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Three-component one-pot synthesis of fused uracils – pyrano[2,3-*d*]-pyrimidine-2,4-diones

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Abstract 5-Arylidene-*N*,*N*-dimethylbarbituric acids undergo smooth hetero-*Diels-Alder* reactions with enol ethers to afford *cis* and *trans* diastereoisomers of 7-alkoxy-5-aryl-2*H*-pyrano[2,3-*d*]pyrimidine-2,4-diones in excellent yields (84–95%). Cycloadducts with *cis*-configuration were the major products. Three-component one-pot reactions of *N*,*N*-dimethylbarbituric acid, aromatic and heteroaromatic aldehydes, and enol ethers in the presence of piperidine gave uracils also in very good yields (87–95%). The structure of the cycloadducts is discussed in terms of configuration and preferred conformation.

Keywords Uracil; Hetero-*Diels-Alder* reaction; l-Oxa-1,3-butadiene; Pyrano[2,3-*d*]pyrimidine-2,4-dione.

Introduction

Uracil [1] is one of the five nucleobases and therefore an important component of nucleic acids, thus uracil and its fused derivatives, such as pyrano[2,3-*d*]pyrimidines, pyrido[2,3-*d*]pyrimidines or pyrimido[4,5-*d*]pyrimidines are well recognized by synthesis as well as biological chemists. Compounds with this ring system have antiallergic [2], antihypertensive [3], cardiotonic [4], bronchiodilator [5], antibronchitic [6], or antitumour [7] activity.

The preparation of naturally occurring complex molecules containing an uracil ring poses significant synthetic challenges. The synthesis exploitation of nucleophilic double bond of uracil is an important strategy for the synthesis of a variety of potential products [8–11]. The synthesis of fused uracils is well described in literature [12–16], but the synthesis methods usually require drastic conditions, long reaction times, complex synthetic pathways and the yields are poor. Recently, a novel approach to the synthesis of fused uracils of biological importance has been made. New synthesis methods rely on a multicomponent reaction in the solid state [17], a stereoselective intramolecular hetero-*Diels-Alder* reaction (H*DA*) [18], an intermolecular [4 + 2] cycloaddition reaction [19], or a photo-induced oxidative cyclization [20]. In our recent work, we have shown that intermolecular and intramolecular H*DA* reactions are a powerful tool in 2*H*-pyrans and policyclic 2*H*-pyran derivatives synthesis [21–26]. Among them, reactions 5-arylidene-*N*,*N*-dimethylbarbituric acids with styrenes [24] or *N*-vinyl-2-oxazolidinone [26] afforded 2*H*-pyrano[2,3-*d*]pyrimidine-2,4-diones with very good yields. It is well-known that a *Knoevenagel* condensation followed by a hetero-*Diels-Alder* reaction can be used in dihydropyran synthesis [27–31]. In the present paper this method was used for the synthesis of fused uracils – pyrano[2,3-*d*]pyrimidine-2,4-dione.

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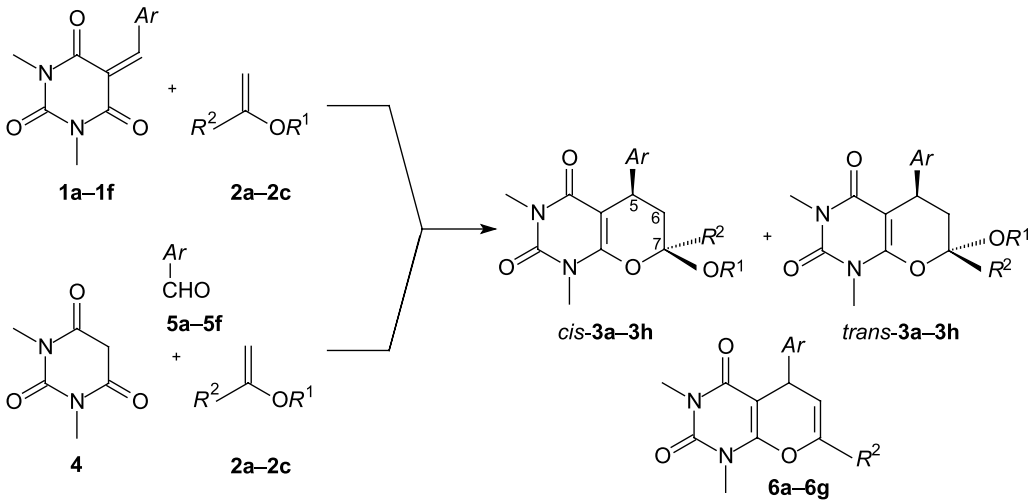
Results and discussion

The aim of the studies was the preparation of fused uracils – pyrano[2,3-*d*]pyrimidine-2,4-diones



					Ar	R^1	R^2
1a	**2a**	**3a**	**5a**	**6a**	*p*-CH_3O-C_6H_4	C_2H_5	H
1a	**2b**	**3b**	**5a**	**6a**	*p*-CH_3O-C_6H_4	*i-Bu*	H
1a	**2c**	**3c**	**5a**	**6b**	*p*-CH_3O-C_6H_4	CH_3	CH_3
1b	**2a**	**3d**	**5b**	**6c**	C_6H_5	C_2H_5	H
1c	**2a**	**3e**	**5c**	**6d**	*p*-NO_2-C_6H_4	C_2H_5	H
1d	**2a**	**3f**	**5d**	**6e**	2-thienyl	C_2H_5	H
1e	**2a**	**3g**	**5e**	**6f**	2-furyl	C_2H_5	H
1f	**2a**	**3h**	**5f**	**6g**	4-pyridinyl	C_2H_5	H

Scheme 1

in a three-component one-pot synthesis. First, it was examined if 5-arylidene-*N*,*N*-dimethylbarbituric acids **1a**–**1f** can act as active heterodienes in H*DA* reaction with enol ethers **2a**–**2c**. Potential heterodienes **1a**–**1f** were synthesized according to the general reaction protocol described in literature [32] by condensation of *N*,*N*-dimethylbarbituric acids with appropriate aromatic or heteroaromatic aldehydes in anhydrous ethanol in the presence of piperidine. The cycloaddition reactions of **1a**–**1f** with a ten-fold excess of **2a**–**2c** were performed with methylene chloride as the solvent at room temperature for 1–5 h and the uracils **3a**–**3h** were obtained in excellent 84–95% yields (Scheme 1, Table 1).

