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Stereospecific Asymmetric N-Heterocyclic Carbene (NHC)-Catalyzed Redox Synthesis of Trifluoromethyl Dihydropyranones and Mechanistic Insights

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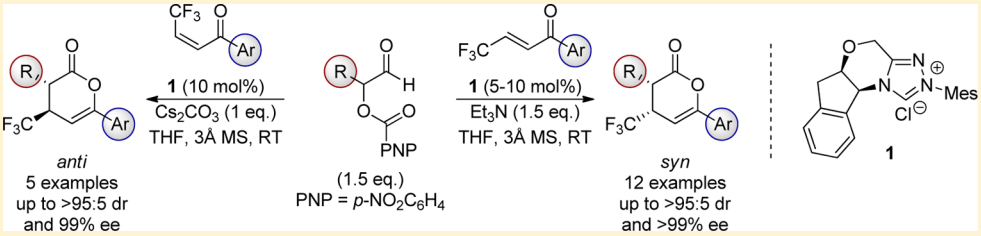
Supporting Information



ABSTRACT: N-Heterocyclic carbene (NHC)-catalyzed redox asymmetric hetero-Diels–Alder reactions of α-aroyloxyaldehydes with β-trifluoromethyl enones generates synthetically useful dihydropyranones containing a stereogenic trifluoromethyl substituent in good yields (up to 81%) and excellent diastereoselectivity and enantioselectivity (up to >95:5 dr and >99% ee). The process is stereospecific, with use of either (*E*)- or (*Z*)-β-trifluoromethyl enones forming *syn*- or *anti*-dihydropyranone products, respectively. Mechanistic studies through in situ kinetic analysis of the reaction reveal key differences in reactivity between chiral NHC precursor **1** and an achiral NHC precursor.

INTRODUCTION

The trifluoromethyl unit is widely employed within the pharmaceutical, agrochemical, and materials industries due to the unique physicochemical properties it can impart onto molecules.[1] In particular, heterocycles containing a stereogenic trifluoromethyl group represent a major structural class of biologically active compounds.[2] The development of new catalytic methodologies for the asymmetric introduction of trifluoromethyl groups into versatile synthetic building blocks is therefore a worthwhile goal.[3] Within the field of organocatalysis, a number of methods have been developed for the asymmetric introduction of fluorine atoms.[4] One general strategy for the organocatalytic construction of stereogenic trifluoromethyl centers is asymmetric functionalization of prochiral trifluoromethylated substrates.[3a] For example, conjugate additions of various nucleophiles into β-trifluoromethyl enones have been catalyzed by proline derivatives,[5a] thioureas,[5b,c] and Cinchona alkaloids.[5d−g]

N-Heterocyclic carbene (NHC)-redox catalysis is a rapidly emerging area of organocatalysis.[6,7] The addition of NHCs to aldehydes bearing an α-reducible functional group allows access to three distinct catalytic intermediates: acyl azoliums, azolium enolates, and homoenolates, which can be used in a range of further reactions. For example, azolium enolates generated through NHC-redox catalysis undergo asymmetric hetero-Diels–Alder reactions with unsaturated ketoesters or ketimines to form dihydropyranones or dihydropyridinones, respectively.[9−11] In this regard, Bode and co-workers showed that either α-chloroaldehydes or their bisulfite adducts could be used as azolium enolate precursors in hetero-Diels–Alder reactions with both (*E*)-β,γ-unsaturated α-ketoesters and (*E*)-α,β-unsaturated γ-ketoesters to form dihydropyranones with high syn diastereoselectivity (Scheme 1).[8a,b] Other NHC-catalyzed redox [4+2] cycloadditions have been performed using azolium enolates generated from α-chloroaldehydes,[8c−e] enals,[9] formyl cyclopropanes,[10] and ketenes.[11] In all these cases, the heterocyclic products are formed preferentially as their syn diastereoisomers. Interestingly, in some cases, cycloadditions of azolium enolates generated by deprotonation of an acyl azolium intermediate give products with preference for the anti diastereoisomer. For example, Chi et al. found that *p*-nitrophenyl esters react with (*E*)-α,β-unsaturated ketimines using NHC catalysis to give *anti*-dihydropyridinones.[12] Additionally, Rovis et al. reported that enolate equivalents generated from aldehydes and NHCs using a stoichiometric oxidant react with (*E*)-α,β-unsaturated ketimines to give *anti*-dihydropyridinones (Scheme 1).[13a] However, azolium enolates formed under identical oxidative conditions react with (*E*)-chalcones to give *syn*-dihydropyranones.[13b] To date, the differing stereoselectivity in these processes has not been rationalized.

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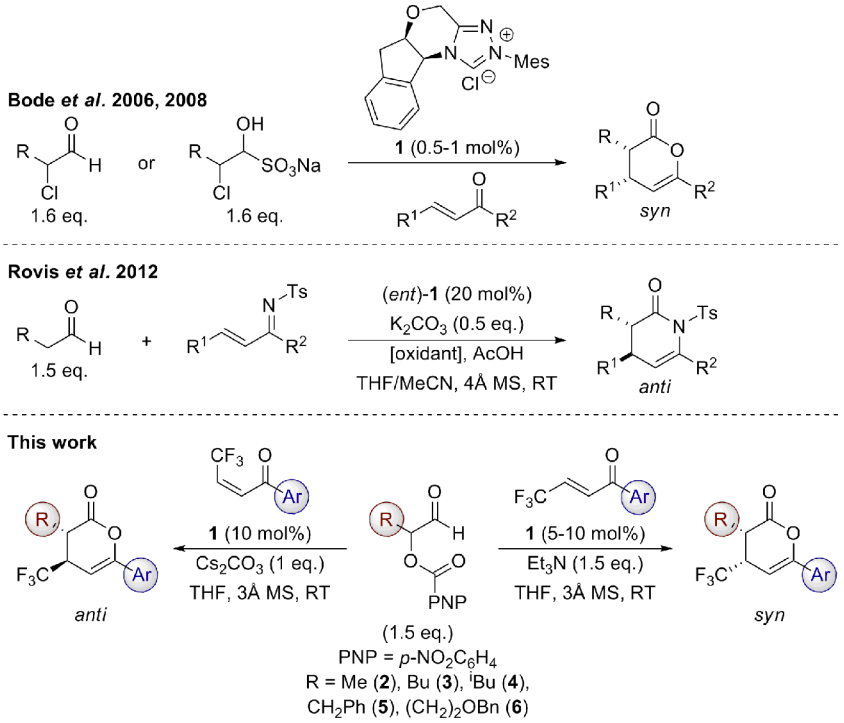
Scheme 1. Hetero-Diels–Alder Reactions of of Enones and α,β-Unsaturated Ketimines with Azolium Enolates



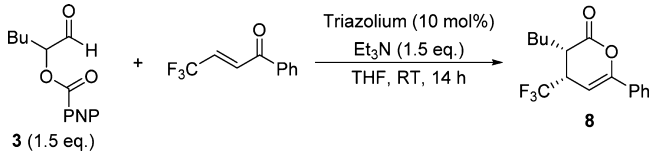
Herein we report the first example of an asymmetric NHC-catalyzed redox [4+2] cycloaddition using β-trifluoromethyl enones to form synthetically useful dihydropyranone products bearing a stereogenic trifluoromethyl substituent. In particular, the stereospecificity of this process has been demonstrated through the use of either (*E*)- or (*Z*)-β-trifluoromethyl enones to form either *syn*- or *anti*-dihydropyranones.[14] We also detail preliminary mechanistic insights into the reaction through kinetic analysis and isolation of key reaction intermediates.

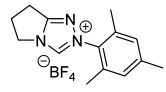
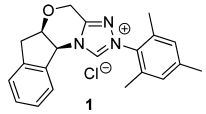
RESULTS AND DISCUSSION

Stereospecific NHC-Catalyzed Redox Hetero-Diels–Alder Reactions with β-Trifluoromethyl Enones. Having previously reported that *p*-nitrobenzoyloxyaldehydes are bench stable alternatives to α-haloaldehydes in NHC-catalyzed redox esterifications,[15] we evaluated their potential as azolium enolate precursors for [4+2] cycloadditions with β-trifluoromethyl enones. α-Aroyloxyaldehydes **2**–**6** are readily prepared in one step on a gram scale from the parent aldehyde and *p*-nitrobenzoic acid using the α-oxyacylation methodology developed by Ishihara and co-workers.[16,17] Initial studies found that α-aroyloxyaldehyde **3** reacted with (*E*)-4,4,4-trifluoro-1-phenylbut-2-en-1-one using 10 mol % achiral triazolium NHC precatalyst **7** and triethylamine in THF at room temperature to give dihydropyranone **8** predominantly as its syn diastereoisomer but in a disappointing 17% yield (Table 1, entry 1). Pleasingly, chiral triazolium precatalyst **1** proved significantly more reactive, giving dihydropyranone **8** in 63% yield as its syn diastereoisomer (>95:5 dr) in >99% ee (Table 1, entry 2). A possible explanation for the surprising difference in reactivity between achiral NHC precatalyst **7** and chiral precatalyst **1** was subsequently found using kinetic analysis (vide infra).

Encouraged by this initial result, the scope of the reaction was explored using a series of aryl substituted (*E*)-β-trifluoromethyl enones (Table 2). The reaction with electron-rich *p*-$MeOC_6H_4$ substituted β-trifluoromethyl enone required 24 h to reach completion, with *syn*-dihydropyranone **9** isolated in 73% yield and >99% ee. The process could be applied to *o*-$MeOC_6H_4$ substituted trifluoromethyl enone, although modified conditions using Cs_2CO_3 and heating the reaction at 40 °C were required to give product **10** in 60% yield as a single enantiomer. The presence of electron-withdrawing *p*-$NO_2C_6H_4$ and *p*-BrC_6H_4 substituents significantly increased the rate of reaction to the extent that *p*-$NO_2C_6H_4$ β-trifluoromethyl enone had to be added slowly via syringe pump to avoid side reactions. The *p*-BrC_6H_4 substituted dihydropyranone **12** provided confirmation of the relative and absolute configuration through X-ray crystallographic analysis.[18] The presence of heteroaromatic 3-pyridyl and 2-furyl substituents was also tolerated, giving the major syn products **13** and **14** in good

Table 1. Initial NHC-Catalyzed Redox [4+2] Cycloaddition Using α-Aroyloxyaldehyde 3



Entry	Triazolium	Yield %	dr[a]	ee %[b]
1	 7	17	94:6	N/A
2	 1	63	>95:5	>99

[a]Values for dr determined by ^{1}H NMR analysis of the crude product. [b]Values for ee determined by HPLC analysis.

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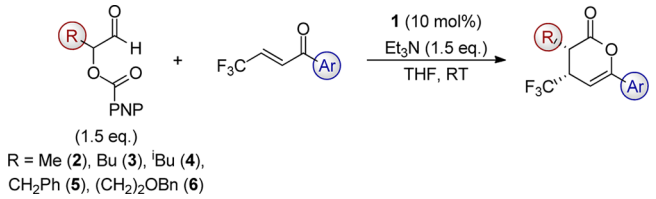
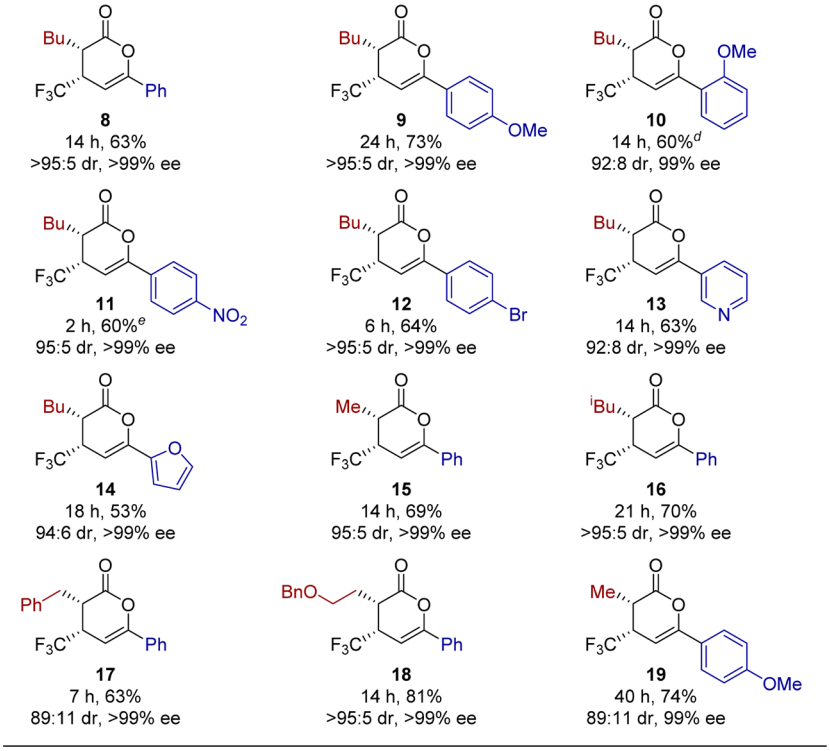
Table 2. [4+2] Cycloadditions with (*E*)-β-Trifluoromethyl Enones[a,b,c]



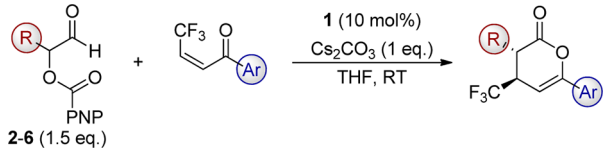


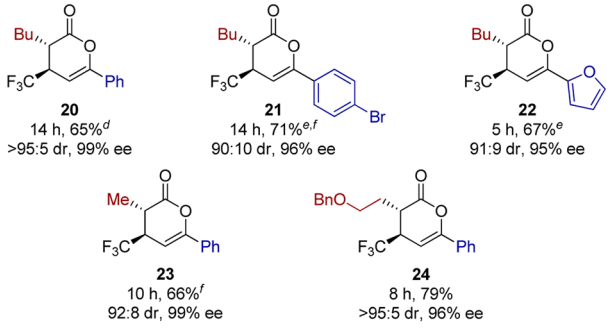
[a]Isolated yields of major diastereoisomer. [b]Values for dr determined by ^{1}H NMR analysis of the crude product. [c]Values for ee determined by HPLC analysis. [d]Reaction using Cs_2CO_3 (1 equiv) at 40 °C. [e]β-Trifluoromethyl enone added via syringe pump over 1 h.

yields (63% and 53%, respectively) and excellent ee (>99%). However, alkyl substituted β-trifluoromethyl enones were significantly less reactive in this process, giving reduced conversion into the desired dihydropyranones.[19] Next, the substituent on the α-aroyloxyaldehyde was varied in reactions with the phenyl substituted β-trifluoromethyl enone. Both methyl and isobutyl substituted α-aroyloxyaldehydes (**2** and **4**) worked well, giving the corresponding *syn*-dihydropyranones (**15** and **16**) in high yields (69% and 70%, respectively) and >99% ee. The reaction using α-aroyloxyaldehyde **6** gave *syn*-dihydropyranone **18** with a pendant *O*-benzyl substituent in 81% yield as a single enantiomer. However, the reaction with α-aroyloxyaldehyde **5** gave reduced diastereoselectivity, with dihydropyranone **17** formed as a 89:11 syn:anti mixture. The reaction of α-aroyloxyaldehyde **2** with *p*-$MeOC_6H_4$ substituted β-trifluoromethyl enone also gave a lower dr, with product **19** obtained as a 89:11 syn:anti mixture after 40 h.

We next probed the stereospecificity of this process using (*Z*)-β-trifluoromethyl enones as substrates. In this case, the reaction of (*Z*)-4,4,4-trifluoro-1-phenylbut-2-en-1-one with α-aroyloxyaldehyde **3** using 10 mol % **1** formed *anti*-dihydropyranone **20** as a single diastereoisomer, which was isolated in 65% yield and 99% ee. This methodology was then applied to a small number of (*Z*)-β-trifluoromethyl enones (Table 3). The reaction of *p*-BrC_6H_4 substituted (*Z*)-β-

Table 3. [4+2] Cycloadditions with (*Z*)-β-Trifluoromethyl Enones[a,b,c]





[a]Isolated yields of major diastereoisomer. [b]Values for dr determined by ^{1}H NMR analysis of the crude product. [c]Values for ee determined by HPLC analysis. [d]Reaction using Et_3N (1.5 equiv). [e]Reaction at 40 °C. [f]Reaction using 2 equiv of aldehyde.

