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Metal-Assisted Aldol Condensation of Chiral 6-Methyl Perihydropyrimidin-4-ones

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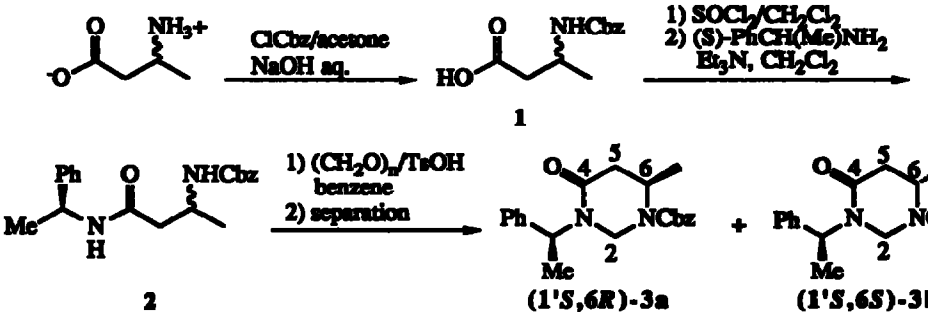
Abstract : The synthesis of 6-methyl perihydropyrimidin-4-ones (1'*S*,6*R*)-3a and (1'*S*,6*S*)-3b is reported starting from *rac*-3-aminobutanoic acid. The aldol condensation of various metal enolates of 3a and 3b with benzaldehyde and acetaldehyde is reported. All reactions afford complete facial diastereoselectivity and good simple diastereoselectivity, depending on the nature of the enolate and of the aldehyde. The reaction yields are generally good and the aldols have been characterized by means of ^{1}H NMR spectroscopy and NOEDIFF experiments.

The use of chiral perihydropyrimidin-4-ones as starting material to enantiomerically pure compounds is particularly attractive and several synthetic approaches to perihydropyrimidin-4-ones in enantiomerically pure form have been developed. Recently β-alanine was converted into *rac*-2-*tert*-butylperihydropyrimidin-4-one and alkylated at the α position in good yield and with d.s. > 96%.[1] 1-Benzoyl-2(*R*)-*tert*-butyl-3,6(*S*)- and 1-benzoyl-2(*S*)-*tert*-butyl-3,6(*S*)-dimethyl perihydropyrimidin-4-ones were obtained enantiomerically pure and alkylated with complete diastereoselection. Acid hydrolysis of the heterocycles afforded chiral 2-methyl and 2-benzyl-3-aminobutanoic acids.[2] Furthermore starting from asparagine the (*R*)- and (*S*)-2-*tert*-butyl-1-carbomethoxy-2,3-dihydro-pyrimidin-4-ones have been prepared which are useful starting material of enantiomerically pure β-aryl-β-amino acids.[3]

In our program directed towards the synthesis of α- and β-amino acids,[4] we have resolved the diastereomeric mixture of (*R*)- and (*S*)-6-methylperihydropyrimidin-4-ones 3a and 3b,[5] obtained *via* the mercuric cyclization of (*S*)-*N*-(1-phenyleth-1-yl)-*N*-benzyloxycarbonyl-aminomethyl allylacetamide utilizing (*S*)-phenylethylamine as the chiral moiety. After few easy steps enantiomerically pure (*R*)- and (*S*)-3-aminobutanoic acids were obtained in good yield. Moreover high diastereoselectivity has been observed in the alkylation of the lithium enolates of the 6-methylperihydropyrimidin-4-ones.[6]

Recently another simple synthesis of 3a and 3b has been envisaged starting from (*S*,*R*)-*N*-benzyloxycarbonyl-3-aminobutanoic acid 1. The acid 1 was converted into the amide 2, which was treated with paraformaldehyde under acid catalysis,[7] to afford a mixture of perihydropyrimidin-4-ones 3a and 3b that were easily separated by flash chromatography.

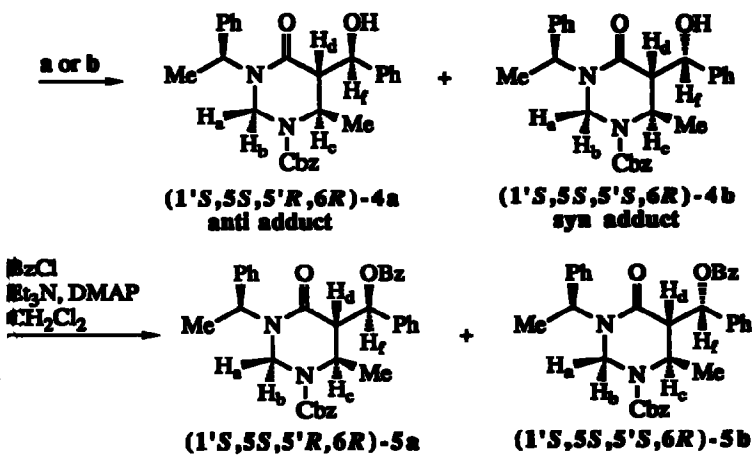


Herein we report our results on the aldol condensation of the enolates of (*R*)- and (*S*)-6-methyl perihydropyrimidin-4-ones **3a** and **3b** with benzaldehyde and acetaldehyde, with particular regard to the stereoselectivity as a function of the nature of the enolate and of the aldehyde.

Results and Discussion

The aldol condensation is a very efficient method for the formation of new carbon-carbon bonds and several laboratories developed methods to carry out the reaction under high stereocontrol.[8] The use of specific metal enolates, prepared by exchange reaction of the corresponding lithium enolates with a salt of the selected metal[9] allows the development of better conditions in order to obtain the desired stereoisomer.

The reaction of benzaldehyde with the lithium enolate of compound **3a** (Method A, see Experimental Section), generated under kinetic conditions by reaction of **3a** with LiHMDS at 0 °C in dry THF afforded aldol products with satisfactory yield. Among the four possible stereoisomers only the products **4a** and **4b** were obtained as a single spot in a 63:37 ratio, as indicated by the ^1H and ^{13}C NMR data. The two adducts were separated and fully characterized through the corresponding benzoates **5a** and **5b**.



a: 1) LiHMDS (1 equiv.), THF, 0 °C, 1h; 2) PhCHO, -78 °C, 1 h. b: 1) LiHMDS (1 equiv.), THF, 0 °C, 1h; 2) MX (1 equiv.), -78 °C, 1 h; 3) PhCHO, -78 °C, 1 h.

Since enolates of chiral perihydropyrimidin-4-ones have not been previously explored under aldol condensation conditions, in an effort to rationalize the selectivity of this reaction, other common metal cations were examined (Method B, see Experimental Section). Table 1 shows the results that we obtained for the aldol reaction of various enolates of **3a** with benzaldehyde. It shows that the zinc mediated aldol reaction (entry 1) improves the stereoselection producing an excess of the anti adduct. Also if the lithium enolate of **3a** is exchanged with $ClTi(Oi\text{-}Pr)_3$ (entry 2), an enrichment of the anti adduct is also observed (anti/syn ratio 81:19) The $ClTi(Oi\text{-}Pr)_3$ was obtained by mixing $TiCl_4$ and $Ti(Oi\text{-}Pr)_4$ in 1:3 ratio according to the Reetz procedure.[10]

Table 1. Diastereomeric Products Ratio and Chemical Yields for Aldol Reactions of (1'*S*,6*R*)-6-Methylperihydropyrimidin-4-one 3a

entry	electrophile	M	solvent	anti/syn ratio [a]	total yield [b]
1	PhCHO	ZnCl	ether/THF	85:15	75
2	PhCHO	$Ti(i\text{-}Pr)_3$	THF	81:19	82
3	PhCHO	Li	THF	67:33	90
4	PhCHO	$AlMe_2$	hexane/THF	50:50	43
5	PhCHO	$B(OMe)_2$	CH_2Cl_2/THF	20:80	80
6	PhCHO	$B(Oi\text{-}Pr)_2$	CH_2Cl_2/THF	20:80	80
7	PhCHO	$B(OBu)_2$	CH_2Cl_2/THF	20:80	80
8	MeCHO	Li	THF	25:75	90

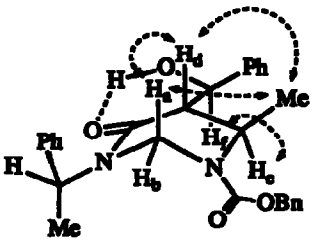
[a] The anti/syn ratios were determined on crude reaction mixtures by means of ^1H NMR and ^{13}C NMR. [b] All reported yields were based on isolated and purified products.

