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Synthesis of Chiral γ-Lactones by One-Pot Sequential Enantioselective Organocatalytic Michael Addition of Boronic Acids and Diastereoselective Intramolecular Passerini Reaction

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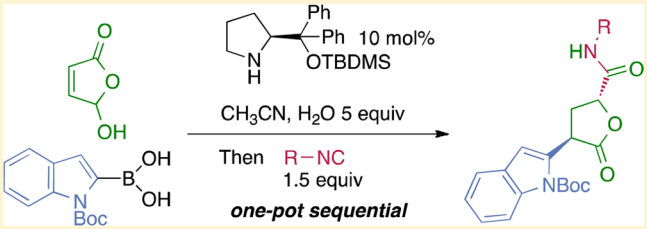
Supporting Information

ABSTRACT: The synthesis of α,γ-substituted chiral γ-lactones was quickly achieved in a one pot sequential process. The procedure involves an enantioselective organocatalysed transfer of boronic acid to 5-hydroxyfuran-2(5*H*)-one, followed by an intramolecular diastereoselective Passerini-type reaction. The methodology was developed and optimized with *N*-Boc-indole-2-boronic acid giving access to α-indole-γ-substituted lactones in high yields and good diastereoisomeric and enantiomeric ratios. By applying the process to other boronic acids, the synthesis of structurally diversified α,γ-substituted chiral lactones was also achieved in good yields albeit with lower enantioselectivities.



INTRODUCTION

The development of synthetic methodologies enabling the increase of molecular diversity starting from simple and readily available materials is an ongoing challenge in organic synthesis. The two main fields of organic synthesis, i.e., target-oriented synthesis (TOS) and diversity-oriented synthesis (DOS),[1,2] are expected to benefit from these new methodologies. The chemical biology and medicinal chemistry areas are especially concerned with the development of new methods allowing efficient functionalization of privileged heterocyclic structures.[3−5] Therein, the exploration of chemical space by increasing the number of sp^3 hybridized carbons is of particular interest,[6] even more so with the stereospecific construction of an sp^3 hybridized asymmetric center.[7,8] A promising strategy to address this task is to combine an enantioselective organocatalytic step and a multicomponent reaction (MCR)[9] to increase chemical diversity on the chiral primary adduct through a tandem one-pot process.[10−14] In this context we recently explored a new synthetic application of γ-hydroxybutenolides.[15] We demonstrated that 5-hydroxyfuran-2(5*H*)-one **1**, a readily available biobased molecule, can be engaged in an efficient one pot sequential process involving an enantioselective organocatalytic Friedel−Crafts and a 4-center 3-component Ugi reaction.[16] In order to further demonstrate the usefulness of **1** as reactant in both organocatalytic and multicomponent reaction processes, we described herein a one pot sequential procedure involving the organocatalytic enantioselective transfer of a boronic acid substituent and the subsequent transformation of the intermediate into an α,γ-substituted chiral lactone via an intramolecular Passerini type reaction (Scheme 1).[17] Inspired by the mechanism of the Petasis reaction,[18−20] efficient enantioselective organocatalytic transfers of boronic acids to α,β-unsaturated carbonyl compounds have been recently reported.[21−29] When the α,β-unsaturated carbonyl compound is activated by the catalyst (i.e., LUMO-lowering activation), the process usually requires activation of the boronic acid by the substrate as an "ate complex". This substrate activation entails the use of a restricted class of α,β-unsaturated carbonyl compounds.[23,25,26,29] The use of vinyl and heteroaryl trifluoroborate salts,[22] even if the use of an hydrofluoric acid additive is required, overcame this limitation and found spectacular application in the total synthesis of natural products.[24] However, the use of polyfunctional α,β-unsaturated carbonyl derivatives able to activate boronic acids is particularly interesting when its functionality is further exploited in a consecutive step. On the basis of our working hypothesis, the carboxylate group on the iminium ion resulting from the activation of 5-hydroxyfuran-2(5*H*)-one **1** by secondary amine catalyst should activate the boronic acid as an "ate complex" (intermediate I, Scheme 1). The chiral adducts obtained after boronic acid substituent migration (intermediate II) should then react with isocyanides to produce the desired variously substituted chiral lactones (Scheme 1).

RESULTS AND DISCUSSION

In view of the biological relevance of the indole moiety,[5,30] the *N*-Boc-indole-2-boronic acid **3** was first chosen as a reaction partner. As we have previously established, the catalysts derived from diphenyl prolinol are suitable to activate the 5-

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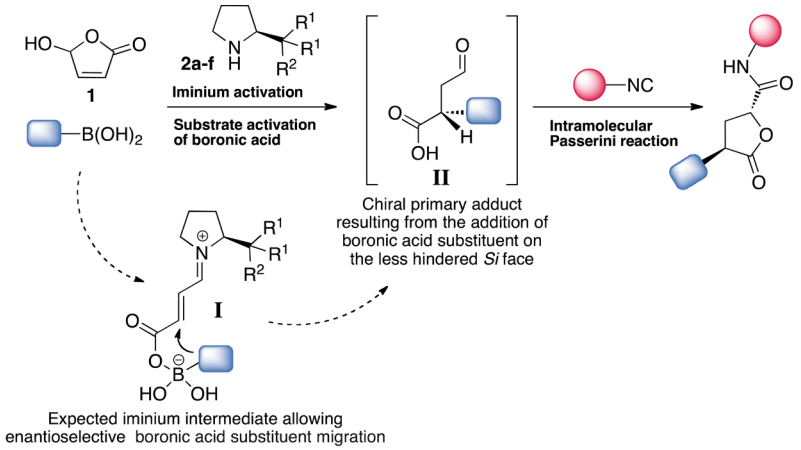
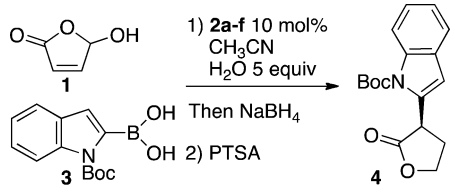
Scheme 1. Approach to Chiral α,γ-Substituted γ-Lactones



	2a	2b	2c	2d	2e	2f
R^1	Ph	Ph	Ph	Ph	Ph	3,5-Ph(CF_3)$_2$
R^2	OH	OCH_3	OTMS	OTBDMS	F	OTBDMS

hydroxyfuran-2(5H)-one **1**.[16] Reactions were conducted on 0.5 mmol scale in the presence of 10 mol % of catalysts **2a–f** and 1.1 equiv of indole boronic acid **3** in acetonitrile at 0 °C. In a first instance, the organocatalytic enantioselective transfer of the boronic acid substituent to 5-hydroxyfuran-2(5*H*)-one **1** was evaluated by conversion of the addition adduct into the monosubstituted lactone **4** (Table 1). In the preliminary

Table 1. Organocatalytic Transfer of Boronic Acid to the 5-Hydroxyfuranone-2(5*H*)-one 1[a]



entry	catalyst	time[b] (h)	yield (%)	er[c]
1	**2a**	6	93	92:8
2	**2b**	10	67	70:30
3	**2c**	12	86	83:17
4	**2d**	2	98	92:8
5	**2e**	3	93	87:13
6	**2f**	4.5	80	91:9
7	**2d**	2	60[d]	99:1[d]

[a]The reactions were carried out at 0 °C with 0.55 mmol of boronic acid, 0.5 mmol of 5-hydroxyfuran-2(5*H*)-one **1**, 0.05 mmol of catalyst **2** in CH_3CN (1.5 mL) and water (45 μL). [b]Reaction time needed for the total consumption of 5-hydroxyfuran-2(5*H*)-one **1** in the organocatalytic boronic acid transfer. [c]Determined by chiral HPLC analysis; absolute configuration was assigned by X-ray crystallography. [d]Reaction carried out on 1 mmol scale; yield and er obtained after recrystallization.

experiments using diphenyl prolinol **2a** as catalyst we were pleased to isolate the expected product **4**, nevertheless we encountered great variation in the reaction time of the boronic acid substituent transfer as well as inconsistencies in the isolated yields of the lactone **4**. After careful examination of the experimental conditions, we found that the amount of water in the reaction medium strongly affected the reaction. When the reaction was carried out under anhydrous conditions, very low conversion of the addition adduct was observed even after prolonged reaction time. The presence of a large excess of water led to sluggish transfer of the boronic acid substituent. In the end, we established that the addition of 5 equiv of water allowed the transformation with reproducible reaction times and isolated yields. When the reaction was performed under these reaction conditions, full consumption of compound **1** was observed after 6 h (entry 1). After in situ reduction by $NaBH_4$ and lactonization of the obtained chiral primary adduct, the lactone **4** was isolated in very good yield (93%) and good enantiomeric ratio (92:8). We have previously established that iminium activation of **1** is efficient in both anhydrous conditions and in the presence of a large excess of water, as exemplified in Friedel–Craft reactions.[16] In the present reaction conditions, the boric acid, which accumulates during the reaction course, can unfavorably interfere with the catalytic cycle. We think that the addition of an optimized amount of water might limit this interference. In order to further improve the process, a broader range of catalysts belonging to the diphenylprolinol family was evaluated. In all cases the reaction was efficient and lactone **4** was isolated in good to excellent yields (from 67 to 98%, entries 2 to 6). Longer reaction time and lower yields of lactone **4** were observed when catalysts **2b** and **2c** containing OCH_3 and OTMS groups instead of the hydroxyl group were used (entries 2 and 3). Lower enantioselectivities were also noticed using these two catalysts; however, the same major enantiomer was obtained, which imply that specific involvement of the hydroxyl group in the catalyst activation mode could be excluded. This fact was confirmed by the good catalytic performance of diphenylprolinol silyl ether **2d**. Indeed when catalyst **2d** was used, a significantly shorter reaction time (2 h) and higher isolated yield (98%) were observed (entry 4) while maintaining a good enantioselectivity (er 92:8). Unfortunately neither the use of catalyst **2e**[31] and **2f** with potentially higher shielding effect (Table 1, entries 5 and 6) nor the use of different solvents (Table 2, entries 2–11) improved the enantiomeric ratio of the lactone **4**. In all other tested solvents this ratio decreased until 71:29 (Table 2). The migration of the boronic acid substituent worked well in a shorter time (from 1.5 h to 6 h) in other

