

SUPPORTING INFORMATION

Methylene C(sp³)–H β , β' -Diarylation of Cyclohexanecarbaldehydes Promoted by a Transient Directing Group and Pyridone Ligand

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General experimental considerations

All nonaqueous reactions were run under an inert atmosphere (argon, balloon) with flame-dried glassware using standard techniques. Anhydrous solvents were obtained by filtration through drying columns (THF, Et₂O, CH₂Cl₂). Hexafluoroisopropanol, Pd(OAc)₂ and AgTFA were purchased from Fluorochem and used as provided. Acetic acid, AgOAc and other Pd catalysts were purchased from Sigma Aldrich and used as provided. Commercial aldehydes were distilled prior to use. All other commercial reagents were used as supplied or purified by standard techniques where necessary. All extractions were conducted three times in equivolume solvent unless stated otherwise.

Reactions in sealed tubes were run using Biotage microwave vials (2–5 mL) and aluminium caps with molded butyl septa.

Heating was achieved by adding the reaction vials to a pre-heated oil bath at the stated temperatures.

Flash column chromatography was performed using 230-400 mesh silica with the indicated solvent system according to standard techniques. Analytical thin-layer chromatography (TLC) was performed on precoated, glass-backed silica gel plates. Visualisation of the developed chromatogram was performed by UV absorbance (254 nm), phosphomolybdic acid, vanillin or *p*-anisaldehyde stains.

Infrared spectra (ν_{\max} , FTIR ATR) were recorded in reciprocal centimeters (cm⁻¹).

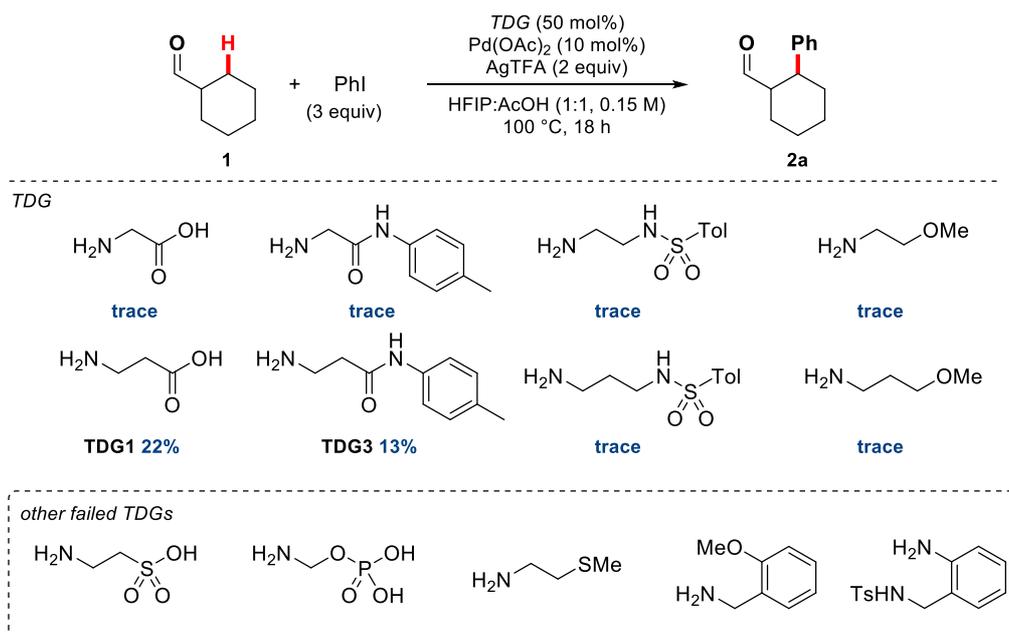
Nuclear magnetic resonance spectra were recorded on 400 MHz spectrometers. Chemical shifts for ¹H NMR spectra are recorded in parts per million from tetramethylsilane with the solvent resonance as the internal standard (chloroform δ = 7.27 ppm, DMSO δ = 2.50 ppm). Data is reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, hept = heptet, m = multiplet and b = broad), coupling constant in Hz, integration, assignment]. ¹³C NMR spectra were recorded with complete proton decoupling. Chemical shifts are reported in parts per million from tetramethylsilane with the solvent resonance as the internal standard (chloroform: δ = 77.00 ppm, DMSO δ = 39.52 ppm). ¹⁹F NMR spectra were recorded with complete proton decoupling. *J* values are reported in Hz. Assignments of ¹H/¹³C spectra were made by the analysis of δ /*J* values, and COSY, HSQC, and HMBC experiments as appropriate. ¹⁹F NMR spectra were recorded with or without complete proton decoupling. Decoupling is indicated as (¹⁹F{¹H}) and where relevant this is stated in each assignment and spectrum. ¹⁹F spectra are indirectly referenced to CFCl₃, automatically via direct measurement of the absolute frequency of the deuterium lock signal by the spectrometer hardware. For clarity NMR spectra are displayed as follows unless this would obscure signals: ¹H NMR spectra are displayed between 10.5 ppm and –0.5 ppm; ¹³C NMR spectra are displayed between 230 ppm and 0 ppm.

Melting points are uncorrected.

The high resolution mass spectrometry (HRMS) analyses were performed using electrospray ion source (ESI) or pneumatically assisted atmospheric pressure chemical ionization (APCI) using an atmospheric solids analysis probe (ASAP). ESI was performed using a Waters LCT Premier equipped with an ESI source operated in positive ion mode. The software used was MassLynx 4.1, this software does not account for the electron and all the calibrations/references are calculated accordingly, i.e. [M+H]⁺ is detected and the mass is calibrated to output [M+H]. APCI was performed using an Orbitrap XL or Xevo G2S using an ASAP to insert samples into the APCI source. The sample was introduced at ambient temperature and the temperature increased until the sample vaporised.

All raw and processed data for this manuscript can be found at the Imperial College London Research Data Repository ([doi: 10.14469/hpc/6480](https://doi.org/10.14469/hpc/6480)).

Initial screen of transient directing groups



Scheme S1: Initial screen of directing groups for the methylene β -C-H arylation of cyclohexanecarboxaldehyde. Yields determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard

Using 50 mol% of the TDG, only β -alanine **TDG1** and the tolyl amide of β -alanine **TDG3** gave significant amounts of product formation in the β -arylation of cyclohexanecarboxaldehyde. The amide group provides a point of diversity to enable optimisation to create a more active TDG.

Before screening the directing group, some changes to conditions were tested to improve the yield and reduce the loading of the TDG (Table S1).

Entry	mol% TDG3	Concentration (M)	Yield mono (2a) (%) ^a	Yield Di (3a) (%) ^a	Total yield (%) ^a
1	50	0.15	13	trace	13
2^b	25	0.075	19	7	22

Table S1: Optimisation using **TDG3**. ^aYields calculated by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard. ^b72 h.

A lower **TDG3** loading and concentration with a longer reaction time gave an improved total yield, and so was used as the conditions to screen the directing groups.

For the screen of TDGs (See manuscript Figure 1), an aqueous work-up was used to remove acetic acid and enable calculation of the yields by the aldehyde signal in the crude ¹H NMR spectra. To improve accuracy, each reaction was conducted twice (ensuring the yields were within 5% of each other for each run) and an average taken.

General procedure for TDG Screen and optimisation: Cyclohexanecarboxaldehyde **1** (24.2 μ L, 0.20 mmol), iodobenzene (67 μ L, 0.6 mmol), **TDG** (25 mol%), palladium acetate (4.5 mg, 0.02 mmol), silver trifluoroacetate (88 mg, 0.40 mmol), HFIP (1.3 mL) and AcOH (1.3 mL) were combined in a flame dried microwave vial. The vial was purged with argon, sealed and heated to 80 °C for 72 h. The reaction was allowed to cool to room temperature and transferred to a separating funnel using CH₂Cl₂. Water was added (20 mL) and the products extracted with CH₂Cl₂ (3 \times 20 mL). The combined organic layers were dried (Na₂SO₄), filtered and the solvent removed under reduced pressure. 10–20 mg of accurately weighed 1,3,5-trimethoxybenzene was added, the residue was fully dissolved in CDCl₃ and the yield of the the arylated products **2a** and **3a** were calculated by ¹H NMR by comparison to the internal standard. The aldehyde signals for **2a** (9.42, d, *J* = 3.1 Hz) and **3a** (9.26, d, *J* = 3.6 Hz) and aromatic 3 H singlet (6.10) for the internal standard were used in yield calculations. NOTE: Iodobenzene and cyclohexanecarboxaldehyde were added after the solid reagents using a Gilson micropipette, then the solvents were added via syringe.

Determination of relative stereochemistry of mono (**2a**) and diarylated (**3a**) aldehyde products

The stereochemistry of both the mono and the diarylated products are proposed to be *trans* by analysis of the *J* coupling values. The large triplet diaxial splitting of 11.5 Hz seen for the *CHPh* and *CHCHO* signals implies the aldehyde and aryl substituents are equatorial leaving the protons axial and *trans*-configured (Figure S1). Ge proposes a *cis*-stereochemistry for monophenylated **2a** through NOE spectra, however the compound **2a** formed by us as Ge are the same by NMR.¹ NOTE: Assignment of H_A and H_B for the monoarylated compound was through known coupling (by COSY NMR) between H_A and the aldehydic proton H_X.

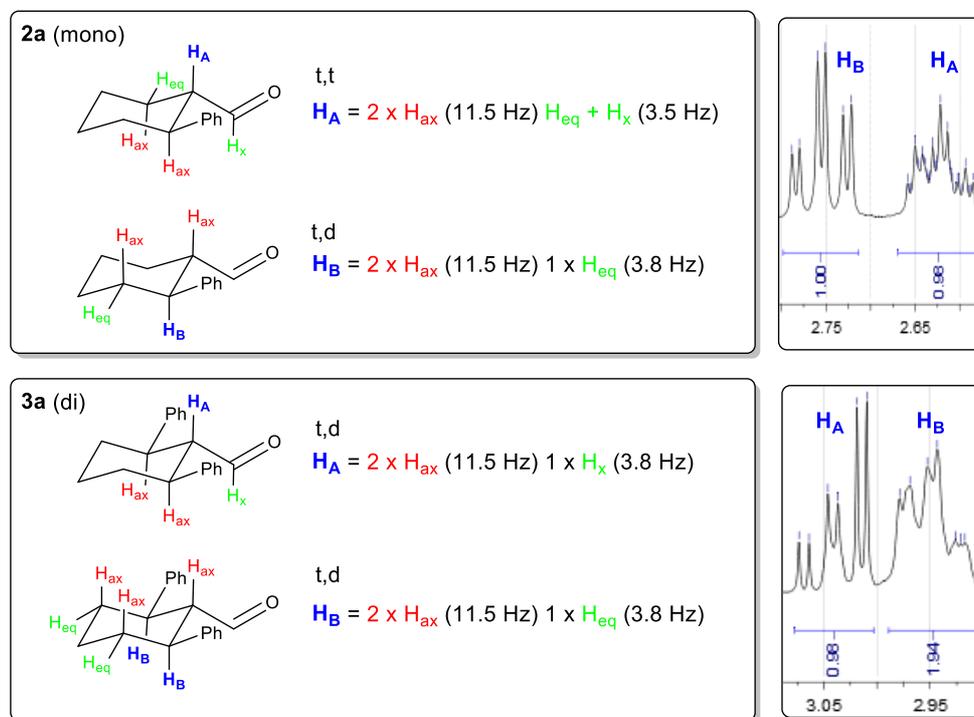


Figure S1: *trans* determination of the arylated products

Optimization table for C(sp³)-H arylation of cyclohexanecarboxaldehyde

Following selection of the TDG, variables considered were Ag salt, solvent, additives and temperature. Alternative ratios of the solvents made little difference to the yield and other silver sources were less effective. A pyridone ligand and higher equivalents of aryl iodide led to increased yields.

Entry	Ag salt	Solvent	Additive (equiv)	Yield 2a (%) ^a	Yield 3a (%) ^a	Total yield (%) ^a
1	AgTFA	HFIP:AcOH (1:1)	none	15	35	50
2	AgTFA	AcOH	-	15	2	17
3	AgTFA	HFIP:AcOH (1:3)	-	21	19	40
4	AgTFA	HFIP:AcOH (3:1)	-	11	40	51
5 ^b	AgTFA	HFIP:AcOH (3:1)	-	10	41	51
6 ^c	AgTFA	HFIP:AcOH (3:1)	-	4	38	42
7	AgTFA	HFIP:AcOH (5:1)	-	10	37	47
9	AgTFA	HFIP:AcOH (9:1)	-	9	42	51
10	AgTFA	HFIP	-	20	3	23
11	AgOAc	HFIP:AcOH (3:1)	-	19	8	27
12	AgF	HFIP:AcOH (3:1)	-	17	21	38
13	Ag ₂ CO ₃	HFIP:AcOH (3:1)	-	16	6	22
14	AgTFA (1.5 equiv)	HFIP:AcOH (3:1)	-	13	27	40
15	AgTFA	HFIP:AcOH (3:1)	H ₂ O (0.5)	12	37	49
16	AgTFA	HFIP:AcOH (3:1)	H ₂ O (2)	10	39	49
17	AgTFA	HFIP:AcOH (3:1)	KF (0.5)	11	38	49
18	AgTFA	HFIP:AcOH (3:1)	KF (2)	11	42	53
19	AgTFA	HFIP:AcOH (3:1)	PivOH (0.5)	13	34	47
20	AgTFA	HFIP:AcOH (3:1)	MesCO ₂ H (0.5)	13	33	46
21	AgTFA	HFIP:AcOH (3:1)	5-(trifluoromethyl)pyridin-2-ol (0.5)	4	60	64
22 ^d	AgTFA	HFIP:AcOH (3:1)	5-(trifluoromethyl)pyridin-2-ol (0.5)	7	65	72

Table S2: Optimisation of direct aldehyde arylation. Conditions: cyclohexanecarboxaldehyde (0.20 mmol), **TDG10** (0.25 equiv), iodobenzene (3 equiv), Pd(OAc)₂ (10 mol%), Ag source (2 equiv), additive (30 mol%), solvent (0.3 M), 120 °C, 24 h unless stated otherwise. ^aYields determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard. ^bDIPA amide **TDG16**. ^c100 °C. ^d4 equiv PhI.

Reaction profiles with TDG1, TDG10 and TDG16

To observe the role of the different TDGs on the rate of the reaction, discrete experiments at different time points were conducted using the best amide TDGs (**TDG10** and **TDG16**) as well as Ge's β -alanine (**TDG1**). This experiment was conducted at a HFIP:ACOH ratio of 5:1.

General procedure for reaction profile experiments: Cyclohexanecarboxaldehyde **1** (24.2 μ L, 0.20 mmol), iodobenzene (67 μ L, 0.6 mmol), **TDG** (25 mol%), palladium acetate (4.5 mg, 0.02 mmol), silver trifluoroacetate (88 mg, 0.40 mmol), HFIP (2.2 mL) and AcOH (0.44 mL) were combined in a flame dried microwave vial. The vial was purged with argon, sealed and heated to 80 °C for a number of hours. The reaction was allowed to cool to room temperature and filtered through a short plug of SiO₂ (eluting with CH₂Cl₂) and the solvent removed under reduced pressure. 10–20 mg of accurately weighed 1,3,5-trimethoxybenzene was added, the residue was fully dissolved in CDCl₃ and the yield of the the arylated products **2a** and **3a** were calculated by ¹H NMR by comparison to the internal standard. The aldehyde signals for **2a** (9.42, d, *J* = 3.1 Hz) and **3a** (9.26, d, *J* = 3.6 Hz) and aromatic 3 H singlet (6.10) for the internal standard were used in yield calculations. NOTE: Iodobenzene and cyclohexanecarboxaldehyde were added after the solid reagents using a Gilson micropipette, then the solvents were added via syringe.

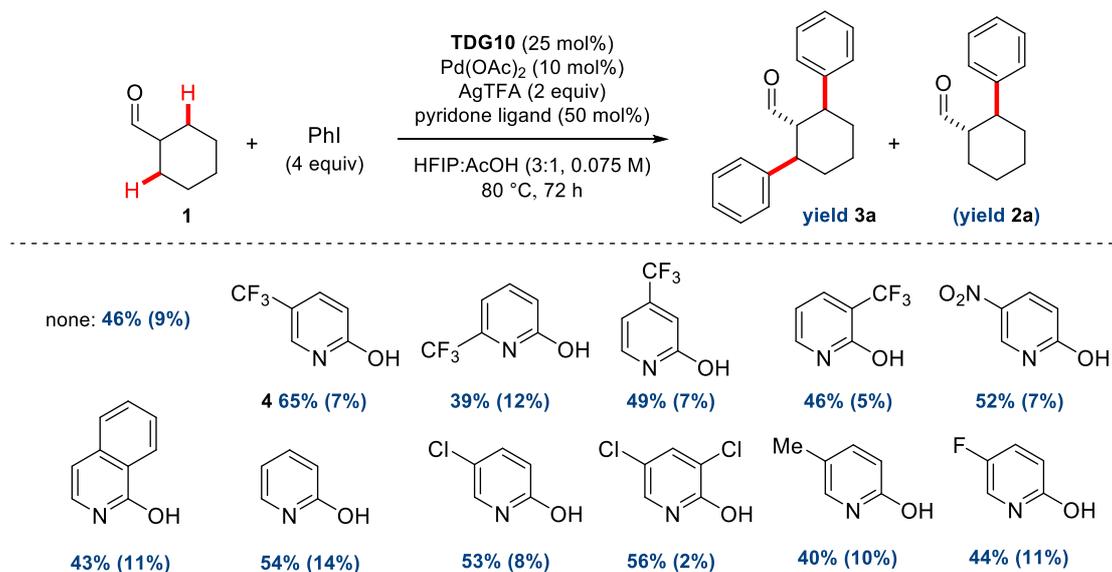
Raw data for reaction profiles (Figure 1b)

t (h)	TDG1 (β -alanine)			TDG10 (<i>t</i> -Bu)			TDG16 (DIPA)		
	Yield 2a (%) ^a	Yield 3a (%) ^a	Total yield (%) ^a	Yield 2a (%) ^a	Yield 3a (%) ^a	Total yield (%) ^a	Yield 2a (%) ^a	Yield 3a (%) ^a	Total yield (%) ^a
3	9	0	9	13	3	16	11	1	12
12	21	2	23	23	10	33	16	9	25
24	22	7	29	16	19	35	24	15	39
48	21	15	36	16	36	52	20	28	48
32	20	18	38	10	42	52	13	38	51

Table S3: Raw data for reaction profiles for different directing groups for arylation of cyclohexanecarboxaldehyde.

Screen of pyridone ligands

Following the improved yield with with pyridone ligand, a selection of alternative pyridone ligands were screened, but none gave a further improvement in yield compared to the 5-CF₃-pyridone **4** (Scheme S2).

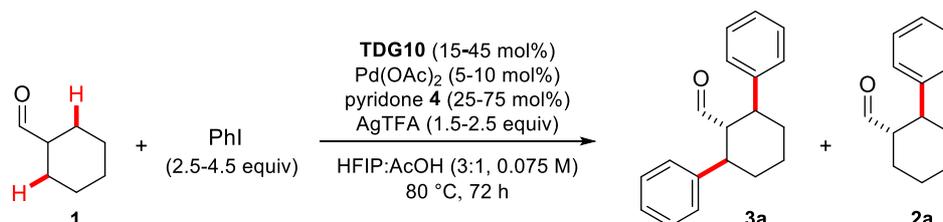


Scheme S2: Screen of pyridone ligands. Yields determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard

Optimisation of continuous reaction parameters using DOE

A DOE study was conducted to identify interactions between the different continuous reaction parameters following selection of the discrete variables, and to potentially achieve greater yields of diarylated product **3a**. The software used for this investigation was JMP Pro 14. The custom design was a response surface methodology with one centre point and 2 replica runs for a default number of runs (27). This design investigated the extremes and midpoints of all factors.

The continuous factors investigated were: TDG loading, catalyst loading, PhI loading, AgTFA loading and pyridone loading. The ranges chosen for all factors selected are given in Table S4. Yield of **3a** was selected as the only response (min = 0, max = 100).



Factor	Role	Min	Max
Pd loading (mol%)	Continuous	5	10
TDG loading (mol%)	Continuous	15	45
Ligand loading (mol%)	Continuous	25	75
PhI loading (equiv)	Continuous	2.5	4.5
AgTFA loading (equiv)	Continuous	1.5	2.5

Table S4: Factors in select ranges investigated for the DOE study.

General procedure for DOE study: Cyclohexanecarboxaldehyde **1** (24.2 μ L, 0.20 mmol), iodobenzene (2.5–4.5 equiv), 3-amino-*N*-(*tert*-butyl)propanamide **TDG10** (15–45 mol%), palladium acetate (5–10 mol%), 5-(trifluoromethyl)pyridine-2-ol (25–75 mol%) silver trifluoroacetate (1.5–2.5 equiv), HFIP (2.00 mL) and AcOH (0.67 mL) were combined in a flame dried microwave vial. The vial was purged with argon, sealed and heated to 80 °C for 72 h. The reaction was allowed to cool to room temperature and transferred to a separating funnel using CH₂Cl₂. Water was added (20 mL) and the products extracted with CH₂Cl₂ (3 \times 20 mL). The combined organic layers were dried (Na₂SO₄), filtered and the solvent removed under reduced pressure. 10–20 mg of accurately weighed 1,3,5-trimethoxybenzene was added, the residue was fully dissolved in CDCl₃ and the yield of the the arylated products **2a** and **3a** were calculated by ¹H NMR by comparison to the internal standard. The aldehyde signals for **2a** (9.42, d, *J* = 3.1 Hz) and **3a** (9.26, d, *J* = 3.6 Hz) and aromatic 3 H singlet (6.10) for the internal standard were used in yield calculations. NOTE: Iodobenzene and cyclohexanecarboxaldehyde were added after the solid reagents using a Gilson micropipette, then the solvents were added via syringe.

These experiments were conducted in a randomised order to minimise systematic error. The original set of experiments as calculated by the DOE is shown in Entries 1–27 with the experimental mono and diarylation yields (Table S5). In addition, other combinations of loadings, conducted prior to or the DOE or after on the basis of the DOE predictions, have been added to the data set in Entries 28-43.

Entry	Pd (mol%)	TDG10 (mol%)	Arl (equiv)	Ag (equiv)	Pyridone (mol%)	Yield Di 3a (%) ^a	Yield mono 2a (%) ^a
1	5	15	4.5	2	50	52	12
2	7.5	45	3.5	2	50	47	3
3	7.5	15	4.5	2.5	25	51	6
4	5	15	2.5	1.5	25	32	17
5	10	45	2.5	1.5	25	21	30
6	7.5	15	3.5	2	75	42	5
7	10	30	4.5	2.5	75	68	1
8	7.5	30	2.5	2	50	52	11
9	10	15	2.5	1.5	75	37	7
10	10	45	4.5	1.5	75	43	24
11	5	45	4.5	1.5	25	27	16
12	5	30	3.5	2.5	25	39	13
13	5	15	2.5	2.5	75	43	11
14	7.5	30	3.5	2	50	54	3
15	7.5	30	2.5	2	50	61	10
16	5	45	4.5	2.5	75	47	15
17	7.5	30	3.5	1.5	50	38	16
18	10	45	4.5	2.5	25	37	2
19	10	30	3.5	2	25	48	3
20	10	15	3.5	2.5	50	40	5
21	10	15	4.5	1.5	25	32	10
22	10	45	2.5	2.5	75	46	1
23	5	45	2.5	1.5	75	24	18
24	5	15	4.5	1.5	75	53	18
25	7.5	30	3.5	1.5	50	47	15
26	10	15	2.5	2.5	25	34	24
27	5	45	2.5	2.5	25	31	20
28	10	25	5	2	50	48	1
29	10	25	4	2	60	55	4
30	10	25	4	2	50	65	7
31	10	25	4	2	25	56	4
32	10	25	4	2	50	62	6
33 ^b	10	25	4	2	50	52	12
34	10	30	4.5	2.5	75	69	1
35	10	30	4.5	2.5	75	62	1
36	8	30	4.5	2.2	75	63	1
37 ^b	8	30	5.5	2.1	70	42	9
38	8	30	5	2.1	70	76	1
39 (repeat)	8	30	5	2.1	70	59	1
40	8	30	5	2.1	100	66	10
41 (repeat)	8	30	5	2.1	100	70	1
42	10	50	1.5	1	14	13	36
43	5	15	5	2.3	70	60	7

Table S5: Results from DOE optimisation. Conditions: cyclohexancarboxaldehyde (0.20 mmol), TDG10, iodobenzene, Pd(OAc)₂, AgTFA, 5-CF₃-pyridone **4**, HFIP:AcOH (3:1, 0.075 M), 80 °C, 72 h, unless stated otherwise. ^a Yields determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard. ^b24 h.

On conducting the initial set of DOE experiments (Entries 1–27), a high (68%) yield was obtained with the conditions outlined in Entry 7, which was later repeated (Entry 34, 69%) to confirm the validity, however a third repeat of this experiment resulted in a reduced 62% yield (Entry 35). At 24 h under these conditions, 52% of the diarylated product was formed with 12% remaining as the monoarylated species (Entry 33). Using the ranges of each factor used within this initial set of experiments (Table S4), the maximum predicted yield was 69%; these conditions (Entry 36) gave a 63% experimental yield.