The progress of the reactions was monitored by TLC. The ratios of the *cis*/*trans* diastereoisomers of the pyrano[2,3-*d*]pyrimidine-2,4-diones **3a**–**3h** were

Table 1 Synthesis of pyrano[2,3-*d*]pyrimidine-2,4-diones **3a**–**3h** by H*DA* reaction of 5-arylidene-*N*,*N*-dimethylbarbituric acids **1a**–**1f** with enol ethers **2a**–**2c**

1	2	3	Reaction time/h	Yield/%[a]	Ratio of *cis*/*trans*[b]
1a	**2a**	**3a**	2 12[c]	94 92[c]	2.6:1 3.6:1[c]
1a	**2b**	**3b**	3	92	2.6:1
1a	**2c**	**3c**	3	89	2:1
1b	**2a**	**3d**	2	90	2:1
1c	**2a**	**3e**	1	95	1.75:1
1d	**2a**	**3f**	5	84	1.25:1
1e	**2a**	**3g**	5	87	1.7:1
1f	**2a**	**3h**	5	89	2.2:1

[a] Isolated yields after column chromatography
[b] Ratio based on ^{1}H NMR (300 MHz) spectra of crude products
[c] The cycloaddition was performed at −35°C

Table 2 One-pot synthesis of pyrano[2,3-*d*]pyrimidine-2,4-diones **3a**–**3h** by reaction of *N*,*N*-dimethylbarbituric acid **4**, aldehydes **5a**–**5f**, and enol ethers **2a**–**2c**

5	2	3	Reaction time/h	Yield/%[a]	Ratio of *cis*/*trans*[b]
5a	**2a**	**3a**	3	95	2.6:1
5a	**2b**	**3b**	4	93	2.4:1
5a	**2c**	**3c**	4	89	2.1:1
5b	**2a**	**3d**	3	92	1.6:1
5c	**2a**	**3e**	2	94	1.1:1
5d	**2a**	**3f**	7	87	2.6:1
5e	**2a**	**3g**	7	90	1.7:1
5f	**2a**	**3h**	7	89	2.9:1

[a] Isolated yields after column chromatography
[b] Ratio based on ^{1}H NMR (300 MHz) spectra of crude products

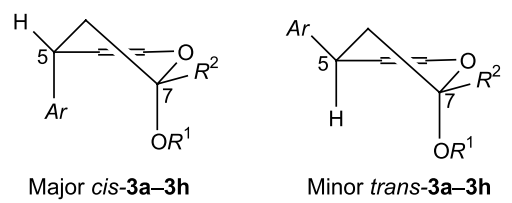
Table 3 Signals of proton 5-H and 7-H in ^{1}H NMR spectra of products **3a–3h**

Compound	dd 5-H δ/ppm $J_{6ax,5}/J_{6eq,5}$/Hz	dd 7-H δ/ppm $J_{6ax,7}/J_{6eq,7}$/Hz	Compound	dd 5-H δ/ppm $J_{6ax,5}/J_{6eq,5}$/Hz	dd 7-H δ/ppm $J_{6ax,7}/J_{6eq,7}$/Hz
cis-**3a**	4.00 6.9/6.6	5.35 5.4/2.7	*trans*-**3a**	4.12 5.4/4.8	5.17 6.9/3.9
cis-**3b**	4.01 7.2/5.7	5.33 4.8/2.7	*trans*-**3b**	4.12 5.4/4.8	5.16 7.5/3.0
cis-**3c**	3.99 6.9/4.5	–	*trans*-**3c**	3.97 11.4/6.9	–
cis-**3d**	4.05 6.9/6.6	5.35 6.0/2.7	*trans*-**3d**	4.17 5.4/4.8	5.18 7.2/3.3
cis-**3e**	4.15 7.5/4.2	5.45 3.9/2.7	*trans*-**3e**	4.21 6.6/6.6	5.27 6.3/2.4
cis-**3f**	4.37 6.0/6.0	5.43 3.6/3.3	*trans*-**3f**	4.43 5.4/2.7	5.32 9.3/2.4
cis-**3g**	4.15 6.6/3.9	5.43 3.3/3.3	*trans*-**3g**	4.21 6.0/2.7	5.37 9.3/2.4
cis-**3h**	4.04 7.5/3.9	5.44 3.6/2.7	*trans*-**3h**	4.09 6.0/5.7	5.20 7.2/2.4

determined on the basis of ^{1}H NMR spectra of crude products, analyzing the signals of protons 5-H and 7-H. All diastereoisomers of **3a–3h** were very easily separated by column chromatography using *t*-butyl-methyl ether as an eluent because the difference between R_f (*cis*) and R_f (*trans*) was approximately 0.2.

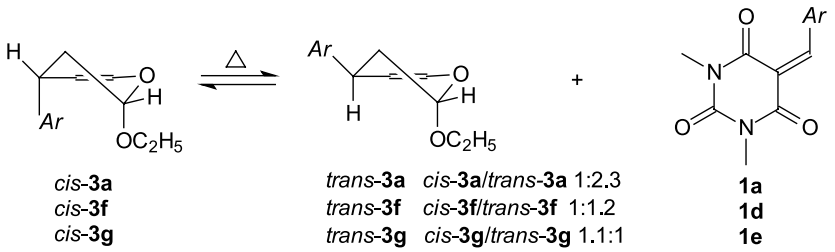
In the next step of studies three-component one-pot synthesis of uracils **3a–3h** was investigated. The experimental procedure was simple: equimolar amounts of *N*,*N*-dimethylbarbituric acid **4** and aromatic or heteroaromatic aldehydes **5a–5f** were mixed with a ten-fold excess of enol ethers **2a–2c** in methylene chloride in the presence of piperidine at room temperature for 2–7 h and the pyrano[2,3-*d*]pyrimidines **3a–3h** were obtained in excellent 87–95% yields (Scheme 1 and Table 2). The progress of the reactions was monitored by TLC. The ratios of the *cis*/*trans* diastereoisomers of pyrano[2,3-*d*]pyrimidines **3a–3h** were determined on the basis of ^{1}H NMR spectra of crude products. Cycloadducts *cis*-**3a–3h** were the major products in all reactions. The preferred formation of the *cis*-diastereoisomers (Tables 1 and 2) results from the *endo* transition state interaction, which is energetically more favorable than the *exo* transition state. Thus, *cis*-products arise from a kinetically controlled process [33]. The cycloaddition reaction of **1a** with a ten-fold excess of **2a** was also performed at a temperature of −35°C (Table 1) and the ratio of *cis*/*trans* isomers of **3a** was 3.6:1. Decreasing the reaction temperature resulted in a slight increase of the reaction diastereoselectivity and the reaction needed longer time to be completed.

