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PAPER

Bifunctional primary amine-thiourea–TfOH (BPAT·TfOH) as a chiral phase-transfer catalyst: the asymmetric synthesis of dihydropyrimidines†

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An enantioselective Biginelli reaction has been developed by using a bifunctional primary amine-thiourea–TfOH (BPAT·TfOH) as a chiral phase-transfer catalyst and *t*-BuNH$_2$·TFA as an additive in saturated brine at room temperature. The corresponding dihydropyrimidines were obtained in moderate-to-good yields with up to 99% ee under mild conditions. A plausible transition state has been proposed to explain the origin of the activation and the asymmetric induction.

Introduction

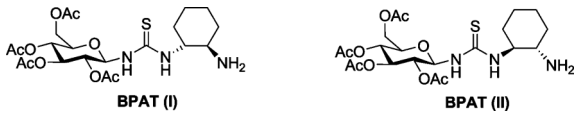
Enantioselective reactions that use chiral phase-transfer catalysts provided some of the most useful methods for practical asymmetric synthesis because of their simple reaction procedures and mild reaction conditions.[1,2] In 1984, the first efficient chiral phase-transfer catalyst, *N*-(*p*-(trifluoromethyl)-benzyl) cinchonidium bromide, was devised by the Merck group for the enantioselective synthesis of (+)-Indacrinone with 92% ee in 95% yield.[3] In 1989, O'Donnell reported a simple stereoselective synthesis of α-amino acid derivatives by the enantioselective alkylation of pro-chiral protected glycine derivatives with a chiral phase-transfer catalyst derived from a Cinchona alkaloid,[4] and recently, Corey,[5] Lygo,[6] Nájera[7] and Jew[8] have developed more efficient Cinchona alkaloid-derived chiral catalysts for this system. Although several efficient chiral phase-transfer catalysts exist,[9,10] the further development of efficient chiral phase-transfer catalysts is of great interest in the field.

The Biginelli reaction, originally described by the Italian chemist Pietro Biginelli in 1893, is one of the most useful multicomponent reactions and allows straightforward access to functionalized 3,4-dihydropyrimidin-2(1*H*)-ones (DHPMs).[11] Compounds containing the DHPM moiety are inherently asymmetric molecules, and the influence of the absolute configuration at the stereogenic center at C4 on their biological activity is well documented.[12] Much effort has been directed towards developing highly efficient asymmetric Biginelli reactions owing to the exhibition of a wide range of biological activities by DHPMs, such as antiviral, antitumor, antibacterial, and antiflammatory properties.[13] In the field of highly enantioselective Biginelli reactions catalyzed by an organocatalytic methodology, Gong has successfully applied BINOL-derived phosphoric acids with excellent enantiocontrol.[14] Feng has also reported an enantioselective Biginelli reaction catalyzed by a *trans*-4-hydroxyproline-derived secondary amine with a Brønsted acid as the combined catalyst.[15] Recently, Zhao and Wang have reported an asymmetric Biginelli reaction catalyzed by substituted 5-(pyrrolidin-2-yl)tetrazoles.[16] In view of these limited successful examples, it remains desirable to develop other new organocatalysts for this important transformation. We now wish to report our efforts in the development of the first enantioselective phase-transfer-catalyzed Biginelli condensation reactions.

Reactions in water have attracted a great deal of attention.[17] Apart from the obvious economic and environmental benefits, aqueous media might have favorable effects on reaction activity and selectivity. Recently, the positive benefits of aqueous solutions have also been discovered for organocatalysts.[18] In light of these successes and with the knowledge of the mechanism of Biginelli reactions, we envisaged that our catalytic system of a chiral bifunctional primary amine-thiourea and an acid could promote asymmetric Biginelli reactions in the presence of water.