However, as the model suggested that increasing the loading of both aryl iodide and pyridone may be beneficial, these experiments were simulated. A 74% yield was predicted when optimising the conditions with an increased 5 equivalents of aryl iodide, which experimentally gave a 76% diarylation yield (Entry 38), which was repeated, unfortunately giving a lower 59% yield (Entry 39). As shown for the 24 h reaction using 5.5 equivalents of PhI (Entry 37), further increasing the amount of aryl iodide was not beneficial, with poor mass recovery and no RSM remaining.

With 5 equivalents of PhI, the amount of pyridone was also increased, resulting in a 66% yield, repeated to give a 70% yield (Entries 40–41). A simulation to maximise monoarylation yield was also conducted (Entry 42, 36% experimental monoarylation yield). Restricting the amount of Pd catalyst to 5 mol% could also give a good experimental yield of the diarylated product (60%), with the computed optimised conditions also using only 15 mol% of **TDG10** (Entry 43).

Excluding the 24 h timepoints, all of this collective data was fitted into a fit least squared model to consider the importance of the reaction components analysed, as well as to observe potential interactions between the reaction components.

In general, the predicted yields had good agreement with the experimental data (Figure S2). This plot also enables the identification of outliers. As shown in the actual vs predicted plot, the highest yield obtained (Entry 38) gave a significantly higher yield than expected, whereas the repeat (Entry 39) was much lower. The conditions given in Entry 40 and 41 were also considered to take forward for scope, as the repeats were constant and aligned with the predicted yields. For both sets of these potential final conditions, the isolated yields for cyclohexanecarboxaldehyde with iodobenzene was identical at 62%, however the conditions which gave the highest *in-situ* yield (Entry 38) gave a higher isolated yield for 4-iodoanisole, so were considered more general and brought forward for the substrate scope. Using the actual vs predicted plot (Figure S2), it was also identified that the initial 65% yield for the pyridone ligand was also an outlier (Entry 30), with a higher than predicted yield, but still a distinct advantage compared to in the absence of the ligand.

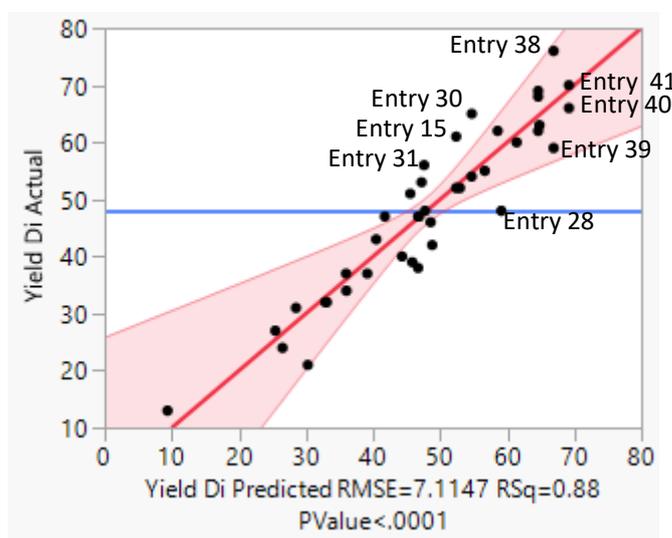


Figure S2: Predicted vs actual yield for diarylation of cyclohexanecarboxaldehyde in a fit least squared model

In comparison to our previous work which demonstrated some key interactions between the reaction components,² the interaction profiler only identified one slight interaction between the loadings of the iodobenzene and the pyridone ligand, where when more PhI was present, more pyridone led to increased diarylation yields (Figure S3).

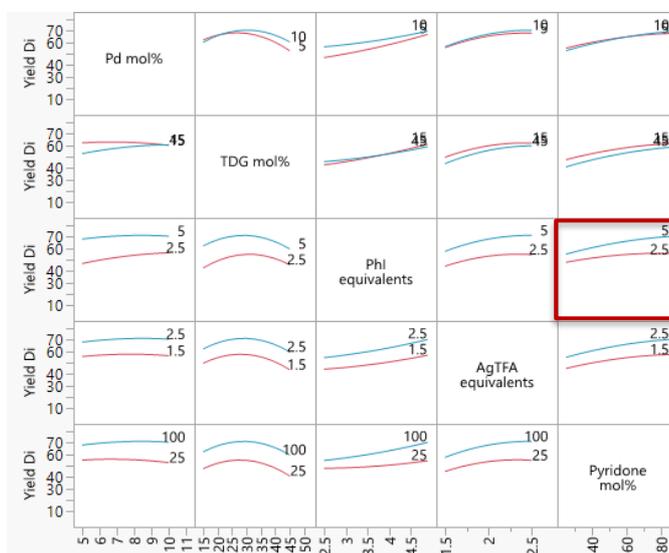


Figure S3: Interaction profiler

Reaction profile with optimised conditions in the presence of pyridone and control reactions

Raw data for reaction profile (Figure 2)

t (h)	Yield RSM 1 (%) ^a	Yield 2a (%) ^a	Yield 3a (%) ^a
1.5	46	16	4
3	36	18	8
6	18	24	24
15	5	19	49
24	2	15	47
48	0	2	55
72	0	0	62

Table S6: Raw data for reaction profiles for different directing groups for arylation of cyclohexanecarboxaldehyde. ^aYields determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard.

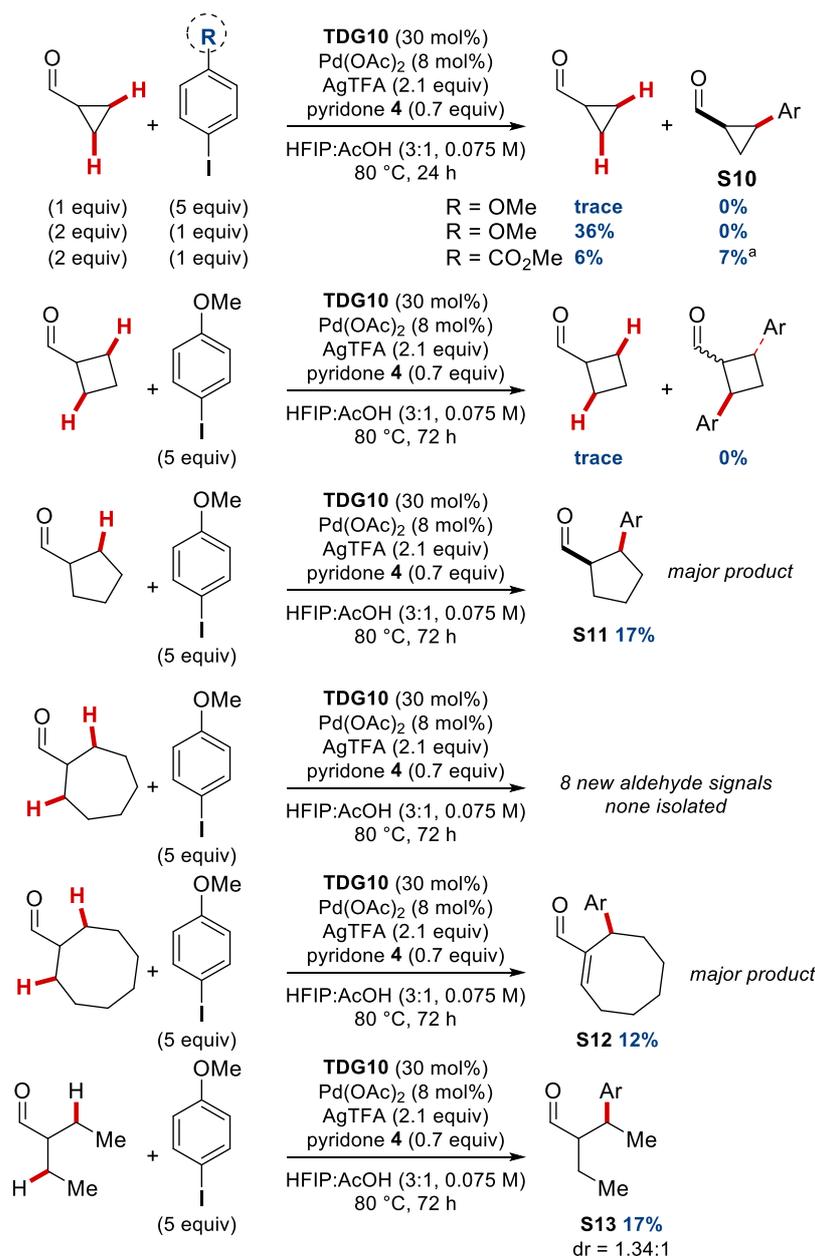
Control reactions

Running the reaction in absence of the directing group (Table S7, Entry 1) led to no product formation as expected. The returned starting material was low, as a result of formation of α,β -unsaturated aldehydes (shown by aldehyde singlets, the major product being cyclohexenecarbaldehyde, as compared with literature data). Under these conditions, removal of the pyridone results in lower yields and poor di-selectivity (Entry 2). Notably we have previously shown in the DOE study that the presence of pyridone **4** enables higher equivalents of aryl iodide to be used (Figure S3).

Entry	Description	RSM (%) ^a	Mono 2a (%) ^a	Di 3a (%) ^a
1	No TDG	22	0	0
2	No pyridone 4	1	13	37

Table S7: Control reactions. ^aYields determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard.

Products observed from arylation of other aldehyde substrates/ring sizes



Scheme S3: C(sp³)-H arylation of other ring size carbaldehydes. Isolated yields. ^aYield determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard, sample isolated for characterisation

Cyclopropanecarboxaldehyde only returned starting material under the standard conditions or when switching the excess to the aldehyde using 4-iodoanisole as the coupling partner. However, some reactivity could be achieved using methyl-4-iodobenzoate, to give monoarylated compound **S10**, assumedly due to more facile oxidative addition.³ No reactivity for the cyclobutyl substrate was achieved under the standard conditions. Arylation of cyclopentanecarbaldehyde yielded the monoarylated species **S11** as the major product, which was isolated in 17% yield. Trace amounts of other aldehydes (potentially di and α,β -unsaturated or *trans* isomers) were observed in the ¹H NMR of the crude reaction mixture. With the 7-membered ring, numerous new aldehyde species were observed in the crude NMR and so isolation was not attempted. The 8-membered ring however resulted in small amounts of one major product, which was isolated and determined to be the α - β -unsaturated monoarylated compound **S12** (where the double bond is on the opposite side to the arylation). This oxidation is likely as a result of β -hydride elimination by palladium. Acyclic 2-ethyl butanal formed monoarylated **S13** as the major product as a mixture of isomers.

Deuteration experiment

The reaction was conducted in deuterated solvents to identify positions of deuterium incorporation (Figure S4).

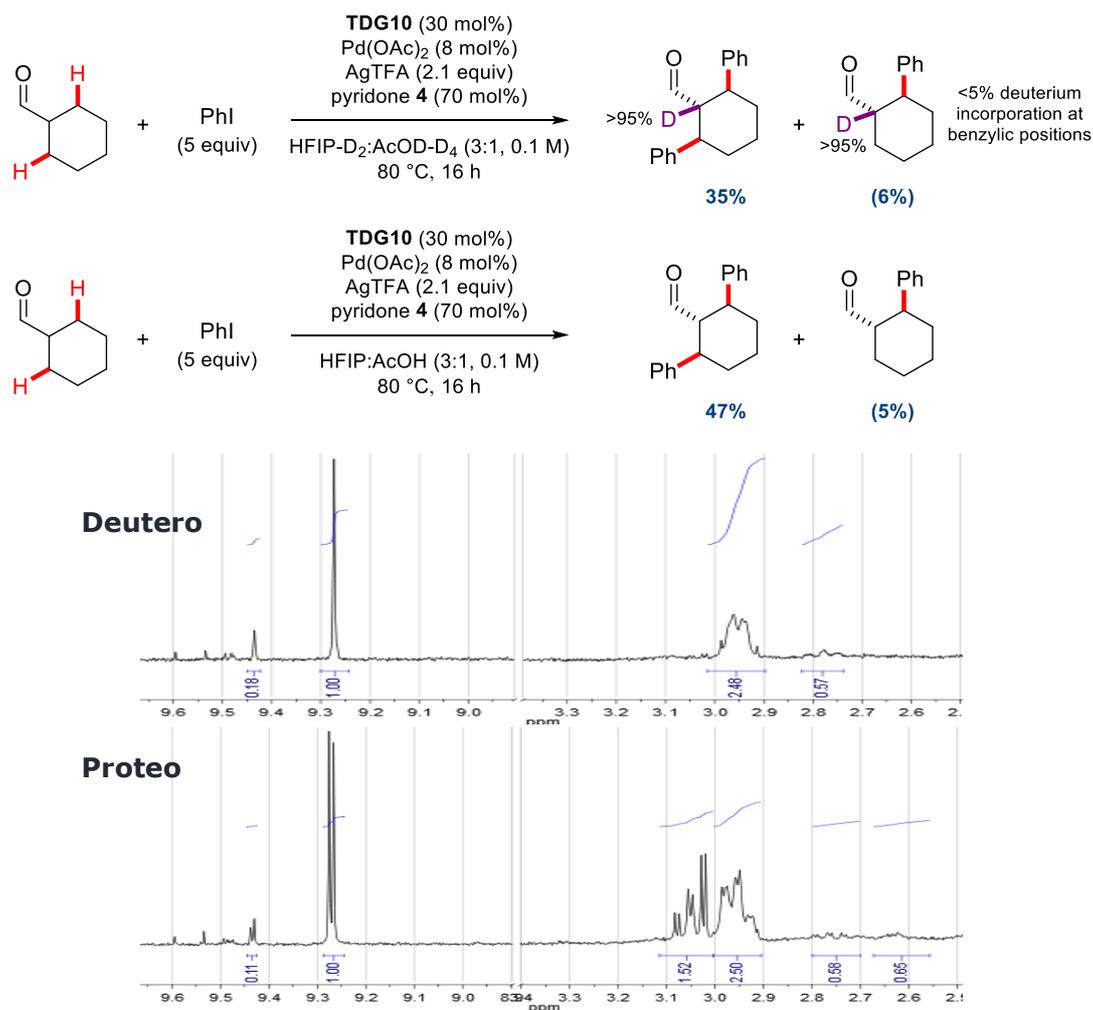


Figure S4: deuteration experiment. Yields determined by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard

Full deuteration occurred at the position α-to the aldehyde in both the mono and diarylated compounds, as shown by loss of splitting of the aldehyde C–H's and disappearance of the α-aldehyde C–H signals. No deuteration occurred at any other site.

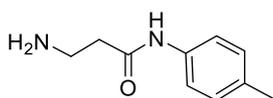
Experimental procedures and characterisation data

Preparation of directing groups (TDG3-TDG17)

General Procedure A for aryl amide formation: *N*-Boc-amino acid (1 equiv), amine (1 equiv), EDC (2.5 equiv), HOBt.H₂O (1.5 equiv) and DIPEA (3.5 equiv) were combined in CH₂Cl₂ (0.3 M) and the reaction was stirred at 25 °C for 20 h. The reaction mixture was diluted with saturated aqueous NaHCO₃ and the product extracted with CH₂Cl₂. The combined organic extracts were dried (MgSO₄), filtered and solvent removed under reduced pressure. Purification by flash chromatography (SiO₂, EtOAc:pentane:MeOH) afforded the corresponding Boc intermediate. HCl (10 equiv, 4 M solution in dioxane) was added and the reaction stirred until complete by TLC. 1 M aqueous NaOH was added and the free amine extracted with CH₂Cl₂, dried (MgSO₄), filtered and solvent removed under reduced pressure to afford the corresponding amide.

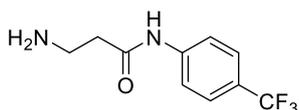
General Procedure B for alkyl amide formation: *N*-Boc-amino acid (1 equiv), amine (2 equiv), EDC (1.5 equiv), HOBt.H₂O (1.5 equiv) and Et₃N (3 equiv) were combined in DMF (0.15 M) and the reaction was stirred at 25 °C overnight. The reaction mixture was diluted with CH₂Cl₂, washed with 1 M aqueous HCl, saturated aqueous sodium bicarbonate solution and brine. The organic phase was dried (MgSO₄), filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (SiO₂) afforded the Boc intermediate. HCl (10 equiv, 4 M solution in dioxane) was added and the reaction stirred until complete by TLC. 1 M aqueous NaOH was added and the free amine extracted with CH₂Cl₂, dried (MgSO₄), filtered and solvent removed under reduced pressure to afford the corresponding amide.

3-amino-*N*-phenylpropanamide (TDG3)



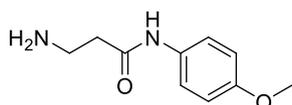
General procedure A was followed using 3-((*tert*-butoxycarbonyl)amino)propanoic acid (946 mg, 5 mmol) and *p*-toluidine (541 mg, 5 mmol), to afford amide **TDG3** as an off white amorphous solid (490 mg, 55%). *R*_f 0.06 (20% (1% NH₃ in MeOH)/CH₂Cl₂). IR (film)/cm⁻¹ 3345, 3290, 2922, 2882, 1660 (C=O), 159, 1539, 1507, 1401, 1298, 1255, 1046. ¹H NMR (400 MHz, CDCl₃) δ 9.81 (bs, 1 H, NH), 7.43 (d, *J* = 8.3 Hz, 2H, Ar-H), 7.11 (d, *J* = 8.3 Hz, 2 H, Ar-H), 3.13–3.10 (m, 2 H, NH₂CH₂), 2.48–2.45 (m, 2 H, O=CCH₂), 2.31 (s, 3 H, Ar-CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 170.8 (C=O), 135.9 (Ar-C_q), 133.3 (Ar-C_q), 129.4 (2 × Ar-C), 119.8 (Ar-C), 119.7 (Ar-C), 38.8 (CH₂), 37.9 (CH₂), 20.8 (Ar-CH₃). HRMS (pNSI) *m/z* Calcd. for C₁₀H₁₅N₂O [M+H]⁺: 179.1179; Found: 179.1178.

3-Amino-*N*-(4-(trifluoromethyl)phenyl)propanamide (TDG4)

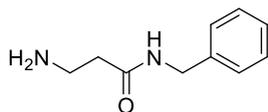


General procedure A was followed using 3-((*tert*-butoxycarbonyl)amino)propanoic acid (378 mg, 2.00 mmol) and 4-(trifluoromethyl)aniline (251 μL, 2.00 mmol) to afford amide **TDG4** as an off white solid (281 mg, 61%) which was further purified by recrystallisation in EtOAc (121 mg, 26%). *R*_f 0.12 (20% (1% NH₃ in MeOH)/CH₂Cl₂). mp = 118–120 °C. IR (film)/cm⁻¹ 2879, 1666 (C=O), 1607, 1561, 1410, 1321, 1307, 1156. ¹H NMR (400 MHz, CDCl₃) δ 10.74 (s, 1 H, NH), 7.68 (d, *J* = 8.5 Hz, 2 H, Ar-H), 7.56 (d, *J* = 8.6 Hz, 2 H, Ar-H), 3.16–3.13 (m, 2 H, NH₂CH₂), 2.51–2.48 (m, 2 H, O=CCH₂). ¹³C NMR (101 MHz, CDCl₃) δ 171.5 (C=O), 141.6 (Ar-C_q), 126.1 (q, ³*J*_{C-F} = 4 Hz, 2 × Ar-C), 125.31 (q, ²*J*_{C-F} = 33 Hz, Ar-C_q), 124.20 (q, ¹*J*_{C-F} = 271 Hz, CF₃), 119.3 (2 × Ar-C), 38.4 (CH₂), 37.7 (CH₂). ¹⁹F NMR (377 MHz, CDCl₃) δ -61.99. HRMS (ESI) *m/z* Calcd. for C₁₀H₁₂N₂OF₃ [M+H]⁺: 233.0902; Found: 233.0904.

3-Amino-*N*-(4-methoxyphenyl)propanamide (TDG5)

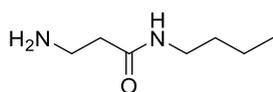


General procedure A was followed using 3-((*tert*-butoxycarbonyl)amino)propanoic acid (378 mg, 2.00 mmol) and 4-methoxyaniline (246 mg, 2.00 mmol) to afford amide **TDG5** as a pale purple solid (176 mg, 45%). *R*_f 0.09 (20% (1% NH₃ in MeOH)/CH₂Cl₂). mp = 141–152 °C. IR (film)/cm⁻¹ 3300, 2835, 1656 (C=O), 1586, 1530, 1510, 1440, 1401, 1364, 1242, 1171, 1027. ¹H NMR (400 MHz, CDCl₃) δ 9.76 (s, 1 H, NH), 7.48–7.44 (m, 2 H, Ar-H), 6.88–6.84 (m, 2 H, Ar-H), 3.79 (s, 3 H, OCH₃), 3.13–3.10 (m, 2 H, NH₂CH₂), 2.48–2.45 (m, 2 H, O=CCH₂). ¹³C NMR (101 MHz, CDCl₃) δ 170.7 (C=O), 156.0 (Ar-C_q), 131.7 (Ar-C_q), 121.5 (2 × Ar-C), 114.1 (2 × Ar-C), 55.5 (OCH₃), 38.7 (CH₂), 38.0 (CH₂). HRMS (ESI) *m/z* Calcd. for C₁₀H₁₅N₂O₂ [M+H]⁺: 195.1134; Found: 195.1139.

3-Amino-*N*-benzylpropanamide (TDG6)

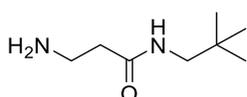
General procedure A was followed using 3-((*tert*-butoxycarbonyl)amino)propanoic acid (946 mg, 5.00 mmol) and benzylamine (546 μ L, 5.00 mmol) to afford amide **TDG6** as an off white solid (403 mg, 45%). R_f 0.09 (20% (1% NH_3 in MeOH)/ CH_2Cl_2). mp = 133–139 °C.

IR (film)/ cm^{-1} 3348, 3302, 2918, 1648 (C=O), 1560, 1439, 1360, 1240, 1040, 1019. ^1H NMR (400 MHz, DMSO) δ 8.42 (s, 1 H, NH), 7.33–7.29 (m, 2 H, Ph-H), 7.25–7.21 (m, 3 H, Ph-H), 4.26 (d, J = 5.9 Hz, 2 H, NHCH_2Ph), 2.78 (t, J = 6.6 Hz, 2 H, CH_2), 2.24 (t, J = 6.6 Hz, 2 H, CH_2). ^{13}C NMR (101 MHz, DMSO) δ 171.3 (C=O), 139.7 (Ph- C_q), 128.3 (Ph-C), 127.2 (Ph-C), 126.7 (Ph-C), 41.9 (NHCH_2Ph), 38.8 (CH_2), 38.2 (CH_2). HRMS (ESI) m/z Calcd. for $\text{C}_{10}\text{H}_{15}\text{N}_2\text{O}$ [$\text{M}+\text{H}$] $^+$: 179.1184; Found: 179.1185.

3-Amino-*N*-butylpropanamide (TDG7)

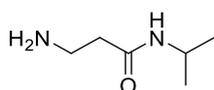
General procedure B was followed using 3-((*tert*-butoxycarbonyl)amino)propanoic acid (460 mg, 2.50 mmol) and butan-1-amine (247 μ L, 2.50 mmol) to afford amide **TDG7** as an off white solid (125 mg, 35%). R_f 0.08 (20% (1% NH_3 in MeOH)/ CH_2Cl_2). mp = 133–138 °C.

IR (film)/ cm^{-1} 3341, 3296, 2927, 1872, 2860, 1644 (C=O), 1541, 1440, 1397, 1365, 1145. ^1H NMR (400 MHz, CDCl_3) δ 6.92 (bs, 1 H, NH), 3.26 (td, J = 7.1, 4.5 Hz, 2 H, CH_2), 3.00 (t, J = 5.8 Hz, 2 H, CH_2), 2.30 (t, J = 5.8 Hz, 2 H, CH_2), 1.52–1.45 (m, 2 H, CH_2), 1.40–1.31 (m, 2 H, CH_2), 0.94–0.91 (m, 3 H, CH_3). ^{13}C NMR (101 MHz, CDCl_3) δ 172.3 (C=O), 39.0 (CH_2), 38.7 (CH_2), 38.3 (CH_2), 31.7 (CH_2), 20.1 (CH_2), 13.7 (CH_3). HRMS (ESI) m/z Calcd. for $\text{C}_7\text{H}_{17}\text{N}_2\text{O}$ [$\text{M}+\text{H}$] $^+$: 145.1341; Found: 145.1335

3-Amino-*N*-neopentylpropanamide (TDG8)

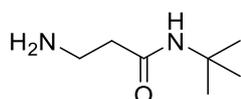
General procedure B was followed using 3-((*tert*-butoxycarbonyl)amino)propanoic acid (553 mg, 3.00 mmol) and 2,2-dimethylpropan-1-amine (420 μ L, 3.57 mmol) to afford amine **TDG8** as a pale yellow amorphous solid (201 mg, 42%). R_f 0.25 (20% (1% NH_3 in MeOH)/ CH_2Cl_2). IR (film)/ cm^{-1} 3318, 2953, 2868, 1645, 1547, 1463, 1365, 1303, 1208. ^1H NMR (400 MHz, CDCl_3)

δ 7.34 (bs, 1 H, NH), 3.08 (d, J = 6.1 Hz, 2 H, NHCH_2), 3.03 (t, J = 5.8 Hz, 2 H, CH_2), 2.34 (t, J = 5.8 Hz, 2 H, CH_2), 0.92 (s, 9 H, $\text{C}(\text{CH}_3)_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 172.6 (C=O), 50.4 (CH_2), 38.5 (CH_2), 38.4 (CH_2), 31.7 ($\text{C}_q(\text{CH}_3)_3$), 27.3 ($\text{C}(\text{CH}_3)_3$). HRMS (ESI) m/z Calcd. for $\text{C}_8\text{H}_{19}\text{N}_2\text{O}$ [$\text{M}+\text{H}$] $^+$: 159.1497; Found: 159.1491.