Compounds **3a–3h** were characterized by ^{1}H, ^{13}C NMR, IR, mass spectra, and elemental analysis. ^{1}H and ^{13}C signal assignments were confirmed by two-dimensional NMR, COSY and HETCOR spectra. The relative *cis* and *trans* configuration of the C-5, C-7 substituents were assigned on the basis of ^{1}H NMR spectra. They were deduced from the chemical shift values and coupling constants of the protons attached to C-5 and C-7 of the dihydropyran ring that exists in a half-chair conformation [34] (Table 3). In the ^{1}H NMR spectra of the major diastereoisomers *cis*-**3a–3h** the signal of 5-H appeared as a doublet of doublets at $\delta = 3.99$–4.37 ppm with coupling constants ($^3J = 6.0$–7.5 and 3.9–6.6 Hz) due to coupling with two protons at C-6 (Table 3). Thus, 5-H occupies the *pseudo-equatorial* position, and the aroma-



Major *cis*-**3a–3h** Minor *trans*-**3a–3h**

Fig. 1 Preferred *cis*/*trans* configurations and conformations of cycloadducts **3a–3h** based on ^{1}H NMR analysis



Scheme 2

tic group adopts the *pseudo-axial* orientation (Fig. 1). The ^{1}H NMR spectra of *cis*-**3a**–**3h** reveal the signals of proton 7-H as a doublet of doublets at $\delta = 5.33$–5.44 ppm with two small coupling constants ($^3J =$ 3.3–6.0 and 2.7–3.3 Hz). Thus, 7-H is in the *equatorial* position and the alkoxy group occupies the *axial* position (Fig. 1).

For the minor diastereoisomers *trans*-**3a**–**3h**, the protons attached to C-5 give rise to a doublet of doublets with coupling constants $^3J = 5.4$–11.4 and 2.7–6.9 Hz at $\delta = 3.97$–4.43 ppm. Thus, 5-H is *pseudo-axial* and the aryl moiety occupies the *pseudo-equatorial* position (Fig. 1). The proton 7-H of *trans*-**3a**–**3h** resonates at $\delta = 5.16$–5.37 ppm as a doublet of doublets with two coupling constants ($^3J = 6.3$–9.3 and 2.4–3.9 Hz). This suggests that for *trans*-**3a**–**3h** the conformation with an *axial* alkoxy group is preferred due to stabilization by the anomeric effect.

It is worth to note that trace amounts of compounds **6a**–**6g** created by a *trans-diaxial*-elimination of the appropriate alcohol were obtained in the above described reactions (^{1}H NMR analysis of crude products, Scheme 1). Only products **6a**, **6e**, and **6f** were isolated in small amounts after column chromatography. Fused uracils **6e** and **6f** are not yet described in literature. Compounds **6a**, **6c**, and **6d** were also obtained in earlier examined reactions of 5-arylidene-*N*,*N*-dimethyl-barbituric acids and *N*-vinyl-2-oxazolidinone [26]. The cycloadditions were conducted in boiling toluene and uracils **6a**, **6c**, and **6d** created as products of 2-oxazolidinone elimination. Taking into account this fact, the *cis*-**3a**, *cis*-**3f**, and *cis*-**3g** diastereoisomers were heated in boiling toluene for 12 h. The mixture of *cis* and *trans* isomers and small amounts of compounds **1a**, **1d**, and **1e** formed in a *retro-Diels-Alder* reaction, were obtained (Scheme 2). Elimination products **6a**, **6e**, and **6f** were absent in reaction mixtures after 12 h of heating. It is known that *cis* diastereoisomers of 3,4-dihydro-2*H*-pyrans derivatives undergo transformation to the thermodynamically more stable *trans* isomers in the presence of *Lewis* acid or under heating [35, 36]. These results corroborated that the *cis* and *trans* configurations were correctly assigned to compound **3a**, **3f**, and **3g**.

In conclusion, fused uracils of potential biological activity, the pyrano[2,3-*d*]pyrimidine-2,4-diones, were obtained by a hetero-*Diels-Alder* reactions between 5-arylidene-*N*,*N*-dimethylbarbituric acids and enol ethers or in a one-pot synthesis in which reagents were: *N*,*N*-dimethylbarbituric acid, aromatic or heteroaromatic aldehydes, and enol ethers. The advantages of the presented reactions are: the excellent yields, short reactions times, and the fact that cycloadditions do not require drastic conditions, but can be carried out at room temperature. The described reactions give easy and rapid access to both *cis* as *trans* diastereoisomers of uracils and pure diastereoisomers can be very easily isolated by column chromatography.

Experimental

Melting points were determined on a *Boetius* hot stage apparatus. IR spectra: Bruker IFS 48 in KBr pellets. NMR spectra: Bruker Avance II 300 (^{1}H: 300.18 MHz, ^{13}C: 75.48 MHz) in $CDCl_3$ with *TMS* as an internal standard. Mass spectra: Finningan Mat 95 (70 eV). Microanalyses were performed with Euro EA 3000 Elemental Analyzer, their results agreed satisfactorily with the calculated values. 5-Arylidene-*N*,*N*-dimethylbarbituric acids **1a**–**1f** were obtained according to the general procedure described in Ref. [32]. Enol ethers **2a**–**2c** were commercially available.

N,N-Dimethyl-5-(2-thienylidene)pyrimidine-2,4,6-trione (**1d**, $C_{11}H_{10}N_2O_3S$)

To a stirred solution of 1.56 g *N*,*N*-dimethylbarbituric acid **4** (10 mmol) in 30 cm^3 anhydrous ethanol, 1 cm^3 tiophene-2-carbaldehyde (10 mmol) and two drops of piperidine were added at room temperature. The mixture was allowed to stir at room temperature for 1 h, then the precipitated light-yellow solid was filtered off and washed with ethanol. Crystallization from methanol gave 2.4 g pale yellow crystals; mp 203°C; yield

96%; IR (KBr): $\bar{\nu} = 3103, 3077, 3058, 2953$ (CH), 1704, 1667, 1652 (C=O), 1560 (C=C) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 3.42$ (s, 3 N–CH_3), 3.43 (s, 3 N–CH_3), 7.29 (dd, $J = 3.9$, 5.1 Hz, 1 thienyl-H), 7.90 (dd, $J = 0.9$, 3.9 Hz, 1 thienyl-H), 8.00 (ddd, $J = 1.3$, 5.1 Hz, 1 thienyl-H), 8.75 (d, $J = 0.6$ Hz, 1 =C–H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 28.1$ (N–CH_3), 28.9 (N–CH_3), 110.6 (=C–H), 128.2, 136.9, 141.8, 145.4 (thienyl-C), 151.3 (C=O), 161.7 (C=O), 162.6 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 250 (100) $[M]^+$, 143 (27), 108 (13).

*Procedures for the synthesis of pyrano[2,3-d]pyrimidine-2,4-diones **3a–3h***

A solution of 4 mmol **1a–1f** in 50 cm^3 anh. CH_2Cl_2 and 40 mmol enol ethers **2a–2c** (10 equivalents) was kept at room temperature for the time given in Table 1. The progress of the reactions was monitored by TLC. The solvent and excess of ethers were evaporated and the mixture was separated and purified by column chromatography on silica gel using *t*-butyl methyl ether (**3a–3g**) or *t*-butyl methyl ether/methanol = 3/1 (**3h**) as an eluent. Recrystallization from *t*-butyl methyl ether (**3a–3g**) or *t*-butyl-methyl ether/methanol = 4/1 (**3h**) gave **3a–3h** with yields listed in Table 1.