Results and discussion

We initially investigated the catalytic asymmetric Biginelli reaction of urea (**5**), benzaldehyde (**6**) and ethyl acetoacetate (**7**) with the bifunctional thiourea catalyst BPAT (I)[19] (Scheme 1) and 2,4,6-trichlorbenzonic acid (TCBA) in the presence of water at room temperature. Based on the previous successful strategy,[15] 10 mol% of *t*-BuNH$_2$·TFA was added as an additive. As shown in Table 1, a series of different amounts of catalyst BPAT (I) was tested. The loaded amount of catalyst (5 and 10 mol%) could catalyze this reaction to provide the desired DHPM product in 83 and



Scheme 1 The structures of BPAT (I) and BPAT (II).

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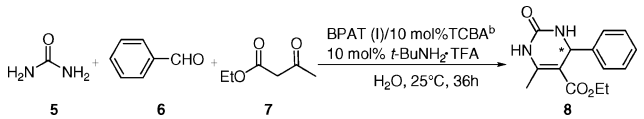
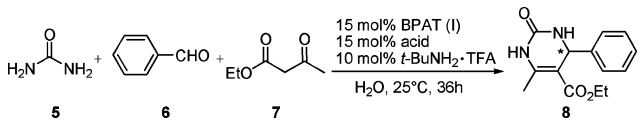
Table 1 Screening the amount of catalyst in an asymmetric Biginelli reaction[a]



Entry	Load of catalyst BPAT (I) (mol%)	Yield (%)[c]	ee (%)[d]
1	5	83	34
2	10	85	36
3	15	88	50
4	20	87	46

[a] The reaction was carried out on a 0.5 mmol scale and the ratio of **5** : **6** : **7** was 1 : 1.5 : 3. [b] TCBA = 2,4,6-trichlorbenzonic acid. [c] Isolated yield based on the urea. [d] Determined by HPLC (Chiralcel OD-H).

Table 2 Investigation of an acid-catalyzed asymmetric Biginelli reaction[a]



Entry	Acid	Yield (%)[b]	ee (%)[c]
1	HAc	16	60
2	HCl	41	54
3	Benzoic acid	33	65
4	*p*-TSA	58	61
5	TFA	72	22
6	TfOH	90	77

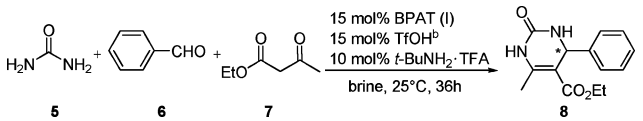
[a] The reaction was carried out on a 0.5 mmol scale and the ratio of **5** : **6** : **7** was 1 : 1.5 : 3. [b] Isolated yield based on the urea. [c] Determined by HPLC (Chiralcel OD-H).

85% yields respectively, but the enantioselectivities were rather poor (Table 1, entries 1 and 2). Next, we explored catalyst BPAT (I) (15 mol%) and found that this reaction worked effectively to provide the DHPM in 88% yield and 50% ee. Furthermore, increasing the loaded amount of catalyst from 15 to 20 mol% did not affect the yield, but resulted in a lower ee (Table 1, entry 4).

The acid additive was found to play another important role in Biginelli reactions.[20] In order to improve the efficiency, various acids combined with catalyst BPAT (I) were then employed to catalyze this reaction. Compared to TCBA, other organic and inorganic acids catalyzed the reaction smoothly. For example, acetic acid, hydrochloric acid, benzoic acid, *p*-toluenesulfonic acid, TFA and trifluoromethane sulfonic acid (TfOH) combined with catalyst BPAT (I) and 10 mol% of *t*-$BuNH_2$·TFA as an additive were employed to catalyze the reaction, and DHPMs in moderate ee were obtained (Table 2, entries 1–5). Within the acids examined, TfOH was found to be the most effective, and the reaction achieved 90% yield with 77% ee (Table 2, entry 6).