3-Amino-*N*-isopropylpropanamide (TDG9)

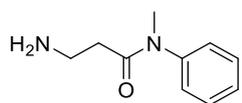
General procedure B was followed using 3-((*tert*-butoxycarbonyl)amino)propanoic acid (553 mg, 3.00 mmol) and propan-2-amine (515 μ L, 6.00 mmol) to afford amine **TDG9** as a pale yellow amorphous solid (120 mg, 31%). R_f 0.25 (20% (1% NH_3 in MeOH)/ CH_2Cl_2). IR (film)/ cm^{-1}

3303, 3025, 2970, 2933, 1637 (C=O), 1568, 1531, 1450, 1359, 1174, 1128. ^1H NMR (400 MHz, CDCl_3) δ 6.59 (b s, 1 H, NH), 4.08 (hept, J = 6.7 Hz, 1 H, $\text{CH}(\text{CH}_3)_2$), 3.01 (t, J = 5.9 Hz, 2 H, CH_2), 2.29 (t, J = 5.9 Hz, 1 H, CH_2), 1.16 (d, J = 6.7 Hz, 6 H, $\text{CH}(\text{CH}_3)_2$). ^{13}C NMR (101 MHz, CDCl_3) δ 171.5 (C=O), 41.1 ($\text{CH}(\text{CH}_3)_2$), 38.8 (CH_2), 38.3 (CH_2), 22.8 ($\text{CH}(\text{CH}_3)_2$). HRMS (ESI) m/z Calcd. for $\text{C}_6\text{H}_{15}\text{N}_2\text{O}$ [$\text{M}+\text{H}$] $^+$: 131.1184; Found: 131.1180.

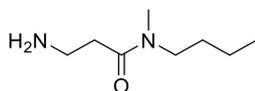
3-Amino-*N*-(*tert*-butyl)propanamide (TDG10)

Triethylamine (2.10 mL, 15.0 mmol) was added to a stirred solution of 3-((*tert*-butoxycarbonyl)amino)propanoic acid (1.04 g, 5.50 mmol), 2-chloro-1-methylpyridinium iodide (3.65 g, 15.0 mmol), 2-methylpropan-2-amine (525 μ L, 5.00 mmol) in CH_2Cl_2 (50 mL)

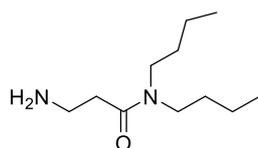
and the reaction was stirred at 25 °C for 24 h. The reaction mixture was diluted with CH_2Cl_2 , washed with saturated aqueous ammonium chloride solution, saturated aqueous sodium bicarbonate solution, dried concentrated and purified by flash column chromatography (silca, 80% diethyl ether/pentane) to afford the Boc intermediate. HCl was added (3.75 mL, 15 mmol, 4 M in dioxane) and the reaction stirred at rt until complete by TLC. 1 M aqueous NaOH was added and the free amine extracted with CH_2Cl_2 , dried (MgSO_4), filtered and solvent removed under reduced pressure to afford amine **TDG10** as a pale yellow oil (535 mg, 74%). R_f 0.14 (20% (1% NH_3 in MeOH)/ CH_2Cl_2). IR (film)/ cm^{-1} 3298, 3074, 2967, 1643 (C=O), 1548, 1454, 1391, 1362, 1224, 1039. ^1H NMR (400 MHz, CDCl_3) δ 6.45 (bs, 1 H, NH), 2.99 (t, J = 5.6 Hz, 2 H, CH_2), 2.26–2.23 (m, 2 H, CH_2), 1.36 (s, 9 H, $\text{C}(\text{CH}_3)_3$). ^{13}C NMR (101 MHz, CDCl_3) δ 171.5 (C=O), 51.0 ($\text{C}(\text{CH}_3)_3$), 39.2 (CH_2), 38.2 (CH_2), 28.8 ($\text{C}(\text{CH}_3)_3$). HRMS (ESI) m/z Calcd. for $\text{C}_7\text{H}_{17}\text{N}_2\text{O}$ [$\text{M}+\text{H}$] $^+$: 145.1341; Found: 145.1340.

3-Amino-*N*-methyl-*N*-phenylpropanamide (TDG11)

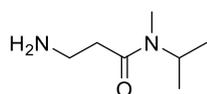
General procedure B was followed using 3-((tert-butoxycarbonyl)amino)propanoic acid (553 mg, 3.00 mmol) and *N*-methylaniline (650 μ L, 6.00 mmol) to afford amine **TDG11** as a brown oil (264 mg, 49%). R_f 0.30 (20% (1% NH_3 in MeOH)/ CH_2Cl_2). IR (film)/ cm^{-1} 3369, 2937, 1644 (C=O), 1593, 1495, 1274, 1117. ^1H NMR (400 MHz, CDCl_3) δ 7.43–7.40 (m, 2 H, Ph-H), 7.36–7.32 (m, 1 H, Ph-H), 7.19–7.18 (m, 2 H, Ph-H), 3.27 (s, 3 H, CH_3), 2.90 (t, $J = 6.1$ Hz, 2 H, CH_2), 2.22 (t, $J = 6.1$ Hz, 2 H, CH_2). ^{13}C NMR (101 MHz, CDCl_3) δ 171.9 (C=O), 143.8 (Ph- C_q), 129.8 (2 \times Ph-C), 127.8 (Ph-C), 127.4 (2 \times Ph-C), 38.2 (CH_2), 37.5 (CH_2), 37.1 (CH_3). HRMS (ESI) m/z Calcd. for $\text{C}_{10}\text{H}_{15}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$: 179.1184; Found: 179.1177.

3-Amino-*N*-butyl-*N*-methylpropanamide (TDG12)

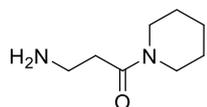
General procedure B was followed using 3-((tert-butoxycarbonyl)amino)propanoic acid (553 mg, 3.00 mmol) and *N*-methylbutan-1-amine (710 μ L, 6.00 mmol) to afford amine **TDG12** as a yellow oil (301 mg, 63%). R_f 0.23 (20% (1% NH_3 in MeOH)/ CH_2Cl_2). IR (film)/ cm^{-1} 2957, 2931, 2872, 1631 (s, C=O), 1459, 1402, 1296, 1130. HT (100 $^\circ\text{C}$) ^1H NMR (400 MHz, DMSO) δ 3.28 (t, $J = 7.3$ Hz, 2 H, CH_2), 2.88 (bs, 3 H, NCH_3), 2.79 (t, $J = 6.5$ Hz, 2 H, CH_2), 2.37 (t, $J = 6.5$ Hz, 2 H, CH_2), 1.52–1.45 (m, 2 H, CH_2), 1.34–1.25 (m, 2 H, CH_2), 0.92 (t, $J = 7.3$ Hz, 3 H, CH_3). HT (100 $^\circ\text{C}$) ^{13}C NMR (101 MHz, DMSO) δ 170.6 (C=O), 48.2 (CH_2), 46.0 (CH_2), 37.6 (CH_2), 36.1 (CH_2), 29.0 (NCH_3), 18.9 (CH_2), 12.9 (CH_3). HRMS (ESI) m/z Calcd. for $\text{C}_8\text{H}_{19}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$: 159.1497; Found: 159.1489.

3-Amino-*N,N*-dibutylpropanamide (TDG13)

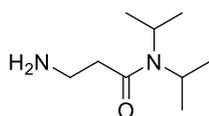
General procedure B was followed using 3-((tert-butoxycarbonyl)amino)propanoic acid (553 mg, 3.00 mmol) and dibutylamine (1.02 mL, 6.00 mmol) to afford amine **TDG13** as a yellow oil (461 mg, 77%). R_f 0.15 (20% (1% NH_3 in MeOH)/ CH_2Cl_2). IR (film)/ cm^{-1} 2957, 2930, 2872, 1632 (C=O), 1456, 1426, 1375, 1214, 1131. ^1H NMR (400 MHz, CDCl_3) δ 3.33–3.29 (m, 2 H, CH_2), 3.23–3.19 (m, 2 H, CH_2), 3.00 (t, $J = 6.0$ Hz, 2 H, CH_2), 2.46 (t, $J = 6.0$ Hz, 1 H, CH_2), 1.58–1.46 (m, 4 H, 2 \times CH_2), 1.35–1.28 (m, 4 H, 2 \times CH_2), 0.97–0.90 (m, 6 H, 2 \times CH_3). ^{13}C NMR (101 MHz, CDCl_3) δ 171.2 (C=O), 47.6 (CH_2), 45.6 (CH_2), 38.2 (CH_2), 36.1 (CH_2), 31.1 (CH_2), 29.9 (CH_2), 20.3 (CH_2), 20.1 (CH_2), 13.8 (CH_3), 13.8 (CH_3). HRMS (ESI) m/z Calcd. for $\text{C}_{11}\text{H}_{25}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$: 201.1967; Found: 201.1966.

3-Amino-*N*-isopropyl-*N*-methylpropanamide (TDG14)

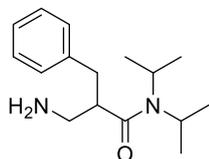
General procedure B was followed using 3-((tert-butoxycarbonyl)amino)propanoic acid (553 mg, 3.00 mmol) and *N*-methylpropan-2-amine (625 μ L, 6.00 mmol) to afford amine **TDG14** as a yellow oil (127 mg, 29%). R_f 0.25 (20% (1% NH_3 in MeOH)/ CH_2Cl_2). IR (film)/ cm^{-1} 3365, 2971, 1620 (C=O), 1458, 1407, 1115. HT (100 $^\circ\text{C}$) ^1H NMR (400 MHz, DMSO) δ 4.46 (bs, 1 H, $\text{CH}(\text{CH}_3)_2$), 2.79 (t, $J = 6.5$ Hz, 2 H, CH_2), 2.74 (bs, 3 H, NCH_3), 2.37 (t, $J = 6.5$ Hz, 2 H, CH_2), 1.09 (d, $J = 6.6$ Hz, 6 H, $\text{CH}(\text{CH}_3)_2$). HT (100 $^\circ\text{C}$) ^{13}C NMR (101 MHz, DMSO) δ 170.2 (C=O), 44.6 ($\text{CH}(\text{CH}_3)_2$), 37.7 (CH_2), 36.7 (CH_2), 26.9 (NCH_3), 19.0 ($\text{CH}(\text{CH}_3)_2$). HRMS (ESI) m/z Calcd. for $\text{C}_7\text{H}_{17}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$: 145.1341; Found: 145.1337.

3-Amino-1-(piperidin-1-yl)propan-1-one (TDG15)

General procedure B was followed using 3-((tert-butoxycarbonyl)amino)propanoic acid (553 mg, 3.00 mmol) and piperidine (593 μ L, 6.00 mmol) to afford amine **TDG15** as a yellow oil (343 mg, 73%). R_f 0.15 (20% (1% NH_3 in MeOH)/ CH_2Cl_2). IR (film)/ cm^{-1} 3367, 2932, 2855, 1623 (C=O), 1440, 1251, 1226, 1136, 1122. ^1H NMR (400 MHz, CDCl_3) δ 3.57–3.54 (m, 2 H, CH_2), 3.40–3.38 (m, 2 H, CH_2), 3.00 (t, $J = 6.0$ Hz, 1 H, CH_2), 2.46 (t, $J = 6.0$ Hz, 1 H, CH_2), 1.66–1.51 (m, 8 H, 3 \times CH_2). ^{13}C NMR (101 MHz, CDCl_3) δ 170.0 (CHO), 46.4 (CH_2), 42.5 (CH_2), 38.1 (CH_2), 36.3 (CH_2), 26.4 (CH_2), 25.5 (CH_2), 24.5 (CH_2). HRMS (ESI) m/z Calcd. for $\text{C}_8\text{H}_{17}\text{N}_2\text{O}$ $[\text{M}+\text{H}]^+$: 157.1341; Found: 157.1339.

3-Amino-*N,N*-diisopropylpropanamide (TDG16)

Triethylamine (4.20 mL, 30.0 mmol) was added to a stirred solution of 3-((*tert*-butoxycarbonyl)amino)propanoic acid (2.10 g, 11.0 mmol), 2-chloro-1-methylpyridinium iodide (7.70 g, 30.0 mmol), diisopropylamine (1.40 mL, 10.0 mmol) in CH₂Cl₂ (100 mL) and the reaction was stirred at 25 °C for 24 h. The reaction mixture was diluted with CH₂Cl₂, washed with saturated aqueous ammonium chloride solution, saturated aqueous sodium bicarbonate solution, dried concentrated and purified by flash column chromatography (silica, 80% diethyl ether/pentane) to afford the Boc intermediate **TDG16-Boc**. HCl was added (7.50 mL, 30 mmol, 4 M in dioxane) and the reaction stirred at rt until complete by TLC. 1 M aqueous NaOH was added and the free amine extracted with CH₂Cl₂, dried (MgSO₄), filtered and solvent removed under reduced pressure to afford amine **TDG16** as a yellow oil (1.25 g, 81%). *R*_f 0.22 (20% (1% NH₃ in MeOH)/CH₂Cl₂). IR (film)/cm⁻¹ 3368, 2967, 2932, 1618 (C=O), 1444, 1370, 1300, 1134, 1043. ¹H NMR (400 MHz, CDCl₃) δ 3.98 (dt, *J* = 13.5, 6.7 Hz, 1 H, CH(CH₃)₂), 3.48 (bs, 1 H, CH(CH₃)₂), 2.99 (t, *J* = 6.0 Hz, 2 H, CH₂), 2.45 (t, *J* = 6.0 Hz, 2 H, CH₂), 1.39 (d, *J* = 6.8 Hz, 6 H, CH(CH₃)₂), 1.20 (d, *J* = 6.7 Hz, 6 H, CH(CH₃)₂). ¹³C NMR (101 MHz, CDCl₃) δ 170.5 (C=O), 48.1 (CH(CH₃)₂), 45.6 (CH(CH₃)₂), 38.0 (CH₂), 37.6 (CH₂), 20.8 (CH(CH₃)₂), 20.7 (CH(CH₃)₂). HRMS (ESI) *m/z* Calcd. for C₉H₂₁N₂O [M+H]⁺: 173.1654; Found: 173.1647.

3-Amino-2-benzyl-*N,N*-diisopropylpropanamide (TDG17)

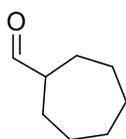
n-Butyllithium (2.12 mL, 4.80 mmol, 2.26 M in hexanes) was added dropwise to a stirred solution of diisopropylamine (673 μL, 4.80 mmol) in THF (6.0 mL) at -78 °C and the reaction was warmed to 0 °C and stirred for 30 minutes. The resulting LDA solution was cooled to -78 °C and *tert*-butyl (3-(diisopropylamino)-3-oxopropyl)carbamate (**TDG16-Boc**) (545 mg, 2.00 mmol) in THF (1.5 mL) was added dropwise and the reaction was stirred for 1 h. Benzyl bromide (952 μL, 8.00 mmol) was added dropwise and the reaction was warmed to 0 °C and stirred for 2 h. The reaction was quenched by addition of saturated aqueous ammonium chloride solution and the product extracted with EtOAc, dried (MgSO₄), filtered and solvent removed under reduced pressure. Purification by flash column chromatography (silica, 20–40% Et₂O:Pentane) afforded over (also *N*-) benzylated intermediate (708 mg, 1.56 mmol, 78%) to which HCl was added (3.90 mL, 15.6 mmol, 4 M solution in dioxane) and the reaction was stirred until complete by TLC. 1 M aqueous NaOH was added and the free amine extracted with CH₂Cl₂, dried (MgSO₄), filtered and solvent removed under reduced pressure to afford the un-Boc-protected *N*-benzylated intermediate (524 mg, 95%). *N*-Debenzylation was achieved by hydrogenation with Pd/C (52 mg, 10 wt%) and a H₂ balloon in MeOH (3 mL) for 24 h followed by filtration through Celite and evaporation of the solvent under reduced pressure, affording benzyl amide analogue **TDG17** (380 mg, 97%, 72% over 3 steps). *R*_f = 0.67 (20% (1% NH₃ in MeOH)/CH₂Cl₂). IR (film)/cm⁻¹ 3485, 3370, 2969, 2932, 1594 (C=O), 1453, 1359, 1333, 1314, 1206, 1137, 1060, 1036. ¹H NMR (400 MHz, CDCl₃) δ 7.29–7.25 (m, 2 H, Ph-H), 7.21–7.17 (m, 3 H, Ph-H), 3.89 (m, 1 H, CH(CH₃)₂), 3.42–3.21 (m, 1 H, CH(CH₃)₂), 3.14–3.01 (m, 2 H, CH + C(H)H), 2.92 (dd, *J* = 13.0, 8.9 Hz, 1 H, C(H)H), 2.80 (dd, *J* = 11.8, 4.0 Hz, 1 H, C(H)H), 2.72 (dd, *J* = 13.0, 5.2 Hz, 1 H, C(H)H), 1.39 (d, *J* = 6.7 Hz, 3 H, CH₃), 1.32 (d, *J* = 6.8 Hz, 3 H, CH₃), 1.10 (d, *J* = 6.7 Hz, 3 H, CH₃), 0.67 (d, *J* = 6.8 Hz, 3 H, CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 173.0 (C=O), 139.4 (Ph-C_q), 129.2 (Ph-C), 128.4 (Ph-C), 126.3 (Ph-C), 48.6 (CH(CH₃)₂), 47.3 (CH(CH₃)₂), 46.0 (CH), 45.0 (CH₂), 37.3 (PhCH₂), 21.3 (CH₃), 20.9 (CH₃), 20.5 (CH₃), 20.2 (CH₃). HRMS (EI⁺) *m/z* Calcd. for C₁₆H₂₆N₂O [M]⁺: 262.2045; Found: 262.2049.

Preparation of aldehydes (S1-S9)

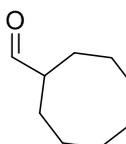
(1*R*,4*R*)-Methyl 4-formylcyclohexane-1-carboxylate was commercial.

Cycloheptanecarbaldehyde and cyclooctanecarbaldehyde were synthesized using the following methods but were not featured in aldehyde scope in the manuscript (Scheme 3) as they did not form the desired diarylated product.

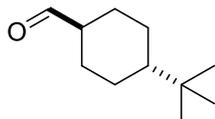
For the Wittig reactions (**S3–S6**, **S8**, **S9**), the major *trans* product was isolated and as a single diastereomer for the C(sp³)-H arylation. However, for 4-phenylcyclohexanecarbaldehyde **S4**, the *cis* and *trans* isomers were combined and used in the arylation as a mixture.

Cycloheptanecarbaldehyde (S1)

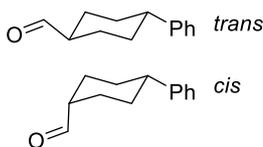
Literature hydroformylation procedure by Shi.⁴ Two reaction batches were prepared using the following procedure: To a mixture of Pd(OAc)₂ (56 mg, 0.25 mmol), dppp (206 mg, 0.50 mmol), Bu₄Ni (46 mg, 0.125 mmol), 4 Å molecular sieves (100 mg, activated by heating under high vacuum), and 1,2-dichloroethane (5.0 mL) in a 20 mL microwave vial was added cycloheptene (584 μL, 5 mmol), Ac₂O (1.45 mL, 15.0 mmol) and HCOOH (770 μL, 20.0 mmol) successively via syringe. The vial was crimped and atmosphere in the vial purged with argon. The reaction mixture was stirred at 80 °C for 24 h and allowed to cooled to rt. Both reaction batches were combined and the crude reaction mixture was directly purified by flash column chromatography (silica, 0–7.5% Et₂O/pentane) to afford the crude aldehyde a yellow oil which was further purified by vacuum distillation to afford aldehyde **S1** as a colourless oil (494 mg, 39%). R_f = 0.42 (2.5% Et₂O/pentane). IR (film)/cm⁻¹ 2922, 2855, 2706, 1722 (C=O), 1461. ¹H NMR (400 MHz, CDCl₃) δ 9.65 (d, *J* = 1.1 Hz, 1 H, CHO), 2.42–2.35 (m, 1 H, CH(CHO)), 2.01–1.94 (m, 2 H, 2 × C(H)H), 1.71 (dt, *J* = 12.2, 7.4 Hz, 2 H, 2 × C(H)H), 1.63–1.50 (m, 8 H, 4 × CH₂). ¹³C NMR (101 MHz, CDCl₃) δ 204.7 (CHO), 51.9 (CH(CHO)), 28.5 (2 × CH₂), 27.2 (2 × CH₂), 26.3 (2 × CH₂). Spectroscopic data for this compound is consistent with that shown in the literature.⁵

Cyclooctanecarbaldehyde (S2)

Literature hydroformylation procedure by Shi.⁴ Two reaction batches were prepared using the following procedure: To a mixture of Pd(OAc)₂ (56 mg, 0.25 mmol), dppp (206 mg, 0.50 mmol), Bu₄Ni (46 mg, 0.125 mmol), 4 Å molecular sieves (100 mg, activated by heating under high vacuum), and 1,2-dichloroethane (5.0 mL) in a 20 mL microwave vial was added cyclooctene (653 μL, 5 mmol), Ac₂O (1.45 mL, 15.0 mmol) and HCOOH (770 μL, 20.0 mmol) successively via syringe. The vial was crimped and atmosphere in the vial purged with argon. The reaction mixture was stirred at 80 °C for 24 h and allowed to cooled to rt. Both reaction batches were combined and the crude reaction mixture was directly purified by flash column chromatography (silica, 0–7.5% Et₂O/pentane) to afford aldehyde **S2** a colorless oil (601 mg, 43%). 476 mg of aldehyde **S2** was further purified by vacuum distillation to afford 95% pure material (326 mg, 68% distillation recovery). R_f = 0.20 (2.5% Et₂O/pentane). IR (film)/cm⁻¹ 2914, 2851, 2702, 1722 (C=O), 1468. ¹H NMR (400 MHz, CDCl₃) δ 9.62 (d, *J* = 1.1 Hz, 1 H, CHO), 2.40–2.36 (m, 1 H, CHCHO), 2.00–1.93 (m, 2 H, 2 × C(H)H), 1.75–1.70 (m, 2 H, 2 × C(H)H), 1.61–1.54 (m, 10 H, 5 × CH₂). ¹³C NMR (101 MHz, CDCl₃) δ 204.9 (CHO), 50.7 (CH(CHO)), 26.7 (2 × CH₂), 26.2 (CH₂), 25.5 (2 × CH₂), 25.2 (2 × CH₂). Spectroscopic data for this compound is consistent with that shown in the literature.⁵

trans-4-(tert-Butyl)cyclohexane-1-carbaldehyde (S3)

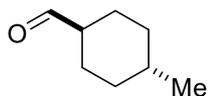
Procedure by Iwasawa:⁶ *n*BuLi (1.25 mL, 2.00 mmol, 1.6 M solution in hexanes) was added to a stirred solution of (Methoxymethyl)triphenylphosphonium chloride (686 mg, 2.00 mmol) in THF (5 mL) at 0 °C and the reaction was stirred at 0 °C for 1 h. A solution of 4-(*tert*-butyl)cyclohexan-1-one (154 mg, 1.00 mmol) in THF (1 mL) was added dropwise to the dark red solution and the reaction stirred at 0 °C for 30 minutes then allowed to warm to room temperature and stirred overnight. The reaction was quenched with addition of brine and the product extracted with EtOAc (3 × 20 mL). The combined organic layers were dried (Na₂SO₄), filtered and solvent removed under reduced pressure. The residue was passed through a short pad of silica (loaded in minimum CH₂Cl₂ and eluted with 2% EtOAc/hexane) and the solvent was removed under reduced pressure. To the intermediate enol ether was added 2 M aqueous HCl (5 mL) and THF (5 mL) and the reaction stirred at 90 °C (with a reflux condenser) for 3 h. The reaction was allowed to cool to room temperature and the product extracted with EtOAc (3 × 20 mL). The combined organic layers were dried (Na₂SO₄), filtered and solvent removed under reduced pressure. Purification by flash column chromatography (silica, 2–3% Et₂O/pentane) afforded *trans*-aldehyde **S3** as a colourless oil (66 mg, 39%). *R*_f = 0.55 (10% Et₂O/pentane). IR (film)/cm⁻¹ 2940, 2858, 2706, 1722 (C=O), 1449, 1362. ¹H NMR (400 MHz, CDCl₃) δ 9.62 (d, *J* = 1.7 Hz, 1 H, CHO), 2.14 (ttd, *J* = 12.2, 3.7, 1.7 Hz, 1 H, CHCHO), 2.05–2.00 (m, 2 H, 2 × C(H)H), 1.94–1.89 (m, 2 H, 2 × C(H)H), 1.29–1.19 (m, 2 H, 2 × C(H)H), 1.09–0.96 (m, 3 H, 2 × C(H)H + CHC(CH₃)₃), 0.86 (s, 9 H, C(CH₃)₃). ¹³C NMR (101 MHz, CDCl₃) δ 205.0 (CHO), 50.5 (CH(CHO)), 47.6 (CHC(CH₃)₃), 32.5 (C(CH₃)₃), 27.5 (C(CH₃)₃), 26.5 (2 × CH₂), 26.2 (2 × CH₂). Spectroscopic data for this compound is consistent with that shown in the literature.⁷

cis/trans-4-(Phenyl)cyclohexane-1-carbaldehyde (S4)