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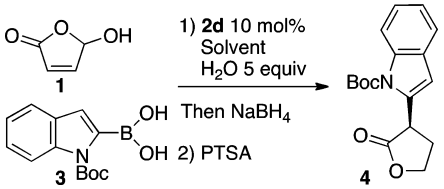
Table 2. Solvent Effect on Boronic Acid Transfer to 5-Hydroxyfuranone-2(5*H*)-one[a]



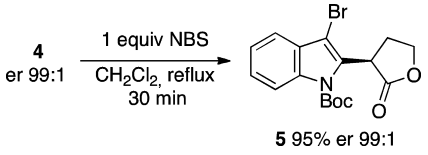
entry	solvent	time[b] (h)	yield (%)	er[c]
1	CH_3CN	2	98	92:8
2	CH_3CH_2CN	1.5	85	82:18
3	nBuCN	2	83	85:15
4	EtOAc	6	76	78:22
5	DCM	2	67	85:15
6	MTBE	48	60	82:18
7	DME	48	55	71:29
8	MeTHF	48	60	78:22
9	EtOH	24	62	84:16
10	DMF	240	42	80:20
11	DMSO	240	20	78:22

[a]The reactions were carried out at room temperature with 0.55 mmol of boronic acid, 0.5 mmol of 5-hydroxyfuran-2(5*H*)-one **1**, 0.05 mmol of catalyst **2d** in solvent (1.5 mL) and water (45 μL). [b]Reaction time needed for the total consumption of 5-hydroxyfuran-2(5*H*)-one **1** in the organocatalytic boronic acid transfer. [c]Determined by chiral HPLC analysis; absolute configuration was assigned by X-ray crystallography.

nitrile solvents (entries 2 and 3), ethyl acetate (entry 4) and dichloromethane (entry 5) but occurred much more slowly in ethereal solvents (entries 6–8) and in ethanol (entry 9). In polar aprotic solvents, DMF and DMSO, the reaction was not complete after prolonged reaction time entailing low yields in lactone **4** (entries 10–11). Finally, the practicality of the process was illustrated by the synthesis of the lactone **4** under optimized conditions in high enantiomeric purity (er 99:1) and in 60% yield after recrystallization (Table 1, entry 7).

In order to assign the absolute configuration of lactone **4**, lactone **5** bearing a bromine atom on the aromatic ring was obtained in 95% yield using *N*-bromosuccinimide as brominating agent (Scheme 2). This transformation proceeded without

Scheme 2. Synthesis of the Brominated Lactone 5



loss of enantiomeric purity. According to the X-ray data obtained for lactone **5**, the absolute configuration of the created stereocenter was assigned as *R* using anomalous dispersion (Figure 1). This stereochemistry is in accordance with our working hypothesis involving the formation of the iminium intermediate **I** and the migration of the boronic acid substituent through the less hindered *Si* face (Scheme 1).

Having established convenient reaction conditions for the asymmetric transfer of the boronic acid substituent, we then explored the one pot synthesis of substituted α,γ-substituted lactones by transformation of the primary adduct by an intramolecular Passerini reaction. The reaction of isocyanide with bifunctional reagents, especially tethered aldehyde and

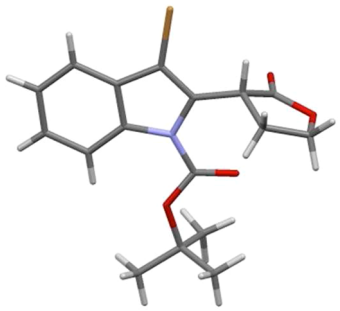


Figure 1. Structure of compound **5** from single-crystal X-ray data.

keto acids, is a commonly used strategy to obtain heterocycles.[32] Despite the numerous studies involving the Ugi reaction,[32] only a few deal with the intramolecular Passerini reaction.[33−36] Notably, and to the best of our knowledge, a direct access to chiral lactone using the intramolecular Passerini reaction as a key step has not been previously reported. In our prototypical synthesis, 1.5 equiv of isocyanide was added after the transfer of the boronic acid substituent under the previously optimized conditions. The reaction mixture was then stirred at room temperature until full consumption of the chiral primary adduct (Scheme 3). When the reaction was carried out with *N*-Boc-indole-2-boronic acid **3** and *tert*-butyl isocyanide, the ^{1}H NMR spectra of the crude reaction mixture showed the formation of the expected γ-lactones **6a** and **6b** in a diastereoisomeric ratio of 72:28. These two diastereoisomeric γ-lactones **6a** and **6b** were easily isolated by chromatography in high yields (56 and 17% respectively). An enantiomeric ratio of 90:10 was obtained for both of them. The X-ray crystallography structure of the minor diastereoisomer **6b** revealed a *cis* relationship between the two substituents of the γ-lactone ring. The compounds **7a** and **7b** bearing a methoxygroup on the indole ring were obtained in the same range of yields, diastereoselectivity (dr 75:25) and enantioselectivity (er 96:4).

The overall process required trivial reaction conditions and only one purification step to obtain γ-lactones in high yields. It is noteworthy that a good level of diastereoselectivity was obtained for this Passerini type reaction.[37] The enantiomeric ratios obtained are in accordance with those observed for the simple transfer of the boronic acid (Table 1) indicating no significant depletion of the chirality during the Passerini reaction. In order to establish the influence of the reaction conditions on the diastereoselectivity of the intermolecular Passerini reaction, an acidic aqueous work up (CH_2Cl_2/HCl 1 N) was done before the addition of the isocyanide to remove the catalyst and the formed boric acid. After evaporation of the solvent, the obtained chiral primary adducts were engaged in the Passerini reaction. In acetonitrile, the same diasteroselectivity was obtained. In dichloromethane, lower diasteroselectivity (dr 60:40) was observed. We also checked to see if the observed diastereoselectivity could be the result of epimerization in the γ position of the final lactone leading to a steady ratio of diastereoisomers. The two diastereoisomers **6a** and **6b** exhibited a configurational stability over a period of 24 h in acetonitrile both in neutral conditions and in the presence of one equivalent of boric acid. These results clearly indicate that diastereoselectivity cannot arise from an epimerization process leading to a thermodynamic mixture of diastereoisiomers. The complexity of Passerini reaction mechanism and the difficulty in establishing a model for such a 1,3-asymmetric induction, make

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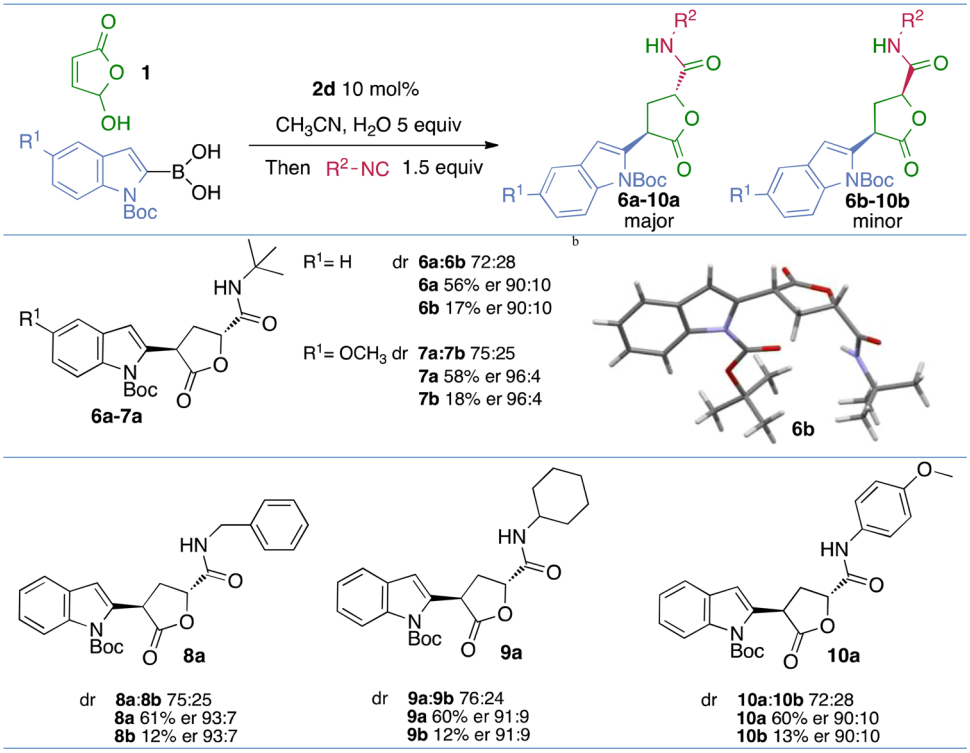
Scheme 3. Access to Indole Substituted Chiral γ-Lactones 6−10 by One Pot Sequential Sequence Enantioselective Organocatalytic Michael Addition of Boronic Acid and Diastereoselective Intramolecular Passerini Reaction[a,b]



[a]The reactions were carried out with 1.1 mmol of boronic acid, 1 mmol of 5-hydroxyfuran-2(5*H*)-one **1**, 0.10 mmol of catalyst **2d** in CH_3CN (1.5 mL) and water (90 μL). The reactions were stirred at 0 °C until full conversion of **1** (TLC analysis). 1.5 mmol of isocyanide and CH_3CN (1.5 mL) were then added, and the reactions were stirred at room temperature until full consumption of primary adduct. dr determined by ^{1}H NMR of the crude mixture and er determined by chiral HPLC analysis. [b]Structure of minor diastereoisomer **6b** from single-crystal X-ray data.

it hard to explain the observed diastereoselectivity. The synthesis of other diversely substituted indole γ-lactones (**8**−**10**) was achieved using various isocyanides. In all cases the formation of lactone rings through the Passerini reaction occurred with a diastereoselectivity higher than 70:30. All diastereoisomers were easily separated by chromatography and were obtained with good enantiomeric ratios in moderate to good yields (Scheme 3).

