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Diastereoselective Synthesis of β-Lactams by Ligand-Controlled Stereodivergent Intramolecular Tsuji–Trost Allylation

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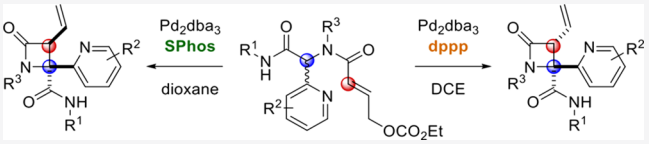
ABSTRACT: The diastereoselective synthesis of highly substituted β-lactams by intramolecular Tsuji–Trost allylation is reported. Judicious selection of the ligand on palladium allows selective access to either the *trans* isomer (in generally good to excellent yield with very high diastereomeric excess) or *cis* isomer (with yields and diastereoselectivity ranging from modest to excellent depending on the substrate). The reaction proceeds under exceedingly mild conditions (rt, no additives) with a broad range of substrates, which are readily accessible by the Ugi reaction.

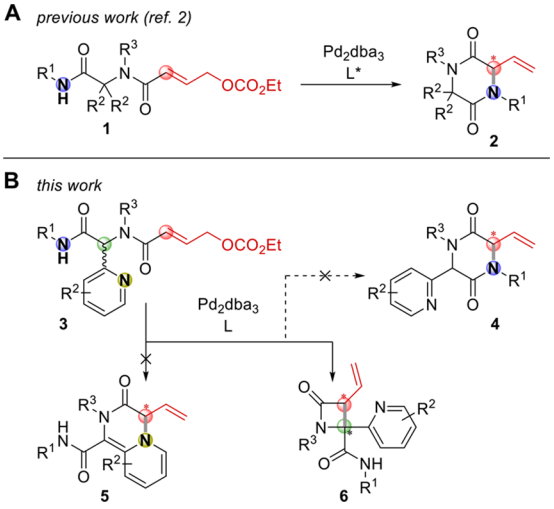


INTRODUCTION

Transition metal-catalyzed formation of C–C, C–N, and C–O bonds has evolved into an essential tool for the construction of medicinally relevant heterocycles. In particular, the Tsuji–Trost reaction and related allylation reactions allow the efficient construction of $C(sp^3)–C(sp^3)$ and $C(sp^3)–N$ bonds, resulting in highly substituted (hetero)cyclic frameworks when conducted in an intramolecular fashion.[1] Recently, we demonstrated that diamides **1** functionalized with an allylic carbonate handle (readily produced by the Ugi four-component reaction [U4CR]) efficiently undergo catalytic asymmetric intramolecular allylation to give highly substituted diketopiperazines **2** (DKPs; Scheme 1A).[2] In continuation of our work in this area, we realized that replacing symmetric (cyclic) ketones with heterocyclic aldehydes presented interesting opportunities for alternative cyclization modes (Scheme 1B). While formation of DKPs **4** may still occur, especially for small R^1 substituents, the presence of the heterocyclic substituent significantly increases the α-acidity of the substrate, allowing cyclization of the π-allylpalladium intermediate either via the heterocyclic N atom (leading to **5**, as reported by You et al. with iridium catalysis,[3] albeit with a nonconjugated electrophile) or the $C_α$ atom (giving **6**). Preliminary experiments (see the Supporting Information) soon revealed that formation of **4** and **5** is outcompeted by the formation of β-lactams **6**.

It is hard to overstate the importance of β-lactams as antibiotics, with a prominent role for the penicillins and cephalosporins, as exemplified by penicillin G (**I**; Figure 1). The rise of antibiotic resistance against first-line antibiotics has led to the development of β-lactamase inhibitors such as

Scheme 1. Intramolecular Tsuji–Trost Reaction of Ugi Products for the Synthesis of Diverse Heterocycles



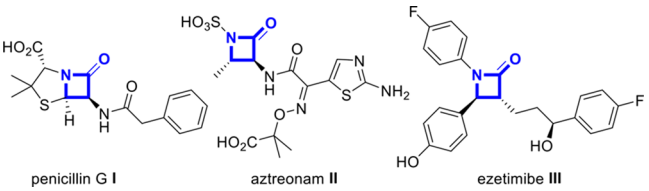


Figure 1. Pharmaceuticals containing β-lactam motifs.

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aztreonam (**II**).[4] In addition, the recently launched cholesterol absorption inhibitor ezetimibe (**III**) also features a β-lactam ring. Consequently, robust and efficient synthetic access to β-lactams with control over relative and absolute stereochemistry is in high demand.

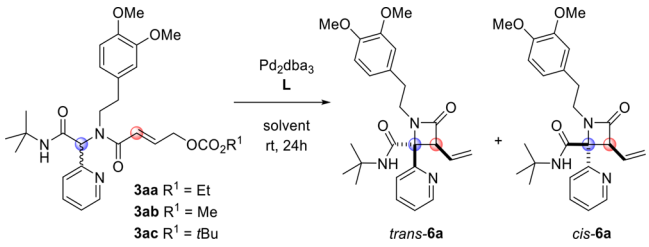
Currently, the production of β-lactam drugs typically relies on semisynthesis starting from simplified penicillin and cephalosporin derivatives obtained by fermentation. In addition to the cyclization of β-amino acids,[5] synthetic methods for the construction of β-lactams include the Staudinger reaction[6] (i.e., the formal [2 + 2] cycloaddition of ketenes and imines), the Kinugasa reaction,[7] intramolecular carbene insertion,[8] and various other methods.[9] In addition, several methods for the synthesis of β-lactams based on the U4CR have been reported,[10−14] but these do not offer the same flexibility, substitution pattern, and stereocontrol. Given the mild conditions of our (likely kinetically controlled) reaction and opportunities to fine-tune the reaction outcome via the Pd ligand, we set about to investigate possibilities to control the relative stereochemistry of the process.

RESULTS AND DISCUSSION

Fortuitously, we soon discovered that the ligand on Pd has a profound effect on the diastereoselectivity of our reaction (Table 1; see the Supporting Information for the full optimization study). Notably, we found that the use of monodentate phosphine ligands afforded predominantly the *trans* isomer, while the *cis* isomer was the major product when bidentate phosphines were used. Thus, while **6a** was obtained as a 31:69 *trans*/*cis* diastereomeric mixture under the initial conditions (Pd_2dba_3, dppe, CH_2Cl_2, rt, 24 h, entry 1), simply replacing the dppe ligand with SPhos gave **6a** in near-quantitative yield as a 91:9 mixture of diastereomers (entry 2). The stereoselectivity was lower in more polar solvents (DMF, MeCN; entries 3 and 4) but even higher in toluene and 1,4-dioxane (entries 5 and 6). Having selected the latter as the optimal solvent, we studied the influence of the carbonate leaving group. As in our previous work,[2] we found that the ethyl carbonate is superior to the corresponding methyl and *tert*-butyl carbonates (**3ab** and **3ac**, entries 7 and 8). Next, we focused on identifying conditions that allow selective access to the *cis* isomer of **6a**. Testing several bidentate phosphine ligands, we noted a marked dependence on the bite angle, with dppp giving the highest selectivity (for details, see the Supporting Information). Thus, simply replacing dppe with dppp increased the diastereoselectivity from 31:69 to 11:89 (entry 9). Interestingly, in this case, solvents such as toluene and 1,4-dioxane gave lower selectivity (entries 10 and 11), while the selectivity was maintained in polar solvents (entries 12 and 13). Performing the reaction in 1,2-dichloroethane gave **6a** with 9:91 dr, albeit still in only modest yield (entry 14). After observing various other reaction parameters not leading to either an improved yield or *dr* (see the Supporting Information), we next performed the reaction at different concentrations (entries 15−17) and found that the reaction performs optimally at 0.066 M. Again, the use of carbonates **3ab** and **3ac** offered no further improvement (entries 18 and 19).

Having identified conditions to selectively access either the *trans* isomer [conditions A: 5 mol % $Pd_2(dba)_3$, 20 mol % SPhos, 1,4-dioxane (0.2 M), rt, 24 h] or the *cis* isomer [conditions B: 5 mol % $Pd_2(dba)_3$, 10 mol % dppp, 1,2-dichloroethane (0.066 M), rt., 24 h], we set out to investigate

Table 1. Optimization of Diastereoselectivity[a]



entry	substrate	ligand	solvent	yield (%)[b]	*trans*:*cis*[c]
1	**3aa**	dppe	CH_2Cl_2	75	31:69
2	**3aa**	SPhos	CH_2Cl_2	99	91:9
3	**3aa**	SPhos	DMF	91	62:38
4	**3aa**	SPhos	MeCN	92	69:31
5	**3aa**	SPhos	PhMe	91	>95:5
6	**3aa**	SPhos	dioxane	92	>95:5
7	**3ab**	SPhos	dioxane	87	>95:5
8	**3ac**	SPhos	dioxane	85	94:6
9	**3aa**	dppp	CH_2Cl_2	45	11:89
10	**3aa**	dppp	PhMe	17	24:76
11	**3aa**	dppp	dioxane	n.d.	
12	**3aa**	dppp	DMF	30	11:89
13	**3aa**	dppp	MeCN	47	11:89
14	**3aa**	dppp	DCE	50	9:91
15[d]	**3aa**	dppp	DCE	42	10:90
16[e]	**3aa**	dppp	DCE	55	9:91
17[f]	**3aa**	dppp	DCE	70	9:91
18	**3ab**	dppp	DCE	73	27:73
19	**3ac**	dppp	DCE	70	10:90

[a]Reagents and conditions: **3a** (0.20 mmol), $Pd_2(dba)_3$ (0.01 mmol), monodentate (0.04 mmol), or bidentate (0.02 mmol) ligand in the indicated solvent (0.2 M). [b]Determined by ^{1}H NMR analysis with an internal standard. [c]Determined by ^{1}H NMR analysis of the crude product. [d]Performed at 0.4 M concentration. [e]Performed at 0.1 M concentration. [f]Performed at 0.066 M concentration. n.d., not detected. DCE, 1,2-dichloroethane.

the scope and limitations of the stereodivergent and chemoselective procedures with respect to R^1 and R^2 as well as the heterocyclic substituent. Thus, we studied the cyclization of diversely substituted Ugi products **3aa**−**3r** under both conditions A and B (Scheme 2). To our delight, nearly all reactants were converted to the corresponding β-lactams **6a**−**6r** under both sets of conditions, often with high selectivity and no trace of either diketopiperazines **4** or dearomatization products **5**.

Pyridine-substituted substrates **3aa**−**3d** were converted to β-lactams **6a**−**6d** in good to excellent yield with (nearly) complete selectivity for the *trans* isomer under conditions A.

Under conditions B, products **6a**−**6d** were formed with moderate selectivity for the *cis* isomer in modest to reasonable yield. Notably, the cyclization of **3d** (featuring a primary R^1 substituent) was accompanied by the formation of the corresponding diketopiperazine **2d** as a side product (15%, 67:33 dr) only under conditions B. Isoxazole-functionalized substrates **3e**−**3h** were also converted to the corresponding β-lactams in modest to excellent yield, always with full diastereoselectivity under conditions A. Under conditions B, the yields were generally lower, and the selectivity for the *cis* isomer ranges from moderate (**6e** and **6f**) to excellent (**6g** and **6h**). The regioisomeric isoxazole substrate **3i** was converted to **6i** under both sets of conditions, in both cases with moderate

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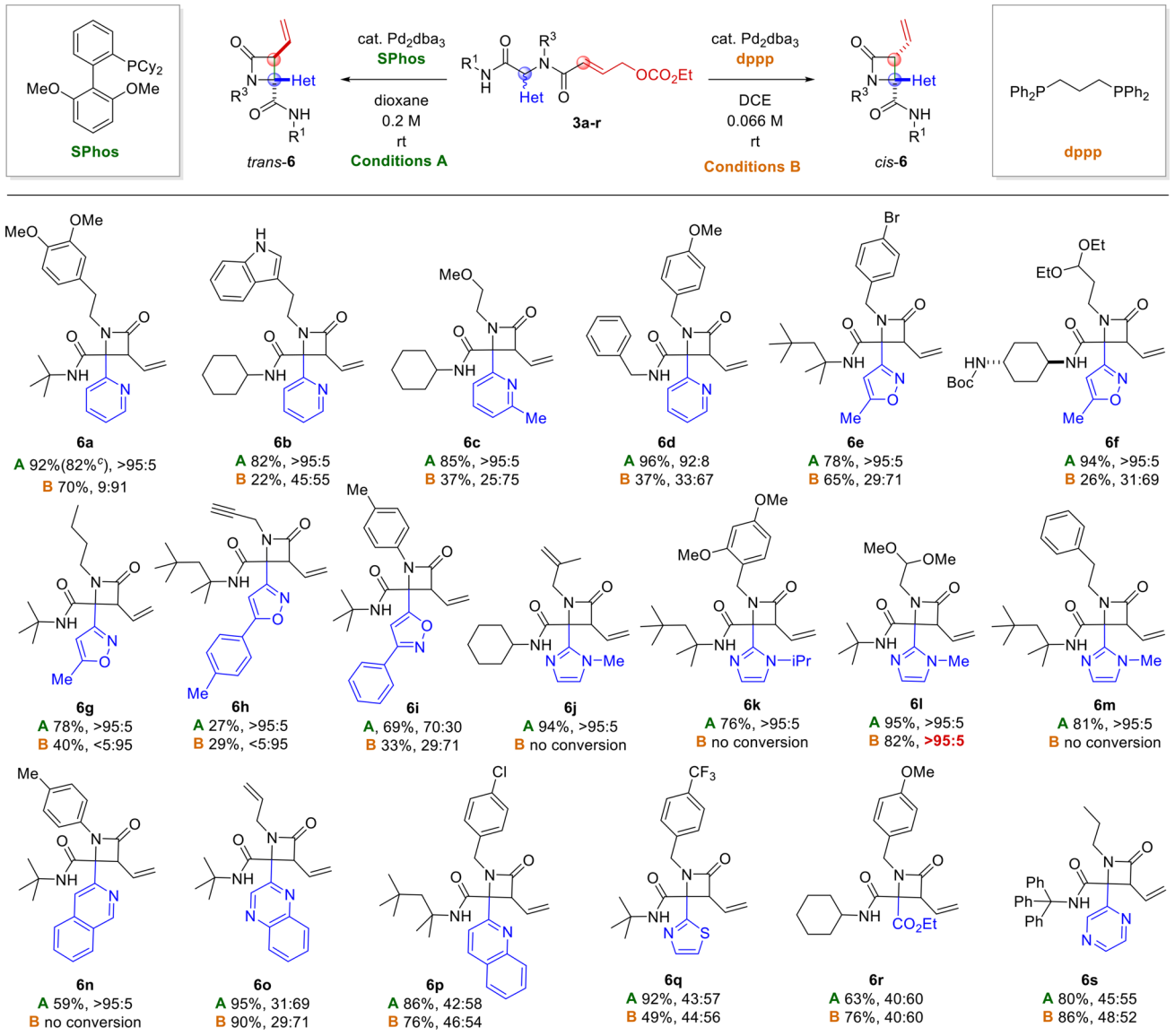
Scheme 2. Scope of the Reaction[a,b,c]



[a]Isolated yields. [b]Diastereomeric ratios are reported as *trans*/*cis* ratios as determined by ^{1}H NMR analysis of the crude reaction product. [c]Yield of 3.0 mmol-scale experiment. [d]Reagents and conditions: A: **3** (0.20 mmol), $Pd_2(dba)_3$ (0.01 mmol), SPhos (0.04 mmol), 1,4-dioxane (1 mL), 24 h, rt. B: **3** (0.20 mmol), $Pd_2(dba)_3$ (0.01 mmol), dppp (0.02 mmol), 1,2-dichloroethane (3 mL), 24 h, rt.

selectivity for the expected diastereomer. Imidazole-substituted substrates **3j**−**3m** were selectively converted to *trans*-β-lactams **6j**−**6m** under conditions A, but no conversion took place under conditions B. The product **6l** was an exception, being formed in good yield under conditions B, curiously with complete selectivity for the *trans* isomer. Isoquinolin-3-yl-substituted β-lactam **6n** was also only formed under conditions A, still with excellent dr. Reactions of substrates with other heterocyclic substituents (**3o**−**3q** and **3s**) or an ester (**3r**) all afforded the corresponding β-lactams in reasonable to excellent yield under both conditions A and B, but the selectivity was completely lost; nearly identical dr's were observed regardless of the conditions. Apparently, the nature of the heterocyclic substituent plays a key role in the diastereoselection. X-ray crystallographic analysis of *cis*-**6s**[15] confirmed the relative stereochemistry assigned by ^{1}H NMR.[16] With regard to the R^1 and R^2 substituents, the mild reaction conditions tolerate a wide variety of functional groups, including nitro groups, ethers, esters, amides, alkenes, alkynes, acetals, and aryl bromides. Intrigued by the stereodivergence of the reaction under conditions A and B, we sought to rationalize this remarkable difference in diastereoselectivity. We speculate that, in reactions employing monodentate ligands (i.e., conditions A), the heterocyclic N atom is actively involved in the mechanism, specifically by intramolecular coordination of the π-allylpalladium(II) complex (Figure 2), thus leading to the *trans* diastereoisomer (with a *syn* arrangement of the vinyl group and heterocycle). Indeed, pyridines and related N-heterocycles are common directing groups in Pd(II)-catalyzed C−H activation.[17] However, we could not find any literature precedent of their use in directing reactions of π-allylpalladium(II) intermediates by intramolecular coordination. In contrast, with bidentate ligands (conditions B), the bidentate complex is proposed to remain intact throughout the catalytic cycle, with C−C bond formation occurring via an outer-sphere mechanism.

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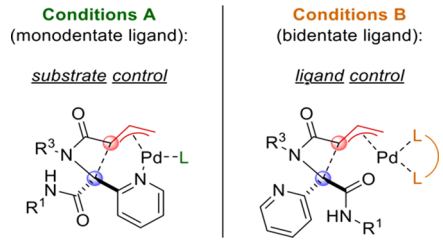


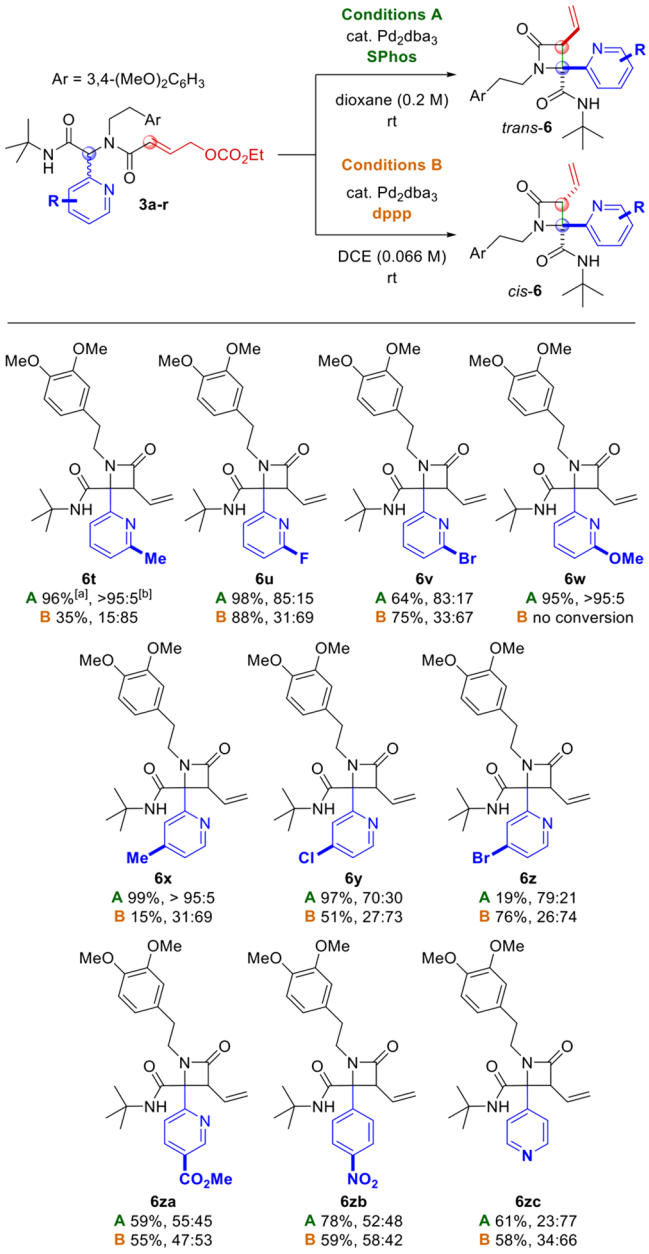
Figure 2. Proposed model for observed diastereodivergence.

This would also explain why substrates bearing heterocycles that are good potential Pd ligands (e.g., pyridines, isoxazoles, and imidazoles) react much more selectively under conditions A than those with heterocycles that are poor ligands for steric or electronic reasons (e.g., quinoline, quinoxaline, and pyrazine). To test this hypothesis, we reacted a series of substrates (**3t**−**3zc**) bearing electronically diverse 2-pyridyl moieties as well as substituents that cannot coordinate to the Pd center. Based on our mechanistic proposal (Figure 2), we expected that the introduction of electron-donating substituents on the pyridine ring would enhance its coordination capacity, thus leading to high *trans* selectivity under conditions A. Conversely, electron-withdrawing substituents would weaken the proposed interaction, leading to lower selectivity and/or yield. Under conditions B, we expected no particular influence of the substituents on the diastereoselectivity based on the proposed mechanism. On the other hand, electron-poor pyridines should increase the acidity of the α-proton, thereby increasing the reaction rate. The results (Scheme 3) are in line with our expectations. Substrates bearing relatively electron-rich pyridines were converted to the corresponding β-lactams (**6t**, **6w**, and **6x**) in excellent yield and selectivity under conditions A, while at best, poor conversion was observed under conditions B. Conversely, β-lactams **6u**, **6v**, **6y**, and **6z** bearing moderately electron-deficient pyridine rings were obtained in good yield under conditions B, while the selectivity (and in some cases the yield) was reduced under conditions A.

