Supporting Information to

Non-Directed, Carbonate-Mediated C-H Activation and Aerobic C-H Oxygenation with Cp*Ir Catalysts

Margaret E. Kerr,^{a,b} Ijaz Ahmed,^a Ahmed Gunay,^a Nicholas J. Venditto,^a Fengfan Zhu,^a Elon A. Ison,^c and M. H. Emmert^{*a}

^aDepartment of Chemistry & Biochemistry, Worcester Polytechnic Institute, 100 Institute Road, Worcester, MA 01609.

^bChemistry Department, Worcester State University, 486 Chandler Street, Worcester, MA 01602

^cDepartment of Chemistry, North Carolina State University, 2620 Yarbrough Drive, Raleigh, NC 27695-8204, United States.

Table of Contents

3
4
7
10
10
11
14
17
19
20
21
23
26

General Procedures

¹H and ¹³C NMR spectra were recorded on Varian Inova 400 MHz NMR spectrometer with the residual solvent peak (CDCI₃: ¹H = 7.27 ppm, ¹³C = 77.23 ppm) as the internal reference unless otherwise noted. Chemical shifts are reported in parts per million (ppm) (δ). Multiplicities are reported as follows: br (broad resonance), s (singlet), t (triplet), q (quartet), d (doublet), m (multiplet), app (apparent). Coupling constants (J) are reported in Hz.

Stock solutions were prepared using volumetric glassware and all liquid reagents were dispensed by difference using gas-tight Hamilton syringes.

MeOH[D₄] for H/D exchange experiments was purchased from Cambridge Isotopes Lab. H/D exchange data for benzene was measured on an Agilent GC-MS Q5000 using a xTi®-5 (serial # 790776) column obtained from Agilent. All raw data were deconvoluted using Periana's benzene H/D exchange worksheet with a reported error of 5%.^[1] An assumption in the worksheet is that the fragmentation pattern of each isotopolog is identical. To obtain the most accurate analysis, pure samples of each isotopolog must be analyzed to determine the exact coefficients of the polynomial expansion for the given instrument. This treatment confirmed that the calculated percents of each isotopolog were within the reported error of the worksheet. All solvents used were dried over activated molecular sieves prior to use.

^[1] V. R. Ziatdinov, J. Oxgaard, O. A. Mironov, K. J. Young, W. A. Goddard, and R. A. Periana, *Journal of the American Chemical Society*, 2006, **128**, 7404-7405.

H/D Exchange Reactions of Benzene

H/D exchange experiments were performed following a literature procedure.^[2]

Table 1. Turnover numbers for H/D exchange between benzene and MeOH[D₄] at 150 °C catalyzed by mixtures of Cp*Ir complexes and additives after 24 h. Conditions: Cp*Ir complex (9.5 µmol [Ir], 2.0 mol % [Ir]), additives (19 µmol, 2.0 mol %), benzene (42 µL, 37 mg, 0.475 mmol, 1.00 equiv), $[D_4]MeOH$ (0.48 mL, 0.43 g, 12 mmol, 25 equiv), 150 °C, 24 h.

Cp*Ir Catalyst Precursor	Additives	TON 24 h
2 mol % Cp*Ir(H ₂ O) ₃ (OTf) ₂	-	11 ± 1
2 mol % Cp*Ir(MeCN) ₃ (OTf) ₂	-	6 ± 3
1 mol % [Cp*lrCl ₂] ₂	-	3 ± 1
11	4 mol % AgOTf	1 ± 0
II	4 mol % AgO ₂ CCF ₃	3 ± 0
11	4 mol % Ag ₂ CO ₃	3 ± 0
II	2 mol % Ag ₂ CO ₃	2 ± 1
11	4 mol % AgBF ₄	5 ± 1
II	4 mol % AgPF ₆	3 ± 1

^[2] M. C. Lehman, J. B. Gary, P. D. Boyle, M. S. Sanford and E. A. Ison, *ACS Catalysis*, 2013, **3**, 2304-2310.

Table 2. Turnover numbers for H/D exchange between benzene and MeOH[D₄] at 150 °C catalyzed by Cp*Ir(H₂O)₃(OTf)₂ /L-type additive combinations after 24 h. Conditions: Cp*Ir(H₂O)₃(OTf)₂ (6.5 mg, 9.5 μ mol, 2.0 mol %), ligand (9.5 μ mol, 2.0 mol %), benzene (42 μ L, 37 mg, 0.475 mmol, 1.00 equiv), [D₄]MeOH (0.48 mL, 0.43 g, 12 mmol, 25 equiv), 150 °C, 24 h.

