#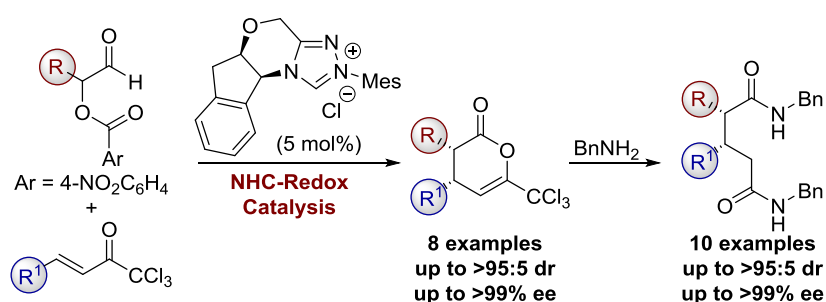 Enantioselective NHC-Catalyzed Redox [4+2]-hetero-Diels-Alder Reactions using α,β-Unsaturated Trichloromethyl ketones as Amide Equivalents

Nassilia Attaba, James E. Taylor, Alexandra M. Z. Slawin, and Andrew D. Smith*

EaStCHEM, School of Chemistry, University of St Andrews, North Haugh, St Andrews, KY16 9ST, U.K.

E-mail: ads10@st-andrews.ac.uk

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-aroyloxyaldehydes. 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 cyclopropanes[6] (Scheme 1a).

We have demonstrated that α-aroyloxyaldehydes 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-aroyloxyaldehydes react with substituted trifluoromethyl ketones to form dihydropyranones with high levels of stereoselectivity (Scheme 1b).[7d] The NHC-catalyzed redox reaction of α-aroyloxyaldehydes and *N*-aryl-*N'*-aroyldiazenes 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 decreased electrophilicity of these substrates. This problem has been overcome in other Lewis based-catalyzed conjugate 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
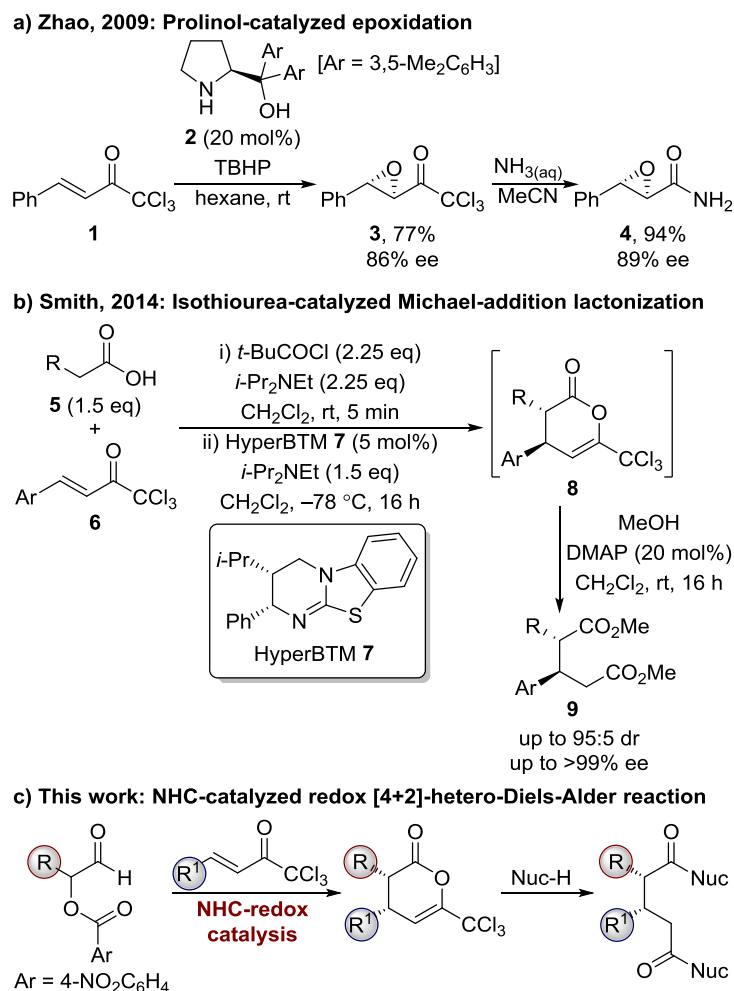
Scheme 1. Azolium enolate precursors for [4+2] hetero-Diels-Alder reactions

a) NHC-catalyzed redox azolium enolate precursors

b) α-Aroyloxyaldehydes in NHC-catalyzed redox [4+2] cycloadditions
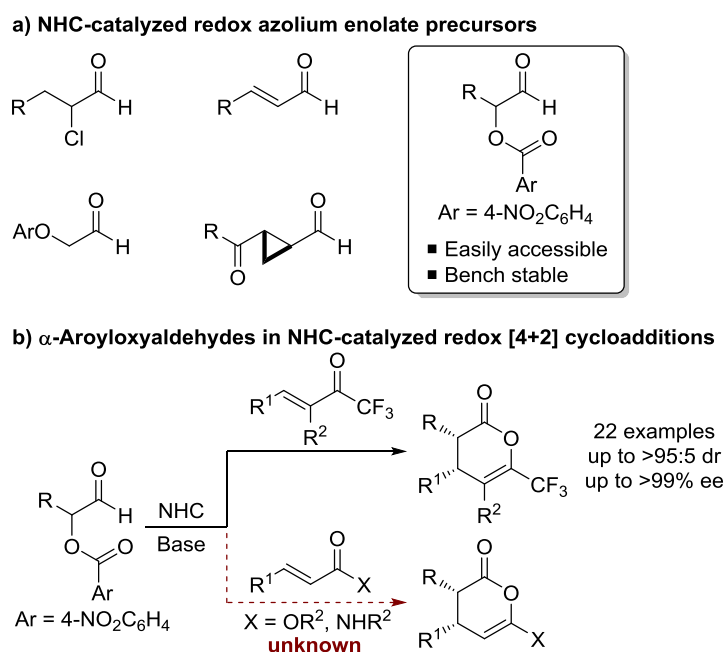
ketones.[16,17] However, the use of α,β-unsaturated amide and ester equivalents in NHC-catalyzed cycloaddition reactions remains unexplored.

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-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

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

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-aroyloxyaldehydes 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 isothiourea-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-aroyloxyaldehyde **10** and α,β-unsaturated trichloromethyl ketone **1** was studied. α-Aroyloxyaldehydes 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-aroyloxyaldehyde **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). 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

Table 1. Reaction optimization[a]
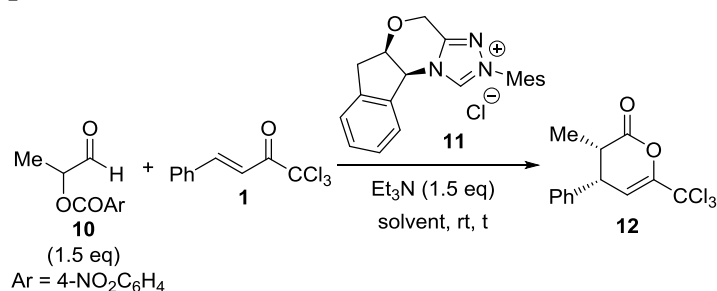
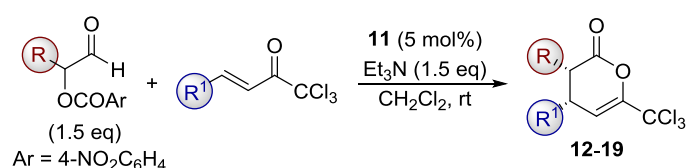| Entry	Solvent	**11** (mol%)	t / h	dr[b]	Yield (%)	ee (%)[c]
1	THF	10	5	>95:5	57	>99
2	Et$_2$O	10	1.5	>95:5	55	>99
3	PhMe	10	1.5	>95:5	55	>99
4	CH$_2$Cl$_2$	10	1	>95:5	67	>99
5	CH$_2$Cl$_2$	5	3.5	>95:5	66	>99
6[d]	CH$_2$Cl$_2$	5	3.5	>95:5	84	>99

[a]Reactions performed on 0.2 mmol scale. [b]Determined by analysis of crude ^{1}H NMR spectra. [c]Determined by chiral HPLC analysis. [d]Reaction performed on a 1.2 mmol scale.

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 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 hours under the standard reaction conditions using 5 mol% **11**, with both diastereoisomers formed with high enantioselectivity (98% ee$_{syn}$, >99% ee$_{anti}$). Increasing

**Table 2. Use of trichloromethyl ketones in NHC-redox catalyzed [4+2] hetero-Diels-Alder reactions**

Product Yield[a] (time)	dr[b] ee[c]	Product Yield[a] (time)	dr[b] 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% (24 h)[e]	85:15 (N/D)[f]	**17** 93% (3 h)	>95:5 (>99%)
18 81% (2 h)	>95:5 (>99%)	**19** 26% (24 h)[d]	>95:5 (>99%)

[a]Isolated yield of major *syn*-diastereoisomer. [b]Determined by analysis of crude ^{1}H NMR spectra. [c]Determined by chiral HPLC analysis. [d]Reaction performed using 10 mol% **11**. [e]Isolated as a mixture of diastereoisomers. [f]ee could not be determined by either chiral HPLC or chiral GC analysis.

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 hours using 5 mol% **11**, whereas increasing the catalyst loading to 10 mol% allowed a single diastereoisomer to be isolated in 65% yield after 4 hours in >99% ee. Within the trichloromethyl ketone, β-aryl groups containing electron-donating (4-MeOC$_6$H$_4$) and electron-withdrawing halogen (4-BrC$_6$H$_4$) 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 CD$_2$Cl$_2$ 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 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.

Scheme 3. Base-promoted epimerization of 14
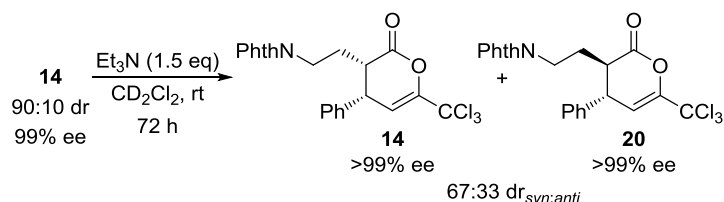
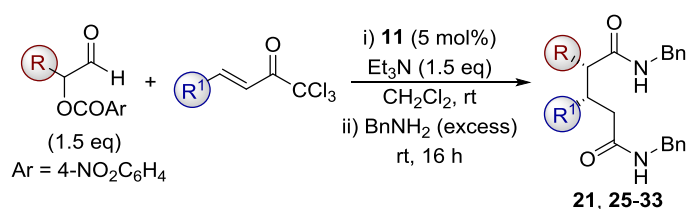## Trichloromethyl ketones as Ester and Amide Equivalents.