In order to clarify the effect of water on this reaction, the Biginelli reaction was further undertaken in unsaturated and saturated NaCl aqueous solutions in the presence of catalyst BPAT (I) combined TfOH and *t*-$BuNH_2$·TFA as an additive (Table 3). Reactions in 5, 10, 15 and 20% NaCl aqueous solutions gave similar stereochemical results and yields. The best result, with a 93% yield and a greater than 99% ee, was obtained after a reaction

Table 3 Optimization of the influence of solvent on an asymmetric Biginelli reaction[a]



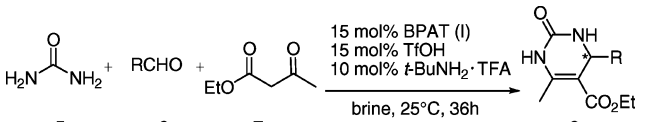
Entry	Concentration of brine (%)	Yield (%)[c]	ee (%)[d]
1	5	82	84
2	10	87	83
3	15	84	87
4	20	80	91
5	26 (saturated)	93	>99

[a] Reagents and conditions: After stirring a solution of acid (15 mol%) and catalyst BPAT (I) (15 mol%) in 2 mL of solvent at 25 °C for 0.5 h, urea (0.5 mmol), benzaldehyde (0.75 mmol), ethyl acetoacetate (1.5 mmol) and *t*-$BuNH_2$·TFA (10 mol%) were added sequentially. [b] TfOH = trifluoromethane sulfonic acid. [c] Isolated yield based on urea. [d] Determined by HPLC (Chiralcel OD-H).

for 36 h when saturated brine was used as the solvent (Table 3, entry 5). Thus, the optimal reaction conditions for this transformation were determined to be 0.5 mmol urea, 1.5 equivalent aldehyde, 3 equivalent ethyl acetoacetate and 15 mol% catalyst BPAT (I) combined with 15 mol% of TfOH containing 10 mol% of *t*-$BuNH_2$·TFA in saturated brine at room temperature. On the other hand, when CH_2Cl_2 was used as the solvent, the reaction afforded the DHPM product with a lower yield and a decreased enantioselectivity, accompanied by a longer reaction time (72 h). Thus, the role of water in the studied reaction is not only *via* the reaction medium, but also by its influence on the reaction rate and stereoselectivity. The beneficial influence of brine over water can be explained only on the basis of ionic complexation;[21] the rate acceleration may be attributed to hydrogen bonding interactions. In addition, a temperature investigation of the reaction established that this reaction is strongly exothermic.[22] Because of the large specific heat capacity of water, it is very efficient for removing the thermal energy from reaction mixtures.

Based on the above optimized reaction conditions, the substrate scope of this reaction was investigated (Table 4). In general, all the examined substrates produced the desired products in good yields. The scope of the aldehyde was investigated by the reaction with urea (**5a**) and ethyl acetoacetate (**7**). It appears that the electronic properties and the position of the substituents on the aromatic aldehyde have a great influence on the enantioselectivity of the reaction. Both the reactions of benzaldehyde and *para*-substituted benzaldehydes with electron-withdrawing groups proceeded in high yields and excellent enantioselectivities (>99 and 88% ee) (Table 4, entries 1 and 2). However, *p*-chlorobenzaldehyde and *p*-bromobenzaldehyde gave lower enantioselectivities (55 and 44% ee) (Table 4, entries 3 and 4), and *para*-substituted benzaldehydes with electron-donating groups underwent the Biginelli reaction with good yields and good enantioselectivities (Table 4, entries 5 and 6). *Meta*-substituted benzaldehydes with both electron-withdrawing and electron-donating groups underwent the reaction with good yields and enantioselectivities (Table 4, entries 7 and 8). The enantioselectivity was improved from 51 to 81% ee when 2 equivalents of TfOH were employed in the Biginelli reaction with *o*-chlorobenzaldehyde (Table 4, entries 9 and 10). Simultaneously,

Table 4 Enantioselective Biginelli reactions catalyzed by chiral bifunctional primary amine-thiourea phase-transfer catalysts in brine[a]



