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SupraBox: Chiral Supramolecular Oxazoline Ligands

Marco Durini,[a,b] Eleonora Russotto,[a] Luca Pignataro,[c] Oliver Reiser,*[b] and Umberto Piarulli*[a]

Dedicated to Professor Cesare Gennari on the occasion of his 60th birthday

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A new class of oxazoline ligands, named SupraBox, was studied. These ligands possess an additional urea functionality to generate supramolecular bidentate ligands in transition-metal complexes, by the establishment of hydrogen bonds between the urea N-hydrogens of one ligand and the carbonyl oxygen of a second one. A library of 16 SupraBox ligands was prepared using 5 differently substituted oxazoline nuclei, 4 linkers and 3 different urea substituents. The formation of copper(II) and palladium(II) complexes was investigated by MS, UV/Vis and ^{1}H-NMR spectroscopy. The SupraBox library was screened in the copper-catalyzed asymmetric benzoylation of *vic*-diols. Good selectivities were obtained in the kinetic resolution of racemic hydrobenzoin [up to 86 % *ee* and selectivity (*s*) = 28] and in the desymmetrization of *meso*-hydrobenzoin (up to 88 % *ee*).

Introduction

The supramolecular assembly of biologically active species through hydrogen bonding is a widely occurring phenomenon in nature, as exemplified by DNA base pairing, the secondary or tertiary structure of proteins, or the mechanism of action of many enzymes. Taking inspiration from nature, chemists have designed and realized supramolecular catalysts in which a receptor or a cavitand is connected to an active site.[1] In a closely related approach, chiral ligands for transition metals have also been developed that possess, as well as centers for coordinating to a metal ion, an additional functionality that is capable of ligand–ligand bonding by non-covalent interactions, such as hydrogen bonding or coordinative bonding. These ligands are usually referred to as "supramolecular bidentate ligands".[2] This approach reduces the number of degrees of freedom in the resulting metal coordination complexes compared to the analogous complexes based on monodentate ligands, and this is expected to give a more pre-organized system with a better capability of controlling a subsequent metal-catalyzed reaction.

Among the different kinds of non-covalent interactions that have been used to date for developing supramolecular ligands, hydrogen bonds are arguably the most practical and efficient for several reasons: (i) functional groups capable of hydrogen bonding (e.g., amides, ureas, guanidines) are stable and relatively easy to introduce; (ii) hydrogen bonds are created dynamically and reversibly in the reaction medium (where catalysis is to take place), are able to self-repair when broken, and often coexist with other interactions in a "non-invasive" manner. In the last few years, several powerful supramolecular bidentate ligands with outstanding reactivity and selectivity have been described, but unfortunately, this concept has so far been exclusively confined to the use of phosphorus ligands.[2]

In this paper, we report the first example of hydrogen-bond-induced assembly of monodentate oxazolines for the formation of supramolecular bis(oxazoline) metal complexes and the use of their copper(II) complexes in asymmetric catalytic transformations.[3]

Results and Discussion

Bis(oxazolines) (Box) have developed into one of the most useful ligand classes for asymmetric catalysis, due to their ability to coordinate a wide variety of metal ions. The resulting complexes can be used in a great number of catalytic processes with excellent reactivity and selectivity.[4] The general structural motif of these ligands can be described

[a] Università degli Studi dell'Insubria, Dipartimento di Scienza e Alta Tecnologia, Via Valleggio 11, 22100 Como, Italy
Fax: +39-031-238-6449
E-mail: Umberto.Piarulli@uninsubria.it
[b] Universität Regensburg, Insitut für Organische Chemie, Universitätstrasse 31, 93053 Regensburg, Germany
Fax: +49-941-943-4121
E-mail: Oliver.Reiser@chemie.uni-regensburg.de
[c] Università degli Studi di Milano Dipartimento di Chimica Organica e Industriale Via G. Venezian 21, 20133 Milano, Italy
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as being two oxazoline units connected by one of a wide range of linkers. These linkers tune the separation and the bite angle of the two oxazolines, and might also introduce additional stereogenic elements (centers or axes) to optimize the enantioselectivity of a given asymmetric reaction.

In our approach, a covalent linker is replaced by a hydrogen-bonding interaction between two urea moieties that are connected to the oxazoline rings by different spacers (Figure 1). The urea functionality has been used before as a self-complementary recognition motif in the formation of supramolecular bidentate phosphane and phosphite ligands.[5]

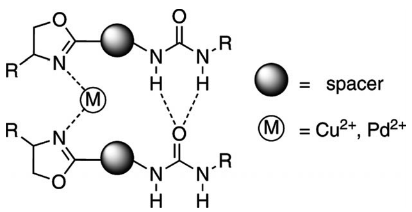
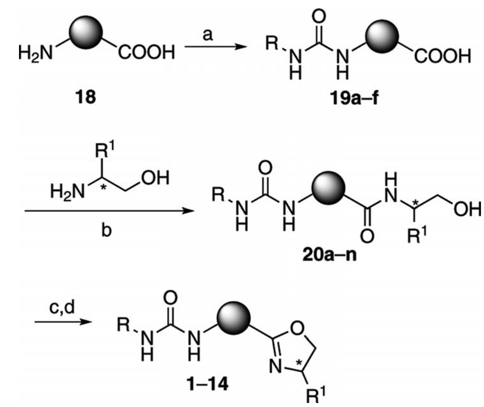


Figure 1. SupraBox: general structure of the ligands and of the supramolecular bidentate complex.

Thus, the synthesis of a library of "SupraBox" ligands (**1**–**16**, Figure 2) was planned. Their structure allows a modular synthetic approach and the introduction of several sites of diversity for steric and electronic tuning of the ligand properties: (i) the spacer between the oxazoline and the urea moiety; (ii) the substituent at the oxazoline stereocenter; (iii) the substitution pattern on the urea moiety.

Synthesis of the Ligands

The ligands were prepared following a straightforward and reliable synthetic protocol involving only one or two chromatographic purifications (Schemes 1 and 2). For the synthesis of ligands **1**–**14** (Scheme 1), the amino acid linkers (i.e., **18**) reacted with different isocyanates in THF or, where the substrate had limited solubility, in 2 N NaOH, to give the corresponding acid ureas (i.e., **19**).[6] These were then coupled to amino alcohols using HBTU (*O*-benzotriazole-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate) in dichloromethane. The ring closure and the formation of oxazolines **1**–**14** was achieved in good yields using DAST (diethylaminosulfur trifluoride), which had to be used in excess (2.2 equiv.), probably because of interference with the urea moiety.



Scheme 1. Synthesis of the SupraBox ligands. Reagents and conditions: (a) RNCO (1 equiv.), THF or aq. NaOH, 60–70%; (b) *i*Pr_2EtN (2.5 equiv.), HBTU (1.3 equiv.), amino alcohol (1.2 equiv.), CH_2Cl_2, 0 °C to r.t., 16 h, 85–99%; (c) DAST (2.2 equiv.), THF, –78 °C to r.t.; (d) K_2CO_3, 75–90%.

For the synthesis of ligands **15** and **16**, featuring the aspartic α-pyrrolidinamide linker, a slightly different protocol was followed (Scheme 2). Starting from L- or D-aspartic acid β-allyl ester **21**,[7] the corresponding phenyl urea **22** was assembled and then treated with pyrrolidine to obtain

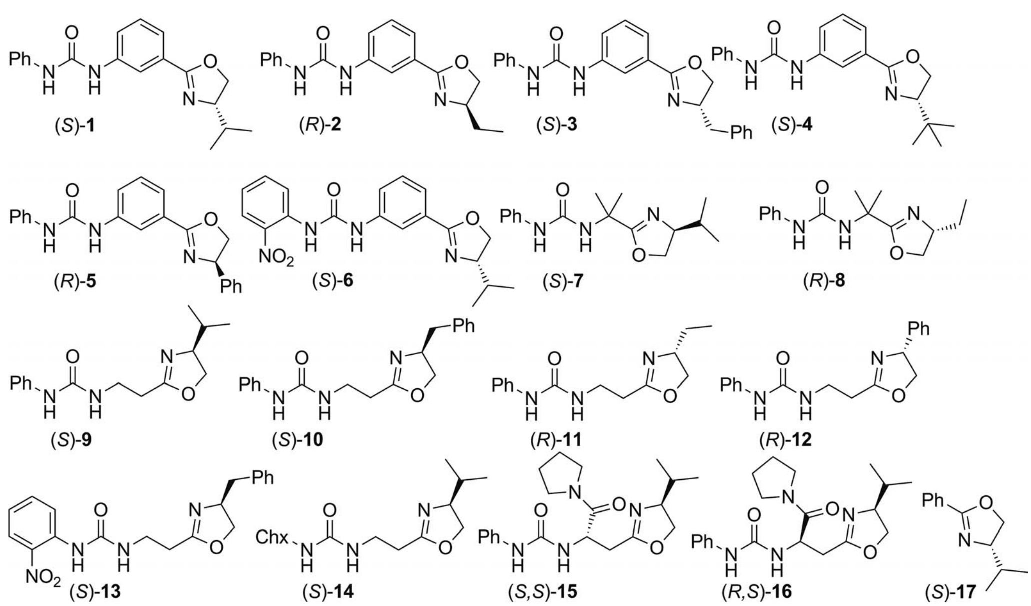


Figure 2. The SupraBox ligand library.

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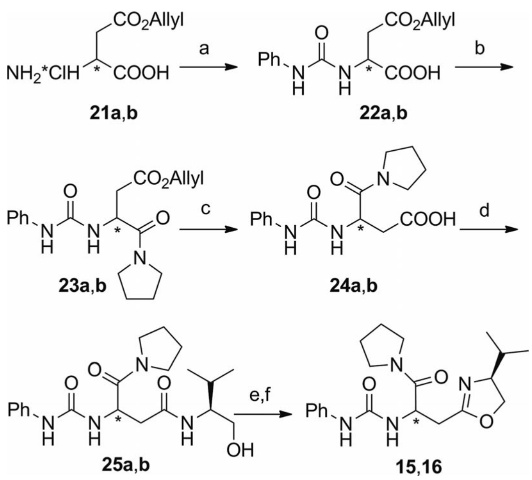


Scheme 2. Synthesis of ligands **15** and **16**. Reagents and conditions: (a) PhNCO (1 equiv.), Et_3N (1 equiv.), THF, r.t., 88%; (b) $i\text{Pr}_2\text{EtN}$ (2.5 equiv.), HBTU (1.3 equiv.), pyrrolidine (1.2 equiv.), DMF, 78%; (c) pyrrolidine (1.2 equiv.), Ph_3P (0.18 equiv.), $[Pd(Ph_3P)]$ (0.04 equiv.), CH_2Cl_2, 77%; (d) $i\text{Pr}_2\text{EtN}$ (2.5 equiv.), HBTU (1.3 equiv.), L-valinol (1.2 equiv.), CH_2Cl_2, 60%; (e) DAST (2.2 equiv.), THF, –78 °C to r.t.; (f) K_2CO_3, 58%.

the α-pyrrolidinamide derivative **23**. The allyl ester was cleaved by reaction with $[Pd(PPh_3)_4]$/pyrrolidine, and the resulting β-carboxylic acid was transformed into the oxazoline nucleus by reaction with (*S*)-valinol and then DAST-mediated ring closure.

Altogether, four different amino-acid spacers (β-alanine, 2-amino-isobutyric acid, *m*-amino benzoic acid and aspartic acid α-pyrrolidine-carboxamide) were used to impart different conformational rigidity to the ligands, and so influence the formation of intramolecular hydrogen bonds between the urea moieties. In addition, three different isocyanates were included in the screening to vary the hydrogen-bond-forming properties of the ligands, as well as five amino alcohols derived from natural α-amino acids to tune the transfer of the stereochemical information. In this way, a small collection of 16 ligands was prepared for testing.

Complexation Studies

Before screening the library of ligands in catalytic applications, we set out to investigate the formation of transition-metal complexes of the SupraBox ligands. The structures of complexes of supramolecular bidentate ligands containing additional functionalities capable of hydrogen-bonding interactions have usually been assessed spectroscopically,[8,5c] by ^{1}H, ^{13}C, and ^{31}P-NMR spectroscopy. ESI-MS has also been used, since this ionization methodology allowed the detection of the ion of the self-assembled complex, as has X-ray structural analysis, which showed the self-organized complex, held together by non-covalent interactions (metal coordination, intermolecular hydrogen bonding, and π-stacking).

