, d_1, and d_2 during 2-phenylpyridine labelling as determined by LC-MS analysis**.**

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