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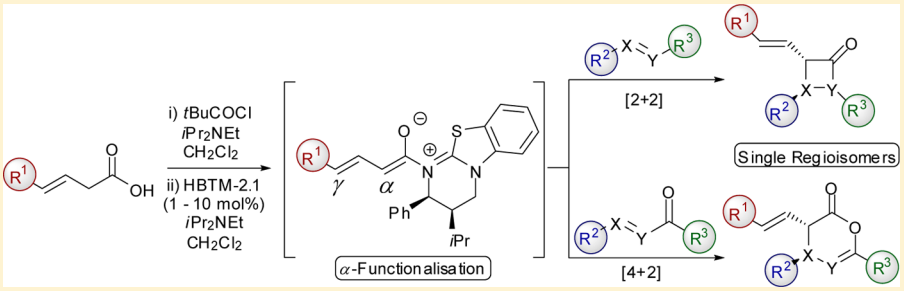
Isothiourea-Mediated Asymmetric Functionalization of 3-Alkenoic Acids

Louis C. Morrill, Samuel M. Smith, Alexandra M. Z. Slawin, and Andrew D. Smith*

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

Supporting Information



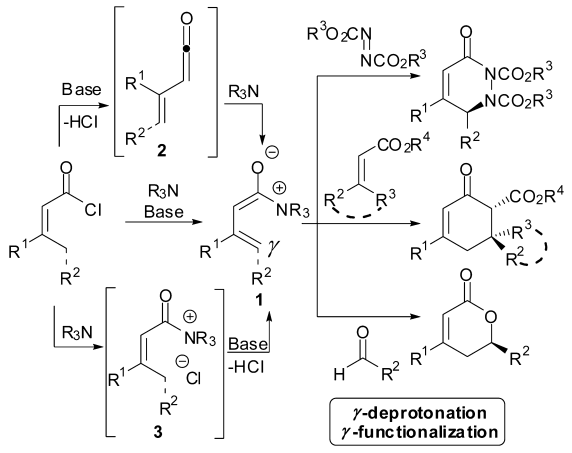
ABSTRACT: Isothiourea HBTM-2.1 promotes the catalytic asymmetric α-functionalization of 3-alkenoic acids through formal [2 + 2] cycloadditions with *N*-tosyl aldimines and formal [4 + 2] cycloadditions with either 4-aryltrifluoromethyl enones or *N*-aryl-*N*-aroyl diazenes, providing useful synthetic building blocks in good yield and with excellent enantiocontrol (up to >99% ee). Stereodefined products are amenable to further synthetic elaboration through manipulation of the olefinic functionality.

INTRODUCTION

The organocatalytic generation of dienolates or their dienamine equivalents is an increasingly popular area of research.[1] These intermediates have powerful synthetic potential due to their ability to react regio- and enantioselectively through either α- or γ-positions, allowing rapid access to diverse molecular scaffolds. In particular, recent research has demonstrated the ability of ammonium and azolium dienolates to participate in asymmetric transformations.[2−11] For example, Peters[2] and Ye[3] have accessed cinchona alkaloid and norephedrine derived C1-ammonium dienolates from α,β-unsaturated acid chloride starting materials and applied these toward the synthesis of a range of stereodefined products (Scheme 1). C1-Ammonium dienolate **1** may form either via initial dehydrohalogenation to form vinyl ketene **2**, which is intercepted by the Lewis base, or from initial attack of the Lewis base to form α,β-acyl ammonium **3** followed by γ-deprotonation. To the best of our knowledge, all catalytically generated β,β-disubstituted C1-ammonium dienolates documented in the literature react to give γ-functionalized products.

C1-Azolium dienolates have also received considerable attention within the past two years. For example, Ye demonstrated that α,β-unsaturated acid chlorides **4**, in the presence of an N-heterocyclic carbene (NHC) and base, afford C1-azolium dienolates **5** that react via the γ-center in asymmetric formal [4 + 2] cycloadditions with 2π electrophiles (Scheme 2a).[4] Chi subsequently disclosed the ability to access the same dienolate via both enals **6** (in presence of a stoichiometric oxidant)[5,6] and α,β-unsaturated esters **7** (Scheme 2b,c).[7] Alternatively, enals bearing an α-bromo leaving group such as **8** have also been demonstrated as

Scheme 1. Generation and Utility of C1-Ammonium Dienolates



suitable azolium dienolate precursors (Scheme 2d).[8] In examples a−d, each process is postulated to involve γ-deprotonation of the corresponding β,β-disubstituted-α,β-acyl azolium intermediate to generate the corresponding dienolate, often depicted in both (*E*)- and (*Z*)-configurations, followed by γ-functionalization of the resulting azolium dienolate.[9] Alternatively, aldehydes that contain a γ-leaving group such as **9** have been used to access C1-azolium dienolates **10** (Scheme 2e). Interestingly, these dienolates give α-functionalization via

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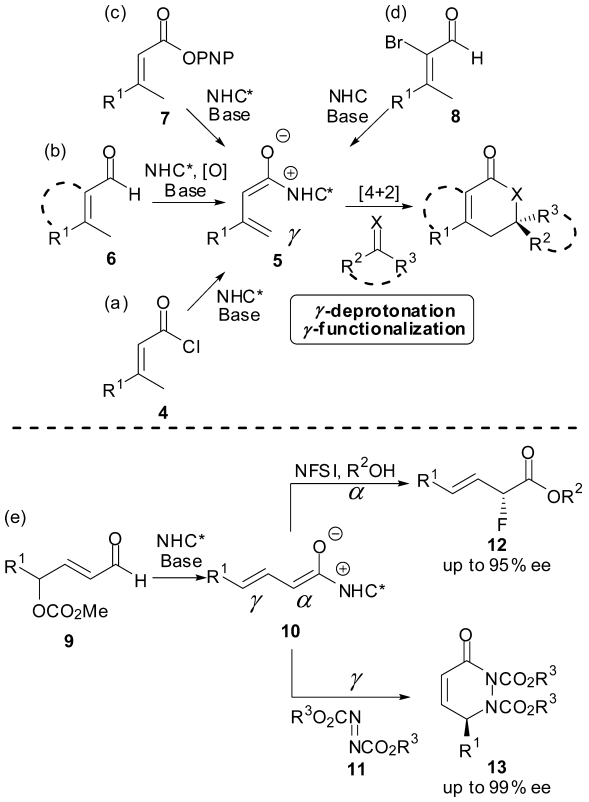
Scheme 2. Generation and Utility of C1-Azolium Dienolates



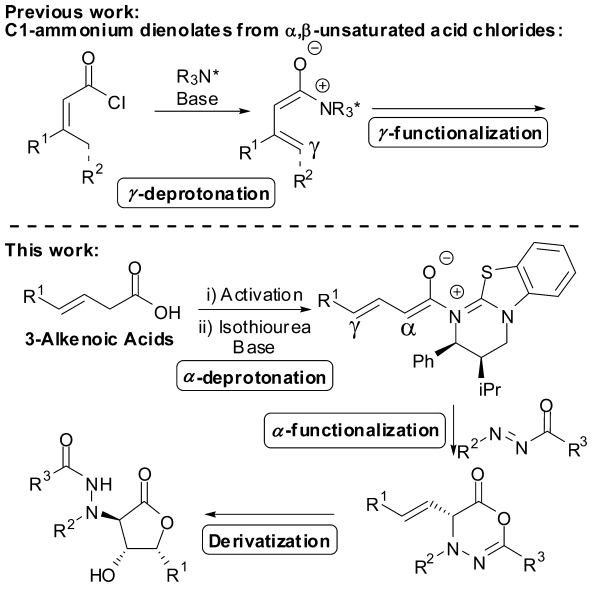
fluorination with NFSI, and γ-functionalization in the formal [4 + 2] cycloaddition with diazodicarboxylates **11**, affording esters **12**[10] and lactams **13**,[11] respectively.

Building upon the elegant nucleophile-catalyzed aldol-lactonization (NCAL) reaction developed by Romo,[12] we have recently shown that isothioureas[13,14] can generate ammonium enolates[15] in situ from carboxylic acids that subsequently undergo a range of intra- and intermolecular Michael addition-lactonization/lactamization reactions to generate stereodefined products.[16] Although powerful, the success of the intermolecular processes often relies upon using arylacetic acids as starting materials,[17,18] which constitutes a limitation of this organocatalytic strategy. To broaden the substrate scope of such processes, the use of 3-alkenoic acids would allow access to extended ammonium dienolates that could give rise to either α- or γ-functionalized products in a stereodefined manner (Scheme 3). In this manuscript, a range of 3-alkenoic acids are shown to act as suitable precursors to isothiourea-derived ammonium dienolates that react in a variety of formal [2 + 2] and [4 + 2] cycloadditions. In contrast to previously accessed C1-ammonium dienolates formed via γ-deprotonation, these ammonium dienolates are formed via α-deprotonation and provide exclusively α-functionalized products. This strategy introduces an additional exocyclic olefin functional handle, allowing for further product functionalization into useful synthetic building blocks.

RESULTS AND DISCUSSION

Generation of Isothiourea Derived Ammonium Dienolates and Reaction with 2π Electrophiles. Initial studies probed the ability of isothioureas to generate an ammonium dienolate from a 3-alkenoic acid, with subsequent reaction with a reactive 2π component used to test if α- or γ-selectivity is

Scheme 3. Proposed Asymmetric Transformations of 3-Alkenoic Acids via Either α- or γ-Functionalization



observed. Encouraged by Ye's report demonstrating diazodicarboxylates as suitable reaction partners with C1-ammonium dienolates,[3a] along with both Ye and Chi who showed that trifluoromethyl ketones are suitable partners in [4 + 2] cycloadditions with C1-azolium dienolates,[4,5] these 2π components were evaluated. Following our report in the previous manuscript, we also evaluated *N*-tosyl aldimines as 2π electrophiles.[19] Using 3-methylbut-3-enoic acid **14** or 2-(cyclopent-1-en-1-yl)acetic acid **15** with pivaloyl chloride as activating agent, achiral DHPB **17** (3,4-dihydro-2*H*-pyrimido-[2,1-*b*]benzothiazole) as catalyst, and trifluoromethyl ketone **18** as the 2π electrophile,[20] no distinguishable cycloaddition products were observed (Table 1). Under the same reaction conditions, (*E*)-4-phenylbut-3-enoic acid **16** reacted with trifluoromethyl ketone **18**, giving solely the [2 + 2] cycloaddition product β-lactone **21** (60:40 dr *anti*:*syn*) derived from α-functionalization[21] in 71% combined yield, while reaction with *N*-tosyl aldimine **19** gave β-lactam **22** (83:17 dr *anti*:*syn*) in 68% yield (*anti* diastereoisomer).[22−24] Unfortunately, diazodicarboxylate **20** proved incompatible with this system, giving no distinguishable product despite full consumption of **20**.

Encouraged by the promising diastereoselectivities observed in the reaction with *N*-tosyl aldimine **19**, further optimization studies focused upon finding a suitable asymmetric variant. Screening of a range of isothiourea catalysts and C(4)-substituted alkenoic acids revealed that chiral isothiourea HBTM-2.1 **23** efficiently promotes the formal [2 + 2] cycloaddition of (*E*)-pent-3-enoic acid **24** and imine **25** at rt, affording β-lactam **26** in moderate diastereoselectivity (68:32 dr *anti*:*syn*), with each separable diastereoisomer isolated in good yield (53% *anti*, 27% *syn*) and enantioselectivity (*anti* 79% ee, *syn* 72% ee) (Table 2). Lowering the temperature to −78 °C resulted in similar diastereoselectivity (71:29 dr *anti*:*syn*) but with each separable diastereoisomer formed in excellent enantioselectivity (*anti* 97% ee, *syn* > 99% ee).[25]

The absolute configuration of *syn*-β-lactam **27** was confirmed unambiguously by X-ray crystallography as (3*S*,4*S*),[26] while that of the *anti*-β-lactam **26** was confirmed by an epimerization

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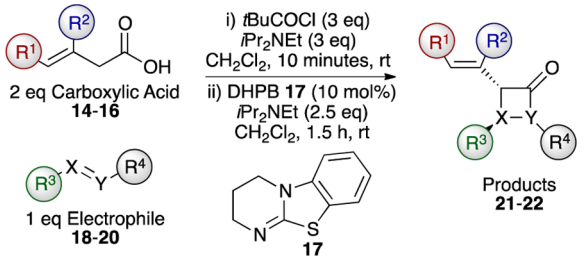
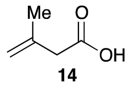
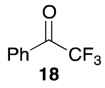
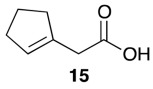
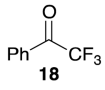
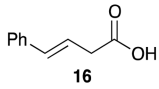
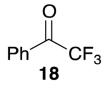
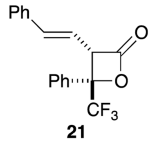
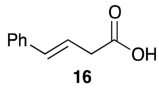
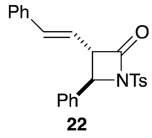
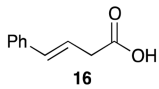
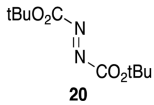
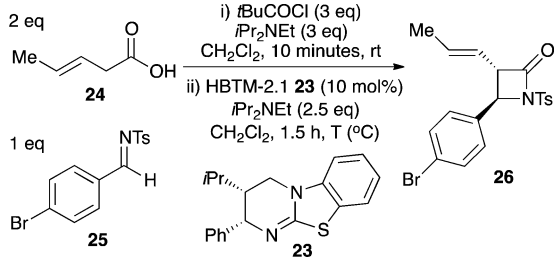
Table 1. Initial Studies



entry	carboxylic acid	electrophile	product (major)	dr[a] (*anti*:*syn*)	Yield[b] (% *anti*, *syn*)
1	 14	 18	None	N/A	N/A
2	 15	 18	None	N/A	N/A
3	 16	 18	 21	60:40	43, 29
4	 16	 19	 22	83:17	68,-
5	 16	 20	None	N/A	N/A

[a]Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [b]Isolated yield (≥95:5 dr).

Table 2. Formal [2 + 2] Cycloaddition Using *N*-Tosyl Aldimine 25

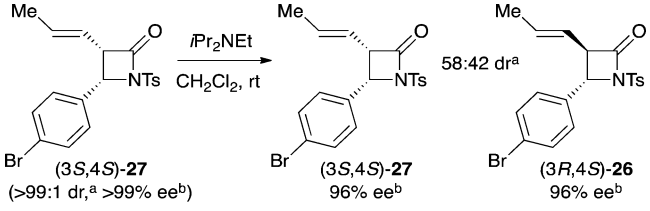


entry	*T* (°C)	dr[a] (*anti*:*syn*)	yield[b] (% *anti*, *syn*)	ee[c] (% *anti*, *syn*)
1	23	68:32	53, 27	79, 72
2	−78	71:29	53, 11	97, >99

[a]Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [b]Isolated yield (≥95:5 dr). [c]Determined by chiral HPLC analysis.

experiment (Scheme 4). Treatment of *syn*-*β*-lactam (3*S*,4*S*)-**27** (>99:1 dr, >99% ee) using *i*Pr$_2$NEt at rt for 16 h gave a (58:42 *syn*:*anti*) mixture comprising of *syn*-*β*-lactam (3*S*,4*S*)-**27** (96% ee) and *anti*-*β*-lactam (3*R*,4*S*)-**26** (96% ee) as determined by Chiral HPLC. The absolute configuration of the *anti*-*β*-lactam formed by epimerization is opposite to that observed experimentally in the catalytic process. Assuming epimerization

Scheme 4. Epimerization Experiment



[a]Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [b]Determined by HPLC analysis.

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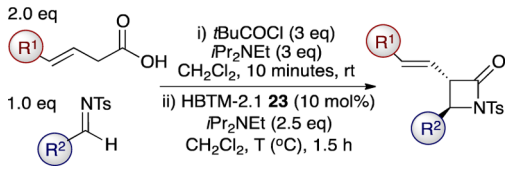
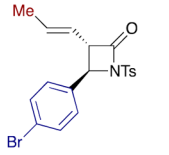
occurs solely at C(3), this allows the absolute configuration of the *anti*-β-lactam formed in Table 2 to be assigned (3*S*,4*R*).[27]

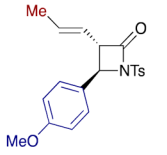
The generality of this protocol was next investigated by variation of both the acid and aldimine components (Table 3).

Table 3. Formal [2 + 2] Cycloaddition Scope

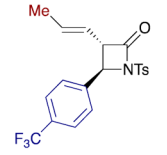




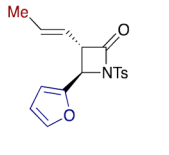
26: At -78 °C
71:29 dr[a] (*anti*:*syn*)
anti: 51% yield,[b] 97% ee[c]
syn: 11% yield,[b] >99% ee[c]



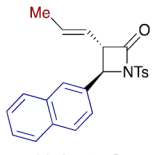
28: At rt
80:20 dr[a] (*anti*:*syn*)
anti: 74% yield,[b] 86% ee[c]



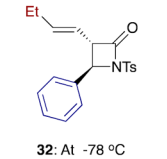
29: At rt
87:13 dr[a] (*anti*:*syn*)
anti: 46% yield,[b] 44% ee[c]



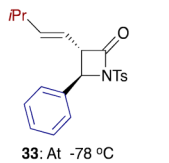
30: At -78 °C
63:37 dr[a] (*anti*:*syn*)
anti: 48% yield,[b] 95% ee[c]



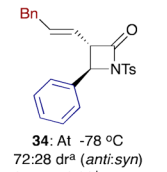
31: At -78 °C
76:24 dr[a] (*anti*:*syn*)
anti: 64% yield,[b] 97% ee[c]
syn: 22% yield,[b] 99% ee[c]



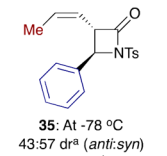
32: At -78 °C
82:18 dr[a] (*anti*:*syn*)
anti: 67% yield,[b] 98% ee[c]
syn: 16% yield,[b] >99% ee[c]



33: At -78 °C
79:21 dr[a] (*anti*:*syn*)
anti: 63% yield,[b] 97% ee[c]



34: At -78 °C
72:28 dr[a] (*anti*:*syn*)
anti: 57% yield,[b] 95% ee[c]
syn: 16% yield,[b] 97% ee[c]



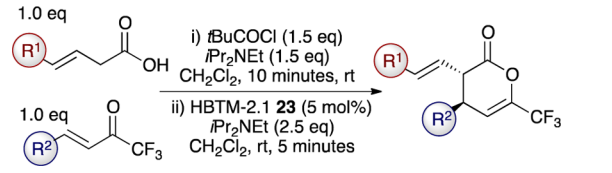
35: At -78 °C
43:57 dr[a] (*anti*:*syn*)
anti: 21% yield,[d] 99% ee[c]
syn: 36% yield,[e] >99% ee[c]

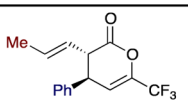
[a]Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [b]Isolated yield (≥95:5 dr). [c]Determined by chiral HPLC analysis. [d]Isolated yield (92:8 dr). [e]Isolated yield (88:12 dr).

Within the aldimine, electron-donating and -withdrawing groups can be incorporated provided the reactions are carried out at rt.[28] 4-OMe substituted β-lactam **28** is formed in good diastereo- and enantioselectivity, while incorporation of the 4-CF_3 group results in a significant reduction in enantioselectivity (44% ee). Heteroaryl substituents (2-furyl) and extended aromatics (2-naphthyl) are tolerated within the aldimine, giving β-lactams **30** and **31** in modest diastereoselectivity with the major (*anti*) diastereoisomer formed in excellent ee (95 and 97%, respectively). In cases where the minor (*syn*) diastereoisomer can be isolated, it is always formed in excellent enantioselectivity (>96% ee). Both the 4-position substituent and the configuration within the acid component can also be varied; for example, (*E*)-4-ethyl, (*E*)-4-isopropyl, and (*E*)-4-benzyl alkenoic acids give the corresponding β-lactams **32**−**34** in high yields and good diastereo- and enantioselectivities. Finally, (*Z*)-pent-3-enoic acid was used as a starting material, giving the usual α-functionalization under the reaction conditions, but generating β-lactam **35** with negligible diastereoselectivity at −78 °C (43:57 dr, *anti*:*syn*), despite both diastereoisomers being formed in exquisite enantioselectivity (>99% ee).[29]

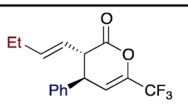
[4 + 2] Cycloadditions of Isothiourea Derived Ammonium Dienolates with 4π Electrophiles. Having established the propensity of these ammonium dienolates to react at the α-position with 2π electrophiles, their ability to partake in formal [4 + 2] cycloadditions with electron-deficient 4π Michael acceptors was investigated. HBTM-2.1 **23** efficiently catalyzes the reaction between (*E*)-pent-3-enoic and (*E*)-1,1,1-trifluoro-4-phenyl-3-buten-2-one in only 5 min at rt, giving δ-lactone **36** in 80% yield with good diastereoselectivity (88:12 dr) and excellent enantioselectivity (96% ee).[30−32] The reaction proceeds efficiently using (*E*)-3-hexenoic acid, giving δ-lactone **37**, although when using (*E*)-styrylacetic acid the reaction has to be carried out at −78 °C to prevent product decomposition and gives the major diastereoisomer of δ-lactone **38** in reduced enantioselectivity (60% ee). Heteroaryl and 4-bromophenyl substituted trifluoromethyl enones are also tolerated giving δ-lactones **39** and **40** in good yields and high diastereo- and enantioselectivity (Table 4).