Entry	8	R	Yield (%)[b]	ee (%)[c]	Configuration[d]
1	**8a**	C_6H_5	93	>99	*S*
2	**8b**	4-(F)-C_6H_4	86	88	*S*
3	**8c**	4-(Cl)-C_6H_4	77	55	*S*
4	**8d**	4-(Br)-C_6H_4	74	44	*S*
5	**8e**	4-(Me)-C_6H_4	89	82	*S*
6	**8f**	4-(OMe)-C_6H_4	66	89	*S*
7	**8g**	3-(F)-C_6H_4	84	87	*S*
8	**8h**	3-(Me)-C_6H_4	82	80	*S*
9	**8i**	2-(Cl)-C_6H_4	62	51	*S*
10[e]	**8i**	2-(Cl)-C_6H_4	72	81	*S*
11[f]	**8j**	C_6H_5	90	>99	*R*

[a] Reagents and conditions: After stirring a solution of TfOH (15 mol%) and catalyst BPAT (I) (15 mol%) in 2 mL of saturated brine at 25 °C for 0.5 h, urea (0.5 mmol), benzaldehyde (0.75 mmol), ethyl acetoacetate (1.5 mmol) and *t*-$BuNH_2$·TFA (10 mol%) were added sequentially. [b] Isolated yield based on urea. [c] Determined by HPLC (Chiralcel OD-H). [d] The absolute configuration was determined by comparison of the optical rotation with literature data.[23] [e] 2 equivalents of TfOH were employed. [f] Catalyst BPAT (II) (15 mol%) was employed in the reaction.

chiral catalyst BPAT (II) exhibited a similar level of stereoselectivity with an opposite mode of asymmetric induction, and up to 99% ee could be obtained. This result indicates that both the (*R*,*R*) and (*S*,*S*)-configurations of 1,2-diaminocyclohexane matched the β-D-glucopyranose and enhanced the stereochemical control (Table 4, entry 11).

A possible mechanism for the reaction is shown in Fig. 1. When the reaction is carried out in an aqueous medium, the water molecules hydrogen bond with the thiourea moiety of bifunctional catalyst BPAT (I) and the acyl group of the benzylideneurea, while the neighbouring primary amine activated ethyl acetoacetate (**7**) forms an enamine intermediate, as shown in transition state I (TS I). The obtained absolute configuration (*S*) of the DHPMs is explained by TS I, in which the *Re*-face of the imine is predominantly approached by the enamine intermediate. The approach of the enamine to the *Si*-face of the benzylideneurea is restricted by the cyclohexyl scaffold of the catalyst. The fact that brine significantly enhances the catalytic performance of the Biginelli reaction suggests that, besides the salt effect, brine could stabilize TS I through a hydrogen bonding interaction with the aid of TfOH and promote the hydrolysis step to complete the catalytic cycle.

Conclusions

In summary, we have developed an enantioselective multicomponent Biginelli reaction catalyzed by a bifunctional primary amine-thiourea–TfOH (BPAT·TfOH) as a chiral phase-transfer catalyst and *t*-$BuNH_2$·TFA as an additive. The catalyst worked efficiently in aqueous media and offered high yields and moderate enantioselectivities. The configuration of the products have been rationalized on the basis of a proposed transition state. Most importantly, saturated brine significantly promoted the reaction's performance. Further studies on the catalytic system in other reactions are now under way.

Experimental

General remarks

All reactions were performed under air. Unless otherwise indicated, all materials were obtained from commercial sources and used as purchased without dehydration. Element analyses were carried out on a Yanaco CHN Corder MT-3 automatic analyzer in the Analysis Center of Nankai University. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ or d_6-DMSO using Bruker

