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Synthesis of nitrogen bicyclic scaffolds: pyrimido[1,2-*a*]pyrimidine-2,6-diones

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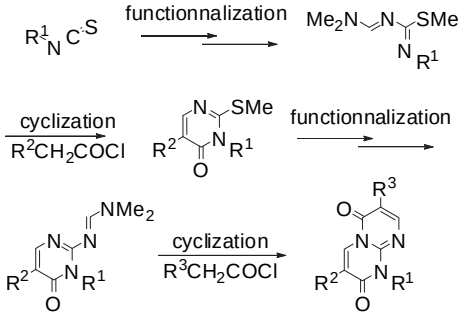
ABSTRACT

The multi-step synthesis of 1,3,7-trisubstituted pyrimido[1,2-*a*]pyrimidinediones starting from isothiocyanates is described. These nitrogen bicycles were prepared by an iterative sequence of functionalization/cyclocondensation reactions. [4+2] Cycloaddition reactions took place between diazadienic chains and various acyl chlorides providing sophisticated heterobicycles.

1. Introduction

Pyrimidopyrimidine moieties are widely represented both in natural and synthetic compounds, and usually display a broad range of biological properties.[1–3] Surprisingly, literature on general access to [1,2-*a*]-analogues—in which one of the three nitrogen atoms is at the junction of the two cycles—is rather limited, with the exception of some examples of specific one-pot or microwave assisted reactions.[4–7] In addition to the potential therapeutic applications, the pyrimido[1,2-*a*]pyrimidine compounds containing a guanidine-like moiety in the structure are also studied as ligands for catalytic activities.[8–10]

In this paper we describe an original and general method for the synthesis of pyrimido[1,2-*a*]pyrimidine-2,6-diones with an isothiocyanate starting material. Both heterocycles of the bicyclic structure are obtained through a cyclocondensation reaction between a diazadiene moiety and an acyl chloride. The synthesis is based on an iterative sequence (diazadiene formation followed by cyclization reaction) and consists of four parts (Scheme 1): functionalization of an isothiocyanate into a diazadienic chain; first cycloaddition reaction providing a pyrimidinone; introduction of a second diazadienic chain onto the structure; and second cycloaddition reaction providing a pyrimidopyrimidinedione.



Scheme 1.

2. Results and discussion

2.1. Pyrimidinone synthesis

The first step of the synthesis involved the conversion of commercially available isothiocyanates into the corresponding thioureas **1**. Reactions were performed in a solution of ammonia in methanol (7 M) in a sealed tube affording thioureas **1**, which then reacted with *N*,*N*-dimethylformamide dimethyl acetal (DMFDMA) in dichloromethane to give thiazadienes **2**. The thiocarbonyl groups were then alkylated with methyl iodide in tetrahydrofuran to afford 2-methylsulfanyl diazadienium iodides **3** in good yields (Scheme 2).

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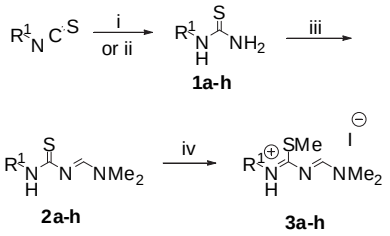


Scheme 2. Three-step synthesis of diazadienium iodides **3** from isothiocyanates. Reagents and conditions: (i) NH_3/MeOH 7 M (excess) for **1a**–**f** and **1h**; (ii) From benzoylisothiocyanate: *N*,*N*-dimethylhydrazine (1 equiv), EtOH, then HCl 4 M, H_2O for **1g**; (iii) DMFDMA (1.2 equiv), CH_2Cl_2; (iv) MeI (1.05 equiv), THF.

The three-step synthetic sequence from isothiocyanates to diazadienium iodides **3** proved to be attractive because of an easy work-up, short reaction times, scalability and high yields. For example 40 g of the compound **3b** (R^1=*p*Tol) was synthesized in one batch in 95% overall yield. Diazadienium iodides **3a**–**h** were obtained with excellent yields independent of the nature of the R^1 group (Table 1): hydrogen (entry 1), aryl (entries 2–4), alkyl (entries 5 and 6), electron donating group (entry 7), and electron withdrawing group (entry 8).[11–13] The compound **1g** (R^1=NMe_2, entry 7) was obtained by a different method in two steps through reaction of *N*,*N*-dimethylhydrazine with benzoylisothiocyanate followed by hydrolysis of the benzoyl group under acidic conditions.

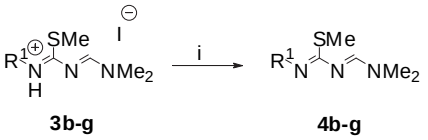
Table 1
Synthesis of thioureas **1**, thiazadienes **2**, diazadienium iodides **3**, and diazadienes **4** (Schemes 2 and 3)

Entry	R^1	Compd (**1**) (%)[a]	Compd (**2**) (%)[d]	Compd (**3**) (%)[e]	Compd (**4**) (%)[f]
1	H	**1a**[b]	**2a** (100)	**3a** (100)	**4a** (—)
2	*p*Tol	**1b** (98)	**2b** (99)	**3b** (100)	**4b** (96)
3	Ph	**1c**[b]	**2c** (94)	**3c** (98)	**4c** (98)
4	*m*Cl_2Ph	**1d** (95)	**2d** (95)	**3d** (99)	**4d** (94)
5	Me	**1e**[b]	**2e** (98)	**3e** (98)	**4e** (76)
6	cHx	**1f** (95)	**2f** (95)	**3f** (98)	**4f** (88)
7	NMe_2	**1g** (68)[c]	**2g** (97)	**3g** (95)	**4g** (78)
8	Ac	**1h**[b]	**2h** (96)	**3h** (98)	**4h** (—)

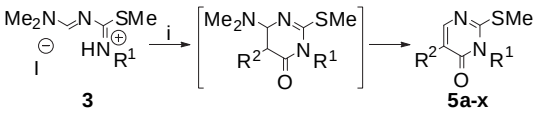
[a] Reagents and conditions: NH_3/MeOH (7 M).
[b] Commercially available.
[c] From benzoylisothiocyanate: *N*,*N*-dimethylhydrazine (1 equiv), EtOH, then HCl 4 M, H_2O.
[d] DMFDMA (1.2 equiv), CH_2Cl_2.
[e] MeI (1.05 equiv), THF.
[f] Saturated aqueous $NaHCO_3$, Et_2O.

A further neutralization step led to the formation of neutral diazadienic chain containing compounds **4b**–**g** (Scheme 3). The reaction was performed under basic conditions using aqueous $NaHCO_3$. However, diazabutadienes **4a** (R^1=H) and **4h** (R^1=Ac) were not obtained, and analogues **4b**–**g** showed rapid degradation. Conversely, all diazadienium salts **3a**–**h** were very stable and proved to be reactive in this ionic form.[13,14] Indeed, the first cyclization reaction took place between the diazadienium iodides **3** and acyl chlorides in basic medium to give pyrimidin-4(3*H*)-ones **5** (Scheme 4).[15] Intermediary cycloadducts were not isolated due to spontaneous loss of dimethylamine; the tandem [4+2] cycloaddition/deamination led to the formation of the expected pyrimidin-4(3*H*)-one together with a secondary product (a *N*,*N*-dimethylamide corresponding to the addition of dimethylamine onto the acyl chloride), but this was easily removed by aqueous wash.

Compounds **5a**–**x** were synthesized with moderate to excellent yields (Table 2). For compounds **5b** (R^1=*p*Tol, R^2=CF_3; entry 2) and **5g** (R^1=*p*Tol, R^2=NMe_2; entry 7), the acyl chlorides were not



Scheme 3. Synthesis of diazadienes **4**. Reagents and conditions: (i) saturated aqueous $NaHCO_3$, Et_2O.



Scheme 4. Synthesis of pyrimidin-4(3*H*)-ones **5** from diazadienium iodides **3**. Reagents and conditions: (i) R^2CH_2COCl (3 equiv), NEt_3 (4 equiv), CH_2Cl_2.

commercially available and were prepared from the corresponding carboxylic acids (1,1,1-trifluoropropionic acid for **5b**; *N*,*N*-dimethylglycine for **5g**). The poor solubility of *N*,*N*-dimethylglycine in common organic solvents is responsible for the dramatic decrease of yield (11%). For compound **5f** (entry 6), microwave irradiation activation[16] allowed us to improve the reaction yield from 65% to 95%. For compounds **5p**–**r** (R^1=Ac, entries 16–18) low yields were obtained due to partial deacetylation of the nitrogen atom.

