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PEG-OSO₃H AS AN EFFICIENT CATALYST IN THE SYNTHESIS OF N3-FUNCTIONALIZED 3,4-DIHYDROPYRIMIDINONE AND QUINAZOLINONE DERIVATIVES

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Abstract – PEG-OSO₃H-catalyzed three-component reaction of 3,4-dihydropyrimidones and quinazolinone with paraformaldehyde and various reagents for synthesis of N3-functionalized 3,4-dihydropyrimidone and quinazolinone derivatives is described. 2-Hydroxy-substituted 3,4-dihydropyrimidone reacts with aldehydes giving benzo[e]pyrimido[1,6-c][1,3]oxazines. This paper explores the versatility and effectiveness of polymer bound sulfonic acids as catalysts in different C-N and C-O bonds formation reactions. The reactions were completed in short times, and the products were obtained in good to excellent yields. The catalysts activity and recyclability were investigated completely.

INTRODUCTION

3,4-Dihydropyrimidinones (DHPMs) and their derivatives are central subunits in a broad range of medicinal agents, which display interesting pharmacological and biological activities, such as calcium channel modulators, α_{1a} adrenergic agonists, mitotic kinesin inhibitors, and hepatitis B virus replication inhibitors.¹⁻⁷ Among DHPM derivatives, most of the pharmacologically attractive forms are N3-substituted analogues.⁸ The N-alkylation of dihydropyrimidin-2-ones is one way of functionalizing the ring to achieve important bioactive properties. Most N-alkylated pyrimidin-2-ones are obtained from S_N2 displacement of an electrophile with the pyrimidine reacting as the nucleophile.⁹ In 2010, we examined

chlorotrimethylsilane (TMSCl) mediated reactions between DHPM with paraformaldehyde and various reagents for the preparation of *N*3-functionalized DHPMs.¹⁰ These reactions were performed in one-pot two-step procedures by treatment of DHPMs with paraformaldehyde and chlorotrimethylsilane (TMSCl), followed by reactions with substituted alcohols, benzoic acids, and acetic acid, respectively. We became interested in whether these reactions were possible in one-step reaction from DHPM with paraformaldehyde and alcohols using acid catalyst.

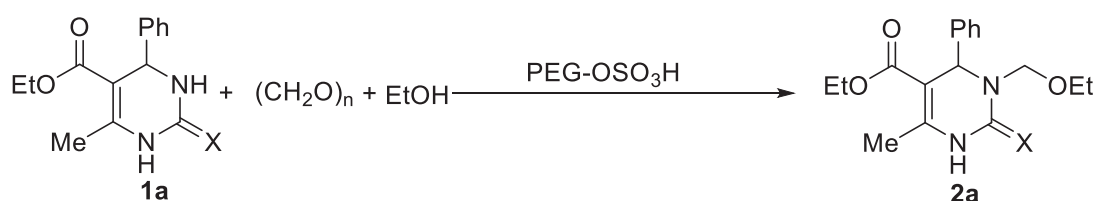
PEGs are soluble in many, mostly polar solvents (including water) and insoluble in a few nonpolar solvents (hexanes, diethyl ether, *tert*-butyl methyl ether). Because of this solubility profile, PEG and its derivatives are considered as ideal supports. In addition, it also combines the advantageous features of homogeneous catalysis such as high reactivity, lack of diffusion phenomena and analytical simplicity.¹¹ We previously reported the preparation and utilization of polyethylene glycol (PEG)-bound sulfonic acid (PEG-OSO₃H) and polystyrene-poly(ethylene glycol) (PS-PEG) resin-supported sulfonic acid in the Biginelli, Mannich, Beckmann rearrangement, multicomponent reactions and conversion of carbohydrates into 5-hydroxymethylfurfural.¹²⁻¹⁵ Recently, the PEG-OSO₃H has been used in several organic transformations.¹⁶⁻²³

In this paper, we wish to report a one-step procedure for *N*3 functionalized 3,4-dihydropyrimidinone derivatives and benzo[*e*]pyrimido[1,6-*c*][1,3]oxazines by a selective reaction between 3,4-dihydropyrimidinones, aldehydes, and nucleophiles (such as alcohols, sodium azide, phenol and 4-methylbenzenethiol) using PEG-OSO₃H as catalyst.

RESULTS AND DISCUSSION

Initially, we chose the reaction of DHPM **1a**, paraformaldehyde and EtOH as a typical reaction to optimize the reaction conditions (Scheme 1). An extensive investigation of arrange of solvents was carried out. The reaction between **1a** (1 mmol), paraformaldehyde (4 mmol) and EtOH (3 mL) using PEG-OSO₃H (0.6 g, 0.2 mmol) as catalyst could occur in DMF, MeCN, 1,4-dioxane, THF, toluene and dichloromethane to give **2a** respectively in yield of 58%, 60%, 65%, 68%, 74% and 78%. Interestingly, the yield of **2a** (86%) was obtained when ethanol itself as the solvent. Lower yields were obtained when the load of catalyst was reduced, such as 0.3 g (0.1 mmol) of catalyst yielding the product **2a** in 61%. Subsequently, we screened different temperatures and found that the temperature has a significant effect on the yield of the reaction. At room temperature, the product **2a** was not detected and at 60 °C, low yield (63%) of **2a** was obtained even the reaction time was prolonged to 24 h. Thus, we decided to use 1 mmol of **1a**, 4 equiv of paraformaldehyde and PEG-OSO₃H (0.6 g, 0.2 mmol) in EtOH (3 mL) at 80 °C as the optimal reaction conditions for the preparation of *N*3-ethoxymethyl DHPM. To evaluate the usefulness of PEG-SO₃H, the comparison experiments using TMSCl, H₂SO₄, TsOH, phosphowolframic acid and phosphomolybdic acid

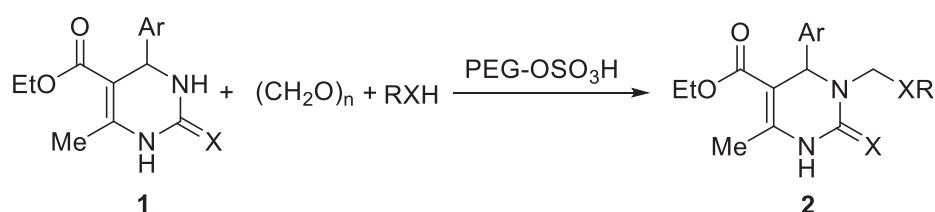
as a catalyst instead of PEG-OSO₃H by a one-step protocol were carried out. TMSCl, H₂SO₄, HCl, TsOH, phosphowolframic acid and phosphomolybdic acid could catalyze the reaction albeit in a lower efficacy resulted the product **2a** in yield of 25%, 35%, 26%, 40% and 45%, respectively. Finally, the silica-supported sulfonic acid was also applied as catalyst and 75% yield of **2a** was obtained. These indicated that PEG-OSO₃H with mild acidity acts simultaneously as an acid catalyst and as a catalyst promoting the release of formaldehyde from paraformaldehyde and subsequently capturing the released formaldehyde.