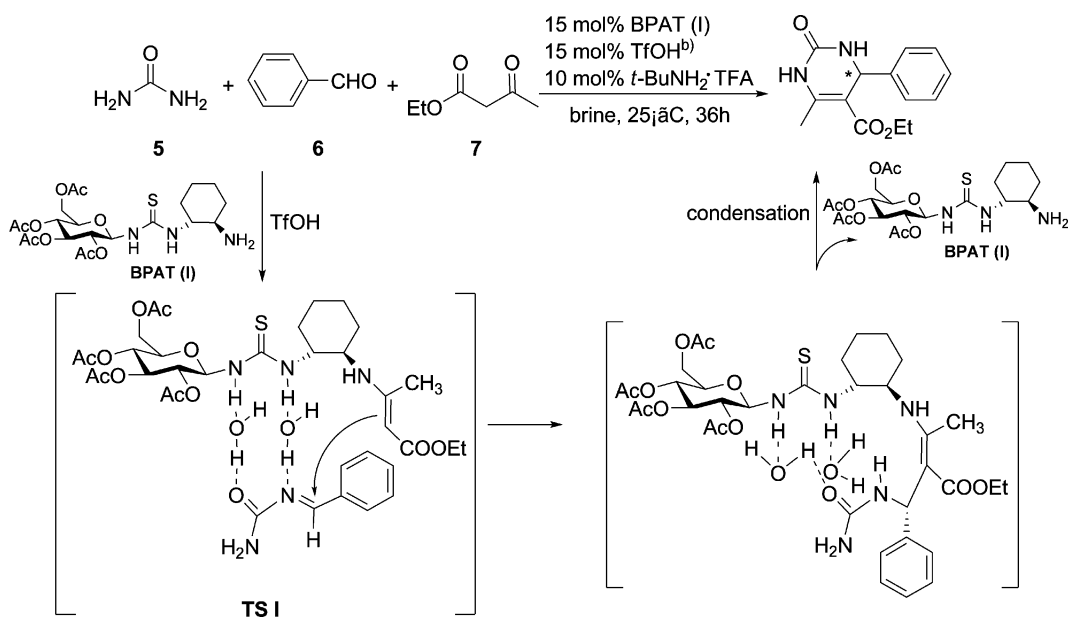


Fig. 1 A plausible reaction mechanism.

400 MHz spectrometers. TMS served as the internal standard (δ = 0) for ^{1}H NMR and DMSO was used as the internal standard (δ = 42.4) for ^{13}C NMR; coupling constants, J, are given in Hz. HPLC analyses were recorded on a chiral column (Daicel Chiralcel OD-H column at 254 nm). Melting points were determined on a T-4 melting point apparatus. Optical rotations were recorded on a Perkin-Elmer 241 polarimeter.

General procedure for the Biginelli reaction

To a suspension of catalyst BPAT (I) (0.039 g, 0.075 mmol) in saturated brine (2 mL) was added TfOH (0.011 g, 0.075 mmol). After stirring for 30 min, aldehyde **6** (0.75 mmol), urea **5** (0.030 g, 0.5 mmol), ethyl acetoacetate **7** (0.195 g, 1.5 mmol) and *t*-BuNH$_2$·TFA (0.009 g, 0.05 mmol) were added sequentially. The reaction mixture was stirred at room temperature for 36 h. After completion of the reaction, the resulting mixture was extracted with AcOEt and dried using anhydrous sodium sulfate. After concentration, the residue was purified by CC (silica gel, AcOEt/petroleum ether (b.p. 60–90 °C) 3 : 2) to afford the DHPM as a white solid.

(*S*)-(+)-5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (8a). White solid; mp 206–207 °C; $[\alpha]_D^{20}$ = 65° (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.16 (t, $^3J_{H,H}$ = 6.8 Hz, 3H, OCH_2CH_3), 2.34 (s, 3H, CH_3), 4.08 (q, $^3J_{H,H}$ = 6.8 Hz, 2H, OCH_2CH_3), 5.40 (d, $^3J_{H,H}$ = 2.4 Hz, 1H, CH), 5.79 (s, 1H, NH), 7.27–7.32 (m, 5H, Ph), 8.25 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.14, 18.67, 55.72, 60.03, 101.32, 126..60, 127.99, 128.71, 143.09, 146.33, 153.35, 165.63; ESI-MS: 259.07 ([M – H]$^-$).