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 CCl_3 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

Scheme 4. Use of trichloromethyl ketones as ester and amide equivalents
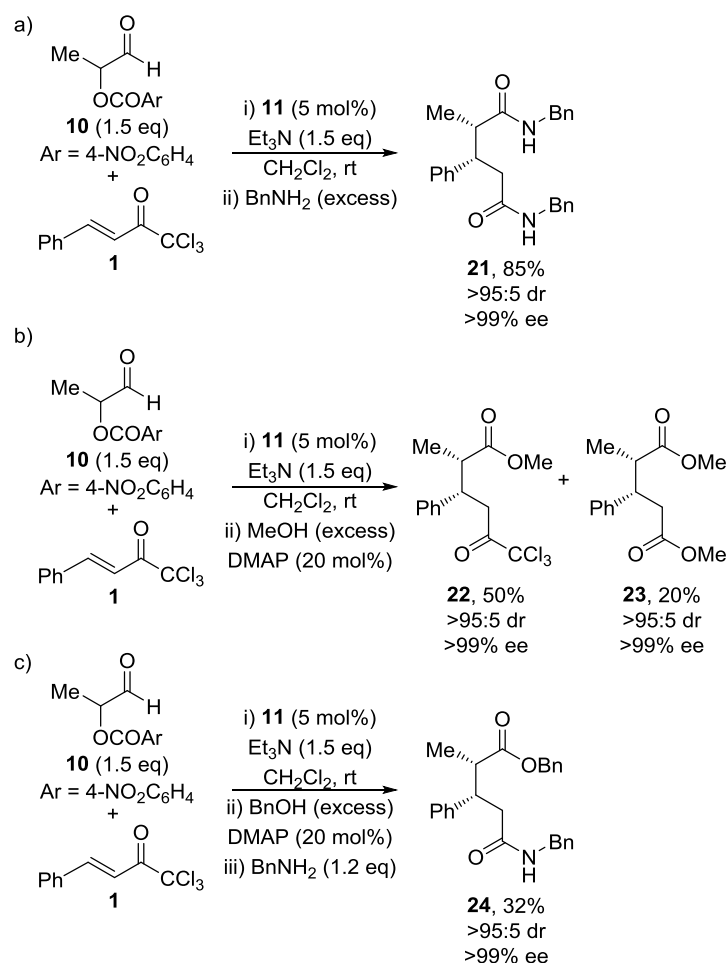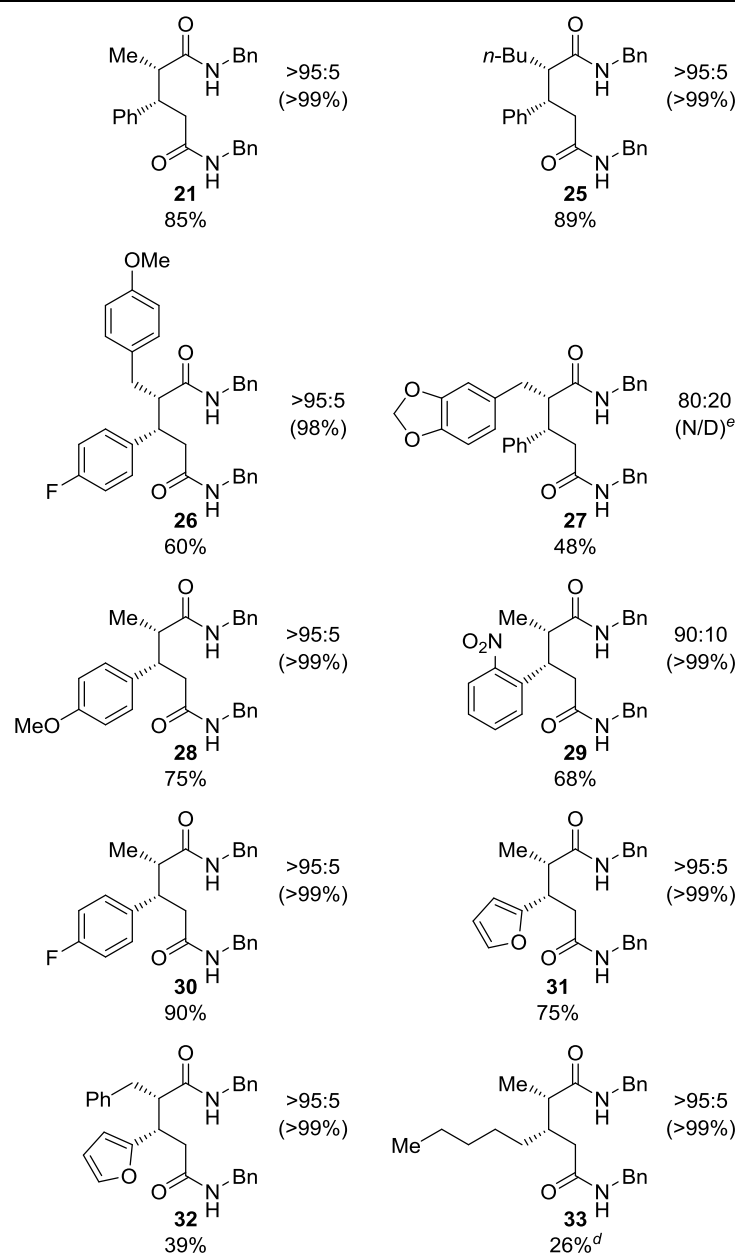
stereoselectivity (Scheme 4b).[24] The observation that only partial alcoholysis of the CCl$_3$ ketone had occurred led to the possibility of a sequential ring-opening and CCl$_3$ ketone displacement using two different nucleophiles. Firstly, benzyl alcohol and DMAP (20 mol%) were used to ring-open the initial *syn*-dihydropyranone product with subsequent addition of benzylamine (1.2 eq) leading to aminolysis of the CCl$_3$ 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 occurs 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 process was

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

Compound	dr	(ee)	yield
21	>95:5	(>99%)	85%
25	>95:5	(>99%)	89%
26	>95:5	(98%)	60%
27	80:20	(N/D)[e]	48%
28	>95:5	(>99%)	75%
29	90:10	(>99%)	68%
30	>95:5	(>99%)	90%
31	>95:5	(>99%)	75%
32	>95:5	(>99%)	39%
33	>95:5	(>99%)	26%[d]

[a]Isolated yield of major *syn*-diastereoisomer. [b]Determined by analysis of crude ^{1}H NMR spectra. [c]Determined by chiral HPLC analysis. [d]Reaction performed using 10 mol% **11**. [e]ee could not be determined by either chiral HPLC or chiral GC analysis.

further assessed using a range of substituted α-aroyloxyaldehydes 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-aroyloxyaldehydes 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-MeOC$_6$H$_4$), electron-withdrawing aryl (2-NO$_2$C$_6$H$_4$) 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-aroyloxyaldehyde, 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-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 using benzylamine or an alcohol, with aminolysis of the resulting trichloromethyl ketone proceeding at a relatively slower rate.

Scheme 5. Proposed mechanism
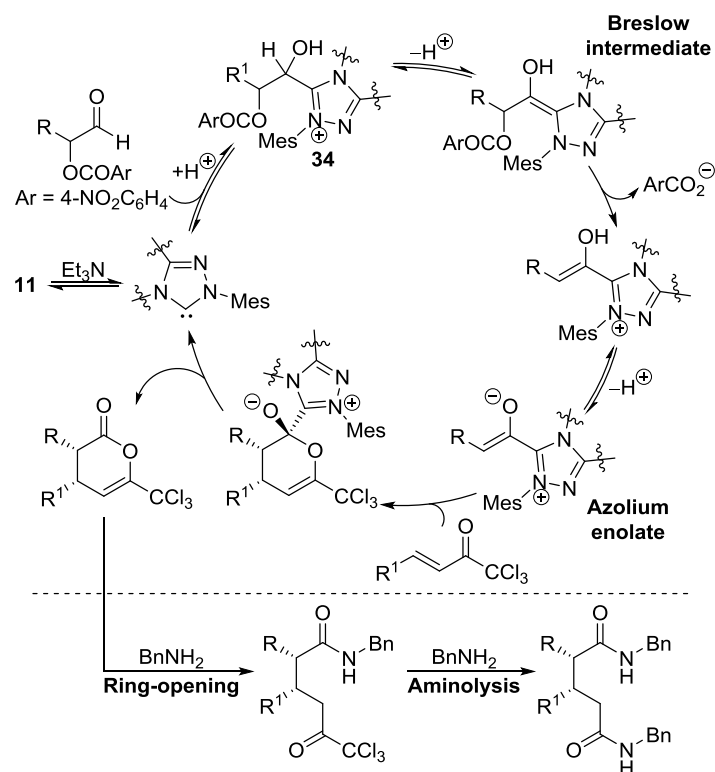
Conclusion

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-aroyloxyaldehydes. 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-aroyloxyaldehydes 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 were 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. ^{1}H NMR spectra were acquired at either 300, 400, 500 or 700 MHz, ^{13}C{^{1}H} NMR spectra were acquired at either 75, 101 or 126 MHz, and ^{19}F{^{1}H} NMR spectra were acquired at either 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 ^{1}H COSY, 2D ^{1}H NOESY, 2D ^{1}H-^{13}C HMBC and 2D ^{1}H-^{13}C HSQC where necessary. Mass spectrometry (*m/z*, HRMS) data were acquired using either atmospheric pressure chemical ionisation (APCI) or nanospray ionisation (NSI) using a TOF mass analyser.

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-Aroyloxyaldehydes

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}; ^{1}H NMR (300 MHz, CDCl$_3$) δ$_H$: 1.59 (3H, d, *J* 7.2, C*H$_3$*), 5.39 (1H, q, *J* 7.2, C*H*CH$_3$), 8.24–8.37 (4H, m, 4-NO$_2$Ar*H*), 9.67 (1H, s, C*H*O).

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}; ^{1}H NMR (300 MHz, CDCl$_3$) δ$_H$: 3.22 (1H, dd, *J* 14.5, 8.4, C*H*^{A}H^B), 3.35 (1H, dd,

J 14.5, 5.0, CH^A*H*^{B}), 5.52 (1H, dd, *J* 8.3, 5.0, C*H*CH$_2$), 7.27–7.38 (4H, m, Ar*H*), 8.15–8.23 (2H, m, 4-NO$_2$Ar*H*), 8.26–8.35 (2H, m, 4-NO$_2$Ar*H*), 9.68 (1H, s, C*H*O).

4-(1,3-Dioxoisoindolin-2-yl)-1-oxobutan-2-yl 4-nitrobenzoate. Phthalic anhydride (4.5 g, 34 mmol, 1.0 eq) and 4-aminobutan-1-ol (3.1 mL, 34 mmol, 1.0 eq) 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-1*H*-isoindole-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}; ^{1}H NMR (500 MHz, CDCl$_3$) δ_H: 1.64 (2H, p, *J* 6.6, NCH$_2$C*H*$_2$), 1.80 (2H, p, *J* 7.3, N(CH$_2$)$_2$C*H*$_2$), 3.71 (2H, t, *J* 6.4, NC*H*$_2$), 3.76 (2H, t, *J* 7.2, N(CH$_2$)$_3$C*H*$_2$), 7.73 (2H, dd, *J* 5.5, 3.0, Ar*H*), 7.86 (2H, dd, *J* 5.4, 3.1, Ar*H*).