The copper(II) complex of ligand (*S*)-**9** was obtained by treating it with $CuCl_2$ in CH_2Cl_2, followed by recrystallization of the crude material from CH_2Cl_2/*n*-hexane. Its molecular composition was assessed by ESI-MS spectroscopy, which revealed one principal peak at m/z = 613.3, corresponding to a copper(I) atom coordinated to two molecules of ligand, i.e., $[CuL_2]^+$. The reduction of Cu^{2+} to Cu^+ has been reported to occur when ESI is used as an ionization source.[9] The presence of two ligands coordinated to Cu^{2+} was further confirmed by a measurement of the complex absorbance as a function of the ligand/metal ratio, also known as Yoe–Jones method[10] (Figure 3). This plot showed a quasi-linear increase of the complex-absorbance value up to a combining ratio of 2:1. Addition of further ligand produced an almost negligible variation in the absorbance. The deviation from linearity could depend on the stability of the complex with respect to ligand dissociation:[11] the more stable the complex, the closer the experimental curve approaches a straight line.

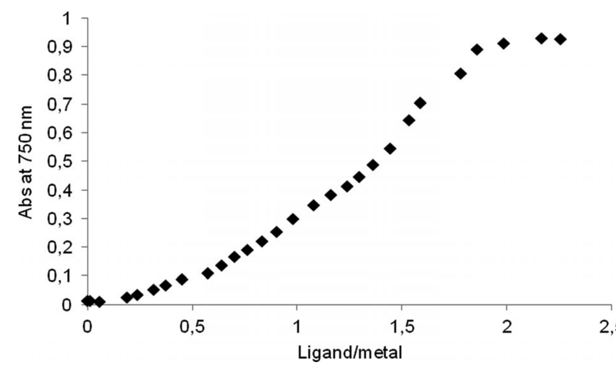


Figure 3. Yoe–Jones plot of complex absorbance as a function of ligand/metal ratio of complex $[Cu(\mathbf{9})_2Cl_2]$. Ligand (*S*)-**9** was added in accurately weighed portions to $CuCl_2$ in CH_2Cl_2, and UV absorption spectra were recorded after each addition.

The formation of palladium(II) complexes was also investigated: palladium chloride was treated with 2 equiv. ligand (*S*)-**9** in dichloromethane, and the complex $[Pd(S\text{-}\mathbf{9})_2Cl_2]$ was isolated by precipitation from hexanes. Since in this case the complex is diamagnetic, the supramolecular bidentate ligand $[Pd(S\text{-}\mathbf{9})_2Cl_2]$ could be studied by ^{1}H NMR spectroscopy. It is important to note that only one set of signals could be detected in the NMR spectra at room temperature, and the two coordinated molecules of **9**, i.e., the one acting as hydrogen-bond donor and the other as acceptor (Figure 4), could not be distinguished. The hydrogen-bonding state of the NH protons for both the free ligand and the Pd complex was also studied. In particular, the variation of the chemical shifts of the NH signals upon dilution was considered for both the ligand and the Pd complex. At 5 mM, the NH protons of the complex resonated at higher chemical shifts than did those of the free ligand (5.74 vs. 5.62 ppm for NH_A, and 7.03 vs. 6.80 ppm for NH_B), and their chemical shifts had a lower concentration dependence over the 5–40 mM range ($\Delta\delta$ = 0.1 vs. 0.27 ppm for NH_A, and $\Delta\delta$ = 0.1 vs. 0.32 ppm for NH_B, see the Supporting Information for the values and graphics) than those of the free ligand. The temperature dependence of the NH signals was also investigated, but on cooling, the signals broadened and coalesced, and two signals appeared at temperatures lower than 268 K, which hampered the measurement of the temperature coefficient ($\Delta\delta/\Delta T$) of each NH proton. These experiments, which are commonly used to differentiate between random-coil peptides and peptides in hydrogen-bonded conformations,[12] indicate that the two ligands coordinated to the metal atom interact intramolecularly by hydrogen bonding.

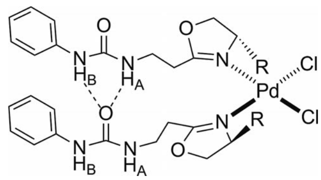
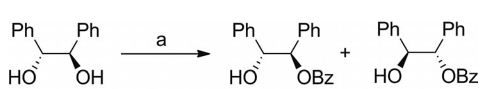


Figure 4. SupraBox: general structure of the ligands and of the supramolecular bidentate complex.

Enantioselective Catalytic Applications

Copper bis(oxazoline) complexes have been shown to be efficient catalysts in the kinetic resolution of racemic diols,[13] and in particular of hydrobenzoin, by benzoylation.[14] For this reason, we decided to screen ligands **1**–**16** in this reaction (Table 1). In addition, mono(oxazoline) **17**[15] (Figure 2) devoid of functional groups capable of forming hydrogen bonds, was added to the screening to confirm the importance of the supramolecular interaction.

Table 1. Screening of the SupraBox ligands in the copper-catalyzed enantioselective benzoylation of hydrobenzoin **23**.[a]



(±) (*R*,*R*)-**26** (*S*,*S*)-**26**

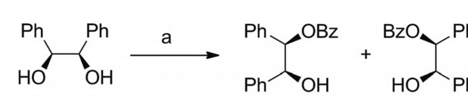
Entry	Ligand	Yield [%][b]	*ee* [%][c] (conf.)[d]	Selectivity (*s*)[e]
1	(*S*)-**1**	17	12 (*R*,*R*)	1.3
2	(*R*)-**2**	35	0	1.0
3	(*S*)-**3**	38	34 (*R*,*R*)	2.5
4	(*S*)-**4**	39	14 (*R*,*R*)	1.4
5	(*R*)-**5**	28	14 (*S*,*S*)	1.4
6	(*S*)-**6**	34	20 (*R*,*R*)	1.7
7	(*S*)-**7**	44	64 (*R*,*R*)	7.4
8	(*R*)-**8**	26	56 (*S*,*S*)	4.3
9	(*S*)-**9**	44	86 (*R*,*R*)	27
10	(*S*)-**10**	43	70 (*R*,*R*)	9.5
11	(*R*)-**11**	45	86 (*S*,*S*)	28
12	(*R*)-**12**	47	20 (*S*,*S*)	1.8
13	(*S*)-**13**	45	2 (*R*,*R*)	1.1
14	(*S*)-**14**	41	44 (*R*,*R*)	3.4
15	(*S*,*S*)-**15**	37	22 (*R*,*R*)	1.8
16	(*R*,*S*)-**16**	35	36 (*R*,*R*)	2.5
17	(*R*,*R*)-PhBox[f]	48	>99 (*S*,*S*)	>645[g]
18	(*S*)-**17**	40	0	1.0

[a] Reagents and conditions: $CuCl_2$ (5 mol-%), ligand (10 mol-%), PhCOCl (0.5 equiv.), *i*$PrEt_2N$ (1 equiv.), CH_2Cl_2, 3 h, 0 °C. [b] Isolated yield after chromatography. [c] Determined by chiral HPLC. [d] Determined according to ref.[14] [e] Determined according to ref.[16] [f] (*R*,*R*)-PhBox = 2,2-isopropylidenebis[(4*R*)-4-phenyl-2-oxazoline]. [g] See ref.[14a]

In the catalytic reactions, the complexes were preformed by stirring a suspension of $CuCl_2$ in a solution of the ligand in CH_2Cl_2 until all of the highly insoluble copper salt became soluble by complexation with the ligand (as seen by the formation of a deeply colored solution). Despite the structural similarities between **1**–**16**, their performance in the asymmetric benzoylation varied considerably, and rather surprisingly, the best selectivities were obtained with ligands **9** and **11**. Ligands **10** and **12**, with benzyl and phenyl substitution at the stereocenters, substituents that had proved most successful in the same reaction with bis(oxazoline) ligands,[13,14] gave inferior results. From a closer inspection of the selectivities, the importance of a fine balance of conformational flexibility, steric hindrance, and electronic properties becomes evident. In particular, the *meta*-disubstituted aromatic linker (Table 1, entries 1–6) and the C_α-tetrasubstituted amino acid (Aib) hamper enantioselectivity, probably because of the high degree of rigidity which does not allow an efficient docking of the two urea functionalities. In fact, the use of a β-alanine linker (Table 1, entries 9–14), which is best combined with an isopropyl or ethyl substitution at the oxazoline moiety, results in a significant increase in selectivity (Table 1, entries 9 and 11, respectively). Finally, no selectivity was obtained with the monodentate ligand **17**, which is not capable of supramolecular interactions (Table 1, entry 18).

Asymmetric catalytic acylation with copper(II) complexes has also been applied to the desymmetrization of *meso* diols,[17] albeit with *ee* values lower than those obtained in the kinetic resolution (58 %*ee* in the asymmetric benzoylation of *meso*-hydrobenzoin[17a]). We tested a selection of ligands in the desymmetrization of *meso*-hydroben-

Table 2. Screening of the SupraBox ligands in the copper-catalyzed desymmetrization of *meso*-hydrobenzoin by benzoylation.[a]



meso (1*R*,2*S*)-**27** (1*S*,2*R*)-**27**

Entry	Ligand	Yield [%][b]	*ee* [%][c] (conf)[d]
1	(*S*)-**1**	68	2 (1*R*,2*S*)
2	(*R*)-**5**	74	7 (1*S*,2*R*)
3	(*S*)-**7**	88	68 (1*R*,2*S*)
4	(*R*)-**8**	99	26 (1*S*,2*R*)
5	(*S*)-**9**	44	88 (1*R*,2*S*)
6	(*S*)-**10**	77	6 (1*R*,2*S*)
7	(*R*)-**11**	92	78 (1*S*,2*R*)
8	(*R*)-**12**	70	24 (1*S*,2*R*)
9	(*S*)-**14**	89	38 (1*R*,2*S*)
10	(*S*,*S*)-**15**	68	40 (1*R*,2*S*)
11	(*R*,*S*)-**16**	62	20 (1*R*,2*S*)
12	(*R*,*R*)-PhBox[e]	86	59[f]
13	(*S*)-**17**	73	0

[a] Reagents and conditions: $CuCl_2$ (5 mol-%), ligand (10 mol-%), PhCOCl (0.5 equiv.), *i*$PrEt_2N$ (1 equiv.), CH_2Cl_2, 3 h, 0 °C. [b] Isolated yield after chromatography. [c] Determined by chiral HPLC. [d] Determined according to ref.[17a] [e] (*R*,*R*)-PhBox = 2,2-isopropylidenebis[(4*R*)-4-phenyl-2-oxazoline]. [f] See ref.[17a]

zoin by benzoylation, and the results are collected in Table 2.

Once again, satisfactory results were obtained with ligands **9** and **11** (Table 2, entries 5 and 7). Notably, the SupraBox ligands outperform the classical methylene-bridged bis(oxazolines) and aza-bis(oxazolines), probably because the flexibility of the non-covalent linker allows these *meso* substrates to be accommodated in the copper(II) coordination sphere. In contrast, the rigidity of the classical bis(oxazolines) creates a cavity where the C_2-symmetric (D,L)-*vic*-diols can fit better than the σ-symmetric *meso* diols. Also in this case, ligand **17**, devoid of functionalities that can as hydrogen-bond donors, catalyzed the benzoylation in an unselective way (Table 2, entry 13).

Conclusions

A new class of supramolecular bidentate nitrogen ligands has been investigated. These ligands feature a chiral oxazoline ring and a urea functionality linked by a spacer. A 16-membered library was prepared, made up of 5 differently substituted oxazoline nuclei, 4 linkers, and 3 different urea substituents. The coordination of these ligands to copper(II) and palladium(II) ions was studied, revealing that: (i) two ligands coordinate to the metal ions via their oxazoline nitrogen atoms; (ii) the NHs of the urea moiety are intramolecularly hydrogen-bonded, as indicated by the downfield values and low concentration dependence of their chemical shifts. The SupraBox library was screened in the kinetic resolution of racemic hydrobenzoin and the desymmetrization of *meso*-hydrobenzoin by copper-catalyzed benzoylation. Good selectivities (*s*) were obtained in the kinetic resolution, while the use of SupraBox ligands proved particularly beneficial in the desymmetrization of hydrobenzoin, outperforming classical bis(oxazolines).

Further studies are currently underway to find further applications for this new class of ligands.