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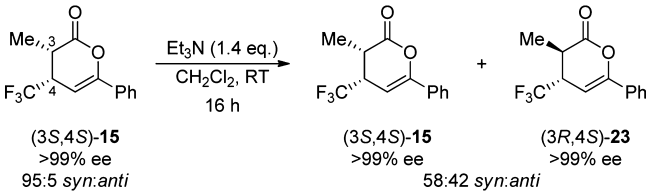
trifluoromethyl enone with α-aroyloxyaldehyde **3** was found to be sluggish under the standard reaction conditions. However, under modified conditions using Cs_2CO_3 as the base and two equiv of α-aroyloxaldehyde **3**, and performing the reaction at 40 °C, *anti*-dihydropyranone **21** could be isolated in 71% yield and 96% ee. These modified conditions also proved to be optimal for the reaction with 2-furyl substituted (*Z*)-β-trifluoromethyl enone, providing *anti*-dihydropyranone **22** in 67% yield and 95% ee. The protocol was used with α-aroyloxyaldehydes **2** and **6**, forming the corresponding *anti*-dihydropyranones **23** and **24** in high yield (66% and 79%, respectively) and excellent ee.

The stereospecific nature of the observed reversal in diastereoselectivity and the absolute configuration of the anti products were confirmed through an epimerization experiment. Treating *syn*-dihydropyranone **15** with triethylamine in CH_2Cl_2 resulted in a 58:42 syn:anti mixture after 16 h with no loss in ee in either diastereoisomer (Scheme 2). In this case, the

Scheme 2. Base Promoted Epimerization of Dihydropyranone 15[a,b]



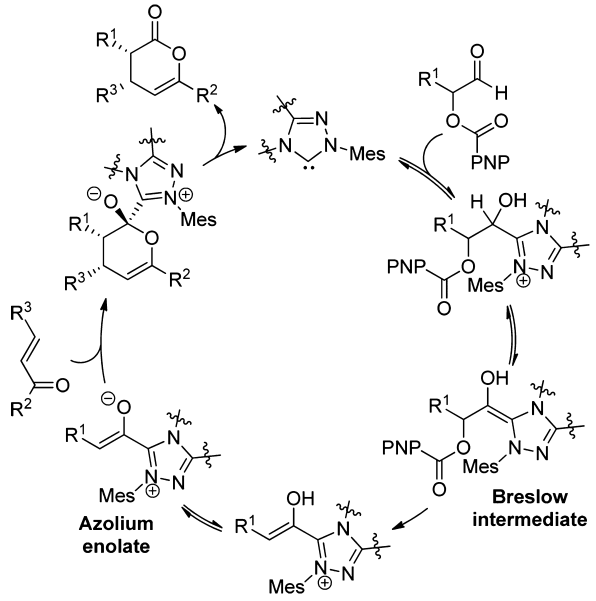
[a]Values for dr determined by ^{1}H NMR analysis of the crude reaction mixture. [b]Values for ee determined by HPLC analysis.

enantiomer of *anti*-dihydropyranone **23** formed was opposite to that obtained using the (*Z*)-β-trifluoromethyl enone. The results are consistent with epimerization of these products occurring at the C(3) position and the configuration of the C(4) stereocenter being dependent upon the enone geometry.

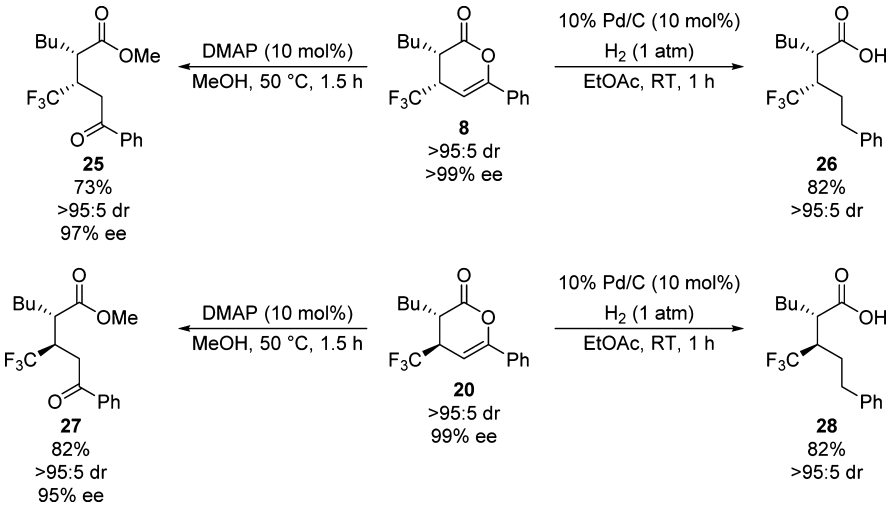
Derivatizations. The utility of the trifluoromethyl substituted dihydropyranones was demonstrated through a series of derivatizations to generate synthetically useful building blocks containing a stereogenic trifluoromethyl group (Scheme 3). First, the NHC-catalyzed redox hetero-Diels–Alder reaction between the phenyl (*E*)-β-trifluoromethyl enone and α-aroyloxyaldehyde **3** was repeated on a gram scale to give *syn*-dihydropyranone **8** (1.92 g) in 74% yield and >99% ee. Treatment of *syn*-dihydropyranone **8** with methanol and 10 mol % 4-dimethylaminopyridine (DMAP) gave the ring-opened ester **25** in good yield and 97% ee. Hydrogenolysis of *syn*-dihydropyranone **8** with Pd/C resulted in reduction of the alkene functionality with concomitant C–O bond cleavage to give acid **26** as a single diastereoisomer.[20] The ring opening with methanol and the reduction could also be performed on *anti*-dihydropyranone **20**, obtained from the cycloaddition using the phenyl (*Z*)-β-trifluoromethyl enone, to give the diastereomeric ester **27** and acid **28**.

Mechanistic Studies. The proposed catalytic cycle for these transformations is based upon that suggested by Bode and co-workers for related [4+2] cycloaddition reactions (Scheme 4).[9b,21] Initially, the active NHC catalyst adds to the

Scheme 4. Proposed Catalytic Cycle



Scheme 3. Derivatization Reactions[a,b]



[a]Values for dr determined by ^{1}H NMR analysis of the crude product. [b]Values for ee determined by HPLC analysis.

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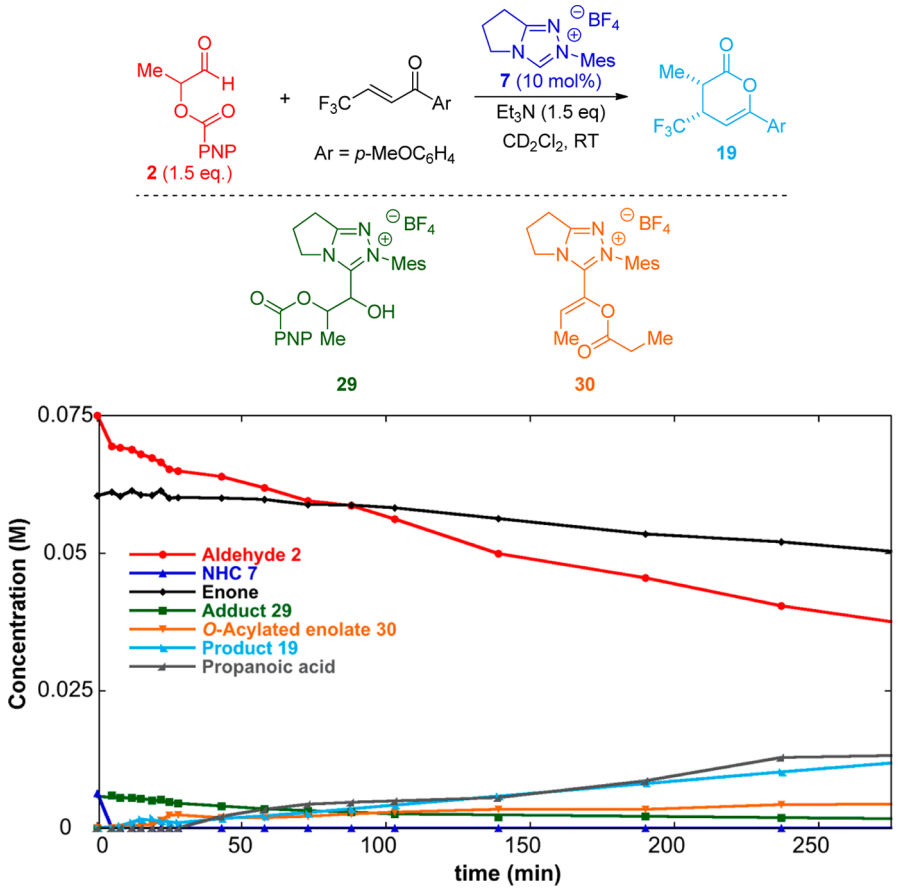
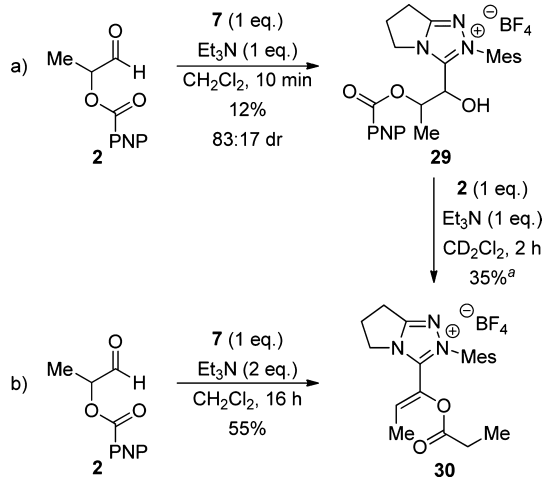


Figure 1. Kinetic profile using achiral NHC precatalyst **7**.

α-aroyloxyaldehyde to form an adduct,[22] which is deprotonated to form the Breslow intermediate. Presumably, rapid elimination of *p*-nitrobenzoate followed by deprotonation forms an azolium enolate, which is thought to undergo an asynchronous endo-hetero-Diels–Alder reaction with the enone.[21a]

Kinetic studies were performed to gain further insight into the mechanism of these NHC-catalyzed cycloadditions. In particular, we were interested in understanding why achiral precatalyst **7** is ineffective compared with **1** and the fate of the excess α-aroyloxyaldehyde during the reaction. To study these observations, kinetic profiles of the reaction between α-aroyloxyaldehyde **2** and *p*-$MeOC_6H_4$ substituted β-trifluoromethyl enone in CD_2Cl_2 were determined using characteristic signals of each species in the ^1H NMR spectrum relative to an internal standard.[23] With achiral salt **7** (Figure 1), the triazolium precatalyst is quickly consumed and forms adduct **29** as a 50:50 mixture of diastereoisomers, which is consistent with our previous mechanistic studies of the benzoin and Stetter reactions.[24] This initial adduct could be isolated and fully characterized from a stoichiometric reaction of precatalyst **7** with aldehyde **2**, with purification enriching the diastereoselectivity to 83:17 (Scheme 5a). The kinetic profile shows that aldehyde **2** is consumed at a faster rate than the enone, with dihydropyranone **19** being formed slowly. Control experiments showed that α-aroyloxyaldehyde **2** undergoes reaction in the absence of the enone, with much of the consumed aldehyde converted into propanoic acid presumably through hydrolysis of the corresponding acyl azolium species with adventitious water. The ^1H NMR spectra of the reaction

Scheme 5. Isolation of (a) Initial NHC–Aldehyde Adduct 29 and (b) O-Acylated Enone 30[a]



[a]Conversion determined by ^1H NMR analysis.

with precatalyst **7** also showed the buildup of another unexpected species over time, which was identified as O-acylated enolate **30**.[25] This side product could be isolated from the stoichiometric reaction of triazolium salt **7** and α-aroyloxyaldehyde **2** if left for extended periods of time (Scheme 5b). Additionally, O-acylated enolate **30** can be observed by ^1H NMR spectroscopy if isolated adduct **29** is re-treated with an excess of aldehyde **2** in CD_2Cl_2.

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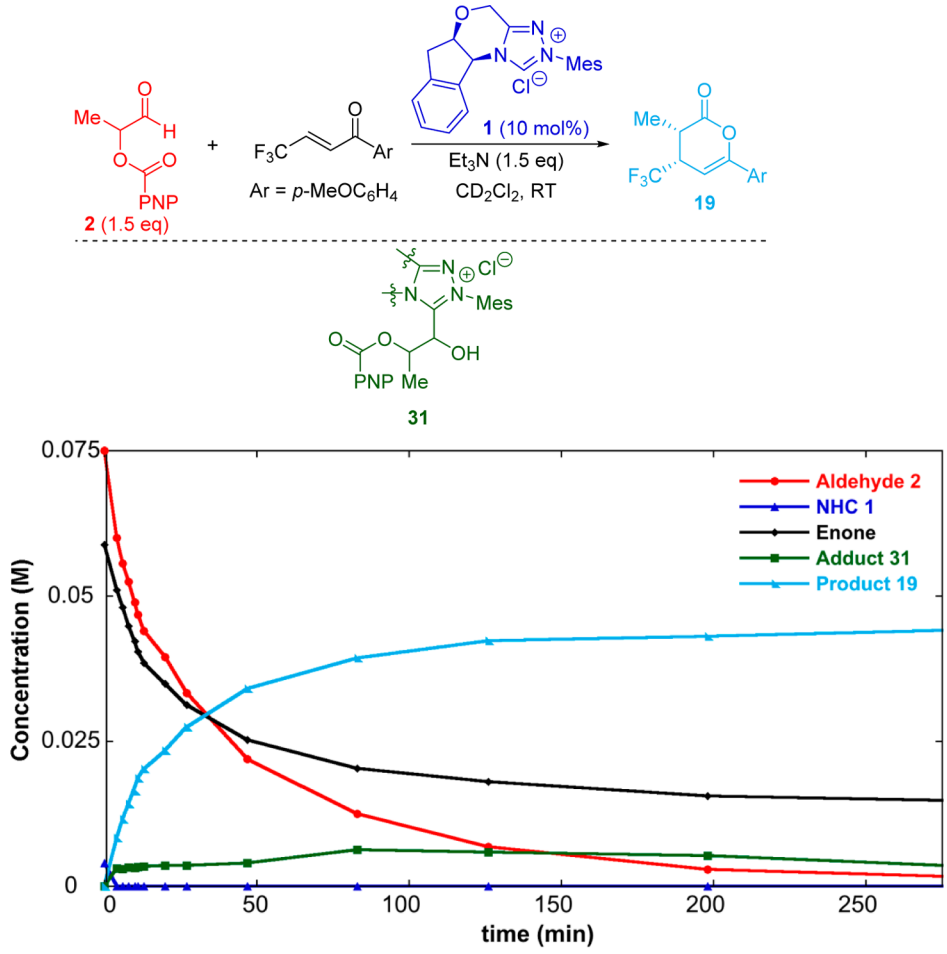


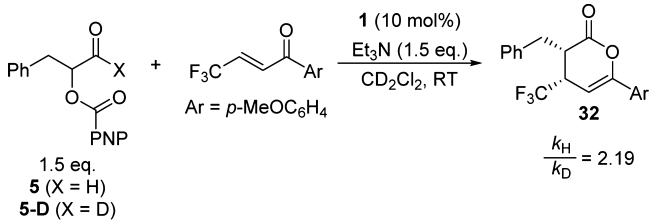
Figure 2. Kinetic profile using chiral NHC precatalyst **1**.

Further studies found that O-acylated enolate **30** is completely unreactive under the reaction conditions and thus represents a catalytic dead end.[26] One possible mechanism for the formation of **30** is through O-acylation of initial adduct **29** with an acyl azolium species, presumably formed through equilibration with the corresponding azolium enolate, followed by base promoted elimination of *p*-nitrobenzoate. The spectroscopic observation of propanoic acid and O-acylated enolate **30** under catalytic conditions using achiral NHC precatalyst **7**, combined with the slow rate of product formation, account for the poor observed activity of this catalyst.

The kinetic experiments were then repeated using chiral NHC salt **1** (Figure 2). The triazolium precatalyst is quickly consumed and forms initial adduct **31** as a single diastereoisomer.[27] The β-trifluoromethyl enone and α-aroyloxyaldehyde **2** are rapidly consumed at the start of the reaction, at a much faster rate than the rate when the achiral catalyst **7** is used, which also correlates with rapid formation of dihydropyranone product **19**. Only after 45 min does the rate of consumption of aldehyde **2** increase beyond that of the enone. However, in this case, the decomposition products of α-aroyloxyaldehyde **2** could not be identified. Importantly, no peaks corresponding to either propanoic acid or the equivalent O-acylated enolate were observed in the ^{1}H NMR spectra of the reaction using chiral NHC **1**, although they could still be present in low concentrations.[28] These results are consistent with the azolium enolate formed with NHC precatalyst **1** being much more reactive toward the hetero-Diels–Alder reaction compared with achiral NHC salt **7**. The rate of product formation is also much greater than those for the unwanted side reactions of the aldehyde with NHC **1**.

