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AZT-prolinamide: the nucleoside derived pyrrolidine catalysts for asymmetric aldol reactions using water as solvent

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ABSTRACT

New pyrrolidine catalysts based on a nucleoside and proline, AZT-prolinamides, were synthesized and successfully employed for the enantioselective direct aldol reaction of aldehydes with ketones. These catalysts proved to be effective in promoting the reaction, in additive free water media with 15 mol % loading. The products, β-hydroxy carbonyl compounds were obtained in high yields and stereoselectivities.

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1. Introduction

Over the past decade, there has been tremendous advancement in the development of organocatalytic methods for carbon–carbon and carbon–heteroatom bond forming reactions. In particular, organocatalysts with additional binding sites, that illustrate the concept of multiple catalyst-substrate interactions during the catalytic mechanism have gained much attention in recent years.[1] Several catalysts designed around proline nuclei bearing a distinct range of functionalities have been reported in the literature.[2,3] Prolinamides were considered to be one such class of organocatalysts, which promote enamine catalysis very effectively for various asymmetric transformations. Several prolinamide derivatives with graded NH acidity and varying levels of steric control have been employed as organocatalysts for a wide range of organic transformations and found to be competent with varied levels of success.[4] Despite these significant advances, still there is a need for the design and development of new and readily accessible organocatalysts to overcome the common drawbacks such as strong substrate dependence, organic solvent medium and catalyst loading associated with most of the organocatalytic protocols. Our literature survey revealed that, synthetic peptides serve as effective catalyst systems for a range of transformations due to their ability for fine-tuning of the reactivity and selectivity.[5] With our continued interest in organocatalysis,[6] we developed two new pyrrolidine derivatives AZT-prolinamide **1** and **2** (Fig. 1) from L-proline and AZT under peptide coupling reaction conditions. To the best of our knowledge these represent the very first examples of nucleoside derived pyrrolidine organocatalysts to be reported. Prolinamides **1** and **2** bearing a nucleoside template were designed

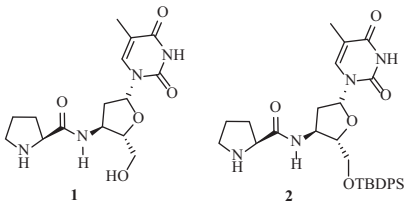

Figure 1. Structure of new nucleoside based prolinamides.

based on the assumption that the pyrrolidine ring would activate the nucleophile, the amide group would activate the electrophile through hydrogen bonding, while the nucleoside motif might serve as the steric controller and also contribute to additional hydrogen bond stabilization as the reaction progresses. In the literature, aldol reactions were found to be particularly suitable for testing the catalytic efficiency of prolinamide organocatalysts. Hence, the aldol reaction of ketones and aldehydes was chosen to evaluate the efficacy of compounds **1** and **2** as organocatalysts. The aldol reaction is one of the most explored fundamental carbon–carbon bond forming reactions in organocatalytic asymmetric synthesis.[7] This reaction offers the formation of chiral adducts with one or more stereogenic centers with the possibility of stereo regulation. The products of this reaction, β-hydroxy carbonyl compounds serve as valuable synthetic intermediates, for the construction of various bio-active natural products and drug molecules.[8] Employing water as the solvent media to perform organic transformations is one of the most fundamental and challenging objectives for organic chemists and substantial progress has been made in this direction in recent times.[9] With these objectives, we report herein the design, synthesis, and application of AZT-prolinamide **1** and **2** as a new catalytic system for the direct asymmetric aldol reaction of aldehydes with ketones under eco-friendly conditions.