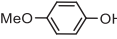


Scheme 1. Three-component reaction of DHPM **1a**, paraformaldehyde and EtOH

With these results in hand we then explored the scope and generality of present three-component reaction using PEG-OSO₃H as catalyst (Table 1). Firstly, we investigated other alcohols, such as methanol, propanol, isopropanol, *n*-butyl alcohol and *tert*-butyl alcohol as a nucleophile and the corresponding *N*³-alkyloxymethyl DHPMs were obtained (Table 1, entries 2-8). In general, *N*³-substituted DHPMs were generated with primary, secondary and tertiary aliphatic alcohol substrates. In fact, when using *tert*-butyl alcohol as a nucleophile substrate, a lower yield of product **2f** resulted (entry 6). Sulfur-containing analogues of DHPMs **1** also exhibited a good reactivity yielding the desired products (entries 9-10). Consistent with previous studies, replacing alcohol with 4-methylbenzenethiol or 4-methoxyphenol allowed the reactions to proceed smoothly and afforded the desired products in high yields (entries 11-12). The products' ¹H NMR and ¹³C NMR data were identical to those reported in the literature.¹⁰ Subsequently, we expanded the nucleophiles of this one-pot reaction such as acetic acid, sodium acetate, benzoic acid, morpholine, sodium benzenesulfinate and sodium azide. However, no products were detected except for a lower yield of an azido group at the *N*³ position of pyrimidone ring. However, some limitations were noted in case of aryl aldehydes, which were unreactive in this reaction instead of paraformaldehyde.

Table 1. Synthesis of DHPM derivatives catalyzed by PEG-OSO₃H

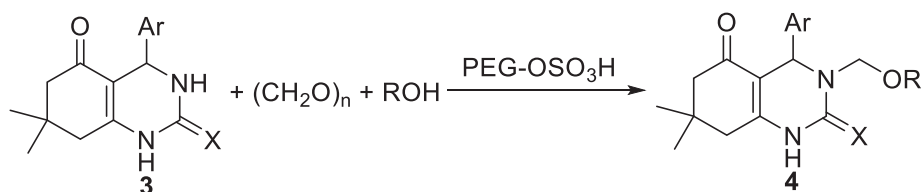


Entry	Ar	X	RXH	Product	Isolated Yield (%)
1	Ph	O	EtOH	2a	86
2	Ph	O	MeOH	2b	78
3	Ph	O	PrOH	2c	76
4	Ph	O	<i>i</i> -PrOH	2d	69
5	Ph	O	<i>n</i> -BuOH	2e	72
6	Ph	O	<i>t</i> -BuOH	2f	61
7	4-MeO-Ph	O	EtOH	2g	88
8	4-Cl-Ph	O	EtOH	2h	83
9	Ph	S	PrOH	2i	78
10	Ph	S	<i>i</i> -PrOH	2j	76
11	Ph	O		2k	83
12	Ph	O		2l	80

^a Conditions: DHPMs (1 mmol), (CH₂O)_n (4 mmol), alcohol (3 mL), PEG-OSO₃H (0.6 g, 0.2 mmol), 80 °C, 8 h.

These promising results promoted us to apply this reaction to other more complicated substrate quinazolinones and their sulfur-containing analogues. To our delight, substrates **3** were also able to transform into the corresponding products **4** in good yields (Table 2, entries 1-7).

Table 2. Synthesis of quinazolinone derivatives catalyzed by PEG-OSO₃H

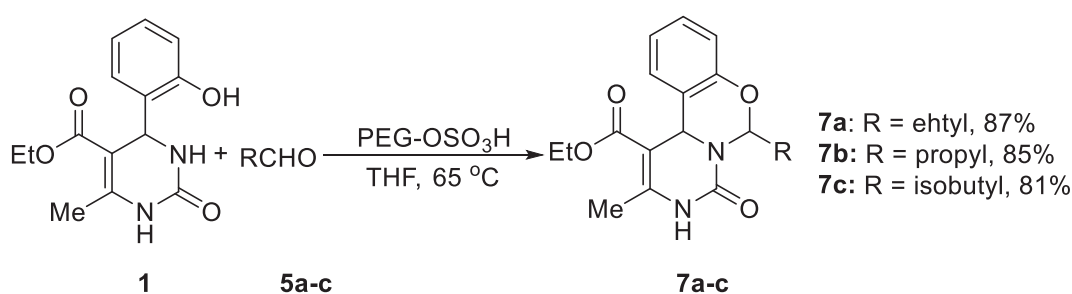


Entry	Ar	X	R	Product	Yield/%
1	Ph	O	Et	4a	83
2	Ph	O	Pr	4b	78
3	Ph	S	Et	4c	85
4	Ph	S	Pr	4d	81
5	Ph	S	<i>i</i> -Pr	4e	76

6	4-MeO-Ph	S	Et	4f	86
7	4-Cl-Ph	S	Et	4g	76

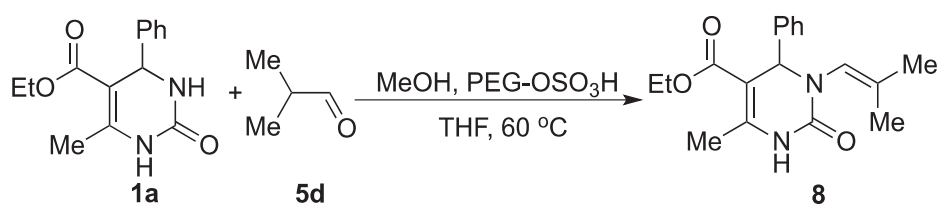
^a Conditions: quinazolinones (1 mmol), (CH₂O)_n (4 mmol), ROH (3 mL), PEG-OSO₃H (0.6 g, 0.2 mmol), 80 °C, 8 h.