A solution of oxalyl chloride (2.3 mL, 27 mmol, 2.0 eq) in CH$_2$Cl$_2$ (50 mL) was cooled to −78 °C before a solution of DMSO (2.14 mL, 30 mmol, 2.2 eq) in CH$_2$Cl$_2$ (10 mL) was added dropwise. After stirring for 15 min a solution of 2-(4-hydroxybutyl)-2,3-dihydro-1*H*-isoindole-1,3-dione (3.0 g, 14 mmol, 1.0 eq) in CH$_2$Cl$_2$ (10 mL) was added dropwise. The reaction mixture was stirred for 15 min before Et$_3$N (5.7 mL, 41 mmol, 3.0 eq) 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$_2$Cl$_2$, washed with 1 M HCl and brine. The organic layer was dried over Na$_2$SO$_4$, 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-1*H*-isoindol-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}; ^{1}H NMR (500 MHz, CDCl$_3$) δ_H: 2.04 (2H, p, *J* 7.0, NCH$_2$C*H*$_2$), 2.51–2.62 (2H, m,

N(CH$_2$)$_2$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-isoindol-2-yl)butanal (1.7 g, 7.9 mmol), 4-nitrobenzoic acid (2.0 g, 12 mmol), *n*-Bu$_4$NI (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$_2$SO$_4$. The phases were separated and the aqueous extracted with EtOAc (× 2). The combined organics were washed with sat. aq. NaHCO$_3$ (× 2) and brine (× 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-dioxoisoindolin-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); ^{1}H NMR (300 MHz, CDCl$_3$) δ$_H$: 2.26–2.38 (1H, m, NCH$_2$CH^AH^B), 2.40–2.51 (1H, m, NCH$_2$CH^AH^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$_2$ArH), 9.62 (1H, s, CHO); ^{13}C{^{1}H} NMR (75 MHz, CDCl$_3$) δ$_C$: 27.4 (NCH$_2$$CH_2$), 34.2 (N$CH_2$), 77.4 ($C$HCHO), 123.5 (NCOAr$C$(2)), 123.7 (Ar$C$(2)), 131.1 (Ar$C$(3)), 131.9 (NCOAr$C$(1)), 134.1 (Ar$C$(1)), 134.4 (NCOAr$C$(1)), 150.9 ($CO_2$), 164.2 (Ar$C$(4)), 168.2 (N$C$OAr), 196.3 ($C$HO); HRMS (APCI$^+$) C$_{19}H_{15}N_2O_7$ [M+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] ^{1}H NMR (300 MHz, CDCl$_3$) 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, ArOCH_3), 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-NO$_2$ArC(2,6)H), 8.31 (2H, d, J 8.6, 4-NO$_2$ArC(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] ^{1}H NMR (300 MHz, CDCl$_3$) 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, OCH_2O), 6.69–6.77 (3H, m, ArCH), 8.21 (2H, d, J 8.9, 4-NO$_2$ArC(2,6)H), 8.32 (2H, d, J 8.9, 4-NO$_2$ArC(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] ^{1}H NMR (400 MHz, CDCl$_3$) δ_H: 0.95 (3H, t, J 7.2, CH_3), 1.37–1.45 (2H, m, CH_2), 1.45–1.54 (2H, m, CH_2), 1.93 (2H, ddd, J 15.5, 14.6, 8.5, CH_2), 5.31 (1H, dd, J 8.3, 4.7, CH)), 8.25–8.35 (4H, m, 4-NO$_2$ArH), 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}; ^{1}H NMR (300 MHz, CDCl$_3$) 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}; ^{1}H NMR (400 MHz, CDCl$_3$) δ_H: 3.87 (3H, s, OCH_3), 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 MnO_2 (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 CH_2Cl_2 (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] ^{1}H NMR (300 MHz, $CDCl_3$) δ_H: 6.70 (1H, dd, *J* 16.0, 7.6, C(2)*H*), 7.43–7.38 (2H, m, Ar*H*), 7.48–7.43 (1H, m, C(3)*H*), 7.62–7.54 (2H, m, Ar*H*), 9.71 (1H, d, *J* 7.6, C*H*O).

Following the procedure by Zhao *et al.*,[16a] (*E*)-3-(4-bromophenyl)acrylaldehyde (387 mg, 1.83 mmol, 1.0 eq) was added to a solution of $CHCl_3$ (293 µL, 3.66 mmol, 2.0 eq) in DMF (1.3 mL) at rt. The reaction mixture was stirred at rt for 20 min then cooled to 0 °C before a solution of KOH (205 mg, 3.66 mmol, 2.0 eq) in EtOH (660 µL) 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 (× 2). The combined organics were washed with water (× 2) and brine (× 3) before being dried over $MgSO_4$, 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. ^{1}H NMR (300 MHz, $CDCl_3$) 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, Ar*H*), 7.43–7.52 (2H, m, Ar*H*).

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 eq) and distilled Et_3N (711 µL, 5.10 mmol, 3.0 eq) were dissolved in anhydrous CH_2Cl_2 (13.5 mL). A solution of sulfur trioxide pyridine complex (812 mg, 5.10 mmol, 3.0 eq) 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 eq). The reaction mixture was stirred at rt for 48 h

before being diluted in water (10 mL), extracted with Et$_2$O (2 × 20 mL) and washed successively with sat. aq. CuSO$_4$ (20 mL), sat. aq. NaHCO$_3$ (2 × 20 mL) and brine (2 × 20 mL). The organic layer was dried over MgSO$_4$, 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] ^{1}H NMR (300 MHz, CDCl$_3$) δ$_H$: 7.32 (1H, d, *J* 15.7, C(2)*H*), 7.48–7.65 (4H, m, Ar*H*), 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] ^{1}H NMR (400 MHz, CDCl$_3$) δ$_H$: 0.87–0.93 (3H, m, C*H*$_3$), 1.28–1.38 (4H, m, C*H*$_2$ × 2), 1.48–1.56 (2H, m, C(6)*H*$_2$), 2.34 (2H, app qd, *J* 7.2, 1.6, C(5)*H*$_2$), 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}; ^{1}H NMR (500 MHz, CDCl$_3$) 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*); ^{19}F{^{1}H} NMR (471 MHz, CDCl$_3$) 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}; ^{1}H NMR (400 MHz, CDCl$_3$) δ$_H$: 7.24 (1H, d, *J* 15.5, C(3)*H*), 7.60–7.66 (1H, m, ArC*H*), 7.70–7.75 (2H, m, ArC*H*), 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}; ^{1}H NMR(400 MHz, CDCl$_3$) 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 eq), the appropriate trichloromethylketone (0.20 mmol, 1.0 eq) and NHC precatalyst **11** (0.010 mmol, 5 mol% or 0.020 mmol, 10 mol%) were dissolved in anhydrous CH_2Cl_2 (2.7 mL). Et_3N (0.30 mmol, 1.5 eq) 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 sodium bisulfite aq. 40% (10 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$, 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 Et_3N (251 μL, 1.80 mmol) in anhydrous CH_2Cl_2 (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; $[\alpha]_D^{20}$ +237.5 (*c* 0.41, CH_2Cl_2); 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); ^{1}H NMR (400 MHz, CDCl$_3$) δ_H: 1.06 (3H, d, *J* 6.9, C*H*$_3$), 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)ArC*H*), 7.28–7.39 (3H, m, C(4)ArC*H*); ^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$) δ_C: 12.1 (*C*H$_3$), 38.2 (*C*(3)), 42.4 (*C*(4)), 90.1 (*C*Cl$_3$), 108.0 (*C*(5)), 128.1 (C(4)Ar*C*H), 128.3 (C(4)Ar*C*H), 129.2 (C(4)Ar*C*H), 135.8 (C(4)Ar*C*(1)), 149.5 (*C*(6)), 168.6 (*C*(2)); *m/z* (APCI$^+$) 307 [(M(^{35}Cl$_2$, ^{37}Cl)+H]$^+$, 100%), 305 [(M(^{35}Cl$_3$)+H]$^+$, 98%); HRMS (APCI$^+$) C$_{13}$H$_{12}$^{35}Cl$_3$O$_2$ [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 Et$_3$N (42 μL, 0.30 mmol) in anhydrous CH$_2$Cl$_2$ (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. $[\alpha]_D^{20}$ +167.7 (*c* 0.43, CH$_2$Cl$_2$); Chiral HPLC AS-H (99:1 hexane : IPA, flow rate 0.5 mL·min^{-1}, 211 nm, 30 °C) t_R minor: 16.6 min, t_R major: 19.2 min, >99% ee; ν_{max} (film, cm^{-1}) 1780 (C=O), 1670 (C=C), 1603 (Ar C=C), 1495 (Ar C=C), 1454 (Ar C=C); ^{1}H NMR (400 MHz, CDCl$_3$) δ$_H$: 2.35–2.46 (1H, m, C(3)C*H*^{A}H^B), 3.21–3.34 (2H, m, C(3)CH^A*H*^{B} and C(3)*H*), 3.65–3.72 (1H, m, C(4)*H*), 6.37 (1H, d, *J* 6.8, C(5)*H*), 7.01–7.08 (2H, m, Ar*H*), 7.11 (2H, m, Ar*H*), 7.29–7.41 (6H, m, Ar*H*); ^{13}C{^{1}H} (101 MHz, CDCl$_3$) δ$_C$: 32.0 (*C*H$_2$), 39.9 (*C*(4)), 44.8 (*C*(3)), 90.1 (*C*Cl$_3$), 108.6 (*C*(5)), 126.8 (Ar*C*H), 128.3 (Ar*C*H × 2), 128.4 (Ar*C*H), 128.7 (Ar*C*H × 2), 128.9 (Ar*C*H × 2), 129.3 (Ar*C*H × 2), 135.9 (C(3)Ar*C*(1)), 137.8 (C(2)CH$_2$Ar*C*(1)), 149.1 (*C*(6)), 167.8 (*C*(2)); *m/z* (APCI$^+$) 381 ([M(^{35}Cl$_3$)+H]$^+$, 100%); HRMS (APCI$^+$) C$_{19}$H$_{16}$O$_2$^{35}Cl$_3$ [M+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-dioxoisoindolin-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$_3$N (42 μL, 0.30 mmol) in anhydrous CH$_2$Cl$_2$ (2.7 mL) at rt for 7 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 °C (*dec*); $[\alpha]_D^{20}$ +271.2 (*c* 0.16, CHCl$_3$); 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; ν_{max} (film,

cm^{-1}) 1772 and 1701 (C=O isoxindole), 1701 (C=O); ^{1}H NMR (500 MHz, CDCl$_3$) δ_H: 1.50–1.60 (1H, m, C(3)CH^AH^B), 2.06–2.16 (1H, m, C(3)CH^AH^B), 2.95 (1H, q, J 7.0, C(3)H), 3.76–3.85 (1H, m, C(3)CH$_2$CH^AH^B), 3.85–3.92 (1H, m, C(3)CH$_2$CH^AH^B), 4.00 (1H, t, J 7.0, C(4)H), 6.42 (1H, d, J 6.9, C(5)H), 7.12–7.16 (2H, m, ArH), 7.29–7.38 (3H, m, ArH), 7.70–7.75 (2H, m, C(3)(CH$_2$)$_2$Ar(2,5)H), 7.83–7.88 (2H, m, C(3)(CH$_2$)$_2$Ar(3,4)H); ^{13}C{^{1}H} (101 MHz, CDCl$_3$) δ_C: 26.3 (CH$_2$), 35.6(CH$_2$), 40.7 (C(3)), 40.9 (C(4)), 90.0 (CCl$_3$), 108.1 (C(5)), 123.4 (ArCH × 2), 128.0 (ArCH × 2), 128.5 (ArCH), 129.4 (ArCH × 2), 132.0 (NPhthArC), 134.1 (ArCH), 135.7 (NPhthArC), 149.3 (C(3)ArC(1)), 167.5 (C(2)), 168.4 (C=O × 2); m/z (NSI$^+$) 951 ([2M(^{35}Cl$_2$,^{37}Cl)+Na]$^+$, 100%), 949 ([2M(^{35}Cl$_3$)+Na]$^+$, 85%), 486 ([M(^{35}Cl$_3$)+Na]$^+$, 85%); HRMS (NSI$^+$) C$_{22}$H$_{16}$O$_4$N$_1$^{35}Cl$_3$Na [M+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$_3$N (42 µL, 0.30 mmol) in anhydrous CH$_2$Cl$_2$ (2.7 mL) at rt for 26 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. [α]$_D^{20}$ +300.0 (*c* 0.81, CHCl$_3$); Chiral HPLC AD-H (99:1 hexane : IPA, flow rate 1.0 mL·min^{-1}, 220 nm, 30 °C) t$_R$ minor: 18.5 min, t$_R$ major: 20.7 min, >99% ee; ν_{max} (film, cm^{-1}) 1780 (C=O), 1612 (C=C), 1514 (Ar C=C), 1456, 1250 (Ph–O–CH$_3$); ^{1}H NMR (500 MHz, CDCl$_3$) δ_H: 2.35 (1H, dd, J 14.4, 9.1, C(3)CH^AH^B), 3.15–3.27 (2H, m, C(3)CH^AH^B and C(3)H), 3.68 (1H, t, J 6.8, C(4)H), 3.81 (3H, s, CH_3O), 6.36 (1H, d, J 6.7, C(5)H), 6.85 (2H, dd, J 9.1, 2.5, C(3)CH$_2$ArC(3,5)H), 6.99–7.08 (4H, m, C(3)CH$_2$ArC(2,6)H and C(4)ArC(3,5)H), 7.31–7.39 (3H, m, C(4)ArC(2,4,6)H); ^{13}C{^{1}H} (126 MHz, CDCl$_3$) δ_C: 31.1 (C(3)CH$_2$), 39.9 (C(4)), 45.0 (C(3)), 55.3 (OCH$_3$), 90.1 (CCl$_3$), 108.6 (C(5)), 114.0