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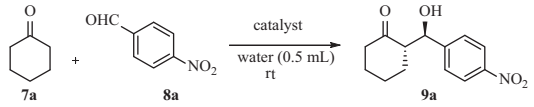
2. Results and discussion

The AZT-prolinamide catalysts **1** and **2** were synthesized from *N*-Cbz-proline **5** and commercially available AZT **3** using standard peptide coupling conditions, followed by deprotection of the protecting groups as depicted in Scheme 1. Accordingly, the primary hydroxy group in AZT was protected as a silyl ether using TBDPSCl/imidazole at room temperature to give compound **4** in 79% yield. The azide group in **4** was reduced to an amine using Pd–C/H_2 in methanol and coupled with acid **5** under EDCI/HOBt conditions to give compound **6**, which on deprotection of the Cbz group using Pd–C/H_2 in methanol resulted in compound **2**. Further removal of the silyl group using ammonium fluoride/methanol resulted in compound **1**. Both compounds **1** and **2** were screened to test their ability as organocatalysts.

Initially catalyst screening studies were conducted for the direct asymmetric aldol reaction by taking cyclohexanone **7a** and *p*-nitrobenzaldehyde **8a** as the model substrates (Scheme 2). The experiments were uniformly conducted with different catalyst loadings at room temperature using water as the reaction medium and the results are summarized in Table 1.

Both the catalysts were found to be equally efficient in carrying out the reaction at different loadings. The reaction performed with 15 mol % of catalyst was found to be more prominent and resulted in aldol adducts with high yields and selectivities (Table 1, entries 5 and 6). Increasing the catalyst loading to 20 mol % had no advantage and therefore 15 mol % was selected as the optimal catalyst loading to proceed to further optimization studies. In the processes of reaction optimization, we then conducted solvent screening experiments for the above transformation at room temperature using 15 mol % of catalyst and the results of this study are summarized in Table 2. As evident from the survey, the reaction proceeded well in all solvents irrespective of their polar/non-polar nature except for slight variations in reaction time, yields, and selectivities. The reactions employing catalyst **2** were found to be slightly inferior to those catalyzed by **1**. Though all solvents worked well, no single solvent proved to be more effective than water in promoting the aldol reaction using catalyst **1** or **2**. Therefore water was chosen as the solvent of choice to carry out aldol reactions using catalyst **1** or **2**.

After solvent screening studies we then tested the effect of additives on the asymmetric aldol reaction catalyzed by **1** or **2**.



7a **8a** **9a**

Scheme 2. Aldol reaction of cyclohexanone and *p*-nitrobenzaldehyde.

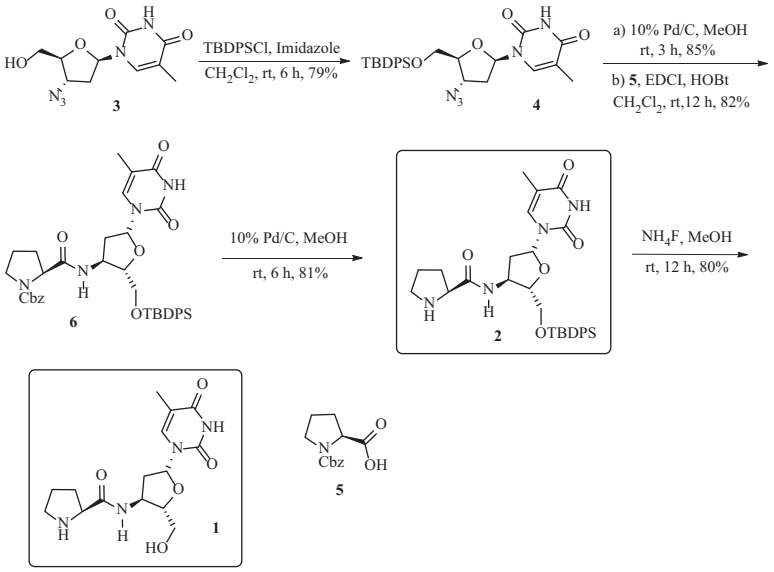
Table 1
Screening of catalysts[a]

Entry	Catalyst	mol%	Time (h)	Yield (%)[b]	*syn/anti*[c]	ee (%)[d]
1	1	5	48	46	91:9	81
2	2	5	48	38	91:9	74
3	1	10	36	71	93:7	92
4	2	10	36	69	91:9	85
5	1	15	24	96	95:5	97
6	2	15	24	94	95:5	94
7	1	20	24	95	96:4	95
8	2	20	24	95	97:3	96

[a] Reaction conditions: cyclohexanone (4 mmol), aldehyde (1 mmol).
[b] Isolated yields.
[c] Determined by the ^{1}H NMR of the crude product.
[d] Determined by chiral HPLC for the *anti*-diastereomer.

