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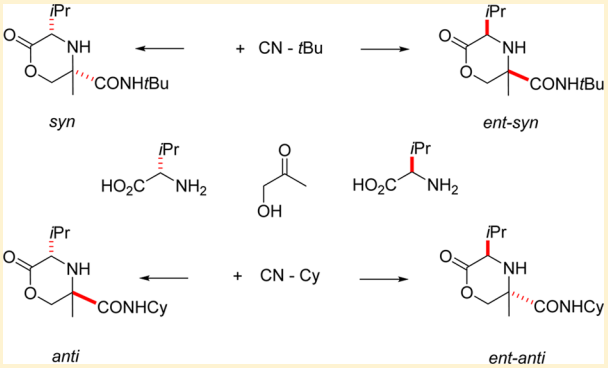
Multicomponent Cascade Reactions of Unprotected Ketoses and Amino Acids – Access to a Defined Configured Quaternary Stereogenic Center

Celin Richter, Minh Nguyen Trung, and Rainer Mahrwald*

Institute of Chemistry, Humboldt University Berlin, Brook-Taylor Str. 2, 12484 Berlin, Germany

Supporting Information

ABSTRACT: A highly stereoselective multicomponent cascade reaction of ketones with unprotected amino acids was developed. This operationally simple methodology was expanded to reactions of unprotected ketohexoses and unprotected amino acids. By the careful choice of amino acid and isonitrile, an optional access to all possible enantiomers is given.



INTRODUCTION

Recently we have demonstrated the utility of unprotected carbohydrates in stereoselective C-C bond formation processes by several operationally simple protocols. In particular these are amine-catalyzed cascade reactions of carbohydrates with 1,3-dicarbonyl or carbonyl compounds.[1] These transformations are characterized by extremely high stereoselectivities. During this investigation we have also elaborated an amine-catalyzed multicomponent reaction of unprotected carbohydrates with amino acids.[2] By application of D- or L-configured amino acids, control over the installation of the configuration at the former anomeric carbon atom can be achieved (Scheme 1).

To demonstrate the power of this transformation, disaccharides (maltose) or dipeptides (aspartame) were reacted under these conditions. By extension of this operationally simple protocol a new methodology for the formation of glycopeptide structures is given (Scheme 2).

The formation of the hemiaminal (**A**) respectively of iminium (**B**) was assumed as the starting reaction of this cascade sequence. The generation of the proposed hemiaminal structure **A** was supported by in-house NMR experiments. When used with 1 equiv proline and 1 equiv ribose structure **A** was formed within 2 h at room temperature. This intermediate **A** is stabilized by an additional equivalent of amine (DBU). Under these conditions we succeeded to detect the hemiaminal structure **A**.[1e]

A subsequent reaction of the isocyanoacetate **2** with iminium **B** yields the corresponding imino ester **D**. A following acyl rearrangement gives rise for the formation of 2,6-diketopiperazine **E**. This diketopiperazine undergoes a nucleophilic attack of the hydroxy groups of the carbohydrate under the reaction conditions. As a result the corresponding lactone **F** was observed (Scheme 3). This consideration was supported by the treatment of isolated diketopiperazine **E** in boiling methanol. After 3 h lactone **F** was detected as the only product. This multicomponent reaction was successfully extended to the application of both aldopentoses and aldohexoses. To explore the scope and limitations of this multicomponent reaction, we considered whether this methodology can be expanded by deployment of ketones in these transformations. In contrast to multicomponent reactions with aldehydes, a relatively small number of reports have been published, potentially due to the lower carbonyl reactivity of ketones.[3] Moreover, to avoid side reactions, ketones were transformed into the corresponding imines in a separate step.[4] Also few multicomponent reactions of unprotected amino acids with aldehydes and isocyanides were reported.[5] Reports on multicomponent reactions of ketones and unprotected amino acids are rare.[6] Multicomponent reactions of unprotected amino acids with unprotected ketoses and isonitriles have not been reported so far. For reviews in this field see ref 7.

RESULTS AND DISCUSSION

In initial experiments we tested the utility of acetone and methyl ethyl ketone in these multicomponent transformations. No reactions were observed when used with simple and unsubstituted ketones or with protected hydroxyacetones (methoxyacetone, dimethoxyacetone). In contrast, hydroxy ketones proved to be useful substrates in these reactions. To this end, we reacted hydroxyacetone with proline and *tert*-butyl isocyanide in boiling methanol in the presence of catalytic amounts of

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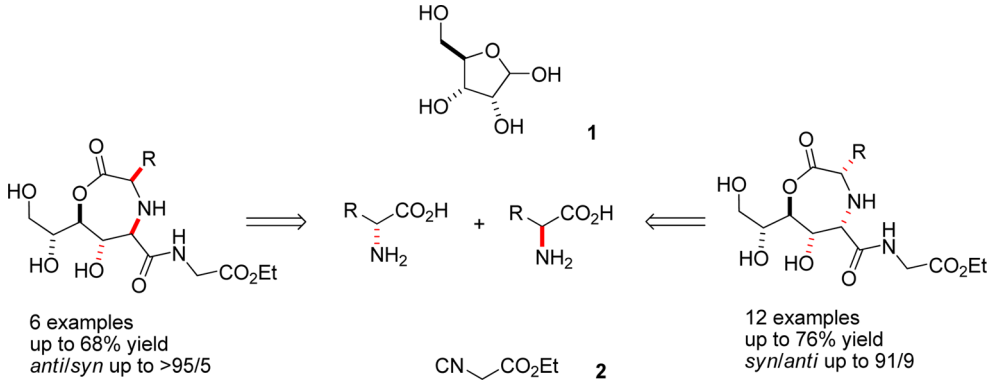
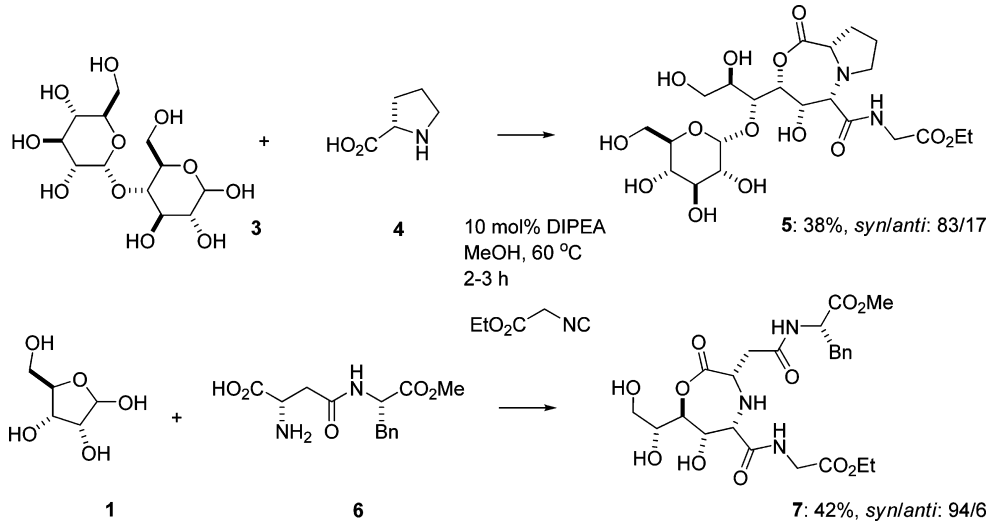
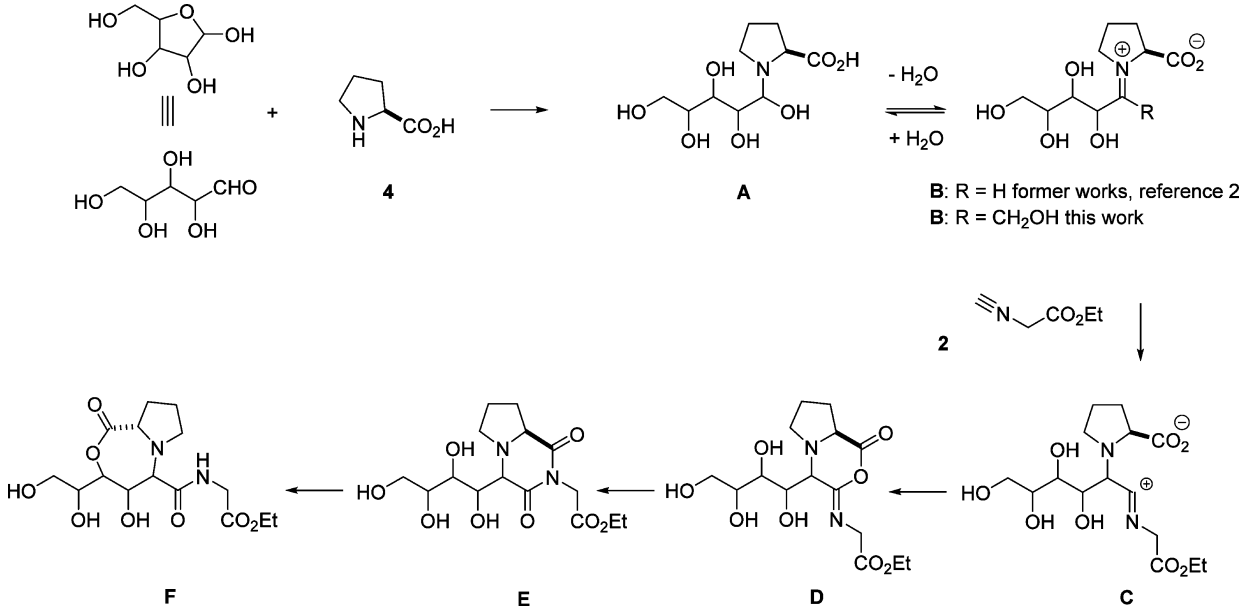
Scheme 1. Multicomponent Reactions of Amino Acids and Carbohydrates



Scheme 2. Multicomponent Reactions with Maltose or Aspartame with Ethyl Isocyanoacetate



Scheme 3. Proposed Reaction Mechanism



diisopropyl ethyl amine (10 mol %). Under these reaction conditions, which were optimized for reactions of carbohydrates (aldoses),[2] a mixture of products was observed in low yields. A subsequent intensive optimization revealed that the highest yields were obtained by deploying trifluoroethanol without any catalyst at room temperature (trifluoroethanol = TFE).[8]

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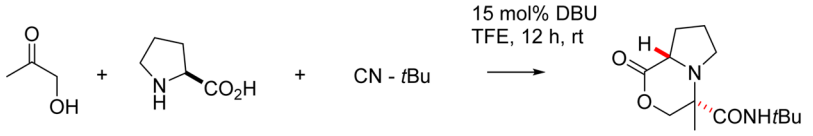
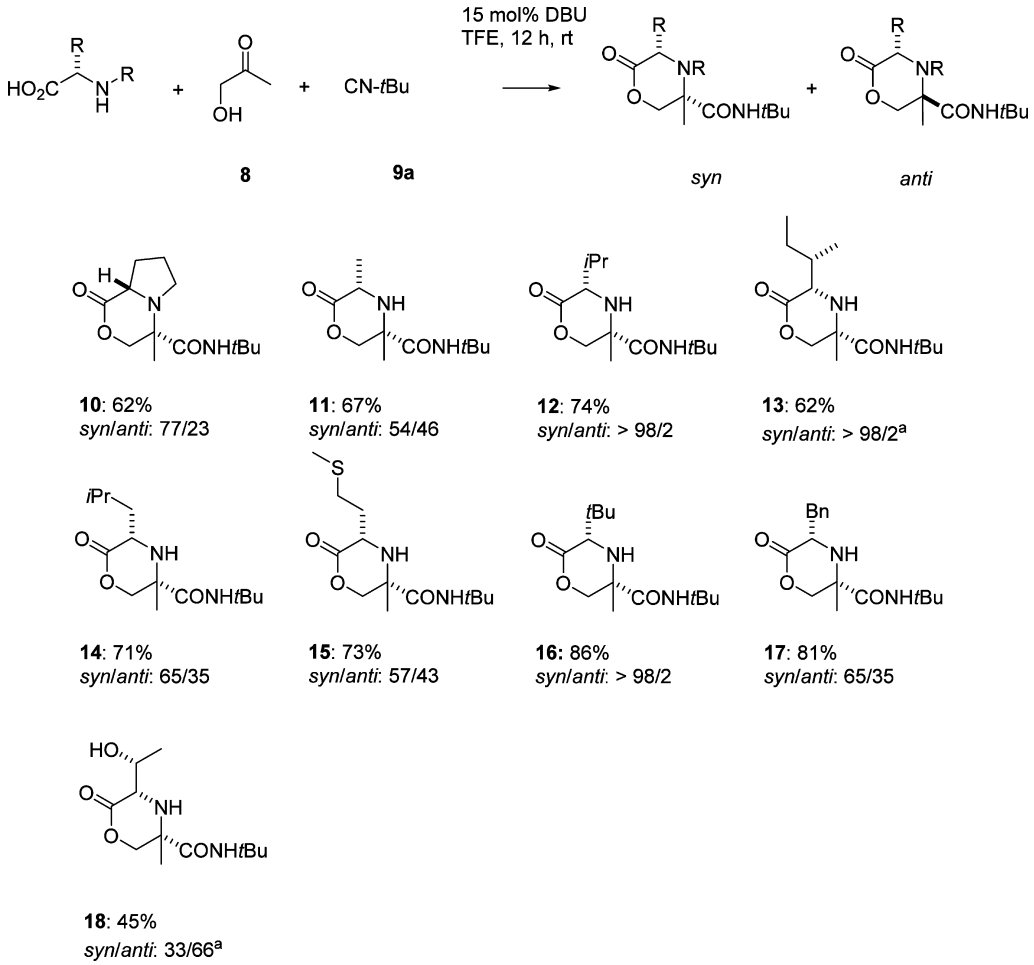
Scheme 4. Multicomponent Reactions of Hydroxyacetone with L-Proline and *tert*-Butyl Isonitrile



8 **4** **9a** **10**: 62 %, *syn*/*anti*: 77/23

Scheme 5. Multicomponent Reactions of Hydroxyacetone with L-Amino Acids[a]



8 **9a**

10: 62%
syn/*anti*: 77/23

11: 67%
syn/*anti*: 54/46

12: 74%
syn/*anti*: > 98/2

13: 62%
syn/*anti*: > 98/2[a]

14: 71%
syn/*anti*: 65/35

15: 73%
syn/*anti*: 57/43

16: 86%
syn/*anti*: > 98/2

17: 81%
syn/*anti*: 65/35

18: 45%
syn/*anti*: 33/66[a]

[a]Ratio of stereoisomers were analyzed by ^{1}H NMR experiments. Due to the second stereogenic center of threonine and isoleucine a divergent description has been used. The configurations of products were determined by NMR-experiments and X-ray structure analysis, see Supporting Information.

Additional catalytic amounts of bases downsize reaction times. Moreover, when used with *tert*-butyl isocyanide, highest yields and diastereoselectivities were obtained. Substituted 2-oxo-morpholine **10** was obtained in good yields (62%) in a diastereomeric mixture of 77/23 (*syn*/*anti*) (Scheme 4).

With these conditions in hand we tested further proteinogenic L-amino acids in reactions with hydroxyacetone and *tert*-butyl isonitrile. The corresponding substituted 2-oxo-morpholines **10**−**18** were isolated in good to high yields (Scheme 5). The diastereoselectivities obtained clearly indicate that the extent of stereoselectivity is dictated by the nature of amino acids deployed. A preference for the formation of *syn*-configured products was detected. Almost no selectivity was detected when used with L-alanine (*syn*/*anti*: 54/46). Whereas, only a single stereoisomer was detected by deployment of L-valine, L-isoleucine, or L-*tert*-leucine, all of which are branched-chain amino acids at the β-carbon atom. In contrast, only a slight diastereoselectivity is observed when used with γ-branched amino acids (leucine, *syn*/*anti*: 65/35). By application of L-threonine the stereoselectivity changed to favor the *anti*-configured product (*anti*/*syn*: 66/33).

No reactions were observed when deploying acidic or basic amino acids. This holds true even when these amino acids were neutralized by additional equivalents of acids or bases.

A similar scenario is observed when used with unnatural D-configured amino acids. Only a single stereoisomer is detected in reactions with D-valine, whereas no stereoselectivity was observed in reactions with D-alanine or D-methionine (Scheme 6). The products were isolated with good to high yields.

In a further series we tested the utility of several different isonitriles in these multicomponent reactions. For this purpose we reacted cyclohexyl isocyanide **9b**, tosylmethyl isocyanide **9c**, and

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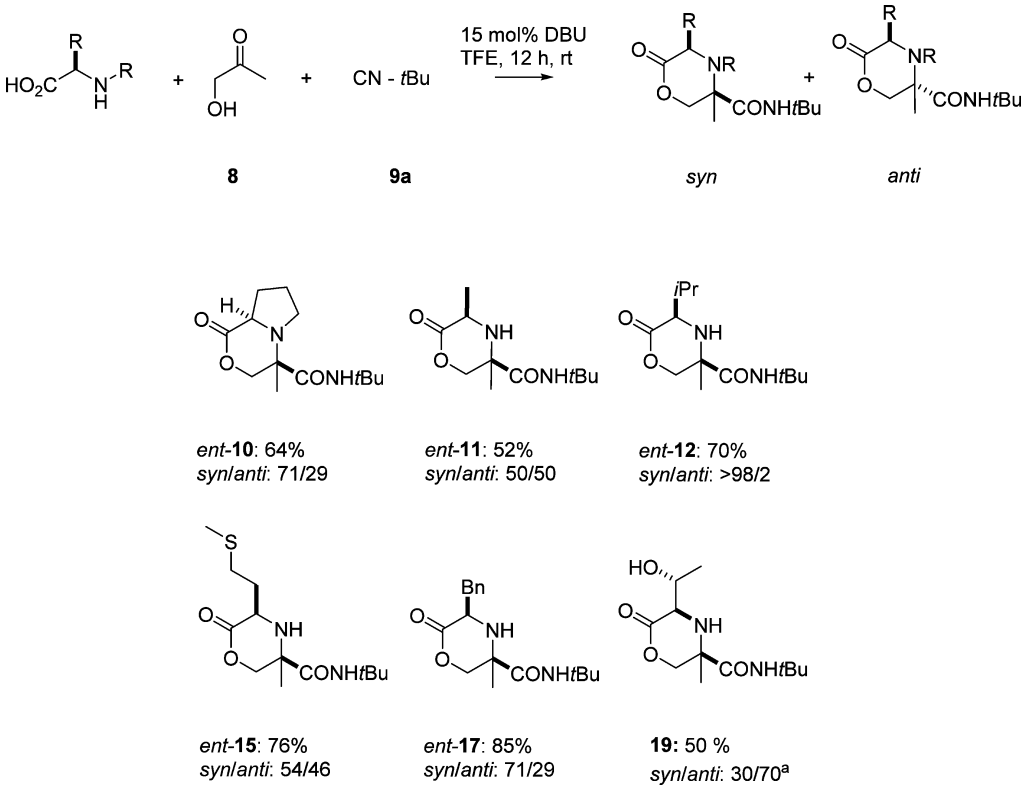
Scheme 6. Multicomponent Reactions of Hydroxyacetone with D-Amino Acids[a]



[a]Due to the second stereogenic center of threonine, a differing configurative description has been used.

ethyl isocyanoacetate **2** with D- and L-configured valine and hydroxyacetone in these multicomponent reactions. Under the optimized conditions the *anti*-configured 2-oxo-morpholines were detected with high degrees of stereoselectivity and isolated as a single stereoisomer. This holds true for both series, L- and D-configured amino acids. Good yields were obtained by the deployment of cyclohexyl isocyanide and ethyl isocyanoacetate, whereas the products of reactions with tosylmethyl isocyanide were isolated only with lower yields.

In the experiments with ethyl isocyanoacetate and valine we observed the formation of 2,6-diketopiperazines **23** and *ent*-**23**, as this was described for multicomponent reactions with unprotected aldoses. They were obtained as a mixture with the corresponding 2-oxo-morpholines **22** and *ent*-**22**. The highest yields of these diketopiperazines were detected after 12 h at room temperature, whereas after 72 h the 2-oxo-morpholines **22** and *ent*-**22** were observed as the only products. This observation identifies 2,6-diketopiperazines **23** and *ent*-**23** as intermediates in these multicomponent reactions (compare with structure **E** in Scheme 3). Again, the initial reaction step—the attack of isonitrile to the intermediate imine—determines the installation of configuration. As a result of that products **22** and **23** as well as *ent*-**22** and *ent*-**23** are configuratively homogeneous.

The configurative outcomes of these experiments contrast strongly with those obtained by reactions with *tert*-butyl isocyanide (compare results of Scheme 7 with those of Schemes 5 and 6). The steric bulkiness of the *tert*-butyl group drives the amide substituent into the relative *syn*-configuration related to the configuration of the amino acids. This implies the more favored axial position of the *tert*-butyl amide at the quaternary stereogenic center, when used with L-valine. As a result, the *S*-configured quaternary stereogenic center is obtained. The *R*-configuration is detected by application of D-valine. In contrast, by deployment of the less bulky cyclohexyl, tosylmethyl, and acetate isocyanides, the corresponding amides occupy the equatorial position at the quaternary stereogenic center, which represents the *anti*-configuration related to the configuration of amino acids (*R*-configuration with L-valine and *S*-configuration with D-valine) (Scheme 8). Based on the extremely high stereoselectivity, this stereochemical behavior acts like a switch by application of D- or L-valine.