By exchanging the lithium enolate of **3a** with a 1M solution of $ClAlMe_2$ in hexanes (entry 4), **4a** and **4b** have been obtained in 50:50 anti/syn ratio, while a ratio of 20:80 anti/syn was observed using boron enolates (entries 5, 6 and 7). The chloroborates were obtained simply by mixing a 1M solution of BCl_3 in CH_2Cl_2 with $B(OR)_3$ in 1:2 molar ratio.[11] This result proves that the simple diastereoselection is regulated by the nature of the metal, in fact the anti/syn ratio improves going from the zinc enolate to the titanium, to the lithium, to the aluminium and to the boron enolate.

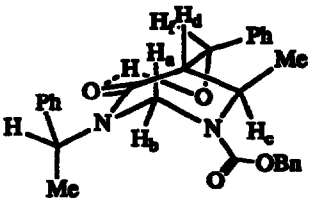
The diastereomeric ratios of **4a** and **4b** have been determined by means of the ^1H and ^{13}C NMR spectra of the crude reaction mixtures and all the hydrogens have been attributed through decoupling experiments. In particular the ^1H NMR signals of H_d of **4a** and **4b** are easily distinguishable as double doublets at δ 2.57 and 2.67 ppm respectively.

As mentioned above, only two compounds have been obtained from all the reactions of enolates of **3a** and benzaldehyde. Both the compounds **4a** and **4b** show a *trans* relationship between the hydrogens H_c and H_d, due to the facial diastereoselection induced by the heterocyclic methyl substituent on C_6. The *trans* relationship was confirmed by means of NOEDIFF experiments performed on **4a**.[12] In fact we noticed the enhancement of H_d and of the Me on C_6 upon irradiation of H_a and *viceversa*, and the enhancement of H_f and

H_b upon irradiation of H_c. Thus, as H_d and the Me on C_6 have a *cis* relationship, the perihydropyrimidin-4-one is 5,6-*trans* disubstituted.



(1'*S*,5*S*,5'*R*,6*R*)-4a



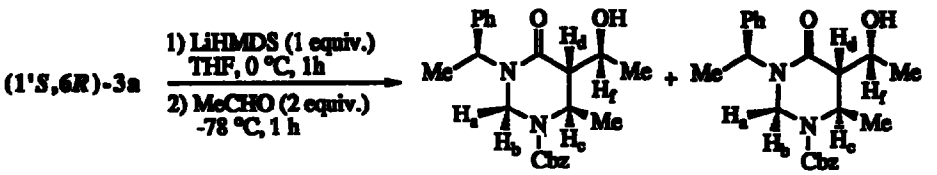
(1'*S*,5*S*,5'*S*,6*R*)-4b

Owing to the carbobenzoxy group, the perihydropyrimidin-4-ones 4a and 4b show the presence of two stable rotamers, already observed for this class of compounds.[4c,5] Unfortunately 20 °C is the coalescence temperature, so we are obliged to record the spectrum at a higher or a lower temperature. At 50 °C the spectrum is nicely resolved, but the hydroxyl group hydrogen was not identified as a doublet. So by recording the spectrum at -40 °C, we obtained a good resolution and the presence of two rotamers. The hydroxyl group signals appear as doublets at δ 4.79 ppm (J = 3.9 Hz) and at δ 3.61 ppm (J = 3.7 Hz) respectively, and do not change upon varying the concentration of the substrate. Thus at -40 °C in both aldol derivatives 4a and 4b a hydrogen bond between the carbonyl of the heterocycle and the hydroxyl group is present and forces the molecule in a preferential conformation that allows us to attribute the relative configuration at the newly introduced stereogenic center C'_6. In fact the ^{1}H NMR spectrum of 4a is characterized by the value of the chemical shift of H_d at δ 2.57 ppm in $CDCl_3$ with $J_{Hd,Hf}$ = 7.4 Hz indicative of an anti stereochemistry, while in the spectrum of 4b H_d resonates at δ 2.67 ppm with $J_{Hd,Hf}$ = 3.7 Hz, typical of a syn stereochemistry (Table 3).[8a] The comparison of the ^{1}H NMR spectra of 4a and 4b at -40 °C and +50 °C shows that the conformation of the molecules is very similar.

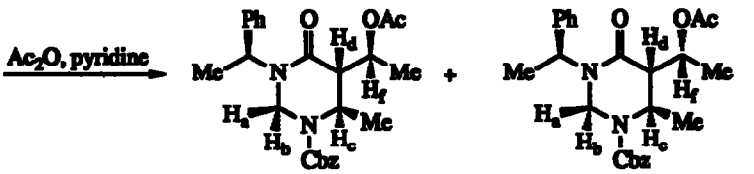
Furthermore the low values of $J_{Hd,Hc}$ for 4a (5.8 Hz) and for 4b (5.5 Hz) show that the heterocyclic rings are rather flat, due to the newly introduced bulky substituent at C_5.

The data are in agreement with a conformation of 4a and 4b similar to that of the starting material 3a with a *trans* relationship between H_d and H_c as well as an anti and a syn stereochemistry between H_d and H_f respectively.

In order to establish the influence of the aldehyde on the simple diastereoselection, the lithium enolate of 3a was reacted with acetaldehyde in THF. The reaction proceeds in high yield and with inversion of diastereoselectivity compared with the aldols of benzaldehyde, giving 6a and 6b in 25:75 anti/syn ratio. The mixture of aldols was acetylated and the two acetates 7a and 7b were separated.

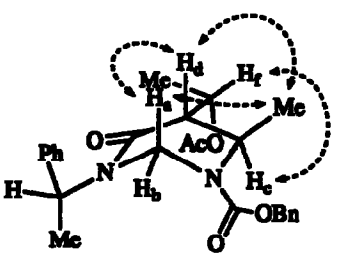


(1'*S*,5*S*,5'*S*,6*R*)-6a anti adduct (1'*S*,5*S*,5'*R*,6*R*)-6b syn adduct

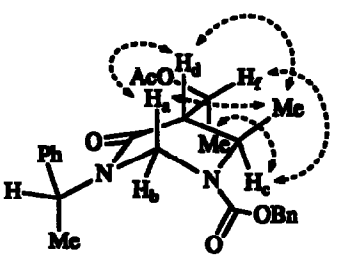


(1'*S*,5*S*,5'*S*,6*R*)-7a (1'*S*,5*S*,5'*R*,6*R*)-7b

In these examples also, the stereochemical attribution is based on the values of the coupling constants of H_c, H_d and H_f. In fact in the minor compound **6a** the $J_{Hd,Hf}$ = 7.3 Hz is in agreement with an anti relationship between H_d and H_f, while for **6b** the value of $J_{Hd,Hf}$ = 5.9 Hz is appropriate for a syn stereochemistry.[8a] Moreover by NOEDIFF experiments both acetates **7a** and **7b** show an enhancement of the Me on C_6 and of H_a, upon irradiation of H_d. This implies a *trans* relationship between H_d and H_c, although a low value of $J_{Hd,Hc}$ (4.6 Hz) was recorded for **6a** and **6b**.