Experimental Section

General Remarks: All reactions were carried out in flame-dried glassware with magnetic stirring under a nitrogen atmosphere unless otherwise stated. Dry solvents (over molecular sieves in bottles with crown cap) were purchased from Fluka and stored under nitrogen. Reactions were monitored by analytical thin-layer chromatography (TLC) using silica gel 60 F_{254} pre-coated glass plates (0.25 mm thickness). Visualization was accomplished by irradiation with a UV lamp and/or staining with a potassium permanganate alkaline solution. Flash column chromatography was performed using silica gel 60 Å, particle size 40–64 µm, following the procedure by Still and co-workers.[18] Proton NMR spectra were recorded with a spectrometer operating at 400.13 MHz. Proton chemical shifts are reported in ppm (δ) with the solvent reference relative to tetramethylsilane (TMS) employed as the internal standard ($CDCl_3$ δ = 7.26 ppm; [D$_6$]DMSO, δ = 2.50 ppm; CD_3OD, δ = 3.33 ppm). The following abbreviations are used to describe spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signal, dd = doublet of doublets. ^{13}C NMR spectra were recorded with a 400 MHz spectrometer operating at 100.56 MHz with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as the internal standard ($CDCl_3$, δ = 77.23 ppm; [D$_6$]DMSO, δ = 39.51 ppm; CD_3OD, δ = 49.05 ppm). Infra-red spectra were recorded with a standard FTIR spectrometer. Optical rotation values were measured with an automatic polarimeter with a 1 dm cell at the sodium D line (λ = 589 nm). HPLC was performed with an instrument equipped with a diode array detector, using a chiral column. High-resolution mass spectra (HRMS) were performed with a Fourier Transform Ion Cyclotron Resonance (FT-ICR) Mass Spectrometer APEX II & Xmass software (Bruker Daltonics) – 4.7 T Magnet (Magnex) equipped with ESI source, available at CIGA (Centro Interdipartimentale Grandi Apparecchiature) c/o Università degli Studi di Milano. Low-resolution mass spectra (MS) were acquired either with a Thermo-Finnigan LCQ Advantage mass spectrometer (ESI ion source) or with a VG Autospec M246 spectrometer (FAB ion source). Elemental analyses were performed with a Perkin–Elmer Series II CHNS/O Analyzer 2000.

Materials: Commercially available reagents were used as received. 4-aspartic acid β-allyl ester[7] (**21**) and (*S*)-4-isopropyl-2-phenyl-4,5-dihydrooxazole[15] (**17**) were prepared according to literature procedures.

3-(3-Phenylureido)benzoic Acid (19a): Phenylisocyanate (1.59 mL, 14.5 mmol, 1.0 equiv.) and 3-aminobenzoic acid (2.0 g, 14.5 mmol, 1.0 equiv.) were dissolved in THF (80 mL), and the reaction mixture was stirred at room temperature for 3 d. The mixture was treated with cold Et_2O to induce precipitation of the product **19a** (2.34 g, 9.15 mmol, 63 %) as a fine white powder. R_f = 0.35 (CH_2Cl_2/MeOH, 95:5). M.p. 152–153 °C. ^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ = 7.03 (m, 1 H), 7.30 (m, 2 H), 7.37–7.46 (m, 3 H), 7.68 (ddd, J = 7.7, 1.5, 1.1 Hz, 1 H), 7.73 (ddd, J = 8.0, 2.3, 1.1 Hz, 1 H), 8.08 (t, J = 1.7 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): δ = 119.1, 119.9, 122.6, 123.2, 123.5, 128.4, 128.6, 131.2, 139.0, 139.5, 151.1, 168.2 ppm. IR: $\tilde{\nu}$ = 3354, 2724, 1738, 1680, 1649, 1556, 1310, 1156, 1066 cm^{-1}. $C_{14}H_{12}N_2O_3$ (256.26): calcd. C 65.62, H 4.72, N 10.93; found C 63.38, H 4.44, N 10.81.

3-[3-(2-Nitrophenyl)ureido]benzoic Acid (19b): 2-nitrophenyl isocyanate (1.0 g, 6.09 mmol, 1.0 equiv.) and 3-aminobenzoic acid (0.84 g, 6.09 mmol, 1.0 equiv.) were dissolved in THF (60 mL), and the reaction mixture was stirred at room temperature for 3 d. The mixture was treated with cold Et_2O to induce precipitation of the product **19b** (1.36 g, 4.50 mmol, 74 %) as a fine yellow powder. R_f = 0.26 (CH_2Cl_2 /MeOH, 95:5). M.p. 174–175 °C. ^{1}H NMR (400 MHz, DMSO, 25 °C): δ = 7.22 (ddd, J = 8.4, 7.2, 1.2 Hz, 1 H), 7.42 (t, J = 7.8 Hz, 1 H), 7.59 (dt, J = 7.7, 1.2 Hz, 1 H), 7.66–7.73 (m, 2 H), 8.09 (dd, J = 8.4, 1.6 Hz, 1 H), 8.15 (t, J = 1.8 Hz, 1 H), 8.29 (dd, J = 8.5, 1.2 Hz, 1 H), 9.61 (s, 1 H), 10.03 (s, 1 H), 12.93 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, DMSO, 25 °C): δ = 119.7, 122.8, 123.0, 123.7, 125.8, 129.6, 131.9, 135.2, 135.4, 138.3, 140.0, 152.3, 167.6 ppm. IR: $\tilde{\nu}$ = 3354, 3281, 2724, 1829, 1739, 1652, 1543, 1310, 1155, 1073, 949 cm^{-1}. $C_{14}H_{11}N_3O_5$ (301.25): calcd. C 55.82, H 3.68, N 13.95; found C 55.54, H 3.34, N 14.30.

2-Methyl-2-(3-phenylureido)propanoic Acid (19c): 2-Aminoisobutyric acid (3.0 g, 29 mmol, 1.3 equiv.) was suspended in 2 M NaOH (10 mL), then phenylisocyanate (2.37 mL, 22 mmol, 1.0 equiv.) was added, and the mixture reaction was stirred for 60 min at room temperature. The mixture was filtered and the product was precipitated from solution by the slow addition of 1 M HCl. The white solid was dissolved in 1 M NaOH (10 mL), and the solution was washed with CH_2Cl_2. Addition of 1 M HCl induced the precipitation of product **19c** (1.73 g, 7.78 mmol, 35 %) as a fine white powder. R_f = 0.37 (CH_2Cl_2/MeOH, 95:5). M.p. 157–158 °C. ^{1}H NMR (400 MHz, CD_3OH, 25 °C): δ = 1.53 (s, 6 H), 6.41 (s, 1 H), 6.95 (m, 1 H), 7.24 (m, 2 H), 7.30 (m, 2 H), 8.19 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): δ = 24.6, 55.3, 118.6, 121.9, 128.3, 139.4, 155.7, 177.3 ppm. IR: $\tilde{\nu}$ = 3381, 2724, 1704, 1648, 1544, 1308, 1158, 1069 cm^{-1}. $C_{11}H_{14}N_2O_3$ (222.24): calcd. C 59.45, H 6.35, N 12.60; found C 59.55, H 5.55, N 12.61.

3-(3-Phenylureido)propanoic Acid (19d): Phenylisocyanate (5.0 mL, 44 mmol, 1.0 equiv.) was dissolved in THF (220 mL), and then β-alanine (3.92 g, 44 mmol, 1.0 equiv.) was added. The reaction mixture was stirred at room temperature for 3 d. The mixture was treated with cold Et_2O to induce precipitation of the product. After filtration, the crude product was purified by flash chromatography eluting with 3→10% MeOH in CH_2Cl_2 to yield product **19d** (8.33 g, 40 mmol, 91%) as a fine white powder. R_f = 0.24 (CH_2Cl_2/MeOH, 95:5). M.p. 160–161 °C. ^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ = 2.55 (t, J = 6.3 Hz, 2 H), 3.47 (t, J = 6.3 Hz, 2 H), 6.98 (t, J = 6.8 Hz, 1 H), 7.25 (dd, J = 8.4, 7.4 Hz, 2 H), 7.33 (m, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 34.1, 35.2, 119.0, 122.0, 128.4, 139.5, 156.8, 174.3 ppm. IR: $\tilde{\nu}$ = 3584, 3329, 2725, 1694, 1638, 1571, 1108 cm^{-1}. $C_{10}H_{12}N_2O_3$ (208.21): calcd. C 57.68, H 5.81, N 13.45; found C 57.73, H 5.57, N 13.81.

3-[3-(2-Nitrophenyl)ureido]propanoic Acid (19e): 2-Nitro-phenylisocyanate (1.000 g, 6.09 mmol, 1.0 equiv.) was dissolved in THF (30 mL), and then β-alanine (1.085 g, 12.18 mmol, 2.0 equiv.) was added. The reaction mixture was stirred at room temperature for 3 d. The mixture was treated with cold Et_2O to induce precipitation of the product. After filtration, the crude product was purified by flash chromatography eluting with 3→5% MeOH in CH_2Cl_2 to yield product **19e** (1.077 g, 4.25 mmol, 67%) as a fine yellow powder. R_f = 0.41 (CH_2Cl_2/MeOH, 95:5). M.p. 160–161 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.56 (t, J = 6.6 Hz, 2 H), 3.48 (t, J = 6.6 Hz, 2 H), 7.13 (ddd, J = 8.5, 7.2, 1.3 Hz, 1 H), 7.61 (ddd, J = 8.6, 7.2, 1.6 Hz, 1 H), 8.12 (dd, J = 8.5, 1.6 Hz, 1 H), 8.35 (dd, J = 8.6, 1.3 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): δ = 33.8, 35.5, 121.4, 122.1, 125.1, 134.6, 135.7, 137.1, 155.4, 174.0 ppm. IR: $\tilde{\nu}$ = 3583, 3393, 3330, 2753, 2360, 1694, 1611, 1582, 1539, 1342, 1258, 1142, 1085, 798 cm^{-1}. $C_{10}H_{11}N_3O_5$ (253.21): calcd. C 47.43, H 4.38, N 16.59; found C 47.62, H 4.23, N 16.29.

3-(3-Cyclohexylureido)propanoic Acid (19f): Cyclohexylisocyanate (2.86 mL, 22 mmol, 1.0 equiv.) was dissolved in THF (150 mL), and then β-alanine (2.00 g, 22.4 mmol, 1.0 equiv.) was added. The reaction mixture was stirred at room temperature for 3 d. The mixture was treated with cold Et_2O to induce precipitation of the product. After filtration, the crude product was purified by flash chromatography eluting with 5→15% MeOH in CH_2Cl_2 to yield product **19f** (3.60 g, 16.8 mmol, 76%) as a fine white powder. R_f = 0.23 (CH_2Cl_2/MeOH, 95:5). M.p. 159–160 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25 °C): δ = 0.97–1.16 (m, 3 H), 1.18–1.30 (m, 2 H), 1.50 (m, 1 H), 1.61 (m, 1 H), 1.70 (m, 1 H), 2.31 (t, J = 6.5 Hz, 2 H), 3.15 (q, J = 6.5 Hz, 2 H), 5.74 (t, J = 5.8 Hz, 1 H), 5.83 (d, J = 7.9 Hz, 1 H), 12.17 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]-DMSO, 25 °C): δ = 24.9, 25.8, 33.7, 35.5, 35.7, 48.1, 157.7, 173.9 ppm. IR: $\tilde{\nu}$ = 3335, 1699, 1626, 1580, 1535, 1307, 1248, 1222, 1080, 921 cm^{-1}. $C_{10}H_{18}N_2O_3$ (214.26): calcd. C 56.06; H 8.47; N 13.07; found C 55.87, H 8.62, N 12.72.

General Procedure for the Synthesis of Products 20a–n, 25a and 25b: Acid **19** or **24** (1.1 equiv.) and *N*,*N*-diisopropylethylamine (3 equiv.) were dissolved in CH_2Cl_2 (0.1 M), and the solution was cooled to 0 °C. HBTU (1.3 equiv.) was added, and the solution was stirred at the same temperature for 30 min. Then the amino alcohol (1.0 equiv.) was added, and the reaction mixture was stirred at 0 °C for 60 min and then overnight at room temperature. The solvent was evaporated under reduced pressure, and the mixture was separated by flash chromatography eluting with MeOH (gradient from 2 to 10%) in CH_2Cl_2 to yield product **20** or **25**.