With these results in hand we investigated the scope of further ketone substrates in this transformation. To this end, we reacted in a next series dihydroxyacetone with amino acids and *tert*-butyl isocyanide **9a** under elaborated standard conditions. The expected 2-oxo-morpholines **26**−**34** were isolated with good yields. But in contrast to reactions with hydroxyacetone, these reactions proceed without stereoselectivity. *Syn*- and *anti*-configured products were isolated with a diastereomeric ratio of about 1/1 to 7/3 (compare results of Schemes 5 and 6 with those described in Scheme 9).

Similar results were obtained by reactions with D-configured amino acids. The corresponding 2-oxo-morpholines were obtained with good yields but without any stereoselectivity (*syn*/*anti*: 1/1 → 3/7, Scheme 10).

In a further series several different isocyanides were tested in multicomponent reactions of dihydroxyacetone with D- and L-valine. Again, only slight stereoselectivities were detected (compare results of Scheme 7 with those described in Scheme 11).

The results obtained with dihydroxyacetone support the mechanism depicted in Scheme 3 and the discussion on the diastereoselectivity observed in reactions with hydroxyacetone (Schemes 5−7). The initial *Re*- or *Si*-side attack of the isocyanide to imine **B** dictates the diastereoselectivity detected in these

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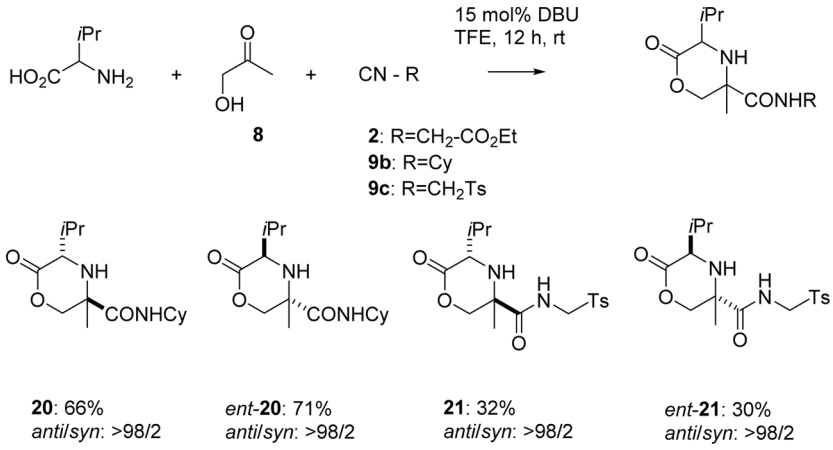
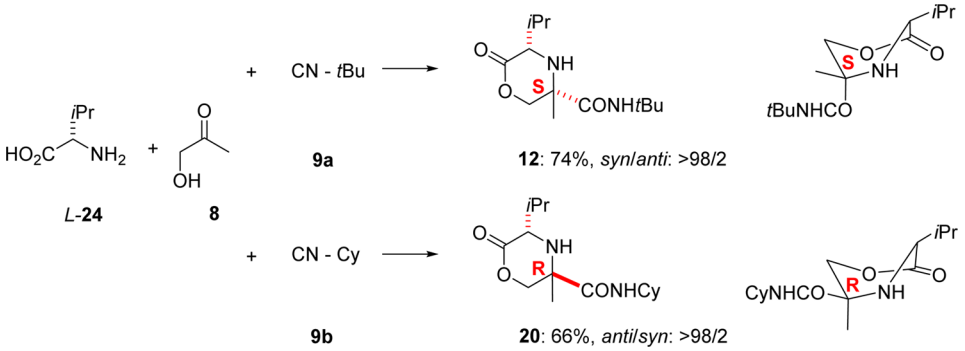
Scheme 7. Multicomponent Reactions of L- or D-Valine and Hydroxyacetone with Different Isonitriles[a]



[a] *anti*/*syn*: > 98/2.

Scheme 8. Stereochemical Results of Multicomponent Reactions of L-Valine and Hydroxyacetone with *tert*-Butyl or Cyclohexyl Isocyanide



reactions. A stereogenic center is not generated in this first step by deployment of dihydroxyacetone. Thus, the observed stereoselectivity resulted only from the subsequent more or less selective cyclization process (formation of intermediate **D** in Scheme 3).

To prove these considerations, we reacted L-erythrulose **39** with L-valine and *tert*-butyl isocyanide **10** in these multicomponent reactions. A change of reaction conditions was necessary for the execution of this reaction. No reactions were observed with trifluoroethanol at room temperature. To this end, we carried out this reaction in boiling methanol and catalytic amounts of trifluoroethanol and DBU. After 16 h a mixture of optically pure 2-oxo-morpholines **40** and **41** alongside the seven-membered lactone **42** was isolated with an overall yield of 62%. These reaction products are homogeneous in terms of the configuration at the quaternary stereogenic center (*R*-configuration, Scheme 12). This result supports a stereochemically homogeneous *Si*-side attack of the *tert*-butyl isocyanide **9a** to the imine-structure of L-erythrulose. Subsequent lactonizations of all three hydroxy groups of erythrulose yield two 2-oxo-morpholines **40** and **41** and lactone **42**. The configuration at the quaternary stereogenic center was not influenced during these maneuvers. Only *R*-configured products were detected, when used with L-valine.[9] By reactions of D-configured valine with L-erythrulose entirely different results were obtained. In contrast to the use of L-valine a mixture of *syn*- and *anti*-configured 2-oxo-morpholines **43** was detected. Moreover, these two diastereoisomers were isolated in low yields (38%). These results indicate a significant matched/mismatched situation: the configuration of L-erythrulose matched that of L-valine. A mismatched

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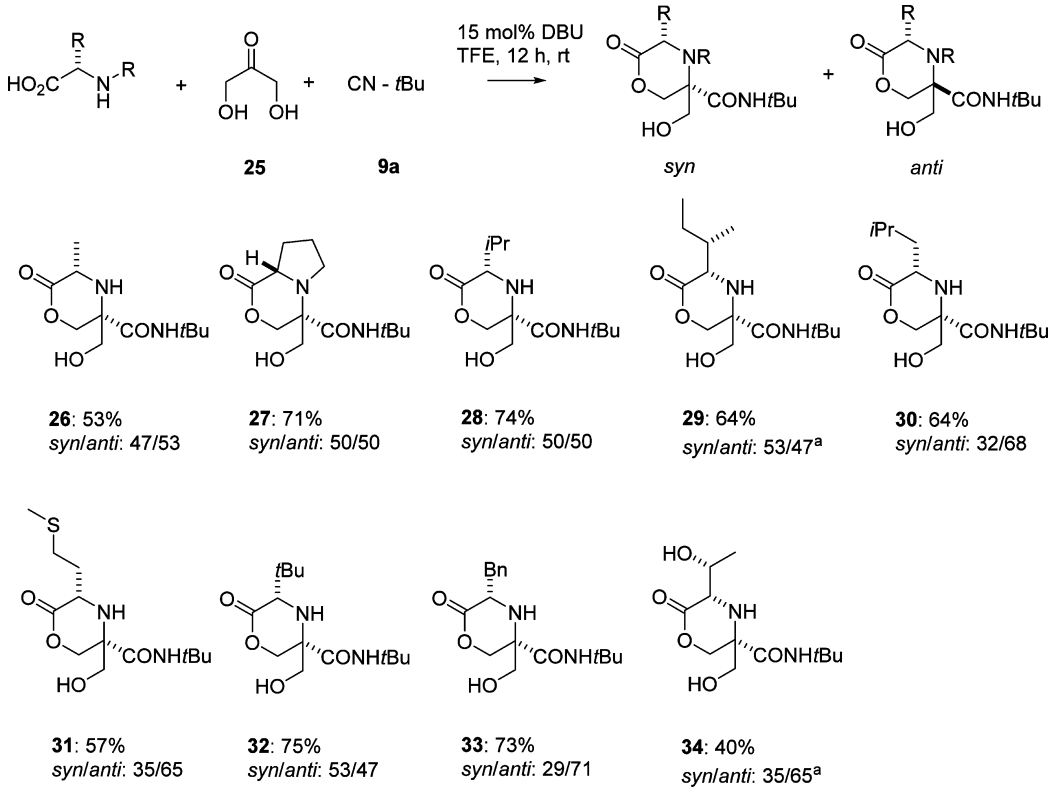
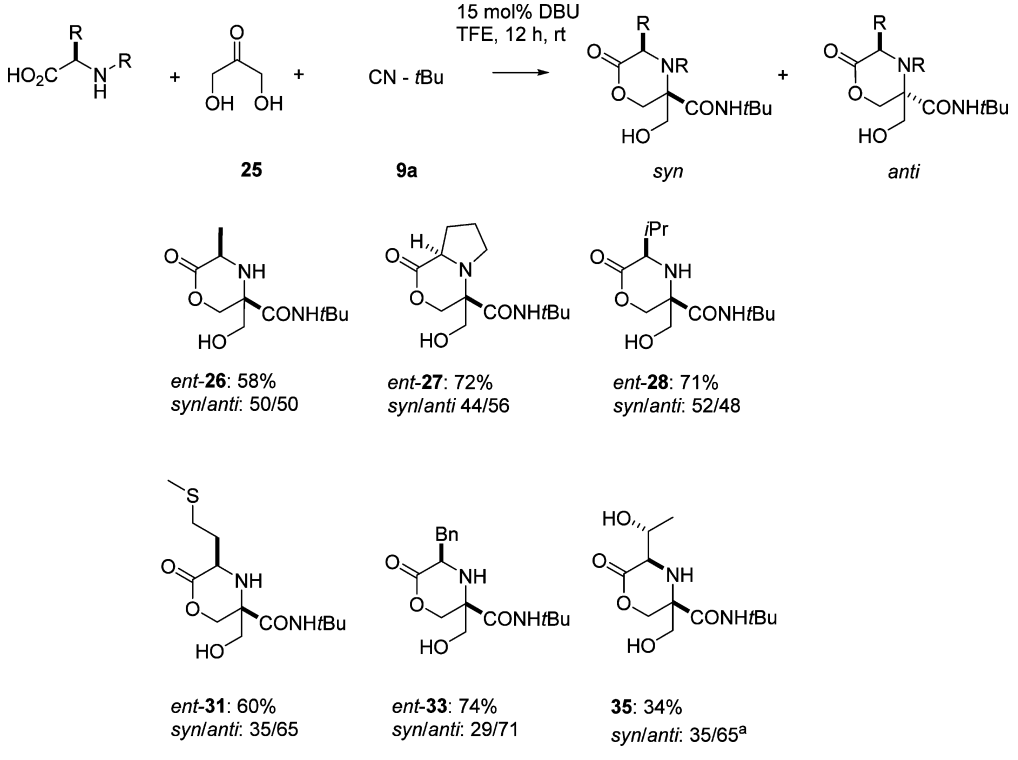
Scheme 9. Multicomponent Reactions of Dihydroxyacetone and *tert*-Butyl Isocyanide with L-Amino Acids[a]



[a]Due to the second stereogenic center of threonine and isoleucine, a divergent description has been used.

Scheme 10. Reactions of D-Configured Amino Acids with Dihydroxyacetone and *tert*-Butyl Isocyanide[a]



[a]Due to the second stereogenic center of threonine, a divergent description has been used.

case is observed when used with L-erythrulose and D-valine (Scheme 12).

To expand these results, unprotected ketoses were reacted with D- and L-valine and *tert*-butyl isocyanide **9a** (Scheme 13).

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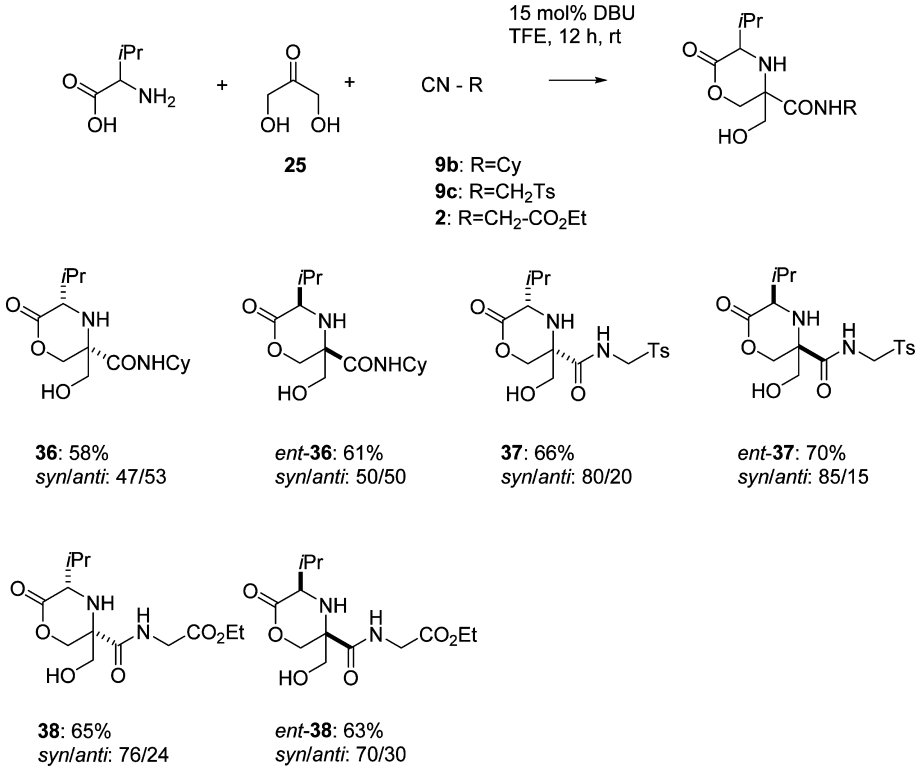
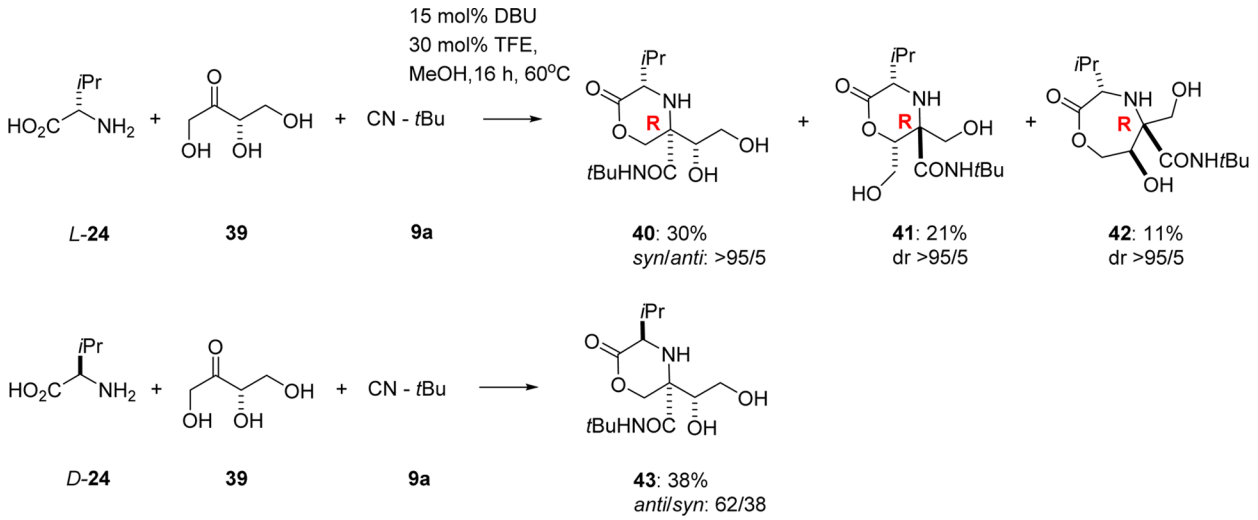
Scheme 11. Multicomponent Reactions of L- or D-Valine and Dihydroxyacetone with Different Isonitriles



Scheme 12. Multicomponent Reactions of D- or L-Valine and L-Erythrulose with *tert*-Butyl Isocyanide



To this end, D-fructose **44**, L-sorbose **45**, and D-tagatose **46** were tested as substrates under the same conditions as described for L-erythrulose **39**.

Different results with regard to yields and stereoselectivities were observed by reactions with ketohexoses. In general, by deployment of unnatural D-configured valine a mismatched case with regard to yields is detected. Roughly, only 60% of the yields of the L-valine series were observed by deployment of D-valine.

By reactions of D-tagatose only a single stereoisomer was detected in both series, in reactions with D- or L-valine. Intermediate **G** seems to be the favored one by evaluation of all possible conformers of imines of L-valine and D-tagatose. A clear *Si*-side attack without any steric hindrance gives rise to the formation of the *syn*-configured product **51** (*syn*/*anti* > 95/5, Scheme 14). In contrast, the bulkiness of D-configured valine (R = valine) prevents an unhindered attack of the isonitrile to imine **G** and drives the imine into the intermediate **H**. An unrestricted *Re*-side attack of the isonitrile to the imine **H** provides *syn*-configured product **52**.

In contrast to reactions with tagatose, the C-4 substituent of D-fructose occupies an axial position in the corresponding conformer **I**. To avoid this unfavored conformation, the conformer **I** switches into the conformer **K** within an equilibrium (Scheme 15). The subsequent *Re*-side attack is then influenced by the steric bulkiness of valine (R = valine). As a result of these different hindrances a mixture of *syn*- and *anti*-configured products was obtained (**47**: *syn*/*anti*: 45/55). These considerations were supported by the following reactions with D-configured

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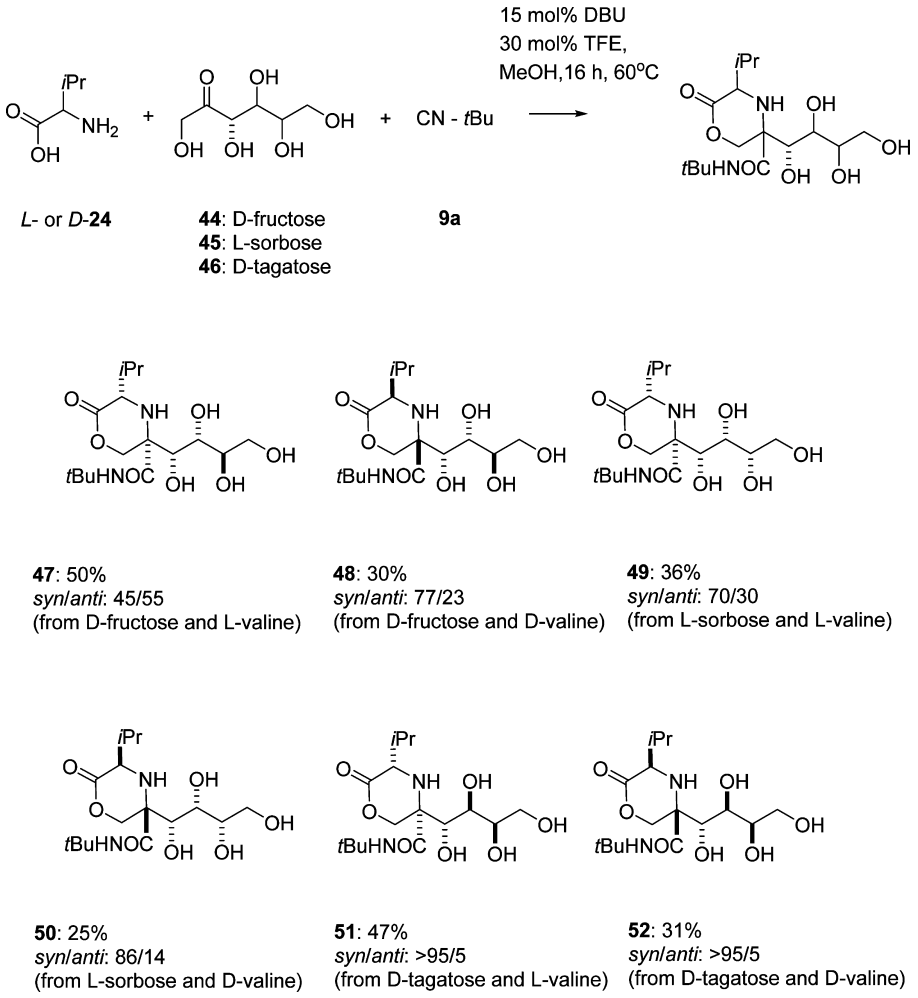
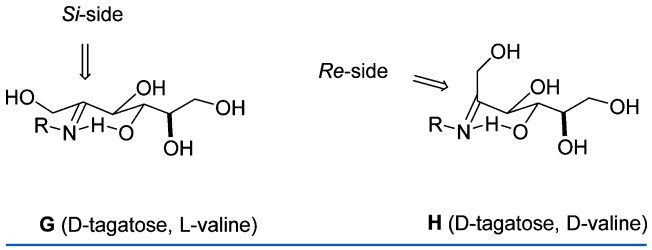
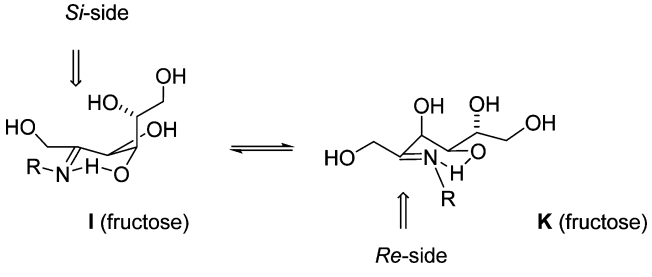
Scheme 13. Multicomponent Reactions of Unprotected Ketoses with D- or L-Valine and *tert*-Butyl Isocyanide



Scheme 14. Stereochemical Outcome of Multicomponent Reactions of D-Tagatose with L- or D-Valine



Scheme 15. Stereochemical Course of Multicomponent Reactions of D-Fructose with L- or D-Valine (R = Valine)



valine. In these experiments an increase of stereoselectivity was noticed, indicating the absence of steric hindrance of L-configured valine (fructose = **47**: 45/55 → **48**: 77/23; sorbose = **49**: 70/30 → **50**: 86/14). For a comprehensive analysis of all possible conformers see Supporting Information.[10]

To demonstrate the usefulness of this reaction, we reacted unprotected and unactivated isomaltulose **53** (6-*O*-(α-D-glucopyranosyl)-D-fructose) with D- and L-valine and *tert*-butyl isocyanide. The stereochemical outcome of this reaction is dictated by the configuration of the fructose unit of isomaltulose. Thus, similar results and tendencies were detected as in the fructose-series (compare yields and stereoselectivities of Scheme 13 with those of Scheme 16).