Table 2
Synthesis of *N*-substituted pyrimidinones **5** from diazadienium iodides **3** (Scheme 4)

Entry	R^1	R^2	Compd (**5**) (%)[a]
1	*p*Tol	CO_2Me	**5a** (97)
2	*p*Tol	CF_3	**5b** (97)[b]
3	*p*Tol	H	**5c** (95)
4	*p*Tol	Ph	**5d** (85)
5	*p*Tol	OMe	**5e** (90)
6	*p*Tol	Me	**5f** (95)[c]
7	*p*Tol	NMe_2	**5g** (11)[b]
8	Me	CO_2Me	**5h** (91)
9	Me	H	**5i** (86)
10	Me	Ph	**5j** (74)
11	Me	OMe	**5k** (62)
12	Me	Me	**5l** (73)
13	H	CO_2Me	**5m** (82)
14	H	H	**5n** (68)
15	H	Ph	**5o** (80)
16	Ac	CO_2Me	**5p** (37)
17	Ac	H	**5q** (47)
18	Ac	Ph	**5r** (10)
19	NMe_2	CO_2Me	**5s** (76)
20	NMe_2	H	**5t** (84)
21	NMe_2	Ph	**5u** (72)
22	*m*Cl_2Ph	CO_2Me	**5v** (79)
23	*m*Cl_2Ph	H	**5w** (78)
24	*m*Cl_2Ph	Ph	**5x** (95)

[a] Reagents and conditions: R^2CH_2COCl (3 equiv), NEt_3 (4 equiv), CH_2Cl_2.
[b] $R^2CH_2CO_2H$ (3 equiv), $(COCl)_2$ (3.3 equiv), DMF (0.1 equiv), CH_2Cl_2, 0 °C; then **4b** (1.0 equiv), NEt_3 (4 equiv), CH_2Cl_2.
[c] Under microwave irradiation: 50 °C, 60 W, 15 min.

2.2. From pyrimidinone rings to bicyclic structures

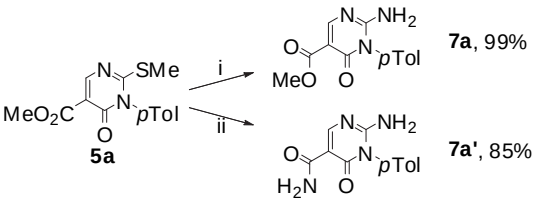
At this point we chose to limit our study to the five compounds **5a**–**e** (R^1=*p*Tol) for the installation of the second ring. The *para*-tolyl group was chosen for two main reasons: this group gave the best general yields for the sequence from *para*-tolylisothiocyanate to pyrimidinones **5** (except for **5g**), and it showed a specific NMR signal (a singlet between 2.4 and 2.6 ppm), which was a practical tool to follow reaction progress.

As the methylsulfanyl group is often considered a leaving group, we thought that the introduction of an amino group on the heterocyclic structure **5** could be achieved by direct nucleophilic displacement with ammonia.[17,18] This nucleophilic substitution reaction proved to be possible only when R^2 group was an electron withdrawing group. In all other cases the reaction substrates were recovered quantitatively. Thus, treatment of compounds **5a** and **5b** (R^2=CO_2Me or CF_3) with ammonia solution in methanol afforded the corresponding 2-aminopyrimidines **7a** and **7b** in quantitative yield (Table 3, entries 1 and 3). In addition, for R^2=CO_2Me, we could efficiently perform the transformation of methyl carboxylate to carboxamide **7a′** using large excess of ammonia (Scheme 5, Table 3, entry 2).

Table 3
Synthesis of compounds **6**, **7**, and **8** (Schemes 5–7)

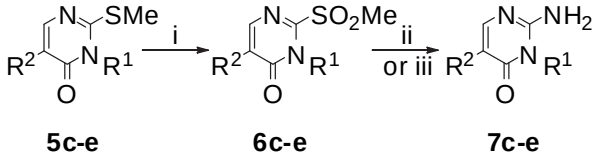
Entry	R^1	R^2	Compd (**6**) (%)[a]	Compd (**7**) (%)	Compd (**8**) (%)[f]
1	*p*Tol	CO_2Me	—	**7a** (99)[b]	**8a** (89)
2	*p*Tol	$CONH_2$	—	**7a′** (85)[c]	**8a′** (90)
3	*p*Tol	CF_3	—	**7b** (100)[c]	**8b** (92)
4	*p*Tol	H	**6c** (100)	**7c** (100)[d]	**8c** (78)
5	*p*Tol	Ph	**6d** (100)	**7d** (100)[d]	**8d** (91)
6	*p*Tol	OMe	**6e** (100)	**7e**[e]	**8e** (44)[g]

[a] Reagents and conditions: DMDO/acetone (0.08 M).
[b] NH_3/MeOH (7 M) (5 equiv).
[c] NH_3/MeOH (7 M) (large excess).
[d] NH_3 (g), toluene.
[e] Under microwave irradiation: formamide, 190 °C, 200 W, 5 min, not isolated.
[f] DMFDMA (1.2 equiv), CH_2Cl_2.
[g] Calculated yield over two steps from sulfone **6e**.



Scheme 5. Synthesis of 2-aminopyrimidinones **7**. Reagents and conditions: (i) NH_3/MeOH (7 M) (5 equiv); (ii) NH_3/MeOH (7 M) (large excess).

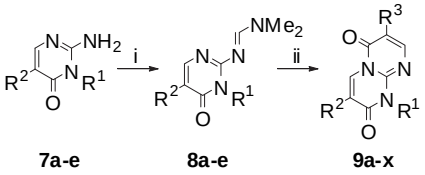
In order to increase the reactivity of the other heterocyclic substrates **5** toward nucleophiles, such as ammonia, we decided to oxidize the methylsulfanyl group to a methylsulfoxide or a methylsulfonyl group. In this way we aimed to increase the electrophilicity of the carbon bearing the methylsulfanyl group. Oxidation was first attempted by use of common oxidizing agents such as *m*-CPBA and H_2O_2; but in these cases reactions only led to carbonylated compounds corresponding to the hydrolysis of the activated sulfur group (pyrimidine-2,4(1*H*,3*H*)-diones).[17] The oxidation reaction was finally achieved without any hydrolysis by using a freshly distilled solution of dimethyldioxirane (DMDO) in acetone, a powerful anhydrous oxidant.[19–22] The use of less than 2 equiv of dioxirane led to a mixture of compounds (SMe, SOMe, and SO_2Me), whereas 2.5 equiv of oxidant afforded the methylsulfone products exclusively and quantitatively (Scheme 6).



Scheme 6. Oxidation and nucleophilic displacement of methylsulfanyl group. Reagents and conditions: (i) DMDO/acetone (0.08 M); (ii) NH_3 (g), toluene for **7c**,**d**; (iii) Under microwave irradiation: formamide, 190 °C, 200 W, 5 min for **7e**.

We then undertook the nucleophilic displacement of the methylsulfonyl group by ammonia on compounds **6c**–**e** (Table 3). Gaseous ammonia was passed for 1 h through a solution of compounds **6** in toluene, and the medium was stirred at room temperature for 24 h. Under these conditions products **7c** (R^2=H, entry 4) and **7d** (R^2=Ph, entry 5) were obtained in quantitative yields. Sulfone **6e** (R^2=OMe, entry 6) on the other hand was nonreactive and recovered after the experiment. This result was attributed to the electron donating effect of the OMe group, deactivating substrate **6e** to nucleophilic attack. However, nucleophilic substitution was finally accomplished by use of formamide in a sealed tube under microwave irradiation at 190 °C.[16] Under these conditions ammonia is produced in situ by thermal decomposition of formamide,[23,24] giving rise to the formation of compound **7e**, which was not isolated but directly engaged in the next step.

With aminopyrimidinones **7** in hand, there were two remaining steps to complete the bicyclic synthesis. Condensation of compounds **7** with DMFDMA led to the formation of formamidines **8** (Scheme 7). Compounds **8a**–**e** were obtained after 3–6 h reaction time in dichloromethane in good to excellent yields (Table 3) except for compound **8e** (R^2=OMe, entry 6), which was isolated in 44% yield over two steps from sulfone **6e**. The second cyclization reaction took place between compounds **8** and acyl chlorides R^3CH_2COCl. We limited our study to three acyl chlorides: acetyl chloride (R^3=H), methylmalonyl chloride (R^3=CO_2Me), and methoxyacetyl chloride (R^3=OMe). In contrast to the first cycloaddition reaction, this second one had to be conducted at the reflux of dichloromethane.



Scheme 7. Two-step synthesis of pyrimido[1,2-*a*]pyrimidine-2,6-diones **9** from 2-aminopyrimidinones **7**. Reagents and conditions: (i) DMFDMA (1.2 equiv), CH_2Cl_2; (ii) R^3CH_2COCl (3 equiv), NEt_3 (3 equiv), CH_2Cl_2, reflux.