As summarized in Table 3, the reaction was practicable in the presence of acid additives, however it was inferior in productivity as compared to the additive free transformation.

With these initial screening experiments we noticed that both compounds **1** and **2** could be employed as organocatalysts to carry out asymmetric aldol reaction between cyclohexanone **7a** and aldehyde **8a** effectively under additive-free conditions employing water as the solvent medium. However, these results clearly indicate that compound **1** is slightly more effective than **2** as an organocatalyst. Having established the optimal reaction conditions, both catalysts were then tested to explore their versatility in this reaction. Several substrate combinations in which a variety of aldehydes **8b–l** were employed as aldol acceptors while cyclohexanone **7a** (Table 4) and other ketones **7b–e** (Table 5) were taken as the donors. As shown in Table 4, aldehydes **8b–l** reacted smoothly with cyclohexanone **7a** under the optimized reaction conditions and the corresponding aldol adducts **9b–l** were obtained in good yields and with high levels of stereoselectivities regardless of the nature of the substitution pattern in the aldehydes (Table 4, entries 1–11).



Scheme 1. Synthesis of AZT-prolinamide **1** and **2**.

Table 2
Screening of solvents[a]

Entry	Solvent	Catalyst	Time (h)	Yield[b] (%)	*anti*/*syn*[c]	ee[d] (%)
1	MeOH	1	24	84	93:7	87
		2	24	81	91:9	85
2	Hexane	1	36	80	95:5	90
		2	36	82	92:8	91
3	CH_3CN	1	36	79	85:15	80
		2	36	75	85:15	81
4	$CHCl_3$	1	36	81	92:8	80
		2	36	83	9:1	76
5	THF	1	36	78	91:9	81
		2	48	71	88:12	77
6	DMF	1	24	70	84:16	85
		2	36	74	8:2	81
7	Dioxan	1	48	76	75:25	78
		2	48	79	72:28	84
8	DMSO	1	24	75	85:15	82
		2	36	71	85:15	75
9	Neat	1	48	83	94:6	90
		2	48	80	92:8	87

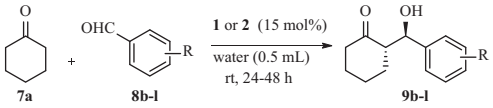
[a] Reaction conditions: catalyst (15 mol %), cyclohexanone (4 mmol), aldehyde (1 mmol), solvent (0.5 mL).
[b] Isolated yields.
[c] Determined by ^{1}H NMR of the crude product.
[d] Determined by chiral HPLC for the *anti*-diastereomer.

Table 3
Screening of additives[a]

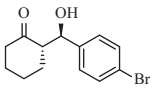
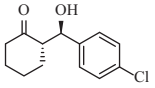
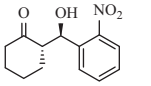
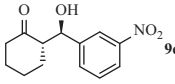
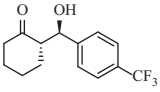
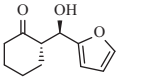
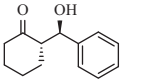
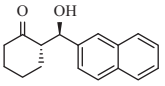
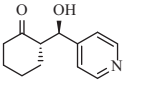
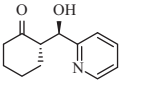
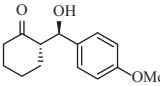
Entry	Additive	Catalyst	Time (h)	Yield[b] (%)	*anti*/*syn*[c]	ee[d] (%)
1	Acetic acid	1	24	72	82:18	75
		2	24	70	85:15	78
2	Formic acid	1	36	76	8:2	83
		2	36	73	8:2	77
3	Benzoic acid	1	24	86	94:6	90
		2	24	81	91:9	84
4	TFA	1	36	69	88:12	82
		2	36	73	85:15	80
5	pTSA	1	36	70	8:2	73
		2	36	71	75:25	76
6	CSA	1	36	74	84:16	81
		2	36	68	7:3	77
7	Anthranilic acid	1	24	89	93:7	89
		2	24	84	9:1	80

