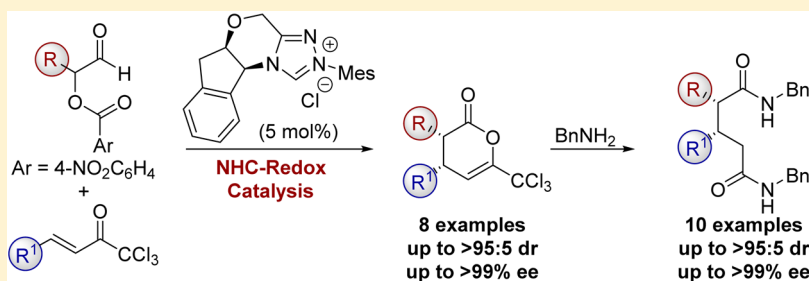


Enantioselective NHC-Catalyzed Redox [4 + 2]-Hetero-Diels–Alder Reactions Using α,β -Unsaturated Trichloromethyl Ketones as Amide Equivalents

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S Supporting Information



ABSTRACT: α,β -Unsaturated trichloromethyl ketones are suitable α,β -unsaturated amide and ester equivalents in N-heterocyclic carbene (NHC)-catalyzed redox hetero-Diels–Alder reactions with azolium enolates generated from α -aryloxyaldehydes. The initially formed *syn*-dihydropyranone products can be isolated or can undergo ring-opening with benzylamine followed by aminolysis of the resulting CCl_3 ketone to form a range of diamides with high diastereo- and enantioselectivity (up to >95:5 dr and >99% ee).

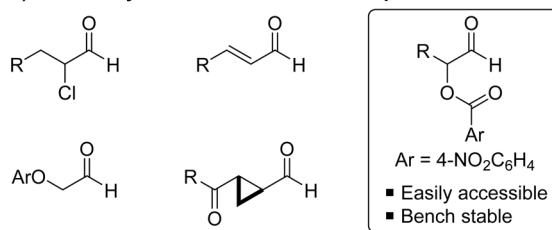
INTRODUCTION

N-Heterocyclic carbenes (NHCs) are valuable Lewis base organocatalysts that can react through a number of distinct catalytic activation modes.¹ For example, azolium enolates are versatile intermediates that react with a range of electrophiles to form a wide variety of synthetically useful products. Azolium enolates have been accessed through reaction of NHCs with ketenes,² α -reducible aldehydes,^{3–7} unfunctionalized aldehydes in the presence of an oxidant,⁸ and activated carboxylic acids or esters in the presence of a base.⁹ NHC-redox catalysis proceeding through addition of an NHC to an aldehyde bearing an α -reducible functional group is a particularly efficient method of forming azolium enolates.¹⁰ α -Reducible aldehydes that have been used for this purpose include α -chloroaldehydes,³ enals,⁴ α -aryloxyaldehydes,⁵ and formyl cyclopropanes⁶ (Scheme 1a).

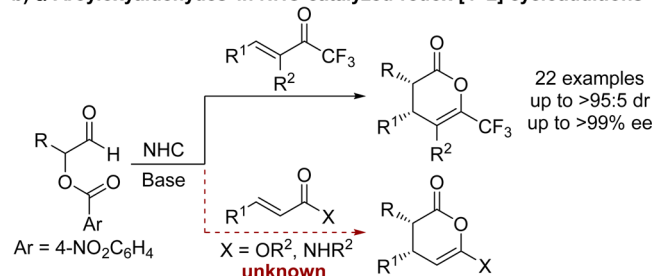
We have demonstrated that α -aryloxyaldehydes are bench-stable azolium enolate precursors that can be utilized in a number of asymmetric NHC-catalyzed redox [4 + 2]-cycloaddition reactions.⁷ For example, azolium enolates generated from α -aryloxyaldehydes react with substituted trifluoromethyl ketones to form dihydropyranones with high levels of stereoselectivity (Scheme 1b).^{7d} The NHC-catalyzed redox reaction of α -aryloxyaldehydes and *N*-aryl-*N'*-aryldiazene to synthesize enantiomerically enriched α -amino acid derivatives has also been explored.^{7c} While NHC-catalyzed asymmetric cycloadditions of azolium enolates with electron-deficient enones are widely reported, the use of α,β -unsaturated amides and esters remains a significant challenge due to the

Scheme 1. Azolium Enolate Precursors for [4 + 2] Hetero-Diels–Alder Reactions

a) NHC-catalyzed redox azolium enolate precursors



b) α -Aryloxyaldehydes in NHC-catalyzed redox [4+2] cycloadditions



decreased electrophilicity of these substrates. This problem has been overcome in other Lewis base-catalyzed conjugate

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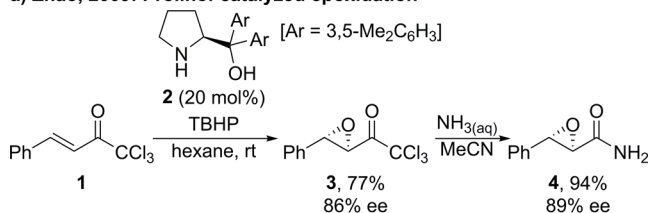
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additions through the use of more reactive α,β -unsaturated amide/ester equivalents such as *N*-acylpyrroles,¹¹ 2-acyl imidazoles,¹² activated imides,¹³ α -ketophosphonates,^{14,15} and trichloromethyl ketones.^{16,17} However, the use of α,β -unsaturated amide and ester equivalents in NHC-catalyzed cycloaddition reactions remains unexplored.

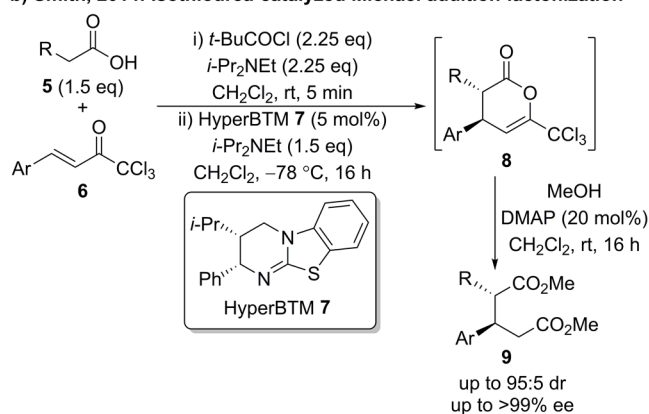
Of particular relevance is the use of trichloromethyl ketones as carboxylic acid, ester, and amide equivalents in processes that use the leaving group ability of the CCl_3 ketone in haloform-type reactions.^{18–20} α,β -Unsaturated trichloromethyl ketones have previously been utilized as Michael acceptors in a small number of organocatalytic reactions.^{16,17} Zhao and co-workers reported the enantioselective epoxidation of α,β -unsaturated trichloromethyl ketones with *tert*-butylhydroperoxide (TBHP) catalyzed by diaryl prolinol **2**.^{16a} Trichloromethyl ketone **3** undergoes either aminolysis or alcoholysis to provide the corresponding amide or ester products without loss in enantioselectivity (Scheme 2a). Various bifunctional H-

Scheme 2. Use of α,β -Unsaturated Trichloromethyl Ketones as Amide and Ester Equivalents

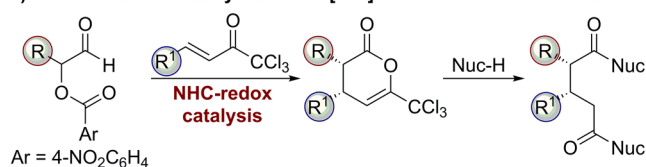
a) Zhao, 2009: Prolinol-catalyzed epoxidation



b) Smith, 2014: Isothiourea-catalyzed Michael addition-lactonization



c) This work: NHC-catalyzed redox [4+2]-hetero-Diels-Alder reaction



bonding/Lewis bases have also been used to catalyze the conjugate addition of nucleophiles including α -cyano ketones,^{16b} α,β -unsaturated γ -butyrolactones,^{16c} and azlactones^{16d} into α,β -unsaturated trichloromethyl ketones. We have reported the isothiurea-catalyzed Michael addition–lactonization of substituted acetic acids and α,β -unsaturated trichloromethyl ketones.¹⁷ The initially formed *anti*-dihydropyranones **8** undergo ring-opening followed by alcoholysis of the CCl_3 ketone with methanol to give a range of diesters **9** with high levels of diastereo- and enantioselectivity (Scheme 2b). This

methodology is limited to the use of either 2-aryl or 2-alkenylacetic acids and gives preferential access to the *anti*-diastereoisomer of the dihydropyranone intermediates.

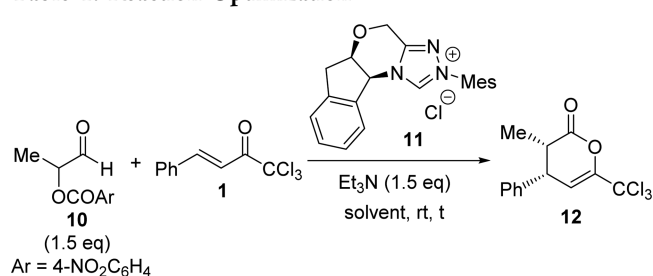
Herein the use of α -aryloxyaldehydes as azolium enolate precursors in [4 + 2] hetero-Diels–Alder reactions with α,β -unsaturated trichloromethyl ketones is investigated, with the *syn*-dihydropyranone products formed in good yields with high levels of diastereo- and enantioselectivity. Subsequent ring-opening followed by aminolysis of the CCl_3 ketone gives access to a wide range of diamide products without loss of enantioselectivity (Scheme 2c). In one case, the sequential addition of two different nucleophiles led to the formation of a differentially substituted diacid derivative. The methodology described is complementary to the related isothiurea-catalyzed process, as it allows access to 3-alkyl-substituted dihydropyranones and preferentially gives the *syn*-diastereoisomer of the products.

RESULTS AND DISCUSSION

[4 + 2] Cycloaddition: Optimization and Generality.

First, the NHC-catalyzed redox [4 + 2] hetero-Diels–Alder reaction between an azolium enolate generated from α -aryloxyaldehyde **10** and α,β -unsaturated trichloromethyl ketone **1** was studied. α -Aryloxyaldehydes were prepared in one step on a gram-scale from the parent aldehyde and 4-nitrobenzoic acid under oxidative conditions using a modified procedure of that described by Ishihara and co-workers.²¹ Trichloromethyl ketones were prepared on a gram-scale using a two-step procedure first reported by Corey and co-workers starting from the corresponding α,β -unsaturated aldehyde and can be stored for a number of months without decomposition.²² Initial studies found that α -aryloxyaldehyde **10** reacts with trichloromethyl ketone **1** using 10 mol % triazolium NHC precatalyst **11** and triethylamine in THF at room temperature, giving dihydropyranone **12** in 57% yield and >95:5 dr, with the major *syn*-diastereoisomer formed in excellent >99% ee (Table 1, entry 1).²³ The reaction proceeds in a number of different solvents, with CH_2Cl_2 giving dihydropyranone **12** in an improved 67% yield without compromising the stereoselectivity (Table 1, entries 2–4).

Table 1. Reaction Optimization^a



Entry	Solvent	11 (mol%)	t / h	dr ^b	Yield (%)	ee (%) ^c
1	THF	10	5	>95:5	57	>99
2	Et_2O	10	1.5	>95:5	55	>99
3	PhMe	10	1.5	>95:5	55	>99
4	CH_2Cl_2	10	1	>95:5	67	>99
5	CH_2Cl_2	5	3.5	>95:5	66	>99
6 ^d	CH_2Cl_2	5	3.5	>95:5	84	>99

^aReactions performed on 0.2 mmol scale. ^bDetermined by analysis of crude ¹H NMR spectra. ^cDetermined by chiral HPLC analysis. ^dReaction performed on a 1.2 mmol scale.

Lowering the catalyst loading to 5 mol % gave comparable results (Table 1, entry 5); however, further decreases in the amount of catalyst led to a significant reduction in isolated yield. Finally, performing the reaction on a larger scale (1.2 mmol) gave *syn*-dihydropyranone **12** in 84% yield as a single diastereoisomer in >99% ee (Table 1, entry 6).

The scope and generality of this procedure was studied through variation of the substituents on both the α -aroyloxyaldehyde and trichloromethyl ketone components (Table 2). A range of α -aroyloxyaldehyde substituents was

Table 2. Use of Trichloromethyl Ketones in NHC-Redox Catalyzed [4 + 2] Hetero-Diels–Alder Reactions

Product	dr ^b	Product	dr ^b
Yield ^a (time)	ee ^c	Yield ^a (time)	ee ^c
 12 84% (4 h)	>95:5 (>99%)	 13 81% (4 h)	>95:5 (>99%)
 14 60% (8 h) ^d	90:10 (99%)	 15 65% (4 h) ^d	>95:5 (>99%)
 16 45% (26 h) ^e	85:15 (N/D) ^f	 17 93% (4 h)	>95:5 (>99%)
 18 81% (2 h)	>95:5 (>99%)	 19 26% (22 h) ^d	>95:5 (>99%)

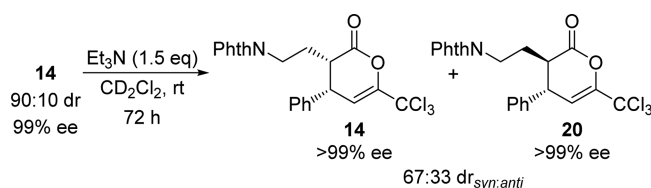
^aIsolated yield of major *syn*-diastereoisomer. ^bDetermined by analysis of crude ¹H NMR spectra. ^cDetermined by chiral HPLC analysis. ^dReaction performed using 10 mol % **11**. ^eIsolated as a mixture of diastereoisomers. ^fee could not be determined by either chiral HPLC or chiral GC analysis.

tolerated under the previously optimized reaction conditions, forming functionalized *syn*-dihydropyranones **12**–**19** with excellent levels of diastereo- and enantioselectivity. A higher catalyst loading (10 mol % **11**) was required to form dihydropyranones **14** and **15**, as lower levels of diastereoselectivity were obtained over extended reaction times with a lower catalyst loading. For example, dihydropyranone **14** was formed in 65:35 dr after 48 h under the standard reaction conditions using 5 mol % **11**, with both diastereoisomers formed with high enantioselectivity (98% ee_{syn}, >99% ee_{anti}). Increasing the catalyst loading to 10 mol % allowed dihydropyranone **14** to be formed in 90:10 dr, with the major *syn*-diastereoisomer isolated in 60% yield and 99% ee. Similarly, dihydropyranone **15** was formed in 90:10 dr after 26

h using 5 mol % **11**, whereas increasing the catalyst loading to 10 mol % allowed a single diastereoisomer to be isolated in 65% yield after 4 h in >99% ee. Within the trichloromethyl ketone, β -aryl groups containing electron-donating (4-MeOC₆H₄) and electron-withdrawing halogen (4-BrC₆H₄) substituents were well tolerated, forming *syn*-dihydropyranones **17** and **18** as single diastereoisomers in excellent yields and >99% ee. However, β -alkyl substitution was less well tolerated, forming *syn*-dihydropyranone **19** in a low 26% yield despite using 10 mol % **11** for an extended reaction time, although the diastereo- and enantioselectivity remained high.