Reaction of compounds **8a**–**e** with acyl chlorides allowed us to isolate 18 novel trisubstituted pyrimido[1,2-*a*]pyrimidine-2,6-diones **9a**–**r** in excellent yields (Table 4). The reactivity of formamidines **8a**,**a′**,**b**, with R^2 being an electron withdrawing group, was sluggish and the supplementary addition of 3 equiv of acyl chloride/NEt_3 after 3 h reaction time was necessary (entries 1–9).

Table 4
Synthesis of trisubstituted pyrimido[1,2-*a*]pyrimidine-2,6-diones **9a**–**r** from compounds **8a**–**e** (Scheme 7)

Entry	R^1	R^2	R^3	Compd (**9**) (%)[a]
1	*p*Tol	CO_2Me	CO_2Me	**9a** (84)[b]
2	*p*Tol	CO_2Me	H	**9b** (89)[b]
3	*p*Tol	CO_2Me	OMe	**9c** (76)[b]
4	*p*Tol	$CONH_2$	CO_2Me	**9d** (72)[b]
5	*p*Tol	$CONH_2$	H	**9e** (71)[b]
6	*p*Tol	$CONH_2$	OMe	**9f** (94)[b]
7	*p*Tol	CF_3	CO_2Me	**9g** (94)[b]
8	*p*Tol	CF_3	H	**9h** (93)[b]
9	*p*Tol	CF_3	OMe	**9i** (95)[b]
10	*p*Tol	H	CO_2Me	**9j** (72)
11	*p*Tol	H	H	**9k** (77)
12	*p*Tol	H	OMe	**9l** (84)
13	*p*Tol	Ph	CO_2Me	**9m** (86)
14	*p*Tol	Ph	H	**9n** (86)
15	*p*Tol	Ph	OMe	**9o** (89)
16	*p*Tol	OMe	CO_2Me	**9p** (99)
17	*p*Tol	OMe	H	**9q** (99)
18	*p*Tol	OMe	OMe	**9r** (89)

[a] Reagents and conditions: R^3CH_2COCl (3 equiv), NEt_3 (3 equiv), CH_2Cl_2, reflux.
[b] The addition of 3 equiv of acyl chloride/NEt_3 was necessary.

The structure of compound **9j** (entry 10) was determined by single crystal X-ray diffraction.[25] The molecular structure depicted in Fig. 1 is in good agreement with the bicyclic structure expected for **9**. However, it should be pointed out that the $-CO_2Me$ (R^3) group slightly deviates from the mean plan of the bicyclic group (maximum deviation of 0.3 Å for O3 and O4 oxygen atoms), while the *para*-tolyl group forms a large dihedral angle of 77.22(5)°.[26]

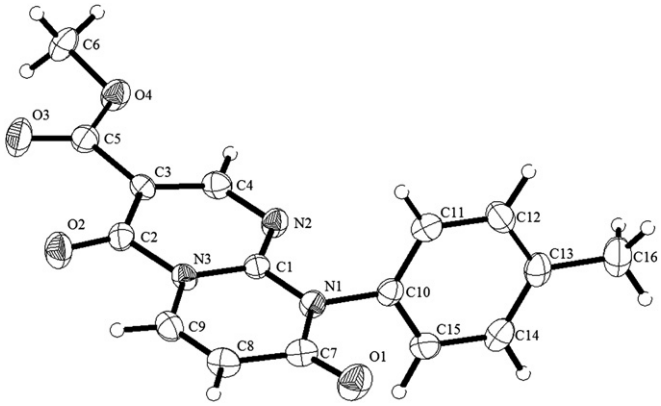


Fig. 1. ORTEP[25] view showing the bicyclic molecular structure of compound **9j** (thermal ellipsoids are plotted at the 50% probability).[26]

In order to confirm these results, we next enlarged the study to the *N*-methyl compounds **5h** and **5j** (R^1=Me; R^2=CO_2Me or Ph) (Table 5). As expected, the electron withdrawing methyl carboxylate group enabled the direct nucleophilic displacement of the methylsulfanyl group (**7f**, entry 1), while the pyrimidinone bearing a phenyl group needed to be activated by oxidation to sulfone **6g** with DMDO to achieve nucleophilic substitution (**7g**, entry 2). Compounds **7f**,**g** were then transformed into the corresponding formamidines **8f**,**g** by condensation with DMFDMA.

Table 5
Synthesis of compounds **6g**, **7f**,**g**, and **8f**,**g** (Schemes 5–7)

Entry	R^1	R^2	Compd (**6**) (%)[a]	Compd (**7**) (%)	Compd (**8**) (%)[d]
1	Me	CO_2Me	—	**7f** (78)[b]	**8f** (99)
2	Me	Ph	**6g** (100)	**7g** (100)[c]	**8g** (96)

[a] Reagents and conditions: DMDO/acetone (0.08 M).
[b] NH_3/MeOH (7 M) (5 equiv).
[c] NH_3 (g), toluene.
[d] DMFDMA (1.2 equiv), CH_2Cl_2.

These compounds were engaged in the last cycloaddition reaction under the same conditions and with the same reaction partners as in the *para*-tolyl study (Table 6). Formamidines **8f** (R^2=CO_2Me) and **8g** (R^2=Ph) afforded the bicyclic compounds **9s**–**u** (entries 1–3) and **9v**–**x** (entries 4–6), respectively in good yields.

Table 6
Synthesis of trisubstituted pyrimido[1,2-*a*]pyrimidinediones **9s**–**x** from compounds **8f**,**g** (Scheme 7)

entry	R^1	R^2	R^3	Compd (**9**) (%)[a]
1	Me	CO_2Me	CO_2Me	**9s** (92)[b]
2	Me	CO_2Me	H	**9t** (66)[b]
3	Me	CO_2Me	OMe	**9u** (72)[b]
4	Me	Ph	CO_2Me	**9v** (98)
5	Me	Ph	H	**9w** (95)
6	Me	Ph	OMe	**9x** (99)

[a] Reagents and conditions: R^3CH_2COCl (3ce:hsp sp="0.25"/>equiv), NEt_3 (3 equiv), CH_2Cl_2, reflux.
[b] The addition of 3 equiv of acyl chloride/NEt_3 was necessary.

3. Conclusions

In conclusion, we have described an efficient multi-step synthesis of 24 sophisticated 1,3,7-trisubstituted pyrimido[1,2-*a*]pyrimidine-2,6-diones in high yields from commercially available sources. This synthetic sequence allowed us to introduce different groups into the structure, such as aryl and alkyl groups, or functional groups with either electron withdrawing or donating effects. One of the key steps of the synthetic pathway is the nucleophilic displacement of the methylsulfanyl group by ammonia. Depending on the electronic properties of the R^1 groups oxidation to the methylsulfonyl is occasionally required. Independent of the activating or deactivating effects of these groups, we were able to perform this substitution reaction. Other key features of our strategy are the elaboration of reactive diazadienic building blocks and subsequent cyclization reactions. We are now focusing on the synthesis of new puric nucleoside analogues from glycosylisothiocyanates using a similar synthetic pathway.

4. Experimental section

4.1. General

NMR spectra were recorded at room temperature with a Brucker AC 300 spectrometer at 300 MHz (^{1}H), 75 MHz (^{13}C) and 300 MHz (^{19}F). Chemical shifts are reported in parts per million (ppm); coupling constant are reported in units of Hertz [Hz]. Infrared (IR) spectra were recorded with a Bruker Vector 22 FTIR using KBr films or KBr pellets. Low-resolution mass spectra (MS) were recorded with a Hewlett Packard 5989 A spectrometer. High-resolution mass spectra (HRMS) were recorded with a Thermofisher hybrid LTQ-orbitrap spectrometer (ESI^+) and with a Bruker Autoflex III SmartBeam spectrometer (MALDI). Melting points were determined in open capillary tubes and are uncorrected. All reagents were purchased from Acros Organics or Aldrich and were used without further purification. Column chromatographies were conducted on silica gel Kieselgel SI60 (40–63 μm) from Merck. Reactions requiring anhydrous conditions were performed under nitrogen. Dichloromethane was distilled from calcium hydride under argon prior to use. Toluene and tetrahydrofuran were distilled from sodium/benzophenone under argon prior to use.

The compounds **1g**, **2a**,**c**,**e**–**g**,**i**,**j**, **3a**,**c**,**e**–**g**,**i**,**j**, **5h**–**j**,**n**–**r** have already been described in the literature.