Added Ligand	TON 24 h	Added Ligand	TON 24 h
-	11 ± 1	NMe ₂	20 ± 1
MeO PCy ₂ C ₆ H ₂ (ⁱ Pr) ₃ OMe	21 ± 10	N	12 ± 1
PCy ₂	17 ± 4	N CF3	9 ± 1
	19 ± 2	N	18 ± 1
	27 ± 12	FN	5 ± 1
	13 ± 2		5 ± 0
		MeON	5 ± 2
		H ₂ N N	6 ± 3
		Me ₂ N N	4 ± 2
			14 ± 1

Table 3. Turnover numbers for H/D exchange between benzene and MeOH[D₄] at 150 °C catalyzed by Cp*Ir(H₂O)₃(OTf)₂/X-type additive combinations after 24 h. Conditions: Cp*Ir(H₂O)₃(OTf)₂ (6.5 mg, 9.5 µmol, 2.0 mol %), additive (2.0 to 16 mol %), benzene (42 µL, 37 mg, 0.475 mmol, 1.00 equiv), [D₄]MeOH (0.48 mL, 0.43 g, 12 mmol, 25 equiv), 150 °C, 24 h.

X-type Additives	TON 24 h
2 mol % Li ₂ CO ₃	18 ± 5
4 mol % Li ₂ CO ₃	53 ± 1
8 mol % Li ₂ CO ₃	49 ± 9
16 mol % Li ₂ CO ₃	65 ± 1
2 mol % Na ₂ CO ₃	32 ± 3
4 mol % Na ₂ CO ₃	46 ± 6
4 mol % NaHCO ₃	37 ± 5
2 mol % Cs ₂ CO ₃	33 ± 8
4 mol % Cs ₂ CO ₃	28 ± 6
2 mol % NaOAc	10 ± 2
2 mol % NaOPiv	10 ± 4
2 mol % NaOTf	9 ± 0
2 mol % KF	10 ± 2
2 mol % Na ₂ SO ₄	23 ± 4
-	11 ± 1

H/D Exchange Reaction of para-Xylene

To a 4 mL resealable schlenk tube was added Cp*Ir(H₂O)₃(OTf)₂ (9.5 µmol, 2.0 mol %), Li₂CO₃ (76 µmol, 16 mol %), and 0.48 mL (0.43 g, 12 mmol, 25 equiv) of [D₄]MeOH. *para*-Xylene (59 µL, 51 mg, 0.48 mmol, 1.0 equiv), stored over 4 Å molecular sieves, was added to the reaction vessel, which was subsequently sealed. The vessel was completely submerged in an oil bath that had been preheated to 150 °C. After 24 h, the vessel was cooled to room temperature and CH₂CICHCl₂ (44.0 µL, 63.0 mg, 0.475 mmol, 1.00 equiv) was added as internal standard for ¹H NMR spectroscopy. The reaction mixture was filtered through a plug of celite and rinsed with [D₄]MeOH (0.05 mL). The resulting filtrate was analyzed by ¹H and ²H NMR spectroscopy.

The % deuterium incorporation was calculated from the loss of signal intensity in quantitative ¹H NMR spectra (NS = 32, D1 = 15 s, AQ = 2.19 s) as referenced to integration from a sample containing standard (1,1,2-trichloroethane) and non-deuterated *p*-xylene in an equimolar ratio. The reported error is the standard deviation of at least two replicate trials.

Table 4. D incorporation after H/D exchange reaction at 150 °C between [D₄]MeOH and *para*-xylene.

Substrate	Posstion Time [h]	D incorpor	ation [%]
		CH ₃	C ₆ H₄
p-H ₃ C(C ₆ H ₄)CH ₃	24	1.7 ± 1.0	17 ± 6



Figure 1. ¹H NMR Spectrum of mixture of 1,1,2-trichloroethane, *p*-xylene, and [D₄]MeOH after H/D exchange.



Figure 2. ²H NMR Spectrum of mixture 1,1,2-trichloroethane, *p*-xylene, and $[D_4]$ MeOH after H/D exchange.