Based on these results, the reactions between DHPM substituted with 2-hydroxy on the aromatic ring and propionaldehyde, butyraldehyde, 3-methylbutanal were examined, and to our delight, the reactions gave the cyclized product 3,4,6,11b-tetrahydrobenzo[*e*]pyrimido[1,6-*c*][1,3]oxazines (**7a**, **7b**, **7c**) with high yields (Scheme 2).



Scheme 2. Reaction of 2-hydroxy-substituted DHPM with aliphatic aldehydes

We finally turn to test the aliphatic aldehydes instead of paraformaldehyde in the three-component reaction. The reaction between 3,4-dihydropyrimidinone (**1a**), isobutyraldehyde (**5d**) and methanol in THF at 60 °C was tested using PEG-OSO₃H as the catalyst. To our great surprise, no any three-component product was detected and after purification of the reaction mixture, a dehydration-isomerization product *N*3-(2-methylprop-1-en-1-yl) substituted product **8** was isolated in 70% yield (Scheme 3).



Scheme 3. The reaction of 3,4-dihydropyrimidinone with isobutyraldehyde

In order to check the recyclability of the catalyst, the reaction for **2a** was tested. The yields of **2a** were 80%, 80%, 76%, 70, 65% and 30% in the second to sixth reuses, respectively. At the end of the reaction, the resulting mixture was cooled, quenched to ice water and filtrated, and then the solution was extracted with dichloromethane (3×10 mL). The white PEG-OSO₃H catalyst can be obtained by adding cooled anhydrous ether into the concentrated organic phase. The recovered catalyst can be used directly in the next run.

CONCLUSIONS

In conclusion, we have developed novel and efficient synthetic methods to prepare *N*3-functionalized DHPMs, and benzo[*e*]pyrimido[1,6-*c*][1,3]oxazines by the selectivity reactions between DHPMs, aldehydes with alcohols, 4-methoxyphenol and 4-methylbenzenethiol using PEG-OSO₃H as inexpensive, and reusable catalysts. Moreover, the simplicity and higher efficiency make this method particularly attractive.

EXPERIMENTAL

Melting points were determined on an XT-4 electrothermal micromelting point apparatus and the thermometer was uncorrected. NMR spectra were recorded at 400 (¹H) and 100 (¹³C) MHz, respectively, on a Varian Mercury plus-400 instrument using CDCl₃ as solvent and TMS as internal standard. Mass-spectra were recorded on a TRACE DSQ instrument. All commercially available substrates were used as received. TLC was performed on 5×10cm aluminum plates coated with silica gel 60F-254 in an appropriate solvent. All reagents were obtained commercially and used without further purification. PEG-OSO₃H were prepared according to our previous procedures.¹²

General procedure for the preparation of compounds 2 and 4 using PEG-OSO₃H as catalyst

A mixture of 3,4-dihydropyrimidinone **1** (1 mmol), paraformaldehyde (4 mmol) and PEG-OSO₃H (0.6 g, 0.2 mmol-SO₃H) in EtOH (5.0 mL) was stirred at 80 °C for 8 h. After completion monitored by TLC, the resulting mixture was cooled and quenched to ice water. Then the precipitation was filtered off and purified by silica gel column chromatography eluted with EtOAc/petroleum ether (1:5) to afford the pure product.

Ethyl 1-(ethoxymethyl)-4-methyl-2-oxo-6-phenyl-1,2,3,6-tetrahydropyrimidine-5-carboxylate (2a).^{10a} White solid; mp 165-167 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.47 (br s, 1H, NH), 7.39-7.26 (m, 5H, H_{Ar}), 5.50 (s, 1H, 4-CH), 5.23 (d, *J* = 10.8 Hz, 1H, NCHH), 4.39 (d, *J* = 10.4 Hz, 1H, NCHH), 4.14-4.06 (m, 2H, OCH₂CH₃), 3.62-3.55 (m, 1H, OCH₂CH₃), 3.46-3.39 (m, 1H, OCH₂CH₃), 2.36 (s, 3H, 6-CH₃), 1.26-1.19 (m, 3H, OCH₂CH₃), 1.14 (t, *J* = 7.2 Hz, 3H, OCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 165.5, 153.2, 146.0, 141.8, 128.5, 127.9, 127.4, 102.3, 74.2, 63.8, 60.0, 58.0, 18.4, 14.9, 14.2. MS: *m/z* = 318 (M⁺). Anal. Calcd for C₁₇H₂₂N₂O₄ (318): C, 64.13; H, 6.97; N, 8.80. Found: C, 63.95; H, 6.88; N, 8.91.

Ethyl 3-(methoxymethyl)-6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (2b).^{10a} White solid; mp 172-174 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.12 (bs, 1H, NH), 7.35-7.27 (m, 5H, H_{Ar}), 5.93 (d, *J* = 10.0 Hz, 1H, NCHH), 5.68 (s, 1H, 4-CH), 4.66 (d, *J* = 10.0 Hz, 1H, NCHH), 4.19-4.12 (m, 2H, OCH₂CH₃), 3.68-3.64 (m, 1H, OCH₂CH₃), 3.56-3.52 (m, 1H, OCH₂CH₃), 2.36 (s, 3H, 6-CH₃), 1.27-1.23 (m, 3H, OCH₂CH₃), 1.19-1.15 (m, 3H, OCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 176.5, 165.2, 142.3, 140.5, 128.7, 128.3, 127.1, 103.7, 79.2, 64.6, 60.4, 57.2, 18.1, 14.9, 14.2.

Ethyl 1-(propoxymethyl)-4-methyl-2-oxo-6-phenyl-1,2,3,6-tetrahydropyrimidine-5-carboxylate (2c).

White solid; mp 142-144 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.60 (br s, 1H, NH), 7.39-7.27 (m, 5H, H_{Ar}), 5.52 (s, 1H, 4-CH), 5.24 (d, *J* = 10.0 Hz, 1H, NCHH), 4.38 (d, *J* = 10.8 Hz, 1H, NCHH), 4.13-4.07 (m, 2H, OCH₂CH₃), 3.50-3.45 (m, 1H, OCH₂CH₂CH₃), 3.37-3.31 (m, 1H, OCH₂CH₂CH₃), 2.36 (s, 3H, 6-CH₃), 1.57-1.51 (m, 2H, OCH₂CH₂CH₃), 1.23-1.19 (m, 3H, OCH₂CH₃), 0.88-0.91 (m, 3H, OCH₂CH₂CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 165.5, 153.3, 146.1, 141.7, 128.5, 127.9, 127.4, 102.2, 74.2, 70.3, 60.0, 57.7, 22.6, 18.4, 14.1, 10.5. MS: *m/z* = 332 (M⁺). Anal. Calcd for C₁₈H₂₄N₂O₄ (332.17): C, 65.04; H, 7.28; N, 8.43. Found: C, 64.85; H, 7.18; N, 8.31.