To investigate the drop in diastereoselectivity observed for the reactions with some of the α -aroyloxyaldehyde substituents, an epimerization experiment was performed. Treating isolated *syn*-dihydropyranone **14** (90:10 dr, 99% ee) with triethylamine in CD₂Cl₂ at room temperature resulted in a mixture of *syn*-**14** and *anti*-**20** (67:33 dr), with both diastereoisomers obtained in >99% ee (Scheme 3). This is consistent with a base-promoted

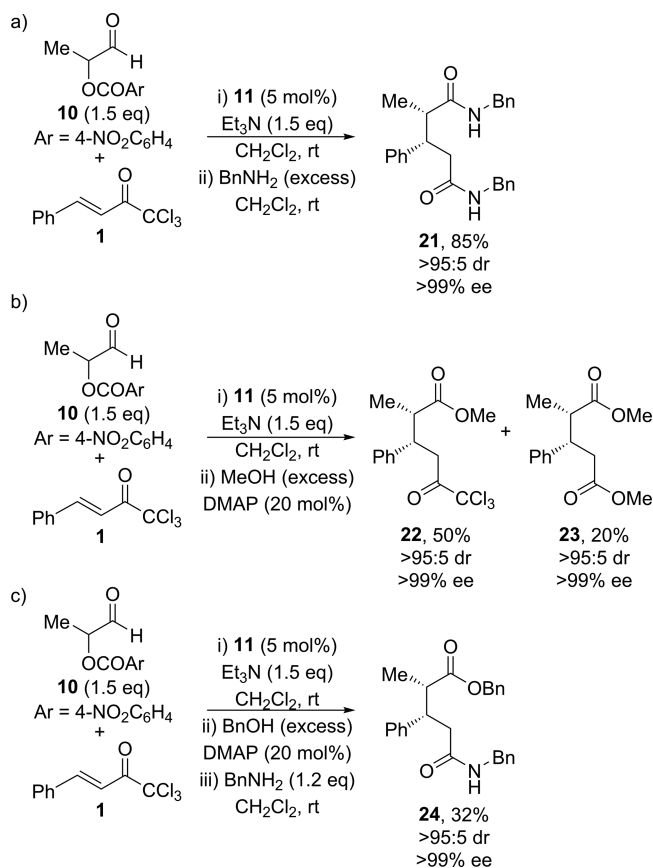
Scheme 3. Base-Promoted Epimerization of **14**



epimerization of the C(3) stereocenter, which accounts for the loss in diastereoselectivity in reactions that required extended reaction times upon changing the α -aroyloxyaldehyde component.

Trichloromethyl Ketones as Ester and Amide Equivalents. Next, the synthetic utility of the trichloromethyl substituent as an ester/amide equivalent was examined. It was hoped that treating the crude *syn*-dihydropyranone products with an excess of a suitable nucleophile (alcohol or amine) would lead to ring-opening followed by alcoholysis/aminolysis of the CCl₃ ketone. Pleasingly, adding an excess of benzylamine to crude *syn*-dihydropyranone **12** led to formation of the expected diamide **21** in excellent 85% yield as a single diastereoisomer in >99% ee (Scheme 4a). In contrast, treating crude *syn*-dihydropyranone **12** with DMAP (20 mol %) and an excess of methanol gave a mixture of trichloroketoester **22** and diester **23**, with both formed with high levels of stereoselectivity (Scheme 4b).²⁴ The observation that only partial alcoholysis of the CCl₃ ketone had occurred led to the possibility of a sequential ring-opening and CCl₃ ketone displacement using two different nucleophiles. First, benzyl alcohol and DMAP (20 mol %) were used to ring-open the initial *syn*-dihydropyranone product with subsequent addition of benzylamine (1.2 equiv) leading to aminolysis of the CCl₃ ketone to give γ -ester amide **24** in 32% yield and >99% ee over the three reaction steps (Scheme 4c). This reactivity is in contrast to the use of α -keto- β,γ -unsaturated phosphonates as ester/amide equivalents in related reactions where both ring-opening and either alcoholysis or aminolysis of the phosphate group occur rapidly and therefore differential substitution is not possible.^{14d} Moreover, dihydropyranones formed from related reactions using α,β -unsaturated trifluoromethyl ketones undergo ring-opening with no alcoholysis/aminolysis of the trifluoromethyl ketone observed.^{7d} The utility of trichloromethyl ketones as amide equivalents in this NHC-catalyzed redox [4 + 2] cycloaddition

Scheme 4. Use of Trichloromethyl Ketones as Ester and Amide Equivalents



process was further assessed using a range of substituted α -aryloxyaldehydes and α,β -unsaturated trichloromethyl ketones (Table 3). The cycloaddition reactions were performed under the previously optimized conditions, and the initially formed *syn*-dihydropyranones underwent ring-opening and aminolysis with benzylamine. The resulting diamide products **21**, **25–33** were conveniently purified by trituration and did not require column chromatography.²⁵

A number of substituted α -aryloxyaldehydes was successfully applied in this process, forming diamides **21**, **25–27** in high yields as single diastereoisomers and in excellent ee. Benzyl substituted diamide **27** was formed with lower diastereoselectivity (80:20 dr), which is consistent with base-promoted epimerization of dihydropyranone **16** under the reaction conditions (cf. Table 2). A wide range of substituted trichloromethyl ketone derivatives was also tolerated, including those containing electron-donating aryl (4-MeOC₆H₄), electron-withdrawing aryl (2-NO₂C₆H₄), and heteroaromatic substituents, forming functionalized diamides **28–32** in good yields with excellent levels of stereocontrol. As observed previously, the incorporation of a β -alkyl substituent led to a significantly lower yield of diamide **33**. The relative and absolute configuration of diamide **28** was confirmed by X-ray crystallographic analysis,²³ with the stereochemistry of all other products assigned by analogy.

Proposed Mechanism. The proposed catalytic cycle starts with nucleophilic addition of the free NHC into the α -aryloxyaldehyde, with the resulting adduct **34** likely to be the resting state of the catalyst (Scheme 5).^{7b,26} Deprotonation forms the Breslow intermediate, which can eliminate 4-

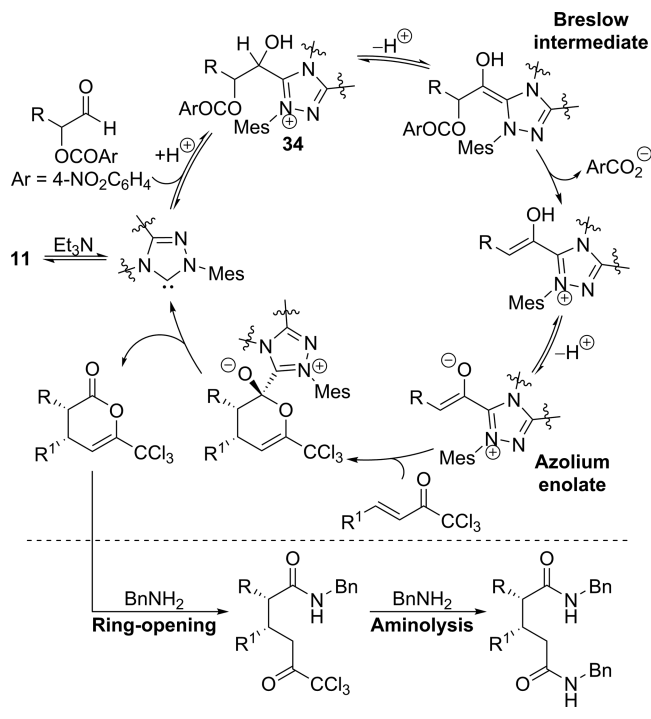
Table 3. NHC-Redox Catalyzed [4 + 2] Cycloaddition Followed by Ring Opening and Aminolysis

Product	dr ^b	Product	dr ^b
Yield ^a (time)	ee ^c	Yield ^a (time)	ee ^c
21 , 85%	>95:5 (>99%)	25 , 89%	>95:5 (>99%)
26 , 60%	>95:5 (98%)	27 , 48%	80:20 (N/D) ^e
28 , 75%	>95:5 (>99%)	29 , 68%	90:10 (>99%)
30 , 90%	>95:5 (>99%)	31 , 75%	>95:5 (>99%)
32 , 39%	>95:5 (>99%)	33 , 26% ^d	>95:5 (>99%)

^aIsolated yield of major *syn*-diastereoisomer. ^bDetermined by analysis of crude ¹H NMR spectra. ^cDetermined by chiral HPLC analysis. ^dReaction performed using 10 mol % **11**. ^eee could not be determined by either chiral HPLC or chiral GC analysis.

nitrobenzoate to form an enol that undergoes further deprotonation into the key azolium enolate intermediate. Consistent with the work of Bode and co-workers,²⁷ the azolium enolate is thought to undergo an asynchronous *endo*-hetero-Diels–Alder reaction with the α,β -unsaturated trichloromethyl ketone. Elimination of the catalyst generates the *syn*-dihydropyranone product, which can undergo ring-opening

Scheme 5. Proposed Mechanism



using benzylamine or an alcohol, with aminolysis of the resulting trichloromethyl ketone proceeding at a relatively slower rate.

CONCLUSION

α,β -Unsaturated trichloromethyl ketones act as amide equivalents in NHC-catalyzed redox [4 + 2] hetero-Diels-Alder reactions with azolium enolates generated from bench-stable α -aryloxyaldehydes. The initially formed *syn*-dihydropyranones can be isolated in good yields with excellent levels of diastereo- and enantioselectivity. The dihydropyranone products undergo facile ring-opening with benzylamine, and further aminolysis of the resulting CCl_3 ketone leads to the formation of diamides. A wide range of both α -aryloxyaldehydes and α,β -unsaturated trichloromethyl ketones can be utilized in this process, generating functionalized diamide products in high yields with excellent levels of stereoselectivity.

EXPERIMENTAL SECTION

General. All reactions were performed in flame-dried glassware using anhydrous solvents. All reagents were obtained from commercial sources and used without further purification. Room temperature (rt) refers to 20–25 °C, with temperatures of 0 °C and –10 °C obtained using ice/water and ice/water/salt baths, respectively. Optical rotations were recorded with a path length of 1 dm, and concentrations, c , are quoted in g/100 mL. All chiral HPLC traces were compared with an authentic racemic trace prepared using (*rac*)-11. Infrared spectra were recorded as thin films using an ATR accessory. ^1H NMR spectra were acquired at 300, 400, 500, or 700 MHz; $^{13}\text{C}\{^1\text{H}\}$ NMR spectra were acquired at 75, 101, or 126 MHz; and $^{19}\text{F}\{^1\text{H}\}$ NMR spectra were acquired at 282, 376, or 471 MHz. Chemical shifts are quoted in parts per million (ppm) relative to the residual solvent peak; coupling constants, J , are quoted in hertz (Hz). NMR peak assignments were confirmed using 2D ^1H COSY, 2D ^1H NOESY, 2D ^1H – ^{13}C HMBC, and 2D ^1H – ^{13}C HSQC where necessary. Mass spectrometry (m/z , HRMS) data were acquired using either atmospheric pressure chemical ionization (APCI) or nanospray ionization (NSI) using a TOF mass analyzer.

NHC-precatalyst **11** was synthesized on a gram-scale according to a literature procedure.²⁸ Commercially available reagents were used as supplied without further purification unless stated otherwise.

Preparation of α -Aryloxyaldehydes. 1-Oxopropan-2-yl 4-Nitrobenzoate (**10**). Prepared according to a previously reported procedure as a beige solid with data in accordance with literature.^{7b} Mp 74–76 °C {lit.^{7b} mp 78–80 °C}; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 1.59 (3H, d, J 7.2, CH_3), 5.39 (1H, q, J 7.2, CHCH_3), 8.24–8.37 (4H, m, 4- NO_2ArH), 9.67 (1H, s, CHO).

1-Oxo-3-phenylpropan-2-yl 4-Nitrobenzoate. Prepared according to a previously reported procedure as a beige solid with data in accordance with literature.^{7b} Mp 91–93 °C {lit.^{7b} mp 85–86 °C}; ^1H NMR (300 MHz, CDCl_3) δ_{H} : 3.22 (1H, dd, J 14.5, 8.4, $\text{CH}^{\text{A}}\text{H}^{\text{B}}$), 3.35 (1H, dd, J 14.5, 5.0, $\text{CH}^{\text{A}}\text{H}^{\text{B}}$), 5.52 (1H, dd, J 8.3, 5.0, CHCH_2), 7.27–7.38 (4H, m, ArH), 8.15–8.23 (2H, m, 4- NO_2ArH), 8.26–8.35 (2H, m, 4- NO_2ArH), 9.68 (1H, s, CHO).

4-(1,3-Dioxoisindolin-2-yl)-1-oxobutan-2-yl 4-Nitrobenzoate. Phthalic anhydride (4.5 g, 34 mmol, 1.0 equiv) and 4-aminobutan-1-ol (3.1 mL, 34 mmol, 1.0 equiv) were heated in toluene (100 mL) at reflux under Dean–Stark conditions for 3 h. The reaction mixture was allowed to cool to rt before being concentrated to give 2-(4-hydroxybutyl)-2,3-dihydro-1H-isindole-1,3-dione as a pale yellow solid (7.0 g, 32 mmol, 95%), with spectroscopic data in accordance with the literature;²⁹ mp 47–49 °C {lit.²⁹ mp 48–49 °C}; ^1H NMR (500 MHz, CDCl_3) δ_{H} : 1.64 (2H, p, J 6.6, NCH_2CH_2), 1.80 (2H, p, J 7.3, $\text{N}(\text{CH}_2)_2\text{CH}_2$), 3.71 (2H, t, J 6.4, NCH_2), 3.76 (2H, t, J 7.2, $\text{N}(\text{CH}_2)_3\text{CH}_2$), 7.73 (2H, dd, J 5.5, 3.0, ArH), 7.86 (2H, dd, J 5.4, 3.1, ArH).

A solution of oxalyl chloride (2.3 mL, 27 mmol, 2.0 equiv) in CH_2Cl_2 (50 mL) was cooled to –78 °C before a solution of DMSO (2.14 mL, 30 mmol, 2.2 equiv) in CH_2Cl_2 (10 mL) was added dropwise. After stirring for 15 min a solution of 2-(4-hydroxybutyl)-2,3-dihydro-1H-isindole-1,3-dione (3.0 g, 14 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was added dropwise. The reaction mixture was stirred for 15 min before Et_3N (5.7 mL, 41 mmol, 3.0 equiv) was added dropwise. The reaction was stirred for 5 min before warming to rt and stirring for an additional 15 min. The reaction was diluted with CH_2Cl_2 and washed with 1 M HCl and brine. The organic layer was dried over Na_2SO_4 , filtered, and concentrated to give the crude product that was purified by flash silica column chromatography (70:30 petrol/EtOAc) to give 4-(1,3-dioxo-2,3-dihydro-1H-isindol-2-yl)butanal as a white solid (1.7 g, 7.9 mmol, 57%), with spectroscopic data in accordance with the literature;³⁰ mp 66–68 °C {lit.³⁰ mp 72–74 °C}; ^1H NMR (500 MHz, CDCl_3) δ_{H} : 2.04 (2H, p, J 7.0, NCH_2CH_2), 2.51–2.62 (2H, m, $\text{N}(\text{CH}_2)_2\text{CH}_2$), 3.73–3.80 (2H, m, NCH_2), 7.74 (2H, dd, J 5.4, 3.1, NCOArH), 7.87 (2H, dd, J 5.5, 3.0, ArH), 9.79 (1H, t, J 1.1, CHO).