Table 4. Formal [4 + 2] Cycloadditions with 4-Aryltrifluoromethyl Enones

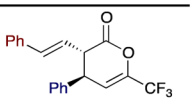




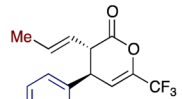
36, dr 88:12[a]
80%,[b] 96% ee[c]



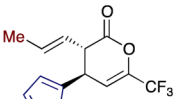
37, dr 90:10[a]
83%,[d] 96% ee[c]



38, At -78 °C, dr 95:5[a]
82%,[e] 60% ee[c]



39, dr 80:20[a]
73%,[e] 92% ee[c]



40, dr 84:16[a]
83%,[f] 93% ee[c]

[a]Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [b]Isolated yield (88:12 dr). [c]Determined by HPLC analysis. [d]Isolated yield (93:7 dr). [e]Isolated yield (≥95:5 dr). [f]Isolated yield (84:16 dr).

The generality of this asymmetric Michael addition-lactonization process was next investigated using *N*-aryl-*N*-aroyldiazenes as Michael acceptors, followed by in situ ring-opening of the intermediate 1,3,4-oxadiazin-6-one formal [4 + 2] cycloaddition adduct with MeOH. Examples including the use of 3-alkenoic acids bearing 4-alkyl (Me, Et, *i*Pr), 4-benzyl and 4-phenyl substituents, in addition to (*E*)- and (*Z*)-alkene configurations are all readily incorporated giving, after in situ ring-opening with methanol,[33] a range of hydrazides **41**−**46** in high yields (71−85%) and excellent enantioselectivity (91−99% ee) (Table 5).[34,35] Diazenes bearing electron deficient (4-FC_6H_4) and heteroaryl (2-furyl) *N*-aroyl substituents are also tolerated, giving products **47** and **48** in excellent ee.

Having developed a highly enantioselective route to hydrazides **41**−**48**, their potential for further elaboration through functionalization of the olefin was probed. Treatment

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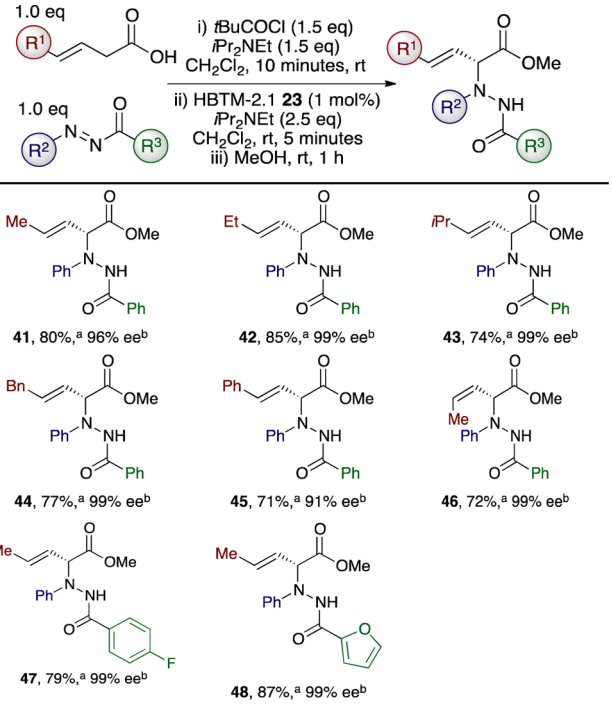
Table 5. Formal [4 + 2] Cycloaddition/Ring-Opening with *N*-Aryl-*N*-aroyldiazenes



[a]Isolated yield. [b]Determined by HPLC analysis.

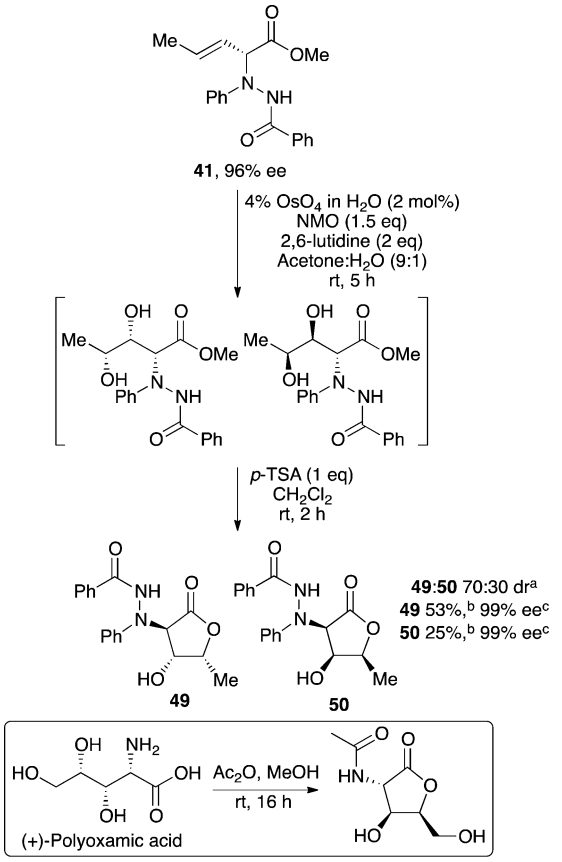
of hydrazide **41** under Upjohn dihydroxylation conditions, followed by acid-catalyzed cyclization, gave a 70:30 mixture of separable diastereomeric 5-membered lactones **49** and **50** in 85% combined yield, both in 99% ee (Scheme 5).[36] These interesting aza-sugar derivatives structurally resemble the cyclized form of (+)-polyoxamic acid, indicating their potential biological significance.

We propose that the catalytic cycle for these transformations proceeds via initial *N*-acylation of HBTM-2.1 **23** with the preformed mixed anhydride to form the corresponding acyl ammonium ion. α-Deprotonation generates the (*Z*,*E*)-enolate (from the (*E*)-alkenoic acid), which undergoes stereoselective Michael addition via α-functionalization with electron-deficient 4π Michael acceptors, followed by intramolecular cyclization, to generate the corresponding heterocyclic species (Figure 1). The sense of stereoinduction in these transformations is consistent with our previous rationale.[16a,c] We tentatively assign the origin of the observed α-functionalization in these processes to preferential reaction via the assumed *s-trans* (*Z*,*E*)-dienolate conformation **51**, in preference to the *s-cis* (*Z*,*E*)-dienolate conformation **52** that is presumably necessary to participate in γ-functionalization.

CONCLUSION

Isothiourea-mediated functionalization of 3-alkenoic acids occurs regioselectively, giving products derived from α-functionalization of an intermediate ammonium enolate in a range of formal [2 + 2] and [4 + 2] cycloadditions. Formal [2 + 2] cycloadditions with *N*-tosyl aldimines proceed readily using HBTM-2.1 (10 mol %) with moderate diastereocontrol (up to 87:13 dr) and excellent enantiocontrol (up to >99% ee). Formal [4 + 2] cycloadditions with either 4-aryl-trifluoromethylenones or *N*-aryl-*N*-aroyldiazenes are also catalyzed by HBTM-2.1 (1−5 mol %), with products obtained in high

Scheme 5. Conversion of Hydrazide 41 to Lactones 49 and 50



[a]Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [b]Isolated yield (>98:2 dr). [c]Determined by HPLC analysis.

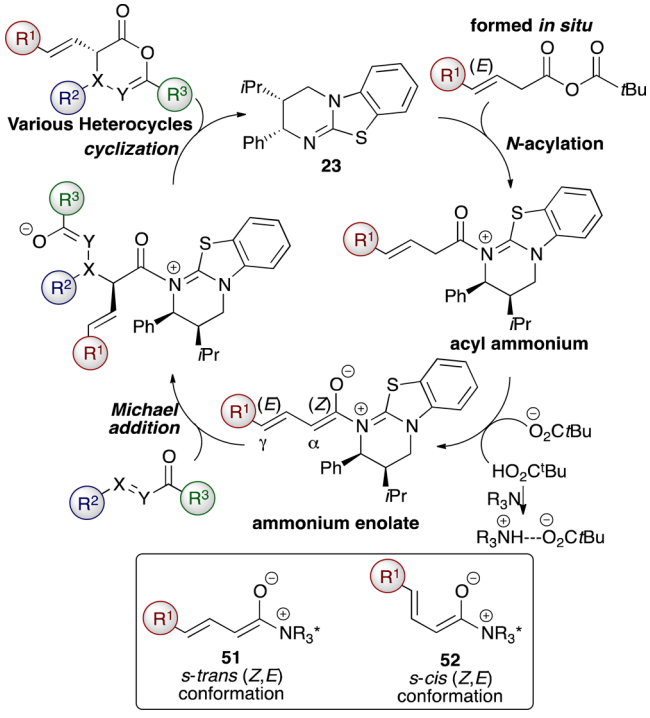


Figure 1. Proposed mechanism of asymmetric heterocycle formation.

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diastereo- and enantiocontrol (up to 95:5 dr, up to 99% ee). The simple, two-step elaboration of stereodefined hydrazides into aza-sugar analogues without erosion of enantiopurity has also been demonstrated. Current research from this laboratory is directed toward developing alternative applications of isothioureas in asymmetric catalysis.

EXPERIMENTAL SECTION

General Information. Reactions involving moisture-sensitive reagents were carried out under an argon atmosphere using standard vacuum line techniques in addition to dry solvents. In these cases, all glassware used was flame-dried and cooled under a vacuum.

For moisture-sensitive reactions, solvents (THF, CH_2Cl_2, toluene, hexane, and Et_2O) were obtained anhydrous and purified by an alumina column. Petrol is defined as petroleum ether 40−60 °C. All other solvents and commercial reagents were used as supplied without further purification unless stated otherwise. 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. Racemic compounds were prepared using general procedure A, employing either DHPB **17** or (±)-HBTM-2.1 **23** as catalyst.

Isothiourea Catalysts Used. DHPB **17**, HBTM-2.1 (±)-**23** and HBTM-2.1 (2*S*,3*R*)-**23** were made to literature procedures.[16d]

***N*-Tosyl Aldimines Used.** 4-Methyl-*N*-[(1*E*)-phenylmethylidene]-benzene-1-sulfonamide **19**, 4-methyl-*N*-[(1*E*)-4-(bromophenyl)-methylidene]benzene-1-sulfonamide **25**, 4-methyl-*N*-[(1*E*)-4-(methoxyphenyl)methylidene]benzene-1-sulfonamide **53**, 4-methyl-*N*-[(1*E*)-4-(trifluoromethylphenyl)methylidene]benzene-1-sulfonamide **54**, *N*-[(1*E*)-furan-2-ylmethylidene]-4-methylbenzene-1-sulfonamide **55**, and 4-methyl-*N*-[(1*E*)-naphthalen-2-ylmethylidene]benzene-1-sulfonamide **56** were made according to literature procedures.[37]

Trifluoromethyl Enones Used. (*E*)-1,1,1-Trifluoro-4-phenyl-3-buten-2-one **57**, (*E*)-1,1,1-trifluoro-4-(4-bromophenyl)-3-buten-2-one **58**, and (*E*)-1,1,1-trifluoro-4-(2-thienyl)-3-buten-2-one **59** were made according to literature procedures.[16d]

***N*-Aryl-*N*-aroyldiazenes Used.** (NE)-*N*-(Phenylimino)-benzamide **60**, (NE)-4-fluoro-*N*-(phenylimino)benzamide **61**, and (NE)-*N*-(phenylimino)furan-2-carboxamide **62** were made according to literature procedures.[16c]

Carboxylic Acids Used. (*E*)-4-Phenylbut-3-enoic acid **16**, (*E*)-pent-3-enoic acid **24**, and (*E*)-hex-3-enoic acid **81** were used as purchased.

3-Methylbut-3-enoic acid 14. Following a literature procedure,[38] to a solution of 3-methylbut-3-en-1-ol (2.00 mL, 19.8 mmol) in acetone (100 mL) at 0 °C was added 2.68 M Jones' reagent (10.4 mL, 27.7 mmol), and the reaction mixture was stirred at 0 °C for 1 h. The reaction mixture was washed with 2 M NaOH, and then the aqueous layer was acidified with conc HCl and extracted with Et_2O (×3). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. The residual oil was purified by distillation to give acid 3-methylbut-3-enoic acid **14** as a colorless oil (1.50 g, 76%): bp 88−90 °C (20 mmHg); {lit.[38] bp 67−70 °C (10 mmHg)}; δ_H (500 MHz, $CDCl_3$) 1.87 (3H, s, CH_3), 3.11 (2H, s, CH_2), 4.92 (1H, s, =C*H*H), 4.99 (1H, s, =CH*H*). Data are in accordance with the literature.[38]

Ethyl 2-cyclopentylideneacetate 63. Following a literature procedure,[39] to a suspension of 60% NaH in mineral oil (1.23 g, 51.4 mmol) in Et_2O (120 mL) at 0 °C was added ethyl 2-(diethoxyphosphoryl)acetate (10.2 mL, 51.4 mmol), and the reaction mixture was stirred for 5 min at 0 °C. A solution of cyclopentanone (4.42 mL, 50.0 mmol) in Et_2O (10 mL) was added, and the reaction mixture was allowed to stir at rt for 4 h. The reaction mixture was diluted with water and extracted with Et_2O (×3). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. Chromatographic purification (eluent Et_2O:petrol 10:90) gave ethyl 2-cyclopentylideneacetate **63** as a colorless oil (7.00 g, 91%): δ_H (500 MHz, $CDCl_3$) 1.30 (3H, t, *J* 7.1, CH_3), 1.68 (2H, quintet, *J* 6.8, CH_2), 1.77 (2H, quintet, *J* 7.0, CH_2), 2.44−2.47 (2H, m, CH_2C=), 2.78−2.81 (2H, m, CH_2C=), 4.17 (2H, q, *J* 7.1, CH_2CH_3), 5.82 (1H, quintet, *J* 2.2, =C*H*). Data are in accordance with the literature.[39]

Ethyl 2-(cyclopent-1-en-1-yl)acetate 64. Following a literature procedure,[40] to a solution of DIPA (5.82 mL, 41.2 mmol) in THF (80 mL) at 0 °C was added 2.5 M *n*-BuLi (16.5 mL, 41.2 mmol), and the reaction mixture was stirred at that temperature for 30 min. The reaction mixture was cooled to −78 °C, and a solution of ethyl 2-(cyclopent-1-en-1-yl)acetate **63** (5.88 g, 38.2 mmol) in THF (25 mL) was added dropwise over 15 min before stirring for a further 20 min. The reaction mixture was quenched by addition of sat. aq. NH_4Cl, and the reaction mixture was warmed to rt before being poured into water and extracted with Et_2O (×3). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo to give ethyl 2-(cyclopent-1-en-1-yl)acetate **64** as a light yellow oil (5.68 g, 97%): δ_H (500 MHz, $CDCl_3$) 1.29 (3H, t, *J* 7.1, CH_3), 1.93 (2H, quintet, *J* 7.5, CH_2), 2.33−2.38 (4H, m, CH_2 and CH_2), 3.14 (2H, s, CH_2CO_2Et), 4.17 (2H, q, *J* 7.1, CH_2CH_3), 5.55−5.57 (1H, m, =C*H*). Data are in accordance with the literature.[40]

2-(Cyclopent-1-en-1-yl)acetic acid 15. Following a literature procedure,[41] a solution of ethyl 2-(cyclopent-1-en-1-yl)acetate **64** (4.15 g, 27.0 mmol) in 0.5 M KOH (80.8 mL, 40.4 mmol) was heated at reflux for 16 h. Once cooled to rt the reaction mixture was extracted with Et_2O (×3). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. Recrystallization from petrol gave 2-(cyclopent-1-en-1-yl)acetic acid **15** as a white solid (2.74 g, 59%): mp 44−46 °C; {lit.[41] mp 48−51 °C}; δ_H (300 MHz, $CDCl_3$) 1.90−2.00 (2H, m, CH_2), 2.37−2.42 (4H, m, CH_2 and CH_2), 3.21 (2H, s, CH_2CO_2H), 5.63 (1H, m, =C*H*). Data are in accordance with the literature.[41]

***(E)*-5-Methylhex-3-enoic acid 65.** Following a literature procedure,[42] a solution of piperidine (39.5 μL, 0.40 mmol) and acetic acid (22.9 μL, 0.40 mmol) in DMSO (1 mL) was stirred at rt for 5 min, after which time a solution of malonic acid (4.16 g, 40.0 mmol) and isovaleraldehyde (4.29 mL, 40.0 mmol) in DMSO (20 mL) was added. The reaction mixture was stirred at rt for 20 min and then at 100 °C for 16 h. Once cooled to rt, the reaction mixture was diluted with H_2O and extracted with Et_2O (×3). The combined organic fractions were washed with H_2O, dried ($MgSO_4$), filtered, and concentrated in vacuo. Chromatographic purification (eluent Et_2O:petrol 30:70) gave (*E*)-5-methylhex-3-enoic acid **65** as a colorless oil (2.93 g, 57%): δ_H (400 MHz, $CDCl_3$) 0.99 (6H, d, *J* 6.8, $CH(CH_3)_2$), 2.26−2.34 (1H, m, C(5)*H*), 3.07 (2H, dt, *J* 6.6, 0.9, $C(2)H_2$), 5.47 (1H, dtd, *J* 15.4, 6.7, 1.1, C(3)*H*), 5.54−5.60 (1H, m, C(4)*H*). Data are in accordance with the literature.[42]

***(E)*-5-Phenylpent-3-enoic acid 66.** Following a literature procedure,[42] a solution of piperidine (39.5 μL, 0.40 mmol) and acetic acid (22.9 μL, 0.40 mmol) in DMSO (1 mL) was stirred at rt for 5 min, after which time a solution of malonic acid (4.16 g, 40.0 mmol) and 3-phenylpropionaldehyde (5.28 mL, 40.0 mmol) in DMSO (20 mL) was added. The reaction mixture was stirred at rt for 20 min and then at 100 °C for 16 h. Once cooled to rt, the reaction mixture was diluted with H_2O and extracted with Et_2O (×3). The combined

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organic fractions were washed with H_2O, dried ($MgSO_4$), filtered, and concentrated in vacuo. Chromatographic purification (eluent Et_2O:petrol 25:75) gave (*E*)-5-phenylpent-3-enoic acid **66** as a colorless oil (4.15 g, 59%): δ_H (400 MHz, $CDCl_3$) 3.13 (2H, dq, *J* 6.8, 1.1, C(5)H_2), 3.40 (2H, d, *J* 6.7, C(2)H_2), 5.63 (1H, dtt, *J* 15.3, 6.9, 1.4, C(3)*H*), 5.77 (1H, dtt, *J* 15.3, 6.7, 1.3, C(4)*H*), 7.18−7.23 (3H, m, Ar(2,6)*H* and Ar(4)*H*), 7.28−7.32 (2H, m, Ar(3,5)*H*). Data are in accordance with the literature.[43]

(*Z*)-Pent-3-en-1-ol 67. Following a literature procedure,[44] Lindlar's catalyst (5% on $CaCO_3$, Pb poisoned, 900 mg (45 mg Pd), 0.43 mmol) was degassed in a RB flask. Quinoline (0.72 mL, 6.04 mmol), Et_2O (150 mL) and pent-3-yn-1-ol (2.74 mL, 29.7 mmol) were added, and a balloon of H_2 gas was appended to the reaction flask. H_2 gas was bubbled through the reaction mixture at rt for 20 h. The reaction mixture was filtered through Celite and concentrated in vacuo, and the residual oil was purified by distillation to give alcohol (*Z*)-pent-3-en-1-ol **67** (94:6 (*Z*):(*E*)) as a colorless oil (1.64 g, 64%): bp 140−141 °C (760 mmHg); {lit.[44] bp 140 °C (760 mmHg)}; Data for (*Z*)-isomer δ_H (500 MHz, $CDCl_3$) 1.65−1.68 (3H, m, CH_3), 2.32−2.37 (2H, m, C(2)H_2), 3.66 (2H, q, *J* 6.2, C(1)H_2), 5.37−5.43 (1H, m, C(4)*H*), 5.62−5.68 (1H, m, C(3)*H*); Selected data for (*E*)-isomer δ_H (500 MHz, $CDCl_3$) 1.68−1.70 (3H, m, CH_3), 2.23−2.28 (2H, m, C(2)H_2). Data are in accordance with the literature.[44]