(*S*)-(+)-5-Ethoxycarbonyl-6-methyl-4-(4-fluorophenyl)-3,4-dihydropyrimidin-2(1*H*)-one (8b). White solid; mp 191–192 °C; $[\alpha]_D^{20}$ = 65° (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.16 (t, $^3J_{H,H}$ = 6.8 Hz, 3H, OCH_2CH_3), 2.32 (s, 3H, CH_3), 4.07 (q, $^3J_{H,H}$ = 6.8 Hz, 2H, OCH_2CH_3), 5.39 (d, $^3J_{H,H}$ = 2.4 Hz, 1H, CH), 6.29 (s, 1H, NH), 6.99–7.29 (m, 4H, Ph), 8.69 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.16, 18.57, 54.92, 60.11, 101.22, 115.52, 128.30, 139.65, 146.44, 153.74, 161.07, 163.52, 165.55; ESI-MS: 277.07 ([M – H]$^-$).

(*S*)-(+)-5-Ethoxycarbonyl-6-methyl-4-(4-chlorophenyl)-3,4-dihydropyrimidin-2(1*H*)-one (8c). White solid; mp 210–212 °C; $[\alpha]_D^{20}$ = 37° (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.17 (t, $^3J_{H,H}$ = 6.8 Hz, 3H, OCH_2CH_3), 2.31 (s, 3H, CH_3), 4.09 (q, $^3J_{H,H}$ = 6.8 Hz, 2H, OCH_2CH_3), 5.36 (s, 1H, CH), 6.32 (s, 1H, NH), 7.22–7.30 (m, 4H, Ph), 8.64 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.19, 18. 62, 54.98, 60.19, 101.10, 128.01, 128.87, 133.70, 142.24, 146.65, 153.72, 165.51; ESI-MS: 293.00 ([M – H]$^-$).

(*S*)-(+)-5-Ethoxycarbonyl-6-methyl-4-(4-bromophenyl)-3,4-dihydropyrimidin-2(1*H*)-one (8d). White solid; mp 209–210 °C; $[\alpha]_D^{20}$ = 38° (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.17 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, OCH_2CH_3), 2.33 (s, 3H, CH_3), 4.09 (q, $^3J_{H,H}$ = 7.2 Hz, 2H, OCH_2CH_3), 5.35 (d, $^3J_{H,H}$ = 2.8 Hz, 1H, CH), 6.15 (s, 1H, NH), 7.18–7.44 (m, 4H, Ph), 8.46 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.19, 18.69, 55.12, 60.19, 100.99, 121.88, 128.38, 131.83, 142.72, 146.58, 153.42, 153.48, 165.47; ESI-MS: 336.93 ([M – H]$^-$).

(*S*)-(+)-5-Ethoxycarbonyl-6-methyl-4-(4-methylphenyl)-3,4-dihydropyrimidin-2(1*H*)-one (8e). White solid; mp 213–214 °C; $[\alpha]_D^{20}$ = 56° (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.17 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, OCH_2CH_3), 2.30 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 4.07 (q, $^3J_{H,H}$ = 7.2 Hz, 2H, OCH_2CH_3), 5.35 (d, $^3J_{H,H}$ = 2.8 Hz, 1H, CH), 6.16 (s, 1H, NH), 7.09–7.26 (m, 4H, Ph), 8.73 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.17, 18.54, 21.12, 55.23, 59.93, 101.36, 126.47, 129.31, 137.59, 140.90, 146.39, 153.90, 165.74; ESI-MS: 273.07 ([M – H]$^-$).

(*S*)-(+)-5-Ethoxycarbonyl-6-methyl-4-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1*H*)-one (8f). White solid; mp 202–205 °C; $[\alpha]_D^{20}$ = 53° (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.17 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, OCH_2CH_3), 2.30 (s, 3H, CH_3), 3.77 (s, 3H, OCH_3), 4.07 (q, $^3J_{H,H}$ = 7.2 Hz, 2H, OCH_2CH_3), 5.33 (d, $^3J_{H,H}$ = 2.4 Hz, 1H, CH), 6.24 (s, 1H, NH), 6.81–7.23 (m, 4H, Ph), 8.77 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.20, 18.53, 54.96, 55.25, 59.98, 101.47, 101.47, 113.94, 127.81, 136.20, 146.26, 153.95, 159.16, 165.78; ESI-MS: 289.07 ([M – H]$^-$).