4.2. General procedure for the preparation of *N*-substituted thiourea 1

A solution of *N*-substituted isothiocyanate (*p*-tolylisothiocyanate for **1b**, 3,5-dichlorophenylisothiocyanate for **1d** and cyclohexylisothiocyanate for **1f**) (1 equiv) in methanolic ammonia (7 M, large excess) was stirred at 50 °C in a sealed tube for 6 h. After concentration under reduced pressure, the resulting solid was washed with a minimum of methanol.

*4.2.1. 1-p-tolylthiourea (**1b**).* White solid (3.768 g, 98%). Mp 185–186 °C. IR (KBr): ν=3428 (s), 3274 (s), 3167 (s), 3078 (m), 3000–2800 (w), 1613, 1583, 1508, 1468 (m), 1535 (s), 1470 (w), 1310–1237 (m), 800 (m) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.27 (s, 3H, PhCH_3), 7.13 and 7.24 (AB system, 4H, J=8.3 Hz, H_{ar}), 7.30 (br s, 2H, NH_2), 9.57 (s, 1H, NH) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ=20.4 (PhCH_3), 123.3 and 129.1 (4CH_{ar}), 133.7 and 136.4 (2C_{ar}), 180.9 (C=S) ppm. MS (EI, 70 eV): m/z (%)=166 (65) $[M]^+$, 133 (17), 106 (100), 91 (21), 65 (11).

*4.2.2. 1-(3,5-Dichlorophenyl)thiourea (**1d**).* White solid (2.655 g, 95%). Mp 175–177 °C. IR (KBr): ν=3447 (m), 3258 (m), 3095 (w),

3069 (w), 3009 (w), 1618 (s), 1577 (s), 1540 (m), 1472 (w), 1434 (m), 1389 (w) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ=7.29 (s, 1H, H_{ar}), 7.60 (s, 2H, H_{ar}), 7.80 (br s, 2H, NH_2), 9.93 (br s, 1H, NH) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ=120.5 (2CH_{ar}), 123.0 (CH_{ar}), 133.6 (2C_{ar}–Cl), 141.9 (C_{ar}), 181.3 (C=S) ppm. MS (EI, 70 eV): m/z (%)=220 (53) $[M]^+$, 187 (20), 161 (100), 145 (15), 90 (38), 75 (22), 63 (57).

*4.2.3. 1-Cyclohexylthiourea (**1f**).* White solid (5.301 g, 95%). Mp 164–165 °C. IR (KBr): ν=3333 (s), 3272 (s), 3076 (w), 2929 (m), 2857 (w), 1619 (s), 1561 (s), 1454 (m), 1370 (m), 1342 (w) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ=1.15–1.31 and 1.51–1.80 (m, 10H, CH_2), 3.89 (br s, 1H, NCH), 6.78 and 7.23 (2br s, 2H, NH_2), 7.47 (d, 1H, J=7.8 Hz, NH) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ=24.5 (2CH_2), 25.1 (CH_2), 32.2 (2CH_2), 52.1 (NCH), 181.8 (C=S) ppm. MS (EI, 70 eV): m/z (%)=159 (20), 158 (100) $[M]^+$, 125 (12), 98 (18), 60 (77).

4.3. General procedure for the preparation of *N*-substituted 1,3-thiazabutadienes 2

N,*N*-Dimethylformamide dimethyl acetal (1.2 equiv) was added to a suspension of substituted thiourea **1** (1.0 equiv) in dichloromethane. The mixture was stirred at room temperature for 2 h for **2b**, 3 h for **2d**, and **2f**. The solvent was removed and the residue was crystallized from ether.

*4.3.1. 4-Dimethylamino-2-p-tolylamino-1,3-thiazabuta-1,3-diene (**2b**).* White crystal (3.970 g, 99%). Mp 155–156 °C. IR (KBr): ν=3198 (m), 3168 (m), 3097 (m), 3030 (m), 2923 (w), 1626 (s), 1593 (m), 1541 (m), 1507 (m), 1479 (m), 1442 (m), 1370 (s), 1324 (m), 1159 (m), 1122 (m), 824 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): *major* (63%) δ=2.31 (s, 3H, PhCH_3), 3.10 and 3.20 (2 s, 6H, N(CH_3)$_2$), 7.09 and 7.33 (AB system, 4H, J=8.1 Hz, H_{ar}), 8.52 (br s, 1H, NH), 8.88 (s, 1H, H^4) ppm. *Minor* (37%) δ=2.33 (s, 3H, PhCH_3), 7.16 and 7.58 (AB system, 4H, J=8.1 Hz, H_{ar}), 8.38 (br s, 1H, NH), 8.94 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): *major* δ=21.0 (PhCH_3), 35.9 and 41.7 (N(CH_3)$_2$), 122.4 and 129.2 (4CH_{ar}), 134.2 and 136.4 (2C_{ar}), 162.8 (C^4), 191.3 (C^2) ppm. *Minor* δ=36.4 and 41.7 (N(CH_3)$_2$), 124.1 and 129.2 (4CH_{ar}), 164.1 (C^4) ppm. MS (EI, 70 eV): m/z (%)=221 (20) $[M]^+$, 115 (100), 91 (11), 65 (9), 44 (15).

*4.3.2. 4-Dimethylamino-2-(3,5-dichlorophenyl)amino-1,3-thiazabuta-1,3-diene (**2d**).* White crystal (2.956 g, 95%). Mp 184–186 °C. IR (KBr): ν=3196 (m), 3095 (w), 3069 (w), 3027 (w), 2923 (w), 1626 (s), 1579 (s), 1479 (w), 1438 (m), 1352 (s), 1311 (m), 1256 (w) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=3.15 and 3.25 (2s, 6H, N(CH_3)$_2$), 7.08 (br s, 1H, H_{ar}), 7.48 (br s, 2H, H_{ar}), 8.57 (br s, 1H, NH), 8.88 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=36.6 and 42.0 (N(CH_3)$_2$), 120.4 (2CH_{ar}), 123.8 (CH_{ar}), 134.8 (2C_{ar}–Cl), 140.6 (C_{ar}), 164.1 (C^4), 191.9 (C^2) ppm. MS (EI, 70 eV): m/z (%)=277 (12), 275 (18) $[M]^+$, 242 (4), 115 (100).

*4.3.3. 2-Cyclohexylamino-4-dimethylamino-1,3-thiazabuta-1,3-diene (**2f**).* White crystal (6.212 g, 95%). Mp 117–119 °C. IR (KBr): ν=3197 (m), 3013 (w), 2919 (m), 2851 (m), 1622 (s), 1531 (m), 1484 (w), 1443 (m), 1372 (s), 1356 (s), 1341 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): *major* (68%) δ=1.23–2.14 (m, 10H, CH_2), 3.03 and 3.13 (2s, 6H, N(CH_3)$_2$), 4.36 (m, 1H, NCH), 6.65 (br s, 1H, NH), 8.89 (s, 1H, H^4) ppm. *Minor* (32%) δ=1.23–2.14 (m, 10H, CH_2), 3.10 and 3.17 (2s, 6H, N(CH_3)$_2$), 4.06 (m, 1H, NCH), 6.76 (br s, 1H, NH), 8.85 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): *major* δ=24.7 and 32.2 (CH_2), 35.5 and 41.2 (N(CH_3)$_2$), 53.2 (NCH), 162.3 (C^4), 191.7 (C^2) ppm. *Minor* δ=25.4 and 32.6 (CH_2), 35.7 and 41.2 (N(CH_3)$_2$), 52.4 (NCH), 163.4 (C^4), 190.5 (C^2) ppm. MS (EI, 70 eV): m/z (%)=214 (13), 213 (46) $[M]^+$, 115 (45), 98 (100), 83 (12), 44 (14).

4.4. General procedure for the preparation of *N*-substituted 1,3-diazabutadienium iodides 3

Methyl iodide (1.05 equiv) was added to a suspension of thiazadiene **2** (1.0 equiv) in THF. The mixture was stirred at room temperature for 3 h for **3b**, 6 h for **3d**, and **3f**. The solvent was removed and the residue was crystallized from ether.

*4.4.1. 4-Dimethylamino-2-methylsulfanyl-1-p-tolyl-1,3-diazabuta-1,3-dienium iodide (**3b**).* White solid (1.598 g, 100%). Mp 150–151 °C. IR (KBr): ν=3141 (m), 3086 (m), 2984 (m), 1638 (s), 1590 (m), 1516 (s), 1502 (s), 1418 (m), 1387 (s), 821 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.35 (s, 3H, PhCH_3), 2.44 (s, 3H, SCH_3), 3.21 and 3.41 (2s, 6H, N(CH_3)$_2$), 7.19 and 7.34 (AB system, 4H, J=8.3 Hz, H_{ar}), 8.99 (s, 1H, H^4), 11.15 (br s, 1H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=15.0 (SCH_3), 21.3 (PhCH_3), 36.7 and 43.3 (N(CH_3)$_2$), 122.6 and 130.1 (4CH_{ar}), 132.8 and 139.0 (2C_{ar}), 157.3 (C^4), 177.6 (C^2) ppm. MS (EI, 70 eV): m/z (%)=236 (4) $[M-I]^+$, 235 (7), 188 (100), 91 (18), 65 (12), 44 (4).