[a] Reaction conditions: catalyst (15 mol %), cyclohexanone (4 mmol), aldehyde (1 mmol), additive (5 mol %), water (0.5 mL).
[b] Isolated yields.
[c] Determined by the ^{1}H NMR of the crude product.
[d] Determined by chiral HPLC for the *anti*-diastereomer.

Table 4
Substrate scope of aldehydes[a]



7a **8b-l** **9b-l**

Entry	Product	Catalyst	Time (h)	Yield[b] (%)	*anti*/*syn*[c]	ee[d] (%)
1	 **9b**	1	24	93	94:6	94
		2	24	87	91:9	91
2	 **9c**	1	24	90	95:5	92
		2	30	84	93:7	87
3	 **9d**	1	24	89	96:4	95
		2	24	87	95:5	93
4	 **9e**	1	24	87	96:4	91
		2	36	81	92:8	85
5	 **9f**	1	24	94	94:6	93
		2	24	85	93:7	93
6	 **9g**	1	36	90	95:5	90
		2	36	83	91:9	84
7	 **9h**	1	36	81	92:8	89
		2	48	74	85:15	87
8	 **9i**	1	36	86	91:9	86
		2	48	73	88:12	81
9	 **9j**	1	36	91	93:7	90
		2	42	83	91:9	92
10	 **9k**	1	36	88	92:8	86
		2	36	85	92:8	81
11	 **9l**	1	42	82	91:9	84
		2	48	75	90:10	87

[a] Reaction conditions: cyclohexanone (4 mmol), aldehyde (1 mmol).
[b] Isolated yields.
[c] Determined by ^{1}H NMR of the crude product.
[d] Determined by chiral HPLC for the *anti*-diastereomer.

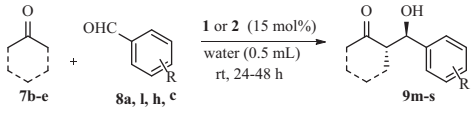
Reactions with other ketones **7b–e** were also found to be equally effective and the resultant products **9m–s** were obtained with good yield and selectivities (Table 5, entries 1–7). The major adducts formed were *anti* diastereomers in all cases except for the reaction of cyclopentanone, which gave the *syn* diastereomer as the major product (Table 5, entry 7). Despite the observed marginal variations in catalytic efficiencies, both compounds **1** and **2** could be employed as organocatalysts to perform asymmetric direct aldol reaction between aldehydes and ketones, as witnessed in the screening experiments. Overall, the observed efficacy of these new catalytic systems is in good agreement with our objectives aimed toward the development of eco-friendly protocols for organocatalytic asymmetric transformations and also in good agreement to those reported for a variety of organocatalysts known in the literature.[4,10]

The absolute stereochemical outcome of this transformation can be explained by considering the possible transition state[2a,11] models depicted in Figure 2. We believe that the pyrrolidine ring of the catalysts activates the ketones to result in enamine formation, while the nucleoside moiety acts as a steric controller and also contributes to hydrogen bond stabilization along with the amide group, and thereby activates the aldehyde substrates. The organocatalyst **1** provides additional hydrogen bond stabilization due to the presence of a free hydroxy group (A), while the catalyst **2** provides extensive steric coverage (B). Overall, positioning of all components results in a perfect architecture during transition state arrangement and lead to the formation of the desired products with high stereoselectivities.

3. Conclusions

In summary, we have developed an enantioselective direct asymmetric aldol reaction between aldehydes and ketones employing newly designed nucleoside based prolinamide organocatalysts.