We then explored the use of other boronic acids in this one-pot process (Scheme 4). The lactones **11**, **12** and **13** were thus obtained in good yields as a mixture of two diastereoismers (79, 63 and 72% respectively) using styrene boronic acid derivatives. However, a lower diastereoselectivity (dr 61:39) was observed using styrene boronic acid instead of indole derivatives. Albeit the enantiomeric ratios obtained for the major diastereoisomers were close to those previously observed (88:12 to 92:8), a significant lower enantiomeric ratio was obtained for the minor diastereoisomers (71:29 to 83:17). We then performed several experiments in acetonitrile to check the configurational stability of diastereoisomers **11**. Neither the enantiomeric nor the diastereoisomeric ratio changed over a period of 24 h under neutral conditions or in the presence of one equivalent of boric acid. These observations indicated that partial racemization of the chiral center occurred during the course of the Passerini reaction rather than after the formation of the final lactone. Despite the lower reactivity of the aryl boronic acid as a reaction partner in the Petasis like reactions, the electron rich aryl boronic acids could be transferred to the 5-hydroxyfuran-2(5*H*)-one **1** and subsequently transformed under one-pot conditions into γ-lactones **14**−**16** by reaction with *tert*-butylisocyanide. The γ-lactone **14** was obtained in a 60% yield and a 88:12 enantiomeric ratio for both diastereoisomers (dr 56:44). When 2,4-dimethoxyphenylboronic acid was used as a reaction partner the reaction sequence proceeded with a good level of diastereoselectivity (80:20). Diastereoisomeric lactones **15a** and **15b** were isolated in good yields (59 and 14%) albeit with a lower enantioselectivity (er 82:18). The diastereoisomeric lactones **16a** and **16b** were obtained in low yields (25 and 15%) under these reaction conditions illustrating the significant lower reactivity of 4-methoxyphenyl boronic acid in this process. Moreover, lactones **16a** and **16b** were obtained with virtually no enantioselectivity. *N*-Boc-pyrrol-2-boronic acid is highly reactive in this process as the addition adduct was obtained in a shorter reaction time on the 1 mmol scale and the conversion into lactones **17a** and **17b** occurred with a good level of diastereoselectivity in this case (dr 75:25). Diastereoisomers **17a** and **17b** were isolated in high yield (64 and 20%, respectively). However, the same low enantiomeric ratio (70:30) was obtained for both diastereoisomers. Finally, the lactone **18** bearing a benzofuran substituent was obtained as a mixture of diastereoisomers in 70% yield but with no enantioselectivity.

CONCLUSION

The transformation of easily available starting materials into chiral γ-lactones exhibiting an original substitution pattern was achieved in a one-pot sequence based on the use of the 5-hydroxyfuran-2(5*H*)-one **1** as a C-4 building block. The process

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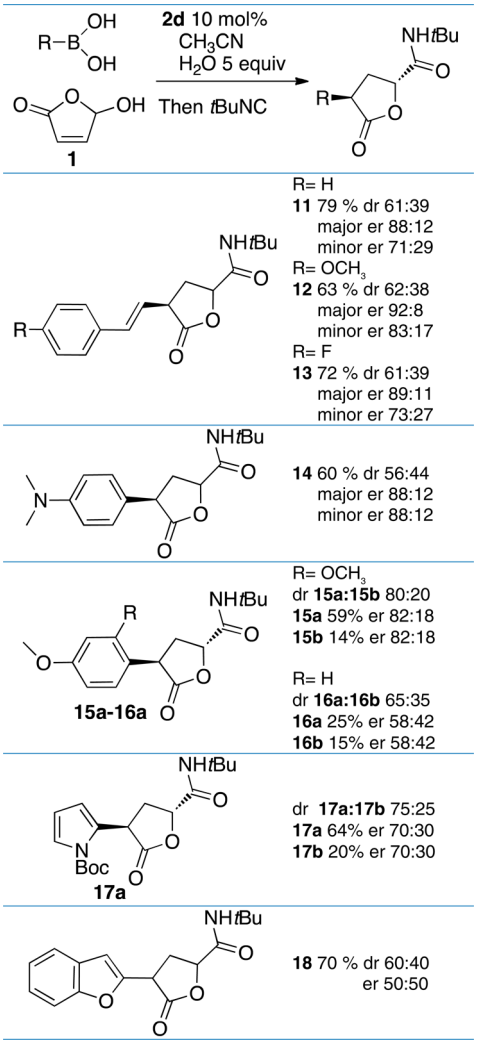
Scheme 4. Synthesis α,γ-Substituted γ-Lactones 11−18[a,b]



[a]The reactions were carried out with 1.1 mmol of boronic acid, 1 mmol of 5-hydroxyfuran-2(5*H*)-one **1**, 0.10 mmol of catalyst **2d** in CH_3CN (1.5 mL) and water (90 μL). The reaction was stirred at 0 °C until full conversion of **1** (TLC analysis). 1.5 mmol of *tert*-butyl isocyanide and CH_3CN (1.5 mL) were then added, and the reaction was stirred at rt until full consumption of primary adduct. dr determined by ^{1}H NMR of the crude mixture. er determined by chiral HPLC analysis. [b]Absolute configuration was assigned by analogy.

involved an enantioselective organocatalytic transfer of boronic acid followed by an intramolecular Passerini reaction. When *N*-Boc-indole-2-boronic acid was used as the reaction partner, the transfer of boronic acid was achieved with a good level of enantioselectivity. Moreover, the intramolecular Passerini reaction, applied for the first time for the synthesis of α,γ-substituted chiral lactones, proceeded diastereoselectively to afford the desired synthons in high yields. The methodology was further extended to several other boronic acids, including styrenes, electron rich phenyl rings and heteroaromatics, leading to structurally diversified γ-lactones in good yield but with moderate enantiomeric and diastereoisomeric selectivity. Further development of merging enantioselective organocatalysis and isocyanide chemistry affording new chiral biologically relevant structures for the generation of structural diversity is currently under investigation in our group.

EXPERIMENTAL SECTION

General Information. Thin-layer chromatography (TLC) analyses were done using aluminum sheets coated with silica gel 60 F_{254}. Flash column chromatography (FC) was carried out using silica gel 60 Å (0.04−0.06 mm). Commercially available products were used without further purification. NMR spectra were recorded with 250 MHz (BBFO + Z-GRD Probe) (^{1}H: 250 and ^{13}C: 63 MHz), 500 MHz (BBFO + Z-GRD Probe) (^{1}H: 500 and ^{13}C: 126 MHz) and 600 MHz (CPTCI Z-GRD CryoProbe) (^{1}H: 600 and ^{13}C: 151 MHz) spectrometers in $CDCl_3$. Chemical shifts are given in ppm, calibrated to the residual solvent peak,[38] and coupling constants "*J*" are expressed in hertz (multiplicity: s = singlet, bs = broad singlet, d = doublet, dd = double doublet, dt = double triplet, t = triplet, m = multiplet). Optical rotations were determined at 20 °C in the specified solvents. High-resolution mass spectra (HRMS) were performed on Q-TOF Micro micromass positive ESI (EV = 30 V). Enantiomeric ratios were determined by high-performance liquid chromatography (HPLC) with a chiral column.

General Procedure for Synthesis of Lactone 4. The catalyst (0.05 mmol) and 5-hydroxyfuran-2(5*H*)-one **1** (0.5 mmol) were dissolved in acetonitrile (1 mL), then H_2O (2.5 mmol) was added. The reaction mixture was cooled to 0 °C and the boronic acid (0.55 mmol) was added. The reaction was stirred until total consumption of the boronic acid (TLC analysis). The reaction mixture was then diluted with CH_3CN (1 mL), and $NaBH_4$ (1 mmol) was added. When the reduction was completed (15 min), 1 M HCl (15 mL) solution was carefully added. The reaction mixture was extracted with CH_2Cl_2 (3 × 15 mL). The organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude mixture was dissolved in $CHCl_3$ (2 mL), and *p*-toluenesulfonic acid was added (0.05 mmol). The reaction mixture was then stirred overnight. The crude material was purified by silica gel column chromatography to yield the desired product.

General Procedure for the One-Pot Sequential Enantioselective Organocatalytic Michael Addition of Boronic Acid and Diastereoselective Intramolecular Passerini Reaction (Compounds 6−18). The catalyst (0.1 mmol) and 5-hydroxyfuran-2(5*H*)-one **1** (1 mmol) were dissolved in acetonitrile (1.5 mL), then H_2O (5 mmol) was added. The reaction mixture was cooled to 0 °C and the boronic acid (1.1 mmol) was added. The reaction was stirred until total consumption of the boronic acid (TLC analysis) (Reaction time A). The isocyanide (1.5 mmol) and acetonitrile (1.5 mL) were then added and the reaction mixture was stirred until total consumption of the primary adduct (TLC analysis) (Reaction time B). After concentration under reduced pressure, the crude residue was purified by silica gel column chromatography to yield the desired products.