To gain further insight into the reaction mechanism, we next performed density functional theory (DFT) calculations at COSMO-ZORA-BLYP/TZ2P[18] on the reaction of **3zd** (Het = 2-pyridyl, R^1 = R^2 = Me) using ADF.[19] Extensive benchmarking of ZORA-BLYP/TZ2P for oxidative addition to palladium shows that the reactivity trends compare very well with ab initio reference from hierarchical series up until CCSD(T).[20] Furthermore, computed trends in reactivity for the studied reactions are the same across multiple level of theories, including when explicit dispersion corrections are applied (COSMO-ZORA-BLYP-D3(BJ)/TZ2P) and when energies are computed at the meta-hybrid level (COSMO-ZORA-M06/TZ2P//COSMO-ZORA-BLYP-D3(BJ)/TZ2P) (see Table S4 in the Supporting Information). An activation strain analysis[21] was performed on the computed transition state structures using the PyFrag 2019 program (Figure S3).[22]

The potential energy surface (PES) in Figure 3 (left) reveals that the reactions involving the monodentate Pd catalyst (conditions A) favor the formation of the *trans*-β-lactam, which is the experimentally obtained diastereomer (kinetic control).[23] The PES in Figure 3 (right) shows that the reactions involving the bidentate Pd catalyst (conditions B) favor the formation of the *cis*-β-lactam. This is also the experimentally obtained diastereomer (kinetically and thermodynamically favored). The mono-TS-*trans* is associated with a

Scheme 3. Further Variation of the Pyridine Ring[a,b]



[a]Isolated yields. [b]Diastereomeric ratios are reported as *trans*/*cis* ratios as determined by ^{1}H NMR analysis of the crude reaction product. [c]Reagents and conditions: A: **3** (0.20 mmol), $Pd_2(dba)_3$ (0.01 mmol), SPhos (0.04 mmol), 1,4-dioxane (1 mL), 24 h, rt. B: **3** (0.20 mmol), $Pd_2(dba)_3$ (0.01 mmol), dppp (0.02 mmol), 1,2-dichloroethane (3 mL), 24 h, rt.

lower activation barrier than mono-TS-*cis* ($\Delta\Delta G^{\ddagger}$ = 4.9 kcal mol^{-1}), supporting the experimentally observed full selectivity for the *trans* isomer. The activation barrier for mono-TS-*cis* is higher due to a more destabilizing activation strain caused by a substantially later and more product-like transition state (Figure S3). The bi-TS-*cis* is associated with a lower barrier than bi-TS-*trans* ($\Delta\Delta G^{\ddagger}$ = 3.7 kcal mol^{-1}), again supporting the experimentally observed selectivity. The activation strain in both bi-TS-*cis* and bi-TS-*trans* is similar and only differs by 0.4 kcal mol^{-1}. A close hydrogen bond contact (2.22 Å) between the carbonyl oxygen of the amide group and a phenyl group on

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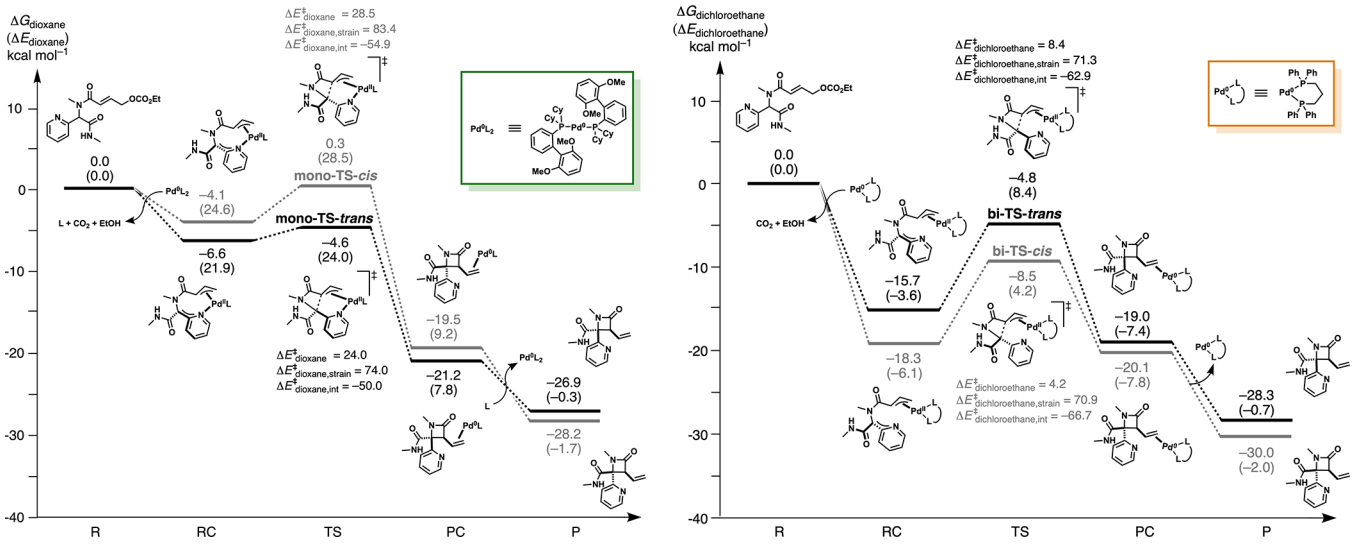


Figure 3. Reaction energy profiles and activation strain analyses for the (left) monodentate (conditions A) and (right) bidentate (conditions B) Pd-catalyzed reactions leading to the *trans*-β-lactam (black) and *cis*-β-lactam (gray) **3zd** computed at COSMO-ZORA-BLYP/TZ2P.

the bidentate ligand was found in the bi-TS-*cis*, which was absent in bi-TS-*trans* (Figure 4).

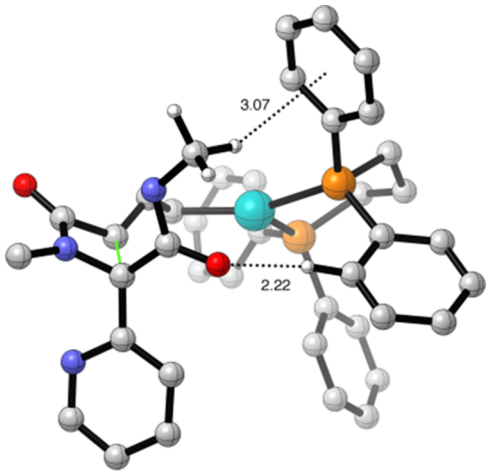
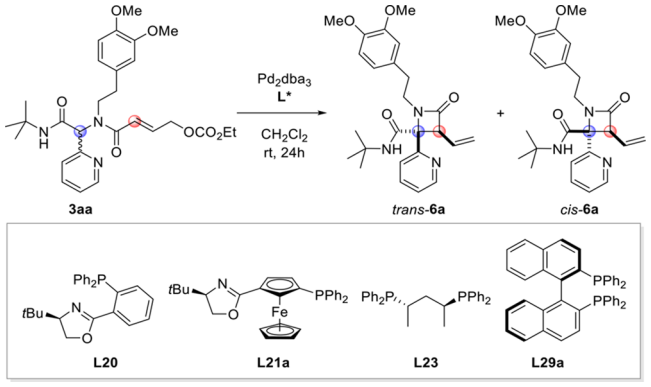


Figure 4. Stabilizing hydrogen bonding and C−H → π interactions in bi-TS-*cis*. All nonessential hydrogens are removed for clarity.

An additional stabilizing C−H → π interaction was identified between the methyl on the amide group and the bidentate ligand. These combined effects (likely even more so when the methyl group is replaced by a *tert*-butyl group) result in a more stabilizing interaction energy ($\Delta\Delta E^{\ddagger}_{int}$ = −3.8 kcal mol^{-1}) for bi-TS-*cis* compared to bi-TS-*trans* and thus a lower activation barrier of the former.

Encouraged by the possibilities to control the relative stereochemistry and to obtain additional insight into the mechanism, we tested a wide variety of chiral mono- and bidentate ligands in an attempt to also control the absolute stereochemistry of the product (see Table S3 for details). Unfortunately, our attempts met with limited success, and only very few ligands gave >50% ee (Table 2). For example, *t*BuPHOX (**L20**), which was highly efficient and selective in the intramolecular allylation of very similar substrates to give diketopiperazines,[2] gave low ee for both the *cis* and *trans* isomers. In this class of ligands, the oxazoline nitrogen is

Table 2. Diastereoselectivity versus Enantioselectivity[a]



entry	ligand	yield (%)[b]	*trans*:*cis*[c]	ee$_{trans}$[d]	ee$_{cis}$[d]
1	**L20**	96	81:19	24%	−33%
2	**L21a**	87	60:40	−72%	−16%
3	**L23**	42	10:90	n.d.	20%
4	**L29a**	22	14:86	n.d.	−56%

[a]All reactions were performed with **3aa** (0.20 mmol), $Pd_2(dba)_3$ (0.01 mmol), monodentate (0.04 mmol), or bidentate (0.02 mmol) ligand in CH_2Cl_2 (0.2 M). [b]Isolated yield. [c]Determined by ^{1}H NMR analysis of the crude product. [d]Determined by chiral HPLC. Positive and negative signs refer to the earlier or later eluting enantiomer, respectively, being the major enantiomer. n.d., not determined.

proposed to act as a hemilabile ligand for palladium. In light of our mechanistic considerations, it is perhaps not surprising that **L20** gives only low ee: the observed dr suggests it acts as a monodentate ligand, and the oxazoline is likely displaced by the pyridine of the substrate. In fact, our DFT calculations suggest that Pd already coordinates to the pyridine prior to generation of the π-allyl complex, which is the enantiodetermining step. Ligand **L21a** proved to be more efficient in controlling the absolute stereochemistry (72% ee for the *trans* isomer), albeit at the expense of the diastereoselectivity. Unfortunately, our attempts to further improve the ee remained fruitless. All chiral bisphosphine ligands appear to follow the bidentate scenario as described above, affording *cis*-**6a** as the main product. However, the conversion was very

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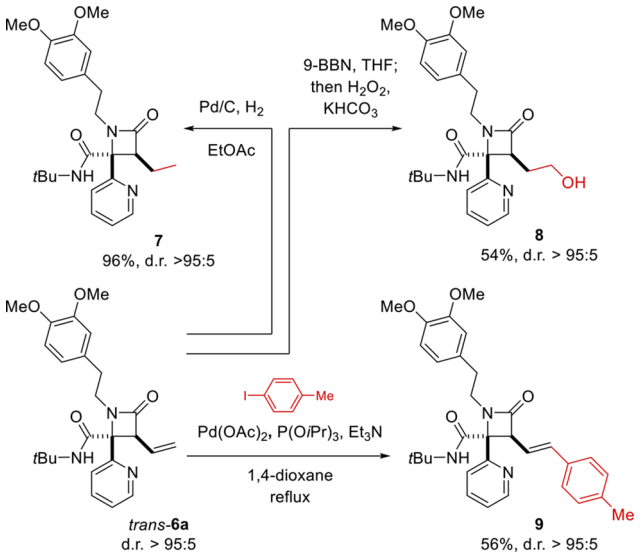
slow, resulting in modest yields even after 1 week of reaction time. (*R*)-BINAP (**L29a**) gave the highest ee for the *cis* isomer, but also in this case, any modifications made to the reaction conditions or the ligand structure proved to be counterproductive.

Finally, to further expand the range of accessible products, we performed some further transformations of the vinyl moiety of *trans*-**6a** (Scheme 4). Catalytic hydrogenation smoothly

Scheme 4. Transformations of the Vinyl Moiety of *trans*-6a



afforded **7** in excellent yield with full retention of the dr. Hydroboration/oxidation furnished **8** in moderate yield as a single diastereomer. Heck reaction with 4-iodotoluene afforded the cross-coupling product **9** without epimerization.

CONCLUSIONS

In conclusion, we developed a new ligand-directed stereodivergent synthesis of β-lactams by Pd-catalyzed intramolecular C(sp^3)–C(sp^3) bond formation. The divergent diastereoselective outcome of the reaction under different conditions is proposed to result from the presence or absence of intramolecular coordination of the Pd(II) π-allyl complex to the heterocyclic moiety. This hypothesis was supported by further studies and DFT calculations. The latter further indicated that the origin of diastereoselectivity in the monodentate scenario primarily results from a difference in activation strain between the two diastereomeric transition states, while a hydrogen bonding interaction in one of the diastereomeric transition states was found to be the origin of the diastereoselectivity in the bidentate scenario. The exceedingly mild reaction conditions tolerate a wide range of functional groups. The accessible product range of our method was further illustrated by various transformations of the vinyl moiety.

EXPERIMENTAL SECTION

General Information. Commercially available reagents were purchased from Sigma-Aldrich, Fischer, Strem Chemicals, or Fluorochem and were used as purchased, unless mentioned otherwise. Solvents were purchased from VWR Chemicals or Sigma-Aldrich and used without purification, unless stated otherwise. Anhydrous, air-free solvents were obtained from a PureSolv MD 5 solvent purification system. The infrared (IR) spectra were recorded neat using a Shimadzu FTIR-8400 s spectrophotometer and wavelengths are reported in cm^{-1}. The nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance 600 (150.90 MHz for ^{13}C), Bruker Avance 500 (125.78 MHz for ^{13}C), or Bruker Avance 300 using the residual $CHCl_3$ as the internal standard (^1H: δ 7.26 ppm; $^{13}C\{^1H\}$: δ 77.16 ppm). Chemical shifts (δ) are given in ppm and coupling constants (J) are quoted in Hertz (Hz). Resonances are described as s (singlet), d (doublet), t (triplet), q (quartet), br (broad singlet), and m (multiplet) or combinations thereof. Electrospray ionization (ESI) high-resolution mass spectrometry was carried out using a Bruker micrOTOF-Q instrument in positive ion mode (capillary potential of 4500 V). Flash chromatography was performed on Silicycle Silica-P Flash Silica Gel (particle size, 40–63 μm; pore diameter, 60 Å) using the indicated eluent. Thin-layer chromatography (TLC) was performed using TLC plates from Merck (SiO_2, Kieselgel 60 F254 neutral, on aluminum with a fluorescence indicator) and compounds were visualized by UV detection (254 nm) and/or $KMnO_4$ stain. SFC-MS analysis was conducted using a Shimadzu Nexera SFC-MS equipped with a Nexera X2 SIL-30 AC autosampler, Nexera UC LC-30 AD SF CO_2 pump, Nexera X2 LC-30 AD liquid chromatograph, Nexera UC SFC-30A back pressure regulator, prominence SPD-M20A diode array detector, prominence CTO-20 AC column oven, and CBM-20A system controller. Enantiomeric excess was determined by SFC-MS analysis using Lux 3 μm Cellulose-1 column (cellulose tris(3,5-dimethylphenylcarbamate) (column 1) and Lux 3 μm Cellulose-3 column (cellulose tris(4-methylbenzoate), 150 × 4.6 mm) (column 3). A gradient of supercritical CO_2 (A) and methanol (B) was used. Method 1 (column 1) was 2% B/98% A to 25% B/75% A over the course of 8 min and was maintained at 25% B/75% A for 1 min (flow: 1.5 mL/min). Method 2 (column 3) was 2% B/98% A to 7% B/93% A over the course of 6 min and then to 30% B/70% A over the course of 1 min and was maintained at 30% B/70% A for 1 min (flow: 1.5 mL/min). The sample injection volume was 5 μL. Mass spectrometry analyses were performed using a Shimadzu LCMS-2020 mass spectrometer. The data were acquired in full-scan APCI mode (MS) from m/z 100 to 800 in positive ionization mode. Data were processed using Shimadzu Labsolutions 5.82. Specific rotations were measured with an Automatic AA-10 polarimeter.

General Procedures. *Procedure A: Synthesis of the Ugi Precursors (GP-A).* A solution of the corresponding aldehyde (3 mmol, 1 equiv) and amine (3 mmol, 1 equiv) in MeOH (1 M, 3 mL) was stirred for 30 min, then the carboxylic acid (3 mmol, 1 equiv) was added, and after 5 min, the corresponding isocyanide (3 mmol, 1 equiv) was added. The reaction mixture was stirred for 24 h or until full conversion of the starting material (monitored by TLC), concentrated, and purified by silica gel column chromatography, as described in the corresponding synthetic procedure.

Procedure B: Diastereoselective Tsuji–Trost Reaction Using Monodentate Ligand (SPhos) (GP-B). A solution of $Pd_2(dba)_3$ (9 mg, 0.01 mmol, 0.05 equiv), SPhos (17 mg, 0.04 mmol, 0.2 equiv), and the corresponding linear precursor (0.2 mmol, 1 equiv) in dioxane (0.2 M, 1 mL) was stirred overnight or until full conversion of the starting material (monitored by TLC). Then, the reaction mixture was filtrated, concentrated, and purified by silica gel column chromatography, as described in the corresponding synthetic procedure.

Procedure C: Diastereoselective Tsuji–Trost Reaction Using Bidentate Ligand (dppp) (GP-C). A solution of $Pd_2(dba)_3$ (9 mg, 0.01 mmol, 0.05 equiv), dppp (9 mg, 0.04 mmol, 0.2 equiv), and the corresponding linear precursor (0.2 mmol, 1 equiv) in DCE (0.066 M, 3 mL) was stirred overnight or until full conversion of the starting material (monitored by TLC). Then, the reaction mixture was filtrated, concentrated, and purified by silica gel column chromatography, as described in the corresponding synthetic procedure.

*Ugi Product **3aa**.* Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (40% EtOAc/*c*Hex) afforded the title compound as a beige solid in 65% yield (1.020 g, 1.93 mmol). R_f = 0.36 (70% EtOAc/*c*Hex). Two rotamers were present on NMR timescale (R^1:R^2 = 4:1), of which the signals of the major rotamer are reported. ^1H NMR (600 MHz, $CDCl_3$) δ 8.60

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(d, J = 4.1 Hz, 1H), 7.70 (t, J = 7.4 Hz, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.24 (s, 1H), 7.08 (s, 1H), 6.91 (dt, J = 15.1, 4.4 Hz, 1H), 6.75 (d, J = 7.8 Hz, 1H), 6.66−6.60 (m, 2H), 6.52 (d, J = 15.1 Hz, 1H), 5.92 (s, 1H), 4.78 (d, J = 3.7 Hz, 2H), 4.25−4.18 (m, 2H), 3.84 (s, 3H), 3.83 (s, 3H), 3.75−3.66 (m, 2H), 2.82−2.73 (m, 1H), 2.55−2.47 (m, 1H), 1.38 (s, 9H), 1.31 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 167.6, 166.5, 160.7, 156.4, 154.9, 149.1, 147.9, 138.9, 137.2, 130.9, 124.1, 123.0, 121.7, 120.8, 112.2, 111.5, 66.3, 64.8, 64.5, 56.0, 56.0, 51.7, 49.6, 36.2, 28.8 (3C), 14.4. IR (neat) ν_{max} (cm^{-1}): 3722, 3296, 2966, 2907, 1740, 1664, 1616, 1514, 1460, 1425, 1257, 1157, 1026, 995, 781, 770, 565, 426. m.p.: 129−134 °C. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{28}H_{37}N_3O_7Na^+$, 550.2524; found, 550.2530.

Ugi Product ***3ab***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (50% EtOAc/*c*Hex) afforded the title compound as a colorless solid in 31% yield (0.471 g, 0.91 mmol). R_f = 0.31 (50% EtOAc/*c*Hex). Two rotamers were present on NMR timescale (R^1:R^2 = 4:1), of which the signals of the major rotamer are reported. ^1H NMR (600 MHz, $CDCl_3$) δ 8.59 (d, J = 7.7 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.24 (d, J = 7.3 Hz, 1H), 7.09 (s, 1H), 6.90 (dt, J = 15.1, 4.5 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 6.66−6.59 (m, 2H), 6.50 (d, J = 15.1 Hz, 1H), 5.93 (s, 1H), 4.78 (d, J = 4.5 Hz, 2H), 3.84 (s, 3H), 3.82 (s, 3H), 3.78 (s, 3H), 3.72−3.68 (m, 2H), 2.79−2.73 (m, 1H), 2.54−2.47 (m, 1H), 1.37 (s, 9H). $^{13}C\{^1H\}$NMR (151 MHz, $CDCl_3$) δ 167.5, 166.4, 156.3, 155.4, 149.1, 149.1, 147.8, 138.7, 137.2, 130.9, 124.1, 123.0, 121.6, 120.7, 112.2, 111.4, 66.5, 64.7, 56.0, 55.9, 55.1, 51.7, 49.6, 36.2, 28.8 (3C). IR (neat) ν_{max} (cm^{-1}): 3298, 2959, 1745, 1663, 1612, 1514, 1427, 1259, 1230, 1157, 1136, 1026, 953. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{27}H_{36}N_3O_7^+$, 514.2548; found. 514.2549.

Ugi Product ***3ac***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (35% EtOAc/*c*Hex) afforded the title compound as a light brown solid in 19% yield (0.320 g, 0.85 mmol). R_f = 0.57 (50% EtOAc/*c*Hex). Two rotamers were present on NMR timescale (R^1:R^2 = 9:4), of which the signals of the major rotamer are reported. ^1H NMR (600 MHz, $CDCl_3$) δ 8.59 (d, J = 4.6 Hz, 1H), 7.70 (t, J = 7.2 Hz, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.24 (t, J = 6.5 Hz, 1H), 7.08 (s, 1H), 6.92 (dt, J = 15.1, 4.5 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 6.66−6.62 (m, 2H), 6.51 (d, J = 15.1 Hz, 1H), 5.91 (s, 1H), 4.71 (d, J = 4.5 Hz, 2H), 3.84 (s, 3H), 3.83 (s, 3H), 3.73−3.69 (m, 2H), 2.79 (t, J = 14.8 Hz, 1H), 2.56−2.50 (m, 1H), 1.47 (s, 9H), 1.38 (s, 9H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 167.6, 166.5, 156.4, 153.1, 149.1, 149.0, 147.9, 139.4, 137.3, 130.9, 124.1, 123.0, 121.6, 120.8, 112.3, 111.5, 82.7, 65.6, 64.9, 56.0 (2C), 51.7, 49.6, 36.2, 28.8 (3C), 27.9 (3C). IR (neat) ν_{max} (cm^{-1}): 3298, 1732, 1666, 1618, 1516, 1421, 1281, 1252, 1236, 1159, 1134, 1030. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{30}H_{42}N_3O_7^+$, 556.3017; found, 556.3015.

Ugi Product ***3b***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (75% EtOAc/*c*Hex) afforded the title compound as a yellow solid in 59% yield (0.937 g, 1.75 mmol). R_f = 0.18 (70% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.49 (d, J = 4.5 Hz, 1H), 7.57 (td, J = 7.7, 1.7 Hz, 1H), 7.42 (d, J = 7.8 Hz, 1H), 7.38−7.28 (m, 2H), 7.21 (d, J = 8.0 Hz, 1H), 7.13 (dd, J = 7.1, 5.1 Hz, 1H), 7.04 (t, J = 7.5 Hz, 1H), 6.98 (t, J = 7.4 Hz, 1H), 6.84 (d, J = 1.7 Hz, 1H), 6.71 (dt, J = 15.1, 4.8 Hz, 1H), 6.24 (d, J = 15.1 Hz, 1H), 5.88 (s, 1H), 4.42 (d, J = 4.8 Hz, 2H), 4.07 (q, J = 7.1 Hz, 2H), 3.83−3.63 (m, 3H), 2.93−2.81 (m, 1H), 2.74−2.60 (m, 1H), 1.84 (s, 2H), 1.59−1.50 (m, 2H), 1.46 (dd, J = 8.9, 3.9 Hz, 1H), 1.30−1.20 (m, 2H), 1.18 (t, J = 7.1 Hz, 3H), 1.13−1.01 (m, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 167.6, 166.5, 156.2, 154.7, 149.0, 138.5, 137.3, 136.3, 127.2, 123.9, 123.00, 122.98, 121.9, 121.7, 119.4, 118.3, 111.8, 111.4, 66.2, 64.6, 64.4, 48.6, 48.5, 32.8, 32.7, 26.0, 25.6, 24.7 (2C), 14.3. IR (neat) ν_{max} (cm^{-1}): 2934, 1749, 1678, 1510, 1375, 1254, 1203, 1032. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{30}H_{36}N_4O_5Na^+$, 555.2578; found, 555.2566.

Ugi Product ***3c***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (60% EtOAc/*c*Hex) afforded the title compound as a colorless solid in 51% yield (0.716 g, 1.53 mmol). R_f = 0.18 (70% EtOAc/*c*Hex). Three rotamers were present on NMR timescale (R^1:R^2:R^3 = 3:2:1), of which the signals of the major rotamer are reported. ^1H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 7.6 Hz, 1H), 7.55 (t, J = 8.0 Hz, 1H), 7.22 (d, J = 7.9 Hz, 1H), 7.09−7.04 (m, 1H), 6.92−6.83 (m, 1H), 6.68 (d, J = 15.2 Hz, 1H), 5.57 (s, 1H), 4.79 (d, J = 3.4 Hz, 2H), 4.21 (q, J = 7.1 Hz, 2H), 3.88−3.81 (m, 1H), 3.78−3.63 (m, 2H), 3.59−3.40 (m, 2H), 3.28 (s, 3H), 2.53 (s, 3H), 2.00−1.86 (m, 2H), 1.71−1.50 (m, 4H), 1.43−1.15 (m, 7H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 167.2, 157.3, 155.7, 150.9, 143.9, 138.8, 137.9, 137.5, 122.5, 120.5, 71.0, 66.5, 64.9, 64.4, 59.0, 48.3, 48.1, 47.4, 32.9 (2C), 25.8 (2C), 24.5, 14.49. IR (neat) ν_{max} (cm^{-1}): 2932, 1746, 1665, 1622, 1452, 1248, 1115, 995, 7317. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{24}H_{35}N_3NaO_6^+$, 484.2418; found, 484.2412.