Finally, the rate-determining step of the process was probed through a ^{2}H kinetic isotope effect (KIE). Measurement of the initial rates of reaction with α-aroyloxyaldehyde **5** and its deuterated analogue **5-D** under the standard reaction conditions revealed a k_H/k_D of 2.19 (Scheme 6).[29,30] This suggests that deprotonation of the adduct formed between NHC **1** and the α-aroyloxyaldehyde to form the Breslow intermediate is a kinetically significant step in these [4+2] cycloadditions.

Scheme 6. Kinetic Isotope Effect Measurement



CONCLUSION

Synthetically useful *syn*- and *anti*-dihydropyranones containing a stereogenic trifluoromethyl substituent can be synthesized

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stereospecifically through NHC-catalyzed redox hetero-Diels–Alder reactions of either (*E*)- or (*Z*)-β-trifluoromethyl enones with α-aroyloxyaldehydes. Kinetic experiments revealed the formation of O-acylated enolate species **30** when achiral precatalyst **7** was used in these reactions, accounting for the differences in reactivity observed compared with chiral precatalyst **1**. The measurement of a positive KIE suggests that deprotonation of the NHC–aldehyde adduct to form the Breslow intermediate is kinetically significant. Current research within this laboratory is focused upon developing novel asymmetric processes utilizing α-aroyloxyaldehydes as azolium enolate precursors.

EXPERIMENTAL SECTION

General Information. 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 and −78 °C obtained using ice/water and CO_2(s)/acetone baths, respectively. ^{1}H NMR spectra were acquired at 300, 400, or 500 MHz, ^{13}C{^{1}H} NMR spectra were acquired at 75, 100, or 125 MHz, and ^{19}F{^{1}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 ^{1}H correlated spectroscopy (COSY), 2D ^{1}H nuclear Overhauser effect spectroscopy (NOESY), 2D ^{1}H–^{13}C heteronuclear multiple-bond correlation spectroscopy (HMBC), and 2D ^{1}H–^{13}C heteronuclear single quantum coherence (HSQC) where necessary. Infrared spectra were recorded as thin films using an attenuated total reflectance (ATR) accessory. Mass spectrometry (*m*/*z*) data was acquired using electrospray ionization (ESI), electron impact (EI), chemical ionization (CI), atmospheric solids analysis probe (ASAP), atmospheric pressure chemical ionization (APCI), or nanospray ionization (NSI) using a time of flight (TOF) mass analyzer. Optical rotations were recorded with a path length of 1 dm and concentrations, *c*, are quoted in g/100 mL. All chiral high-performance liquid chromatography (HPLC) traces were compared with an authentic racemic trace prepared using racemic **1**.

General Procedure for the Synthesis of α-Aroyloxyaldehydes. On the basis of a literature procedure,[16] *tert*-butyl hydroperoxide (5–6 M in decane) was added to a solution of the appropriate aldehyde (1.5 equiv), *p*-nitrobenzoic acid (1 equiv), tetrabutylammonium iodide (20 mol %), and piperidine (10 mol %) in ethyl acetate (to make 0.2 M solution of acid). The resulting solution was heated at 50 °C for 5 h before being cooled to room temperature and quenched with $Na_2S_2O_3$ and $NaHCO_3$. The phases were separated, the aqueous phase was extracted with ethyl acetate (×2), and the combined organics were washed with brine before being dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography.

*1-Oxopropan-2-yl 4-Nitrobenzoate (**2**).* Propionaldehyde (2.71 mL, 37.5 mmol), *p*-nitrobenzoic acid (4.18 g, 25 mmol), tetrabutylammonium iodide (1.85 g, 5.00 mmol) and piperidine (0.25 mL, 2.50 mmol) in ethyl acetate (125 mL), and *tert*-butyl hydroperoxide (5.00 mL, 27.5 mmol) were reacted as described in the general procedure and purified by column chromatography on silica (70:30 petrol:EtOAc) to give 1-oxopropan-2-yl 4-nitrobenzoate **2** as a light yellow solid (4.35 g, 78%): mp 78–80 °C; IR ν_{max} (film) 1722 (C═O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 1.53 (3H, d, *J* 7.2, CH_3), 5.32 (1H, q, *J* 7.2, CH_3CH), 8.21 (2H, d, *J* 8.9, C(2)*H*), 8.26 (2H, d, *J* 8.9, C(3)*H*), 9.60 (1H, s, C*H*O); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C 14.2 (CH_3), 75.9 (CH_3CH), 123.7 (ArC(2)), 131.0 (ArC(3)), 134.5 (ArC(1)), 150.8 (CO_2), 164.1 (ArC(4)), 197.2 (CHO); HRMS (NSI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{10}H_{10}O_5N$ 224.0553, found 224.0556.

*1-Oxohexan-2-yl 4-Nitrobenzoate (**3**).* Hexanal (4.50 mL, 37.5 mmol), *p*-nitrobenzoic acid (4.18 g, 25 mmol), tetrabutylammonium iodide (1.85 g, 5.00 mmol) and piperidine (0.25 mL, 2.50 mmol) in ethyl acetate (125 mL), and *tert*-butyl hydroperoxide (5.00 mL, 27.5 mmol) were reacted as described in the general procedure and purified by column chromatography on silica (85:15 petrol:EtOAc) to give 1-oxohexan-2-yl 4-nitrobenzoate **3** as an orange oil (4.22 g, 15.9 mmol, 64%): IR ν_{max} (film) 2958 (C—H), 1724 (CHO), 1525 (NO_2), 1346 (NO_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.88 (3H, t, *J* 7.2, CH_2CH_3), 1.30–1.38 (2H, m, CH_2), 1.39–1.50 (2H, m, CH_2), 1.80–2.03 (2H, m, CH_2), 5.22–5.27 (1H, m, CHCHO), 8.20 (2H, d, *J* 8.8, ArC(3)*H*), 8.26 (2H, d, *J* 8.8, ArC(2)*H*), 9.57 (1H, s, C*H*O); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ_C 13.8 (CH_2CH_3), 22.4 (CH_2), 27.1 (CH_2), 28.3 (CH_2), 79.6 (CHCHO), 123.7 (ArC(2)), 131.0 (ArC(3)), 134.6 (OCOAr), 150.8 (ArC(1)), 164.2 (ArC(4)), 197.1 (CHO); HRMS (NSI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{16}O_5N$ 266.1023, found 266.1020.

*4-Methyl-1-oxopentan-2-yl 4-Nitrobenzoate (**4**).* Compound (**4**) was made via an alternative route. First, to a stirred solution of isovaleraldehyde (2.79 mL, 26.0 mmol) in THF (50 mL) was added vinyl magnesium bromide (0.7 M in THF, 40.9 mL, 28.6 mmol) dropwise at −78 °C, and the resulting solution was stirred for 30 min. Lithium chloride (1.32 g, 31.2 mmol) was added, followed by *p*-nitrobenzoyl chloride (5.79 g, 31.2 mmol), and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was quenched with water, separated with ethyl acetate, dried with sodium sulfate, filtered, and concentrated in vacuo to give the crude product, which was purified by column chromatography on silica (95:5 petrol:EtOAc) to give 5-methylhex-1-en-3-yl 4-nitrobenzoate as a yellow oil (2.32 g, 8.82 mmol, 35%): ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 0.90 (6H, dd, *J* 6.5, 4.1, CH_3), 1.49 (1H, ddd, *J* 12.9, 7.1, 5.6, $(CH_3)_2CH$), 1.61–1.77 (2H, m, CH_2), 5.17 (1H, dt, *J* 10.5, 1.1, H_aH_bC═CH), 5.28 (1H, dt, *J* 17.2, 1.2, H_aH_bC═CH), 5.52 (1H, ddd, *J* 8.2, 6.8, 5.6, H_2C═CHCH), 5.81 (1H, ddd, *J* 17.2, 10.5, 6.7, H_2C═CH), 8.15 (2H, d, *J* 8.8, ArH), 8.22 (2H, d, *J* 8.8, ArH).

5-Methylhex-1-en-3-yl 4-nitrobenzoate (1.00 g, 3.80 mmol) was dissolved in CH_2Cl_2 (400 mL), subjected to ozonolysis, and then quenched with dimethyl sulfide (0.558 mL, 7.60 mmol). The resulting mixture was concentrated in vacuo to give the crude product and purified using column chromatography on silica (80:20 petrol:EtOAc) to give 4-methyl-1-oxopentan-2-yl 4-nitrobenzoate **4** as a pale yellow oil (0.560 g, 2.11 mmol, 56%) with spectroscopic data in accordance with the literature:[15] ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 0.86–0.98 (3H, m, CH_3), 1.02 (3H, dd, *J* 13.3, 6.4, CH_3), 1.76–1.94 (3H, m, $(CH_3)_2CH$ and CH_2), 5.37 (1H, dd, *J* 9.2, 4.4, CHCHO), 8.27 (2H, d, *J* 8.8, ArH), 8.33 (2H, d, *J* 8.8, ArH), 9.63 (1H, s, CHO).

*1-Oxo-3-phenylpropan-2-yl 4-Nitrobenzoate (**5**).* 3-Phenylpropionaldehyde (4.93 mL, 37.5 mmol), *p*-nitrobenzoic acid (4.18 g, 25 mmol), tetrabutylammonium iodide (1.85 g, 5.00 mmol) and piperidine (0.25 mL, 2.50 mmol) in ethyl acetate (125 mL), and *tert*-butyl hydroperoxide (5.00 mL, 27.5 mmol) were reacted as described in the general procedure and purified by column chromatography on silica (60:40 hexane: EtOAc) to give 1-oxo-3-phenylpropan-2-yl 4-nitrobenzoate **5** as a pale yellow solid (3.40 g, 45%), with spectroscopic data in accordance with the literature:[15] mp 85–86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 3.15 (1H, dd, *J* 14.5, 8.4, $PhCH_aH_b$), 3.28 (1H, dd, *J* 14.5, 4.9, $PhCH_aH_b$), 5.45 (1H, dd, *J* 8.4, 4.9, CHCHO), 7.14–7.31 (5H, m, PhH), 8.11 (2H, d, *J* 8.9, ArH), 8.23 (2H, d, *J* 8.8, ArH), 9.61 (1H, s, CHO).

*1-Oxo-3-phenyl(1-^{2}H)propan-2-yl 4-Nitrobenzoate (**5-D**).* To a flamed-dried two-neck round-bottomed flask fitted with a dropping funnel under an atmosphere of N_2 was added $LiAlD_4$ (1 M in THF, 20 mL, 20 mmol) and THF (20 mL) before the solution was cooled to 0 °C. A solution of methyl 3-phenylpropanoate (2.18 g, 13.3 mmol) in THF (18 mL) was added dropwise to the mixture via a dropping funnel over ca. 30 min. After the reaction mixture was stirred at 0 °C for 3 h, the reaction mixture was quenched by adding 1 M KOH (10 mL) dropwise via a dropping funnel. The resulting suspension was stirred for 1 h before being filtered through a pad of Celite, washing with EtOAc. The filtrate was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to give the deuterated alcohol as a colorless oil (1.60 g, 87%) with spectroscopic data in accordance with the literature:[31] ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 1.35 (1H, br s, OH),

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1.89 (2H, t, *J* 7.7, CH_2CD_2), 2.71 (2H, t, *J* 7.7, PhCH_2), 7.17−7.23 (3H, m, Ar*H*), 7.25−7.31 (2H, m, Ar*H*).

Deuterated alcohol (1.60 g, 11.7 mmol) was added to a two-neck round-bottomed flask containing DMSO (7.9 mL, 35.1 mmol), Et_3N (11.4 mL, 111.2 mmol), and CH_2Cl_2 (100 mL), and the resulting solution was cooled to 0 °C. Sulfur trioxide pyridine complex (5.6 g, 35.1 mmol) was added portionwise for ca. 15 min, and the solution was stirred at 0 °C for 1 h before being warmed to rt. After the mixture was stirred for 2 h, TLC analysis showed complete consumption of the starting material, and the reaction mixture was quenched with saturated aq NH_4Cl (50 mL), the organic layer was separated and washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by column chromatography on silica (90:10 petrol:EtOAc, R_f 0.38) to give a deuterated aldehyde as a colorless oil (1.10 g, 69%) with spectroscopic data in accordance with the literature:[31] ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 2.79−2.84 (2H, m, CH_2COD), 2.99 (2H, br t, *J* 7.6, PhCH_2), 7.20−7.27 (3H, m, Ar*H*), 7.28−7.36 (2H, m, Ar*H*).

Deuterated aldehyde (1.10 g, 8.1 mmol), *p*-nitrobenzoic acid (2.04 g, 12.2 mmol), tetrabutylammonium iodide (0.60 g, 1.6 mmol), piperidine (0.08 mL, 0.08 mmol), ethyl acetate (40 mL), and *tert*-butyl hydroperoxide (1.6 mL, 8.9 mmol) were reacted as described in the general procedure and purified by column chromatography on silica (neat CH_2Cl_2 to 99:1 CH_2Cl_2:Et_2O, R_f 0.33) to give 1-oxo-3-phenyl(1-^{2}H)propan-2-yl 4-nitrobenzoate **5-D** as a white solid (1.06 g, 43%): mp 94−95 °C; IR ν_{max} (film) 1728 (C═O), 1709 (C═O), 1524; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 3.22 (1H, dd, *J* 14.5, 8.4, C$H_a$$H_b$Ph), 3.35 (1H, dd, *J* 14.7, 4.9, C$H_a$$H_b$Ph), 5.52 (1H, dd, *J* 8.4, 4.9, C*H*CH_aCH_bPh), 7.25−7.30 (3H, m, Ph*H*), 7.31−7.36 (2H, m, Ph*H*), 8.19 (2H, app dt, *J* 9.0, 2.0, Ar*H*), 8.30 (2H, app dt, *J* 9.0, 2.1, Ar*H*); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C 35.3, 79.8 (t, *J* 3.5), 123.8, 127.5, 129.0, 129.4, 131.1, 134.5, 135.1, 164.2, *C*OD not observed; HRMS (NSI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{13}DO_5N$ 301.0935, found 301.0923.

*4-(Benzyloxy)-1-oxobutan-2-yl 4-Nitrobenzoate (**6**).* Sodium hydride (60% dispersion in mineral oil, 1.60 g, 39.9 mmol) was washed with hexane and then suspended in THF (60 mL), and the mixture was cooled to 0 °C. Butanediol (15.0 g, 166 mmol) was added slowly via a dropping funnel, and the resulting mixture was warmed to rt and stirred for 2 h. The mixture was cooled to 0 °C, benzyl bromide (4.00 mL, 33.3 mmol) in THF (8 mL) was added via a dropping funnel, and the reaction was left stirring for 16 h while warming to rt. The reaction mixture was quenched with saturated aq NH_4Cl solution (50 mL) and extracted with ethyl acetate, the organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo to give the crude product, which was purified by column chromatography on silica (70:30 petrol:EtOAc), and pure fractions were evaporated to dryness to give 4-(benzyloxy)butan-1-ol as a colorless oil (5.66 g, 31.4 mmol, 94%) with spectroscopic data in accordance with the literature:[32] ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 1.57−1.87 (4H, m, CH_2 ×2), 3.52 (2H, t, *J* 5.8, OCH_2), 3.65 (2H, t, *J* 5.8, OCH_2), 4.52 (2H, s, ArCH_2), 7.27−7.39 (5H, m, Ar*H*).

Oxalyl chloride (5.31 mL, 62.8 mmol) was dissolved in CH_2Cl_2 (125 mL) and the solution was cooled to −78 °C. DMSO (4.91 mL, 69.1 mmol) was added dropwise via a dropping funnel, and the reaction mixture was left to stir for 15 min. 4-(Benzyloxy)butan-1-ol (5.66 g, 31.4 mmol) in CH_2Cl_2 (15 mL) was added to the mixture dropwise via a dropping funnel, and the reaction mixture was left to stir for 15 min. To the reaction mixture was added triethylamine (13.1 mL, 94.2 mmol) dropwise. The resulting mixture was stirred for 5 min, and the solution was warmed to rt and stirred for 15 min. The mixture was diluted with ethyl acetate and washed with saturated aq NH_4Cl solution and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo to give the crude product, which was purified by column chromatography on silica (85:15 petrol:EtOAc), and pure fractions were evaporated to dryness to give 4-(benzyloxy)-butanal as a pale yellow oil (4.18 g, 23.5 mmol, 75%) with spectroscopic data in accordance with the literature:[32] ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 1.95 (2H, tt, *J* 7.1, 6.1, CH_2), 2.55 (2H, td, *J* 7.1, 1.6, CH_2), 3.51 (2H, t, *J* 6.1, OCH_2), 4.49 (2H, s, ArCH_2), 7.26−7.38 (5H, m, Ar*H*), 9.79 (1H, t, *J* 1.6, C*H*O).