(*S*)-*N*-(1-Hydroxy-3-methylbutan-2-yl)-3-(3-phenylureido)benzamide (20a): According to the general procedure, product **20a** (0.578 g, 1.69 mmol, 96%) was obtained as a white solid, starting from acid **19a** (0.500 g, 1.95 mmol) and L-valinol. R_f = 0.38 (CH_2Cl_2/MeOH, 95:5). M.p. 167–168 °C. $[\alpha]_D^{20}$ = –44.37 (c = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ = 1.00 (d, J = 6.8 Hz, 3 H), 1.03 (d, J = 6.8 Hz, 3 H), 2.00 (m, 1 H), 3.67–3.76 (m, 2 H), 3.91 (m, 1 H), 7.03 (t, J = 7.3 Hz, 1 H), 7.30 (m, 2 H), 7.39 (t, J = 7.9 Hz, 1 H), 7.44 (dd, J = 8.7, 1.2 Hz, 2 H), 7.48 (dt, J = 7.7, 1.3 Hz, 1 H), 7.58 (ddd, J = 8.1, 2.1, 1.0 Hz, 1 H), 7.88 (t, J = 1.8 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): δ = 17.8, 18.7, 28.9, 57.4, 61.7, 117.9, 119.0, 121.2, 121.8, 122.6, 128.4, 128.6, 135.7, 138.9, 139.4, 153.9, 169.2 ppm. IR: $\tilde{\nu}$ = 3266, 3200, 2722, 1656, 1609, 1565, 1501, 1310, 1221, 1167, 1089, 989, 840 cm^{-1}. $C_{19}H_{23}N_3O_3$ (341.40): calcd. C 66.84, H 6.79, N 12.31; found C 66.62, H 7.14, N 12.14.

(*R*)-*N*-(1-Hydroxybutan-2-yl)-3-(3-phenylureido)benzamide (20b): According to the general procedure, product **20b** (0.565 g, 1.72 mmol, 97%) was obtained as a white solid, starting from acid **19a** (0.500 g, 1.95 mmol) and (*R*)-2-aminobutan-1-ol. R_f = 0.40 (CH_2Cl_2/MeOH, 95:5). M.p. 146–147 °C. $[\alpha]_D^{20}$ = +42.58 (c = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ = 1.00 (t, J = 7.5 Hz, 3 H), 1.56 (m, 1 H), 1.76 (m, 1 H), 3.63 (dd, J = 5.6, 0.9 Hz, 2 H), 4.03 (m, 2 H), 7.03 (t, J = 7.3 Hz, 1 H), 7.29 (dd, J = 8.5, 7.5 Hz, 2 H), 7.36 (t, J = 7.8 Hz, 1 H), 7.44 (dd, J = 8.7, 1.2 Hz, 2 H), 7.48 (dt, J = 7.7, 1.3 Hz, 1 H), 7.58 (ddd, J = 7.9, 2.2, 1.1 Hz, 1 H), 7.88 (t, J = 1.8 Hz, 1 H), 8.05 (d, J = 8.3 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): δ = 9.6, 23.66, 53.7, 63.43, 117.9, 119.1, 121.2, 121.9, 122.6, 128.5, 128.7, 135.6, 138.9, 139.4, 153.9, 169.2 ppm. IR: $\tilde{\nu}$ = 3383, 2724, 1697, 1648, 1542, 1154, 1069 cm^{-1}. $C_{18}H_{21}N_3O_3$ (327.38): calcd. C 66.04, H 6.47, N 12.84; found C 65.93, H 6.70, N 12.58.

(*S*)-N-(1-Hydroxy-3-phenylpropan-2-yl)-3-(3-phenylureido)benzamide (20c): According to the general procedure, product **20c** (0.689 g, 1.77 mmol, 100%) was obtained as a white solid, starting from acid **19a** (0.500 g, 1.95 mmol) and (*S*)-2-amino-3-phenylpropan-1-ol. R_f = 0.34 (CH_2Cl_2/MeOH, 95:5). M.p. 157–158 °C. $[\alpha]_D^{20}$ = –50.29 (c = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ = 2.87 (dd, J = 13.7, 8.6 Hz, 1 H), 3.03 (dd, J = 13.7, 6.2 Hz, 1 H), 3.66 (d, J = 5.5 Hz, 2 H), 4.34 (m, 1 H), 7.04 (t, J = 7.5 Hz, 1 H), 7.17 (m, 1 H), 7.29 (m, 6 H), 7.37 (m, 2 H), 7.45 (dd, J = 8.6, 1.0 Hz, 2 H), 7.56 (dt, J = 7.0, 2.2 Hz, 1 H), 7.79 (m, 1 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): δ = 36.6, 53.6, 62.9, 117.8, 119.0, 121.1, 121.8, 122.6, 125.9, 128.0, 128.5, 128.6, 129.0, 134.7, 135.5, 138.5, 139.0, 139.3, 153.9, 168.8 ppm. IR: $\tilde{\nu}$ = 3324, 2724, 1739, 1648, 1543, 1310, 1265, 1155, 1069, 876, 840 cm^{-1}. $C_{23}H_{23}N_3O_3$ (389.45): calcd. C 70.93, H 5.95, N 10.79; found C 70.88, H 6.18, N 7.78.

(*S*)-*N*-(1-Hydroxy-3,3-dimethylbutan-2-yl)-3-(3-phenylureido)benzamide (20d): According to the general procedure, product **20d** (0.552 g, 1.55 mmol, 88%) was obtained as a white solid, starting from acid **19a** (0.500 g, 1.95 mmol) and (*S*)-2-amino-3,3-dimethylbutan-1-ol. R_f = 0.37 (CH_2Cl_2/MeOH, 95:5). M.p. 97–98 °C. $[\alpha]_D^{20}$ = –49.69 (c = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ = 1.02 (s, 9 H), 3.63 (dd, J = 11.4, 8.8 Hz, 1 H), 3.68 (dd, J = 11.4, 3.5 Hz, 1 H), 4.04 (dd, J = 8.8, 3.5 Hz, 1 H), 7.04 (m, 1 H), 7.30 (m, 1 H), 7.40 (t, J = 7.7 Hz, 1 H), 7.42–7.50 (m, 3 H), 7.59 (ddd, J = 7.9, 2.2, 1.1 Hz, 1 H) 7.87 (t, J = 1.7 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): δ = 26.0, 33.9, 54.4, 60.9, 117.9, 119.1, 121.3, 121.8, 122.6, 128.5, 128.7, 136.0, 138.9, 139.2, 153.9, 169.9 ppm. IR: ṽ = 3278, 3204, 2727, 1670, 1625, 1589, 1553, 1500, 1310, 1233, 1134, 1088, 1047, 840 cm^{-1}. $C_{20}H_{25}N_3O_3$ (355.43): calcd. C 67.58, H 7.09, N 11.82; found C 67.44, H 7.16, N 12.11.

(*R*)-*N*-(2-Hydroxy-1-phenylethyl)-3-(3-phenylureido)benzamide (20e): According to the general procedure, product **20e** (0.420 g, 1.12 mmol, 98%) was obtained as a white solid, starting from acid **19a** (0.320 g, 1.25 mmol) and (*R*)-2-amino-2-phenylethanol. R_f = 0.39 (CH_2Cl_2/MeOH, 95:5). M.p. 112–113 °C. $[\alpha]_D^{20}$ = –46.89 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, CD_3OD, 25 °C): *δ* = 3.87 (d, *J* = 6.6 Hz, 2 H), 5.21 (t, *J* = 6.6 Hz, 1 H), 7.02 (t, *J* = 7.3 Hz, 1 H), 7.23–7.45 (m, 10 H), 7.51 (d, *J* = 7.7 Hz, 1 H), 7.58 (dd, *J* = 8.0, 1.1 Hz, 1 H), 7.90 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): *δ* = 56.4, 64.7, 118.0, 119.1, 121.3, 122.0, 122.6, 126.6, 127.0, 128.1, 128.5, 128.7, 135.3, 138.9, 139.4, 139.9, 153.9, 168.9 ppm. IR: ṽ = 3300, 3205, 2727, 1646, 1621, 1599, 1563, 1348, 1298, 1235, 1175, 1065, 844 cm^{-1}. $C_{22}H_{21}N_3O_3$ (375.42): calcd. C 70.38, H 5.64, N 11.19; found C 70.37, H 5.73, N 12.11.

(*S*)-*N*-(1-Hydroxy-3-methylbutan-2-yl)-3-[3-(2-nitrophenyl)ureido]-benzamide (20f): According to the general procedure, product **20f** (0.568 g, 1.47 mmol, 97%) was obtained as a yellow solid, starting from acid **19b** (0.500 g, 1.66 mmol) and L-valinol. R_f = 0.36 (CH_2Cl_2/MeOH, 95:5). M.p. 140–141 °C. $[\alpha]_D^{20}$ = –47.64 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, CD_3OD, 25 °C): *δ* = 1.00 (d, *J* = 6.8 Hz, 1 H), 1.03 (d, *J* = 6.8 Hz, 1 H), 2.01 (m, 1 H), 3.71 (m, 2 H), 3.92 (m, 1 H), 7.19 (ddd, *J* = 8.4, 7.4, 1.3 Hz, 1 H), 7.42 (t, *J* = 7.8 Hz, 1 H), 7.51 (dt, *J* = 7.8, 1.3 Hz, 1 H), 7.67 (m, 2 H), 7.97 (t, *J* = 1.8 Hz, 1 H), 8.19 (dd, *J* = 8.4, 1.4 Hz, 1 H), 8.48 (dd, *J* = 8.6, 1.2 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): *δ* = 17.8, 18.7, 28.9, 57.4, 61.7, 118.2, 121.6, 122.0, 122.3, 125.2, 128.7, 134.7, 135.2, 135.8, 153.2, 169.2 ppm. IR: ṽ = 3296, 3205, 1722, 1697, 1628, 1604, 1565, 1340, 1252, 1194, 1141, 1074, 1028, 846 cm^{-1}. $C_{19}H_{22}N_4O_5$ (386.41): calcd. C 59.06, H 5.74, N 14.50; found C 59.27, H 6.09, 14.83.

(*S*)-*N*-(1-Hydroxy-3-methylbutan-2-yl)-2-methyl-2-(3-phenylureido)-propanamide (20g): According to the general procedure, product **20g** (0.630 g, 2.04 mmol, 100%) was obtained as a white solid, starting from acid **19c** (0.500 g, 2.25 mmol) and L-valinol. R_f = 0.25 (CH_2Cl_2/MeOH, 95:5). M.p. 135–136 °C. $[\alpha]_D^{20}$ = –38.27 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C): *δ* = 0.86 (d, *J* = 6.8 Hz, 3 H), 0.89 (d, *J* = 6.7 Hz, 3 H), 1.52 (s, 3 H), 1.53 (s, 3 H), 1.70 (m, 1 H), 3.39 (t, *J* = 10.2 Hz, 1 H), 3.70 (m, 2 H), 3.98 (br. s, 1 H), 6.43 (s, 1 H), 6.86 (d, *J* = 9.8 Hz, 1 H), 6.94 (t, *J* = 7.2 Hz, 1 H), 7.15 (t, *J* = 7.6 Hz, 2 H), 7.28 (d, *J* = 7.7 Hz, 2 H), 8.09 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CHCl_3$, 25 °C): *δ* = 19.2, 19.7, 24.7, 26.9 29.1, 56.8, 57.9, 64.2, 120.1, 123.0, 128.7, 138.7, 156.1, 177.4 ppm. IR: ṽ = 3358, 2724, 1649, 1578, 1542, 1310, 1150, 1133, 1087, 965 cm^{-1}. $C_{16}H_{25}N_3O_3$ (307.39): calcd. C 62.52, H 8.20, N 13.67; found C 62.22, H 8.06, N 14.01.

(*R*)-*N*-(1-Hydroxybutan-2-yl)-2-methyl-2-(3-phenylureido)propan-amide (20h): According to the general procedure, product **20h** (0.630 g, 2.04 mmol, 100%) was obtained as a white solid, starting from acid **19c** (0.500 g, 2.25 mmol) and (*R*)-2-aminobutan-1-ol. R_f = 0.27 (CH_2Cl_2/MeOH, 95:5). M.p. 137–138 °C. $[\alpha]_D^{20}$ = +39.99 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, CD_3OD, 25 °C): *δ* = 0.94 (t, *J* = 7.6 Hz, 3 H), 1.46 (m, 1 H), 1.50 (s, 6 H), 1.62 (m, 1 H), 3.52 (d, *J* = 5.4 Hz, 2 H), 3.81 (m, 1 H), 6.97 (t, *J* = 7.3 Hz, 1 H), 7.23 (m, 2 H), 7.33 (dd, *J* = 8.5, 1.0 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CHCl_3$, 25 °C): *δ* = 10.6, 23.4, 24.8, 26.9, 53.9, 56.7, 65.6, 120.0, 123.0, 128.7, 138.7, 156.0, 177.4 ppm. IR: ṽ = 3382, 3271, 3133, 2724, 1648, 1598, 1542, 1494, 1312, 1253, 1220, 1168, 1062, 845 cm^{-1}. $C_{15}H_{23}N_3O_3$ (293.36): calcd. C 61.41, H 7.90, N 14.32; found C 61.22, H 8.01, N 13.97.