Ugi Product ***3d***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (75% EtOAc/*c*Hex) afforded the title compound as a yellow oil in 60% yield (0.923 g, 1.80 mmol). R_f = 0.20 (70% EtOAc/*c*Hex). Two rotamers were present on NMR timescale (R^1:R^2 = 7:1), of which the signals of the major rotamer are reported. ^1H NMR (500 MHz, $CDCl_3$) δ 8.45 (d, J = 4.1 Hz, 1H), 7.68−7.56 (m, 2H), 7.42−7.37 (m, 1H), 7.32−7.27 (m, 2H), 7.26−7.21 (m, 3H), 7.18−7.13 (m, 1H), 7.05 (d, J = 8.1 Hz, 2H), 6.98 (dt, J = 15.2, 4.8 Hz, 1H), 6.74 (d, J = 8.3 Hz, 2H), 6.52 (d, J = 15.1 Hz, 1H), 5.86 (s, 1H), 4.85−4.80 (m, 2H), 4.74 (d, J = 3.0 Hz, 2H), 4.56−4.42 (m, 2H), 4.16 (q, J = 7.2 Hz, 2H), 3.75 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 168.2, 167.1, 164.9, 159.0, 154.7, 148.5, 139.9, 138.3, 137.3, 128.9, 128.7 (2C), 128.2 (2C), 127.7 (2C), 127.4, 123.0, 121.9, 114.1 (2C), 114.0, 66.3, 64.5, 64.5, 55.4, 51.2, 43.8, 14.4. IR (neat) ν_{max} (cm^{-1}): 3300, 2957, 1744, 1664, 1612, 1512, 1433, 1244, 1202, 1175, 1028, 995. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{29}H_{31}N_3NaO_6^+$, 540.2105; found, 540.2101.

Ugi Product ***3e***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a yellow oil in 57% yield (1.005 g, 1.67 mmol). R_f = 0.71 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.3 Hz, 2H), 6.97 (dt, J = 15.1, 4.6 Hz, 1H), 6.31 (dd, J = 15.4, 1.8 Hz, 1H), 6.22 (s, 1H), 6.10 (s, 1H), 5.65 (s, 1H), 4.76−4.69 (m, 3H), 4.64 (d, J = 17.8 Hz, 1H), 4.14 (q, J = 7.1 Hz, 2H), 2.33 (s, 3H), 1.68 (d, J = 15.0 Hz, 1H), 1.62 (d, J = 17.2 Hz, 1H), 1.36 (s, 3H), 1.35 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H), 0.92 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 170.2, 166.9, 165.2, 159.9, 154.6, 140.6, 135.9, 131.9 (2C), 128.5 (2C), 121.6, 121.3, 102.9, 66.1, 64.5, 57.3, 55.9, 52.2, 50.8, 31.7, 31.5 (3C), 28.9, 28.7, 14.3, 12.4. IR (neat) ν_{max} (cm^{-1}): 2953, 1747, 1666, 1624, 1398, 1366, 1252, 1227, 1203, 1011, 791. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{28}H_{38}BrN_3NaO_6^+$, 614.1836; found, 614.1828.

Ugi Product ***3f***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (70% EtOAc/*c*Hex) afforded the title compound as an amber oil in 47% yield (0.894 g, 1.40 mmol). R_f = 0.13 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 6.94 (dt, J = 15.2, 4.7 Hz, 1H), 6.67 (d, J = 7.9 Hz, 1H), 6.61 (dt, J = 15.0, 1.6 Hz, 1H), 6.13 (s, 1H), 5.33 (s, 1H), 4.80−4.77 (m, 2H), 4.52 (t, J = 5.1 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 4.03−3.89 (m, 3H), 3.63 (ddt, J = 14.2, 8.9, 7.1 Hz, 3H), 3.56−3.41 (m, 3H), 2.86 (s, 2H), 2.40 (s, 3H), 1.98−1.81 (m, 5H), 1.72 (s, 1H), 1.45−1.41 (m, 11H), 1.31 (d, J = 14.3 Hz, 3H), 1.19 (t, J = 7.1 Hz, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 170.2, 166.1, 166.0, 160.5, 154.7, 154.7, 139.8, 121.1, 102.6, 100.6, 79.6, 66.1, 64.4, 62.2, 61.9, 58.1, 47.2 (2C), 44.7, 33.6, 31.6 (4C), 28.4 (3C), 15.3, 15.3, 14.3, 12.4. IR (neat) ν_{max} (cm^{-1}): 2974, 1747, 1666, 1423, 1366, 1252, 1171, 1138, 1059, 1005, 7317. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{31}H_{51}N_4O_{10}^+$, 639.3600; found, 639.3605.

Ugi Product ***3g***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a colorless waxy solid in 86% yield (1.094 mg, 2.58 mmol). R_f = 0.38 (50% EtOAc/*c*Hex). ^1H NMR (600 MHz, $CDCl_3$) δ 6.94 (dt, J = 15.1, 4.6 Hz, 1H), 6.52−6.43 (m, 2H), 6.17 (s, 1H), 5.55 (s, 1H), 4.81 (d, J = 4.3 Hz, 2H), 4.22 (d, J = 7.2 Hz, 2H), 3.43 (t, J = 8.1 Hz, 2H), 2.42 (s, 3H), 1.67−1.57 (m, 1H), 1.47 (dq, J = 14.2, 6.9 Hz, 1H), 1.35−1.31 (m, 12H), 1.30−1.24

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(m, 2H), 0.89 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, CDCl3) δ 170.0, 166.2, 166.1, 160.7, 154.8, 139.5, 121.5, 102.8, 66.2, 64.5, 58.0, 51.8, 48.5, 32.0, 28.7 (3C), 20.1, 14.4, 13.7, 12.5. IR (neat): ν_{max} (cm^{-1}): 3286, 2964, 2934, 2872, 1738, 1688, 1663, 1605, 1549, 1477, 1454, 1454, 1367, 1288, 1246, 1217, 1136, 995, 918, 851, 797, 662, 471, 401. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{21}H_{33}N_3NaO_6^+$, 446.2262; found, 446.2268.

Ugi Product ***3h***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (15% EtOAc/*c*Hex) afforded the title compound as a light yellow solid in 56% yield (0.908 g, 1.69 mmol). R_f = 0.78 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 7.01 (dt, J = 15.1, 4.4 Hz, 1H), 6.70 (s, 1H), 6.68 (d, J = 15.6 Hz, 1H), 6.46 (s, 1H), 6.07 (s, 1H), 4.84 (d, J = 3.2 Hz, 2H), 4.29 (s, 2H), 4.23 (q, J = 7.0 Hz, 2H), 2.39 (s, 3H), 2.30 (s, 1H), 1.76−1.66 (m, 2H), 1.44 (s, 3H), 1.43 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H), 0.98 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 170.5, 166.5, 165.0, 160.2, 154.8, 140.8, 140.6, 129.8 (2C), 125.9 (2C), 124.5, 121.1, 100.2, 79.1, 73.8, 66.2, 64.6, 56.4, 56.1, 52.1, 37.3, 31.7, 31.5 (3C), 28.9, 28.9, 21.6, 14.4. IR (neat) ν_{max} (cm^{-1}): 2953, 1747, 1666, 1618, 1452, 1252, 1227, 1211, 1188, 822. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{30}H_{39}N_3NaO_6^+$, 560.2731; found, 560.2721.

Ugi Product ***3i***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a colorless solid in 59% yield (0.305 g, 0.59 mmol). R_f = 0.40 (50% EtOAc/*c*Hex). ^1H NMR (600 MHz, $CDCl_3$) δ 7.72 (dd, J = 6.7, 3.0 Hz, 2H), 7.44−7.38 (m, 3H), 7.09 (d, J = 7.9 Hz, 2H), 7.00−6.93 (m, 3H), 6.71 (s, 1H), 6.51 (s, 1H), 6.23 (s, 1H), 5.87 (dt, J = 15.3, 1.7 Hz, 1H), 4.66 (dt, J = 5.0, 2.9, 1.7 Hz, 2H), 4.13 (q, J = 7.1 Hz, 2H), 2.30 (s, 3H), 1.40 (s, 9H), 1.25 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 166.1, 165.9, 165.5, 162.5, 154.7, 139.5, 139.2, 136.1, 130.2 (2C), 130.2, 129.1 (2C), 129.0 (2C), 128.9, 126.9 (2C), 122.5, 104.8, 66.2, 64.4, 58.0, 52.0, 28.7 (3C), 21.3, 14.3. IR (neat) ν_{max} (cm^{-1}): 3313, 2972, 2935, 1740, 1693, 1668, 1605, 1541, 1512, 1464, 1447, 1371, 1269, 1246, 993, 764, 687, 590, 509. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{29}H_{34}N_3O_6^+$, 520.2442; found, 520.2463.

Ugi Product ***3j***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (65% EtOAc/*c*Hex) afforded the title compound as an off-white solid in 74% yield (0.991 g, 2.22 mmol). R_f = 0.11 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 7.95−7.88 (m, 1H), 6.85−6.74 (m, 3H), 6.56 (s, 1H), 6.22 (d, J = 15.2 Hz, 1H), 4.66−4.61 (m, 2H), 4.52 (s, 1H), 4.32 (s, 1H), 4.06 (q, J = 7.1 Hz, 2H), 3.97 (d, J = 18.6 Hz, 1H), 3.81 (d, J = 18.6 Hz, 1H), 3.70−3.60 (m, 1H), 3.53 (s, 3H), 1.80 (d, J = 9.4 Hz, 1H), 1.70 (d, J = 11.4 Hz, 1H), 1.59−1.49 (m, 2H), 1.47−1.41 (m, 1H), 1.33 (s, 3H), 1.25−1.21 (m, 2H), 1.17 (t, J = 7.1 Hz, 3H), 1.08 (dq, J = 25.9, 11.9, 11.4 Hz, 3H).$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 166.7, 165.2, 154.5, 142.6, 141.0, 139.4, 127.5, 121.9, 121.6, 110.1, 66.0, 64.2, 51.8, 50.0, 48.5, 33.0, 32.5, 25.5 (2), 24.6 (2C), 19.8, 14.2. IR (neat) ν_{max} (cm^{-1}): 3259, 2932, 2853, 1745, 1651, 1618, 1562, 1377, 1249, 1202, 993. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{23}H_{34}N_4NaO_5^+$, 469.2421; found, 469.2427.

Ugi Product ***3k***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (50% EtOAc/*c*Hex) afforded the title compound as a light yellow oil in 65% yield (0.935 g, 1.56 mmol). R_f = 0.38 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 8.47 (s, 1H), 6.97−6.89 (m, 3H), 6.64 (s, 1H), 6.48 (d, J = 8.4 Hz, 1H), 6.34 (d, J = 2.0 Hz, 1H), 6.29 (d, J = 15.2 Hz, 1H), 6.25 (dd, J = 8.4, 1.9 Hz, 1H), 4.83−4.73 (m, 2H), 4.65 (d, J = 4.7 Hz, 2H), 4.42 (d, J = 18.0 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.78 (s, 3H), 3.73 (s, 3H), 1.76 (d, J = 14.9 Hz, 1H), 1.48 (d, J = 14.9 Hz, 1H), 1.38 (d, J = 6.6 Hz, 3H), 1.35 (d, J = 6.6 Hz, 3H), 1.29 (s, 3H), 1.27 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H), 0.87 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 167.1, 164.8, 159.9, 157.2, 154.7, 142.2, 139.1, 128.04, 127.99, 122.4, 118.0, 116.3, 103.8, 98.1, 66.4, 64.3, 55.5, 55.4, 55.3, 53.2, 52.2, 47.4, 43.2, 31.6, 31.5 (3C), 28.5, 28.5, 24.7, 23.3, 14.3. IR (neat) ν_{max} (cm^{-1}): 2949, 1747, 1672, 1614, 1508, 1462, 1454, 1254, 1207, 1157, 1119, 1032, 7301. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{32}H_{49}N_4O_7^+$, 601.3596; found, 601.3588.

Ugi Product ***3l***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (80% EtOAc/*c*Hex) afforded the title compound as a brown oil in 65% yield (0.295 g, 0.65 mmol). R_f = 0.18 (100% EtOAc). ^1H NMR (600 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.01 (s, 1H), 6.95−6.89 (m, 2H), 6.78 (d, J = 15.3 Hz, 1H), 6.60 (s, 1H), 4.78 (d, J = 4.6 Hz, 2H), 4.20 (q, J = 7.1 Hz, 2H), 3.65−3.51 (m, 4H), 3.39−3.28 (m, 2H), 3.25 (s, 3H), 3.18 (s, 3H), 1.38 (s, 9H), 1.30 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 167.7, 165.1, 154.9, 143.2, 138.8, 127.5, 123.1, 122.3, 103.5, 66.5, 64.4, 55.6, 55.4, 52.8, 51.8, 47.5, 33.2, 28.8 (3C), 14.4. IR (neat) ν_{max} (cm^{-1}): 3298, 2968, 2920, 1749, 1659, 1616, 1553, 1454, 1423, 1394, 1367, 1254, 1223, 1176, 1121, 1051, 989, 920, 795, 756, 602, 401. m.p.: 111−112 °C. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{21}H_{35}N_4O_7^+$, 455.2500; found, 455.2510.

Ugi Product ***3m***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (60% EtOAc/*c*Hex) afforded the title compound as a colorless solid in 37% yield (0.587 g, 1.11 mmol). R_f = 0.45 (70% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.23−7.11 (m, 3H), 7.05−6.99 (m, 3H), 6.96 (dt, J = 15.4, 4.4 Hz, 1H), 6.89 (d, J = 1.0 Hz, 1H), 6.55 (s, 1H), 6.52 (dt, J = 15.4, 1.8 Hz, 1H), 4.76 (dd, J = 4.4, 1.8 Hz, 2H), 4.17 (q, J = 7.1 Hz, 2H), 3.62 (ddd, J = 16.7, 11.6, 4.7 Hz, 1H), 3.58 (s, 3H), 3.42 (dt, J = 15.4, 5.8 Hz, 1H), 2.57 (td, J = 12.5, 5.3 Hz, 1H), 1.98 (td, J = 13.1, 12.5, 5.4 Hz, 1H), 1.80 (d, J = 14.8 Hz, 1H), 1.62 (d, J = 14.8 Hz, 1H), 1.42 (s, 3H), 1.40 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H), 0.92 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 165.8, 164.8, 154.6, 142.9, 139.5, 137.9, 128.6 (2C), 128.5 (2C), 127.4, 126.5, 122.2, 120.7, 66.0, 64.3, 55.5, 52.4, 52.0, 46.9, 36.2, 33.0, 31.5, 31.4 (3C), 28.8, 28.6, 14.2. IR (neat) ν_{max} (cm^{-1}): 3306, 2949, 1738, 1657, 1610, 1547, 1421, 1281, 1250, 1178, 1032, 762, 746. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{29}H_{43}N_4O_5^+$, 527.3228; found, 527.3216.

Ugi Product ***3n***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (40% EtOAc/*c*Hex) afforded the title compound as a brown oil in 63% yield (0.318 mg, 0.63 mmol). R_f = 0.35 (70% EtOAc/*c*Hex). ^1H NMR (600 MHz, $CDCl_3$) δ 9.15 (s, 1H), 7.92 (d, J = 8.2 Hz, 1H), 7.82 (s, 1H), 7.76 (d, J = 8.3 Hz, 1H), 7.65 (t, J = 7.5 Hz, 1H), 7.58 (t, J = 7.5 Hz, 1H), 7.38 (s, 1H), 7.17−7.10 (m, 2H), 7.04 (d, J = 8.0 Hz, 2H), 6.86 (dt, J = 15.3, 5.2 Hz, 1H), 6.10 (s, 1H), 5.89 (d, J = 15.3 Hz, 1H), 4.60 (d, J = 5.2 Hz, 2H), 4.09 (q, J = 7.1 Hz, 2H), 2.27 (s, 3H), 1.28 (s, 9H), 1.22 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 167.3, 165.5, 154.6, 151.7, 148.8, 138.1, 137.93, 137.91, 136.3, 130.7, 129.7 (2C), 127.74, 127.73, 127.4 (2C), 127.2 (2C), 123.5, 121.5, 68.0, 66.3, 64.2, 51.4, 28.6 (3C), 21.1, 14.3. IR (neat) ν_{max} (cm^{-1}): 3325, 2970, 2928, 1670, 1628, 1543, 1510, 1450, 1366, 1248, 1005, 960, 789, 754, 604, 532, 472. M.p.: 136−138 °C. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{29}H_{33}N_3O_5Na^+$, 526.2312; found, 526.2318.

Ugi Product ***3o***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (40% EtOAc/*c*Hex) afforded the title compound as an orange solid in 45% yield (0.406 g, 0.89 mmol). R_f = 0.23 (50% EtOAc/*c*Hex). Two rotamers were present on NMR timescale (R^1:R^2 = 4:1), of which the signals of the major rotamer are reported. ^1H NMR (600 MHz, $CDCl_3$) δ 13.06 (s, 1H), 8.00 (d, J = 2.1 Hz, 1H), 7.60 (d, J = 7.9 Hz, 1H), 7.42−7.32 (m, 1H), 7.18−7.12 (m, 1H), 7.09 (dd, J = 8.1, 0.9 Hz, 1H), 6.98 (dt, J = 15.3, 5.0 Hz, 1H), 6.30 (dt, J = 15.3, 1.7 Hz, 1H), 6.04 (ddt, J = 17.1, 10.0, 7.1 Hz, 1H), 5.50 (s, 1H), 5.32−5.27 (m, 1H), 5.25−5.20 (m, 1H), 4.74−4.64 (m, 2H), 4.30 (dd, J = 13.8, 7.0 Hz, 1H), 4.09 (qd, J = 7.1, 1.9 Hz, 2H), 4.04 (dd, J = 13.7, 7.2 Hz, 1H), 1.37 (s, 9H), 1.22 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 169.0, 168.0, 154.7, 146.9, 140.1, 139.8, 134.1, 132.1, 131.3, 130.1, 129.4, 123.3, 121.7, 121.1, 115.7, 66.1, 64.4, 62.8, 53.0, 51.6, 29.2 (3C), 14.3. IR (neat) ν_{max} (cm^{-1}): 3304, 2968, 2930, 1744, 1663, 1628, 1556, 1456, 1406, 1364, 1261, 1200, 1119, 987, 945, 793, 762, 677, 507. m.p.: 101−107 °C. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{24}H_{31}N_4O_5^+$, 455.2289; found, 455.2276.

Ugi Product ***3p***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (20% EtOAc/*c*Hex) afforded the title compound as an orange solid in 87% yield

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(1.550 mg, 2.61 mmol). R_f = 0.73 (70% EtOAc/*c*Hex). ^{1}H NMR (500 MHz, $CDCl_3$) δ 13.70 (s, 1H), 7.44−7.38 (m, 3H), 7.33 (d, J = 7.6 Hz, 1H), 7.27 (d, J = 7.7 Hz, 2H), 7.24−7.18 (m, 2H), 7.06 (t, J = 7.5 Hz, 1H), 6.96 (dt, J = 15.3, 5.2 Hz, 1H), 6.39−6.33 (m, 1H), 6.10 (dd, J = 9.6, 1.6 Hz, 1H), 5.11 (d, J = 13.3 Hz, 1H), 4.94 (s, 1H), 4.66 (d, J = 5.0 Hz, 2H), 4.21 (d, J = 13.3 Hz, 1H), 4.13−4.04 (m, 2H), 1.67 (d, J = 14.8 Hz, 1H), 1.30 (s, 3H), 1.24−1.18 (m, 4H), 1.15 (s, 3H), 0.89 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 169.0, 168.8, 154.7, 148.0, 139.6, 137.9, 136.2, 135.3, 134.2, 131.9 (2C), 131.1, 129.1 (2C), 127.7, 122.4, 122.1, 120.8, 117.0, 116.3, 96.9, 66.3, 64.3, 55.0, 53.0, 52.4, 31.6 (3C), 29.3, 28.4 (2C), 14.3. IR (neat) ν_{max} (cm^{-1}): 3350, 2959, 2943, 1742, 1622, 1585, 1506, 1443, 1373, 1250, 1213, 1148, 1094, 987, 847, 802, 748, 613. m.p.: 106−108 °C. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{33}H_{41}ClN_3O_5^+$, 594.2729; found, 594.2737.

Ugi Product ***3q***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (60% EtOAc/*c*Hex) afforded the title compound as an amber oil in 56% yield (0.880 g, 1.67 mmol). R_f = 0.22 (50% EtOAc/*c*Hex). Two rotamers were present on NMR timescale (R^1:R^2 = 5:1), of which the signals of the major rotamer are reported. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, J = 3.2 Hz, 1H), 7.45 (d, J = 8.1 Hz, 2H), 7.25−7.20 (m, 4H), 6.97 (dt, J = 15.1, 4.5 Hz, 1H) 6.28 (d, J = 15.2 Hz, 1H), 6.15 (s, 1H), 4.86 (d, J = 17.6 Hz, 1H), 4.78 (d, J = 17.6 Hz, 1H), 4.67 (dd, J = 4.3, 1.6 Hz, 2H), 4.05 (q, J = 7.1 Hz, 2H), 1.25 (s, 9H), 1.17 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 167.0, 165.6, 164.3, 154.5, 142.2, 140.95, 140.91, 129.6 (q, J = 32.4 Hz), 126.9 (2C), 125.4 (q, J = 3.6 Hz, 2H), 124.0 (q, J = 272.0 Hz), 121.1, 120.8, 65.9, 64.3, 59.9, 51.8, 50.2, 28.4 (3C), 14.1. IR (neat) ν_{max} (cm^{-1}): 1747, 1666, 1323, 1254, 1202, 1163, 1121, 1113, 1067, 1016, 733, 625, 590. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{24}H_{28}F_3N_3NaO_5S^+$, 550.1594; found, 550.1592.

Ugi Product ***3r***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a clear oil in 37% yield (0.367 g, 0.73 mmol). R_f = 0.31 (50% EtOAc/*c*Hex). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (d, J = 7.8 Hz, 1H), 7.25 (d, J = 8.5 Hz, 2H), 6.94 (dd, J = 15.2, 4.5 Hz, 1H), 6.85 (d, J = 8.5 Hz, 2H), 6.49 (d, J = 15.2 Hz, 1H), 4.82 (d, J = 16.7 Hz, 1H), 4.75 (d, J = 4.5 Hz, 2H), 4.62 (d, J = 16.7 Hz, 1H), 4.46 (s, 1H), 4.25−4.07 (m, 4H), 3.77 (s, 3H), 3.74−3.68 (m, 1H), 1.81 (t, J = 13.9 Hz, 2H), 1.68−1.59 (m, 1H), 1.56−1.49 (m, 1H), 1.34−1.24 (m, 6H), 1.23−1.13 (m, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 167.6, 167.0, 164.8, 159.3, 154.6, 140.1, 128.7 (2C), 127.7, 120.9, 114.1 (2C), 66.0, 64.4, 63.8, 62.0, 55.3, 52.7, 48.4, 32.6, 32.4, 25.5 (2C), 24.5, 14.2, 13.9. IR (neat) ν_{max} (cm^{-1}): 3306, 2979, 2932, 2854, 1745, 1664, 1616, 1539, 1514, 1447, 1371, 1246, 1203, 1176, 1097, 1028, 966, 868, 818, 791, 555, 509, 459. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{26}H_{37}F_3N_2O_8^+$, 505.2544; found, 505.2541.