(1'*S*,5*S*,5'*S*,6*R*)-7a



(1'*S*,5*S*,5'*R*,6*R*)-7b

These results confirm the capability of the lithium enolate to afford an anti selectivity for aromatic and a syn selectivity for aliphatic aldehydes, already reported in the literature.[9b,c,d]

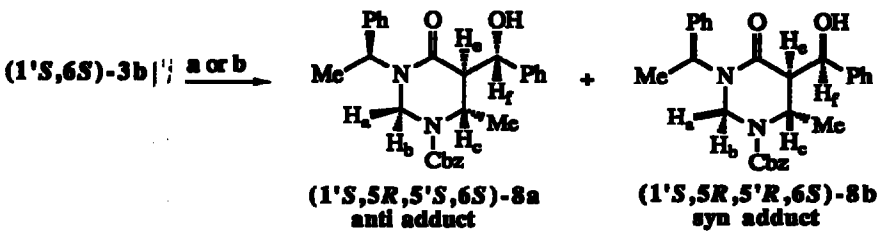
In order to establish the reactivity of perihydropyrimidin-4-one **3b** towards aldol condensation, the lithium and zinc enolates of **3b** have been reacted with benzaldehyde and acetaldehyde and the results are reported in Table 2.

Table 2. Diastereomeric Products Ratio and Chemical Yields for Aldol Reactions of (1'*S*,6*S*)-6-Methylperihydropyrimidin-4-one 3b

entry	electrophile	M	solvent	anti/syn ratio [a]	total yield [b]
1	PhCHO	Li	THF	66 :34	82
2	PhCHO	ZnCl	ether/THF	90 : 10	76
3	MeCHO	Li	THF	25 : 75	85
4	MeCHO	ZnCl	ether/THF	67 : 33	82

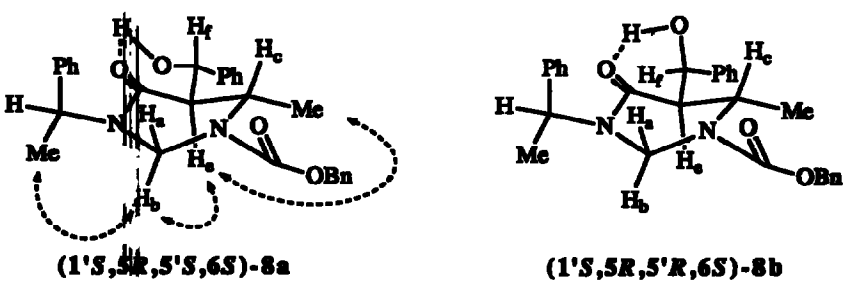
[a] The anti/syn ratios were determined on crude reaction mixtures by means of ^{1}H NMR and ^{13}C NMR. [b] All reported yields were based on isolated and purified products.

The metal enolates of 3b react with benzaldehyde affording the aldols 8a and 8b in good yield and these are easily separable by flash chromatography. The compounds were characterized by means of ^{1}H and ^{13}C NMR spectroscopy.



a: 1) LiHMDS (1 equiv.), THF, 0 °C, 1h; 2) PhCHO, -78 °C, 1 h.
b: 1) LiHMDS (1 equiv.), THF, 0 °C, 1h; 2) MX (1 equiv.), -78 °C, 1 h; 3) PhCHO, -78 °C, 1 h.

The NOEDIFF experiments performed on 8a[12] show the enhancement of the Me on C_6 and H_b upon irradiation of H_e and vice-versa, which implies a *trans* relationship between the substituents on C_5 and C_6 as previously observed.



Furthermore the ^{1}H NMR spectra of the compounds 8a and 8b recorded in $CDCl_3$ at -40 °C show a preferential conformation with a hydrogen bond between the hydroxyl group and the carbonyl of the heterocycle. This

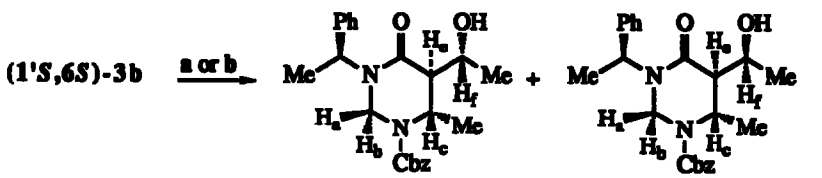
conformation was confirmed by the hydroxyl hydrogen signal of the rotamers, which appears as a doublet at δ 4.41 and 4.35 (J = 6.0 and 6.3 Hz) and δ 3.93 and 4.17 (J = 5.7 and 6.7 Hz) respectively and does not change upon varying the concentration of the sample (Table 3). The values of the coupling constant $J_{He,Hf}$ of 6.9 Hz and 3.2-3.6 Hz accounts for the anti and for the syn stereochemistry respectively.[8a]

Table 3. Significant ^{1}H NMR Data of Aldols 4 and 8 in $CDCl_3$ at 300 MHz at -40 °C

Product	d_{Hd}	$J_{Hd,Hf}$	d_{He}	$J_{He,Hf}$	d_{Hf}	d_{OH}	$J_{OH,Hf}$
4a	2.57	7.4	-	-	4.81 4.87[a]	4.79	3.9
4b	2.67	3.7	-	-	5.46	3.61	3.7
8a	-	-	2.60	6.9	4.74	4.35 4.41[a]	6.3 6.0[a]
8b	-	-	2.71 2.75[a]	3.6 3.2[a]	5.37	3.93 4.17[a]	5.7 6.7[a]

[a] Owing to the presence of two conformers, two chemical shifts values have been reported.

The aldols 9a and 9b were obtained in good yield by reaction of the lithium enolate of 3b with acetaldehyde (Method A, see Experimental Section) with the prefential formation of the syn adduct 9b, as previously observed for 3a (Equation 5). In contrast the aldol condensation of the zinc enolate of 3b with acetaldehyde (Method B, see Experimental Section) affords a mixture of aldols 9a and 9b in 67:33 anti/syn ratio.

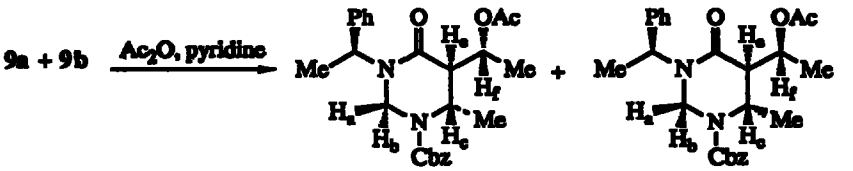


(1'S,5R,5'R,6S)-9a
anti adduct

(1'S,5R,5'S,6S)-9b
syn adduct

a: 1) LiHMDS (1 equiv.), THF, 0 °C, 1h; 2) MeCHO (2 equiv.), -78 °C, 1 h.
b: 1) LiHMDS (1 equiv.), THF, 0 °C, 1h; 2) MX (1 equiv.), -78 °C, 1 h; 3) MeCHO (2 equiv.), -78 °C, 1 h.