(*S*)-(+)-5-Ethoxycarbonyl-6-methyl-4-(3-fluorophenyl)-3,4-dihydropyrimidin-2(1*H*)-one (8g). White solid; mp 212–213 °C; $[\alpha]_D^{20}$ = 58° (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.18 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, OCH_2CH_3), 2.37 (s, 3H, CH_3), 4.10 (q, $^3J_{H,H}$ = 7.2 Hz, 2H, OCH_2CH_3), 5.41 (s, 1H, CH), 5.53 (s, 1H, NH), 6.95–7.27 (m, 4H, Ph), 7.34(s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.17, 18.77, 55.28, 60.20, 100.96, 113.61, 114.92, 122.19, 130.30, 146.09, 146.67, 153.10, 161.72, 165.45; ESI-MS: 277.07 ([M – H]$^-$).

(*S*)-(+)-5-Ethoxycarbonyl-6-methyl-4-(3-methylphenyl)-3,4-dihydropyrimidin-2(1*H*)-one (8h). White solid; mp 209–210 °C; $[\alpha]_D^{20}$ = 56° (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.17 (t, $^3J_{H,H}$ = 6.8 Hz, 3H, OCH_2CH_3), 2.33 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 4.07 (q, $^3J_{H,H}$ = 6.8 Hz, 2H, OCH_2CH_3), 5.36 (s, 1H, NH), 5.72 (s, 1H, CH), 7.06–7.26 (m, 4H, Ph), 8.25 (s, 1H, NH); ^{13}C NMR (75 MHz, DMSO): δ 14.15, 18.70, 21.51, 55.75, 60.01, 101.34, 123.71, 127. 28, 128.58, 128.74, 138.39, 143.66, 146.24, 153.39, 165.70; ESI-MS: 273.13 ([M – H]$^-$).

(*S*)-(+)-5-Ethoxycarbonyl-6-methyl-4-(2-chlorophenyl)-3,4-dihydropyrimidin-2(1*H*)-one (8i). White solid; mp 228–230 °C; $[\alpha]_D^{20}$ = 46° (c = 0.5, MeOH); ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ 1.06 (t, $^3J_{H,H}$ = 6.8 Hz, 3H, OCH_2CH_3), 2.45 (s, 3H, CH_3), 4.01 (q, $^3J_{H,H}$ = 6.8 Hz, 2H, OCH_2CH_3), 5.73 (s, 1H, CH), 5.89 (s, 1H, NH), 7.21–7.39 (m, 4H, Ph), 8.36 (s, 1H, NH); ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ 13.99, 18.43, 52.15, 60.02, 98. 94, 127.56, 127.98,129.32, 129.82, 132. 58, 139.43, 148.33, 152.84, 165.30; ESI-MS: 293.00 ([M + H]$^+$).

(*R*)-(–)-5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (8j). White solid; mp 202–204 °C; $[\alpha]_D^{20}$ = –64° (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.16 (t, $^3J_{H,H}$ = 6.8 Hz, 3H, OCH_2CH_3), 2.32 (s, 3H, CH_3), 4.07 (q, $^3J_{H,H}$ = 6.8 Hz, 2H, OCH_2CH_3), 5.39(d, $^3J_{H,H}$ = 2.4 Hz, 1H, CH), 6.11(s, 1H, NH), 7.26–7.31 (m, 5H, Ph), 8.64 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.16, 18.70, 55.73, 60.05, 101.35, 126.62, 127.98, 128.73, 143.71, 145.33, 153.33, 165.66. ESI-MS: 259.07 ([M – H]$^-$).

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