Aerobic C-H Oxygenation of para-Xylene: Optimizations

General Procedure

Cp*Ir catalyst ([Cp*IrCl₂]₂ or Cp*Ir(H₂O)₃(OTf)₂; 1.5 to 15 μ mol [Ir]), carbonate additive (0 to 0.94 mmol, 0 to 160 equiv.), *p*-xylene (0.1 to 5.0 mL), and carboxylic acid (0.041 to 1.75 mmol, 7.0 to 344 equiv.) were mixed in a 20 mL scintillation vial. The vial was tightly sealed with a Teflon®-lined vial cap and heated to 125 °C for 18 h on a preheated vial plate. After the reaction time was complete, the mixture was allowed to cool to room temperature and PhBr (10 μ L, 95 μ mol) was added as GC standard. The mixture was extracted with H₂O (5 mL), the organic phase was filtered through celite, and the resulting filtrated was analyzed by GC-FID and/or GC-MS. Yields were determined by quantitative GC-FID analysis.

Background Reactions and Initial Reactivity



In analogy to the general procedure, Cp*Ir catalyst ($[Cp*IrCl_2]_2$ or Cp*Ir(H₂O)₃(OTf)₂; 0 or 6 µmol [Ir]), Na₂CO₃ (0 or 47 µmol, 0 or 8 equiv.), *p*-xylene (1.5 mL, 1.3 g, 12.2 mmol), and benzoic acid (0 or 0.49 mmol, 0 or 82 equiv.) were reacted at 125 °C for 18 h. Workup and GC analysis were performed as described in the general procedure above.

Catalyst	Equiv. Na₂CO₃ ^b	Equiv. PhCO₂H ^ь	µmol O ₂ CPh	µmol ОН	µmol 0
-	8	82	1 ± 1	45 ± 10	122 ±10
-	-	-	0	66 ± 46	113 ± 28
-	-	82	2 ± 1	46 ± 1	139 ± 6
-	8	-	0	31 ± 5	123 ± 15
3 µmol [Cp*lrCl ₂] ₂	8	82	6.4 ± 1.7 (1 TON/[Ir])	42 ± 10 (0 TON/[lr])	108 ± 47 (0 TON/[lr])
п	-	82	2 ± 1 (0 TON/[Ir])	1.5 ± 1.3 (0 TON/[lr])	76 ± 1 (0 TON/[lr])
n	8	-	0 (0 TON/[Ir])	21 ± 3 (0 TON/[Ir])	101 ± 18 (0 TON/[lr])
$6 \ \mu mol$ [Cp*lr(H ₂ O) ₃](OTf) ₂	8	82	12 ± 4 (2 TON/[Ir])	47 ± 7 (0 TON/[Ir])	147 ± 86 (4 TON/[lr])
6 µmol	8	82	3 ± 1 (0 TON/[Ir])	16 ± 11 (0 TON/[lr])	89 ± 20 (0 TON/[Ir])
$\begin{array}{c} \overbrace{H_2O \ H_2O \ Me}^{Ir} \\ H_2O \ Me \end{array} $	8	82	8 ± 3 (1 TON/[lr])	23 ± 15 (0 TON/[lr])	118 ± 46 (0 TON/[Ir])

Table 5. Background Reactions in *p*-Xylene.^a

^aAll values for TON/[Ir] are corrected for background reactivity by subtracting the values for mmol products in the respective cell of entry 1. Conditions: Ir catalyst (6 μmol [Ir], 1 equiv.), Na₂CO₃ (0 or 8 equiv.), *p*-xylene (1.5 mL, 2033 equiv.), benzoic acid (0 or 83 equiv.), 125 °C, 18 h. ^bBased on 6 μmol [Ir] = 1 equiv.