Ugi Product ***3s***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (40% EtOAc/*c*Hex) afforded the title compound as a yellow solid in 78% yield (1.236 g, 2.09 mmol). R_f = 0.34 (60% EtOAc/*c*Hex). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.60 (s, 1H), 8.50 (d, J = 5.3 Hz, 2H), 7.31−7.27 (m, 12H), 7.25−7.21 (m, 3H), 6.90 (dt, J = 15.6, 4.5 Hz, 1H), 6.50 (d, J = 15.6 Hz, 1H), 5.54 (s, 1H), 4.81 (d, J = 4.5 Hz, 2H), 4.23 (q, J = 7.1 Hz, 2H), 3.52−3.34 (m, 2H), 1.58−1.46 (m, 1H), 1.43−1.35 (m, 1H), 1.33 (t, J = 7.1 Hz, 3H), 0.80 (t, J = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 166.8, 166.3, 154.8, 152.0, 144.6, 144.5 (3C), 143.6, 143.1, 139.8, 128.8 (6C), 128.0 (6C), 127.0 (3C), 121.4, 70.9, 66.2, 65.7, 64.5, 51.5, 23.3, 14.4, 11.3. IR (neat) ν_{max} (cm^{-1}): 3722, 3263, 2974, 2303, 1745, 1688, 1672, 1599, 1529, 1433, 1366, 1248, 1219, 1030, 756, 698, 633, 590, 430. m.p.: 110−114 °C. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{35}H_{37}N_4O_5^+$, 593.2578; found, 593.2588.

Ugi Product ***3t***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (40% EtOAc/*c*Hex) afforded the title compound as a beige solid in 70% yield (1.134 g, 2.10 mmol). R_f = 0.30 (70% EtOAc/*c*Hex). Two rotamers were present on NMR timescale (R^1:R^2 = 7:3), of which the signals of the major rotamer are reported. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.58 (t, J = 7.2 Hz, 1H), 7.23 (d, J = 7.5 Hz, 1H), 7.12−7.06 (m, 1H), 6.90 (dt, J = 15.1, 4.4 Hz, 1H), 6.79−6.70 (m, 1H), 6.66−6.61 (m, 2H), 6.50 (d, J = 15.1 Hz, 1H), 5.86 (s, 1H), 4.77 (d, J = 4.4 Hz, 2H), 4.20 (q, J = 7.1 Hz, 2H), 3.87−3.81 (m, 6H), 3.67 (dt, J = 14.0, 7.3 Hz, 2H), 2.83−2.74 (m, 1H), 2.60−2.53 (m, 4H), 1.38 (s, 9H), 1.30 (d, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 167.2, 166.3, 157.5, 155.8, 154.8, 149.0, 147.8, 138.7, 137.6, 131.0, 123.2, 122.4, 121.7, 120.7, 112.1, 111.3, 66.3, 64.5, 64.2, 56.0, 56.0, 51.5, 49.6, 36.2, 28.8 (3C), 24.5, 14.4. IR (neat) ν_{max} (cm^{-1}): 3304, 2959, 2932, 1742, 1664, 1624, 1560, 1514, 1456, 1416, 1364, 1246, 1153, 1024, 959, 864, 787, 644, 557, 473. m.p.: 118−121 °C. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{29}H_{39}N_3O_7Na^+$, 564.2680; found, 564.2701.

Ugi Product ***3u***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (40% EtOAc/*c*Hex) afforded the title compound as a colorless solid in 81% yield (1.330 g, 2.44 mmol). R_f = 0.23 (50% EtOAc/*c*Hex). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 (q, J = 7.9 Hz, 1H), 7.33 (d, J = 7.1 Hz, 1H), 6.92−6.87 (m, 2H), 6.76 (d, J = 8.1 Hz, 2H), 6.71 (d, J = 1.8 Hz, 1H), 6.68 (d, J = 8.1 Hz, 1H), 6.50 (d, J = 15.1 Hz, 1H), 5.77 (s, 1H), 4.78 (s, 2H), 4.21 (q, J = 7.1 Hz, 2H), 3.86 (s, 3H), 3.84 (s, 3H), 3.73 (d, J = 8.5 Hz, 2H), 2.81 (t, J = 14.0, 8.5 Hz, 1H), 2.62 (dd, J = 14.0, 8.5 Hz, 1H), 1.38 (s, 9H), 1.31 (d, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 167.3, 166.6, 162.9 (d, J = 241.5 Hz), 154.9 (d, J = 9.8 Hz), 154.8, 149.2, 147.9, 142.0 (d, J = 7.3 Hz), 139.3, 130.7, 121.4, 121.0 (d, J = 3.8 Hz), 120.8, 112.2, 111.5, 108.9 (d, J = 36.6 Hz), 66.2, 65.1, 64.5, 56.03 55.98, 51.8, 50.1, 36.2, 28.7 (3C), 14.4. IR (neat) ν_{max} (cm^{-1}): 3290, 2966, 1742, 1664, 1618, 1574, 1555, 1514, 1450, 1425, 1362, 1254, 1240, 1157, 1024, 991, 933, 878, 787, 764, 656, 577, 555, 467, 432.03. m.p.: 122−128 °C. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{28}H_{36}N_3O_7FNa^+$, 568.2429; found, 568.2446.

Ugi Product ***3v***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (40% EtOAc/*c*Hex) afforded the title compound as a colorless solid in 68% yield (1.241 g, 2.05 mmol). R_f = 0.42 (50% EtOAc/*c*Hex). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (t, J = 7.8 Hz, 1H), 7.41 (dd, J = 16.8, 7.7 Hz, 2H), 7.04 (s, 1H), 6.90 (dt, J = 15.1, 4.5 Hz, 1H), 6.77 (d, J = 8.2 Hz, 1H), 6.70 (d, J = 6.5 Hz, 2H), 6.50 (d, J = 15.1 Hz, 1H), 5.75 (s, 1H), 4.78 (d, J = 4.5 Hz 2H), 4.22 (q, J = 7.1 Hz, 2H), 3.86 (s, 3H), 3.84 (s, 3H), 3.71 (t, J = 7.9 Hz, 2H), 2.81 (dt, J = 15.1, 7.8 Hz, 1H), 2.65 (dt, J = 14.6, 7.8 Hz, 1H), 1.38 (s, 9H), 1.31 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 166.8, 166.5, 157.6, 154.8, 149.2, 147.9, 141.2, 139.4, 139.2, 130.7, 127.3, 122.7, 121.5, 120.9, 112.2, 111.5, 66.2, 65.0, 64.5, 56.0, 51.8, 50.2, 36.2, 28.8 (3C), 14.4. IR (neat) ν_{max} (cm^{-1}): 3304, 2966, 2908, 1744, 1663, 1628, 1555, 1514, 1445, 1414, 1259, 1232, 1157, 1130, 1028, 997, 787, 741, 640, 567, 434. m.p.: 130−132 °C. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{28}H_{36}O_7N_3BrNa^+$, 628.1629; found, 628.1633.

Ugi Product ***3w***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (40% EtOAc/*c*Hex) afforded the title compound as a beige solid in 87% yield (1.456 g, 2.61 mmol). R_f = 0.33 (50% EtOAc/*c*Hex). Two rotamers were present on NMR timescale (R^1:R^2 = 4:1), of which the signals of the major rotamer are reported. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (t, J = 7.8 Hz, 1H), 7.01 (d, J = 7.2 Hz, 1H), 6.93 (dt, J = 15.1, 4.4 Hz, 1H), 6.73 (dd, J = 16.9, 8.2 Hz, 2H), 6.59 (d, J = 8.2 Hz, 1H), 6.55 (d, J = 13.0 Hz, 2H), 6.40 (s, 1H), 5.92 (s, 1H), 4.80 (d, J = 4.5 ,2H), 4.21 (q, J = 7.1 Hz, 2H), 3.87 (s, 3H), 3.83 (s, 6H), 3.73 (t, J = 8.3 Hz, 2H), 2.77 (dt, J = 15.7, 8.3 Hz, 1H), 2.35 (dd, J = 15.7, 8.3 Hz, 1H), 1.37 (s, 9H), 1.30 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 167.7, 166.3, 163.7, 154.8, 153.3, 149.1, 147.8, 139.6, 138.9, 130.9, 121.6, 120.6, 116.8, 112.0, 111.4, 110.5, 66.3, 64.45, 64.43, 56.0, 55.9, 53.5, 51.6, 49.3, 36.4, 28.8 (3C), 14.4. IR (neat) ν_{max} (cm^{-1}): 3306, 2968, 2935, 1747, 1686, 1663, 1595, 1553, 1514, 1460, 1420, 1254, 1157, 1026, 991, 816, 789, 733, 648, 567, 548. m.p.: 99−101 °C. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{29}H_{39}N_3O_8Na^+$, 580.2629; found, 580.2655.

Ugi Product ***3x***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (40% EtOAc/

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*c*Hex) afforded the title compound as a beige solid in 66% yield (1.079 g, 2.00 mmol). R_f = 0.31 (70% EtOAc/*c*Hex). Two rotamers were present on NMR timescale (R^1:R^2 = 3:1), of which the signals of the major rotamer are reported. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (d, *J* = 4.5 Hz, 1H), 7.25 (s, 1H), 7.17 (s, 1H), 7.07 (d, *J* = 4.5 Hz, 1H), 6.92 (dd, *J* = 15.1, 3.9 Hz, 1H), 6.74 (d, *J* = 7.9 Hz, 1H), 6.66−6.60 (m, 2H), 6.52 (d, *J* = 15.1 Hz, 1H), 5.93 (s, 1H), 4.78 (d, *J* = 3.9 Hz, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.84 (s, 3H), 3.83 (s, 3H), 3.69 (tt, *J* = 15.4, 7.9 Hz, 2H), 2.77 (td, *J* = 13.7, 10.3, 6.1 Hz, 1H), 2.50 (ddd, *J* = 13.7, 10.3, 6.1 Hz, 1H), 2.34 (s, 3H), 1.37 (s, 9H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 167.6, 166.3, 156.3, 156.1, 154.8, 149.0, 148.7, 147.8, 138.8, 130.9, 125.1, 124.1, 121.6, 120.7, 112.2, 111.3, 66.3, 64.5, 64.3, 56.0, 55.9, 51.6, 49.4, 36.2, 28.8 (3C), 21.4, 14.4. IR (neat) ν_{max} (cm^{-1}): 3300, 2968, 2930, 1742, 1680, 1599, 1545, 1514, 1431, 1259, 1155, 1026, 820, 781, 646, 569, 467, 430. m.p.: 118−121 °C. HRMS (ESI) *m*/*z*: $[M + Na]^+$ calcd. for $C_{29}H_{39}N_3O_7Na^+$, 564.2680; found, 564.2683.

Ugi Product ***3y***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (40% EtOAc/*c*Hex) afforded the title compound as a colorless solid in 83% yield (1.401 g, 2.50 mmol). R_f = 0.34 (70% EtOAc/*c*Hex). Two rotamers were present on NMR timescale (R^1:R^2 = 7:1), of which the signals of the major rotamer are reported. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.46 (d, *J* = 5.2 Hz, 1H), 7.43 (s, 1H), 7.24 (dd, *J* = 5.2, 1.6 Hz, 1H), 7.04 (s, 1H), 6.92 (dt, *J* = 15.2, 4.5 Hz, 1H), 6.75 (d, *J* = 8.6 Hz, 1H), 6.69−6.62 (m, 2H), 6.52 (d, *J* = 15.2 Hz, 1H), 5.82 (s, 1H), 4.80−4.76 (m, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 3.83 (s, 3H), 3.72 (d, *J* = 7.9 Hz, 2H), 2.81 (dt, *J* = 14.4, 8.0 Hz, 1H), 2.59 (dd, *J* = 14.4, 7.9 Hz, 1H), 1.37 (s, 9H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 167.0, 166.5, 157.9, 154.8, 149.8, 149.1, 147.8, 145.3, 139.4, 130.6, 124.1, 123.4, 121.2, 120.8, 112.03, 111.3, 66.2, 64.8, 64.5, 56.0, 55.9, 51.8, 49.9, 36.2, 28.7 (3C), 14.4. IR (neat) ν_{max} (cm^{-1}): 3294, 2964, 2939, 1745, 1688, 1664, 1595, 1570, 1545, 1514, 1470, 1448, 1423, 1389, 1360, 1254, 1230, 1190, 1159, 1103, 1028, 966, 868, 818, 787, 764, 706, 567, 467. m.p.: 118−122 °C. HRMS (ESI) *m*/*z*: $[M + Na]^+$ calcd. for $C_{28}H_{36}N_3O_7ClNa^+$, 584.2134; found, 584.2135.

Ugi Product ***3z***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (40% EtOAc/*c*Hex) afforded the title compound as a colorless solid in 50% yield (0.913 g, 1.50 mmol). R_f = 0.33 (70% EtOAc/*c*Hex). Two rotamers were present on NMR timescale (R^1:R^2 = 3:1), of which the signals of the major rotamer are reported. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (d, *J* = 5.3 Hz, 1H), 7.62 (s, 1H), 7.45−7.39 (m, 1H), 7.00 (s, 1H), 6.93 (dt, *J* = 15.1, 4.5 Hz, 1H), 6.76 (d, *J* = 8.6 Hz, 1H), 6.69−6.63 (m, 2H), 6.53 (d, *J* = 15.1 Hz, 1H), 5.84 (s, 1H), 4.83−4.77 (m, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 3.84 (s, 3H), 3.73 (d, *J* = 7.5 Hz, 2H), 2.81 (dd, *J* = 14.0, 7.5 Hz, 1H), 2.60 (dd, *J* = 14.0, 7.5 Hz, 1H), 1.38 (s, 9H), 1.31 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 167.0, 166.6, 157.7, 154.8, 149.5, 149.13, 147.90, 147.88, 139.5, 130.6, 127.2, 126.5, 121.2, 120.8, 112.1, 111.4, 66.2, 64.7, 64.5, 56.0 (2C), 51.8, 49.9, 36.2, 28.8 (3C), 14.4. IR (neat) ν_{max} (cm^{-1}): 3269, 2962, 2930, 1738, 1663, 1622, 1560, 1514, 1460, 1418, 1389, 1366, 1296, 1259, 1159, 1030, 993, 962, 870, 835, 793, 702, 679, 571, 546, 465, 436. m.p.: 106−109 °C. HRMS (ESI) *m*/*z*: $[M + Na]^+$ calcd. for $C_{28}H_{36}N_3O_7BrNa^+$, 628.1629; found, 628.1636.

Ugi Product ***3za***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (60% EtOAc/*c*Hex) afforded the title compound as an amber oil in 94% yield (1.691 g, 2.8 mmol). R_f = 0.22 (50% EtOAc/*c*Hex). Two rotamers were present on NMR timescale (R^1:R^2 = 5:2), of which the signals of the major rotamer are reported. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.16 (s, 1H), 8.26 (d, *J* = 8.2 Hz, 1H), 7.49 (d, *J* = 8.2 Hz, 1H), 7.11 (s, 1H), 6.90 (dt, *J* = 15.1, 4.4 Hz, 1H), 6.75 (dd, *J* = 13.7, 6.2 Hz, 1H), 6.65 (s, 2H), 6.51 (d, *J* = 15.2 Hz, 1H), 5.83 (s, 1H), 4.78 (d, *J* = 4.5 Hz, 2H), 4.20 (q, *J* = 7.0 Hz, 2H), 3.94 (s, 3H), 3.84−3.80 (m, 6H), 3.73 (t, *J* = 7.9 Hz, 2H), 2.82 (dt, *J* = 13.5, 6.1 Hz, 1H), 2.61 (dt, *J* = 14.8, 7.9 Hz, 1H), 1.37 (s, 9H), 1.29 (t, *J* = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.1, 167.1, 164.7, 160.5, 154.8, 150.2, 149.1, 147.7, 138.1, 134.8, 130.5, 125.1, 123.2, 121.2, 112.0 (2C), 111.4, 66.2, 65.5, 64.5, 56.0, 55.97, 55.9, 50.3, 36.1, 34.1, 28.7 (3C), 14.4. IR (neat) ν_{max} (cm^{-1}): 2959, 1728, 1514, 1256, 1236, 1190, 1157, 1140, 1117, 1025, 731. HRMS (ESI) *m*/*z*: $[M + Na]^+$ calcd. for $C_{30}H_{39}N_3NaO_9^+$, 608.2579; found, 608.2573.

Ugi Product ***3zb***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (40% EtOAc/*c*Hex) afforded the title compound as a yellow solid in 60% yield (1.031 g, 1.80 mmol). R_f = 0.42 (70% EtOAc/*c*Hex). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.6 Hz, 2H), 7.59 (d, *J* = 8.6 Hz, 2H), 7.00 (dt, *J* = 15.0, 4.0 Hz, 1H), 6.73 (d, *J* = 8.1 Hz, 1H), 6.61−6.51 (m, 3H), 6.16 (s, 1H), 6.01 (s, 1H), 4.88−4.79 (m, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 3H), 3.82 (s, 3H), 3.61 (t, *J* = 8.1 Hz, 2H), 2.77 (dd, *J* = 15.5, 6.9 Hz, 1H), 2.42 (dd, *J* = 15.5, 8.1 Hz, 1H), 1.38 (s, 9H), 1.31 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 167.9, 166.7, 154.8, 149.2, 148.1, 147.8, 143.2, 140.2, 130.2, 129.8 (2C), 123.9 (2C), 120.9, 120.7, 112.0, 111.5, 66.1, 64.6, 62.2, 56.05, 55.99, 52.1, 49.0, 36.5, 28.7 (3C), 14.4. IR (neat) ν_{max} (cm^{-1}): 3302, 2962, 1738, 1661, 1610, 1516, 1460, 1421, 1348, 1246, 1153, 1001, 953, 851, 793, 696, 596, 544, 473, 424. M.p.: 138−139 °C. HRMS (ESI) *m*/*z*: $[M + Na]^+$ calcd. for $C_{29}H_{37}N_3O_9Na^+$, 594.2422; found, 594.2438.

Ugi Product ***3zc***. Prepared according to GP-A. Purification of the crude material by silica gel column chromatography (60% EtOAc/*c*Hex) afforded the title compound as an orange solid in 27% yield (0.424 g, 0.81 mmol). R_f = 0.21 (100% EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, *J* = 5.9 Hz, 1H), 7.31 (d, *J* = 5.7 Hz, 2H), 7.00 (dd, *J* = 15.1, 4.2 Hz, 2H), 6.73 (d, *J* = 8.1 Hz, 1H), 6.62−6.50 (m, 3H), 6.17 (s, 1H), 5.90 (s, 1H), 4.84 (dd, *J* = 4.2, 1.7 Hz, 2H), 4.22 (d, *J* = 7.1 Hz, 2H), 3.83 (s, 3H), 3.83 (s, 3H), 3.59 (t, *J* = 8.3 Hz, 2H), 2.82−2.72 (m, 1H), 2.51−2.35 (m, 1H), 1.38 (s, 9H), 1.31 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 167.7, 166.6, 154.8, 150.3 (2C), 149.1, 147.9, 144.8, 140.0, 130.3, 123.6 (2C), 120.9, 120.7, 111.9, 111.4, 66.1, 64.6, 62.0, 56.02, 55.98, 52.1, 49.0, 36.5, 28.7 (3C), 14.4. IR (neat) ν_{max} (cm^{-1}): 3302, 2972, 1740, 1661, 1620, 1551, 1514, 1456, 1420, 1369, 1254, 1159, 1024, 995, 947, 874, 783, 550, 432. m.p.: 110−112 °C. HRMS (ESI) *m*/*z*: $[M + Na]^+$ calcd. for $C_{28}H_{37}N_3O_7Na^+$, 550.2524; found, 550.2524.

β-Lactam Synthesis. trans-β-Lactam ***6a***. Prepared according to GP-B using **3a**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 92% yield (77 mg, 0.18 mmol).

*Three Millimole-Scale Experiment (trans-**6a**)*. Prepared according to GP-B. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 82% yield (1115.7 mg, 2.55 mmol).

R_f = 0.67 (60% EtOAc/*c*Hex). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.56−8.54 (m, 1H), 7.58 (td, *J* = 7.8, 1.8 Hz, 1H), 7.21 (ddd, *J* = 7.8, 4.8, 1.2 Hz, 1H), 7.02 (d, *J* = 7.8 Hz, 1H), 6.84 (s, 1H), 6.82−6.77 (m, 2H), 5.22 (dd, *J* = 15.2, 1.7 Hz, 1H), 5.07−4.88 (m, 2H), 4.09 (d, *J* = 7.3 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.72 (ddd, *J* = 13.9, 9.6, 4.8 Hz, 1H), 3.42 (ddd, *J* = 13.9, 9.6, 4.8 Hz, 1H), 3.38−3.32 (m, 1H), 3.16 (ddd, *J* = 13.9, 9.6, 4.8 Hz, 1H), 1.38 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 168.5, 168.0, 156.4, 149.0, 148.5, 147.7, 137.4, 132.1, 128.5, 122.8, 122.6, 121.1, 120.9, 112.4, 111.4, 69.9, 65.7, 56.1, 55.9, 51.5, 46.6, 33.6, 28.7 (3C). IR (neat): ν_{max} (cm^{-1}): 2964, 2930, 1751, 1672, 1585, 1545, 1512, 1460, 1261, 1230, 1148, 1028, 995, 930, 808, 758, 650, 623, 463, 401. HRMS (ESI) *m*/*z*: $[M + Na]^+$ calcd. for $C_{25}H_{31}N_3O_4Na^+$, 460.2207; found, 460.2216.

cis-β-Lactam ***6a***. Prepared according to GP-C using **3a**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 64% yield (55 mg, 0.12 mmol). R_f = 0.61 (60% EtOAc/*c*Hex). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 (d, *J* = 5.8 Hz, 1H), 7.96 (s, 1H), 7.63 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.25 (t, *J* = 7.8, 5.8 Hz, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 6.79−6.76 (m, 3H), 5.91 (dt, *J* = 17.1, 10.3, 8.6 Hz, 1H), 5.37 (d, *J* = 17.1 Hz, 1H), 5.33 (d, *J* = 10.3 Hz, 1H), 3.96 (d, *J* = 8.6 Hz, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.66 (dd, *J* = 14.0, 7.8 Hz, 1H), 3.44 (dd, *J* = 14.0, 7.8 Hz, 1H), 3.16 (t, *J* = 7.8 Hz, 2H), 1.33 (s, 9H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 168.8, 166.5, 158.3, 149.1,

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148.9, 147.8, 137.6, 131.9, 128.9, 123.0, 121.9, 121.2, 120.9, 112.3, 111.4, 70.6, 66.2, 56.1, 56.0, 51.7, 46.4, 33.9, 28.9 (3C). IR (neat) ν_{max} (cm^{-1}): 2964, 2926, 2339, 1751, 1672, 1583, 1545, 1512, 1458, 1261, 1230, 1148, 1028, 995, 922, 806, 762, 733, 640. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd. for $C_{25}H_{31}N_3O_4Na^+$, 460.2207; found, 460.2216.

trans-β-Lactam **6b**. Prepared according to GP-B using **3db**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a light yellow solid in 82% yield (0.073 g, 0.16 mmol). R_f = 0.62 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 8.72 (d, *J* = 7.1 Hz, 1H), 8.56−8.53 (m, 1H), 8.48 (s, 1H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.40−7.35 (m, 2H), 7.21−7.14 (m, 2H), 7.13 (d, *J* = 2.2 Hz, 1H), 7.12−7.06 (m, 2H), 5.24 (dt, *J* = 17.0, 1.3 Hz, 1H), 5.05 (ddd, *J* = 16.8, 10.3, 8.0 Hz, 1H), 4.97 (dd, *J* = 10.3, 1.5 Hz, 1H), 4.14 (d, *J* = 8.0 Hz, 1H), 3.88−3.75 (m, 2H), 3.65 (ddd, *J* = 13.6, 8.8, 7.2 Hz, 1H), 3.55 (ddd, *J* = 16.0, 8.8, 7.4 Hz, 1H), 3.42 (ddd, *J* = 14.4, 8.7, 5.5 Hz, 1H), 1.97−1.91 (m, 1H), 1.83−1.77 (m, 1H), 1.72−1.66 (m, 1H), 1.65−1.54 (m, 2H), 1.43−1.07 (m, 5H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 168.6, 168.4, 155.9, 148.5, 137.2, 136.4, 128.5, 127.4, 122.8, 122.8, 122.7, 122.0, 121.3, 119.4, 118.9, 113.0, 111.4, 69.6, 65.9, 48.6, 45.1, 32.6, 25.6 (2C), 24.6, 23.7 (2C). IR (neat) ν_{max} (cm^{-1}): 3290, 2932, 2851, 1730, 1672, 1649, 1529, 1431, 1402, 1339, 924, 750, 729. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd. for $C_{27}H_{30}N_4NaO_2^+$, 465.2261; found, 465.2260.