(*Z*)-Pent-3-enoic acid 68. Following a literature procedure,[44] to $K_2Cr_2O_7$ (56.1 mg, 0.19 mmol), HNO_3 (343 mg, 3.81 mmol) and $NaIO_4$ (8.97 g, 42.0 mmol) in H_2O (25 mL) was added a solution of (*Z*)-pent-3-en-1-ol **67** (1.64 g, 19.1 mmol) in MeCN (50 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 8 h followed by rt for 16 h. The inorganic salts were filtered and washed with Et_2O. H_2O was added, and the reaction mixture was extracted with Et_2O (×3). The combined organic fractions were dried ($MgSO_4$), filtered, and concentrated in vacuo. The residual oil was purified by distillation to give (*Z*)-pent-3-enoic acid **68** (94:6 (*Z*):(*E*)) as a colorless oil (0.69 g, 36%): bp 100−102 °C (22 mmHg); {lit.[44] bp 100 °C (20 mmHg)}; Data for (*Z*)-isomer δ_H (500 MHz, $CDCl_3$) 1.64 (3H, dt, *J* 6.8, 0.8, CH_3), 3.14 (2H, dd, *J* 7.2, 0.4, C(2)H_2), 3.66 (2H, q, *J* 6.2, C(1)H_2), 5.56 (1H, dtq, *J* 10.7, 7.1, 1.8, C(3)*H*), 5.66−5.73 (1H, m, C(4)*H*); Selected data for (*E*)-isomer δ_H (500 MHz, $CDCl_3$) 1.70 (3H, dt, *J* 6.3, 1.3, CH_3), 3.06 (2H, dt, *J* 6.7, 1.2, C(2)H_2). Data are in accordance with the literature.[44]

(*E*)-Ethyl 3-phenylbut-2-enoate 69. Following a literature procedure,[45] to a suspension of 60% NaH in mineral oil (1.00 g, 41.6 mmol) in THF (35 mL) at 0 °C was added ethyl 2-(diethoxyphosphoryl)acetate (8.26 mL, 41.6 mmol) dropwise over 30 min, and the reaction mixture was stirred for 30 min at rt. A solution of acetophenone (4.85 mL, 41.6 mmol) in THF (15 mL) was added dropwise, and the reaction mixture was allowed to stir at rt for 4 h. The reaction mixture was diluted with water and extracted with Et_2O (×3). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. Chromatographic purification (eluent Et_2O:petrol 5:95) gave (*E*)-ethyl 3-phenylbut-2-enoate **69** as a colorless oil (2.35 g, 30%): δ_H (500 MHz, $CDCl_3$) 1.35 (3H, t, *J* 7.1, CH_2CH_3), 2.61 (3H, d, *J* 1.3, CH_3), 4.25 (2H, q, *J* 7.1, CH_2CH_3), 6.16 (1H, q, *J* 1.2, =C*H*), 7.38−7.42 (3H, m, Ar*H*), 7.50−7.52 (2H, m, Ar*H*). Data are in accordance with the literature.[45]

(*E*)-3-Phenylbut-2-enoic acid 70. Following a literature procedure,[41] a solution of (*E*)-ethyl 3-phenylbut-2-enoate **69** (2.35 g, 12.4 mmol) in 0.5 M KOH (37.1 mL, 18.6 mmol) was heated at reflux for 16 h. Once cooled to rt the reaction mixture was extracted with Et_2O (×3). The reaction mixture was treated with 1 M H_2SO_4 until acidic and extracted with Et_2O (×3). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. Recrystallization from Et_2O gave (*E*)-3-phenylbut-2-enoic acid **70** as a white solid (1.39 g, 70%): mp 94−96 °C; {lit.[46] mp 95−97 °C}; δ_H (500 MHz, $CDCl_3$) 2.64 (3H, d, *J* 1.2, CH_3), 6.21 (1H, q, *J* 1.2, =C*H*), 7.41−7.44 (3H, m, Ar*H*), 7.51−7.54 (2H, m, Ar*H*). Data are in accordance with the literature.[47]

(*E*)-Ethyl 3,4-diphenylbut-2-enoate 71. Following a literature procedure,[45] to a suspension of 60% NaH in mineral oil (2.04 g, 51.0 mmol) in THF (50 mL) at 0 °C was added ethyl 2-(diethoxyphosphoryl)acetate (10.1 mL, 51.0 mmol) dropwise over 30 min, and the reaction mixture was stirred for 30 min at rt. A solution of 1,2-diphenylethanone (10 g, 51.0 mmol) in THF (20 mL) was added dropwise, and the reaction mixture was allowed to stir at rt for 4 h. The reaction mixture was diluted with water and extracted with Et_2O (×3). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. Chromatographic purification (eluent Et_2O:petrol 5:95) gave (*E*)-ethyl 3,4-diphenylbut-2-enoate **71** as a colorless oil (2.35 g, 17%): δ_H (300 MHz, $CDCl_3$) 1.35 (3H, t, *J* 7.1, CH_2CH_3), 4.27 (2H, q, *J* 7.1, CH_2CH_3), 4.55 (2H, s, CH_2Ph), 6.29 (1H, d, =C*H*), 7.14−7.27 (5H, m, Ar*H*), 7.33−7.36 (3H, m, Ar*H*), 7.42−7.48 (2H, m, Ar*H*). Data are in accordance with the literature.[48]

(*E*)-3,4-Diphenylbut-2-enoic acid 72. Following a literature procedure,[41] a solution of (*E*)-ethyl 3,4-diphenylbut-2-enoate **71** (2.35 g, 8.84 mmol) in 0.5 M KOH (26.8 mL, 13.3 mmol) was heated at reflux for 16 h. Once cooled to rt the reaction mixture was extracted with Et_2O (×3). The reaction mixture was treated with 1 M H_2SO_4 until acidic and extracted with Et_2O (×3). The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. Chromatographic purification (eluent Et_2O:petrol 25:75) gave (*E*)-3,4-diphenylbut-2-enoic acid **72** as a white solid (210 mg, 10%): mp 122−124 °C; {lit.[49] mp 138−139 °C}; δ_H (300 MHz, $CDCl_3$) 4.59 (2H, s, CH_2Ph), 6.34 (1H, s, =C*H*), 7.18−7.29 (5H, m, Ar*H*), 7.34−7.39 (3H, m, Ar*H*), 7.46−7.49 (2H, m, Ar*H*). Data are in accordance with the literature.[49]

General Procedure A: Isothiourea-Catalyzed Intermolecular Reactions. To a solution of acid (1−2 equiv) in CH_2Cl_2 (~1 mL per 0.2 mmol of acid) were added *i*Pr_2NEt (1.5 equiv based upon acid) and activating agent (1.5 equiv based upon acid) at rt. The reaction mixture was allowed to stir at rt for 10 min. The requisite isothiourea (1−10 mol %), Michael acceptor/ketone/imine (1 equiv), and *i*Pr_2NEt (2.5 equiv) were then added at the required temperature. The reaction mixture was stirred at the required temperature until complete by TLC. The reaction mixture was subsequently quenched by addition of HCl (1 M in H_2O). The reaction mixture was poured into H_2O and extracted with CH_2Cl_2 (×3). The combined organics were dried ($MgSO_4$), filtered, and concentrated in vacuo to give the crude reaction mixture.

(3*S*,4*S*)-4-Phenyl-3-[(*E*)-2-phenylethynyl]-4-(trifluoromethyl)-oxetan-2-one 21 and (3*S*,4*R*)-4-Phenyl-3-[(*E*)-2-phenylethynyl]-4-(trifluoromethyl)oxetan-2-one 73. Following general procedure A, (*E*)-4-phenylbut-3-enoic acid **16** (259 mg, 1.60 mmol), *i*Pr_2NEt (0.42 mL, 2.40 mmol) and pivaloyl chloride (296 μL, 2.40 mmol) in CH_2Cl_2 (10 mL), DHPB **17** (15.2 mg, 0.08 mmol, 10 mol %), 2,2,2-trifluoro-1-phenylethan-1-one **18** (109 μL, 0.80 mmol) and *i*Pr_2NEt (0.35 mL, 2.00 mmol) for 1.5 h at rt gave crude lactones **21** and **73** (60:40 dr). Chromatographic purification (eluent Et_2O:petrol 2.5:97.5) gave lactone **21** (>98:2 dr) as a white solid (110 mg, 43%) and lactone **73** (>98:2 dr) as a white solid (73.4 mg, 29%).

Following general procedure A, (*E*)-4-phenylbut-3-enoic acid **16** (259 mg, 1.60 mmol), *i*Pr_2NEt (0.42 mL, 2.40 mmol) and pivaloyl chloride (296 μL, 2.40 mmol) in CH_2Cl_2 (10 mL), HBTM-2.1 (2*S*,3*R*)-**23** (24.6 mg, 0.08 mmol, 10 mol %), 2,2,2-trifluoro-1-phenylethan-1-one **18** (109 μL, 0.80 mmol) and *i*Pr_2NEt (0.35 mL, 2.00 mmol) for 1.5 h at −78 °C gave crude lactones (3*S*,4*S*)-**21** and (3*R*,4*R*)-**73** (65:35 dr). Chromatographic purification (eluent Et_2O:petrol 2.5:97.5) gave lactone (3*S*,4*S*)-**21** (>98:2 dr) as a white solid (98.3 mg, 39%) and lactone (3*R*,4*R*)-**73** (>98:2 dr) as a white solid (52.6 mg, 21%):

Data for lactone (3*S*,4*S*)-**21**: mp 66−67 °C; $[\alpha]_D^{20}$ −14.8 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralcel OD-H (0.5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*R*,4*R*) 9.6 min, t_R(3*S*,4*S*) 12.6 min, 79% ee; ν_{max} (ATR)/cm^{-1} 3080, 3030 (C−H), 1847 (C=O), 1698; δ_H (400 MHz, $CDCl_3$) 4.95−4.98 (1H, m, C(3)*H*), 5.64 (1H, dd, *J* 15.7, 9.4, PhCH=C*H*), 6.71 (1H, d, *J* 15.7, PhC*H*=CH), 7.20−7.23 (2H, m, Ar*H*), 7.27−7.31 (3H, m, Ar*H*), 7.46−7.49 (5H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 60.9 (C(3)), 79.5 (q, *J* 32.8, C(4)), 116.1 (PhCH=CH), 123.6 (q, *J* 280, CF_3), 126.9 (*ArC*), 127.3 (*ArC*), 128.8 (*ArC*), 128.8 (*ArC*), 128.9 (4ry *ArC*), 129.0 (*ArC*), 130.1 (*ArC*), 135.3

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(C(4)*ArC*(1), 138.4 (PhCH=CH), 165.9 (*C*(2)=O); δ_F (376 MHz, $CDCl_3$) −78.7 (*C*F_3); *m*/*z* (APCI$^+$) 319 ([M + H]$^+$, 100%); HRMS (APCI$^+$) $C_{18}H_{14}F_3O_2^+$ ([M + H]$^+$) requires 319.0940, found 319.0940 (−0.1 ppm).

Data for lactone (3*S*,4*R*)-**73**: mp 110−112 °C; $[\alpha]_D^{20}$ −93.0 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralcel OD-H (2% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*R*,4*S*) 13.1 min, t_R(3*S*,4*R*) 14.9 min, 77% ee; ν_{max} (ATR)/cm^{-1} 3080, 2944 (C−H), 1834 (C=O), 1692; δ_H (400 MHz, $CDCl_3$) 4.77 (1H, d, *J* 8.7, C(3)*H*), 6.38−6.47 (1H, m, PhCH=C*H*), 6.83−6.88 (1H, m, PhC*H*=CH), 7.34−7.50 (9H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 64.9 (*C*(3)), 79.6 (q, *J* 30.1, *C*(4)), 115.1 (PhCH=*C*H), 123.3 (q, *J* 281, *C*F_3), 126.3 (*ArC*), 127.1 (*ArC*), 128.9 (*ArC*), 128.9 (*ArC*), 129.1 (*ArC*), 130.2 (*ArC*), 132.9 (4ry *ArC*), 135.4 (C(4)*ArC*(1)), 139.0 (PhCH=CH), 165.9 (*C*(2)=O); δ_F (376 MHz, $CDCl_3$) −74.2 (*C*F_3); *m*/*z* (APCI$^+$) 319 ([M + H]$^+$, 100%); HRMS (APCI$^+$) $C_{18}H_{14}F_3O_2^+$ ([M + H]$^+$) requires 319.0940, found 319.0941 (+0.2 ppm).

(3*S*,4*R*)-1-[(4-Methylbenzene)sulfonyl]-4-phenyl-3-[(*E*)-2-phenylethenyl]azetidin-2-one 22. Following general procedure A, (*E*)-4-phenylbut-3-enoic acid **16** (259 mg, 1.60 mmol), *i*Pr$_2$NEt (0.42 mL, 2.40 mmol) and pivaloyl chloride (296 μL, 2.40 mmol) in CH_2Cl_2 (10 mL), DHPB **17** (15.2 mg, 0.08 mmol, 10 mol %), imine **19** (207 mg, 0.80 mmol) (109 μL, 0.80 mmol) and *i*Pr$_2$NEt (0.35 mL, 2.00 mmol) for 1.5 h at rt gave crude lactam **22** (83:17 dr). Chromatographic purification (eluent Et$_2$O:petrol 20:80) gave lactam **22** (>98:2 dr) as a white solid (219 mg, 68%).

Following general procedure A, (*E*)-4-phenylbut-3-enoic acid **16** (260 mg, 1.60 mmol), *i*Pr$_2$NEt (420 μL, 2.40 mmol) and pivaloyl chloride (296 μL, 2.40 mmol) in CH_2Cl_2 (10 mL), HBTM-2.1 (2*S*,3*R*)-**23** (24.6 mg, 0.08 mmol, 10 mol %), imine **19** (207 mg, 0.80 mmol) and *i*Pr$_2$NEt (348 μL, 2.00 mmol) for 1.5 h at rt gave crude lactam (3*S*,4*R*)-**22** (85:15 dr). Chromatographic purification (eluent Et$_2$O:petrol 20:80) gave lactam (3*S*,4*R*)-**22** (>98:2 dr) as a white solid (125 mg, 39%): mp 137−139 °C; $[\alpha]_D^{20}$ +9.8 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*) 24.4 min, t_R(3*R*,4*S*) 40.9 min, 72% ee; ν_{max} (ATR)/cm^{-1} 3024, 2924 (C−H), 1790 (C=O), 1450, 1359 (S=O), 1165 (S=O); Data for major diastereoisomer δ_H (300 MHz, $CDCl_3$) 2.44 (3H, s, *C*H$_3$), 3.91 (1H, ddd, *J* 8.0, 3.3, 1.1 Hz, C(3)*H*), 4.90 (1H, d, *J* 3.3 Hz, C(4)*H*), 6.16 (1H, dd, *J* 15.9, 8.0 Hz, PhCH=C*H*), 6.53 (1H, dd, *J* 15.9, 1.1 Hz, PhC*H*=CH), 7.24−7.36 (12H, m, Ar*H*), 7.65−7.69 (2H, m, SO$_2$Ar(2,6)*H*); δ_C (100 MHz, $CDCl_3$) 21.8 (*C*H$_3$), 62.9 (C(3)), 64.3 (*C*(4)), 119.3 (*H*C=CHPh), 126.6 (*ArC*), 126.8 (*ArC*), 127.7 (*ArC*), 128.4 (*ArC*), 128.8 (*ArC*), 129.1 (*ArC*), 129.1 (*ArC*), 130.0 (*ArC*), 135.8 (HC=*C*HPh), 135.8 (4ry *ArC*), 135.8 (4ry *ArC*), 135.8 (4ry *ArC*), 145.4 (C(4)*ArC*(1)), 165.2 (*C*(2)=O); *m*/*z* (NSI) 404 ([M + H]$^+$, 65%); HRMS (NSI) $C_{24}H_{22}NO_3S^+$ ([M + H]$^+$) requires 404.1315, found 404.1313 (−0.5 ppm).

(3*S*,4*S*)-1-[(4-Methylbenzene)sulfonyl]-4-phenyl-3-[(*E*)-2-phenylethenyl]azetidin-2-one 74. Following general procedure A, (*E*)-4-phenylbut-3-enoic acid **16** (260 mg, 1.60 mmol), *i*Pr$_2$NEt (420 μL, 2.40 mmol) and pivaloyl chloride (296 μL, 2.40 mmol) in CH_2Cl_2 (10 mL), HBTM-2.1 (2*S*,3*R*)-**23** (24.6 mg, 0.08 mmol, 10 mol %), imine **19** (207 mg, 0.80 mmol) and *i*Pr$_2$NEt (348 μL, 2.00 mmol) for 2.5 h at −78 °C gave crude lactam (3*S*,4*S*)-**74** (83:17 dr). Chromatographic purification (eluent Et$_2$O:petrol 20:80) gave lactam (3*S*,4*S*)-**74** (>98:2 dr) as a white solid (136 mg, 42%): mp 127−129 °C; $[\alpha]_D^{20}$ −6.4 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*S*) 23.0 min, t_R(3*R*,4*R*) 46.8 min, 16% ee; ν_{max} (ATR)/cm^{-1} 3024, 2924 (C−H), 1790 (C=O), 1450, 1359 (S=O), 1165 (S=O); Data for major diastereoisomer δ_H (500 MHz, $CDCl_3$) 2.48 (3H, s, *C*H$_3$), 4.40−4.42 (1H, m, C(3)*H*), 5.38 (1H, d, *J* 6.7 Hz, C(4)*H*), 5.49 (1H, dd, *J* 15.9, 7.3 Hz, PhCH=C*H*), 6.61 (1H, d, *J* 15.8 Hz, PhC*H*=CH), 7.06−7.07 (2H, m, Ar*H*), 7.16−7.24 (5H, m, Ar*H*), 7.28−7.34 (5H, m, Ar*H*), 7.80 (2H, d, *J* 8.4 Hz, SO$_2$Ar(2,6)*H*); δ_C (100 MHz, $CDCl_3$) 21.9 (*C*H$_3$), 58.1 (*C*(4)), 61.8 (C(3)), 118.4 (*H*C=CHPh), 126.5 (C(4)*ArC*(2,6)), 127.5 (*ArC*), 127.8 (*ArC*), 128.2 (*ArC*), 128.6 (*ArC*), 128.6 (*ArC*), 128.9 (*ArC*), 130.0 (*ArC*), 133.7 (4ry *ArC*), 135.8 (4ry *ArC*), 135.9 (HC=CHPh), 136.1 (4ry *ArC*), 145.5 (C(4)*ArC*(1)), 165.0 (C(2)=O); *m*/*z* (NSI) 404 ([M + H]$^+$, 70%); HRMS (NSI) $C_{24}H_{22}NO_3S^+$ ([M + H]$^+$) requires 404.1314, found 404.1313 (−0.2 ppm).

(3*S*,4*R*)-4-(4-Bromophenyl)-1-[(4-methylbenzene)sulfonyl]-3-[(1*E*)-prop-1-en-1-yl]azetidin-2-one 26 and (3*S*,4*S*)-4-(4-Bromophenyl)-1-[(4-methylbenzene)sulfonyl]-3-[(1*E*)-prop-1-en-1-yl]azetidin-2-one 27. Following general procedure A, (*E*)-pent-3-enoic acid **24** (162 μL, 1.60 mmol), *i*Pr$_2$NEt (420 μL, 2.40 mmol) and pivaloyl chloride (296 μL, 2.40 mmol) in CH_2Cl_2 (10 mL), HBTM-2.1 (2*S*,3*R*)-**23** (24.6 mg, 0.08 mmol, 10 mol %), imine **25** (270 mg, 0.80 mmol) and *i*Pr$_2$NEt (348 μL, 2.00 mmol) for 1.5 h at rt gave crude lactams (3*S*,4*R*)-**26** and (3*S*,4*S*)-**27** (68:32 dr). Chromatographic purification (eluent Et$_2$O:petrol 20:80) gave lactam (3*S*,4*R*)-**26** (>98:2 dr) as a colorless oil (177 mg, 53%) and lactam (3*S*,4*S*)-**27** (>98:2 dr) as a white solid (91 mg, 27%).