(*R*)-*tert*-Butyl 2-(2-oxotetrahydrofuran-3-yl)-1*H*-indole-1-carboxylate (4). (Table 1, Entry 4) The title compound (150 mg, 0.49 mmol, 98%) was prepared as a white solid by the general procedure and eluted from silica gel with CH_2Cl_2/Hexanes (90/10) (R_f = 0.6 CH_2Cl_2/Hexanes 80/20): mp 108−109 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.02 (d, J = 8.0 Hz, 1H), 7.58−7.40 (m, 1H), 7.36−7.10 (m, 2H), 6.59 (s, 1H), 4.61 (t, J = 9.5 Hz, 1H), 4.49 (td, J = 8.5, 4.0 Hz, 1H), 4.38 (td, J = 9.0, 7.0 Hz, 1H), 2.74 (dddd, J = 12.5, 9.0, 7.0, 4.0 Hz, 1H), 2.50 (ddt, J = 12.5, 10.0, 8.5 Hz, 1H), 1.70 (s, 9H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 175.9, 150.6, 136.6, 135.6, 128.8, 124.5, 123.1, 120.7, 115.9, 109.7, 84.9, 66.6, 41.3, 30.5, 28.3; IR (KBr plate) ν_{max} 3005, 2976, 2935, 2913, 1914, 1770, 1732, 1570, 1481, 1546, 1379, 1344, 1323, 1307, 1304, 1258, 1225, 1171, 1161, 1127, 1097, 1021, 951, 904, 840, 748 (cm^{-1}); ESI-HRMS m/z calcd for $C_{17}H_{19}NNaO_4^+$ ($[M + Na]^+$) 324.1212, found 324.1196; er (8:92); The enantiomeric ratio was determined by HPLC with a CHIRALCEL OD-H column (hexane/*i*PrOH = 83:17, 254 nm, 1 mL/min), t_R (minor) = 6.7 min, t_R (major) = 8.1 min.

Reaction carried out on 1 mmol scale, compound **4** (180 mg, 0.6 mmol, 60%): $[\alpha]^{20}_D$ = +52.5 (c 1, $CHCl_3$), er (1:99).

(*R*)-*tert*-Butyl 3-bromo-2-(2-oxotetrahydrofuran-3-yl)-1*H*-indole-1-carboxylate (5). The compound **4** (50 mg, 0.17 mmol) was dissolved in dichloromethane (2 mL) then the NBS (31 mg, 0.174 mmol) was added. The mixture was heated to reflux for 2 h. Water (10

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mL) was added, and the reaction mixture was extracted twice with dichloromethane (15 mL), and then washed with 1 M NaOH (10 mL). The organic layers were dried over $MgSO_4$, filtered, concentrated under reduced pressure and purified on silica gel chromatography (CH_2Cl_2/Hexanes 90/10) to afford compound **5** (61 mg, 0.16 mmol, 95%) as a white solid (90/10) (R_f = 0.5 CH_2Cl_2/Hexanes 80/20): mp 180 °C dec; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (d, J = 8.5 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.36 (t, J = 7.5 Hz, 1H), 7.31 (t, J = 7.5 Hz, 1H), 4.64 (t, J = 9.0 Hz, 1H), 4.59 (bs, 1H), 4.43 (dt, J = 9.0, 8.5 Hz, 1H), 2.74 (ddd, J = 21.5, 11.5, 10.0 Hz, 1H), 2.57 (s, 1H), 1.69 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.1, 150.1, 135.0, 131.8, 128.1, 125.8, 123.5, 119.5, 115.8, 104.0, 85.8, 66.8, 40.1, 28.2, 27.8; ESI-HRMS m/z calcd for $C_{17}H_{18}BrNNaO_4^+$ ([M + Na]$^+$) 402.0317, found 402.0312; $[\alpha]^{20}_D$ = +6.1 (c 1, $CHCl_3$), er (99:1). The enantiomeric ratio was determined by HPLC with a CHIRALCEL IC column (hexane/iPrOH = 60:40, 254 nm, 1 mL/min), t_R (major) = 9.5 min, t_R (minor) = 27.3 min.

***tert*-Butyl 2-((3*R*,5*R*)-5-(*tert*-butylcarbamoyl)-2-oxotetrahydrofuran-3-yl)-1*H*-indole-1-carboxylate (6a).** The title compound (225 mg, 0.56 mmol, 56%) was prepared as a white solid by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 4 h; Reaction time B: 12 h) (R_f = 0.4 CH_2Cl_2/AcOEt 98/2): mp 116−118 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.02 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 8.0 Hz, 1H), 7.38−7.16 (m, 2H), 6.57 (s, 1H), 6.24 (bs, 1H), 4.92 (dd, J = 9.0, 5.0 Hz, 1H), 4.46 (t, J = 9.0 Hz, 1H), 2.96−2.71 (m, 2H), 1.66 (s, 9H), 1.41 (s, 9H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 174.7, 168.9, 150.7, 136.6, 134.2, 128.6, 124.8, 123.2, 120.7, 116.0, 111.0, 85.2, 76.2, 51.9, 41.0, 32.8, 28.9, 28.3; IR (KBr plate) ν_{max} 3338, 3078, 2974, 2929, 2855, 1786, 1732, 1685, 1550, 1545, 1455, 1425, 1376, 1330, 1257, 1224, 1159, 1122, 1091, 1056, 965, 851, 820 (cm^{-1}); ESI-HRMS m/z calcd for $C_{22}H_{28}N_2NaO_5^+$ ([M + Na]$^+$) 423.1896, found 423.1894; $[\alpha]^{20}_D$ = −4.2 (c 1, $CHCl_3$), er (90:10). The enantiomeric ratio was determined by HPLC with a CHIRALCEL OD-H column (hexane/EtOH = 92:8, 254 nm, 1 mL/min), t_R (major) = 6.6 min, t_R (minor) = 7.6 min.

***tert*-Butyl 2-((3*R*,5*S*)-5-(*tert*-butylcarbamoyl)-2-oxotetrahydrofuran-3-yl)-1*H*-indole-1-carboxylate (6b).** The title compound (70 mg, 0.17 mmol, 17%) was prepared as a white solid by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 4 h; Reaction time B: 12 h) (R_f = 0.2 CH_2Cl_2/AcOEt 98/2): mp 146 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.96 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 7.0 Hz, 1H), 7.36−7.16 (m, 2H), 6.62 (s, 1H), 6.42 (bs, 1H), 4.80 (dd, J = 10.0, 7.5 Hz, 1H), 4.56−4.35 (m, 1H), 2.97 (dt, J = 12.0, 9.0 Hz, 1H), 2.62 (dt, J = 12.0, 11.5 Hz, 1H), 1.70 (s, 9H), 1.41 (s, 9H).^{13}C NMR (63 MHz, $CDCl_3$) δ 174.1, 168.5, 150.9, 136.4, 133.9, 128.7, 124.8, 123.3, 120.7, 116.0, 112.0, 85.1, 76.0, 51.6, 42.6, 33.4, 28.9, 28.4; IR (KBr plate) ν_{max} 3402, 2978, 2934, 1791, 1711, 1685, 1529, 1455, 1381, 1321, 1327, 1273, 1223, 1182, 1157, 1130, 1097, 1044, 1005, 968, 925, 845, 814, 762 (cm^{-1}); ESI-HRMS m/z calcd for $C_{22}H_{28}N_2NaO_5^+$ ([M + Na]$^+$) 423.1896, found 423.1896; $[\alpha]^{20}_D$ = −9 (c 1, $CHCl_3$), er (90:10). The enantiomeric ratio was determined by HPLC with a CHIRALCEL OD-H column (hexane/EtOH = 92:8, 254 nm, 1 mL/min), t_R (minor) = 8.0 min, t_R (major) = 12.5 min.

***tert*-Butyl 2-((3*R*,5*R*)-5-(*tert*-butylcarbamoyl)-2-oxotetrahydrofuran-3-yl)-5-methoxy-1*H*-indole-1-carboxylate (7a).** The title compound was prepared (250 mg, 0.58 mmol, 58%) as a white solid by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 7 h; Reaction time B: 12 h) (R_f = 0.4 CH_2Cl_2/AcOEt 97/3): mp 65−67 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89 (d, J = 9.0 Hz, 1H), 6.95 (d, J = 2.5 Hz, 1H), 6.90 (dd, J = 9.0, 2.5 Hz, 1H), 6.49 (s, 1H), 6.23 (bs, 1H), 4.90 (dd, J = 9.5, 4.5 Hz, 1H), 4.43 (bs, 1H), 3.83 (s, 3H), 2.86 (ddd, J = 14.5, 10.0, 4.5 Hz, 1H), 2.78 (dt, J = 13.0, 9.0 Hz, 1H), 1.67 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.7, 168.9, 156.2, 150.6, 134.8, 131.2, 129.4, 116.8, 113.6, 110.9, 103.0, 85.0, 76.2, 55.8, 51.8, 41.0, 32.5, 28.8, 28.3; IR (KBr plate) ν_{max} 3347, 2974, 2935, 1784, 1729, 1684, 1618, 1541, 1479, 1451, 1379, 1323, 1256, 1219, 1160, 1126, 1093, 1035, 965, 901, 850 (cm^{-1}); ESI-HRMS m/z calcd for $C_{23}H_{30}N_2NaO_6^+$ ([M + Na]$^+$) 453.2002, found 453.2005; $[\alpha]^{20}_D$ = +9.9 (c 1, $CHCl_3$), er (96:4). The enantiomeric ratio was determined by HPLC with a CHIRALCEL IC column (hexane/EtOH = 70:30, 254 nm, 1 mL/min), t_R (major) = 9.9 min, t_R (minor) = 16.4 min.