From an adapted procedure of Ishihara et al.,²¹ 4-(1,3-dioxo-2,3-dihydro-1H-isindol-2-yl)butanal (1.7 g, 7.9 mmol), 4-nitrobenzoic acid (2.0 g, 12 mmol), *n*- Bu_4NI (0.58 g, 1.6 mmol), and piperidine (78 μL , 0.79 mmol) were dissolved in EtOAc (40 mL) and *t*- BuOOH (5–6 M solution in decane, 1.57 mL) was added. The reaction mixture was heated at 50 °C for 5 h before being cooled to rt and quenched with Na_2SO_4 . The phases were separated, and the aqueous phase was extracted with EtOAc ($\times 2$). The combined organics were washed with sat. aq. NaHCO_3 ($\times 2$) and brine ($\times 2$) before being dried over MgSO_4 , filtered, and concentrated. The crude product was purified by flash silica column chromatography (70:30 petrol/EtOAc) to give 4-(1,3-dioxoisindolin-2-yl)-1-oxobutan-2-yl 4-nitrobenzoate as a pale orange solid (1.9 g, 4.8 mmol, 62%); mp 38–41 °C; ν_{max} (film) 1705 (br, C=O); ^1H NMR (300 MHz, CDCl_3) δ_{H} : 2.26–2.38 (1H, m, $\text{NCH}_2\text{CH}^{\text{A}}\text{H}^{\text{B}}$), 2.40–2.51 (1H, m, $\text{NCH}_2\text{CH}^{\text{A}}\text{H}^{\text{B}}$), 3.95 (2H, t, J 6.5, NCH_2), 5.35 (1H, dd, J 9.3, 3.7, CHCHO), 7.65–7.84 (4H, m, ArH), 8.19–8.26 (4H, m, 4- NO_2ArH), 9.62 (1H, s, CHO); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3) δ_{C} : 27.4 (NCH_2CH_2), 34.2 (NCH_2), 77.4 (CHCHO), 123.5 ($\text{NCOArC}(2)$), 123.7 ($\text{ArC}(2)$), 131.1 ($\text{ArC}(3)$), 131.9 ($\text{NCOArC}(1)$), 134.1 ($\text{ArC}(1)$), 134.4 ($\text{NCOArC}(1)$), 150.9 (CO_2), 164.2 ($\text{ArC}(4)$), 168.2 (NCOAr), 196.3 (CHO); HRMS (APCI⁺) $\text{C}_{19}\text{H}_{15}\text{N}_2\text{O}_7$ [$\text{M} + \text{H}$]⁺ found 383.0874, requires 383.0874 (+0.1 ppm).

1-(4-Methoxyphenyl)-3-oxopropan-2-yl 4-Nitrobenzoate. Prepared according to a previously reported procedure as a viscous yellow oil with data in accordance with the literature.^{7c} ¹H NMR (300 MHz, CDCl₃) δ_{H} : 3.17 (1H, dd, *J* 14.6, 8.1, C(1)H^AH^B), 3.29 (1H, dd, *J* 14.6, 5.1, C(1)H^AH^B), 3.78 (3H, s, ArOCH₃), 5.47 (1H, dd, *J* 8.0, 5.0, C(2)H), 6.85 (2H, d, *J* 8.6, MeOArC(3,5)H), 7.19 (2H, d, *J* 8.6, MeOArC(2,6)H), 8.20 (2H, d, *J* 8.6, 4-NO₂ArC(2,6)H), 8.31 (2H, d, *J* 8.6, 4-NO₂ArC(3,5)H), 9.66 (1H, s, CHO).

1-(Benzo[d][1,3]dioxol-5-yl)-3-oxopropan-2-yl 4-Nitrobenzoate. Prepared according to a previously reported procedure as a viscous orange oil with data in accordance with the literature.^{7c} ¹H NMR (300 MHz, CDCl₃) δ_{H} : 3.14 (1H, dd, *J* 14.6, 8.2, C(1)H^AH^B), 3.26 (1H, dd, *J* 14.6, 5.0, C(1)H^AH^B), 5.46 (1H, dd, *J* 8.1, 5.0, C(2)H), 5.94 (2H, s, OCH₂O), 6.69–6.77 (3H, m, ArCH), 8.21 (2H, d, *J* 8.9, 4-NO₂ArC(2,6)H), 8.32 (2H, d, *J* 8.9, 4-NO₂ArC(3,5)H), 9.66 (1H, s, CHO).

1-Oxohexan-2-yl 4-Nitrobenzoate. Prepared according to a previously reported procedure as a yellow oil with data in accordance with literature.^{7b} ¹H NMR (400 MHz, CDCl₃) δ_{H} : 0.95 (3H, t, *J* 7.2, CH₃), 1.37–1.45 (2H, m, CH₂), 1.45–1.54 (2H, m, CH₂), 1.93 (2H, ddd, *J* 15.5, 14.6, 8.5, CH₂), 5.31 (1H, dd, *J* 8.3, 4.7, CH), 8.25–8.35 (4H, m, 4-NO₂ArH), 9.64 (1H, d, *J* 0.5, CHO).

Preparation of α,β -Unsaturated Trichloromethyl Ketones. **(E)-1,1,1-Trichloro-4-phenylbut-3-en-2-one (1).** Prepared according to a previously reported procedure as a white solid with data in accordance with literature.¹⁷ Mp 57–59 °C [lit.¹⁷ mp 59 °C]; ¹H NMR (300 MHz, CDCl₃) δ_{H} : 7.34 (1H, d, *J* 15.6, C(3)H), 7.41–7.52 (3H, m, ArH), 7.61–7.70 (2H, m, ArH), 8.01 (1H, d, *J* 15.6, C(4)H).

(E)-1,1,1-Trichloro-4-(4-methoxyphenyl)but-3-en-2-one. Prepared according to a previously reported procedure as a white solid with data in accordance with literature.¹⁷ Mp 98–100 °C [lit.¹⁷ mp 98–100 °C]; ¹H NMR (400 MHz, CDCl₃) δ_{H} : 3.87 (3H, s, OCH₃), 6.92–6.99 (2H, m, ArH), 7.21 (1H, d, *J* 15.6, C(3)H), 7.58–7.65 (2H, m, ArH), 7.97 (1H, d, *J* 15.5, C(4)H).

(E)-4-(4-Bromophenyl)-1,1,1-trichlorobut-3-en-2-one. From an adapted procedure of Patil and Singh,³¹ reactivated MnO₂ (2.0 g, 23 mmol)³² was added portion-wise to a solution of (E)-3-(4-bromophenyl)prop-2-en-1-ol (491 mg, 2.3 mmol) and in CH₂Cl₂ (9.8 mL) and stirred at rt for 3.5 h. The mixture was filtered through Celite and concentrated to give (E)-3-(4-bromophenyl)acrylaldehyde (413 mg, 88%) as a brown solid that was used without further purification with data in accordance with literature.³³ ¹H NMR (300 MHz, CDCl₃) δ_{H} : 6.70 (1H, dd, *J* 16.0, 7.6, C(2)H), 7.43–7.38 (2H, m, ArH), 7.48–7.43 (1H, m, C(3)H), 7.62–7.54 (2H, m, ArH), 9.71 (1H, d, *J* 7.6, CHO).

Following the procedure by Zhao et al.,^{16a} (E)-3-(4-bromophenyl)acrylaldehyde (387 mg, 1.83 mmol, 1.0 equiv) was added to a solution of CHCl₃ (293 μ L, 3.66 mmol, 2.0 equiv) in DMF (1.3 mL) at rt. The reaction mixture was stirred at rt for 20 min and then cooled to 0 °C before a solution of KOH (205 mg, 3.66 mmol, 2.0 equiv) in EtOH (660 μ L) was added dropwise. The reaction was stirred at 0 °C for 2 h. The reaction mixture was acidified with 1 M HCl and extracted with EtOAc (\times 2). The combined organics were washed with water (\times 2) and brine (\times 3) before being dried over MgSO₄, filtered, and concentrated to give ((E)-4-(4-bromophenyl)-1,1,1-trichlorobut-3-en-2-ol (562 mg, 93%) as a brown oil that was used without further purification. ¹H NMR (300 MHz, CDCl₃) δ_{H} : 4.76 (1H, dd, *J* 5.9, 1.3, C(1)H), 6.37 (1H, dd, *J* 15.9, 5.9, C(2)H), 6.85 (1H, br d, C(3)H), 7.27–7.35 (2H, m, ArH), 7.43–7.52 (2H, m, ArH).

Following the procedure described by Evans et al.,³⁴ ((E)-4-(4-bromophenyl)-1,1,1-trichlorobut-3-en-2-ol (562 mg, 1.70 mmol, 1.0 equiv) and distilled Et₃N (711 μ L, 5.10 mmol, 3.0 equiv) were dissolved in anhydrous CH₂Cl₂ (13.5 mL). A solution of sulfur trioxide pyridine complex (812 mg, 5.10 mmol, 3.0 equiv) in distilled DMSO (2.7 mL) was added dropwise at 0 °C. The reaction mixture was stirred at 0 °C for 24 h before adding again sulfur trioxide pyridine complex (812 mg, 5.10 mmol, 3.0 equiv). The reaction mixture was stirred at rt for 48 h before being diluted in water (10 mL), extracted with Et₂O (2 \times 20 mL), and washed successively with sat. aq. CuSO₄ (20 mL), sat. aq. NaHCO₃ (2 \times 20 mL), and brine (2 \times 20 mL). The organic layer was dried over MgSO₄, filtered, and concentrated to give

(E)-4-(4-bromophenyl)-1,1,1-trichlorobut-3-en-2-one (583 mg, quant.) as a brown solid that was used without further purification with data in accordance with literature.^{16a} ¹H NMR (300 MHz, CDCl₃) δ_{H} : 7.32 (1H, d, *J* 15.7, C(2)H), 7.48–7.65 (4H, m, ArH), 7.93 (1H, d, *J* 15.6, C(3)H).

(E)-1,1,1-Trichloronon-3-en-2-one. Prepared according to a previously reported procedure as a yellow oil with data in accordance with literature.¹⁷ ¹H NMR (400 MHz, CDCl₃) δ_{H} : 0.87–0.93 (3H, m, CH₃), 1.28–1.38 (4H, m, CH₂ \times 2), 1.48–1.56 (2H, m, C(6)H₂), 2.34 (2H, app qd, *J* 7.2, 1.6, C(5)H₂), 6.73 (1H, dt, *J* 15.3, 1.6, C(3)H), 7.34 (1H, dt, *J* 15.4, 7.0, C(4)H).

(E)-1,1,1-Trichloro-4-(4-fluorophenyl)but-3-en-2-one. Prepared according to a previously reported procedure as a white solid with data in accordance with literature.¹⁷ Mp 66–64 °C [lit.^{16a} mp 60–62 °C]; ¹H NMR (500 MHz, CDCl₃) δ_{H} : 7.10–7.18 (2H, m, ArC(3,5)H), 7.26 (1H, d, *J* 15.6, C(3)H), 7.62–7.70 (2H, m, ArC(2,6)H), 7.97 (1H, d, *J* 15.6, C(4)H); ¹⁹F{¹H} NMR (471 MHz, CDCl₃) δ_{F} : –106.65(ArC(4)F).

(E)-1,1,1-Trichloro-4-(2-nitrophenyl)but-3-en-2-one. Prepared according to a previously reported procedure as a white solid with data in accordance with literature.¹⁷ Mp 56–58 °C [lit.¹⁷ mp 56–58 °C]; ¹H NMR (400 MHz, CDCl₃) δ_{H} : 7.24 (1H, d, *J* 15.5, C(3)H), 7.60–7.66 (1H, m, ArCH), 7.70–7.75 (2H, m, ArCH), 8.10–8.12 (1H, m, ArC(3)H), 8.43 (1H, d, *J* 15.5, C(4)H).

(E)-1,1,1-Trichloro-4-(furan-2-yl)but-3-en-2-one. Prepared according to a previously reported procedure as a white solid with data in accordance with literature.¹⁷ Mp 40–42 °C [lit.^{16a} mp 42–44 °C]; ¹H NMR (400 MHz, CDCl₃) δ_{H} : 6.56 (1H, dd, *J* 3.5, 1.8, ArC(4)H), 6.84 (1H, d, *J* 3.6, ArC(3)H), 7.21 (1H, d, *J* 15.3, C(3)H), 7.57–7.60 (1H, m, ArC(5)H), 7.73 (1H, d, *J* 15.3, C(4)H).

General Procedure for the NHC-Catalyzed Redox Synthesis of *syn*-Dihydropyranones. The appropriate α -aroyloxyaldehyde (0.30 mmol, 1.5 equiv), the appropriate trichloromethylketone (0.20 mmol, 1.0 equiv), and NHC precatalyst **11** (0.010 mmol, 5 mol % or 0.020 mmol, 10 mol %) were dissolved in anhydrous CH₂Cl₂ (2.7 mL). Et₃N (0.30 mmol, 1.5 equiv) was added, and the reaction mixture was stirred at rt until determined complete by TLC analysis. The mixture was diluted in EtOAc (10 mL) and washed with sodium bisulfite aq. 40% (10 mL) and brine (10 mL). The organic layer was dried over MgSO₄, filtered, and concentrated to give the crude product that was purified by flash silica column chromatography.

(3S,4S)-3-Methyl-4-phenyl-6-(trichloromethyl)-3,4-dihydro-2H-pyran-2-one (12). Following the general procedure, 1-oxopropan-2-yl 4-nitrobenzoate **10** (402 mg, 1.80 mmol), (E)-1,1,1-trichloro-4-phenylbut-3-en-2-one **1** (300 mg, 1.20 mmol), NHC precatalyst **11** (22.1 mg, 0.060 mmol), and Et₃N (251 μ L, 1.80 mmol) in anhydrous CH₂Cl₂ (16.2 mL) at rt for 3.5 h gave a crude brown solid (>95:5 dr) that was purified by flash silica column chromatography (90:10 hexane/EtOAc) to give the title compound (307 mg, 84%) as a white solid. Mp 142–145 °C; [α]_D²⁰ +237.5 (*c* 0.41, CH₂Cl₂); Chiral HPLC AD-H (95:5 hexane/IPA, flow rate 1.0 mL·min^{–1}, 220 nm, 30 °C) *t*_R major: 5.9 min, *t*_R minor: 7.1 min, >99% ee; ν_{max} (film, cm^{–1}) 1776 (C=O), 1674 (C=C), 1601 (Ar C=C), 1493 (Ar C=C), 1454 (Ar C=C); ¹H NMR (400 MHz, CDCl₃) δ_{H} : 1.06 (3H, d, *J* 6.9, CH₃), 3.08 (1H, p, *J* 6.9, C(3)H), 3.75 (1H, t, *J* 6.8, C(4)H), 6.42 (1H, d, *J* 6.5, C(5)H), 7.04–7.14 (2H, m, C(4)ArCH), 7.28–7.39 (3H, m, C(4)ArCH); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ_{C} : 12.1 (CH₃), 38.2 (C(3)), 42.4 (C(4)), 90.1 (CCl₃), 108.0 (C(5)), 128.1 (C(4)ArCH), 128.3 (C(4)ArCH), 129.2 (C(4)ArCH), 135.8 (C(4)ArC(1)), 149.5 (C(6)), 168.6 (C(2)); *m/z* (APCI⁺) 307 [(M(³⁵Cl₂, ³⁷Cl) + H)⁺, 100%], 305 [(M(³⁵Cl₃) + H)⁺, 98%]; HRMS (APCI⁺) C₁₃H₁₂³⁵Cl₃O₂ [M + H]⁺ found 304.9903, requires 304.9897 (+1.5 ppm).