CONCLUSION

We have demonstrated an operationally simple methodology for the application of ketones and unprotected amino acids in multicomponent reactions. The elaborated conditions were successfully extended to the application of unprotected ketohexoses. Matched/mismatched situations were detected. The stereochemical course of these reactions was analyzed, and a rough rule for the prediction of installation of configuration is given.

EXPERIMENTAL SECTION

General Methods. ^{1}H NMR, ^{13}C NMR, DEPT, and correlation experiments H,H-COSY, HSQC, NOESY and JRES were carried out at 600, 500, and 125 MHz. The residual protonated solvent was used as the internal standard: ^{1}H NMR: 7.26 ppm for $CDCl_3$; ^{13}C NMR: 77.0 ppm for $CDCl_3$; ^{1}H NMR: 3.31 ppm for MeOD; ^{13}C NMR: 49.0 ppm for

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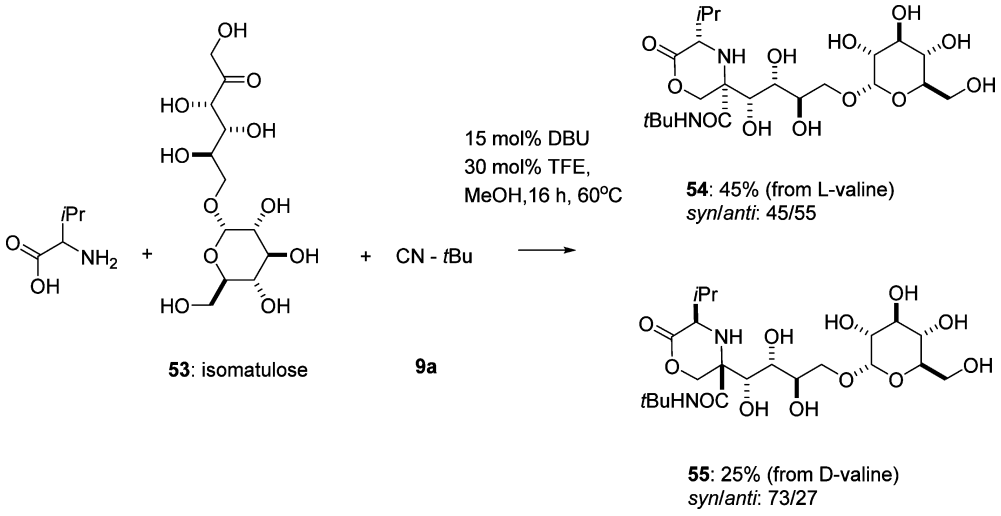
Scheme 16. Multicomponent Reactions of Isomaltulose with D- or L-Valine and *tert*-Butyl Isocyanide



MeOD; ^{1}H NMR: 2.05 ppm for acetone-d_6; ^{13}C NMR: 206.3/29.8 ppm for acetone-d_6. Chemical shifts are given in ppm, coupling constants in Hz. High-resolution mass spectroscopy was performed out on a LTQ-FT-ICR machine (ESI-MS). Purification of products was accomplished by flash chromatography (particle size 0.04−0.063 mm). Yields were determined after column chromatography. The solvent mixtures of CH_2Cl_2 (DCM) and methanol in ratio 80/20 → 95/5 and hexane/acetone 7/3 → 1/1 and hexane/ethyl acetate 6/4 → 4/6 were used as eluent (hexane/acetone or hexane/ethyl acetate for compounds **10**−**23**; DCM/MeOH 95/5 for compounds **24**−**43**; 90/10 for compounds **47**−**52**; 8/2 for compounds **54**−**55**). Development was performed with cer(IV) sulfate/phosphormolybdic acid.

Procedure A. In a 10 mL round-bottom flask, 1.0 mmol ketone and 0.7 mmol amino acid were suspended in 3.0 mL trifluoroethanol. 0.7 mmol of isonitril and 0.1 mmol DBU were added, and the mixture was stirred at room temperature overnight. After removal of volatile compounds, the residue was directly purified by column chromatography.

Procedure B. In a 10 mL round-bottom flask, 1.0 mmol ketose and 0.7 mmol amino acid were suspended in 5.0 mL MeOH. 0.2 mmol of trifluoroethanol, 0.7 mmol of isonitril, and 0.1 mmol DBU were added, and the mixture heated under reflux for 3 h (L-erythrulose) or 24 h (ketohexoses). After removal of volatile compounds, the residue was directly purified by column chromatography.

Representative Synthesis for Compounds. *(4S,8S)-N-(tert-Butyl)-4-methyl-1-oxohexahydro-1H-pyrrolo[2,1][1,4]oxazine-4-carboxamide (syn-**10**).* Inseparable mixture (*syn*/*anti*: 77/23). Overall yield: 109.7 mg; 62%. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 7.23 (s, 1H), 4.34 (d, J = 11.8 Hz, 1H), 4.10 (d, J = 11.8 Hz, 1H,), 3.71 (t, J = 7.8 Hz), 2.82−2.76 (m, 1H), 2.65 (dd, J = 16.1, 7.8 Hz), 1.97−1.91 (m, 2H), 1.83−1.70 (m, 2H), 1.26 (s, 3H), 1.23 (s, 9H). ^{13}C NMR (126 MHz, DMSO-d_6): δ 172.9, 172.0, 72.1, 59.0, 56.3, 49.9, 45.8, 28.3, 25.0, 22.3, 16.6. HRMS (ESI-MS) m/z: [M + H]$^+$, calcd for $C_{13}H_{23}O_3N_2$, 255.1703; found, 255.1701; [M + Na]$^+$, $C_{13}H_{22}O_3N_2Na$, 277.1523; found: 277.1520.

*(4R,8S)-N-(tert-Butyl)-4-methyl-1-oxohexahydro-1H-pyrrolo[2,1]-[1,4]oxazine-4-carboxamide (anti-**10**).* ^{1}H NMR (500 MHz, DMSO) δ 7.43 (s, 1H), 4.46 (d, J = 11.1 Hz, 1H), 4.25 (d, J = 11.1 Hz, 1H), 3.96 (t, J = 7.9 Hz, 1H), 2.92 (t, J = 7.3 Hz, 1H), 2.73−2.64 (m, 1H), 2.18 (dd, J = 19.1, 7.4 Hz, 1H), 1.94−1.78 (m, 2H), 1.78−1.65 (m, 1H), 1.26 (s, 9H), 1.17 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 172.0, 170.7, 68.9, 60.2, 56.9, 50.0, 47.2, 28.9, 28.2, 24.1, 18.8. HRMS calcd for $C_{13}H_{23}O_3N_2$ [M + H]$^+$: 255.1703 found: 255.1701; $C_{13}H_{22}O_3N_2Na$ [M + Na]$^+$: 277.1523 found: 277.1520.

*(4R,8R)-N-(tert-Butyl)-4-methyl-1-oxohexahydro-1H-pyrrolo[2,1]-[1,4]oxazine-4-carboxamide (syn-ent-**10**).* Yield: 96.0 mg (20% *trans*-product); 45%. ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.23 (s, 1H), 4.34 (d, J = 11.8 Hz, 1H), 4.10 (d, J = 11.8 Hz, 1H,), 3.71 (t, J = 7.8 Hz), 2.82−2.76 (m, 1H), 2.65 (dd, J = 16.1, 7.8 Hz), 1.97−1.91 (m, 2H), 1.83−1.70 (m, 2H), 1.26 (s, 3H), 1.23 (s, 9H). ^{13}C NMR (126 MHz, DMSO-d_6): δ 172.9, 172.0, 72.1, 59.0, 56.3, 49.9, 45.8, 28.3, 25.0, 22.3, 16.6. HRMS calcd for $C_{13}H_{23}O_3N_2$ [M + H]$^+$: 255.1703 found: 255.1701; $C_{13}H_{22}O_3N_2Na$ [M + Na]$^+$: 277.1523 found: 277.1520.

*(4S,8R)-N-(tert-Butyl)-4-methyl-1-oxohexahydro-1H-pyrrolo[2,1]-[1,4]oxazine-4-carboxamide (anti-ent-**10**).* Yield: 36.8 mg (10% *cis*-product); 19%. ^{1}H NMR (500 MHz, DMSO) δ 7.43 (s, 1H), 4.46 (d, J = 11.1 Hz, 1H), 4.25 (d, J = 11.1 Hz, 1H), 3.96 (t, J = 7.9 Hz, 1H), 2.92 (t, J = 7.3 Hz, 1H), 2.73−2.64 (m, 1H), 2.18 (dd, J = 19.1, 7.4 Hz, 1H), 1.94−1.78 (m, 2H), 1.78−1.65 (m, 1H), 1.26 (s, 9H), 1.17 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 172.0, 170.7, 68.9, 60.2, 56.9, 50.0, 47.2, 28.9, 28.2, 24.1, 18.8. HRMS calcd for $C_{13}H_{23}O_3N_2$ [M + H]$^+$: 255.1703 found: 255.1701; $C_{13}H_{22}O_3N_2Na$ [M + Na]$^+$: 277.1523 found: 277.1520.

*(3S,5S)-N-(tert-Butyl)-3,5-dimethyl-6-oxomorpholine-3-carboxamide (syn-**11**).* Yield: 56.7 mg; 36%;^{1}H NMR (500 MHz, DMSO) δ 7.81 (s, 1H), 4.45 (d, J = 11.0 Hz, 1H), 4.22 (d, J = 11.0 Hz, 1H), 3.86 (p, J = 6.4 Hz, 1H), 3.42 (d, J = 6.9 Hz, 1H), 1.21 (s, 9H), 1.15 (s, 3H), 1.15 (d, J = 6.4 Hz, 6H). ^{13}C NMR (126 MHz, DMSO) δ 173.2, 173.0, 71.6, 57.6, 49.8, 47.4, 28.2, 21.3, 17.6. $[\alpha]_D^{25}$ = −67 (c = 0.7, methanol). HRMS (ESI) calcd for $C_{11}H_{21}O_3N_2$ [M + H]$^+$: 229.1547, found: 229.1545 $C_{11}H_{20}O_3N_2Na$ [M + Na]$^+$: 251.1366, found: 251.1363.

*(3R,5S)-N-(tert-Butyl)-3,5-dimethyl-6-oxomorpholine-3-carboxamide (anti-**11**).* Yield: 49.4 mg; 31%. ^{1}H NMR (500 MHz, DMSO) δ 7.68 (s, 1H), 4.37 (d, J = 11.5 Hz, 1H), 4.07 (d, J = 11.5 Hz, 1H), 3.49 (dq, J = 11.1, 6.7 Hz, 1H), 3.09 (d, J = 11.0 Hz, 1H), 1.27 (s, 9H), 1.20 (d, J = 6.8 Hz, 3H), 1.18 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 173.0, 172.7, 71.0, 57.1, 49.8, 48.2, 28.3, 23.3, 16.2. $[\alpha]_D^{25}$ = −66 (c = 1, methanol). HRMS (ESI) calcd for $C_{11}H_{21}O_3N_2$ [M + H]$^+$: 229.1547, found: 229.1545 $C_{11}H_{20}O_3N_2Na$ [M + Na]$^+$: 251.1366, found: 251.1363.

*(3R,5R)-N-(tert-Butyl)-3,5-dimethyl-6-oxomorpholine-3-carboxamide (syn-ent-**11**).* Yield: 40.4 mg; 26%. ^{1}H NMR (500 MHz, DMSO) δ 7.81 (s, 1H), 4.45 (d, J = 11.0 Hz, 1H), 4.22 (d, J = 11.0 Hz, 1H), 3.86 (p, J = 6.4 Hz, 1H), 3.42 (d, J = 6.9 Hz, 1H), 1.21 (s, 9H), 1.15 (s, 3H), 1.15 (d, J = 6.4 Hz, 6H). ^{13}C NMR (126 MHz, DMSO) δ 173.2, 173.0, 71.6, 57.6, 49.8, 47.4, 28.2, 21.3, 17.6. $[\alpha]_D^{25}$ = +70 (c = 0.9, methanol). HRMS (ESI) calcd for $C_{11}H_{21}O_3N_2$ [M + H]$^+$: 229.1547, found: 229.1545 $C_{11}H_{20}O_3N_2Na$ [M + Na]$^+$: 251.1366, found: 251.1363.

*(3S,5R)-N-(tert-Butyl)-3,5-dimethyl-6-oxomorpholine-3-carboxamide (anti-ent-**11**).* Yield: 40.9 mg; 26%. ^{1}H NMR (500 MHz, DMSO) δ 7.68 (s, 1H), 4.37 (d, J = 11.5 Hz, 1H), 4.07 (d, J = 11.5 Hz, 1H), 3.49 (dq, J = 11.1, 6.7 Hz, 1H), 3.09 (d, J = 11.0 Hz, 1H), 1.27 (s, 9H), 1.20 (d, J = 6.8 Hz, 3H), 1.18 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 173.0, 172.7, 71.0, 57.1, 49.8, 48.2, 28.3, 23.3, 16.2. $[\alpha]_D^{25}$ = +57 (c = 1, methanol). HRMS (ESI) calcd for $C_{11}H_{21}O_3N_2$ [M + H]$^+$: 229.1547,

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found: 229.1545 $C_{11}H_{20}O_3N_2Na$ $[M + Na]^+$: 251.1366, found: 251.1363.

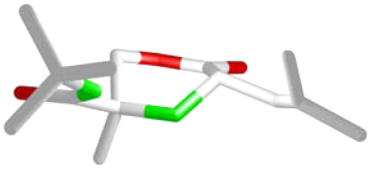
*(3S,5S)-N-(tert-Butyl)-3-methyl-5-isopropyl-6-oxomorpholine-3-carboxamide (syn-**12**).* Yield: 131.4 mg; 74%. ^{1}H NMR (400 MHz, DMSO) δ 7.80 (s, 1H, C(O)NH), 4.41 (d, J = 10.9 Hz, 1H, H-2eq), 4.18 (d, J = 10.9 Hz, 1H, H-2ax), 3.66 (dd, J = 6.3, 3.5 Hz, 1H, H-5), 2.97 (d, J = 6.8 Hz, 1H, H-4), 2.09−1.98 (m, 1H, CH-$(CH_3)_2$), 1.21 (s, 9H, C$(CH_3)_3$), 1.19 (s, 3H, CH_3-CN), 0.97 (d, J = 7.3 Hz, 3H, CH_3-CH), 0.95 (d, J = 7.1 Hz, 3H, CH_3-CH). ^{13}C NMR (101 MHz, DMSO) δ 173.1 (C(O)NH), 171.4 (C-6), 71.0 (C-2), 57.4 (C-3), 56.4 (C-5), 49.7 (C-$(CH_3)_3$), 28.7 (CH-$(CH_3)_2$), 28.2 ($(CH_3)_3$), 21.5 (CH_3-C), 18.4 (CH_3-CH), 17.5 (CH_3-CH). $[\alpha]_D^{25}$ = −120 (c = 1.0, methanol). HRMS calcd for $C_{13}H_{25}O_3N_2$ $[M + H]^+$: 257.1860 found: 257.1857; $C_{13}H_{24}O_3N_2Na$ $[M + Na]^+$: 279.1679 found: 279.1676.

*(3R,5R)-N-(tert-Butyl)-3-methyl-5-isopropyl-6-oxomorpholine-3-carboxamide (syn-ent-**12**).* Yield: 125.1 mg; 70%. ^{1}H NMR (400 MHz, DMSO) δ 7.80 (s, 1H), 4.41 (d, J = 10.9 Hz, 1H), 4.18 (d, J = 10.9 Hz, 1H), 3.66 (dd, J = 6.3, 3.5 Hz, 1H), 2.97 (d, J = 6.8 Hz, 1H), 2.09−1.98 (m, 1H), 1.21 (s, 9H), 1.19 (s, 3H), 0.97 (d, J = 7.3 Hz, 3H), 0.95 (d, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 173.1, 171.4, 71.0, 57.4, 56.4, 49.7, 28.7, 28.2, 21.5, 18.4, 17.5. $[\alpha]_D^{25}$ = +113 (c = 1.0, methanol). HRMS calcd for $C_{13}H_{25}O_3N_2$ $[M + H]^+$: 257.1860 found: 257.1857; $C_{13}H_{24}O_3N_2Na$ $[M + Na]^+$: 279.1679 found: 279.1676.

*(3S,5S)-5-((S)-sec-Butyl)-N-(tert-butyl)-3-methyl-6-oxomorpholine-3-carboxamide (syn-**13**).* Yield: 116.6 mg; 62%. ^{1}H NMR (500 MHz, DMSO) δ 7.81 (s, 1H), 4.41 (d, J = 11.0 Hz, 1H), 4.19 (d, J = 11.0 Hz, 1H), 3.69 (dd, J = 6.9, 3.7 Hz, 1H), 3.04 (d, J = 7.0 Hz, 1H), 1.79−1.68 (m, 1H), 1.51 (dqd, J = 15.1, 7.5, 3.7 Hz, 1H), 1.36−1.23 (m, 1H), 1.22 (s, 9H), 1.19 (s, 3H), 0.97 (d, J = 7.0 Hz, 3H), 0.89 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 173.1, 171.4, 70.8, 57.3, 56.4, 49.7, 35.8, 28.2, 24.9, 21.6, 14.8, 12.1. $[\alpha]_D^{25}$ = −116 (c = 1, methanol). HRMS calcd for $C_{14}H_{27}O_3N_2$ $[M + H]^+$: 271.2016 found: 271.2016; $C_{14}H_{26}O_3N_2Na$ $[M + Na]^+$: 293.1836 found: 293.1834.

*(3S,5S)-N-(tert-Butyl)-3-methyl-5-isobutyl-6-oxomorpholine-3-carboxamide (syn-**14**).* Yield: 86.1 mg; 46%. ^{1}H NMR (400 MHz, DMSO) δ 7.72 (s, 1H), 4.44 (d, J = 11.0 Hz, 1H), 4.24 (d, J = 11.1 Hz, 1H), 3.74 (dd, J = 12.7, 7.1 Hz, 1H), 3.23 (d, J = 7.3 Hz, 1H), 1.89−1.72 (m, 1H), 1.60 (ddd, J = 13.5, 8.1, 5.5 Hz, 1H), 1.35−1.25 (m, 2H), 1.22 (s, 9H), 1.18 (s, 3H), 0.90 (d, J = 6.7 Hz, 4H), 0.88 (d, J = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 173.0, 172.8, 71.3, 57.5, 49.9, 49.8, 41.0, 28.1, 23.8, 23.1, 22.1, 21.6. $[\alpha]_D^{25}$ = −109 (c = 1, methanol). HRMS calcd for $C_{14}H_{27}O_3N_2$ $[M + H]^+$: 271.2016 found: 271.2015; $C_{14}H_{26}O_3N_2Na$ $[M + Na]^+$: 293.1836 found: 293.1833.