*4.4.2. 4-Dimethylamino-1-(3,5-dichlorophenyl)-2-methylsulfanyl-1,3-diazabuta-1,3-dienium iodide (**3d**).* Yellow solid (4.190 g, 99%). Mp 114–116 °C. IR (KBr): ν=3142 (w), 3090 (w), 3050 (w), 2961 (w), 2920 (w), 1643 (s), 1586 (m), 1507 (s), 1440 (m), 1417 (m), 1395 (s), 1307 (w) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.52 (s, 3H, SCH_3), 3.26 and 3.47 (2s, 6H, N(CH_3)$_2$), 7.36 (s, 1H, H_{ar}), 7.44 (s, 2H, H_{ar}), 8.96 (s, 1H, H^4), 11.42 (br s, 1H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.0 (PhCH_3), 37.0 and 43.5 (N(CH_3)$_2$), 124.7 (2CH_{ar}), 128.6 (CH_{ar}), 135.5 (2C_{ar}–Cl), 137.3 (C_{ar}), 157.9 (C^4), 176.9 (C^2) ppm. MS (EI, 70 eV): m/z (%)=291 (5) $[M-I]^+$, 289 (8), 244 (59), 242 (100), 127 (13), 44 (13), 42 (23).

*4.4.3. 1-Cyclohexyl-4-dimethylamino-2-methylsulfanyl-1,3-diazabuta-1,3-dienium iodide (**3f**).* Yellow solid (9.786 g, 98%). Mp 109–111 °C. IR (KBr): ν=3200 (m), 2967 (m), 2938 (w), 2915 (w), 2943 (w), 1643 (s), 1536 (s), 1499 (s), 1453 (m), 1398 (m), 1362 (w) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=1.25 and 1.82–2.00 (m, 10H, CH_2), 2.48 (s, 3H, SCH_3), 3.14 and 3.39 (2s, 6H, N(CH_3)$_2$), 3.62 (m, 1H, NCH), 8.83 (s, 1H, H^4), 9.63 (br s, 1H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=14.3 (SCH_3), 24.7 and 31.6 (4 CH_2), 36.1 and 42.6 (N(CH_3)$_2$), 56.4 (NCH), 156.2 (C^4), 175.6 (C^2) ppm. MS (EI, 70 eV): m/z (%)=228 (11) $[M-I]^+$, 213 (8), 180 (47), 127 (14), 115 (10), 98 (100), 44 (7).

4.5. General procedure for the preparation of *N*-substituted 1,3-diazabutadienes 4

To a suspension of compound **3** (1.0 equiv) in ether was added a saturated solution of potassium hydrogencarbonate. The mixture was stirred at room temperature for 2 h. After extraction with ethyl acetate, the combined organic layers were washed with brine, dried over magnesium sulfate, and concentrated under reduced pressure to give **4**.

*4.5.1. 4-Dimethylamino-2-methylsulfanyl-1-p-tolyl-1,3-diazabuta-1,3-diene (**4b**).* White solid (610 mg, 96%). Mp 86–87 °C. IR (KBr): ν=3077 (w), 3041 (w), 3022 (w), 2995 (w), 2956 (w), 2877 (w), 1624 (s), 1548 (s), 1501 (m), 1486 (m), 1418 (s), 1342 (s), 1155 (m), 1086 (s), 858 (w), 822 (w) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): *major* (80%) δ=2.31 (s, 3H, PhCH_3), 2.39 (s, 3H, SCH_3), 3.06 and 3.10 (2s, 6H, N(CH_3)$_2$), 6.81 and 7.10 (AB system, 4H, J=7.7 Hz, H_{ar}), 8.24 (s, 1H, H^4) ppm. *Minor* (20%) δ=2.31 (s, 3H, PhCH_3), 2.47 (s, 3H, SCH_3), 2.85 and 2.98 (2 s, 6H, N(CH_3)$_2$), 6.97 (br s, 4H, H_{ar}), 7.78 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=14.8 (SCH_3), 20.8 (PhCH_3), 34.5 and 40.5 (N(CH_3)$_2$), 121.4 and 129.3 (4CH_{ar}), 132.3 and 147.6 (2C_{ar}), 153.9 (C^4),

164.6 (C^2) ppm. MS (EI, 70 eV): m/z (%)=235 (7) $[M]^+$, 188 (100), 91 (17), 65 (12), 44 (13).

*4.5.2. 4-Dimethylamino-1-(3,5-dichlorophenyl)-2-methylsulfanyl-1,3-diazabuta-1,3-diene (**4d**).* Colorless oil (65 mg, 94%). IR (neat): ν=3061 (w), 2960 (w), 2927 (w), 2896 (w), 1691 (s), 1573 (w), 1486 (s), 1443 (m), 1330 (w), 1260 (w) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.43 (s, 3H, SCH_3), 3.03 and 3.09 (2s, 6H, N(CH_3)$_2$), 6.86 (s, 1H, H_{ar}), 6.99 (s, 2H, H_{ar}), 8.17 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=15.0 (SCH_3), 34.8 and 40.9 (N(CH_3)$_2$), 120.9 and 122.6 (CH_{ar}), 134.5 (2C_{ar}—Cl), 152.4 (C_{ar}), 157.9 (C^4), 176.9 (C^2) ppm. MS (EI, 70 eV): m/z (%)=292 (2), 291 (7), 290 (3), 289 (10) $[M]^+$, 245 (8), 244 (63), 243 (12), 242 (100), 44 (5).

*4.5.3. 4-Dimethylamino-1-methyl-2-methylsulfanyl-1,3-diazabuta-1,3-diene (**4e**).* Colorless oil (115 mg, 76%). IR (neat): ν=2924 (w), 2856 (w), 1432 (m), 1390 (m), 1359 (m), 1258 (w) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): *major* (60%) δ=2.32 (s, 3H, SCH_3), 2.86 (s, 3H, NCH_3), 2.99 and 3.18 (2 s, 6H, N(CH_3)$_2$), 8.72 (s, 1H, H^4) ppm. *Minor* (40%) δ=2.72 (s, 3H, SCH_3), 3.04 and 3.22 (2s, 6H, N(CH_3)$_2$), 8.15 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): *major* δ=14.2 (SCH_3), 30.7 (NCH_3), 35.5 and 41.8 (N(CH_3)$_2$), 157.3 (C^4), 177.7 (C^2) ppm. *Minor* δ=15.7 (SCH_3), 31.5 (NCH_3), 36.0 and 42.2 (N(CH_3)$_2$), 158.4 (C^4), 173.4 (C^2) ppm. MS (EI, 70 eV): m/z (%)=159 (2) $[M]^+$, 112 (100), 86 (63), 58 (20).

*4.5.4. 1-Cyclohexyl-4-dimethylamino-2-methylsulfanyl-1,3-diazabuta-1,3-diene (**4f**).* Colorless oil (339 mg, 88%). IR (neat): ν=2930 (w), 2854 (w), 1670 (m), 1653 (m), 1386 (w), 1344 (w) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): *major* (80%) δ=1.26–1.31 and 1.83–1.99 (m, 10H, CH_2), 2.39 (s, 3H, SCH_3), 2.95 and 3.01 (2s, 6H, N(CH_3)$_2$), 3.56–3.63 (m, 1H, NC*H*), 7.90 (s, 1H, H^4) ppm. *Minor* (20%) δ=2.32 (s, 3H, SCH_3), 2.92 and 2.98 (2s, 6H, N(CH_3)$_2$), 3.75–3.85 (m, 1H, NC*H*), 7.69 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=13.7 (SCH_3), 24.5–27.5 (3 CH_2), 31.5 (N(CH_3)$_2$), 32.8 and 34.0 (2CH_2), 36.5 (N(CH_3)$_2$), 52.5 (NCH), 162.6 (C^4), 164.1 (C^2) ppm. MS (CI^+, NH_3): m/z=228 (100) $[M+H]^+$.