(C(3)CH$_2$ArC(3,5)), 128.3 (ArCH), 128.4 (ArCH), 129.2 (ArCH), 129.7(ArCH), 129.7 (ArCH), 129.9 (ArCH), 136.0 (C(4)ArC(1)), 149.1 (C(6)), 158.4 (C(3)CH$_2$ArC(4)), 167.9 (C(2)); m/z (NSI$^+$) 462 ([M(^{35}Cl$_2$, ^{37}Cl)+MeOH+NH$_4$]$^+$, 51%), 460 ([M(^{35}Cl$_3$)+MeOH+NH$_4$]$^+$, 52%), 445 ([M(^{35}Cl$_2$, ^{37}Cl)+MeOH+H]$^+$, 65%), 443 ([M(^{35}Cl$_3$)+MeOH+H]$^+$, 67%), 432 ([M(^{35}Cl^{37}Cl$_2$)+NH$_4$]$^+$, 30%), 430 ([M(^{35}Cl$_2$, ^{37}Cl)+NH$_4$]$^+$, 97%), 428 ([M(^{35}Cl$_3$)+NH$_4$]$^+$, 100%), 411 ([M(^{35}Cl$_2$, ^{37}Cl)+H]$^+$, 43%); HRMS (NSI$^+$) C$_{20}$H$_{18}$O$_3$Cl$_3$ [M+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$_3$N (42 μL, 0.30 mmol) in anhydrous CH$_2$Cl$_2$ (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 °C; [α]$_D^{20}$ +230.4 (*c* 0.51, CH$_2$Cl$_2$); ee could not be determined by either chiral HPLC or GC; ν$_{max}$ (film, cm^{-1}) 1780 (C=O), 1504, 1489 and 1445 (Ar C=C), 1246 (C-O); ^{1}H NMR (500 MHz, CDCl$_3$) δ$_H$: 2.33 (1H, dd, *J* 14.5, 9.1, C(3)CH^{A}H^B), 3.15 (1H, dd, *J* 14.5, 5.3, C(3)CH^{A}H^B), 3.18–3.22 (1H, m, C(3)*H*), 3.71 (1H, t, *J* 6.7, C(4)*H*), 5.96 (2H, dd, *J* 4.6, 1.4, OCH$_2$O), 6.37 (1H, d, *J* 6.8, C(5)*H*), 6.53 (1H, dd, *J* 7.9, 1.5, C(3)CH$_2$ArC(6)*H*), 6.61 (1H, *app* d, *J* 1.6, C(3)CH$_2$ArC(4)*H*), 6.75 (1H, d, *J* 7.9, C(3)CH$_2$ArC(7)*H*), 7.05–7.07 (2H, m, C(4)ArC(3,5)*H*), 7.32–7.39 (3H, m, C(4)ArC(2,4,6)*H*); ^{13}C{^{1}H} (126 MHz, CDCl$_3$) δ$_C$: 31.8 (C(4)CH$_2$), 39.9 (C(4)), 45.1 (C(3)), 90.1 (CCl$_3$), 101.0 (OCH$_2$O), 108.4 (C(3)CH$_2$ArC(7)), 108.6 (C(5)), 109.1 (C(3)CH$_2$ArC(4)), 122.0 (C(3)CH$_2$ArC(6)), 128.3 (C(4)ArCH), 128.4 (C(4)ArCH), 129.3 (C(4)ArCH), 131.4 (C(3)CH$_2$ArC(5)), 135.9 (C(4)ArC(1)), 146.4 (C(3)CH$_2$ArC(3a)), 147.8 (C(3)CH$_2$ArC(7a)), 149.0 (C(6)), 167.8 (C(2)); m/z (NSI$^+$) 481 ([M(^{35}Cl$_2$, ^{37}Cl)+MeOH+Na]$^+$, 65%), 479

([M(^{35}Cl$_3$)+MeOH+Na]$^+$, 67%), 449 ([M(^{35}Cl$_2$, ^{37}Cl)+Na]$^+$, 50%), 447 ([M(^{35}Cl$_3$) +Na]$^+$, 52%), 444 ([M(^{35}Cl$_2$, ^{37}Cl)+NH$_4$]$^+$, 31%), 442 ([M(^{35}Cl$_3$)+NH$_4$]$^+$, 34%), 429 ([M(^{35}Cl, ^{37}Cl$_2$)+H]$^+$, 30%), 427 ([M(^{35}Cl$_2$, ^{37}Cl)+H]$^+$, 94%), 425 [M(^{35}Cl$_3$)+H]$^+$, 100%); HRMS (NSI$^+$) C$_{20}$H$_{16}$O$_4$^{35}Cl$_3$ [M+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$_3$N (126 µL, 0.90 mmol) in anhydrous CH$_2$Cl$_2$ (8.2 mL) at rt for 3 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 solide. mp 109–111 °C; [α]$_D^{20}$ +369.6 (*c* 0.575, CH$_2$Cl$_2$); Chiral HPLC AD-H (98:2 hexane : IPA, flow rate 1.0 mL·min^{-1}, 220 nm, 30 °C) t$_R$ minor: 11.2 min, t$_R$ major: 12.6 min, 99% ee; ν$_{max}$ (film, cm^{-1}) 1778 (C=O), 1609 (C=C), 1512 (Ar C=C), 1252 (Ph-O-CH$_3$); ^{1}H NMR (500 MHz, CDCl$_3$) δ$_H$: 2.41 (1H, dd, *J* 15.8, 10.6, C(3)C*H*^{A}H^B), 3.23–3.30 (2H, m, C(3)CH^A*H*^{B} and C(3)*H*), 3.62 (1H, t, *J* 6.7, C(4)*H*), 3.82 (3H, s, C*H*$_3$), 6.35 (1H, d, *J* 6.8, C(5)*H*), 6.87–6.97 (4H, m, C(4)Ar*H*), 7.10–7.14 (2H, m, Ar*H*), 7.24–7.28 (1H, m, Ar*H*), 7.30–7.35 (2H, m, Ar*H*); ^{13}C{^{1}H} (126 MHz, CDCl$_3$) δ$_C$: 32.0 (*C*H$_2$), 39.1 (*C*(4)), 45.0 (*C*(3)), 55.3 (*C*H$_3$O), 90.1 (*C*Cl$_3$), 108.9 (*C*(5)), 114.6 (C(4)Ar*C*H), 126.8 (C(3)CH$_2$Ar*C*H), 127.6 (C(4)Ar*C*(1)), 128.7 (C(3)CH$_2$Ar*C*H), 129.0 (C(3)CH$_2$Ar*C*H), 129.4 (C(4)Ar*C*H), 137.9 (C(3)CH$_2$Ar*C*), 148.8 (*C*(6)), 159.6 (C(4)Ar*C*(4)), 168.0 (*C*(2)); *m/z* (APCI$^+$) 411 ([M(^{35}Cl$_3$)+H]$^+$, 100%), 303 ([M(^{35}Cl$_3$)–4-OMeC$_6$H$_4$]$^+$, 70%); HRMS (APCI$^+$) C$_{20}$H$_{17}$^{35}Cl$_3$O$_3$ [M+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. $[\alpha]_D^{20}$ +71.4 (*c* 0.29, CH_2Cl_2); Chiral HPLC OD-H (97:3 hexane : IPA, flow rate 1.0 mL·min^{-1}, 220 nm, 30 °C) t_R major: 10.3 min, t_R minor: 11.7 min, >99% ee; ν_{max} (film, cm^{-1}) 1780 (C=O), 1661 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.33–2.42 (1H, m, C(3)CH^AH^B), 3.24–3.35 (2H, m, C(3)CH^AH^B and C(3)*H*), 3.64 (1H, t, *J* 6.7, C(4)*H*), 6.33 (1H, d, *J* 6.8, C(5)*H*), 6.86–6.93 (2H, m, C(4)ArC(2,6)*H*), 7.07–7.12 (2H, m, C(3)Ar*H*), 7.27–7.36 (3H, m, C(3)Ar*H*), 7.46–7.52 (2H, m, C(4)ArC(3,5)*H*); ^{13}C{^{1}H}(101 MHz, $CDCl_3$) δ_C: 32.0 (*C*H$_2$), 39.2 (*C*(4)), 44.4 (*C*(3)), 90.2 (*C*Cl$_3$), 108.0 (*C*(5)), 123.0 (C(4)Ar*C*(1)), 127.0 (C(3)CH$_2$Ar*C*H), 128.8 (C(3)CH$_2$Ar*C*H), 128.9 (C(3)CH$_2$Ar*C*H), 129.9 (C(4)Ar*C*(2,6)), 132.4 (C(4)Ar*C*(3,5)), 135.1 (C(4)Ar*C*(4)), 137.8 (C(3)CH$_2$Ar*C*), 146.6 (*C*(6)), 167.7 (*C*(2)); *m/z* (APCI$^+$) 463 ([M(^{35}Cl,^{37}Cl$_2$,^{79}Br)+H]$^+$, 60%), 461 ([M(^{35}Cl$_2$,^{37}Cl,^{79}Br)+H]$^+$, 100%), 458 ([M(^{35}Cl$_3$,^{79}Br)+H]$^+$, 50%); HRMS (APCI$^+$) $C_{19}H_{15}O_2{}^{79}Br^{35}Cl_3$ [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-trichloronon-3-en-2-one (49 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 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. $[\alpha]_D^{20}$ +8.9 (*c* 0.44, CHCl$_3$); 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); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 0.88 (3H, t, *J* 6.9, C*H*$_3$), 1.26 (3H, d,