(3S,4S)-3-Benzyl-4-phenyl-6-(trichloromethyl)-3,4-dihydro-2H-pyran-2-one (13). Following the general procedure, 1-oxo-3-phenylpropan-2-yl 4-nitrobenzoate (90 mg, 0.30 mmol), (E)-1,1,1-trichloro-4-phenylbut-3-en-2-one **1** (50 mg, 0.20 mmol), NHC precatalyst **11** (3.7 mg, 0.010 mmol), and Et₃N (42 μ L, 0.30 mmol) in anhydrous CH₂Cl₂ (2.7 mL) at rt for 4 h gave a brown oil (>95:5 dr) that was purified by column chromatography (90:10 petrol/EtOAc) to give the title compound (62 mg, 95% pure, 81%) as a light red oil. [α]_D²⁰ +167.7

(c 0.43, CH_2Cl_2); Chiral HPLC AS-H (99:1 hexane/IPA, flow rate 0.5 $\text{mL}\cdot\text{min}^{-1}$, 211 nm, 30 $^\circ\text{C}$) t_{R} minor: 16.6 min, t_{R} major: 19.2 min, >99% ee; ν_{max} (film, cm^{-1}) 1780 ($\text{C}=\text{O}$), 1670 ($\text{C}=\text{C}$), 1603 ($\text{Ar C}=\text{C}$), 1495 ($\text{Ar C}=\text{C}$), 1454 ($\text{Ar C}=\text{C}$); ^1H NMR (400 MHz, CDCl_3) δ_{H} : 2.35–2.46 (1H, m, $\text{C}(3)\text{CH}^{\text{A}}\text{H}^{\text{B}}$), 3.21–3.34 (2H, m, $\text{C}(3)\text{CH}^{\text{A}}\text{H}^{\text{B}}$ and $\text{C}(3)\text{H}$), 3.65–3.72 (1H, m, $\text{C}(4)\text{H}$), 6.37 (1H, d, J 6.8, $\text{C}(5)\text{H}$), 7.01–7.08 (2H, m, ArH), 7.11 (2H, m, ArH), 7.29–7.41 (6H, m, ArH); $^{13}\text{C}\{^1\text{H}\}$ (101 MHz, CDCl_3) δ_{C} : 32.0 (CH_2), 39.9 ($\text{C}(4)$), 44.8 ($\text{C}(3)$), 90.1 (CCl_3), 108.6 ($\text{C}(5)$), 126.8 (ArCH), 128.3 ($\text{ArCH} \times 2$), 128.4 (ArCH), 128.7 ($\text{ArCH} \times 2$), 128.9 ($\text{ArCH} \times 2$), 129.3 ($\text{ArCH} \times 2$), 135.9 ($\text{C}(3)\text{ArC}(1)$), 137.8 ($\text{C}(2)\text{CH}_2\text{ArC}(1)$), 149.1 ($\text{C}(6)$), 167.8 ($\text{C}(2)$); m/z (APCI $^+$) 381 ($[\text{M}(^{35}\text{Cl}_3) + \text{H}]^+$, 100%); HRMS (APCI $^+$) $\text{C}_{19}\text{H}_{16}\text{O}_2^{35}\text{Cl}_3$ $[\text{M} + \text{H}]^+$ found 381.0204, requires 381.0210 (–1.7 ppm).

2-(2-((3S,4S)-2-Oxo-4-phenyl-6-(trichloromethyl)-3,4-dihydro-2H-pyran-3-yl)ethyl)iso-indoline-1,3-dione (14). Following the general procedure 4-(1,3-dioxoisindolin-2-yl)-1-oxobutan-2-yl 4-nitrobenzoate (115 mg, 0.30 mmol), (*E*)-1,1,1-trichloro-4-phenylbut-3-en-2-one **1** (50 mg, 0.20 mmol), NHC precatalyst **11** (7.4 mg, 0.020 mmol, 10 mol %), and Et_3N (42 μL , 0.30 mmol) in anhydrous CH_2Cl_2 (2.7 mL) at rt for 8 h gave a brown solid (90:10 dr) that was purified by column chromatography (90:10 petrol/ EtOAc) to give the title compound (55 mg, 60%) as a white solid. Mp 132 $^\circ\text{C}$ (*dec*); $[\alpha]_{\text{D}}^{20} +271.2$ (c 0.16, CHCl_3); Chiral HPLC OD-H (97:3 hexane/IPA, flow rate 1.0 $\text{mL}\cdot\text{min}^{-1}$, 211 nm, 30 $^\circ\text{C}$) *syn*: t_{R} minor: 34.3 min, t_{R} major: 42.2 min, >99% ee, *anti*: t_{R} major: 51.3 min, t_{R} minor: 59.2 min, >99% ee; ν_{max} (film, cm^{-1}) 1772 and 1701 ($\text{C}=\text{O}$ isoxindole), 1701 ($\text{C}=\text{O}$); ^1H NMR (500 MHz, CDCl_3) δ_{H} : 1.50–1.60 (1H, m, $\text{C}(3)\text{CH}^{\text{A}}\text{H}^{\text{B}}$), 2.06–2.16 (1H, m, $\text{C}(3)\text{CH}^{\text{A}}\text{H}^{\text{B}}$), 2.95 (1H, q, J 7.0, $\text{C}(3)\text{H}$), 3.76–3.85 (1H, m, $\text{C}(3)\text{CH}_2\text{CH}^{\text{A}}\text{H}^{\text{B}}$), 3.85–3.92 (1H, m, $\text{C}(3)\text{CH}_2\text{CH}^{\text{A}}\text{H}^{\text{B}}$), 4.00 (1H, t, J 7.0, $\text{C}(4)\text{H}$), 6.42 (1H, d, J 6.9, $\text{C}(5)\text{H}$), 7.12–7.16 (2H, m, ArH), 7.29–7.38 (3H, m, ArH), 7.70–7.75 (2H, m, $\text{C}(3)(\text{CH}_2)_2\text{ArC}(2,5)\text{H}$), 7.83–7.88 (2H, m, $\text{C}(3)(\text{CH}_2)_2\text{ArC}(3,4)\text{H}$); $^{13}\text{C}\{^1\text{H}\}$ (101 MHz, CDCl_3) δ_{C} : 26.3 (CH_2), 35.6 (CH_2), 40.7 ($\text{C}(3)$), 40.9 ($\text{C}(4)$), 90.0 (CCl_3), 108.1 ($\text{C}(5)$), 123.4 ($\text{ArCH} \times 2$), 128.0 ($\text{ArCH} \times 2$), 128.5 (ArCH), 129.4 ($\text{ArCH} \times 2$), 132.0 (NPhthArC), 134.1 (ArCH), 135.7 (NPhthArC), 149.3 ($\text{C}(3)\text{-ArC}(1)$), 167.5 ($\text{C}(2)$), 168.4 ($\text{C}=\text{O} \times 2$); m/z (NSI^+) 951 ($[\text{M}(^{35}\text{Cl}_2, ^{37}\text{Cl}) + \text{Na}]^+$, 100%), 949 ($[\text{M}(^{35}\text{Cl}_3) + \text{Na}]^+$, 85%), 486 ($[\text{M}(^{35}\text{Cl}_3) + \text{Na}]^+$, 85%); HRMS (NSI^+) $\text{C}_{22}\text{H}_{16}\text{O}_4\text{N}_1^{35}\text{Cl}_3\text{Na}$ $[\text{M} + \text{Na}]^+$ found 486.0041, requires 486.0037 (+0.8 ppm).

(3S,4S)-3-(4-Methoxybenzyl)-4-phenyl-6-(trichloromethyl)-3,4-dihydro-2H-pyran-2-one (15). Following the general procedure, 1-(4-methoxyphenyl)-3-oxopropan-2-yl 4-nitrobenzoate (99 mg, 0.30 mmol), (*E*)-1,1,1-trichloro-4-phenylbut-3-en-2-one **1** (50 mg, 0.20 mmol), NHC precatalyst **11** (7.4 mg, 0.020 mmol), and Et_3N (42 μL , 0.30 mmol) in anhydrous CH_2Cl_2 (2.7 mL) at rt for 4 h gave a brown oil (>95:5 dr) that was purified by column chromatography (95:5 petrol/ EtOAc) to give the title compound (53 mg, 65%) as a yellow oil. $[\alpha]_{\text{D}}^{20} +300.0$ (c 0.81, CHCl_3); Chiral HPLC AD-H (99:1 hexane/IPA, flow rate 1.0 $\text{mL}\cdot\text{min}^{-1}$, 220 nm, 30 $^\circ\text{C}$) t_{R} minor: 18.5 min, t_{R} major: 20.7 min, >99% ee; ν_{max} (film, cm^{-1}) 1780 ($\text{C}=\text{O}$), 1612 ($\text{C}=\text{C}$), 1514 ($\text{Ar C}=\text{C}$), 1456, 1250 (Ph-O-CH_3); ^1H NMR (500 MHz, CDCl_3) δ_{H} : 2.35 (1H, dd, J 14.4, 9.1, $\text{C}(3)\text{CH}^{\text{A}}\text{H}^{\text{B}}$), 3.15–3.27 (2H, m, $\text{C}(3)\text{CH}^{\text{A}}\text{H}^{\text{B}}$ and $\text{C}(3)\text{H}$), 3.68 (1H, t, J 6.8, $\text{C}(4)\text{H}$), 3.81 (3H, s, CH_3O), 6.36 (1H, d, J 6.7, $\text{C}(5)\text{H}$), 6.85 (2H, dd, J 9.1, 2.5, $\text{C}(3)\text{CH}_2\text{ArC}(3,5)\text{H}$), 6.99–7.08 (4H, m, $\text{C}(3)\text{CH}_2\text{ArC}(2,6)\text{H}$ and $\text{C}(4)\text{ArC}(3,5)\text{H}$), 7.31–7.39 (3H, m, $\text{C}(4)\text{ArC}(2,4,6)\text{H}$); $^{13}\text{C}\{^1\text{H}\}$ (126 MHz, CDCl_3) δ_{C} : 31.1 ($\text{C}(3)\text{CH}_2$), 39.9 ($\text{C}(4)$), 45.0 ($\text{C}(3)$), 55.3 (OCH_3), 90.1 (CCl_3), 108.6 ($\text{C}(5)$), 114.0 ($\text{C}(3)\text{CH}_2\text{ArC}(3,5)$), 128.3 (ArCH), 128.4 (ArCH), 129.2 (ArCH), 129.7 (ArCH), 129.7 (ArCH), 129.9 (ArCH), 136.0 ($\text{C}(4)\text{ArC}(1)$), 149.1 ($\text{C}(6)$), 158.4 ($\text{C}(3)\text{CH}_2\text{ArC}(4)$), 167.9 ($\text{C}(2)$); m/z (NSI^+) 462 ($[\text{M}(^{35}\text{Cl}_2, ^{37}\text{Cl}) + \text{MeOH} + \text{NH}_4]^+$, 51%), 460 ($[\text{M}(^{35}\text{Cl}_3) + \text{MeOH} + \text{NH}_4]^+$, 52%), 445 ($[\text{M}(^{35}\text{Cl}_2, ^{37}\text{Cl}) + \text{MeOH} + \text{H}]^+$, 65%), 443 ($[\text{M}(^{35}\text{Cl}_3) + \text{MeOH} + \text{H}]^+$, 67%), 432 ($[\text{M}(^{35}\text{Cl}_2, ^{37}\text{Cl}_2) + \text{NH}_4]^+$, 30%), 430 ($[\text{M}(^{35}\text{Cl}_2, ^{37}\text{Cl}) + \text{NH}_4]^+$, 97%), 428 ($[\text{M}(^{35}\text{Cl}_3) + \text{NH}_4]^+$, 100%), 411 ($[\text{M}(^{35}\text{Cl}_2, ^{37}\text{Cl}) + \text{H}]^+$, 43%); HRMS (NSI^+) $\text{C}_{20}\text{H}_{18}\text{O}_3\text{Cl}_3$ $[\text{M} + \text{H}]^+$ found 411.0321, requires 411.0316 (+1.2 ppm).