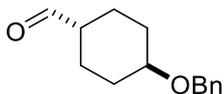
Procedure modified from Falck:⁸ KOtBu (359 mg, 3.20 mmol) was added portionwise to a stirred solution of (Methoxymethyl)triphenylphosphonium chloride (1.09 g, 3.20 mmol) in THF (4 mL) at 0 °C and the reaction was stirred at 0 °C for 30 mins. 4-(Phenyl)cyclohexan-1-one (349 mg, 2.00 mmol) was added portionwise to the dark red solution and the reaction was stirred at 0 °C for 30 minutes then allowed to warm to room temperature and stirred overnight. The reaction was quenched with addition of water and the product extracted with EtOAc (3 × 20 mL). The combined organic layers were dried (Na₂SO₄), filtered and solvent removed under reduced pressure. Purification by flash column chromatography (silica, 5% Et₂O/pentane) afforded the enol ether intermediate (374 mg, 92%, *R*_f = 0.52 (5% Et₂O/pentane)). Water (0.5 mL) followed by aqueous HCl (0.5 mL, 12 M (37%)) was added to a solution of the enol ether in THF (4 mL) at 0 °C and the reaction was stirred for 2 h until complete by TLC. Brine was added and the product extracted with EtOAc (3 × 20 mL). The combined organic layers were dried (Na₂SO₄), filtered and solvent removed under reduced pressure. Purification by flash column chromatography (silica, 10% Et₂O/pentane) afforded aldehyde **S4** as a colourless oil as a mixture of *trans* and *cis* isomers (285 mg, 76%, 4:1 *trans*:*cis*, >95% purity). IR (film)/cm⁻¹ 2926, 2855, 2706, 1722 (C=O), 1490, 1446.

trans: *R*_f = 0.25 (10% Et₂O/pentane). ¹H NMR (400 MHz, CDCl₃) δ 9.69 (d, *J* = 1.5 Hz, 1 H, CHO), 7.34–7.29 (m, 2 H, Ph-H), 7.23–7.15 (m, 3 H, Ph-H), 2.58–2.47 (m, 1 H, CHPh), 2.36–2.28 (m, 1 H, CHCHO), 2.17–2.12 (m, 2 H, 2 × C(H)H), 2.07–2.03 (m, 2 H, 2 × C(H)H), 1.59–1.42 (m, 4 H, 2 × CH₂). ¹³C NMR (101 MHz, CDCl₃) δ 204.5 (CHO), 146.6 (Ph-C_q), 128.4 (2 × Ph-C), 126.7 (2 × Ph-C), 126.2 (Ph-C), 50.0 (CH(CHO)), 43.8 (CHPh), 32.9 (2 × CH₂), 26.3 (2 × CH₂). Spectroscopic data for this compound is consistent with that shown in the literature.⁸

cis: *R*_f = 0.30 (10% Et₂O/pentane). ¹H NMR (400 MHz, CDCl₃) δ 9.80 (s, 1 H, CHO), 7.34–7.29 (m, 2 H, Ph-H), 7.23–7.16 (m, 3 H, Ph-H), 2.57–2.50 (m, 2 H, CHPh + CHCHO), 2.39–2.32 (m, 2 H, 2 × C(H)H), 1.85–1.80 (m, 2 H, 2 × C(H)H), 1.78–1.69 (m, 2 H, 2 × C(H)H). Spectroscopic data for this compound is consistent with that shown in the literature.⁸

trans-4-(Methyl)cyclohexane-1-carbaldehyde (S5)

Procedure by Iwasawa:⁶ *n*BuLi (5.0 mL, 8.00 mmol, 1.6 M solution in hexanes) was added to a stirred solution of (Methoxymethyl)triphenylphosphonium chloride (2.74 g, 8.00 mmol) in THF (20 mL) at 0 °C and the reaction was stirred at 0 °C for 1 h. A solution of 4-(methyl)cyclohexan-1-one (491 μL, 4.00 mmol) in THF (1 mL) was added dropwise to the dark red solution and the reaction stirred at 0 °C for 30 minutes then allowed to warm to room temperature and stirred overnight. The reaction was quenched with addition of brine and the product extracted with EtOAc (3 × 20 mL). The combined organic layers were dried (Na₂SO₄), filtered and solvent removed under reduced pressure. The residue was passed through a short pad of silica (loaded in minimum CH₂Cl₂ and eluted with 2% EtOAc/hexane) and the solvent was removed under reduced pressure. To the intermediate enol ether was added 2 M aqueous HCl (5 mL) and THF (5 mL) and the reaction stirred at 90 °C (with a reflux condenser) for 3 h. The reaction was allowed to cool to room temperature and the product extracted with EtOAc (3 × 20 mL). The combined organic layers were dried (Na₂SO₄), filtered and solvent removed under reduced pressure. Purification by flash column chromatography (silica, 2% Et₂O/pentane) afforded *trans*-aldehyde **S5** as a colourless oil (55 mg, 11%). *R*_f = 0.50 (10% Et₂O/pentane). IR (film)/cm⁻¹ 2922, 2847, 2706, 1722 (C=O), 1449. ¹H NMR (400 MHz, CDCl₃) δ 9.62 (d, *J* = 1.6 Hz, 1 H, CHO), 2.16 (ttd, *J* = 12.2, 3.6, 1.7 Hz, 1 H, CHCHO), 1.99–1.94 (m, 2 H, 2 × C(H)H), 1.83–1.79 (m, 2 H, 2 × C(H)H), 1.39–1.22 (m, 3 H, CHCH₃ + 2 × C(H)H), 1.02–0.93 (m, 2 H, 2 × C(H)H), 0.92 (d, *J* = 6.6 Hz, 3 H, CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 204.9 (CHO), 50.2 (CH(CHO)), 33.9 (2 × CH₂), 32.2 (CH(CH₃)), 26.0 (2 × CH₂), 22.4 (CH₃). Spectroscopic data for this compound is consistent with that shown in the literature.⁹

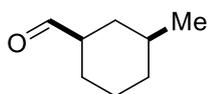
trans-4-(Benzyloxy)cyclohexane-1-carbaldehyde (S6)

Procedure modified from Falck:⁸ KOtBu (359 mg, 3.20 mmol) was added portionwise to a stirred solution of (Methoxymethyl)triphenylphosphonium chloride (1.09 g, 3.20 mmol) in THF (4 mL) at 0 °C and the reaction was stirred at 0 °C for 30 mins. 4-(Benzyloxy)cyclohexan-1-one (387 μL, 2.00 mmol) was added dropwise to the dark red solution and the reaction was stirred at 0 °C for 30 minutes then allowed to warm to room temperature and stirred overnight. The reaction was quenched with addition of water and the product extracted with EtOAc (3 × 20 mL). The combined organic layers were dried (Na₂SO₄), filtered and solvent removed under reduced pressure. Purification by flash column chromatography (silica, 2.5% Et₂O/pentane) afforded the enol ether intermediate (151 mg, 32%, *R*_f = 0.39 (5% Et₂O/pentane)). Water (0.5 mL) followed by aqueous HCl (0.5 mL, 12 M (37%)) was added to a solution of the enol ether in THF (4 mL) at 0 °C and the reaction was stirred for 2 h until complete by TLC. Brine was added and the product extracted with EtOAc (3 × 20 mL). The combined organic layers were dried (Na₂SO₄), filtered and solvent removed under reduced pressure. Purification by flash column chromatography (silica, 10% Et₂O/pentane) afforded *trans* aldehyde **S6** as a colourless oil (48 mg, 11%). The *cis* isomer of aldehyde **S6** was also isolated as a colourless oil (43 mg, 10%, *R*_f = 0.30 (10% Et₂O/pentane)). ¹H NMR (400 MHz, CDCl₃) δ 9.65 (d, *J* = 1.0 Hz, 1 H, CHO), 7.35 (d, *J* = 4.4 Hz, 4 H, Ph-H), 7.31–7.26 (m, 1 H, Ph-H), 4.52 (s, 2 H, OCH₂), 3.61–3.58 (m, 1 H, CHOBn), 2.31–2.25 (m, 1 H, CHCHO), 1.97–1.90 (m, 2 H, 2 × C(H)H), 1.89–1.80 (m, 2 H, 2 × C(H)H), 1.73–1.59 (m, 4 H, 2 × CH₂).

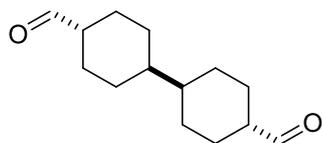
trans: *R*_f = 0.25 (10% Et₂O/pentane). IR (film)/cm⁻¹ 2933, 2858, 2709, 1722 (CHO), 1453, 1356, 1095. ¹H NMR (400 MHz, CDCl₃) δ 9.65 (d, *J* = 1.2 Hz, 1 H, CHO), 7.35 (d, *J* = 4.4 Hz, 4 H, Ph-H), 7.33–7.28 (m, 1 H, Ph-H), 4.57 (s, 2 H, OCH₂), 3.35 (tt, *J* = 9.7, 3.9 Hz, 1 H, CHOPh), 2.29–2.21 (m, 1 H, CHCHO), 2.17–2.11 (m, 2 H, 2 × C(H)H), 2.08–2.02 (m, 2 H, 2 × C(H)H), 1.47–1.32 (m, 4 H, 2 × CH₂). ¹³C NMR (101 MHz, CDCl₃) δ 204.1 (CHO), 138.9 (Ph-C_q), 128.4 (2 × Ph-C), 127.5 (3 × Ph-C), 76.3 (CH(OBn)), 70.1 (OCH₂), 49.3 (CH(CHO)), 30.7 (2 × CH₂), 23.8 (2 × CH₂). Spectroscopic data for this compound is consistent with that shown in the literature.¹⁰

4,4-Difluorocyclohexane-1-carbaldehyde (S7)

(4,4-Difluorocyclohexyl)methanol (130 μ L, 1.00 mmol) was added to a stirred solution of Dess-Martin Periodinane (636 mg, 1.50 mmol) in CH_2Cl_2 (2 mL) at 0 $^\circ\text{C}$. The reaction was allowed to warm to room temperature and stirred for 2.5 h. Saturated sodium bicarbonate solution was added and the product extracted with CH_2Cl_2 . The combined organic extracts were dried (Na_2SO_4), filtered and solvent removed under reduced pressure. Purification by flash column chromatography (silica, 20% Et_2O /pentane) afforded aldehyde **S7** as a colourless oil (141 mg, 95%). R_f = 0.32 (20% Et_2O /pentane). IR (film)/ cm^{-1} 2944, 2821, 1722 (C=O), 1449, 1360, 1110. ^1H NMR (400 MHz, CDCl_3) δ 9.68 (d, J = 0.5 Hz, 1 H, CHO), 2.39–2.32 (m, 1 H, $\text{CH}(\text{CHO})$), 2.12–2.00 (m, 4 H, $2 \times \text{CH}_2$), 1.92–1.76 (m, 4 H, $2 \times \text{CH}_2$). ^{13}C NMR (101 MHz, CDCl_3) δ 202.7 (CHO), 122.6 (t, $^1J_{\text{C-F}}$ = 242.3 Hz, CF_2), 47.2 ($\text{CH}(\text{CHO})$), 32.2 (t, $^2J_{\text{C-F}}$ = 24.6 Hz, $2 \times \text{CH}_2$), 22.1 (dd, $^3J_{\text{C-F}}$ = 5.8, 4.5 Hz, $2 \times \text{CH}_2$). ^{19}F NMR (377 MHz, CDCl_3) δ -94.9 (d, J = 236 Hz), -98.8 (d, J = 236 Hz). Spectroscopic data for this compound is consistent with that shown in the literature.¹¹

cis-3-(Methyl)cyclohexane-1-carbaldehyde (S8)

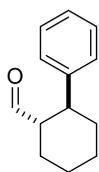
Procedure by Iwasawa:⁶ $n\text{BuLi}$ (5.00 mL, 8.00 mmol, 1.6 M solution in hexanes) was added to a stirred solution of (Methoxymethyl)triphenylphosphonium chloride (2.74 g, 9.00 mmol) in THF (20 mL) at 0 $^\circ\text{C}$ and the reaction was stirred at 0 $^\circ\text{C}$ for 1 h. A solution of 3-(methyl)cyclohexan-1-one (419 μ L, 4.00 mmol) in THF (4 mL) was added dropwise to the dark red solution and the reaction stirred at 0 $^\circ\text{C}$ for 30 minutes then allowed to warm to room temperature and stirred overnight. The reaction was quenched with addition of brine and the product extracted with EtOAc (3×20 mL). The combined organic layers were dried (Na_2SO_4), filtered and solvent removed under reduced pressure. The residue was passed through a short pad of silica (loaded in minimum CH_2Cl_2 and eluted with 2% EtOAc/hexane) and the solvent was removed under reduced pressure. To the intermediate enol ether was added 2 M aqueous HCl (20 mL) and THF (20 mL) and the reaction stirred at 90 $^\circ\text{C}$ (with a reflux condenser) for 3 h. The reaction was allowed to cool to room temperature and the product extracted with EtOAc (3×20 mL). The combined organic layers were dried (Na_2SO_4), filtered and solvent removed under reduced pressure. Purification by flash column chromatography (silica, 2–3% Et_2O /pentane then 10% CH_2Cl_2 /pentane) afforded aldehyde **S8** as a colourless oil (78 mg, 15%). R_f = 0.47 (10% Et_2O /pentane). IR (film)/ cm^{-1} 2922, 2855, 1722 (C=O), 1457. ^1H NMR (400 MHz, CDCl_3) δ 9.60 (d, J = 1.6 Hz, 1 H, CHO), 2.26 (ttd, J = 12.3, 3.5, 1.6 Hz, 1 H, CHCHO), 1.98–1.90 (m, 2 H, $2 \times \text{C}(\text{H})\text{H}$), 1.86 (ddt, J = 13.2, 6.5, 3.3 Hz, 1 H, $\text{C}(\text{H})\text{H}$), 1.76–1.68 (m, 1 H, $\text{C}(\text{H})\text{H}$), 1.51–1.39 (m, 1 H, CHCH_3), 1.38–1.26 (m, 1 H, $\text{C}(\text{H})\text{H}$), 1.15 (ddd, J = 25.4, 12.9, 3.6 Hz, 1 H, $\text{C}(\text{H})\text{H}$), 0.95 (d, J = 6.5 Hz, 3 H, CH_3), 0.94–0.81 (m, 2 H, $2 \times \text{C}(\text{H})\text{H}$). ^{13}C NMR (101 MHz, CDCl_3) δ 204.7 (CHO), 50.6 ($\text{CH}(\text{CHO})$), 34.6 (CH_2), 34.3 (CH_2), 31.9 ($\text{CH}(\text{CH}_3)$), 25.7 (CH_2), 25.2 (CH_2), 22.7 (CH_3). Spectroscopic data for this compound is consistent with that shown in the literature.¹²

trans-[1,1'-Bi(cyclohexane)]-4,4'-dicarbaldehyde (S9)

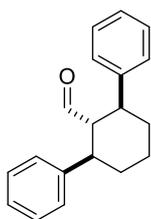
Procedure modified from Falck:⁸ KOtBu (359 mg, 3.20 mmol) was added portionwise to a stirred solution of (Methoxymethyl)triphenylphosphonium chloride (1.09 g, 3.20 mmol) in THF (4 mL) at 0 $^\circ\text{C}$ and the reaction was stirred at 0 $^\circ\text{C}$ for 30 mins. [1,1'-Bi(cyclohexane)]-4,4'-dione (194 mg, 1.00 mmol) was added dropwise to the dark red solution and the reaction was stirred at 0 $^\circ\text{C}$ for 30 minutes then allowed to warm to room temperature and stirred overnight. The reaction was quenched with addition of water and the product extracted with EtOAc (3×20 mL). The combined organic layers were dried (Na_2SO_4), filtered and solvent removed under reduced pressure. Purification by flash column chromatography (silica, 2.5% Et_2O /pentane) afforded the enol ether intermediate (165 mg, 65%, R_f = 0.42 (5% Et_2O /pentane)). Water (0.5 mL) followed by aqueous HCl (0.5 mL, 12 M (37%)) was added to a solution of the enol ether in THF (4 mL) at 0 $^\circ\text{C}$ and the reaction was stirred for 2 h until complete by TLC. Brine was added and the product extracted with EtOAc (3×20 mL). The combined organic layers were dried (Na_2SO_4), filtered and solvent removed under reduced pressure. Purification by flash column chromatography (silica, 10% Et_2O /pentane) afforded *trans* aldehyde **S9** as a white solid (45 mg, 20%). Other mixed isomers were present but not isolated. R_f = 0.21 (20% Et_2O /pentane). MP = 54–56 $^\circ\text{C}$. IR (film)/ cm^{-1} 2922, 2847, 2724, 1718 (C=O), 1446, 1364. ^1H NMR (400 MHz, CDCl_3) δ 9.62 (d, J = 1.6 Hz, 2 H, $2 \times \text{CHO}$), 2.16 (ttd, J = 12.2, 3.6, 1.6 Hz, 2 H, $2 \times \text{CHCHO}$), 2.06–2.00 (m, 4 H, $4 \times \text{C}(\text{H})\text{H}$), 1.89–1.83 (m, 4 H, $4 \times \text{C}(\text{H})\text{H}$), 1.31–1.20 (m, 4 H, $4 \times \text{C}(\text{H})\text{H}$), 1.13–1.01 (m, 6 H, $4 \times \text{C}(\text{H})\text{H} + 2 \times \text{CHCy}$). ^{13}C NMR (101 MHz, CDCl_3) δ 204.7 ($2 \times \text{CHO}$), 50.5 ($2 \times \text{CH}(\text{CHO})$), 42.5 ($2 \times \text{CHCy}$), 28.7 ($4 \times \text{CH}_2$), 26.2 ($4 \times \text{CH}_2$). HRMS (pAPCI) m/z Calcd. for $\text{C}_{14}\text{H}_{23}\text{O}_2$ [$\text{M}+\text{H}$] $^+$: 223.1693; Found: 223.1691.

C(sp³)–H arylation of cyclohexanecarbaldehydes (2a-p, 3a-o, 5-11)

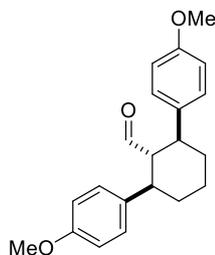
General procedure C for C(sp³)–H arylation of aldehydes: Aldehyde (0.20 mmol), aryl iodide (1.00 mmol), **TDG10** (8.6 mg, 0.06 mmol, 30 mol%), 5-(trifluoromethyl)pyridin-2-ol (23 mg, 0.14 mmol, 70 mol%), palladium acetate (3.6 mg, 0.016 mmol, 8 mol%), silver trifluoroacetate (92 mg, 0.42 mmol), HFIP (2.0 mL) and AcOH (0.67 mL) were combined in a flame dried microwave vial. The vial was purged with argon, sealed and heated to 80 °C for 72 h. The reaction was allowed to cool to room temperature and transferred to a separating funnel using CH₂Cl₂. Water was added (20 mL) and the products extracted with CH₂Cl₂ (3 × 20 mL). The combined organic layers were dried (Na₂SO₄), filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (silica) afforded the arylated aldehyde products. NOTE: Brine was used when the organic and aqueous phases failed to fully separate.

***trans*-2-Phenylcyclohexane-1-carbaldehyde (2a)**

A sample of monoarylated product was isolated from a number of mixed optimisation crudes for characterisation. R_f = 0.36 (2.5% acetone/pentane). IR (film)/cm⁻¹ 2926, 2855, 1722 (s, C=O), 1409, 1446. ¹H NMR (400 MHz, CDCl₃) δ 9.42 (d, *J* = 3.0 Hz, 1 H, CHO), 7.33–7.27 (m, 2 H, Ph-H), 7.26–7.17 (m, 3 H, Ph-H), 2.75 (td, *J* = 11.6, 3.6 Hz, 1 H, PhCH), 2.65–2.56 (m, 1 H, CHCHO), 2.07–1.88 (m, 4 H, 2 × CH₂), 1.69–1.38 (m, 4 H, 2 × CH₂). ¹³C NMR (101 MHz, CDCl₃) δ 204.7 (CHO), 144.1 (Ph-C_q), 128.7 (Ph-C), 127.4 (Ph-C), 126.6 (Ph-C), 55.3 (CHCHO), 45.2 (PhCH), 34.9 (CH₂), 26.7 (CH₂), 26.1 (CH₂), 24.9 (CH₂). Spectroscopic data for this compound is consistent with that shown in the literature.¹

***trans*-2,6-Diphenylcyclohexane-1-carbaldehyde (3a)**

General procedure C was followed using cyclohexanecarboxaldehyde (24 μL, 0.20 mmol), and iodobenzene (112 μL, 1.00 mmol) to afford arylated aldehyde **3a** as a white solid (33 mg, 62%). R_f = 0.30 (10% Et₂O/hexane). MP = 160–170 °C. IR (film)/cm⁻¹ 2922, 2851, 1714 (C=O), 1490, 1453, 1028. ¹H NMR (400 MHz, CDCl₃) δ 9.26 (d, *J* = 3.6 Hz, 1 H, CHO), 7.33–7.27 (m, 4 H, Ph-H), 7.26–7.17 (m, 6 H, Ph-H), 3.09–3.00 (m, 1 H, CHCHO), 2.94 (td, *J* = 10.5, 3.8 Hz, 2 H, PhCH), 2.06–1.95 (m, 2 H, CH₂), 1.72–1.62 (m, 4 H, 2 × CH₂). ¹³C NMR (101 MHz, CDCl₃) δ 204.3 (CHO), 143.3 (Ph-C_q), 128.7 (Ph-C), 127.4 (Ph-C), 126.8 (Ph-C), 60.7 (CHCHO), 45.8 (2 × PhCH), 34.4 (2 × CH₂), 26.3 (CH₂). HRMS (pAPCI) *m/z* Calcd. for C₁₉H₂₁O [M+H]⁺: 265.1587; Found: 265.1589.

***trans*-2,6-bis(4-Methoxyphenyl)cyclohexane-1-carbaldehyde (3b)****1 mmol scale**

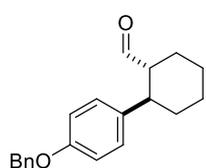
Cyclohexanecarboxaldehyde (132 μL, 1.00 mmol), 4-iodoanisole (1.17 g, 5.00 mmol), **TDG10** (34.3 mg, 0.3 mmol, 30 mol%), 5-(trifluoromethyl)pyridin-2-ol (114 mg, 0.70 mmol, 70 mol%), palladium acetate (18 mg, 0.08 mmol, 8 mol%), silver trifluoroacetate (462 mg, 2.1 mmol), HFIP (10.0 mL) and AcOH (3.33 mL) were combined in a flame dried microwave vial (25 mL capacity). The vial was purged with argon, sealed and heated to 80 °C for 72 h. The reaction was allowed to cool to room temperature and transferred to a separating funnel using CH₂Cl₂. Water was added (50 mL) and the products extracted with CH₂Cl₂ (3 × 50 mL). The combined organic layers were dried (Na₂SO₄), filtered and the solvent removed under reduced pressure. Purification by flash column chromatography (silica, 20% Et₂O/hexane) afforded arylated aldehyde **3b** as an off-white solid (219 mg, 68%).

0.2 mmol scale: General procedure C was followed using cyclohexanecarboxaldehyde (24 μL, 0.20 mmol), and 4-iodoanisole (234 mg, 1.00 mmol) to afford aldehyde **3b** as a white solid (39 mg, 60%). Data collected was equivalent.