(*S*)-*N*-(1-Hydroxy-3-methylbutan-2-yl)-3-(3-phenylureido)propan-amide (20i): According to the general procedure, product **20i** (0.569 g, 1.94 mmol, 89%) was obtained as a white solid solid, starting from acid **19d** (0.500 g, 2.4 mmol) and L-valinol. R_f = 0.22 (CH_2Cl_2/MeOH, 95:5). M.p. 121–122 °C. $[\alpha]_D^{20}$ = –31.01 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C): *δ* = 0.89 (d, *J* = 6.8 Hz, 3 H), 0.91 (d, *J* = 6.8 Hz, 3 H), 1.83 (m, 1 H), 2.57 (m, 2 H), 2.90 (br. s, 1 H), 3.47–3.59 (m, 3 H), 3.67 (dd, *J* = 11.6, 3.2 Hz, 1 H), 3.75 (m, 1 H), 6.85 (d, *J* = 8.5 Hz, 1 H), 6.98 (m, 1 H), 7.21 (m, 2 H), 7.28 (m, 1 H), 7.44 (m, 1 H), 7.55 (m, 1 H), 7.86 (br. s, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): *δ* = 18.9, 19.4, 29.1, 36.5, 37.2, 57.4, 63.3, 119.8, 123.1, 128.9, 138.7, 156.9, 173.4 ppm. IR: ṽ = 3337, 3243, 3087, 2478, 2419, 1670, 1632, 1560, 1503, 1354, 1295, 1260, 1141, 1117, 1063, 1029, 970, 760 cm^{-1}. $C_{15}H_{23}N_3O_3$ (293.36): calcd. C 61.41, H 7.90, N 14.32; found C 61.21, H 8.02, N 14.72.

(*S*)-*N*-(1-Hydroxy-3-phenylpropan-2-yl)-3-(3-phenylureido)propan-amide (20j): According to the general procedure, product **20j** (0.802 g, 2.35 mmol, 98%) was obtained as a white solid, starting from acid **19d** (0.500 g, 2.4 mmol) and (*S*)-2-amino-3-phenylpro-pan-1-ol. R_f = 0.30 (CH_2Cl_2/MeOH, 95:5). M.p. 131–132 °C. $[\alpha]_D^{20}$ = –34.68 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, CD_3OD, 25 °C): *δ* = 2.38 (t, *J* = 6.4 Hz, 2 H), 2.71 (dd, *J* = 13.8, 8.1 Hz, 1 H), 2.90 (dd, *J* = 13.8, 6.2 Hz, 1 H), 3.38 (m, 2 H), 3.53 (m, 2 H), 4.12 (m, 1 H), 6.97 (m, 1 H), 7.15 (m, 1 H), 7.21–7.27 (m, 6 H), 7.33 (m, 2 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): *δ* = 35.9, 36.1, 36.6, 52.8, 62.9, 118.8, 122.1, 125.9, 126.9, 127.9, 128.4, 128.9, 138.4, 139.5, 156.8, 172.5 ppm. IR: ṽ = 3320, 2724, 2453, 1829, 1738, 1625, 1545, 1308, 1263, 1156, 1071, 1036 cm^{-1}. $C_{19}H_{23}N_3O_3$ (341.40): calcd. C 66.84, H 6.79, N 12.31; found C 67.01, H 6.46, N 12.37.

(*R*)-*N*-(1-Hydroxybutan-2-yl)-3-(3-phenylureido)propanamide (20k): According to the general procedure, product **20k** (0.604 g, 2.16 mmol, 99%) was obtained as a white solid, starting from acid **19d** (0.500 g, 2.4 mmol) and (*R*)-2-aminobutan-1-ol. R_f = 0.23 (CH_2Cl_2/MeOH, 94:6). M.p. 131–132 °C. $[\alpha]_D^{20}$ = +32.01(*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, CD_3OD, 25 °C): *δ* = 0.93 (t, *J* = 7.4 Hz, 3 H), 1.42 (m, 1 H), 1.63 (m, 1 H), 2.46 (m, 2 H), 3.43–3.52 (m, 4 H), 3.80 (m, 1 H), 6.97 (m, 1 H), 7.23 (m, 2 H), 7.33 (m, 2 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): *δ* = 18.6, 23.9, 36.5, 37.3, 53.9, 64.8, 119.8, 123.0, 128.9, 138.9, 157.0, 173.3 ppm. IR: ṽ = 3327, 3265, 2724, 1738, 1647, 1557, 1307, 1154, 1070 cm^{-1}. $C_{14}H_{21}N_3O_3$ (279.33): calcd. C 60.20, H 7.58, N 15.04; found C 60.42, H 7.59, N 14.79.

(*R*)-*N*-(2-Hydroxy-1-phenylethyl)-3-(3-phenylureido)propanamide (20l): According to the general procedure, product **20l** (0.505 g, 1.54 mmol, 64%) was obtained as a white solid, starting from acid **19d** (0.500 g, 2.4 mmol) and (*R*)-2-amino-2-phenylethanol. R_f = 0.31 (CH_2Cl_2/MeOH, 95:5). M.p. 119–120 °C. $[\alpha]_D^{20}$ = –37.23 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, CD_3OD, 25 °C): *δ* = 2.53 (m, 2 H), 3.47 (t, *J* = 6.5 Hz, 2 H), 3.77 (dd, *J* = 11.2, 7.7 Hz, 1 H), 3.75 (dd, *J* = 11.2, 5.3 Hz, 1 H), 5.01 (dd, *J* = 7.7, 5.3 Hz, 1 H), 6.97 (tt, *J* = 7.3, 1.2 Hz, 1 H), 7.20–7.35 (m, 9 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): *δ* = 35.9, 36.0 55.6, 64.9, 118.8, 122.0, 126.6, 127.0, 128.1, 128.4, 139.5, 139.9, 156.8, 172.5 ppm. IR: ṽ = 3382, 3308, 2462, 2364, 1644, 1598, 1544, 1313, 1243, 1153, 1125, 1078, 1056, 905 cm^{-1}. $C_{18}H_{21}N_3O_3$ (327.38): calcd. C 66.04, H 6.47, N 12.84; found C 65.89, H 6.75, N 12.56.

(*S*)-*N*-(1-Hydroxy-3-phenylpropan-2-yl)-3-[3-(2-nitrophenyl)-ureido]propanamide (20m): According to the general procedure, product **20m** (0.211 g, 0.546 mmol, 46%) was obtained as a yellow solid, starting from acid **19e** (0.300 g, 1.18 mmol) and (*S*)-2-amino-3-phenylpropan-1-ol. R_f = 0.31 (CH_2Cl_2/MeOH, 95:5). M.p. 146–147 °C. $[\alpha]_D^{20}$ = –43.40 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, CD_3OD, 25 °C): δ = 2.40 (t, *J* = 6.6 Hz, 2 H), 2.72 (dd, *J* = 13.7, 8.3 Hz, 1 H), 2.90 (dd, *J* = 13.7, 6.1 Hz, 1 H), 3.41 (m, 2 H), 3.51 (dd, *J* = 11.1, 5.6 Hz, 1 H), 3.56 (dd, *J* = 10.6, 5.1 Hz, 1 H), 4.14 (m, 1 H), 7.13 (m, 2 H), 7.23 (m, 4 H), 7.61 (ddd, *J* = 8.7, 7.2, 1.6 Hz, 1 H), 8.13 (dd, *J* = 8.4, 1.6 Hz, 1 H), 8.35 (dd, *J* = 8.6, 1.2 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): δ = 35.9, 36.2, 36.6, 52.8, 62.8, 121.4, 122.1, 125.1, 125.9, 127.8, 128.9, 134.6, 135.7, 137.1, 138.4, 155.4, 172.2 ppm. IR: ṽ = 3371, 3329, 3282, 2368, 1676, 1649, 1585, 1556, 1155, 1116, 1082, 960, 840 cm^{-1}. $C_{19}H_{22}N_4O_5$ (386.41): calcd. C 59.06, H 5.74, N 14.50; found C 59.23, H 6.00, 14.76.

(*S*)-3-(3-Cyclohexylureido)-*N*-(1-hydroxy-3-methylbutan-2-yl)-propanamide (20n): According to the general procedure, product **20n** (0.688 g, 2.19 mmol, 99%) was obtained as a white solid, starting from acid **19f** (0.500 g, 2.3 mmol) and L-valinol. R_f = 0.44 (CH_2Cl_2/MeOH, 95:5). M.p. 140–141 °C. $[\alpha]_D^{20}$ = –30.12 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, CD_3OD, 25 °C): δ = 0.91 (d, *J* = 6.7 Hz, 3 H), 0.94 (d, *J* = 6.7 Hz, 3 H), 1.17 (m, 3 H), 1.34 (m, 3 H), 1.60 (dt, *J* = 12.6, 3.8 Hz, 1 H), 1.72 (dt, *J* = 13.3, 3.8 Hz, 1 H), 1.85 (m, 3 H), 2.42 (m, 2 H), 3.39 (m, 2 H), 3.53 (dd, *J* = 11.4, 6.6 Hz, 1 H), 3.61 (dd, *J* = 11.3, 4.4 Hz, 1 H), 3.71 (m, 1 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): δ = 17.4, 18.6, 24.6, 25.3, 28.6, 33.3, 36.1, 36.5, 56.6, 61.9, 158.9, 172.9 ppm. IR: ṽ = 3312, 3278, 2409, 1623, 1578, 1545, 1345, 1214, 1123, 1076, 965 cm^{-1}. $C_{15}H_{29}N_3O_3$ (299.41): calcd. C 60.17; H 9.76; N 14.03; found C 59.89, H 10.09, 14.33.

General Procedure for the Synthesis of Products 1–16: Peptide **20** (1.0 equiv.) was dissolved in THF (0.1 M solution) and cooled to –78 °C; then DAST (2.2 equiv.) was added dropwise, and the reaction mixture was stirred at the same temperature for 90 min. The mixture was filtered, and the solvent was evaporated under reduced pressure. The product was purified by flash chromatography eluting with MeOH (gradient from 1 to 5%) in CH_2Cl_2.

(*S*)-1-[3-(4-Isopropyl-4,5-dihydrooxazol-2-yl)phenyl]-3-phenylurea (1): According to the general procedure, product **1** (0.458 g, 1.42 mmol, 91%) was obtained as a white solid starting from precursor **20a** (0.530 g, 1.55 mmol). R_f = 0.49 (CH_2Cl_2/MeOH, 95:5). M.p. 138–139 °C. $[\alpha]_D^{20}$ = –35.05 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, CD_2Cl_2, 25 °C): δ = 0.92 (d, *J* = 6.8 Hz, 3 H), 1.01 (d, *J* = 6.7 Hz, 3 H), 1.84 (m, 1 H), 4.09 (ddd, *J* = 9.5, 8.2, 6.4 Hz, 1 H), 4.16 (t, *J* = 8.2 Hz, 1 H), 4.43 (dd, *J* = 9.5, 8.3 Hz, 1 H), 7.10 (m, 1 H), 7.14 (br. s, 1 H), 7.25 (br. s, 1 H), 7.28–7.37 (m, 5 H), 7.50 (ddd, *J* = 8.0, 2.1, 0.9 Hz, 1 H), 7.60 (dt, *J* = 7.7, 1.1 Hz, 1 H), 7.95 (t, *J* = 1.7 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 17.6, 18.8, 32.4, 70.6, 71.2, 119.4, 120.8, 123.2, 123.6, 123.9, 128.9, 129.1, 129.3, 138.0, 138.8, 139.0, 153.6, 165.0 ppm. IR: ṽ = 3319, 2725, 1743, 1646, 1595, 1567, 1309, 1262, 1155, 1069, 801 cm^{-1}. $C_{19}H_{21}N_3O_2$ (323.39): calcd. C 70.57, H 6.55, N 12.99; found C 70.19, H 6.41, N 12.83.