Ethyl 3-(isopropoxymethyl)-6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (2d).^{10a}

White solid; mp 127-129 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.56 (bs, 1H, NH), 7.39-7.32 (m, 3H, H_{Ar}), 7.31-7.32 (m, 2H, H_{Ar}), 5.53 (s, 1H, 4-CH), 5.26 (d, *J* = 10.4 Hz, 1H, NCHH), 4.34 (d, *J* = 10.4 Hz, 1H, NCHH), 4.13-4.07 (m, 2H, OCH₂CH₃), 3.74-3.68 (m, 1H, OCHCH₃CH₃), 2.35 (s, 3H, 6-CH₃), 1.26-1.18 (m, 6H, CH(CH₃)₂), 1.07-1.05 (m, 3H, OCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 165.5, 153.3, 146.1, 141.9, 128.5, 127.9, 127.4, 102.2, 71.9, 68.8, 59.9, 57.7, 22.7, 21.4, 18.4, 14.2.

Ethyl 1-(butoxymethyl)-4-methyl-2-oxo-6-phenyl-1,2,3,6-tetrahydropyrimidine-5-carboxylate (2e).

White solid; mp 111-113 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.69 (br s, 1H, NH), 7.38-7.28 (m, 5H, H_{Ar}), 5.51 (s, 1H, 4-CH), 5.23 (d, *J* = 10.4 Hz, 1H, NCHH), 4.36 (d, *J* = 10.4 Hz, 1H, NCHH), 4.13-4.07 (m, 2H, OCH₂CH₃), 3.54-3.48 (m, 1H, OCH₂CH₂CH₂CH₃), 3.39-3.36 (m, 1H, OCH₂CH₂CH₂CH₃), 2.36 (s, 3H, 6-CH₃), 1.53-1.44 (m, 2H, OCH₂CH₂CH₂CH₃), 1.37-1.32 (m, 2H, OCH₂CH₂CH₂CH₃), 1.22 (t, *J* = 7.2 Hz, 3H, OCH₂CH₃), 0.89 (t, *J* = 7.2 Hz, 3H, OCH₂CH₂CH₂CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 165.4, 152.8, 145.7, 141.6, 128.5, 128.0, 127.3, 102.5, 74.3, 68.1, 60.1, 57.7, 31.5, 19.2, 18.6, 14.2, 13.8. MS: *m/z* = 346 (M⁺). Anal. Calcd for C₁₉H₂₆N₂O₄ (346.19): C, 65.87; H, 7.56; N, 8.09. Found: C, 65.93; H, 7.48; N, 8.18.

Ethyl 3-(tert-butoxymethyl)-6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (2f).^{10a}

White solid; mp 142-144 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.76 (bs, 1H, NH), 7.38-7.24 (m, 5H, H_{Ar}), 5.60 (s, 1H, 4-CH), 5.40 (d, *J* = 10.0 Hz, 1H, NCHH), 4.12 (d, *J* = 10.0 Hz, 1H, NCHH), 4.10-4.06 (m, 2H, OCH₂CH₃), 2.32 (s, 3H, CH₃), 1.29-1.19 (m, 9H, CH₃), 1.18-1.14 (m, 3H, OCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 165.6, 152.7, 146.3, 141.8, 128.4, 127.9, 127.5, 102.0, 74.1, 67.9, 59.9, 57.0, 28.0, 18.4, 14.2.

Ethyl 3-(ethoxymethyl)-4-(4-methoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (2g).^{10a}

White solid; mp 134-136 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.51 (bs, 1H, NH), 7.30-7.27 (m, 2H, H_{Ar}), 6.83-6.81 (m, 2H, H_{Ar}), 5.45 (s, 1H, 4-CH), 5.34 (d, *J* = 10.4 Hz, 1H, NCHH), 4.35 (d, *J* = 10.4 Hz, 1H, NCHH), 4.11-4.05 (m, 2H, OCH₂CH₃), 3.80 (s, 3H, OCH₃), 3.61-3.57 (m, 1H, OCH₂CH₃), 3.52-3.42 (m, 1H, OCH₂CH₃), 2.37 (s, 3H, CH₃), 1.24-1.16 (m, 6H, OCH₂CH₃×2). ¹³C NMR

(100 MHz, CDCl₃): δ 165.5, 153.3, 145.9, 138.9, 137.7, 129.1, 127.3, 102.4, 73.9, 63.8, 60.0, 57.6, 21.1, 18.4, 14.9, 14.2.

Ethyl 4-(4-chlorophenyl)-3-(ethoxymethyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (2h).^{10a} White solid; mp 175-177 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.69 (bs, 1H, NH), 7.33-7.26 (m, 4H, H_{Ar}), 5.48 (s, 1H, C4-CH), 5.19 (d, J = 10.8 Hz, 1H, NCHH), 4.37 (d, J = 10.8 Hz, 1H, NCHH), 4.15-4.06 (m, 2H, OCH₂CH₃), 3.59-3.53 (m, 1H, OCH₂CH₃), 3.43-3.39 (m, 1H, OCH₂CH₃), 2.36 (s, 3H, 6-CH₃), 1.26-1.20 (m, 3H, OCH₂CH₃), 1.18-1.12 (m, 3H, OCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 165.3, 153.2, 146.3, 140.4, 133.7, 128.8, 128.6, 101.9, 74.2, 63.8, 60.1, 57.4, 18.4, 14.8, 14.2.