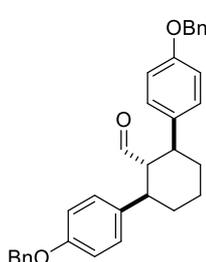
R_f = 0.16 (20% Et₂O/hexane). MP = 154–159 °C. IR (film)/cm⁻¹ 2929, 1725 (C=O), 1610, 1513, 1248, 1177, 1036. ¹H NMR (400 MHz, CDCl₃) δ 9.25 (d, *J* = 2.2 Hz, 1 H, CHO), 7.16–7.12 (m, 4 H, Ar-H), 6.85–6.81 (m, 4 H, Ar-H), 3.77 (s, 6 H, OCH₃), 2.92–2.85 (m, 3 H, 2 × CH(Ar) + CH(CHO)), 2.01–1.93 (m, 3 H, 3 × C(H)H), 1.65–1.58 (m, 3 H, 3 × C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 204.6 (CHO), 158.3 (2 × Ar-C_q), 135.5 (2 × Ar-C_q), 128.3 (4 × Ar-C), 114.0 (4 × Ar-C), 61.4 (CH(CHO)), 55.2 (2 × OCH₃), 44.9 (2 × CH(Ar)), 34.5 (2 × CH₂), 26.4 (CH₂). HRMS (pAPCI) *m/z* Calcd. for C₂₁H₂₅O₃ [M+H]⁺: 325.1798; Found: 325.1801.

trans-2-(4-(Benzyloxy)phenyl)cyclohexane-1-carbaldehyde (2c) and 2,6-bis(4-(benzyloxy)phenyl)cyclohexane-1-carbaldehyde (3c)

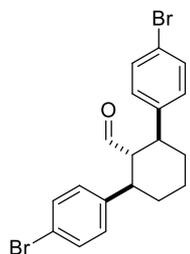
General procedure C was followed using cyclohexanecarboxaldehyde (24 μ L, 0.20 mmol), and 1-(benzyloxy)-4-iodobenzene (280 mg, 1.00 mmol) to afford monoarylated aldehyde **2c** as an amorphous off-white solid (5 mg, 8%) followed by diarylated aldehyde **3c** as an off-white solid (45 mg, 47%).



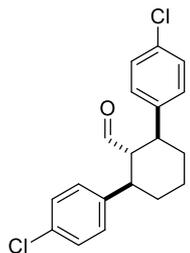
trans-2-(4-(Benzyloxy)phenyl)cyclohexane-1-carbaldehyde (2c): Rf = 0.27 (50% Et₂O/pentane). IR (film)/cm⁻¹ 2926, 2855, 1722 (C=O), 1509, 1244, 1021. ¹H NMR (400 MHz, CDCl₃) δ 9.42 (d, *J* = 3.1 Hz, 1 H, CHO), 7.45–7.33 (m, 5 H, Ph), 7.14–7.12 (m, 2 H, Ar-H), 6.93–6.90 (m, 2 H, Ar-H), 5.03 (s, 2 H, OCH₂), 2.71 (td, *J* = 11.5, 3.5 Hz, 1 H, CHAr), 2.55 (tt, *J* = 11.4, 3.3 Hz, 1 H, CHCHO), 1.96–1.85 (m, 4 H, 2 \times CH₂), 1.54–1.36 (m, 4 H, 2 \times CH₂). ¹³C NMR (101 MHz, CDCl₃) δ 204.9 (CHO), 157.5 (Ar-C_q), 137.1 (Ar-C_q), 136.5 (Ar-C_q), 128.6 (2 \times Ar-C), 128.3 (2 \times Ar-C), 127.9 (Ph-C), 127.5 (2 \times Ar-C), 115.0 (2 \times Ar-C), 70.0 (OCH₂), 55.6 (CH(CHO)), 44.3 (CH(Ar)), 35.0 (CH₂), 26.7 (CH₂), 26.1 (CH₂), 24.8 (CH₂). HRMS (pAPCI) *m/z* Calcd. for C₂₀H₂₃O₂ [M+H]⁺: 295.1693; Found: 295.1679.



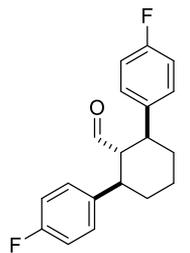
trans-2,6-bis(4-(Benzyloxy)phenyl)cyclohexane-1-carbaldehyde (3c): Rf = 0.21 (50% Et₂O/pentane). MP = 183–186 °C. IR (film)/cm⁻¹ 2922, 2855, 1722 (C=O), 1610, 1509, 1241, 1013. ¹H NMR (400 MHz, CDCl₃) δ 9.26 (d, *J* = 2.8 Hz, 1 H, CHO), 7.44–7.30 (m, 10 H, Ph-H), 7.17–7.13 (m, 4 H, Ar-H), 6.92–6.89 (m, 4 H, Ar-H), 5.02 (s, 4 H, 2 \times OCH₂), 2.92–2.86 (m, 3 H, 2 \times CHAr + CHCHO), 2.00–1.93 (m, 3 H, 3 \times C(H)H), 1.65–1.60 (m, 3 H, 3 \times C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 204.6 (CHO), 157.5 (2 \times Ar-C_q), 137.0 (2 \times Ar-C_q), 135.7 (2 \times Ar-C_q), 128.6 (4 \times Ar-C), 128.4 (4 \times Ar-C), 127.9 (2 \times Ph-C), 127.5 (4 \times Ar-C), 114.9 (4 \times Ar-C), 70.0 (2 \times OCH₂), 61.3 (CH(CHO)), 44.9 (2 \times CH(Ar)), 34.5 (2 \times CH₂), 26.6 (CH₂). HRMS (pAPCI) *m/z* Calcd. for C₃₃H₃₃O₃ [M+H]⁺: 477.2424; Found: 477.2432.

trans-2,6-bis(4-Bromophenyl)cyclohexane-1-carbaldehyde (3d)

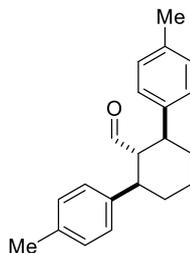
General procedure C was followed using cyclohexanecarboxaldehyde (24 μ L, 0.20 mmol), and 1-bromo-4-iodobenzene (283 mg, 1.00 mmol) to afford arylated aldehyde **3d** as a white solid (43 mg, 51%). Rf = 0.18 (10% Et₂O/hexane). MP = 146–147 °C. IR (film)/cm⁻¹ 2927, 2853, 1723 (C=O), 1488, 1073, 1009. ¹H NMR (400 MHz, CDCl₃) δ 9.23 (d, *J* = 2.7 Hz, 1 H, CHO), 7.44–7.40 (m, 4 H, Ar-H), 7.12–7.09 (m, 4 H, Ar-H), 2.94–2.85 (m, 3 H, 2 \times CH(Ar) + CH(CHO)), 2.02–1.94 (m, 3 H, 3 \times C(H)H), 1.65–1.58 (m, 3 H, 3 \times C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 203.7 (CHO), 142.1 (2 \times Ar-C_q), 131.8 (4 \times Ar-C), 129.1 (4 \times Ar-C), 120.6 (2 \times Ar-C_q), 60.5 (CH(CHO)), 45.1 (2 \times CH(Ar)), 34.2 (2 \times CH₂), 26.1 (CH₂). HRMS (pAPCI) *m/z* Calcd. for C₁₉H₁₉O⁷⁹Br₂ [M+H]⁺: 420.9797; Found: 420.9795.

trans-2,6-bis(4-Chlorophenyl)cyclohexane-1-carbaldehyde (3e)

General procedure C was followed using cyclohexanecarboxaldehyde (24 μ L, 0.20 mmol), and 4-chloriodobenzene (238 mg, 1.00 mmol) to afford arylated aldehyde **3e** as an off white solid (37 mg, 56%). Rf = 0.23 (10% Et₂O/hexane). MP = 141–145 °C. IR (film)/cm⁻¹ 2929, 2854, 1720 (C=O), 1490, 1089, 1013. ¹H NMR (400 MHz, CDCl₃) δ 9.23 (d, *J* = 1.9 Hz, 1 H, CHO), 7.29–7.25 (m, 4 H, Ar-H), 7.18–7.14 (m, 4 H, Ar-H), 2.92–2.91 (m, 3 H, CHCHO + 2 \times CHAr), 2.01–1.95 (m, 3 H, 3 \times C(H)H), 1.65–1.59 (m, 3 H, 3 \times C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 203.7 (CHO), 141.6 (2 \times Ar-C_q), 132.5 (2 \times Ar-C_q), 128.9 (4 \times Ar-C), 128.8 (4 \times Ar-C), 60.7 (CH(CHO)), 45.1 (2 \times CHAr), 34.2 (2 \times CH₂), 26.1 (CH₂). HRMS (pAPCI) *m/z* Calcd. for C₁₉H₁₉³⁵Cl₂O [M+H]⁺: 333.0807; Found: 333.0791.

trans-2,6-bis(4-Fluorophenyl)cyclohexane-1-carbaldehyde (3f)

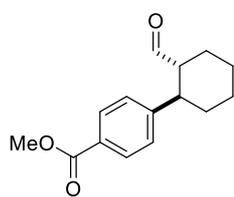
General procedure C was followed using cyclohexanecarboxaldehyde (24 μ L, 0.20 mmol), and 1-fluoro-4-iodobenzene (115 μ L, 1.00 mmol) to afford arylated aldehyde **3f** as a white solid (29 mg, 48%). Rf = 0.18 (10% Et₂O/hexane). MP = 155 °C. IR (film)/cm⁻¹ 2933, 2855, 1714 (C=O), 1509, 1226. ¹H NMR (400 MHz, CDCl₃) δ 9.24 (d, *J* = 2.9 Hz, 1 H, CHO), 7.20–7.17 (m, 4 H, Ar-H), 7.00–6.96 (m, 4 H, Ar-H), 2.94–2.88 (m, 3 H, CHCHO + 2 \times CHAr), 2.02–1.96 (m, 3 H, 3 \times C(H)H), 1.66–1.59 (m, 3 H, 3 \times C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 203.9 (CHO), 161.6 (d, ¹*J*_{C-F} = 245.0 Hz, 2 \times Ar-C_q), 138.9 (d, ⁴*J*_{C-F} = 3.1 Hz, 2 \times Ar-C_q), 128.8 (d, ³*J*_{C-F} = 7.9 Hz, 4 \times Ar-C), 115.5 (d, ²*J*_{C-F} = 21.1 Hz, 4 \times Ar-C), 61.2 (CH(CHO)), 45.0 (2 \times CHAr), 34.4 (2 \times CH₂), 26.2 (CH₂). ¹⁹F NMR (377 MHz, CDCl₃) δ -116.0. HRMS (pAPCI) *m/z* Calcd. for C₁₉H₁₉F₂O [M+H]⁺: 301.1398; Found: 301.1404.

trans-2,6-Di-p-tolylcyclohexane-1-carbaldehyde (3g)

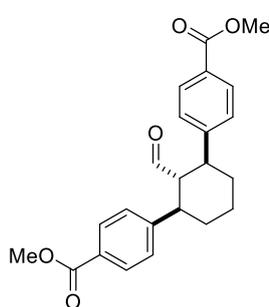
General procedure C was followed using cyclohexanecarboxaldehyde (24 μ L, 0.20 mmol), and 1-iodo-4-methylbenzene (218 mg, 1.00 mmol) to afford arylated aldehyde **3g** as a white solid (32 mg, 55%). Rf = 0.37 (10% Et₂O/hexane). MP = 110–120 °C. IR (film)/cm⁻¹ 2926, 2855, 1725 (C=O), 1513. ¹H NMR (400 MHz, CDCl₃) δ 9.26 (d, *J* = 3.6 Hz, 1 H, CHO), 7.14–7.09 (m, 8 H, Ar-H), 3.01–2.95 (m, 1 H, CH(CHO)), 2.93–2.86 (m, 2 H, 2 \times CH(Ar)), 2.30 (s, 6 H, 2 \times CH₃), 2.01–1.95 (m, 3 H, 3 \times C(H)H), 1.65–1.60 (m, 3 H, 3 \times C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 204.5 (CHO), 140.3 (2 \times Ar-C_q), 136.2 (2 \times Ar-C_q), 129.3 (4 \times Ar-C), 127.3 (4 \times Ar-C), 60.9 (CH(CHO)), 45.3 (2 \times CH(Ar)), 34.5 (2 \times CH₂), 26.4 (CH₂), 21.0 (2 \times CH₃). HRMS (pAPCI) *m/z* Calcd. for C₂₁H₂₅O [M+H]⁺: 293.1900; Found: 293.1905.

Methyl 4-((*trans*)-2-formylcyclohexyl)benzoate (2h) and dimethyl 4,4'-((*trans*)-2-formylcyclohexane-1,3-diyl)dibenzoate (3h)

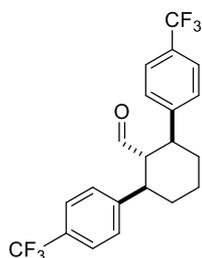
General procedure C was followed using cyclohexanecarboxaldehyde (24 μ L, 0.20 mmol), and methyl 4-iodobenzoate (262 mg, 1.00 mmol) to afford monoarylated aldehyde **2h** as a colourless oil (6 mg, 12%) followed by diarylated aldehyde **3h** as a white solid (32 mg, 42%).



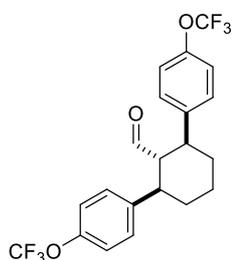
Methyl 4-((*trans*)-2-formylcyclohexyl)benzoate (2h): Rf = 0.24 (20% Et₂O/hexane). IR (film)/cm⁻¹ 2931, 2856, 1722 (C=O), 1278, 1112. ¹H NMR (400 MHz, CDCl₃) δ 9.42 (d, *J* = 2.8 Hz, 1 H, CHO), 7.99–7.96 (m, 2 H, Ar-H), 7.30–7.28 (m, 2 H, Ar-H), 3.90 (s, 3 H, OCH₃), 2.83 (td, *J* = 11.4, 3.5 Hz, 1 H, CH(Ar)), 2.65 (tt, *J* = 11.4, 3.2 Hz, 1 H, CH(CHO)), 2.04–1.99 (m, 1 H, C(H)H), 1.95–1.87 (m, 3 H, C(H)H + 2 \times C(H)H), 1.56–1.39 (m, 4 H, 2 \times CH₂). ¹³C NMR (101 MHz, CDCl₃) δ 203.8 (CHO), 166.9 (C=O), 149.6 (Ar-C_q), 130.0 (2 \times Ar-C), 128.6 (Ar-C_q), 127.4 (2 \times Ar-C), 55.1 (CH(CHO)), 52.0 (OCH₃), 44.9 (CH(Ar)), 34.5 (CH₂), 26.5 (CH₂), 25.9 (CH₂), 24.8 (CH₂). HRMS (pAPCI) *m/z* Calcd. for C₁₅H₁₉O₃ [M+H]⁺: 247.1329; Found: 247.1320.



Dimethyl 4,4'-((*trans*)-2-formylcyclohexane-1,3-diyl)dibenzoate (3h): Rf = 0.12 (20% Et₂O/hexane). MP = 170–179 $^{\circ}$ C. IR (film)/cm⁻¹ 2933, 2855, 1722 (C=O), 1282, 1110. ¹H NMR (400 MHz, CDCl₃) δ 9.23 (d, *J* = 3.0 Hz, 1 H, CHO), 7.98 (d, *J* = 8.2 Hz, 4 H, Ar-H), 7.32 (d, *J* = 8.2 Hz, 4 H, Ar-H), 3.90 (s, 6 H, 2 \times OCH₃), 3.11–2.98 (m, 3 H, CHCHO + 2 \times CHAr), 2.05–2.01 (m, 3 H, 3 \times C(H)H), 1.75–1.65 (m, 3 H, 3 \times C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 203.4 (CHO), 176.4 (2 \times C=O), 148.4 (2 \times Ar-C_q), 130.1 (4 \times Ar-C), 128.8 (2 \times Ar-C_q), 127.5 (4 \times Ar-C), 60.1 (CH(CHO)), 52.1 (2 \times OCH₃), 45.7 (2 \times CH(Ar)), 34.0 (2 \times CH₂), 26.1 (CH₂). HRMS (pAPCI) *m/z* Calcd. for C₂₃H₂₅O₅ [M+H]⁺: 381.1697; Found: 381.1706.

***trans*-2,6-bis(4-(Trifluoromethyl)phenyl)cyclohexane-1-carbaldehyde (3i)**

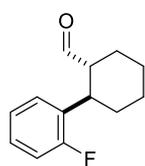
General procedure C was followed using cyclohexanecarboxaldehyde (24 μ L, 0.20 mmol), and 1-iodo-4-(trifluoromethyl)benzene (147 μ L, 1.00 mmol) to afford arylated aldehyde **3i** as a white solid (34 mg, 42%). Rf = 0.15 (10% Et₂O/hexane). MP = 116–121 $^{\circ}$ C. IR (film)/cm⁻¹ 2937, 1725 (C=O), 1617, 1326, 1162, 1118, 1069. ¹H NMR (400 MHz, CDCl₃) δ 9.24 (d, *J* = 2.8 Hz, 1 H, CHO), 7.57 (d, *J* = 8.0 Hz, 4 H, Ar-H), 7.36 (d, *J* = 8.0 Hz, 4 H, Ar-H), 3.08–2.98 (m, 3 H, 2 \times CH(Ar) + CH(CHO)), 2.06–2.00 (m, 3 H, 3 \times C(H)H), 1.71–1.65 (m, 3 H, 3 \times C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 203.2 (CHO), 147.0 (2 \times Ar-C_q), 129.2 (q, ²*J*_{C-F} = 32.5 Hz, 2 \times Ar-C_q), 127.8 (4 \times Ar-C), 125.8 (q, ³*J*_{C-F} = 3.4 Hz, 4 \times Ar-C), 124.1 (q, ¹*J*_{C-F} = 272.0 Hz, CF₃), 60.1 (CH(CHO)), 45.5 (2 \times CH(Ar)), 34.1 (2 \times CH₂), 26.1 (CH₂). ¹⁹F NMR (377 MHz, CDCl₃) δ -62.5. HRMS (pAPCI) *m/z* Calcd. for C₂₁H₁₉F₆O [M+H]⁺: 401.1335; Found: 401.1331.

***trans*-2,6-bis(4-(Trifluoromethoxy)phenyl)cyclohexane-1-carbaldehyde (3j)**

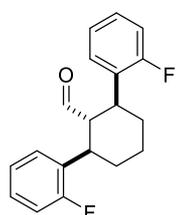
General procedure C was followed using cyclohexanecarboxaldehyde (24 μ L, 0.20 mmol), and 1-iodo-4-(trifluoromethoxy)benzene (151 μ L, 1.00 mmol) to afford arylated aldehyde **3j** as a white solid (37 mg, 43%). Rf = 0.52 (20% Et₂O/hexane). MP = 98–100 $^{\circ}$ C. IR (film)/cm⁻¹ 2933, 2858, 1725 (C=O), 1509, 1252, 1207, 1148, 1021. ¹H NMR (400 MHz, CDCl₃) δ 9.28 (d, *J* = 1.8 Hz, 1 H, CHO), 7.30–7.26 (m, 4 H, Ar-H), 7.19–7.16 (m, 4 H, Ar-H), 3.00–2.98 (m, 3 H, 2 \times CH(Ar) + CH(CHO)), 2.05–1.99 (m, 3 H, 3 \times C(H)H), 1.70–1.64 (m, 3 H, 3 \times C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 203.7 (CHO), 148.0 (2 \times Ar-C_q), 141.8 (2 \times Ar-C_q), 128.7 (4 \times Ar-C), 121.2 (4 \times Ar-C), 120.4 (q, ¹*J*_{C-F} = 257 Hz, OCF₃), 60.7 (CH(CHO)), 45.1 (2 \times CH(Ar)), 34.3 (2 \times CH₂), 26.1 (CH₂). ¹⁹F NMR (377 MHz, CDCl₃) δ -57.9. HRMS (pAPCI) *m/z* Calcd. for C₂₁H₁₉F₆O₃ [M+H]⁺: 433.1233; Found: 433.1213.

trans-2-(2-Fluorophenyl)cyclohexane-1-carbaldehyde (2k) and trans-2,6-bis(2-fluorophenyl)cyclohexane-1-carbaldehyde (3k)

General procedure C was followed using cyclohexanecarboxaldehyde (24 μL , 0.20 mmol), and 2-fluoriodobenzene (117 μL , 1.00 mmol) to afford monoarylated aldehyde **2k** as a colourless oil (7 mg, 17%) followed by diarylated aldehyde **3k** as an off-white amorphous solid (9 mg, 15%).



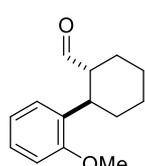
trans-2-(2-Fluorophenyl)cyclohexane-1-carbaldehyde (2k): $R_f = 0.28$ (7.5% Et_2O /pentane). IR (film)/ cm^{-1} 2929, 2855, 1722 (C=O), 1490, 1449, 1226. ^1H NMR (400 MHz, CDCl_3) δ 9.43 (dd, $J = 3.1, 0.6$ Hz, 1 H, CHO), 7.24–7.15 (m, 2 H, Ar-H), 7.09 (td, $J = 7.5, 1.3$ Hz, 1 H, Ar-H), 7.01 (ddd, $J = 10.6, 8.1, 1.3$ Hz, 1 H, Ar-H), 3.10 (td, $J = 11.5, 3.6$ Hz, 1 H, CH(Ar)), 2.67 (tt, $J = 11.5, 3.3$ Hz, 1 H, CHCHO), 2.01–1.86 (m, 4 H, 2 \times CH_2), 1.62–1.52 (m, 1 H, C(H)H), 1.50–1.38 (m, 3 H, C(H)H + CH_2). ^{13}C NMR (101 MHz, CDCl_3) δ 204.1 (CHO), 160.4 (d, $^1J_{\text{C-F}} = 244.5$ Hz, $\text{C}_q\text{-F}$), 130.7 (d, $^2J_{\text{C-F}} = 14.5$ Hz, $^{\text{F}}\text{Ar-C}_q$), 128.5 (d, $^3J_{\text{C-F}} = 4.9$ Hz, $^{\text{F}}\text{Ar-C}$), 128.0 (d, $^3J_{\text{C-F}} = 8.5$ Hz, $^{\text{F}}\text{Ar-C}$), 124.4 (d, $^4J_{\text{C-F}} = 3.3$ Hz, $^{\text{F}}\text{Ar-C}$), 115.7 (d, $^2J_{\text{C-F}} = 22.8$ Hz, $^{\text{F}}\text{Ar-C}$), 54.5 (CH(CHO)), 37.7 (CH(Ar)), 32.9 (CH_2), 26.7 (CH_2), 26.0 (CH_2), 24.8 (CH_2). ^{19}F NMR (377 MHz, CDCl_3) δ -118.2. HRMS (pAPCI) m/z Calcd. for $\text{C}_{13}\text{H}_{16}\text{OF}$ $[\text{M}+\text{H}]^+$: 207.1180; Found: 207.1183.



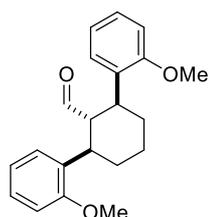
trans-2,6-bis(2-Fluorophenyl)cyclohexane-1-carbaldehyde (3k): $R_f = 0.22$ (7.5% Et_2O /pentane). IR (film)/ cm^{-1} 2933, 2858, 1729 (C=O), 1490, 1449, 1226. ^1H NMR (400 MHz, CDCl_3) δ 9.29 (d, $J = 4.3$ Hz, 1 H, CHO), 7.28 (td, $J = 7.4, 1.7$ Hz, 2 H, Ar-H), 7.18 (tdd, $J = 7.4, 5.3, 1.7$ Hz, 2 H, Ar-H), 7.10 (td, $J = 7.4, 1.1$ Hz, 2 H, Ar-H), 7.01 (ddd, $J = 10.4, 8.2, 1.1$ Hz, 2 H, Ar-H), 3.34–3.28 (m, 2 H, 2 \times CH(Ar)), 3.09 (td, $J = 11.2, 4.1$ Hz, 1 H, CHCHO), 2.02–2.00 (m, 3 H, 3 \times C(H)H), 1.79–1.66 (m, 3 H, 3 \times C(H)H). ^{13}C NMR (101 MHz, CDCl_3) δ 202.9 (CHO), 160.4 (d, $^1J_{\text{C-F}} = 244.9$ Hz, 2 \times $\text{C}_q\text{-F}$), 129.8 (d, $^2J_{\text{C-F}} = 14.1$ Hz, 2 \times $^{\text{F}}\text{Ar-C}_q$), 128.7 (d, $^3J_{\text{C-F}} = 4.6$ Hz, 2 \times $^{\text{F}}\text{Ar-C}$), 128.3 (d, $^3J_{\text{C-F}} = 8.5$ Hz, 2 \times $^{\text{F}}\text{Ar-C}$), 124.4 (d, $^4J_{\text{C-F}} = 3.3$ Hz, 2 \times $^{\text{F}}\text{Ar-C}$), 115.7 (d, $^2J_{\text{C-F}} = 22.9$ Hz, 2 \times $^{\text{F}}\text{Ar-C}$), 58.9 (CH(CHO)), 38.3 (2 \times CH(Ar)), 32.4 (2 \times CH_2), 26.2 (CH_2). ^{19}F NMR (377 MHz, CDCl_3) δ -118.0. HRMS (pAPCI) m/z Calcd. for $\text{C}_{19}\text{H}_{19}\text{OF}_2$ $[\text{M}+\text{H}]^+$: 301.1398; Found: 301.1395.

trans-2-(2-Methoxyphenyl)cyclohexane-1-carbaldehyde (2l) and trans-2,6-bis(2-methoxyphenyl)cyclohexane-1-carbaldehyde (3l)

General procedure C was followed using cyclohexanecarboxaldehyde (24 μL , 0.20 mmol), and 2-iodoanisole (130 μL , 1.00 mmol) to afford monoarylated aldehyde **2l** as a colourless oil (7 mg, 16%) followed by diarylated aldehyde **3l** as a white solid (4 mg, 6%).