J 7.0, C(3)CH_3), 1.27–1.40 (7H, m, C(4)CH^AH^B and CH_3(CH_2)$_3$), 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}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ_C: 11.3 (C(3)CH_3), 14.0 (CH_3), 22.4 (CH$_3$$CH_2$), 26.0 (CH$_3$(CH$_2$)$_2$$CH_2$), 28.8 (C(4)$CH_2$), 31.8 (CH$_3CH_2$$CH_2$), 35.3 ($C$(4)), 36.9 ($C$(3)), 90.1 ($CCl_3$), 109.2 ($C$(5)), 148.4 ($C$(6)), 169.9 ($C$(2)); m/z (APCI$^+$) 319 ([M(^{35}Cl$_2$,^{37}Cl)+H$_3$O]$^+$, 62%), 317 ([M(^{35}Cl$_3$)+H$_3$O]$^+$, 65%), 303 ([M(^{35}Cl,^{37}Cl$_2$)+H]$^+$, 30%), 301 ([M(^{35}Cl$_2$,^{37}Cl)+H]$^+$, 95%), 299 ([M(^{35}Cl$_3$)+H]$^+$, 100%); HRMS (APCI$^+$) C$_{12}$H$_{17}$^{35}Cl$_3$O$_2$$^+$ [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)isoindo-line-1,3-dione **14** (13.2 mg, 0.028 mmol, 1.0 eq) was dissolved in CD$_2$Cl$_2$ before Et$_3$N (5.9 μL, 0.42 mmol, 1.5 eq) was added. The ratio between the two diastereoisomers were monitored by ^{1}H 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 eq), the appropriate trichloromethyl ketone (0.20 mmol, 1.0 eq) and NHC precatalyst **11** (0.010 mmol, 5 mol% or 0.020 mmol, 10 mol%) were dissolved in anhydrous CH$_2$Cl$_2$ (2.7 mL). Et$_3$N (0.30 mmol, 1.5 eq) 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 × 2), sodium bisulfite aq. 40% (10 mL × 2), and brine (10 mL × 2). The organic layer was dried over MgSO$_4$, filtered and concentrated. The crude *syn*-dihydropyranone was dissolved in anhydrous CH$_2$Cl$_2$ (6.6 mL) and benzylamine (60 mmol, 300 eq, 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 × 3), sat. aq. NaHCO$_3$ (20 mL × 3) and brine (20 mL × 3). The organic layer was dried over MgSO$_4$, filtered and concentrated to give the crude product that was triturated in Et$_2$O then dispersed in CHCl$_3$ and concentrated to give the desired diamide.

(2S,3S)-N^1,N^5-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 Et$_3$N (42 μL, 0.30 mmol) in anhydrous CH$_2$Cl$_2$ (2.7 mL) at rt for 3.5 h gave a crude orange solid (>95:5 dr). The crude was stirred in anhydrous CH$_2$Cl$_2$ (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 Et$_2$O to give the title compound (70 mg, 85%) as a white solid. mp 172–174 °C; [α]$_D^{20}$ −8.7 (*c* 0.53, CHCl$_3$); 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; ^{1}H NMR (400 MHz, CDCl$_3$) δ$_H$: 1.20 (3H, d, *J* 6.9, C(2)C*H*$_3$), 2.48 (1H, dd, *J* 13.8, 8.6, C(4)*H*^{A}H^B), 2.67 (1H, p, *J* 7.0, C(2)*H*), 2.91 (1H, dd, *J* 13.8, 6.9, C(4)H^A*H*^{B}), 3.36 (1H, q, *J* 7.7, C(3)*H*), 4.14 (1H, dd, *J* 14.7, 5.2, N^{1}C*H*^{A}H^B), 4.24 (1H, dd, *J* 14.9, 5.4, N^{5}C*H*^{A}H^B), 4.31 (1H, dd, *J* 14.7, 6.1, N^{1}CH^A*H*^{B}), 4.38 (1H, dd, *J* 14.8, 6.1, N^{5}CH^A*H*^{B}), 5.58 (1H, br t, *J* 5.0, N^1*H*), 6.10 (1H, br t, *J* 5.0, N^5*H*), 6.87–6.96 (3H, dd, *J* 6.6, 2.8, Ar*H*), 6.97–7.02 (3H, m, Ar*H*), 7.11–7.18 (3H, m, ArH), 7.19–7.26 (8H, m); ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ$_C$: 16.0 (C(2)*C*H$_3$), 40.5 (*C*(4)), 43.3 (N*C*H$_2$), 43.4 (N*C*H$_2$), 45.7 (*C*(2)), 46.4 (*C*(3)), 127.1 (Ar*C*H), 127.27 (Ar*C*H), 127.33 (Ar*C*H), 127.5 (Ar*C*H), 127.7 (Ar*C*H), 128.3 (Ar*C*H), 128.6 (Ar*C*H), 137.9 (NCH$_2$Ar*C*(1)), 138.1 (NCH$_2$Ar*C*(1)), 141.3 (C(3)Ar*C*), 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$^+$) C$_{26}$H$_{29}$O$_2$N$_2$ [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 eq), (*E*)-1,1,1-trichloro-4-phenylbut-3-en-2-one **1** (0.20 mmol, 50 mg, 1.0 eq) and NHC precatalyst **11** (0.010 mmol, 3.7 mg, 5 mol%) were dissolved in anhydrous CH_2Cl_2 (2.7 mL). Et_3N (0.30 mmol, 42 µL, 1.5 eq) 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 × 2), sodium bisulfte aq. 40% (10 mL × 2) and brine (10 mL × 2). The organic layer was dried with $MgSO_4$, filtered and concentrated to give a crude orange solid (>95:5 dr). The crude was dissolved in anhydrous CH_2Cl_2 (2.4 mL) with MeOH (60 mmol, 2.4 mL, 300 eq) 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 (35 mg, 50%) as a colourless oil. $[\alpha]_D^{20}$ −17.3 (*c* 1.60, $CHCl_3$); 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; v_{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)C*H*$_3$), 2.86 (1H, p, *J* 7.0, C(2)*H*), 3.49 (2H, dd, *J* 6.9, 2.7, C(4)*H*$_2$), 3.52 (3H, s, C(1)OC*H*$_3$), 3.54–3.62 (1H, m, C(3)*H*), 7.17–7.24 (3H, m, Ar*H*), 7.24–7.31 (2H, m, Ar*H*); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ_C: 14.8 (C(2)*C*H$_3$), 36.8 (*C*(4)), 44.0 (*C*(3)), 44.7 (*C*(2)), 51.6 (C(1)O*C*H$_3$), 96.2 (*C*(6)), 127.3 (Ar*C*H), 128.1 (Ar*C*H × 2), 128.4 (Ar*C*H × 2), 140.3 (C(3)Ar*C*(1)), 174.9 (*C*(1)), 188.7 (*C*(5)); *m/z* (APCI$^+$) 356 ([M($^{35}Cl_2$,^{37}Cl)+NH$_4$]$^+$, 34%), 354 ([M($^{35}Cl_3$)+ NH$_4$]$^+$, 34%), 341 ([M(^{35}Cl,$^{37}Cl_2$)+H]$^+$, 34%), 339 ([M($^{35}Cl_2$,^{37}Cl)+H]$^+$, 99%), 337 ([M($^{35}Cl_3$)+H]$^+$, 100%); HRMS (APCI$^+$) $C_{14}H_{15}O_3{}^{35}Cl_3$ [M+H]$^+$ found 337.0160, requires 337.0164 (+1.3 ppm).

23 (10 mg, 20%, 85% pure) as a yellow oil.[35,36] $[\alpha]_D^{20}$ +0.46 (*c* 0.44, CHCl$_3$); 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; ^{1}H NMR (400 MHz, CDCl$_3$) δ_H: 1.18 (3H, d, *J* 7.0, C(2)C*H*$_3$), 2.69 (1H, dd, *J* 15.7, 9.7, C(4)*H*^{A}H^B), 2.74–2.87 (2H, m, C(4)H^A*H*^{B} and C(2)*H*), 3.41–3.48 (1H, m, C(3)*H*), 3.50 (3H, s, C(1)OC*H*$_3$), 3.54 (3H, s, C(5)OC*H*$_3$), 7.14–7.23 (3H, m, Ar*H*), 7.24–7.30 (2H, m, Ar*H*); ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ_C: 14.4 (C(2)*C*H$_3$), 37.0 (*C*(4)), 44.5 (*C*(3)), 45.1 (*C*(2)), 51.5 (C(1)O*C*H$_3$), 51.6 (*C*(5)O*C*H$_3$), 126.9 (C(3)Ar*C*H), 127.8 (C(3)Ar*C*H × 2), 128.3 (C(3)Ar*C*H × 2), 141.3 (C(3)Ar*C*(1)), 172.4 *C*(5), 175.2 *C*(2); *m/z* (NSI$^+$) 251 ([M+H]$^+$, 100%); HRMS (NSI$^+$) C$_{14}$H$_{19}$O$_4$ [M+H]$^+$ found 251.1279, requires 251.1278 (+0.5 ppm).

*(2S,3S)-Benzyl 5-(benzylamino)-2-methyl-5-oxo-3-phenylpentanoate (**24**).* 1-Oxopropan-2-yl 4-nitrobenzoate **10** (0.30 mmol, 67 mg, 1.5 eq), (*E*)-1,1,1-trichloro-4-phenylbut-3-en-2-one **1** (0.20 mmol, 50 mg, 1.0 eq) and NHC precatalyst **11** (0.010 mmol, 3.7 mg, 5 mol%) were dissolved in anhydrous CH$_2$Cl$_2$ (2.7 mL). Et$_3$N (0.30 mmol, 42 µL, 1.5 eq) 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 × 2), sodium bisulfite aq. 40% (10 mL × 2), and brine (10 mL × 2). The organic layer was dried over MgSO$_4$, filtered and concentrated to give a crude orange solid (77 mg, >95:5 dr). The crude was dissolved in anhydrous CH$_2$Cl$_2$ (6.6 mL) with BnOH (60 mmol, 6.6 mL, 300 eq) 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 CH$_2$Cl$_2$ (2.6 mL) with benzylamine (2.6 mL, 0.24 mmol, 1.2 eq) at rt for 16 h. The reaction mixture was diluted in EtOAc (20 ml) and wash with 1 M HCl (20 mL × 3), sat. aq. NaHCO$_3$ (20 mL × 3) and brine (20 mL × 3). The organic layer was dried over MgSO$_4$, 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;

$[\alpha]_D^{20}$ +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; ^{1}H 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); ^{13}C{^{1}H} 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).

(2S,3S)-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 µL, 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; $[\alpha]_D^{20}$ –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; ^{1}H NMR (400 MHz, CDCl$_3$) δ$_H$: 0.87 (3H, t, J 6.9, CH_3), 1.19–1.34 (4H, m, C(2)CH$_2$(CH_2)$_2$), 1.52–1.60 (2H, m, C(2)CH_2), 2.41–2.51 (2H, m, C(2)H and C(4)H^{A}H^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, N^{1}CH^{A}H^B), 4.26 (1H, dd, J 14.8, 5.4, N^{5}CH^{A}H^B), 4.30 (1H, dd, J 14.8, 6.2, N^{1}CH^AH^B), 4.36 (1H, dd, J 14.8, 6.1, N^{5}CH^AH^B), 5.48 (1H, t, J 5.3, N^1H), 5.96 (1H, t, J 5.1, N^5H), 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); ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) 14.0 (CH$_3$), 22.7 (CH$_2$), 29.8 (CH$_2$), 30.2 (C(2)CH$_2$), 40.7 (C(4)), 43.3(NCH$_2$), 43.5 (NCH$_2$), 45.3 (C(3)), 52.2 (C(2)), 127.0 (ArCH), 127.28 (ArCH), 127.32 (ArCH), 127.6 (ArCH × 2), 127.8 (ArCH × 2), 128.3 (ArCH × 2), 128.50 (ArCH × 2), 128.53 (ArCH × 2), 128.6 (ArCH × 2), 138.0 (NCH$_2$ArC), 138.1 (NCH$_2$ArC), 141.4 (C(3)ArC(1)), 171.4 (C(5)), 173.2 (C(1)); m/z (NSI$^+$) 443 ([M+H]$^+$, 100%); HRMS (NSI$^+$) C$_{29}$H$_{35}$O$_2$N$_2$ [M+H]$^+$ found 443.2692, requires 443.2653 (–0.2 ppm).