*(3R,5S)-N-(tert-Butyl)-3-methyl-5-isobutyl-6-oxomorpholine-3-carboxamide (anti-**14**).*



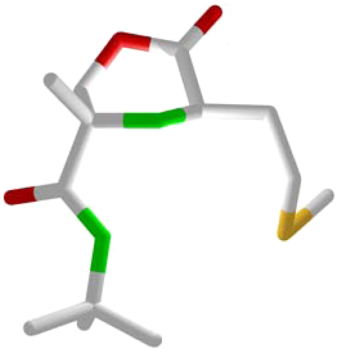
Yield: 46.2 mg; 25%. ^{1}H NMR (400 MHz, DMSO) δ 7.75 (s, 1H), 4.36 (d, J = 11.7 Hz, 1H), 4.06 (d, J = 11.7 Hz, 1H), 3.41−3.33 (m, 1H), 2.97 (d, J = 11.9 Hz, 1H), 1.89−1.75 (m, 1H), 1.53 (ddd, J = 13.8, 10.0, 3.8 Hz, 1H), 1.43 (ddd, J = 14.2, 10.0, 4.4 Hz, 1H), 1.26 (s, J = 6.2 Hz, 9H), 1.19 (s, 3H), 0.92 (d, J = 6.7 Hz, 3H), 0.88 (d, J = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 173.3, 173.1, 70.4, 57.0, 50.1, 49.6, 38.5, 28.2, 23.8, 23.5, 23.5, 21.1. $[\alpha]_D^{25}$ = −68 (c = 1, methanol). HRMS calcd for $C_{14}H_{27}O_3N_2$ $[M + H]^+$: 271.2016 found: 271.2015; $C_{14}H_{26}O_3N_2Na$ $[M + Na]^+$: 293.1836 found: 293.1833.

*(3S,5S)-N-(tert-Butyl)-3-methyl-5-(2-(methylthio)ethyl)-6-oxomorpholine-3-carboxamide (syn-**15**).* Yield: 84.6 mg; 42%.^{1}H NMR (500 MHz, DMSO) δ 7.71 (s, 1H, C(O)NH), 4.45 (d, J = 11.0 Hz, 1H, H-2eq), 4.20 (d, J = 11.0 Hz, 1H, H-2ax), 3.86 (dd, J = 12.8, 5.8 Hz, 1H, H-5), 3.36 (d, J = 7.3 Hz, 1H, H-4), 2.63−2.51 (m, 2H, CH_2−S), 2.04 (s, 3H, CH_3−S), 1.94 (ddt, J = 15.0, 12.2, 5.7 Hz, 1H, CH_2-CH_2S), 1.73 (ddt, J = 14.8, 9.1, 5.7 Hz, 1H, CH_2-CH_2S), 1.20 (s, 9H, $(CH_3)_3$), 1.16 (s, 3H, CH_3-CN). ^{13}C NMR (126 MHz, DMSO) δ 172.9 (C(O)NH), 172.2 (C-6), 71.5 (C-2), 57.5 (C-3), 50.8 (C-5), 49.8 (C-$(CH_3)_3$), 31.2 (CH_2-CH_2S), 29.3 (CH_2S-CH_2), 28.2 ($(CH_3)_3$), 21.4 (CH_3-CN), 14.7 (CH_3S). $[\alpha]_D^{25}$ = +80 (c = 1.0, methanol). HRMS calcd for $C_{13}H_{25}O_3N_2S$ $[M + H]^+$: 289.1580 found: 289.1577; $C_{13}H_{24}O_3N_2SNa$ $[M + Na]^+$: 311.1400 found: 311.1397.

*(3R,5S)-N-(tert-Butyl)-3-methyl-5-(2-(methylthio)ethyl)-6-oxomorpholine-3-carboxamide (anti-**15**).* Yield: 62.0 mg; 31%. ^{1}H NMR (400 MHz, DMSO) δ 7.69 (s, 1H, C(O)NH), 4.34 (d, J = 11.6 Hz, 1H, H-2ax), 4.09 (d, J = 11.7 Hz, 1H, H-2eq), 3.52 (ddd, J = 11.8, 9.7, 3.9 Hz, 1H, H-5), 3.08 (d, J = 11.8 Hz, 1H, H-4), 2.64 (ddd, J = 8.5, 6.0, 2.4 Hz, 2H, CH_2-S), 2.04 (s, 3H, CH_3S), 2.10−1.98 (m, 1H, CH_2-CH_2S), 1.81−1.69 (m, 1H, CH_2-CH_2S), 1.28 (s, 9H, $(CH_3)_3$), 1.21 (s, 3H, CH_3-CN). ^{13}C NMR (101 MHz, DMSO) δ 172.7 (C(O)NH), 172.7 (C-6), 70.8 (C-2), 56.9 (C-3), 50.6 (C-5), 49.8 (C-$(CH_3)_3$), 29.7 (CH_2-CH_2S), 28.5 (CH_2S-CH_2), 28.2 ($(CH_3)_3$), 23.5 (CH_3-CN), 14.4 (CH_3S). $[\alpha]_D^{25}$ = −93 (c = 0.7, methanol). HRMS calcd for $C_{13}H_{25}O_3N_2S$ $[M + H]^+$: 289.1580 found: 289.1578; $C_{13}H_{24}O_3N_2SNa$ $[M + Na]^+$: 311.1400 found: 311.1399.

*(3R,5R)-N-(tert-Butyl)-3-methyl-5-(2-(methylthio)ethyl)-6-oxomorpholine-3-carboxamide (syn-ent-**15**).* Yield: 82.0 mg; 41%. ^{1}H NMR (500 MHz, DMSO) δ 7.71 (s, 1H), 4.45 (d, J = 11.0 Hz, 1H), 4.20 (d, J = 11.0 Hz, 1H), 3.86 (dd, J = 12.8, 5.8 Hz, 1H), 3.36 (d, J = 7.3 Hz, 1H), 2.63−2.51 (m, 2H), 2.04 (s, 3H), 1.94 (ddt, J = 15.0, 12.2, 5.7 Hz, 1H), 1.73 (ddt, J = 14.8, 9.1, 5.7 Hz, 1H), 1.20 (s, 9H), 1.16 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 172.9, 172.2, 71.5, 57.5, 50.8, 49.8, 31.2, 29.3, 28.2, 21.4, 14.7. $[\alpha]_D^{25}$ = −79 (c = 1.0, methanol). HRMS calcd for $C_{13}H_{25}O_3N_2S$ $[M + H]^+$: 289.1580 found: 289.1579; $C_{13}H_{24}O_3N_2SNa$ $[M + Na]^+$: 311.1400 found: 311.1397.

*(3S,5R)-N-(tert-Butyl)-3-methyl-5-(2-(methylthio)ethyl)-6-oxomorpholine-3-carboxamide (anti-ent-**15**).*



Yield: 69.2 mg; 35%. ^{1}H NMR (400 MHz, DMSO) δ 7.69 (s, 1H), 4.34 (d, J = 11.6 Hz, 1H), 4.09 (d, J = 11.7 Hz, 1H), 3.52 (ddd, J = 11.8, 9.7, 3.9 Hz, 1H), 3.08 (d, J = 11.8 Hz, 1H), 2.64 (ddd, J = 8.5, 6.0, 2.4 Hz, 2H), 2.04 (s, 3H), 2.10−1.98 (m, 1H), 1.81−1.69 (m, 1H), 1.28 (s, 9H), 1.21 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 172.7, 172.7, 70.8, 56.9, 50.6, 49.8, 29.7, 28.5, 28.2, 23.5, 14.4. $[\alpha]_D^{25}$ = +98 (c = 0.7, methanol). HRMS calcd for $C_{13}H_{25}O_3N_2S$ $[M + H]^+$: 289.1580 found: 289.1577; $C_{13}H_{24}O_3N_2SNa$ $[M + Na]^+$: 311.1400 found: 311.1397.

*(3S,5S)-N,5-Di-tert-butyl-3-methyl-6-oxomorpholine-3-carboxamide (syn-**16**).* Yield: 162.6 mg; 86%. ^{1}H NMR (400 MHz, DMSO) δ 7.75 (s, 1H), 4.40 (d, J = 10.9 Hz, 1H), 4.21 (d, J = 10.9 Hz, 1H), 3.50 (d, J = 7.3 Hz, 1H), 2.77 (d, J = 7.3 Hz, 1H), 1.22 (s, 9H), 1.21 (s, 3H), 1.03 (s, 9H). ^{13}C NMR (101 MHz, DMSO) δ 172.8, 170.3, 71.1, 59.5, 57.9, 49.8, 33.1, 28.2, 26.0, 21.2. $[\alpha]_D^{25}$ = −70 (c = 1.0, methanol). HRMS calcd for $C_{14}H_{27}O_3N_2$ $[M + H]^+$: 271.2016 found: 271.2013; $C_{14}H_{26}O_3N_2Na$ $[M + Na]^+$: 293.1836 found: 293.1832.

*(3S,5S)-5-Benzyl-N-(tert-butyl)-3-methyl-6-oxomorpholine-3-carboxamide (syn-**17**).* Yield: 111.2 mg; 53%. ^{1}H NMR (500 MHz, DMSO) δ 7.52 (s, 1H), 7.35−7.30 (m, 2H), 7.30−7.26 (m, 2H), 7.21−7.17 (m, 1H), 4.42 (d, J = 11.0 Hz, 1H), 4.25 (d, J = 11.0 Hz, 1H), 4.13 (dd, J = 12.7, 5.8 Hz, 1H), 3.18 (d, J = 7.1 Hz, 1H), 3.02 (dd, J = 14.1, 5.8 Hz, 1H), 2.86 (dd, J = 14.1, 5.6 Hz, 1H), 1.16 (s, 3H), 1.11 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 172.9, 172.0, 137.8, 130.0, 128.1, 126.2, 71.3, 57.5, 52.8, 49.6, 36.9, 28.1, 21.5. $[\alpha]_D^{25}$ = −100 (c = 0.7, methanol). HRMS calcd for $C_{17}H_{25}O_3N_2$ $[M + H]^+$: 305.1860 found: 305.1858; $C_{17}H_{24}O_3N_2Na$ $[M + Na]^+$: 327.1679 found: 327.1676.

*(3R,5S)-5-Benzyl-N-(tert-butyl)-3-methyl-6-oxomorpholine-3-carboxamide (anti-**17**).* Yield: 59.0 mg; 28%. ^{1}H NMR (400 MHz, DMSO)

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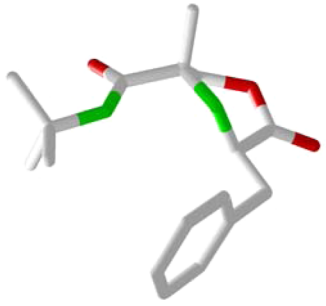
δ 7.34−7.24 (m, 1H), 7.20 (ddd, *J* = 5.6, 4.3, 1.9 Hz, 1H), 7.10 (s, 1H), 4.21 (d, *J* = 11.9 Hz, 1H), 4.08 (d, *J* = 11.9 Hz, 1H), 3.61−3.50 (m, 1H), 3.17 (d, *J* = 12.9 Hz, 1H), 3.11 (dd, *J* = 14.0, 3.1 Hz, 1H), 2.60 (dd, *J* = 14.0, 11.2 Hz, 1H), 1.19 (s, *J* = 8.1 Hz, 1H), 0.91 (s, 2H). ^{13}C NMR (101 MHz, DMSO) δ 173.2, 172.9, 138.9, 129.2, 128.2, 126.2, 70.1, 56.9, 53.9, 49.1, 35.1, 28.0, 23.6. $[\alpha]_D^{25}$ = −23 (*c* = 1, methanol). HRMS calcd for $C_{17}H_{25}O_3N_2$ [M + H]$^+$: 305.1860 found: 305.1858; $C_{17}H_{24}O_3N_2$ [M + Na]$^+$: 327.1679 found: 327.1676.

*(3R,5R)-5-Benzyl-N-(tert-butyl)-3-methyl-6-oxomorpholine-3-carboxamide (syn-ent-**17**).* Yield: 127.4 mg; 60%. ^{1}H NMR (500 MHz, DMSO) δ 7.52 (s, 1H), 7.35−7.30 (m, 2H), 7.30−7.26 (m, 2H), 7.21−7.17 (m, 1H), 4.42 (d, *J* = 11.0 Hz, 1H), 4.25 (d, *J* = 11.0 Hz, 1H), 4.13 (dd, *J* = 12.7, 5.8 Hz, 1H), 3.18 (d, *J* = 7.1 Hz, 1H), 3.02 (dd, *J* = 14.1, 5.8 Hz, 1H), 2.86 (dd, *J* = 14.1, 5.6 Hz, 1H), 1.16 (s, 3H), 1.11 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 172.9, 172.0, 137.8, 130.0, 128.1, 126.2, 71.3, 57.5, 52.8, 49.6, 36.9, 28.1, 21.5. $[\alpha]_D^{25}$ = +107 (*c* = 0.8, methanol). HRMS calcd for $C_{17}H_{25}O_3N_2$ [M + H]$^+$: 305.1860 found: 305.1859; $C_{17}H_{24}O_3N_2Na$ [M + Na]$^+$: 327.1679 found: 327.1677.

*(3S,5R)-5-Benzyl-N-(tert-butyl)-3-methyl-6-oxomorpholine-3-carboxamide (anti-ent-**17**).*



Yield: 52.0 mg; 25%. ^{1}H NMR (500 MHz, DMSO) δ 7.34−7.24 (m, 1H), 7.20 (ddd, *J* = 5.6, 4.3, 1.9 Hz, 1H), 7.10 (s, 1H), 4.21 (d, *J* = 11.9 Hz, 1H), 4.08 (d, *J* = 11.9 Hz, 1H), 3.61−3.50 (m, 1H), 3.17 (d, *J* = 12.9 Hz, 1H), 3.11 (dd, *J* = 14.0, 3.1 Hz, 1H), 2.60 (dd, *J* = 14.0, 11.2 Hz, 1H), 1.19 (s, *J* = 8.1 Hz, 1H), 0.91 (s, 2H). ^{13}C NMR (126 MHz, DMSO) δ 173.2, 172.9, 138.9, 129.2, 128.2, 126.2, 70.1, 56.9, 53.9, 49.1, 35.1, 28.0, 23.6. $[\alpha]_D^{25}$ = +58 (*c* = 0.75, methanol). HRMS calcd for $C_{17}H_{25}O_3N_2$ [M + H]$^+$: 305.1860 found: 305.1860; $C_{17}H_{24}O_3N_2$ [M + Na]$^+$: 327.1679 found: 327.1677.

*(3S,5S)-N-(tert-Butyl)-5-((R)-1-hydroxyethyl)-3-methyl-6-oxomorpholine-3-carboxamide (syn-**18**).* Yield: 26.4 mg; 15%. ^{1}H NMR (400 MHz, DMSO) δ 8.38 (s, 1H), 5.06 (d, *J* = 5.0 Hz, 1H), 4.40 (d, *J* = 10.4 Hz, 1H), 4.15−4.05 (m, 1H), 4.09 (d, *J* = 10.4 Hz, 1H), 3.60 (dd, *J* = 8.5, 2.4 Hz, 1H), 3.02 (d, *J* = 8.5 Hz, 1H), 1.19 (s, 9H), 1.18 (s, 3H), 1.09 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 172.8, 170.8, 72.5, 64.7, 57.1, 56.8, 49.9, 28.1, 21.3, 20. $[\alpha]_D^{25}$ = −76 (*c* = 0.7, methanol). HRMS calcd for $C_{12}H_{23}O_4N_2$ [M + H]$^+$: 259.1652 found: 259.1650; $C_{12}H_{22}O_4N_2Na$ [M + Na]$^+$: 281.1472 found: 281.1468.

*(3R,5S)-N-(tert-Butyl)-5-((R)-1-hydroxyethyl)-3-methyl-6-oxomorpholine-3-carboxamide (anti-**18**).* Yield: 53.0 mg; 30%. ^{1}H NMR (400 MHz, DMSO) δ 7.56 (s, 1H), 4.93 (d, *J* = 5.6 Hz, 1H), 4.40 (d, *J* = 11.0 Hz, 1H), 4.10 (pd, *J* = 6.3, 2.8 Hz, 1H), 4.04 (d, *J* = 11.1 Hz, 1H), 3.36−3.31 (m, 1H), 2.67 (d, *J* = 10.0 Hz, 1H), 1.24 (s, 9H), 1.20 (s, 3H), 1.17 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 172.2, 170.7, 71.5, 65.4, 58.6, 56.6, 49.9, 28.3, 23.1, 20.2. $[\alpha]_D^{25}$ = −31 (*c* = 1.0, methanol). HRMS calcd for $C_{12}H_{23}O_4N_2$ [M + H]$^+$: 259.1652 found: 259.1650; $C_{12}H_{22}O_4N_2Na$ [M + Na]$^+$: 281.1472 found: 281.1468.

*(3R,5R)-N-(tert-Butyl)-5-((R)-1-hydroxyethyl)-3-methyl-6-oxomorpholine-3-carboxamide (syn-**19**).* Yield: 25.5 mg; 15%. ^{1}H NMR (400 MHz, DMSO) δ 8.38 (s, 1H), 5.06 (d, *J* = 5.0 Hz, 1H), 4.40 (d, *J* = 10.4 Hz, 1H), 4.15−4.05 (m, 1H), 4.09 (d, *J* = 10.4 Hz, 1H), 3.60 (dd, *J* = 8.5, 2.4 Hz, 1H), 3.02 (d, *J* = 8.5 Hz, 1H), 1.19 (s, 9H), 1.18 (s, 3H), 1.09 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 172.8, 170.8, 72.5, 64.7, 57.1, 56.8, 49.9, 28.1, 21.3, 20.2. $[\alpha]_D^{25}$ = +86 (*c* = 0.7, methanol). HRMS calcd for $C_{12}H_{23}O_4N_2$ [M + H]$^+$: 259.1652 found: 259.1651; $C_{12}H_{22}O_4N_2Na$ [M + Na]$^+$: 281.1472 found: 281.1470.

*(3S,5R)-N-(tert-Butyl)-5-((R)-1-hydroxyethyl)-3-methyl-6-oxomorpholine-3-carboxamide (anti-**19**).* Yield: 62.7 mg; 35%. ^{1}H NMR (400 MHz, DMSO) δ 7.56 (s, 1H), 4.93 (d, *J* = 5.6 Hz, 1H), 4.40 (d, *J* = 11.0 Hz, 1H), 4.10 (pd, *J* = 6.3, 2.8 Hz, 1H), 4.04 (d, *J* = 11.1 Hz, 1H), 3.36−3.31 (m, 1H), 2.67 (d, *J* = 10.0 Hz, 1H), 1.24 (s, 9H), 1.20 (s, 3H), 1.17 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 172.2, 170.7, 71.5, 65.4, 58.6, 56.6, 49.9, 28.3, 23.1, 20.2. $[\alpha]_D^{25}$ = +31 (*c* = 1.0, methanol). HRMS calcd for $C_{12}H_{23}O_4N_2$ [M + H]$^+$: 259.1652 found: 259.1651; $C_{12}H_{22}O_4N_2Na$ [M + Na]$^+$: 281.1472 found: 281.1470.

*(3R,5S)-N-Cyclohexyl-3-methyl-5-isopropyl-6-oxomorpholine-3-carboxamide (anti-**20**).* Yield: 129.5 mg; 66%. ^{1}H NMR (400 MHz, DMSO) δ 7.77 (d, *J* = 8.1 Hz, 1H), 4.43 (d, *J* = 11.1 Hz, 1H), 3.99 (d, *J* = 11.1 Hz, 1H), 3.61−3.42 (m, 1H), 3.26 (dd, *J* = 9.2, 4.9 Hz, 1H), 2.88 (d, *J* = 9.4 Hz, 1H), 2.05 (qd, *J* = 13.3, 6.7 Hz, 1H), 1.75−1.60 (m, 4H), 1.58−1.45 (m, 1H), 1.34−1.08 (m, 5H), 1.18 (s, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 172.2, 171.1, 71.7, 58.3, 56.8, 47.3, 32.4, 32.2, 29.5, 25.2, 24.4, 23.2, 19.4, 17.6. $[\alpha]_D^{25}$ = −57 (*c* = 1.0, methanol). HRMS calcd for $C_{15}H_{27}O_3N_2$ [M + H]$^+$: 283.2016 found: 283.2018; $C_{15}H_{26}O_3N_2Na$ [M + Na]$^+$: 305,1836 found: 305.1837.

*(3S,5R)-N-Cyclohexyl-3-methyl-5-isopropyl-6-oxomorpholine-3-carboxamide (anti-ent-**20**).* Yield: 139.9 mg; 71%. ^{1}H NMR (400 MHz, DMSO) δ 7.77 (d, *J* = 8.1 Hz, 1H), 4.43 (d, *J* = 11.1 Hz, 1H), 3.99 (d, *J* = 11.1 Hz, 1H), 3.61−3.42 (m, 1H), 3.26 (dd, *J* = 9.2, 4.9 Hz, 1H), 2.88 (d, *J* = 9.4 Hz, 1H), 2.05 (qd, *J* = 13.3, 6.7 Hz, 1H), 1.75−1.60 (m, 4H), 1.58−1.45 (m, 1H), 1.34−1.08 (m, 5H), 1.18 (s, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 172.2, 171.1, 71.7, 58.3, 56.8, 47.3, 32.4, 32.2, 29.5, 25.2, 24.4, 23.2, 19.4, 17.6. $[\alpha]_D^{25}$ = +62 (*c* = 1.0, methanol). HRMS calcd for $C_{15}H_{27}O_3N_2$ [M + H]$^+$: 283.2016 found: 283.2018; $C_{15}H_{26}O_3N_2Na$ [M + Na]$^+$: 305,1837. found: 305.1837.