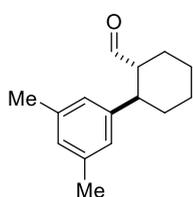
trans-2-(2-Methoxyphenyl)cyclohexane-1-carbaldehyde (2l): $R_f = 0.45$ (14% Et_2O /pentane). IR (film)/ cm^{-1} 2929, 2855, 1722 (C=O), 1490, 1461, 1244. ^1H NMR (400 MHz, CDCl_3) δ 9.36 (d, $J = 3.3$ Hz, 1 H, CHO), 7.20–7.16 (m, 2 H, Ar-H), 6.93 (td, $J = 7.5, 1.0$ Hz, 1 H, Ar-H), 6.85 (d, $J = 8.0$ Hz, 1 H, Ar-H), 3.82 (s, 3 H, OCH_3), 3.23 (td, $J = 11.7, 3.3$ Hz, 1 H, CH(Ar)), 2.57 (tt, $J = 11.7, 3.3$ Hz, 1 H, CHCHO), 1.95–1.84 (m, 4 H, 2 \times CH_2), 1.56–1.36 (m, 4 H, 2 \times CH_2). ^{13}C NMR (101 MHz, CDCl_3) δ 205.3 (CHO), 156.6 (Ar- C_q), 132.0 (Ar- C_q), 127.5 (Ar-C), 127.4 (Ar-C), 120.9 (Ar-C), 110.6 (Ar-C), 55.3 (CH(CHO) or OCH_3), 55.1 (CH(CHO) or OCH_3), 37.2 (CH(Ar)), 32.8 (CH_2), 26.8 (CH_2), 26.2 (CH_2), 24.9 (CH_2). HRMS (pAPCI) m/z Calcd. for $\text{C}_{14}\text{H}_{19}\text{O}_2$ $[\text{M}+\text{H}]^+$: 219.1380; Found: 219.1375.



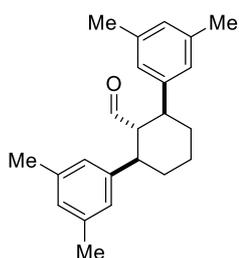
trans-2,6-bis(2-Methoxyphenyl)cyclohexane-1-carbaldehyde (3l): $R_f = 0.24$ (15% Et_2O /pentane). MP = 115–119 $^\circ\text{C}$. IR (film)/ cm^{-1} 2933, 2855, 1725 (C=O), 1490, 1461, 1241, 1028. ^1H NMR (400 MHz, CDCl_3) δ 9.20 (d, $J = 5.1$ Hz, 1 H, CHO), 7.24 (dd, $J = 7.5, 1.6$ Hz, 2 H, Ar-H), 7.16 (td, $J = 8.2, 1.6$ Hz, 2 H, Ar-H), 6.92 (td, $J = 7.5, 0.9$ Hz, 2 H, Ar-H), 6.83 (dd, $J = 8.2, 0.9$ Hz, 2 H, Ar-H), 3.82 (s, 6 H, 2 \times OCH_3), 3.51 (t, $J = 11.4$ Hz, 2 H, 2 \times CHAr), 2.89 (td, $J = 11.4, 5.1$ Hz, 1 H, CHCHO), 2.00–1.92 (m, 3 H, 3 \times C(H)H), 1.73–1.59 (m, 3 H, 3 \times C(H)H). ^{13}C NMR (101 MHz, CDCl_3) δ 203.4 (CHO), 156.5 (2 \times Ar- C_q), 131.6 (2 \times Ar- C_q), 127.7 (2 \times Ar-C), 127.4 (2 \times Ar-C), 120.8 (2 \times Ar-C), 110.6 (2 \times Ar-C), 60.7 (CH(CHO)), 55.3 (2 \times OCH_3), 37.3 (2 \times CH(Ar)), 32.4 (2 \times CH_2), 26.6 (CH_2). HRMS (pAPCI) m/z Calcd. for $\text{C}_{21}\text{H}_{25}\text{O}_3$ $[\text{M}+\text{H}]^+$: 325.1798; Found: 325.1804.

trans-2-(3,5-Dimethylphenyl)cyclohexane-1-carbaldehyde (2m) and **trans-2,6-bis(3,5-dimethylphenyl)cyclohexane-1-carbaldehyde (3m)**

General procedure C was followed using cyclohexanecarboxaldehyde (24 μ L, 0.20 mmol), and 1-iodo-3,5-dimethylbenzene (144 μ L, 1.00 mmol) to afford monoarylated aldehyde **2m** (3 mg, 7%) as a mixture with diarylated aldehyde **3m** as a white solid (23 mg, 36%). R_f = 0.11 (2% Et₂O/pentane). IR (film)/cm⁻¹ 3015, 2922, 1725 (C=O), 1602, 1446, 1036.



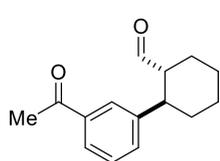
trans-2-(3,5-Dimethylphenyl)cyclohexane-1-carbaldehyde (2m): ¹H NMR (400 MHz, CDCl₃) δ 9.43 (d, *J* = 3.1 Hz, 1 H, CHO), 6.85 (s, 2 H, Ar-H), 6.84 (s, 1 H, Ar-H), 2.67 (td, *J* = 11.4, 3.4 Hz, 1 H, CH(Ar)), 2.59 (ddd, *J* = 11.4, 7.1, 3.1 Hz, 1 H, CHCHO), 2.30 (s, 6 H, 2 \times Ar-CH₃), 2.02–1.36 (m, 8 H, 4 \times CH₂). HRMS (pAPCI) *m/z* Calcd. for C₁₅H₁₈O [M-H₂]⁺: 214.1352; Found: 214.1349.



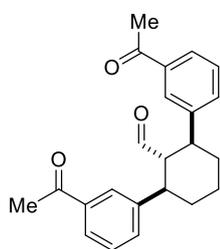
trans-2,6-bis(3,5-Dimethylphenyl)cyclohexane-1-carbaldehyde (3m): ¹H NMR (400 MHz, CDCl₃) δ 9.28 (d, *J* = 3.8 Hz, 1 H, CHO), 6.85 (s, 4 H, Ar-H), 6.84 (s, 2 H, Ar-H), 3.05–2.97 (m, 1 H, CHCHO), 2.87–2.81 (m, 2 H, 2 \times CH(Ar)), 2.30 (s, 12 H, 4 \times Ar-CH₃), 1.99–1.92 (m, 3 H, 3 \times C(H)H), 1.66–1.61 (m, 3 H, 3 \times C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 204.6 (CHO), 143.4 (2 \times Ar-C_q), 138.0 (4 \times Ar-C_q), 128.4 (2 \times Ar-C), 125.2 (4 \times Ar-C), 60.5 (CH(CHO)), 45.7 (2 \times CH(Ar)), 34.5 (2 \times CH₂), 26.4 (CH₂), 21.3 (4 \times Ar-CH₃). HRMS (pAPCI) *m/z* Calcd. for C₂₃H₂₉O [M+H]⁺: 321.2213; Found: 321.2212.

trans-2-(3-Acetylphenyl)cyclohexane-1-carbaldehyde (2n) and **trans-2,6-bis(3-acetylphenyl)cyclohexane-1-carbaldehyde (3n)**

General procedure C was followed using cyclohexanecarboxaldehyde (24 μ L, 0.20 mmol), and 1-(3-iodophenyl)ethan-1-one (139 μ L, 1.00 mmol) to afford monoarylated aldehyde **2n** as a yellow oil (8 mg, 17%) followed by diarylated aldehyde **3n** as a yellow oil (20 mg, 29%).



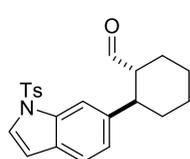
trans-2-(3-Acetylphenyl)cyclohexane-1-carbaldehyde (2n): R_f = 0.50 (50% Et₂O/pentane). IR (film)/cm⁻¹ 3015, 2922, 2855, 1725 (C=O, CHO), 1684 (C=O, COMe). ¹H NMR (400 MHz, CDCl₃) δ 9.43 (d, *J* = 2.8 Hz, 1 H, CHO), 7.83 (s, 1 H, Ar-H), 7.79 (dt, *J* = 6.8, 1.8 Hz, 1 H, Ar-H), 7.44–7.38 (m, 2 H, Ar-H), 2.84 (td, *J* = 11.6, 3.5 Hz, 1 H, CH(Ar)), 2.72–2.65 (m, 1 H, CHCHO), 2.60 (s, 3H), 2.04–1.86 (m, 4 H, 2 \times CH₂), 1.59–1.35 (m, 4 H, 2 \times CH₂). ¹³C NMR (101 MHz, CDCl₃) δ 204.0 (CHO), 198.1 (C=O), 144.9 (Ar-C_q), 137.4 (Ar-C_q), 132.3 (Ar-C), 128.9 (Ar-C), 126.9 (Ar-C), 126.9 (Ar-C), 55.2 (CH(CHO)), 44.7 (CH(Ar)), 34.7 (CH₂), 26.7 (CH₃), 26.6 (CH₂), 26.0 (CH₂), 24.8 (CH₂). HRMS (pAPCI) *m/z* Calcd. for C₁₅H₁₉O₂ [M+H]⁺: 231.1380; Found: 231.1372.



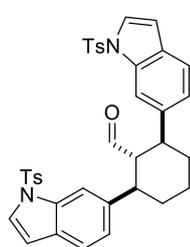
trans-2,6-bis(3-Acetylphenyl)cyclohexane-1-carbaldehyde (3n): R_f = 0.12 (50% Et₂O/pentane). IR (film)/cm⁻¹ 2929, 2855, 1722 (C=O, CHO), 1681 (2 \times C=O, COMe), 1360, 1274. ¹H NMR (400 MHz, CDCl₃) δ 9.24 (d, *J* = 3.4 Hz, 1 H, CHO), 7.86 (t, *J* = 1.6 Hz, 2 H, Ar-H), 7.79 (dt, *J* = 7.6, 1.6 Hz, 2 H, Ar-H), 7.46 (dt, *J* = 7.6, 1.6 Hz, 2 H, Ar-H), 7.40 (t, *J* = 7.6 Hz, 2 H, Ar-H), 3.11 (td, *J* = 10.9, 3.3 Hz, 1 H, CHCHO), 3.02 (td, *J* = 10.6, 2.2 Hz, 2 H, 2 \times CH(Ar)), 2.61 (s, 6 H, 2 \times CH₃), 2.04–2.01 (m, 3 H, 3 \times C(H)H), 1.77–1.63 (m, 3 H, 3 \times C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 203.7 (CHO), 198.1 (2 \times C=O), 143.8 (2 \times Ar-C_q), 137.5 (2 \times Ar-C_q), 132.4 (2 \times Ar-C), 129.0 (2 \times Ar-C), 127.2 (2 \times Ar-C), 126.9 (2 \times Ar-C), 60.3 (CH(CHO)), 45.6 (2 \times CH(Ar)), 34.1 (2 \times CH₂), 26.7 (2 \times CH₃), 26.1 (CH₂). HRMS (pAPCI) *m/z* Calcd. for C₂₃H₂₅O₃ [M+H]⁺: 349.1798; Found: 349.1804.

trans-2-(1-Tosyl-1H-indol-6-yl)cyclohexane-1-carbaldehyde (2o) and **trans-2,6-bis(1-tosyl-1H-indol-6-yl)cyclohexane-1-carbaldehyde (3o)**

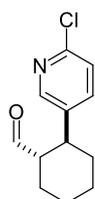
General procedure X was followed using cyclohexanecarboxaldehyde (24 μ L, 0.20 mmol), and 5-iodo-1-tosyl-1H-indole (397 mg, 1.00 mmol) to afford monoarylated aldehyde **2o** as a pale yellow amorphous solid (6 mg, 8%) followed by diarylated aldehyde **3o** as an off-white solid (27 mg, 21%).



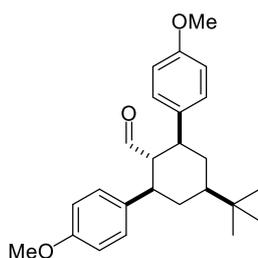
trans-2-(1-Tosyl-1H-indol-6-yl)cyclohexane-1-carbaldehyde (2o): Rf = 0.34 (40% Et₂O/pentane). IR (film)/cm⁻¹ 2929, 2855, 1722 (C=O), 1461, 1371, 1174, 1133. ¹H NMR (400 MHz, CDCl₃) δ 9.37 (d, *J* = 3.1 Hz, 1 H, CHO), 7.89 (d, *J* = 8.6 Hz, 1 H, Ar-H), 7.77 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.53 (d, *J* = 3.7 Hz, 1 H, Ar-H), 7.35 (d, *J* = 1.7 Hz, 1 H, Ar-H), 7.24 (d, *J* = 8.3 Hz, 2 H, Ar-H), 7.16 (dd, *J* = 8.6, 1.7 Hz, 1 H, Ar-H), 6.59 (dd, *J* = 3.7, 0.7 Hz, 1 H, Ar-H), 2.81 (td, *J* = 11.6, 3.5 Hz, 1 H, CH(Ar)), 2.62 (tt, *J* = 11.3, 3.3 Hz, 1 H, CHCHO), 2.36 (s, 3 H, ArCH₃), 1.97–1.85 (m, 4 H, 2 \times CH₂), 1.53–1.39 (m, 4 H, 2 \times CH₂). ¹³C NMR (101 MHz, CDCl₃) δ 204.8 (CHO), 144.9 (Ar-C_q), 139.2 (Ar-C_q), 135.3 (Ar-C_q), 133.6 (Ar-C_q), 131.0 (Ar-C_q), 129.9 (2 \times Ar-C), 126.8 (2 \times Ar-C), 126.6 (Ar-C), 124.2 (Ar-C), 119.8 (Ar-C), 113.6 (Ar-C), 108.8 (Ar-C), 55.6 (CH(CHO)), 45.0 (CH(Ar)), 35.2 (CH₂), 26.7 (CH₂), 26.1 (CH₂), 24.9 (CH₂), 21.6(Ar-CH₃). HRMS (pAPCI) *m/z* Calcd. for C₂₂H₂₄NO₃S [M+H]⁺: 382.1471; Found: 382.1472.



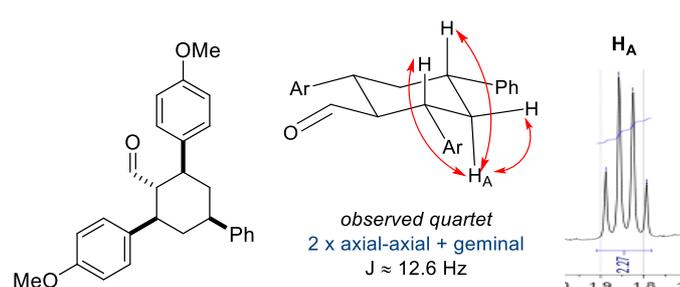
trans-2,6-bis(1-Tosyl-1H-indol-6-yl)cyclohexane-1-carbaldehyde (3o): Rf = 0.08 (40% Et₂O/pentane). MP = 110–119 $^{\circ}$ C. IR (film)/cm⁻¹ 2926, 2855, 1722 (C=O), 1461, 1367, 1170, 1133. ¹H NMR (400 MHz, CDCl₃) δ 9.16 (d, *J* = 3.4 Hz, 1 H, CHO), 7.89 (d, *J* = 8.6 Hz, 2 H, Ar-H), 7.77–7.74 (m, 4 H, Ar-H), 7.52 (d, *J* = 3.7 Hz, 2 H, Ar-H), 7.38 (d, *J* = 1.7 Hz, 2 H, Ar-H), 7.22 (d, *J* = 8.1 Hz, 4 H, Ar-H), 7.19 (dd, *J* = 8.6, 1.7 Hz, 2 H, Ar-H), 6.58 (dd, *J* = 3.7, 0.6 Hz, 2 H, Ar-H), 3.10–3.04 (m, 1 H, CHCHO), 3.03–2.97 (m, 2 H, 2 \times CHAr), 2.33 (s, 6 H, 2 \times Ar-CH₃), 2.01–1.97 (m, 3 H, 3 \times C(H)H), 1.72–1.60 (m, 3 H, C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 204.5 (CHO), 144.9 (2 \times Ar-C_q), 138.4 (2 \times Ar-C_q), 135.3 (2 \times Ar-C_q), 133.7 (2 \times Ar-C_q), 131.0 (2 \times Ar-C_q), 129.9 (4 \times Ar-C), 126.8 (4 \times Ar-C), 126.6 (2 \times Ar-C), 124.2 (2 \times Ar-C), 119.9 (2 \times Ar-C), 113.6 (2 \times Ar-C), 108.8 (2 \times Ar-C), 61.2 (CH(CHO)), 45.7 (2 \times CH(Ar)), 34.8 (2 \times CH₂), 26.4 (CH₂), 21.5 (2 \times Ar-CH₃). HRMS (pAPCI) *m/z* Calcd. for C₃₇H₃₅N₂O₅S₂ [M+H]⁺: 651.1982; Found: 651.1968.

trans-2-(6-Chloropyridin-3-yl)cyclohexane-1-carbaldehyde (2p)

General procedure C was followed using cyclohexanecarboxaldehyde (24 μ L, 0.20 mmol), and 2-chloro-5-iodopyridine (239 mg, 1.00 mmol) to afford arylated aldehyde **2x** as a yellow oil (8 mg, 18%). Rf = 0.25 (40% Et₂O/pentane). IR (film)/cm⁻¹ 2929, 2855, 1722 (C=O), 1457, 1103. ¹H NMR (400 MHz, CDCl₃) δ 9.45 (d, *J* = 2.6 Hz, 1 H, CHO), 8.26 (d, *J* = 2.5 Hz, 1 H, Ar-H), 7.50 (dd, *J* = 8.1, 2.5 Hz, 1 H, Ar-H), 7.26 (d, *J* = 8.1 Hz, 1 H, Ar-H), 2.82 (td, *J* = 11.4, 3.5 Hz, 1 H, CH(Ar)), 2.62 (tt, *J* = 11.4, 3.0 Hz, 1 H, CHCHO), 2.08–2.04 (m, 1 H, C(H)H), 1.98–1.88 (m, 3 H, C(H)H + 2 \times C(H)H), 1.52–1.31 (m, 4 H, 2 \times CH₂). ¹³C NMR (101 MHz, CDCl₃) δ 202.8 (CHO), 149.5 (Ar-C_q), 148.9 (Ar-C), 138.7 (Ar-C_q), 137.7 (Ar-C), 124.2 (Ar-C), 55.1 (CH(CHO)), 41.2 (CH(Ar)), 34.4 (CH₂), 26.5 (CH₂), 25.8 (CH₂), 24.8 (CH₂). HRMS (pAPCI) *m/z* Calcd. for C₁₂H₁₅ON³⁵Cl [M+H]⁺: 224.0837; Found: 224.0847.

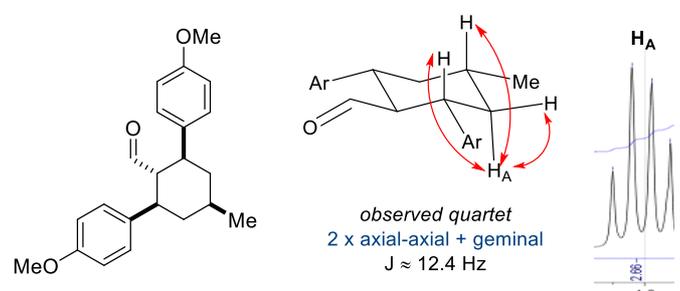
4-(tert-Butyl)-2,6-bis(4-methoxyphenyl)cyclohexane-1-carbaldehyde (5-di)

General procedure C was followed using *trans*-4-(*tert*-butyl)cyclohexane-1-carbaldehyde (**S3**) (34 mg, 0.20 mmol) and 4-iodoanisole (234 mg, 1.00 mmol) to afford arylated aldehyde **5-di** as a white solid (39 mg, 51%). Rf = 0.24 (20% Et₂O/pentane). MP = 200–207 $^{\circ}$ C. IR (film)/cm⁻¹ 2944, 2866, 1714 (C=O), 1610, 1513, 1244, 1177, 1032. ¹H NMR (400 MHz, CDCl₃) δ 9.27 (d, *J* = 3.4 Hz, 1 H, CHO), 7.18–7.14 (m, 4 H, Ar-H), 6.86–6.82 (m, 4 H, Ar-H), 3.78 (s, 6 H, 2 \times OCH₃), 2.94–2.82 (m, 3 H, CHCHO + 2 \times CHAr), 2.03–1.99 (m, 2 H, 2 \times C(H)H), 1.48–1.26 (m, 3 H, 2 \times C(H)H + CHCH₃), 0.89 (s, 9 H, C(CH₃)₃). ¹³C NMR (101 MHz, CDCl₃) δ 204.8 (CHO), 158.3 (2 \times Ar-C_q), 135.6 (2 \times Ar-C_q), 128.4 (4 \times Ar-C), 114.1 (4 \times Ar-C), 61.2 (CH(CHO)), 55.2 (2 \times OCH₃), 47.9 (CH(*t*Bu)), 45.1 (2 \times CH(Ar)), 35.9 (2 \times CH₂), 32.5 (C(CH₃)₃), 27.5 (C(CH₃)₃). HRMS (pAPCI) *m/z* Calcd. for C₂₅H₃₃O₃ [M+H]⁺: 381.2424; Found: 381.2424.

2,6-bis(4-Methoxyphenyl)-4-phenylcyclohexane-1-carbaldehyde (6-di):

General procedure C was followed using *cis/trans*-4-(phenyl)cyclohexane-1-carbaldehyde **S4** (38 mg, 0.20 mmol) and 4-iodoanisole (234 mg, 1.00 mmol) to afford diarylated aldehyde **6-di** as a white solid (41 mg, 51%). Rf = 0.15 (20% Et₂O/pentane). MP = 120–121 °C. IR (film)/cm⁻¹ 2922, 2836, 1725 (C=O), 1610, 1513, 1248, 1177, 1032. ¹H NMR (400 MHz, CDCl₃) δ 9.34 (d, $J = 3.7$ Hz, 1 H, CHO), 7.32–7.25 (m, 4 H, Ph-H), 7.22–7.17 (m, 5 H, Ph-H + 4 x Ar-H), 6.86–6.82 (m, 4 H, Ar-H), 3.77 (s, 6

H, 2 x OCH₃), 3.13 (td, $J = 11.7, 3.3$ Hz, 2 H, 2 x CHAr), 3.06–2.93 (m, 2 H, CHCHO + CHPh), 2.19 (dt, $J = 5.6, 2.4$ Hz, 2 H, 2 x C(H)H), 1.89–1.79 (m, 2 H, 2 x C(H_A)H). ¹³C NMR (101 MHz, CDCl₃) δ 204.5 (CHO), 158.4 (2 x Ar-C_q), 145.4 (Ph-C_q), 134.8 (2 x Ar-C_q), 128.5 (2 x Ph-C), 128.3 (4 x Ar-C), 126.6 (2 x Ph-C), 126.3 (Ph-C), 114.1 (4 x Ar-C), 60.8 (CH(CHO)), 55.2 (2 x OCH₃), 45.1 (2 x CH(Ar)), 43.9 (CH(Ph)), 41.9 (2 x CH₂). HRMS (pAPCI) *m/z* Calcd. for C₂₇H₂₉O₃ [M+H]⁺: 401.2111; Found: 401.2107.

4-(Methyl)-2,6-bis(4-methoxyphenyl)cyclohexane-1-carbaldehyde (7-di)

General procedure C was followed using *trans*-4-(methyl)cyclohexane-1-carbaldehyde (**S5**) (25 mg, 0.20 mmol) and 4-iodoanisole (234 mg, 1.00 mmol) to afford arylated aldehyde **7-di** as a white solid (30 mg, 44%, 90:10 ratio of major and minor (Me *cis* to aldehyde) data given for major isomer only). Rf = 0.25 (20% Et₂O/pentane). MP = 182–186 °C. IR (film)/cm⁻¹ 2944, 2903, 2712, 1718 (C=O), 1610, 1513, 1244, 1177, 1032.