(2S,3S)-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 Et$_3$N (42 μL, 0.30 mmol) in anhydrous CH$_2$Cl$_2$ (2.7 mL) at rt for 6 h gave a crude brown oil (>95:5 dr). The crude was stirred in anhydrous CH$_2$Cl$_2$ (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 Et$_2$O to give the title compound (61 mg, 60%) as a beige solid. mp 221–223 °C; [α]$_D^{20}$ –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; ^{1}H NMR (700 MHz, CDCl$_3$) 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^{A}H^B and C(2)CH^AH^B), 3.48 (1H, q, J 8.1, C(3)H), 3.79 (3H, s, OCH_3), 4.00 (1H, dd, J 14.8, 5.6,

N^{1}CH^{A}H^B), 4.12 (1H, dd, J 14.9, 6.0, N^{1}CH^{A}H^B), 4.28 (1H, dd, J 14.7, 5.5, N^{5}CH^{A}H^B), 4.38 (1H, dd, J 14.7, 6.0, N^{5}CH^{A}H^B), 5.41 (1H, t, J 5.6, N^{1}H), 5.78 (1H, t, J 5.1, N^{5}H), 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); ^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$) δ_C: 35.7 (C(2)CH$_2$), 40.7 (C(4)), 43.0 (N^{1}CH$_2$), 43.5 (N^{5}CH$_2$), 44.4 (C(3)), 54.4 (C(2)), 55.2 (OCH$_3$), 113.9 (C(2)CH$_2$ArC(3,5)), 115.3 (d, J_{CF} 21.2, C(3)ArC(3,5)), 127.2 (NCH$_2$ArC(4)), 127.5 (NCH$_2$ArC(4) and N^{1}CH$_2$ArC(2,6)), 127.6 (N^{5}CH$_2$ArC(2,6)), 128.4 (NCH$_2$ArC(3,5)), 128.6 (NCH$_2$ArC(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 (NCH$_2$ArC), 137.9 (NCH$_2$ArC), 158.2 (C(2)CH$_2$ArC(4)), 161.9 (d, J_{CF} 245.3, C(3)ArC(4)), 170.9 (C(5)), 172.2 (C(1)); ^{19}F NMR (376 MHz, CDCl$_3$) δ_F: −115.57 (s, C(3)ArC(4)F); m/z (NSI$^+$) 547 ([M+Na]$^+$, 43%), 525 ([M+H]$^+$, 100%); HRMS (NSI$^+$) C$_{33}$H$_{34}$O$_3$N$_2$F [M+H]$^+$ found 525.2554, requires 525.2548 (+1.1 ppm).

(2S,3S)-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 Et$_3$N (42 μL, 0.30 mmol) in anhydrous CH$_2$Cl$_2$ (2.7 mL) at rt for 27 h gave a crude brown oil (85:15 dr). The crude was stirred in anhydrous CH$_2$Cl$_2$ (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 Et$_2$O to give the title compound (50 mg, 48%) as an off-white solid. mp 198 °C (*dec*); $[\alpha]_D^{20}$ −39.4 (*c* 0.18, CHCl$_3$); 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; ^{1}H NMR (400 MHz, CDCl$_3$) δ_H: 2.57 (1H, dd, J 14.0, 8.3, C(4)H^{A}H^B), 2.74–2.84 (2H, m, C(2)H and C(2)CH^{A}H^B), 2.84–2.96 (2H, m, C(2)H^{A}H^B and C(4)H^{A}H^B), 3.43–3.52 (1H, m, C(3)H), 4.01–4.15 (2H, m, NCH$_2$), 4.26–4.40

(2H, m, NCH_2), 5.43 (1H, t, J 5.2, NH), 5.83 (1H, t, J 5.3, *NH*), 5.88–5.94 (2H, m, OCH_2O), 6.56–6.62 (1H, m, C(2)CH$_2$ArH), 6.62–6.70 (2H, m, C(2)CH$_2$ArH), 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); ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ_C: 36.2 (C(2)CH$_2$), 40.5 (C(4)), 43.0 (NCH$_2$), 43.5 (NCH$_2$), 45.2 (C(3)), 54.4 (C(2)), 100.8 (OCH$_2$O), 109.3 (C(2)CH$_2$ArCH), 121.9 (C(2)CH$_2$ArCH), 127.1 (ArCH × 2), 127.4 (ArCH), 127.5 (ArCH × 2), 127.6 (ArCH × 2), 128.3 (ArCH × 2), 128.4 (ArCH × 2), 128.6 (ArCH × 2), 128.6 (ArCH × 2), 133.1 (C(2)CH$_2$ArC(1)), 137.8 (NCH$_2$ArC(1)), 138.0 (NCH$_2$ArC(1)), 141.2 (C(3)ArC(1)), 146.0 (C(2)CH$_2$ArC(2a or 6a)), 147.6 (C(2)CH$_2$ArC(6a or 2a)), 171.2 (C=O), 172.2 (C=O); *m/z* (NSI$^+$) 543 ([M+Na]$^+$, 31%), 521 ([M+H]$^+$, 100%); HRMS (NSI$^+$) C$_{33}$H$_{33}$O$_4$N$_2$ [M+H]$^+$ found 521.2440, requires 521.2435 (+1.0 ppm).

*(2S,3S)-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 Et$_3$N (42 μL, 0.30 mmol) in anhydrous CH$_2$Cl$_2$ (2.7 mL) at rt for 22 h gave a crude yellow solid (>95:5 dr). The crude was stirred in anhydrous CH$_2$Cl$_2$ (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 Et$_2$O to give the title compound (64 mg, 75%) as a white solid. mp 176–178 °C; $[\alpha]_D^{20}$ −12.8 (*c* 0.56, CHCl$_3$); 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; ^{1}H NMR (400 MHz, CDCl$_3$) δ_H: 1.22 (3H, d, J 6.9, C(2)CH_3), 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, OCH_3), 4.15 (1H, dd, J 14.7, 5.1, N^{1}CH^AH^B), 4.25 (1H, dd, J 14.9, 5.3, N^{5}CH^AH^B), 4.37 (1H, dd, J 14.8, 6.4, N^{1}CH^AH^B), 4.42 (1H, dd, J 14.9, 6.3, N^{5}CH^AH^B), 5.60

(1H, t, J 5.5, N^{1}H), 6.08 (1H, t, J 5.4, N^{5}H), 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); ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ_C: 16.0 (C(2)CH$_3$), 40.8 (C(4)), 43.3 (N^{1}CH$_2$), 43.4 (N^{5}CH$_2$), 45.6 (C(3)), 45.9 (C(2)), 55.2 (OCH$_3$), 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 (NCH$_2$ArC(1)), 138.1 (NCH$_2$ArC(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$^+$) C$_{27}$H$_{31}$O$_3$N$_2$ [M+H]$^+$ found 431.2328, requires 431.2329 (–0.3 ppm).

(2S,3S)-N^1,N^5-Dibenzyl-2-methyl-3-(2-nitrophenyl)pentanediamide (**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 Et$_3$N (42 μL, 0.30 mmol) in anhydrous CH$_2$Cl$_2$ (2.7 mL) at rt for 2 h gave a crude brown oil (>95:5 dr). The crude was stirred in anhydrous CH$_2$Cl$_2$ (6.6 mL) with benzylamine (6.6 mL, 60 mmol) at rt for 16 h to give a crude light yellow solid (approx. 90:10 dr) that was triturated in Et$_2$O to give the title compound (60 mg, 68%) as a brown solid. mp 176 °C (*dec.*); $[\alpha]_D^{20}$ –2.3 (*c* 0.61, CHCl$_3$); 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; ^{1}H NMR (400 MHz, CDCl$_3$) δ_H: 1.21 (3H, d, J 6.9, C(2)CH$_3$), 2.60 (1H, dd, J 15.0, 9.3, C(4)H^{A}H^B), 2.80 (1H, p, J 7.1, C(2)H), 2.87 (1H, dd, J 15.0, 5.9, C(4)H^{A}H^B), 3.94–4.04 (1H, m, C(3)H), 4.21–4.34 (4H, m, NCH$_2$ × 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); ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ_C: 15.1 (C(2)CH$_3$), 38.6 (C(4)), 43.4 (NCH$_2$), 43.5 (NCH$_2$), 45.2 (C(2)), 124.6 (C(3)ArC(6)), 127.3 (ArCH), 127.4 (ArCH), 127.6

(Ar*C*H), 127.6 (Ar*C*H), 128.6 (Ar*C*H), 132.6 (C(3)Ar*C*(4)), 135.9 (C(3)Ar*C*(1)), 137.9 (NCH$_2$Ar*C*(1)), 138.1 (NCH$_2$Ar*C*(1)), 150.3 (C(3)Ar*C*(2)), 170.4 (*C*(5)), 173.8 (*C*(1)), *C*(3) and C(3)Ar*C*(3) not observed; *m/z* (NSI$^+$) 468 ([M+Na]$^+$, 33%), 446 ([M+H]$^+$, 100%); HRMS (NSI$^+$) found C$_{26}$H$_{28}$O$_4$N$_3$ found 446.2072, requires 446.2074 (–0.5 ppm).

(2S,3S)-N^1,N^5-Dibenzyl-3-(4-fluorophenyl)-2-methylpentanediamide *(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 Et$_3$N (42 μL, 0.30 mmol) in anhydrous CH$_2$Cl$_2$ (2.7 mL) at rt for 3 h gave a crude brown oil (>95:5 dr). The crude was stirred in anhydrous CH$_2$Cl$_2$ (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 Et$_2$O to give the title compound (76 mg, 90%) as a white solid. mp 204–206 °C; $[\alpha]_D^{20}$ –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; ^{1}H NMR (400 MHz, CDCl$_3$) δ$_H$: 1.22 (3H, d, *J* 6.9, C(2)C*H$_3$*), 2.45 (1H, dd, *J* 13.8, 8.7, C(4)*H^A*H^B), 2.65 (1H, p, *J* 7.0, C(2)*H*), 2.91 (1H, dd, *J* 13.8, 6.8, C(4)H^A*H^B*), 3.38 (1H, q, *J* 8.0, C(3)H), 4.16 (1H, dd, *J* 14.7, 5.1, N^{1}C*H^A*H^B), 4.26 (1H, dd, *J* 14.7, 5.3, N^{5}C*H^A*H^B), 4.37 (1H, dd, *J* 15.1, 6.8, N^{1}CH^A*H^B*), 4.42 (1H, dd, *J* 14.9, 6.4, N^{5}CH^A*H^B*), 5.61 (1H, t, *J* 5.5, N^1*H*), 6.01 (1H, t, *J* 5.5, N^5*H*), 6.88–6.94 (1H, m, C(3)ArC(3)*H*), 6.94–6.98 (2H, m, Ar*H* ×1 and C(3)ArC(5)*H*), 7.00–7.06 (2H, m, Ar*H*), 7.09–7.16 (2H, m, C(3)ArC(2,6)*H*), 7.23–7.28 (7H, m, Ar*H*); ^{13}C{^{1}H} NMR (126 MHz, CDCl$_3$) δ$_C$: 16.1 (C(2)*C*H$_3$), 40.7 (*C*(4)), 43.3 (N*C*H$_2$), 43.5 (N*C*H$_2$), 45.7 (*C*(2)), 45.7 (*C*(3)), 115.3 (d, *J*$_{CF}$ 21.1, C(2)Ar*C*(3,5)), 127.4 (NCH$_2$Ar*C*(4)), 127.5 (NCH$_2$Ar*C*(4)), 127.6 (Ar*C*H × 2), 127.7 (Ar*C*H × 2), 128.6 (Ar*C*H × 4), 129.8 (d, *J*$_{CF}$ 7.9, C(3)Ar*C*(2,6)), 136.9 (d, *J*$_{CF}$ 3.1, C(3)Ar*C*(1)), 137.8 (NCH$_2$Ar*C*(1)), 138.0 (NCH$_2$Ar*C*(1)), 161.9 (d, *J*$_{CF}$ 245.3, C(3)Ar*C*(4)), 171.2 (*C*(5)), 173.8 (*C*(1)); ^{19}F (376 MHz,

CDCl$_3$) 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]$^+$ C$_{26}$H$_{28}$O$_2$N$_2$F found 419.2129, requires 419.2129 (−0.1 ppm).