(3S,4S)-(-3-(Benzo[d][1,3]dioxol-5-ylmethyl)-4-phenyl-6-(trichloromethyl)-3,4-dihydro-2H-pyran-2-one (16). Following the general procedure, 1-(benzo[d][1,3]dioxol-5-yl)-3-oxopropan-2-yl 4-nitrobenzoate (103 mg, 0.30 mmol), (*E*)-1,1,1-trichloro-4-phenylbut-3-en-2-one **1** (50 mg, 0.20 mmol), NHC precatalyst **11** (3.7 mg, 0.010 mmol), and Et_3N (42 μL , 0.30 mmol) in anhydrous CH_2Cl_2 (2.7 mL) at rt for 26 h gave a brown oil (85:15 dr) that was purified by column chromatography (95:5 petrol/ EtOAc) to give the title compound (38 mg, 45%) as a white solid. Mp 145–147 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{20} +230.4$ (c 0.51, CH_2Cl_2); ee could not be determined by either chiral HPLC or GC; ν_{max} (film, cm^{-1}) 1780 ($\text{C}=\text{O}$), 1504, 1489, and 1445 ($\text{Ar C}=\text{C}$), 1246 (C-O); ^1H NMR (500 MHz, CDCl_3) δ_{H} : 2.33 (1H, dd, J 14.5, 9.1, $\text{C}(3)\text{CH}^{\text{A}}\text{H}^{\text{B}}$), 3.15 (1H, dd, J 14.5, 5.3, $\text{C}(3)\text{CH}^{\text{A}}\text{H}^{\text{B}}$), 3.18–3.22 (1H, m, $\text{C}(3)\text{H}$), 3.71 (1H, t, J 6.7, $\text{C}(4)\text{H}$), 5.96 (2H, dd, J 4.6, 1.4, OCH_2O), 6.37 (1H, d, J 6.8, $\text{C}(5)\text{H}$), 6.53 (1H, dd, J 7.9, 1.5, $\text{C}(3)\text{CH}_2\text{ArC}(6)\text{H}$), 6.61 (1H, app d, J 1.6, $\text{C}(3)\text{CH}_2\text{ArC}(4)\text{H}$), 6.75 (1H, d, J 7.9, $\text{C}(3)\text{CH}_2\text{ArC}(7)\text{H}$), 7.05–7.07 (2H, m, $\text{C}(4)\text{ArC}(3,5)\text{H}$), 7.32–7.39 (3H, m, $\text{C}(4)\text{ArC}(2,4,6)\text{H}$); $^{13}\text{C}\{^1\text{H}\}$ (126 MHz, CDCl_3) δ_{C} : 31.8 ($\text{C}(4)\text{CH}_2$), 39.9 ($\text{C}(4)$), 45.1 ($\text{C}(3)$), 90.1 (CCl_3), 101.0 (OCH_2O), 108.4 ($\text{C}(3)\text{CH}_2\text{ArC}(7)$), 108.6 ($\text{C}(5)$), 109.1 ($\text{C}(3)\text{CH}_2\text{ArC}(4)$), 122.0 ($\text{C}(3)\text{CH}_2\text{ArC}(6)$), 128.3 ($\text{C}(4)\text{ArCH}$), 128.4 ($\text{C}(4)\text{ArCH}$), 129.3 ($\text{C}(4)\text{ArCH}$), 131.4 ($\text{C}(3)\text{CH}_2\text{ArC}(5)$), 135.9 ($\text{C}(4)\text{ArC}(1)$), 146.4 ($\text{C}(3)\text{CH}_2\text{ArC}(3a)$), 147.8 ($\text{C}(3)\text{-CH}_2\text{ArC}(7a)$), 149.0 ($\text{C}(6)$), 167.8 ($\text{C}(2)$); m/z (NSI^+) 481 ($[\text{M}(^{35}\text{Cl}_2, ^{37}\text{Cl}) + \text{MeOH} + \text{Na}]^+$, 65%), 479 ($[\text{M}(^{35}\text{Cl}_3) + \text{MeOH} + \text{Na}]^+$, 67%), 449 ($[\text{M}(^{35}\text{Cl}_2, ^{37}\text{Cl}) + \text{Na}]^+$, 50%), 447 ($[\text{M}(^{35}\text{Cl}_3) + \text{Na}]^+$, 52%), 444 ($[\text{M}(^{35}\text{Cl}_2, ^{37}\text{Cl}) + \text{NH}_4]^+$, 31%), 442 ($[\text{M}(^{35}\text{Cl}_3) + \text{NH}_4]^+$, 34%), 429 ($[\text{M}(^{35}\text{Cl}_2, ^{37}\text{Cl}_2) + \text{H}]^+$, 30%), 427 ($[\text{M}(^{35}\text{Cl}_2, ^{37}\text{Cl}) + \text{H}]^+$, 94%), 425 ($[\text{M}(^{35}\text{Cl}_3) + \text{H}]^+$, 100%); HRMS (NSI^+) $\text{C}_{20}\text{H}_{16}\text{O}_4^{35}\text{Cl}_3$ $[\text{M} + \text{H}]^+$ found 425.0107, requires 425.0109 (–0.4 ppm).

(3S,4S)-3-Benzyl-4-(4-methoxyphenyl)-6-(trichloromethyl)-3,4-dihydro-2H-pyran-2-one (17). Following the general procedure, 1-oxo-3-phenylpropan-2-yl 4-nitrobenzoate (270 mg, 0.90 mmol), (*E*)-1,1,1-trichloro-4-(4-methoxyphenyl)but-3-en-2-one (168 mg, 0.60 mmol), NHC precatalyst **11** (11.1 mg, 0.030 mmol), and Et_3N (126 μL , 0.90 mmol) in anhydrous CH_2Cl_2 (8.2 mL) at rt for 4 h gave a brown oil (>95:5 dr) that was purified by column chromatography (90:10 petrol/ EtOAc) to give the title compound (229 mg, 93%) as a white solid. Mp 109–111 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{20} +369.6$ (c 0.575, CH_2Cl_2); Chiral HPLC AD-H (98:2 hexane/IPA, flow rate 1.0 $\text{mL}\cdot\text{min}^{-1}$, 220 nm, 30 $^\circ\text{C}$) t_{R} minor: 11.2 min, t_{R} major: 12.6 min, 99% ee; ν_{max} (film, cm^{-1}) 1778 ($\text{C}=\text{O}$), 1609 ($\text{C}=\text{C}$), 1512 ($\text{Ar C}=\text{C}$), 1252 (Ph-O-CH_3); ^1H NMR (500 MHz, CDCl_3) δ_{H} : 2.41 (1H, dd, J 15.8, 10.6, $\text{C}(3)\text{CH}^{\text{A}}\text{H}^{\text{B}}$), 3.23–3.30 (2H, m, $\text{C}(3)\text{CH}^{\text{A}}\text{H}^{\text{B}}$ and $\text{C}(3)\text{H}$), 3.62 (1H, t, J 6.7, $\text{C}(4)\text{H}$), 3.82 (3H, s, CH_3), 6.35 (1H, d, J 6.8, $\text{C}(5)\text{H}$), 6.87–6.97 (4H, m, $\text{C}(4)\text{ArH}$), 7.10–7.14 (2H, m, ArH), 7.24–7.28 (1H, m, ArH), 7.30–7.35 (2H, m, ArH); $^{13}\text{C}\{^1\text{H}\}$ (126 MHz, CDCl_3) δ_{C} : 32.0 (CH_2), 39.1 ($\text{C}(4)$), 45.0 ($\text{C}(3)$), 55.3 (CH_3O), 90.1 (CCl_3), 108.9 ($\text{C}(5)$), 114.6 ($\text{C}(4)\text{ArCH}$), 126.8 ($\text{C}(3)\text{CH}_2\text{ArCH}$), 127.6 ($\text{C}(4)\text{ArC}(1)$), 128.7 ($\text{C}(3)\text{CH}_2\text{ArCH}$), 129.0 ($\text{C}(3)\text{CH}_2\text{ArCH}$), 129.4 ($\text{C}(4)\text{ArCH}$), 137.9 ($\text{C}(3)\text{CH}_2\text{ArC}$), 148.8 ($\text{C}(6)$), 159.6 ($\text{C}(4)\text{ArC}(4)$), 168.0 ($\text{C}(2)$); m/z (APCI $^+$) 411 ($[\text{M}(^{35}\text{Cl}_3) + \text{H}]^+$, 100%), 303 ($[\text{M}(^{35}\text{Cl}_3) - 4\text{OMeC}_6\text{H}_4]^+$, 70%); HRMS (APCI $^+$) $\text{C}_{20}\text{H}_{17}^{35}\text{Cl}_3\text{O}_3$ $[\text{M} + \text{H}]^+$ found 411.0313, requires 411.0316 (–0.7 ppm).

(3S,4S)-3-Benzyl-4-(4-bromophenyl)-6-(trichloromethyl)-3,4-dihydro-2H-pyran-2-one (18). Following the general procedure, 1-oxo-3-phenylpropan-2-yl 4-nitrobenzoate (90 mg, 0.30 mmol), (*E*)-4-(4-bromophenyl)-1,1,1-trichlorobut-3-en-2-one (70 mg, 0.20 mmol), NHC precatalyst **11** (3.7 mg, 0.010 mmol), and Et_3N (42 μL , 0.30 mmol) in anhydrous CH_2Cl_2 (2.7 mL) at rt for 1.5 h gave a brown oil (>95:5 dr) that was purified by column chromatography (90:10 petrol/ EtOAc) to give the title compound (60 mg, 95% pure, 55%) as a yellow oil. $[\alpha]_{\text{D}}^{20} +71.4$ (c 0.29, CH_2Cl_2); Chiral HPLC OD-H (97:3 hexane/IPA, flow rate 1.0 $\text{mL}\cdot\text{min}^{-1}$, 220 nm, 30 $^\circ\text{C}$) t_{R} major: 10.3 min, t_{R} minor: 11.7 min, >99% ee; ν_{max} (film, cm^{-1}) 1780 ($\text{C}=\text{O}$), 1661 ($\text{C}=\text{C}$); ^1H NMR (400 MHz, CDCl_3) δ_{H} : 2.33–2.42 (1H, m, $\text{C}(3)\text{CH}^{\text{A}}\text{H}^{\text{B}}$), 3.24–3.35 (2H, m, $\text{C}(3)\text{CH}^{\text{A}}\text{H}^{\text{B}}$ and $\text{C}(3)\text{H}$), 3.64 (1H, t, J 6.7, $\text{C}(4)\text{H}$), 6.33 (1H, d, J 6.8, $\text{C}(5)\text{H}$), 6.86–6.93 (2H, m,

C(4)ArC(2,6)H), 7.07–7.12 (2H, m, C(3)ArH), 7.27–7.36 (3H, m, C(3)ArH), 7.46–7.52 (2H, m, C(4)ArC(3,5)H); $^{13}\text{C}\{^1\text{H}\}$ (101 MHz, CDCl_3) δ_{C} : 32.0 (CH_2), 39.2 (C(4)), 44.4 (C(3)), 90.2 (CCl_3), 108.0 (C(5)), 123.0 (C(4)ArC(1)), 127.0 (C(3)CH₂ArCH), 128.8 (C(3)-CH₂ArCH), 128.9 (C(3)CH₂ArCH), 129.9 (C(4)ArC(2,6)), 132.4 (C(4)ArC(3,5)), 135.1 (C(4)ArC(4)), 137.8 (C(3)CH₂ArC), 146.6 (C(6)), 167.7 (C(2)); m/z (APCI⁺) 463 ([M(^{35}Cl , ^{37}Cl , ^{79}Br) + H]⁺, 60%), 461 ([M(^{35}Cl , ^{37}Cl , ^{79}Br) + H]⁺, 100%), 458 ([M(^{35}Cl , ^{79}Br) + H]⁺, 50%); HRMS (APCI⁺) C₁₉H₁₅O₂⁷⁹Br³⁵Cl₃ [M + H]⁺ found 458.9312, requires 458.9316 (−0.8 ppm).

(3S,4S)-3-Methyl-4-pentyl-6-(trichloromethyl)-3,4-dihydro-2H-pyran-2-one (19). Following the general procedure, 1-oxopropan-2-yl 4-nitrobenzoate **10** (67 mg, 0.30 mmol), (E)-1,1,1-trichloro-2-nitro-2-one (49 mg, 0.20 mmol), NHC precatalyst **11** (7.4 mg, 0.020 mmol), and Et₃N (42 μL , 0.30 mmol) in anhydrous CH₂Cl₂ (2.7 mL) at rt for 22 h gave a crude brown solid (>95:5 dr) that was purified by flash silica column chromatography (95:5 hexane/EtOAc) to give the title compound (15 mg, >95% pure, 26%) as a yellow oil. $[\alpha]_{\text{D}}^{20}$ +8.9 (c 0.44, CHCl₃); Chiral GC analysis Restek Rt-bDEXcst (length: 30 m, thickness: 0.250 mm, film thickness: 0.25 μm) carrier gas: He, linear velocity: 20.0 cm·s^{−1}, temperature: 160 °C, t_{R} minor: 105.3 min, t_{R} major: 106.9 min, >99% ee; ν_{max} (film, cm^{−1}) 1782 (C=O), 1668 (C=C), 1458 (Ar C=C); ^1H NMR (400 MHz, CDCl_3) δ_{H} : 0.88 (3H, t, J 6.9, CH₃), 1.26 (3H, d, J 7.0, C(3)CH₃), 1.27–1.40 (7H, m, C(4)CH^AH^B and CH₃(CH₂)₃), 1.50–1.55 (1H, m, C(4)CH^AH^B), 2.53–2.64 (1H, m, C(4)H), 2.81 (1H, p, J 7.0, C(3)H), 6.18 (1H, d, J 5.8, C(5)H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ_{C} : 11.3 (C(3)CH₃), 14.0 (CH₃), 22.4 (CH₃CH₂), 26.0 (CH₃(CH₂)₂CH₂), 28.8 (C(4)CH₂), 31.8 (CH₃CH₂CH₂), 35.3 (C(4)), 36.9 (C(3)), 90.1 (CCl_3), 109.2 (C(5)), 148.4 (C(6)), 169.9 (C(2)); m/z (APCI⁺) 319 ([M(^{35}Cl , ^{37}Cl) + H₃O]⁺, 62%), 317 ([M(^{35}Cl , ^{37}Cl) + H₃O]⁺, 65%), 303 ([M(^{35}Cl , ^{37}Cl) + H]⁺, 30%), 301 ([M(^{35}Cl , ^{37}Cl) + H]⁺, 95%), 299 ([M(^{35}Cl) + H]⁺, 100%); HRMS (APCI⁺) C₁₂H₁₇³⁵Cl₃O₂⁺ [M + H]⁺ found 299.0366, requires 299.0367 (−0.3 ppm).

Epimerization of 14. In an NMR tube, 2-(2-((3S,4S)-2-oxo-4-phenyl-6-(trichloromethyl)-3,4-dihydro-2H-pyran-3-yl)ethyl)isoidoline-1,3-dione **14** (13.2 mg, 0.028 mmol, 1.0 equiv) was dissolved in CD₂Cl₂ before Et₃N (5.9 μL , 0.42 mmol, 1.5 equiv) was added. The ratio between the two diastereoisomers were monitored by ^1H NMR comparing the ratio between *syn*-C(5)H (δ_{H} 6.21 (1H, d, J 3.7)) and *anti*-C(5)H (δ_{H} 6.45 (1H, d, J 6.9)). Chiral HPLC OD-H (97:3 hexane/IPA, flow rate 1.0 mL·min^{−1}, 211 nm, 30 °C) *syn*: t_{R} minor: 34.3 min, t_{R} major: 42.2 min, >99% ee, *anti*: t_{R} major: 51.3 min, t_{R} minor: 59.2 min, >99% ee.

General Procedure for the NHC-Catalyzed Redox [4 + 2]-Hetero-Diels–Alder Reaction Followed by Ring-Opening and Aminolysis. The appropriate α -aroyloxyaldehyde (0.30 mmol, 1.5 equiv), the appropriate trichloromethyl ketone (0.20 mmol, 1.0 equiv), and NHC precatalyst **11** (0.010 mmol, 5 mol % or 0.020 mmol, 10 mol %) were dissolved in anhydrous CH₂Cl₂ (2.7 mL). Et₃N (0.30 mmol, 1.5 equiv) was added, and the reaction mixture was stirred at rt until complete by TLC analysis. The mixture was diluted in EtOAc (10 mL) and washed with water (10 mL \times 2), sodium bisulfite aq. 40% (10 mL \times 2), and brine (10 mL \times 2). The organic layer was dried over MgSO₄, filtered, and concentrated. The crude *syn*-dihydropyranone was dissolved in anhydrous CH₂Cl₂ (6.6 mL), and benzylamine (60 mmol, 300 equiv, 6.6 mL) was added. The reaction mixture was stirred at rt for 16 h before being diluted in EtOAc (20 mL) and washed with 1 M HCl (20 mL \times 3), sat. aq. NaHCO₃ (20 mL \times 3), and brine (20 mL \times 3). The organic layer was dried over MgSO₄, filtered, and concentrated to give the crude product that was triturated in Et₂O then dispersed in CHCl₃ and concentrated to give the desired diamide.