Ethyl 1-(propoxymethyl)-4-methyl-2-thioxo-6-phenyl-1,2,3,6-tetrahydropyrimidine-5-carboxylate (2i). White solid; mp 108-110 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.29 (br s, 1H, NH), 7.34-7.27 (m, 5H, H_{Ar}), 5.97 (d, J = 10.4 Hz, 1H, NCHH), 5.70 (s, 1H, 4-CH), 4.64 (d, J = 10.0 Hz, 1H, NCHH), 4.18-4.13 (m, 2H, OCH₂CH₃), 3.54-3.43 (m, 2H, OCH₂CH₂CH₃), 2.37 (s, 3H, 6-CH₃), 1.60-1.54 (m, 2H, OCH₂CH₂CH₃), 1.25 (t, J = 7.2 Hz, 3H, OCH₂CH₃), 0.93 (t, J = 7.2 Hz, 3H, OCH₂CH₂CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 176.4, 165.2, 142.5, 140.4, 128.7, 128.3, 127.1, 103.6, 79.2, 70.7, 60.4, 56.9, 22.7, 18.0, 14.1, 10.5. MS: m/z = 348 (M⁺). Anal. Calcd for C₁₈H₂₄N₂O₃S (348.15): C, 62.04; H, 6.94; N, 8.04. Found: C, 62.12; H, 7.01; N, 8.09.

Ethyl 1-(isopropoxymethyl)-4-methyl-2-thioxo-6-phenyl-1,2,3,6-tetrahydropyrimidine-5-carboxylate (2j). White solid; mp 80-82 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.01 (br s, 1H, NH), 7.34-7.27 (m, 5H, H_{Ar}), 6.00 (d, J = 10.8 Hz, 1H, NCHH), 5.74 (s, 1H, 4-CH), 4.62 (d, J = 10.4 Hz, 1H, NCHH), 4.19-4.14 (m, 2H, OCH₂CH₃), 3.86-3.80 (m, 1H, OCHCH₃CH₃), 2.36 (s, 3H, 6-CH₃), 1.28-1.24 (m, 3H, OCH₂CH₃), 1.22 (d, J = 6.0 Hz, 3H, CH₃CHCH₃), 1.13 (d, J = 6.0 Hz, 3H, CH₃CHCH₃). ¹³C NMR (100 MHz, CDCl₃) δ 176.2, 165.2, 142.4, 140.4, 128.8, 128.3, 127.0, 103.6, 76.7, 69.9, 60.4, 56.7, 22.8, 21.5, 18.1, 14.2. MS: m/z = 348 (M⁺). Anal. Calcd for C₁₈H₂₄N₂O₃S (348.15): C, 62.04; H, 6.94; N, 8.04. Found: C, 62.12; H, 7.01; N, 8.09.

Ethyl 1-(*p*-tolylthiomethyl)-4-methyl-2-oxo-6-phenyl-1,2,3,6-tetrahydropyrimidine-5-carboxylate (2k).^{10a} White solid; mp 147-149 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.56 (br s, 1H, NH), 7.40-7.09 (m, 9H, H_{Ar}), 5.61 (s, 1H, 4-CH), 5.54 (d, J = 13.6 Hz, 1H, NCHH), 4.12-4.03 (m, 2H, OCH₂CH₃), 3.83 (d, J = 14.0 Hz, 1H, NCHH), 2.31 (s, 3H, Ar-CH₃), 2.27 (s, 3H, 6-CH₃), 1.20 (t, J = 7.2 Hz, 3H, OCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 165.4, 152.3, 146.0, 141.0, 137.8, 132.6, 129.9, 129.7, 128.5, 128.1, 127.5, 101.4, 59.9, 58.0, 49.6, 21.1, 18.2, 14.1.

Ethyl 1-((4-methoxyphenoxy)methyl)-4-methyl-2-oxo-6-phenyl-1,2,3,6-tetrahydropyrimidine-5-carboxylate (2l). White solid; mp 175-177 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.63 (br s, 1H, NH), 7.43-6.62 (m, 9H, H_{Ar}), 5.48 (s, 1H, 4-CH), 4.72 (d, J = 14.8 Hz, 1H, NCHH), 4.15-4.03 (m, 2H, OCH₂CH₃), 3.90 (d, J = 14.8 Hz, 1H, NCHH), 3.74 (s, 3H, Ar-OCH₃), 2.33 (s, 3H, 6-CH₃), 1.23-1.19 (m,

3H, OCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 165.2, 154.4, 152.6, 149.7, 145.0, 141.3, 128.7, 128.3, 127.6, 122.2, 118.0, 117.0, 115.1, 102.3, 61.0, 60.2, 55.8, 45.7, 18.4, 14.2. MS: *m/z* = 396 (M⁺). Anal. Calcd for C₂₂H₂₄N₂O₅ (396.17): C, 66.65; H, 6.10; N, 7.07. Found: C, 66.78; H, 6.06; N, 7.16.

Ethyl 3-(azidomethyl)-6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (2m).^{10a}

White solid; mp 136-138 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.24 (br, 1H, NH), 7.35-7.26 (m, 5H, H_{Ar}), 5.54 (s, 1H, 4-CH), 5.17 (d, *J* = 12.0 Hz, 1H, NCHH), 4.26 (d, *J* = 12.0 Hz, 1H, NCHH), 4.11-4.08 (m, 2H, OCH₂CH₃), 2.37 (s, 3H, 6-CH₃), 1.23-1.19 (m, 3H, OCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 165.2, 152.9, 145.5, 141.2, 128.8, 128.4, 127.3, 102.4, 60.9, 60.3, 60.2, 18.5, 14.1.

3-(Ethoxymethyl)-7,7-dimethyl-4-phenyl-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (4a).

White solid; mp 168-170 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.67 (br s, 1H, NH), 7.40-7.25 (m, 5H, H_{Ar}), 5.61 (s, 1H, 4-CH), 5.28 (d, *J* = 10.4 Hz, 1H, NCHH), 4.35 (d, *J* = 10.4 Hz, 1H, NCHH), 3.56-3.54 (m, 1H, OCH₂CH₃), 3.46-3.45 (m, 1H, OCH₂CH₃), 2.43-2.18 (m, 4H, 6-CH₂, 8-CH₂), 1.15 (t, *J* = 7.2 Hz, 3H, OCH₂CH₃), 1.11 (s, 3H, CH₃), 0.95 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 193.6, 153.2, 149.4, 141.2, 128.6, 127.9, 127.1, 110.1, 74.4, 63.9, 56.1, 50.3, 40.0, 32.8, 29.3, 27.2, 14.9. MS: *m/z* = 328 (M⁺). Anal. Calcd for C₁₉H₂₄N₂O₃ (328.18): C, 69.49; H, 7.37; N, 8.53. Found: C, 69.61; H, 7.42; N, 8.42.