(2S,3S)-N^1,N^5-Dibenzyl-3-(furan-2-yl)-2-methylpentanediamide (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 Et$_3$N (42 μL, 0.30 mmol) in anhydrous CH$_2$Cl$_2$ (2.7 mL) at rt for 3 h gave a crude brown crystallised oil (95:5 dr). The crude was stirred in anhydrous CH$_2$Cl$_2$ (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 Et$_2$O to give the title compound (58 mg, 75%) as a beige solid. mp 192–194 °C; [α]$_D^{20}$ −1.4 (*c* 0.50, CHCl$_3$); 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; ^{1}H NMR (400 MHz, CDCl$_3$) δ$_H$: 1.19 (3H, d, *J* 7.0, C(2)C*H*$_3$), 2.53 (1H, dd, *J* 13.9, 8.5, C(4)*H*^{A}H^B), 2.71 (1H, p, *J* 7.0, C(2)*H*), 2.80 (1H, dd, *J* 13.9, 6.7, C(4)H^A*H*^{B}), 3.49–3.58 (1H, m, C(3)*H*), 4.25–4.36 (3H, m, N^{1}C*H*$_2$ and N^{5}C*H*^{A}H^B), 4.41 (1H, dd, *J* 14.8, 6.0, N^{5}CH^A*H*^{B}), 5.76 (1H, t, *J* 5.2, N^1*H*), 6.06–6.10 (1H, m, C(3)ArC(5)*H*), 6.15 (1H, t, *J* 4.9, N^5*H*), 6.25 (1H, dd, *J* 3.2, 1.9, C(3)ArC(4)*H*), 7.10–7.18 (4H, m, Ar*H*), 7.22 (1H, dd, *J* 1.8, 0.8, C(3)ArC(3)*H*), 7.23–7.32 (6H, m, Ar*H*); ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ$_C$: 15.2 (C(2)*C*H$_3$), 38.2 (*C*(4)), 39.8 (*C*(3)), 45.54 (N*C*H$_2$Ph), 45.55 (N*C*H$_2$Ph), 43.9 (*C*(2)), 107.3 (C(3)Ar*C*(5)), 110.3 (C(3)Ar*C*(4)), 127.4 (Ar*C*H), 127.5 (Ar*C*H), 127.7 (Ar*C*H), 127.9 (Ar*C*H), 128.60 (Ar*C*H), 128.61 (Ar*C*H), 138.0 (NCH$_2$Ar*C*(1)), 138.2 (NCH$_2$Ar*C*(1)), 141.4 (C(3)Ar*C*(3)), 154.6 (C(3)Ar*C*(1)), 171.1 (*C*(5)), 173.9 (*C*(1)); m/z (NSI$^+$) 413 ([M+Na]$^+$, 41%), 391 ([M+H]$^+$, 100%); HRMS (NSI$^+$) C$_{24}$H$_{27}$O$_3$N$_2$ [M+H]$^+$ found 391.2016, requires 391.2016 (+0.0 ppm).

(2S,3S)-N^1,N^5,2-Tribenzyl-3-(furan-2-yl)pentanediamide (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 Et$_3$N (42 μL, 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 CH$_2$Cl$_2$ (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 Et$_2$O to give the title compound (36 mg, 39%) as a off-white solid. mp 192–194 °C; $[\alpha]_D^{20}$ −17.3 (*c* 0.48, CHCl$_3$); 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; ^{1}H NMR (400 MHz, CDCl$_3$) δ$_H$: 2.61 (1H, dd, *J* 14.0, 8.3, C(4)*H*^{A}H^B), 2.83–2.99 (4H, m, C(4)H^A*H*^{B}, C(2)*H*, C(2)C*H$_2$*), 3.59–3.68 (1H, m, C(3)*H*), 4.14 (1H, dd, *J* 14.8, 5.6, N^{1}C*H*^{A}H^B), 4.21 (1H, dd, *J* 14.8, 5.9, N^{1}CH^A*H*^{B}), 4.31–4.42 (2H, m, N^{5}C*H$_2$*), 5.62 (1H, t, *J* 5.5, N^1*H*), 5.98 (1H, t, *J* 5.5, N^5*H*), 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, Ar*H*), 7.10–7.17 (4H, m, Ar*H*), 7.17–7.21 (4H, m, Ar*H*), 7.21–7.25 (3H, m, Ar*H*), 7.26–7.33 (3H, m, Ar*H*); ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ$_C$: 35.8 (C(2)*C*H$_2$), 38.2 (*C*(4)), 38.6 (*C*(3)), 43.3 (N^1*C*H$_2$), 43.6 (N^5*C*H$_2$), 52.1 (*C*(2)), 107.5 (C(3)Ar*C*(4)), 110.4 (C(3)Ar*C*(5)), 126.4 (Ar*C*H), 127.2 (Ar*C*H), 127.4 (Ar*C*H), 127.6 (Ar*C*H × 2), 127.8 (Ar*C*H × 2), 128.4 (Ar*C*H × 2), 128.5 (Ar*C*H × 2), 128.6 (Ar*C*H × 2), 128.9 (Ar*C*H × 2), 137.9 (NCH$_2$Ar*C*(1)), 138.1 (NCH$_2$Ar*C*(1)), 139.3 (C(2)CH$_2$Ar*C*(1)), 141.4 (C(3)Ar*C*(3)), 154.4 (C(3)Ar*C*(1)), 170.9 (*C*(5)), 172.2 (*C*(1)); *m/z* (NSI$^+$) 489 ([M+Na]$^+$, 34%), 467 ([M+H]$^+$, 100%); HRMS (NSI$^+$) C$_{30}$H$_{31}$O$_3$N$_2$ [M+H]$^+$ found 467.2326, requires 467.2329 (−0.7 ppm).

*(2S,3S)-N^1,N^5-Dibenzyl-2-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 Et$_3$N (42 μL, 0.30 mmol) in anhydrous CH$_2$Cl$_2$ (2.7 mL) at rt for 24 h gave a crude brown oil (>95:5 dr). The crude was stirred in anhydrous CH$_2$Cl$_2$ (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 Et_2O to give the title compound (21 mg, 26%) as a white solid. mp 168–170°C; $[\alpha]_D^{20}$ +15.0 (*c* 0.40, $CHCl_3$); 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; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 0.86 (3H, t, *J* 6.8, C*H*$_3$), 1.12 (3H, d, *J* 7.0, C(2)C*H*$_3$), 1.16–1.36 (7H, m, $CH_3(CH_2)_3$ and C(3)C*H*^{A}H^B), 1.43–1.53 (1H, m, C(3)CH^A*H*^{B}), 1.95–2.07 (1H, m, C(3)*H*), 2.22 (1H, dd, *J* 13.9, 6.1, C(4)*H*^{A}H^B), 2.29 (1H, dd, *J* 13.9, 8.0, C(4)H^A*H*^{B}), 2.50–2.59 (1H, m, C(2)*H*), 4.39–4.44 (4H, m, NC*H*$_2$ × 2), 6.14 (1H, t, *J* 4.8, N^5*H*), 6.48 (1H, t, *J* 5.1, N^1*H*), 7.23–7.35 (10H, m, Ar*H*); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C: 14.0 (C(2)*C*H$_3$), 14.1 (*C*H$_3$), 22.6 (CH_3*C*H$_2$), 27.3 ($CH_3(CH_2)_2$*C*H$_2$), 31.1 (C(3)*C*H$_2$), 31.9 (CH_3CH_2*C*H$_2$), 38.7 (*C*(4)), 40.0 (*C*(3)), 42.1 (*C*(2)), 43.4 (N*C*H$_2$), 43.5 (N*C*H$_2$), 127.4 (Ar*C*H), 127.5 (Ar*C*H), 127.7 (Ar*C*H), 127.8 (Ar*C*H), 128.7 (Ar*C*H), 128.7 (Ar*C*H), 138.4 (NCH$_2$Ar*C*(1)), 138.6 (NCH$_2$Ar*C*(1)), 172.9 (*C*(5)), 174.7 (*C*(1)); *m/z* (NSI$^+$) ([2M+Na]$^+$, 34%), 395 ([M+H]$^+$, 100%); HRMS (NSI$^+$) $C_{25}H_{35}O_2N_2$ [M+H]$^+$ found 395.2690, requires 395.2693.

Supporting Information: ^{1}H and ^{13}C{^{1}H} NMR spectra and HPLC trances of all novel compounds. CIF file giving X-ray crystallographic data for **28**. This material is available free of charge *via* the Internet at http://pubs.acs.org.

References

(1) For reviews of NHC organocatalysis, see: (a) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606-5655. (b) Marion, N.; Diez-Gonzalez, S.; Nolan, S. P. *Angew. Chem. Int. Ed.* **2007**, *46*, 2988-3000. (c) Moore, J. L.; Rovis, T. *Top. Curr. Chem.* **2010**, *291*, 77-144. (d) Ryan, S. J.; Candish, L.; Lupton, D. W. *Chem. Soc. Rev.* **2013**, *42*, 4906-4917. (e) Flanigan, D. M.; Romanov-Michailidis, F.; White, N. A.; Rovis, T. *Chem. Rev.* **2015**, DOI: 10.1021/acs.chemrev.5b00060.

(2) For selected examples, see: (a) Huang, X. L.; He, L.; Shao, P. L.; Ye, S. *Angew. Chem. Int. Ed.* **2009**, *48*, 192-195. (b) Lv, H.; Chen, X.-Y.; Sun, L.-h.; Ye, S. *J. Org. Chem.* **2010**, *75*, 6973-6976. (c) Jian, T.-Y.; Shao, P.-L.; Ye, S. *Chem. Commun.* **2011**, *47*, 2381-2383. (d) Leckie, S. M.; Brown, T. B.; Pryde, D.; Lebl, T.; Slawin, A. M. Z.; Smith, A. D. *Org. Biomol. Chem.* **2013**, *11*, 3230-3246.