Data for lactam (3*S*,4*R*)-**26**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 220 nm, 30 °C) t_R(3*S*,4*R*) 18.6 min, t_R(3*R*,4*S*) 47.0 min, 79% ee; ν_{max} (ATR)/cm^{-1} 3032, 2965 (C−H), 1794 (C=O), 1595, 1366 (S=O), 1169 (S=O); δ_H (400 MHz, $CDCl_3$) 1.68 (3H, ddd, *J* 6.5, 1.6, 0.8 Hz, *C*H$_3$CH=CH), 2.44 (3H, s, ArC*H*$_3$), 3.64 (1H, ddt, *J* 8.0, 3.3, 0.9 Hz, C(3)*H*), 4.70 (1H, d, *J* 3.3 Hz, C(4)*H*), 5.38−5.45 (1H, m, CH$_3$CH=C*H*), 5.62−5.69 (1H, m, CH$_3$C*H*=CH), 7.07−7.11 (2H, m, Ar*H*), 7.26−7.29 (2H, m, SO$_2$Ar(3,5)*H*), 7.40−7.43 (2H, m, Ar*H*), 7.64−7.67 (2H, m, SO$_2$Ar(2,6)*H*); δ_C (125 MHz, $CDCl_3$) 18.2 (*C*H$_3$CH=CH), 21.8 (ArC*H*$_3$), 62.8 (*C*(3)), 63.4 (*C*(4)), 121.0 (CH$_3$*C*H=CH), 123.0 (C(4)*ArC*(4)), 127.6 (*ArC*), 128.2 (*ArC*), 130.0 (*ArC*), 132.1 (*ArC*), 133.1 (CH$_3$*C*H=CH)), 135.1 (4ry *ArC*), 135.5 (4ry *ArC*), 145.5 (C(4)*ArC*(1)), 165.4 (C(2)=O); *m*/*z* (APCI) 420 ([M + H]$^+$, 98%); HRMS (APCI) $C_{19}H_{18}BrNO_3S^+$ ([M + H]$^+$) requires 420.0264, found 420.0266 (+0.6 ppm).

Data for lactam (3*S*,4*S*)-**27**: mp 92−94 °C; Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*S*) 20.9 min, t_R(3*R*,4*R*) 23.0 min, 72% ee; ν_{max} (ATR)/cm^{-1} 2941, 2926, (C−H), 1786 (C=O), 1487, 1368 (S=O), 1125 (S=O); δ_H (400 MHz, $CDCl_3$) 1.51 (3H, ddd, *J* 6.6, 1.7, 1.0 Hz, *C*H$_3$CH=CH), 2.46 (3H, s, ArC*H*$_3$), 4.16 (1H, ddt, *J* 7.8, 6.7, 1.1, C(3)*H*), 4.78 (1H, ddq, *J* 15.3, 7.7, 1.7 Hz, CH$_3$CH=C*H*), 5.17 (1H, d, *J* 6.7 Hz, C(4)*H*), 5.69 (1H, dqd, *J* 15.3, 6.6, 1.3 Hz, CH$_3$*C*H=CH), 6.97−7.00 (2H, m, Ar*H*), 7.31−7.33 (2H, m, SO$_2$Ar(3,5)*H*), 7.40−7.42 (2H, m, Ar*H*), 7.75−7.77 (2H, m, SO$_2$Ar(2,6)*H*); δ_C (125 MHz, $CDCl_3$) 18.2 (*C*H$_3$CH=CH), 21.9 (ArC*H*$_3$), 58.3 (*C*(3)), 61.1 (*C*(4)), 119.4 (CH$_3$*C*H=CH), 122.7 (C(4)*ArC*(4)), 127.7 (*ArC*), 129.1 (*ArC*), 130.1 (*ArC*), 131.7 (*ArC*), 133.2 (4ry *ArC*), 133.9 (CH$_3$*C*H=CH)), 135.6 (4ry *ArC*), 145.7 (C(4)*ArC*(1)), 165.4 (*C*(2)=O); *m*/*z* (NSI) 420 ([M + H]$^+$, 100%); HRMS (NSI) $C_{19}H_{18}BrNO_3S^+$ ([M + H]$^+$) requires 420.0264, found 420.0263 (−0.1 ppm).

Reaction carried out for 1.5 h at −78 °C gave crude lactams (3*S*,4*R*)-**26**:(3*S*,4*S*)-**27** (71:29 dr). Chromatographic purification (eluent Et$_2$O:petrol 20:80) gave lactam (3*S*,4*R*)-**26** (>98:2 dr) as a colorless oil (179 mg, 53%) with identical spectroscopic properties as before in 97% ee; $[\alpha]_D^{20}$ 0.6 (*c* 0.5, CH_2Cl_2) and lactam (3*S*,4*S*)-**27** (>98:2 dr) as a white solid (35.6 mg, 11%) with identical spectroscopic properties as before in >99% ee; $[\alpha]_D^{20}$ −14.6 (*c* 0.5, CH_2Cl_2).

(3*S*,4*R*)-4-(4-Methoxyphenyl)-1-[(4-methylbenzene)-sulfonyl]-3-[(1*E*)-prop-1-en-1-yl]azetidin-2-one 28. Following general procedure A, (*E*)-pent-3-enoic acid **24** (162 μL, 1.60 mmol), *i*Pr$_2$NEt (420 μL, 2.40 mmol) and pivaloyl chloride (296 μL, 2.40 mmol) in CH_2Cl_2 (10 mL), HBTM-2.1 (2*S*,3*R*)-**23** (24.6 mg, 0.08 mmol, 10 mol %), imine **53** (231 mg, 0.80 mmol) and *i*Pr$_2$NEt (348 μL, 2.00 mmol) for 1.5 h at rt gave crude lactam (3*S*,4*R*)-**28** (80:20 dr). Chromatographic purification (eluent Et$_2$O:petrol 30:70) gave lactam (3*S*,4*R*)-**28** (96:4 dr) as a yellow oil (220 mg, 74%): $[\alpha]_D^{20}$ −11.2 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*) 17.6 min, t_R(3*R*,4*S*) 53.0 min, 86% ee; ν_{max} (ATR)/cm^{-1} 2966 (C−H), 1790 (C=O), 1612, 1516, 1364 (S=O), 1167 (S=O); Data for major diastereomer δ_H (500 MHz, $CDCl_3$) 1.68 (3H, ddd, *J* 6.5, 1.6,

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0.8 Hz, CH_3CH=CH), 2.42 (3H, s, ArCH_3), 3.67 (1H, ddt, *J* 8.0, 3.3, 0.9 Hz, C(3)*H*), 3.80 (3H, s, OCH_3), 4.73 (1H, d, *J* 3.3 Hz, C(4)*H*), 5.43 (1H, ddq, *J* 15.3, 8.0, 1.6 Hz, CH_3CH=C*H*), 5.63−5.70 (1H, m, CH_3C*H*=CH), 6.80−6.81 (2H, m, C(4)Ar(3,5)*H*), 7.12−7.14 (2H, m, C(4)Ar(2,6)*H*), 7.24 (2H, d, *J* 8.6 Hz, SO_2Ar(3,5)*H*), 7.60−7.61 (2H, m, SO_2Ar(2,6)*H*); δ_C (125 MHz, $CDCl_3$) 18.2 (*C*H_3CH=CH), 21.8 (ArCH_3), 55.5 (OCH_3), 62.6 (*C*(3)), 64.0 (*C*(4)), 114.3 (C(4)*ArC*(3,5)), 121.4 (CH_3CH=*C*H), 127.6 (SO_2*ArC*(2,6)), 127.8 (C(4)*ArC*(1)), 128.2 (C(4)*ArC*(2,6)), 129.8 (SO_2*ArC*(3,5)), 132.6 (CH_3CH=*C*H)), 135.9 (SO_2*ArC*(1)), 145.1 (SO_2*ArC*(4)), 160.2 (C(4)*ArC*(4)), 165.9 (*C*(2)=O); *m*/*z* (ESI) 394 ([M + Na]$^+$, 80%); HRMS (ESI) $C_{20}H_{21}NNaO_4S^+$ ([M + Na]$^+$) requires 394.1089, found 394.1075 (−2.2 ppm).

(3*S*,4*R*)-1-[(4-Methylbenzene)sulfonyl]-3-[(1*E*)-prop-1-en-1-yl]-4-[4-(trifluoromethyl)phenyl]azetidin-2-one 29. Following general procedure A, (*E*)-pent-3-enoic acid **24** (162 μL, 1.60 mmol), *i*Pr$_2$NEt (420 μL, 2.40 mmol) and pivaloyl chloride (296 μL, 2.40 mmol) in CH_2Cl_2 (10 mL), HBTM-2.1 (2*S*,3*R*)-**23** (24.6 mg, 0.08 mmol, 10 mol %), imine **54** (262 mg, 0.80 mmol) and *i*Pr$_2$NEt (348 μL, 2.00 mmol) for 1.5 h at rt gave crude lactam (3*S*,4*R*)-**29** (87:13 dr). Chromatographic purification (eluent Et_2O:petrol 20:80) gave lactam (3*S*,4*R*)-**29** (>98:2 dr) as a colorless oil (151 mg, 46%): $[\alpha]_D^{20}$ +1.0 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*) 20.3 min, t_R(3*R*,4*S*) 48.4 min, 44% ee; ν_{max} (ATR)/cm^{-1} 2970 (C−H), 1796 (C=O), 1597, 1323 (S=O), 1165 (S=O); Data for major diastereomer δ_H (400 MHz, $CDCl_3$) 1.69 (3H, ddd, *J* 6.5, 1.6, 0.8 Hz, *C*H_3CH=CH), 2.44 (3H, s, ArCH_3), 3.67 (1H, ddt, *J* 8.0, 3.3, 0.9 Hz, C(3)*H*), 4.79 (1H, d, *J* 3.3 Hz, C(4)*H*), 5.39−5.46 (1H, m, CH_3CH=C*H*), 5.64−5.73 (1H, m, CH_3C*H*=CH), 7.25−7.28 (2H, m, SO_2Ar(3,5)*H*), 7.35 (2H, d, *J* 8.3 Hz, C(4)Ar(3,5)*H*), 7.55 (2H, d, *J* 8.1 Hz, C(4)Ar(2,6)*H*), 7.65−7.68 (2H, m, SO_2Ar(2,6)*H*); δ_C (125 MHz, $CDCl_3$) 18.2 (*C*H_3CH=CH), 21.8 (ArCH_3), 63.0 (*C*(3) or *C*(4)), 63.2 (*C*(3) or C(4)), 120.8 (CH_3CH=*C*H), 123.9 (q, *J* 271 Hz, *C*F$_3$), 125.9 (q, *J* 3.5 Hz, C(4)*ArC*(3,5)), 126.9 (C(4)*ArC*(2,6)), 127.6 (SO_2*ArC*(2,6)), 130.0 (SO_2*ArC*(3,5)), 131.2 (q, *J* 32.5 Hz, C(4)*ArC*(4)), 133.4 (CH_3CH=*C*H), 135.4 (SO_2*ArC*(1)), 140.2 (C(4)*ArC*(1)), 145.7 (SO_2*ArC*(4)), 165.2 (*C*(2)=O); δ_F (376 MHz, $CDCl_3$) −63.3 (*C*F$_3$); *m*/*z* (NSI) 410 ([M + H]$^+$, 15%); HRMS (NSI) $C_{20}H_{19}F_3NO_3S^+$ ([M + H]$^+$) requires 410.1032, found 410.1030 (−0.5 ppm).

(3*S*,3*R*)-4-(Furan-2-yl)-1-[(4-methylbenzene)sulfonyl]-3-[(1*E*)-prop-1-en-1-yl]azetidin-2-one 30. Following general procedure A, (*E*)-pent-3-enoic acid **24** (162 μL, 1.60 mmol), *i*Pr$_2$NEt (420 μL, 2.40 mmol) and pivaloyl chloride (296 μL, 2.40 mmol) in CH_2Cl_2 (10 mL), HBTM-2.1 (2*S*,3*R*)-**23** (24.6 mg, 0.08 mmol, 10 mol %), imine **55** (199 mg, 0.80 mmol) and *i*Pr$_2$NEt (348 μL, 2.00 mmol) for 1.5 h at rt gave crude lactam (3*S*,4*R*)-**30** (73:27 dr). Chromatographic purification (eluent Et_2O:petrol 20:80) gave lactam (3*S*,4*R*)-**30** (95:5 dr) as a white solid (171 mg, 65%): mp 137−139 °C; Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*) 11.6 min, t_R(3*R*,4*S*) 13.4 min, 45% ee; ν_{max} (ATR)/cm^{-1} 2976 (C−H), 1788 (C=O), 1595, 1362 (S=O), 1165 (S=O); Data for major diastereoisomer δ_H (400 MHz, $CDCl_3$) 1.71 (3H, ddd, *J* 6.5, 1.6, 0.9 Hz, *C*H_3CH=CH), 2.42 (3H, s, ArCH_3), 4.00−4.03 (1H, m, C(3)*H*), 4.86−4.87 (1H, m, C(4)*H*), 5.45−5.52 (1H, m, CH_3CH=C*H*), 5.71−5.80 (1H, m, CH_3C*H*=CH), 6.35 (1H, dd, *J* 3.3, 1.9 Hz, C(4)ArC(4)*H*), 6.50 (1H, dd, *J* 3.3, 0.7 Hz, C(4)ArC(3)*H*), 7.20 (1H, dt, *J* 1.0, 0.5 Hz, C(4)ArC(5)*H*), 7.22−7.24 (2H, m, SO_2Ar(3,5)*H*), 7.52−7.55 (2H, m, SO_2Ar(2,6)*H*); δ_C (125 MHz, $CDCl_3$) 18.2 (*C*H_3CH=CH), 21.8 (ArCH_3), 56.7 (*C*(3)), 58.7 (*C*(4)), 110.9 (C(4)*ArC*), 112.0 (C(4)*ArC*), 121.1 (CH_3CH=*C*H), 127.4 (SO_2*ArC*(2,6)), 129.8 (SO_2*ArC*(3,5)), 133.0 (CH_3CH=*C*H)), 135.7 (C(4)*ArC*(1)), 143.5 (C(4)*ArC*(5)), 145.0 (SO_2*ArC*(1)), 147.6 (SO_2*ArC*(4)), 164.9 (*C*(2)=O); *m*/*z* (APCI) 332 ([M + H]$^+$, 100%); HRMS (APCI) $C_{17}H_{18}NO_4S^+$ ([M + H]$^+$) requires 332.0951, found 332.0954 (+0.9 ppm).

Reaction carried out for 1.5 h at −78 °C gave crude lactam (3*S*,4*R*)-**30** (63:37 dr). Chromatographic purification (eluent Et_2O:petrol 20:80) gave lactam (3*S*,4*R*)-**30** (95:5 dr) as a white solid (126 mg, 48%) with identical spectroscopic properties as before in 95% ee; $[\alpha]_D^{20}$ −6.4 (*c* 0.5, CH_2Cl_2).

(3*S*,4*R*)-1-[(4-Methylbenzene)sulfonyl]-4-(naphthalen-2-yl)-3-[(1*E*)-prop-1-en-1-yl]azetidin-2-one 31 and (3*S*,4*S*)-1-[(4-Methylbenzene)sulfonyl]-4-(naphthalen-2-yl)-3-[(1*E*)-prop-1-en-1-yl]azetidin-2-one 75. Following general procedure A, (*E*)-pent-3-enoic acid **24** (162 μL, 1.60 mmol), *i*Pr$_2$NEt (420 μL, 2.40 mmol) and pivaloyl chloride (296 μL, 2.40 mmol) in CH_2Cl_2 (10 mL), HBTM-2.1 (2*S*,3*R*)-**23** (24.6 mg, 0.08 mmol, 10 mol %), imine **56** (247 mg, 0.80 mmol) and *i*Pr$_2$NEt (348 μL, 2.00 mmol) for 1.5 h at rt gave crude lactams (3*S*,4*R*)-**31** and (3*S*,4*S*)-**75** (67:33 dr). Chromatographic purification (eluent Et_2O:petrol 20:80) gave lactam (3*S*,4*R*)-**31** (>98:2 dr) as a colorless oil (188 mg, 60%) and lactam (3*S*,4*S*)-**75** (94:6 dr) as a colorless oil (96 mg, 31%).

Data for lactam (3*S*,4*R*)-**31**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*) 17.1 min, t_R(3*R*,4*S*) 37.0 min, 81% ee; ν_{max} (ATR)/cm^{-1} 2972 (C−H), 1792 (C=O), 1699, 1364 (S=O), 1167 (S=O); δ_H (500 MHz, $CDCl_3$) 1.71 (3H, ddd, *J* 6.5, 1.5, 0.7 Hz, *C*H_3CH=CH), 2.38 (3H, s, ArCH_3), 3.77 (1H, ddd, *J* 7.9, 2.4, 0.8 Hz, C(3)*H*), 4.95 (1H, d, *J* 3.3 Hz, C(4)*H*), 5.48−5.53 (1H, m, CH_3C*H*=CH), 5.68−5.72 (1H, m, CH_3CH=C*H*), 7.14−7.16 (2H, m, SO_2Ar(3,5)*H*), 7.23 (1H, dd, *J* 8.5, 1.8 Hz, C(4)Ar*H*), 7.49−7.53 (2H, m, Ar*H*), 7.60−7.63 (2H, m, SO_2Ar(2,6)*H*), 7.70−7.72 (1H, m, C(4)Ar(1)*H*), 7.74 (1H, d, *J* 8.5, C(4)Ar*H*), 7.81−7.84 (1H, m, C(4)Ar*H*); δ_C (125 MHz, $CDCl_3$) 18.2 (*C*H_3CH=CH), 21.7 (ArCH_3), 62.9 (*C*(3)), 64.4 (*C*(4)), 121.3 (CH_3CH=*C*H), 123.3 (*ArC*), 126.6 (*ArC*), 126.7 (*ArC*), 126.8 (*ArC*), 127.6 (SO_2*ArC*(2,6)), 127.8 (*ArC*), 128.1 (*ArC*), 129.0 (*ArC*), 129.8 (SO_2*ArC*(3.5)), 132.9 (CH_3CH=*C*H)), 133.0 (4ry *ArC*), 133.1 (4ry *ArC*), 133.5 (4ry *ArC*), 135.7 (4ry *ArC*), 145.4 (C(4)*ArC*(1)), 165.7 (*C*(2)=O); *m*/*z* (APCI) 392 ([M + H]$^+$, 26%); HRMS (APCI) $C_{23}H_{22}NO_3S^+$ ([M + H]$^+$) requires 392.1315, found 392.1318 (+0.8 ppm).

Data for lactam (3*S*,4*S*)-**75**: Chiral HPLC Chiralcel OD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*S*) 19.2 min, t_R(3*R*,4*R*) 25.0 min, 81% ee; ν_{max} (ATR)/cm^{-1} 2972 (C−H), 1790 (C=O), 1597, 1364 (S=O), 1169 (S=O); δ_H (400 MHz, $CDCl_3$) 1.43 (3H, ddd, *J* 6.6, 1.7, 1.0 Hz, *C*H_3CH=CH), 2.43 (3H, s, ArCH_3), 4.26 (1H, ddq, *J* 7.8, 6.8, 1.0, C(3)*H*), 4.84 (1H, ddq, *J* 15.3, 7.8, 1.7 Hz, CH_3CH=C*H*), 5.42 (1H, d, *J* 6.7 Hz, C(4)*H*), 5.66−5.75 (1H, m, CH_3C*H*=CH), 7.13 (1H, dd, *J* 8.5, 1.9 Hz, C(4)Ar*H*), 7.24−7.27 (2H, m, SO_2Ar(3,5)*H*), 7.48−7.52 (2H, m, Ar*H*), 7.55 (1H, dd, *J* 1.2, 0.5, C(4)Ar(1)*H*), 7.66−7.68 (1H, m, C(4)Ar*H*), 7.72−7.77 (3H, m, Ar*H*), 7.81−7.84 (1H, m, C(4)Ar*H*); δ_C (100 MHz, $CDCl_3$) 18.1 (*C*H_3CH=CH), 21.8 (ArCH_3), 58.6 (*C*(3)), 62.0 (*C*(4)), 119.7 (CH_3CH=*C*H), 124.8 (*ArC*), 126.6 (*ArC*), 126.6 (*ArC*), 127.1 (*ArC*), 127.8 (*ArC*), 127.8 (SO_2*ArC*(2,6)), 128.1 (*ArC*), 128.3 (*ArC*), 130.0 (SO_2*ArC*(3,5)), 131.5 (4ry *ArC*), 133.0 (4ry *ArC*), 133.4 (4ry *ArC*), 133.6 (CH_3CH=*C*H), 135.9 (4ry *ArC*), 145.4 (C(4)*ArC*(1)), 165.7 (*C*(2)=O); *m*/*z* (APCI) 392 ([M + H]$^+$, 83%); HRMS (APCI) $C_{23}H_{22}NO_3S^+$ ([M + H]$^+$) requires 392.1315, found 392.1316 (+0.3 ppm).

Reaction carried out for 1.5 h at −78 °C gave crude lactams (3*S*,4*R*)-**31**:(3*S*,4*S*)-**75** (76:24 dr). Chromatographic purification (eluent Et_2O:petrol 20:80) gave lactam (3*S*,4*R*)-**31** (>98:2 dr) as a colorless oil (201 mg, 64%) with identical spectroscopic properties as before in 97% ee; $[\alpha]_D^{20}$ −10.6 (*c* 0.5, CH_2Cl_2) and lactam (3*S*,4*S*)-**75** (95:5 dr) as a colorless oil (69.0 mg, 22%) with identical spectroscopic properties as before in 99% ee; $[\alpha]_D^{20}$ +0.6 (*c* 0.5, CH_2Cl_2).