3-(Propoxymethyl)-7,7-dimethyl-4-phenyl-3,4,7,8-tetrahydroquinazoline-2,5(1H,6H)-dione (4b).

White solid; mp 166-168 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.96 (br s, 1H, NH), 7.40-7.23 (m, 5H, H_{Ar}), 5.61 (s, 1H, 4-CH), 5.28 (d, *J* = 10.0 Hz, 1H, NCHH), 4.35 (d, *J* = 10.0 Hz, 1H, NCHH), 3.47-3.32 (m, 2H, OCH₂CH₂CH₃), 2.43-2.13 (m, 4H, 6-CH₂, 8-CH₂), 1.57-1.51 (m, 2H, OCH₂CH₂CH₃), 1.10 (s, 3H, CH₃), 0.95 (s, 3H, CH₃), 0.89 (t, *J* = 7.2 Hz, 3H, OCH₂CH₂CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 193.6, 153.4, 149.6, 141.2, 128.6, 127.9, 127.1, 110.0, 74.6, 70.3, 55.9, 50.3, 39.9, 32.8, 29.2, 27.2, 22.7, 10.6. MS: *m/z* = 342 (M⁺). Anal. Calcd for C₂₀H₂₆N₂O₃ (342.19): C, 70.15; H, 7.65; N, 8.18. Found: C, 70.26; H, 7.62; N, 8.26.

3-(Ethoxymethyl)-7,7-dimethyl-4-phenyl-2-thioxo-1,2,3,4,7,8-hexahydroquinazolin-5(6H)-one (4c).

White solid; mp 153-155 °C; ¹H NMR (400 MHz, CDCl₃): δ 7.98 (br s, 1H, NH), 7.36-7.28 (m, 4H, H_{Ar}), 5.98 (d, *J* = 10.4 Hz, 1H, NCHH), 5.76 (s, 1H, 4-CH), 4.63 (d, *J* = 10.0 Hz, 1H, NCHH), 3.65-3.49 (m, 2H, OCH₂CH₃), 2.43-2.17 (m, 4H, 6-CH₂, 8-CH₂), 1.18 (t, *J* = 7.2 Hz, 3H, OCH₂CH₃), 1.11 (s, 3H, CH₃), 0.93 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 193.9, 176.7, 145.2, 140.1, 128.8, 128.2, 126.9, 110.9, 79.6, 64.8, 55.5, 50.3, 39.6, 32.9, 29.3, 27.1, 15.0. MS: *m/z* = 344 (M⁺). Anal. Calcd for C₁₉H₂₄N₂O₂S (344.16): C, 66.25; H, 7.02; N, 8.13. Found: C, 66.37; H, 7.10; N, 8.02.

3-(Propoxymethyl)-7,7-dimethyl-4-phenyl-2-thioxo-1,2,3,4,7,8-hexahydroquinazolin-5(6H)-one (4d).

White solid; mp 148-150 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.73 (br s, 1H, NH), 7.36-7.26 (m, 5H, H_{Ar}), 5.99 (d, *J* = 10.4 Hz, 1H, NCHH), 5.77 (s, 1H, 4-CH), 4.62 (d, *J* = 10.4 Hz, 1H, NCHH), 3.55-3.42 (m, 2H, OCH₂CH₂CH₃), 2.44-2.17 (m, 4H, 6-CH₂, 8-CH₂), 1.59-1.52 (m, 2H, OCH₂CH₂CH₃), 1.11 (s, 3H,

CH₃), 0.93 (s, 3H, CH₃), 0.89 (t, $J = 7.2$ Hz, 3H, OCH₂CH₂CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 193.9, 176.7, 145.5, 140.1, 128.8, 128.2, 126.9, 110.8, 79.5, 71.0, 55.3, 50.3, 39.4, 32.9, 29.2, 27.1, 22.7, 10.5. MS: $m/z = 358$ (M⁺). Anal. Calcd for C₂₀H₂₆N₂O₂S (358.17): C, 67.01; H, 7.31; N, 7.81. Found: C, 67.13; H, 7.27; N, 7.94.

3-(Isopropoxymethyl)-7,7-dimethyl-4-phenyl-2-thioxo-1,2,3,4,7,8-hexahydroquinazolin-5(6H)-one (4e). Light yellow solid; mp 118-120 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.59 (br s, 1H, NH), 7.36-7.24 (m, 5H, H_{Ar}), 6.03 (d, $J = 10.4$ Hz, 1H, NCHH), 5.81 (s, 1H, 4-CH), 4.59 (d, $J = 10.4$ Hz, 1H, NCHH), 3.83-3.77 (m, 1H, OCH(CH₃)₂), 2.43-2.17 (m, 4 H, 6-CH₂, 8-CH₂), 1.19 (d, $J = 6.0$ Hz, 3H, CH₃CHCH₃), 1.14 (d, $J = 6.0$ Hz, 3H, CH₃CHCH₃), 1.10 (s, 3H, CH₃), 0.93 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 193.9, 176.4, 145.5, 140.1, 128.8, 128.2, 126.9, 110.7, 77.5, 70.4, 55.1, 50.3, 39.4, 32.9, 29.2, 27.2, 22.8, 21.7. MS: $m/z = 358$ (M⁺). Anal. Calcd for C₂₀H₂₆N₂O₂S (358.17): C, 67.01; H, 7.31; N, 7.81. Found: C, 67.12; H, 7.28; N, 7.93.

3-(Ethoxymethyl)-4-(4-methoxyphenyl)-7,7-dimethyl-2-thioxo-1,2,3,4,7,8-hexahydroquinazolin-5(6H)-one (4f). Light yellow solid; mp 161-163 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.64 (br s, 1H, NH), 7.28-6.82 (m, 4H, H_{Ar}), 5.96 (d, $J = 7.6$ Hz, 1H, NCHH), 5.69 (s, 1H, 4-CH), 4.59 (d, $J = 7.2$ Hz, 1H, NCHH), 3.79 (s, 3H, Ar-OCH₃), 3.67-3.52 (m, 2H, OCH₂CH₃), 2.43-2.16 (m, 4H, 6-CH₂, 8-CH₂), 1.27-1.23 (m, 3H, OCH₂CH₃), 1.21 (s, 3H, CH₃), 0.94 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 194.1, 176.4, 159.4, 145.3, 145.2, 132.4, 128.3, 114.1, 110.9, 79.2, 64.7, 54.9, 50.3, 39.3, 32.9, 29.3, 27.1, 15.0. MS: $m/z = 374$ (M⁺). Anal. Calcd for C₂₀H₂₆N₂O₃S (374.17): C, 64.14; H, 7.00; N, 7.48. Found: C, 64.25; H, 6.97; N, 7.59.