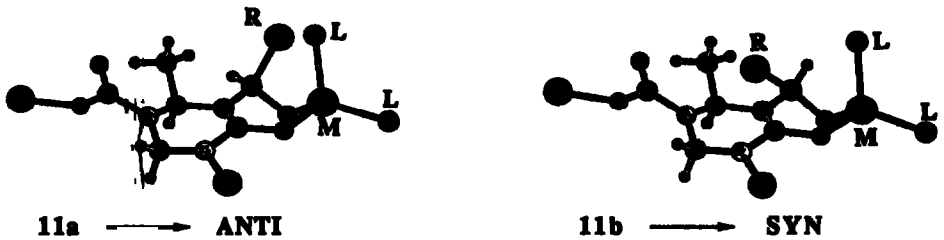
The mixtures of **9a** and **9b** were transformed into the corresponding acetates **10a** and **10b** in 90% yield and easily separated by silica gel chromatography. The structural assignment is made on the basis of the ^1H NMR spectra of **9a** and **9b**.



(1'*S*,5*R*,5'*R*,6*S*)-**10a** (1'*S*,5*R*,5'*S*,6*S*)-**10b**

Although the origin of the different stereoselection among zinc, lithium, titanium, aluminium and boron enolates is not completely understood, we propose a possible rationalization of the results obtained for **3a** with various aldehydes. The model takes in account the interactions between the enolate and the electrophile in the transition state, as a function of the metal nature.

To explain the stereochemical outcome we propose the closed transition states **11a** and **11b** both for aliphatic and for aromatic aldehydes. In the transition state **11a** a 1,3 repulsive interaction between the ligand L and the aldehyde side chain R is present. On the other hand in the trasition state **11b** the side chain R, lying in the more stable quasi-equatorial position, suffers from the 1,3 repulsive interaction with the adjacent methyl group.



11a ⟶ ANTI **11b** ⟶ SYN

The magnitude of the 1,3 R-L interaction in **11a** is dependent from the length of the metal-oxygen bond and increases with its decrease. For instance in the case of the bulky phenyl group of benzaldehyde, for metals with longer metal-oxygen distances like zinc, titanium and lithium (1.7 - 2.0 Å)[8a,9e], the phenyl-methyl 1,3 interaction disfavors **11b**, favoring the formation of the anti adduct, while, for the shorter oxygen-boron bond (1.3 - 1.4 Å),[8a,9e] the 1,3 L-R interaction becames predominant, disfavoring the transition state **11a** and favoring the formation of the syn adduct.

Furthermore entries 1 and 8 of Table 1 show a reversal of diastereoselectivity if acetaldehyde or benzaldehyde is used as electrophile. This result has already been observed[9b,c,d] and can be ascribed to the differences of steric hindrance between the methyl and the phenyl group. In fact, when the electrophile is acetaldehyde, the transition state **11b** is preferred, lying the smaller methyl substituent in the equatorial position free from steric interactions.

Thus the facial diastereoselectivity is controlled by the substituent on the perihydropyrimidin-4-one, while the simple diastereoselectivity is under the control of the metal, due to the length of the metal-oxygen bond, and strongly depends on the bulk of the aldehyde.

In conclusion, we have explored: (1) the diastereoselectivity of metal-mediated aldol reactions of chiral perihydropyrimidin-4-ones; (2) the preferential conformations assumed by the aldols, by means of ^{1}H NMR and NOEDIFF experiments; (3) a model that interprets the different results obtained on varying both the nature of the enolate and the aldehyde.

Experimental

^{1}H NMR and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz, respectively. Chemical shifts are reported in ppm relative to the solvent. Infrared spectra were recorded with a NICOLET 205 FT infrared spectrometer. Melting points were determined in open capillaries and are uncorrected. Flash chromatography was performed with silica gel 60 (230-400 mesh). Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Methylene chloride was distilled over CaH_2 and stored over molecular sieves. Other solvents were used as purchased. $ZnCl_2$ was purchased by Aldrich as 1M solution in ether, $ClAlMe_2$ was purchased by Aldrich as 1M solution in hexanes, and BCl_3 was purchased by Aldrich as 1M solution in CH_2Cl_2. $TiCl_4$, $Ti(Oi\text{-}Pr)_4$, $B(OMe)_3$, $B(Oi\text{-}Pr)_3$, $B(OBu)_3$ were purchased as pure liquids.

(*S*,*R*)-*N*-Benzyloxycarbonyl-3-aminobutanoic acid (1). To a stirring solution of (*S*,*R*)-3-aminobutanoic acid (48.5 mmol, 5.0 g) in H_2O (30 mL) were added NaOH pellets (97 mmol, 3.88 g). When the solution was clear, benzyl chloroformate (50.0 mmol, 7.14 mL) in acetone (30 ml) was added at 0 °C. The mixture was stirred at room temperature for 1 h, then the acetone was evaporated, and the aqueous layer was extracted with ethyl acetate. HCl (6M) was added to the aqueous layer until a pH = 2 was obtained and the mixture was extracted twice with ethyl acetate. The second organic layer was dried and concentrated under reduced pressure to give 1 as a white solid in 91% yield (44.1 mmol, 10.45 g): mp 122 °C; IR (film): 3300, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (d, 3H, J = 6.8 Hz, C*H*$_3$-CHN), 2.58 (d, 2H, J = 4.4 Hz, C*H*$_2$-CHN), 4.12 (m, 1H, CHN), 5.11 (s, 2H, OC*H*$_2$Ph), 5.27 (bs, 1H, NH), 7.35 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ 20.3, 40.2, 43.8, 66.7, 128.0, 128.1, 128.5, 136.3, 155.7, 176.2. Anal. Calcd. for $C_{12}H_{15}NO_4$: C, 60.73; H, 6.38; N, 5.91. Found: C, 60.77; H, 6.31; N, 5.83.

[*S*,(*S*,*R*)]-*N*-(1-Phenyleth-1-yl)-3-benzyloxycarbonylaminobutanamide (2). To a stirring solution of compound 1 (43.9 mmol, 10.42 g) in dry CH_2Cl_2 (80 mL), a solution of $SOCl_2$ (87.8 mmol, 3.2 mL) in dry CH_2Cl_2 (20 mL) was added dropwise at room temperature. The mixture was stirred for 30 min and the excess of $SOCl_2$ and the solvent were removed under vacuum. A waxy solid was obtained, and dry CH_2Cl_2 (30 mL) was added. The solution was added dropwise to a stirring solution of (*S*)-1-phenylethylamine (43.9 mmol, 5.59 mL) and triethylamine (48.2 mmol, 6.7 ml) in dry CH_2Cl_2 (10 mL) at 0 °C and stirred at room temperature for 2 hours. The mixture was washed with 1M HCl (40 mL), then with water, dried over Na_2SO_4 and concentrated under vacuum. Flash chromatography (cyclohexane/ethyl acetate 8:2 as eluant) of the residue afforded a white solid in 80% overall yield (35.1 mmol, 11.94 g): IR (film) 3300, 1680, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$) (mixture of diastereoisomers) δ 1.22 and 1.26 (d, 3H, J = 6.6 Hz, CH_2-CHN-C*H*$_3$), 1.45 and 1.47 (d, 3H, J = 6.9 Hz, Ph-CHN-C*H*$_3$), 2.41 (m, 2H, C*H*$_2$-CHN), 4.04 (m, 1H, CH_2-C*H*N-CH_3), 5.08 (s, 2H, OC*H*$_2$Ph), 5.11 (dq, 1H, J = 6.9 Hz, Ph-C*H*N-CH_3), 5.54 (bs, 1H, NH), 6.05 (bs, 1H, NH), 7.32 (m, 10H,

Ph); ^{13}C NMR ($CDCl_3$) (mixture of diastereoisomers) δ 20.5, 21.7, 42.6, 44.8, 48.8, 66.6, 126.1, 127.4, 127.9, 128.0, 128.5, 128.7, 136.5, 143.1, 155.8, 169.7. Anal. Calcd. for $C_{20}H_{24}N_2O_3$: C, 70.55; H, 7.11; N, 8.23. Found: C, 70.51; H, 7.14; N, 8.24.