^aConditions for esterification background: Cp*Ir(H₂O)₃(OTf)₂ (0 or 6 μmol [Ir]), Na₂CO₃ (47 μmol, 8 equiv.), and benzoic acid (0.49 mmol, 82 equiv.), 125 °C, 18 h. ^bBased on 6 μmol [Ir] = 1 equiv

Table 7. Effect of Water Addition.^a

	82 e	Ir catalyst equiv. $PhCO_2H$ quiv. Na_2CO_3 air, H_2O 8 h, 125 °C	O ₂ CPh	
Catalyst	added water	μmol O ₂ CPh	µmol ОН	µmol
3 µmol [Cp*IrCl ₂] ₂	0 μL	6.4 ± 1.7 (1 TON/[lr])	42 ± 10 (0 TON/[Ir])	108 ± 47 (0 TON/[lr])
II	100 µL	1 ± 1 (0 TON/[lr])	7 ± 12 (0 TON/[lr])	36 ± 42 (0 TON/[Ir])
6 µmol [Cp*Ir(H ₂ O) ₃](OTf) ₂	0 μL	12 ± 4 (2 TON/[Ir])	47 ± 7 (0 TON/[Ir])	147 ± 86 (4 TON/[lr])
" "	100 µL	3 ± 1 (0 TON/[Ir])	28 ± 9 (0 TON/[Ir])	112 ± 28 (0 TON/[Ir])

^aAll values for TON/[Ir] are corrected for background reactivity by subtracting the values for mmol products in the respective cell of Table 5, entry 1. Conditions: Ir catalyst (6 μmol [Ir], 1 equiv.), Na₂CO₃ (8 equiv.), *p*-xylene (1.5 mL, 2033 equiv.), benzoic acid (82 equiv.), 125 °C, 18 h.

	+ or O	Ir catalyst 82 equiv. PhCO ₂ H 8 equiv. Na ₂ CO ₃ air or N ₂ 18 h, 125 °C		<u>v</u> CPh
Catalyst	Additive	µmol O ₂ CPh	µmol ОН	µmol O
3 µmol [Cp*lrCl ₂] ₂	-	6.4 ± 1.7 (1 TON/[lr])	42 ± 10 (0 TON/[Ir])	108 ± 47 (0 TON/[lr])
н	50 µmol OH	6.7 ± 5 (1 TON/[lr])	not determined	112 ± 33 (0 TON/[Ir])
	150 µmol	5.4 ± 1 (1 TON/[Ir])	24 ± 11 (0 TON/[Ir])	not determined
6 µmol [Cp*lr(H ₂ O) ₃](OTf) ₂	-	12 ± 4 (2 TON/[lr])	47 ± 7 (0 TON/[Ir])	147 ± 86 (4 TON/[lr])
II	50 µmol	4 ± 1 (0 TON/[lr])	not determined	87 ± 3 (0 TON/[lr])
н	150 μmol	11 ± 0 (2 TON/[Ir])	19 ± 2 (0 TON/[Ir])	not determined
пр	150 µmol	0 ± 0 ^b (0 TON/[lr])	3 ± 1 ^b (0 TON/[Ir])	not determined

Table 8. Effect of other Additives & N₂ Atmosphere.^a

^aAll values for TON/[Ir] are corrected for background reactivity by subtracting the values for mmol products in the respective cell of Table 5, entry 1. Conditions: Ir catalyst (6 μmol [Ir], 1 equiv.), Na₂CO₃ (8 equiv.), *p*-xylene (1.5 mL, 2033 equiv.), benzoic acid (82 equiv.), 125 °C, 18 h. ^bReaction under N₂ atmosphere.

Optimization of Ester Formation: Na₂CO₃ and Li₂CO₃ Loading



In analogy to the general procedure, Ir catalyst (6 μ mol [Ir]), Na₂CO₃ (0 to 160 equiv.) or Li₂CO₃ (9 to 68 equiv.), *p*-xylene (1.5 mL, 1.3 g, 12.2 mmol, 2033 equiv.), and benzoic acid (60 mg, 0.49 mmol, 83 equiv.) were reacted at 125 °C for 18 h. Workup and GC analysis were performed as described in the general procedure above; TONs and μ mol of ester product are shown in Table 9.