3-(Ethoxymethyl)-4-(4-chlorophenyl)-7,7-dimethyl-2-thioxo-1,2,3,4,7,8-hexahydroquinazolin-5(6H)-one (4g). Light yellow solid; mp 179-181 °C; ¹H NMR (400 MHz, CDCl₃): δ 8.55 (br s, 1H, NH), 7.31-7.27 (m, 4H, H_{Ar}), 5.95 (d, $J = 10.4$ Hz, 1H, NCHH), 5.74 (s, 1H, 4-CH), 4.63 (d, $J = 10.0$ Hz, 1H, NCHH), 3.64-3.50 (m, 2H, OCH₂CH₃), 2.44-2.17 (m, 4H, 6-CH₂, 8-CH₂), 1.18 (t, $J = 6.8$ Hz, 3H, OCH₂CH₃), 1.11 (s, 3H, CH₃), 0.92 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 193.9, 176.6, 145.6, 138.7, 134.1, 129.0, 128.3, 110.4, 79.5, 64.9, 54.8, 50.2, 39.4, 32.9, 29.3, 27.0, 14.9. MS: $m/z = 378$ (M⁺), 380 (M+2). Anal. Calcd for C₁₉H₂₃ClN₂O₂S (378.12): C, 60.23; H, 6.12; N, 7.39. Found: C, 60.35; H, 6.07; N, 7.46.

Ethyl 6-methyl-3-(2-methylprop-1-en-1-yl)-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (6a). White solid, mp 151-153 °C, yield: 70%. ¹H NMR (400 MHz, CDCl₃): δ 8.90 (s, 1H), 7.38-7.24 (m, 5H), 5.61 (s, 1H), 5.30 (s, 1H), 4.12-4.08 (m, 2H), 2.37 (s, 3H), 1.71 (s, 3H), 1.61 (s, 3H), 1.21 (t, $J = 7.2$, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 165.6, 152.7, 147.1, 141.3, 133.9, 128.4, 127.6, 127.0, 120.6, 101.4, 61.9, 59.9, 22.1, 18.4, 18.0, 14.1. MS: m/z 314 (M⁺). Anal. Calcd for C₁₈H₂₂N₂O₃ (314.38): C 68.77, H 7.05, N 8.91. Found: C 68.70, H 7.08, N 8.87.

General procedure for the synthesis of products 7a-c

A mixture of 2-hydroxy-substituted 3,4-dihydropyrimidinone (**1**, 1 mmol), propionaldehyde (**4a**, 1.5 mmol) and PEG-OSO₃H (0.6 g) in THF (3.0 mL) was stirred at 65 °C for 6 h. After completion monitored by TLC, the resulting mixture was cooled and quenched to ice water. Then the precipitation was filtered off and purified by silica gel column chromatography eluted with EtOAc/petroleum ether (1:5) to afford the pure product **7**.

Ethyl 6-ethyl-2-methyl-4-oxo-3,4,6,11b-tetrahydrobenzo[e]pyrimido[1,6-c][1,3]oxazine-1-carboxylate (7a). White solid; mp 246-248 °C; yield: 87%; ¹H NMR (400 MHz, CDCl₃): δ 8.46 (br s, 1H, NH), 7.17-6.80 (m, 4H, H_{Ar}), 6.15 (t, *J* = 7.2 Hz, 1H, OCHN), 5.62 (s, 1H, CH), 4.35-4.23 (m, 2H, OCH₂CH₃), 2.36 (s, 3H, 2-CH₃), 2.10-1.86 (m, 2H, CH₂CH₃), 1.31 (t, *J* = 7.2 Hz, 3H, CH₂CH₃), 1.04 (t, *J* = 7.2 Hz, 3H, OCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 166.3, 154.1, 152.4, 148.2, 128.8, 124.6, 124.4, 120.3, 117.1, 98.3, 82.8, 60.4, 47.4, 25.0, 18.6, 14.4, 8.8. MS: *m/z* = 316 (M⁺). Anal. Calcd for C₁₇H₂₀N₂O₄ (316): C, 64.54; H, 6.37; N, 8.86. Found: C, 64.63; H, 6.35; N, 8.94.

Ethyl 2-methyl-4-oxo-6-propyl-3,4,6,11b-tetrahydrobenzo[e]pyrimido[1,6-c][1,3]oxazine-1-carboxylate (7b). White solid; mp 185-187 °C; yield: 85%; ¹H NMR (400 MHz, CDCl₃): δ 8.33 (br s, 1H, NH), 7.26-6.79 (m, 4H, H_{Ar}), 6.24 (t, *J* = 7.2 Hz, 1H, OCHN), 5.64 (s, 1H, CH), 4.35-4.24 (m, 2H, OCH₂CH₃), 2.36 (s, 3H, 2-CH₃), 2.04-1.83 (m, 2H, CH₂CH₂CH₃), 1.54-1.47 (m, 2H, CH₂CH₂CH₃), 1.33 (t, *J* = 7.2 Hz, 3H, CH₂CH₂CH₃), 1.01 (t, *J* = 7.2 Hz, 3H, OCH₂CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 166.3, 154.0, 152.4, 148.1, 128.8, 124.6, 124.4, 120.3, 117.2, 98.4, 81.5, 60.4, 47.5, 33.8, 18.6, 17.8, 14.4, 13.7. MS: *m/z* = 330 (M⁺). Anal. Calcd for C₁₈H₂₂N₂O₄ (330.16): C, 65.44; H, 6.71; N, 8.48. Found: C, 65.52; H, 6.68; N, 8.55.