***tert*-Butyl 2-((3*R*,5*S*)-5-(*tert*-butylcarbamoyl)-2-oxotetrahydrofuran-3-yl)-5-methoxy-1*H*-indole-1-carboxylate (7b).** The title compound was prepared (77 mg, 0.18 mmol, 18%) as a white solid by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 7 h; Reaction time B: 12 h) (R_f = 0.2 CH_2Cl_2/AcOEt 97/3): mp 148 °C dec; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 (d, J = 9.0 Hz, 1H), 6.95 (d, J = 2.5 Hz, 1H), 6.90 (dd, J = 9.0, 2.5 Hz, 1H), 6.54 (s, 1H), 6.42 (bs, 1H), 4.79 (dd, J = 10.0, 7.5 Hz, 1H), 4.40 (bs, 1H), 3.84 (s, 3H), 2.96 (m, 1H), 2.61 (q, J = 11.5 Hz, 1H), 1.68 (s, 9H), 1.41 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.2, 168.6, 156.2, 150.7, 134.4, 131.0, 129.5, 116.8, 113.6, 112.1, 103.0, 84.9, 76.0, 55.8, 51.5, 42.6, 33.3, 28.8, 28.4; IR (KBr plate) ν_{max} 3430, 2974, 2925, 1786, 1684, 1618, 1528, 1480, 1450, 1380, 1317, 1289, 1255, 1216, 1177, 1157, 1128, 1099, 1042, 1008, 968, 852 (cm^{-1}); ESI-HRMS m/z calcd for $C_{23}H_{30}N_2NaO_6^+$ ([M + Na]$^+$) 453.2002, found 453.2004; $[\alpha]^{20}_D$ = +1.3 (c 1.2, $CHCl_3$), er (96:4). The enantiomeric ratio was determined by HPLC with a CHIRALCEL OD-H column (hexane/EtOH = 70:30, 254 nm, 1 mL/min), t_R (minor) = 5.6 min, t_R (major) = 9.3 min.

***tert*-Butyl 2-((3*R*,5*R*)-5-(benzylcarbamoyl)-2-oxotetrahydrofuran-3-yl)-1*H*-indole-1-carboxylate (8a).** The title compound (266 mg, 0.61 mmol, 61%) was prepared as a white solid by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 4 h; Reaction time B: 72 h) (R_f = 0.5 CH_2Cl_2/AcOEt 98/2): mp 75−76 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.00 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 9.0 Hz, 1H), 7.43−7.15 (m, 7H), 6.85 (t, J = 5.5 Hz, 2H), 6.56 (s, 1H), 5.06 (dd, J = 8.5, 5.0 Hz, 2H), 4.63−4.36 (m, 3H), 3.00−2.78 (m, 2H), 1.68 (s, 9H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 174.5, 169.8, 150.8, 137.4, 136.5, 134.1, 129.0, 128.6, 128.0, 124.8, 123.3, 120.8, 116.0, 111.1, 85.3, 76.0, 43.6, 40.8, 33.0, 28.3; IR (KBr plate) ν_{max} 3312, 2978, 2932, 1787, 1730, 1670, 1539, 1454, 1377, 1329, 1252, 1225, 1159, 1122, 1089, 1056, 1029, 964, 850, 819, 747 (cm^{-1}); ESI-HRMS m/z calcd for $C_{25}H_{26}N_2NaO_5^+$ ([M + Na]$^+$) 457.1739, found 457.1757; $[\alpha]^{20}_D$ = −9 (c 1, $CHCl_3$), er (93:7). The enantiomeric ratio was determined by HPLC with a CHIRALCEL OD-H column (hexane/EtOH = 70:30, 254 nm, 1 mL/min), t_R (major) = 10.2 min, t_R (minor) = 11.5 min.

***tert*-Butyl 2-((3*R*,5*S*)-5-(benzylcarbamoyl)-2-oxotetrahydrofuran-3-yl)-1*H*-indole-1-carboxylate (8b).** The title compound (51 mg, 0.12 mmol, 12%) was prepared as a light brown gum by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 4 h; Reaction time B: 72 h) (R_f = 0.2 CH_2Cl_2/AcOEt 98/2): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.93 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.38−7.15 (m, 7H), 7.03 (bs, 1H), 6.61 (s, 1H), 4.97 (t, J = 8.5 Hz, 1H), 4.60 (dd, J = 14.5, 6.0 Hz, 1H), 4.52−4.35 (m, 2H), 3.03 (dt, J = 12.0, 9.0 Hz, 1H), 2.66 (q, J = 11.5 Hz, 1H), 1.59 (s, 9H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 173.90, 169.4, 150.8, 137.4, 136.2, 133.7, 128.8, 128.6, 127.9, 127.7 124.7, 123.2, 120.7, 115.9, 112.2, 85.2, 75.8, 43.4, 42.3, 33.1, 28.2; IR (KBr plate) ν_{max} 3420, 2976, 2921, 2856, 1790, 1723, 1680, 1533, 1452, 1379, 1324, 1271, 1221, 1155, 1122, 1092, 1049, 963, 904, 837, 754 (cm^{-1}); ESI-HRMS m/z calcd for $C_{25}H_{26}N_2NaO_5^+$ ([M + Na]$^+$) 457.1739, found 457.1729; $[\alpha]^{20}_D$ = +10 (c 1, $CHCl_3$), er (93:7). The enantiomeric ratio was determined by HPLC with a CHIRALCEL IC column (hexane/EtOH = 60:40, 254 nm, 1 mL/min), t_R (minor) = 7.3 min, t_R (major) = 23.0 min.

***tert*-Butyl 2-((3*R*,5*R*)-5-(cyclohexylcarbamoyl)-2-oxotetrahydrofuran-3-yl)-1*H*-indole-1-carboxylate (9a).** The title compound (254 mg, 0.6 mmol, 60%) was prepared as a white solid by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 4 h; Reaction time B: 12 h) (R_f = 0.5 CH_2Cl_2/AcOEt 98/2): mp 78−80 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.01 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 6.5 Hz, 1H), 7.38−7.15 (m, 2H), 6.57 (s, 1H), 6.35 (d, J = 8.5 Hz, 1H), 5.00 (dd, J = 8.0, 6.0 Hz, 1H), 4.44 (t, J = 9.5 Hz, 1H), 3.94−3.69 (m, 1H), 3.03−2.68 (m, 2H), 1.93 (bs, 2H), 1.69 (s, 9H), 1,68 (m, 2H), 1.50−1.04 (m, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 174.7, 168.8, 150.7, 136.5, 134.2, 128.6, 124.8, 123.3, 120.7,

116.0, 111.2, 85.3, 76.0, 48.6, 40.9, 33.2, 33.0, 28.3, 25.5, 25.0; IR (KBr plate) ν_{max} 3222, 2975, 2933, 2856, 1786, 1731, 1665, 1542, 1454, 1377, 1330, 1254, 1224, 1159, 1123, 1092, 1056, 1033, 965, 851, 748 (cm^{-1}); ESI-HRMS m/z calcd for $C_{24}H_{30}N_2NaO_5^+$ ($[M + Na]^+$) 449.2052, found 449.2050; $[\alpha]^{20}_D$ = +1,4 (c 1, $CHCl_3$), er (91:9). The enantiomeric ratio was determined by HPLC with a CHIRALCEL IC column (hexane/EtOH = 70:30, 254 nm, 1 mL/min), t_R (major) = 10.0 min, t_R (minor) = 18.1 min.

***tert*-Butyl 2-((3*R*,5*S*)-5-(cyclohexylcarbamoyl)-2-oxotetrahydrofuran-3-yl)-1*H*-indole-1-carboxylate (9b).** The title compound (51 mg, 0.12 mmol, 12%) was prepared as a white solid by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 4 h; Reaction time B: 12 h) (R_f = 0.2 CH_2Cl_2/AcOEt 98/2): mp 176 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.96 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 7.5 Hz, 1H), 7.37−7.11 (m, 2H), 6.62 (s, 1H), 6.51 (d, J = 8.0 Hz, 1H), 4.89 (dd, J = 10.0, 8.0 Hz, 1H), 4.53−4.35 (m, 1H), 3.93−3.63 (m, 1H), 3.12−2.81 (m, 1H), 2.63 (dt, J = 12.0, 11.5 Hz, 1H), 1.94 (s, 2H), 1.70 (m, 2H), 1.69 (s, 9H), 1.48−1.05 (m, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 174.1, 168.4, 150.9, 136.4, 133.9, 128.7, 124.8, 123.3, 120.7, 116.0, 112.0, 85.1, 75.9, 48.3, 42.5, 33.2, 33.1, 28.4, 25.6, 25.0; IR (KBr plate) ν_{max} 3391, 2929, 2855, 1790, 1723, 1673, 1532, 1479, 1452, 1379, 1325, 1271, 1222, 1157, 1123, 1095, 1049, 967, 925, 895, 868, 841, 810, 754 (cm^{-1}); ESI-HRMS m/z calcd for $C_{24}H_{30}N_2NaO_5^+$ ($[M + Na]^+$) 449.2052, found 449.2060; $[\alpha]^{20}_D$ = +15 (c 1, $CHCl_3$), er (9:91). The enantiomeric ratio was determined by HPLC with a CHIRALCEL OD-H column (hexane/*i*PrOH = 77:23, 254 nm, 1 mL/min), t_R (minor) = 5.2 min, t_R (major) = 7.5 min.