Catalyst	Equiv. Na₂CO₃ ^c	µmol O ₂ CPh
3 µmol [Cp*lrCl ₂] ₂	0	0 (0 TON/[lr])
п	3.8	2.0 ± 1.3 (0.4 TON/[Ir])
п	9.4	4.5 ± 1.6 (0.9 TON/[Ir])
I	18.8	6.8 ± 3.4 (1.4 TON/[Ir])
II	25.1	3.0 ± 0.4 (0.6 TON/[Ir])
II	37.6	1.2 ± 0.6 (0.3 TON/[Ir])
II	50.2	0 (0 TON/[Ir])
6 µmol [Cp*lr(H ₂ O) ₃](OTf) ₂	0	0.9 ± 1.6 (0.15 TON/[Ir])
п	3.2	7.5 ± 2.3 (1.3 TON/[Ir])
II	8	10.2 ± 3.5 (1.7 TON/[Ir])
II	32	9.0 ± 1.0 (1.5 TON/[Ir])
	64	10.7 ± 0.6 (1.8 TON/[Ir])
I	96	5.4 ± 0.8 (0.9 TON/[Ir])
I	160	0 (0 TON/[lr])

Table 9. Optimization of Na₂CO₃ Loading.^{a,b}

^aAll values for TON/[Ir] and µmol product are corrected for background reactivity by subtracting the values for µmol products in Table 5, entry 1. ^bConditions: Ir catalyst (6 µmol [Ir]), Na₂CO₃ (0 to 100 mg, 0 to 0.94 mmol, 0 to 160 equiv.), *p*-xylene (1.5 mL, 1.3 g, 12.2 mmol, 2033 equiv.), benzoic acid (60 mg, 0.49 mmol, 83 equiv.), 125 °C, 18 h. ^cBased on 6 µmol [Ir] = 1 equiv.

Catalyst	Equiv. Li₂CO₃ ^c	μmol
3 µmol [Cp*lr(H ₂ O) ₃](OTf) ₂	9	8.9 ± 0.6 (3 TON/[Ir])
п	18	8.4 ± 1.5 (2.8 TON/[Ir])
п	23	12.9 ± 2.0 (4.3 TON/[Ir])
п	32	8.1 ± 1.0 (2.7 TON/[Ir])
	45	11.0 ± 4.0 (3.1 TON/[Ir])
п	59	9.7 ± 3.0 (3.2 TON/[Ir])
n	68	11.5 ± 0.7 (3.8 TON/[Ir])

Table 10. Optimization of Li₂CO₃ Loading.^{a,b}

^aAll values for TON/[Ir] and µmol product are corrected for background reactivity by subtracting the values for µmol products in Table 5, entry 1. ^bConditions: Ir catalyst (3 µmol [Ir]), Li₂CO₃ (5 to 150 mg, 0.07 to 0.20 mmol, 9 to 68 equiv.), *p*-xylene (1.5 mL, 1.3 g, 12.2 mmol, 4066 equiv.), benzoic acid (60 mg, 0.49 mmol, 163 equiv.), 125 °C, 18 h. ^cBased on 3 µmol [Ir] = 1 equiv.

Optimization of Ester Formation: PhCO₂H Loading



In analogy to the general procedure, Ir catalyst (6 μ mol [Ir]), Na₂CO₃ (5.0 mg, 0.047 mmol, 8.0 equiv.), *p*-xylene (1.5 mL, 1.3 g, 12 mmol, 2033 equiv.), and benzoic acid (5 to 210 mg, 0.041 to 1.8 mmol, 7 to 344 equiv.) were reacted at 125 °C for 18 h. Workup and GC analysis were performed as described in the general procedure above; TONs and μ mol of ester product are shown in Table 9 below.

Catalyst	Equiv. PhCO₂H ^c	μ mol
3 µmol [Cp*lrCl ₂] ₂	16	0 (0 TON/[Ir])
п	82	2.0 ±0.5 (0.40 TON/[lr])
п	98	4.5 ± 1.6 (0.89 TON/[Ir])
п	197	4.2 ± 1.4 (0.84 TON/[Ir])
II	246	4.8 ± 0.5 (0.96 TON/[Ir])
II	344	2.8 ± 1.1 (0.56 TON/[Ir])
6 µmol [Cp*lr(H ₂ O) ₃](OTf) ₂	7	0 (0 TON/[Ir])
II	83	8.9 ± 1.3 (1.5 TON/[Ir])
II	111	10.2 ± 0.7 (1.7 TON/[Ir])
II	139	13.6 ± 2.5 (2.3 TON/[Ir])
II	166	10.2 ± 0.007 (1.7 TON/[Ir])
"	195	4.9 ± 1.9 (0.8 TON/[Ir])

Table 11. Optimization of PhCO₂H Loading.^{a,b}

^aAll values for TON/[Ir] and µmol products are corrected for background reactivity by subtracting the values for µmol products in Table 5, entry 1. ^bConditions: Ir catalyst (6 µmol [Ir]), Na₂CO₃ (5.0 mg, 0.047 mmol, 8.0 equiv.), *p*-xylene (1.5 mL, 1.3 g, 12 mmol, 2033 equiv.), benzoic acid (5 to 210 mg, 0.041 to 1.8 mmol, 7 to 344 equiv.), 125 °C, 18 h. ^cBased on 6 µmol [Ir] = 1 equiv.