Ethyl 6-isobutyl-2-methyl-4-oxo-3,4,6,11b-tetrahydrobenzo[e]pyrimido[1,6-c][1,3]oxazine-1-carboxylate (7c). White solid; mp 180-182 °C; yield: 81%; ¹H NMR (400 MHz, CDCl₃): δ 8.29 (br s, 1H, NH), 7.26-6.79 (m, 4H, H_{Ar}), 6.33 (t, *J* = 6.8 Hz, 1H, OCHN), 5.65 (s, 1H, CH), 4.35-4.25 (m, 2H, OCH₂CH₃), 2.36 (s, 3H, 2-CH₃), 1.90-1.78 (m, 3H, CH₂CH(CH₃)₂), 1.33 (t, *J* = 6.8 Hz, 3H, OCH₂CH₃), 1.24-0.98 (m, 6H, CH₂CH(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 166.3, 153.9, 152.4, 148.1, 128.8, 124.7, 124.2, 120.3, 117.2, 98.5, 80.4, 60.4, 47.5, 40.3, 24.2, 22.9, 22.2, 18.6, 14.4. MS: *m/z* = 344 (M⁺). Anal. Calcd for C₁₉H₂₄N₂O₄ (344.17): C, 66.26; H, 7.02; N, 8.13. Found: C, 66.35; H, 7.05; N, 8.21.

Ethyl 4-methyl-1-(2-methylprop-1-enyl)-2-oxo-6-phenyl-1,2,3,6-tetrahydropyrimidine-5-carboxylate (8). White solid, yield: 70%, mp 151-153 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.90 (s, 1H), 7.38-7.24 (m, 5H), 5.61 (s, 1H), 5.30 (s, 1H), 4.12-4.08 (m, 2H), 2.37 (s, 3H), 1.71 (s, 3H), 1.61 (s, 3H), 1.21 (t, *J* = 7.2, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 165.6, 152.7, 147.1, 141.3, 133.9, 128.4, 127.6, 127.0, 120.6, 101.4, 61.9, 59.9, 22.1, 18.4, 18.0, 14.1. MS: *m/z* 314 (M⁺). Anal. Calcd for C₁₈H₂₂N₂O₃ (314): C 68.77, H 7.05, N 8.91. Found: C 68.70, H 7.08, N 8.87.

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REFERENCES

1. C. O. Kappe, *Acc. Chem. Res.*, 2000, **33**, 879.
2. D. Dallinger, A. Stadler, and C. O. Kappe, *Pure Appl. Chem.*, 2004, **76**, 1017.
3. L. Z. Gong, X. H. Chen, and X. Y. Xu, *Chem. Eur. J.*, 2007, **13**, 8920.
4. M. A. Kolosov and V. D. Orlov, *Mol. Divers.*, 2009, **13**, 5.
5. C. O. Kappe, *Eur. J. Med. Chem.*, 2000, **35**, 1043.
6. K. Singh, D. Arora, K. Singh, and S. Singh, *Mini-Rev. Med. Chem.*, 2009, **9**, 95.
7. K. Deres, C. H. Schroeder, A. Paessens, S. Goldmann, H. J. Hacke, O. Weber, T. Kramer, U. Niewoehner, U. Pleiss, J. Stoltefuss, E. Graef, D. Koletzki, R. N. A. Masantschek, A. Reimann, R. Jaeger, R. Grob, B. Beckermann, K. H. Schlemmer, D. Haebich, and H. Ruebsamen-Waigmann, *Science*, 2003, **299**, 893.
8. C. O. Kappe, *Tetrahedron*, 1993, **49**, 6937.
9. (a) X.-C. Wang, Z.-J. Quan, and Z. Zhang, *Tetrahedron*, 2007, **63**, 8227; (b) X.-C. Wang, Z.-J. Quan, J.-K. Wang, Z. Zhang, and M.-G. Wang, *Bioorg. Med. Chem. Lett.*, 2006, **16**, 4592; (c) Z.-J. Quan, R.-G. Ren, X.-D. Jia, Y.-X. Da, Z. Zhang, and X.-C. Wang, *Tetrahedron*, 2011, **67**, 2462.
10. (a) Z.-J. Quan, R.-G. Ren, Y.-X. Da, Z. Zhang, X.-D. Jia, C.-X. Yang, and X.-C. Wang, *Heterocycles*, 2010, **81**, 1827; (b) Z.-J. Quan, R.-G. Ren, X.-D. Jia, Y.-X. Da, Z. Zhang, and X.-C. Wang, *Lett. Org. Chem.*, 2011, **8**, 188.
11. L. A. Thompson and J. A. Ellman, *Chem. Rev.*, 1996, **96**, 555.
12. X.-C. Wang, Z.-J. Quan, F. Wang, M.-G. Wang, Z. Zhang, and Z. Li, *Synth. Commun.*, 2006, **36**, 451.
13. Z.-J. Quan, Y.-X. Da, Z. Zhang, and X.-C. Wang, *Catal. Commun.*, 2009, **10**, 1146.
14. X.-C. Wang, L. Li, Z.-J. Quan, H.-P. Gong, H.-L. Ye, and X.-F. Cao, *Chin. Chem. Lett.*, 2009, **20**, 651.
15. Z. Zhang, Z. B. Du, B. L.-J. Zhang, Y.-X. Da, Z.-J. Quan, L.-J. Yang, and X.-C. Wang, *RSC Adv.*, 2013, **3**, 9201.
16. A. R. Kiasat and M. F. Mehrjardi, *Catal. Commun.*, 2008, **9**, 1497.
17. S. R. Sheng, Q. Y. Wang, Y. Ding, X. L. Liu, and M. Z. Cai, *Catal. Lett.*, 2009, **128**, 418.
18. A. Hasaninejad, A. Zare, M. Shekouhy, and J. Ameri-Rad, *Green Chem.*, 2011, **13**, 958.
19. A. Hasaninejad, A. Zare, and M. Shekouhy, *Tetrahedron*, 2011, **67**, 390.

20. C. B. Reddy, K. S. Kumar, M. A. Kumar, M. V. N. Reddy, B. S. Krishna, M. Naveen, M. K. Arunasree, C. S. Reddy, C. NagaRaju, and C. D. Reddy, *Eur. J. Med. Chem.*, 2012, **47**, 553.
21. Z. N. Siddiqui and T. Khan, *Tetrahedron Lett.*, 2013, **54**, 3759.
22. K. R. M. Naidu, B. S. Krishna, M. A. Kumar, P. Arulselvan, S. L. Khalivulla, and O. Lasekan, *Molecules*, 2012, **17**, 7543.
23. (a) K. Debnath, S. Pathak, and A. Pramanik, *Tetrahedron Lett.*, 2013, **54**, 4110; (b) R. H. Vekariya and H. D. Patel, *RSC Adv.*, 2015, **5**, 49006.