cis-β-Lactam **6b**. Prepared according to GP-C using **3b**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a yellow solid in 9.9% *trans* diastereoisomer (0.009 g, 0.020 mmol) and 12.1% *cis* diastereoisomer (0.011 g, 0.024 mmol). R_f = 0.66 (50% EtOAc/*c*Hex). Two diastereoisomers were present in NMR (*trans*: *cis* = 1: 4.5) of which the signals of the *trans* diastereoisomer are marked with ■ and *cis* diastereoisomer are marked with ●. ^1H NMR (500 MHz, $CDCl_3$) ■ δ 8.66 (d, *J* = 6.6 Hz, 1H), ●■ 8.61−8.56 (m, 1H), 8.55 ■ (dd, *J* = 4.1, 1.6 Hz, 1H), ● 8.23 (s, 1H), ■ 8.19 (s, 1H), ■ 7.62 (d, *J* = 8.0 Hz, 1H), ● 7.56 (d, *J* = 7.9 Hz, 1H), ● 7.51 (td, *J* = 7.8, 1.8 Hz, 1H), ●■ 7.40−7.33 (m, ● 2H, ■ 1H), ● 7.26 (d, *J* = 7.9 Hz, 1H), ●■ 7.23−7.16 (m, 3H), ●■ 7.12−7.08 (m, ● 1H, ■ 2H), ● 5.84 (ddd, *J* = 17.2, 10.3, 8.2 Hz, 1H), ● 5.39 (dt, *J* = 17.1, 1.2 Hz, 1H), ● 5.29 (d, *J* = 10.3 Hz, 1H), ■ 5.24 (dt, *J* = 17.0, 1.3 Hz, 1H), ■ 5.09−4.94 (m, 2H), ● 4.28 (d, *J* = 8.2 Hz, 1H), ■ 4.13 (d, *J* = 7.9 Hz, 1H), ■ 3.87−3.75 (m, 2H), ●■ 3.73−3.63 (m, ● 2H, ■ 1H), ■ 3.59−3.52 (m, 1H), ●■ 3.50−3.40 (m, 1H), ● 3.35 (dt, *J* = 13.4, 6.6 Hz, 1H), ● 3.26 (dt, *J* = 15.1, 7.6 Hz, 1H), ■ 1.96−1.90 (m, 1H), ■ 1.84−1.76 (m, 1H), ●■ 1.70 (d, *J* = 8.4 Hz, ● 2H, ■ 1H), ●■ 1.61−1.45 (m, ● 3H, ■ 2H), ●■ 1.28−1.15 (m, ● 2H, ■ 5H), ● 0.97−0.87 (m, 1H), ● 0.74−0.56 (m, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ ● 169.6, ■ 168.6, ■ 168.4, ● 166.9, ● 156.8, ■ 156.0, ● 149.2, ■ 148.5, ■ 137.2, ● 137.2, ● 136.5, ■ 136.4, ● 128.7, ■ 128.5, ■ 127.4, ● 127.4, ● 123.1, ■ 122.83, ■ 122.80, ■ 122.7, ● 122.5, ● 122.4, ● 122.3, ■ 122.2, ● 121.6, ■ 121.3, ● 119.7, ■ 119.5, ■ 119.0, ● 118.9, ■ 113.3, ● 112.9, ● 111.4, ■ 111.3, ● 70.7, ■ 69.7, ■ 65.9, ● 65.3, ■ 48.6, ● 48.2, ■ 45.1, ● 44.0, ● 32.7, ■ 32.5, ■ 25.7 (2C), ● 25.3 (2C), ● 24.83, ● 24.77, ■ 24.7, ●■ 23.8 (● 1C, ■ 2C). IR (neat) ν_{max} (cm^{-1}): 3290, 2932, 2851, 1730, 1672, 1649, 1529, 1431, 1402, 1339, 924, 750, 729. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd. for $C_{27}H_{30}N_4NaO_2^+$, 465.2261; found, 465.2263.

trans-β-Lactam **6c**. Prepared according to GP-B using **3c**. Purification of the crude material by silica gel column chromatography (35% EtOAc/*c*Hex) afforded the title compound as a yellow oil in 87% yield (0.070 g, 0.188 mmol). R_f = 0.50 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 8.78 (d, *J* = 7.3 Hz, 1H), 7.61−7.51 (m, 2H), 7.09−6.99 (m, 1H), 5.30−5.16 (m, 2H), 5.06−4.97 (m, 1H), 4.10 (d, *J* = 7.2 Hz, 1H), 3.87−3.78 (m, 2H), 3.75−3.62 (m, 2H), 3.49−3.42 (m, 1H), 3.30 (s, 3H), 2.50 (s, 3H), 1.95−1.86 (m, 2H), 1.76−1.67 (m, 2H), 1.60 (dt, *J* = 12.5, 3.6 Hz, 1H), 1.41−1.31 (m, 2H), 1.26−1.12 (m, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 169.4, 168.9, 157.2, 154.6, 136.9, 128.6, 122.2, 121.4, 120.8, 70.0, 69.8, 65.7, 58.5, 48.5, 44.2, 32.9, 32.8, 25.7, 24.9, 24.8, 24.5. IR (neat) ν_{max} (cm^{-1}): 2930, 2853, 1757, 1663, 1649, 1535, 1456, 1340, 1107, 1094, 924, 750. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd. for $C_{21}H_{29}N_3NaO_3^+$, 394.2101; found, 394.2109.

cis-β-Lactam **6c**. Prepared according to GP-C using **3c**. Purification of the crude material by silica gel column chromatography (35% EtOAc/*c*Hex) afforded the title compound as a yellow oil in 9% *trans* diastereoisomer and 28% *cis* diastereoisomer (0.017 g, 0.045 mmol). R_f = 0.50 (50% EtOAc/*c*Hex). Two diastereoisomers were present in NMR (*trans*:*cis* = 1:4), of which the signals of the *trans* diastereoisomer are marked with ■ and *cis* diastereoisomer are marked with ●. ^1H NMR (500 MHz, $CDCl_3$) δ ■ 8.78 (d, *J* = 6.8 Hz, 1H), ● 8.41 (d, *J* = 7.6 Hz, 1H), ●■ 7.63−7.53 (m, ● 1H, ■ 2H), ● 7.38 (d, *J* = 7.8 Hz, 1H), ●■ 7.07 (d, *J* = 7.7 Hz, 1H), ● 5.87 (ddd, *J* = 17.9, 10.3, 8.0 Hz, 1H), ● 5.39 (d, *J* = 17.2 Hz, 1H), ● 5.29 (d, *J* = 10.4 Hz, 1H), ■ 5.25−5.16 (m, 2H), ■ 5.02 (dd, *J* = 9.6, 2.1 Hz, 1H), ● 4.39 (d, *J* = 7.9 Hz, 1H), ■ 4.12 (d, *J* = 7.3 Hz, 1H), ●■ 3.96−3.81 (m, 2H), ■ 3.77−3.67 (m, 2H), ● 3.61−3.53 (m, 2H), ■ 3.51−3.46 (m, 1H), ● 3.43 (s, 3H), ■ 3.33 (s, 3H), ● 3.06 (ddd, *J* = 15.3, 9.6, 5.2 Hz, 1H), ■ 2.52 (s, 3H), ● 2.51 (s, 3H), ●■ 1.98−1.93 (m, 2H), ●■ 1.78−1.71 (m, 2H), ●■ 1.68−1.60 (m, 1H), ●■ 1.44−1.31 (m, 2H), ●■ 1.26−1.12 (m, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$ δ ● 170.3, ■ 169.5, ■ 168.9, ● 167.4, ● 158.1, ■ 157.2, ● 155.7, ■ 154.7, ● 137.0, ■ 136.9, ● 129.0, ■ 128.7, ● 122.7, ■ 122.3, ■ 121.5, ● 120.9, ●■ 120.2, ■ 70.9, ● 69.9, ●■ 69.7, ■ 65.8, ● 64.9, ● 58.7, ■ 58.6, ■ 48.6, ● 48.5, ■ 44.3, ● 43.6, ● 33.6, ● 33.3, ■ 33.0, ■ 32.9, ●■ 25.7, ● 25.2 (2C), ■ 24.95, ■ 24.92, ● 24.64, ■ 24.58. IR (neat) ν_{max} (cm^{-1}): 2928, 1757, 1663, 1533, 1454, 1342, 1103, 995, 625, 442. HRMS (ESI) *m/z*: $[M + Na]^+$ calcd. for $C_{21}H_{29}N_3NaO_3^+$, 394.2101; found, 394.2112.

trans-β-Lactam **6d**. Prepared according to GP-B using **3d**. Purification of the crude material by silica gel column chromatography (50% EtOAc/*c*Hex) afforded the title compound as a yellow oil in 85% yield (0.078 g, 0.176 mmol). R_f = 0.38 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 9.04 (t, *J* = 5.8 Hz, 1H), 8.53−8.48 (m, 1H), 7.50 (td, *J* = 7.8, 1.8 Hz, 1H), 7.35−7.31 (m, 2H), 7.28 (d, *J* = 6.7 Hz, 2H), 7.25 (s, 1H), 7.24−7.20 (m, 2H), 7.20−7.16 (m, 2H), 6.78 (d, *J* = 8.7 Hz, 2H), 5.26 (dt, *J* = 16.9, 1.3 Hz, 1H), 5.07 (ddd, *J* = 16.9, 10.3, 7.9 Hz, 1H), 4.98 (ddd, *J* = 10.2, 1.7, 0.7 Hz, 1H), 4.86 (d, *J* = 15.3 Hz, 1H), 4.49 (d, *J* = 2.8 Hz, 1H), 4.48 (d, *J* = 3.0 Hz, 1H), 4.41 (d, *J* = 15.2 Hz, 1H), 4.24 (d, *J* = 8.0 Hz, 1H), 3.76 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 169.4, 168.5, 159.2, 155.6, 148.3, 138.1, 137.0, 130.6 (2C), 128.7 (2C), 128.4, 128.2, 127.6 (2C), 127.5, 123.6, 122.8, 121.6, 114.1 (2C), 70.4, 66.3, 55.3, 46.7, 43.9. IR (neat) ν_{max} (cm^{-1}): 2930, 1751, 1666, 1512, 1433, 1244, 1176, 1030, 727. HRMS (ESI) *m/z*: $[M + H]^+$ calcd. for $C_{27}H_{28}N_3O_3^+$, 442.2125; found, 442.2130.

cis-β-Lactam **6d** *and Diketopiperazine* **2d**. Prepared according to GP-C using **3d**. Purification of the crude material by silica gel column chromatography (50% EtOAc/*c*Hex) afforded the title compound as a yellow oil in 37% **6d** and 15% **2d** (0.046 g, 0.10 mmol). R_f = 0.38 (50% EtOAc/*c*Hex). Two products were present in NMR (**18b**:**18c** = 2:1), of which the signals of **2d** are marked with ■ and **6d** are marked with ●. ^1H NMR (500 MHz, $CDCl_3$) δ ●■ 8.62−8.55 (m, 1H), ●■ 7.77−7.69 (m, 1H), ● 7.60 (td, *J* = 7.8, 1.8 Hz, 1H), ●■ 7.35−7.27 (m, ● 3H, ■ 4H), ●■ 7.25−7.21 (m, ● 1H, ■ 3H), ● 7.18 (d, *J* = 8.6 Hz, 2H), ● 7.16−7.11 (m, 2H), ■ 7.04 (d, *J* = 8.6 Hz, 2H), ● 7.03−6.99 (m, 1H), ■ 6.83 (d, *J* = 8.7 Hz, 2H), ● 6.72 (d, *J* = 8.6 Hz, 2H), ●■ 5.93−5.77 (m, 1H), ■ 5.51 (d, *J* = 10.0 Hz, 1H), ●■ 5.42−5.35 (m, ● 1H, ■ 2H), ■ 5.33−5.29 (m, 1H), ● 5.29−5.24 (m, 1H), ■ 4.98 (s, 1H), ■ 4.74 (d, *J* = 8.4 Hz, 1H), ● 4.54 (d, *J* = 15.3 Hz, 1H), ● 4.38 (dd, *J* = 14.7, 5.9 Hz, 1H), ● 4.35−4.29 (m, 2H), ● 4.27 (d, *J* = 8.1 Hz, 1H), ■ 3.95 (d, *J* = 15.0 Hz, 1H), ■ 3.80 (s, 3H), ● 3.75 (s, 3H), ■ 3.39 (d, *J* = 14.7 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ ● 168.0, ● 166.9, ■ 165.4, ■ 164.1, ■ 158.4, ● 158.2, ● 155.8, ■ 155.0, ■ 149.1, ● 148.1, ● 136.7, ● 136.2, ■ 136.2, ■ 134.4, ● 132.2, ■ 129.6, ● 129.3 (2C), ■ 129.1 (2C), ● 127.65 (2C), ■ 127.60 (2C), ● 127.55, ■ 127.02 (2C), ● 126.96 (2C), ■ 126.64, ● 126.57, ■ 126.2, ■ 123.1, ■ 122.8, ● 122.2, ● 121.7, ■ 121.0, ● 120.9, ●■ 113.3 (2C), ● 70.8, ● 65.3, ■ 62.9, ■ 61.2, ● 54.4, ■ 54.3, ■ 46.0, ■ 45.7, ● 44.9, ● 42.8. IR (neat)

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ν_{max} (cm^{-1}): 2932, 1753, 1663, 1512, 1452, 1433, 1302, 1244, 1176, 1030, 930, 731. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{27}H_{28}N_3O_3^+$, 442.2125; found, 442.2130.

trans-β-Lactam **6e**. Prepared according to GP-B using **3e**. Purification of the crude material by silica gel column chromatography (20% EtOAc/*c*Hex) afforded the title compound as a yellow solid in 78% yield (0.079 g, 0.15 mmol). R_f = 0.34 (20% EtOAc/*c*Hex). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 6.61 (s, 1H), 5.86 (s, 1H), 5.37−5.32 (m, 2H), 5.19−5.16 (m, 1H), 4.62 (d, J = 15.6 Hz, 1H), 4.58 (d, J = 15.6 Hz, 1H), 4.17 (d, J = 6.2 Hz, 1H), 2.37 (s, 3H), 1.59 (d, J = 14.9 Hz, 1H), 1.52 (d, J = 14.9 Hz, 1H), 1.21 (s, 3H), 1.20 (s, 3H), 0.90 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 169.9, 168.0, 166.4, 160.9, 135.4, 132.2 (2C), 131.0 (2C), 127.7, 122.5, 122.3, 103.3, 65.9, 65.7, 56.0, 51.5, 46.0, 31.7, 31.5 (3C), 28.8, 28.3, 12.3. IR (neat) ν_{max} (cm^{-1}): 3369, 2945, 1759, 1672, 1522, 1377, 1364, 1155, 1013, 908, 839, 806, 721, 573. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{25}H_{32}BrN_3NaO_3^+$, 524.1519; found, 524.1516.

cis-β-Lactam **6e**. Prepared according to GP-C using **3e**. Purification of the crude material by silica gel column chromatography (20% EtOAc/*c*Hex) afforded the title compound as a light yellow solid in 21% *trans* diastereoisomer and 44% *cis* diastereoisomer (0.065 g, 0.13 mmol). R_f = 0.29 (20% EtOAc/*c*Hex). Two diastereoisomers were present in NMR (*trans*:*cis* = 1:2), of which the signals of the *trans* diastereoisomer are marked with ■ and *cis* diastereoisomer are marked with ●. ^{1}H NMR (500 MHz, $CDCl_3$) δ ■ 7.46 (d, J = 8.4 Hz, 2H), ● 7.43 (d, J = 8.4 Hz, 2H), ■ 7.24 (d, J = 8.4 Hz, 2H), ● 7.19 (d, J = 8.4 Hz, 2H), ■ 6.61 (s, 1H), ● 6.26 (s, 1H), ●■ 5.90−5.80 (m, 1H), ● 5.78−5.74 (m, 1H), ● 5.44 (dt, J = 17.1, 1.2 Hz, 1H), ●■ 5.37−5.32 (m, ● 1H, ■ 2H), ■ 5.18 (dd, J = 8.5, 3.2 Hz, 1H), ●■ 4.65−4.56 (m, ● 1H, ■ 2H), ● 4.50 (d, J = 15.6 Hz, 1H), ● 4.21 (d, J = 8.1 Hz, 1H), ■ 4.17 (d, J = 6.2 Hz, 1H), ■ 2.37 (s, 3H), ● 2.35 (s, 3H), ■ 1.59 (d, J = 14.9 Hz, 1H), ●■ 1.55−1.50 (m, 1H), ● 1.44 (d, J = 14.9 Hz, 1H), ● 1.27 (s, 3H), ● 1.25 (s, 3H), ■ 1.22 (s, 3H), ■ 1.20 (s, 3H), ■ 0.90 (s, 9H), ● 0.88 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ ● 170.5, ■ 169.9, ■ 168.0, ● 167.9, ■ 166.4, ● 165.0, ● 162.3, ■ 161.0, ● 135.4, ■ 135.4, ■ 132.2 (2C), ● 132.1 (2C), ■ 131.0 (2C), ● 130.8 (2C), ●■ 127.7, ● 122.6, ■ 122.5, ■ 122.3, ● 122.2, ■ 103.3, ● 101.8, ■ 65.9, ● 65.8, ● 65.73, ■ 65.71, ● 56.4, ■ 56.0, ● 52.6, ■ 51.5, ■ 46.0, ● 45.8, ■ 31.7, ● 31.6, ●■ 31.5 (3C), ■ 28.8, ● 28.8, ■ 28.3, ● 28.1, ■ 12.33, ● 12.31. IR (neat) ν_{max} (cm^{-1}): 2955, 1763, 1678, 1601, 1514, 1489, 1474, 1445, 1383, 1366, 1350, 1225, 1070, 1013, 914. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{25}H_{32}BrN_3NaO_3^+$, 512.1519; found, 524.1513.

trans-β-Lactam **6f**. Prepared according to GP-B using **3f**. Purification of the crude material by silica gel column chromatography (35% EtOAc/*c*Hex) afforded the title compound as an off-white solid in 94% yield (0.104 g, 0.189 mmol). R_f = 0.63 (50% EtOAc/*c*Hex). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, J = 7.1 Hz, 1H), 6.24 (s, 1H), 5.35−5.22 (m, 2H), 5.16−5.09 (m, 1H), 4.61 (dd, J = 6.0, 4.5 Hz, 1H), 4.13−3.97 (br, 3H), 3.97−3.89 (m, 1H), 3.72−3.64 (m, 1H), 3.64−3.56 (m, 2H), 3.56−3.45 (m, 2H), 3.34 (dt, J = 14.3, 6.3 Hz, 1H), 2.89−2.75(br, 2H), 2.41 (s, 3H), 2.08 (dt, J = 14.4, 5.4 Hz, 1H), 1.96 (tt, J = 14.3, 6.4 Hz, 2H), 1.92−1.83 (br, 2H), 1.50−1.32 (br, 12H), 1.17 (td, J = 7.0, 4.9 Hz, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 170.0, 167.9, 167.7, 160.8, 154.7, 127.7, 122.4, 103.3, 102.3, 79.7, 66.0 (2C), 64.8, 63.1 (2C), 62.0, 47.8 (2C), 39.3, 31.5 (2C), 28.4 (3C), 26.9, 15.5, 15.4, 12.4. IR (neat) ν_{max} (cm^{-1}): 3313, 2974, 1749, 1686, 1653, 1427, 1364, 1167, 1136, 1124, 1057. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{28}H_{45}N_4O_7^+$, 549.3283; found, 549.3284.

cis-β-Lactam **6f**. Prepared according to GP-C using **3f**. Purification of the crude material by silica gel column chromatography (50% EtOAc/*c*Hex) afforded the title compound as a light yellow oil in 19% *cis* stereoisomer and 7% *trans* stereoisomer (0.028 g, 0.052 mmol). R_f = 0.31 (50% EtOAc/*c*Hex). Two diastereoisomers were present in NMR (*trans*:*cis* = 2:5), of which the signals of the *trans* diastereoisomer are marked with ■ and *cis* diastereoisomer are marked with ●. ^{1}H NMR (500 MHz, $CDCl_3$) ■ δ 7.90 (d, J = 7.2 Hz, 1H), ● 7.68 (d, J = 7.7 Hz, 1H), ■ 6.26 (q, J = 0.8 Hz, 1H), ● 6.21 (q, J = 0.8 Hz, 1H), ● 5.77 (ddd, J = 17.9, 10.3, 7.7 Hz, 1H), ● 5.42 (dt, J = 17.2, 1.2 Hz, 1H), ●■ 5.35−5.28 (m, ● 1H, ■ 2H), ■ 5.20−5.09 (m, 1H), ●■ 4.67−4.60 (m, 1H), ●■ 4.25−3.89 (m, 4H), ●■ 3.77−3.42 (m, ● 5H, ■ 6H), ● 3.26 (dd, J = 13.3, 7.3 Hz, 1H), ●■ 2.88−2.78 (m, 2H), ●■ 2.44 (s, 3H), ● 2.42−2.38 (m, 1H), ●■ 2.13−1.81 (m, ● 4H, ■ 5H), ●■ 1.49−1.37 (m, 12H), ●■ 1.25−1.15 (m, 6H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ ● 170.6, ■ 170.0, ■ 168.0, ● 167.9, ■ 167.8, ● 166.5, ● 161.9, ■ 160.9, ●■ 154.8, ■ 127.7, ● 127.4, ■ 122.5, ● 122.4, ■ 103.4, ● 102.7, ■ 102.4, ● 102.0, ■ 79.8, ● 79.8, ■ 66.1, ● 65.3, ● 65.1, ■ 64.9, ● 63.6 (2C), ■ 63.1 (2C), ■ 62.14 (2C), ● 62.07 (2C), ■ 47.85 (2C), ● 47.80 (2C), ■ 39.3 (2C), ● 39.0 (2C), ● 31.7 (2C), ■ 31.6 (2C), ●■ 28.5 (3C), ● 15.6, ■ 15.6, ●■ 15.4, ● 12.5, ■ 12.4. IR (neat) ν_{max} (cm^{-1}): 2978, 1761, 1420, 1366, 1169, 1138, 1059, 629, 467. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{28}H_{45}N_4O_7^+$, 549.3283; found, 549.3282.

trans-β-Lactam **6g**. Prepared according to GP-B using **3g**. Purification of the crude material by silica gel column chromatography (20% EtOAc/*c*Hex) afforded the title compound as a brown oil in 78% yield (52 mg, 0.16 mmol). R_f = 0.47 (50% EtOAc/*c*Hex). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (s, 1H), 6.08 (s, 1H), 5.35−5.31 (m, 2H), 5.15 (dd, J = 7.5, 4.3 Hz, 1H), 4.18−4.14 (m, 1H), 3.37 (ddd, J = 14.0, 9.8, 6.2 Hz, 1H), 3.26 (ddd, J = 14.0, 9.8, 6.2 Hz, 1H), 2.46 (s, 3H), 1.75−1.64 (m, 2H), 1.38 (s, 9H), 1.37−1.30 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 170.2, 167.8, 166.8, 161.6, 128.1, 122.2, 103.0, 65.1 (2C), 52.2, 43.3, 30.1, 28.6 (3C), 20.7, 13.8, 12.4. IR (neat) ν_{max} (cm^{-1}): 3366, 2959, 2930, 2878, 1753, 1672, 1601, 1518, 1450, 1360, 1223, 941, 816, 594, 465. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{18}H_{27}N_3O_3Na^+$, 356.1945; found, 356.1958.