(3*S*,4*R*)-3-[(1*E*)-But-1-en-1-yl]-1-[(4-methylbenzene)-sulfonyl]-4-phenylazetidin-2-one 32 and (3*S*,4*S*)-3-[(1*E*)-But-1-en-1-yl]-1-[(4-methylbenzene)sulfonyl]-4-phenylazetidin-2-one 76. Following general procedure A, (*E*)-hex-3-enoic acid **81** (190 μL, 1.60 mmol), *i*Pr$_2$NEt (420 μL, 2.40 mmol) and pivaloyl chloride (296 μL, 2.40 mmol) in CH_2Cl_2 (10 mL), HBTM-2.1 (2*S*,3*R*)-**23** (24.6 mg, 0.08 mmol, 10 mol %), imine **19** (207 mg, 0.80 mmol) and *i*Pr$_2$NEt (348 μL, 2.00 mmol) for 1.5 h at rt gave crude lactams (3*S*,4*R*)-**32** and (3*S*,4*S*)-**76** (84:16 dr). Chromatographic purification (eluent Et_2O:petrol 20:80) gave lactam (3*S*,4*R*)-**32** (>98:2 dr) as a

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colorless oil (158 mg, 55%) and lactam (3*S*,4*S*)-**76** (98:2 dr) as a white solid (22 mg, 8%).

Data for lactam (3*S*,4*R*)-**32**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*) 11.5 min, t_R(3*R*,4*S*) 17.8 min, 81% ee; ν_{max} (ATR)/cm^{-1} 2967 (C−H), 1794 (C═O), 1699, 1366 (S═O), 1169 (S═O); Data for major diastereomer δ_H (500 MHz, $CDCl_3$) 0.95 (3H, t, *J* 7.5 Hz, CH_2CH_3), 2.00−2.07 (2H, m, CH_2CH_3), 2.42 (3H, s, $ArCH_3$), 3.70 (1H, ddt, *J* 7.8, 2.4, 0.9 Hz, C(3)*H*), 4.77 (1H, d, *J* 3.3 Hz, C(4)*H*), 5.42 (1H, ddt, *J* 15.4, 7.8, 1.6 Hz, EtCH═C*H*), 5.70 (1H, dtd, *J* 15.4, 6.3, 1.1 Hz, EtC*H*═CH), 7.21−7.25 (4H, m, Ar*H*), 7.27−7.34 (3H, m, Ar*H*), 7.62−7.64 (2H, m, $SO_2Ar(2,6)H$); δ_C (125 MHz, $CDCl_3$) 13.1 (CH_2CH_3), 21.8 ($ArCH_3$), 25.6 (CH_2CH_3), 62.6 (*C*(3) or *C*(4)), 64.2 (*C*(3) or *C*(4)), 119.1 (EtCH═*C*H), 126.7 (C(4)*ArC*(2,6)), 127.6 (SO_2ArC(2,6)), 128.9 (C(4)*ArC*(3,5)), 129.0 (C(4)*ArC*(4)), 129.9 (SO_2ArC(3.5)), 135.7 (4ry *ArC*), 136.0 (4ry *ArC*), 139.3 (EtCH═CH)), 145.2 (C(4)*ArC*(1)), 165.8 (*C*(2)═O); *m*/*z* (NSI) 356 ([M + H]$^+$, 37%); HRMS (NSI) $C_{20}H_{22}NO_3S^+$ ([M + H]$^+$) requires 356.1315, found 356.1316 (+0.3 ppm).

Data for lactam (3*S*,4*S*)-**76**: mp 85−87 °C; Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*S*) 14.9 min, t_R(3*R*,4*R*) 27.9 min, 74% ee; ν_{max} (ATR)/cm^{-1} 2967 (C−H), 1788 (C═O), 1456, 1368 (S═O), 1171 (S═O); Data for major diastereomer δ_H (500 MHz, $CDCl_3$) 0.72 (3H, t, *J* 7.4 Hz, CH_3CH_2), 1.78−1.84 (2H, m, CH_3CH_2), 2.45 (3H, s, $ArCH_3$), 4.16 (1H, ddd, *J* 7.6, 6.7, 1.0, C(3)*H*), 4.76 (1H, ddt, *J* 15.5, 7.6, 1.6 Hz, EtCH═C*H*), 5.24 (1H, d, *J* 6.7 Hz, C(4)*H*), 5.69 (1H, dtd, *J* 15.5, 6.4, 1.2 Hz, EtC*H*═CH), 7.08−7.11 (2H, m, Ar*H*), 7.25−7.31 (5H, m, Ar*H*), 7.76−7.78 (2H, m, $SO_2Ar(2,6)H$); δ_C (100 MHz, $CDCl_3$) 13.1 (CH_3CH_2), 21.8 ($ArCH_3$), 25.6 (CH_3CH_2), 58.2 (*C*(3), 61.8 (*C*(4)), 117.7 (EtCH═CH), 127.5 (C(4)*ArC*(2,6)), 127.8 (SO_2ArC(2,6)), 128.4 (C(4)*ArC*(3,5)), 128.6 (C(4)*ArC*(4)), 130.0 (SO_2ArC(3.5)), 134.0 (4ry *ArC*), 135.8 (4ry *ArC*), 140.0 (EtCH═CH)), 145.4 (C(4)*ArC*(1)), 165.7 (*C*(2)═O); *m*/*z* (NSI) 356 ([M + H]$^+$, 39%); HRMS (NSI) $C_{20}H_{22}NO_3S^+$ ([M + H]$^+$) requires 356.1315, found 356.1316 (+0.3 ppm).

Reaction carried out for 1.5 h at −78 °C gave crude lactams (3*S*,4*R*)-**32**:(3*S*,4*S*)-**76** (82:18 dr). Chromatographic purification (eluent Et_2O:petrol 20:80) gave lactam (3*S*,4*R*)-**32** (>98:2 dr) as a colorless oil (189 mg, 67%) with identical spectroscopic properties as before in 98% ee; $[\alpha]_D^{20}$ +2.4 (*c* 0.5, CH_2Cl_2) and lactam (3*S*,4*S*)-**76** (98:2 dr) as a white solid (47.0 mg, 16%) with identical spectroscopic properties as before in >99% ee; $[\alpha]_D^{20}$ −9.3 (*c* 0.5, CH_2Cl_2).

(3*S*,4*R*)-1-[(4-Methylbenzene)sulfonyl]-3-[(1*E*)-3-methylbut-1-en-1-yl]-4-phenylazetidin-2-one 33. Following general procedure A, (*E*)-5-methylhex-3-enoic acid **65** (205 mg, 1.60 mmol), *i*Pr_2NEt (420 μL, 2.40 mmol) and pivaloyl chloride (296 μL, 2.40 mmol) in CH_2Cl_2 (10 mL), HBTM-2.1 (2*S*,3*R*)-**23** (24.6 mg, 0.08 mmol, 10 mol %), imine **19** (207 mg, 0.80 mmol) and *i*Pr_2NEt (348 μL, 2.00 mmol) for 1.5 h at rt gave crude lactam (3*S*,4*R*)-**33** (73:27 dr). Chromatographic purification (eluent Et_2O:petrol 15:85) gave lactam (3*S*,4*R*)-**33** (>98:2 dr) as a colorless solid (155 mg, 53%): Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 220 nm, 30 °C) t_R(3*S*,4*R*) 9.9 min, t_R(3*R*,4*S*) 14.4 min, 82% ee; ν_{max} (ATR)/cm^{-1} 2961 (C−H), 1794 (C═O), 1597, 1435, 1366 (S═O), 1169 (S═O); Data for major diastereomer δ_H (500 MHz, $CDCl_3$) 0.95 (6H, d, *J* 6.8 Hz, $CH(CH_3)_2$), 2.23−2.30 (1H, m, $CH(CH_3)_2$), 2.42 (3H, s, $ArCH_3$), 3.68−3.70 (1H, m, C(3)*H*), 4.77 (1H, d, *J* 3.3 Hz, C(4)*H*), 5.38 (1H, ddd, *J* 15.5, 7.7, 1.4 Hz, *i*PrCH═*C*H), 5.62 (1H, ddd, *J* 15.5, 6.5, 1.1 Hz, *i*PrC*H*═CH), 7.21−7.25 (4H, m, Ar*H*), 7.27−7.34 (3H, m, Ar*H*), 7.62−7.64 (2H, m, $SO_2Ar(2,6)H$); δ_C (125 MHz, $CDCl_3$) 21.8 ($ArCH_3$), 22.0 (CH-($CH_3)_2$), 31.2 ($CH(CH_3)_2$), 62.5 (*C*(3)), 64.3 (*C*(4)), 117.3 (*i*PrCH═CH), 126.7 (C(4)*ArC*(2,6)), 127.6 (SO_2ArC(2,6)), 128.9 (C(4)*ArC*(3,5)), 129.0 (C(4)*ArC*(4)), 129.8 (SO_2ArC(3,5)), 135.7 (4ry *ArC*), 136.0 (4ry *ArC*), 144.4 (*i*PrCH═CH), 145.2 (C(4)*ArC*(1)), 165.8 (*C*(2)═O); *m*/*z* (NSI) 370 ([M + H]$^+$, 32%); HRMS (NSI) $C_{21}H_{24}NO_3S^+$ ([M + H]$^+$) requires 370.1471, found 370.1472 (+0.2 ppm).

Reaction carried out for 1.5 h at −78 °C gave crude lactam (3*S*,4*R*)-**33** (79:21 dr). Chromatographic purification (eluent Et_2O:petrol 15:85) gave lactam (3*S*,4*R*)-**33** (>98:2 dr) as a colorless oil (185 mg, 63%) with identical spectroscopic properties as before in 97% ee; $[\alpha]_D^{20}$ +1.6 (*c* 0.5, CH_2Cl_2).

(3*S*,4*R*)-1-[(4-Methylbenzene)sulfonyl]-4-phenyl-3-[(1*E*)-3-phenylprop-1-en-1-yl]azetidin-2-one 34 and (3*S*,4*S*)-1-[(4-Methylbenzene)sulfonyl]-4-phenyl-3-[(1*E*)-3-phenylprop-1-en-1-yl]azetidin-2-one 77. Following general procedure A, (*E*)-5-phenylpent-3-enoic acid **66** (282 mg, 1.60 mmol), *i*Pr_2NEt (420 μL, 2.40 mmol) and pivaloyl chloride (296 μL, 2.40 mmol) in CH_2Cl_2 (10 mL), HBTM-2.1 (2*S*,3*R*)-**23** (24.6 mg, 0.08 mmol, 10 mol %), imine **19** (207 mg, 0.80 mmol) and *i*Pr_2NEt (348 μL, 2.00 mmol) for 1.5 h at rt gave crude lactams (3*S*,4*R*)-**34** and (3*S*,4*S*)-**77** (72:28 dr). Chromatographic purification (eluent Et_2O:petrol 25:75) gave lactam (3*S*,4*R*)-**34** (>98:2 dr) as a colorless oil (197 mg, 59%) and lactam (3*S*,4*S*)-**77** (95:5 dr) as a colorless oil (61 mg, 18%).

Data for lactam (3*S*,4*R*)-**34**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*) 18.4 min, t_R(3*R*,4*S*) 25.3 min, 62% ee; ν_{max} (ATR)/cm^{-1} 3028 (C−H), 1792 (C═O), 1597, 1364 (S═O), 1169 (S═O); Data for major diastereoisomer δ_H (500 MHz, $CDCl_3$) 2.42 (3H, s, $ArCH_3$), 3.37 (2H, d. *J* 6.7 Hz, $PhCH_2$), 3.76 (1H, ddd, *J* 7.7, 3.3, 0.9 Hz, C(3)*H*), 4.81 (1H, d, *J* 3.3 Hz, C(4)*H*), 5.51 (1H, ddt, *J* 15.4, 7.7, 1.5 Hz, BnCH═C*H*), 5.84 (1H, dtd, *J* 15.3, 6.7, 1.2 Hz, BnC*H*═CH), 7.12−7.14 (2H, m, Ar*H*), 7.20−7.23 (5H, m, Ar*H*), 7.28−7.35 (5H, m, Ar*H*), 7.62−7.64 (2H, m, $SO_2(2,6)H$); δ_C (125 MHz, $CDCl_3$) 21.8 ($ArCH_3$), 38.9 ($PhCH_2CH$═CH), 62.3 (C(3)), 64.1 (*C*(4)), 121.4 (BnCH═*C*H), 126.4 (*ArC*), 126.7 (*ArC*), 127.5 (*ArC*), 128.6 (*ArC*), 128.6 (*ArC*), 128.9 (*ArC*), 129.1 (C(4)*ArC*(4)), 129.8 (SO_2ArC(3,5)), 135.7 (4ry *ArC*), 135.8 (4ry *ArC*), 136.1 (BnCH═CH), 139.0 (SO_2ArC(1)), 145.2 (C(4)*ArC*(1)), 165.4 (*C*(2)═O); *m*/*z* (NSI) 418 ([M + H]$^+$, 20%); HRMS (NSI) $C_{25}H_{24}NO_3S^+$ ([M + H]$^+$) requires 418.1471, found 418.1467 (−1.1 ppm).

Data for lactam (3*S*,4*S*)-**77**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*S*) 14.4 min, t_R(3*R*,4*R*) 26.7 min, 39% ee; ν_{max} (ATR)/cm^{-1} 3028, 2924 (C−H), 1788 (C═O), 1595, 1359 (S═O), 1167 (S═O); Data for minor diastereoisomer δ_H (500 MHz, $CDCl_3$) 2.45 (3H, s, $ArCH_3$), 3.12 (2H, d. *J* 6.7 Hz, $PhCH_2$), 4.18−4.21 (1H, m, C(3)*H*), 4.85 (1H, ddt, *J* 15.4, 7.7, 1.5 Hz, BnCH═C*H*), 5.26 (1H, d, *J* 6.7 Hz, C(4)*H*), 5.78 (1H, dtd, *J* 15.4, 6.8, 1.2, BnC*H*═CH), 6.76−6.79 (2H, m, Ar*H*), 7.08−7.23 (5H, m, Ar*H*), 7.27−7.35 (5H, m, Ar*H*), 7.77−7.79 (2H, m, $SO_2(2,6)H$); δ_C (125 MHz, $CDCl_3$) 21.9 ($ArCH_3$), 38.9 ($PhCH_2$), 58.1 (C(3)), 61.8 (C(4)), 120.4 (BnCH═CH), 126.2 (*ArC*), 127.4 (*ArC*), 127.8 (*ArC*), 128.4 (*ArC*), 128.6 (*ArC*), 128.7 (*ArC*), 128.7 (*ArC*), 130.0 (SO_2ArC(3,5)), 134.0 (4ry *ArC*), 135.7 (4ry *ArC*), 136.8 (BnCH═CH), 138.9 (SO_2ArC(1)), 145.5 (C(4)*ArC*(1)), 165.4 (*C*(2)═O); *m*/*z* (NSI) 418 ([M + H]$^+$, 28%); HRMS (NSI) $C_{25}H_{24}NO_3S^+$ ([M + H]$^+$) requires 418.1471, found 418.1459 (−3.0 ppm).

Reaction carried out for 1.5 h at −78 °C gave crude lactams (3*S*,4*R*)-**34**:(3*S*,4*S*)-**77** (72:28 dr). Chromatographic purification (eluent Et_2O:petrol 25:75) gave lactam (3*S*,4*R*)-**34** (>98:2 dr) as a colorless oil (189 mg, 57%) with identical spectroscopic properties as before in 95% ee; $[\alpha]_D^{20}$ +0.8 (*c* 0.5, CH_2Cl_2) and lactam (3*S*,4*S*)-**77** (95:5 dr) as a colorless oil (53.0 mg, 16%) with identical spectroscopic properties as before in 97% ee; $[\alpha]_D^{20}$ −6.8 (*c* 0.5, CH_2Cl_2).

(3*S*,4*R*)-1-[(4-Methylbenzene)sulfonyl]-4-phenyl-3-[(1*Z*)-prop-1-en-1-yl]azetidin-2-one 35 and (3*S*,4*S*)-1-[(4-Methylbenzene)sulfonyl]-4-phenyl-3-[(1*Z*)-prop-1-en-1-yl]-azetidin-2-one 78. Following general procedure A, (*Z*)-pent-3-enoic acid **68** (160 mg, 1.60 mmol), *i*Pr_2NEt (420 μL, 2.40 mmol) and pivaloyl chloride (296 μL, 2.40 mmol) in CH_2Cl_2 (10 mL), HBTM-2.1 (2*S*,3*R*)-**23** (24.6 mg, 0.08 mmol, 10 mol %), imine **19** (207 mg, 0.80 mmol) and *i*Pr_2NEt (348 μL, 2.00 mmol) for 1.5 h at rt gave crude lactams (3*S*,4*R*)-**35** and (3*S*,4*S*)-**78** (48:52 dr). Chromatographic purification (eluent Et_2O:petrol 20:80) gave lactam (3*S*,4*R*)-**35** (92:8 dr) as a colorless oil (89 mg, 33%) and lactam (3*S*,4*S*)-**78** (88:12 dr) as a white solid (97 mg, 36%).

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Data for lactam (3*S*,4*R*)-**35**: Chiral HPLC Chiralpak AD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*R*,4*S*) 14.5 min, t_R(3*S*,4*R*) 16.0 min, 92% ee; ν_{max} (ATR)/cm^{-1} 3030, 2967 (C−H), 1788 (C═O), 1456, 1362 (S═O), 1167 (S═O); Data for major diastereoisomer δ_H (500 MHz, $CDCl_3$) 1.51 (3H, dd, *J* 6.9, 1.8 Hz, CH_3CH═CH), 2.43 (3H, s, ArCH_3), 4.00−4.02 (1H, m, C(3)*H*), 4.75 (1H, d, *J* 3.2 Hz, C(4)*H*), 5.44 (1H, ddq, *J* 10.6, 8.8, 1.8 Hz, CH_3CH═C*H*), 5.78 (1H, dqd, *J* 10.7, 6.9, 1.4 Hz, CH_3C*H*═CH), 7.23−7.25 (4H, m, Ar*H*), 7.28−7.35 (3H, m, Ar*H*), 7.62−7.65 (2H, m, SO_2Ar(2,6)*H*); δ_C (125 MHz, $CDCl_3$) 14.0 (CH_3CH═CH), 21.8 (ArCH_3), 58.2 (*C*(3)), 64.4 (*C*(4)), 120.5 (CH_3CH═*C*H), 126.7 (C(4)*ArC*(3,5)), 127.6 (SO_2*ArC*(3,5)), 128.9 (SO_2*ArC*(2,6)), 129.1 (C(4)*ArC*(4)), 129.9 (C(4)*ArC*(2,6)), 132.1 (CH_3CH═CH), 135.7 (4ry *ArC*), 136.0 (4ry *ArC*), 145.3 (C(4)*ArC*(1)), 165.9 (*C*(2)═O); *m*/*z* (NSI) 342 ([M + H]$^+$, 42%); HRMS (NSI) $C_{19}H_{20}NO_3S^+$ ([M + H]$^+$) requires 342.1158, found 342.1159 (+0.2 ppm).

Data for lactam (3*S*,4*S*)-**78**: mp 83−85 °C; Chiral HPLC Chiralcel OD-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*S*) 12.0 min, t_R(3*R*,4*R*) 15.8 min, 98% ee; ν_{max} (ATR)/cm^{-1} 3032, 2922 (C−H), 1788 (C═O), 1458, 1354 (S═O), 1165 (S═O); Data for minor diastereoisomer δ_H (500 MHz, $CDCl_3$) 1.55−1.57 (3H, m, CH_3CH═CH), 2.46 (3H, s, ArCH_3), 4.47−4.50 (1H, m, C(3)*H*), 4.89−4.94 (1H, m, CH_3CH═C*H*), 5.31 (1H, d, *J* 6.8 Hz, C(4)*H*), 5.54 (1H, dqd, *J* 10.8, 6.9, 1.5 Hz, CH_3C*H*═CH), 7.09−7.11 (2H, m, Ar*H*), 7.23−7.34 (5H, m, Ar*H*), 7.76−7.78 (2H, m, SO_2Ar(2,6)*H*); δ_C (125 MHz, $CDCl_3$) 13.9 (CH_3CH═CH), 21.9 (ArCH_3), 53.7 (*C*(3)), 61.8 (*C*(4)), 118.6 (CH_3CH═*C*H), 127.4 (C(4)*ArC*(3,5)), 127.8 (SO_2*ArC*(3,5)), 128.5 (SO_2*ArC*(2,6)), 128.7 (C(4)*ArC*(4)), 130.0 (C(4)*ArC*(2,6)), 132.1 (CH_3CH═CH), 134.0 (4ry *ArC*), 135.7 (4ry *ArC*), 145.4 (C(4)*ArC*(1)), 165.9 (*C*(2)═O); *m*/*z* (NSI) 342 ([M + H]$^+$, 30%); HRMS (NSI) $C_{19}H_{20}NO_3S^+$ ([M + H]$^+$) requires 342.1158, found 342.1160 (+0.5 ppm).