One-pot synthesis: Equimolar amounts (4 mmol) of *N*,*N*-dimethylbarbituric acid (**4**) and aromatic aldehydes **5a–5f** were mixed with a ten-fold excess of enol ethers **2a–2c** (40 mmol) in 50 cm^3 anh. CH_2Cl_2 in the presence of 2 drops of piperidine at room temperature for the time given in Table 2. The progress of the reactions was monitored by TLC. The solvent and excess of ethers were evaporated and the mixture was separated and purified by column chromatography on silica gel and recrystallized. Products **3a–3h** were obtained with yields listed in Table 2.

(5RS,7SR)-7-Ethoxy-1,5,6,7-tetrahydro-5-(4-methoxyphenyl)-1,3-dimethyl-2H-pyrano[2,3-d]pyrimidine-2,4(3H)-dione (*cis*-**3a**, $C_{18}H_{22}N_2O_5$)

Colorless crystals; mp 120°C; yield 68%; IR (KBr): $\bar{\nu} = 2974$, 2940, 2888 (CH), 1707, 1652 (C=O), 1247, 1177, 1131 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.17$ (t, $J = 7.05$ Hz, 3H, OCH_2CH_3), 2.13 (ddd, $J = 5.7$, 6.0, 14.1 Hz, 1H, 6-H), 2.34 (ddd, $J = 2.7$, 7.2, 14.1 Hz, 1H, 6-H), 3.27 (s, 3H, N–CH_3), 3.43 (s, 3H, N–CH_3), 3.61 (dq, $J = 7.2$, 9.3 Hz, 1H, OCH_2CH_3), 3.76 (s, 3H, OCH_3), 3.89 (dq, $J = 7.2$, 9.3 Hz, 1H, OCH_2CH_3), 4.00 (dd $J = 6.6$, 6.9 Hz, 1H, 5-H), 5.35 (dd, $J = 2.7$, 5.4 Hz, 1H, 7-H), 6.78 (ddd, $J = 1.8$, 3.0, 9.0 Hz, 2H, *Ar*H), 7.10 (ddd, $J = 1.8$, 3.0, 8.4 H, 2H, *Ar*H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.9$ (OCH_2CH_3), 27.9 (N–CH_3), 28.7 (N–CH_3), 33.7 (C-6), 36.3 (C-5), 55.2 (OCH_3), 65.5 (OCH_2CH_3), 90.0 (C-4a), 102.4 (C-7), 113.5, 128.2, 135.7, 151.3 (*Ar*C), 154.9 (C-8a), 157.9 (C=O), 162.1 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 300 (10) $[M]^+$, 300 (5), 273 (10), 134 (2), 73 (100).

(5RS,7RS)-7-Ethoxy-1,5,6,7-tetrahydro-5-(4-methoxyphenyl)-1,3-dimethyl-2H-pyrano[2,3-d]pyrimidine-2,4(3H)-dione (*trans*-**3a**, $C_{18}H_{22}N_2O_5$)

Colorless crystals; mp 141°C; yield 26%; IR (KBr): $\bar{\nu} = 2982$, 2944, 2906, 2890 (CH), 1699, 1646 (C=O), 1243, 1190, 1150 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.25$ (t, $J = 7.05$ Hz, $3OCH_2CH_3$), 2.14 (m, 2 6-H), 3.30 (s, 3N–CH_3), 3.43 (s, 3N–CH_3), 3.64 (dq, $J = 7.05$, 9.6 Hz, $1OCH_2CH_3$), 3.77 (s, $3OCH_3$), 3.97 (dq, $J = 7.05$, 9.5 Hz, $1OCH_2CH_3$), 4.12 (dd, $J = 4.8$, 5.4 Hz, 1 5-H), 5.17 (dd, $J = 3.9$, 6.9 Hz, 1 7-H), 6.84 (ddd, $J = 1.8$, 3.0, 8.7 Hz, 2*Ar*H), 7.08 (ddd, $J =$ 1.8, 3.0, 8.4 Hz, 2*Ar*H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta =$ 15.1 (OCH_2CH_3), 27.9 (N–CH_3), 28.6 (N–CH_3), 33.3 (C-6), 36.0 (C-5), 55.2 (OCH_3), 65.9 (OCH_2CH_3), 88.7 (C-4a), 101.5 (C-7), 114.1, 128.1, 135.6, 151.3 (*Ar*C), 155.2 (C-8a), 158.3 (C=O), 162.1 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 346 (95) $[M]^+$, 300 (63), 273 (100), 243 (10), 134 (14), 73 (17).

(5RS,7SR)-1,5,6,7-Tetrahydro-7-isobutoxy-5-(4-methoxyphenyl)-1,3-dimethyl-2H-pyrano[2,3-d]pyrimidine-2,4(3H)-dione (*cis*-**3b**, $C_{20}H_{26}N_2O_5$)

Colorless crystals; mp 121°C; yield 67%; IR (KBr): $\bar{\nu} = 2956$, 2911, 2876 (CH), 1707, 1641 (C=O), 1240, 1175, 1128 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.80$ (d, $J = 6.6$ Hz, 6 $OCH_2CH(CH_3)_2$), 1.75 (m, $J = 6.6$ Hz, $1OCH_2CH(CH_3)_2$), 2.18 (ddd, $J = 5.4$, 5.4, 14.1 Hz, 1 6-H), 2.33 (ddd, $J = 2.7$, 7.2, 14.1 Hz, 1 6-H), 3.28 (s, 3N–CH_3), 3.29 (dd, $J = 6.6$, 9.0 Hz, $1OCH_2CH(CH_3)_2$), 3.42 (s, 3N–CH_3), 3.60 (dd, $J = 6.6$, 9.0 Hz, $1OCH_2CH(CH_3)_2$), 3.76 (s, $3OCH_3$), 4.01 (dd, $J = 5.7$, 7.2 Hz, 1 5-H), 5.33 (dd, $J = 2.7$, 4.8 Hz, 1 7-H), 6.77 (ddd, $J = 2.1$, 3.0, 8.7 Hz, 2*Ar*H), 7.09 (ddd, $J = 1.8$, 3.0, 8.4 Hz, 2*Ar*H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 19.0$ ($OCH_2CH(CH_3)_2$), 27.9 (N–CH_3), 28.3 ($OCH_2CH(CH_3)_2$), 28.6 (N–CH_3), 33.2 (C-6), 35.9 (C-5), 55.2 (OCH_3), 77.2 ($OCH_2CH(CH_3)_2$), 89.7 (C-4a), 102.8 (C-7), 113.5, 128.0, 135.6, 151.3 (*Ar*C), 154.9 (C-8a), 157.8 (C=O), 162.1 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 374 (75) $[M]^+$, 300 (69), 289 (19), 274 (100), 243 (8), 134 (14), 73 (64).