*(3R,5S)-3-Methyl-5-isopropyl-6-oxo-N-(tosylmethyl)morpholine-3-carboxamide (anti-**21**).* Yield: 80.5 mg; 32%. ^{1}H NMR (400 MHz, DMSO) δ 8.83 (t, *J* = 6.6 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.40 (d, *J* = 8.3 Hz, 2H), 4.80−4.63 (m, 2H), 4.29 (d, *J* = 11.1 Hz, 1H), 3.91 (d, *J* = 11.2 Hz, 1H), 3.21 (dd, *J* = 8.5, 4.6 Hz, 1H), 2.88 (d, *J* = 8.6 Hz, 1H), 2.37 (s, 3H), 2.16−1.95 (m, 1H), 1.07 (s, 3H), 0.94 (d, *J* = 6.9 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 173.4, 170.3, 144.8, 134.6, 129.8, 128.5, 71.5, 60.2, 58.3, 57.0, 29.9, 22.8, 21.1, 19.1, 17.6. $[\alpha]_D^{25}$ = −24 (*c* = 1.0, methanol). HRMS calcd for $C_{17}H_{24}O_5N_2SNa$ [M + Na]$^+$: 391.1298 found: 391.1298.

*(3S,5R)-3-Methyl-5-isopropyl-6-oxo-N-(tosylmethyl)morpholine-3-carboxamide (anti-ent-**21**).* Yield: 77.1 mg; 30%. ^{1}H NMR (400 MHz, DMSO) δ 8.83 (t, *J* = 6.6 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.40 (d, *J* = 8.3 Hz, 2H), 4.80−4.63 (m, 2H), 4.29 (d, *J* = 11.1 Hz, 1H), 3.91 (d, *J* = 11.2 Hz, 1H), 3.21 (dd, *J* = 8.5, 4.6 Hz, 1H), 2.88 (d, *J* = 8.6 Hz, 1H), 2.37 (s, 3H), 2.16−1.95 (m, 1H), 1.07 (s, 3H), 0.94 (d, *J* = 6.9 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 173.4, 170.3, 144.8, 134.6, 129.8, 128.5, 71.5, 60.2, 58.3, 57.0, 29.9, 22.8, 21.1, 19.1, 17.6. $[\alpha]_D^{25}$ = +24 (*c* = 1.0, methanol). HRMS calcd for $C_{17}H_{24}O_5N_2SNa$ [M + Na]$^+$: 391.1298 found: 391.1299.

*Ethyl ((3R,5S)-3-Methyl-5-isopropyl-6-oxomorpholine-3-carbonyl)glycinate (anti-**22**).* Yield: 141.5 mg; 71% (72 h rt). ^{1}H NMR (500 MHz, DMSO) δ 8.42 (t, *J* = 6.0 Hz, 1H), 4.49 (d, *J* = 11.0 Hz, 1H), 4.11−4.04 (m, 2H), 4.02 (d, *J* = 11.1 Hz, 1H), 3.92 (dd, *J* = 17.4, 6.3 Hz, 1H), 3.84 (dd, *J* = 17.4, 5.8 Hz, 1H), 3.44 (dd, *J* = 9.1, 4.6 Hz, 1H), 2.87 (d, *J* = 9.1 Hz, 1H), 2.12−2.03 (m, 1H), 1.22 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 174.0, 170.7, 169.7, 71.9, 60.6, 58.3, 56.7, 40.8, 29.8, 23.1, 19.1, 17.7, 14.0. $[\alpha]_D$ = −44 (*c* = 1.0, methanol). HRMS calcd for $C_{13}H_{23}O_5N_2$ [M + H]$^+$: 287.1601 found: 287.1603; $C_{13}H_{22}O_5N_2Na$ [M + Na]$^+$: 309.1421 found: 309.1420.

*Ethyl-2-((3R,5S)-3-(Hydroxymethyl)-5-isopropyl-3-methyl-2,6-dioxopiperazin-1-yl)acetate (**23**).* Yield: 75.8 mg; 38% (12 h rt). ^{1}H NMR (500 MHz, DMSO) δ 5.21 (t, *J* = 5.4 Hz, 1H), 4.40 (d, *J* = 16.8 Hz, 1H), 4.29 (d, *J* = 16.8 Hz, 1H), 4.11−4.00 (m, 2H), 3.88 (dd, *J* = 10.3, 5.6 Hz, 1H), 3.68 (dd, *J* = 12.0, 3.1 Hz, 1H), 3.28 (dd, *J* = 10.4, 5.2 Hz, 1H), 2.46−2.42 (m, 1H), 2.40 (d, *J* = 12.1 Hz, 1H), 1.15 (t, *J* = 7.1 Hz, 3H), 1.13 (s, 3H), 1.01 (d, *J* = 7.0 Hz, 3H), 0.83 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 174.7, 172.7, 167.6, 66.7, 60.9, 59.9, 57.4, 40.2, 28.5, 19.1, 18.6, 16.4, 14.0. $[\alpha]_D$ = −21 (*c* = 1.0,

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methanol). HRMS calcd for $C_{13}H_{23}O_5N_2$ $[M + H]^+$: 287.1601 found: 287.1603; $C_{13}H_{22}O_5N_2Na$ $[M + Na]^+$: 309.1421 found: 309.1421.

*Ethyl-((3S,5R)-3-Methyl-5-isopropyl-6-oxomorpholine-3-carbonyl)glycinate (anti-ent-**22**).* Yield: 135.1 mg; 68% (72 h rt). ^{1}H NMR (500 MHz, DMSO) δ 8.42 (t, J = 6.0 Hz, 1H), 4.49 (d, J = 11.0 Hz, 1H), 4.11−4.04 (m, 2H), 4.02 (d, J = 11.1 Hz, 1H), 3.92 (dd, J = 17.4, 6.3 Hz, 1H), 3.84 (dd, J = 17.4, 5.8 Hz, 1H), 3.44 (dd, J = 9.1, 4.6 Hz, 1H), 2.87 (d, J = 9.1 Hz, 1H), 2.12−2.03 (m, 1H), 1.22 (s, 3H), 1.17 (t, J = 7.1 Hz, 3H), 0.99 (d, J = 6.9 Hz, 3H), 0.94 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 174.0, 170.7, 169.7, 71.9, 60.6, 58.3, 56.7, 40.8, 29.8, 23.1, 19.1, 17.7, 14.0. $[\alpha]_D$ = +51 (c = 1.0, methanol). HRMS calcd for $C_{13}H_{23}O_5N_2$ $[M + H]^+$: 287.1601 found: 287.1603; $C_{13}H_{22}O_5N_2Na$ $[M + Na]^+$: 309.1421 found: 309.1420.

*Ethyl-2-((3S,5R)-3-(Hydroxymethyl)-5-isopropyl-3-methyl-2,6-dioxopiperazin-1-yl)acetate (ent-**23**).* Yield: 30.7 mg; 16% (12 h rt). ^{1}H NMR (500 MHz, DMSO) δ 5.21 (t, J = 5.4 Hz, 1H), 4.40 (d, J = 16.8 Hz, 1H), 4.29 (d, J = 16.8 Hz, 1H), 4.11−4.00 (m, 2H), 3.88 (dd, J = 10.3, 5.6 Hz, 1H), 3.68 (dd, J = 12.0, 3.1 Hz, 1H), 3.28 (dd, J = 10.4, 5.2 Hz, 1H), 2.46−2.42 (m, 1H), 2.40 (d, J = 12.1 Hz, 1H), 1.15 (t, J = 7.1 Hz, 3H), 1.13 (s, 3H), 1.01 (d, J = 7.0 Hz, 3H), 0.83 (d, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 174.7, 172.7, 167.6, 66.7, 60.9, 59.9, 57.4, 40.2, 28.5, 19.1, 18.6, 16.4, 14.0. $[\alpha]_D$ = +20 (c = 1.0, methanol). HRMS calcd for $C_{13}H_{23}O_5N_2$ $[M + H]^+$: 287.1601 found: 287.1603; $C_{13}H_{22}O_5N_2Na$ $[M + Na]^+$: 309.1421 found: 309.1421.

*(3S,5S)-N-(tert-Butyl)-3-(hydroxymethyl)-5-methyl-6-oxomorpholine-3-carboxamide (syn-**26**).* Inseparable mixture *syn*/*anti* (47/53); Overall yield: 90.3 mg; 53%. ^{1}H NMR (500 MHz, DMSO) δ 7.77 (s, 1H), 5.14 (t, J = 5.7 Hz, 1H), 4.45 (d, J = 11.3 Hz, 1H), 4.37 (d, J = 11.3 Hz, 1H), 3.84 (p, J = 6.2 Hz, 1H), 3.47 (dd, J = 5.7, 2.5 Hz, 2H), 3.26 (d, J = 6.6 Hz, 1H), 1.23 (s, 9H), 1.20 (d, J = 6.3 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 173.2, 171.6, 68.7, 63.1, 62.3, 50.0, 47.8, 28.3, 17.2. HRMS calcd for $C_{11}H_{21}O_4N_2$ $[M + H]^+$: 245.1496 found: 245.1494; $C_{11}H_{20}O_4N_2Na$ $[M + Na]^+$: 267.1315 found: 267.1312.

*(3R,5S)-N-(tert-Butyl)-3-(hydroxymethyl)-5-methyl-6-oxomorpholine-3-carboxamide (anti-**26**).* ^{1}H NMR (500 MHz, DMSO) δ 7.69 (s, 1H), 5.02 (t, J = 5.8 Hz, 1H), 4.34 (d, J = 11.9 Hz, 1H), 4.19 (d, J = 12.0 Hz, 1H), 3.59 (dd, J = 10.8, 5.9 Hz, 1H), 3.57 (dq, J = 11.2, 6.6 Hz, 1H), 3.43 (dd, J = 10.8, 5.6 Hz, 1H), 2.89 (d, J = 11.2 Hz, 1H), 1.27 (s, 9H), 1.23 (d, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 173.2, 171.0, 68.1, 64.7, 61.5, 50.0, 47.8, 28.4, 16.2.

*(3R,5R)-N-(tert-Butyl)-3-(hydroxymethyl)-5-methyl-6-oxomorpholine-3-carboxamide (syn-ent-**26**).* Inseparable mixture *syn*/*anti* (50:50); Overall yield: 99.0 mg; 58%. ^{1}H NMR (500 MHz, DMSO) δ 7.77 (s, 1H), 5.14 (t, J = 5.7 Hz, 1H), 4.45 (d, J = 11.3 Hz, 1H), 4.37 (d, J = 11.3 Hz, 1H), 3.84 (p, J = 6.2 Hz, 1H), 3.47 (dd, J = 5.7, 2.5 Hz, 2H), 3.26 (d, J = 6.6 Hz, 1H), 1.23 (s, 9H), 1.20 (d, J = 6.3 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 173.2, 171.6, 68.7, 63.1, 62.3, 50.0, 47.8, 28.3, 17.2. HRMS calcd for $C_{11}H_{21}O_4N_2$ $[M + H]^+$: 245.1496 found: 245.1495; $C_{11}H_{20}O_4N_2Na$ $[M + Na]^+$: 267.1315 found: 267.1312.

*(3S,5R)-N-(tert-Butyl)-3-(hydroxymethyl)-5-methyl-6-oxomorpholine-3-carboxamide (anti-ent-**26**).* ^{1}H NMR (500 MHz, DMSO) δ 7.69 (s, 1H), 5.02 (t, J = 5.8 Hz, 1H), 4.34 (d, J = 11.9 Hz, 1H), 4.19 (d, J = 12.0 Hz, 1H), 3.59 (dd, J = 10.8, 5.9 Hz, 1H), 3.57 (dq, J = 11.2, 6.6 Hz, 1H), 3.43 (dd, J = 10.8, 5.6 Hz, 1H), 2.89 (d, J = 11.2 Hz, 1H), 1.27 (s, 9H), 1.23 (d, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 173.2, 171.0, 68.1, 64.7, 61.5, 50.0, 47.8, 28.4, 16.2.

*(4S,8S)-N-(tert-Butyl)-4-(hydroxymethyl)-1-oxohexahydro-1H-pyrrolo[2,1][1,4]oxazine-4-carboxamide (syn-**27**).* Inseparable mixture *syn*/*anti* (50/50). Overall yield: 133.2 mg; 71%. ^{1}H NMR (500 MHz, DMSO) δ 7.36 (s, 1H), 5.33 (t, J = 5.0 Hz, 1H), 4.40 (d, J = 11.8 Hz, 1H), 4.37 (d, J = 11.7 Hz, 1H), 3.86 (t, J = 7.8 Hz, 1H), 3.73 (dd, J = 11.7, 5.1 Hz, 1H), 3.61 (dd, J = 11.7, 4.8 Hz, 1H), 2.90−2.87 (m, 2H), 1.99−1.92 (m, 2H), 1.74−1.68 (m, 2H), 1.24 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 172.8, 170.6, 69.1, 62.5, 61.6, 57.6, 50.0, 46.0, 28.3, 25.7, 22.7. HRMS calcd for $C_{13}H_{23}O_4N_2$ $[M + H]^+$: 271.1652 found: 271.1653; $C_{13}H_{22}O_4N_2Na$ $[M + Na]^+$: 293.1472 found: 293.1473.

*(4R,8S)-N-(tert-Butyl)-4-(hydroxymethyl)-1-oxohexahydro-1H-pyrrolo[2,1][1,4]oxazine-4-carboxamide (anti-**27**)* . ^{1}H NMR (500 MHz, DMSO) δ 7.37 (s, 1H), 5.01 (t, J = 5.1 Hz, 1H), 4.45 (d, J = 11.2 Hz, 1H), 4.33 (d, J = 11.3 Hz, 1H), 3.93 (dd, J = 8.2, 7.4 Hz, 1H), 3.65 (dd, J = 11.4, 4.7 Hz, 1H), 3.57 (dd, J = 11.4, 5.6 Hz, 1H), 3.02−2.99 (m, 1H), 2.85−2.78 (m, 1H), 2.16−2.09 (m, 1H), 1.90−1.84 (m, 1H) 1.74−1.68 (m, 2H), 1.26 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 172.2, 169.3, 67.6, 63.6, 62.5, 57.3, 50.2, 46.8, 28.3, 28.1, 23.9.

*(4R,8R)-N-(tert-Butyl)-4-(hydroxymethyl)-1-oxohexahydro-1H-pyrrolo[2,1][1,4]oxazine-4-carboxamide (syn-ent-**27**).* Inseparable mixture *syn*/*anti* (44/56). Overall yield: 134.9 mg; 72%. ^{1}H NMR (500 MHz, DMSO) δ 7.36 (s, 1H), 5.33 (t, J = 5.0 Hz, 1H), 4.40 (d, J = 11.8 Hz, 1H), 4.37 (d, J = 11.7 Hz, 1H), 3.86 (t, J = 7.8 Hz, 1H), 3.73 (dd, J = 11.7, 5.1 Hz, 1H), 3.61 (dd, J = 11.7, 4.8 Hz, 1H), 2.90−2.87 (m, 2H), 1.99−1.92 (m, 2H), 1.74−1.68 (m, 2H), 1.24 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 172.8, 170.6, 69.1, 62.5, 61.6, 57.6, 50.0, 46.0, 28.3, 25.7, 22.7. HRMS calcd for $C_{13}H_{23}O_4N_2$ $[M + H]^+$: 271.1652 found: 271.1653; $C_{13}H_{22}O_4N_2Na$ $[M + Na]^+$: 293.1472 found: 293.1473.

*(4S,8R)-N-(tert-Butyl)-4-(hydroxymethyl)-1-oxohexahydro-1H-pyrrolo[2,1][1,4]oxazine-4-carboxamide (anti-ent-**27**).* ^{1}H NMR (500 MHz, DMSO) δ 7.37 (s, 1H), 5.01 (t, J = 5.1 Hz, 1H), 4.45 (d, J = 11.2 Hz, 1H), 4.33 (d, J = 11.3 Hz, 1H), 3.93 (dd, J = 8.2, 7.4 Hz, 1H), 3.65 (dd, J = 11.4, 4.7 Hz, 1H), 3.57 (dd, J = 11.4, 5.6 Hz, 1H), 3.02−2.99 (m, 1H), 2.85−2.78 (m, 1H), 2.16−2.09 (m, 1H), 1.90−1.84 (m, 1H) 1.74−1.68 (m, 2H), 1.26 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 172.2, 169.3, 67.6, 63.6, 62.5, 57.3, 50.2, 46.8, 28.3, 28.1, 23.9.

*(3S,5S)-N-(tert-Butyl)-3-(hydroxymethyl)-5-isopropyl-6-oxomorpholine-3-carboxamide (syn-**28**).* Inseparable mixture *syn*/*anti* (50/50). Overall yield: 140.1 mg; 74%. ^{1}H NMR (500 MHz, DMSO) δ 7.78 (s, 1H), 5.20 (t, J = 5.8 Hz, 1H), 4.42 (d, J = 11.2 Hz, 1H), 4.33 (d, J = 11.7 Hz, 1H), 3.64 (dd, J = 6.9, 3.8 Hz, 1H), 3.50 (d, J = 5.8 Hz, 2H), 2.92 (d, J = 7.0 Hz, 1H), 2.15−2.05 (m, 1H), 1.23 (s, 9H), 1.00 (d, J = 7.0 Hz, 3H), 0.98 (d, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.5, 171.4, 68.2, 63.0, 62.0, 56.7, 50.0, 28.7, 28.3, 18.6, 17.4. HRMS calcd for $C_{13}H_{25}O_4N_2$ $[M + H]^+$: 273.1809 found: 273.1810; $C_{13}H_{24}O_4N_2Na$ $[M + Na]^+$: 295.1628 found: 295.1629.

*(3R,5S)-N-(tert-Butyl)-3-(hydroxymethyl)-5-isopropyl-6-oxomorpholine-3-carboxamide (anti-**28**).* ^{1}H NMR (500 MHz, DMSO) δ 7.66 (s, 1H), 5.10 (t, J = 5.9 Hz, 1H), 4.33 (d, J = 11.7 Hz, 1H), 4.15 (d, J = 11.8 Hz, 1H), 3.57 (dd, J = 10.9, 6.0 Hz, 1H), 3.45 (dd, J = 10.9, 5.8 Hz, 1H), 3.29 (dd, J = 11.6, 5.1 Hz, 1H), 2.71 (d, J = 11.6 Hz, 1H), 2.15−2.05 (m, 1H), 1.27 (s, 9H), 1.03 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.9, 171.1, 68.2, 65.0, 61.6, 56.7, 50.0, 28.7, 28.4, 19.7, 17.3.

*(3R,5R)-N-(tert-Butyl)-3-(hydroxymethyl)-5-isopropyl-6-oxomorpholine-3-carboxamide (syn-ent-**28**).* Inseparable mixture *syn*/*anti* (52/48). Overall yield: 133.8 mg; 71%. ^{1}H NMR (500 MHz, DMSO) δ 7.78 (s, 1H), 5.20 (t, J = 5.8 Hz, 1H), 4.42 (d, J = 11.2 Hz, 1H), 4.33 (d, J = 11.7 Hz, 1H), 3.64 (dd, J = 6.9, 3.8 Hz, 1H), 3.50 (d, J = 5.8 Hz, 2H), 2.92 (d, J = 7.0 Hz, 1H), 2.15−2.05 (m, 1H), 1.23 (s, 9H), 1.00 (d, J = 7.0 Hz, 3H), 0.98 (d, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.5, 171.4, 68.2, 63.0, 62.0, 56.7, 50.0, 28.7, 28.3, 18.6, 17.4. HRMS calcd for $C_{13}H_{25}O_4N_2$ $[M + H]^+$: 273.1809 found: 273.1809; $C_{13}H_{24}O_4N_2Na$ $[M + Na]^+$: 295.1628 found: 295.1629.

*(3S,5R)-N-(tert-Butyl)-3-(hydroxymethyl)-5-isopropyl-6-oxomorpholine-3-carboxamide (anti-ent-**28**).* ^{1}H NMR (500 MHz, DMSO) δ 7.66 (s, 1H), 5.10 (t, J = 5.9 Hz, 1H), 4.33 (d, J = 11.7 Hz, 1H), 4.15 (d, J = 11.8 Hz, 1H), 3.57 (dd, J = 10.9, 6.0 Hz, 1H), 3.45 (dd, J = 10.9, 5.8 Hz, 1H), 3.29 (dd, J = 11.6, 5.1 Hz, 1H), 2.71 (d, J = 11.6 Hz, 1H), 2.15−2.05 (m, 1H), 1.27 (s, 9H), 1.03 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.9, 171.1, 68.2, 65.0, 61.6, 56.7, 50.0, 28.7, 28.4, 19.7, 17.3.

*(3S,5S)-5-((S)-sec-Butyl)-N-(tert-butyl)-3-(hydroxymethyl)-6-oxomorpholine-3-carboxamide (syn-**29**).* Inseparable mixture *syn*/*anti* (53/47). Overall yield: 127.5 mg; 64%. ^{1}H NMR (500 MHz, DMSO) δ 7.78 (s, 1H), 5.18 (t, J = 5.7 Hz, 1H), 4.41 (d, J = 11.3 Hz, 1H), 4.32 (d, J = 11.3 Hz, 1H), 3.65 (dd, J = 6.9, 4.0 Hz, 1H), 3.50 (dd, J = 5.7, 2.7 Hz, 2H), 2.97 (d, J = 6.9 Hz, 1H), 1.82−1.74 (m, 1H), 1.60−1.47 (m, 1H), 1.33−1.27 (m, 1H), 1.23 (s, 9H), 0.99 (d, J = 7.0 Hz, 3H), 0.90 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.6, 171.3, 68.1, 63.1, 61.9, 56.7, 49.9, 35.8, 28.3, 24.8, 15.0, 12.1. HRMS calcd for $C_{14}H_{27}O_4N_2$ $[M + H]^+$: 287.1965 found: 287.1966; $C_{14}H_{26}O_4N_2Na$ $[M + Na]^+$: 309.1785 found: 309.1785.