1-Benzyloxycarbonyl-3-(1'-phenyleth-1'-yl)-6-methylperihydropyrimi-din-4-ones (3a) and (3b). To a stirring solution of amide 3 (35.1 mmol, 11.94 g) in benzene (200 mL) was added paraformaldehyde (351 mmol, 10.54 g) and *p*-toluenesulfonic acid monohydrate (35.1 mmol, 6.78 g). The mixture was refluxed for 1 h in a Markuson apparatus, washed with aqueous Na_2CO_3, dried over Na_2SO_4 and concentrated. After flash chromatography (cyclohexane/ethyl acetate 9:1 as eluant) of the residue (1'*S*,6*R*)-(3a) and (1'*S*,6*S*)-(3b) were obtained in 40% yield (14.0 mmol, 4.94 g) and 38% yield (13.3 mmol, 4.68 g) respectively. For the analytical and spectroscopic data see ref. 5.

Aldol condensation of (1'*S*,6*R*)-6-methylperihydropyrimidin-4-one (3a) and benzaldehyde
Method A - To a stirring solution of pyrimidin-4-one (3a) (1 mmol, 0.35 g) in dry THF (10 ml) was added dropwise LiHMDS (1M solution in THF, 1 mmol, 1 mL) in dry THF (2 ml) under argon at 0 °C. After 1 hour the mixture was cooled to -78 °C and freshly distilled benzaldehyde (1 mmol, 0.1 mL) in dry THF (2 ml) was added dropwise at -78 °C. After 1 h the reaction was quenched with absolute EtOH (1 mL), the solvent was removed under reduced pressure, replaced with CH_2Cl_2 and washed twice with water. The organic layer was dried over Na_2SO_4, concentrated and chromatographed on silica gel (cyclohexane/ethyl acetate 9:1 as eluant) to give the mixture of aldols (4a) and (4b), obtained as a single spot.
Method B - To a stirring solution of pyrimidin-4-one (3a) (1 mmol, 0.35 g) in dry THF (10 ml) was added dropwise LiHMDS (1M solution in THF, 1 mmol, 1 mL) in dry THF (2 ml) under argon at 0 °C. After 1 hour the mixture was cooled at -78 °C and MX (1 mmol) in dry THF (2 ml) was added dropwise. The mixture was stirred for an additional hour, then freshly distilled benzaldehyde (1 mmol, 0.1 mL) in dry THF (2 ml) was added dropwise at -78 °C. After 1 h the reaction was quenched with absolute EtOH (1 mL), the solvent was removed under reduced pressure, replaced with CH_2Cl_2 and washed twice with water. The organic layer was dried over Na_2SO_4, concentrated and chromatographed on silica gel (cyclohexane/ethyl acetate 9:1 as eluant) to give the mixture of aldols (4a) and (4b), obtained as a single spot.
(1'*S*,5*S*,5'*R*,6*R*)-(4a) : IR (film) 3405, 1704, 1646, 1620 cm^{-1}; ^1H NMR ($CDCl_3$, 50 °C) δ 0.92 (d, 3H, J = 6.3 Hz, CH-CHN-CH_3), 1.58 (d, 3H, J = 7.2 Hz, Ph-CHN-CH_3), 2.57 (dd, 1H, $J_{Hd,Hc}$ = 5.8 Hz, $J_{Hd,Hf}$ = 7.1 Hz, H_d), 3.97 (d, 1H, J = 12.9 Hz, H_a), 4.17 (m, 1H, H_c), 4.86 (d, 1H, $J_{Hf,Hd}$ = 7.1 Hz, H_f), 4.92 (d, 1H, J = 12.9 Hz, H_b), 5.10 (m, 2H, OCH_2Ph), 5.95 (q, 1H, J = 7.2 Hz, Ph-CHN-CH$_3$), 7.32 (m, 15H, Ph); ^{13}C NMR ($CDCl_3$, 50 °C) δ 15.8, 20.0, 47.9, 50.6, 51.0, 54.5, 67.8, 73.6, 126.1, 126.9, 127.3, 127.5, 127.7, 127.9, 128.2, 128.3, 128.4, 128.5, 128.7, 136.2, 139.2, 141.7, 153.6, 169.6.
(1'*S*,5*S*,5'*S*,6*R*)-(4b) : IR (film) 3405, 1704, 1646, 1620 cm^{-1}; ^1H NMR ($CDCl_3$, 50 °C) δ 0.80 (d, 3H, J = 6.5 Hz, CH-CHN-CH_3), 1.58 (d, 3H, J = 7.2 Hz, Ph-CHN-CH_3), 2.67 (dd, 1H, $J_{Hd,Hc}$ = 5.5 Hz, $J_{Hd,Hf}$ = 3.4 Hz, H_d), 3.95 (d, 1H, J = 12.8 Hz, H_a), 4.44 (m, 1H, H_c), 5.01 (d, 1H, J = 12.8 Hz, H_b), 5.12 (m, 2H, OCH_2Ph), 5.47 (d, 1H, $J_{Hf,Hd}$ = 3.4 Hz, H_f), 5.92 (q, 1H, J = 7.2 Hz, N-CH-CH$_3$), 7.32 (m, 15H, Ph); ^{13}C NMR ($CDCl_3$) δ 15.8, 20.0, 46.5, 50.6, 50.9, 54.9, 67.6, 72.5, 126.1, 126.9, 127.3, 127.5, 127.8, 127.9, 128.2, 128.3, 128.4, 128.5, 128.7, 136.2, 139.5, 141.2, 153.6, 169.6.

Benzoates (1'*S*,5*S*,5'*R*,6*R*)-(5a) and (1'*S*,5*S*,5'*S*,6*R*)-(5b). To a stirring solution of aldols (4a) and (4b) (0.68 mmol, 0.31 g) in dry CH_2Cl_2 (20 mL), was added triethylamine (1.36 mmol, 0.19 mL), 4-dimethylaminopyridine (0.07 mmol, 9 mg) and a solution of benzoyl chloride (1.02 mmol, 0.12 mL) in dry CH_2Cl_2 (10 mL) added dropwise under argon atmosphere at 0 °C. The reaction mixture was stirred overnight at room temperature, then washed twice with water, dried over Na_2SO_4 and concentrated. After flash chromatography (cyclohexane/ethyl acetate 9:1 as eluant) benzoates (5a) and (5b) were obtained separately in 85% overall yield.