(5RS,7RS)-1,5,6,7-Tetrahydro-7-isobutoxy-5-(4-methoxyphenyl)-1,3-dimethyl-2H-pyrano[2,3-d]pyrimidine-2,4(3H)-dione (*trans*-**3b**, $C_{20}H_{26}N_2O_5$)

Colorless crystals; mp 143°C; yield 26%; IR (KBr): $\bar{\nu} = 2955$, 2899, 2870, 2831 (CH), 1708, 1648 (C=O), 1252, 1158, 1106 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.90$ (d, $J = 6.6$ Hz, $6OCH_2CH(CH_3)_2$), 1.88 (m, $J = 6.6$ Hz, $1OCH_2CH(CH_3)_2$), 2.15 (m, 2 6-H), 3.30 (s, 3N–CH_3), 3.34 (dd, $J = 6.6$, 9.0 Hz, $1OCH_2CH(CH_3)_2$), 3.42 (s, 3N–CH_3), 3.66 (dd, $J = 6.6$, 9.3 Hz, $1OCH_2CH(CH_3)_2$), 3.77 (s, $3OCH_3$), 4.12 (dd, $J = 4.8$, 5.4 Hz, 1 5-H), 5.16 (dd, $J = 3.0$, 7.5 Hz, 1 7-H), 6.84 (d, $J = 8.7$ Hz, 2*Ar*H), 7.08 (d, $J = 8.7$ Hz, 2*Ar*H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 19.1$ ($OCH_2CH(CH_3)_2$), 27.9 (N–CH_3), 28.4 ($OCH_2CH(CH_3)_2$), 28.6 (N–CH_3), 33.2 (C-6), 36.0 (C-5), 55.2 (OCH_3), 77.3 ($OCH_2CH(CH_3)_2$), 88.7 (C-4a), 101.8 (C-7), 114.1, 128.1, 135.6, 151.4 (*Ar*C), 155.2 (C-8a), 158.3 (C=O), 162.1 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 374 (79) $[M]^+$, 300 (74), 289 (21), 274 (100), 243 (9), 134 (14), 73 (31).

(5RS,7SR)-1,5,6,7-Tetrahydro-7-methoxy-5-(4-methoxyphenyl)-1,3,7-trimethyl-2H-pyrano[2,3-d]pyrimidine-2,4(3H)-dione (*cis*-**3c**, $C_{18}H_{22}N_2O_5$)

Colorless crystals; mp 170°C; yield 59%; IR (KBr): $\bar{\nu} = 2999$, 2946, 2872, 2836 (CH), 1699, 1639 (C=O), 1248, 1182, 1055

(C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.56$ (s, 3 7-CH_3), 2.17 (dd, $J = 7.2$, 14.1 Hz, 1 6-H), 2.28 (dd, $J = 4.5$, 14.1 Hz, 1 6-H), 3.25 (s, 3 7-OCH_3), 3.25 (s, 3N–CH_3), 3.44 (s, 3N–CH_3), 3.76 (s, 3 4-CH_3O–C_6H_4), 3.99 (dd, $J = 4.5$, 6.9 Hz, 1 5-H), 6.79 (d, $J = 8.7$ Hz, 2*Ar*H), 7.08 (d, $J = 8.4$ Hz, 2*Ar*H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 22.3$ (7-CH_3), 28.0 (N–CH_3), 28.6 (N–CH_3), 33.9 (C-6), 40.1 (C-5), 49.6 (7-OCH_3), 55.1 (4-CH_3O–C_6H_4), 89.1 (C-4a), 105.5 (C-7), 113.5, 128.1, 135.7, 151.4 (*Ar*C), 155.1 (C-8a), 157.8 (C=O), 162.3 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 346 (28) $[M]^+$, 314 (9), 274 (100), 273 (79), 191 (19), 159 (9), 72 (8).

(5RS,7RS)-1,5,6,7-Tetrahydro-7-methoxy-5-(4-methoxyphenyl)-1,3,7-trimethyl-2H-pyrano[2,3-d]pyrimidine-2,4(3H)-dione (*trans*-**3c**, $C_{18}H_{22}N_2O_5$)
Colorless crystals; mp 143°C; yield 29%; IR (KBr): $\bar{\nu} = 2999$, 2947, 2872, 2836 (CH), 1699, 1639 (C=O), 1247, 1182, 1055 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.59$ (s, 3 7-CH_3), 1.83 (dd, $J = 11.4$, 14.1 Hz, 1 6-H), 2.34 (dd, $J = 6.9$, 14.1 Hz, 1 6-H), 3.24 (s, 3 7-OCH_3), 3.33 (s, 3N–CH_3), 3.42 (s, 3N–CH_3), 3.77 (s, 3 4-CH_3O–C_6H_4), 3.97 (dd $J = 6.9$, 11.4 Hz, 1 5-H), 6.82 (d, $J = 8.4$ Hz, 2*Ar*H), 7.10 (d, $J = 8.4$ Hz, 2*Ar*H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 22.2$ (7-CH_3), 27.9 (N–CH_3), 28.5 (N–CH_3), 33.8 (C-6), 43.5 (C-5), 50.0 (7-OCH_3), 55.1 (4-CH_3O–C_6H_4), 91.2 (C-4a), 104.0 (C-7), 114.0, 127.8, 136.0, 151.4 (*Ar*C), 154.6 (C-8a), 158.0 (C=O), 161.9 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 346 (30) $[M]^+$, 314 (8), 274 (100), 273 (80), 191 (19), 159 (10), 72 (6).

(5RS,7SR)-7-Ethoxy-1,5,6,7-tetrahydro-1,3-dimethyl-5-phenyl-2H-pyrano[2,3-d]pyrimidine-2,4(3H)-dione (*cis*-**3d**, $C_{17}H_{20}N_2O_4$)
Colorless crystals; mp 164°C; yield 60%; IR (KBr): $\bar{\nu} = 3057$, 3021, 2978, 2887 (CH), 1702, 1631 (C=O), 1178, 1132 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.15$ (t, $J = 7.05$ Hz, 3OCH_2CH_3), 2.16 (ddd, $J = 6.0$, 6.6, 14.1 Hz, 1 6-H), 2.36 (ddd, $J = 2.7$, 7.5, 14.1 Hz, 1 6-H), 3.27 (s, 3N–CH_3), 3.43 (s, 3N–CH_3), 3.60 (dq, $J = 6.9$, 9.3 Hz, 1OCH_2CH_3), 3.88 (dq, $J = 6.9$, 9.6 Hz, 1OCH_2CH_3), 4.05 (dd, $J = 6.6$, 6.9 Hz, 1 5-H), 5.35 (dd, $J = 2.7$, 6.0 Hz, 1 7-H), 7.13–7.27 (m, 5*Ph*H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.9$ (OCH_2CH_3), 27.9 (N–CH_3), 28.7 (N–CH_3), 34.4 (C-6), 36.1 (C-5), 65.5 (OCH_2CH_3), 89.7 (C-4a), 102.3 (C-7), 126.2, 127.3, 128.1, 143.5 (*Ph*C), 151.3 (C-8a), 155.0 (C=O), 162.1 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 316 (96) $[M]^+$, 287 (14), 270 (41), 259 (47), 243 (100), 186 (15), 161 (16), 115 (25), 72 (30).