cis-β-Lactam **6g**. Prepared according to GP-C using **3g**. Purification of the crude material by silica gel column chromatography (20% EtOAc/*c*Hex) afforded the title compound as a brown oil in 28% yield (26 mg, 0.08 mmol). R_f = 0.52 (50% EtOAc/*c*Hex). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.56 (s, 1H), 6.11 (s, 1H), 5.83 (ddd, J = 17.1, 10.3, 8.2 Hz, 1H), 5.39 (dt, J = 17.1, 1.2 Hz, 1H), 5.31 (dd, J = 10.3, 1.2 Hz, 1H), 4.12 (d, J = 8.2 Hz, 1H), 3.28 (t, J = 7.9 Hz, 2H), 2.45 (s, 3H), 1.70−1.59 (m, 2H), 1.34 (s, 9H), 1.34−1.28 (m, 2H), 0.89 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 170.7, 167.7, 165.5, 162.6, 128.01122.4, 101.4, 65.1 (2C), 52.3, 43.2, 30.4, 28.8 (3C), 20.7, 13.8, 12.4. IR (neat) ν_{max} (cm^{-1}): 3366, 2959, 2930, 2878, 1753, 1672, 1601, 1518, 1450, 1361, 1223, 941, 816, 594, 465. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{18}H_{27}N_3O_3Na^+$, 356.1945; found, 356.1958.

trans-β-Lactam **6h**. Prepared according to GP-B using **3h**. Purification of the crude material by silica gel column chromatography (15% EtOAc/*c*Hex) afforded the title compound as a light yellow oil in 27% yield (0.024 g, 0.05 mmol). R_f = 0.86 (50% EtOAc/*c*Hex). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, J = 8.2 Hz, 2H), 7.36 (s, 1H), 7.28 (d, J = 8.0 Hz, 2H), 6.88 (s, 1H), 5.40−5.35 (m, 2H), 5.22−5.17 (m, 1H), 4.44 (dd, J = 18.3, 2.6 Hz, 1H), 4.37 (dd, J = 18.3, 2.5 Hz, 1H), 4.19 (d, J = 7.1 Hz, 1H), 2.41 (s, 3H), 2.33 (t, J = 2.6 Hz, 1H), 1.88 (d, J = 14.9 Hz, 1H), 1.75 (d, J = 14.9 Hz, 1H), 1.48 (s, 3H), 1.47 (s, 3H), 1.00 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 170.5, 167.4, 166.4, 161.4, 141.2, 129.9 (2C), 127.3, 126.0 (2C), 124.2, 122.8, 100.8, 78.1, 74.2, 66.4, 66.0, 56.6, 51.5, 31.9, 31.6 (3C), 31.5, 29.4, 28.8, 21.7. IR (neat) ν_{max} (cm^{-1}): 2955, 1774, 1678, 1510, 1423, 1364, 932, 822, 824, 625. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{27}H_{33}N_3NaO_3^+$, 470.2414; found, 470.2423.

cis-β-Lactam **6h**. Prepared according to GP-C using **3h**. Purification of the crude material by silica gel column chromatography (15% EtOAc/*c*Hex) afforded the title compound as a light yellow oil in 7.5% *trans* diastereoisomer and 21.5% *cis* diastereoisomer (0.026 g, 0.05 mmol). R_f = 0.42 (20% EtOAc/*c*Hex). Two diastereoisomers were present in NMR (*trans*:*cis* = 1:3), of which the signals of the *trans* diastereoisomer are marked. ^{1}H NMR (500 MHz, $CDCl_3$) δ ●■ 7.67 (d, J = 8.2 Hz, 2H), ■ 7.35 (s, 1H), ●■ 7.28 (d, J = 8.0 Hz, 2H), ● 7.09 (s, 1H), ■ 6.88 (s, 1H), ● 6.87 (s, 1H), ● 5.88 (ddd, J = 17.2, 10.3, 8.0 Hz, 1H), ● 5.46 (dt, J = 17.2, 1.1 Hz, 1H), ●■ 5.41−5.35 (m, ● 1H, ■ 2H), ■ 5.20−5.16 (m,

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1H), ●■ 4.47−4.29 (m, 2H), ●■ 4.21−4.13 (m, 1H), ●■ 2.41 (s, 3H), ■ 2.33 (t, J = 2.6 Hz, 1H), ● 2.32 (t, J = 2.6 Hz, 1H), ■ 1.88 (d, J = 14.9 1H), ●■ 1.79−1.69 (m, ● 2H, ■ 1H), ■ 1.48 (s, 3H), ■ 1.47 (s, 3H), ● 1.44 (s, 3H), ● 1.42 (s, 3H), ■ 1.00 (s, 9H), ● 0.97 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ ● 170.9, ■ 170.5, ■ 167.3, ● 167.3, ■166.4, ● 164.8, ● 163.0, ■ 161.4, ● 141.3, ■ 141.2, ● 129.93 (2C), ■ 129.91 (2C), ●■ 127.3, ● 126.0 (2C), ■ 125.9 (2C), ■ 124.24, ● 124.19, ● 122.85, ■ 122.82, ■ 100.8, ● 99.4, ● 78.12, ■ 78.09, ■ 74.2, ● 74.0, ● 67.0, ■ 66.4, ■ 66.0, ● 65.6, ● 56.8, ■ 56.6, ● 52.5, ■ 51.5, ■ 31.9, ● 31.8, ●■ 31.6 (3C), ● 31.5, ■ 31.3, ■ 29.4, ● 29.2, ■ 28.8, ● 28.5, ●■ 21.7. IR (neat) ν_{max} (cm^{-1}): 2955, 1772, 1678, 1510, 1452, 1423, 1366, 1354, 1225, 932, 733. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{27}H_{33}N_3NaO_3^+$, 470.2414; found, 470.2414.

trans/cis-β-Lactam ***6i***. Prepared according to GP-B using **3i**. Purification of the crude material by silica gel column chromatography (20% EtOAc/*c*Hex) afforded the title compound as a brown oil in 48% yield *trans* diastereoisomer and 21% yield *cis* diastereoisomer (63 mg, 0.15 mmol). Also prepared according to GP-C using **3i**. Purification of the crude material by silica gel column chromatography (20% EtOAc/*c*Hex) afforded the title compound as a brown oil in 10% yield *cis* diastereoisomer and 23% yield *trans* diastereoisomer (35 mg, 0.08 mmol). R_f = 0.55 (50% EtOAc/*c*Hex). Two diastereoisomers were present in NMR (*trans*:*cis* = 5:2), of which the signals of the *trans* diastereoisomer are marked with ● and *cis* diastereoisomer are marked with ■. ^1H NMR (500 MHz, $CDCl_3$) δ ■ 7.82−7.77 (m, 5H), ● 7.47−7.43 (m, 5H), ●■ 7.26−7.21 (m, 2H), ●■ 7.13−7.07 (m, 2H), ■ 7.02 (s, 1H), ● 7.00 (s, 1H), ● 6.20 (s, 1H), ■ 6.12 (s, 1H), ■ 5.97−5.87 (m, 1H), ●■ 5.60−5.51 (m, 1H), ●■ 5.49−5.41 (d, J = 1.6 Hz, 1H), ● 5.30−5.25 (m, 1H), ■ 4.41 (d, J = 7.5 Hz, 1H), ● 4.32 (d, J = 7.7 Hz, 1H), ● 2.30 (s, 3H), ■ 2.28 (s, 3H), ● 1.36 (s, 9H), ■ 1.35 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ ■ 167.0, ● 165.6, ● 165.5, ■ 164.05, ● 164.04, ■ 163.8, ● 162.9, ■ 162.8, ■ 135.1, ● 135.0, ● 133.8, ■ 133.6, ● 130.55, ■ 130.50, ■ 130.1 (2C), ● 130.0 (2C), ● 129.1 (2C), ■ 129.0 (2C), ■ 128.4, ● 128.3, 127.1 (2C), ■ 127.0 (2C), ■ 126.6, ● 126.5, ● 123.8, ■ 123.2, ● 117.35 (2C), ■ 117.33 (2C), ● 104.6, ■ 103.9, ● 66.2, ■ 65.5, ● 65.0, ■ 64.8, ■ 52.7, ● 52.5, ■ 28.8 (3C), ● 28.6 (3C), ●■ 21.1. IR (neat) ν_{max} (cm^{-1}): 3354, 2966, 2926, 2311, 1757, 1680, 1516, 1367, 1221, 1192, 943, 916, 818, 766, 727,689, 592, 507, 401. m.p.: 170−172 °C. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{26}H_{27}N_3O_3Na^+$, 452.1945; found, 452.1958.

trans-β-Lactam ***6j***. Prepared according to GP-B using **3j**. Purification of the crude material by silica gel column chromatography (50% EtOAc/*c*Hex) afforded the title compound as a yellow solid in 94% yield (0.067 g, 0.18 mmol). R_f = 0.31 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 7.03 (d, J = 1.2 Hz, 1H), 6.91 (d, J = 1.1 Hz, 1H), 5.74 (d, J = 7.2 Hz, 1H), 5.40−5.33 (m, 1H), 5.24−5.12 (m, 2H), 4.86 (s, 1H), 4.81 (s, 1H), 4.79 (d, J = 9.3 Hz, 1H), 4.36 (d, J = 16.5 Hz, 1H), 4.17 (d, J = 16.4 Hz, 1H), 3.71 (dtd, J = 10.8, 7.4, 4.0 Hz, 1H), 3.40 (s, 3H), 1.84−1.76 (m, 1H), 1.73 (s, 3H), 1.64−1.50 (m, 3H), 1.35−1.21 (m, 3H), 1.13−0.93 (m, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 167.5, 166.1, 142.9, 140.4, 128.3, 128.1, 123.4, 122.7, 113.5, 66.1, 62.2, 49.4, 48.3, 33.9, 33.0, 32.2, 25.4, 24.73, 24.66, 20.5. IR (neat) ν_{max} (cm^{-1}): 2931, 2854, 1749, 1655, 1518, 1377, 1281, 914, 729. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{20}H_{28}N_4NaO_2^+$, 379.2104; found, 379.2117.

trans-β-Lactam ***6k***. Prepared according to GP-B using **3k**. Purification of the crude material by silica gel column chromatography (35% EtOAc/*c*Hex) afforded the title compound as an off-white solid in 76% yield (0.078 g, 0.15 mmol). R_f = 0.57 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, J = 8.4 Hz, 1H), 7.09−7.06 (m, 1H), 7.00 (d, J = 1.2 Hz, 1H), 6.42 (dd, J = 8.4, 2.3 Hz, 1H), 6.37 (d, J = 2.3 Hz, 1H), 5.72 (s, 1H), 5.39 (dd, J = 16.8, 1.7 Hz, 1H), 5.33−5.24 (m, 1H), 5.21 (dd, J = 9.9, 1.8 Hz, 1H), 5.11 (d, J = 17.3 Hz, 1H), 4.87 (d, J = 17.4 Hz, 1H), 4.80 (d, J = 9.4 Hz, 1H), 4.10 (hept, J = 6.9 Hz, 1H), 3.73 (s, 6H), 1.32 (s, 3H), 1.30 (s, 3H), 1.20−1.15 (m, 4H), 1.10 (d, J = 14.9 Hz, 1H), 0.79 (s, 3H), 0.73 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 168.2, 165.9, 160.3, 157.5, 142.1, 129.4, 129.3, 128.8, 122.4, 117.5, 117.3, 104.3, 98.5, 67.7, 61.6, 56.3, 55.5, 55.3, 53.9, 48.1, 40.5, 31.4 (3C), 31.3, 27.1, 26.8, 24.5, 24.4. IR (neat) ν_{max} (cm^{-1}): 2955, 1751, 1678, 1508, 1375, 1256, 1203, 1124, 1032, 932. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{29}H_{43}N_4O_4^+$, 511.3279; found, 511.3270.

trans-β-Lactam ***6l***. Prepared according to GP-B using **3l**. Purification of the crude material by silica gel column chromatography (50% EtOAc/*c*Hex) afforded the title compound as a brown oil in 95% yield (69 mg, 0.19 mmol). R_f = 0.18 (70% EtOAc/*c*Hex). ^1H NMR (600 MHz, $CDCl_3$) δ 7.46 (s, 1H), 6.97 (s, 1H), 6.87 (s, 1H), 5.38−5.31 (m, 1H), 5.27−5.18 (m, 1H), 5.15 (dd, J = 10.2, 1.3 Hz, 1H), 5.05 (t, J = 5.6 Hz, 1H), 4.39 (d, J = 9.0 Hz, 1H), 3.72 (dd, J = 14.8, 5.6 Hz, 1H), 3.66 (dd, J = 14.8, 5.6 Hz, 1H), 3.57 (s, 3H), 3.42 (s, 3H), 3.31 (s, 3H), 1.34 (s, 9H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 167.8, 166.7, 143.3, 128.4, 127.2, 123.6, 122.4, 101.8, 67.5, 63.9, 55.1, 54.2, 52.0, 45.7, 35.1, 28.6 (3C). IR (neat) ν_{max} (cm^{-1}): 2966, 2934, 2340, 1759, 1676, 1528, 1367, 1121, 1067, 984, 760, 652. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{18}H_{29}N_4O_4^+$, 365.2183; found, 365.2190.

trans-β-Lactam ***6m***. Prepared according to GP-B using **3m**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a yellow solid in 81% yield (0.075 g, 0.162 mmol). R_f = 0.76 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 7.40 (s, 1H), 7.30−7.24 (m, 2H), 7.20 (d, J = 7.5 Hz, 3H), 7.01 (d, J = 1.1 Hz, 1H), 6.88 (d, J = 1.1 Hz, 1H), 5.39−5.34 (m, 1H), 5.31−5.22 (m, 1H), 5.16−5.12 (m, 1H), 4.57 (d, J = 7.9 Hz, 1H), 3.75 (ddd, J = 13.9, 11.7, 5.5 Hz, 1H), 3.54 (ddd, J = 13.9, 11.6, 5.4 Hz, 1H), 3.49 (s, 3H), 3.25 (td, J = 12.5, 11.7, 5.5 Hz, 1H), 3.04 (ddd, J = 13.3, 11.9, 5.4 Hz, 1H), 1.65 (d, J = 15.0 Hz, 1H), 1.58 (d, J = 15.0 Hz, 1H), 1.47 (s, 3H), 1.45 (s, 3H), 0.90 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 167.6, 166.2, 142.7, 138.8, 128.7 (2C), 128.6 (2C), 128.4, 127.8, 126.5, 123.7, 122.0, 66.4, 62.7, 56.2, 53.5, 45.1, 34.5, 34.0, 31.7, 31.5 (3C), 28.4, 28.2. IR (neat) ν_{max} (cm^{-1}): 2955, 1753, 1670, 1510, 1454, 1364, 1281, 1223, 731, 700, 501, 457. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{26}H_{36}N_4NaO_2^+$, 459.2730; found, 459.2733.

trans-β-Lactam ***6n***. Prepared according to GP-B using **3n**. Purification of the crude material by silica gel column chromatography (20% EtOAc/*c*Hex) afforded the title compound as a brown oil in 59% yield (49 mg, 0.12 mmol). R_f = 0.65 (60% EtOAc/*c*Hex). ^1H NMR (600 MHz, $CDCl_3$) δ 9.37 (s, 1H), 9.29 (s, 1H), 8.03 (d, J = 8.1 Hz, 1H), 7.75 (s, 1H), 7.73−7.65 (m, 3H), 7.32 (d, J = 8.5 Hz, 2H), 7.09 (d, J = 8.2 Hz, 2H), 5.32 (td, J = 17.0, 1.4 Hz, 1H), 5.06 (ddd, J = 17.0, 10.3, 8.1 Hz, 1H), 4.96 (td, J = 10.3, 1.4 Hz, 1H), 4.32 (td, J = 8.1 Hz, 1H), 2.29 (s, 3H), 1.42 (s, 9H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 166.8, 164.7, 151.6, 148.2, 136.3, 135.3, 133.6, 131.5, 129.6 (2C), 128.5, 128.1, 127.6, 127.5, 127.4, 121.8, 120.4, 117.7(2C), 69.0, 65.9, 51.7, 28.7 (3C), 21.1. IR (neat) ν_{max} (cm^{-1}): 2966, 2926, 2339, 2312, 1755, 1678, 1541, 1514, 1366, 1273, 1221, 1188, 933, 812, 752, 521, 471. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{26}H_{27}N_3O_2Na^+$, 436.1995; found, 436.2003.

trans/cis-β-Lactam ***6o***. Prepared according to GP-B using **3o**. Purification of the crude material by silica gel column chromatography (20% EtOAc/*c*Hex) afforded the title compound as a brown oil in 66% yield *cis* diastereoisomer and 29% yield *trans* diastereoisomer (55 mg, 0.15 mmol). Also prepared according to GP-C using **3o**. Purification of the crude material by silica gel column chromatography (20% EtOAc/*c*Hex) afforded the title compound as a brown oil in 64% yield *cis* diastereoisomer and 26% yield *trans* diastereoisomer (60 mg, 0.16 mmol). R_f = 0.39 (50% EtOAc/*c*Hex). Two diastereoisomers were present in NMR (*cis*:*trans* = 7:3), of which the signals of the *trans* diastereoisomer are marked with ■ and *cis* diastereoisomer are marked with ●. ^1H NMR (600 MHz, $CDCl_3$) δ ■ 9.10 (s, 1H), ● 9.08 (s, 1H), ■ 8.16−8.12 (m, 3H), ●■ 8.07−7.99 (m, 1H), ■ 7.98 (s, 1H), ● 7.84−7.80 (m, 3H), ● 7.32 (s, 1H), ■ 6.08 (ddq, J = 15.0, 10.1, 6.6, 4.0 Hz, 1H), ● 5.99−5.90 (m, 2H), ● 5.47 (d, J = 17.1 Hz, 1H), ● 5.39 (d, J = 10.1 Hz, 1H), ■ 5.36−5.29 (m, 2H), ● 5.24 (d, J = 16.9 Hz, 1H), ■ 5.22 (d, J = 9.0 Hz, 1H), ● 5.18 (d, J = 10.1 Hz, 1H), ■ 5.13 (dt, J = 17.5, 10.3, 8.0 Hz, 1H), ■ 5.02 (d, J = 10.3 Hz, 1H), ● 4.46 (d, J = 7.9 Hz, 1H), ■

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4.34 (dd, J = 15.4, 6.6 Hz, 1H), ■ 4.30 (d, J = 7.9 Hz, 1H), ■ 4.25 (dd, J = 15.4, 6.6 Hz, 1H), ● 4.16 (dd, J = 15.6, 6.5 Hz, 1H), ● 4.02 (dd, J = 15.6, 6.5 Hz, 1H), ■ 1.42 (s, 9H), ● 1.40 (s, 9H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ ● 168.3, ■ 167.9, ■ 167.5, ● 166.3, ● 152.7, ■ 151.7, ■ 145.4, ● 144.5, ● 141.9, ■ 141.5, ● 140.9, ■ 140.5, ● 132.3, ■ 132.2, ●■ 130.9, ●■ 130.8, ■ 129.6, ● 129.5, ● 129.2, ■ 128.9, ● 128.1, ■ 127.8, ■ 122.6, ● 122.2, ■ 120.2, ● 120.0, ● 69.9, ■ 69.2, ■ 66.3, ● 65.6, ●52.5, ■ 52.2, ■ 46.6, ● 45.9, ● 28.9 (3C), ■ 28.7 (3C). IR (neat) ν_{max} (cm^{-1}): 3340, 2976, 2922, 2339, 1753, 1668, 1520, 1385, 1215, 1124, 951, 837, 756, 619, 563, 411. m.p.: 101−106 °C. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{21}H_{24}N_4O_2Na^+$, 387.1791; found, 387.1810.

trans/cis-β-Lactam ***6p***. Prepared according to GP-B using **3p**. Purification of the crude material by silica gel column chromatography (20% EtOAc/*c*Hex) afforded the title compound as a brown oil in 50% yield (*cis* diastereoisomer) and 36% yield (*trans* diastereoisomer) (93 mg, 0.18 mmol). Also prepared according to GP-C using **3p.** Purification of the crude material by silica gel column chromatography (20% EtOAc/*c*Hex) afforded the title compound as a brown oil in 41% yield *cis* diastereoisomer and 35% yield *trans* diastereoisomer (80 mg, 0.16 mmol). R_f = 0.56 (60% EtOAc/*c*Hex). Two diastereoisomers were present in NMR (*cis*:*trans* = 5:4), of which the signals of the *trans* diastereoisomer are marked with ● and *cis* diastereoisomer are marked with ■. ^1H NMR (500 MHz, $CDCl_3$) δ ■ 9.25 (s, 1H), ● 8.29 (s, 1H), ●■ 8.03−7.97 (m, 2H), ●■ 7.80 (d, J = 8.2 Hz, 1H), ●■ 7.78−7.74 (m, 1H), ●■ 7.60−7.56 (m, 1H), ■ 7.35 (d, J = 8.4 Hz, 2H), ● 7.30 (d, J = 8.6 Hz, 1H), ●■ 7.28−7.25 (m, 2H), ■ 7.22 (d, J = 8.7 Hz, 1H), ● 7.20 (d, J = 8.4 Hz, 2H), ● 6.04−5.95 (m, 1H), ● 5.42 (dt, J = 17.1, 1.1 Hz, 1H), ● 5.37 (d, J = 10.3 Hz, 1H), ■ 5.25 (dt, J = 17.0, 1.2 Hz, 1H), ■ 5.06 (ddd, J = 17.0, 10.4, 7.9 Hz, 1H), ■ 5.00 (d, J = 15.5 Hz, 1H), ■ 4.91 (d, J = 10.4 Hz, 1H), ● 4.85 (d, J = 15.6 Hz, 1H), ● 4.47 (d, J = 7.6 Hz, 1H), ■ 4.44 (d, J = 7.9 Hz, 1H), ■ 4.30 (d, J = 7.9 Hz, 1H), ● 4.24 (d, J = 8.5 Hz, 1H), ■ 1.85 (d, J = 14.9 Hz, 1H), ● 1.81 (d, J = 14.9 Hz, 1H), ■ 1.73 (d, J = 14.9 Hz, 1H), ● 1.50 (d, J = 14.9 Hz, 1H), ■ 1.46 (s, 3H), ●■ 1.43 (s, 3H), ● 1.41 (s, 3H), ■ 0.97 (s, 9H), ● 0.88 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ ● 169.1, ■ 168.7, ■ 167.3, ● 166.0, ● 158.0, ■ 156.6, ■ 146.5, ● 146.3, ● 137.4, ■ 136.8, ● 135.1, ■ 135.0, ■ 133.64, ● 133.58, ■ 130.7 (2C), ● 130.42 (2C), ■ 130.39, ● 130.37, ■ 128.9 (2C), ●■ 128.8 (● 2C, ■ 1C), ● 128.7, ● 128.5, ■ 128.1, ■ 127.8, ● 127.7, ■ 127.32, ● 127.31, ● 126.9, ■ 126.7, ● 122.3, ■ 121.5, ■ 120.7, ● 119.3, ● 71.3, ■ 70.7, ● 66.8, ■ 66.2, ● 55.9, ■ 55.6, ● 52.5, ■ 51.6, ■ 46.9, ● 46.4, ■ 31.7, ● 31.6, ■ 31.52 (3C), ● 31.47 (3C), ■ 29.2, ■ 29.0, ● 28.8, ● 28.7. IR (neat) ν_{max} (cm^{-1}): 2955, 2907, 2341, 2309, 1759, 1672, 1499, 1371, 1225, 1143, 1094, 924, 825, 731, 642, 623, 505, 453, 401. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{30}H_{34}N_3O_2ClNa^+$, 526.2232; found, 526.2249.