(1'*S*,5*S*,5'*R*,6*R*)-(5a) : mp = 69 °C; IR (film) 1714, 1658 cm^{-1}; ^1H NMR ($CDCl_3$, 50 °C) δ 1.12 (d, 3H, J = 6.7 Hz, CH-CHN-CH_3), 1.47 (d, 3H, J = 7.3 Hz, Ph-CHN-CH_3), 3.08 (dd, 1H, $J_{Hd,Hc}$ = 2.5 Hz, $J_{Hd,Hf}$ = 7.8 Hz, H_d), 4.23 (d, 1H, J = 11.8 Hz, H_a), 4.26 (m, 1H, H_c), 4.82 (d, 1H, J = 11.8 Hz, H_b), 5.08 (m, 2H, OCH_2Ph), 6.04 (q, 1H, J = 7.3 Hz, Ph-C*H*N-CH$_3$), 6.44 (d, 1H, $J_{Hf,Hd}$ = 7.8 Hz, H_f), 7.33 (m, 18H, Ph), 8.15 (m, 2H, Ph); ^{13}C NMR ($CDCl_3$, 50 °C) δ 15.2, 19.7, 47.0, 50.1, 52.0, 54.7, 67.5, 74.1, 127.0, 127.4, 127.8, 127.9, 128.2, 128.4, 128.5, 128.6, 129.8, 133.1, 136.2, 137.6, 139.3, 153.5, 165.3, 166.2; $[\alpha]_D$ = -4.3 (c 1, $CHCl_3$). Anal. Calcd. for $C_{35}H_{34}N_2O_5$: C, 74.7; H, 6.09; N, 4.98. Found: C, 74.72; H, 6.11; N, 4.89.

(1'*S*,5*S*,5'*S*,6*R*)-(5b) : mp = 114 °C; IR (film) 1708, 1656 cm^{-1}; ^1H NMR ($CDCl_3$, 50 °C) δ 0.99 (d, 3H, J = 6.9 Hz, CH-CHN-CH_3), 1.44 (d, 3H, J = 7.1 Hz, Ph-CHN-CH_3), 2.85 (dd, 1H, $J_{Hd,Hc}$ = 2.3 Hz, $J_{Hd,Hf}$ = 4.3 Hz, H_d), 4.04 (d, 1H, J = 11.8 Hz, H_a), 4.73 (m, 1H, H_c), 4.97 (d, 1H, J = 11.8 Hz, H_b), 5.13 (s, 2H, OCH_2Ph), 6.04 (q, 1H, J = 7.1 Hz, Ph-C*H*N-CH$_3$), 6.68 (d, 1H, $J_{Hf,Hd}$ = 4.3 Hz, H_f), 7.35 (m, 18H, Ph), 8.05 (m, 2H, Ph); ^{13}C NMR ($CDCl_3$, 50 °C) δ 15.3, 19.8, 45.8, 50.2, 51.2, 54.2, 67.8, 75.7, 126.0, 127.4, 127.8, 128.0, 128.2, 128.4, 128.5, 128.6, 129.7, 133.0, 136.0, 138.2, 139.2, 153.6, 165.0, 166.3; $[\alpha]_D$ = +24.2 (c 1, $CHCl_3$). Anal. Calcd. for $C_{35}H_{34}N_2O_5$: C, 74.7; H, 6.09; N, 4.98. Found: C, 74.65; H, 6.15; N, 5.01.

Aldol condensation of (1'*S*,6*R*)-6-methylperihydropyrimidin-4-ones (3a) and acetaldehyde. To a stirring solution of pyrimidin-4-one (3a) (0.27 mmol, 95 mg) in dry THF (5 ml) was added dropwise LiHMDS (1M solution in THF, 0.27 mmol, 0.27 mL) in dry THF (2 ml) under argon at 0 °C. After 1 hour the mixture was cooled to -78 °C and freshly twice distilled acetaldehyde (0.54 mmol, 15 mL) in dry THF (2 ml) was added dropwise at -78 °C. After 1 h the reaction was quenched with absolute EtOH (1 mL), the solvent was removed under reduced pressure, replaced with CH_2Cl_2 and washed twice with water. The organic layer was dried over Na_2SO_4, concentrated and chromatographed on silica gel (cyclohexane/ethyl acetate 9:1 as eluant) to give the aldols (6a) and (6b), obtained as a mixture.

(1'*S*,5*S*,5'*S*,6*R*)-(6a) : IR (film) 3465, 1705, 1648 cm^{-1}; ^1H NMR ($CDCl_3$, 50 °C) δ 1.26 (d, 3H, J = 6.4 Hz, CH-CHN-CH_3), 1.31 (d, 3H, J = 7.1 Hz, HO-CH-CH_3), 1.58 (d, 3H, J = 7.1 Hz, Ph-CHN-CH_3), 2.09 (dd, 1H, $J_{Hd,Hc}$ = 4.6 Hz, $J_{Hd,Hf}$ = 7.3 Hz, H_d), 3.96 (d, 1H, J = 12.6 Hz, H_a), 4.16 (m, 1H, H_f), 4.21 (m, 1H, H_c), 4.62 (bs, 1H, OH), 5.07 (d, 1H, J = 12.6 Hz, H_b), 5.14 (m, 2H, OCH_2Ph), 5.97 (q, 1H, J = 7.1 Hz, Ph-C*H*N-CH$_3$), 7.32 (m, 10H, Ph); ^{13}C NMR ($CDCl_3$, 50 °C) δ 16.5, 19.4, 20.9, 48.5, 50.3, 50.9, 52.5, 67.0, 67.5, 127.2, 127.9, 128.0, 128.6, 128.7, 128.8, 136.2, 139.3, 155.0, 170.9.

(1'*S*,5*S*,5'*R*,6*R*)-(6b) : IR (film) 3457, 1702, 1654 cm^{-1}; ^1H NMR ($CDCl_3$, 50 °C) δ 1.23 (d, 3H, J = 6.4 Hz, HO-CH-CH_3), 1.32 (d, 3H, J = 6.4 Hz, CH-CHN-CH_3), 1.51 (d, 3H, J = 7.1 Hz, Ph-CHN-CH_3), 2.46 (dd, 1H, $J_{Hd,Hc}$ = 4.6 Hz, $J_{Hd,Hf}$ = 5.9 Hz, H_d), 3.74 (bs, 1H, OH), 3.97 (d, 1H, J = 12.9 Hz, H_a), 4.05 (dq, 1H, $J_{Hf,CH3}$ = 6.4 Hz, $J_{Hf,Hd}$ = 4.6 Hz, H_f), 4.23 (dq, 1H, $J_{Hc,CH3}$ = 6.4 Hz, $J_{Hc,Hd}$ = 5.9 Hz, H_c), 5.00 (d,

1H, J = 12.9 Hz, H_b), 5.18 (AB, J = 12.1 Hz, 2H, OCH_2Ph), 5.92 (q, 1H, J = 7.1 Hz, Ph-CHN-CH$_3$), 7.31 (m, 10H, Ph); ^{13}C NMR (CDCl$_3$, 50 °C) δ 16.0, 19.5, 47.8, 50.0, 50.8, 53.7, 67.3, 67.9, 127.3, 127.8, 128.1, 128.3, 128.5, 128.7, 136.1, 139.4, 153.9, 169.8.

Acetylation procedure of aldols (6a-b). A solution of aldol (6a-b) (0.25 mmol, 100 mg) in pyridine (1 ml) and acetic anhydride (1 ml) was stirred at room temperature overnight. The mixture was concentrated, the residue was chromatographed on silica gel (cyclohexane/ethyl acetate 9:1) and two acetates easily separated. The products were obtained in about 90 % overall yield.