(5RS,7RS)-7-Ethoxy-1,5,6,7-tetrahydro-1,3-dimethyl-5-phenyl-2H-pyrano[2,3-d]pyrimidine-2,4(3H)-dione (*trans*-**3d**, $C_{17}H_{20}N_2O_4$)
Colorless crystals; mp 162°C; yield 30%; IR (KBr): $\bar{\nu} = 3057$, 3019, 2977, 2891 (CH), 1700, 1629 (C=O), 1177, 1149 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.25$ (t, $J = 7.05$ Hz, 3OCH_2CH_3), 2.16 (m, 2 6-H), 3.30 (s, 3N–CH_3), 3.43 (s, 3N–CH_3), 3.64 (dq, $J = 7.05$, 9.6 Hz, 1OCH_2CH_3), 3.97 (dq, $J = 7.05$, 9.6 Hz, 1OCH_2CH_3), 4.17 (dd $J = 4.8$, 5.4 Hz, 1 5-H), 5.18 (dd, $J = 3.3$, 7.2 Hz, 1 7-H), 7.16–7.34 (m, 5*Ph*H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 15.1$ (OCH_2CH_3), 28.0 (N–CH_3), 28.7 (N–CH_3), 34.1 (C-6), 35.9 (C-5), 66.0 (OCH_2CH_3), 88.5 (C-4a), 101.5 (C-7), 126.7, 127.2, 128.7, 143.6 (*Ph*C), 151.4 (C-8a), 155.3 (C=O), 162.1 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 316 (100) $[M]^+$, 287 (13), 270 (40), 259 (40), 243 (93), 186 (14), 161 (14), 115 (17), 72 (30).

(5RS,7SR)-7-Ethoxy-1,5,6,7-tetrahydro-1,3-dimethyl-5-(4-nitrophenyl)-2H-pyrano[2,3-d]pyrimidine-2,4(3H)-dione (*cis*-**3e**, $C_{17}H_{19}N_3O_6$)
Colorless crystals; mp 141°C; yield 60%; IR (KBr): $\bar{\nu} = 2987$, 2956, 2893 (CH), 1707, 1639 (C=O), 1516, 1343 (NO_2), 1175, 1130, 1108 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.08$ (t, $J = 7.05$ Hz, 3 OCH_2CH_3), 2.23 (ddd, $J = 3.9$, 4.2, 14.1 Hz, 1 6-H), 2.39 (ddd, $J = 2.7$, 7.5, 14.1 Hz, 1 6-H), 3.30 (s, 3N–CH_3), 3.45 (s, 3N–CH_3), 3.56 (dq, $J = 7.05$, 9.3 Hz, 1OCH_2CH_3), 3.83 (dq, $J = 7.05$, 9.3 Hz, 1OCH_2CH_3), 4.15 (dd, $J = 4.2$, 7.5 Hz, 1 5-H), 5.45 (dd, $J = 2.7$, 3.9 Hz, 1 7-H), 7.35 (ddd, $J = 1.8$, 2.4, 8.7 Hz, 2*Ar*H), 8.11 (ddd, $J = 1.8$, 2.4, 8.7 Hz, 2*Ar*H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.8$ (OCH_2CH_3), 28.0 (N–CH_3), 28.8 (N–CH_3), 33.4 (C-6), 34.6 (C-5), 65.6 (OCH_2CH_3), 88.1 (C-4a), 101.5 (C-7), 123.3, 128.4, 146.4, 151.1 (*Ar*C), 151.6 (C-8a), 155.3 (C=O), 162.2 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 361 (85) $[M]^+$, 332 (15), 304 (37), 288 (5), 206 (14), 84 (100), 72 (44).

(5RS,7RS)-7-Ethoxy-1,5,6,7-tetrahydro-1,3-dimethyl-5-(4-nitrophenyl)-2H-pyrano[2,3-d]pyrimidine-2,4(3H)-dione (*trans*-**3e**, $C_{17}H_{19}N_3O_6$)
Colorless crystals; mp 141°C; yield 35%; IR (KBr): $\bar{\nu} = 2987$, 2958, 2893 (CH), 1702, 1637 (C=O), 1518, 1346 (NO_2), 1159, 1092 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.27$ (t, $J = 7.05$ Hz, 3OCH_2CH_3), 2.05 (ddd, $J = 2.4$, 6.6, 14.1 Hz, 1 6-H), 2.29 (ddd, $J = 6.3$, 6.3, 14.1 Hz, 1 6-H), 3.27 (s, 3N–CH_3), 3.44 (s, 3N–CH_3), 3.68 (dq, $J = 7.05$, 9.3 Hz, 1OCH_2CH_3), 3.94 (dq, $J = 7.05$, 9.3 Hz, 1OCH_2CH_3), 4.21 (t, $J = 6.6$ Hz, 1 5-H), 5.27 (dd, $J = 2.4$, 6.3 Hz, 1 7-H), 7.37 (ddd, $J = 1.8$, 2.4, 8.4 Hz, 2*Ar*H), 8.17 (ddd, $J = 1.8$, 2.4, 8.7 Hz, 2*Ar*H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 15.0$ (OCH_2CH_3), 28.0 (N–CH_3), 28.8 (N–CH_3), 33.9 (C-6), 35.9 (C-5), 66.0 (OCH_2CH_3), 88.2 (C-4a), 100.7 (C-7), 124.0, 128.0, 146.8, 151.2 (*Ar*C), 151.7 (C-8a), 155.5 (C=O), 162.0 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 361 (100) $[M]^+$, 332 (17), 304 (42), 288 (6), 206 (16), 84 (20), 72 (53).

(5RS,7SR)-7-Ethoxy-1,5,6,7-tetrahydro-1,3-dimethyl-5-(2-thienyl)-2H-pyrano[2,3-d]pyrimidine-2,4(3H)-dione (*cis*-**3f**, $C_{15}H_{18}N_2O_4S$)
Colorless crystals; mp 120°C; yield 47%; IR (KBr): $\bar{\nu} = 2972$, 2930, 2893 (CH), 1704, 1633 (C=O), 1490 (C=C), 1272, 1180, 1116 (C–O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.16$ (t, $J = 7.05$ Hz, 3OCH_2CH_3), 2.35 (dd, $J = 3.3$, 6.0 Hz, 2 6-H), 3.31 (s, 3N–CH_3), 3.41 (s, 3N–CH_3), 3.61 (dq, $J = 7.05$, 9.3 Hz, 1OCH_2CH_3), 3.86 (dq, $J = 7.05$, 9.3 Hz, 1OCH_2CH_3), 4.37 (t, $J = 6.0$ Hz, 1 5-H), 5.43 (t, $J = 3.3$ Hz, 1 7-H), 6.87 (m,

2 thienyl-H), 7.07 (dd, $J = 1.8$, 4.2 Hz, 1 thienyl-H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.8$ ($OCH_2\mathit{C}H_3$), 28.0 (N–CH_3), 28.7 (N–CH_3), 29.0 (C-6), 35.5 (C-5), 65.5 ($O\mathit{C}H_2CH_3$), 90.0 (C-4a), 101.6 (C-7), 122.9, 124.4, 126.2, 147.8 (thienyl-C), 151.2 (C-8a), 154.5 (C=O), 162.1 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 322 (100) $[M]^+$, 276 (27), 265 (24), 250 (95), 167 (17), 136 (26), 108 (15), 73 (13).