trans-β-Lactam ***6q***. Prepared according to GP-B using **3q**. Purification of the crude material by silica gel column chromatography (15% EtOAc/*c*Hex) afforded the title compound as a colorless solid in 40% yield (0.035 g, 0.079 mmol). R_f = 0.84 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 3.3 Hz, 1H), 7.77 (s, 1H), 7.60 (d, J = 8.1 Hz, 2H), 7.51 (d, J = 8.1 Hz, 2H), 7.33 (d, J = 3.3 Hz, 1H), 5.33 (d, J = 17.0 Hz, 1H), 5.22 (ddd, J = 17.1, 10.2, 7.5 Hz, 1H), 5.10 (d, J = 10.1 Hz, 1H), 4.73 (d, J = 15.5 Hz, 1H), 4.59 (d, J = 15.5 Hz, 1H), 4.18 (d, J = 7.5 Hz, 1H), 1.25 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 168.6, 166.6, 166.0, 142.9, 140.3, 130.4 (q, J = 32.6 Hz), 129.7 (2C), 126.7, 125.9 (q, J = 3.7 Hz, 2C), 124.1 (d, J = 272.2 Hz), 122.8, 121.3, 69.0, 67.8, 51.9, 46.7, 28.4 (3C). IR (neat) ν_{max} (cm^{-1}): 2968, 1767, 1672, 1366, 1321, 1163, 1242, 1113, 1067, 1020. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{21}H_{22}F_3N_3NaO_2S^+$, 460.1277; found, 460.1282.

cis-β-Lactam ***6q***. Prepared according to GP-C using **3q**. Purification of the crude material by silica gel column chromatography (15% EtOAc/*c*Hex) afforded the title compound as a colorless solid in 27% yield (0.013 g, 0.027 mmol). R_f = 0.82 (50% EtOAc/*c*Hex). ^1H NMR (600 MHz, $CDCl_3$) δ 7.80 (d, J = 3.3 Hz, 1H), 7.59 (d, J = 8.1 Hz, 2H), 7.47 (d, J = 8.0 Hz, 2H), 7.37 (s, 1H), 7.34 (d, J = 3.3 Hz, 1H), 5.87 (ddd, J = 17.2, 10.3, 8.1 Hz, 1H), 5.41 (dt, J = 17.2, 1.2 Hz, 1H), 5.35 (dd, J = 10.3, 0.9 Hz, 1H), 4.60 (d, J = 1.9 Hz, 2H), 4.04 (d, J = 8.0 Hz, 1H), 1.21 (s, 9H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 168.7, 167.7, 165.1, 142.9, 140.3, 130.4 (q, J = 32.5 Hz), 129.6 (2C), 127.3, 126.0 (q, J = 3.7 Hz, 2C), 124.1 (d, J = 272.2 Hz), 122.9, 121.2, 69.4, 69.2, 52.1, 46.4, 28.5 (3C). IR (neat) ν_{max} (cm^{-1}): 3265, 2920, 1761, 1672, 1560, 1321, 1313, 1223, 1161, 1138, 1111, 1065, 1013, 943. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{21}H_{22}F_3N_3NaO_2S^+$, 460.1277; found 460.1290.

trans/cis-β-Lactam ***6r***. Prepared according to GP-B using **3r**. Purification of the crude material by silica gel column chromatography (20% EtOAc/*c*Hex) afforded the title compound as a clear oil in 63% yield as a mixture of diastereoisomers (ratio, 2:1) (47 mg, 0.11 mmol). Also prepared according to GP-C using **3r**. Purification of the crude material by silica gel column chromatography (20% EtOAc/*c*Hex) afforded the title compound as a clear oil in 76% yield as a mixture of diastereoisomers (ratio, 3:2) (61 mg, 0.15 mmol). R_f = 0.43 (50% EtOAc/*c*Hex). Two diastereoisomers were present in NMR (ratio, 2: 1), of which the signals of the major diastereoisomer are marked with ● and minor diastereoisomer are marked with ■. ^1H NMR (600 MHz, chloroform-*d*) δ ● 7.29 (d, J = 8.6 Hz, 2H), ■ 7.23 (d, J = 8.6 Hz, 2H), ■ 7.18 (d, J = 7.7 Hz, 2H), ● 6.86 (d, J = 8.6 Hz, 2H), ■ 6.82 (d, J = 8.6 Hz, 1H), ● 6.20 (d, J = 7.7 Hz, 1H), ■● 5.76−5.62 (m, 1H), ■● 5.41 (d, J = 17.1 Hz, 1H), ■● 5.30 (d, J = 12.0 Hz, 1H), ■ 4.58 (d, J = 14.7 Hz, 1H), ● 4.54 (d, J = 15.0 Hz, 1H), ● 4.42 (d, J = 15.0 Hz, 1H), ●■ 4.37 (d, J = 14.7 Hz, 1H), ● 4.25 (d, J = 7.9 Hz, 1H), ● 4.21−4.13 (m, 1H), ■● 4.13−4.08 (m, 1H), ■ 4.04 (d, J = 7.9 Hz, 1H), ■ 3.93 (dq, J = 10.8, 7.2 Hz, 1H), ● 3.79 (s, 3H), ■ 3.77 (s, 3H), ■ 3.75−3.69 (m, 1H), ● 3.64 (ddt, J = 14.7, 7.8, 4.1 Hz, 1H), ■● 1.89−1.51 (m, 5H), ■● 1.43−1.02 (m, 7H), ● 0.91 (qd, J = 11.9, 3.1 Hz, 1H), ■ 0.82−0.74 (m, 1H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ ■ 169.7, ● 169.0, ● 167.4, ■ 166.4, ■ 164.8, ● 163.9, ● 159.6, ■ 159.3, ■ 130.8 (2C), ● 130.5 (2C), ● 128.1, ● 127.4, ■ 127.2, ■ 127.0, ■ 123.1, ● 122.6, ● 114.4 (2C), ■ 113.9 (2C), ● 68.9, ■ 67.8, ■ 64.5, ● 62.7, ● 62.6, ■ 62.5, ● 55.5, ■ 55.4, ■ 48.8, ● 48.5, ■ 46.1, ● 45.6, ■ 32.8, ● 32.7, ● 32.62, ■ 32.58, ● 25.6, ■ 25.50, ■ 24.8, ● 24.7, ● 24.6, ■● 14.07, ■ 14.03. IR (neat) ν_{max} (cm^{-1}): 3339, 2930, 2854, 2338, 1757, 1668, 1612, 1516, 1450, 1381, 1246, 1175, 1103, 1034, 814, 623, 513. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{23}H_{30}N_2O_5Na^+$, 437.2047; found, 437.2057.

trans-β-Lactam ***6s***. Prepared according to GP-B using **3s**. Purification of the crude material by silica gel column chromatography (20% EtOAc/*c*Hex) afforded the title compound as yellow crystals in 36% yield (36 mg, 0.07 mmol). R_f = 0.57 (60% EtOAc/*c*Hex). ^1H NMR (600 MHz, $CDCl_3$) δ 10.07 (s, 1H), 8.84 (s, 1H), 8.63 (d, J = 2.1 Hz, 1H), 8.56−8.42 (m, 1H), 7.39−7.13 (m, 15H), 5.32−5.20 (m, 1H), 5.16−4.93 (m, 2H), 4.04 (d, J = 6.8 Hz, 1H), 3.37 (ddd, J = 13.8, 9.8, 6.5 Hz, 1H), 3.24 (dd, J = 10.0, 6.7 Hz, 1H), 1.80 (dq, J = 13.8, 3.9, 0.9 Hz, 2H), 0.90 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 167.5, 166.9, 152.3, 144.9, 144.5 (3C), 144.3, 142.5, 128.6 (6C), 128.1 (6C), 127.8 (3C), 127.3, 122.6, 71.3, 68.5, 65.9, 46.2, 21.3, 12.1. IR (neat) ν_{max} (cm^{-1}): 3227, 3057, 2930, 2336, 1751, 1688, 1551, 1483, 1447, 1391, 1263, 1022, 930, 758, 700, 602, 401. m.p.: 193−198 °C. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{32}H_{30}N_4O_2Na^+$, 525.2261; found, 525.2279.

cis-β-Lactam ***6s***. Prepared according to GP-C using **3s**. Purification of the crude material by silica gel column chromatography (20% EtOAc/*c*Hex) afforded the title compound as yellow crystals in 45% yield (40 mg, 0.08 mmol). R_f = 0.51 (60% EtOAc/*c*Hex). ^1H NMR (600 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.74 (d, J = 1.4 Hz, 1H), 8.63 (d, J = 2.4 Hz, 1H), 8.57−8.46 (m, 1H), 7.36−7.19 (m, 15H), 5.73 (ddd, J = 17.1, 10.3, 8.6 Hz, 1H), 5.37 (d, J = 17.1 Hz, 1H), 5.26 (d, J = 10.3 Hz, 1H), 4.08 (d, J = 8.6 Hz, 1H), 3.33−3.25 (m, 1H), 3.22−3.12 (m, 1H), 1.64 (dddd, J = 24.8, 14.6, 8.1, 5.0 Hz, 2H), 0.83 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 168.1, 165.7, 153.9, 144.5, 144.2 (3C), 143.7, 143.0, 128.8 (6C), 128.6, 128.1 (6C), 127.3 (3C), 122.7, 71.5, 69.4, 67.1, 45.9, 21.7, 11.9. IR (neat) ν_{max} (cm^{-1}): 3225, 3053, 2925, 1783, 1664, 1651, 1485, 1448, 1391, 1263, 1022, 930, 757, 700, 602, 401. m.p.: 193−

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198 ° C. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{32}H_{30}N_4O_2Na^+$, 525.2261; found, 525.2279.

trans-β-Lactam ***6t***. Prepared according to GP-B using **3t**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 93% yield (87 mg, 0.19 mmol). R_f = 0.37 (60% EtOAc/*c*Hex). ^1H NMR (600 MHz, $CDCl_3$) δ 9.41 (s, 1H), 7.47 (t, J = 7.8 Hz, 1H), 7.06 (d, J = 7.8 Hz, 1H), 6.85 (d, J = 7.8 Hz, 1H), 6.83 (s, 1H), 6.79 (s, 2H), 5.22 (d, J = 16.7 Hz, 1H), 5.06−4.97 (m, 1H), 4.95 (d, J = 10.3 Hz, 1H), 4.05 (d, J = 7.6 Hz, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.70 (ddd, J = 13.7, 9.9, 4.8 Hz, 1H), 3.45−3.38 (m, 1H), 3.34 (dt, J = 13.7, 9.9, 7.4 Hz, 1H), 3.17 (ddd, J = 13.7, 9.9, 4.8 Hz, 1H), 2.53 (s, 3H), 1.40 (s, 9H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 168.4, 168.2, 157.3, 155.7, 149.0, 147.7, 137.6, 132.2, 128.6, 122.3, 120.93, 120.92, 119.7, 112.4, 111.4, 69.7, 65.8, 56.1, 56.0, 51.4, 46.5, 33.6, 28.8 (3C), 24.3. IR (neat) ν_{max} (cm^{-1}): 2962, 2934, 2341, 1753, 1674, 1585, 1547, 1512, 1456, 1360, 1261, 1230, 1149, 1028, 991, 922, 731, 646, 536, 501, 461. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{26}H_{33}N_3O_4Na^+$, 474.2363; found, 474.2381.

cis-β-Lactam ***6t***. Prepared according to GP-C using **3t**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 30% yield (29 mg, 0.06 mmol). R_f = 0.33 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 8.78 (s, 1H), 7.52 (t, J = 7.8 Hz, 1H), 7.10 (d, J = 7.8 Hz, 1H), 6.99 (d, J = 7.8 Hz, 1H), 6.81−6.77 (m, 3H), 5.92 (ddd, J = 17.1, 10.2, 8.8 Hz, 1H), 5.39−5.29 (m, 2H), 3.85 (s, 3H), 3.84 (s, 3H), 3.81 (d, J = 8.7 Hz, 1H), 3.68 (dt, J = 14.0, 9.3, 6.9 Hz, 1H), 3.44 (dt, J = 14.0, 9.3, 6.9 Hz, 1H), 3.27−3.13 (m, 2H), 2.55 (s, 3H), 1.36 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 168.7, 166.4, 157.8, 157.6, 149.0, 147.7, 138.0, 132.0, 128.9, 122.5, 121.9, 120.9, 117.8, 112.2, 111.3, 70.3, 66.8, 56.1, 56.0, 51.6, 46.4, 33.8, 28.9 (3C), 24.4. IR (neat) ν_{max} (cm^{-1}): 3381, 2959, 2926, 2858, 2297, 1745, 1664, 1583, 1514, 1448, 1358, 1259, 1232, 1026, 935, 798, 579, 462, 401. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{26}H_{33}N_3O_4Na^+$, 474.2363; found, 474.2381.

trans-β-Lactam ***6u***. Prepared according to GP-B using **3u**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 83% yield (70 mg, 0.15 mmol). R_f = 0.37 (50% EtOAc/*c*Hex). ^1H NMR (600 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.67 (q, J = 7.9 Hz, 1H), 6.90 (d, J = 7.5 Hz, 1H), 6.87−6.84 (m, 2H), 6.84−6.74 (m, 2H), 5.26 (d, J = 16.8 Hz, 1H), 5.13−5.04 (m, 1H), 5.02 (d, J = 10.3 Hz, 1H), 4.10 (d, J = 7.8 Hz, 1H), 3.86 (d, J = 2.5 Hz, 3H), 3.84 (d, J = 2.5 Hz, 3H), 3.78−3.67 (m, 1H), 3.49−3.42 (m, 1H), 3.39−3.28 (m, 1H), 3.21−3.09 (m, 1H), 1.38 (s, 9H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 168.2, 167.7, 162.3 (d, J = 243.3 Hz), 154.9 (d, J = 11.8 Hz), 149.1, 147.8, 142.3 (d, J = 7.6 Hz), 132.0, 128.1, 121.7, 121.0, 120.1 (d, J = 4.0 Hz), 112.4, 111.4, 108.9 (d, J = 35.6 Hz), 69.9, 65.6, 56.1, 56.0, 51.9, 46.7, 33.7, 28.7 (3C). IR (neat) ν_{max} (cm^{-1}): 2964, 2934, 2301, 1751, 1674, 1591, 1514, 1450, 1261, 1229, 1148, 1028, 802, 731, 646, 461, 401. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{25}H_{31}N_3O_4F^+$, 456.2293; found, 456.2306.

cis-β-Lactam ***6u***. Prepared according to GP-C using **3u**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 61% yield (57 mg, 0.13 mmol). R_f = 0.32 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, J = 7.9 Hz, 1H), 7.10 (dd, J = 7.9, 2.4 Hz, 1H), 7.02 (s, 1H), 6.89 (dd, J = 7.9, 2.4 Hz, 1H), 6.78−6.73 (m, 3H), 5.87 (ddd, J = 17.1, 10.4, 8.5 Hz, 1H), 5.42 (dt, J = 17.1, 1.2 Hz, 1H), 5.35 (d, J = 10.4 Hz, 1H), 4.09 (d, J = 8.4 Hz, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.62 (ddd, J = 13.8, 8.8, 5.8 Hz, 1H), 3.46 (dt, J = 13.8, 8.8, 7.5 Hz, 1H), 3.18−3.02 (m, 2H), 1.31 (s, 9H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 168.4, 166.3, 162.5 (d, J = 243.0 Hz), 156.4 (d, J = 11.9 Hz), 149.1, 147.8, 142.3 (d, J = 7.7 Hz), 131.6, 128.5, 122.1, 120.9, 119.2 (d, J = 4.1 Hz), 112.2, 111.4, 109.3 (d, J = 36.0 Hz), 70.3, 65.2, 56.04, 55.96, 52.1, 46.1, 33.9, 28.8 (3C). IR (neat) ν_{max} (cm^{-1}): 3377, 2961, 2934, 2328, 1749, 1668, 1599, 1576, 1516, 1448, 1151, 1026, 941, 860, 802, 744, 584, 463, 401. HRMS (ESI) m/z: $[M + H]^+$ calcd. for $C_{25}H_{31}N_3O_4F^+$, 456.2293; found, 456.2306.

trans-β-Lactam ***6v***. Prepared according to GP-B using **3v**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 54% yield (53 mg, 0.10 mmol). R_f = 0.40 (50% EtOAc/*c*Hex). ^1H NMR (600 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.43−7.35 (m, 2H), 6.92 (dd, J = 7.4, 1.1 Hz, 1H), 6.84 (d, J = 1.5 Hz, 1H), 6.82−6.79 (m, 2H), 5.29−5.23 (m, 1H), 5.11−5.00 (m, 2H), 4.08 (d, J = 6.9 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.78−3.70 (m, 1H), 3.42−3.32 (m, 2H), 3.18−3.11 (m, 1H), 1.39 (s, 9H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 168.1, 167.6, 157.5, 149.1, 147.8, 140.5, 139.4, 132.0, 128.1, 127.2, 121.69, 121.66, 121.0, 112.4, 111.4, 69.7, 65.7, 56.1, 56.0, 51.8, 46.7, 33.6, 28.7 (3C). IR (neat) ν_{max} (cm^{-1}): 3377, 2951, 2330, 1749, 1668, 1587, 1516, 1447, 1231, 1149, 1028, 939, 800, 744, 581, 463. m.p.: 115−125 °C. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{25}H_{30}N_3O_4BrNa^+$, 538.1312; found, 538.1334.

cis-β-Lactam ***6v***. Prepared according to GP-C using **3v**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 50% yield (56 mg, 0.11 mmol). R_f = 0.32 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.48 (t, J = 7.6 Hz, 1H), 7.43 (d, J = 7.6 Hz, 1H), 7.12 (d, J = 7.6 Hz, 1H), 6.83−6.74 (m, 3H), 5.88 (ddd, J = 17.1, 10.3, 8.4 Hz, 1H), 5.41 (d, J = 17.1 Hz, 1H), 5.35 (d, J = 10.3 Hz, 1H), 3.96 (d, J = 8.4 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.68 (ddd, J = 13.9, 9.0, 6.0 Hz, 1H), 3.43 (ddd, J = 13.9, 9.0, 6.0 Hz, 1H), 3.24−3.09 (m, 2H), 1.34 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 168.3, 165.9, 159.2, 149.0, 147.7, 140.9, 139.6, 131.6, 128.3, 127.5, 122.2, 120.9, 120.4, 112.1, 111.3, 70.2, 66.1, 56.01, 55.97, 51.9, 46.3, 33.8, 28.8 (3C). IR (neat) ν_{max} (cm^{-1}): 3377, 2951, 2330, 1749, 1668, 1587, 1516, 1447, 1231, 1149, 1028, 939, 800, 744, 581, 463. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{25}H_{30}N_3O_4BrNa^+$, 538.1312; found, 538.1331.

trans-β-Lactam ***6w***. Prepared according to GP-B using **3w**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 95% yield (88 mg, 0.19 mmol). R_f = 0.33 (50% EtOAc/*c*Hex). ^1H NMR (600 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.50−7.47 (m, 1H), 6.83 (s, 1H), 6.80 (s, 2H), 6.68 (t, J = 7.9 Hz, 2H), 5.24 (d, J = 17.0 Hz, 1H), 5.10 (ddd, J = 17.0, 10.2, 8.1 Hz, 1H), 4.99 (d, J = 10.2 Hz, 1H), 4.11 (d, J = 8.1 Hz, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 3.84 (s, 3H), 3.70−3.63 (m, 1H), 3.51 (ddd, J = 13.6, 10.1, 7.0 Hz, 1H), 3.32 (ddd, J = 13.6, 10.1, 7.0 Hz, 1H), 3.22−3.15 (m, 1H), 1.39 (s, 9H). $^{13}C\{^1H\}$ NMR (600 MHz, $CDCl_3$) δ 168.4, 168.3, 163.4, 153.5, 149.1, 147.7, 139.7, 132.0, 128.7, 121.0, 120.9, 115.3, 112.4, 111.4, 110.6, 70.5, 65.4, 56.1, 56.0, 53.7, 51.7, 46.5, 33.8, 28.9 (3C). IR (neat) ν_{max} (cm^{-1}): 2964, 2934, 1751, 1674, 1580, 1514, 1464, 1414, 1327, 1261, 1232, 1153, 1026, 989, 924, 800, 733, 644, 617, 544, 503, 463. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{26}H_{33}N_3O_5Na^+$, 490.2312; found, 490.2328.

trans-β-Lactam ***6x***. Prepared according to GP-B using **3x**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 99% yield (90 mg, 0.20 mmol). R_f = 0.40 (50% EtOAc/*c*Hex). ^1H NMR (600 MHz, $CDCl_3$) δ 8.92 (s, 1H), 8.40 (d, J = 5.0 Hz, 1H), 7.03 (d, J = 5.0 Hz, 1H), 6.87 (s, 2H), 6.85−6.77 (m, 2H), 5.23 (d, J = 16.5 Hz, 1H), 5.06−4.90 (m, 2H), 4.09 (d, J = 7.5 Hz, 1H), 3.85 (s, 3H), 3.85 (s, 3H), 3.75−3.70 (m, 1H), 3.48−3.38 (m, 2H), 3.19−3.12 (m, 1H), 2.22 (s, 3H), 1.38 (s, 9H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 168.7, 168.5, 156.2, 149.05, 149.01, 148.2, 147.7, 132.3, 128.6, 123.8, 123.3, 121.0, 120.9, 112.4, 111.4, 69.8, 65.8, 56.03, 55.97, 51.5, 46.7, 33.5, 28.8 (3C), 21.5. IR (neat) ν_{max} (cm^{-1}): 2962, 2930, 2309, 1753, 1674, 1601, 1545, 1514, 1456, 1261, 1230, 1148, 1028, 926, 810, 644, 451, 401. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{26}H_{33}N_3O_4Na^+$, 474.2363; found, 474.2375.

cis-β-Lactam ***6x***. Prepared according to GP-C using **3x**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 10% yield (10 mg, 0.02 mmol). R_f = 0.33 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 8.40 (d, J = 4.9 Hz, 1H), 8.30 (s, 1H), 7.06 (d, J = 4.9 Hz, 1H), 7.00 (s, 1H), 6.83−6.78 (m, 3H), 5.92 (ddd, J = 17.1, 10.2, 8.7 Hz, 1H), 5.41−5.30 (m, 2H), 3.88−3.84 (m, 7H),

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3.71 (ddd, J = 13.8, 9.3, 5.3 Hz, 1H), 3.46 (dt, J = 13.8, 9.3, 7.3 Hz, 1H), 3.25 (dt, J = 13.8, 9.3, 7.3 Hz, 1H), 3.17 (ddd, J = 13.8, 9.3, 5.3 Hz, 1H), 2.27 (s, 3H), 1.34 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 168.8, 166.5, 158.2, 149.2, 149.0, 148.4, 147.7, 132.1, 128.9, 123.9, 122.0, 121.8, 120.8, 112.2, 111.3, 70.4, 66.5, 56.02, 55.99, 51.7, 46.5, 33.8, 28.9 (3C), 21.5. IR (neat) ν_{max} (cm^{-1}): 2962, 2930, 2309, 1753, 1674, 1601, 1545, 1514, 1456, 1261, 1230, 1148, 1028, 926, 810, 644, 451, 401. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{26}H_{33}N_3O_4Na^+$, 474.2363; found, 474.2375.