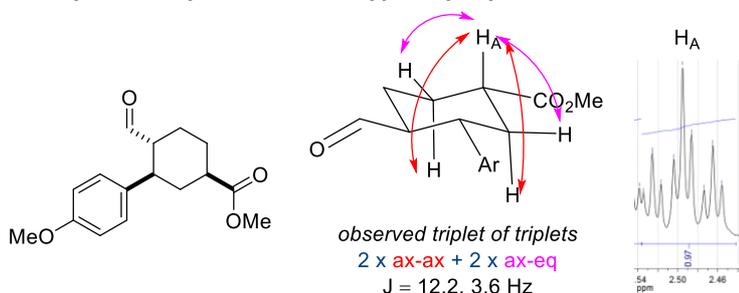
¹H NMR (400 MHz, CDCl₃) δ 9.27 (d, $J = 3.8$ Hz, 1 H, CHO), 7.16–7.12 (m, 4 H, Ar-H), 6.85–6.81 (m, 4 H, Ar-H), 3.77 (s, 6 H, 2 x OCH₃), 2.98–2.91 (m, 2 H, 2 x CHAr), 2.85 (td, $J = 10.9, 3.8$ Hz, 1 H, CHCHO), 1.97–1.92 (m, 2 H, 2 x C(H)H), 1.83–1.74 (m, 1 H, CHCH₃), 1.35–1.26 (m, 2 H, 2 x C(H_A)H), 0.99 (d, $J = 6.6$ Hz, 3 H, CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 204.9 (CHO), 158.2 (2 x Ar-C_q), 135.3 (2 x Ar-C_q), 128.3 (4 x Ar-C), 114.0 (4 x Ar-C), 61.0 (CH(CHO)), 55.2 (2 x OCH₃), 44.8 (2 x CH(Ar) or 2 x CH₂), 43.1 (2 x CH(Ar) or 2 x CH₂), 32.7 (CH(CH₃)), 22.1 (CH₃). HRMS (pAPCI) *m/z* Calcd. for C₂₂H₂₇O₃ [M+H]⁺: 339.1955; Found: 339.1957. Observed signals for minor isomer of di: ¹H NMR (400 MHz, CDCl₃) δ 3.14 (td, $J = 12.5, 3.7$ Hz, 2 H, 2 x CHAr), 2.31–2.24 (m, 1 H, CHMe). NOTE: Signal for CHMe is majorly shifted downfield in *cis* isomer due to equatorial confirmation, suggesting Me group is axial.

Methyl-4-formyl-3-(4-methoxyphenyl)cyclohexane-1-carboxylate (8-mono) and methyl-4-formyl-3,5-bis(4-methoxyphenyl)cyclohexane-1-carboxylate (8-di)

General procedure C was followed using (1R,4R)-methyl 4-formylcyclohexanecarboxylate (34 mg, 0.20 mmol) and 4-iodoanisole (234 mg, 1.00 mmol) to afford monoarylated aldehyde **8-mono** as a white solid (5 mg, 9%) followed by diarylated aldehyde **8-di** as a white solid (31 mg, 41%, 3:1 *trans:cis*).

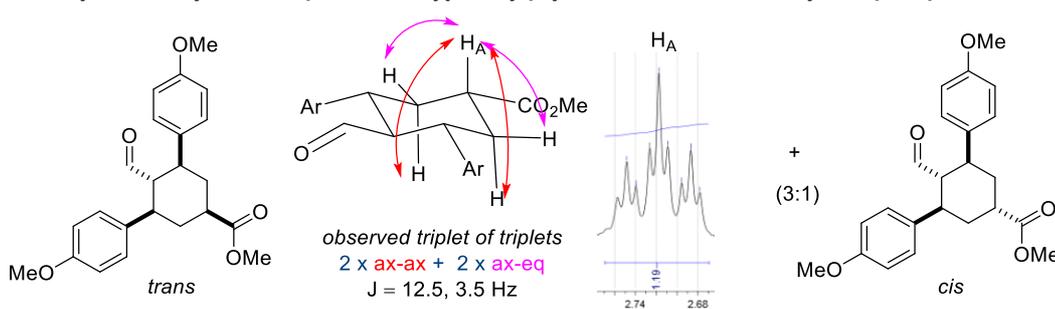
Methyl-4-formyl-3-(4-methoxyphenyl)cyclohexane-1-carboxylate (8-mono): R_f = 0.43 (50% Et₂O/pentane). IR

(film)/cm⁻¹ 2948, 1729 (C=O), 1610, 1513, 1248, 1177, 1036. ¹H NMR (400 MHz, CDCl₃) δ 9.44 (d, *J* = 2.7 Hz, 1 H, CHO), 7.16–7.11 (m, 2 H, Ar-H), 6.87–6.83 (m, 2 H, Ar-H), 3.79 (s, 3 H, OCH₃), 3.68 (s, 3 H, OCH₃), 2.76 (td, *J* = 12.0, 3.5 Hz, 1 H, CHAr), 2.61–2.54 (m, 1 H, CHCHO), 2.50 (tt, *J* = 12.2, 3.6 Hz, 1 H, CH_ACO₂CH₃), 2.20–2.15 (m, 2 H, 2 × C(H)H), 2.08–2.03 (m, 1 H, C(H)H), 1.72–1.43 (m, 3 H, C(H)H + CH₂). ¹³C NMR (101 MHz, CDCl₃) δ 204.2 (CHO), 158.5 (Ar-C_q), 134.7 (Ar-C_q), 128.3 (2 × Ar-C), 114.2 (2 × Ar-C), 55.2 (CH(CHO) or OCH₃), 54.6 (CH(CHO) or OCH₃), 51.7 (CH(CHO) or OCH₃), 43.6 (CH(Ar) or CH(CO₂CH₃)), 42.9 (CH(Ar) or CH(CO₂CH₃)), 37.0 (CH₂), 27.3 (CH₂), 25.8 (CH₂). HRMS (pAPCI) *m/z* Calcd. for C₁₆H₂₀O₄ [M+H]⁺: 276.1356; Found: 276.1365.



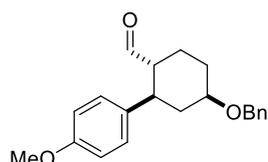
Methyl-4-formyl-3,5-bis(4-methoxyphenyl)cyclohexane-1-carboxylate (8-di): R_f = 0.28 (50% Et₂O/pentane). MP =

163–168 °C. IR (film)/cm⁻¹ 2952, 2836, 1729 (C=O), 1610, 1513, 1252, 1177, 1036. *Trans*: ¹H NMR (400 MHz, CDCl₃) δ 9.26 (d, *J* = 2.0 Hz, 1 H, CHO), 7.15 (d, *J* = 8.7 Hz, 4 H, Ar-H), 6.83 (d, *J* = 8.7 Hz, 4 H, Ar-H), 3.78 (s, 6 H, 2 × OCH₃), 3.67 (s, 3 H, CO₂CH₃), 2.99–2.92 (m, 3 H, CHCHO + 2 × CH(Ar)), 2.72 (tt, *J* = 12.3, 3.5 Hz, 1 H, CH_ACO₂CH₃), 2.23 (d, *J* = 14.0 Hz, 2 H, 2 × C(H)H), 1.85–1.77 (m, 2 H, 2 × C(H)H). *Cis*: ¹H NMR (400 MHz, CDCl₃) δ 9.22 (d, *J* = 4.2 Hz, 1 H, CHO), 7.15 (d, *J* = 8.7 Hz, 4 H, Ar-H), 6.83 (d, *J* = 8.7 Hz, 4 H, Ar-H), 3.82 (s, 3 H, CO₂CH₃), 3.78 (s, 3 H, OCH₃), 3.13 (td, *J* = 12.5, 3.4 Hz, 2 H, 2 × CH(Ar)), 2.91–2.84 (m, 1 H, CHCO₂CH₃), 2.99–2.92 (m, 1 H, CHCHO), 2.41 (d, *J* = 13.7 Hz, 2 H, C(H)H), 1.86–1.76 (m, 2 H, C(H)H). NOTE: Downfield shift of the CHCO₂CH₃ signal for this isomer is consistent with an axial configuration of the ester group. ¹³C NMR (101 MHz, CDCl₃) δ 204.2 (CHO, *trans*), 203.7 (CHO, *cis*), 174.9 (C=O), 158.5 (2 × Ar-C_q), 134.1 (2 × Ar-C_q), 128.4 (4 × Ar-C), 114.1 (4 × Ar-C), 60.8 (CH(CHO) *cis*), 60.5 (CH(CHO) *trans*), 55.2 (2 × OCH₃), 51.8 (CO₂CH₃), 44.2 (2 × CH(Ar)), 43.1 (CHCO₂CH₃, *trans*), 40.8 (CHCO₂CH₃, *cis*), 36.4 (2 × CH₂, *trans*), 34.8 (2 × CH₂, *cis*). HRMS (pAPCI) *m/z* Calcd. for C₂₃H₂₇O₅ [M+H]⁺: 383.1853; Found: 383.1850.



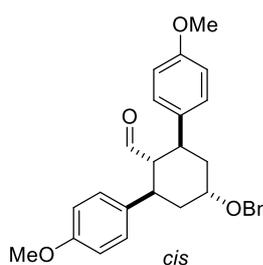
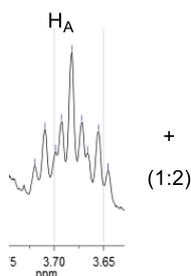
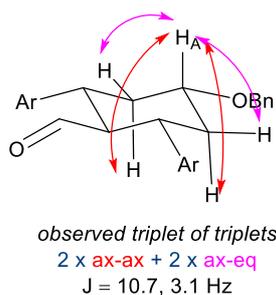
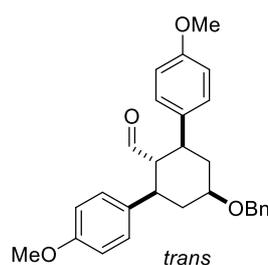
4-(Benzyloxy)-2-(4-methoxyphenyl)cyclohexane-1-carbaldehyde (9-mono) and 4-(benzyloxy)-2,6-bis(4-methoxyphenyl)cyclohexane-1-carbaldehyde (9-di)

General procedure C was followed using *trans*-4-(benzyloxy)cyclohexane-1-carbaldehyde **S6** (44 mg, 0.20 mmol) and 4-iodoanisole (234 mg, 1.00 mmol) to afford monoarylated aldehyde **9-mono** (8 mg, 12%) as a mixture with diarylated aldehyde **9-di** as a yellow oil (34 mg, 40%, 1:2 *trans*:*cis*). NOTE: *cis* isomer of the monoarylated product was also observed but coeluted with the starting material. R_f = 0.21 (30% Et₂O/pentane). IR (film)/cm⁻¹ 2933, 1722 (C=O), 1610, 1513, 1453, 1244, 1177, 1095, 1032. ¹³C NMR (101 MHz, CDCl₃) δ 204.4 (CHO, 9-mono), 204.3 (CHO, 9-di-*trans*), 203.8 (CHO, 9-di-*cis*), 158.4, 158.3, 138.8, 134.8, 134.6, 134.1, 128.5, 128.42, 128.39, 128.32, 128.25, 127.6, 127.49, 127.45, 114.18, 114.14, 114.06, 76.4 (CHOBn, 9-mono), 76.0 (CHOBn, 9-di-*trans*), 72.8 (CHOBn, xx-di-*cis*), 70.2, 70.0, 61.3 (CH(CHO, xx-di-*cis*), 61.2, 55.2, 55.0, 43.1, 43.0, 40.4, 40.1 (2 × CH₂ 9-di-*trans*), 38.5 (2 × CH(Ar) 9-di-*cis*), 37.7 (2 × CH₂, 9-di-*cis*), 31.0, 30.3, 24.7.



4-(Benzyloxy)-2-(4-methoxyphenyl)cyclohexane-1-carbaldehyde (9-mono): ¹H NMR (400 MHz, CDCl₃) δ 9.43 (d, *J* = 2.8 Hz, 1 H, CHO), 7.46–7.28 (m, 5 H, Ph-H), 7.15 (d, *J* = 7.7 Hz, 2 H, Ar-H), 6.88–6.82 (m, 2 H, Ar-H), 4.60 (d, *J* = 2.0 Hz, 2 H, OCH₂), 3.80 (s, 3 H, OCH₃), 3.54–3.46 (m, 1 H, CHOPh), 2.78 (td, *J* = 12.2, 3.4 Hz, 1 H, CHAr), 2.55 (tt, *J* = 11.5, 3.1 Hz, 1 H, CHCHO), 2.34–2.29 (m, 2 H, 2 × C(H)*H*^{eq}), 2.06–1.97 (m, 1 H, C(H)*H*^{eq}), 1.65–1.56 (m, 1 H, C(*H*^{ax})H), 1.50–1.44 (m, 2 H, 2 × C(*H*^{ax})H). NOTE: Chemical shift of the CHOBn signal for this isomer is similar to *trans* isomer of the diarylated product. HRMS (pAPCI) *m/z* Calcd. for C₂₁H₂₄O₃ [M-H]⁺: 323.1642; Found: 323.1641.

4-(Benzyloxy)-2,6-bis(4-methoxyphenyl)cyclohexane-1-carbaldehyde (9-di): *Trans*: ¹H NMR (400 MHz, CDCl₃) δ

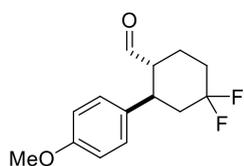


9.25 (d, *J* = 3.1 Hz, 1 H, CHO), 7.46–7.29 (m, 5 H, Ph-H), 7.15 (d, *J* = 7.7 Hz, 4 H, Ar-H), 6.86–6.82 (m, 4 H, Ar-H), 4.61 (s, 2 H, OCH₂), 3.78 (s, 6 H, 2 × OCH₃), 3.68 (tt, *J* = 10.7, 4.1 Hz, 1 H, CHOBn), 2.99–2.91 (m, 3 H, 2 ×

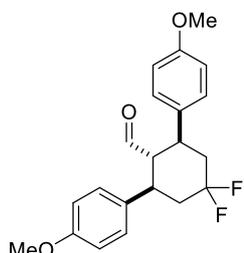
CHPh + CHCHO), 2.39 (d, *J* = 12.4 Hz, 2 H, 2 × C(H)*H*^{eq}), 1.76 (dd, *J* = 19.0, 7.3 Hz, 2 H, 2 × C(*H*^{ax})H). *cis*: ¹H NMR (400 MHz, CDCl₃) δ 9.27 (d, *J* = 4.4 Hz, 1 H, CHO), 7.47–7.28 (m, 5 H, Ph-H), 7.15 (d, *J* = 7.7 Hz, 4 H, Ar-H), 6.86–6.83 (m, 4 H, Ar-H), 4.63 (s, 2 H, OCH₂), 3.95–3.91 (m, 1 H, CHOBn), 3.78 (s, 6 H, 2 × OCH₃), 3.43 (td, *J* = 12.7, 3.3 Hz, 2 H, 2 × CHAr), 2.87 (td, *J* = 11.4, 4.4 Hz, 1 H, CHCHO), 2.25 (d, *J* = 13.5 Hz, 2 H, 2 × C(H)*H*^{eq}), 1.79–1.71 (m, 2 H, 2 × C(*H*^{ax})H). NOTE: Downfield shift of the CHOBn signal for this isomer is consistent with an axial configuration of the ether group. HRMS (pAPCI) *m/z* Calcd. for C₂₈H₃₁O₄ [M+H]⁺: 431.2217; Found: 431.2206.

4,4-Difluoro-2-(4-methoxyphenyl)cyclohexane-1-carbaldehyde (10-mono) and **4,4-difluoro-2,6-bis(4-methoxyphenyl)cyclohexane-1-carbaldehyde (10-di)**

General procedure C was followed using 4,4-Difluorocyclohexane-1-carbaldehyde (**S7**) (30 mg, 0.20 mmol) and 4-iodoanisole (234 mg, 1.00 mmol) to afford monoarylated aldehyde **10-mono** as a white solid (12 mg, 24%) followed by diarylated aldehyde **10-di** as a white solid (4 mg, 6%).



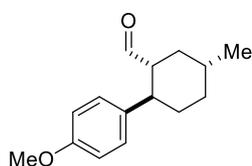
4,4-Difluoro-2-(4-methoxyphenyl)cyclohexane-1-carbaldehyde (10-mono): Rf = 0.36 (50% CH₂Cl₂/pentane). MP = 91–94 °C. IR (film)/cm⁻¹ 2955, 2825, 2735, 1710 (C=O), 1610, 1513, 1461, 1367, 1263, 1073, 1025. ¹H NMR (400 MHz, CDCl₃) δ 9.43 (d, *J* = 2.7 Hz, 1 H, CHO), 7.17–7.13 (m, 2 H, Ar-H), 6.89–6.86 (m, 2 H, Ar-H), 3.80 (s, 3 H, OCH₃), 3.10 (td, *J* = 11.9, 2.4 Hz, 1 H, CHAr), 2.60 (tt, *J* = 11.7, 2.7 Hz, 1 H, CHCHO), 2.37–2.26 (m, 2 H, 2 × C(H)H), 2.06–1.98 (m, 1 H, C(H)H), 1.96–1.85 (m, 1 H, C(H)H), 1.83–1.72 (m, 2 H, C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 204.1 (CHO), 158.8 (Ar-C_q), 132.6 (Ar-C_q), 122.36 (dd, ¹*J*_{C-F} = 244.0, 239.4 Hz, CF₂), 128.3 (2 × Ar-C), 114.4 (2 × Ar-C), 55.3 (CH(CHO)), 53.7 (OCH₃), 41.5 (dd, ²*J*_{C-F} = 25.9, 22.5 Hz, CH₂), 41.0 (d, ³*J*_{C-F} = 10.2 Hz, CH(Ar)), 32.4 (t, ²*J*_{C-F} = 24.5 Hz, CH₂), 22.9 (d, ³*J*_{C-F} = 10.5 Hz, CH₂). ¹⁹F NMR (377 MHz, CDCl₃) δ -91.1 (d, *J* = 240 Hz), -101.7 (d, *J* = 240 Hz). HRMS (pAPCI) *m/z* Calcd. for C₁₄H₁₇F₂O₂ [M+H]⁺: 255.1191; Found: 255.1199.



4,4-Difluoro-2,6-bis(4-methoxyphenyl)cyclohexane-1-carbaldehyde (10-di): Rf = 0.25 (50% CH₂Cl₂/pentane). IR (film)/cm⁻¹ 2963, 2840, 1714 (C=O), 1610, 1513, 1248, 1177. ¹H NMR (400 MHz, CDCl₃) δ 9.24 (d, *J* = 3.8 Hz, 1 H, CHO), 7.17–7.13 (m, 4 H, Ar-H), 6.87–6.83 (m, 4 H, Ar-H), 3.78 (s, 6 H, 2 × CH₃), 3.30–3.23 (m, 2 H, 2 × CHAr), 2.95 (td, *J* = 11.4, 3.8 Hz, 1 H, CHCHO), 2.43–2.36 (m, 2 H, 2 × C(H)H), 2.07 (dtd, *J* = 33.9, 13.6, 3.0 Hz, 2 H, 2 × C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 202.8 (CHO), 158.8 (2 × Ar-C_q), 132.2 (2 × Ar-C_q), 128.4 (4 × Ar-C), 114.4 (4 × Ar-C), 60.0 (CH(CHO)), 55.2 (2 × CH₃), 41.26 (d, ³*J*_{C-F} = 10.8 Hz, 2 × CH(Ar)), 41.08 (dd, ²*J*_{C-F} = 24.8, 21.8 Hz, 2 × CH₂). CF₂ signal not observed. ¹⁹F NMR (377 MHz, CDCl₃) δ -90.7 (d, *J* = 242 Hz), -100.1 (d, *J* = 242 Hz). HRMS (pAPCI) *m/z* Calcd. for C₂₁H₂₃F₂O₃ [M+H]⁺: 361.1610; Found: 361.1603.

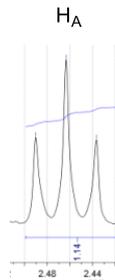
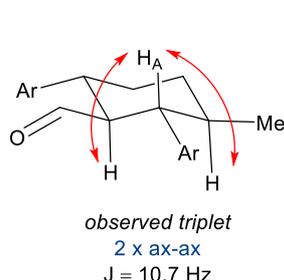
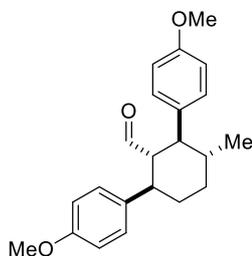
2-(4-Methoxyphenyl)-5-methylcyclohexane-1-carbaldehyde (11-mono) and 2,6-bis(4-methoxyphenyl)-3-methylcyclohexane-1-carbaldehyde (11-di)

General procedure C was followed using *cis*-3-(methyl)cyclohexane-1-carbaldehyde **S8** (25 mg, 0.20 mmol) and 4-iodoanisole (234 mg, 1.00 mmol) to afford monoarylated aldehyde **11-mono** as a colourless oil (11 mg, 24%) followed by diarylated aldehyde **11-di** as an off-white solid (8 mg, 12%).

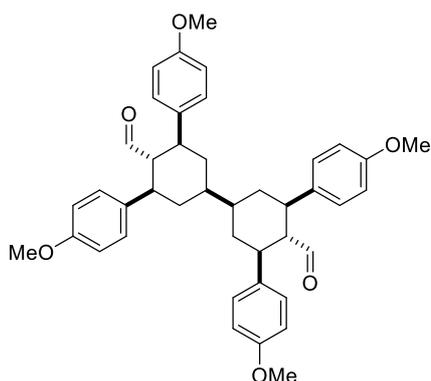


2-(4-Methoxyphenyl)-5-methylcyclohexane-1-carbaldehyde (11-mono): Rf = 0.48 (20% Et₂O/pentane). IR (film)/cm⁻¹ 2922, 2987, 1722 (C=O), 1513, 1248, 1036. ¹H NMR (400 MHz, CDCl₃) δ 9.41 (d, *J* = 2.9 Hz, 1 H, CHO), 7.14–7.11 (m, 2 H, Ar-H), 6.86–6.82 (m, 2 H, Ar-H), 3.78 (s, 3 H, OCH₃), 2.70–2.56 (m, 2 H, CHAr + CHCHO), 1.94–1.86 (m, 2 H, 2 × C(H)H), 1.86–1.79 (m, 1 H, C(H)H), 1.63–1.48 (m, 2 H, C(H)H + CHCH₃), 1.16–1.04 (m, 2 H, CH₂), 1.00 (d, *J* = 6.5 Hz, 3 H, CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 204.8 (CHO), 158.2 (Ar-C_q), 135.9 (Ar-C_q), 128.3 (2 × Ar-C), 114.1 (2 × Ar-C), 55.6 (OCH₃ or CH(CHO)), 55.2 (OCH₃ or CH(CHO)), 44.0 (CH(Ar)), 35.1 (CH(CH₃) or CH₂), 34.9 (CH(CH₃) or CH₂), 34.8 (CH(CH₃) or CH₂), 31.4 (CH₂), 22.4 (CH₃). HRMS (pAPCI) *m/z* Calcd. for C₁₅H₂₁O₂ [M+H]⁺: 233.1536; Found: 233.1532.

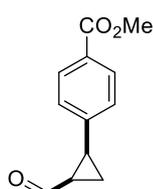
2,6-Bis(4-methoxyphenyl)-3-methylcyclohexane-1-carbaldehyde (11-di): Rf = 0.25 (20% Et₂O/pentane). IR



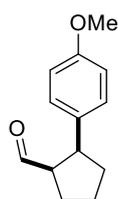
(film)/cm⁻¹ 2922, 2836, 1722 (C=O), 1610, 1509, 1244, 1177, 1032. ¹H NMR (400 MHz, CDCl₃) δ 9.18 (d, *J* = 3.7 Hz, 1 H, CHO), 7.15–7.11 (m, 2 H, Ar-H), 7.11–7.06 (m, 2 H, Ar-H), 6.84–6.79 (m, 4 H, Ar-H), 3.78 (s, 3 H, OCH₃), 3.77 (s, 3 H, OCH₃), 2.96–2.84 (m, 2 H, CHAr + CHCHO), 2.46 (t, *J* = 10.7 Hz, 1 H, CH_AAr), 2.00–1.94 (m, 2 H, 2 × C(H)H), 1.79–1.67 (m, 2 H, C(H)H + CHCH₃), 1.41–1.26 (m, 1 H, C(H)H), 0.73 (d, *J* = 6.5 Hz, 3 H, CH₃). ¹³C NMR (101 MHz, CDCl₃) δ 204.6 (CHO), 158.2 (2 × Ar-C_q), 135.4 (Ar-C_q), 133.8 (Ar-C_q), 128.3 (4 × Ar-C), 114.0 (4 × Ar-C), 62.0 (CH(CHO)), 55.2 (OCH₃), 55.1 (OCH₃), 51.7 (CH(Ar)), 45.1 (CH(Ar)), 37.3 (CHCH₃), 35.2 (CH₂), 34.7 (CH₂), 20.0 (CH₃). HRMS (pAPCI) *m/z* Calcd. for C₂₂H₂₇O₃ [M+H]⁺: 339.1955; Found: 339.1940.

***trans*-3,3',5,5'-Tetrakis(4-methoxyphenyl)-[1,1'-bi(cyclohexane)]-4,4'-dicarbaldehyde (12):**


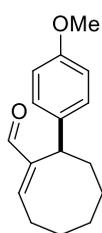
General procedure C was followed using *trans*-[1,1'-bi(cyclohexane)]-4,4'-dicarbaldehyde **S9** (22 mg, 0.10 mmol) and 4-iodoanisole (234 mg, 1.00 mmol) to afford terta-arylated aldehyde **12** as a white solid (21 mg, 32%). Rf = 0.28 (30% EtOAc/pentane). MP = decomposes at 240 °C. IR (film)/cm⁻¹ 2937, 2836, 1714 (C=O), 1610, 1513, 1248, 1177, 1032. ¹H NMR (400 MHz, CDCl₃) δ 9.25 (d, *J* = 2.3 Hz, 2 H, 2 × CHO), 7.13–7.09 (m, 8 H, Ar-H), 6.83–6.80 (m, 8 H, Ar-H), 3.77 (s, 12 H, 4 × OCH₃), 2.94–2.82 (m, 6 H, 2 × CHCHO + 4 × CHAr), 1.99 (d, *J* = 12.8 Hz, 4 H, 4 × C(H)H), 1.67–1.62 (m, 2 H, 2 × CHCy), 1.45–1.37 (m, 4 H, 4 × C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 204.4 (2 × CHO), 158.4 (4 × Ar-C_q), 135.1 (4 × Ar-C_q), 128.3 (8 × Ar-C), 114.1 (8 × Ar-C), 60.8 (2 × CH(CHO)), 55.2 (4 × OCH₃), 44.9 (4 × CH(Ar)), 42.6 (2 × CHCy), 38.3 (4 × CH₂). HRMS (ES⁺) *m/z* Calcd. for C₄₂H₄₇O₆ [M+H]⁺: 647.3373; Found: 647.3367.