(5RS,7RS)-7-Ethoxy-1,5,6,7-tetrahydro-1,3-dimethyl-5-(2-thienyl)-2H-pyrano[2,3-d]pyrimidine-2,4(3H)-dione (*trans*-**3f**, $C_{15}H_{18}N_2O_4S$)

Colorless crystals; mp 125°C; yield 37%; IR (KBr): $\bar{\nu} = 2973$, 2943, 2904 (CH), 1705, 1630 (C=O), 1501 (C=C), 1165, 1094 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.30$ (t, $J = 7.05$ Hz, $3OCH_2C\mathit{H}_3$), 2.14 (ddd, $J = 5.7$, 9.3, 13.8 Hz, 1 6-H), 2.31 (ddd, $J = 2.7$, 2.7, 13.8 Hz, 1 6-H), 3.33 (s, 3N–CH_3), 3.41 (s, 3N–CH_3), 3.70 (dq, $J = 7.05$, 9.6 Hz, $1OC\mathit{H}_2CH_3$), 4.01 (dq, $J = 7.05$, 9.3 Hz, $1OC\mathit{H}_2CH_3$), 4.43 (dd $J = 2.7$, 5.4 Hz, 1 5-H), 5.32 (dd, $J = 2.4$, 9.3 Hz, 1 7-H), 6.83 (dd, $J = 1.2$, 3.3 Hz, 1 thienyl-H), 6.93 (dd, $J = 3.6$, 5.1 Hz, 1 thienyl-H), 7.14 (dd, $J = 1.2$, 5.1 Hz, 1 thienyl-H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 15.1$ ($OCH_2\mathit{C}H_3$), 28.0 (N–CH_3), 28.6 (N–CH_3), 29.8 (C-6), 35.8 (C-5), 66.2 ($O\mathit{C}H_2CH_3$), 89.1 (C-4a), 102.0 (C-7), 123.7, 124.4, 127.0, 147.8 (thienyl-C), 151.2 (C-8a), 155.0 (C=O), 162.1 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 322 (100) $[M]^+$, 276 (23), 265 (20), 250 (97), 167 (15), 136 (22), 108 (11), 73 (26).

(5RS,7SR)-7-Ethoxy-5-(2-furyl)-1,5,6,7-tetrahydro-1,3-dimethyl-2H-pyrano[2,3-d]pyrimidine-2,4(3H)-dione (*cis*-**3g**, $C_{15}H_{18}N_2O_5$)

Colorless crystals; mp 141°C; yield 55%; IR (KBr): $\bar{\nu} = 2977$, 2949, 2901 (CH), 1705, 1642 (C=O), 1485 (C=C), 1179, 1056 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.19$.(t, $J = 7.05$ Hz, $3OCH_2C\mathit{H}_3$), 2.15 (ddd, $J = 3.0$, 6.9, 14.1 Hz, 1 6-H), 2.51 (ddd, $J = 3.6$, 3.9, 14.1 Hz, 1 6-H), 3.33 (s, 3N–CH_3), 3.39 (s, 3N–CH_3), 3.55 (dq, $J = 7.05$, 9.3 Hz, $1OC\mathit{H}_2CH_3$), 3.80 (dq, $J = 7.05$, 9.3 Hz, $1OC\mathit{H}_2CH_3$), 4.15 (dd, $J = 3.9$, 6.6 Hz, 1 5-H), 5.43 (t, $J = 3.3$ Hz, 1 7-H), 5.93 (d, $J = 3.0$ Hz, 1 furyl-H), 6.25 (dd, $J = 1.8$, 3.3 Hz, 1 furyl-H), 7.26 (d, $J = 1.8$ Hz, 1 furyl-H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.7$ ($OCH_2\mathit{C}H_3$), 26.9 (N–CH_3), 28.0 (N–CH_3), 28.6 (C-6), 31.4 (C-5), 65.2 ($O\mathit{C}H_2CH_3$), 87.7 (C-4a), 101.3 (C-7), 105.0, 110.3, 140.2, 151.2 (furyl-C), 154.6 (C-8a), 155.6 (C=O), 162.2 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 306 (100) $[M]^+$, 249 (21), 234 (46), 206 (27), 151 (12), 120 (16), 92 (10), 72 (5).

(5RS,7RS)-7-Ethoxy-5-(2-furyl)-1,5,6,7-tetrahydro-1,3-dimethyl-2H-pyrano[2,3-d]pyrimidine-2,4(3H)-dione (*trans*-**3g**, $C_{15}H_{18}N_2O_5$)

Colorless crystals; mp 125°C; yield 32%; IR (KBr): $\bar{\nu} = 2979$, 2951, 2824 (CH), 1706, 1648 (C=O), 1504 (C=C), 1177, 1095 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.30$ (t, $J = 7.05$ Hz, $3OCH_2C\mathit{H}_3$), 2.03 (ddd, $J = 5.7$, 9.3, 13.8 Hz, 1 6-H), 2.37 (ddd, $J = 2.4$, 2.7, 13.8 Hz, 1 6-H), 3.32 (s, 3N–CH_3), 3.40 (s, 3N–CH_3), 3.73 (dq, $J = 7.05$, 9.6 Hz, $1OC\mathit{H}_2CH_3$), 4.03 (dq, $J = 7.05$, 9.3 Hz, $1OC\mathit{H}_2CH_3$), 4.21 (dd $J = 2.7$, 6.0 Hz, 1 5-H), 5.37 (dd, $J = 2.4$, 9.3 Hz, 1 7-H), 6.07 (d, $J = 3.3$ Hz, 1 furyl-H), 6.28 (dd, $J = 1.8$, 3.3 Hz, 1 furyl-H), 7.31 (d, $J = 1.8$ Hz, 1 furyl-H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 15.1$ ($OCH_2\mathit{C}H_3$), 27.9 (N–CH_3), 28.4 (N–CH_3), 28.6 (C-6), 32.4 (C-5), 66.1 ($O\mathit{C}H_2CH_3$), 86.8 (C-4a), 102.4 (C-7), 106.4, 110.4, 141.4, 151.2 (furyl-C), 155.1 (C-8a), 155.6 (C=O), 162.0 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 306 (100) $[M]^+$, 249 (23), 234 (52), 206 (29), 151 (13), 120 (19), 92 (12), 73 (9).