(R)-1-[3-(4-Ethyl-4,5-dihydrooxazol-2-yl)phenyl]-3-phenylurea (2): According to the general procedure, product **2** (0.370 g, 1.20 mmol, 78%) was obtained as a white solid starting from precursor **20b** (0.500 g, 1.53 mmol). R_f = 0.46 (CH_2Cl_2/MeOH, 95:5). M.p. 147–148 °C. $[\alpha]_D^{20}$ = +43.30 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, CD_3OD, 25 °C): δ = 0.99 (t, *J* = 7.3 Hz, 3 H), 1.63 (m, 1 H), 1.74 (m, 1 H), 4.14 (t, *J* = 7.7 Hz, 1 H), 4.24 (m, 1 H), 4.54 (dd, *J* = 9.4, 8.2 Hz, 1 H), 7.02 (m, 1 H), 7.29 (m, 2 H), 7.37 (t, *J* = 8.2 Hz, 1 H), 7.43 (dd, *J* = 8.7, 1.1 Hz, 2 H), 7.58 (dt, *J* = 7.7, 1.3 Hz, 1 H), 7.68 (ddd, *J* = 8.1, 2.3, 1.0 Hz, 1 H), 7.96 (t, *J* = 2.0 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): δ = 8.52, 28.0, 67.1, 72.0, 118.4, 119.0, 122.1, 122.6, 127.8, 128.5, 128.7, 138.9, 139.6, 153.8, 164.6 ppm. IR: ṽ = 3309, 3281, 1644, 1612, 1592, 1572, 1448, 1311, 1298, 1237, 1168, 1080, 1059, 973, 926 cm^{-1}. $C_{18}H_{19}N_3O_2$ (309.36): calcd. C 69.98, H 6.19, N 13.58; found C 70.01, H 6.15, N 13.54.

(*S*)-1-[3-(4-Benzyl-4,5-dihydrooxazol-2-yl)phenyl]-3-phenylurea (3): According to the general procedure, product **3** (0.518 g, 1.39 mmol, 78%) was obtained as a white solid starting from precursor **20c** (0.693 g, 1.78 mmol). R_f = 0.52 (CH_2Cl_2/MeOH, 95:5). M.p. 106–107 °C. $[\alpha]_D^{20}$ = –37.89 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, $CHCl_3$, 25 °C): δ = 2.64 (dd, *J* = 13.7, 9.0 Hz, 1 H), 3.12 (dd, *J* = 13.7, 5.1 Hz, 1 H), 4.02 (t, *J* = 7.8 Hz, 1 H), 4.22 (t, *J* = 8.8 Hz, 1 H), 4.47 (m, 1 H), 6.95 (t, *J* = 7.1 Hz, 1 H), 7.11–7.27 (m, 11 H), 7.54 (d, *J* = 7.1 Hz, 1 H), 7.94 (d, *J* = 8.1 Hz, 2 H), 8.04 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 41.8, 67.6, 72.0, 119.8, 120.5, 123.0, 123.1, 123.6, 126.6, 128.1, 128.6, 128.9, 129.0, 129.1, 137.8, 138.2, 138.7, 154.0, 164.4 ppm. IR: ṽ = 3353, 2724, 2360, 1649, 1597, 1555, 1310, 1264, 1201, 1154, 1074, 896, 845 cm^{-1}. $C_{23}H_{21}N_3O_2$ (371.43): calcd. C 74.37, H 5.70, N 11.31; found C 77.37, H 5.68, N 10.95.

(*S*)-1-[3-(4-*tert*-Butyl-4,5-dihydrooxazol-2-yl)phenyl]-3-phenylurea (4): According to the general procedure, product **4** (0.436 g, 1.29 mmol, 83%) was obtained as a white solid starting from precursor **20d** (0.552 g, 1.55 mmol). R_f = 0.48 (CH_2Cl_2/MeOH, 95:5). M.p. 170–171 °C. $[\alpha]_D^{20}$ = –47.13 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, CD_3OD, 25 °C): δ = 1.02 (s, 9 H), 3.63 (dd, *J* = 11.5, 8.9 Hz, 1 H), 3.88 (dd, *J* = 11.5, 3.4 Hz, 1 H), 4.04 (dd, *J* = 8.9, 3.4 Hz, 1 H), 7.03 (t, *J* = 7.4 Hz, 1 H), 7.30 (dd, *J* = 8.4, 7.4 Hz, 2 H), 7.40 (t, *J* = 7.7 Hz, 1 H), 7.44 (m, 2 H), 7.48 (ddd, *J* = 7.7, 1.7, 1.1 Hz, 1 H), 7.59 (ddd, *J* = 8.2, 2.2, 1.1 Hz, 1 H), 7.82 (t, *J* = 1.7 Hz, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 25.8, 33.9, 68.8, 75.9, 119.8, 120.6, 123.0, 123.1, 123.6, 128.3, 129.0, 138.1, 138.6, 154.0, 163.7 ppm. IR: ṽ = 3352, 2724, 2360, 1740, 1647, 1596, 1560, 1309, 1264, 1204, 1154, 1073, 897, 799 cm^{-1}. $C_{20}H_{23}N_3O_2$ (337.42): calcd. C 71.19, H 6.87, N 12.45; found C 71.44, H 7.10, N 12.47.

(*R*)-1-Phenyl-3-[3-(4-phenyl-4,5-dihydrooxazol-2-yl)phenyl]urea (5): According to the general procedure, product **5** (0.103 g, 0.29 mmol, 30%) was obtained as a white solid starting from precursor **20e** (0.400 g, 1.06 mmol). R_f = 0.45 (CH_2Cl_2/MeOH, 95:5). M.p. 134–135 °C. $[\alpha]_D^{20}$ = –51.78 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 4.25 (t, *J* = 8.3 Hz, 1 H), 4.90 (dd, *J* = 10.1, 8.3 Hz, 1 H), 5.45 (dd, *J* = 10.1, 8.3 Hz, 1 H), 6.98 (t, *J* = 7.3 Hz, 1 H), 7.24–7.31 (m, 3 H), 7.34–7.41 (m, 5 H), 7.55 (dd, *J* = 8.7, 1.1 Hz, 2 H), 7.65 (dt, *J* = 7.7, 1.3 Hz, 1 H), 7.73 (ddd, *J* = 8.2, 2.3, 1.1 Hz, 1 H), 8.23 (t, *J* = 1.9 Hz, 1 H), 8.36 (s, 1 H), 8.52 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 69.5, 74.9, 118.2, 118.5, 118.6, 121.5, 121.6, 121.9, 122.1, 126.7, 127.3, 128.1, 128.5, 128.7, 128.9, 139.9, 140.4, 142.9, 152.5, 164.3 ppm. IR: ṽ = 3321, 3278, 2725, 1709, 1656, 1611, 1561, 1311, 1223, 1189, 1063, 970, 840 cm^{-1}. $C_{22}H_{19}N_3O_2$ (357.41): calcd. C 73.93, H 5.36, N 11.76; found C 73.57, H 5.63, N 11.46.

(*S*)-1-[3-(4-Isopropyl-4,5-dihydrooxazol-2-yl)phenyl]-3-(2-nitrophenyl)urea (6): According to the general procedure, product **6** (0.441 g, 1.20 mmol, 82%) was obtained as a yellow solid starting from precursor **20f** (0.565 g, 1.46 mmol). R_f = 0.38 (CH_2Cl_2/MeOH, 95:5). M.p. 166–167 °C. $[\alpha]_D^{20}$ = –49.37 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, CD_2Cl_2, 25 °C): δ = (d, *J* = 6.7 Hz, 3 H), 1.05 (d, *J* = 6.7 Hz, 3 H), 1.84 (m, 1 H), 4.07–4.18 (m, 2 H), 4.45 (dd, *J* = 9.2, 7.8 Hz, 1 H), 7.10 (br. s, 1 H), 7.15 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1 H), 7.43 (t, J = 7.7 Hz, 1 H), 7.64 (ddd, J = 7.9, 2.1, 1.0 Hz, 1 H), 7.68 (ddd, J = 8.7, 7.1, 1.6 Hz, 1 H), 7.72 (dt, J = 7.7, 1.2 Hz, 1 H), 8.04 (t, J = 2.0 Hz, 1 H), 8.22 (dd, J = 8.6, 1.6 Hz, 1 H), 8.68 (dd, J = 8.7, 1.1 Hz, 1 H), 9.94 (br. s, 1 H) ppm. ^{13}C NMR (100.6 MHz, CH_2Cl_2, 25 °C): δ = 17.8, 18.6, 32.8, 70.3, 72.5, 119.7, 121.9, 122.1, 122.9, 123.4, 125.5, 128.8, 129.1, 135.4, 136.0, 136.7, 138.4, 151.8, 163.1 ppm. IR: $\tilde{\nu}$ = 3339, 3281, 2724, 1650, 1591, 1557, 1309, 1278, 1155, 1066, 823 cm^{-1}. $C_{19}H_{20}N_4O_4$ (368.39): calcd. C 61.95, H 5.47, N 15.21; found C 61.71, H 5.84, N 13.47.

(*S*)-1-[2-(4-Isopropyl-4,5-dihydrooxazol-2-yl)propan-2-yl]-3-phenylurea (7): According to the general procedure, product **7** (0.501 g, 1.73 mmol, 84%) was obtained as a white solid starting from precursor **20g** (0.635 g, 2.06 mmol). R_f = 0.50 (CH_2Cl_2/MeOH, 95:5). M.p. 189–190 °C. $[\alpha]_D^{20}$ = –43.12 (c = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ = 0.89 (d, J = 6.7 Hz, 3 H), 0.95 (d, J = 6.8 Hz, 3 H), 1.56 (s, 3 H), 1.59 (s, 3 H), 1.82 (m, 1 H), 4.00 (ddd, J = 9.8, 7.2, 5.5 Hz, 1 H), 4.12 (dd, J = 8.6, 7.2 Hz, 1 H), 4.32 (dd, J = 9.8, 8.6 Hz, 1 H), 6.96 (m, 1 H), 7.23 (dd, J = 8.6, 7.5 Hz, 2 H), 7.31 (dd, J = 8.6, 1.2 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): δ = 16.4, 17.5, 25.5, 25.7, 31.9, 51.5, 70.0, 71.2, 118.6, 121.9, 128.9, 139.4, 155.5, 172.2 ppm. IR: $\tilde{\nu}$ = 3338, 2725, 1646, 1600, 1557, 1543, 1310, 1264, 1152, 1071, 800 cm^{-1}. $C_{16}H_{23}N_3O_2$ (289.37): calcd. C 66.41, H 8.01, N 14.52; found C 66.53, H 8.11, 14.77.

(*S*)-1-[2-(4-Ethyl-4,5-dihydrooxazol-2-yl)propan-2-yl]-3-phenylurea (8): According to the general procedure, product **8** (0.441 g, 1.60 mmol, 74%) was obtained as a white solid starting from precursor **20h** (0.636 g, 2.17 mmol). R_f = 0.49 (CH_2Cl_2/MeOH, 95:5). M.p. 122–123 °C. $[\alpha]_D^{20}$ = +40.82 (c = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ = 0.94 (t, J = 7.3 Hz, 3 H), 1.55 (s, 3 H), 1.56 (m, 1 H), 1.57 (s, 3 H), 1.66 (m, 1 H), 4.01 (t, J = 7.6 Hz, 1 H), 4.08 (m, 1 H), 4.39 (dd, J = 9.0, 7.8 Hz, 1 H), 6.96 (t, J = 7.3 Hz, 1 H), 7.23 (t, J = 7.9 Hz, 2 H), 7.30 (dd, J = 8.8, 1.2 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): δ = 8.3 25.5, 25.6, 27.6, 51.3, 66.8, 72.3, 118.6, 122.0, 128.3, 139.3, 155.4, 172.2 ppm. IR: $\tilde{\nu}$ = 3321, 2725, 1661, 1641, 1596, 1587, 1500, 1302, 1250, 1218, 1132, 1082, 1068, 979, 955, 924, 843 cm^{-1}. $C_{15}H_{21}N_3O_2$ (275.35): calcd. C 65.43, H 7.69, N 15.26; found C 65.57, H 7.66, N 15.37.