4-(Benzyloxy)butanal (4.18 g, 23.5 mmol), *p*-nitrobenzoic acid (2.62 g, 15.7 mmol), tetrabutylammonium iodide (1.16 g, 3.14 mmol) and piperidine (155 μL, 1.57 mmol) in ethyl acetate (100 mL), and *tert*-butyl hydroperoxide (3.15 mL, 17.3 mmol) were reacted as described in the general procedure and purified by column chromatography on silica (80:20 petrol:EtOAc) to give 4-(benzyloxy)-1-oxobutan-2-yl 4-nitrobenzoate **6** as a yellow oil (4.26 g, 12.4 mmol, 79%): IR ν_{max} (film) 2800 (C—H), 1732 (C═O), 1716 (C═O), 1521 (NO_2), 1269 (NO_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 2.29 (2H, q, *J* 5.8, CH_2), 3.53−3.77 (2H, m, CH_2), 4.47 (2H, d, *J* 1.4, ArCH_2), 5.47 (1H, t, *J* 5.8, C*H*CHO), 7.20−7.36 (5H, m, Ph*H*), 8.12−8.16 (2H, m, Ar*H*), 8.23−8.28 (2H, m, Ar*H*), 9.63 (1H, s, C*H*O); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C 29.7 (CH_2), 64.6 (OCH_2), 73.2 (PhCH_2), 77.0 (CHCHO), 123.6 (ArC(3)), 127.8 (PhC(4)), 127.9 (PhC(2) or PhC(3)), 128.5 (PhC(2) or PhC(3)), 131.0 (ArC(2)), 134.6 (ArC(1)), 137.6 (PhC(1)), 150.8 (ArC(4)), 164.0 (*C*O_2Ar), 196.6 (*C*HO); HRMS (NSI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{18}O_6N$ 344.1129, found 344.1131.

General Procedure for the Synthesis of *β*-Trifluoromethyl Enones. Following the procedure of Yamazaki et al.,[33a] *n*-butyl lithium (2.5 M in hexane, 2.2 equiv) was added to a solution of diisopropylamine (2.2 equiv) in THF (0.8 M) at −78 °C, and the solution was stirred for 20 min. A precooled solution of 2-bromo-3,3,3-trifluoroprop-1-ene (1.0 equiv) in THF (0.5 M) was added dropwise at −78 °C, and the reaction mixture was stirred for 5 min before the appropriate aldehyde (1.2 equiv) was added dropwise. The reaction mixture was stirred for 30 min before being quenched with aqueous 1 M HCl (10 equiv). The resulting solution was extracted with ethyl acetate (×3), and the combined organics were dried over Na_2SO_4, filtered, and concentrated in vacuo to give the crude trifluoropropargylic alcohol, which was used without further purification.

Following the procedure of Yamazaki et al.,[33b] triethylamine (4.0 equiv) was added to a solution of the appropriate trifluoropropargylic alcohol (1.0 equiv) in THF (0.2 M) and heated at reflux for 16 h. The reaction mixture was cooled, quenched with 1 M HCl (5.0 equiv), and extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo to give the crude *β*-trifluoromethyl enone, which was purified by column chromatography.

(E)-4,4,4-Trifluoro-1-phenylbut-2-en-1-one and (Z)-4,4,4-Trifluoro-1-phenylbut-2-en-1-one. *n*-Butyl lithium (2.5 M in hexane, 25.1 mmol, 10.0 mL), diisopropylamine (3.52 mL, 25.1 mmol) in THF (30 mL), 2-bromo-3,3,3-trifluoroprop-1-ene (1.20 mL, 11.4 mmol) in THF (20 mL), and benzaldehyde (1.39 mL, 13.7 mmol) were reacted as described in the general procedure to give (*E*)-4,4,4-trifluoro-1-phenylbut-2-yn-1-ol as an orange oil (1.97 g, 9.83 mmol, 86%) with spectroscopic data in accordance with the literature:[33a] ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 2.31 (1H, br s), 5.57 (1H, q, *J* 3.0, ArC*H*OH), 7.39−7.47 (3H, m, Ar*H*), 7.49−7.54 (2H, m, Ar*H*); ^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$) δ_F −50.6 (CF_3).

4,4,4-Trifluoro-1-phenylbut-2-yn-1-ol (3.25 g, 16.2 mmol), triethylamine (9.03 mL, 64.8 mmol), and THF (85 mL) were reacted as described in the general procedure and purified by column chromatography (98:2 petrol: Et_2O) to give (*E*)-4,4,4-trifluoro-1-phenylbut-2-en-1-one as a pale yellow crystalline solid (1.21 g, 6.02 mmol, 37%) with spectroscopic data in accordance with the literature:[34a] mp 27−29 °C {lit. 28 °C}; ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 6.75 (1H, dq, *J* 15.6, 6.6, F_3CC*H*═CH), 7.43−7.51 (3H, m, F_3CCH═C*H* and Ar(3)*H*), 7.54−7.63 (1H, m, Ar(4)*H*), 7.89−7.94 (2H, m, Ar(2)*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −65.6 (dd, *J* 6.6, 2.0, CF_3).

(*Z*)-4,4,4-Trifluoro-1-phenylbut-2-en-1-one was isolated as a yellow oil (0.340 g, 1.71 mmol, 11%): IR ν_{max} (film) 1678 (C═O); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.02 (1H, dq, *J* 12.7, 7.9, F_3CC*H*═CH), 6.80 (1H, dd, *J* 12.7, 0.7, F_3CCH═C*H*), 7.39−7.48 (2H, m, ArC(3)*H*), 7.52−7.67 (1H, m, ArC(4)*H*), 7.81−7.93 (2H, m, ArC(2)*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −61.3 (d, *J* 7.9, CF_3); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C 121.8 (q, *J* 272, CF_3), 123.4 (q, *J* 35.6, F_3CCH═CH), 128.9 (ArC(3)), 129.0 (ArC(2)), 134.3 (ArC(4)),

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135.5 (ArC(1)), 136.7 (q, *J* 5.0, $F_3CCH{=}CH$), 191.9 (COAr); HRMS (NSI$^+$) *m*/*z* $[M + NH_4]^+$ calcd for $C_{10}H_{11}F_3ON$ 218.0787, found 218.0788.

(E)-4,4,4-Trifluoro-1-(4-methoxyphenyl)but-2-en-1-one and (Z)-4,4,4-Trifluoro-1-(4-methoxy-phenyl)but-2-en-1-one. *n*-Butyl lithium (2.5 M in hexane, 25.1 mmol, 10.0 mL), diisopropylamine (3.52 mL, 25.1 mmol) in THF (30 mL), 2-bromo-3,3,3-trifluoroprop-1-ene (1.20 mL, 11.4 mmol) in THF (20 mL), and 4-methoxybenzaldehyde (1.67 mL, 13.7 mmol) were reacted as described in the general procedure to give 4,4,4-trifluoro-1-(4-methoxyphenyl)but-2-yn-1-ol as an orange oil (2.62 g, 11.4 mmol, quantitative) with spectroscopic data in accordance with the literature:[33b] ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 3.76 (3H, s, ArC(4)OCH_3), 5.44 (1H, d, *J* 3.0, ArC*H*OH), 6.87 (2H, d, *J* 8.0, ArC(3)*H*), 7.36 (2H, d, *J* 8.9, ArC(2)*H*); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ_F −51.0 (CF_3).

4,4,4-Trifluoro-1-(4-methoxyphenyl)but-2-yn-1-ol (2.62 g, 11.4 mmol), triethylamine (6.36 mL, 45.6 mmol), and THF (50 mL) were reacted as described in the general procedure and purified by column chromatography (98:2 petrol:EtOAc) to give (*E*)-4,4,4-trifluoro-1-(4-methoxyphenyl)but-2-en-1-one as a pale yellow crystalline solid (0.920 g, 4.02 mmol, 35%) with spectroscopic data in accordance with the literature:[33b] mp 41−43 °C {lit. 36 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 3.90 (3H, s, ArC(4)OCH_3), 6.80 (1H, dq, *J* 15.6, 6.7, $F_3CCH{=}CH$), 6.99 (2H, d, *J* 8.9, $F_3CCH{=}CH$), 7.53 (1H, dd, *J* 15.5, 2.1, ArC(3)*H*), 7.98 (2H, d, *J* 9.0, ArC(2)*H*); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F −65.5 (dd, *J* 6.6, 1.9, CF_3).

(*Z*)-4,4,4-Trifluoro-1-(4-methoxyphenyl)but-2-en-1-one was isolated as a yellow oil (0.150 g, 0.655 mmol, 6%): ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 3.82 (3H, s, ArC(4)OCH_3), 5.97 (1H, dq, *J* 12.7, 7.9, $F_3CCH{=}CH$), 6.76 (1H, dd, *J* 12.7, 0.7, $F_3CCH{=}CH$), 6.90 (2H, d, *J* 9.0, ArC(2)*H*), 7.83 (2H, d, *J* 9.0, ArC(3)*H*); ^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$) δ_F −61.3 (CF_3).

(E)-4,4,4-Trifluoro-1-(2-methoxyphenyl)but-2-en-1-one. *n*-Butyl lithium (2.5 M in hexane, 25.1 mmol, 10.0 mL), diisopropylamine (3.52 mL, 25.1 mmol) in THF (30 mL), 2-bromo-3,3,3-trifluoroprop-1-ene (1.20 mL, 11.4 mmol) in THF (20 mL), and 2-methoxybenzaldehyde (1.66 mL, 13.7 mmol) were reacted as described in the general procedure to give 4,4,4-trifluoro-1-(2-methoxyphenyl)but-2-yn-1-ol as an orange oil (2.54 g, 11.1 mmol, 97%) with spectroscopic data in accordance with the literature:[33c] ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 3.92 (3H, s, ArC(2)OCH_3), 5.67 (1H, q, *J* 3.1, ArC*H*OH), 6.92−7.08 (2H, m, Ar*H*), 7.32−7.44 (2H, m, Ar*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −50.9 (d, *J* 2.9, CF_3).

4,4,4-Trifluoro-1-(2-methoxyphenyl)but-2-yn-1-ol (2.54 g, 11.1 mmol), triethylamine (6.19 mL, 44.4 mmol), and toluene (50 mL) were heated at reflux in a modified version of the general procedure and purified by column chromatography (98:2 petrol:EtOAc) to give (*E*)-4,4,4-trifluoro-1-(2-methoxyphenyl)but-2-en-1-one as a yellow oil (1.06 g, 4.59 mmol, 41%) with spectroscopic data in accordance with the literature:[35] ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 3.92 (3H, s, ArC(2)CH_3), 6.66 (1H, dq, *J* 15.6, 6.8, $F_3CCH{=}CH$), 7.00 (1H, dd, *J* 8.5, 0.9, ArC(3)*H*), 7.05 (1H, td, *J* 7.4, 1.0, ArC(5)*H*), 7.47 (1H, dq, *J* 15.7, 2.0, $F_3CCH{=}CH$), 7.54 (1H, ddd, *J* 8.4, 7.3, 1.8, ArC(4)*H*), 7.72 (1H, dd, *J* 7.5, 1.7, ArC(6)*H*); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F −65.4 to −65.3 (m, CF_3).

(E)-4,4,4-Trifluoro-1-(4-nitrophenyl)but-2-en-1-one and (Z)-4,4,4-Trifluoro-1-(4-nitrophenyl)-but-2-en-1-one. Following the procedure of Yamazaki et al.,[33b] *n*-butyl lithium (2.5 M in hexane, 25.1 mmol, 10.0 mL, 2.2 equiv) was added to a solution of diisopropylamine (3.52 mL, 25.1 mmol, 2.2 equiv) in THF (30 mL) at −78 °C, and the solution was stirred for 20 min. A precooled solution of 2-bromo-3,3,3-trifluoroprop-1-ene (1.56 mL, 14.8 mmol, 1.3 equiv) in THF (30 mL) was added dropwise at −78 °C, and the reaction mixture was stirred for 5 min. A solution of *tert*-butyldimethylsilyl chloride (6.71 g, 44.5 mmol, 3.9 equiv) and 4-nitrobenzaldehyde (1.72 g, 11.4 mmol, 1.0 equiv) in THF (30 mL) was then added dropwise at −78 °C, and the reaction mixture was stirred for 30 min. The reaction mixture was quenched with aqueous 1 M HCl (100 mL), and the resulting solution was extracted with ethyl acetate (×3). The combined organics were dried over Na_2SO_4, filtered, and concentrated in vacuo to give the crude product, which was purified by column chromatography (80:20 petrol:EtOAc) to give 4,4,4-trifluoro-1-(4-nitrophenyl)but-2-yn-1-ol as an orange oil (0.428 g, 1.75 mmol, 15%), with spectroscopic data in accordance with the literature:[33b] ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 5.64 (1H, d, *J* 2.9, ArC*H*OH), 7.64 (1H, d, *J* 8.2, ArC(3)*H*), 8.23 (1H, d, *J* 8.8, ArC(4)*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −51.4 (d, *J* 3.1, CF_3).

4,4,4-Trifluoro-1-(4-nitrophenyl)but-2-yn-1-ol (0.428 g, 1.75 mmol), triethylamine (0.980 mL, 7.00 mmol), and THF (10 mL) were reacted as described in the general procedure and purified by column chromatography (95:5 petrol:EtOAc) to give (*E*)-4,4,4-trifluoro-1-(4-nitrophenyl)but-2-en-1-one as a yellow crystalline solid (0.206 g, 0.838 mmol, 48%) with spectroscopic data in accordance with the literature:[33b] mp 58−60 °C {lit. 66−70 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.90 (1H, dq, *J* 15.6, 6.5, $F_3CCH{=}CH$), 7.52 (1H, dq, *J* 15.6, 2.0, $F_3CCH{=}CH$), 8.14 (1H, d, *J* 9.0, ArC(2)*H*), 8.39 (1H, d, *J* 9.0, ArC(3)*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −65.8 (dd, *J* 6.5, 1.9, CF_3).

(*Z*)-4,4,4-Trifluoro-1-(4-nitrophenyl)but-2-en-1-one was isolated as an orange oil (0.144 g, 0.590 mmol, 34%) with spectroscopic data in accordance with the literature:[12] ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.20 (1H, dq, *J* 12.8, 7.8, $F_3CCH{=}CH$), 6.86 (1H, dd, *J* 12.7, 0.7, $F_3CCH{=}CH$), 8.10 (1H, d, *J* 9.1, ArC(2)*H*), 8.37 (2H, d, *J* 9.0, ArC(3)*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −61.3 (d, *J* 7.9, CF_3).

(E)-1-(4-Bromophenyl)-4,4,4-trifluorobut-2-en-1-one and (Z)-1-(4-Bromophenyl)-4,4,4-trifluorobut-2-en-1-one. *n*-Butyl lithium (2.5 M in hexane, 37.6 mmol, 15.0 mL), diisopropylamine (5.27 mL, 37.6 mmol) in THF (45 mL), 2-bromo-3,3,3-trifluoroprop-1-ene (1.81 mL, 17.1 mmol) in THF (30 mL), and 4-bromobenzaldehyde (3.78 g, 20.5 mmol) were reacted as described in the general procedure to give 4,4,4-trifluoro-1-phenylbut-2-yn-1-ol as an orange solid (3.18 g, 11.4 mmol, quant) with spectroscopic data in accordance with the literature:[33c] ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 5.54 (1H, q, *J* 2.9, ArC*H*OH), 7.67−7.71 (2H, m, Ar*H*), 7.73−7.77 (2H, m, Ar*H*); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ_F −51.2 (CF_3).

1-(4-Bromophenyl)-4,4,4-trifluorobut-2-yn-1-ol (4.77 g, 17.1 mmol), triethylamine (9.53 mL, 68.4 mmol), and THF (100 mL) were reacted as described in the general procedure and purified by column chromatography (99:1 petrol:EtOAc) to give (*E*)-1-(4-bromophenyl)-4,4,4-trifluorobut-2-en-1-one as a pale yellow crystalline solid (2.31 g, 8.26 mmol, 48%) with spectroscopic data in accordance with the literature:[33b] mp 59−61 °C {lit. 51−52 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.83 (1H, dq, *J* 15.5, 6.6, $F_3CCH{=}CH$), 7.49 (1H, dq, *J* 15.5, 2.0, $F_3CCH{=}CH$), 7.63−7.72 (2H, m, Ar*H*), 7.80−7.89 (2H, m, Ar*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −65.7 (dd, *J* 6.6, 1.9, CF_3).