Products observed from arylation of other ring sizes (S10–S12)**Methyl 4-((1S,2R)-2-formylcyclopropyl)benzoate (S10)**

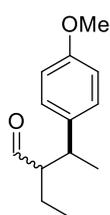
General procedure C was followed using cyclopropanecarboxaldehyde (30 μ L, 0.40 mmol), and methyl 4-iodobenzoate (52 mg, 0.20 mmol) to afford arylated aldehyde **S10** as a yellow oil. Rf = 0.10 (20% Et₂O/pentane). IR (film)/cm⁻¹ 1722 (C=O), 1282, 1110. ¹H NMR (400 MHz, CDCl₃) δ 8.74 (d, *J* = 6.3 Hz, 1 H, CHO), 8.00–7.97 (m, 2 H, Ar-H), 7.40 (d, *J* = 8.0 Hz, 2 H, Ar-H), 3.92 (s, 3 H, OCH₃), 2.86 (dd, *J* = 16.3, 8.2 Hz, 1 H, CHAr), 2.27–2.22 (m, 1 H, CHCHO), 1.94 (dt, *J* = 7.4, 5.5 Hz, 1 H, C(H)H), 1.65 (td, *J* = 8.2, 5.5 Hz, 2 H, C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 200.3 (CHO), 166.7 (C=O), 141.0 (Ar-C_q), 129.8 (2 \times Ar-C), 129.2 (2 \times Ar-C), 129.0 (Ar-C_q), 52.1 (OCH₃), 29.9 (CH(CHO)), 26.5 (CH(Ar)), 11.7 (CH₂). Spectroscopic data for this compound is consistent with that shown in the literature.³

cis-2-(4-Methoxyphenyl)cyclopentane-1-carbaldehyde (S11)

General procedure C was followed using cyclopentanecarboxaldehyde (21 μ L, 0.20 mmol), and 4-iodoanisole (234 mg, 1.00 mmol) to afford arylated aldehyde **S11** as a yellow oil (7 mg, 17%). Rf = 0.43 (20% Et₂O/pentane). ¹H NMR (400 MHz, CDCl₃) δ 9.66 (d, *J* = 2.7 Hz, 1 H, CHO), 7.19–7.15 (m, 2 H, Ar-H), 6.87–6.83 (m, 2 H, CHO), 3.80 (s, 3 H, OCH₃), 3.28 (dd, *J* = 16.9, 9.3 Hz, 1 H, CHAr), 2.85 (ddd, *J* = 17.1, 8.5, 2.7 Hz, 1 H, CHCHO), 2.20–2.15 (m, 1 H, C(H)H), 2.05–1.99 (m, 2 H, 2 \times C(H)H), 1.94–1.87 (m, 1 H, C(H)H), 1.78–1.69 (m, 2 H, 2 \times C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 203.3 (CHO), 158.2 (Ar-C_q), 135.5 (Ar-C_q), 128.1 (2 \times Ar-C), 114.0 (2 \times Ar-C), 59.5 (OCH₃), 55.3 (CH(CHO)), 46.2 (CH(Ar)), 35.6 (CH₂), 26.7 (CH₂), 25.1 (CH₂).

8-(4-Methoxyphenyl)cyclooct-1-ene-1-carbaldehyde (S12)

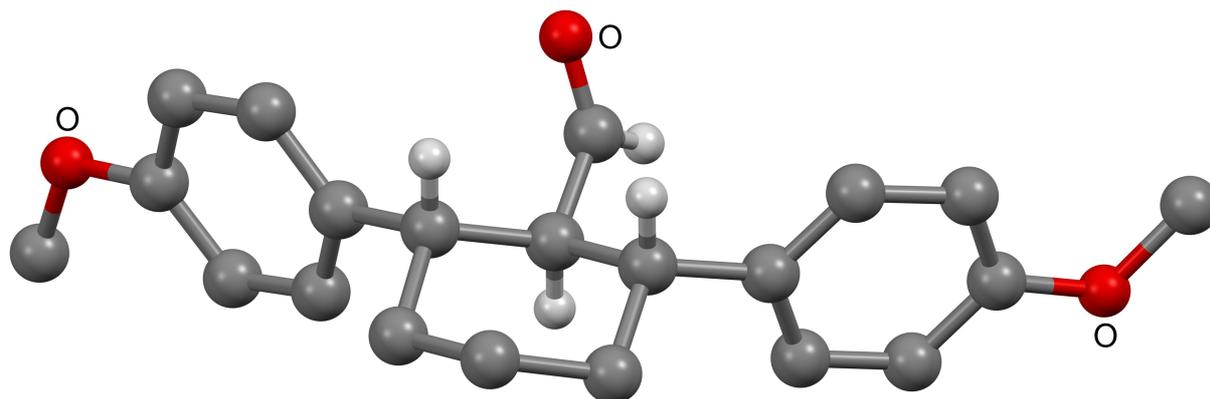
General procedure C was followed using cyclooctanecarboxaldehyde (**S2**) (29 μ L, 0.20 mmol), and 4-iodoanisole (234 mg, 1.00 mmol) to afford arylated aldehyde **S12** as a yellow oil (6 mg, 12%). Rf = 0.32 (20% Et₂O/hexane). ¹H NMR (400 MHz, CDCl₃) δ 9.34 (s, 1 H, CHO), 7.18–7.14 (m, 2 H, Ar-H), 6.85–6.80 (m, 3 H, 2 \times Ar-C + CH=C), 4.10 (dd, *J* = 11.8, 4.8 Hz, 1 H, CHAr), 3.78 (s, 3 H, OCH₃), 2.74–2.65 (m, 1 H, C(H)H), 2.55–2.46 (m, 1 H, C(H)H), 2.29–2.22 (m, 1 H, C(H)H), 1.96–1.88 (m, 1 H, C(H)H), 1.82–1.70 (m, 3 H, 3 \times C(H)H), 1.66–1.59 (m, 1 H, C(H)H), 1.49–1.44 (m, 2 H, 2 \times C(H)H). ¹³C NMR (101 MHz, CDCl₃) δ 194.2 (CHO), 157.7 (Ar-C_q), 153.8 (CH=C), 146.5 (CH=C), 135.1 (Ar-C_q), 128.4 (2 \times Ar-C), 113.6 (2 \times Ar-C), 55.2 (OCH₃), 39.5 (CH(Ar)), 33.4 (CH₂), 28.3 (CH₂), 27.6 (CH₂), 26.4 (CH₂), 25.4 (CH₂).

2-Ethyl-3-(4-methoxyphenyl)butanal (S13)

General procedure C was followed using 2-ethylbutanal (29 μ L, 0.20 mmol), and 4-iodoanisole (234 mg, 1.00 mmol) to afford arylated aldehyde **S13** as a yellow oil (7 mg, 17%, 1.34:1 dr, contains grease). Rf = 0.51 (20% Et₂O/hexane). ¹H NMR (400 MHz, CDCl₃) δ 9.60 (d, *J* = 4.3 Hz, 1 H, CHO major), 9.48 (d, *J* = 3.7 Hz, 1 H, CHO minor), 7.10 (dd, *J* = 8.8, 2.6 Hz, 2 H, Ar-H major and minor), 6.89–6.83 (m, 2 H, Ar-H major and minor), 3.81 (s, 3 H, OCH₃ major), 3.79 (s, 2 H, OCH₃ minor), 3.06 (p, *J* = 7.3 Hz, 1 H, CHAr minor), 2.95 (dq, *J* = 9.3, 7.0 Hz, 1 H, CHAr major), 2.41–2.28 (m, 2 H, CHCHO major and minor), 1.73–1.59 (m, 2 H, CH₂CH₃ major), 1.52–1.32 (m, 2 H, CH₂CH₃ minor), 1.30 (d, *J* = 7.1 Hz, 3 H, CH(Ar)CH₃ minor), 1.24 (d, *J* = 7.0 Hz, 3 H, CH(Ar)CH₃ major), 0.90 (t, *J* = 7.5 Hz, 3 H, CH₂CH₃ minor), 0.79 (t, *J* = 7.5 Hz, 3 H, CH₂CH₃ major). ¹³C NMR (101 MHz, CDCl₃, mix of diastereomers) δ 205.6, 205.4, 158.2, 157.6, 136.1, 135.9, 128.5, 128.4, 113.9, 60.5, 59.8, 55.2, 39.0, 20.9, 20.5, 19.8, 18.9, 11.8.

References

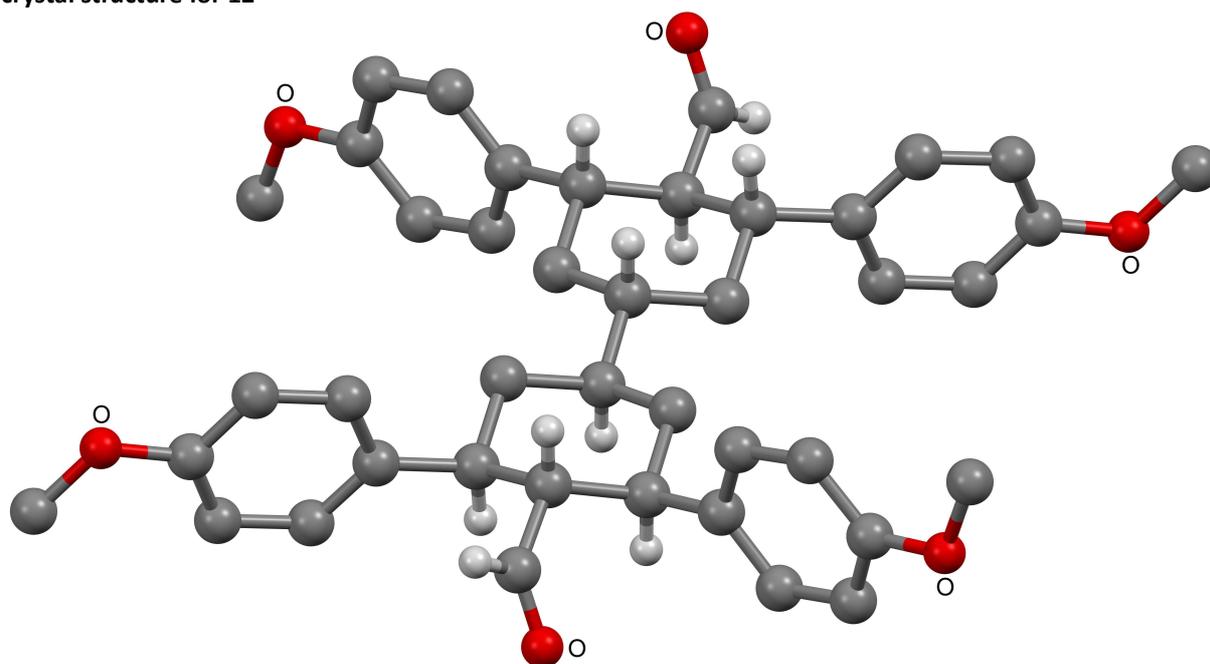
- (1) Yang, K.; Li, Q.; Liu, Y.; Li, G.; Ge, H. Catalytic C–H Arylation of Aliphatic Aldehydes Enabled by a Transient Ligand. *J. Am. Chem. Soc.* **2016**, *138* (39), 12775–12778.
- (2) St John-Campbell, S.; Bull, J. A. Intramolecular Palladium(II)/(IV) catalysed Catalysed C(sp³)–H Arylation of Tertiary Aldehydes Using a Transient Imine Directing Group. *Chem. Commun.* **2019**, *55* (62), 9172–9175.
- (3) Dong, C.; Wu, L.; Yao, J.; Wei, K. Palladium-Catalyzed β -C–H Arylation of Aliphatic Aldehydes and Ketones Using Amino Amide as a Transient Directing Group. *Org. Lett.* **2019**, *21* (7), 2085–2089.
- (4) Ren, W.; Chang, W.; Dai, J.; Shi, Y.; Li, J.; Shi, Y. An Effective Pd-Catalyzed Regioselective Hydroformylation of Olefins with Formic Acid. *J. Am. Chem. Soc.* **2016**, *138* (45), 14864–14867.
- (5) Rodríguez, J. G.; Benito, Y.; Temprano, F. Synthesis of Spiro[Cycloalkane-1,3'-[3 H]Indoles] from Cycloalkanecarbaldehydes. Acid-Catalyzed Rearrangement to Cycloalkano[b]Indoles. *J. Heterocycl. Chem.* **1985**, *22* (5), 1207–1210.
- (6) Watanabe, E.; Kaiho, A.; Kusama, H.; Iwasawa, N. Cobalt–Salen Complex-Catalyzed Oxidative Generation of Alkyl Radicals from Aldehydes for the Preparation of Hydroperoxides. *J. Am. Chem. Soc.* **2013**, *135* (32), 11744–11747.
- (7) DiLabio, G. A.; Ingold, K. U.; Roydhouse, M. D.; Walton, J. C. Axial and Equatorial Cyclohexylacyl and Tetrahydropyranyl-2-Acyl Radicals. An Experimental and Theoretical Study. *Org. Lett.* **2004**, *6* (23), 4319–4322.
- (8) Munnuri, S.; Adebessin, A. M.; Paudyal, M. P.; Yousufuddin, M.; Dalipe, A.; Falck, J. R. Catalyst-Controlled Diastereoselective Synthesis of Cyclic Amines via C-H Functionalization. *J. Am. Chem. Soc.* **2017**, *139* (50), 18288–18294.
- (9) Brace, G. N.; Chappell, R. E.; Deboves, H. J. C.; Foley, A. M.; Foulkes, G.; Jones, E. P.; Lecomte, F. C.; Quincey, J. R.; Schulze, M.-S. E. D.; Selby, M. D.; et al. Spirocyclic Indolines as IL-17 Modulators, WIPO (PCT) WO2018229079A1. **2018**.
- (10) Takayama, T.; Shibata, T.; Shiozawa, F.; Kawabe, K.; Shimizu, Y.; Hamada, M.; Hiratate, A.; Takahashi, M.; Ushiyama, F.; Oi, T.; et al. Partially Saturated Nitrogen-Containing Heterocyclic Compound, European Patent EP2881384A1. **2015**.
- (11) Tseng, C.; Noordali, H.; Sani, M.; Madhani, M.; Grant, D. M.; Frenneaux, M. P.; Zanda, M.; Greig, I. R. Development of Fluorinated Analogues of Perhexiline with Improved Pharmacokinetic Properties and Retained Efficacy. *J. Med. Chem.* **2017**, *60* (7), 2780–2789.
- (12) Hoepfner, W.; Weyerstahl, P. Struktur Und Geruch, IV1) Synthese Und Riechstoff-Eigenschaften von Rosenoxid-Analoga. *Liebigs Ann. der Chemie* **1986**, *1986* (1), 99–113.

X-Ray crystal structure for **3b**

Crystal data for **3b**: $C_{21}H_{24}O_3$, $M = 324.40$, monoclinic, $P2_1/c$ (no. 14), $a = 15.7637(3)$, $b = 5.62343(11)$, $c = 19.2702(4)$ Å, $\beta = 92.7203(18)^\circ$, $V = 1706.30(6)$ Å³, $Z = 4$, $D_c = 1.263$ g cm⁻³, $\mu(\text{Cu-K}\alpha) = 0.660$ mm⁻¹, $T = 173$ K, colourless platy needles, Agilent Xcalibur PX Ultra A diffractometer; 3241 independent measured reflections ($R_{\text{int}} = 0.0273$), F^2 refinement,^[X1,X2] $R_1(\text{obs}) = 0.0383$, $wR_2(\text{all}) = 0.1062$, 2481 independent observed absorption-corrected reflections [$|F_o| > 4\sigma(|F_o|)$], completeness to $\theta_{\text{full}}(67.7^\circ) = 98.3\%$, 220 parameters. CCDC 1970804.

Table S8 Bond lengths [Å] and angles [°] for JAB1905.

C(1)-C(7)	1.5049(19)		
C(1)-C(2)	1.5384(19)		
C(1)-C(6)	1.5587(18)		
C(2)-C(8)	1.5215(19)		
C(2)-C(3)	1.541(2)		
C(3)-C(4)	1.526(2)		
C(4)-C(5)	1.527(2)		
C(5)-C(6)	1.533(2)		
C(6)-C(16)	1.516(2)		
C(7)-O(7)	1.1948(19)		
C(8)-C(13)	1.392(2)		
C(8)-C(9)	1.395(2)		
C(9)-C(10)	1.385(2)		
C(10)-C(11)	1.388(2)		
C(11)-O(14)	1.3721(18)		
C(11)-C(12)	1.387(2)		
C(12)-C(13)	1.396(2)		
O(14)-C(15)	1.423(2)		
C(16)-C(21)	1.387(2)		
C(16)-C(17)	1.403(2)		
C(17)-C(18)	1.385(2)		
C(18)-C(19)	1.395(2)		
C(19)-O(22)	1.3712(18)		
C(19)-C(20)	1.388(2)		
C(20)-C(21)	1.399(2)		
O(22)-C(23)	1.424(2)		
C(7)-C(1)-C(2)	112.06(11)	O(14)-C(11)-C(12)	124.29(14)
C(7)-C(1)-C(6)	106.95(11)	O(14)-C(11)-C(10)	116.06(13)
C(2)-C(1)-C(6)	112.14(11)	C(12)-C(11)-C(10)	119.65(14)
C(8)-C(2)-C(1)	112.04(11)	C(11)-C(12)-C(13)	119.34(13)
C(8)-C(2)-C(3)	110.65(12)	C(8)-C(13)-C(12)	121.85(13)
C(1)-C(2)-C(3)	110.35(11)	C(11)-O(14)-C(15)	117.15(13)
C(4)-C(3)-C(2)	112.11(13)	C(21)-C(16)-C(17)	117.61(13)
C(3)-C(4)-C(5)	111.31(12)	C(21)-C(16)-C(6)	120.40(12)
C(4)-C(5)-C(6)	111.01(13)	C(17)-C(16)-C(6)	121.96(12)
C(16)-C(6)-C(5)	113.45(12)	C(18)-C(17)-C(16)	121.16(13)
C(16)-C(6)-C(1)	111.11(11)	C(17)-C(18)-C(19)	120.13(13)
C(5)-C(6)-C(1)	109.81(11)	O(22)-C(19)-C(20)	124.05(13)
O(7)-C(7)-C(1)	124.63(13)	O(22)-C(19)-C(18)	116.04(13)
C(13)-C(8)-C(9)	117.47(13)	C(20)-C(19)-C(18)	119.90(13)
C(13)-C(8)-C(2)	121.34(12)	C(19)-C(20)-C(21)	119.09(13)
C(9)-C(8)-C(2)	121.13(12)	C(16)-C(21)-C(20)	122.10(13)
C(10)-C(9)-C(8)	121.32(14)	C(19)-O(22)-C(23)	116.82(12)
C(9)-C(10)-C(11)	120.30(13)		

X-Ray crystal structure for **12**

Crystal data for 12: $C_{42}H_{46}O_6 \cdot 1.35(CH_2Cl_2)$, $M = 761.44$, monoclinic, $P2_1/n$ (no. 14), $a = 16.2239(8)$, $b = 5.6038(2)$, $c = 24.4539(17)$ Å, $\beta = 96.377(5)^\circ$, $V = 2209.5(2)$ Å³, $Z = 2$ [C_i symmetry], $D_c = 1.145$ g cm⁻³, $\mu(Cu-K\alpha) = 2.046$ mm⁻¹, $T = 173$ K, colourless needles, Agilent Xcalibur PX Ultra A diffractometer; 6656 independent measured reflections ($R_{int} = 0.0448$), F^2 refinement,^[X1,X2] $R_1(obs) = 0.0637$, $wR_2(all) = 0.1946$, 3328 independent observed absorption-corrected reflections [$|F_o| > 4\sigma(|F_o|)$], completeness to $\theta_{full}(67.7^\circ) = 98.1\%$, 221 parameters. CCDC 1970805.

The crystal of **12** that was studied was found to be a two component twin in a *ca.* 74:26 ratio, with the two lattices related by the approximate twin law $[-1.00 \ 0.00 \ 0.00 \ 0.00 \ -1.00 \ 0.00 \ 0.34 \ 0.00 \ 1.00]$. The structure was found to sit across a centre of symmetry at the middle of the C1–C1A bond.

The included solvent was found to be highly disordered, and the best approach to handling this diffuse electron density was found to be the SQUEEZE routine of PLATON.^[X3] This suggested a total of 114 electrons per unit cell, equivalent to 57 electrons per molecule. Before the use of SQUEEZE the solvent most resembled dichloromethane (CH_2Cl_2 , 42 electrons), and 1.35 dichloromethane molecules corresponds to 56.7 electrons, so this was used as the solvent present. As a result, the atom list for the asymmetric unit is low by $0.5 \times 1.35(CH_2Cl_2) = C_{0.675}H_{1.35}Cl_{1.35}$ (and that for the unit cell low by $C_{2.7}H_{5.4}Cl_{5.4}$) compared to what is actually presumed to be present.

References

[X1] SHELXTL v5.1, Bruker AXS, Madison, WI, 1998.

[X2] SHELX-2013, G.M. Sheldrick, *Acta Cryst.*, 2015, **C71**, 3-8.

[X3] A.L. Spek (2003, 2009) PLATON, A Multipurpose Crystallographic Tool, Utrecht University, Utrecht, The Netherlands. See also A.L. Spek, *Acta Cryst.*, 2015, **C71**, 9-18.

Table S9. Bond lengths [Å] and angles [°] for JAB1908.

C(1)-C(6)	1.531(5)
C(1)-C(2)	1.532(4)
C(1)-C(1)#1	1.545(6)
C(2)-C(3)	1.536(4)
C(3)-C(7)	1.518(4)
C(3)-C(4)	1.553(4)
C(4)-C(15)	1.501(4)
C(4)-C(5)	1.535(4)
C(5)-C(6)	1.527(4)
C(5)-C(16)	1.529(5)
C(7)-C(12)	1.370(4)
C(7)-C(8)	1.403(4)
C(8)-C(9)	1.387(5)
C(9)-C(10)	1.391(5)
C(10)-C(11)	1.375(5)
C(10)-O(13)	1.380(4)
C(11)-C(12)	1.398(5)
O(13)-C(14)	1.418(4)
C(15)-O(15)	1.197(4)
C(16)-C(21)	1.373(5)
C(16)-C(17)	1.379(5)
C(17)-C(18)	1.385(5)
C(18)-C(19)	1.385(6)
C(19)-O(22)	1.367(4)
C(19)-C(20)	1.395(5)
C(20)-C(21)	1.378(5)
O(22)-C(23)	1.429(5)

C(6)-C(1)-C(2)	110.2(3)
C(6)-C(1)-C(1)#1	113.0(3)
C(2)-C(1)-C(1)#1	111.5(3)
C(1)-C(2)-C(3)	112.9(3)
C(7)-C(3)-C(2)	112.5(3)
C(7)-C(3)-C(4)	113.4(3)
C(2)-C(3)-C(4)	109.7(2)
C(15)-C(4)-C(5)	112.4(3)
C(15)-C(4)-C(3)	107.6(3)
C(5)-C(4)-C(3)	110.7(3)
C(6)-C(5)-C(16)	110.1(3)
C(6)-C(5)-C(4)	110.9(3)
C(16)-C(5)-C(4)	113.3(3)
C(5)-C(6)-C(1)	114.9(3)
C(12)-C(7)-C(8)	118.2(3)
C(12)-C(7)-C(3)	120.4(3)
C(8)-C(7)-C(3)	121.4(3)
C(9)-C(8)-C(7)	120.7(3)
C(8)-C(9)-C(10)	119.9(3)
C(11)-C(10)-O(13)	124.6(3)
C(11)-C(10)-C(9)	120.0(3)

O(13)-C(10)-C(9)	115.4(3)
C(10)-C(11)-C(12)	119.4(3)
C(7)-C(12)-C(11)	121.8(3)
C(10)-O(13)-C(14)	116.6(3)
O(15)-C(15)-C(4)	124.7(3)
C(21)-C(16)-C(17)	117.9(3)
C(21)-C(16)-C(5)	121.4(3)
C(17)-C(16)-C(5)	120.5(3)
C(16)-C(17)-C(18)	121.5(4)
C(17)-C(18)-C(19)	119.9(4)
O(22)-C(19)-C(18)	116.5(3)
O(22)-C(19)-C(20)	124.7(4)
C(18)-C(19)-C(20)	118.9(4)
C(21)-C(20)-C(19)	119.6(4)
C(16)-C(21)-C(20)	122.1(3)
C(19)-O(22)-C(23)	117.1(3)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y,-z+1

^1H and ^{13}C NMR spectra of selected compounds