***tert*-Butyl 2-((3*R*,5*R*)-5-((4-methoxyphenyl)carbamoyl)-2-oxotetrahydrofuran-3-yl)-1*H*-indole-1-carboxylate (10a).** The title compound (270 mg, 0.6 mmol, 60%) was prepared as a pale yellow solid by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 4 h; Reaction time B: 144 h) (R_f = 0.5 CH_2Cl_2/AcOEt (98/2): mp 86−88 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.19 (s, 1H), 8.01 (d, J = 8.5 Hz, 1H), 7.56−7.42 (m, 3H), 7.37−7.10 (m, 2H), 6.86 (m, 2H), 6.59 (s, 1H), 5.16 (dd, J = 9.0, 5.0 Hz, 1H), 4.50 (t, J = 9.5 Hz, 1H), 3.80 (s, 3H), 3.07−2.81 (m, 2H), 1.69 (s, 9H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 174.5, 167.7, 157.0, 150.7, 136.4, 133.8, 129.8, 128.5, 124.7, 123.2, 121.9, 120.7, 115.9, 114.3, 111.4, 85.2, 75.9, 55.5, 40.8, 32.7, 28.2; IR (KBr plate) ν_{max} 3327, 3139, 3072, 2977, 2935, 2837, 1785, 1729, 1687, 1605, 1543, 1513, 1454, 1416, 1377, 1330, 1245, 1158, 1122, 1092, 1034, 964, 830, 748 (cm^{-1}); ESI-HRMS m/z calcd for $C_{25}H_{26}N_2NaO_6^+$ ($[M + Na]^+$) 473.1689, found 473.1679; $[\alpha]^{20}_D$ = −1.1 (c 1, $CHCl_3$), er (90:10). The enantiomeric ratio was determined by HPLC with a CHIRALCEL OD-H column (hexane/EtOH = 85:15, 254 nm, 1 mL/min), t_R (major) = 14.6 min, t_R (minor) = 18.4 min.

***tert*-Butyl 2-((3*R*,5*S*)-5-((4-methoxyphenyl)carbamoyl)-2-oxotetrahydrofuran-3-yl)-1*H*-indole-1-carboxylate (10b).** The title compound (60 mg, 0.13 mmol, 13%) was prepared as a brown gum by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 4 h; Reaction time B: 144 h) (R_f = 0.2 CH_2Cl_2/AcOEt 98/2): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (bs, 1H), 7.92 (d, J = 8.5 Hz, 1H), 7.54 (d, J = 9.0 Hz, 2H), 7.50 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 8.0 Hz, 1H), 7.23 (t, J = 7.5 Hz, 1H), 6.88 (d, J = 9.0 Hz, 2H), 6.65 (s, 1H), 5.03 (t, J = 9.0 Hz, 1H), 4.42 (s, 1H), 3.81 (s, 3H), 3.07 (dt, J = 10.5, 9.5 Hz, 1H), 2.70 (q, J = 11.0 Hz, 1H), 1.57 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 167.6, 156.8, 151.1, 136.2, 133.6, 130.3, 128.7, 124.9, 123.4, 121.7, 120.8, 116.0, 114.3, 112.9, 85.5, 75.6, 55.6, 42.4, 32.9, 28.2; IR (KBr plate) ν_{max} 3405, 3339, 3045, 2974, 2931, 2837, 1789, 1725, 1683, 1601, 1539, 1513, 1453, 1414, 1381, 1329, 1246, 1159, 1125, 1036, 964, 916, 831, 744 (cm^{-1}); ESI-HRMS m/z calcd for $C_{25}H_{26}N_2NaO_6^+$ ($[M + Na]^+$) 473.1689, found 473.1683; $[\alpha]^{20}_D$ = +21.4 (c 0.2, $CHCl_3$), er (90:10). The enantiomeric ratio was determined by HPLC with a CHIRALCEL OD-H column (hexane/EtOH = 85:15, 254 nm, 1 mL/min), t_R (minor) = 12.2 min, t_R (major) = 21.4 min.

(4*R*)-*N*-(*tert*-Butyl)-5-oxo-4-((*E*)-styryl)tetrahydrofuran-2-carboxamide (11). The title compound (mixture of diastereoisomers 61:39)) was prepared (228 mg, 0.79 mmol, 79%) as a white solid by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 6 h; Reaction time B: 12 h) (R_f = 0.4 and 0.6 CH_2Cl_2/AcOEt 97/3): ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.47−7.16 (m), 6.61 (dd, J = 6.5, 1.5 Hz, 1H, minor), 6.55 (dd, J = 6.5, 1.5 Hz, 1H, major), 6.31−6.09 (m), 4.81 (dd, J = 8.5, 4.5 Hz, 1H, major), 4.73 (dd, J = 9.5, 7.0 Hz, 1H, minor), 3.63−3.37 (m), 2.95 (ddd, J = 13.0, 8.0, 7.0 Hz, 1H, minor), 2.79 (ddd, J = 13.0, 9.0, 4.5 Hz, 1H, major), 2.56 (dt, J = 13.0, 8.5 Hz, 1H, major), 2.27 (ddd, J = 13.0, 11.0, 9.5 Hz, 1H, minor), 1.38 (s, 9H, major), 1.37 (s, 9H, minor); ^{13}C NMR (63 MHz, $CDCl_3$) δ 176.0 (major), 175.5 (minor), 168.3 (major), 168.1 (minor), 136.1, 134.1 (major), 134.0 (minor), 128.8, 128.3 (major), 128.2 (minor), 126.6, 123.0 (minor), 122.8 (major), 76.2 (major), 76.1 (minor), 51.9 (major), 51.8 (minor), 43.5 (minor), 42.0 (major), 32.8 (minor), 32.2 (major), 28.8; IR (KBr plate) ν_{max} 3276, 3091, 3029, 2970, 2932, 1785, 1683, 1658, 1565, 1490, 1454, 1391, 1365, 1327, 1266, 1220, 1154, 1120, 1052, 1008, 966, 924, 864, 835, 792 (cm^{-1}); ESI-HRMS m/z calcd for $C_{17}H_{21}NNaO_3^+$ ($[M + Na]^+$) 310.1419, found 310.1427; er (12:88 major ; 29:71 minor). The enantiomeric ratio was determined by HPLC with a CHIRALCEL OD-H column (hexane/EtOH = 80:20, 254 nm, 1 mL/min), t_R (major, major) = 12.6 min, t_R (minor, major) = 16.2 min, t_R (minor, minor) = 14.3 min, t_R (major, minor) = 23.6 min.

(4*R*)-*N*-(*tert*-Butyl)-4-((*E*)-4-methoxystyryl)-5-oxotetrahydrofuran-2-carboxamide (12). The title compound (mixture of diastereoisomers 62:38) was prepared (200 mg, 0.6 mmol, 60%) as a pale yellow solid by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 3 h; Reaction time B: 12 h) (R_f = 0.4 and 0.5 CH_2Cl_2/AcOEt 97/3): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32−7.28 (m), 6.87−6.83 (m), 6.56−6.47 (m), 6.16 (s, 1H, minor), 6.15 (s, 1H, major), 6.07 (dd, J = 16.0, 6.5 Hz, 1H, minor), 6.02 (dd, J = 16.0, 6.5 Hz, 1H, major), 4.80 (dd, J = 8.5, 4.5 Hz, 1H, major), 4.72 (dd, J = 9.5, 7.0 Hz, 1H, minor), 3.80 (s, 3H, major), 3.80 (s, 3H, minor), 3.50 (dddd, J = 10.5, 8.5, 6.5, 1.5 Hz, 1H, minor), 3.43 (tdd, J = 8.5, 6.5, 1.5 Hz, 1H, major), 2.94 (ddd, J = 13.0, 9.0, 7.0 Hz, 1H, minor), 2.77 (ddd, J = 13.5, 9.0, 5.0 Hz, 1H, major), 2.54 (dt, J = 13.0, 8.5 Hz, 1H, major), 2.26 (ddd, J = 13.0, 10.5, 9.5 Hz, 1H, minor), 1.38 (s, 9H, major), 1.36 (s, 9H, minor); ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.2 (major), 175.8 (minor), 168.4 (major), 168.1 (minor), 159.74 (major), 159.70 (minor), 133.50 (major), 133.47 (minor), 128.90 (minor), 128.88 (major), 127.8, 120.6 (minor), 120.4 (major), 114.18 (major), 114.16 (minor), 76.2 (major), 76.0 (minor), 55.43 (major), 55.41 (minor), 51.9 (major), 51.8 (minor), 43.6 (minor), 42.0 (major), 32.9 (minor), 32.3 (major), 28.80 (major), 28.78 (minor); IR (KBr plate) ν_{max} 3277, 3093, 3036, 2968, 2933, 2841, 1782, 1659, 1608, 1564, 1513, 1457, 1393, 1365, 1294, 1252, 1225, 1172, 1155, 1035, 965, 928, 821 (cm^{-1}); ESI-HRMS m/z calcd for $C_{18}H_{23}NNaO_4^+$ ($[M + Na]^+$) 340.1525, found 340.1521; er (93:7 major ; 17:83 minor). The enantiomeric ratio was determined by HPLC with a CHIRALCEL OD-H column (hexane/EtOH = 70:30, 254 nm, 1 mL/min), t_R (major, major) = 9.2 min, t_R (minor, major) = 11.7 min, t_R (major, minor) = 9.8 min, t_R (minor, minor) = 16.0 min.