*(3R,5S)-5-((S)-sec-Butyl)-N-(tert-butyl)-3-(hydroxymethyl)-6-oxomorpholine-3-carboxamide (anti-**29**).* ^{1}H NMR (500 MHz, DMSO)

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δ 7.63 (s, 1H), 5.10 (t, J = 5.8 Hz, 1H), 4.37 (d, J = 11.7 Hz, 1H), 4.15 (d, J = 11.8 Hz, 1H), 3.56 (dd, J = 10.9, 5.9 Hz, 1H), 3.45 (dd, J = 10.9, 5.8 Hz, 1H), 3.36 (dd, J = 11.1, 5.2 Hz, 1H), 2.70 (d, J = 11.3 Hz, 1H), 1.89−1.81 (m, 1H), 1.60−1.47 (m, 1H), 1.27 (s, 9H), 1.24−1.17 (m, 1H), 1.01 (d, J = 6.8 Hz, 3H), 0.88 (t, J = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.7, 171.0, 68.2, 64.9, 61.6, 56.5, 50.0, 35.0, 28.4, 24.0, 16.0, 11.5.

*(3S,5S)-N-(tert-Butyl)-3-(hydroxymethyl)-5-isobutyl-6-oxomorpholine-3-carboxamide (syn-**30**).* Inseparable mixture *syn*/*anti* (32/68). Overall yield: 126.7 mg; 64%. ^{1}H NMR (500 MHz, DMSO) δ = 7.70 (s, 1H), 5.20 (t, J = 5.6 Hz, 1H), 4.44 (d, J = 11.4 Hz, 1H), 4.38 (d, J = 11.4 Hz, 1H), 3.73 (m, 1H), 3.49 (dd, J = 5.6, 3.0 Hz, 2H), 3.06 (d, J = 7.2 Hz, 1H), 1.84−1.77 (m, 1H), 1.65−1.59 (m, 1H), 1.40−1.33 (m, 1H), 1.23 (s, 9H), 0.93 (d, J = 6.7 Hz, 3H), 0.90 (d, J = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 172.9, 171.6, 68.4, 63.3, 61.9, 50.2, 50.0, 40.5, 28.3, 24.0, 23.1, 22.0. HRMS calcd for $C_{14}H_{27}O_4N_2$ [M + H]$^+$: 287.1965 found: 287.1967; $C_{14}H_{26}O_4N_2Na$ [M + Na]$^+$: 309.1785 found: 309.1786

*(3R,5S)-N-(tert-Butyl)-3-(hydroxymethyl)-5-isobutyl-6-oxomorpholine-3-carboxamide (anti-**30**).* ^{1}H NMR (500 MHz, DMSO) δ 7.75 (s, 1H), 4.96 (t, J = 5.8 Hz, 1H), 4.35 (d, J = 12.0 Hz, 1H), 4.17 (d, J = 12.1 Hz, 1H), 3.59 (dd, J = 10.8, 6.0 Hz, 1H), 3.46 (dd, J = 10.8, 5.7 Hz, 1H), 3.47−3.42 (m, 1H), 2.78 (d, J = 12.2 Hz, 1H), 1.91−1.84 (m, 1H), 1.59−1.54 (m, 1H), 1.47−1.40 (m, 1H), 1.27 (s, 9H), 0.95 (d, J = 6.7 Hz, 3H), 0.91 (d, J = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 173.4, 171.4, 67.6, 65.1, 61.5, 49.8, 49.8, 38.5, 28.3, 23.9, 23.5, 21.2.

*(3S,5S)-N-(tert-Butyl)-3-(hydroxymethyl)-5-(2-(methylthio)ethyl)-6-oxomorpholine-3-carboxamide (syn-**31**).* Inseparable mixture *syn*/*anti* (35/65). Overall yield: 121.0 mg; 57%. ^{1}H NMR (500 MHz, DMSO) δ 7.71 (s, 1H), 5.16 (t, J = 5.6 Hz, 1H), 4.46 (d, J = 11.3 Hz, 1H), 4.35 (d, J = 11.3 Hz, 1H), 3.85 (dd, J = 12.6, 5.9 Hz, 1H), 3.48 (dd, J = 5.7, 1.2 Hz, 2H), 3.22 (d, J = 7.1 Hz, 1H), 2.63−2.58 (m, 2H), 2.07 (s, 3H), 2.02−1.95 (m, 1H), 1.83−1.79 (m, 1H), 1.23 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 172.3, 171.4, 68.7, 63.1, 62.2, 51.1, 50.1, 30.9, 29.3, 28.3, 14.7. HRMS calcd for $C_{13}H_{25}O_4N_2S$ [M + H]$^+$: 305.1530 found: 305.1531; $C_{13}H_{24}O_4N_2SNa$ [M + Na]$^+$: 327.1349 found: 327.1350.

*(3R,5S)-N-(tert-Butyl)-3-(hydroxymethyl)-5-(2-(methylthio)ethyl)-6-oxomorpholine-3-carboxamide (anti-**31**).* ^{1}H NMR (500 MHz, DMSO) δ 7.70 (s, 1H), 4.99 (t, J = 5.7 Hz, 1H), 4.32 (d, J = 12.0 Hz, 1H), 4.20 (d, J = 12.0 Hz, 1H), 3.59 (dd, J = 10.8, 6.0 Hz, 1H), 3.58−3.53 (m, 1H), 3.45 (dd, J = 10.9, 5.7 Hz, 1H), 2.91 (d, J = 12.0 Hz, 1H), 2.65 (ddd, J = 8.2, 6.0, 3.7 Hz, 2H), 2.11−2.07 (m, 1H), 2.05 (s, 3H), 1.79−1.73 (m, 1H), 1.28 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 172.8, 171.1, 68.0, 65.1, 61.5, 50.4, 50.0, 29.7, 28.7, 28.3, 14.4.

*(3R,5R)-N-(tert-Butyl)-3-(hydroxymethyl)-5-(2-(methylthio)ethyl)-6-oxomorpholine-3-carboxamide (syn-ent-**31**).* Inseparable mixture *syn*/*anti* (35/65). Overall yield: 126.6 mg; 60%. ^{1}H NMR (500 MHz, DMSO) δ 7.71 (s, 1H), 5.16 (t, J = 5.6 Hz, 1H), 4.46 (d, J = 11.3 Hz, 1H), 4.35 (d, J = 11.3 Hz, 1H), 3.85 (dd, J = 12.6, 5.9 Hz, 1H), 3.48 (dd, J = 5.7, 1.2 Hz, 2H), 3.22 (d, J = 7.1 Hz, 1H), 2.63−2.58 (m, 2H), 2.07 (s, 3H), 2.02−1.95 (m, 1H), 1.83−1.79 (m, 1H), 1.23 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 172.3, 171.4, 68.7, 63.1, 62.2, 51.1, 50.1, 30.9, 29.3, 28.3, 14.7. HRMS calcd for $C_{13}H_{25}O_4N_2S$ [M + H]$^+$: 305.1530 found: 305.1530; $C_{13}H_{24}O_4N_2SNa$ [M + Na]$^+$: 327.1349 found: 327.1350.

*(3S,5R)-N-(tert-Butyl)-3-(hydroxymethyl)-5-(2-(methylthio)ethyl)-6-oxomorpholine-3-carboxamide (anti-ent-**31**).* ^{1}H NMR (500 MHz, DMSO) δ 7.70 (s, 1H), 4.99 (t, J = 5.7 Hz, 1H), 4.32 (d, J = 12.0 Hz, 1H), 4.20 (d, J = 12.0 Hz, 1H), 3.59 (dd, J = 10.8, 6.0 Hz, 1H), 3.58−3.53 (m, 1H), 3.45 (dd, J = 10.9, 5.7 Hz, 1H), 2.91 (d, J = 12.0 Hz, 1H), 2.65 (ddd, J = 8.2, 6.0, 3.7 Hz, 2H), 2.11−2.07 (m, 1H), 2.05 (s, 3H), 1.79−1.73 (m, 1H), 1.28 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 172.8, 171.1, 68.0, 65.1, 61.5, 50.4, 50.0, 29.7, 28.7, 28.3, 14.4.

*(3S,5S)-N,5-Di-tert-butyl-3-(hydroxymethyl)-6-oxomorpholine-3-carboxamide (syn-**32**).* Inseparable mixture *syn*/*anti* (53/47). Overall yield: 148.5 mg; 75%. ^{1}H NMR (500 MHz, DMSO) δ 7.75 (s, 1H), 5.30 (t, J = 5.6 Hz, 1H), 4.40 (d, J = 11.2 Hz, 1H), 4.37 (d, J = 11.1 Hz, 1H), 3.50 (d, J = 5.6 Hz, 2H), 3.47 (d, J = 7.4 Hz, 1H), 2.86 (d, J = 7.5 Hz, 1H), 1.23 (s, 9H), 1.06 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 171.4, 170.3, 68.5, 62.7, 62.1, 59.7, 50.0, 33.1, 28.2, 26.0. HRMS calcd for $C_{14}H_{27}O_4N_2$ [M + H]$^+$: 287.1965 found: 287.1966; $C_{14}H_{26}O_4N_2Na$ [M + Na]$^+$: 309.1785 found: 309.1784.

*(3R,5S)-N,5-Di-tert-butyl-3-(hydroxymethyl)-6-oxomorpholine-3-carboxamide (anti-**32**).* ^{1}H NMR (500 MHz, DMSO) δ 7.63 (s, 1H), 5.12 (t, J = 6.0 Hz, 1H), 4.31 (d, J = 11.9 Hz, 1H), 4.13 (d, J = 11.9 Hz, 1H), 3.59 (dd, J = 11.0, 6.2 Hz, 1H), 3.46 (dd, J = 11.0, 5.9 Hz, 1H), 3.21 (d, J = 12.3 Hz, 1H), 2.66 (d, J = 12.3 Hz, 1H), 1.27 (s, 9H), 1.07 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 171.3, 170.8, 67.9, 65.1, 62.3, 59.6, 50.0, 33.0, 28.4, 26.3.

*(3S,5S)-5-Benzyl-N-(tert-butyl)-3-(hydroxymethyl)-6-oxomorpholine-3-carboxamide (syn-**33**).* Inseparable mixture *syn*/*anti* (29/71). Overall yield: 162.8 mg; 73%. ^{1}H NMR (500 MHz, DMSO) δ 7.58 (s, 1H), 7.25−7.18 (m, 5H), 5.17 (t, J = 5.4 Hz, 1H), 4.43 (d, J = 11.3 Hz, 1H), 4.38 (d, J = 11.3 Hz, 1H), 4.13 (dd, J = 6.5, 6.3, 5.3 Hz, 1H), 3.47 (dd, J = 5.3, 3.0 Hz, 2H), 3.11 (dd, J = 14.1, 5.3 Hz, 1H), 3.05 (d, J = 6.7 Hz, 1H), 2.89 (dd, J = 14.1, 6.5 Hz, 1H), 1.15 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 172.0, 171.4, 137.7, 129.8, 128.2, 126.4, 68.5, 62.8, 62.1, 53.0, 49.9, 36.9, 28.2. HRMS calcd for $C_{17}H_{25}O_4N_2$ [M + H]$^+$: 321.1809 found: 321.1807; $C_{17}H_{24}O_4N_2Na$ [M + Na]$^+$: 343.1628 found: 343.1626.

*(3R,5S)-5-Benzyl-N-(tert-butyl)-3-(hydroxymethyl)-6-oxomorpholine-3-carboxamide (anti-**33**).* ^{1}H NMR (500 MHz, DMSO) δ 7.36−7.28 (m, 5H), 7.14 (s, 1H), 4.98 (t, J = 5.8 Hz, 1H), 4.25 (d, J = 12.2 Hz, 1H), 4.20 (d, J = 12.2 Hz, 1H), 3.66 (ddd, J = 12.9, 11.2, 3.2 Hz, 1H), 3.59 (dd, J = 10.8, 6.0 Hz, 1H), 3.48 (dd, J = 10.8, 5.6 Hz, 1H), 3.19 (dd, J = 14.1, 3.2 Hz, 1H), 3.05 (d, J = 12.8 Hz, 1H), 2.67 (dd, J = 14.1, 11.1 Hz, 1H), 0.95 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 173.0, 171.2, 138.9, 129.2, 128.3, 126.3, 67.6, 65.2, 61.6, 53.7, 49.4, 35.3, 28.1.

*(3R,5R)-5-Benzyl-N-(tert-butyl)-3-(hydroxymethyl)-6-oxomorpholine-3-carboxamide (syn-ent-**33**).* Inseparable mixture *syn*/*anti* (29/71). Overall yield: 165.7 mg; 74%. ^{1}H NMR (500 MHz, DMSO) δ 7.58 (s, 1H), 7.25−7.18 (m, 5H), 5.17 (t, J = 5.4 Hz, 1H), 4.43 (d, J = 11.3 Hz, 1H), 4.38 (d, J = 11.3 Hz, 1H), 4.13 (dd, J = 6.5, 6.3, 5.3 Hz, 1H), 3.47 (dd, J = 5.3, 3.0 Hz, 2H), 3.11 (dd, J = 14.1, 5.3 Hz, 1H), 3.05 (d, J = 6.7 Hz, 1H), 2.89 (dd, J = 14.1, 6.5 Hz, 1H), 1.15 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 172.0, 171.4, 137.7, 129.8, 128.2, 126.4, 68.5, 62.8, 62.1, 53.0, 49.9, 36.9, 28.2. HRMS calcd for $C_{17}H_{25}O_4N_2$ [M + H]$^+$: 321.1809 found: 321.1808; $C_{17}H_{24}O_4N_2Na$ [M + Na]$^+$: 343.1628 found: 343.1627.

*(3S,5R)-5-Benzyl-N-(tert-butyl)-3-(hydroxymethyl)-6-oxomorpholine-3-carboxamide (anti-ent-**33**).* ^{1}H NMR (500 MHz, DMSO) δ 7.36−7.28 (m, 5H), 7.14 (s, 1H), 4.98 (t, J = 5.8 Hz, 1H), 4.25 (d, J = 12.2 Hz, 1H), 4.20 (d, J = 12.2 Hz, 1H), 3.66 (ddd, J = 12.9, 11.2, 3.2 Hz, 1H), 3.59 (dd, J = 10.8, 6.0 Hz, 1H), 3.48 (dd, J = 10.8, 5.6 Hz, 1H), 3.19 (dd, J = 14.1, 3.2 Hz, 1H), 3.05 (d, J = 12.8 Hz, 1H), 2.67 (dd, J = 14.1, 11.1 Hz, 1H), 0.95 (s, 9H). ^{13}C NMR (126 MHz, DMSO) δ 173.0, 171.2, 138.9, 129.2, 128.3, 126.3, 67.6, 65.2, 61.6, 53.7, 49.4, 35.3, 28.1.

*(3S,5S)-N-(tert-Butyl)-5-((R)-1-hydroxyethyl)-3-(hydroxymethyl)-6-oxomorpholine-3-carboxamide (syn-**34**).* Inseparable mixture *syn*/*anti* (35/65). Overall yield: 75.8 mg; 40%. ^{1}H NMR (500 MHz, DMSO) δ 8.25 (s, 1H), 5.18 (t, J = 5.7 Hz, 1H), 5.12 (d, J = 5.1 Hz, 1H), 4.42 (d, J = 10.9 Hz, 1H), 4.27 (d, J = 10.9 Hz, 1H), 4.11−4.03 (m, 1H), 3.60 (dd, J = 8.4, 3.1 Hz, 1H), 3.51 (d, J = 5.7 Hz, 2H), 3.05 (d, J = 8.0 Hz, 1H), 1.21 (s, 9H), 1.16 (d, J = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.4, 170.9, 69.4, 65.1, 62.8, 61.5, 57.3, 50.1, 28.2, 20.4. HRMS calcd for $C_{12}H_{23}O_5N_2$ [M + H]$^+$: 275.1601 found: 275.1602; $C_{12}H_{22}O_5N_2Na$ [M + Na]$^+$: 297.1421 found: 297.1422.

*(3R,5S)-N-(tert-Butyl)-5-((R)-1-hydroxyethyl)-3-(hydroxymethyl)-6-oxomorpholine-3-carboxamide (anti-**34**).* ^{1}H NMR (500 MHz, DMSO) δ 7.65 (s, 1H), 5.25 (t, J = 5.4 Hz, 1H), 5.03 (d, J = 4.8 Hz, 1H), 4.36 (d, J = 11.5 Hz, 1H), 4.23−4.20 (m, 1H), 4.19 (d, J = 11.6 Hz, 1H), 3.59 (dd, J = 10.8, 5.4 Hz, 1H), 3.43 (dd, J = 10.7, 5.4 Hz, 1H), 3.38 (dd, J = 10.9, 2.4 Hz, 1H), 2.94 (d, J = 11.0 Hz, 1H), 1.26 (s, 9H), 1.21 (d, J = 6.4 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.1, 170.7, 68.3, 64.6, 64.4, 60.9, 57.5, 50.0, 28.3, 20.3.

*(3R,5R)-N-(tert-Butyl)-5-((R)-1-hydroxyethyl)-3-(hydroxymethyl)-6-oxomorpholine-3-carboxamide (syn-**35**).* Inseparable mixture *syn*/*anti* (35/65); Overall yield: 63.8 mg; 34%; ^{1}H NMR (500 MHz, DMSO) δ 8.25 (s, 1H), 5.18 (t, J = 5.7 Hz, 1H), 5.12 (d, J = 5.1 Hz, 1H), 4.42 (d, J = 10.9 Hz, 1H), 4.27 (d, J = 10.9 Hz, 1H), 4.11−4.03 (m, 1H),

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3.60 (dd, J = 8.4, 3.1 Hz, 1H), 3.51 (d, J = 5.7 Hz, 2H), 3.05 (d, J = 8.0 Hz, 1H), 1.21 (s, 9H), 1.16 (d, J = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.4, 170.9, 69.4, 65.1, 62.8, 61.5, 57.3, 50.1, 28.2, 20.4. HRMS calcd for $C_{12}H_{23}O_5N_2$ $[M + H]^+$: 275.1601 found: 275.1603; $C_{12}H_{22}O_5N_2Na$ $[M + Na]^+$: 297.1421 found: 297.1422.

*(3S,5R)-N-(tert-Butyl)-5-((R)-1-hydroxyethyl)-3-(hydroxymethyl)-6-oxomorpholine-3-carboxamide (anti-**35**).* ^{1}H NMR (500 MHz, DMSO) δ 7.65 (s, 1H), 5.25 (t, J = 5.4 Hz, 1H), 5.03 (d, J = 4.8 Hz, 1H), 4.36 (d, J = 11.5 Hz, 1H), 4.23−4.20 (m, 1H), 4.19 (d, J = 11.6 Hz, 1H), 3.59 (dd, J = 10.8, 5.4 Hz, 1H), 3.43 (dd, J = 10.7, 5.4 Hz, 1H), 3.38 (dd, J = 10.9, 2.4 Hz, 1H), 2.94 (d, J = 11.0 Hz, 1H), 1.26 (s, 9H), 1.21 (d, J = 6.4 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.1, 170.7, 68.3, 64.6, 64.4, 60.9, 57.5, 50.0, 28.3, 20.3.

*(3S,5S)-N-Cyclohexyl-3-(hydroxymethyl)-5-isopropyl-6-oxomorpholine-3-carboxamide (syn-**36**).* Inseparable mixture *syn*/*anti* (47/53). Overall yield: 120.5 mg; 58%. ^{1}H NMR (400 MHz, DMSO) δ 7.81 (d, J = 8.3 Hz, 1H), 5.18 (t, J = 5.8 Hz, 1H), 4.43 (d, J = 11.4 Hz, 1H), 4.34 (d, J = 11.3 Hz, 1H), 3.62 (dd, J = 6.8, 4.0 Hz, 1H), 3.55−3.48 (m, 1H), 3.51 (d, J = 5.8 Hz, 2H), 2.93 (d, J = 7.0 Hz, 1H), 2.15−2.04 (m, 1H), 1.76−1.48 (m, 5H), 1.34−1.10 (m, 5H), 1.01 (d, J = 7.4 Hz, 3H), 0.99 (d, J = 7.7 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 171.4, 171.3, 68.2, 63.1, 61.8, 56.9, 47.4, 32.3, 32.2, 28.8, 25.1, 24.4, 24.1, 18.7, 17.5. HRMS calcd for $C_{15}H_{27}O_4N_2$ $[M + H]^+$: 299.1965 found: 299.1967; $C_{15}H_{26}O_4N_2Na$ $[M + Na]^+$: 321.1785 found: 321.1787.