Optimization of Ester Formation: p-Xylene Loading



In analogy to the general procedure, Ir catalyst (6 μ mol [Ir]), Na₂CO₃ (5.0 mg, 47 μ mol, 8.0 equiv.), *p*-xylene (0.1 to 5 mL, 0.09 to 4.3 g, 0.8 to 41 mmol, 162 to 8120 equiv.), and benzoic acid (60 mg, 0.49 mmol, 83 equiv.) were reacted at 125 °C for 18 h. Workup and GC analysis were performed as described in the general procedure above.

Catalyst	Equiv. p-xylene ^c	µmol O ₂ CPh
3 µmol [Cp*IrCl ₂] ₂	162	0 (0 TON/[Ir])
n	820	4.8 ± 3 (1.6 TON/[Ir])
n	1624	1.9 ± 1.7 (0.39 TON/[Ir])
n	2440	4.5 ± 1.6 (0.89 TON/[Ir])
n	3240	1.9 ± 1.7 (0.37 TON/[Ir])
n	4860	3.7 ± 3.9 (0.74 TON/[Ir])
n	6500	1.2 ± 1.2 (0.27 TON/[Ir])
n	8120	1.4 ± 1.2 (0.27 TON/[Ir])

Table 12. Optimization of *p*-Xylene Loading.^{a,b}

^aAll values for TON/[Ir] and mmol products are corrected for background reactivity by subtracting the values for μmol products in Table 5, entry 1. ^bConditions: 3 μmol [Cp*IrCl₂]₂ (6 μmol [Ir]), Na₂CO₃ (5.0 mg, 47 μmol, 8.0 equiv.), *p*-xylene (0.1 to 5 mL, 0.09 to 4.3 g, 0.8 to 41 mmol, 162 to 8120 equiv.), benzoic acid (60 mg, 0.49 mmol, 83 equiv.), 125 °C, 18 h. ^cBased on 6 μmol [Ir] = 1 equiv.

Optimization of Ester Formation: Catalyst Loading



In analogy to the general procedure, Ir catalyst (1.5 μ mol to 15 μ mol [Ir]), Na₂CO₃ (5 mg, 0.047 mmol), *p*-xylene (1.5 mL, 1.3 g, 12.2 mmol), and benzoic acid (1.5 mL, 1.3 g, 12.2 mmol), were reacted at 125 °C for 18 h. Workup and GC analysis were performed as described in the general procedure above.

Catalyst Loading	μmol
2.5 µmol [Cp*lrCl ₂] ₂	5.9 ± 1.0 (2.4 TON/[Ir])
5 µmol [Cp*lrCl ₂] ₂	4.5 ± 1.6 (0.9 TON/[Ir])
7.5 μmol [Cp*lrCl ₂] ₂	3.2 ± 2.4 (0.3 TON/[Ir])
10 μmol [Cp*lrCl ₂] ₂	0 (0 TON/[Ir])
13 μmol [Cp*lrCl ₂] ₂	0 (0 TON/[Ir])
1.5 μmol [Cp*lr(H ₂ O) ₃](OTf) ₂	6.8 ± 0.8 (4.5 TON/[Ir])
3 µmol [Cp*lr(H ₂ O) ₃](OTf) ₂	8.9 ± 0.7 (3 TON/[Ir])
6 µmol [Cp*lr(H ₂ O) ₃](OTf) ₂	10 ± 3 (1.7 TON/[Ir])
9 µmol [Cp*lr(H ₂ O) ₃](OTf) ₂	9.4 ± 2 (1.1 TON/[Ir])
15 μmol [Cp*lr(H ₂ O) ₃](OTf) ₂	6.3 ± 0.3 (0.4 TON/[Ir])

Table 13. Optimization of Catalyst Loading.^{a,b}

^aAll values for TON/[Ir] and μmol products are corrected for background reactivity by subtracting the values for μmol products in Table 5, entry 1. ^bConditions: Ir catalyst (1.5 μmol to 15 μmol [Ir]), Na₂CO₃ (5 mg, 0.047 mmol), *p*-xylene (1.5 mL, 1.3 g, 12.2 mmol), benzoic acid (1.5 mL, 1.3 g, 12.2 mmol), 125 °C, 18 h.