4.6. General procedure for the preparation of pyrimidin-4 (3*H*)-ones 5

Method A (from acyl chlorides). Triethylamine (4.0 equiv) was added to a solution of diazadienium iodide salt **3** (1.0 equiv) in dichloromethane. Acyl chloride (3.0 equiv) was added dropwise to the reaction medium at 0 °C, and the reaction mixture was stirred at room temperature over a period of 3–8 h (3 h for **5e**,**f**,**h**,**l**,**n**,**x**; 6 h for **5a**,**d**,**s**–**v**; 8 h for **5c**,**w**). The solvent was then removed and the residue was dissolved in dichloromethane, washed with water, brine, dried with magnesium sulfate, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (ethyl acetate/petroleum ether: (6:4) for **5a**, **5c**, **5f**, and **5h**; ethyl acetate/petroleum ether: (5:5) for **5w**; ethyl acetate/petroleum ether: (4:6) for **5e** and **5v**; ethyl acetate/petroleum ether: (3:7) for **5l** and **5x**; ethyl acetate/petroleum ether: (2:8) for **5d**). *Method B* (from carboxylic acids). Oxalyl chloride (3.3 equiv) was added at 0 °C to a solution of carboxylic acid (3,3,3-trifluoropropionic acid for **5b**; *N*,*N*-dimethylglycine for **5g**) (3.0 equiv) in dichloromethane. A catalytic amount of *N*,*N*-dimethylformamide (0.1 equiv) was added to the reaction medium and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was then introduced to a solution of diazadiene **3b** (1.0 equiv) in dichloromethane, and triethylamine (4.0 equiv) was added dropwise to the reaction medium at 0 °C, and the reaction mixture was stirred at room temperature for 3 h. The solvent was then removed and the residue was dissolved in dichloromethane, washed with water, brine, dried with magnesium sulfate, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (ethyl acetate/petroleum ether: (6:4) for **5g**; dichloromethane/petroleum ether: (4:6) for **5b**).

*4.6.1. 5-Methoxycarbonyl-2-methylsulfanyl-3-p-tolylpyrimidin-4 (3H)-one (**5a**).* White solid (3.089 g, 97%). Mp 204–205 °C. IR (KBr): ν=3098 (w), 3069 (w), 3057 (w), 3017 (w), 2962 (w), 2852 (w), 1743 (s), 1679 (m), 1568 (m), 1481 (s), 1375 (m), 1131 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.44 (s, 3H, SCH_3), 2.49 (s, 3H, PhCH_3), 3.88 (s, 3H, CO_2CH_3), 7.11 and 7,34 (AB system, 4H, J=8.0 Hz, H_{ar}), 8.65 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=15.8 (SCH_3), 21.5 (PhCH_3), 52.3 (CO_2CH_3), 112.3 (C^5), 128.0 and 130.7 (4 CH_{ar}), 132.7 and 140.8 (2C_{ar}), 158.2 (C^6), 158.7 (C^2), 165.1 (C^4), 170.3 (CO_2CH_3) ppm. MS (EI, 70 eV): m/z (%)=290 (56) $[M]^+$, 259 (16), 243 (100), 175 (50), 91 (55), 59 (34), 47 (13).

*4.6.2. 2-Methylsulfanyl-3-p-tolyl-5-trifluoromethylpyrimidin-4(3H)-one (**5b**).* White solid (1.106 g, 97%). Mp 183–184 °C. IR (KBr): ν=3052 (w), 2983 (w), 2925 (w), 1697 (s), 1595 (m), 1501 (s), 1430 (w), 1388 (m), 1142 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.44 (s, 3H, PhCH_3), 2.47 (s, 3H, SCH_3), 7.14 and 7.35 (AB system, 4H, J=8.1 Hz, H_{ar}), 8.20 (q, 1H, J=1.0 Hz, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=15.7 (SCH_3), 21.5 (PhCH_3), 112.8 (C^5, q, J=31 Hz), 122.8 (CF_3, q, J=270 Hz), 128.0 and 130.8 (4CH_{ar}), 132.0 and 141.0 (2C_{ar}), 151.6 (C^6), 157.8 (C^2), 169.6 (C^4) ppm. ^{19}F NMR (300 MHz, $CDCl_3$): δ=–64.6 (CF_3) ppm. MS (EI, 70 eV): m/z (%)=301 (21), 300 (93) $[M]^+$, 267 (20), 253 (100), 163 (74), 105 (15), 91 (34), 65 (17).

*4.6.3. 2-Methylsulfanyl-3-p-tolylpyrimidin-4(3H)-one (**5c**).* Yellow solid (1.218 g, 95%). Mp 124–126 °C. IR (KBr): ν=3099 (w), 3050 (w), 3024 (w), 2948 (w), 2925 (w), 2857 (w), 1689 (s), 1571 (m), 1483 (s), 1377 (w), 1322 (m), 817 (w) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.42 (s, 3H, SCH_3), 2.43 (s, 3H, PhCH_3), 6.30 (d, 1H, J=6.5 Hz, H^5), 7.15 and 7.34 (AB system, 4H, J=8.1 Hz, H_{ar}), 7.83 (d, 1H, J=6.5 Hz, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=15.5 (SCH_3), 21.4 (PhCH_3), 111.0 (C^5), 128.1–130.6 (4CH_{ar}), 133.0 and 140.4 (2C_{ar}), 152.4 (C^6), 162.2 (C^4), 164.8 (C^2) ppm. MS (EI, 70 eV): m/z (%)=233 (9), 232 (67) $[M]^+$, 199 (21), 185 (100), 91 (10), 77 (4).

*4.6.4. 2-Methylsulfanyl-5-phenyl-3-p-tolylpyrimidin-4(3H)-one (**5d**).* White solid (1.087 g, 85%). Mp 168–169 °C. IR (KBr): ν=3064 (w), 3030 (w), 2988 (w), 2927 (w), 1684 (s), 1597 (w), 1581 (w), 1498 (s), 1485 (s), 1447 (m), 1367 (m), 813 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.44 (s, 3H, PhCH_3), 2.48 (s, 3H, SCH_3), 7.20 and 7.38 (m, 5H, H_{ar}), 7.35 and 7.70 (AB system, J=7.8 Hz, 4H, H_{ar}), 8.07 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=15.5 (SCH_3), 21.5 (PhCH_3), 122.7 (C^5), 128.1–130.7 (9 CH_{ar}), 133.6 (2C_{ar}), 140.4 (C_{ar}), 150.0 (C^6), 161.6 (C^2), 163.2 (C^4) ppm. MS (EI, 70 eV): m/z (%)=309 (4), 308 (18) $[M]^+$, 116 (100), 91 (16), 89 (28), 77 (9), 65 (12).

*4.6.5. 5-Methoxy-2-methylsulfanyl-3-p-tolylpyrimidin-4(3H)-one (**5e**).* White solid (1.941 g, 90%). Mp 149–150 °C. IR (KBr): ν=3057 (w), 3027 (w), 3000 (w), 2974 (w), 2926 (w), 1690 (s), 1589 (s), 1518 (m), 1505 (s), 1459 (w), 1387 (w), 1305 (m), 1283 (s), 1024 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.40 (s, 3H, SCH_3), 2.43 (s, 3H, PhCH_3), 3.85 (s, 3H, OCH_3), 7.14 and 7.33 (AB system, 4H, J=8.3 Hz, H_{ar}), 7.46 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=15.4 (SCH_3), 21.5 (PhCH_3), 56.7 (OCH_3), 128.3 (2CH_{ar}), 129.6 (C^6), 130.6 (2CH_{ar}), 132.9 and 140.5 (2C_{ar}), 144.3 (C^5), 154.5 (C^2), 158.6 (C^4) ppm. MS (EI, 70 eV): m/z (%)=263 (16), 262 (100) $[M]^+$, 229 (40), 215 (24), 172 (17), 164 (24), 149 (20), 117 (26), 106 (50), 91 (32).

*4.6.6. 5-Methyl-2-methylsulfanyl-3-p-tolylpyrimidin-4(3H)-one (**5f**).* White solid (881 mg, 95%). Mp 179 °C. IR (KBr): ν=3060 (w), 3042 (w), 3000 (w), 2976 (w), 1677 (s), 1604 (w), 1499 (s), 1383 (w), 1310 (m), 1271 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.05 (s, 3H,

CH_3), 2.41 (s, 3H, SCH_3), 2.43 (s, 3H, PhCH_3), 7.13 and 7.32 (AB system, 4H, J=8.0 Hz, H_{ar}), 7.73 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=13.4 (CH_3), 15.4 (SCH_3), 21.5 (PhCH_3), 120.5 (C^5), 128.3 and 130.6 (4CH_{ar}), 133.5 and 140.3 (2C_{ar}), 149.5 (C^6), 154.5 and 158.6 (C^2 and C^4) ppm. MS (EI, 70 eV): m/z (%)=246 (92) $[M]^+$, 213 (37), 199 (100), 171 (10), 105 (17), 91 (30), 65 (13).