(*S*)-1-[2-(4-Isopropyl-4,5-dihydrooxazol-2-yl)ethyl]-3-phenylurea (9): According to the general procedure, product **9** (0.519 g, 1.88 mmol, 99%) was obtained as a white solid starting from precursor **20i** (0.560 g, 1.91 mmol). R_f = 0.59 (CH_2Cl_2/MeOH, 95:5). M.p. 81–81 °C. $[\alpha]_D^{20}$ = –29.80 (c = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ = 0.89 (d, J = 6.8 Hz, 3 H), 0.94 (d, J = 6.7 Hz, 3 H), 1.74 (m, 1 H), 2.52 (m, 2 H), 3.49 (m, 2 H), 3.91 (m, 1 H), 4.07 (t, J = 7.9 Hz, 1 H), 4.31 (dd, J = 9.8, 8.7 Hz, 1 H), 6.97 (m, 1 H), 7.24 (m, 2 H), 7.33 (dd, J = 8.7, 1.2 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): δ = 17.4, 18.6, 28.6, 36.1, 36.2, 56.6, 61.8, 118.8, 122, 128.4, 139.5, 156.8, 172.8 ppm. IR: $\tilde{\nu}$ = 3205, 2728, 1694, 1639, 1594, 1527, 1380, 1353, 1168, 1077, 1029, 920, 832 cm^{-1}. $C_{15}H_{21}N_3O_2$ (273.35): calcd. C 65.43, H 7.69, N 15.26; found C 65.61, H 7.99, N 14.61.

(*S*)-1-[2-(4-Benzyl-4,5-dihydrooxazol-2-yl)ethyl]-3-phenylurea (10): According to the general procedure, product **10** (0.175 g, 0.541 mmol, 53%) was obtained as a pale yellow solid starting from precursor **20j** (0.350 g, 1.03 mmol). R_f = 0.51 (CH_2Cl_2/MeOH, 95:5). M.p. 130–131 °C. $[\alpha]_D^{20}$ = –44.65 (c = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CHCl_3$, 25 °C): δ = 2.44 (t, J = 5.8 Hz, 2 H), 2.64 (dd, J = 13.7, 7.8 Hz, 1 H), 2.96 (dd, J = 13.7, 5.6 Hz, 1 H), 3.43–3.62 (m, 2 H), 3.98 (t, J = 7.4 Hz, 1 H), 4.20 (t, J = 8.4 Hz, 1 H), 4.29 (m, 1 H), 6.06 (br. s, 1 H), 7.03 (t, J = 7.3 Hz, 1 H), 7.13 (m, 2 H), 7.16–7.40 (m, 8 H), 7.63 (br. s, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 28.8, 36.6, 41.6, 66.7, 71.9, 120.5, 123.3, 126.6, 128.6, 129.1, 129.2, 137.7, 139.0, 156.2, 167.4 ppm. IR: $\tilde{\nu}$ = 3331, 2724, 1679, 1632, 1595, 1565, 1497, 1444, 1349, 1311, 1242, 1191, 1084, 975, 924 cm^{-1}. $C_{19}H_{21}N_3O_2$ (323.39): calcd. C 70.57, H 6.55, N 12.99; found C 70.78, H 6.32, N 13.04.

(*R*)-1-[2-(4-Ethyl-4,5-dihydrooxazol-2-yl)ethyl]-3-phenylurea (11): According to the general procedure, product **11** (0.410 g, 1.57 mmol, 77%) was obtained as a pale yellow solid starting from precursor **20k** (0.570 g, 2.04 mmol). R_f = 0.57 (CH_2Cl_2/MeOH, 95:5). M.p. 68–69 °C. $[\alpha]_D^{20}$ = +29.07 (c = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CHCl_3$, 25 °C): δ = 0.91 (t, J = 7.3 Hz, 3 H), 1.56 (m, 1 H), 1.67 (m, 1 H), 2.69 (t, J = 5.6 Hz, 1 H), 3.57 (m, 2 H), 4.06–4.20 (m, 2 H), 4.63 (t, J = 8.8 Hz, 1 H), 6.38 (br. s, 1 H), 7.02 (t, J = 7.7 Hz, 1 H), 7.25 (m, 2 H), 7.39 (d, J = 7.3 Hz, 2 H), 7.75 (br. s, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 9.8, 24.0, 36.5, 37.3, 53.6, 64.6, 119.6, 122.8, 128.9, 139.2, 156.8, 173.0 ppm. IR: $\tilde{\nu}$ = 3321, 2725, 1640, 1556, 1309, 1243, 1156, 1070 cm^{-1}. $C_{14}H_{19}N_3O_2$ (261.32): calcd. C 64.35, H 7.33, N 16.08; found C 64.44, H 7.43, N 15.41.

(*R*)-1-Phenyl-3-[2-(4-phenyl-4,5-dihydrooxazol-2-yl)ethyl]urea (12): According to the general procedure, product **12** (0.257 g, 0.83 mmol, 77%) was obtained as a white solid starting from precursor **20l** (0.500 g, 1.54 mmol). R_f = 0.59 (CH_2Cl_2/MeOH, 95:5). M.p. 122–123 °C. $[\alpha]_D^{20}$ = +38.08 (c = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CHCl_3$, 25 °C): δ = 2.51 (t, J = 5.8 Hz, 2 H), 3.54 (m, 2 H), 4.06 (t, J = 8.3 Hz, 1 H), 4.56 (dd, J = 10.1, 8.6 Hz, 1 H), 5.09 (t, J = 9.2 Hz, 1 H), 6.18 (t, J = 6.0 Hz, 1 H), 6.97 (m, 1 H), 7.13–7.36 (m, 10 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 28.9, 36.6, 67.7, 69.4, 120.1, 122.9, 127.8, 128.8, 129.0, 139.1, 141.8, 156.4, 171.8 ppm. IR: $\tilde{\nu}$ = 3310, 2726, 1678, 1620, 1567, 1541, 1310, 1245, 1180, 1076, 978, 845 cm^{-1}. $C_{18}H_{19}N_3O_2$ (309.36): calcd. C 69.88, H 6.12, N 13.58; found C 69.58, H 6.34, N 13.89.

(*S*)-1-[2-(4-Benzyl-4,5-dihydrooxazol-2-yl)ethyl]-3-(2-nitrophenyl)urea (13): According to the general procedure, product **13** (0.101 g, 0.274 mmol, 50%) was obtained as a yellow solid starting from precursor **20m** (0.210 g, 0.543 mmol). R_f = 0.34 (CH_2Cl_2/MeOH, 95:5). M.p. 154–155 °C. $[\alpha]_D^{20}$ = –42.12 (c = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.56 (t, J = 5.7 Hz, 2 H), 2.78 (dd, J = 13.7, 7.9 Hz, 1 H), 3.08 (dd, J = 13.7, 5.4 Hz, 1 H), 3.61 (m, 2 H), 4.10 (dd, J = 8.3, 7.4 Hz, 1 H), 4.33 (t, J = 8.9 Hz, 1 H), 4.49 (m, 1 H), 6.17 (br. s, 1 H), 7.04 (m, 1 H), 7.20–7.35 (m, 5 H), 7.58 (ddd, J = 8.7, 7.3, 1.6 Hz, 1 H), 8.16 (dd, J = 8.4, 1.5 Hz, 1 H), 8.58 (d, J = 8.6 Hz, 1 H), 9.72 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 28.1, 36.6, 41.5, 66.6, 71.9, 121.3, 121.5, 125.7, 126.7, 128.6, 129.3, 134.7, 135.8, 137.0, 137.4, 153.9, 172.2 ppm. IR: $\tilde{\nu}$ = 3353, 2724, 1651, 1613, 1543, 1309, 1264, 1140, 1104, 794 cm^{-1}. $C_{19}H_{20}N_4O_4$ (368.38): calcd. C 61.95, H 5.47, N 15.21; found C 61.66, H 5.78, N 14.99.

(*S*)-1-Cyclohexyl-3-[2-(4-isopropyl-4,5-dihydrooxazol-2-yl)ethyl]urea (14): According to the general procedure, product **14** (0.402 g, 1.42 mmol, 62%) was obtained as a white solid starting from precursor **20n** (0.688 g, 2.30 mmol). R_f = 0.54 (CH_2Cl_2/MeOH, 95:5). M.p. 103–104 °C. $[\alpha]_D^{20}$ = –39.45 (c = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.90 (d, J = 6.8 Hz, 3 H), 0.98 (d, J = 6.8 Hz, 3 H), 1.08–1.39 (m, 6 H), 1.59 (dt, J = 12.8, 3.8 Hz, 1 H), 1.71 (m, 2 H), 1.77 (m, 1 H), 1.92 (m, 2 H), 2.50 (m, 2 H), 3.51 (m, 2 H), 3.92 (m, 1 H), 4.02 (t, J = 8.1 Hz, 1 H), 4.32 (dd, J = 9.5, 8.5 Hz, 1 H), 4.61 (d, J = 7.5 Hz, 1 H), 5.49 (br. s, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 18.1, 18.7, 24.9, 25.6, 28.6, 32.5, 33.9, 36.6, 49.4, 70.3, 71.3, 157.6, 167.4 ppm. IR: $\tilde{\nu}$ =

3351, 3305, 2350, 1669, 1624, 1579, 1532, 1309, 1251, 1167, 1082, 982, 939, 891, 791 cm^{-1}. $C_{15}H_{27}N_3O_2$ (281.39): calcd. C 64.02, H 9.67, N 14.93; found C 63.89, H 9.90, N 14.79.

4-(Allyloxy)-4-oxo-2-(3-phenylureido)butanoic Acid (22a–b): 4-(Allyloxy)-2-amino-4-oxobutanoic acid hydrochloride **21a**–**b** (1.20 g, 5.72 mmol, 1.0 equiv.) was suspended in THF (57 mL), and triethylamine (0.79 mL, 5.72 mmol, 1.0 equiv.) was added dropwise. The reaction mixture was vigorously stirred for 30 min, then phenylisocyanate (0.65 mL, 5.72 mmol, 1.0 equiv.) was added and the mixture was stirred for 3 d at room temperature. The mixture was treated with cold Et_2O to induce precipitation of a white powder. The solid was washed with $KHSO_4$ 1 M to obtain products **22a** and **22b** as fine white powders (*R*-enantiomer: 1.394 g, 4.77 mmol, 83%. *S*-enantiomer: 1.407 g, 4.81 mmol, 84%). R_f = 0.28 (CH_2Cl_2/MeOH, 95:5). M.p. 186–187 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.86 (br. s, 2 H), 4.54 (br. s, 2 H), 4.78 (br. s, 1 H), 5.19 (d, *J* = 10.4 Hz, 1 H), 5.26 (d, *J* = 17.1 Hz, 1 H), 5.84 (m, 1 H), 6.8 (br. s, 1 H), 6.96 (t, *J* = 6.8 Hz, 1 H), 7.20 (t, *J* = 7.1 Hz, 2 H), 7.39 (d, *J* = 7.0 Hz, 2 H), 8.46 (br. s, 1 H), 11.23 (br. s, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 36.5, 49.9, 65.6, 118.4, 119.4, 122.6, 128.8, 131.8, 139.1, 156.5, 170.9 ppm. IR: $\tilde{\nu}$ = 3311, 2738, 2603, 2531, 2496, 1716, 1702, 1596, 1547, 1397, 1172, 1072, 1036, 851, 807 cm^{-1}. $C_{14}H_{16}N_2O_5$ (292.29): calcd. C 57.53, H 5.52, N 9.58; found C 57.89, H 5.87, N 9.34.