Optimization of Ester Formation: AcOH Loading



In analogy to the general procedure, $[Cp^*Ir(H_2O)_3](OTf)_2$ (2.0 mg, 3.0 µmol [Ir]), Na₂CO₃ (5 mg, 47 µmol, 16 equiv.), *p*-xylene (1.5 mL, 1.3 g, 12.2 mmol, 4066 equiv.), and AcOH (0.03 to 0.18 mL, 31.5 to 189 mg, 0.52 to 3.1 mmol, 181 to 1085 equiv.) were reacted at 125 °C for 18 h. Workup and GC analysis were performed as described in the general procedure above.

Catalyst	Equiv. AcOH ^c	μmol
3 µmol [Cp*lr(H ₂ O) ₃](OTf) ₂	181	0 (0 TON/[Ir]) ^d
n	362	13.2 ± 7 (4.6 TON/[Ir]) ^d
п	482	17.3 ± 2 (5.9 TON/[Ir]) ^d
п	723	12.3 ± 9 (4.2 TON/[Ir]) ^d
п	904	10.5 ± 8 (3.6 TON/[Ir]) ^d
II	1085	0 (0 TON/[Ir]) ^d

Table 14. Optimization of AcOH Loading.^{a,b}

^aAll values for TON/[Ir] and μmol products are corrected for background reactivity by subtracting the values for μmol products in Table 12, entries 1-8, respectively. ^bConditions: [Cp*Ir(H₂O)₃](OTf)₂ (2.0 mg, 3.0 μmol [Ir]), Na₂CO₃ (5 mg, 47 μmol, 16 equiv.), *p*-xylene (1.5 mL, 1.3 g, 12.2 mmol, 4066 equiv.), AcOH (0.03 to 0.18 mL, 31.5 to 189 mg, 0.52 to 3.1 mmol, 181 to 1085 equiv.), 18 h, 125 °C. ^cBased on 3 μmol [Ir] = 1 equiv.

Catalyst	Equiv. AcOH ^c	μmol
None	181	0
n	362	21 ± 15
I	482	16 ± 4
n	723	42 ± 22
n	904	56 ± 13
n	1085	0

Table 15. Background Formation of Acetate Ester in the Absence of Ir Catalyst.^a

^aNa₂CO₃ (5 mg, 47 μmol, 16 equiv.), *p*-xylene (1.5 mL, 1.3 g, 12.2 mmol, 4066 equiv.), AcOH (0.03 to 0.18 mL, 31.5 to 189 mg, 0.52 to 3.1 mmol, 181 to 1085 equiv.), 18 h, 125 °C.

Scope of Carboxylic Acids

Original samples of each ester were synthesized independently according to literature procedures.³

Conditions A: Carboxylic Acid Scope using Low Carboxylic Acid Loading (546 equiv.)



In analogy to the general procedure, $[Cp^*Ir(H_2O)_3](OTf)_2$ (1.0 mg, 1.5 µmol [Ir]), Na₂CO₃ (5.0 mg, 47 µmol, 31 equiv.), *p*-xylene (1.5 mL, 1.3 g, 12.2 mmol, 8133 equiv.), and carboxylic acid (0.819 mmol, 546 equiv.) were reacted at 125 °C for 18 h. Workup and GC analysis were performed as described in the general procedure above, using PhBr as GC standard.

Conditions B: Carboxylic Acid Scope using High Carboxylic Acid Loading (1747 equiv.)



In analogy to the general procedure, $[Cp*Ir(H_2O)_3](OTf)_2$ (1.0 mg, 1.5 µmol [Ir]), Na₂CO₃ (5.0 mg, 47 µmol, 31 equiv.), *p*-xylene (1.5 mL, 1.3 g, 12.2 mmol, 8133 equiv.), and carboxylic acid (2.62 mmol, 1747 equiv.) were reacted at 125 °C for 18 h. Workup and GC analysis were performed as described in the general procedure above, using PhBr as GC standard.