(1'*S*,5*S*,5'*S*,6*R*)-(7a) : IR (film) 1739, 1706, 1662 cm^{-1}; ^{1}H NMR (CDCl$_3$, 50 °C) δ 1.19 (d, 3H, J = 6.6 Hz, CH-CHN-CH_3), 1.34 (d, 3H, J = 6.4 Hz, O-CH-CH_3), 1.55 (d, 3H, J = 7.1 Hz, Ph-CHN-CH_3), 2.03 (s, 3H, OCOCH$_3$), 2.57 (dd, 1H, $J_{Hd,Hc}$ = 4.2 Hz, $J_{Hd,Hf}$ = 5.2 Hz, H_d), 4.07 (d, 1H, J = 11.5 Hz, H_a), 4.37 (dq, 1H, $J_{Hc,CH3}$ = 6.6 Hz, $J_{Hc,Hd}$ = 4.2 Hz, H_c), 4.94 (d, 1H, J = 11.5 Hz, H_b), 5.14 (AB, J = 12.1 Hz, 2H, OCH_2Ph), 5.44 (dq, 1H, $J_{Hf,CH3}$ = 6.4 Hz, $J_{Hf,Hd}$ = 5.2 Hz, H_f), 5.96 (q, 1H, J = 7.1 Hz, Ph-CHN-CH$_3$), 7.32 (m, 10H, Ph); ^{13}C NMR (CDCl$_3$, 50 °C) δ 15.6, 17.4, 20.0, 21.1, 47.7, 50.1, 51.3, 52.3, 67.8, 69.8, 127.4, 127.7, 128.0, 128.3, 128.6, 128.7, 136.2, 139.5, 153.8, 166.9, 170.0; $[\alpha]_D$ = -40.7° (c 0.3, CHCl$_3$). Anal. Calcd. for $C_{25}H_{30}N_2O_5$: C, 68.47; H, 6.9; N, 6.39. Found: C, 68.49; H, 6.88; N, 6.28.

(1'*S*,5*S*,5'*R*,6*R*)-(7b) : IR (film) 1740, 1706, 1652 cm^{-1}; ^{1}H NMR (CDCl$_3$, 50 °C) δ 1.08 (d, 3H, J = 6.7 Hz, CH-CHN-CH_3), 1.38 (d, 3H, J = 6.3 Hz, O-CH-CH_3), 1.46 (d, 3H, J = 6.9 Hz, Ph-CHN-CH_3), 1.83 (s, 3H, OCOCH$_3$), 2.37 (m, 1H, H_d), 3.99 (d, 1H, J = 10 Hz, H_a), 4.45 (m, 1H, H_c), 4.90 (d, 1H, J = 10 Hz, H_b), 5.05 (AB, J = 12.3 Hz, 2H, OCH_2Ph), 5.15 (dq, 1H, $J_{Hf,CH3}$ = 6.3 Hz, $J_{Hf,Hd}$ = 6.6 Hz, H_f), 5.99 (q, 1H, J = 6.9 Hz, Ph-CHN-CH$_3$), 7.27 (m, 10H, Ph); ^{13}C NMR (CDCl$_3$, 50 °C) δ 15.5, 18.3, 19.1, 20.9, 45.8, 49.7, 51.2, 53.2, 67.7, 69.4, 127.4, 127.8, 128.1, 128.3, 128.5, 128.6, 135.9, 138.9, 153.5, 167.0, 169.3; $[\alpha]_D$ = -13.4 (c 1.6, CHCl$_3$). Anal. Calcd. for $C_{25}H_{30}N_2O_5$: C, 68.47; H, 6.9; N, 6.39. Found: C, 68.41; H, 6.78; N, 6.38.

Aldol condensation of (1'*S*,6*S*)-6-methylperihydropyrimidin-4-one (3b) and benzaldehyde. The reaction procedure was the same followed for compound (3a) and benzaldehyde, according to method A or method B. The reaction products (8a) and (8b) were easily separated by flash chromatography (cyclohexane/ethyl acetate 85:15 as eluant) as waxy solids.

(1'*S*,5*R*,5'*S*,6*S*)-(8a) : IR (film) 3419, 1706, 1650 cm^{-1}; ^{1}H NMR (CDCl$_3$, 50 °C) δ 1.03 (d, 3H, J = 6.6 Hz, CH-CHN-CH_3), 1.37 (d, 3H, J = 7.1 Hz, Ph-CHN-CH_3), 2.60 (dd, 1H, $J_{He,Hc}$ = 4.4 Hz, $J_{He,Hf}$ = 7.6 Hz, H_e), 4.18 (m, 1H, H_c), 4.40 (d, 1H, J = 12.1 Hz, H_b), 4.82 (d, 1H, $J_{Hf,He}$ = 7.6 Hz, H_f), 4.88 (d, 1H, J = 12.1 Hz, H_a), 5.05 (m, 2H, OCH_2Ph), 6.02 (q, 1H, J = 7.1 Hz, Ph-CHN-CH$_3$), 7.32 (m, 15H, Ph); ^{13}C NMR (CDCl$_3$, 50 °C) δ 16.2, 19.0, 47.2, 50.5, 54.8, 67.6, 73.7, 127.0, 127.1, 127.2, 127.8, 127.9, 127.9, 128.2, 128.4, 128.5, 128.7, 136.0, 139.2, 141.7, 169.9; $[\alpha]_D$ = -14.6 ° (c 0.8, CHCl$_3$). Anal. Calcd. for $C_{28}H_{30}N_2O_4$: C, 73.33; H, 6.6; N, 6.11. Found: C, 73.37; H, 6.71; N, 6.14.

(1'*S*,5*R*,5'*R*,6*S*)-(8b) : IR (film) 3430, 1707, 1644 cm^{-1}; ^{1}H NMR (CDCl$_3$, 50 °C) δ 1.01 (d, 3H, J = 6.7 Hz, CH-CHN-CH_3), 1.36 (d, 3H, J = 7.1 Hz, Ph-CHN-CH_3), 2.71 (dd, 1H, $J_{He,Hc}$ = 3.9 Hz, $J_{He,Hf}$ = 3.9 Hz, H_e), 4.34 (d, 1H, J = 12.1 Hz, H_b), 4.49 (dq, 1H, $J_{Hc,He}$ = 3.9 Hz, $J_{Hc,CH3}$ = 6.7 Hz, H_c), 4.80 (d, 1H, J = 12.1 Hz, H_a), 4.98 (m, 2H, OCH_2Ph), 5.32 (d, 1H, $J_{Hf,He}$ = 3.9 Hz, H_f), 5.98 (q, 1H, J = 7.1 Hz, Ph-CHN-CH$_3$), 7.32 (m, 15H, Ph); ^{13}C NMR (CDCl$_3$, 50 °C) δ 16.3, 19.7, 46.3, 50.6, 50.8, 67.5, 73.7, 126.3,

127.2, 127.6, 127.7, 127.8, 128.1, 128.3, 128.4, 128.6, 136.6, 139.3, 141.3, 153.5, 169.0; $[\alpha]_D$ = -2.3 (c 1, $CHCl_3$). Anal. Calcd. for $C_{28}H_{30}N_2O_4$: C, 73.33; H, 6.6; N, 6.11. Found: C, 73.4; H, 6.58; N, 6.2.