Table 5
Substrate scope of ketones[a]



Entry	Product	Catalyst	Time (h)	Yield[b] (%)	*anti*/*syn*[c]	ee[d] (%)
1	**9m**	1	36	81	---	91
		2	36	78	---	90
2	**9n**	1	36	77	---	75
		2	48	72	---	77
3	**9o**	1	36	74	---	79
		2	48	73	---	81
4	**9p**	1	36	83	---	86
		2	36	75	---	87
5	**9q**	1	24	85	93:7	89[e]
		2	36	84	91:9	85[e]
6	**9r**	1	24	83	91:9	86[e]
		2	36	80	94:6	83[e]
7	**9s**	1	36	79	15:85	88[f]
		2	36	76	15:85	83[f]

[a] Reaction conditions: cyclohexanone (4 mmol), aldehyde (1 mmol).
[b] Isolated yields.
[c] Determined by ^{1}H NMR of the crude product.
[d] Determined by chiral HPLC.
[e] Determined by chiral HPLC for the *anti*-diastereomer.
[f] Determined by chiral HPLC for the *syn*-diastereomer.

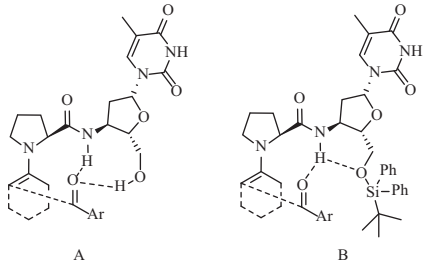


Figure 2. Possible transition state structures.

These catalysts exhibit great catalytic efficacy and led to the formation of aldol adducts with high yields and stereoselectivities. The best results were obtained under additive free water mediated reaction conditions. Further investigations on catalyst structure modification to extend the catalytic capacity of these new proline derivatives toward other organocatalytic asymmetric transformations are in progress.

4. Experimental

4.1. General

All solvents and reagents were purified by standard techniques. Crude products were purified by column chromatography on silica gel of 60–120 mesh. IR spectra were recorded on a Perkin–Elmer 683 spectrometer. Optical rotations were obtained on a Jasco Dip 360 digital polarimeter. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution on a Varian Gemini 200 and Brucker Avance 300. Chemical shifts were reported in parts per million with respect to internal TMS. Coupling constants j are quoted in Hz. Mass spectra were obtained on an Agilent Technologies LC/MSD Trap SL. Chiral HPLC analysis was carried out on chiral pak OD-H, IC, IA or AD-H columns using a mixture of isopropanol and hexanes as the eluent.

4.1.1. 1-((2*R*,4*S*,5*S*)-4-Azido-5-(((*tert*-butyldiphenylsilyl)oxy)-methyl) tetrahydrofuran-2-yl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione 4

To a stirred solution of azidothymidine **3** (5 g, 18.7 mmol) in CH_2Cl_2 (50 mL), were added imidazole (1.91 g, 28.8 mmol) and TBDPSCl (5.2 ml, 20.5 mmol) at 0 °C and allowed to stir at room temperature. After 6 h, the reaction mixture was quenched with saturated solution of NH_4Cl (40 mL) and extracted with ethyl acetate (2 × 50 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. Silica gel column chromatography (EtOAc/hexanes, 7:3) of the residue gave the silylether of azidothymidine **4** (7.5 g, 79% yield) as a colorless liquid. $[\alpha]_D^{20}$ = +213.14 (*c* 0.7, MeOH); IR (Neat): ν = 3185, 3044, 2933, 2860, 2106, 1677, 1468, 1266, 1111, 771, 105 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.05–8.95 (br s, 1H), 7.71–7.60 (m, 4H), 7.51–7.31 (m, 7H), 6.26 (t, *J* = 6.798 Hz, 1H), 4.37–4.27 (m, 1H), 4.06–3.91 (m, 2H), 3.87–3.76 (m, 1H), 2.50–2.40 (m, 1H), 2.35–2.21 (m, 1H), 1.63 (s, 3H), 1.10 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.0, 150.4, 135.2, 135.0, 134.6, 132.3, 131.9, 129.9, 129.8, 127.7, 127.7, 111.1, 84.0, 83.9, 63.2, 60.1, 37.4, 26.7, 19.0, 11.8; ESIMS: *m*/*z* 506 [M+H]$^+$; HRMS Calcd for $C_{26}H_{32}N_5O_4Si$: 506.2218, found 506.2221.