(4*R*)-*N*-(*tert*-Butyl)-4-((*E*)-4-fluorostyryl)-5-oxotetrahydrofuran-2-carboxamide (13). The title compound (mixture of diastereoisomers 61:39) was prepared (220 mg, 0.72 mmol, 72%) as a white solid by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 5 h; Reaction time B: 12 h) (R_f = 0.4 and 0.6 CH_2Cl_2/AcOEt 97/3): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38−7.31 (m), 7.05−6.98 (m), 6.60−6.50 (m), 6.17−6.12 (m), 6.09 (dd, J = 16.0, 6.5 Hz, 1H, major), 4.81 (dd, J = 8.5, 4.5 Hz, 1H, major), 4.74 (dd, J = 9.5, 7.0 Hz, 1H, minor), 3.52 (dddd, J = 10.5, 8.5, 6.0, 1.5 Hz, 1H, minor), 3.44 (tdd, J = 8.5, 6.5, 1.5 Hz, 1H, major), 2.95 (ddd, J = 13.0, 8.5, 7.0 Hz, 1H, minor), 2.81 (ddd, J = 13.5, 9.0, 4.5 Hz, 1H, major), 2.55 (dt, J = 13.0, 8.5 Hz, 1H, major), 2.27 (dt, J = 13.0, 10.0 Hz, 1H, minor), 1.39 (s, 9H, major), 1.37 (s, 9H, minor); ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.0 (major), 175.5 (minor), 168.3 (major), 168.0 (minor), 162.9 (d, J_{C-F} = 248.5 Hz, major), 162.8 (d, J_{C-F} = 248.5 Hz, minor), 133.0 (major), 132.9 (minor), 132.30 (d, J_{C-F} = 4.0 Hz, minor), 132.27 (d, J_{C-F} = 4.0 Hz, major) 128.21 (d, J_{C-F} = 2.0 Hz, major), 128.20 (d, J_{C-F} = 2.0 Hz, minor), 122.7 (d, J_{C-F} = 2.0 Hz, minor), 122.6 (d, J_{C-F} = 2.0 Hz, major), 115.8 (major), 115.7 (minor),

76.2 (major), 76.1 (minor), 52.0 (major), 51.8 (minor), 43.5 (minor), 41.9 (major), 32.8 (minor), 32.2 (major), 28.81 (major), 28.78 (minor); ^{19}F NMR (235 MHz, $CDCl_3$) δ −113.79 − −114.04 (m). IR (KBr plate) ν_{max} 3341, 3277, 3089, 2973, 2931, 1891, 1765, 1683, 1662, 1602, 1558, 1510, 1456, 1393, 1366, 1329, 1266, 1232, 1172, 1095, 1045, 967, 924, 820 (cm^{-1}); ESI-HRMS m/z calcd for $C_{17}H_{20}FNNaO_3^+$ ($[M + Na]^+$) 328.1325, found 328.1328; er (89:11 major ; 73:27 minor). The enantiomeric ratio was determined by HPLC with a CHIRALCEL IC column (Hexane/EtOH = 88:12, 254 nm, 1 mL/min), t_R (major, major) = 16.4 min, t_R (minor, major) = 21.5 min, t_R (major, minor) = 18.2 min, t_R (minor, minor) = 25.8 min.

(4*R*)-*N*-(*tert*-Butyl)-4-(4-(dimethylamino)phenyl)-5-oxotetrahydrofuran-2-carboxamide (14). The title compound (mixture of diastereoisomers 56:44) was prepared (183 mg, 0.59 mmol, 60%) as a white solid by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 3 h; Reaction time B: 12 h) (R_f = 0.4 and 0.45 CH_2Cl_2/AcOEt 97/3): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.17−7.08 (m), 6.75−6.66 (m), 6.23 (bs), 4.83 (dd, J = 8.5, 5.0 Hz, 1H, major), 4.73 (dd, J = 9.5, 7.0 Hz, 1H, minor), 3.81 (dd, J = 11.5, 9.0 Hz, 1H, minor), 3.74 (t, J = 9.0 Hz, 1H, major), 3.03 (ddd, J = 13.0, 9.0, 7.0 Hz, 1H, minor), 2.93 (s, 6H, minor), 2.93 (s, 6H, major), 2.87 (ddd, J = 13.5, 9.0, 5.0 Hz, 1H, major), 2.65 (dt, J = 13.5, 8.5 Hz, 1H, major), 2.37 (ddd, J = 13.0, 11.5, 9.5 Hz, 1H, minor), 1.38 (s, 9H, major), 1.37 (s, 9H, minor); ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.9 (major), 176.3 (minor), 168.6 (major), 168.2 (minor), 150.22 (minor), 150.17 (major), 128.5 (minor), 128.3 (major), 123.1 (major), 122.6 (minor), 112.9 (major), 112.8 (minor), 76.0 (major), 75.6 (minor), 51.8 (major), 51.6 (minor), 45.3 (minor), 43.7 (major), 40.58 (minor), 40.55 (major), 34.7 (minor), 34.4 (major), 28.73 (major), 28.71 (minor); IR (KBr plate) ν_{max} 3338, 3280, 3091, 2967, 2928, 2886, 2800, 1782, 1659, 1618, 1561, 1525, 1454, 1393, 1361, 1271, 1225, 1194, 1149, 1056, 1015, 935, 899, 820, 799 (cm^{-1}); ESI-HRMS m/z calcd for $C_{17}H_{25}N_2O_3^+$ ($[M + H]^+$) 305.1865, found 305.1863; er (12:88). The enantiomeric ratio was determined by HPLC with a CHIRALCEL IC column (hexane/EtOH = 60:40, 254 nm, 1 mL/min), t_R (major, major) = 9.3 min, t_R (minor, minor) = 11.6 min, t_R (minor, minor) = 10.2 min, t_R (major, minor) = 21.7 min.

(2*R*,4*R*)-*N*-(*tert*-Butyl)-4-(2,4-dimethoxyphenyl)-5-oxotetrahydrofuran-2-carboxamide (15a). The title compound was prepared (190 mg, 0.59 mmol, 59%) as a pale yellow gum by the general procedure and eluted from silica gel with Hexanes/AcOEt (85/15) (Reaction time A: 6 h; Reaction time B: 12 h) (R_f = 0.6 CH_2Cl_2/AcOEt 95/5): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (d, J = 8.0 Hz, 1H), 6.47 (d, J = 2.5 Hz, 1H), 6.44 (dd, J = 8.5, 2.5 Hz, 1H), 6.22 (bs, 1H), 4.85 (dd, J = 9.5, 4.5 Hz, 1H), 3.92−3.67 (m, 7H), 2.78 (ddd, J = 13.0, 10.5, 4.5 Hz, 1H), 2.62 (dt, J = 13.0, 9.0 Hz, 1H), 1.39 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.3, 169.2, 161.0, 157.8, 130.8, 117.8, 104.6, 99.4, 76.1, 55.6, 55.5, 51.8, 41.4, 33.0, 28.8; IR (KBr plate) ν_{max} 3420, 3355, 3079, 2967, 2933, 2842, 1778, 1672, 1615, 1588, 1547, 1510, 1459, 1388, 1365, 1296, 1265, 1210, 1157, 1033, 933, 899, 834, 796, 754 (cm^{-1}); ESI-HRMS m/z calcd for $C_{17}H_{24}NO_5^+$ ($[M + H]^+$) 322.1654, found 322.1653; $[\alpha]^{20}_D$ = −6.8 (c 1, $CHCl_3$), er (82:18). The enantiomeric ratio was determined by HPLC with a CHIRALCEL IC column (hexane/EtOH = 60:40, 254 nm, 1 mL/min), t_R (major) = 6.6 min, t_R (minor) = 8.9 min.

(2*R*,4*S*)-*N*-(*tert*-Butyl)-4-(2,4-dimethoxyphenyl)-5-oxotetrahydrofuran-2-carboxamide (15b). The title compound was prepared (46 mg, 0.14 mmol, 14%) as a pale yellow solid by the general procedure and eluted from silica gel with Hexanes/AcOEt (85/15) (Reaction time A: 6 h; Reaction time B: 12 h) (R_f = 0.4 CH_2Cl_2/AcOEt 95/5): mp 127−129 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.06 (d, J = 8.0 Hz, 1H), 6.54−6.39 (m, 2H), 6.28 (bs, 1H), 4.72 (dd, J = 10.0, 7.5 Hz, 1H), 3.86 (dd, J = 11.5, 9.5 Hz, 1H), 3.81−3.74 (m, 6H), 2.92 (ddd, J = 13.0, 9.5, 7.5 Hz, 1H), 2.37 (ddd, J = 13.0, 11.5, 10.0 Hz, 1H), 1.41 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.6, 168.8, 161.1, 157.9, 130.9, 117.2, 104.7, 99.5, 75.8, 55.59, 55.57, 51.56, 43.1, 33.7, 28.9; IR (NaCl film) ν_{max} 3422, 3353, 2964, 2929, 1781, 1679, 1614, 1587, 1530, 1511, 1458, 1393, 1363, 1291, 1266, 1209, 1152, 1036, 936, 834 (cm^{-1}); ESI-HRMS m/z calcd for $C_{17}H_{23}NNaO_5^+$ ($[M + Na]^+$) 344.1474, found 344.1484; $[\alpha]^{20}_D$ = −6 (c 0.6, $CHCl_3$), er (84:16). The enantiomeric ratio was determined by HPLC with a CHIRALCEL IC column (hexane/EtOH = 60:40, 254 nm, 1 mL/min), t_R (minor) = 7.7 min, t_R (minor) = 25.0 min.