(2S,3S)-N¹,N⁵-Dibenzyl-2-methyl-3-phenylpentanediamide (21). Following the general procedure, 1-oxopropan-2-yl 4-nitrobenzoate **10** (67 mg, 0.30 mmol), (E)-1,1,1-trichloro-4-phenylbut-3-en-2-one **1** (50 mg, 0.20 mmol), NHC precatalyst **11** (3.7 mg, 0.010 mmol), and Et₃N (42 μL , 0.30 mmol) in anhydrous CH₂Cl₂ (2.7 mL) at rt for 3.5 h gave a crude orange solid (>95:5 dr). The crude was stirred in anhydrous CH₂Cl₂ (6.6 mL) with benzylamine (6.6 mL, 60 mmol) at rt for 16 h to give a crude beige solid (dr >95:5) that was triturated in

Et₂O to give the title compound (70 mg, 85%) as a white solid. Mp 172–174 °C; $[\alpha]_{\text{D}}^{20}$ −8.7 (c 0.53, CHCl₃); Chiral HPLC AD-H (90:10 hexane/IPA, flow rate 1.0 mL·min^{−1}, 211 nm, 30 °C) t_{R} minor: 15.3 min, t_{R} major: 19.1 min, >99% ee; ν_{max} (film, cm^{−1}) 3283 (N–H), 3258 (N–H), 1636 (C=O), 1558 (N–C=O), 1541 (N–C=O), 1495, 1454, 1435; ^1H NMR (400 MHz, CDCl_3) δ_{H} : 1.20 (3H, d, J 6.9, C(2)CH₃), 2.48 (1H, dd, J 13.8, 8.6, C(4)H^AH^B), 2.67 (1H, p, J 7.0, C(2)H), 2.91 (1H, dd, J 13.8, 6.9, C(4)H^AH^B), 3.36 (1H, q, J 7.7, C(3)H), 4.14 (1H, dd, J 14.7, 5.2, N¹CH^AH^B), 4.24 (1H, dd, J 14.9, 5.4, N⁵CH^AH^B), 4.31 (1H, dd, J 14.7, 6.1, N¹CH^AH^B), 4.38 (1H, dd, J 14.8, 6.1, N⁵CH^AH^B), 5.58 (1H, br t, J 5.0, N¹H), 6.10 (1H, br t, J 5.0, N⁵H), 6.87–6.96 (3H, dd, J 6.6, 2.8, ArH), 6.97–7.02 (3H, m, ArH), 7.11–7.18 (3H, m, ArH), 7.19–7.26 (8H, m); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ_{C} : 16.0 (C(2)CH₃), 40.5 (C(4)), 43.3 (NCH₂), 43.4 (NCH₂), 45.1 (C(2)), 46.4 (C(3)), 127.1 (ArCH), 127.7 (ArCH), 127.33 (ArCH), 127.5 (ArCH), 127.7 (ArCH), 128.3 (ArCH), 128.6 (ArCH), 137.9 (NCH₂ArC(1)), 138.1 (NCH₂ArC(1)), 141.3 (C(3)ArC), 171.4 (C(5)), 174.0 (C(1)); m/z (NSI⁺) 823 ([2M + Na]⁺, 44%), 423 ([M + Na]⁺, 42%), 401 ([M + H]⁺, 100%); HRMS (NSI⁺) C₂₆H₂₉O₂N₂ [M + H]⁺ found 401.2221, requires 401.2224 (−0.6 ppm).

(2S,3S)-Methyl 6,6,6-Trichloro-2-methyl-5-oxo-3-phenylhexanoate (22) and (2S,3S)-Dimethyl 2-methyl-3-phenylpentanedioate (23). 1-Oxopropan-2-yl 4-nitrobenzoate **10** (0.30 mmol, 67 mg, 1.5 equiv), (E)-1,1,1-trichloro-4-phenylbut-3-en-2-one **1** (0.20 mmol, 50 mg, 1.0 equiv), and NHC precatalyst **11** (0.010 mmol, 3.7 mg, 5 mol %) were dissolved in anhydrous CH₂Cl₂ (2.7 mL). Et₃N (0.30 mmol, 42 μL , 1.5 equiv) was added, and the reaction mixture was stirred at rt for 3.5 h. The mixture was diluted in EtOAc (10 mL) and washed with water (10 mL \times 2), sodium bisulfite aq. 40% (10 mL \times 2), and brine (10 mL \times 2). The organic layer was dried with MgSO₄, filtered, and concentrated to give a crude orange solid (>95:5 dr). The crude was dissolved in anhydrous CH₂Cl₂ (2.4 mL) with MeOH (60 mmol, 2.4 mL, 300 equiv) and DMAP (0.04 mmol, 5.0 mg, 20 mol %). The reaction mixture was stirred at rt for 16 h before being concentrated to give a crude orange oil (>95:5 dr) that was purified by flash silica column chromatography (98:2 to 90:10 hexane/EtOAc) to give **22** and **23**.

22 (35 mg, 50%) as a colorless oil. $[\alpha]_{\text{D}}^{20}$ −17.3 (c 1.60, CHCl₃); Chiral HPLC AD-H (99:1 hexane/IPA, flow rate 1.0 mL·min^{−1}, 211 nm, 30 °C) t_{R} minor: 8.0 min, t_{R} major: 9.7 min, >99% ee; ν_{max} (film, cm^{−1}) 1734 (C=O), 1456, 1198, 1167; ^1H NMR (400 MHz, CDCl_3) δ_{H} : 1.23 (3H, d, J 7.0, C(2)CH₃), 2.86 (1H, p, J 7.0, C(2)H), 3.49 (2H, dd, J 6.9, 2.7, C(4)H₂), 3.52 (3H, s, C(1)OCH₃), 3.54–3.62 (1H, m, C(3)H), 7.17–7.24 (3H, m, ArH), 7.24–7.31 (2H, m, ArH); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ_{C} : 14.8 (C(2)CH₃), 36.8 (C(4)), 44.0 (C(3)), 44.7 (C(2)), 51.6 (C(1)OCH₃), 96.2 (C(6)), 127.3 (ArCH), 128.1 (ArCH \times 2), 128.4 (ArCH \times 2), 140.3 (C(3)ArC(1)), 174.9 (C(1)), 188.7 (C(5)); m/z (APCI⁺) 356 ([M(^{35}Cl , ^{37}Cl) + NH₄]⁺, 34%), 354 ([M(^{35}Cl) + NH₄]⁺, 34%), 341 ([M(^{35}Cl , ^{37}Cl) + H]⁺, 34%), 339 ([M(^{35}Cl , ^{37}Cl) + H]⁺, 99%), 337 ([M(^{35}Cl) + H]⁺, 100%); HRMS (APCI⁺) C₁₄H₁₅O₃³⁵Cl₃ [M + H]⁺ found 337.0160, requires 337.0164 (+1.3 ppm).

23 (10 mg, 20%, 85% pure) as a yellow oil. $[\alpha]_{\text{D}}^{20}$ +0.46 (c 0.44, CHCl₃); Chiral HPLC AD-H (99:1 hexane/IPA, flow rate 1.0 mL·min^{−1}, 211 nm, 30 °C) major diastereoisomer: t_{R} minor: 13.8 min, t_{R} major: 15.1 min, 98% ee, minor diastereoisomer: t_{R} minor: 12.3 min, t_{R} major: 13.0 min, >99% ee; ν_{max} (film, cm^{−1}) 1734 (C=O), 1456, 1453, 1258, 1198, 1161; ^1H NMR (400 MHz, CDCl_3) δ_{H} : 1.18 (3H, d, J 7.0, C(2)CH₃), 2.69 (1H, dd, J 15.7, 9.7, C(4)H^AH^B), 2.74–2.87 (2H, m, C(4)H^AH^B and C(2)H), 3.41–3.48 (1H, m, C(3)H), 3.50 (3H, s, C(1)OCH₃), 3.54 (3H, s, C(5)OCH₃), 7.14–7.23 (3H, m, ArH), 7.24–7.30 (2H, m, ArH); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ_{C} : 14.4 (C(2)CH₃), 37.0 (C(4)), 44.5 (C(3)), 45.1 (C(2)), 51.5 (C(1)OCH₃), 51.6 (C(5)OCH₃), 126.9 (C(3)ArCH), 127.8 (C(3)ArCH \times 2), 128.3 (C(3)ArCH \times 2), 141.3 (C(3)ArC(1)), 172.4 (C(5)), 175.2 (C(2)); m/z (NSI⁺) 251 ([M + H]⁺, 100%); HRMS (NSI⁺) C₁₄H₁₉O₄ [M + H]⁺ found 251.1279, requires 251.1278 (+0.5 ppm).

(2*S*,3*S*)-Benzyl 5-(Benzylamino)-2-methyl-5-oxo-3-phenylpentanoate (**24**). 1-Oxopropan-2-yl 4-nitrobenzoate **10** (0.30 mmol, 67 mg, 1.5 equiv), (*E*)-1,1,1-trichloro-4-phenylbut-3-en-2-one **1** (0.20 mmol, 50 mg, 1.0 equiv), and NHC precatalyst **11** (0.010 mmol, 3.7 mg, 5 mol %) were dissolved in anhydrous CH₂Cl₂ (2.7 mL). Et₃N (0.30 mmol, 42 μ L, 1.5 equiv) was added, and the reaction mixture was stirred at rt for 3.5 h. The mixture was diluted in EtOAc (10 mL) and washed with water (10 mL \times 2), sodium bisulfite aq. 40% (10 mL \times 2), and brine (10 mL \times 2). The organic layer was dried over MgSO₄, filtered, and concentrated to give a crude orange solid (77 mg, >95:5 dr). The crude was dissolved in anhydrous CH₂Cl₂ (6.6 mL) with BnOH (60 mmol, 6.6 mL, 300 equiv) and DMAP (0.04 mmol, 5 mg, 20 mol %). The reaction mixture was stirred at rt for 16 h before being concentrated. Excess BnOH was removed by Kugelrohr distillation to give a crude orange oil (105 mg, >95:5 dr). The oil was stirred in anhydrous CH₂Cl₂ (2.6 mL) with benzylamine (2.6 mL, 0.24 mmol, 1.2 equiv) at rt for 16 h. The reaction mixture was diluted in EtOAc (20 mL) and wash with 1 M HCl (20 mL \times 3), sat. aq. NaHCO₃ (20 mL \times 3), and brine (20 mL \times 3). The organic layer was dried over MgSO₄, filtered, and concentrated to give a crude orange oil (105 mg, >95:5 dr) that was purified by Biotage Isolera 4 [SNAP Ultra 10 g, 36 mL min⁻¹, hexane/EtOAc (80:20 1 CV, 80:20 to 50:50 15 CV, 50:50 5 CV)] to give the title compound (26 mg, 32%) as a yellow solid. Mp 98–100 °C; [α]_D²⁰ +6.92 (*c* 0.52, CHCl₃); Chiral HPLC AD-H (90:10 hexane/IPA, flow rate 1.0 mL min⁻¹, 211 nm, 30 °C) *t*_R minor: 19.7 min, *t*_R major: 26.2 min, >99% ee; ν_{\max} (film, cm⁻¹) 3319, 3269, 1720 (C(1)=O), 1643 (C(5)=O), 1549 (N–C=O), 1495, 1454, 1256; ¹H NMR (400 MHz, CDCl₃) δ _H: 1.24 (3H, d, *J* 7.0, C(2)CH₃), 2.44 (1H, dd, *J* 14.0, 9.8, C(4)H^AH^B), 2.79 (1H, dd, *J* 14.0, 5.6, C(4)H^AH^B), 2.82–2.92 (1H, m, C(2)H), 3.40–3.50 (1H, m, C(3)H), 4.18 (1H, dd, *J* 14.8, 5.3, NCH^AH^B), 4.34 (1H, dd, *J* 14.8, 6.2, NCH^AH^B), 4.88 (1H, d, *J* 12.3, OCH^AH^B), 4.93 (1H, d, *J* 12.3, OCH^AH^B), 5.51 (1H, t, *J* 5.1, NH), 6.87–6.94 (2H, m, ArH), 7.09–7.17 (4H, m, ArH), 7.18–7.25 (6H, m, ArH), 7.26–7.32 (3H, m, ArH); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ _C: 15.3 (C(2)CH₃), 40.5 (C(4)), 43.4 (NCH₂), 44.8 (C(2)), 45.8 (C(3)), 66.2 (OCH₂), 127.1 (ArCH), 127.3 (ArCH), 127.5 (ArCH), 128.1 (ArCH), 128.2 (ArCH), 128.48 (ArCH), 128.54 (ArCH), 135.7 (OCH₂ArC(1)), 137.9 (NCH₂ArC(1)), 141.1 (C(3)ArC(1)), 170.9 (C(5)), 174.6 (C(1)); *m/z* (NSI⁺) 424 ([M + Na]⁺, 33%), 402 ([M + H]⁺, 100%); HRMS (NSI⁺) C₂₆H₂₈O₃N₁ [M + H]⁺ found 402.2062, requires 402.2064 (–0.4 ppm).

(2*S*,3*S*)-*N*¹,*N*⁵-Dibenzyl-2-butyl-3-phenylpentanediamide (**25**). Following the general procedure, 1-oxohexan-2-yl 4-nitrobenzoate (80 mg, 0.30 mmol), (*E*)-1,1,1-trichloro-4-phenylbut-3-en-2-one **1** (50 mg, 0.20 mmol), NHC precatalyst **11** (7.4 mg, 0.020 mmol), and Et₃N (42 μ L, 0.30 mmol) in anhydrous THF (2.7 mL) at rt for 3 h gave a crude brown-green oil (>95:5 dr). The crude was stirred in anhydrous CH₂Cl₂ (6.6 mL) with benzylamine (6.6 mL, 60 mmol) at rt for 16 h to give a crude beige solid (>95:5 dr) that was triturated in Et₂O to give the title compound (78 mg, 89%) as a white solid. Mp 205–207 °C; [α]_D²⁰ –21.6 (*c* 0.63, CHCl₃); Chiral HPLC AD-H (90:10 hexane/IPA, flow rate 1.0 mL min⁻¹, 211 nm, 30 °C) *t*_R minor: 11.9 min, *t*_R major: 17.7 min, >99% ee; ν_{\max} (film, cm⁻¹) 3279 (N–H), 3252 (N–H), 1636 (C=O), 1558 (N–C=O), 1495, 1454; ¹H NMR (400 MHz, CDCl₃) δ _H: 0.87 (3H, t, *J* 6.9, CH₃), 1.19–1.34 (4H, m, C(2)CH₂(CH₂)₂), 1.52–1.60 (2H, m, C(2)CH₂), 2.41–2.51 (2H, m, C(2)H and C(4)H^AH^B), 2.89 (1H, dd, *J* 13.8, 7.0, C(4)H^AH^B), 3.38 (1H, q, *J* 8.0, C(3)H), 4.13 (1H, dd, *J* 14.7, 5.1, N¹CH^AH^B), 4.26 (1H, dd, *J* 14.8, 5.4, N⁵CH^AH^B), 4.30 (1H, dd, *J* 14.8, 6.2, N¹CH^AH^B), 4.36 (1H, dd, *J* 14.8, 6.1, N⁵CH^AH^B), 5.48 (1H, t, *J* 5.3, N¹H), 5.96 (1H, t, *J* 5.1, N⁵H), 6.90–6.95 (2H, m, ArH), 6.98–7.03 (2H, m, ArH), 7.11–7.16 (2H, m, ArH), 7.19–7.26 (9H, m, ArH); ¹³C{¹H} NMR (101 MHz, CDCl₃) 14.0 (CH₃), 22.7 (CH₂), 29.8 (CH₂), 30.2 (C(2)CH₂), 40.7 (C(4)), 43.3 (NCH₂), 43.5 (NCH₂), 45.3 (C(3)), 52.2 (C(2)), 127.0 (ArCH), 127.28 (ArCH), 127.32 (ArCH), 127.6 (ArCH \times 2), 127.8 (ArCH \times 2), 128.3 (ArCH \times 2), 128.50 (ArCH \times 2), 128.53 (ArCH \times 2), 128.6 (ArCH \times 2), 138.0 (NCH₂ArC), 138.1 (NCH₂ArC), 141.4 (C(3)ArC(1)), 171.4 (C(5)), 173.2 (C(1)); *m/z*

(NSI⁺) 443 ([M + H]⁺, 100%); HRMS (NSI⁺) C₂₉H₃₅O₂N₂ [M + H]⁺ found 443.2692, requires 443.2653 (–0.2 ppm).