4.1.2. (*S*)-Benzyl 2-(((2*S*,3*S*,5*R*)-2-(((*tert*-butyldiphenylsilyl)oxy)-methyl)-5-(5-methyl-2,4-dioxo-3,4 dihydropyrimidin-1(2*H*) yl)-tetrahydrofuran-3 yl) carbamoyl)pyrrolidine-1-carboxylate 6

To a stirred solution of azidosilylether **4** (3 g, 13.5 mmol) in methanol (30 mL), was added 10% Pd/C (120 mg) at room temperature. The reaction mixture was subjected to hydrogen pressure (atmospheric) for 6 h. The reaction mixture was diluted with $CHCl_3$ (50 mL), filtered through a small pad of Celite, and concentrated under reduced pressure to obtain the free amine (2.4 g, 85% yield) as a white solid which was used for the next step without purification. To the solution of *N*-Cbz-proline **5** (900 mg, 3.4 mmol) in dry CH_2Cl_2 (15 mL), HOBt (690 mg, 5.1 mmol) and EDCI (976 mg, 5.1 mmol) were added sequentially at 0 °C and stirred at the same temperature for 15 min. Then, the solution of the above obtained free amine in dry CH_2Cl_2 was added to the reaction mixture and stirred at room temperature for 12 h. Ethyl acetate (30 ml) was added to dilute the reaction mixture, which was washed with saturated NH_4Cl solution (30 mL), aqueous $NaHCO_3$ solution (20 mL), and brine (20 mL). The combined organic layer was dried over Na_2SO_4, concentrated in vacuo, and purified by silica gel chromatography using ethylacetate/hexane (96:4) to afford dipeptide **6** (2 g, 82% yield) as a white solid. Mp: 115–118 °C; $[\alpha]_D^{20}$ = +8.40 (*c* 0.5, MeOH); IR (Neat): ν = 3322, 3191, 3069, 2956, 2930, 1690, 1467, 1422, 1114, 753, 703 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.02–9.90 (br s, 1H), 8.20–8.33 (m, 1H), 7.75–7.60 (m, 5H), 7.54–7.26 (m, 12H), 6.64–6.51 (m, 1H), 5.25 (s, 2H), 4.75–4.60 (br, 1H), 4.35–4.20 (br, 1H), 4.08–3.98 (m, 2H) 3.68–3.41 (m, 3H), 2.42–2.21 (m, 2H), 1.95–1.81 (m, 2H), 1.38 (s, 3H), 1.10 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.4, 163.6, 156.1, 151.3, 136.2, 135.5, 135.1, 134.9, 133.5, 132.2, 130.0, 129.8, 128.4, 128.2, 128.0, 127.9, 127.8, 112.1, 86.6, 84.0, 67.8, 65.0, 60.1, 51.2, 47.0,

36.9, 29.6, 28.9, 27.1, 24.8, 19.5, 11.6; ESIMS: m/z 711 $[M+H]^+$; HRMS Calcd for $C_{39}H_{47}N_4O_7Si$: 711.3209, found 711.3219.