Aldol condensation of (1'*S*,6*S*)-6-methylperhydropyrimidin-4-ones (3b) and acetaldehyde
Method A - To a stirring solution of pyrimidin-4-one (3b) (0.27 mmol, 95 mg) in dry THF (5 ml) was added dropwise LiHMDS (1M solution in THF, 0.27 mmol, 0.27 mL) in dry THF (2 ml) under argon at 0 °C. After 1 hour the mixture was cooled to -78 °C and freshly twice distilled acetaldehyde (0.54 mmol, 15 mL) in dry THF (2 ml) was added dropwise at -78 °C. After 1 h the reaction was quenched with absolute EtOH (1 mL), the solvent was removed under reduced pressure, replaced with CH_2Cl_2 and washed twice with water. The organic layer was dried over Na_2SO_4, concentrated and chromatographed on silica gel (cyclohexane/ethyl acetate 9:1 as eluant) to give the aldols (9a) and (9b), obtained as a mixture.
Method B - To a stirring solution of pyrimidin-4-one (3b) (0.27 mmol, 95 mg) in dry THF (5 ml) was added dropwise LiHMDS (1M solution in THF, 0.27 mmol, 0.27 mL) in dry THF (2 ml) under argon at 0 °C. After 1 hour the mixture was cooled to -78 °C and $ZnCl_2$ (1M solution in ether, 0.27 mmol, 0.27 mL) in dry THF (2 ml) was added dropwise. After 1 hour, freshly twice distilled acetaldehyde (0.54 mmol, 15 mL) in dry THF (2 ml) was added dropwise at -78 °C. After 1 h the reaction was quenched with absolute EtOH (1 mL), the solvent was removed under reduced pressure, replaced with CH_2Cl_2 and washed twice with water. The organic layer was dried over Na_2SO_4, concentrated and chromatographed on silica gel (cyclohexane/ethyl acetate 9:1 as eluant) to give the aldols (9a) and (9b), obtained as a mixture.
(1'*S*,5*R*,5'*R*,6*S*)-(9a) : IR (film) 3438, 1701, 1646 cm^{-1}; ^1H NMR ($CDCl_3$, 50 °C) δ 1.29 (d, 3H, J = 6.6 Hz, CH-CHN-CH_3), 1.40 (d, 3H, J = 6.3 Hz, HO-CH-CH_3), 1.55 (d, 3H, J = 7.1 Hz, Ph-CHN-CH_3), 2.22 (dd, 1H, $J_{He,Hc}$ = 5.4 Hz, $J_{He,Hf}$ = 5.4 Hz, H_e), 3.68 (bs, 1H, OH), 3.98 (dq, 1H, $J_{Hf,He}$ = 5.4 Hz, $J_{Hf,CH3}$ = 6.3 Hz, H_f), 4.35 (m, 1H, H_c), 4.39 (d, 1H, J = 12.1 Hz, H_b), 4.90 (m, 2H, OCH_2Ph), 5.01 (d, 1H, J = 12.1 Hz, H_a), 5.98 (q, 1H, J = 7.1 Hz, Ph-C*H*N-CH$_3$), 7.32 (m, 10H, Ph); ^{13}C NMR ($CDCl_3$, 50 °C) δ 16.3, 19.3, 22.0, 47.8, 50.0, 50.6, 54.3, 67.4, 67.5, 127.0, 127.6, 127.7, 128.0, 128.4, 128.5, 135.9, 139.4, 153.8, 169.8.
(1'*S*,5*R*,5'*S*,6*S*)-(9b) : IR (film) 3438, 1701, 1646 cm^{-1}; ^1H NMR ($CDCl_3$, 50 °C) δ 1.29 (d, 3H, J = 6.6 Hz, CH-CHN-CH_3), 1.31 (d, 3H, J = 6.3 Hz, HO-CH-CH_3), 1.55 (d, 3H, J = 7.1 Hz, Ph-CHN-CH_3), 2.47 (dd, 1H, $J_{He,Hc}$ = 4.7 Hz, $J_{He,Hf}$ = 4.7 Hz, H_e), 3.68 (bs, 1H, OH), 3.98 (dq, 1H, $J_{Hf,He}$ = 4.7 Hz, $J_{Hf,CH3}$ = 6.3 Hz, H_f), 4.35 (m, 1H, H_c), 4.40 (d, 1H, J = 12.1 Hz, H_b), 4.93 (m, 2H, OCH_2Ph), 5.03 (d, 1H, J = 12.1 Hz, H_a), 5.98 (q, 1H, J = 7.1 Hz, Ph-C*H*N-CH$_3$), 7.31 (m, 10H, Ph); ^{13}C NMR ($CDCl_3$, 50 °C) δ 16.0, 19.1, 19.9, 47.3, 50.0, 50.6, 54.2, 67.4, 67.5, 127.0, 127.6, 127.7, 128.0, 128.4, 128.5, 135.9, 139.4, 153.8, 169.3.

Acetylation procedure of aldols (9a-b). See the acetylation procedure of aldols (6a-b).
(1'*S*,5*R*,5'*R*,6*S*)-(10a) : IR (film) 1737, 1707, 1642 cm^{-1}; ^1H NMR ($CDCl_3$, 50 °C) δ 1.27 (d, 3H, J = 6.8 Hz, CH-CHN-CH_3), 1.33 (d, 3H, J = 6.5 Hz, O-CH-CH_3), 1.56 (d, 3H, J = 7.1 Hz, Ph-CHN-CH_3), 1.97 (s, 3H, OCOCH$_3$), 2.58 (dd, 1H, $J_{He,Hf}$ = 4.5 Hz, $J_{He,Hc}$ = 2.9 Hz, H_e), 4.43 (d, 1H, J = 11.8 Hz, H_b), 4.48 (m, 1H, H_c), 4.78 (d, 1H, J = 11.8 Hz, H_a), 5.06 (m, 2H, OCH_2Ph), 5.39 (dq, 1H, $J_{Hf,CH3}$ = 6.5 Hz, $J_{Hf,He}$ = 4.5 Hz, H_f), 6.02 (q, 1H, J = 7.1 Hz, Ph-C*H*N-CH$_3$), 7.31 (m, 10H, Ph); ^{13}C NMR ($CDCl_3$, 50 °C) δ 15.7, 17.7, 19.7, 21.0, 50.2, 51.5, 52.4, 53.3, 67.6, 70.6, 127.3, 127.7, 127.9, 128.5, 128.6, 128.7,

139.5, 142.8, 158.2, 169.9; $[\alpha]_D$ = -23.5 (c 0.2, $CHCl_3$). Anal. Calcd. for $C_{25}H_{30}N_2O_5$: C, 68.47; H, 6.9; N, 6.39. Found: C, 68.55; H, 6.92; N, 6.35.

(1'*S*,5*R*,5'*S*,6*S*)-(10b) : IR (film) 1740, 1709, 1647 cm^{-1}; ^1H NMR ($CDCl_3$, 50 °C) δ 1.28 (d, 3H, *J* = 6.8 Hz, CH-CHN-C*H*$_3$), 1.36 (d, 3H, *J* = 6.4 Hz, O-CH-C*H*$_3$), 1.57 (d, 3H, *J* = 7.1 Hz, Ph-CHN-C*H*$_3$), 1.81 (s, 3H, $OCOCH_3$), 2.45 (dd, 1H, $J_{He,Hf}$ = 6.9 Hz, $J_{He,Hc}$ = 1.6 Hz, H_e), 4.48 (d, 1H, *J* = 11.7 Hz, H_b), 4.58 (m, 1H, H_c), 4.72 (d, 1H, *J* = 11.8 Hz, H_a), 5.02 (m, 2H, OC*H*$_2$Ph), 5.19 (dq, 1H, $J_{Hf,CH3}$ = 6.4 Hz, $J_{Hf,He}$ = 6.9 Hz, H_f), 6.04 (q, 1H, *J* = 7.1 Hz, Ph-C*H*N-CH_3), 7.30 (m, 10H, Ph); ^{13}C NMR ($CDCl_3$, 50 °C) δ 15.3, 18.5, 19.1, 20.8, 45.9, 50.2, 51.6, 53.9, 67.6, 69.4, 127.8, 128.2, 128.5, 128.6, 128.7, 136.1, 139.3, 153.7, 166.7, 169.8; $[\alpha]_D$ = -52.2 (c 0.5, $CHCl_3$). Anal. Calcd. for $C_{25}H_{30}N_2O_5$: C, 68.47; H, 6.9; N, 6.39. Found: C, 68.49; H, 6.85; N, 6.41.

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References and Notes

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