(*Z*)-1-(4-Bromophenyl)-4,4,4-trifluorobut-2-en-1-one was also isolated as a pale orange solid (0.370 g, 1.33 mmol, 8%) with spectroscopic data in accordance with the literature:[33b] mp 47−49 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.11 (1H, dq, *J* 12.7, 7.9, $F_3CCH{=}CH$), 6.81 (1H, dd, *J* 12.7, 0.7, $F_3CCH{=}CH$), 7.63−7.70 (2H, m, Ar*H*), 7.74−7.84 (2H, m, Ar*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −61.3 (d, *J* 7.9, CF_3).

(E)-4,4,4-Trifluoro-1-(pyridin-3-yl)but-2-en-1-one. *n*-Butyl lithium (2.5 M in hexane, 25.1 mmol, 10.0 mL), diisopropylamine (3.52 mL, 25.1 mmol) in THF (30 mL), 2-bromo-3,3,3-trifluoroprop-1-ene (1.20 mL, 11.4 mmol) in THF (20 mL), and nicotinaldehyde (1.29 mL, 13.7 mmol) were reacted as described in the general procedure and quenched with saturated aq NH_4Cl to give 4,4,4-trifluoro-1-(pyridin-3-yl)but-2-yn-1-ol as a brown oil (1.82 g, 9.06 mmol, 79%): ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 5.59 (1H, q, *J* 2.8, ArC*H*OH), 7.32 (1H, ddd, *J* 7.9, 4.9, 0.9, ArC(5)*H*), 7.83 (1H, dt, *J* 7.9, 1.7, ArC(4)*H*), 8.53 (1H, dd, *J* 4.9, 1.6, ArC(6)*H*), 8.64 (1H, d, *J* 1.8, ArC(2)*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −51.2 (d, *J* 2.9, CF_3).

4,4,4-Trifluoro-1-(pyridin-3-yl)but-2-yn-1-ol (0.428 g, 1.75 mmol), triethylamine (0.980 mL, 7.00 mmol), and THF (10 mL) were reacted as described in the general procedure and purified by column chromatography (95:5 petrol:EtOAc) to give (*E*)-4,4,4-trifluoro-1-(pyridin-3-yl)but-2-en-1-one as an orange crystalline solid (0.560 g, 2.78 mmol, 31%) with spectroscopic data in accordance with the

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literature:[34a] mp 52−53 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 6.82 (1H, dq, *J* 15.5, 6.5, F_3CCH=CH), 7.41−7.48 (2H, m, F_3CCH=C*H* and ArC()*H*), 8.22 (1H, ddd, *J* 8.0, 2.3, 1.7, ArC()*H*), 8.80 (1H, dd, *J* 4.8, 1.7, ArC(6)*H*), 9.14 (1H, dd, *J* 2.3, 0.9, ArC(2)*H*); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F −65.7 (dd, *J* 6.6, 1.9, CF_3).

(E)-4,4,4-Trifluoro-1-(furan-2-yl)but-2-en-1-one and (Z)-4,4,4-Trifluoro-1-(furan-2-yl)but-2-en-1-one. *n*-Butyl lithium (2.5 M in hexane, 25.1 mmol, 10.0 mL), diisopropylamine (3.52 mL, 25.1 mmol) in THF (30 mL), 2-bromo-3,3,3-trifluoroprop-1-ene (1.20 mL, 11.4 mmol) in THF (20 mL), and furfural (1.14 mL, 13.7 mmol) were reacted as described in the general procedure to give 4,4,4-trifluoro-1-(furan-2-yl)but-2-yn-1-ol as a yellow oil (0.930 g, 4.90 mmol, 43%) with spectroscopic data in accordance with the literature:[33b] ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 5.57 (2H, q, *J* 2.9, ArC*H*OH), 6.40 (1H, dd, *J* 3.3, 1.9, ArC(3)*H*), 6.50 (1H, d, *J* 3.3, ArC(4)*H*), 7.46 (1H, dd, *J* 1.9, 0.8, ArC(5)*H*); ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ_F −51.4 (CF_3).

4,4,4-Trifluoro-1-(furan-2-yl)but-2-yn-1-ol (0.930 g, 4.90 mmol), triethylamine (2.73 mL, 19.6 mmol), and THF (30 mL) were reacted as described in the general procedure and purified by column chromatography (95:5 petrol:EtOAc) to give (*E*)-4,4,4-trifluoro-1-(furan-2-yl)but-2-en-1-one as a pale yellow crystalline solid (0.510 g, 2.66 mmol, 54%) with spectroscopic data in accordance with the literature:[34b] mp 68−70 °C {lit. 64−66 °C}; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.64 (1H, dd, *J* 3.6, 1.7, ArC(3)*H*), 6.90 (1H, dq, *J* 15.6, 6.7, F_3CCH=CH), 7.39 (1H, dd, *J* 3.7, 0.7, ArC(4)*H*), 7.42 (1H, dq, *J* 15.7, 2.0, F_3CCH=C*H*), 7.71 (1H, dd, *J* 1.7, 0.7, ArC(5)*H*); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F −65.6 (dd, *J* 6.7, 2.0, CF_3).

(*Z*)-4,4,4-Trifluoro-1-(furan-2-yl)but-2-en-1-one was isolated as a yellow oil (0.120 g, 0.631 mmol, 13%): IR ν_{max} (film) 1672 (C=O); ^{1}H NMR (400 MHz, CD_2Cl_2) δ_H 6.02 (1H, dq, *J* 12.6, 8.3, F_3CCH=CH), 6.54 (1H, dd, *J* 3.7, 1.7, ArC(4)*H*), 6.82 (1H, d, *J* 12.6, F_3CCH=C*H*), 7.17 (1H, dd, *J* 3.7, 0.8, ArC(3)*H*), 7.62 (1H, dd, *J* 1.7, 0.8, ArC(5)*H*); ^{19}F NMR (376 MHz, CD_2Cl_2) δ_F −61.2 (d, *J* 8.2, CF_3); ^{13}C{^{1}H} NMR (101 MHz, CD_2Cl_2) δ_C 112.7 (ArC(4)), 119.9 (ArC(3)), 121.7 (q, *J* 272, CF_3), 125.2 (q, *J* 36.1, F_3CCH=CH), 134.6 (q, *J* 5.2, F_3CCH=CH), 148.1 (ArC(5)), 151.7 (ArC(2)), 177.6 (ArC(2)C=O); HRMS (CI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_8H_6F_3O_2$ 191.0320, found 191.0323.

General Procedure for NHC-Catalyzed Hetero-Diels−Alder Reactions. The appropriate α-aroyloxyaldehyde (1.5 equiv), β-trifluoromethyl enone (1.0 equiv), and NHC precatalyst **1** (10 mol %) were dissolved in anhydrous THF (0.075 M) in a sealed vial containing 4 Å molecular sieves. Triethylamine (1.5 equiv) or cesium carbonate (1 equiv) was added as stated, and the reaction mixture was stirred at rt until complete by TLC analysis. The mixture was diluted with EtOAc and washed successively with 1 M HCl, saturated $NaHCO_3$, and brine. The organic layer was dried with $MgSO_4$, filtered, and concentrated in vacuo to give the crude product that was purified by flash silica column chromatography.

*(3S,4S)-3-Butyl-6-phenyl-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**8**).* 1-Oxohexan-2-yl 4-nitrobenzoate **3** (199 mg, 0.750 mmol), (*E*)-4,4,4-trifluoro-1-phenylbut-2-en-1-one (100 mg, 0.500 mmol), precatalyst **1** (18.4 mg, 50.0 μmol), triethylamine (105 μL, 0.750 mmol), and THF (10 mL) were reacted as described in the general procedure for 14 h and then purified by column chromatography (95:5 petrol:Et_2O) to give (3*S*,4*S*)-3-butyl-6-phenyl-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **8** as a white crystalline solid (93.3 mg, 0.313 mmol, 63%): mp 109−111 °C; $[\alpha]_D^{20}$ +70.8 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralcel OJ-H 99.8:0.2 hexane:IPA, flow rate 1 mL min^{-1}, 254 nm, 30 °C) t_R(3*S*,4*S*) 33.1 min, t_R(3*R*,4*R*) 54.2 min, >99% ee; IR ν_{max} (solid) 2959 (C—H), 1761 (C=O); δ_H (500 MHz, $CDCl_3$) 0.94 (3H, t, *J* 7.1, CH_2CH_3), 1.27−1.56 (4H, m, $(CH_2)_2$), 1.64−1.79 (1H, m, C(3)CH_aH_b), 2.07 (1H, dd, *J* 14.3, 7.5, C(3)CH_aH_b), 2.88 (1H, q, *J* 7.1, C(3)*H*), 3.24−3.48 (1H, m, C(4)*H*), 5.76 (1H, d, *J* 6.3, C(5)*H*), 7.33−7.50 (3H, m, ArC(2)*H* and ArC(4)*H*), 7.56−7.75 (2H, m, ArC(3)*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −67.5 (d, *J* 8.6, C(4)CF_3); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C 13.8 (CH_2CH_3), 22.5 (CH_2), 26.1 (C(3)CH_2), 29.7 (CH_2), 39.4 (q, *J* 28.3, *C*(4)), 39.8 (*C*(3)), 94.6 (*C*(5)), 125.0 (ArC(3)), 125.9 (q, *J* 282, C(4)CF_3), 128.6 (ArC(2)), 130.0 (ArC(4)), 131.4 (ArC(1)), 153.4 (*C*(6)), 168.2 (*C*(2)); HRMS (NSI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{18}F_3O_2$ 299.1253, found 299.1261.

*(3S,4S)-3-Butyl-6-(4-methoxyphenyl)-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**9**).* 1-Oxohexan-2-yl 4-nitrobenzoate **3** (80 mg, 0.300 mmol), (*E*)-4,4,4-trifluoro-1-(4-methoxyphenyl)but-2-en-1-one (44 mg, 0.200 mmol), precatalyst **1** (7.4 mg, 20.0 μmol), triethylamine (42 μL, 0.30 mmol), and THF (4 mL) were reacted as described in the general procedure for 24 h and then purified by column chromatography (95:5 petrol:Et_2O) to give (3*S*,4*S*)-3-butyl-6-(4-methoxyphenyl)-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **9** as a white crystalline solid (47.5 mg, 0.145 mmol, 73%): mp 105−107 °C; $[\alpha]_D^{20}$ +66.2 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralpak AD-H 95:5 hexane:IPA, flow rate 1 mL min^{-1}, 254 nm, 30 °C) t_R(3*S*,4*S*) 14.2 min, t_R(3*R*,4*R*) 16.5 min, >99% ee; IR ν_{max} (solid) 2957 (C—H), 1761 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 0.93 (3H, t, *J* 7.1, CH_2CH_3), 1.30−1.55 (4H, m, $(CH_2)_2$), 1.68 (1H, dd, *J* 14.9, 6.9, C(3)CH_aH_b), 2.02−2.16 (1H, m, C(3)CH_aH_b), 2.86 (1H, q, *J* 7.2, C(3)*H*), 3.33 (1H, qt, *J* 8.7, 6.4 C(4)*H*), 3.83 (3H, s, ArC(4)OCH_3), 5.62 (1H, d, *J* 6.5, C(5)*H*), 6.91 (2H, d, *J* 8.9, ArC(3)*H*), 7.58 (2H, d, *J* 8.9, ArC(2)*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −67.7 (d, *J* 8.7, C(4)CF_3); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 13.9 (CH_2CH_3), 22.5 (CH_2), 26.1 (C(3)CH_2), 29.7 (CH_2), 39.3 (q, *J* 28.2, *C*(4)), 39.8 (*C*(3)), 55.4 (ArC(4)OCH_3), 92.7 (d, *J* 2.6, *C*(5)), 114.0 (ArC(3)), 123.9 (ArC(1)), 125.9 (q, *J* 282, C(4)CF_3), 126.5 (ArC(2)), 153.2 (*C*(6)), 161.0 (ArC(4)), 168.4 (*C*(2)); HRMS (CI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{20}F_3O_3$ 329.1365, found 329.1357.

*(3S,4S)-3-Butyl-6-(2-methoxyphenyl)-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**10**).* 1-Oxohexan-2-yl 4-nitrobenzoate **3** (80 mg, 0.300 mmol), (*E*)-4,4,4-trifluoro-1-(2-methoxyphenyl)but-2-en-1-one (46 mg, 0.200 mmol), precatalyst **1** (7.3 mg, 20.0 μmol), cesium carbonate (65 mg, 0.200 mmol), and THF (4 mL) were reacted as described in the general procedure for 14 h and then purified by column chromatography (97:3 petrol:EtOAc) to give (3*S*,4*S*)-3-butyl-6-(2-methoxyphenyl)-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **10** as a white crystalline solid (39.2 mg, 0.119 mmol, 60%): mp 46−48 °C; $[\alpha]_D^{20}$ +64.4 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralpak IA 98:2 hexane:IPA, flow rate 1 mL min^{-1}, 254 nm, 30 °C) t_R(3*S*,4*S*) 7.5 min, t_R(3*R*,4*R*) 16.4 min, 99% ee; IR ν_{max} (solid) 2961 (C—H), 1763 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.94 (3H, t, *J* 7.1, CH_2CH_3), 1.32−1.54 (4H, m, $(CH_2)_2$), 1.64−1.77 (1H, m, C(3)-CH_aH_b), 2.02−2.14 (1H, m, C(3)CH_aH_b), 2.89 (1H, q, *J* 7.3, C(3)*H*), 3.36 (1H, qt, *J* 8.9, 6.4, C(4)*H*), 6.13 (1H, d, *J* 6.4, C(5)*H*), 6.95 (1H, dd, *J* 8.3, 1.0, ArC(6)*H*), 7.00 (1H, td, *J* 7.6, 1.1, ArC(4)*H*), 7.35 (1H, ddd, *J* 8.3, 7.4, 1.8, ArC(5)*H*), 7.67 (1H, dd, *J* 7.8, 1.8, ArC(3)*H*); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F −67.5 (d, *J* 9.2, C(4)CF_3); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C 13.9 (CH_2CH_3), 22.5 (CH_2), 25.9 (C(3)CH_2), 29.7 (CH_2), 39.6 (q, *J* 28.0, *C*(4)), 39.7 (*C*(3)), 55.6 (ArC(4)OCH_3), 99.9 (q, *J* 2.9, *C*(5)), 111.2 (ArC(6)), 120.2 (ArC(1)), 120.5 (ArC(4)), 126.0 (q, *J* 281.7, C(4)CF_3), 128.4 (ArC(3)), 130.7 (ArC(5)), 150.0 (*C*(6)), 157.2 (ArC(2)), 168.5 (*C*(2)); HRMS (NSI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{20}F_3O_3$ 329.1359, found 329.1359.

*(3S,4S)-3-Butyl-6-(4-nitrophenyl)-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**11**).* 1-Oxohexan-2-yl 4-nitrobenzoate **3** (200 mg, 0.750 mmol), precatalyst **1** (18.4 mg, 50.0 μmol), triethylamine (105 μL, 0.750 mmol), and THF (6 mL) were reacted via a modified version of the general procedure, utilizing syringe pump addition of a solution of (*E*)-4,4,4-trifluoro-1-(4-nitrophenyl)but-2-en-1-one (123 mg, 0.500 mmol) in THF (4 mL) over 1 h followed by stirring for 1 h. The crude product was purified by column chromatography (97:3 petrol:EtOAc) to give (3*S*,4*S*)-3-butyl-6-(4-nitrophenyl)-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **11** as a white crystalline solid (103 mg, 0.299 mmol, 60%): mp 95−98 °C; $[\alpha]_D^{20}$ +72.5 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralpak IA 95:5 hexane:IPA, flow rate 1 mL min^{-1}, 220 nm, 30 °C) t_R(3*S*,4*S*) 25.1 min, t_R(3*R*,4*R*) 32.8 min, >99% ee; IR ν_{max} (solid) 2961 (C—H), 1771 (C=O), 1516 (NO_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.93 (3H, t, *J* 7.0, CH_2CH_3), 1.31−1.55 (4H, m, $(CH_2)_2$), 1.65−1.81 (1H, m, C(3)CH_aH_b), 2.00−2.17 (1H, m, C(3)CH_aH_b), 2.91 (1H, q, *J* 7.1, C(3)*H*), 3.44 (1H, qt, *J* 8.6, 6.4, C(4)*H*), 5.96 (1H, d, *J* 6.4, C(5)*H*), 7.82 (1H, d, *J* 9.0,

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ArC(3)*H*), 8.25 (1H, d, *J* 9.1, ArC(2)*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −67.2 (d, *J* 8.6, C(4)C*F*$_3$); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C 13.8 (CH_2*C*H$_3$), 22.4 (*C*H$_2$), 26.0 (C(3)*C*H$_2$), 29.7 (*C*H$_2$), 39.6 (*C*(3)), 39.6 (q, *J* 28.5, *C*(4)), 98.4 (*C*(5)), 123.9 (Ar*C*(3)), 125.6 (d, *J* 282.0, C(4)*C*F$_3$), 125.9 (Ar*C*(2)), 137.2 (Ar*C*(1)), 148.5 (Ar*C*(4)), 151.6 (*C*(6)), 167.2 (*C*(2)); HRMS (CI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{17}F_3O_4N$ 344.1110, found 344.1117.