Allyl 4-Oxo-3-(3-phenylureido)-4-(pyrrolidin-1-yl)butanoate (23a,b): 4-(Allyloxy)-4-oxo-2-(3-phenylureido)butanoic acid **22a**,**b** (1.300 g, 4.45 mmol, 1.0 equiv.) and *N*,*N*-diisopropylethylamine (1.90 mL, 11.1 mmol, 2.5 equiv.) were dissolved in DMF (45 mL), and the solution was cooled to 0 °C. HBTU (1.3 equiv.) was added, and the solution was stirred at the same temperature for 30 min. Then pyrrolidine (0.44 mL, 5.34 mmol, 1.2 equiv.) was added, and the reaction mixture was stirred at 0 °C for 60 min and then overnight at room temperature. The solvent was evaporated under reduced pressure, and the mixture was separated by flash chromatography eluting with MeOH (gradient from 2 to 6%) in CH_2Cl_2 to yield products **23a**,**b** as pale yellow oils (*R*-enantiomer: 1.122 g, 3.24 mmol, 73%. *S*-enantiomer: 1.199 g, 3.47 mmol, 78%). R_f = 0.28 (CH_2Cl_2/MeOH, 95:5). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.88 (m, 2 H), 1.99 (m, 2 H), 2.68 (dd, *J* = 15.8, 6.7 Hz, 1 H), 2.89 (dd, *J* = 15.8, 7.4 Hz, 1 H), 3.42 (m, 2 H), 3.67 (m, 1 H), 3.78 (m, 1 H), 4.59 (t, *J* = 1.3 Hz, 1 H), 4.61 (t, *J* = 1.3 Hz, 1 H), 5.01 (t, *J* = 7.0 Hz, 1 H), 5.20 (ddd, *J* = 10.5, 2.7, 1.2 Hz, 1 H), 5.31 (ddd, *J* = 17.2, 3.0, 1.6 Hz, 1 H), 5.92 (m, 1 H), 6.98 (m, 1 H), 7.24 (m, 2 H), 7.34 (dd, *J* = 8.8, 1.0 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 23.7, 25.5, 36.6, 46.0, 46.5, 48.2, 65.1, 117.2, 118.8, 122.3, 128.4, 132.1, 139.2, 155.7, 170.2, 170.4 ppm. IR: $\tilde{\nu}$ = 2721, 2656, 2512, 2345, 1721, 1678, 1600, 1329, 1178, 1109, 1074, 997, 856 cm^{-1}. $C_{18}H_{23}N_3O_4$ (345.39): calcd. C 62.59, H 6.71, N 12.17; found C 62.33, H 6.57, N 11.99.

4-Oxo-3-(3-phenylureido)-4-(pyrrolidin-1-yl)butanoic Acid (24a,b): Allyl 4-oxo-3-(3-phenylureido)-4-(pyrrolidin-1-yl)butanoate **23a**,**b** (1.10 g, 3.18 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (30 mL), and the solution was cooled to 0 °C. Pyrrolidine (0.31 mL, 3.82 mmol, 1.2 equiv.), triphenylphosphane (0.149 g, 0.57 mmol, 0.18 equiv.) and tetrakis(triphenylphosphane)palladium(0) (0.147 g, 0.13 mmol, 0.04 equiv.) were added, and the reaction mixture was stirred for 1 h at 0 °C. The mixture was poured into EtOAc (200 mL) and extracted with satd. $NaHCO_3$ solution (5× 30 mL). The combined organic layers were acidified to pH 2 with 1 M $KHSO_4$ solution. The acidified aqueous solution was extracted with CH_2Cl_2 (3× 25 mL), and the combined organic layers were dried with Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash chromatography eluting with 6% MeOH in CH_2Cl_2 to yield products **24a**,**b** as yellow solids [(*R*)-enantiomer 0.754 g, 2.47 mmol, 77%. (*S*)-enantiomer 0.778 g, 2.55 mmol, 80%]. R_f = 0.30 (CH_2Cl_2/MeOH, 95:5). M.p. 168–169 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.85 (m, 2 H), 1.96 (m, 2 H), 2.73 (dd, *J* = 15.7, 6.2 Hz, 1 H), 2.84, (dd, *J* = 15.7, 6.1 Hz, 1 H), 3.44 (m, 2 H), 3.62 (m, 1 H), 3.80 (m, 1 H), 5.13 (m, 1 H), 6.75 (d, *J* = 8.8 Hz, 1 H), 6.97 (t, *J* = 7.5 Hz, 1 H), 7.21 (t, *J* = 7.5 Hz, 2 H), 7.34 (d, *J* = 7.7 Hz, 2 H), 8.08 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 24.1, 25.9, 37.5, 46.6, 47.1, 48.2, 119.5, 122.7, 128.8, 139.1, 155.4, 170.6, 173.7 ppm. IR: $\tilde{\nu}$ = 3347, 3202, 3145, 1728, 1685, 1615, 1553, 1518, 1481, 1312, 1203, 1119, 1046, 997 cm^{-1}. $C_{15}H_{19}N_3O_4$ (305.33): calcd. C 59.01, H 6.27, N 13.76; found C 59.34, H 5.99, N 13.44.

(*S*)-*N*-[(*S*)-1-Hydroxy-3-methylbutan-2-yl]-4-oxo-3-(3-phenylureido)-4-(pyrrolidin-1-yl)butanamide (25a): According to the general procedure, product **25a** (0.154 g, 0.39 mmol, 60%) was obtained as a yellow pale oil starting from acid **24a** (0.200 g, 0.65 mmol) and L-valinol. R_f = 0.33 (CH_2Cl_2/MeOH, 95:5). $[\alpha]_D^{20}$ = –78.04 (*c* = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ = 0.91 (d, *J* = 6.8 Hz, 3 H), 0.94 (d, *J* = 6.7 Hz, 3 H), 1.82–1.93 (m, 2 H), 2.00 (m, 1 H), 2.57 (dd, *J* = 14.4, 7.4 Hz, 1 H), 2.72 (dd, *J* = 14.4, 6.7 Hz, 1 H), 3.38–3.60 (m, 4 H), 3.69 (m, 2 H), 3.79 (m, 1 H), 5.02 (t, *J* = 7.2 Hz, 1 H), 6.98 (m, 1 H), 7.24 (m, 2 H), 7.33 (m, 2 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): δ = 17.4, 18.6, 23.7, 25.5, 28.5, 38.4, 45.9, 46.5, 48.8, 56.7, 61.7, 118.8, 122.2, 128.4, 139.2, 155.8, 170.7 ppm. IR: $\tilde{\nu}$ = 3310, 3259, 2767, 2456, 2412, 1665, 1565, 1508, 1459, 1334, 1300, 1211, 1098, 980, 876 cm^{-1}. $C_{20}H_{30}N_4O_4$ (390.48): calcd. C 61.52, H 7.74, N 14.35; found C 61.66, H 7.60, N 14.53.

(*R*)-*N*-[(*S*)-1-Hydroxy-3-methylbutan-2-yl]-4-oxo-3-(3-phenylureido)-4-(pyrrolidin-1-yl)butanamide (25b): According to the general procedure, product **25b** (0.144 g, 0.37 mmol, 56%) was obtained as a yellow pale oil starting from acid **24b** (0.200 g, 0.65 mmol) and L-valinol. R_f = 0.33 (CH_2Cl_2/MeOH, 95:5). $[\alpha]_D^{20}$ = –12.35 (*c* = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, CD_3OD, 25 °C): δ = 0.89 (d, *J* = 6.8 Hz, 3 H), 0.93 (d, *J* = 6.7 Hz, 3 H), 1.80–1.92 (m, 3 H), 2.00 (m, 2 H), 2.58 (dd, *J* = 14.3, 6.8 Hz, 1 H), 2.73 (dd, *J* = 14.3, 7.4 Hz, 1 H), 3.35–3.63 (m, 4 H), 3.70 (m, 2 H), 3.82 (m, 1 H), 4.99 (t, *J* = 7.0 Hz, 1 H), 6.98 (m, 1 H), 7.24 (m, 2 H), 7.33 (dd, *J* = 8.8, 1.2 Hz, 2 H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD, 25 °C): δ = 17.3, 18.6, 23.7, 25.5, 28.5, 38.3, 45.9, 46.5, 48.7, 56.7, 61.7, 118.7, 122.2, 128.4, 139.2, 155.8, 170.6, 170.8 ppm. IR: $\tilde{\nu}$ = 3300, 3256, 2789, 2481, 2426, 1656, 1599, 1548, 1499, 1315, 1224, 1100, 978, 856 cm^{-1}. $C_{20}H_{30}N_4O_4$ (390.48): calcd. C 61.52, H 7.74, N 14.35; found C 61.84, H 7.70, N 14.39.

1-[(*S*)-3-{(*S*)-4-Isopropyl-4,5-dihydrooxazol-2-yl}-1-oxo-1-(pyrrolidin-1-yl)propan-2-yl]-3-phenylurea (15): According to the general procedure, product **15** (0.083 g, 0.22 mmol, 58%) was obtained as a yellow solid starting from precursor **25a** (0.150 g, 0.38 mmol). R_f = 0.43 (CH_2Cl_2/MeOH, 95:5). M.p. 122–123 °C. $[\alpha]_D^{20}$ = –71.70 (*c* = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.84 (d, *J* = 6.7 Hz, 3 H), 0.92 (d, *J* = 6.7 Hz, 3 H), 1.66 (m, 1 H), 1.87 (m, 2 H), 1.96 (m, 2 H), 2.68 (dd, *J* = 15.2, 6.4 Hz, 1 H), 2.82 (dd, *J* = 15.2, 8.0 Hz, 1 H), 3.49 (m, 2 H), 3.78–3.92 (m, 4 H), 4.20 (dd, *J* = 9.4, 8.2 Hz, 1 H), 5.20 (m, 1 H), 6.88–6.96 (m, 2 H), 7.22 (t, *J* = 7.6 Hz, 2 H), 7.36 (d, *J* = 7.6 Hz, 2 H), 8.26 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 18.3, 18.7, 24.3, 25.9, 31.8, 32.6, 46.3, 47.1, 48.3, 70.3, 72.2, 118.8, 122.1, 128.7, 139.6, 155.2, 163.7, 170.9 ppm. IR: $\tilde{\nu}$ = 3330, 3223, 2721, 1656, 1623, 1567, 1504, 1398, 1311, 1214, 1200, 1178, 1123, 1083, 1034, 970 cm^{-1}. $C_{20}H_{28}N_4O_3$ (372.46): calcd. C 64.49, H 7.58, N 15.04; found C 64.67, H 7.30, N 14.99.

1-{(*R*)-3-[(*S*)-4-Isopropyl-4,5-dihydrooxazol-2-yl]-1-oxo-1-(pyrrolidin-1-yl)propan-2-yl}-3-phenylurea (16): According to the general procedure, product **16** (0.074 g, 0.20 mmol, 58%) was obtained as a yellow solid starting from precursor **25b** (0.134 g, 0.34 mmol). R_f = 0.43 (CH_2Cl_2/MeOH, 95:5). M.p. 126–127 °C. $[\alpha]_D^{20}$ = –13.76 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.83 (d, *J* = 6.7 Hz, 3 H), 0.87 (d, *J* = 6.7 Hz, 3 H), 1.65 (m, 1 H), 1.88 (m, 2 H), 1.97 (m, 2 H), 2.67 (dd, *J* = 15.6, 6.6 Hz, 1 H), 2.81 (dd, *J* = 15.6, 8.3 Hz, 1 H), 3.42–3.55 (m, 2 H), 3.83–3.93 (m, 4 H), 4.19 (dd, *J* = 8.7, 7.9 Hz, 1 H), 5.23 (m, 1 H), 6.89 (d, *J* = 9.5 Hz, 1 H), 6.94 (t, *J* = 7.3 Hz, 1 H), 7.21 (t, *J* = 7.7 Hz, 2 H), 7.35 (d, *J* = 7.8 Hz, 2 H), 8.35 (s, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$, 25 °C): δ = 18.2, 18.4, 24.3, 25.9, 31.9, 32.4, 46.3, 47.1, 48.0, 70.2, 72.1, 118.8, 122.0, 128.7, 139.8, 155.1, 163.9, 171.0 ppm. IR: $\tilde{\nu}$ = 3312, 2729, 1678, 1634, 1603, 1593, 1549, 1334, 1212, 1150, 1115, 1084, 1065, 991, 840 cm^{-1}. $C_{20}H_{28}N_4O_3$ (372.46): calcd. C 64.49, H 7.58, N 15.04; found C 64.71, H 7.44, N 14.81.

Supporting Information (see footnote on the first page of this article): Copies of the ^1H NMR and ^{13}C NMR spectra of all important intermediates and final products.

Acknowledgments

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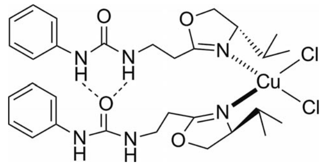
Supramolecular Catalysts

SupraBox ligands feature a chiral oxazoline ring and a urea functionality linked by a spacer and form supramolecular bidentate assemblies when coordinated to a metal. A small SupraBox library was prepared and tested in the kinetic resolution of racemic hydrobenzoin and the desymmetrization of *meso*-hydrobenzoin by copper-catalyzed benzoylation.



M. Durini, E. Russotto, L. Pignataro, O. Reiser,* U. Piarulli* 1–12

SupraBox: Chiral Supramolecular Oxazoline Ligands

Keywords: Supramolecular chemistry / Self-assembly / N ligands / Asymmetric catalysis / Acylation