Reaction carried out for 1.5 h at −78 °C gave crude lactams (3*S*,4*R*)-**35**:(3*S*,4*S*)-**78** (43:57 dr). Chromatographic purification (eluent Et_2O:petrol 20:80) gave lactam (3*S*,4*R*)-**35** (92:8 dr) as a colorless oil (58 mg, 21%) with identical spectroscopic properties as before in 99% ee; $[\alpha]_D^{20}$ +4.2 (*c* 0.5, CH_2Cl_2) and lactam (3*S*,4*S*)-**78** (88:12 dr) as a white solid (99.0 mg, 36%) with identical spectroscopic properties as before in 99% ee; $[\alpha]_D^{20}$ −14.2 (*c* 0.5, CH_2Cl_2).

(3*S*,4*R*)-4-Phenyl-3-((*E*)-prop-1-en-1-yl)-6-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one 36. Following general procedure A, (*E*)-pent-3-enoic acid **24** (40.6 μL, 0.40 mmol), *i*Pr_2NEt (104 μL, 0.60 mmol) and pivaloyl chloride (74.0 μL, 0.60 mmol) in CH_2Cl_2 (2 mL), HBTM-2.1 (2*S*,3*R*)-**23** (6.16 mg, 0.02 mmol, 5 mol %), (*E*)-1,1,1-trifluoro-4-phenyl-3-buten-2-one **57** (80.0 mg, 0.40 mmol) and *i*Pr_2NEt (174 μL, 1.0 mmol) for 5 min at rt gave crude lactone (3*S*,4*R*)-**36** (88:12 dr). Chromatographic purification (eluent Et_2O:petrol 4:96) gave lactone (3*S*,4*R*)-**36** (88:12 dr) as a colorless oil (89.8 mg, 80%): $[\alpha]_D^{20}$ −212.4 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralcel OD-H (1% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) major diastereoisomer t_R(3*S*,4*R*) 9.7 min, t_R(3*R*,4*S*) 13.2 min, 96% ee; minor diastereoisomer t_R 10.7 min, t_R 14.8 min, 15% ee; ν_{max} (ATR)/cm^{-1} 3060, 3027 (C−H), 1784 (C═O), 1699; Data for major diastereoisomer δ_H (500 MHz, $CDCl_3$) 1.68 (3H, t, *J*, 5.9, CH_3), 3.43 (1H, t, *J* 6.9, C(3)*H*), 3.70−3.75 (1H, m, C(4)*H*), 5.44−5.56 (2H, m, C(3)C*H*═CHCH$_3$ and C(3)CH═C*H*CH$_3$), 6.09 (1H, d, *J* 4.5, C(5)*H*), 7.11 (2H, d, *J* 7.8, C(4)Ar(2,6)*H*), 7.31−7.40 (3H, m, C(4)Ar(3,5)*H* and C(4)Ar(4)*H*); δ_C (75 MHz, $CDCl_3$) 18.1 (CH_3), 43.2 (*C*(4)), 49.9 (*C*(3)), 109.7 (q, *J* 3.5, *C*(5)), 118.5 (q, *J* 270, CF_3), 123.8 (C(3)*CH*═CHCH$_3$), 127.4 (*ArC*), 128.1 (*ArC*), 129.2 (*ArC*), 132.1 (C(3)CH═*CH*CH$_3$), 138.7 (4ry C(4)ArC(1)), 140.8 (q, *J* 37.9, *C*(6)), 166.1 (*C*(2)); δ_F (376 MHz, $CDCl_3$) −72.6 (CF_3); Selected data or minor diastereoisomer δ_H (500 MHz, $CDCl_3$) 3.63 (1H, t, *J* 7.8, C(3)*H*), 3.86−3.88 (1H, m, C(4)*H*), 5.13 (1H, dd, *J* 15.4, 8.6, C(3)C*H*═CHCH$_3$), 5.69 (1H, dq, *J* 14.7, 7.1, C(3)CH═*CH*CH$_3$), 6.23 (1H, d, *J* 5.7, C(5)*H*), 7.11 (2H, d, *J* 7.7, Ar(2,6)*H*); δ_C (75 MHz, $CDCl_3$) 18.0 (CH_3), 43.0 (*C*(4)), 47.7 (*C*(3)), 110.8 (q, *J* 3.5, *C*(5)), 122.6 (C(3)CH═CHCH$_3$), 128.2 (*ArC*), 128.3 (*ArC*), 129.1 (*ArC*), 132.2 (C(3)CH═CHCH$_3$), 166.6 (*C*(2)); δ_F (376 MHz, $CDCl_3$) −72.7 (CF_3); *m*/*z* (NSI$^+$) 300 ([M + NH_4]$^+$, 100%); HRMS (NSI$^+$) $C_{15}H_{17}F_3NO_2^+$ ([M + NH_4]$^+$) requires 300.1206, found 300.1206 (+0.0 ppm).

(3*S*,4*R*)-4-Phenyl-3-((*E*)-but-1-en-1-yl)-6-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one 37. Following general procedure A, (*E*)-hex-3-enoic acid **81** (47.4 μL, 0.40 mmol), *i*Pr_2NEt (104 μL, 0.60 mmol) and pivaloyl chloride (74.0 μL, 0.60 mmol) in CH_2Cl_2 (2 mL), HBTM-2.1 (2*S*,3*R*)-**23** (6.16 mg, 0.02 mmol, 5 mol %), (*E*)-1,1,1-trifluoro-4-phenyl-3-buten-2-one **57** (80.0 mg, 0.40 mmol) and *i*Pr_2NEt (174 μL, 1.0 mmol) for 5 min at rt gave crude lactone (3*S*,4*R*)-**37** (90:10 dr). Chromatographic purification (eluent Et_2O:petrol 3:97) gave lactone (3*S*,4*R*)-**37** (93:7 dr) as a colorless oil (98.7 mg, 83%): $[\alpha]_D^{20}$ −191.0 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralcel OD-H (1% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) major diastereoisomer t_R(3*S*,4*R*) 8.9 min, t_R(3*R*,4*S*) 12.4 min, 96% ee; minor diastereoisomer t_R 9.9 min, t_R 14.4 min, 12% ee; ν_{max} (ATR)/cm^{-1} 3065, 2968 (C−H), 1786 (C═O), 1699; Data for major diastereoisomer δ_H (500 MHz, $CDCl_3$) 0.92 (3H, t, *J* 7.5, CH_3), 2.00−2.06 (2H, m, CH_2CH_3), 3.42 (1H, t, *J* 7.1, C(3)*H*), 3.71−3.74 (1H, m, C(4)*H*), 5.41−5.45 (1H, m, C(3)C*H*═CHCH$_2$CH$_3$ or C(3)CH═C*H*CH$_2$CH$_3$), 5.49−5.54 (1H, m, C(3)C*H*═CHCH$_2$CH$_3$ or C(3)CH═C*H*CH$_2$CH$_3$), 6.10 (1H, d, *J* 4.6, C(5)*H*), 7.14−7.16 (2H, m, C(4)Ar(2,6)*H*), 7.31−7.40 (3H, m, C(4)Ar(3,5)*H* and C(4)Ar(4)*H*); δ_C (125 MHz, $CDCl_3$) 13.2 (CH_3), 25.6 (CH_2CH_3), 43.3 (*C*(4)), 49.9 (*C*(3)), 109.7 (q, *J* 3.5, *C*(5)), 118.5 (q, *J* 270, CF_3), 121.6 (C(3)*CH*═CHCH$_2$CH$_3$), 127.5 (*ArC*), 128.1 (*ArC*), 129.2 (*ArC*), 138.7 (4ry C(4)ArC(1)), 138.8 (C(3)CH═*C*HCH$_2$CH$_3$), 140.8 (q, *J* 37.9, *C*(6)), 166.2 (*C*(2)); δ_F (376 MHz, $CDCl_3$) −72.6 (CF_3); Selected data or minor diastereoisomer δ_H (500 MHz, $CDCl_3$) 3.63 (1H, t, *J* 7.7, C(3)*H*), 3.87−3.90 (1H, m, C(4)*H*), 5.10 (1H, ddt, *J* 15.5, 8.5, 1.6, C(3)C*H*═CHCH$_2$CH$_3$), 5.70 (1H, dt, *J* 15.4, 6.4, C(3)CH═C*H*CH$_2$CH$_3$), 6.23 (1H, d, *J* 5.7, C(5)*H*), 7.11 (2H, d, *J* 8.0, Ar(2,6)*H*); δ_C (125 MHz, $CDCl_3$) 43.0 (*C*(4)), 47.6 (*C*(3)), 110.7 (q, *J* 3.5, *C*(5)), 120.5 (C(3)CH═CHCH$_2$CH$_3$), 128.2 (*ArC*), 128.2 (*ArC*), 129.0 (*ArC*), 138.9 (C(3)CH═CHCH$_2$CH$_3$), 166.6 (*C*(2)); δ_F (376 MHz, $CDCl_3$) −72.6 (CF_3); *m*/*z* (NSI$^+$) 297 ([M + H]$^+$, 20%); HRMS (NSI$^+$) $C_{16}H_{16}F_3O_2^+$ ([M + H]$^+$) requires 297.1097, found 297.1101 (+1.4 ppm).

(3*S*,4*R*)-4-Phenyl-3-((*E*)-styryl)-6-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one 38. Following general procedure A, (*E*)-4-phenylbut-3-enoic acid **16** (64.9 mg, 0.40 mmol), *i*Pr_2NEt (104 μL, 0.60 mmol) and pivaloyl chloride (74.0 μL, 0.60 mmol) in CH_2Cl_2 (2 mL), HBTM-2.1 (2*S*,3*R*)-**23** (6.16 mg, 0.02 mmol, 5 mol %), (*E*)-1,1,1-trifluoro-4-phenyl-3-buten-2-one **57** (80.0 mg, 0.40 mmol) and *i*Pr_2NEt (174 μL, 1.0 mmol) for 5 min at −78 °C gave crude lactone (3*S*,4*R*)-**38** (95:5 dr). Chromatographic purification (eluent Et_2O:petrol 7.5:92.5) gave lactone (3*S*,4*R*)-**38** (95:5 dr) as a colorless oil (113 mg, 82%): $[\alpha]_D^{20}$ −159.6 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IB (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) major diastereoisomer t_R(3*R*,4*S*) 12.3 min, t_R(3*S*,4*R*) 13.9 min, 60% ee; minor diastereoisomer t_R 8.00 min, t_R 10.6 min, 52% ee; ν_{max} (ATR)/cm^{-1} 3063, 3030 (C−H), 1782 (C═O), 1699, 1601; Data for major diastereoisomer δ_H (500 MHz, $CDCl_3$) 3.65 (1H, t, *J* 7.6, C(3)*H*), 3.85−3.90 (1H, m, C(4)*H*), 6.15−6.20 (2H, m, C(5)*H* and C(3)C*H*═CHPh), 6.36 (1H, d, *J* 15.9, C(3)CH═C*H*Ph), 7.21 (2H, d, *J* 7.5, Ar*H*), 7.28−7.42 (8H, m, Ar*H*); δ_C (125 MHz, $CDCl_3$) 43.3 (*C*(4)), 50.0 (*C*(3)), 109.9 (q, *J* 3.3, *C*(5)), 118.5 (q, *J* 270, CF_3), 122.0 (C(3)CH═CHPh), 126.6 (*ArC*), 127.5 (*ArC*), 128.3 (*ArC*), 128.4 (*ArC*), 128.7 (ArC), 129.4 (ArC), 135.7 (C(3)CH═CHPh), 135.8 (4ry *ArC*), 138.5 (4ry *ArC*), 141.0 (q, *J* 38.0, *C*(6)), 165.6 (*C*(2)); δ_F (376 MHz, $CDCl_3$) −72.6 (CF_3); Selected data for minor diastereoisomer δ_H (500 MHz, $CDCl_3$) 3.99 (1H, t, *J* 6.2, C(4)*H*), 5.84 (1H, dd, *J* 16.0, 8.6, C(3)C*H*═CHPh), 6.30 (1H, d, *J* 5.9, C(5)*H*), 6.59 (1H, d, *J* 16.0, C(3)CH═C*H*Ph), 7.16 (2H, d, *J* 7.6, Ar*H*); δ_C (125 MHz, $CDCl_3$) 47.9 (*C*(3)), 110.7 (q, *J* 3.4, *C*(5)), 121.4 (C(3)CH═CHPh), 128.2 (*ArC*), 128.5 (*ArC*), 129.3 (*ArC*), 135.4 (C(3)CH═CHPh), 166.2 (*C*(2)); δ_F (376 MHz, $CDCl_3$) −72.7 (CF_3); *m*/*z* (NSI$^+$) 345 ([M + H]$^+$, 15%); HRMS (NSI$^+$) $C_{20}H_{16}F_3O_2^+$ ([M + H]$^+$) requires 345.1097, found 345.1098 (+0.3 ppm).

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(3*S*,4*R*)-4-(4-Bromophenyl)-3-((*E*)-prop-1-en-1-yl)-6-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one 39. Following general procedure A, (*E*)-pent-3-enoic acid **24** (40.6 μL, 0.40 mmol), *i*Pr$_2$NEt (104 μL, 0.60 mmol) and pivaloyl chloride (74.0 μL, 0.60 mmol) in CH_2Cl_2 (2 mL), HBTM-2.1 (2*S*,3*R*)-**23** (6.16 mg, 0.02 mmol, 5 mol %), (*E*)-1,1,1-trifluoro-4-(4-bromophenyl)-3-buten-2-one **58** (112 mg, 0.40 mmol) and *i*Pr$_2$NEt (174 μL, 1.0 mmol) for 5 min at rt gave crude lactone (3*S*,4*R*)-**39** (80:20 dr). Chromatographic purification (eluent Et$_2$O:petrol 3:97) gave lactone (3*S*,4*R*)-**39** (95:5 dr) as a colorless oil (105 mg, 73%): $[\alpha]_D^{20}$ −201.0 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralcel OD-H (1% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) major diastereoisomer t_R(3*R*,4*S*) 10.1 min, t_R(3*S*,4*R*) 11.8 min, 92% ee; minor diastereoisomer t_R 9.3 min, t_R 12.8 min, 90% ee; ν_{max} (ATR)/cm^{-1} 2987 (C−H), 1786 (C=O), 1753, 1660; Data for major diastereoisomer δ_H (500 MHz, $CDCl_3$) 1.69 (3H, t, *J*, 6.4, CH_3), 3.37 (1H, t, *J* 7.4, C(3)*H*), 3.68−3.71 (1H, m, C(4)*H*), 5.43 (1H, ddd, *J* 15.3, 7.5, 1.3, C(3)C*H*=CHCH$_3$), 5.52 (1H, dq, *J* 15.4, 6.3, C(3)CH=C*H*CH$_3$), 6.03 (1H, d, *J* 4.4, C(5)*H*), 7.02−7.04 (2H, m, C(4)Ar(3,5)*H*), 7.50−7.52 (2H, m, C(4)Ar(2,6)*H*); δ_C (125 MHz, $CDCl_3$) 18.1 (*C*H$_3$), 42.7 (*C*(4)), 49.7 (*C*(3)), 109.2 (q, *J* 3.5, *C*(5)), 118.4 (q, *J* 270, *C*F$_3$), 122.1 (C(4)*ArC*(4)), 123.4 (C(3)CH=CHCH$_3$), 129.1 (C(4)*ArC*(3,5)), 132.3 (C(4)*ArC*(2,6)), 132.6 (C(3)CH=*C*HCH$_3$), 137.7 (4ry C(4)ArC(1)), 141.1 (q, *J* 38, *C*(6)), 165.8 (*C*(2)); δ_F (376 MHz, $CDCl_3$) −72.7 (*C*F$_3$); Selected data or minor diastereoisomer δ_H (500 MHz, $CDCl_3$) 3.62 (1H, t, *J* 7.8, C(3)*H*), 3.82−3.85 (1H, m, C(4)*H*), 5.09−5.14 (1H, m, C(3)C*H*=CHCH$_3$), 5.65−5.72 (1H, m, C(3)CH=C*H*CH$_3$), 6.18 (1H, d, *J* 5.7, C(5)*H*); δ_C (75 MHz, $CDCl_3$) 18.0 (*C*H$_3$), 44.4 (*C*(4)), 47.4 (*C*(3)); δ_F (376 MHz, $CDCl_3$) −72.8 (*C*F$_3$); *m*/*z* (NSI$^+$) 378 ([M + NH$_4$]$^+$, 56%); HRMS (NSI$^+$) $C_{15}H_{16}{}^{78}BrF_3NO_2^+$ ([M + NH$_4$]$^+$) requires 378.0311, found 378.0311 (+0.0 ppm).

(3*S*,4*R*)-4-(Thiophen-2-yl)-3-((*E*)-prop-1-en-1-yl)-6-(trifluoromethyl)-3,4-dihydro-2*H*-pyran-2-one 40. Following general procedure A, (*E*)-pent-3-enoic acid **24** (40.6 μL, 0.40 mmol), *i*Pr$_2$NEt (104 μL, 0.60 mmol) and pivaloyl chloride (74.0 μL, 0.60 mmol) in CH_2Cl_2 (2 mL), HBTM-2.1 (2*S*,3*R*)-**23** (6.16 mg, 0.02 mmol, 5 mol %), (*E*)-1,1,1-trifluoro-4-(2-thienyl)-3-buten-2-one **59** (82.4 mg, 0.40 mmol) and *i*Pr$_2$NEt (174 μL, 1.0 mmol) for 5 min at rt gave crude lactone (3*S*,4*R*)-**40** (84:16 dr). Chromatographic purification (eluent Et$_2$O:petrol 4:96) gave lactone (3*S*,4*R*)-**40** (84:16 dr) as a colorless oil (95.8 mg, 83%): $[\alpha]_D^{20}$ −187.0 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak AS-H (0.5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) major diastereoisomer t_R(3*S*,4*R*) 14.1 min, t_R(3*R*,4*S*) 16.1 min, 93% ee; ν_{max} (ATR)/cm^{-1} 2998 (C−H), 1784 (C=O), 1699, 1674; Data for major diastereoisomer δ_H (300 MHz, $CDCl_3$) 1.72−1.74 (3H, m, *CH*$_3$), 3.55 (1H, td, *J* 6.7, 0.7, C(3)*H*), 4.00−4.04 (1H, m, C(4)*H*), 5.47 (1H, ddq, *J* 15.4, 8.4, 1.7, C(3)C*H*=CHCH$_3$), 5.63−5.75 (1H, m, C(3)CH=C*H*CH$_3$), 6.16 (1H, d, *J* 5.0, C(5)*H*), 6.89−6.90 (1H, m, Ar*H*), 6.98−7.03 (1H, m, Ar*H*), 7.27−7.30 (1H, m, Ar*H*); δ_C (125 MHz, $CDCl_3$) 18.1 (*C*H$_3$), 38.2 (*C*(4)), 50.6 (*C*(3)), 109.2 (q, *J* 3.5, *C*(5)), 118.4 (q, *J* 270, *C*F$_3$), 123.2 (C(3)CH=CHCH$_3$), 125.4 (*ArC*), 125.4 (*ArC*), 127.4 (*ArC*), 132.4 (C(3)CH=*C*HCH$_3$), 140.7 (q, *J* 37.9, *C*(6)), 141.2 (C(4)ArC(1)), 165.5 (*C*(2)); δ_F (376 MHz, $CDCl_3$) −72.4 (*C*F$_3$); Selected data or minor diastereoisomer δ_H (500 MHz, $CDCl_3$) 3.64 (1H, t, *J* 7.5, C(3)*H*), 4.13−4.18 (1H, m, C(4)*H*), 5.35 (1H, ddq, *J* 15.4, 8.4, 1.7, C(3)C*H*=CHCH$_3$), 6.28 (1H, d, *J* 5.8, C(5)*H*); δ_C (75 MHz, $CDCl_3$) 18.1 (*C*H$_3$), 38.0 (*C*(4)), 48.0 (*C*(3)), 110.7 (q, *J* 3.5, *C*(5)), 122.5 (C(3)*C*H=CHCH$_3$), 125.7 (*ArC*), 126.3 (*ArC*), 127.4 (*ArC*), 132.7 (C(3)CH=*C*HCH$_3$), 166.2 (*C*(2)); δ_F (376 MHz, $CDCl_3$) −72.6 (*C*F$_3$); *m*/*z* (APCI$^+$) 289 ([M + H]$^+$, 100%); HRMS (APCI$^+$) $C_{13}H_{12}F_3O_2S^+$ ([M + H]$^+$) requires 289.0505, found 289.0507 (+0.8 ppm).