*(3S,4S)-6-(4-Bromophenyl)-3-butyl-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**12**).* 1-Oxohexan-2-yl 4-nitrobenzoate **3** (200 mg, 0.750 mmol), (*E*)-1-(4-bromophenyl)-4,4,4-trifluorobut-2-en-1-one (140 mg, 0.500 mmol), precatalyst **1** (13.4 mg, 50.0 μmol), triethylamine (150 μL, 0.750 mmol), and THF (10 mL) were reacted as described in the general procedure for 6 h and then purified by column chromatography (98:2 petrol:EtOAc) to give (3*S*,4*S*)-6-(4-bromophenyl)-3-butyl-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **12** as a white crystalline solid (121 mg, 0.321 mmol, 64%): mp 126−128 °C; $[\alpha]_D^{20}$ +56.6 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralpak IB 99:1 hexane:IPA, flow rate 1 mL min^{-1}, 254 nm, 40 °C) t_R(3*S*,4*S*) 8.3 min, t_R(3*R*,4*R*) 10.3 min, >99% ee; IR ν_{max} (solid) 2961 (C—H), 1769 (C═O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.93 (3H, t, *J* 7.1, CH_2CH_3), 1.33−1.52 (4H, m, $(CH_2)_2$), 1.65−1.76 (1H, m, C(3)C*H*$_a$H$_b$), 2.00−2.14 (1H, m, C(3)CH$_a$*H*$_b$), 2.87 (1H, q, *J* 7.2, C(3)*H*), 3.27−3.43 (1H, m, C(4)*H*), 5.76 (1H, d, *J* 6.4, C(5)*H*), 7.48−7.56 (4H, m, Ar*H*); ^{19}F NMR (470 MHz, $CDCl_3$) δ_F −67.0 (d, *J* 8.6, C(4)C*F*$_3$); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C 13.8 (CH_2CH_3), 22.5 (*C*H$_2$), 26.0 (C(3)*C*H$_2$), 29.7 (*C*H$_2$), 39.4 (q, *J* 28.2, *C*(4)), 39.7 (*C*(3)), 95.1 (*C*(5)), 124.3 (Ar*C*(4)), 125.7 (d, *J* 282, C(4)*C*F$_3$), 126.6 (Ar*C*(2) or Ar*C*(3)), 130.3 (Ar*C*(1)), 131.9 (Ar*C*(2) or Ar*C*(3)), 152.6 (*C*(6)), 167.8 (*C*(2)); HRMS (CI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{16}{}^{79}BrF_3O_2$ 377.0364, found 377.0356.

*(3S,4S)-3-Butyl-6-(pyridin-3-yl)-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**13**).* 1-Oxohexan-2-yl 4-nitrobenzoate **3** (200 mg, 0.750 mmol), (*E*)-4,4,4-trifluoro-1-(pyridin-3-yl)but-2-en-1-one (115 mg, 0.500 mmol), precatalyst **1** (18.4 mg, 50.0 μmol), triethylamine (105 μL, 0.750 mmol), and THF (10 mL) were reacted as described in the general procedure for 14 h and then purified by column chromatography (85:15 petrol:EtOAc) to give (3*S*,4*S*)-3-butyl-6-(pyridin-3-yl)-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **13** as a white crystalline solid (94.9 mg, 0.317 mmol, 63%): mp 62−65 °C; $[\alpha]_D^{20}$ +63.2 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralpak IA 90:10 hexane:IPA, flow rate 1 mL min^{-1}, 254 nm, 30 °C) t_R(3*S*,4*S*) 9.5 min, t_R(3*R*,4*R*) 13.9 min, >99% ee; IR ν_{max} (solid) 2963 (C—H), 1761 (C═O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 0.93 (3H, t, *J* 7.1, CH_2CH_3), 1.29−1.53 (4H, m, $(CH_2)_2$), 1.64−1.79 (1H, m, C(3)-C*H*$_a$H$_b$), 2.00−2.17 (1H, m, C(3)CH$_a$*H*$_b$), 2.89 (1H, q, *J* 7.1, C(3)*H*), 3.29−3.50 (1H, m, C(4)*H*), 5.84 (1H, d, *J* 6.4, C(5)*H*), 7.34 (1H, dd, *J* 8.0, 4.8, ArC(4)*H*), 7.93 (1H, dt, *J* 8.1, 2.0, ArC(5)*H*), 8.55−8.70 (1H, m, ArC(6)*H*), 8.88 (1H, d, *J* 1.8, ArC(2)*H*); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F −67.4 (d, *J* 7.9, C(4)C*F*$_3$); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C 13.8 (CH_2CH_3), 22.4 (*C*H$_2$), 26.0 (C(3)*C*H$_2$), 29.7 (*C*H$_2$), 39.4 (q, *J* 28.4, *C*(4)), 39.7 (*C*(3)), 96.2 (d, *J* 2.8, *C*(5)), 123.4 (Ar*C*(4)), 125.7 (q, *J* 282.0, C(4)*C*F$_3$), 127.4 (Ar*C*(3)), 132.5 (Ar*C*(5)), 146.5 (Ar*C*(2)), 150.8 (Ar*C*(6)), 151.4 (*C*(6)), 167.5 (*C*(2)); HRMS (NSI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{17}F_3NO_2$ 300.1206, found 300.1206.

*(3S,4S)-3-Butyl-6-(furan-2-yl)-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**14**).* 1-Oxohexan-2-yl 4-nitrobenzoate **3** (200 mg, 0.750 mmol), (*E*)-4,4,4-trifluoro-1-(furan-2-yl)but-2-en-1-one (95.1 mg, 0.500 mmol), catalyst **1** (18.4 mg, 50.0 mmol), triethylamine (105 μL, 0.750 mmol), and THF (10 mL) were reacted as described in the general procedure for 18 h and then purified by column chromatography (97:3 petrol: Et$_2$O) to give (3*S*,4*S*)-3-butyl-6-(furan-2-yl)-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **14** as a white crystalline solid (76.1 mg, 0.337 mmol, 53%): mp 59−60 °C; $[\alpha]_D^{20}$ +83.4 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralpak AD-H 98:2 hexane:IPA, flow rate 1 mL min^{-1}, 254 nm, 30 °C) t_R(3*S*,4*S*) 7.4 min, t_R(3*R*,4*R*) 10.4 min, >99% ee; IR ν_{max} (solid) 2966 (C—H), 1763 (C═O); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.93 (3H, t, *J* 7.0, CH_2CH_3), 1.29−1.62 (3H, m, $(CH_2)_2$), 1.62−1.87 (1H, m, C(3)-C*H*$_a$H$_b$), 2.07 (1H, ddt, *J* 5.9, 2.8, 1.5, C(3)CH$_a$*H*$_b$), 2.86 (1H, q, *J* 7.1, C(3)*H*), 3.35 (1H, qt, *J* 8.6, 6.4, C(4)*H*), 5.72 (1H, d, *J* 6.5, C(5)*H*), 6.46 (1H, dd, *J* 3.4, 1.8, ArC(4)*H*), 6.68 (1H, d, *J* 3.5, ArC(3)*H*), 7.44 (1H, dd, *J* 1.9, 0.9, ArC(5)*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −67.6 (d, *J* 8.6, C(4)C*F*$_3$); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C 13.8 (CH_2CH_3), 22.5 (*C*H$_2$), 26.2 (C(3)*C*H$_2$), 29.7 (*C*H$_2$), 39.2 (q, *J* 28.5, *C*(4)), 40.1 (*C*(3)), 92.9 (q, *J* 2.9, *C*(5)), 109.3 (Ar*C*(4)), 111.6 (Ar*C*(3)), 125.8 (q, *J* 282, C(4)*C*F$_3$), 143.9 (Ar*C*(5)), 145.9 (Ar*C*(1)), 146.0 (*C*(6)), 167.7 (*C*(2)); HRMS (NSI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{16}F_3O_3$ 289.1046, found 289.1049.

*(3S,4S)-3-Methyl-6-phenyl-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**15**).* 1-Oxopropan-2-yl 4-nitrobenzoate **2** (167 mg, 0.750 mmol), (*E*)-4,4,4-trifluoro-1-phenylbut-2-en-1-one (100 mg, 0.500 mmol), precatalyst **1** (18.4 mg, 50.0 μmol), triethylamine (105 μL, 0.750 mmol), and THF (10 mL) were reacted as described in the general procedure for 14 h and then purified by column chromatography (95:5 petrol: Et$_2$O) to give (3*S*,4*S*)-3-methyl-6-phenyl-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **15** as a white crystalline solid (86.6 mg, 0.343 mmol, 69%): mp 90−93 °C; $[\alpha]_D^{20}$ +87.4 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralcel OD-H 99:1 hexane:IPA, flow rate 1 mL min^{-1}, 254 nm, 30 °C) t_R(3*S*,4*S*) 24.0 min, t_R(3*R*,4*R*) 41.3 min, >99% ee; IR ν_{max} (solid) 2961 (C—H), 1769 (C═O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 1.47 (3H, dd, *J* 7.2, 1.8, C(3)C*H*$_3$), 3.09 (1H, p, *J* 7.1, C(3)*H*), 3.31 (1H, tdd, *J* 8.9, 6.5, 2.4, C(4)*H*), 5.75 (1H, d, *J* 6.2, C(5)*H*), 7.38−7.44 (3H, m, ArC(2)*H* and ArC(4)*H*), 7.62−7.69 (2H, m, ArC(3)*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −67.4 (dd, *J* 8.9, 1.9, C(4)C*F*$_3$); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C 12.2 (C(3)*C*H$_3$), 34.4 (*C*(3)), 41.0 (q, *J* 28.4, *C*(4)), 94.3 (*C*(5)), 125.1 (Ar*C*(3)), 125.9 (q, *J* 281, C(4)*C*F$_3$), 128.7 (Ar*C*(2)), 130.0 (Ar*C*(4)), 131.4 (Ar*C*(1)), 153.5 (*C*(6)), 168.7 (*C*(2)); HRMS (NSI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{12}F_3O_2$ 257.0784, found 257.0788.

*(3S,4S)-3-Isobutyl-6-phenyl-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**16**).* 4-Methyl-1-oxopentan-2-yl 4-nitrobenzoate **4** (199 mg, 0.750 mmol), (*E*)-4,4,4-trifluoro-1-phenylbut-2-en-1-one (100 mg, 0.500 mmol), precatalyst **1** (18.4 mg, 50.0 μmol), triethylamine (105 μL, 0.750 mmol), and THF (10 mL) were reacted as described in the general procedure for 21 h and then purified by column chromatography (98:2 petrol:EtOAc) to give (3*S*,4*S*)-3-isobutyl-6-phenyl-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **16** as a white crystalline solid (104.8 mg, 0.351 mmol, 70%): mp 109−111 °C; $[\alpha]_D^{20}$ +78.4 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralcel OJ-H 99.8:0.2 hexane:IPA, flow rate 1 mL min^{-1}, 254 nm, 30 °C) t_R(3*S*,4*S*) 24.5 min, t_R(3*R*,4*R*) 35.1 min, >99% ee; IR ν_{max} (solid) 2957 (C—H), 1765 (C═O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 0.97 (6H, dd, *J* 8.4, 6.6, $(CH_3)_2$CH), 1.53−1.64 (1H, m, C(3)C*H*$_a$H$_b$), 1.81 (1H, dp, *J* 13.4, 6.6, $(CH_3)_2$C*H*), 1.95 (1H, dt, *J* 14.5, 7.4, C(3)CH$_a$*H*$_b$), 2.98 (1H, q, *J* 7.2, C(3)*H*), 3.27−3.37 (1H, m, C(4)*H*), 5.77 (1H, d, *J* 6.4, C(5)*H*), 7.38−7.43 (3H, m, Ar*H*), 7.63−7.68 (2H, m, Ar*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −67.4 (d, *J* 8.6, C(4)C*F*$_3$); ^{13}C{^{1}H} (126 MHz, $CDCl_3$) δ_C 22.2 ((CH_3)$_2$CH), 22.5 (CH_3)$_2$CH), 25.4 ((CH_3)$_2$CH), 35.1 (C(3)CH_2), 37.5 (*C*(3)), 39.5 (q, *J* 28.4, *C*(4)), 94.6 (d, *J* 3.1, *C*(5)), 125.1 (Ar*C*(2)), 125.8 (q, *J* 282, C(4)*C*F$_3$), 128.6 (Ar*C*(3)), 130.0 (Ar*C*(4)), 131.3 (Ar*C*(1)), 153.5 (*C*(6)), 168.3 (*C*(2)); HRMS (NSI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{18}F_3O_2$ 299.1253, found 299.1259.

*(3S,4S)-3-Benzyl-6-phenyl-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**17**).* 1-Oxo-3-phenylpropan-2-yl 4-nitrobenzoate **5** (224 mg, 0.750 mmol), (*E*)-4,4,4-trifluoro-1-phenylbut-2-en-1-one (100 mg, 0.500 mmol), precatalyst **1** (18.4 mg, 50.0 mmol), triethylamine (105 μL, 0.750 mmol), and THF (10 mL) were reacted as described in the general procedure for 7 h and then purified by column chromatography (98:2 petrol: Et$_2$O) to give (3*S*,4*S*)-3-benzyl-6-phenyl-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **17** as a white crystalline solid (105.7 mg, 0.316 mmol, 63%): mp 110−111 °C; $[\alpha]_D^{20}$ +32.3 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralpak AD-H 99:1 hexane:IPA, flow rate 1 mL min^{-1}, 254 nm, 30 °C) t_R(3*R*,4*R*) 35.0 min, t_R(3*S*,4*S*) 44.6 min, >99% ee; IR ν_{max} (solid) 2963 (C—H), 1769 (C═O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 2.99 (1H, dd, *J* 14.1, 9.5, C(3)C*H*$_a$H$_b$), 3.17−3.31 (2H, m, C(3)*H* and C(4)*H*), 3.54 (1H, dd, *J* 14.6, 5.7, C(3)CH$_a$*H*$_b$), 5.74 (1H, d, *J* 6.6, C(5)*H*), 7.25−7.30 (3H, m,

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C(3)CH_2ArC(2)*H* and C(3)CH_2ArC(4)*H*), 7.32−7.37 (2H, m, C(3)CH_2ArC(3)*H*), 7.40 (3H, dd, *J* 5.1, 1.7, C(6)ArC(2)*H* and C(6)ArC(4)*H*), 7.64 (2H, dd, *J* 6.8, 3.0, C(6)ArC(3)*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −66.6 (d, *J* 8.0, C(4)CF_3); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C 32.0 (C(3)CH_2), 38.5 (q, *J* 28.3, *C*(4)), 42.0 (*C*(3)), 95.0 (d, *J* 2.6, *C*(5)), 125.1 (C(6)ArC(3)), 125.9 (q, *J* 282, C(4)CF_3), 126.9 (C(3)CH_2Ar*C*(4)), 128.7 (C(6)Ar*C*(2)), 128.8 (C(3)-CH_2Ar*C*(3)), 128.9 (C(3)CH_2Ar*C*(2)), 130.1 (C(6)Ar*C*(4)), 131.2 (C(6)Ar*C*(1)), 137.8 (C(3)CH_2Ar*C*(1)), 153.8 (*C*(6)), 167.8 (*C*(2)); HRMS (NSI$^+$) *m*/*z* [M + NH_4]$^+$ calcd for $C_{19}H_{19}F_3O_2N$ 350.1362, found 350.1368.