(2*S*,3*S*)-*N*¹,*N*⁵-Dibenzyl-3-(4-fluorophenyl)-2-(4-methoxybenzyl)pentanediamide (**26**). Following the general procedure, 1-(4-methoxyphenyl)-3-oxopropan-2-yl 4-nitrobenzoate (99 mg, 0.30 mmol), (*E*)-1,1,1-trichloro-4-(4-fluorophenyl)but-3-en-2-one (54 mg, 0.20 mmol), NHC precatalyst **11** (3.7 mg, 0.010 mmol), and Et₃N (42 μ L, 0.30 mmol) in anhydrous CH₂Cl₂ (2.7 mL) at rt for 6 h gave a crude brown oil (>95:5 dr). The crude was stirred in anhydrous CH₂Cl₂ (6.6 mL) with benzylamine (6.6 mL, 60 mmol) at rt for 16 h to give a crude yellow solid (>95:5 dr) that was triturated in Et₂O to give the title compound (61 mg, 60%) as a beige solid. Mp 221–223 °C; [α]_D²⁰ –23.9 (*c* 0.41, DMSO); Chiral HPLC AD-H (90:10 hexane/IPA, flow rate 1.5 mL min⁻¹, 211 nm, 40 °C) *t*_R major: 16.9 min, *t*_R minor: 21.2 min, 98% ee; ν_{\max} (film, cm⁻¹) 3343 (N–H), 3296 (N–H), 1639 (C=O), 1553 (N–C=O), 1454, 1422, 1356; ¹H NMR (700 MHz, CDCl₃) δ _H: 2.52 (1H, dd, *J* 14.0, 8.5, C(4)H^AH^B), 2.71–2.78 (1H, m, C(2)H), 2.77–2.83 (1H, m, C(2)CH^AH^B), 2.85–2.93 (2H, m, C(4)H^AH^B and C(2)CH^AH^B), 3.48 (1H, q, *J* 8.1, C(3)H), 3.79 (3H, s, OCH₃), 4.00 (1H, dd, *J* 14.8, 5.6, N¹CH^AH^B), 4.12 (1H, dd, *J* 14.9, 6.0, N¹CH^AH^B), 4.28 (1H, dd, *J* 14.7, 5.5, N⁵CH^AH^B), 4.38 (1H, dd, *J* 14.7, 6.0, N⁵CH^AH^B), 5.41 (1H, t, *J* 5.6, N¹H), 5.78 (1H, t, *J* 5.1, N⁵H), 6.67–6.71 (2H, m, ArH), 6.75–6.80 (2H, m, ArH), 6.89–6.95 (1H, m, ArH), 7.00–7.03 (1H, m, ArH), 7.03–7.06 (1H, m, ArH), 7.12–7.18 (4H, m, ArH), 7.24–7.28 (6H, m, ArH); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ _C: 35.7 (C(2)CH₂), 40.7 (C(4)), 43.0 (N¹CH₂), 43.5 (N⁵CH₂), 44.4 (C(3)), 54.4 (C(2)), 55.2 (OCH₃), 113.9 (C(2)CH₂ArC(3,5)), 115.3 (d, *J*_{CF} 21.2, C(3)ArC(3,5)), 127.2 (NCH₂ArC(4)), 127.5 (NCH₂ArC(4) and N¹CH₂ArC(2,6)), 127.6 (N⁵CH₂ArC(2,6)), 128.4 (NCH₂ArC(3,5)), 128.6 (NCH₂ArC(3,5)), 129.87 (C(2)ArC(2,6)), 129.93 (d, *J*_{CF} 7.8, C(3)ArC(2,6)), 131.1 (C(2)ArC(1)), 137.0 (d, *J*_{CF} 3.0, C(3)ArC(1)), 137.8 (NCH₂ArC), 137.9 (NCH₂ArC), 158.2 (C(2)CH₂ArC(4)), 161.9 (d, *J*_{CF} 245.3, C(3)ArC(4)), 170.9 (C(5)), 172.2 (C(1)); ¹⁹F NMR (376 MHz, CDCl₃) δ _F: –115.57 (s, C(3)ArC(4)F); *m/z* (NSI⁺) 547 ([M + Na]⁺, 43%), 525 ([M + H]⁺, 100%); HRMS (NSI⁺) C₃₃H₃₄O₃N₂F [M + H]⁺ found 525.2554, requires 525.2548 (+1.1 ppm).

(2*S*,3*S*)-2-(Benzo[d][1,3]dioxol-5-ylmethyl)-*N*¹,*N*⁵-dibenzyl-3-phenylpentanediamide (**27**). Following the general procedure, 1-(benzo[d][1,3]dioxol-5-yl)-3-oxopropan-2-yl 4-nitrobenzoate (103 mg, 0.30 mmol), (*E*)-1,1,1-trichloro-4-phenylbut-3-en-2-one **1** (50 mg, 0.20 mmol), NHC precatalyst **11** (3.7 mg, 0.010 mmol), and Et₃N (42 μ L, 0.30 mmol) in anhydrous CH₂Cl₂ (2.7 mL) at rt for 27 h gave a crude brown oil (85:15 dr). The crude was stirred in anhydrous CH₂Cl₂ (6.6 mL) with benzylamine (6.6 mL, 60 mmol) at rt for 16 h to give a crude brown solid (80:20 dr) that was triturated in Et₂O to give the title compound (50 mg, 48%) as an off-white solid. Mp 198 °C (*dec*); [α]_D²⁰ –39.4 (*c* 0.18, CHCl₃); no ee could be determined by either chiral HPLC or chiral GC; ν_{\max} (film, cm⁻¹) 3296 (N–H), 1643 (C=O), 1553 (N–C=O), 1499, 1487, 1354; ¹H NMR (400 MHz, CDCl₃) δ _H: 2.57 (1H, dd, *J* 14.0, 8.3, C(4)H^AH^B), 2.74–2.84 (2H, m, C(2)H and C(2)CH^AH^B), 2.84–2.96 (2H, m, C(2)H^AH^B and C(4)H^AH^B), 3.43–3.52 (1H, m, C(3)H), 4.01–4.15 (2H, m, NCH₂), 4.26–4.40 (2H, m, NCH₂), 5.43 (1H, t, *J* 5.2, NH), 5.83 (1H, t, *J* 5.3, NH), 5.88–5.94 (2H, m, OCH₂O), 6.56–6.62 (1H, m, C(2)CH₂ArH), 6.62–6.70 (2H, m, C(2)CH₂ArH), 6.70–6.75 (2H, m, ArH), 6.99–7.05 (2H, m, ArH), 7.12–7.21 (5H, m, ArH), 7.22–7.25 (6H, m, ArH); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ _C: 36.2 (C(2)CH₂), 40.5 (C(4)), 43.0 (NCH₂), 43.5 (NCH₂), 45.2 (C(3)), 54.4 (C(2)), 100.8 (OCH₂O), 109.3 (C(2)CH₂ArCH), 121.9 (C(2)CH₂ArCH), 127.1 (ArCH \times 2), 127.4 (ArCH), 127.5 (ArCH \times 2), 127.6 (ArCH \times 2), 128.3 (ArCH \times 2), 128.4 (ArCH \times 2), 128.6 (ArCH \times 2), 128.6 (ArCH \times 2), 133.1 (C(2)CH₂ArC(1)), 137.8 (NCH₂ArC(1)), 138.0 (NCH₂ArC(1)), 141.2 (C(3)ArC(1)), 146.0 (C(2)CH₂ArC(2a or 6a)), 147.6 (C(2)CH₂ArC(6a or 2a)), 171.2 (C=O), 172.2 (C=O); *m/z* (NSI⁺) 543 ([M + Na]⁺, 31%), 521 ([M + H]⁺, 100%); HRMS (NSI⁺) C₃₃H₃₅O₄N₂ [M + H]⁺ found 521.2440, requires 521.2435 (+1.0 ppm).

(2*S*,3*S*)-*N*¹,*N*⁵-Dibenzyl-3-(4-methoxyphenyl)-2-methylpentanediamide (**28**). Following the general procedure, 1-oxopropan-2-yl 4-

nitrobenzoate **10** (67 mg, 0.30 mmol), (*E*)-1,1,1-trichloro-4-(4-methoxyphenyl)but-3-en-2-one (56 mg, 0.20 mmol), NHC precatalyst **11** (3.7 mg, 0.010 mmol), and Et₃N (42 μ L, 0.30 mmol) in anhydrous CH₂Cl₂ (2.7 mL) at rt for 22 h gave a crude yellow solid (>95:5 dr). The crude was stirred in anhydrous CH₂Cl₂ (6.6 mL) with benzylamine (6.6 mL, 60 mmol) at rt for 16 h to give a crude light yellow solid (>95:5 dr) that was triturated in Et₂O to give the title compound (64 mg, 75%) as a white solid. Mp 176–178 °C; [α]_D²⁰ –12.8 (c 0.56, CHCl₃); Chiral HPLC AD-H (90:10 hexane/IPA, flow rate 1.0 mL·min^{–1}, 211 nm, 30 °C) *t*_R minor: 18.1 min, *t*_R major: 24.8 min, >99% ee; ν_{max} (film, cm^{–1}) 3273 (N–H), 1636 (C=O), 1558 (N–C=O), 1508, 1454, 1429, 1350, 1242; ¹H NMR (400 MHz, CDCl₃) δ_{H} : 1.22 (3H, d, *J* 6.9, C(2)CH₃), 2.46 (1H, dd, *J* 13.8, 8.8, C(4)H^AH^B), 2.64 (1H, p, *J* 6.9, C(2)H), 2.91 (1H, dd, *J* 13.8, 6.8, C(4)H^AH^B), 3.32 (1H, q, *J* 8.0, C(3)H), 3.81 (3H, s, OCH₃), 4.15 (1H, dd, *J* 14.7, 5.1, N¹CH^AH^B), 4.25 (1H, dd, *J* 14.9, 5.3, N⁵CH^AH^B), 4.37 (1H, dd, *J* 14.8, 6.4, N¹CH^AH^B), 4.42 (1H, dd, *J* 14.9, 6.3, N⁵CH^AH^B), 5.60 (1H, t, *J* 5.5, N¹H), 6.08 (1H, t, *J* 5.4, N⁵H), 6.74–6.82 (2H, m, C(3)ArC(3,5)H), 6.91–6.98 (2H, m, ArH), 6.99–7.05 (2H, m, ArH), 7.05–7.11 (2H, m, C(3)ArC(2,6)H), 7.21–7.28 (6H, m, ArH); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ_{C} : 16.0 (C(2)CH₃), 40.8 (C(4)), 43.3 (N¹CH₂), 43.4 (N⁵CH₂), 45.6 (C(3)), 45.9 (C(2)), 55.2 (OCH₃), 113.9 (C(3)ArC(3,5)), 127.26 (ArCH), 127.33 (ArCH), 127.5 (ArCH), 127.7 (ArCH), 128.5 (ArCH), 129.2 (C(3)ArC(2,6)), 133.2 (C(3)ArC(1)), 137.9 (NCH₂ArC(1)), 138.1 (NCH₂ArC(1)), 158.6 (C(3)ArC(4)), 171.5 (C(5)), 174.1 (C(1)); *m/z* (NSI⁺) 883 ([2M + Na]⁺, 30%), 453 ([M + Na]⁺, 58%), 431 ([M + H]⁺, 100%); HRMS (NSI⁺) C₂₇H₃₁O₃N₂ [M + H]⁺ found 431.2328, requires 431.2329 (–0.3 ppm).

(2*S*,3*S*)-*N*¹,*N*⁵-Dibenzyl-2-methyl-3-(2-nitrophenyl)pentanedi-
amide (**29**). Following the general procedure, 1-oxopropan-2-yl 4-nitrobenzoate **10** (67 mg, 0.30 mmol), (*E*)-1,1,1-trichloro-4-(2-nitrophenyl)but-3-en-2-one (59 mg, 0.20 mmol), NHC precatalyst **11** (3.7 mg, 0.010 mmol), and Et₃N (42 μ L, 0.30 mmol) in anhydrous CH₂Cl₂ (2.7 mL) at rt for 2 h gave a crude brown oil (>95:5 dr). The crude was stirred in anhydrous CH₂Cl₂ (6.6 mL) with benzylamine (6.6 mL, 60 mmol) at rt for 16 h to give a crude light yellow solid (approximately 90:10 dr) that was triturated in Et₂O to give the title compound (60 mg, 68%) as a brown solid. Mp 176 °C (*dec.*); [α]_D²⁰ –2.3 (c 0.61, CHCl₃); Chiral HPLC AD-H (95:5 hexane/IPA, flow rate 1.5 mL·min^{–1}, 211 nm, 30 °C) *t*_R major: 63.9 min, *t*_R minor: 70.9 min, 99% ee; ν_{max} (film, cm^{–1}) 3292 (N–H), 1636 (C=O), 1558 (N–C=O), 1541 (N–C=O), 1522, 1456, 1354; ¹H NMR (400 MHz, CDCl₃) δ_{H} : 1.21 (3H, d, *J* 6.9, C(2)CH₃), 2.60 (1H, dd, *J* 15.0, 9.3, C(4)H^AH^B), 2.80 (1H, p, *J* 7.1, C(2)H), 2.87 (1H, dd, *J* 15.0, 5.9, C(4)H^AH^B), 3.94–4.04 (1H, m, C(3)H), 4.21–4.34 (4H, m, NCH₂ × 2), 6.06 (1H, t, *J* 4.9, NH), 6.31 (1H, t, *J* 5.4, NH), 6.98–7.08 (4H, m, ArH), 7.18–7.25 (5H, m, ArH), 7.2–7.36 (1H, m, C(3)ArC(5)H), 7.36–7.41 (1H, m, C(3)ArC(3)H), 7.42–7.49 (1H, m, C(3)ArC(4)H), 7.66 (2H, dd, *J* 8.1, 1.2, C(3)ArC(6)H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ_{C} : 15.1 (C(2)CH₃), 38.6 (C(4)), 43.4 (NCH₂), 43.5 (NCH₂), 45.2 (C(2)), 124.6 (C(3)ArC(6)), 127.3 (ArCH), 127.4 (ArCH), 127.6 (ArCH), 127.6 (ArCH), 128.6 (ArCH), 132.6 (C(3)ArC(4)), 135.9 (C(3)ArC(1)), 137.9 (NCH₂ArC(1)), 138.1 (NCH₂ArC(1)), 150.3 (C(3)ArC(2)), 170.4 (C(5)), 173.8 (C(1)), C(3) and C(3)ArC(3) not observed; *m/z* (NSI⁺) 468 ([M + Na]⁺, 33%), 446 ([M + H]⁺, 100%); HRMS (NSI⁺) found C₂₆H₂₈O₄N₃ found 446.2072, requires 446.2074 (–0.5 ppm).