(2*R*)-(*E*)-Methyl 2-(2-benzoyl-1-phenylhydrazinyl)pent-3-enoate 41. Following general procedure A, (*E*)-pent-3-enoic acid **24** (40.6 μL, 0.40 mmol), *i*Pr$_2$NEt (104 μL, 0.60 mmol) and pivaloyl chloride (74.0 μL, 0.60 mmol) in CH_2Cl_2 (2 mL), HBTM-2.1 (2*S*,3*R*)-**23** (1.23 mg, 0.004 mmol, 1 mol %), (NE)-*N*-(phenylimino)-benzamide **60** (84.0 mg, 0.40 mmol) and *i*Pr$_2$NEt (174 μL, 1.00 mmol) for 15 min at rt, followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave after chromatographic purification (eluent Et$_2$O:petrol 40:60) a rotameric mixture (ratio 95:5) of (2*R*)-**41** as a white solid (105 mg, 80%): mp 108−110 °C; $[\alpha]_D^{20}$ −67.0 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IB (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*) 13.2 min, t_R(2*R*) 17.3 min, 96% ee; ν_{max} (ATR)/cm^{-1} 3350 (N−H), 2949 (C−H), 1721 (C=O), 1698 (C=O), 1597; Data for major rotamer δ_H (500 MHz, $CDCl_3$) 1.72 (3H, d, *J* 4.7, *CH*$_3$CH=), 3.78 (3H, s, OC*H*$_3$), 5.25−5.26 (1H, m, C(2)*H*), 5.79−5.89 (2H, m, *CH*=CHCH$_3$ and CH=*CH*CH$_3$), 6.94−6.97 (3H, m, NAr(2,6)*H* and NAr(4)*H*), 7.27−7.30 (2H, m, NAr(3,5)*H*), 7.50 (2H, t, *J* 7.6, C(O)Ar(3,5)*H*), 7.58 (1H, t, *J* 7.4, C(O)Ar(4)*H*), 7.86−7.88 (2H, m, C(O)Ar(2,6)*H*), 8.64 (1H, s, N*H*); δ_C (125 MHz, $CDCl_3$) 18.2 (*CH*$_3$CH=), 52.4 (OCH$_3$), 64.6 (*C*(2)), 114.7 (N*ArC*(2,6)), 121.5 (N*ArC*(4)), 123.6 (*CH*=CHCH$_3$), 127.2 (C(O)*ArC*(2,6)), 128.8 (C(O)*ArC*(3,5)), 129.4 (N*ArC*(3,5)), 132.0 (C(O)*ArC*(4) or CH=*CH*CH$_3$), 132.3 (C(O)*ArC*(4)) or CH=*CH*CH$_3$), 133.0 (4ry C(O)*ArC*(1)), 148.1 (N*ArC*(1)), 167.4 (NHC=O), 173.3 (MeOC=O); Selected data for minor rotamer δ_H (500 MHz, $CDCl_3$) 1.65 (3H, d, *J* 5.9, *CH*$_3$CH=), 3.67 (3H, s, OC*H*$_3$), 4.97 (1H, d, *J* 7.1, C(2)*H*); δ_C (125 MHz, $CDCl_3$) 18.1 (*CH*$_3$CH=), 52.3 (OCH$_3$), 65.8 (*C*(2)), 115.0 (N*ArC*(2,6)); *m*/*z* (NSI$^+$) 325 ([M + H]$^+$, 100%); HRMS (NSI$^+$) $C_{19}H_{21}N_2O_3^+$ ([M + H]$^+$) requires 325.1547, found 325.1548 (+0.4 ppm).

(2*R*)-(*E*)-Methyl 2-(2-benzoyl-1-phenylhydrazinyl)hex-3-enoate 42. Following general procedure A, (*E*)-hex-3-enoic acid **81** (47.4 μL, 0.40 mmol), *i*Pr$_2$NEt (104 μL, 0.60 mmol) and pivaloyl chloride (74.0 μL, 0.60 mmol) in CH_2Cl_2 (2 mL), HBTM-2.1 (2*S*,3*R*)-**23** (1.23 mg, 0.004 mmol, 1 mol %), (NE)-*N*-(phenylimino)-benzamide **60** (84.0 mg, 0.40 mmol) and *i*Pr$_2$NEt (174 μL, 1.00 mmol) for 15 min at rt, followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave after chromatographic purification (eluent Et$_2$O:petrol 40:60) a rotameric mixture (ratio 95:5) of (2*R*)-**42** as a white solid (115 mg, 85%): mp 98−100 °C; $[\alpha]_D^{20}$ −54.8 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IB (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*) 11.3 min, t_R(2*R*) 15.6 min, 99% ee; ν_{max} (ATR)/cm^{-1} 3352 (N−H), 2990 (C−H), 1721 (C=O), 1688 (C=O), 1597, 1508; Data for major rotamer δ_H (500 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.4, *CH*$_3$CH$_2$), 2.03−2.09 (2H, m, CH$_3$*CH*$_2$) 3.78 (3H, s, OC*H*$_3$), 5.26−5.27 (1H, m, C(2)*H*), 5.77−5.88 (2H, m, *CH*=CHCH$_2$CH$_3$ and CH=*CH*CH$_2$CH$_3$), 6.93−6.97 (3H, m, NAr(2,6)*H* and NAr(4)*H*), 7.26−7.29 (2H, m, NAr(3,5)*H*), 7.47−7.50 (2H, m, C(O)Ar(3,5)*H*), 7.55−7.58 (1H, m, C(O)Ar(4)*H*), 7.85−7.87 (2H, m, C(O)Ar(2,6)*H*), 8.62 (1H, s, N*H*); δ_C (125 MHz, $CDCl_3$) 13.1 (*CH*$_3$CH$_2$), 25.6 (CH$_3$*CH*$_2$), 52.4 (OCH$_3$), 64.5 (*C*(2)), 114.7 (N*ArC*(2,6)), 121.6 (N*ArC*(4) or *CH*=CHCH$_2$CH$_3$), 121.7 (N*ArC*(4) or *CH*=CHCH$_2$CH$_3$), 127.3 (C(O)*ArC*(2,6)), 128.9 (C(O)*ArC*(3,5)), 129.4 (N*ArC*(3,5)), 132.1 (C(O)*ArC*(4)), 133.1 (C(O)*ArC*(1)), 138.8 (CH=*CH*CH$_2$CH$_3$), 148.2 (N*ArC*(1)), 167.4 (NHC=O), 173.4 (MeOC=O); Selected data for minor rotamer δ_H (500 MHz, $CDCl_3$) 3.67 (3H, s, OC*H*$_3$), 4.99−5.00 (1H, m, C(2)*H*); δ_C (125 MHz, $CDCl_3$) 12.5 (*CH*$_3$CH$_2$), 52.3 (OCH$_3$), 66.1 (*C*(2)), 115.1 (N*ArC*(2,6)), 141.1 (CH=*CH*CH$_2$CH$_3$), 148.7 (N*ArC*(1)), 167.4 (NHC=O), 173.4 (MeOC=O); *m*/*z* (NSI$^+$) 339 ([M + H]$^+$, 100%); HRMS (NSI$^+$) $C_{20}H_{23}N_2O_3^+$ ([M + H]$^+$) requires 339.1703, found 339.1708 (+1.4 ppm).

(2*R*)-(*E*)-Methyl 2-(2-benzoyl-1-phenylhydrazinyl)-5-methylhex-3-enoate 43. Following general procedure A, (*E*)-5-methylhex-3-enoic acid **65** (51.2 mg, 0.40 mmol), *i*Pr$_2$NEt (104 μL, 0.60 mmol) and pivaloyl chloride (74.0 μL, 0.60 mmol) in CH_2Cl_2 (2 mL), HBTM-2.1 (2*S*,3*R*)-**23** (1.23 mg, 0.004 mmol, 1 mol %), (NE)-*N*-(phenylimino)benzamide **60** (84.0 mg, 0.40 mmol) and *i*Pr$_2$NEt (174 μL, 1.00 mmol) for 15 min at rt, followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave after chromatographic purification (eluent Et$_2$O:petrol 40:60) a rotameric mixture (ratio 95:5) of (2*R*)-**43** as a white solid (104 mg, 74%): mp 128−130 °C; $[\alpha]_D^{20}$ −66.6 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IB (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*) 14.5 min, t_R(2*R*) 19.0 min, 99% ee; ν_{max} (ATR)/cm^{-1} 3326 (N−H), 2988 (C−H), 1719 (C=O Ester), 1678 (C=O Amide), 1597, 1506; Data for major rotamer δ_H (500 MHz, $CDCl_3$) 0.89 (3H, t, *J* 6.8, CH(*CH*$_3$)*CH*$_3$), 0.92 (3H, t, *J* 6.8,

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$CH(CH_3)CH_3$), 2.27−2.34 (1H, m, $CH(CH_3)CH_3$), 3.78 (3H, s, OCH_3), 5.27−5.28 (1H, m, C(2)*H*), 5.72−5.80 (2H, m, *CH*=CHCH(CH_3)CH_3 and CH=*CH*CH(CH_3)CH_3), 6.93−6.97 (3H, m, NAr(2,6)*H* and NAr(4)*H*), 7.26−7.30 (2H, m, NAr(3,5)*H*), 7.46−7.49 (2H, m, C(O)Ar(3,5)*H*), 7.54−7.58 (1H, m, C(O)Ar(4)*H*), 7.85−7.88 (2H, m, C(O)Ar(2,6)*H*), 8.64 (1H, s, N*H*); δ_C (100 MHz, $CDCl_3$) 21.8 (CH(CH_3)CH_3), 22.0 (CH(CH_3)CH_3), 31.1 (*CH*(CH_3)CH_3), 52.3 (OCH_3), 64.4 (*C*(2)), 114.8 (NA*rC*(2,6)), 120.0 (*CH*=CHCH(CH_3)CH_3), 121.5 (NA*rC*(4)), 127.3 (C(O)*ArC*(2,6)), 128.8 (C(O)*ArC*(3,5)), 129.4 (NA*rC*(3,5)), 132.1 (C(O)*ArC*(4)), 133.0 (C(O)*ArC*(1)), 143.9 (CH=*CH*CH(CH_3)CH_3), 148.2 (NA*rC*(1)), 167.3 (NH*C*=O), 173.4 (MeO*C*=O); Selected data for minor rotamer δ_H (500 MHz, $CDCl_3$) 3.66 (3H, s, OCH_3), 5.01 (1H, d, *J* 7.0, C(2)*H*); δ_C (100 MHz, $CDCl_3$) 21.4 (CH(CH_3)CH_3), 21.5 (CH(CH_3)CH_3), 31.1 (*CH*(CH_3)CH_3), 52.2 (OCH_3), 66.3 (*C*(2)), 115.2 (NA*rC*(2,6)), 146.1 (CH=*CH*CH_2CH_3), 148.8 (NA*rC*(1)), 172.0 (MeOC=O); *m*/*z* (NSI^+) 353 ($[M + H]^+$, 100%); HRMS (NSI^+) $C_{21}H_{25}N_2O_3^+$ ($[M + H]^+$) requires 353.1860, found 353.1862 (+0.7 ppm).

(2*R*)-(*E*)-Methyl 2-(2-benzoyl-1-phenylhydrazinyl)-5-phenylpent-3-enoate 44. Following general procedure A, (*E*)-5-phenylpent-3-enoic acid **66** (70.4 mg, 0.40 mmol), *i*Pr_2NEt (104 μL, 0.60 mmol) and pivaloyl chloride (74.0 μL, 0.60 mmol) in CH_2Cl_2 (2 mL), HBTM-2.1 (2*S*,3*R*)-**23** (1.23 mg, 0.004 mmol, 1 mol %), (NE)-*N*-(phenylimino)benzamide **60** (84.0 mg, 0.40 mmol) and *i*Pr_2NEt (174 μL, 1.00 mmol) for 15 min at rt, followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 96:4) of (2*R*)-**44** as a white solid (123 mg, 77%): mp 136−138 °C; $[\alpha]_D^{20}$ −70.8 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IB (5% IPA:hexane, flow rate 1 mL min^{-1}, 220 nm, 30 °C) t_R(2*S*) 28.5 min, t_R(2*R*) 41.2 min, 99% ee; ν_{max} (ATR)/cm^{-1} 3323 (N−H), 2890 (C−H), 1730 (C=O Ester), 1686 (C=O Amide), 1599, 1514; Data for major rotamer δ_H (500 MHz, $CDCl_3$) 3.41 (2H, d, *J* 6.1, C*H*HPh and CH*H*Ph), 3.78 (3H, s, OCH_3), 5.34−5.35 (1H, m, C(2)*H*), 5.89−6.00 (2H, m, *CH*=CHBn and CH=*CH*Bn), 6.96−6.99 (3H, m, NAr(2,6)*H* and NAr(4)*H*), 7.05−7.03 (CH_2Ar(2,6)*H*), 7.12−7.15 (CH_2Ar(3,5)*H* and CH_2Ar(4)*H*), 7.28−7.32 (2H, m, NAr(3,5)*H*), 7.48−7.51 (2H, m, C(O)Ar(3,5)*H*), 7.58−7.62 (1H, m, C(O)Ar(4)*H*), 7.85−7.86 (2H, m, C(O)Ar-(2,6)*H*), 8.68 (1H, s, N*H*); δ_C (100 MHz, $CDCl_3$) 38.9 (CH_2Ph), 52.4 (OCH_3), 64.5 (*C*(2)), 114.7 (NA*rC*(2,6)), 121.6 (NA*rC*(4)), 124.1 (CH=CHBn), 126.2 (CH_2A*rC*(4)), 127.3 (C(O)*ArC*(2,6)), 128.4 (*ArC*), 128.6 (*ArC*), 128.8 (C(O)*ArC*(3,5)), 129.4 (NA*rC*(3,5)), 132.1 (C(O)*ArC*(4)), 132.8 (C(O)*ArC*(1)), 135.7 (CH=CHBn), 138.9 (CH_2A*rC*(1)), 148.1 (NA*rC*(1)), 167.1 (NHC=O), 173.1 (MeO*C*=O); Selected data for minor rotamer δ_H (500 MHz, $CDCl_3$) 3.67 (3H, s, OCH_3), 5.06−5.08 (1H, m, C(2)*H*); δ_C (100 MHz, $CDCl_3$) 38.8 (CH_2Ph), 52.3 (OCH_3), 66.2 (*C*(2)), 115.2 (NA*rC*(2,6)), 148.7 (NA*rC*(1)); *m*/*z* (NSI^+) 401 ($[M + H]^+$, 100%); HRMS (NSI^+) $C_{25}H_{25}N_2O_3^+$ ($[M + H]^+$) requires 401.1860, found 401.1859 (−0.2 ppm).

(2*R*)-(*E*)-Methyl 2-(2-benzoyl-1-phenylhydrazinyl)-4-phenylbut-3-enoate 45. Following general procedure A, (*E*)-4-phenylbut-3-enoic acid **16** (64.9 mg, 0.40 mmol), *i*Pr_2NEt (104 μL, 0.60 mmol) and pivaloyl chloride (74.0 μL, 0.60 mmol) in CH_2Cl_2 (2 mL), HBTM-2.1 (2*S*,3*R*)-**23** (1.23 mg, 0.004 mmol, 1 mol %), (NE)-*N*-(phenylimino)benzamide **60** (84.0 mg, 0.40 mmol) and *i*Pr_2NEt (174 μL, 1.00 mmol) for 15 min at rt, followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave after chromatographic purification (eluent Et_2O:petrol 40:60) a rotameric mixture (ratio 95:5) of (2*R*)-**45** as an off-white solid (109 mg, 71%): mp 116−118 °C; $[\alpha]_D^{20}$ −19.6 (*c* 0.25, CH_2Cl_2); Chiral HPLC Chiralpak IB (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*) 22.0 min, t_R(2*R*) 27.9 min, 91% ee; ν_{max} (ATR)/cm^{-1} 3325 (N−H), 3057, 2959 (C−H), 1728 (C=O), 1693 (C=O), 1599; Data for major rotamer δ_H (500 MHz, $CDCl_3$) 3.84 (3H, s, CH_3), 5.50 (1H, d, *J* 5.1, C(2)*H*), 6.54 (1H, dd, *J* 16.3, 5.7, *CH*=CHPh), 6.76 (1H, d, *J* 16.3, CH=*CH*Ph), 6.99−7.04 (3H, m, Ar*H*), 7.24−7.41 (7H, m, Ar*H*), 7.44 (2H, t, *J* 8.7, C(O)Ar(3,5)*H*), 7.54 (1H, t, *J* 7.4, C(O)Ar(4)*H*), 7.83 (2H, d, *J* 7.4, C(O)Ar(2,6)*H*), 8.72 (1H, s, N*H*); δ_C (125 MHz, $CDCl_3$) 52.6 (CH_3), 64.9 (*C*(2)), 114.8 (NA*rC*(2,6)), 121.7 (NA*rC*(4)), 122.1 (CH=CHPh), 126.8 (=CHA*rC*(4)), 127.2 (C(O)*ArC*(2,6)), 128.3 (*ArC*), 128.7 (*ArC*), 128.8 (C(O)*ArC*(3,5)), 129.5 NA*rC*(3,5)), 132.1 (C(O)*ArC*(4)), 133.0 (C(O)*ArC*(1)), 135.0 (CH=CHPh), 135.9 (=CHA*rC*(1)), 148.0 (NA*rC*(1)), 167.6 (NHC=O), 172.8 (MeOC=O); Selected data for minor rotamer δ_H (500 MHz, $CDCl_3$) 3.73 (3H, s, CH_3), 5.21 (1H, d, *J* 7.2, C(2)*H*), 6.02 (1H, dd, *J* 16.1, 7.2, C*H*=CHPh), 7.98 (1H, s, N*H*); δ_C (125 MHz, $CDCl_3$) 52.5 (CH_3), 66.1 (*C*(2)), 115.1 (NA*rC*(2,6)), 137.5 (CH=CHPh); *m*/*z* (NSI^+) 387 ($[M + H]^+$, 100%); HRMS (NSI^+) $C_{24}H_{23}N_2O_3^+$ ($[M + H]^+$) requires 387.1703, found 387.1704 (−0.2 ppm).

(2*R*)-(*Z*)-Methyl 2-(2-benzoyl-1-phenylhydrazinyl)pent-3-enoate 46. Following general procedure A, (*Z*)-pent-3-enoic acid **68** (40.0 mg, 0.40 mmol), *i*Pr_2NEt (104 μL, 0.60 mmol) and pivaloyl chloride (74.0 μL, 0.60 mmol) in CH_2Cl_2 (2 mL), HBTM-2.1 (2*S*,3*R*)-**23** (1.23 mg, 0.004 mmol, 1 mol %), (NE)-*N*-(phenylimino)-benzamide **60** (84.0 mg, 0.40 mmol) and *i*Pr_2NEt (174 μL, 1.00 mmol) for 15 min at rt, followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 95:5) of (2*R*)-**46** (94:6 (*Z*):(*E*)) as a colorless oil (93.7 mg, 72%): $[\alpha]_D^{20}$ −76.8 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak AD-H (20% IPA:hexane, flow rate 1 mL min^{-1}, 220 nm, 30 °C) t_R(2*S*) 19.1 min, t_R(2*R*) 23.6 min, 99% ee; ν_{max} (ATR)/cm^{-1} 3291 (N−H), 2953 (C−H), 1732 (C=O Ester), 1674 (C=O Amide), 1599; Data for major isomer (*Z*) and major rotamer δ_H (400 MHz, $CDCl_3$) 1.88 (3H, dd, *J* 7.0, 1.8, CH_3CH=), 3.75 (3H, s, OCH_3), 5.48 (1H, d, *J* 8.2, C(2)*H*), 5.61−5.67 (1H, m, *CH*=CHCH$_3$), 5.91 (1H, dqd, *J* 10.7, 7.0, 1.0, CH=*CH*CH_3), 6.93−6.99 (3H, m, NAr(2,6)*H* and NAr(4)*H*), 7.26−7.30 (2H, m, NAr(3,5)*H*), 7.46−7.51 (2H, m, C(O)Ar(3,5)*H*), 7.54−7.59 (1H, m, C(O)Ar(4)*H*), 7.88−7.91 (2H, m, C(O)Ar(2,6)*H*), 8.67 (1H, s, N*H*); δ_C (100 MHz, $CDCl_3$) 14.1 (CH_3CH=), 52.6 (OCH_3), 59.8 (*C*(2)), 114.7 (NA*rC*(2,6)), 121.6 (NA*rC*(4)), 121.7 (CH=CHCH$_3$), 127.4 (C(O)*ArC*(2,6)), 128.9 (C(O)*ArC*(3,5)), 129.5 (NA*rC*(3,5)), 132.2 (C(O)*ArC*(4), 132.7 (CH=*CH*CH$_3$), 132.8 (C(O)*ArC*(1)), 148.3 (NA*rC*(1)), 167.0 (NHC=O), 173.6 (MeO*C*=O); *m*/*z* (NSI^+) 325 ($[M + H]^+$, 100%); HRMS (NSI^+) $C_{19}H_{21}N_2O_3^+$ ($[M + H]^+$) requires 325.1547, found 325.1548 (+0.4 ppm).