*(3S,4S)-3-(2-(Benzyloxy)ethyl)-6-phenyl-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**18**).* 4-(Benzyloxy)-1-oxobutan-2-yl 4-nitrobenzoate **6** (256 mg, 0.750 mmol), (*E*)-4,4,4-trifluoro-1-phenylbut-2-en-1-one (100 mg, 0.500 mmol), precatalyst **1** (18.4 mg, 50.0 mmol), triethylamine (105 μL, 0.750 mmol), and THF (10 mL) were reacted as described in the general procedure for 14 h and then purified by column chromatography (97:3 petrol:EtOAc) to give (3*S*,4*S*)-3-(2-(benzyloxy)ethyl)-6-phenyl-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **18** as a white crystalline solid (152.5 mg, 0.405 mmol, 81%): mp 64−66 °C; $[\alpha]_D^{20}$ +34.6 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralpak AD-H 98:2 hexane:IPA, flow rate 1 mL min^{-1}, 254 nm, 30 °C) t_R(3*S*,4*S*): 15.5 min, t_R(3*R*,4*R*): 24.5 min, >99% ee; IR ν_{max} (solid) 2880 (C—H), 1765 (C═O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 1.93−2.05 (1H, m, C(3)CH_aH_b), 2.36−2.47 (1H, m, C(3)CH_aH_b), 3.17−3.36 (2H, m, C(3)*H* and C(4)*H*)), 3.63−3.77 (2H, m, C(3)CH_2CH_2), 4.51 (2H, q, *J* 11.8, OCH_2Ar), 5.74 (1H, d, *J* 6.5, C(5)*H*), 7.27−7.38 (5H, m, Ar*H*), 7.38−7.43 (3H, m, Ar*H*), 7.65 (3H, ddd, *J* 5.2, 2.4, 1.4, Ar*H*); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F −67.4 (d, *J* 8.2, C(4)CF_3); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C 27.1 (C(3)CH_2), 35.9 (*C*(3)), 39.5 (q, *J* 28.2, *C*(4)), 67.0 (C(3)CH_2CH_2), 73.2 (OCH_2Ar), 94.7 (q, *J* 2.6, C(5)), 125.1 (C(6)Ar*C*(2, 3 or 4)), 125.9 (q, *J* 281.8, C(4)CF_3), 127.8 (OCH_2ArC(2, 3 or 4)), 127.8 (OCH_2ArC(2, 3 or 4)), 128.5 (OCH_2ArC(2, 3 or 4)), 128.6 (C(6)ArC(2, 3 or 4)), 130.0 (C(6)Ar*C*(2, 3 or 4)), 131.4 (C(6)ArC(1)), 138.1 (OCH_2Ar*C*(1)), 153.6 (*C*(6)), 168.3 (*C*(2)); HRMS (NSI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{20}F_3O_3$ 377.1359, found 377.1360.

*(3S,4S)-6-(4-Methoxyphenyl)-3-methyl-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**19**).* 1-Oxopropan-2-yl 4-nitrobenzoate **2** (167 mg, 0.750 mmol), (*E*)-4,4,4-trifluoro-1-(4-methoxyphenyl)but-2-en-1-one (115 mg, 0.500 mmol), precatalyst **1** (18.4 mg, 50.0 mmol), triethylamine (105 μL, 0.750 mmol), and THF (10 mL) were reacted as described in the general procedure for 40 h and then purified by column chromatography (95:5 petrol:EtOAc) to give (3*S*,4*S*)-6-(4-methoxyphenyl)-3-methyl-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **19** as a colorless crystalline solid (106 mg, 0.369 mmol, 74%): mp 92−94 °C; $[\alpha]_D^{20}$ +78.0 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralcel OD-H 95:5 hexane:IPA, flow rate 1 mL min^{-1}, 254 nm, 30 °C) t_R(3*S*,4*S*) 13.2 min, t_R(3*R*,4*R*) 18.7 min, 99% ee; IR ν_{max} (solid) 2957 (C—H), 1780 (C═O); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 1.46 (2H, dd, *J* 7.1, 1.9, C(3)CH_3), 3.07 (1H, p, *J* 7.0, C(3)*H*), 3.27 (1H, qt, *J* 8.9, 6.5, C(4)*H*), 3.83 (3H, s, ArC(4)OCH_3), 5.60 (1H, d, *J* 6.3, C(5)*H*), 6.90 (1H, d, *J* 9.0, ArC(3)*H*), 7.58 (1H, d, *J* 8.9, ArC(2)*H*); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F −67.5 (dd, *J* 8.8, 2.0, C(4)CF_3); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C 12.2 (C(3)*C*H_3), 24.4 (*C*(3)), 41.0 (q, *J* 28.2, *C*(4)), 55.4 (ArC(4)O*C*H_3), 92.3 (q, *J* 3.1, *C*(5)), 114.0 (Ar*C*(3)), 123.9 (ArC(1)), 126.6 (Ar*C*(2)), 129.6 (q, *J* 282, C(4)CF_3), 153.2 (*C*(6)), 161.0 (Ar*C*(4)), 168.9 (*C*(2)); HRMS (CI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{14}F_3O_3$ 287.0895, found 287.0899.

*(3S,4R)-3-Butyl-6-phenyl-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**20**).* 1-Oxohexan-2-yl 4-nitrobenzoate **3** (995 mg, 3.75 mmol), (*Z*)-4,4,4-trifluoro-1-phenylbut-2-en-1-one (500 mg, 2.50 mmol), precatalyst **1** (92 mg, 0.25 mmol), triethylamine (0.53 mL, 3.75 mmol), and THF (50 mL) were reacted as described in the general procedure for 14 h to give crude lactone **20** (94:6 dr). Column chromatography on silica (95:5 petrol:Et_2O) gave (3*S*,4*R*)-3-butyl-6-phenyl-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **20** (>99:1 dr) as a colorless oil (487 mg, 1.63 mmol, 65%): $[\alpha]_D^{20}$ −90.3 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralcel OJ-H 99.8:0.2 hexane:IPA, flow rate 1 mL min^{-1}, 254 nm, 30 °C) t_R(3*S*,4*S*) 31.9 min, t_R(3*R*,4*R*) 50.6 min, >99% ee; IR ν_{max} (film) 2961 (C—H), 1773 (C═O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.84 (3H, t, *J* 7.2, CH_2CH_3), 1.20−1.47 (4H, m, $(CH_2)_2$), 1.60 (1H, dd, *J* 9.4, 7.5, C(3)CH_aH_b), 1.66−1.82 (1H, m, C(3)CH_aH_b), 2.87−2.97 (1H, m, C(3)*H*), 2.96−3.09 (1H, m, C(4)*H*), 5.56 (1H, dd, *J* 6.4, 1.3, C(5)*H*), 7.31−7.37 (3H, m, Ar*H*), 7.56−7.63 (2H, m, Ar*H*); ^{19}F NMR (470 MHz, $CDCl_3$) δ_F −72.2 (d, *J* 8.8, C(4)CF_3); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C 14.2 (CH_2CH_3), 22.5 (CH_2), 29.2 (CH_2), 31.1 (C(3)CH_2), 38.6 (*C*(3)), 42.2 (q, *J* 28.8, *C*(4)), 91.3 (*C*(5)), 125.5 (ArC(1)), 126.1 (d, *J* 280, C(4)CF_3), 129.1 (ArC(2)), 130.5 (ArC(4)), 131.1 (ArC(3)), 153.7 (*C*(6)), 168.0 (*C*(2)); HRMS (NSI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{18}F_3O_2$ 299.1253, found 299.1258.

*(3S,4R)-6-(4-Bromophenyl)-3-butyl-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**21**).* 1-Oxohexan-2-yl 4-nitrobenzoate **3** (265 mg, 1.00 mmol), (*Z*)-1-(4-bromophenyl)-4,4,4-trifluorobut-2-en-1-one (140 mg, 0.500 mmol), precatalyst **1** (18.4 mg, 50.0 μmol), cesium carbonate (163 mg, 0.500 mmol), and THF (10 mL) were reacted in a modified version of the general procedure for 14 h at 40 °C and then purified by column chromatography (98:2 petrol:EtOAc) to give (3*S*,4*R*)-6-(4-bromophenyl)-3-butyl-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **21** as a colorless oil (133.7 mg, 0.354 mmol, 71%): $[\alpha]_D^{20}$ −78.6 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralpak IA 99:1 hexane:IPA, flow rate 1 mL min^{-1}, 30 °C, 254 nm) t_R(3*R*,4*S*) 9.9 min, t_R(3*S*,4*R*) 12.5 min, 96% ee; IR ν_{max} (film) 2934 (C—H), 1775 (C═O); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 0.91 (2H, t, *J* 7.1, CH_2CH_3), 1.28−1.49 (3H, m, $(CH_2)_2$), 1.57−1.85 (2H, m, C(3)CH_2), 2.94−3.02 (1H, m, C(3)*H*), 3.09 (1H, qdd, *J* 8.6, 6.4, 1.7, C(4)*H*), 5.62 (1H, dd, *J* 6.4, 1.3, C(5)*H*), 7.54 (4H, s, Ar*H*); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F −72.6 (d, *J* 8.6, C(4)CF_3); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C 14.2 (CH_2CH_3), 22.5 (CH_2), 29.1 (CH_2), 31.1 (C(3)CH_2), 38.5 (*C*(3)), 42.3 (q, *J* 29.2, *C*(4)), 91.8 (*C*(5)), 124.8 (Ar*C*(4)), 126.0 (d, *J* 280, C(4)CF_3), 127.0 (Ar*C*(2) or Ar*C*(3)), 130.6 (Ar*C*(1)), 132.3 (Ar*C*(2) or Ar*C*(3)), 152.9 (*C*(6)), 167.7 (*C*(2)); HRMS (CI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{17}{}^{79}BrF_3O_2$ 377.0364, found 377.0372.

*(3S,4R)-3-Butyl-6-(furan-2-yl)-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**22**).* 1-Oxohexan-2-yl 4-nitrobenzoate **3** (184 mg, 0.695 mmol), (*Z*)-4,4,4-trifluoro-1-(furan-2-yl)but-2-en-1-one (88.0 mg, 0.463 mmol), precatalyst **1** (17.0 mg, 46.3 μmol), cesium carbonate (151 mg, 0.463 mmol), and THF (9 mL) were reacted in a modified version of the general procedure for 5 h at 40 °C and then purified by column chromatography on silica (99.5:0.5 petrol:EtOAc) to give (3*S*,4*R*)-3-butyl-6-(furan-2-yl)-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **22** (dr 93:7) as a colorless oil (88.9 mg, 0.308 mmol, 67%): $[\alpha]_D^{20}$ −119.2 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralpak IA 99.8:0.2 hexane:IPA, flow rate 1 mL min^{-1}, 30 °C, 220 nm) t_R(3*R*,4*S*) 10.8 min, t_R(3*S*,4*R*) 13.8 min, 95% ee; IR ν_{max} (film) 2961 (C—H), 1778 (C═O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.83 (3H, t, *J* 7.1, CH_2CH_3), 1.21−1.43 (4H, m, CH_2 × 2), 1.51−1.65 (1H, m, C(3)CH_aH_b), 1.65−1.79 (1H, m, C(3)CH_aH_b), 2.84−2.94 (1H, m, C(3)*H*), 3.02 (1H, ddd, *J* 8.4, 6.6, 1.6, C(4)*H*), 5.51 (1H, dd, *J* 6.5, 1.4, C(5)*H*), 6.39 (1H, dd, *J* 3.4, 1.8, ArC(4)*H*), 6.63 (1H, d, *J* 3.4, ArC(3)*H*), 7.38 (1H, dd, *J* 1.8, 0.8, ArC(5)*H*); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F −72.8 (d, *J* 8.6); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C 13.7 (CH_2CH_3), 22.1 (CH_2), 28.8 (CH_2), 30.7 (C(3)CH_2), 38.5 (*C*(3)), 41.6 (q, *J* 29.1, *C*(4)), 89.0 (*C*(5)), 109.5 (Ar*C*(3)), 111.6 (Ar*C*(4)), 125.7 (q, *J* 280.2, C(4)CF_3), 144.0 (Ar*C*(5)), 145.8 (Ar*C*(2)), 145.9 (*C*(6)), 167.0 (*C*(2)); HRMS (NSI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{16}F_3O_3$ 289.1046, found 289.1048.

*(3S,4R)-3-Methyl-6-phenyl-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**23**).* 1-Oxopropan-2-yl 4-nitrobenzoate **2** (223 mg, 1.00 mmol), (*Z*)-4,4,4-trifluoro-1-phenylbut-2-en-1-one (100 mg, 0.500 mmol), precatalyst **1** (18.4 mg, 50.0 μmol), cesium carbonate (163 mg, 0.500 mmol), and THF (10 mL) were reacted in a modified version of the general procedure for 10 h and then purified by column chromatography on silica (98:2 petrol:EtOAc) to give (3*S*,4*R*)-3-methyl-6-phenyl-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **23** as a white crystalline solid (84.9 mg, 0.331 mmol, 66%): mp 71−73 °C; $[\alpha]_D^{20}$ −58.3 (*c* 0.4, $CHCl_3$); chiral HPLC analysis (Chiralcel OD-H 99:1 hexane:IPA, flow rate 1 mL min^{-1}, 30 °C, 254 nm) t_R(3*R*,4*S*)

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12.6 min, t_R(3*S*,4*R*) 16.0 min, 99% ee; IR ν_{max} (film) 2918 (C—H), 1767 (C═O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 1.47 (3H, d, *J* 7.1, C(3)CH_3), 3.01−3.13 (2H, m, C(3)*H* and C(4)*H*), 5.67 (1H, dd, *J* 5.2, 1.1, C(5)*H*), 7.38−7.45 (3H, m, ArC(3)*H* and ArC(4)*H*), 7.64−7.70 (2H, m, ArC(2)*H*); ^{19}F NMR (470 MHz, $CDCl_3$) δ_F −67.8 (d, *J* 9.8, C(4)CF_3); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ_C 16.4 (C(3)*C*H$_3$), 33.2 (*C*(3)), 43.6 (q, *J* 28.6, *C*(4)), 91.6 (q, *J* 3.0, *C*(5)), 125.0 (Ar*C*(2)), 125.7 (q, *J* 280, C(4)*C*F$_3$), 128.7 (Ar*C*(3)), 130.1 (Ar*C*(4)), 131.3 (Ar*C*(1)), 153.0 (*C*(6)), 168.5 (*C*(2)); HRMS (CI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{12}F_3O_2$ 257.0789, found 257.0789.

*(3S,4R)-3-(2-(Benzyloxy)ethyl)-6-phenyl-4-(trifluoromethyl)-3,4-dihydro-2H-pyran-2-one (**24**).* 4-(Benzyloxy)-1-oxobutan-2-yl 4-nitrobenzoate **6** (256 mg, 0.750 mmol), (*Z*)-4,4,4-trifluoro-1-phenylbut-2-en-1-one (100 mg, 0.500 mmol), precatalyst **1** (18.4 mg, 50.0 mmol), cesium carbonate (163 mg, 0.500 mmol), and THF (10 mL) were reacted in a modified version of the general procedure for 8 h and then purified by column chromatography on silica (95:5 petrol:EtOAc) to give (3*S*,4*R*)-3-(2-(benzyloxy)ethyl)-6-phenyl-4-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one **24** as a colorless oil (149.2 mg, 0.396 mmol, 79%): $[\alpha]_D^{20}$ −86.5 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralcel OD-H 98:2 hexane:IPA, flow rate 1 mL min^{-1}, 30 °C, 254 nm) t_R(3*S*,4*R*) 20.0 min, t_R(3*R*,4*S*) 24.7 min, 96% ee; IR ν_{max} (film) 2866 (C—H), 1771 (C═O); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 1.95−2.13 (2H, m, C(3)CH_2), 3.17−3.36 (2H, m, C(3)*H* and C(4)*H*), 3.55−3.69 (2H, m, C(3)CH$_2$CH_2), 4.42−4.62 (2H, m, OCH_2Ar), 5.57−5.70 (1H, m, C(5)*H*), 7.27−7.46 (8H, m, Ar*H*), 7.60−7.74 (2H, m, C(6)ArC(2)*H*); ^{19}F NMR (376 MHz, $CDCl_3$) δ_F −72.5 (d, *J* 8.7, C(4)CF_3); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C 31.0 (C(3)*C*H$_2$), 35.9 (*C*(3)), 41.7 (q, *J* 29.0, *C*(4)), 66.9(C(3)CH$_2$*C*H$_2$), 73.3 (OCH$_2$Ar), 91.1 (*C*(5)), 125.1 (C(6)Ar*C*(2)), 125.8 (q, *J* 280, C(4)CF_3), 127.8 (OCH$_2$Ar*C*(2)), 127.8 (OCH$_2$Ar*C*(4)), 128.5 (OCH$_2$Ar*C*(3)), 128.6 (C(6)Ar*C*(3)), 130.1 (C(6)Ar*C*(4)), 131.3 (C(6)Ar*C*(1)), 137.8 (OCH$_2$Ar*C*(1)), 153.4 (*C*(6)), 167.5 (*C*(2)); HRMS (NSI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{20}F_3O_3$ 377.1359, found 377.1363.