*4.6.7. 5-Dimethylamino-2-methylsulfanyl-3-p-tolylpyrimidin-4(3H)-one (**5g**).* White solid (95 mg, 11%). Mp 139–141 °C. IR (KBr): ν=3060 (w), 3033 (w), 2980 (w), 2923 (w), 2862 (w), 1671 (s), 1570 (s), 1508 (s), 1459 (w), 1380 (m), 1336 (w), 1248 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.41 (s, 3H, PhCH_3), 2.44 (s, 3H, SCH_3), 2.86 (s, 6H, N(CH_3)$_2$), 7.15 and 7.34 (AB system, J=8,7 Hz, 4H, H_{ar}), 7.36 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=15.1 (SCH_3), 21.3 (PhCH_3), 41.6 (N(CH_3)$_2$), 128.3 and 130.3 (4CH_{ar}), 133.3 (C_{ar}), 134.4 (C^6), 136.0 (C^5), 140.0 (C_{ar}), 153.8 and 159.6 (C^2 and C^4) ppm. MS (EI, 70 eV): m/z (%)=276 (18), 275 (100) $[M]^+$, 260 (22), 116 (13), 91 (57), 69 (23), 68 (27), 65 (19).

*4.6.8. 5-Methoxycarbonyl-3-methyl-2-methylsulfanylpyrimidin-4(3H)-one (**5h**).* White solid (680 mg, 91%). Mp 110–111 °C. IR (KBr): ν=3022 (w), 2995 (w), 2948 (w), 2850 (w), 1739 (s), 1697 (s), 1685 (s), 1563 (m), 1492 (s), 1377 (m), 1365 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.64 (s, 3H, SCH_3), 3.55 (s, 3H, NCH_3), 3.89 (s, 1H, OCH_3), 8,55 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=15.4 (SCH_3), 30.8 (NCH_3), 52.3 (OCH_3), 111.1 (C^5), 157.4 (C^6), 158.6 (C^4), 165.1 (CO_2CH_3), 168.9 (C^2) ppm. MS (EI, 70 eV): m/z (%)=214 (61) $[M]^+$, 183 (75), 169 (100), 167 (44), 136 (21), 99 (86), 88 (57), 73 (20).

*4.6.9. 3,5-Dimethyl-2-methylsulfanylpyrimidin-4(3H)-one (**5l**).* White solid (345 mg, 73%). Mp 86–88 °C. IR (KBr): ν=2997 (w), 2921 (w), 2892 (w), 1670 (s), 1511 (s), 1407 (s), 1382 (m), 1326 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.99 (s, 3H, CH_3), 2.51 (s, 3H, SCH_3), 3.49 (s, 3H, NCH_3), 7.62 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=13.4 (CH_3), 14.8 (SCH_3), 30.4 (NCH_3), 118.7 (C^5), 149.0 (C^6), 160.5 and 163.0 (C^2 and C^4) ppm. MS (EI, 70 eV): m/z (%)=171 (39), 170 (100) $[M]^+$, 169 (13), 125 (76), 124 (35), 96 (10), 95 (16), 57 (15).

*4.6.10. 2-Methylsulfanylpyrimidin-4(3H)-one (**5n**).* White solid (440 mg, 68%). Mp 189–190 °C. IR (KBr): ν=3440 (s), 3085 (w), 2926 (w), 1668 (s), 1546 (s), 1454 (m), 1372 (w), 1329 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.56 (s, 3H, SCH_3), 6.12 (d, 1H, J=6.6 Hz, H^5), 7.84 (d, 1H, J=6.6 Hz, H^6), 12.97 (br s, 1H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=13.4 (SCH_3), 110.8 (C^5), 154.2 (C^6), 158.2 and 161.1 (C^2 and C^4) ppm. MS (EI, 70 eV): m/z (%)=143 (35), 142 (100) $[M]^+$, 114 (8), 96 (12), 95 (33), 44 (9).

*4.6.11. 3-Dimethylamino-5-methoxycarbonyl-2-methylsulfanylpyrimidin-4(3H)-one (**5s**).* White solid (87 mg, 76%). Mp 96–97 °C. IR (KBr): ν=2952 (w), 2929 (w), 1741 (s), 1687 (m), 1570 (m), 1472 (s), 1446 (m), 1375 (m), 1290 (s), 1188 (w) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.29 (s, 3H, SCH_3), 2.91 (s, 6H, N(CH_3)$_2$), 3.78 (s, 3H, CO_2CH_3), 8.40 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=14.7 (SCH_3), 42.4 (N(CH_3)$_2$), 52.1 (CO_2CH_3), 112.3 (C^5), 157.5 (C^6), 158.4 (C^4), 164.6 (CO_2CH_3), 173.1 (C^2) ppm. MS (CI^+, NH_3): m/z=261 (100) $[M+NH_4]^+$.

*4.6.12. 3-Dimethylamino-2-methylsulfanylpyrimidin-4(3H)-one (**5t**).* White solid (64 mg, 84%). Mp 92–94 °C. IR (KBr): ν=3067 (w), 2924 (w), 1621 (s), 1592 (m), 1545 (s), 1486 (w), 1424 (s), 1350 (m), 1286 (w) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.31 (s, 3H, SCH_3), 2.97 (s, 6H, N(CH_3)$_2$), 6.08 (d, 1H, J=6.5 Hz, H^5), 7.65 (d, 1H, J=6.5 Hz, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=14.7 (SCH_3), 42.7 (N(CH_3)$_2$), 111.7 (C^5), 151.7 (C^6), 162.1 (C^2), 168.1 (C^4) ppm. MS (EI, 70 eV): m/z (%)=186 (7), 185 (6) $[M]^+$, 184 (10), 143 (31), 142 (100), 112 (13), 95 (23), 84 (17), 43 (19). MS (CI^+, NH_3): m/z=186 (100) $[M+H]^+$.

*4.6.13. 3-Dimethylamino-2-methylsulfanyl-5-phenylpyrimidin-4(3H)-one (**5u**).* White solid (89 mg, 72%). Mp 88–90 °C. IR (KBr): ν=3057 (w), 3025 (w), 2980 (w), 2950 (w), 2887 (w), 1676 (s), 1566 (w), 1500 (s), 1439 (m), 1366 (s), 1285 (w) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.29 (s, 3H, SCH_3), 2.96 (s, 6H, N(CH_3)$_2$), 7.26–7.34 (m, 2H, H_{ar}), 7.52–7.55 (m, 3H, H_{ar}), 7.81 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=14.6 (SCH_3), 42.6 (N(CH_3)$_2$), 123.3 (C^5), 127.9 (CH_{ar}), 128.4 (4CH_{ar}), 133.2 (C_{ar}), 149.3 (C^6), 161.2 (C^2), 166.4 (C^4) ppm. MS (EI, 70 eV): m/z (%)=261 (12) $[M]^+$, 219 (23), 218 (100), 164 (14), 116 (47), 91 (32), 77 (9), 44 (19).

*4.6.14. 3-(3,5-Dichlorophenyl)-5-methoxycarbonyl-2-methylsulfanylpyrimidin-4(3H)-one (**5v**).* White solid (326 mg, 79%). Mp 191–193 °C. IR (KBr): ν=3077 (m), 2998 (w), 2948 (w), 2843 (w), 1738 (s), 1717 (m), 1676 (m), 1574 (s), 1565 (m), 1475 (s), 1432 (m), 1372 (m), 1328 (m), 806 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.54 (s, 3H, SCH_3), 3.89 (s, 3H, OCH_3), 7.19 (s, 2H, H_{ar}), 7.53 (s, 1H, H_{ar}), 8.63 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=15.8 (SCH_3), 52.5 (OCH_3), 112.5 (C^5), 127.4 and 130.9 (3CH_{ar}), 136.3 (2C_{ar}–Cl), 136.9 (C_{ar}), 158.3 (C^2 and C^6), 164.6 (C^4), 169.3 (CO_2CH_3) ppm. MS (EI, 70 eV): m/z (%)=346 (30), 344 (42) $[M]^+$, 314 (31), 312 (43), 299 (64), 297 (100), 231 (46), 229 (61), 203 (38), 59 (34), 53 (92).