³ O. Ohno, M. Ye, T. Koyama, K. Yazawa, E. Mura, H. Matsumoto, T. Ichino, K. Yamada, K. Nakamura, T. Ohno, K. Yamaguchi, J. Ishida, A. Fukamizu and D. Uemura, *Bioorganic & Medicinal Chemistry*, 2008, **16**, 7843-7852.

Carboxylic Acid	Product	Product Yield (Conditions A) ^{a,c}	Product Yield (Conditions B) ^{b,c}
HO Ph	O Ph	12 ± 1 μmol (8 TON/[lr])	8 ± 5 µmol (5 TON/[Ir])
НО		9 ± 5 µmol (6 TON/[lr])	16 ± 3 μmol (11 TON/[Ir])
но		10 ± 1 μmol (7 TON/[Ir])	25 ± 1 μmol (11 TON/[lr])
но		4.5 ± 0.3 μmol (3.0 TON/[Ir])	7.5 ± 0.1 μmol (5 TON/[lr])
HO CF ₃	CF3	10 ± 1 μmol (7 TON/[lr])	13 ± 1 μmol (9 TON/[lr])
НО		4.2 ± 0.1 μmol (2.8 TON/[Ir])	2.4 ± 2.9 μmol (1.4 TON/[Ir])

Table 16. Carboxylic Acid Scope.

^aConditions: [Cp*Ir(H₂O)₃](OTf)₂ (1.0 mg, 1.5 μmol [Ir]), Na₂CO₃ (5.0 mg, 47 μmol, 31 equiv.), *p*-xylene (1.5 mL, 1.3 g, 12.2 mmol, 8133 equiv.), carboxylic acid (0.819 mmol, 546 equiv.), 125 °C, 18 h.
 ^bConditions: [Cp*Ir(H₂O)₃](OTf)₂ (1.0 mg, 1.5 μmol [Ir]), Na₂CO₃ (5.0 mg, 47 μmol, 31 equiv.), *p*-xylene (1.5 mL, 1.3 g, 12.2 mmol, 8133 equiv.), carboxylic acid (2.62 mmol, 1747 equiv.), 125 °C, 18 h.
 ^cValues for TONs and µmol product are corrected for the values of the background reactivity (see Table 17).

Carboxylic Acid	Product	µmol Product under Conditions Aª	µmol Product under Conditions B [♭]
O HO Ph	O Ph	1.7 ± 0.6	0
НО		0	60 ± 14
НО		7.5 ± 7	17.5 ± 5
но		9.3 ± 5	23 ± 7
HO CF3	CF3	0.3 ± 0.4	0.8 ± 1
НО		6.8 ± 0.6	0.5 ± 0.8

Table 17. Background Reactions for Carboxylic Acid Scope in the Absence of Ir Catalyst.

^aConditions: Na₂CO₃ (5.0 mg, 47 μmol, 31 equiv.), *p*-xylene (1.5 mL, 1.3 g, 12.2 mmol, 8133 equiv.), carboxylic acid (0.819 mmol, 546 equiv.), 125 °C, 18 h. ^bNa₂CO₃ (5.0 mg, 47 μmol, 31 equiv.), *p*-xylene (1.5 mL, 1.3 g, 12.2 mmol, 8133 equiv.), carboxylic acid (2.62 mmol, 1747 equiv.), 125 °C, 18 h.

Scope of Alkyl Arenes



In analogy to the general procedure, $Cp^*(H_2O)_3(OTf)_2$ (1.5 µmol), Na_2CO_3 (47.2 µmol, 31 equiv.), alkyl arene (12.2 mmol, 8133 equiv.), and AcOH (2.62 mmol, 1747 equiv.) were reacted at 125 °C for 18 h. Workup and GC analysis (using PhBr as GC standard) were performed as described in the general procedure above.



Table 18. Aryl Arene Scope.^a

Alkyl Arene	Product	µmol Product under Conditions B ^ª
		60 ± 14
	OAc	22 ± 8
	OAc	11 ± 3
	OAc	151 ± 8

 Table 19. Aryl Arene Background Reactions in the Absence of Ir Catalyst.

^aConditions: Conditions: Na₂CO₃ (47.2 µmol), alkyl arene (12.2 mmol), AcOH (2.62 mmol), 125 °C, 18 h.