trans-β-Lactam **6y**. Prepared according to GP-B using **3y**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 68% yield (60 mg, 0.13 mmol). R_f = 0.46 (50% EtOAc/*c*Hex). ^1H NMR (600 MHz, $CDCl_3$) δ 8.47−8.43 (m, 2H), 7.24 (dd, J = 5.3, 1.7 Hz, 1H), 7.08 (s, 1H), 6.84 (s, 1H), 6.82 (d, J = 7.6 Hz, 2H), 5.27−5.23 (m, 1H), 5.08−4.98 (m, 2H), 4.10 (d, J = 7.1 Hz, 1H), 3.85 (s, 6H), 3.79−3.72 (m, 1H), 3.40 (tt, J = 16.4, 8.1 Hz, 2H), 3.19−3.10 (m, 1H), 1.37 (s, 9H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 168.4, 167.5, 158.2, 149.3, 149.1, 147.9, 146.0, 131.8, 128.2, 123.4, 123.2, 121.6, 120.8, 112.2, 111.5, 69.9, 65.9, 56.00, 55.96, 51.7, 46.8, 33.6, 28.7 (3C). IR (neat) ν_{max} (cm^{-1}): 2964, 2932, 1755, 1674, 1566, 1551, 1514, 1456, 1261, 1231, 1148, 1028, 920, 729, 644, 457, 401. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{25}H_{30}N_3O_4ClNa^+$, 494.1817; found, 494.1827.

cis-β-Lactam **6y**. Prepared according to GP-C using **3y**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 37% yield (35 mg, 0.07 mmol). R_f = 0.42 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 8.46 (d, J = 5.3 Hz, 1H), 7.73 (s, 1H), 7.29−7.24 (m, 1H), 7.21 (d, J = 1.8 Hz, 1H), 6.82−6.76 (m, 3H), 5.89 (ddd, J = 17.1, 10.3, 8.5 Hz, 1H), 5.39 (d, J = 17.1 Hz, 1H), 5.34 (d, J = 10.3 Hz, 1H), 3.98 (d, J = 8.5 Hz, 1H), 3.88−3.83 (m, 6H), 3.75−3.64 (m, 1H), 3.48−3.38 (m, 1H), 3.17 (ttd, J = 16.9, 8.4, 5.3 Hz, 2H), 1.32 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 168.6, 166.0, 159.8, 149.7, 149.1, 147.8, 145.9, 131.6, 128.5, 123.5, 122.2, 122.0, 120.8, 112.0, 111.4, 70.3, 66.2, 56.00, 55.95, 51.91, 46.5, 33.8, 28.8 (3C). IR (neat) ν_{max} (cm^{-1}): 2964, 2932, 1755, 1674, 1566, 1551, 1514, 1456, 1261, 1230, 1148, 1028, 920, 729, 644, 457, 401. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{25}H_{30}N_3O_4ClNa^+$, 494.1817; found, 494.1825.

trans-β-Lactam **6z**. Prepared according to GP-B using **3z**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 15% yield (15 mg, 0.03 mmol). R_f = 0.38 (50% EtOAc/*c*Hex). ^1H NMR (600 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.38 (d, J = 5.2 Hz, 1H), 7.42 (dd, J = 5.2, 1.7 Hz, 1H), 7.31 (d, J = 1.7 Hz, 1H), 6.83 (dd, J = 5.8, 1.8 Hz, 2H), 6.81 (d, J = 8.7 Hz, 1H), 5.31−5.23 (m, 1H), 5.09−5.00 (m, 2H), 4.11 (d, J = 7.4 Hz, 1H), 3.86 (s, 3H), 3.86 (s, 3H), 3.78−3.71 (m, 1H), 3.44 (ddd, J = 13.5, 9.4, 7.5 Hz, 1H), 3.38 (dt, J = 13.5, 9.4, 7.5 Hz, 1H), 3.17 (td, J = 8.8, 4.4 Hz, 1H), 1.38 (s, 9H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 168.4, 167.5, 158.0, 149.2, 149.1, 147.9, 134.7, 131.8, 128.2, 126.4, 126.2, 121.7, 120.8, 112.2, 111.5, 69.9, 66.0, 56.03, 55.98, 51.7, 46.7, 33.6, 28.8 (3C). IR (neat) ν_{max} (cm^{-1}): 2962, 2932, 2339, 1753, 1674, 1553, 1514, 1456, 1387, 1261, 1230, 1148, 1028, 920, 729, 453. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{25}H_{30}N_3O_4BrNa^+$, 538.1312; found, 538.1332.

cis-β-Lactam **6z**. Prepared according to GP-C using **3z**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 56% yield (59 mg, 0.11 mmol). R_f = 0.33 (50% EtOAc/*c*Hex). ^1H NMR (600 MHz, $CDCl_3$) δ 8.37 (d, J = 5.6 Hz, 1H), 7.66 (s, 1H), 7.43 (d, J = 7.1 Hz, 2H), 6.84−6.70 (m, 3H), 5.89 (ddd, J = 17.1, 10.3, 8.5 Hz, 1H), 5.38 (d, J = 17.1 Hz, 1H), 5.34 (d, J = 10.3 Hz, 1H), 3.99 (d, J = 8.5 Hz, 1H), 3.85 (s, 3H), 3.85 (s, 3H), 3.72−3.60 (m, 1H), 3.50−3.38 (m, 1H), 3.20−3.09 (m, 2H), 1.32 (s, 9H). $^{13}C\{^1H\}$ NMR (600 MHz, $CDCl_3$) δ 168.6, 166.0, 159.6, 149.5, 149.1, 147.8, 134.5, 131.6, 128.6, 126.5, 125.0, 122.2, 120.8, 112.1, 111.5, 70.3, 66.1, 56.02, 55.96, 51.9, 46.4, 33.8, 28.8 (3C). IR (neat) ν_{max} (cm^{-1}): 2962, 2932, 2339, 1753, 1674, 1555, 1514, 1456, 1387, 1261, 1230, 1145, 1028, 920, 729, 453. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{25}H_{30}N_3O_4BrNa^+$, 538.1312; found, 538.1331.

trans/cis-β-Lactam **6za**. Prepared according to GP-B using **3za**. Purification of the crude material by silica gel column chromatography (40% EtOAc/*c*Hex) afforded the title compound as an amber oil in 27% *trans* diastereoisomer and 32% *cis* diastereoisomer yield (0.059 g, 0.11 mmol). R_f = 0.35 (50% EtOAc/*c*Hex). Two diastereoisomers were present in NMR (*trans*: *cis* = 1: 2.8) of which the signals of the *cis* diastereoisomer are marked with ■ and *trans* diastereoisomer are marked with ●. ^1H NMR (500 MHz, $CDCl_3$) δ ●■ 9.14 (s, 1H), ■ 8.48 (s, 1H), ● 8.19 (dd, J = 8.3, 2.0 Hz, 1H), ■ 8.14 (dd, J = 8.3, 2.0 Hz, 1H), ● 7.68 (s, 1H), ● 7.26 (d, J = 4.9 Hz, 1H), ■ 7.08 (d, J = 8.3 Hz, 1H), ●■ 6.88−6.73 (m, 3H), ● 5.96−5.83 (m, 1H), ● 5.38 (d, J = 17.1 Hz, 1H), ● 5.35 (d, J = 10.3 Hz, 1H), ■ 5.27−5.19 (m, 1H), ■ 5.02−4.92 (m, 2H), ■ 4.12 (d, J = 6.5 Hz, 1H), ● 3.98 (d, J = 8.5 Hz, 1H), ● 3.96 (s, 3H), ■ 3.95 (s, 3H), ■ 3.87 (s, 3H), ● 3.85 (s, 3H), ■ 3.84 (s, 3H), ● 3.83 (s, 3H), ■ 3.79−3.74 (m, 1H), ● 3.67 (td, J = 15.1, 14.6, 7.0 Hz, 1H), ●■ 3.43 (dq, J = 14.3, 7.3, 6.6 Hz, 1H), ■ 3.37 (dd, J = 8.0, 4.7 Hz, 1H), ●■ 3.21−3.11 (m, ● 2H, ■ 1H), ■ 1.38 (s, 9H), ● 1.32 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ ● 168.5, ■ 168.2, ■ 167.4, ● 166.0, ● 165.14, ■ 165.13, ● 162.2, ■ 160.6, ● 150.0, ■ 149.6, ■ 149.03, ● 149.00, ●■ 147.8, ● 138.5, ■ 138.3, ■ 131.9, ● 131.6, ● 128.5, ■ 128.1, ● 125.3, ■ 125.1, ■ 122.33, ● 122.28, ■ 121.6, ● 121.0, ■ 120.9, ● 120.8, ■ 112.4, ● 112.1, ●■ 111.3, ● 70.7, ■ 70.6, ● 66.1, ■ 66.0, ■ 56.05, ● 56.01, ●■ 55.95, ●■ 52.7, ● 51.9, ■ 51.7, ■ 46.9, ● 46.5, ■ 33.8, ● 33.6, ● 28.8 (3C), ■ 28.7 (3C). IR (neat) ν_{max} (cm^{-1}): 2955, 1751, 1728, 1676, 1514, 1290, 1261, 1236, 1142. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{27}H_{32}N_3NaO_6^+$, 518.2262; found, 518.2257.

trans-β-Lactam **6zb**. Prepared according to GP-B using **3zb**. Purification of the crude material by silica gel column chromatography (40% EtOAc/*c*Hex) afforded the title compound as a brown oil in 41% yield (25 mg, 0.05 mmol). R_f = 0.38 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, J = 8.9 Hz, 2H), 7.21 (d, J = 8.9 Hz, 2H), 6.84 (d, J = 8.1 Hz, 1H), 6.81 (d, J = 1.9 Hz, 1H), 6.77 (dd, J = 8.1, 1.9 Hz, 1H), 5.30 (dt, J = 16.8, 1.2 Hz, 1H), 5.25 (s, 1H), 5.09−5.02 (m, 1H), 4.95 (ddd, J = 16.8, 10.3, 8.3 Hz, 1H), 4.66 (d, J = 8.3 Hz, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.52 (ddd, J = 13.7, 9.1, 7.7 Hz, 1H), 3.44 (dd, J = 9.1, 4.9 Hz, 1H), 3.34−3.23 (m, 1H), 2.98 (ddd, J = 13.7, 9.1, 4.9 Hz, 1H), 1.38 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 168.7, 167.7, 149.2, 148.1, 147.9, 142.8, 130.9, 128.5 (2C), 128.4, 124.1 (2C), 122.3, 120.7, 112.2, 111.4, 71.1, 63.1, 56.1, 56.0, 52.9, 45.7, 33.8, 28.8 (3C). IR (neat) ν_{max} (cm^{-1}): 2966, 2932, 1747, 1676, 1599, 1514, 1454, 1346, 1261, 1230, 1148, 1026, 918, 851, 808, 729, 401. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{26}H_{31}N_3O_6Na^+$, 504.2105; found, 504.2119.

cis-β-Lactam **6zb**. Prepared according to GP-C using **3zb**. Purification of the crude material by silica gel column chromatography (40% EtOAc/*c*Hex) afforded the title compound as a brown oil in 31% yield (41 mg, 0.09 mmol). R_f = 0.40 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, J = 8.9 Hz, 2H), 7.49 (d, J = 8.9 Hz, 2H), 6.71 (d, J = 8.1 Hz, 1H), 6.65−6.57 (m, 2H), 5.89 (ddd, J = 17.2, 10.3, 8.1 Hz, 1H), 5.50−5.44 (m, 2H), 5.39 (d, J = 10.3 Hz, 1H), 4.18 (d, J = 8.1 Hz, 1H), 3.84 (s, 3H), 3.81 (s, 3H), 3.42 (ddd, J = 14.2, 8.1, 6.1 Hz, 1H), 3.33 (dq, J = 14.0, 7.8, 6.8 Hz, 1H), 3.00−2.86 (m, 2H), 1.32 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 168.0, 167.0, 149.0, 148.0, 147.8, 144.0, 130.6, 128.8, 128.3 (2C), 124.1 (2C), 122.3, 120.6, 111.9, 111.3, 69.8, 65.1, 56.01, 55.97, 52.7, 45.2, 33.7, 28.8 (3C). IR (neat) ν_{max} (cm^{-1}): 2966, 2932, 1747, 1676, 1599, 1514, 1454, 1346, 1261, 1230, 1148, 1026, 918, 851, 808, 729, 401. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{26}H_{31}N_3O_6Na^+$, 504.2105; found, 504.2116.

trans-β-Lactam **6zc**. Prepared according to GP-B using **3zc**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 16% yield (12 mg, 0.03 mmol). R_f = 0.24 (100% EtOAc). Two diastereoisomers were present in NMR (*trans*:*cis* = 5:2), of which the signals of the *cis* diastereoisomer are marked with ■ and *trans* diastereoisomer are marked with ●. ^1H NMR (500 MHz, $CDCl_3$) δ

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■ 8.61 (d, J = 6.1 Hz, 2H), ● 8.58 (d, J = 6.0 Hz, 2H), ■ 7.24 (d, J = 6.2 Hz, 2H), ● 6.96 (d, J = 6.1 Hz, 2H), ● 6.83−6.75 (m, 3H), ■ 6.73 (d, J = 8.1 Hz, 1H), ■ 6.66−6.60 (m, 2H), ■ 5.87 (ddd, J = 17.2, 10.2, 8.2 Hz, 1H), ■ 5.47 (s, 1H), ■ 5.44 (d, J = 17.1 Hz, 1H), ■ 5.37 (d, J = 10.3 Hz, 1H), ● 5.32−5.26 (m, 2H), ● 5.07−5.03 (m, 1H), ● 4.97 (ddd, J = 16.9, 10.2, 8.3 Hz, 1H), ● 4.61 (d, J = 8.2 Hz, 1H), ■ 4.13 (d, J = 8.2 Hz, 1H), ● 3.86 (s, 3H), ● 3.85 (s, 3H), ■ 3.82 (s, 3H), ■ 3.82 (s, 3H), ● 3.52 (ddd, J = 13.7, 9.5, 7.4 Hz, 1H), ●■ 3.44−3.32 (m, ● 1H, ■ 2H), ● 3.24 (ddd, J = 13.6, 9.5, 7.4 Hz, 1H), ●■ 3.01−2.93 (m, 1H), ■ 2.92−2.85 (m, 1H), ● 1.37 (s, 9H), ■ 1.31 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ ● 168.7, ■ 168.1, ● 167.5, ■ 166.6, ■ 150.6 (2C), ● 150.5 (2C), ● 149.1, ■ 149.0, ● 148.0, ■ 147.9, ■ 145.9, ● 144.6, ● 130.9, ■ 130.7, ■ 128.9, ● 128.4, ● 122.2 (2C), ●■ 122.1, ■ 122.0 (2C), ● 120.7, ■ 120.6, ● 112.2, ■ 111.9, ● 111.40, ■ 111.38, ● 70.6, ■ 69.2, ■ 64.7, ● 62.8, ● 56.05, ■ 56.01, ● 56.00, ■ 55.96, ● 52.8, ■ 52.6, ● 45.5, ■ 45.1, ● 33.8, ■ 33.7, ■ 28.8 (3C), ● 28.7 (3C). IR (neat) ν_{max} (cm^{-1}): 2964, 2934, 1747, 1672, 1595, 1512, 1456, 1263, 1232, 1148, 1028, 916, 731, 644, 519. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{25}H_{31}N_3O_4Na^+$, 460.2207; found, 460.2215.

cis-β-Lactam ***6zc***. Prepared according to GP-C using **3zc**. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound as a brown oil in 35% yield (37 mg, 0.09 mmol). R_f = 0.12 (100% EtOAc). ^1H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, J = 6.2 Hz, 2H), 7.32−7.14 (m, 2H), 6.73 (d, J = 8.1 Hz, 1H), 6.63 (dd, J = 8.1, 1.8 Hz, 2H), 5.88 (ddd, J = 17.2, 10.2, 8.2 Hz, 1H), 5.53−5.33 (m, 3H), 4.14 (d, J = 8.2 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.36 (d, J = 7.5 Hz, 2H), 2.98 (dd, J = 14.3, 7.5 Hz, 1H), 2.89 (dd, J = 14.3, 7.5 Hz, 1H), 1.32 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 168.1, 166.7, 150.7 (2C), 149.1, 147.9, 145.9, 130.7, 128.9, 122.2, 122.0 (2C), 120.6, 111.9, 111.4, 69.3, 64.8, 56.05, 56.00, 52.6, 45.2, 33.7, 28.8 (3C). IR (neat) ν_{max} (cm^{-1}): 2964, 2934, 1747, 1672, 1595, 1512, 1456, 1263, 1232, 1148, 1028, 916, 731, 644, 519. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{25}H_{31}N_3O_4Na^+$, 460.2207; found, 460.2212.

*trans-N-(tert-Butyl)-1-(3,4-dimethoxyphenethyl)-3-ethyl-4-oxo-2-(pyridin-2-yl)azetidine-2-carboxamide (****7****).* To a stirred solution of **6a** (44 mg, 0.1 mmol, 1 equiv) in EtOAc (2 mL, 0.05 M) was added Pd/C (11 mg; 25%, w/w). The suspension was filled with H_2 and then degassed and backfilled with H_2: the procedure was repeated three times and stirred overnight at room temperature. The crude was filtrated over a Celite pad with EtOAc, and the solvent was removed under vacuum, affording the title compound **7** as a yellow oil in 96% yield (0.044 g, 0.096 mmol). R_f = 0.43 (80% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.55 (d, J = 4.7 Hz, 1H), 7.58 (td, J = 7.8, 1.7 Hz, 1H), 7.23 (dd, J = 7.4, 4.9 Hz, 1H), 7.06 (d, J = 8.0 Hz, 1H), 6.86−6.76 (m, 3H), 3.85 (s, 3H), 3.83 (s, 3H), 3.66 (ddd, J = 17.9, 9.3, 5.6 Hz, 1H), 3.42−3.30 (m, 3H), 3.16 (td, J = 11.1, 9.6, 4.9 Hz, 1H), 1.37 (s, 9H), 1.05 (ddq, J = 28.5, 14.1, 7.3 Hz, 2H), 0.81 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 171.1, 168.7, 156.8, 148.9, 148.2, 147.6, 137.3, 132.2, 122.8, 122.6, 120.9, 112.3, 111.2, 69.6, 63.9, 56.0, 55.9, 51.3, 46.4, 33.7, 28.7 (3C), 19.6, 11.7. IR (neat) ν_{max} (cm^{-1}): 2964, 2933, 1747, 1672, 1514, 1261, 1234, 1155, 1140, 1028, 729, 646, 461, 401. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{25}H_{33}N_3NaO_4^+$, 462.2363; found, 462.2362.

*trans-N-(tert-Butyl)-1-(3,4-dimethoxyphenethyl)-3-(2-hydroxyethyl)-4-oxo-2-(pyridin-2-yl)azetidine-2-carboxamide (****8****).* To a solution of **6a** (44 mg, 0.1 mmol, 1 equiv) in THF (1 mL, 0.1 M) cooled at 0 °C was added a solution of 9-BBN (0.5 M in THF, 0.6 mL, 3 equiv), and the mixture was stirred for 3 h at room temperature. Then, 3 M $KHCO_3$ (150 μL) and 30% H_2O_2 (400 μL) were added to the mixture, which was stirred at room temperature for 1 h. EtOAc (5 mL) and a saturated solution of NH_4Cl (2 mL) were added and the organic layer was washed with H_2O (2 mL) and brine (2 mL) and dried over Na_2SO_4 and the solvent was removed under vacuum. Purification of the crude material by silica gel column chromatography (70% EtOAc/*c*Hex) afforded the title compound **87** as a clear oil in 54% yield (0.032 g, 0.054 mmol). R_f = 0.13 (80% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 8.58 (d, J = 4.1 Hz, 1H), 8.45 (s, 1H), 7.62 (td, J = 7.8, 1.8 Hz, 1H), 7.27−7.23 (m, 1H), 7.09 (d, J = 8.0 Hz, 1H), 6.84−6.80 (m, 3H), 3.86 (s, 3H), 3.85 (s, 3H), 3.70 (ddd, J = 14.4, 10.0, 5.0 Hz, 1H), 3.64−3.50 (m, 4H), 3.30 (ddd, J = 13.4, 9.8, 7.2 Hz, 1H), 3.16 (ddd, J = 14.1, 9.7, 5.1 Hz, 1H), 2.16 (s, 1H), 1.44−1.39 (m, 1H), 1.37 (s, 9H), 1.30−1.21 (m, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 171.2, 168.7, 156.7, 149.1, 148.9, 147.8, 137.9, 132.0, 123.2, 122.7, 121.0, 112.4, 111.4, 69.6, 61.1, 60.1, 56.2, 56.1, 51.7, 46.8, 33.9, 28.8 (3C), 28.4. IR (neat) ν_{max} (cm^{-1}): 3302, 2957, 1744, 1663, 1514, 1431, 1259, 1230, 1157, 1138, 1026. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{25}H_{33}N_3NaO_5^+$, 478.2312; found, 478.2314.

*trans-N-(tert-Butyl)-1-(3,4-dimethoxyphenethyl)-3-((E)-4-methylstyryl)-4-oxo-2-(pyridine-2-yl)azetidine-2-carboxamide (****9****).* A solution of **6a** (44 mg, 0.1 mmol, 1.0 equiv), $Pd(OAc)_2$ (5 mg, 0.02 mmol, 0.2 equiv), $P(OiPr)_3$ (5.5 μL, 0.02 mmol, 0.2 equiv), *p*-iodotoluene (44 mg, 0.2 mmol, 2.0 equiv), and TEA (27.9 μL, 0.25 mmol, 2.5 equiv) in dioxane (0.05 M, 2 mL) was refluxed overnight. The reaction mixture was diluted with DCM (5 mL), washed with 1 M HCl (5 mL) and brine (5 mL), and dried over Na_2SO_4 and the solvent was removed under vacuum. Purification of the crude material by silica gel column chromatography (30% EtOAc/*c*Hex) afforded the title compound **9** as a clear oil in 56% yield (0.014 g, 0.027 mmol). R_f = 0.71 (50% EtOAc/*c*Hex). ^1H NMR (500 MHz, $CDCl_3$) δ 8.85 (s, 1H), 8.55−8.53 (m, 1H), 7.58 (td, J = 7.8, 1.8 Hz, 1H), 7.22−7.18 (m, 1H), 7.09 (d, J = 8.0 Hz, 1H), 6.99 (d, J = 8.0 Hz, 2H), 6.89 (d, J = 8.1 Hz, 2H), 6.87−6.80 (m, 3H), 6.49 (d, J = 15.8 Hz, 1H), 5.27 (dd, J = 15.8, 8.3 Hz, 1H), 4.26 (d, J = 8.3 Hz, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.76 (ddd, J = 14.1, 9.9, 4.8 Hz, 1H), 3.53−3.45 (m, 1H), 3.43−3.35 (m, 1H), 3.21 (ddd, J = 13.9, 9.6, 4.8 Hz, 1H), 2.26 (s, 3H), 1.41 (s, 9H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 168.8, 168.1, 156.6, 149.0, 148.5, 147.7, 137.8, 137.4, 135.5, 133.7, 132.1, 129.2 (2C), 126.3 (2C), 122.8, 122.6, 120.9, 118.8, 112.4, 111.3, 70.5, 65.6, 56.1, 56.0, 51.6, 46.7, 33.7, 28.8 (3C), 21.3. IR (neat) ν_{max} (cm^{-1}): 2930, 1753, 1672, 1514, 1261, 1234, 1157, 1142, 1028, 808, 731, 457, 401. HRMS (ESI) m/z: $[M + Na]^+$ calcd. for $C_{32}H_{37}N_3NaO_4^+$, 550.2676; found, 550.2676.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c00575.

X-ray crystallographic data for *cis*-**6s** (CIF)

Additional optimization data, crystallographic data for *cis*-**6s**, computational data and figures, and ^1H and ^{13}C NMR spectra of all new compounds (PDF)

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Author Contributions

The manuscript was written through contributions of all authors.

Notes

The authors declare no competing financial interest.

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