(2*R*,4*R*)-*N*-(*tert*-Butyl)-4-(4-methoxyphenyl)-5-oxotetrahydrofuran-2-carboxamide (16a). The title compound was prepared (73 mg, 0.25 mmol, 25%) as a white solid by the general procedure and eluted from silica gel with Hexanes/AcOEt (85/15) (Reaction time A: 48 h; Reaction time B: 12 h) (R_f = 0.7 CH_2Cl_2/AcOEt 97/3): mp 109−111 °C ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.19 (d, J = 8.5 Hz, 2H), 6.90 (d, J = 8.5 Hz, 2H), 6.19 (bs, 1H), 4.84 (dd, J = 8.5, 4.5 Hz, 1H), 3.82−3.75 (m, 4H), 2.93 (ddd, J = 13.5, 9.5, 4.5 Hz, 1H), 2.66 (dt, J = 13.5, 8.5 Hz, 1H), 1.39 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.6, 168.4, 159.4, 128.9, 127.7, 114.6, 76.0, 55.5, 52.0, 43.9, 34.4, 28.8; IR (KBr plate) ν_{max} 3529, 3280, 3096, 2967, 2929, 2848, 2794, 1775, 1661, 1616, 1565, 1517, 1458, 1393, 1366, 1307, 1255, 1225, 1177, 1149, 1040, 1013, 983, 900, 831, 800, 773 (cm^{-1}); ESI-HRMS m/z calcd for $C_{16}H_{21}NNaO_4^+$ ($[M + Na]^+$) 314.1368, found 314.1367; er (58:42). The enantiomeric ratio was determined by HPLC with a CHIRALCEL IC column (hexane/EtOH = 60:40, 280 nm, 1 mL/min), t_R (major) = 6.0 min, t_R (minor) = 7.5 min.

(2*R*,4*S*)-*N*-(*tert*-Butyl)-4-(4-methoxyphenyl)-5-oxotetrahydrofuran-2-carboxamide (16b). The title compound was prepared (42 mg, 0.15 mmol, 15%) as a colorless gum by the general procedure and eluted from silica gel with Hexanes/AcOEt (85/15) (Reaction time A: 48 h; Reaction time B: 12 h) (R_f = 0.55 CH_2Cl_2/AcOEt 97/3): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, J = 8.5 Hz, 2H), 6.90 (d, J = 8.5 Hz, 2H), 6.20 (bs, 1H), 4.76 (dd, J = 9.5, 7.0 Hz, 1H), 3.87 (dd, J = 11.5, 9.0 Hz, 1H), 3.80 (s, 3H), 3.07 (ddd, J = 13.5, 9.0, 7.0 Hz, 1H), 2.40 (ddd, J = 13.5, 11.5, 9.5 Hz, 1H), 1.38 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 168.1, 159.4, 129.0, 127.2, 114.5, 75.6, 55.5, 51.8, 45.4, 34.7, 28.8; IR (KBr plate) ν_{max} 3420, 3273, 3095, 2964, 2927, 2856, 1776, 1729, 1664, 1615, 1569, 1514, 1456, 1383, 1327, 1303, 1253, 1179, 1153, 1036, 936, 833, 805 (cm^{-1}); ESI-HRMS m/z calcd for $C_{16}H_{21}NNaO_4^+$ ($[M + Na]^+$) 314.1368, found 314.1357; er (58:42). The enantiomeric ratio was determined by HPLC with a CHIRALCEL IC column (hexane/EtOH = 60:40, 280 nm, 1 mL/min), t_R (minor) = 6.5 min, t_R (minor) = 11.5 min.

***tert*-Butyl 2-((3*R*,5*R*)-5-(*tert*-butylcarbamoyl)-2-oxotetrahydrofuran-3-yl)-1*H*-pyrrole-1-carboxylate (17a).** The title compound was prepared (224 mg, 0.64 mmol, 64%) as a colorless gum by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 1 h; Reaction time B: 12 h) (R_f = 0.4 CH_2Cl_2/AcOEt 97:3): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 (dd, J = 3.5, 2.0 Hz, 1H), 6.22 (bs, 1H), 6.15 (dd, J = 3.5, 2.0 Hz, 1H), 6.12 (t, J = 3.5 Hz, 1H), 4.86 (dd, J = 9.0, 4.5 Hz, 1H), 4.30 (bs, 1H), 2.80 (ddd, J = 13.0, 10.0, 4.5 Hz, 1H), 2.70 (dt, J = 13.0, 9.0 Hz, 1H), 1.58 (s, 9H), 1.39 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.0, 168.9, 149.2, 128.0, 122.6, 114.6, 110.3, 84.5, 76.0, 51.7, 39.6, 32.6, 28.7, 27.9; IR (KBr plate) ν_{max} 3421, 3358, 2975, 2933, 1787, 1741, 1683, 1547, 1486, 1457, 1413, 1372, 1336, 1257, 1227, 1141, 1064, 977, 900, 846, 769, 728, 686 (cm^{-1}); ESI-HRMS m/z calcd for $C_{18}H_{26}N_2NaO_5^+$ ($[M + Na]^+$) 373.1739, found 373.1733; $[\alpha]^{20}_D$ = +8 (c 1, $CHCl_3$), er (70:30). The enantiomeric ratio was determined by HPLC with a CHIRALCEL IC column (hexane/*i*PrOH = 70:30, 254 nm, 1 mL/min), t_R (major) = 6.9 min, t_R (minor) = 8.8 min.

***tert*-Butyl 2-((3*R*,5*S*)-5-(*tert*-butylcarbamoyl)-2-oxotetrahydrofuran-3-yl)-1*H*-pyrrole-1-carboxylate (17b).** The title compound was prepared (70 mg, 0.2 mmol, 20%) as a white solid by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 1 h; Reaction time B: 12 h) (R_f = 0.25 CH_2Cl_2/AcOEt 97/3): mp 106−108 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21 (dd, J = 3.5, 2.0 Hz, 1H), 6.40 (bs, 1H), 6.20 (dd, J = 3.5, 2.0 Hz, 1H), 6.12 (t, J = 3.5 Hz, 1H), 4.74 (dd, J = 10.0, 7.5 Hz, 1H), 4.28 (m, 1H), 2.90 (dt, J = 12.0, 9.0 Hz, 1H), 2.49 (q, J = 12.0 Hz, 1H), 1.58 (s, 9H), 1.40 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.7, 168.6, 149.4, 127.9, 122.7, 115.7, 110.5, 84.5, 75.9, 51.5, 41.4, 33.3, 28.8, 28.1; IR (KBr plate) ν_{max} 3426, 3117, 2973, 2934, 2878, 1793, 1734, 1678, 1529, 1495, 1478, 1453, 1413, 1365, 1342, 1256, 1227, 1143, 1072, 1052, 987, 929, 881, 846, 829, 728 (cm^{-1}); ESI-HRMS m/z calcd for $C_{18}H_{26}N_2NaO_5^+$ ($[M + Na]^+$) 373.1739, found 373.1733; $[\alpha]^{20}_D$ =

−5.5 (*c* 0.9, $CHCl_3$), er (70:30). The enantiomeric ratio was determined by HPLC with a CHIRALCEL OD-H column (hexane/*i*PrOH = 70:30, 254 nm, 1 mL/min), t_R (minor) = 6.7 min, t_R (major) = 8.1 min.

4-(Benzofuran-2-yl)-*N*-(*tert*-butyl)-5-oxotetrahydrofuran-2-carboxamide (18). The title compound (mixture of diastereoisomers (dr 60:40)) was prepared (210 mg, 0.7 mmol, 70%) as a white solid by the general procedure and eluted from silica gel with CH_2Cl_2/AcOEt (98/2) (Reaction time A: 5 h; Reaction time B: 12 h) (R_f = 0.15 and 0.25 CH_2Cl_2/AcOEt 95/5): ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56−7.51 (m), 7.48−7.40 (m), 7.32−7.25 (m), 7.25−7.20 (m), 6.74 (s, 1H, minor), 6.71 (s, 1H, major), 6.25−6.13 (m), 5.00 (dd, *J* = 8.0, 5.5 Hz, 1H, major), 4.83 (dd, *J* = 9.0, 7.5 Hz, 1H, minor), 4.15 (t, *J* = 9.5 Hz, 1H, minor), 4.10 (dd, *J* = 9.5, 7.5 Hz, 1H, major), 3.11 (ddd, *J* = 13.5, 9.5, 7.5 Hz, 1H, minor), 2.99−2.85 (m, 2H, major), 2.69 (ddd, *J* = 13.5, 10.5, 9.5 Hz, 1H, minor), 1.40 (s, 9H, major), 1.38 (s, 9H, minor); ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.3 (major), 172.8 (minor), 168.0 (major), 167.6 (minor), 155.15 (minor), 155.12 (major), 151.0 (major), 150.7 (minor), 128.01 (minor), 127.96 (major), 124.8 (major), 124.7 (minor), 123.3 (major), 123.2 (minor), 121.20 (major), 121.17 (minor), 111.3, 105.6 (minor), 105.4 (major), 76.6 (major), 76.0 (minor), 52.0 (major), 51.9 (minor), 40.8 (minor), 39.8 (major), 32.0 (minor), 31.6 (major), 28.8 (major), 28.7 (minor); IR (KBr plate) ν_{max} 3289, 3089, 2968, 2930, 2785, 1779, 1664, 1609, 1561, 1455, 1395, 1369, 1323, 1271, 1255, 1225, 1185, 1043, 1013, 954, 924, 874, 816, 799, 744 (cm^{-1}); ESI-HRMS *m*/*z* calcd for $C_{17}H_{19}NNaO_4^+$ ($[M + Na]^+$) 324.1212, found 324.1220; er (50:50). The enantiomeric ratio was determined by HPLC with a CHIRALCEL IC column (hexane/EtOH = 70:30, 254 nm, 1 mL/min), t_R (major, major) = 5.2 min, t_R (minor, major) = 6.6 min, t_R (major, minor) = 6.1 min, t_R (minor, minor) = 8.9 min.

■ ASSOCIATED CONTENT

Supporting Information

Copies of NMR spectra and HPLC chromatograms of all new compounds. X-ray structural data (CIF) of compounds **4**, **5** and **6b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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