(3) For seminal examples, see: (a) Reynolds, N. T.; Rovis, T. *J. Am. Chem. Soc.* **2005**, *127*, 16406-16407. (b) He, M.; Uc, G. J.; Bode, J. W. *J. Am. Chem. Soc.* **2006**, *128*, 15088-15089. (c) He, M.; Beahm, B. J.; Bode, J. W. *Org. Lett.* **2008**, *10*, 3817-3820.

(4) For seminal examples, see: (a) He, M.; Struble, J. R.; Bode, J. W. *J. Am. Chem. Soc.* **2006**, *128*, 8418-8420. (b) He, M.; Bode, J. W. *J. Am. Chem. Soc.* **2007**, *130*, 418-419. (c) Phillips, E. M.; Wadamoto, M.; Chan, A.; Scheidt, K. A. *Angew. Chem. Int. Ed.* **2007**, *46*, 3107-3110. (d) Wadamoto, M.; Phillips, E. M.; Reynolds, T. E.; Scheidt, K. A. *J. Am. Chem. Soc.* **2007**, *129*, 10098-10099.

(5) (a) Kawanaka, Y.; Phillips, E. M.; Scheidt, K. A. *J. Am. Chem. Soc.* **2009**, *131*, 18028-18029. (b) Phillips, E. M.; Wadamoto, M.; Roth, H. S.; Ott, A. W.; Scheidt, K. A. *Org. Lett.* **2009**, *11*, 105-108.

(6) (a) Li, G.-Q.; Dai, L.-X.; You, S.-L. *Org. Lett.* **2009**, *11*, 1623-1625. (b) Lv, H.; Mo, J. M.; Fang, X. Q.; Chi, Y. R. *Org. Lett.* **2011**, *13*, 5366-5369.

(7) (a) Ling, K. B.; Smith, A. D. *Chem. Commun.* **2011**, *47*, 373-375. (b) Davies, A. T.; Taylor, J. E.; Douglas, J.; Collett, C. J.; Morrill, L. C.; Fallan, C.; Slawin, A. M. Z.; Churchill, G.; Smith, A. D. *J. Org. Chem.* **2013**, *78*, 9243-9257. (c) Taylor, J. E.; Daniels, D. S. B.; Smith, A. D. *Org. Lett.* **2013**, *15*, 6058-6061. (d) Davies, A. T.; Pickett, P. M.; Slawin, A. M. Z.; Smith, A. D. *ACS Catal.* **2014**, *4*, 2696-2700.

(8) For selected examples, see: (a) Zhao, X.; Ruhl, K. E.; Rovis, T. *Angew. Chem. Int. Ed.* **2012**, *51*, 12330-12333. (b) Mo, J.; Yang, R.; Chen, X.; Tiwari, B.; Chi, Y. R. *Org. Lett.* **2013**, *15*, 50-53. (c) Lin, L.; Yang, Y.; Wang, M.; Lai, L.; Guo, Y.; Wang, R. *Chem. Commun.* **2015**, *51*, 8134-8137.

(9) For selected examples, see: (a) Hao, L.; Du, Y.; Lv, H.; Chen, X. K.; Jiang, H. S.; Shao, Y. L.; Chi, Y. R. *Org. Lett.* **2012**, *14*, 2154-2157. (b) Lee, A.; Younai, A.; Price, C. K.; Izquierdo, J.; Mishra, R. K.; Scheidt, K. A. *J. Am. Chem. Soc.* **2014**, *136*, 10589-10592. (c) Cheng, J.-T.; Chen, X.-Y.; Ye, S. *Org. Biomol. Chem.* **2015**, *13*, 1313-1316. (d) Lee, A.; Scheidt, K. A. *Chem. Commun.* **2015**, *51*, 3407-3410.

(10) For reviews on NHC-redox catalysis, see: (a) Rong, Z. Q.; Zhang, W.; Yang, G. Q.; You, S. L. *Curr. Org. Chem.* **2011**, *15*, 3077-3090. (b) Douglas, J.; Churchill, G.; Smith, A. D. *Synthesis* **2012**, *44*, 2295-2309. (c) Vora, H. U.; Wheeler, P.; Rovis, T. *Adv. Synth. Catal.* **2012**, *354*, 1617-1639.

(11) Matsunaga, S.; Kinoshita, T.; Okada, S.; Harada, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 7559-7570.

(12) Evans, D. A.; Fandrick, K. R.; Song, H.-J. *J. Am. Chem. Soc.* **2005**, *127*, 8942-8943.

(13) Vanderwal, C. D.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2004**, *126*, 14724-14725.

(14) (a) Evans, D. A.; Scheidt, K. A.; Fandrick, K. R.; Lam, H. W.; Wu, J. *J. Am. Chem. Soc.* **2003**, *125*, 10780-10781. (b) Evans, D. A.; Johnson, J. S. *J. Am. Chem. Soc.* **1998**, *120*, 4895-4896. (c) Jiang, H.; Paixão, M. W.; Monge, D.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2010**, *132*, 2775-2783. (d) Smith, S. R.; Leckie, S. M.; Holmes, R.; Douglas, J.; Fallan, C.; Shapland, P.; Pryde, D.; Slawin, A. M. Z.; Smith, A. D. *Org. Lett.* **2014**, *16*, 2506-2509.

(15) For an example of α-keto-β,γ-unsaturated phosphonates in NHC catalysis, see: Leckie, S. M.; Fallan, C.; Taylor, J. E.; Brown, T. B.; Pryde, D.; Lébl, T.; Slawin, A. M. Z.; Smith, A. D. *Synlett* **2013**, 1243-1249.

(16) (a) Zheng, C.; Li, Y.; Yang, Y.; Wang, H.; Cui, H.; Zhang, J.; Zhao, G. *Adv. Synth. Catal.* **2009**, *351*, 1685-1691. (b) Wang, H.-F.; Li, P.; Cui, H.-F.; Wang, X.-W.; Zhang, J.-K.; Liu, W.; Zhao, G. *Tetrahedron* **2011**, *67*, 1774-1780. (c) Zhang, J.; Liu, X.; Ma, X.; Wang, R. *Chem. Commun.* **2013**, *49*, 9329-9331. (d) Zhang, J.; Liu, X.; Wu, C.; Zhang, P.; Chen, J.; Wang, R. *Eur. J. Org. Chem.* **2014**, 7104-7108.

(17) Morrill, L. C.; Stark, D. G.; Taylor, J. E.; Smith, S. R.; Squires, J. A.; D'Hollander, A. C. A.; Simal, C.; Shapland, P.; O'Riordan, T. J. C.; Smith, A. D. *Org. Biomol. Chem.* **2014**, *12*, 9016-9027.

(18) For mechanistic studies on the reactivity of trichloromethyl ketones in haloform-type reactions, see: (a) Uieara, M.; Zucco, C.; Zanette, D.; Rezende, M. C.; Nome, F. *J. Chem. Soc., Perkin Trans. 2* **1987**, 175-179. (b) Zucco, C.; Lima, C. F.; Rezende, M. C.; Vianna, J. F.; Nome, F. *J. Org. Chem.* **1987**, *52*, 5356-5359.

(19) For seminal examples, see: (a) Signaigo, F. K.; Adkins, H. *J. Am. Chem. Soc.* **1936**, *58*, 1122-1124. (b) Treibs, A.; Dietl, A. *Justus Liebigs Ann. Chem.* **1958**, *619*, 80-95. (c)

Bailey, D. M.; Johnson, R. E.; Albertson, N. F. *Org. Synth.* **1971**, *51*, 100. (d) Bailey, D. M.; Johnson, R. E. *J. Med. Chem.* **1973**, *16*, 1300-1302. (e) Barker, P.; Gendler, P.; Rapoport, H. *J. Org. Chem.* **1978**, *43*, 4849-4853.

(20) For selected recent uses of trichloromethyl ketones in natural product synthesis and medicinal chemistry, see: (a) Wu, P.; Zhang, J.; Meng, Q.; Nare, B.; Jacobs, R. T.; Zhou, H. *Eur. J. Med. Chem.* **2014**, *81*, 59-75. (b) Rodriguez, R. A.; Barrios Steed, D.; Kawamata, Y.; Su, S.; Smith, P. A.; Steed, T. C.; Romesberg, F. E.; Baran, P. S. *J. Am. Chem. Soc.* **2014**, *136*, 15403-15413. (c) Hirata, A.; Nokihara, K.; Kawamoto, Y.; Bando, T.; Sasaki, A.; Ide, S.; Maeshima, K.; Kasama, T.; Sugiyama, H. *J. Am. Chem. Soc.* **2014**, *136*, 11546-11554. (d) Grosse, S.; Mathieu, V.; Pillard, C.; Massip, S.; Marchivie, M.; Jarry, C.; Bernard, P.; Kiss, R.; Guillaumet, G. *Eur. J. Med. Chem.* **2014**, *84*, 718-730.

(21) Uyanik, M.; Suzuki, D.; Yasui, T.; Ishihara, K. *Angew. Chem. Int. Ed.* **2011**, *50*, 5331-5334.

(22) Corey, E. J.; Link, J. O.; Shao, Y. *Tetrahedron Lett.* **1992**, *33*, 3435-3438.

(23) The relative and absolute configuration of the products was assigned by X-ray crystallographic analysis of diamide **28**, with all other products assigned by analogy. See supporting information for details. Crystallographic data for **28** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC 1410758.

(24) Further attempts to promote complete alcoholysis of the trichloromethyl ketone using alternative alcohols and catalysts were unsuccessful.

(25) The ee of diamide **21** was the same before and after purification (>99% ee) showing that the trituration process did not enhance the observed enantioselectivity.

(26) For work regarding the pKa's of various NHC catalysts, see: Massey, R. S.; Collett, C. J.; Lindsay, A. G.; Smith, A. D.; O'Donoghue, A. C. *J. Am. Chem. Soc.* **2012**, *134*, 20421-20432.

(27) (a) Allen, S. E.; Mahatthananchai, J.; Bode, J. W.; Kozlowski, M. C. *J. Am. Chem. Soc.* **2012**, *134*, 12098-12103. (b) Mahatthananchai, J.; Bode, J. W. *Acc. Chem. Res.* **2014**, *47*, 696-707.

(28) For the synthesis of NHC-precatalyst **11**, see: Struble, J. R.; Bode, J. W. *Org. Synth.* **2010**, *87*, 362-376.

(29) Xiao, X.; Antony, S.; Kohlhagen, G.; Pommier, Y.; Cushman, M. *Bioorg. Med. Chem.* **2004**, *12*, 5147-5160.

(30) Wada, M.; Nakai, H.; Sato, Y.; Hatanaka, Y.; Kanoaka, Y. *Tetrahedron* **1983**, *39*, 2691-2698.

(31) Patil, N. T.; Singh, V. *Chem. Commun.* **2011**, *47*, 11116-11118.

(32) MnO_2 was reactivated by washing with distilled water several times before drying in an oven at 120 °C.

(33) Noole, A.; Borissova, M.; Lopp, M.; Kanger, T. *J. Org. Chem.* **2011**, *76*, 1538-1545.

(34) Johnson, J. S.; Olhava, E. J; Evans, D. A. *J. Am. Chem. Soc.* **2000**, *122*, 1635-1649.

(35) Kawai, M.; Onaka, M.; Izumi, Y. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2157-2164.

(36) Tsukamoto, M.; Tananka, S.; Hirao, I.; Yamaguchi, M. *Tetrahedron Lett.* **1984***, 25,* 5661-5664.