(5RS,7SR)-7-Ethoxy-1,5,6,7-tetrahydro-1,3-dimethyl-5-(4-pyridinyl)-2H-pyrano[2,3-d]pyrimidine-2,4(3H)-dione (*cis*-**3h**, $C_{16}H_{19}N_3O_4$)

Colorless crystals; mp 152°C; yield 61%; IR (KBr): $\bar{\nu} = 3032$, 2977, 2943, 2886 (CH), 1701, 1640 (C=O), 1598 (C=C), 1200, 1056 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.03$ (t, $J = 7.05$ Hz, $3OCH_2C\mathit{H}_3$), 2.36 (ddd, $J = 2.7$, 7.5, 14.4 Hz, 1 6-H), 2.26 (ddd, $J = 3.6$, 3.9, 13.8 Hz, 1 6-H), 3.27 (s, 3N-CH_3), 3.44 (s, 3N–CH_3), 3.54 (dq, $J = 7.05$, 9.3 Hz, $1OC\mathit{H}_2CH_3$), 3.81 (dq, $J = 7.05$, 9.3 Hz, $1OC\mathit{H}_2CH_3$), 4.04 (dd, $J = 3.9$, 7.5 Hz, 1 5-H), 5.44 (dd, $J = 2.7$, 3.6 Hz, 1 7-H), 7.13 (dd, $J = 1.5$, 4.5 Hz, 2 pyridinyl-H), 8.46 (dd, $J = 1.5$, 4.5 Hz, 2 pyridinyl-H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 15.0$ ($OCH_2\mathit{C}H_3$), 27.9 (N–CH_3), 28.7 (N–CH_3), 33.4 (C-6), 35.3 (C-5), 66.0 ($O\mathit{C}H_2CH_3$), 87.4 (C-4a), 100.9 (C-7), 122.4, 150.0, 151.1 (pyridinyl-C), 152.7 (C-8a), 155.5 (C=O), 161.9 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 317 (100) $[M]^+$, 260 (20), 245 (16), 217 (24), 131 (12), 103 (14), 72 (5).

(5RS,7RS)-7-Ethoxy-1,5,6,7-tetrahydro-1,3-dimethyl-5-(4-pyridinyl)-2H-pyrano[2,3-d]pyrimidine-2,4(3H)-dione (*trans*-**3h**, $C_{16}H_{19}N_3O_4$)

Colorless crystals; mp 131°C; yield 28%; IR (KBr): $\bar{\nu} = 3031$, 2979, 2943, 2888 (CH), 1702, 1645 (C=O), 1593 (C=C), 1196, 1056 (C–O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$ 1.27 (t, $J = 7.05$ Hz, $3OCH_2C\mathit{H}_3$), 2.08 (ddd, $J = 2.4$, 5.7, 13.8 Hz, 1 6-H), 2.25 (ddd, $J = 6.0$, 7.2, 13.8 Hz, 1 6-H), 3.32 (s, 3N–CH_3), 3.44 (s, 3N–CH_3), 3.67 (dq, $J = 7.05$, 9.3 Hz, $1OC\mathit{H}_2CH_3$), 3.96 (dq, $J = 7.05$, 9.3 Hz, $1OC\mathit{H}_2CH_3$), 4.12 (dd, $J = 5.7$, 6.0 Hz, 1 5-H), 5.20 (dd, $J = 2.4$, 7.2 Hz, 1 7-H), 7.12 (dd, $J = 1.5$, 4.5 Hz, 2 pyridinyl-H), 8.54 (dd, $J = 1.5$, 4.5 Hz, 2 pyridinyl-H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.7$ ($OCH_2\mathit{C}H_3$), 27.9 (N–CH_3), 28.7 (N–CH_3), 32.6 (C-6), 34.1 (C-5), 65.4 ($O\mathit{C}H_2CH_3$), 87.6 (C-4a), 101.3 (C-7), 122.7, 149.3, 151.1 (pyridyl-C), 152.6 (C-8a), 155.2 (C=O), 162.1 (C=O) ppm; MS (EI, 70 eV): m/z (%) = 317 (100) $[M]^+$, 260 (27), 245 (23), 217 (15), 131 (17), 103 (21), 72 (14).

1,5-Dihydro-1,3-dimethyl-5-thienyl-2H-pyrano[2,3-d]-pyrimidine-2,4(3H)-dione (**6e**, $C_{13}H_{12}N_2O_3S$)

Orange crystals; mp 195°C; 21 mg (2%); IR (KBr): $\bar{\nu} = 2973$, 2932, 2899 (CH), 1705, 1639 (C=O), 1600, 1489 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 3.34$ (s, 3N–CH_3), 3.41 (s, 3N–CH_3), 7.12 (d, $J = 15.0$ Hz, 1 5-H), 7.21 (dd, $J =$ 3.9, 5.0 Hz, 1 thienyl-H), 7.77 (dd, $J = 1.2$, 5.1 Hz, 1 thienyl-H), 7.78 (dd, $J = 1.2$, 3.9 Hz, 1 thienyl-H), 8.13 (d, $J =$ 12.3 Hz, 1 7-H), 8.36 (dd, $J = 12.0$, 15.0 Hz, 1 6-H) ppm;

^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 28.0$ (CH_3), 28.5 (CH_3), 98.7 (C-5), 117.7, 123.4, 123.9, 124.4, 127.5, 138.7, 148.0, 156.6 (C-4a, C-6, C-7, C-8a, thienyl-C), 159.0 (C-4), 160.2 (C-2) ppm; MS (EI, 70 eV): m/z (%) = 267 (100) $[M]^+$, 161 (32), 115 (19).

5-Furyl-1,5-dihydro-1,3-dimethyl-2H-pyrano[2,3-d]-pyrimidine-2,4(3H)-dione (**6f**, $C_{13}H_{12}N_2O_4$)
Orange crystals; mp 199°C; 19 mg (2%); IR (KBr): $\bar{\nu} = 2978$, 2951, 2903 (CH), 1706, 1645 (C=O), 1599, 1485 (C=C) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 3.38$ (s, 3N–CH_3), 3.39 (s, 3N–CH_3), 6.56 (dd, $J = 1.5$, 3.6 Hz, 1 furyl-H), 6.83 (d, $J = 3.6$ Hz, 1 furyl-H), 7.17 (d, $J = 15.3$ Hz, 1 5-H), 7.61 (d, $J = 1.5$ Hz, 1 furyl-H), 8.13 (d, $J = 12.3$ Hz, 1 7-H), 8.41 (dd, $J = 12.3$, 15.3 Hz, 1 6-H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 28.0$ (CH_3), 28.4 (CH_3), 96.8 (C-5), 102.4, 113.4, 117.7, 123.4, 138.7, 146.8, 156.5, 156.6 (C-4a, C-6, C-7, C-8a, furyl-C), 158.5 (C-4), 160.0 (C-2) ppm; MS (EI, 70 eV): m/z (%) = 260 (100) $[M]^+$, 145 (29), 115 (21).

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