*(3R,5S)-N-Cyclohexyl-3-(hydroxymethyl)-5-isopropyl-6-oxomorpholine-3-carboxamide (anti-**36**).* ^{1}H NMR (400 MHz, DMSO) δ 7.77 (d, J = 8.3 Hz, 1H), 5.11 (t, J = 5.9 Hz, 1H), 4.40 (d, J = 11.7 Hz, 1H), 4.16 (d, J = 11.6 Hz, 1H), 3.54 (dd, J = 10.9, 5.9 Hz, 1H), 3.53−3.50 (m, 1H), 3.45 (dd, J = 10.9, 5.9 Hz, 1H), 3.33 (dd, J = 10.5, 4.8 Hz, 1H), 2.72 (d, J = 10.6 Hz, 1H), 2.15−2.04 (m, 1H), 1.76−1.48 (m, 5H), 1.34−1.10 (m, 5H), 1.01 (d, J = 6.8 Hz, 3H), 0.94 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 171.6, 170.7, 68.5, 65.0, 61.4, 57.5, 47.4, 32.4, 32.2, 29.0, 25.2, 24.4, 24.1, 19.5, 17.4.

*(3R,5R)-N-Cyclohexyl-3-(hydroxymethyl)-5-isopropyl-6-oxomorpholine-3-carboxamide (syn-ent-**36**).* Inseparable mixture *syn*/*anti* (50/50); Overall yield: 127.2 mg; 61%; ^{1}H NMR (400 MHz, DMSO) δ 7.81 (d, J = 8.3 Hz, 1H), 5.18 (t, J = 5.8 Hz, 1H), 4.43 (d, J = 11.4 Hz, 1H), 4.34 (d, J = 11.3 Hz, 1H), 3.62 (dd, J = 6.8, 4.0 Hz, 1H), 3.55−3.48 (m, 1H), 3.51 (d, J = 5.8 Hz, 2H), 2.93 (d, J = 7.0 Hz, 1H), 2.15−2.04 (m, 1H), 1.76−1.48 (m, 5H), 1.34−1.10 (m, 5H), 1.01 (d, J = 7.4 Hz, 3H), 0.99 (d, J = 7.7 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 171.4, 171.3, 68.2, 63.1, 61.8, 56.9, 47.4, 32.3, 32.2, 28.8, 25.1, 24.4, 24.1, 18.7, 17.5. HRMS calcd for $C_{15}H_{27}O_4N_2$ $[M + H]^+$: 299.1965 found: 299.1966; $C_{15}H_{26}O_4N_2Na$ $[M + Na]^+$: 321.1785 found: 321.1785.

*(3S,5R)-N-Cyclohexyl-3-(hydroxymethyl)-5-isopropyl-6-oxomorpholine-3-carboxamide (anti-ent-**36**).* ^{1}H NMR (400 MHz, DMSO) δ 7.77 (d, J = 8.3 Hz, 1H), 5.11 (t, J = 5.9 Hz, 1H), 4.40 (d, J = 11.7 Hz, 1H), 4.16 (d, J = 11.6 Hz, 1H), 3.54 (dd, J = 10.9, 5.9 Hz, 1H), 3.53−3.50 (m, 1H), 3.45 (dd, J = 10.9, 5.9 Hz, 1H), 3.33 (dd, J = 10.5, 4.8 Hz, 1H), 2.72 (d, J = 10.6 Hz, 1H), 2.15−2.04 (m, 1H), 1.76−1.48 (m, 5H), 1.34−1.10 (m, 5H), 1.01 (d, J = 6.8 Hz, 3H), 0.94 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 171.6, 170.7, 68.5, 65.0, 61.4, 57.5, 47.4, 32.4, 32.2, 29.0, 25.2, 24.4, 24.1, 19.5, 17.4.

*(3S,5S)-3-(Hydroxymethyl)-5-isopropyl-6-oxo-N-(tosylmethyl)-morpholine-3-carboxamide (syn-**37**).* Inseparable mixture *syn*/*anti* (80/20). Overall yield: 176.8 mg; 66%. ^{1}H NMR (500 MHz, DMSO) δ 8.63 (t, J = 6.8 Hz, 1H), 7.68 (d, J = 8.2 Hz, 2H), 7.40 (d, J = 8.2 Hz, 2H), 5.26 (t, J = 5.7 Hz, 1H), 4.79 (dd, J = 14.0, 7.6 Hz, 1H), 4.61 (dd, J = 14.0, 6.2 Hz, 1H), 4.29 (d, J = 11.6 Hz, 1H), 4.23 (d, J = 11.7 Hz, 1H), 3.60 (dd, J = 6.3, 4.2 Hz, 1H), 3.44 (dd, J = 11.0, 5.8 Hz, 1H), 3.40 (dd, J = 11.0, 5.8 Hz, 1H), 2.84 (d, J = 6.5 Hz, 1H), 2.40 (s, 3H), 2.07−2.03 (m, 1H), 0.99 (d, J = 7.0 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 172.8, 171.3, 144.6, 134.4, 129.8, 128.6, 67.6, 62.9, 62.0, 60.3, 56.8, 28.9, 21.2, 18.7, 17.4. HRMS calcd for $C_{17}H_{25}O_6N_2S$ $[M + H]^+$: 385.1428 found: 385.1430; $C_{17}H_{24}O_6N_2SNa$ $[M + Na]^+$: 407.1247 found: 407.1247.

*(3R,5S)-3-(Hydroxymethyl)-5-isopropyl-6-oxo-N-(tosylmethyl)-morpholine-3-carboxamide (anti-**37**).* ^{1}H NMR (500 MHz, DMSO) δ 8.78 (t, J = 6.8 Hz, 1H), 7.73 (d, J = 6.0 Hz, 1H), 7.72 (d, J = 6.1 Hz, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.42 (d, J = 8.7 Hz, 1H), 5.19 (t, J = 5.8 Hz, 1H), 4.80 (dd, J = 14.3, 7.3 Hz, 1H), 4.64 (dd, J = 14.5, 5.9 Hz, 1H), 4.24 (d, J = 11.5 Hz, 1H), 4.07 (d, J = 11.6 Hz, 1H), 3.50−3.45 (m, 1H), 3.42−3.38 (m, 1H), 3.27 (dd, J = 9.6, 4.6 Hz, 1H), 2.70 (d, J = 9.7 Hz, 1H), 2.40 (s, 3H), 2.12−2.07 (m, 1H), 1.01 (d, J = 6.9 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 172.0, 170.9, 144.7, 134.7, 129.9, 128.6, 68.3, 64.7, 61.5, 58.6, 57.4, 29.4, 21.2, 19.1, 17.5.

*(3R,5R)-3-(Hydroxymethyl)-5-isopropyl-6-oxo-N-(tosylmethyl)-morpholine-3-carboxamide (syn-ent-**37**).* Inseparable mixture *syn*/*anti* (85/15). Overall yield: 186.0 mg; 70%. ^{1}H NMR (500 MHz, DMSO) δ 8.63 (t, J = 6.8 Hz, 1H), 7.68 (d, J = 8.2 Hz, 2H), 7.40 (d, J = 8.2 Hz, 2H), 5.26 (t, J = 5.7 Hz, 1H), 4.79 (dd, J = 14.0, 7.6 Hz, 1H), 4.61 (dd, J = 14.0, 6.2 Hz, 1H), 4.29 (d, J = 11.6 Hz, 1H), 4.23 (d, J = 11.7 Hz, 1H), 3.60 (dd, J = 6.3, 4.2 Hz, 1H), 3.44 (dd, J = 11.0, 5.8 Hz, 1H), 3.40 (dd, J = 11.0, 5.8 Hz, 1H), 2.84 (d, J = 6.5 Hz, 1H), 2.40 (s, 3H), 2.07−2.03 (m, 1H), 0.99 (d, J = 7.0 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 172.8, 171.3, 144.6, 134.4, 129.8, 128.6, 67.6, 62.9, 62.0, 60.3, 56.8, 28.9, 21.2, 18.7, 17.4. HRMS calcd for $C_{17}H_{25}O_6N_2S$ $[M + H]^+$: 385.1428 found: 385.1428; $C_{17}H_{24}O_6N_2SNa$ $[M + Na]^+$: 407.1247 found: 407.1246.

*(3S,5R)-3-(Hydroxymethyl)-5-isopropyl-6-oxo-N-(tosylmethyl)-morpholine-3-carboxamide (anti-ent-**37**).* ^{1}H NMR (500 MHz, DMSO) δ 8.78 (t, J = 6.8 Hz, 1H), 7.73 (d, J = 6.0 Hz, 1H), 7.72 (d, J = 6.1 Hz, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.42 (d, J = 8.7 Hz, 1H), 5.19 (t, J = 5.8 Hz, 1H), 4.80 (dd, J = 14.3, 7.3 Hz, 1H), 4.64 (dd, J = 14.5, 5.9 Hz, 1H), 4.24 (d, J = 11.5 Hz, 1H), 4.07 (d, J = 11.6 Hz, 1H), 3.50−3.45 (m, 1H), 3.42−3.38 (m, 1H), 3.27 (dd, J = 9.6, 4.6 Hz, 1H), 2.70 (d, J = 9.7 Hz, 1H), 2.40 (s, 3H), 2.12−2.07 (m, 1H), 1.01 (d, J = 6.9 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 172.0, 170.9, 144.7, 134.7, 129.9, 128.6, 68.3, 64.7, 61.5, 58.6, 57.4, 29.4, 21.2, 19.1, 17.5.

*Ethyl-((3S,5S)-3-(Hydroxymethyl)-5-isopropyl-6-oxomorpholine-3-carbonyl)glycinate (syn-**38**).* Inseparable mixture *syn*/*anti* (76/24). Overall yield: 137.1 mg; 65%. ^{1}H NMR (400 MHz, DMSO) δ 8.33 (t, J = 5.9 Hz, 1H), 5.23 (t, J = 5.8 Hz, 1H), 4.43 (d, J = 11.5 Hz, 1H), 4.36 (d, J = 11.5 Hz, 1H), 4.08 (q, J = 7.1 Hz, 2H), 3.89 (dd, J = 10.4, 5.9 Hz, 2H), 3.60 (dd, J = 6.9, 4.5 Hz, 1H), 3.53 (dd, J = 10.9, 5.8 Hz, 2H), 2.90 (d, J = 7.0 Hz, 1H), 2.12−2.03 (m, 1H), 1.18 (t, J = 7.1 Hz, 3H), 1.02 (d, J = 4.6 Hz, 3H), 1.00 (d, J = 4.4 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 173.2, 171.4, 169.5, 67.9, 63.2, 61.7, 60.6, 57.1, 41.2, 29.0, 18.8, 17.6, 14.0. HRMS calcd for $C_{13}H_{23}O_6N_2$ $[M + H]^+$: 303.1551 found: 303.1552; $C_{13}H_{22}O_6N_2Na$ $[M + Na]^+$: 325.1370 found: 325.1372.

*Ethyl-((3R,5S)-3-(Hydroxymethyl)-5-isopropyl-6-oxomorpholine-3-carbonyl)glycinate (anti-**38**).* ^{1}H NMR (400 MHz, DMSO) δ 8.40 (t, J = 5.9 Hz, 1H), 5.19 (t, J = 6.0 Hz, 1H), 4.47 (d, J = 11.4 Hz, 1H), 4.19 (d, J = 11.5 Hz, 1H), 4.09 (q, J = 7.1 Hz, 2H), 3.99−3.92 (m, 1H), 3.86−3.80 (m, 1H), 3.57 (dd, J = 8.4, 5.6 Hz, 1H), 3.54−3.49 (m, 1H), 3.49−3.45 (m, 1H), 2.70 (d, J = 10.0 Hz, 1H), 2.19−2.11 (m, 1H), 1.18 (t, J = 7.1 Hz, 3H), 1.02 (d, J = 6.8 Hz, 3H), 0.96 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 172.4, 171.1, 169.7, 68.8, 64.9, 61.3, 60.6, 57.5, 41.0, 29.4, 19.2, 17.5, 14.0.

*Ethyl-((3R,5R)-3-(Hydroxymethyl)-5-isopropyl-6-oxomorpholine-3-carbonyl)glycinate (syn-ent-**38**).* Inseparable mixture *syn*/*anti* (70:30). Overall yield: 132.5 mg; 63%. ^{1}H NMR (400 MHz, DMSO) δ 8.33 (t, J = 5.9 Hz, 1H), 5.23 (t, J = 5.8 Hz, 1H), 4.43 (d, J = 11.5 Hz, 1H), 4.36 (d, J = 11.5 Hz, 1H), 4.08 (q, J = 7.1 Hz, 2H), 3.89 (dd, J = 10.4, 5.9 Hz, 2H), 3.60 (dd, J = 6.9, 4.5 Hz, 1H), 3.53 (dd, J = 10.9, 5.8 Hz, 2H), 2.90 (d, J = 7.0 Hz, 1H), 2.12−2.03 (m, 1H), 1.18 (t, J = 7.1 Hz, 3H), 1.02 (d, J = 4.6 Hz, 3H), 1.00 (d, J = 4.4 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 173.2, 171.4, 169.5, 67.9, 63.2, 61.7, 60.6, 57.1, 41.2, 29.0, 18.8, 17.6, 14.0. HRMS calcd for $C_{13}H_{23}O_6N_2$ $[M + H]^+$: 303.1551 found: 303.1553; $C_{13}H_{22}O_6N_2Na$ $[M + Na]^+$: 325.1370 found: 325.1371.

*Ethyl-((3S,5R)-3-(Hydroxymethyl)-5-isopropyl-6-oxomorpholine-3-carbonyl)glycinate (anti-ent-**38**).* ^{1}H NMR (400 MHz, DMSO) δ 8.40 (t, J = 5.9 Hz, 1H), 5.19 (t, J = 6.0 Hz, 1H), 4.47 (d, J = 11.4 Hz, 1H), 4.19 (d, J = 11.5 Hz, 1H), 4.09 (q, J = 7.1 Hz, 2H), 3.99−3.92 (m, 1H), 3.86−3.80 (m, 1H), 3.57 (dd, J = 8.4, 5.6 Hz, 1H), 3.54−3.49 (m, 1H), 3.49−3.45 (m, 1H), 2.70 (d, J = 10.0 Hz, 1H), 2.19−2.11 (m, 1H), 1.18 (t, J = 7.1 Hz, 3H), 1.02 (d, J = 6.8 Hz, 3H), 0.96 (d, J = 6.8 Hz, 3H).

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^{13}C NMR (101 MHz, DMSO) δ 172.4, 171.1, 169.7, 68.8, 64.9, 61.3, 60.6, 57.5, 41.0, 29.4, 19.2, 17.5, 14.0.

*(3R,5S)-N-(tert-Butyl)-3-((R)-1,2-dihydroxyethyl)-5-isopropyl-6-oxomorpholine-3-carboxamide (**40**).* Inseparable mixture of **40**/**41**/**42** (49/34/18). Overall yield: 130.6 mg; 62%. ^{1}H NMR (500 MHz, DMSO) δ 7.68 (s, 1H), 5.48 (d, J = 5.4 Hz, 1H), 4.81 (s, 1H), 4.48 (d, J = 11.7 Hz, 1H), 4.42 (d, J = 11.6 Hz, 1H), 3.67 (dd, J = 9.7, 5.4 Hz, 1H), 3.59 (d, J = 11.1 Hz, 1H), 3.56−3.52 (m, 1H), 3.35−3.32 (m, 1H), 3.02 (d, J = 8.9 Hz, 1H), 2.12−2.05 (m, 1H), 1.24 (s, 9H), 1.00 (d, J = 6.9 Hz, 3H), 0.96 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 172.1, 171.7, 73.1, 69.1, 62.3, 62.3, 55.9, 50.2, 28.3, 28.0, 18.9, 17.2. HRMS calcd for $C_{14}H_{27}O_5N_2$ $[M + H]^+$: 303.1914 found: 303.1916; $C_{14}H_{26}O_5N_2Na$ $[M + Na]^+$: 325.1734 found: 325.1735

*(2R,3R,5S)-N-(tert-Butyl)-2,3-bis(hydroxymethyl)-5-isopropyl-6-oxomorpholine-3-carboxamide (**41**).* ^{1}H NMR (500 MHz, DMSO) δ 7.80 (s, 1H), 5.09 (s, 1H), 5.00 (t, J = 5.5 Hz, 1H), 4.36 (dd, J = 7.4, 2.7 Hz, 1H), 4.05 (d, J = 11.7 Hz, 1H), 3.77−3.70 (m, 1H), 3.54 (dd, J = 10.7, 5.9 Hz, 1H), 3.47 (dd, J = 11.2, 5.5 Hz, 1H), 3.27 (dd, J = 12.8, 5.2 Hz, 1H), 2.66 (d, J = 12.9 Hz, 1H), 2.19−2.11 (m, 1H), 1.27 (s, 9H), 1.06 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 172.4, 170.9, 79.3, 63.7, 62.2, 60.5, 56.4, 49.9, 28.3, 27.4, 20.0, 17.2.

*(3S,5R,6R)-N-(tert-Butyl)-6-hydroxy-5-(hydroxymethyl)-3-isopropyl-2-oxo-1,4-oxazepane-5-carboxamide (**42**).* ^{1}H NMR (500 MHz, DMSO) δ 7.60 (s, 1H), 5.26 (s, 1H), 4.68 (s, 1H), 4.33 (s, 2H), 3.77−3.70 (m, 1H), 3.42−3.37 (m, 1H), 3.34−3.27 (m, 1H), 3.22 (dd, J = 11.2, 4.9 Hz, 1H), 2.74 (d, J = 11.3 Hz, 1H), 2.15−2.10 (m, 1H), 1.26 (s, 9H), 1.02 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 6.8 Hz, 3H). ^{13}C NMR (125 MHz, DMSO) δ 171.7, 170.7, 74.5, 69.6, 62.9, 61.8, 57.3, 50.1, 28.5, 28.3, 19.6, 17.2.

*(3S,5R)-N-(tert-Butyl)-3-((R)-1,2-dihydroxyethyl)-5-isopropyl-6-oxomorpholine-3-carboxamide (syn-**43**).* Yield: 49.1 mg; 24%. ^{1}H NMR (500 MHz, DMSO) δ 7.91 (s, 1H), 5.36 (d, J = 6.1 Hz, 1H), 4.84 (t, J = 5.3 Hz, 1H), 4.52 (d, J = 10.9 Hz, 1H), 4.45 (d, J = 11.0 Hz, 1H), 3.67−3.63 (m, 1H), 3.63 (dd, J = 6.5, 3.4 Hz, 1H), 3.43−3.38 (m, 2H), 3.15 (d, J = 6.6 Hz, 1H), 2.13−2.05 (m, 1H), 1.23 (s, 9H), 1.00 (d, J = 7.0 Hz, 3H), 0.97 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.5, 71.2, 69.1, 64.1, 61.9, 56.7, 49.9, 28.5, 28.1, 18.6, 17.1. $[\alpha]_D$ = +54 (c = 1.0, methanol). HRMS calcd for $C_{14}H_{27}O_5N_2$ $[M + H]^+$: 303.1914 found: 303.1917; $C_{14}H_{26}O_5N_2Na$ $[M + Na]^+$: 325.1734 found: 325.1737.

*(3R,5R)-N-(tert-Butyl)-3-((R)-1,2-dihydroxyethyl)-5-isopropyl-6-oxomorpholine-3-carboxamide (anti-**43**).* Yield: 28.6 mg; 14%. ^{1}H NMR (500 MHz, DMSO) δ 7.60 (s, 1H), 5.27 (t, J = 6.2 Hz, 1H), 4.77 (t, J = 5.1 Hz, 1H), 4.34 (d, J = 11.9 Hz, 1H), 4.29 (d, J = 11.9 Hz, 1H), 3.62−3.57 (m, 1H), 3.57−3.52 (m, 1H), 3.43−3.38 (m, 1H), 3.33 (m, 1H), 3.16 (d, J = 5.1 Hz, 1H), 2.13−2.02 (m, 1H), 1.27 (s, 9H), 1.00 (d, J = 6.6, 3H), 0.90 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.9, 171.0, 73.2, 67.8, 62.6, 62.0, 57.0, 50.1, 28.7, 28.3, 19.5, 17.0. $[\alpha]_D$ = +82 (c = 1.0, methanol). HRMS calcd for $C_{14}H_{27}O_5N_2$ $[M + H]^+$: 303.1914 found: 303.1917; $C_{14}H_{26}O_5N_2Na$ $[M + Na]^+$: 325.1734 found: 325.1737.