(2*S*,3*S*)-*N*¹,*N*⁵-Dibenzyl-3-(4-fluorophenyl)-2-methylpentanedi-
amide (**30**). Following the general procedure, 1-oxopropan-2-yl 4-nitrobenzoate **10** (67 mg, 0.30 mmol), (*E*)-1,1,1-trichloro-4-(4-fluorophenyl)but-3-en-2-one (54 mg, 0.20 mmol), NHC precatalyst **11** (3.7 mg, 0.010 mmol), and Et₃N (42 μ L, 0.30 mmol) in anhydrous CH₂Cl₂ (2.7 mL) at rt for 3 h gave a crude brown oil (>95:5 dr). The crude was stirred in anhydrous CH₂Cl₂ (6.6 mL) with benzylamine (6.6 mL, 60 mmol) at rt for 16 h to give a crude beige solid (>95:5 dr) that was triturated in Et₂O to give the title compound (76 mg, 90%) as a white solid. Mp 204–206 °C; [α]_D²⁰ –2.5 (c 0.52, DMSO); Chiral HPLC AD-H (90:10 hexane/IPA, flow rate 1.0 mL·min^{–1}, 211 nm, 30 °C) *t*_R minor: 12.8 min, *t*_R major: 19.1 min, > 99% ee; ν_{max} (film,

cm^{–1}) 3292 (N–H), 1645 (C=O), 1541 (N–C=O), 1508, 1495, 1456, 1219; ¹H NMR (400 MHz, CDCl₃) δ_{H} : 1.22 (3H, d, *J* 6.9, C(2)CH₃), 2.45 (1H, dd, *J* 13.8, 8.7, C(4)H^AH^B), 2.65 (1H, p, *J* 7.0, C(2)H), 2.91 (1H, dd, *J* 13.8, 6.8, C(4)H^AH^B), 3.38 (1H, q, *J* 8.0, C(3)H), 4.16 (1H, dd, *J* 14.7, 5.1, N¹CH^AH^B), 4.26 (1H, dd, *J* 14.7, 5.3, N⁵CH^AH^B), 4.37 (1H, dd, *J* 15.1, 6.8, N¹CH^AH^B), 4.42 (1H, dd, *J* 14.9, 6.4, N⁵CH^AH^B), 5.61 (1H, t, *J* 5.5, N¹H), 6.01 (1H, t, *J* 5.5, N⁵H), 6.88–6.94 (1H, m, C(3)ArC(3)H), 6.94–6.98 (2H, m, ArH × 1 and C(3)ArC(5)H), 7.00–7.06 (2H, m, ArH), 7.09–7.16 (2H, m, C(3)ArC(2,6)H), 7.23–7.28 (7H, m, ArH); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ_{C} : 16.1 (C(2)CH₃), 40.7 (C(4)), 43.3 (NCH₂), 43.5 (NCH₂), 45.7 (C(2)), 45.7 (C(3)), 115.3 (d, *J*_{CF} 21.1, C(2)ArC(3,5)), 127.4 (NCH₂ArC(4)), 127.5 (NCH₂ArC(4)), 127.6 (ArCH × 2), 127.7 (ArCH × 2), 128.6 (ArCH × 4), 129.8 (d, *J*_{CF} 7.9, C(3)ArC(2,6)), 136.9 (d, *J*_{CF} 3.1, C(3)ArC(1)), 137.8 (NCH₂ArC(1)), 138.0 (NCH₂ArC(1)), 161.9 (d, *J*_{CF} 245.3, C(3)ArC(4)), 171.2 (C(5)), 173.8 (C(1)); ¹⁹F (376 MHz, CDCl₃) δ_{F} : –115.60 (s, C(3)ArC(4)F); *m/z* (NSI⁺) 441 ([M + Na]⁺, 51%), 419 ([M + H]⁺, 100%); HRMS (NSI⁺) [M + H]⁺ C₂₆H₂₈O₂N₂F found 419.2129, requires 419.2129 (–0.1 ppm).

(2*S*,3*S*)-*N*¹,*N*⁵-Dibenzyl-3-(furan-2-yl)-2-methylpentanedi-
amide (**31**). Following the general procedure, 1-oxopropan-2-yl 4-nitrobenzoate **10** (67 mg, 0.30 mmol), (*E*)-1,1,1-trichloro-4-(furan-2-yl)but-3-en-2-one (48 mg, 0.20 mmol), NHC precatalyst **11** (3.7 mg, 0.010 mmol), and Et₃N (42 μ L, 0.30 mmol) in anhydrous CH₂Cl₂ (2.7 mL) at rt for 3 h gave a crude brown crystallized oil (95:5 dr). The crude was stirred in anhydrous CH₂Cl₂ (6.6 mL) with benzylamine (6.6 mL, 60 mmol) at rt for 16 h to give a crude beige solid (>95:5 dr) that was triturated in Et₂O to give the title compound (58 mg, 75%) as a beige solid. Mp 192–194 °C; [α]_D²⁰ –1.4 (c 0.50, CHCl₃); Chiral HPLC AD-H (90:10 hexane/IPA, flow rate 1.0 mL·min^{–1}, 211 nm, 30 °C) *t*_R major: 19.8 min, *t*_R minor: 27.6 min, >99% ee; ν_{max} (film, cm^{–1}) 3279 (N–H), 1645 (C=O), 1562 (N–C=O), 1541 (N–C=O), 1506, 1456; ¹H NMR (400 MHz, CDCl₃) δ_{H} : 1.19 (3H, d, *J* 7.0, C(2)CH₃), 2.53 (1H, dd, *J* 13.9, 8.5, C(4)H^AH^B), 2.71 (1H, p, *J* 7.0, C(2)H), 2.80 (1H, dd, *J* 13.9, 6.7, C(4)H^AH^B), 3.49–3.58 (1H, m, C(3)H), 4.25–4.36 (3H, m, N¹CH₂ and N⁵CH^AH^B), 4.41 (1H, dd, *J* 14.8, 6.0, N⁵CH^AH^B), 5.76 (1H, t, *J* 5.2, N¹H), 6.06–6.10 (1H, m, C(3)ArC(5)H), 6.15 (1H, t, *J* 4.9, N⁵H), 6.25 (1H, dd, *J* 3.2, 1.9, C(3)ArC(4)H), 7.10–7.18 (4H, m, ArH), 7.22 (1H, dd, *J* 1.8, 0.8, C(3)ArC(3)H), 7.23–7.32 (6H, m, ArH); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ_{C} : 15.2 (C(2)CH₃), 38.2 (C(4)), 39.8 (C(3)), 45.54 (NCH₂Ph), 45.55 (NCH₂Ph), 43.9 (C(2)), 107.3 (C(3)ArC(5)), 110.3 (C(3)ArC(4)), 127.4 (ArCH), 127.5 (ArCH), 127.7 (ArCH), 127.9 (ArCH), 128.60 (ArCH), 128.61 (ArCH), 138.0 (NCH₂ArC(1)), 138.2 (NCH₂ArC(1)), 141.4 (C(3)ArC(3)), 154.6 (C(3)ArC(1)), 171.1 (C(5)), 173.9 (C(1)); *m/z* (NSI⁺) 413 ([M + Na]⁺, 41%), 391 ([M + H]⁺, 100%); HRMS (NSI⁺) C₂₄H₂₇O₃N₂ [M + H]⁺ found 391.2016, requires 391.2016 (+0.0 ppm).

(2*S*,3*S*)-*N*¹,*N*⁵-2-Tribenzyl-3-(furan-2-yl)pentanedi-
amide (**32**). Following the general procedure, 1-oxo-3-phenylpropan-2-yl 4-nitrobenzoate (90 mg, 0.30 mmol), (*E*)-1,1,1-trichloro-4-(furan-2-yl)but-3-en-2-one (48 mg, 0.20 mmol), NHC precatalyst **11** (3.7 mg, 0.010 mmol), and Et₃N (42 μ L, 0.30 mmol) in anhydrous THF (2.7 mL) at rt for 4 h gave a crude brown oil (>95:5 dr). The crude was stirred in anhydrous CH₂Cl₂ (6.6 mL) with benzylamine (6.6 mL, 60 mmol) at rt for 16 h to give a crude orange solid (>95:5 dr) that was triturated in Et₂O to give the title compound (36 mg, 39%) as an off-white solid. Mp 192–194 °C; [α]_D²⁰ –17.3 (c 0.48, CHCl₃); Chiral HPLC AD-H (80:20 hexane/IPA, flow rate 1.5 mL·min^{–1}, 211 nm, 40 °C) *t*_R major: 5.6 min, *t*_R minor: 13.0 min, >99% ee; ν_{max} (film, cm^{–1}) 3275 (N–H), 1638 (C=O), 1560 (N–C=O), 1533, 1495, 1452; ¹H NMR (400 MHz, CDCl₃) δ_{H} : 2.61 (1H, dd, *J* 14.0, 8.3, C(4)H^AH^B), 2.83–2.99 (4H, m, C(4)H^AH^B, C(2)H, C(2)CH₂), 3.59–3.68 (1H, m, C(3)H), 4.14 (1H, dd, *J* 14.8, 5.6, N¹CH^AH^B), 4.21 (1H, dd, *J* 14.8, 5.9, N¹CH^AH^B), 4.31–4.42 (2H, m, N⁵CH₂), 5.62 (1H, t, *J* 5.5, N¹H), 5.98 (1H, t, *J* 5.5, N⁵H), 6.12–6.17 (1H, m, C(3)ArC(5)H), 6.29 (1H, dd, *J* 3.2, 1.9, C(3)ArC(4)H), 6.84–6.90 (2H, m, ArH), 7.10–7.17 (4H, m, ArH), 7.17–7.21 (4H, m, ArH), 7.21–7.25 (3H, m, ArH), 7.26–7.33 (3H, m, ArH); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ_{C} : 35.8

(C(2)CH₂), 38.2 (C(4)), 38.6 (C(3)), 43.3 (N¹CH₂), 43.6 (N⁵CH₂), 52.1 (C(2)), 107.5 (C(3)ArC(4)), 110.4 (C(3)ArC(5)), 126.4 (ArCH), 127.2 (ArCH), 127.4 (ArCH), 127.6 (ArCH × 2), 127.8 (ArCH × 2), 128.4 (ArCH × 2), 128.5 (ArCH × 2), 128.6 (ArCH × 2), 128.9 (ArCH × 2), 137.9 (NCH₂ArC(1)), 138.1 (NCH₂ArC(1)), 139.3 (C(2)CH₂ArC(1)), 141.4 (C(3)ArC(3)), 154.4 (C(3)ArC(1)), 170.9 (C(5)), 172.2 (C(1)); *m/z* (NSI⁺) 489 ([M + Na]⁺, 34%), 467 ([M + H]⁺, 100%); HRMS (NSI⁺) C₃₀H₃₁O₃N₂ [M + H]⁺ found 467.2326, requires 467.2329 (−0.7 ppm).

(2*S*,3*S*)-*N*¹,*N*⁵-Dibenzyl-3-methyl-3-pentylpentanediamide (**33**). Following the general procedure, 1-oxopropan-2-yl 4-nitrobenzoate **10** (67 mg, 0.30 mmol), (E)-1,1,1-trichloronon-3-en-2-one (**56** mg, 0.20 mmol), NHC precatalyst **11** (7.4 mg, 0.020 mmol), and Et₃N (42 μL, 0.30 mmol) in anhydrous CH₂Cl₂ (2.7 mL) at rt for 24 h gave a crude brown oil (>95:5 dr). The crude was stirred in anhydrous CH₂Cl₂ (6.6 mL) with benzylamine (6.6 mL, 60 mmol) at rt for 16 h to give a crude orange paste (>95:5 dr) that was triturated in Et₂O to give the title compound (21 mg, 26%) as a white solid. Mp 168–170 °C; [α]_D²⁰ +15.0 (c 0.40, CHCl₃); Chiral HPLC AD-H (90:10 hexane/IPA, flow rate 1.0 mL·min^{−1}, 211 nm, 40 °C) *t*_R minor: 5.3 min, *t*_R major: 5.8 min, >99% ee; *ν*_{max} (film, cm^{−1}) 3287 (N–H), 1636 (C=O), 1541 (N–C=O), 1535 (N–C=O), 1454; ¹H NMR (400 MHz, CDCl₃) δ_H: 0.86 (3H, t, *J* 6.8, CH₃), 1.12 (3H, d, *J* 7.0, C(2)CH₃), 1.16–1.36 (7H, m, CH₃(CH₂)₃ and C(3)CH^AH^B), 1.43–1.53 (1H, m, C(3)CH^AH^B), 1.95–2.07 (1H, m, C(3)H), 2.22 (1H, dd, *J* 13.9, 6.1, C(4)H^AH^B), 2.29 (1H, dd, *J* 13.9, 8.0, C(4)H^AH^B), 2.50–2.59 (1H, m, C(2)H), 4.39–4.44 (4H, m, NCH₂ × 2), 6.14 (1H, t, *J* 4.8, N⁵H), 6.48 (1H, t, *J* 5.1, N¹H), 7.23–7.35 (10H, m, ArH); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ_C: 14.0 (C(2)CH₃), 14.1 (CH₃), 22.6 (CH₃CH₂), 27.3 (CH₃(CH₂)₂CH₂), 31.1 (C(3)CH₂), 31.9 (CH₃CH₂CH₂), 38.7 (C(4)), 40.0 (C(3)), 42.1 (C(2)), 43.4 (NCH₂), 43.5 (NCH₂), 127.4 (ArCH), 127.5 (ArCH), 127.7 (ArCH), 127.8 (ArCH), 128.7 (ArCH), 128.7 (ArCH), 138.4 (NCH₂ArC(1)), 138.6 (NCH₂ArC(1)), 172.9 (C(5)), 174.7 (C(1)); *m/z* (NSI⁺) ([2M + Na]⁺, 34%), 395 ([M + H]⁺, 100%); HRMS (NSI⁺) C₂₅H₃₅O₂N₂ [M + H]⁺ found 395.2690, requires 395.2693.

■ ASSOCIATED CONTENT

■ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01820.

¹H and ¹³C{¹H} NMR spectra and HPLC traces of all novel compounds (PDF)

X-ray crystallographic data for **28** (CIF)

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Notes

The authors declare no competing financial interest.

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