(2*R*)-(*E*)-Methyl 2-(2-(4-fluorobenzoyl)-1-phenylhydrazinyl)-pent-3-enoate 47. Following general procedure A, (*E*)-pent-3-enoic acid **24** (40.6 μL, 0.40 mmol), *i*Pr_2NEt (104 μL, 0.60 mmol) and pivaloyl chloride (74.0 μL, 0.60 mmol) in CH_2Cl_2 (2 mL), HBTM-2.1 (2*S*,3*R*)-**23** (1.23 mg, 0.004 mmol, 1 mol %), (NE)-4-fluoro-*N*-(phenylimino)benzamide **61** (91.2 mg, 0.40 mmol) and *i*Pr_2NEt (174 μL, 1.00 mmol) for 15 min at rt, followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave after chromatographic purification (eluent Et_2O:petrol 40:60) a rotameric mixture (ratio 92:8) of (2*R*)-**47** as a white solid (109 mg, 79%): mp 102−104 °C; $[\alpha]_D^{20}$ −57.8 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IB (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*) 13.2 min, t_R(2*R*) 17.1 min, 99% ee; ν_{max} (ATR)/cm^{-1} 3522 (N−H), 2951 (C−H), 1751 (C=O), 1661 (C=O), 1599; Data for major rotamer δ_H (500 MHz, $CDCl_3$) 1.68−1.69 (3H, m, CH_3CH=), 3.76 (3H, s, OCH_3), 5.21−5.22 (1H, m, C(2)*H*), 5.74−5.84 (2H, m, *CH*=CHCH$_3$ and CH=*CH*CH$_3$), 6.91−6.95 (3H, m, NAr(2,6)*H* and NAr(4)*H*), 7.13−7.17 (2H, t, *J* 8.4, NAr(3,5)*H*), 7.24−7.27 (2H, m, C(O)Ar(3,5)*H*), 7.84−7.87 (2H, m, C(O)Ar(2,6)*H*), 8.60 (1H, s, N*H*); δ_C (125 MHz, $CDCl_3$) 18.2 (CH_3CH=), 52.4 (OCH_3), 64.6 (*C*(2)), 114.8 (NA*rC*(2,6)), 116.0 (d, *J* 21.8, C(O)*ArC*(3,5)), 121.7 (NA*rC*(4)), 123.7 (CH=CHCH$_3$), 129.2 (d, *J* 3.5, C(O)*ArC*(1)), 129.5 (NA*rC*(3,5)), 129.7 (d, *J* 8.7, C(O)*ArC*(2,6)), 132.4 (CH=*CH*CH$_3$), 148.1 (NA*rC*(1)), 165.2 (d, *J* 252, C(O)*ArC*(4)), 166.4 (NHC=O), 173.4 (MeOC=O); δ_F (376 MHz, $CDCl_3$) −107.6 (Ar*F*); Selected data for minor rotamer δ_H (500 MHz, $CDCl_3$) 1.61−1.62 (3H, m, CH_3CH=), 3.65 (3H, s, OCH_3), 4.95 (1H, d, *J* 7.3, C(2)*H*), 7.36 (2H, dd, *J* 8.8, 7.4, C(O)Ar(3,5)*H*), 7.58−7.61 (2H, C(O)Ar(2,6)*H*); δ_C (125 MHz, $CDCl_3$) 18.2 (CH_3CH=), 52.4 (OCH_3), 66.0 (*C*(2)), 114.8 (NA*rC*(2,6)); δ_F (376 MHz, $CDCl_3$) −108.8 (Ar*F*); *m*/*z* (NSI^+) 343 ($[M + H]^+$, 100%); HRMS (NSI^+) $C_{19}H_{20}FN_2O_3^+$ ($[M + H]^+$) requires 343.1452, found 343.1458 (+1.6 ppm).

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(2*R*)-(*E*)-Methyl 2-(2-(furan-2-yl)-1-phenylhydrazinyl)pent-3-enoate 48. Following general procedure A, (*E*)-pent-3-enoic acid **24** (40.6 μL, 0.40 mmol), iPr$_2$NEt (104 μL, 0.60 mmol) and pivaloyl chloride (74.0 μL, 0.60 mmol) in CH_2Cl_2 (2 mL), HBTM-2.1 (2*S*,3*R*)-**23** (1.23 mg, 0.004 mmol, 1 mol %), (NE)-*N*-(phenylimino)-furan-2-carboxamide **62** (80.0 mg, 0.40 mmol) and iPr$_2$NEt (174 μL, 1.00 mmol) for 15 min at rt, followed by addition of MeOH (2 mL) and stirring for 1 h at rt gave after chromatographic purification (eluent Et_2O:petrol 50:50) a rotameric mixture (ratio 94:6) of (2*R*)-**48** as a colorless oil (109 mg, 87%): $[\alpha]_D^{20}$ −82.4 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IB (5% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(2*S*) 16.0 min, t_R(2*R*) 22.2 min, 99% ee; ν_{max} (ATR)/cm^{-1} 3335 (N−H), 2953 (C−H), 1730 (C═O), 1688 (C═O), 1589; Data for major rotamer δ_H (500 MHz, $CDCl_3$) 1.70 (3H, dt, *J* 6.4, 1.3, CH_3CH═), 3.76 (3H, s, OCH_3), 5.20−5.21 (1H, m, C(2)*H*), 5.75 (1H, ddq, *J* 15.6, 6.0, 1.5, C*H*═CHCH$_3$), 5.74 (1H, dqd, *J* 15.6, 6.4, 1.2, CH═C*H*CH$_3$), 6.56 (1H, dd, *J* 3.5, 1.8, C(O)Ar(4)*H*), 6.92−6.95 (3H, m, NAr(2,6)*H* and NAr(4)*H*), 7.24−7.27 (3H, m, NAr(3,5)*H* and C(O)Ar(3)*H*), 7.52 (1H, dd, *J* 1.7, 0.8, C(O)Ar(5)*H*), 8.75 (1H, s, N*H*); δ_C (125 MHz, $CDCl_3$) 18.2 (*C*H$_3$CH═), 52.4 (O*C*H$_3$), 64.7 (*C*(2)), 112.2 (C(O)*ArC*(4)), 114.8 (N*ArC*(2,6)), 115.9 (C(O)*ArC*(3)), 121.6 (N*ArC*(4)), 123.3 (*C*H═CHCH$_3$), 129.4 (N*ArC*(3,5)), 132.8 (CH═*C*HCH$_3$), 144.7 (C(O)*ArC*(5)), 146.6 (C(O)*ArC*(2)), 148.1 (N*ArC*(1)), 158.2 (NH*C*═O), 173.0 (MeO*C*═O); Selected data for minor rotamer δ_H (500 MHz, $CDCl_3$) 3.69 (3H, s, OCH_3), 5.10 (1H, d, *J* 7.1, C(2)*H*), 6.38 (1H, dd, *J* 3.5, 1.7, C(O)Ar(3)*H*); δ_C (125 MHz, $CDCl_3$) 18.1 (*C*H$_3$CH═), 52.4 (O*C*H$_3$), 65.5 (*C*(2)), 111.6 (C(O)*ArC*(4)), 115.0 (N*ArC*(2,6)), 129.8 (N*ArC*(3,5)), 145.6 (C(O)*ArC*(5)); *m*/*z* (NSI$^+$) 315 ([M + H]$^+$, 100%); HRMS (NSI$^+$) $C_{17}H_{19}N_2O_4^+$ ([M + H]$^+$) requires 315.1339, found 315.1335 (−1.4 ppm).

(3*R*,4*R*,5*R*)-*N*′-(4-Hydroxy-5-methyl-2-oxooxolan-3-yl)-*N*′-phenylbenzohydrazide amine 49 and (3*R*,4*S*,5*S*)-*N*′-(4-Hydroxy-5-methyl-2-oxooxolan-3-yl)-*N*′-phenylbenzohydrazide amine 50. To a solution of hydrazide (2*R*)-**41** (1.12 g, 3.44 mmol) in acetone:water (9:1, 40 mL) was added 2,6-lutidine (0.80 mL, 6.88 mmol), *N*-methylmorpholine-*N*-oxide (0.60 g, 5.16 mmol) and OsO_4 (4 wt % in H_2O, 0.44 mL, 0.07 mmol), and the reaction mixture was stirred at rt for 5 h, after which time it was quenched by addition of sat. aq. $Na_2S_2O_3$. The reaction mixture was extracted with EtOAc (×3), and the combined organic fractions were washed with HCl (2 M in H_2O), dried ($MgSO_4$), filtered, and concentrated in vacuo to give a mixture of crude diols (2*R*,3*R*,4*R*)-**49** and (2*R*,3*S*,4*S*)-**50**, which were used directly in the next reaction without purification. The crude reaction mixture was dissolved in CH_2Cl_2 (50 mL) and treated with *p*-toluenesulfonic acid (0.65 g, 3.44 mmol). The reaction mixture was stirred at rt for 2 h before being quenched by addition of H_2O. The reaction mixture was extracted with CH_2Cl_2 (×3), and the combined organic fractions were dried ($MgSO_4$), filtered, and concentrated in vacuo to give crude lactones (3*R*,4*R*,5*R*)-**49** and (3*R*,4*S*,5*S*)-**50** (70:30 dr).

Major diastereoisomer. Chromatographic purification (eluent Et_2O:petrol 60:40 to 100% Et_2O) gave lactone (3*R*,4*R*,5*R*)-**49** (>99:1 dr) as a white solid (0.59 g, 53%): mp 58−60 °C; $[\alpha]_D^{20}$ +37.0 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralcel OJ-H (10% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*S*,5*S*) 13.5 min, t_R(3*R*,4*R*,5*R*) 19.3 min, 99% ee; ν_{max} (ATR)/cm^{-1} 3306 (N−H and O−H), 2980 (C−H), 1767 (lactone C═O), 1661 (amide C═O), 1597; δ_H (500 MHz, $CDCl_3$) 1.44 (3H, d, *J* 6.3, CH_3), 4.73−4.79 (3H, m, C(3)*H*, C(4)*H* and C(5)*H*), 5.02 (1H, br s, O*H*), 6.93−6.96 (3H, m, NAr(2,6)*H* and NAr(4)*H*), 7.24 (2H, td, *J* 9.1, 1.7, NAr(3,5)*H*), 7.43−7.46 (2H, m, C(O)Ar(3,5)*H*), 7.58 (1H, tt, *J* 7.5, 1.4, C(O)Ar(4)*H*), 7.79−7.81 (2H, m, C(O)Ar(2,6)*H*), 8.58 (1H, br s, N*H*); δ_C (125 MHz, $CDCl_3$) 14.9 (*C*H$_3$), 66.8 (*C*(3)), 69.3 (*C*(4)), 77.3 (*C*(5)), 114.7 (N*ArC*(2,6)), 121.7 (N*ArC*(4)), 127.6 (*ArC*), 129.0 (*ArC*), 129.5 (*ArC*), 131.4 (C═O*ArC*(1)), 133.0 (C═O*ArC*(4)), 148.0 (N*ArC*(1)), 168.8 (NH*C*═O), 172.0 (MeO*C*═O); *m*/*z* (NSI$^+$) 327 ([M + H]$^+$, 86%); HRMS (NSI$^+$) $C_{18}H_{19}N_2O_4^+$ ([M + H]$^+$) requires 327.1339, found 327.1345 (+1.7 ppm).

Minor diastereoisomer. Chromatographic purification (eluent Et_2O:petrol 60:40 to 100% Et_2O) gave lactone (3*R*,4*S*,5*S*)-**50** (>99:1 dr) as a white solid (0.28 g, 25%): mp 110−112 °C; $[\alpha]_D^{20}$ −266.4 (*c* 0.5, CH_2Cl_2); Chiral HPLC Chiralpak IA (40% IPA:hexane, flow rate 1 mL min^{-1}, 211 nm, 30 °C) t_R(3*S*,4*R*,5*R*) 8.9 min, t_R(3*R*,4*S*,5*S*) 14.8 min, 99% ee; ν_{max} (ATR)/cm^{-1} 3238 (N−H and O−H), 2938 (C−H), 1776 (lactone C═O), 1668 (amide C═O), 1597, 1510; δ_H (500 MHz, $CDCl_3$) 1.51 (3H, d, *J* 6.3, CH_3), 4.61−4.65 (2H, m, C(4)*H* and C(5)*H*), 4.76 (1H, d, *J* 4.3, C(3)*H*), 4.95 (1H, s, O*H*), 6.88 (2H, d, *J* 8.0, NAr(2,6)*H*), 6.97 (1H, t, *J* 7.4, NAr(4)*H*), 7.30 (2H, tt, *J* 7.2, 1.8, NAr(3,5)*H*), 7.48−7.51 (2H, m, C(O)Ar(3,5)*H*), 7.58−7.62 (1H, m, C(O)Ar(4)*H*), 7.89−7.91 (2H, m, C(O)Ar(2,6)*H*), 8.92 (1H, s, N*H*); δ_C (125 MHz, $CDCl_3$) 13.9 (*C*H$_3$), 67.7 (*C*(3)), 70.3 (*C*(4)), 79.4 (*C*(5)), 113.0 (N*ArC*(2,6)), 121.5 (N*ArC*(4)), 127.6 (*ArC*), 129.1 (*ArC*), 129.8 (*ArC*), 131.4 (C═O*ArC*(1)), 133.1 (C═O*ArC*(4)), 147.3 (N*ArC*(1)), 168.9 (NH*C*═O), 172.0 (MeO*C*═O); *m*/*z* (NSI$^+$) 327 ([M + H]$^+$, 100%); HRMS (NSI$^+$) $C_{18}H_{19}N_2O_4^+$ ([M + H]$^+$) requires 327.1339, found 327.1346 (+2.0 ppm).

(3*R*,4*R*,5*R*)-4-Hydroxy-5-methyl-2-(phenylamino)-dihydrofuran-2(3*H*)-one 79. To a solution of lactone (3*R*,4*R*,5*R*)-**49** (65.2 g, 0.20 mmol) in MeOH (2 mL) at −78 °C was added SmI_2 (0.1 M in THF, 6.00 mL, 0.60 mmol), and the reaction mixture was stirred at −78 °C for 10 min, after which time it was quenched by addition of sat. aq. $NaHCO_3$. The reaction mixture was extracted with EtOAc (×3), and the combined organic fractions were dried ($MgSO_4$), filtered, and concentrated in vacuo. Chromatographic purification (eluent Et_2O:petrol 60:40) gave lactone (3*R*,4*R*,5*R*)-**79** as a colorless oil (29.0 mg, 70%): $[\alpha]_D^{20}$ +18.0 (*c* 0.1, CH_2Cl_2); ν_{max} (ATR)/cm^{-1} 3381 (N−H or O−H), 2986 (C−H), 1761 (C═O), 1603, 1499; δ_H (500 MHz, $CDCl_3$) 1.45 (3H, d, *J* 6.8, CH_3), 2.74 (1H, d, *J* 4.9, O*H* or N*H*), 4.13 (1H, s, O*H* or N*H*), 4.18−4.19 (1H, m, C(3)*H*), 4.41 (1H, td, *J* 7.0, 4.8, C(4)*H*), 4.73 (1H, app. quintet, *J* 6.7, C(5)*H*), 6.80−6.85 (3H, m, NAr(2,6)*H* and NAr(4)*H*), 7.19−7.23 (2H, m, NAr(3,5)*H*); δ_C (125 MHz, $CDCl_3$) 14.7 (*C*H$_3$), 59.6 (*C*(3)), 74.9 (*C*(4)), 77.4 (*C*(5)), 114.1 (N*ArC*(2,6)), 119.6 (N*ArC*(4)), 129.6 (N*ArC*(3,5)), 146.8 (N*ArC*(1)), 174.2 (C═O); *m*/*z* (NSI$^+$) 208 ([M + H]$^+$, 100%); HRMS (NSI$^+$) $C_{11}H_{14}NO_3^+$ ([M + H]$^+$) requires 208.0968, found 208.0968 (−0.1 ppm).

(3*R*,4*S*,5*S*)-4-Hydroxy-5-methyl-2-(phenylamino)-dihydrofuran-2(3*H*)-one 80. To a solution of lactone (3*R*,4*S*,5*S*)-**50** (65.2 g, 0.20 mmol) in MeOH (2 mL) at −78 °C was added SmI_2 (0.1 M in THF, 6.00 mL, 0.60 mmol), and the reaction mixture was stirred at −78 °C for 10 min, after which time it was quenched by addition of sat. aq. $NaHCO_3$. The reaction mixture was extracted with EtOAc (×3), and the combined organic fractions were dried ($MgSO_4$), filtered, and concentrated in vacuo. Chromatographic purification (eluent Et_2O:petrol 60:40) gave lactone (3*R*,4*S*,5*S*)-**80** as a colorless oil (31.4 mg, 76%): $[\alpha]_D^{20}$ −98.0 (*c* 0.1, CH_2Cl_2); ν_{max} (ATR)/cm^{-1} 3389 (N−H or O−H), 2982 (C−H), 1761 (C═O), 1603, 1506; δ_H (400 MHz, $CDCl_3$) 1.47 (3H, d, *J* 6.5, CH_3), 2.76 (1H, br s, O*H* or N*H*), 4.08 (1H, d, *J* 4.4, C(3)*H*), 4.40 (1H, dd, *J* 4.4, 2.9, C(4)*H*), 4.58 (1H, qd, *J* 6.5, 2.9, C(5)*H*), 6.67−6.70 (2H, m, NAr(2,6)*H*), 6.84 (1H, tt, *J* 7.4, 1.0, NAr(4)*H*), 7.16−7.21 (2H, m, NAr(3,5)*H*); δ_C (100 MHz, $CDCl_3$) 13.8 (*C*H$_3$), 60.4 (*C*(3)), 69.8 (*C*(4)), 78.6 (*C*(5)), 114.2 (N*ArC*(2,6)), 120.5 (N*ArC*(4)), 129.6 (N*ArC*(3,5)), 146.0 (N*ArC*(1)), 174.6 (C═O); *m*/*z* (NSI$^+$) 208 ([M + H]$^+$, 100%); HRMS (NSI$^+$) $C_{11}H_{14}NO_3^+$ ([M + H]$^+$) requires 208.0968, found 208.0968 (−0.1 ppm).

■ ASSOCIATED CONTENT

Supporting Information

β-Lactam epimerization studies, assignments of aza-sugar relative configurations, X-ray structural data, spectral and HPLC data for all new compounds are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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AUTHOR INFORMATION

Corresponding Author

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

Notes

The authors declare no competing financial interest.

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(20) All experiments were carried out under air using bench grade solvents as standard.

(21) Other carboxylic acid starting materials, namely, (*E*)-3-phenylbut-2-enoic acid **70** and (*E*)-3,4-diphenylbut-2-enoic acid **72**, were tested to attempt to access ammonium dienolates, which react at the γ-position, but none were successful.

(22) The relative configurations of β-lactones (*anti* **21**, *syn* **73**) and β-lactams (*anti* **22**, *syn* **74**) in Table 1 were confirmed unambiguously by X-ray crystallography. Crystallographic data for all diastereoisomers **21**, **22**, **73**, and **74** have been deposited with the Cambridge Crystalographic Data Centre as supplementary publication numbers CCDC 968689, 968690, 968692, and 968693.

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(25) Racemic samples of all β-lactams in Tables 2 and 3 were prepared using achiral catalyst DHPB **17**.
(26) The absolute configuration of *syn*-β-lactam **27** was confirmed unambiguously by X-ray crystallography as (3*S*,4*S*). Crystallographic data for **27** has been deposited with the Cambridge Crystalographic Data Centre as supplementary publication number CCDC 968691.
(27) See Supporting Information for full details of the epimerization experiment.
(28) Poor conversion to β-lactams **28** and **29** is observed when the reactions are carried out at −78 °C.
(29) All reactions quoted at −78 °C were also carried out at rt, typically giving lower enantioselectivities for β-lactam products. See Supporting Information for these results.
(30) Racemic (±)-**36** was prepared using (±)-HBTM-2.1 **23**. Racemic samples of all products in Table 4 were made using (±)-HBTM-2.1 **23** as a catalyst.
(31) The minor diastereoisomer was formed in 15% ee. The enantioselectivities of all minor diastereoisomers in Table 4 can be found in the Supporting Information.
(32) The relative and absolute configuration of δ-lactone **36** was assigned by comparison with the literature ref 16d. All other products in Table 4 were assigned by analogy.
(33) The initial heterocyclic products were immediately ring-opened with methanol because of their instability toward chromatographic purification on silica.
(34) The absolute configuration of hydrazide **41** was assigned by comparison with the literature ref 16c. All other products in Table 5 were assigned by analogy.
(35) Racemic (±)-**41** was prepared using the achiral isothiourea DHPB **17**. Racemic samples of all products in Table 5 were made using DHPB **17** as a catalyst.
(36) The N−N bond in lactones **49** and **50** were cleaved using SmI_2 in 70 and 76% yield, respectively. Coupling constant analysis in addition to NOE studies of these products allowed the relative configurations of lactones **49** and **50** to be assigned. See Supporting Information for details.
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