*(S)-Methyl 2-((S)-1,1,1-trifluoro-4-oxo-4-phenylbutan-2-yl)-hexanoate (**25**).* To a solution of lactone **8** (59.6 mg, 0.20 mmol) (97:3 dr) in MeOH (2 mL) was added DMAP (2.44 mg, 0.02 mmol), and the reaction mixture was heated at 50 °C for 1.5 h before being concentrated in vacuo to give crude ester **25** (90:10 dr). Column chromatography on silica (97:3 petrol:Et$_2$O) gave (*S*)-methyl 2-((*S*)-1,1,1-trifluoro-4-oxo-4-phenylbutan-2-yl)hexanoate **25** (97:3 dr) as a colorless oil (48.5 mg, 0.147 mmol, 73%): $[\alpha]_D^{20}$ −27.0 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralcel OJ-H 95:5 hexane:IPA, flow rate 0.5 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*,3*S*) 10.0 min, t_R(2*R*,3*R*) 11.3 min, 97% ee; IR ν_{max} (oil) 2957 (C—H), 2934, 1740 (C═O), 1690 (C═O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.79 (3H, t, *J* 7.0, CH$_2$CH_3), 1.09−1.28 (4H, m, CH_2 ×2), 1.39−1.47 (1H, m, C(2)CH_aH$_b$), 1.64−1.73 (1H, m, C(2)CH$_a$*H*$_b$), 2.68 (1H, ddd, *J* 11.3, 4.9, 3.6, C(2)*H*), 3.12 (1H, dd, *J* 18.3, 4.6, C(O)CH$_a$*H*$_b$), 3.33 (1H, dd, *J* 18.3, 6.8, C(O)CH_aH$_b$), 3.47−3.57 (1H, m, F$_3$CC*H*), 3.61 (3H, s, CH_3), 7.39−7.43 (2H, m, ArC(3)*H*), 7.50−7.55 (1H, m, ArC(4)*H*), 7.88−7.91 (2H, m, ArC(2)*H*); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C 13.9 (CH$_2$*C*H$_3$), 22.5 (*C*H$_2$), 27.9 (*C*H$_2$), 29.9 (*C*H$_2$), 34.3 (q, *J* 2.0, C(O)*C*H$_2$), 40.0 (q, *J* 26.1, F$_3$C*C*), 43.9 (q, *J* 1.73, *C*(2)), 52.1 (O*C*H$_3$), 127.5 (q, *J* 279, *C*F$_3$), 128.1 (Ar*C*), 128.8 (Ar*C*), 133.6 (Ar*C*(4)), 136.3 (Ar*C*(1)), 173.6 (*C*(1)), 195.7 (*C*OPh); HRMS (CI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{22}F_3O_3$ 311.1521, found 311.1524.

*(±)-2-(1,1,1-Trifluoro-4-phenylbutan-2-yl)hexanoic Acid (**26**).* To a solution of lactone (±)-**8** (59.6 mg, 0.20 mmol) (97:3 dr) in EtOAc (5 mL) was added 10% Pd/C (21.3 mg, 0.02 mmol), and a balloon of H_2(g) was appended. The reaction mixture was stirred at rt for 1 h before being filtered through Celite and concentrate in vacuo to give the crude acid (±)-**26** (95:5 dr). Column chromatography on silica (50:50 petrol:Et$_2$O) gave 2-(1,1,1-trifluoro-4-phenylbutan-2-yl)-hexanoic acid (±)-**26** (95:5 dr) as a colorless oil (49.0 mg, 0.163 mmol, 82%): IR ν_{max} (oil) 3500−2600 (O—H), 2959 (C—H), 2874, 1712 (C═O); ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 0.83 (3H, t, *J* 7.0, CH$_2$CH_3), 1.14−1.34 (4H, m, CH_2 × 2), 1.45−1.54 (1H, m, C(2)CH_aH$_b$), 1.59−1.69 (1H, m, C(2)CH$_a$*H*$_b$), 1.84−1.94 (2H, m, CH_2), 2.54−2.74 (4H, m, C(2)*H*, F$_3$CC*H* and CH_2), 7.09−7.15 (3H, m, ArC*H*), 7.19−7.24 (2H, m, ArC*H*); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ_C 13.9 (CH$_2$*C*H$_3$), 22.5 (*C*H$_2$), 27.1 (*C*H2), 27.2 (*C*H$_2$), 30.0 (*C*H$_2$), 33.4 (*C*H$_2$), 43.7 (*C*(2)), 44.2 (q, *J* 25.0, F$_3$*C*C), 126.3 (Ar*C*(4)), 127.7 (q, *J* 280, *C*F$_3$), 128.4 (Ar*C*), 128.6 (Ar*C*), 140.8 (Ar*C*(1)), 179.9 (*C*(1)); HRMS (CI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{22}F_3O_2$ 303.1572, found 303.1576.

*(S)-Methyl 2-((R)-1,1,1-trifluoro-4-oxo-4-phenylbutan-2-yl)-hexanoate (**27**).* To a solution of lactone **20** (59.6 mg, 0.20 mmol) (>99:1 dr) in MeOH (2 mL) was added DMAP (2.44 mg, 0.02 mmol), and the reaction mixture was heated at 50 °C for 1.5 h before being concentrated in vacuo to give crude ester **27** (94:6 dr). Column chromatography on silica (95:5 petrol:Et$_2$O) gave (*S*)-methyl 2-((*R*)-1,1,1-trifluoro-4-oxo-4-phenylbutan-2-yl)hexanoate **27** (98:2 dr) as a white solid (54.0 mg, 0.164 mmol, 82%): mp 64−66 °C; $[\alpha]_D^{20}$ −2.2 (*c* 0.5, $CHCl_3$); chiral HPLC analysis (Chiralpak AD-H 98:2 hexane:IPA, flow rate 1 mL min^{-1}, 254 nm, 30 °C) t_R(2*R*,3*S*) 5.4 min, t_R(2*S*,3*R*) 6.5 min, >95% ee; IR ν_{max} (solid) 2957 (C—H), 2934, 1740 (C═O), 1690 (C═O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 0.88 (3H, t, *J* 7.0, CH$_2$CH_3), 1.24−1.34 (4H, m, CH_2 × 2), 1.46−1.53 (1H, m, C(2)CH_aH$_b$), 1.63−1.70 (1H, m, C(2)CH$_a$*H*$_b$), 2.90 (1H, dt, *J* 9.4, 4.7, C(2)*H*), 3.26−3.31 (1H, m, C(O)CH$_a$*H*$_b$), 3.55−3.61 (2H, m, C(O)CH$_a$*H*$_b$ and F$_3$CC*H*), 3.73 (3H, s, OCH_3), 7.52 (2H, t, *J* 7.7, ArC(3)*H*), 7.62 (1H, t, *J* 7.4, ArC(4)*H*), 8.03−8.04 (2H, m, ArC(2)*H*); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ_C 13.9 (CH$_2$*C*H$_3$), 22.3 (*C*H$_2$), 29.6 (*C*H$_2$), 30.1 (*C*H$_2$), 33.3 (*C*H$_2$), 40.0 (q, *J* 26.3, F$_3$*C*C), 42.7 (*C*(2)), 51.9 (O*C*H$_3$), 127.3 (q, *J* 279, *C*F$_3$), 128.2 (Ar*C*), 128.8 (Ar*C*), 133.6 (Ar*C*(4)), 136.2 (Ar*C*(1)), 174.3 (*C*(1)), 196.2 (*C*OPh); HRMS (CI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{22}F_3O_3$ 311.1521, found 311.1524.

*(±)-2-(1,1,1-Trifluoro-4-phenylbutan-2-yl)hexanoic Acid (**28**).* To a solution of lactone (±)-**20** (59.6 mg, 0.20 mmol) (>99:1 dr) in EtOAc (5 mL) was added 10% Pd/C (21.3 mg, 0.02 mmol), and a balloon of H_2(g) was appended. The reaction mixture was stirred at rt for 1 h before being filtered through Celite and concentrated in vacuo to give the crude acid (±)-**28** (>99:1 dr). Column chromatography on silica (Et$_2$O) gave 2-(1,1,1-trifluoro-4-phenylbutan-2-yl)hexanoic acid (±)-**28** (>99:1 dr) as a colorless oil (50.0 mg, 0.164 mmol, 82%): IR ν_{max} (oil) 3500−2600 (O—H), 2959 (C—H), 2874, 1712 (C═O); ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 0.92 (3H, t, *J* 7.2, CH$_2$CH_3), 1.15−1.39 (4H, m, CH_2 × 2), 1.47−1.52 (1H, m, C(2)CH_aH$_b$), 1.74−1.80 (1H, m, C(2)CH$_a$*H*$_b$), 1.93−2.09 (2H, m, CH_2), 2.55−2.61 (1H, m, C*H*), 2.69−2.75 (2H, m, C*H* × 2), 2.82−2.88 (1H, m, C*H*), 7.21−7.27 (3H, m, ArC(2)*H* and ArC(4)*H*), 7.34 (2H, t, *J* 7.5, ArC(3)*H*); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ_C 13.9 (CH$_2$*C*H$_3$), 22.5 (*C*H$_2$), 28.1 (*C*H$_2$), 30.0 (*C*H$_2$), 30.4 (*C*(2)), 33.7 (*C*H$_2$), 44.2 (q, *J* 25.1, F$_3$*C*C), 126.4 (Ar*C*(4)), 127.8 (q, *J* 280, CF3), 128.6 (Ar*C*), 128.6 (Ar*C*), 140.7 (Ar*C*(1)), 179.8 (*C*(1)); HRMS (CI$^+$) *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{22}F_3O_2$ 303.1572, found 303.1576.

*3-(1-Hydroxy-2-(4-nitrophenoxy)propyl)-2-mesityl-6,7-dihydro-5H-pyrrolo[2,1-c][1,2,4]triazol-2-ium Tetrafluoroborate (**29**).* To a solution of NHC precatalyst **7** (100 mg, 0.32 mmol) and aldehyde **2** (62 mg, 0.32 mmol) in CH_2Cl_2 (10 mL) was added NEt$_3$ (49 μL, 0.35 mmol). After 10 min, the solution was concentrated in vacuo and purified by column chromatography (20:80 CH_2Cl_2:acetone) to give the combined diastereoisomers of **29** (dr 83:17) as a white solid (20.0 mg, 0.04 mmol, 12%): mp 123−126 °C; IR ν_{max} (neat) 1724 (C═O), 1593 (C═C), 1525 (N−O), 1348 (N−O), 1269 (C−O), 1078 (C−O); *m*/*z* (NSI$^+$) 451 ([M − BF_4^-]$^+$, 100%); HRMS (NSI$^+$) *m*/*z* [M − BF_4^-]$^+$ calcd for $C_{24}H_{27}N_4O_5$ 451.1976, found 451.1973.

Major: ^{1}H NMR (500 MHz, CD_2Cl_2) δ_H 1.41−1.44 (3H, m, CHCH_3), 1.91 (3H, s, CH_3), 2.11 (3H, s, CH_3), 2.37 (3H, s, CH_3), 2.86−2.98 (2H, m, NCH$_2$CH_2CH$_2$), 3.22−3.28 (2H, m, NCH$_2$CH$_2$CH_2), 4.55−4.61 (1H, m, NCH_AH$_B$CH$_2$CH$_2$), 4.83−4.90 (1H, m, NCH$_A$*H*$_B$CH$_2$CH$_2$), 5.11−5.05 (2H, m, CH$_3$C*H*C(OH)(*H*)), 7.02 (1H, s, MesC*H*), 7.11 (1H, s, MesC*H*), 8.05−8.06 (2H, m, 2,6-Ar*H*), 8.24−8.26 (2H, m, 3,5-Ar*H*); ^{13}C{^{1}H} NMR (125 MHz, CD_2Cl_2) δ_C 15.2, 17.2, 17.7, 21.3, 22.2, 27.3, 49.5, 67.9, 71.6, 123.9, 130.3, 130.6, 130.9, 131.2, 135.4, 135.5, 143.1, 151.2, 151.8, 163.5, 164.0.

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Minor: ^{1}H NMR (500 MHz, CD_2Cl_2, characteristic signals) δ_H 2.03 (3H, s, CH_3), 2.14 (3H, s, CH_3), 2.33 (3H, s, CH_3), 4.34−4.40 (1H, m, $NCH_AH_BCH_2CH_2$), 4.83−4.90 (1H, m, $NCH_AH_BCH_2CH_2$), 5.11−5.05 (2H, m, $CH_3CHC(OH)(H)$), 6.98 (1H, s, MesC*H*), 7.08 (1H, s, MesC*H*), 8.12−8.16 (2H, m, 2,6-Ar*H*), 8.29−8.32 (2H, m, 3,5-Ar*H*), $^{13}C\{^1H\}$ NMR (125 MHz, CD_2Cl_2, characteristic signals) δ_C 49.7, 124.2, 131.1.

*(Z)-2-Mesityl-3-(1-(propionyloxy)prop-1-en-1-yl)-6,7-dihydro-5H-[2,1-c][1,2,4]triazol-2-ium Tetrafluoroborate (**30**).* To a solution of NHC precatalyst **7** (100 mg, 0.32 mmol) and aldehyde **2** (62 mg, 0.32 mmol) in CH_2Cl_2 (10 mL) was added NEt_3 (88 μL, 0.64 mmol). After 16 h, the solution was concentrated in vacuo and purified by column chromatography (50:50 CH_2Cl_2:acetone) to give **30** as a white solid (37 mg, 0.18 mmol, 55%): mp 55−60 °C; IR ν_{max} (neat) 2924, 1775 (C═O), 1589 (C═C), 1487, 1449, 1033 (C—O); ^{1}H NMR (500 MHz, MeOD-d_4) δ_H 0.94 (3H, t, *J* 7.4, CH_2CH_3), 1.78 (3H, d, *J* 7.1, $CHCH_3$), 2.11 (3H, s, CH_3), 2.04−2.08 (8H, m, $ArCH_3$ and CH_2CH_3), 2.38 (3H, s, $ArCH_3$), 2.92 (2H, quintet, *J* 7.5, NCH_2CH_2), 3.26 (2H, t, *J* 7.8, $NCH_2CH_2CH_2$), 4.57 (2H, t, *J* 7.3, NCH_2), 6.55 (1H, q, *J* 7.1, $CHCH_3$), 7.13 (2H, s, ArC*H*); $^{13}C\{^1H\}$ NMR (125 MHz, MeOD-d_4) δ_C 8.6, 12.7, 17.4, 21.2, 22.8, 26.7, 27.7, 50.2, 130.8, 131.2, 133.6, 134.4, 137.0, 143.6, 145.7, 164.5, 172.0; *m*/*z* (NSI$^+$) 340 ([M − BF_4^-]$^+$, 100%); HRMS (NSI$^+$) *m*/*z* [M − BF_4^-]$^+$ calcd for $C_{20}H_{26}N_3O_2$ 340.2020, found 340.2020.

■ ASSOCIATED CONTENT

Supporting Information

Epimerization of *syn*-**15**, kinetic profiles, and kinetic isotope effect, ^{1}H and $^{13}C\{^1H\}$ NMR spectra and HPLC trances of all dihydropyranones and derivatization products. CIF file giving X-ray crystallographic data for *syn*-**12**. Representative spectra from mechanistic studies. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(17) α-Aroyloxyaldehydes are stable for a number of months when stored in a fridge.

(18) Crystallographic data for **12** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 933076.

(19) For example, reaction of a pentyl substituted β-trifluoromethyl enone with **2** gave the corresponding *syn*-dihydropyranone in 27% yield.

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(22) We have recently isolated a number of these aldehyde-NHC adducts for related Stetter and benzoin reactions; see ref 24a.

(23) Control experiments found that reactions performed in CH_2Cl_2 gave comparable dr and ee to those performed in THF.

(24) (a) Collett, C. J.; Massey, R. S.; Maguire, O. R.; Batsanov, A. S.; O'Donoghue, A. C.; Smith, A. D. *Chem. Sci.* **2013**, *4*, 1514−1522. (b) Massey, R. S.; Collett, C. J.; Lindsay, A. G.; Smith, A. D.; O'Donoghue, A. C. *J. Am. Chem. Soc.* **2012**, *134*, 20421−20432.

(25) α-Aroyloxyaldehyde **2** is likely to undergo other decomposition pathways as the formation of initial adduct **29**, product **19**, O-acylated enolate **30**, and propanoic acid does not fully account for the rate of decomposition observed.
(26) Chi et al. have observed deactivation of a related achiral NHC-catalyst through a different pathway in reactions with activated esters; see ref 12.
(27) Attempts to isolate adduct **31** from a stoichiometric reaction of chiral NHC precatalyst **1** and **2** were unsuccessful due to the rapid forward reaction.
(28) In this case, aldehyde decomposition products could not be observed by ^{1}H NMR spectroscopy.
(29) KIE is an average over two experiments. For full details of kinetic experiments see the Supporting Information.
(30) This value is comparable with that observed by Rovis et al. for an intramolecular Stetter reaction in which proton transfer is rate-determining (k_H/k_D = 2.62); see: Moore, J. L.; Silvestri, A. P.; de Alaniz, J. R.; DiRocco, D. A.; Rovis, T. *Org. Lett.* **2011**, *13*, 1742−1745.
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