*(3R,5S)-N-(tert-Butyl)-5-isopropyl-6-oxo-3-((1R,2S,3R)-1,2,3,4-tetrahydroxybutyl)morpholine-3-carboxamide (syn-**47**).* Overall yield: 126.6 mg; 50%. Inseparable mixture *syn*/*anti* (45/55). ^{1}H NMR (500 MHz, DMSO) δ 7.88 (s, 1H), 5.05 (d, J = 7.2 Hz, 1H), 4.91 (d, J = 7.2 Hz, 1H), 4.55 (d, J = 5.4 Hz, 1H), 4.46 (d, J = 11.3 Hz, 1H), 4.45 (t, J = 5.5 Hz, 1H), 4.38 (d, J = 11.1 Hz, 1H), 4.01 (d, J = 7.2 Hz, 1H), 3.62−3.59 (m, 1H), 3.59−3.56 (m, 1H), 3.51−3.47 (m, 1H), 3.47−3.43 (m, 1H), 3.40 (dd, J = 11.9, 4.4 Hz, 1H), 3.38−3.31 (m, 1H), 2.13−2.04 (m, 1H), 1.22 (s, 9H), 0.97 (d, J = 7.0 Hz, 6H), 0.96 (d, J = 6.7 Hz, 6H). ^{13}C NMR (126 MHz, DMSO) δ 172.2, 172.0, 71.1, 70.7, 68.7, 68.4, 64.3, 63.3, 56.0, 49.9, 28.3, 28.3, 18.8, 17.1. HRMS calcd for $C_{16}H_{31}O_7N_2$ $[M + H]^+$: 363.2126 found: 363.2128; $C_{16}H_{30}O_7N_2Na$ $[M + Na]^+$: 385.1945 found: 385.1947.

*(3S,5S)-N-(tert-Butyl)-5-isopropyl-6-oxo-3-((1R,2S,3R)-1,2,3,4-tetrahydroxybutyl)morpholine-3-carboxamide (anti-**47**).* ^{1}H NMR (500 MHz, DMSO) δ = 7.94 (s, 1H), 4.93 (d, J = 7.6 Hz, 1H), 4.69 (d, J = 7.7 Hz, 1H), 4.45 (d, J = 5.1 Hz, 1H), 4.38 (d, J = 11.9 Hz, 1H), 4.35 (t, J = 5.6 Hz, 1H), 4.30 (d, J = 11.8 Hz, 1H), 4.02 (d, J = 7.6 Hz, 1H) 3.65−3.58 (m, 1H), 3.54 (ddd, J = 10.8, 5.5, 2.8 Hz, 1H), 3.43−3.38 (m, 1H), 3.34−3.29 (m, 1H), 3.21 (dd, J = 11.4, 4.6 Hz, 1H), 3.13 (d, J = 11.4 Hz, 1H), 2.12−2.04 (m, 1H), 1.27 (s, 9H), 1.02 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.8, 171.3, 71.1, 70.9, 70.7, 70.0, 64.7, 63.3, 57.2, 50.0, 28.4, 28.3, 19.7, 17.1.

*(3S,5R)-N-(tert-Butyl)-5-isopropyl-6-oxo-3-((1R,2S,3R)-1,2,3,4-tetrahydroxybutyl)morpholine-3-carboxamide (syn-**48**).* Inseparable mixture *syn*/*anti* (77/32). Overall yield: 74.6 mg; 30%. ^{1}H NMR (500 MHz, DMSO) δ 8.07 (s, 1H), 5.13 (d, J = 7.6 Hz, 1H), 5.05 (d, J = 7.0 Hz, 1H), 4.54 (d, J = 10.9 Hz, 1H), 4.51 (d, J = 5.4 Hz, 1H), 4.46 (d, J = 11.0 Hz, 1H), 4.40 (t, J = 5.7 Hz, 1H), 3.95 (d, J = 7.5 Hz, 1H), 3.73 (d, J = 6.0 Hz, 1H), 3.61−3.58 (m, 1H), 3.57−3.52 (m, 1H), 3.44−3.38 (m, 1H), 3.36−3.32 (m, 1H), 3.31 (dd, J = 13.2, 6.4 Hz, 1H), 2.08 (dtd, J = 13.7, 6.8, 3.3 Hz, 1H), 1.23 (s, 9H), 0.97 (d, J = 12.7 Hz, 3H), 0.96 (d, J = 12.4 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.8, 171.8, 71.4, 71.0, 69.2, 67.6, 65.5, 63.2, 56.8, 49.9, 28.5, 28.1, 18.8, 17.0. HRMS calcd for $C_{16}H_{31}O_7N_2$ $[M + H]^+$: 363.2126 found: 363.2126; $C_{16}H_{30}O_7N_2Na$ $[M + Na]^+$: 385.1945 found: 385.1944.

*(3R,5R)-N-(tert-Butyl)-5-isopropyl-6-oxo-3-((1R,2S,3R)-1,2,3,4-tetrahydroxybutyl)morpholine-3-carboxamide (anti-**48**).* ^{1}H NMR (500 MHz, DMSO) δ 7.75 (s, 1H), 4.86 (d, J = 7.5 Hz, 1H), 4.82 (d, J = 7.3 Hz, 1H), 4.58 (d, J = 6.0 Hz, 1H), 4.48 (t, J = 5.5 Hz, 1H), 4.26 (d, J = 12.4 Hz, 1H), 4.20 (d, J = 12.5 Hz, 1H), 3.99 (d, J = 7.5 Hz, 1H), 3.57−3.52 (m, 1H), 3.55−3.51 (m, 1H), 3.44−3.38 (m, 2H), 3.36−3.32 (m, 1H), 3.21 (dd, J = 12.6, 3.9 Hz, 1H), 2.19−2.10 (m, 1H), 1.27 (s, 9H), 1.04 (d, J = 6.9 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 172.5, 171.9, 71.1, 70.6, 70.5, 67.6, 63.9, 63.1, 56.5, 49.8, 28.4, 27.5, 19.8, 16.5.

*(3R,5S)-N-(tert-Butyl)-5-isopropyl-6-oxo-3-((1R,2S,3S)-1,2,3,4-tetrahydroxybutyl) morpholine-3-carboxamide (syn-**49**).* Inseparable mixture *syn*/*anti* (70/30). Overall yield: 90.6 mg; 36%. ^{1}H NMR (500 MHz, DMSO) δ 7.83 (s, 1H), 5.14 (d, J = 5.8 Hz, 1H), 4.84 (d, J = 4.8 Hz, 1H), 4.79 (d, J = 6.7 Hz, 1H), 4.61 (t, J = 5.5 Hz, 1H), 4.47 (d, J = 11.2 Hz, 1H), 4.38 (d, J = 11.2 Hz, 1H), 3.84 (dd, J = 5.7, 1.4 Hz, 1H), 3.65 (t, J = 5.1 Hz, 1H), 3.61 (dd, J = 7.9, 3.6 Hz, 1H), 3.53−3.51 (m, 1H), 3.46 (dd, J = 11.0, 5.3 Hz, 1H), 3.39 (d, J = 7.8 Hz, 2H), 2.15−1.99 (m, 1H), 1.22 (s, 9H), 0.98 (d, J = 7.3 Hz, 3H), 0.96 (d, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 172.0, 171.8, 73.6, 71.3, 69.8, 68.7, 63.9, 62.2, 56.0, 50.0, 28.4, 28.3, 18.9, 17.1. HRMS calcd for $C_{16}H_{31}O_7N_2$ $[M + H]^+$: 363.2126 found: 363.2128; $C_{16}H_{30}O_7N_2Na$ $[M + Na]^+$: 385.1945 found: 385.1946.

*(3S,5S)-N-(tert-Butyl)-5-isopropyl-6-oxo-3-((1R,2S,3S)-1,2,3,4-tetrahydroxybutyl)morpholine-3-carboxamide (anti-**49**).* ^{1}H NMR (500 MHz, DMSO) δ 7.93 (s, 1H), 4.96 (d, J = 6.5 Hz, 1H), 4.66 (d, J = 4.4 Hz, 1H), 4.64 (d, J = 7.1 Hz, 1H), 4.51−4.48 (m, 1H), 4.39 (d, J = 11.9 Hz, 1H), 4.29 (d, J = 11.8 Hz, 1H), 3.84 (d, J = 6.0 Hz, 1H), 3.48−3.45 (m, 1H), 3.45−3.41 (m, 1H), 3.40−3.37 (m, 1H), 3.27−3.23 (m, 1H), 3.22 (d, J = 4.8 Hz, 1H), 3.12 (d, J = 11.4 Hz, 1H), 2.15−1.99 (m, 1H), 1.22 (s, 9H), 0.98 (d, J = 7.3 Hz, 3H), 0.96 (d, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.9, 171.2, 74.1, 73.0, 69.8, 69.5, 64.6, 62.2, 56.0, 50.0, 28.4, 28.2, 19.7, 17.0.

*(3S,5R)-N-(tert-Butyl)-5-isopropyl-6-oxo-3-((1R,2S,3S)-1,2,3,4-tetrahydroxybutyl)morpholine-3-carboxamide (syn-**50**).* Inseparable mixture *syn*/*anti* (86/14). Overall yield: 62.9 mg; 25%. ^{1}H NMR (500 MHz, DMSO) δ 8.07 (s, 1H), 5.13 (d, J = 6.4 Hz, 1H), 4.97 (d, J = 5.9 Hz, 1H), 4.81 (d, J = 4.4 Hz, 1H), 4.54 (t, J = 5.4 Hz, 1H), 4.53 (d, J = 10.8 Hz, 1H), 4.43 (d, J = 11.0 Hz, 1H), 3.77 (d, J = 6.2 Hz, 1H), 3.72 (d, J = 5.9 Hz, 1H), 3.61 (dd, J = 6.6, 4.3 Hz, 1H), 3.47−3.41 (m, 2H), 3.39 (dd, J = 10.6, 5.4 Hz, 1H), 3.26 (dd, J = 10.7, 5.2 Hz, 1H), 2.08 (dtd, J = 13.7, 6.8, 3.4 Hz, 1H), 1.23 (s, 9H), 0.99 (d, J = 7.0 Hz, 3H), 0.96 (d, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.7, 171.6, 73.9, 70.0, 70.0, 68.8, 65.3, 62.1, 56.7, 49.8, 28.4, 28.0, 18.7, 16.9. HRMS calcd for $C_{16}H_{31}O_7N_2$ $[M + H]^+$: 363.2126 found: 363.2124; $C_{16}H_{30}O_7N_2Na$ $[M + Na]^+$: 385.1945 found: 385.1945.

*(3R,5R)-N-(tert-Butyl)-5-isopropyl-6-oxo-3-((1R,2S,3S)-1,2,3,4-tetrahydroxybutyl)morpholine-3-carboxamide (anti-**50**).* ^{1}H NMR (500 MHz, DMSO) δ 7.75 (s, 1H), 4.92 (d, J = 6.3 Hz, 1H), 4.84 (d, J = 4.7 Hz, 1H), 4.76 (d, J = 6.1 Hz, 1H), 4.64 (t, J = 5.4 Hz, 1H), 4.26 (d, J = 12.4 Hz, 1H), 4.22 (d, J = 12.5 Hz, 1H), 3.83 (d, J = 6.3 Hz, 1H), 3.73 (d, J = 7.0 Hz, 1H), 3.56−3.52 (m, 1H), 3.53−3.48 (m, 1H),

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3.49−3.46 (m, 1H), 3.24−3.20 (m, 1H), 2.18−2.12 (m, 1H), 1.27 (s, 9H), 1.04 (d, J = 6.9 Hz, 3H), 0.89 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.5, 171.3, 73.7, 72.6, 69.6, 67.6, 63.8, 62.0, 56.4, 49.8, 28.3, 28.3, 19.7, 16.4.

*(3R,5S)-N-(tert-Butyl)-5-isopropyl-6-oxo-3-((1R,2R,3R)-1,2,3,4-tetrahydroxybutyl)morpholine-3-carboxamide (syn-**51**).* Yield: 118.2 mg; 47%. ^{1}H NMR (500 MHz, DMSO) δ 7.84 (s, 1H), 5.21 (d, J = 8.2 Hz, 1H), 4.97 (d, J = 5.9 Hz, 1H), 4.58 (d, J = 11.8 Hz, 1H), 4.51 (d, J = 11.9 Hz, 1H), 4.47 (t, J = 5.6 Hz, 1H), 4.30 (d, J = 6.8 Hz, 1H), 3.78−3.73 (m, 1H), 3.70 (q, J = 7.2 Hz, 1H), 3.63 (dd, J = 7.6, 3.9 Hz, 1H), 3.51 (ddd, J = 9.2, 5.8, 1.0 Hz, 1H), 3.43 (d, J = 7.7 Hz, 1H), 3.38−3.34 (m, 2H), 2.18−2.06 (m, 1H), 1.26 (s, 9H), 0.99 (d, J = 7.0 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 172.8, 171.9, 71.4, 71.0, 69.9, 69.8, 62.4, 62.3, 55.5, 50.3, 28.2, 28.1, 18.9, 17.1. $[\alpha]_D$ = −90 (c = 0.7, methanol. HRMS calcd for $C_{16}H_{31}O_7N_2$ $[M + H]^+$: 363.2126 found: 363.2126; $C_{16}H_{30}O_7N_2Na$ $[M + Na]^+$: 385.1945 found: 385.1945.

*(3S,5R)-N-(tert-Butyl)-5-isopropyl-6-oxo-3-((1R,2R,3R)-1,2,3,4-tetrahydroxybutyl)morpholine-3-carboxamide (syn-**52**).* Yield: 76.6 mg; 31%. ^{1}H NMR (500 MHz, DMSO) δ 7.68 (s, 1H), 5.29 (d, J = 7.2 Hz, 1H), 4.53 (d, J = 11.1 Hz, 1H), 4.52−4.48 (m, 1H), 4.49 (d, J = 11.0 Hz, 1H), 4.34 (d, J = 7.0 Hz, 1H), 4.17 (d, J = 8.1 Hz, 1H), 3.85 (dd, J = 8.3, 7.4 Hz, 1H), 3.67 (d, J = 6.7 Hz, 1H), 3.65 (dd, J = 6.9, 3.4 Hz, 1H), 3.59−3.54 (m, 1H), 3.44−3.32 (m, 2H), 2.97 (d, J = 7.0 Hz, 1H), 2.16−2.07 (m, 1H), 1.20 (s, 9H), 1.02 (d, J = 7.0 Hz, 3H), 1.00 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.7, 171.6, 71.6, 70.6, 70.0, 69.4, 63.4, 62.5, 56.5, 49.9, 28.6, 28.2, 18.6, 17.3. $[\alpha]_D$ = +80 (c = 0.6, methanol). HRMS calcd for $C_{16}H_{31}O_7N_2$ $[M + H]^+$: 363.2126 found: 363.2127; $C_{16}H_{30}O_7N_2Na$ $[M + Na]^+$: 385.1945 found: 385.1947.

*(3R,5S)-N-(tert-Butyl)-5-isopropyl-6-oxo-3-((1R,2S,3R)-1,2,3-trihydroxy-4-(((2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)-tetrahydro-2H-pyran-2-yl)oxy)butyl)morpholine-3-carboxamide (syn-**54**).* Inseparable mixture *syn*/*anti* (44/56). Overall yield: 162.7 mg; 45%. ^{1}H NMR (500 MHz, DMSO) δ 7.89 (s, 1H), 5.14 (d, J = 7.3 Hz, 1H), 4.91 (d, J = 8.0 Hz, 1H), 4.86 (d, J = 5.5 Hz, 1H), 4.76 (d, J = 4.8 Hz, 1H), 4.68 (d, J = 8.3 Hz, 1H), 4.66 (d, J = 3.9 Hz, 1H), 4.62−4.60 (m, 1H), 4.47 (d, J = 11.2 Hz, 1H), 4.46−4.43 (m, 1H), 4.43 (d, J = 11.5 Hz, 1H), 4.05 (d, J = 7.6 Hz, 1H), 3.65−3.39 (m, 8H), 3.18−3.05 (m, 4H), 2.13−2.03 (m, 1H), 1.23 (s, 9H), 0.97 (d, J = 7.0 Hz, 3H), 0.97 (d, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 172.3, 172.0, 98.8, 73.6, 72.6, 72.2, 71.2, 70.7, 70.2, 69.5, 69.1, 68.5, 64.4, 60.9, 56.1, 50.0, 28.4, 28.3, 18.9, 17.1. HRMS calcd for $C_{22}H_{41}O_{12}N_2$ $[M + H]^+$: 525.2654 found: 525.2651; $C_{22}H_{40}O_{12}N_2Na$ $[M + Na]^+$: 547.2473 found: 547.2466.

*(3S,5S)-N-(tert-Butyl)-5-isopropyl-6-oxo-3-((1R,2S,3R)-1,2,3-trihydroxy-4-(((2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)-tetrahydro-2H-pyran-2-yl)oxy)butyl)morpholine-3-carboxamide (anti-**54**).* ^{1}H NMR (500 MHz, DMSO) δ 7.95 (s, 1H), 5.04 (d, J = 7.7 Hz, 1H), 4.83 (d, J = 5.1 Hz, 1H), 4.71 (d, J = 4.8 Hz, 1H), 4.67 (d, J = 2.6 Hz, 1H), 4.67−4.65 (m, 1H), 4.63−4.59 (m, 1H), 4.62 (d, J = 8.2 Hz, 1H), 4.45−4.40 (m, 1H), 4.39 (d, J = 11.8 Hz, 1H), 4.31 (d, J = 11.8 Hz, 1H), 4.05 (d, J = 7.6 Hz, 1H), 3.67−3.39 (m, 8H), 3.22 (dd, J = 11.3, 4.8 Hz, 1H), 3.16−3.14 (m, 1H), 3.14−3.05 (m, 2H), 2.13−2.03 (m, 1H), 1.27 (s, 9H), 1.02 (d, J = 6.8 Hz, 3H), 0.93 (d, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.8, 171.3, 98.9, 73.7, 72.6, 72.2, 71.2, 70.6, 70.2, 69.7, 69.0, 68.5, 64.7, 60.9, 57.3, 50.1, 28.4, 28.3, 19.7, 17.2.

*(3S,5R)-N-(tert-Butyl)-5-isopropyl-6-oxo-3-((1R,2S,3R)-1,2,3-trihydroxy-4-(((2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)-tetrahydro-2H-pyran-2-yl)oxy)butyl)morpholine-3-carboxamide (syn-**55**).* Inseparable mixture *syn*/*anti* (73/27). Overall yield: 90.0 mg; 25%. ^{1}H NMR (500 MHz, DMSO) δ 8.09 (s, 1H), 5.24 (d, J = 7.7 Hz, 1H), 5.02 (d, J = 7.7 Hz, 1H), 4.83 (d, J = 5.0 Hz, 1H), 4.72 (d, J = 4.7 Hz, 1H), 4.66−4.64 (m, 1H), 4.63−4.61 (m, 1H), 4.54 (d, J = 10.8 Hz, 1H), 4.46 (d, J = 11.1 Hz, 1H), 4.44 (t, J = 5.7 Hz, 1H), 3.98 (d, J = 7.8 Hz, 1H), 3.68 (d, J = 5.9 Hz, 1H), 3.62−3.38 (m, 8H), 3.19−3.04 (m, 4H), 2.10−2.04 (m, 1H), 1.23 (s, 9H), 0.99 (d, J = 7.0 Hz, 3H), 0.96 (d, J = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 171.8, 171.7, 99.0, 73.6, 72.5, 72.2, 71.5, 70.2, 69.7, 69.3, 68.9, 67.5, 65.3, 60.8, 56.8, 49.9, 28.5, 28.2, 18.8, 17.0. HRMS calcd for $C_{22}H_{41}O_{12}N_2$ $[M + H]^+$: 525.2654 found: 525.2653; $C_{22}H_{40}O_{12}N_2Na$ $[M + Na]^+$: 547.2473 found: 547.2468.

*(3R,5R)-N-(tert-Butyl)-5-isopropyl-6-oxo-3-((1R,2S,3R)-1,2,3-trihydroxy-4-(((2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)-tetrahydro-2H-pyran-2-yl)oxy)butyl)morpholine-3-carboxamide (anti-**55**).* ^{1}H NMR (500 MHz, DMSO) δ 7.74 (s, 1H), 4.99 (d, J = 7.6 Hz, 1H), 4.82 (d, J = 4.0 Hz, 1H), 4.80 (d, J = 5.5 Hz, 1H), 4.76 (d, J = 4.8 Hz, 1H), 4.70 (d, J = 6.0 Hz, 1H), 4.66−4.64 (m, 1H), 4.63−4.61 (m, 1H), 4.44−4.41 (m, 1H), 4.29 (d, J = 12.3 Hz, 1H), 4.22 (d, J = 12.4 Hz, 1H), 4.00 (d, J = 7.7 Hz, 1H), 3.62−3.38 (m, 8H), 3.23 (dd, J = 12.2, 4.1 Hz, 1H), 3.19−3.04 (m, 3H), 2.17−2.10 (m, 1H), 1.27 (s, 9H), 1.03 (d, J = 6.7 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 172.3, 171.8, 98.7, 73.4, 72.4, 72.1, 70.7, 70.3, 70.1, 69.8, 69.0, 67.7, 63.7, 60.7, 56.6, 49.8, 28.3, 28.2, 19.7, 16.5.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02003.

Crystallographic data for *anti*-**14** (CIF)
Crystallographic data for *anti-ent*-**15** (CIF)
Crystallographic data for *anti-ent*-**17** (CIF)
X-ray structure analysis for compounds *anti*-**14** (CCDC 1422155), *anti-ent*-**15** (CCDC 1422156) and *anti-ent*-**17** (CCDC 1423243). This data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Conformation analysis, proof of configuration, and copies of ^{1}H NMR and ^{13}C NMR spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: rainer.mahrwald@rz.hu-berlin.de.

Notes

The authors declare no competing financial interest.

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