4.1.3. (*S*)-*N*-((2*S*,3*S*,5*R*)-2-(((*tert*-Butyldiphenylsilyl)oxy)methyl)-5-(5-methyl-2,4-dioxo-3,4 dihydropyrimidin-1(2*H*) yl)tetrahydrofuran-3-yl)pyrrolidine-2-carboxamide 2

To a stirred solution of dipeptide **6** (2 g, 2.8 mmol) in methanol (30 mL), was added 10% Pd/C (120 mg) at room temperature. The reaction mixture was subjected to hydrogen pressure (atmospheric) for 6 h. The reaction mixture was diluted with $CHCl_3$ (50 mL), filtered through a small pad of Celite, and concentrated under reduced pressure to obtain the free amine compound **2** (1.3 g, 81% yield) as a colorless liquid. $[\alpha]_D^{20}$ = +1.86 (*c* 0.7, MeOH); IR (Neat): ν = 2924, 2853, 1745, 1680, 1460, 1219, 772 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.09 (d, J = 6.798 Hz, 1H), 7.75–7.62 (m, 4H), 7.50–7.33 (m, 7H), 6.42 (t, J = 7.55, 6.043 Hz, 1H), 4.77–4.63 (m, 1H), 4.05–3.88 (m, 2H), 3.76–3.66 (m, 1H), 3.09–2.86 (m, 1H), 2.42–2.21 (m, 2H), 2.01–1.86 (m, 2H), 1.80–1.65 (m, 4H), 1.53 (br s, 4H), 1.10 (br s, 10H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.6, 164.1, 151.3, 135.4, 135.0, 134.6, 133.2, 132.1, 129.8, 129.7, 129.2, 127.8, 127.4, 111.7, 80.0, 83.9, 64.4, 60.9, 49.7, 46.8, 37.7, 29.9, 29.5, 26.8, 26.4, 25.6, 19.3, 11.7; ESIMS: m/z 577 $[M+H]^+$; HRMS Calcd for $C_{31}H_{41}N_4O_5Si$: 577.2841, found 577.2839.

4.1.4. (*S*)-*N*-((2*S*,3*S*,5*R*)-2-(Hydroxymethyl)-5-(5-methyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)tetrahydrofuran-3-yl)pyrrolidine-2-carboxamide 1

To a stirred solution of compound **2** (2 g, 34.7 mmol) in methanol (20 mL), was added NH_4F (192 mg, 52 mmol) at 0 °C and allowed to stir at room temperature for 12 h. The reaction mixture was diluted with $CHCl_3$ (50 mL), filtered through a small pad of Celite, and concentrated under reduced pressure to obtain free amino alcohol **1** (940 mg, 80% yield) as a white solid. Mp: 170–173 °C; $[\alpha]_D^{20}$ = −7.60 (*c* 0.5, MeOH); IR (Neat): ν = 3340, 3062, 2928, 1684, 1548, 1472, 1272, 1099, 1059, 875, 771, 560 cm^{-1}; ^1H NMR (DMSO-d_6, 300 MHz): δ 7.92 (br, s, 1H), 7.60–7.45 (m, 1H), 6.10–5.90 (m, 1H), 4.65 (br, s, 3H), 4.42 (br, s, 1H), 3.67–3.57 (m, 3H), 3.55–3.42 (m, 2H), 2.16–2.01 (m, 2H), 1.95–1.82 (m, 1H), 1.70–1.58 (m, 4H), 1.54–1.39 (m, 2H), 1.05–0.95 (m, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 172.9, 164.2, 150.8, 136.7, 109.9, 85.0, 83.9, 61.6, 60.2, 49.2, 46.8, 37.3, 30.6, 25.4, 12.6; ESIMS: m/z 339 $[M+H]^+$; HRMS Calcd for $C_{15}H_{23}N_4O_5$: 339.1663, found 339.1651.

4.1.5. General procedure for the aldol reaction of ketones to aldehydes

To a mixture of catalyst **1** or **2** (15 mol %) and cyclohexanone (4 mmol) in H_2O (0.5 mL) was added aldehyde (1 mmol) and the resulting mixture was stirred for the appropriate time (Tables 4 and 5) at room temperature. After completion of the reaction (monitored by TLC), the mixture was purified by silica-gel column chromatography to afford the desired product. The relative and absolute configurations of the products were determined by comparison of ^1H NMR, ^{13}C NMR, and specific rotation values with those reported in the literature.[4]

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