*4.6.15. 3-(3,5-Dichlorophenyl)-2-methylsulfanylpyrimidin-4(3H)-one (**5w**).* White solid (537 mg, 78%). Mp 214–216 °C. IR (KBr): ν=3075 (m), 3058 (m), 1684 (s), 1575 (m), 1487 (s), 1419 (w), 1314 (m), 820 (m), 808 (m), 683 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.47 (s, 3H, SCH_3), 6.29 (d, 1H, J=6.6 Hz, H^5), 7.20 (s, 2H, H_{ar}), 7.51 (s, 1H, H_{ar}), 7.82 (d, 1H, J=6.6 Hz, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=15.6 (SCH_3), 111.2 (C^5), 127.7 (2 CH_{ar}), 130.7 (CH_{ar}), 136.2 (2C_{ar}–Cl), 137.5 (C_{ar}), 152.6 (C^6), 161.5 and 163.9 (C^2 and C^4) ppm. MS (EI, 70 eV): m/z (%)=288 (28), 287 (7), 286 (43) $[M]^+$, 255 (20), 253 (38), 241 (59), 240 (12), 239 (100).

*4.6.16. 3-(3,5-Dichlorophenyl)-2-methylsulfanyl-5-phenylpyrimidin-4(3H)-one (**5x**).* White solid (207 mg, 95%). Mp 213–215 °C. IR (KBr): ν=3075 (w), 3025 (w), 2928 (w), 1674 (s), 1598 (w), 1575 (m), 1495 (s), 1363 (m), 1321 (m), 808 (m), 700 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.52 (s, 3H, SCH_3), 7.26 (s, 2H, H_{ar}), 7.35–7.43 (m, 3H, H_{ar}), 7.53 (m, 1H, H_{ar}), 7.66 (m, 2H, H_{ar}), 8.06 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=15.5 (SCH_3), 122.9 (C^5), 127.7–128.5 (8CH_{ar}), 130.6 and 133.0 (2C_{ar}), 136.1 and 137.6 (2C_{ar}), 150.1 (C^6), 161.0 and 162.1 (C^2 and C^4) ppm. MS (EI, 70 eV): m/z (%)=363 (37), 362 (100) $[M]^+$, 331 (18), 329 (25), 315 (12), 116 (44).

4.7. General procedure for the preparation of 2-methylsulfonylpyrimidinones 6

General procedure for the preparation of: a solution of dimethyldioxirane in acetone (2.5 equiv) was added to compound **5** (1.0 equiv) and the mixture was stirred at room temperature for 1 h for **6c**–**e**, 30 min for **6g**. The corresponding methylsulfonylpyrimidinone **6** was obtained as pure material after removal of the solvent under reduced pressure.

*4.7.1. 2-Methylsulfonyl-3-p-tolylpyrimidin-4(3H)-one (**6c**).* White solid (82 mg, 100%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.43 (s, 3H, PhCH_3), 3.32 (s, 3H, SO_2CH_3), 6.68 (d, 1H, J=6.6 Hz, H^5), 7.23 and 7.33 (AB system, 4H, J=8.3 Hz, H_{ar}), 7.91 (d, 1H, J=6.6 Hz, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5 (PhCH_3), 41.2 (SO_2CH_3), 118.5 (C^5), 128.7 (2CH_{ar}), 129.6 (C_{ar}), 129.8 (2CH_{ar}), 140.8 (C_{ar}), 150.4 (C^6), 156.3

(C^2), 160.8 (C^4) ppm. MS (EI, 70 eV): *m*/*z* (%)=264 (15) $[M]^+$, 202 (100), 185 (78), 104 (47), 78 (34), 65 (25).

*4.7.2. 2-Methylsulfonyl-5-phenyl-3-p-tolylpyrimidin-4(3H)-one (**6d**).* White solid (335 mg, 100%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.44 (s, 3H, PhCH_3), 3.36 (s, 3H, SO_2CH_3), 7.28 and 7.34 (AB system, 4H, *J*=8.4 Hz, H_{ar}), 7.44 and 7.72 (m, 5H, H_{ar}), 8.09 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.6 (PhCH_3), 41.3 (SO_2CH_3), 128.7–130.1 (9CH_{ar}), 130.5 and 132.0 (C_{ar} and C^5), 140.8 (C_{ar}), 147.2 (C^6), 154.8 (C^2), 160.6 (C^4) ppm. MS (EI, 70 eV): *m*/*z* (%)=340 (3) $[M]^+$, 279 (18), 278 (100), 161 (28), 144 (77), 117 (56), 105 (32), 90 (36), 89 (31).

*4.7.3. 5-Methoxy-2-methylsulfonyl-3-p-tolylpyrimidin-4(3H)-one (**6e**).* White solid (150 mg, 100%). Mp 260–261 °C. IR (KBr): ν=2922 (w), 1643 (s), 1514 (m), 1476 (m), 1441 (w), 1280 (m), 1049 (w) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.43 (s, 3H, PhCH_3), 3.29 (s, 3H, SO_2CH_3), 3.94 (s, 3H, OCH_3), 7.23 and 7.32 (AB system, 4H, *J*=8.1 Hz, H_{ar}), 7.39 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.6 (PhCH_3), 41.5 (SO_2CH_3), 56.9 (OCH_3), 124.7 (C^6), 128.9 and 130.0 (4CH_{ar}), 132.9 and 140.8 (2C_{ar}), 158.3 (C^6), 158.8 (C^2), 165.1 (C^4) ppm. MS (EI, 70 eV): *m*/*z* (%)=295 (6), 294 (44) $[M]^+$, 216 (14), 215 (100), 172 (56), 132 (18), 117 (64), 116 (28), 91 (25).

*4.7.4. 3-Methyl-2-methylsulfonyl-5-phenylpyrimidin-4(3H)-one (**6g**).* White solid (83 mg, 100%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.47 (s, 3H, SO_2CH_3), 3.92 (s, 3H, NCH_3), 7.44–7.46 and 7.66–7.68 (m, 5H, H_{ar}), 7.97 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=30.7 (NCH_3), 40.8 (SO_2CH_3), 128.6 and 129.3 (5CH_{ar}), 129.6 and 132.1 (C_{ar} and C^5), 146.9 (C^6), 154.6 (C^2), 160.2 (C^4) ppm. MS (EI, 70 eV): *m*/*z* (%)=264 (79) $[M]^+$, 185 (46), 116 (100), 89 (14).

4.8. General procedure for the preparation of 2-aminopyrimidinones 7

Method A (from 2-methylsulfanylpyrimidinones **5**). A solution of compound **5** (1.0 equiv) in methanolic ammonia (7 M, 5.0 equiv for **7a** and **7f**, large excess for **7a′** and **7b**) was stirred at 50 °C in a sealed tube for 3–12 h (3 h for **7b**; 12 h for **7a**,**a′**,**f**). After concentration under reduced pressure, the resulting solid was washed with a minimum of methanol. *Method B* (from 2-methylsulfonylpyrimidinones **6**). Gaseous ammonia was passed for 1 h through a solution of compound **6** in toluene, and the medium was stirred at room temperature for 24 h. The corresponding aminopyrimidinone **7** was obtained as pure material after removal of the solvent under reduced pressure.

*4.8.1. 2-Amino-5-methoxycarbonyl-3-p-tolylpyrimidin-4(3H)-one (**7a**).* White solid (352 mg, 99%). Mp 245 °C. IR (KBr): ν=3358 (m), 3025 (m), 2999 (m), 2950 (m), 1737 (s), 1672 (s), 1654 (s), 1571 (s), 1508 (s), 1484 (s), 1433 (m), 1376 (w), 1057 (m), 801 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.43 (s, 3H, PhCH_3), 3.82 (s, 3H, CO_2CH_3), 7.14 and 7.37 (AB system, 4H, *J*=8.3 Hz, H_{ar}), 7.87 (br s, 2H, NH_2), 8.54 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.4 (PhCH_3), 51.9 (CO_2CH_3), 106.2 (C^5), 127.8 and 131.5 (4CH_{ar}), 131.4 and 140.8 (2C_{ar}), 158.3 and 159.0 (C^2 and C^6), 161.6 (C^4), 165.1 (CO_2CH_3) ppm. MS (EI, 70 eV): *m*/*z* (%)=259 (10) $[M]^+$, 228 (18), 133 (47), 91 (100), 77 (22), 65 (38). HRMS (ESI^+): calcd for $C_{13}H_{13}N_3NaO_3$ $[M+Na]^+$ 282.0849; found 282.0846.

*4.8.2. 2-Amino-5-carbamoyl-3-p-tolylpyrimidin-4(3H)-one (**7a′**).* White solid (381 mg, 85%). Mp 330 °C. IR (KBr): ν=3467 (m), 3357 (m), 3118 (w), 3044 (w), 1689 (s), 1650 (s), 1572 (m), 1476 (s), 1406 (m), 1310 (s), 821 (m) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ=2.39 (s, 3H, PhCH_3), 7.14 (d, 1H, *J*=3.9 Hz, NH_2), 7.20 and 7.37 (AB system, 4H, *J*=8.3 Hz, H_{ar}), 8.11 (d, 1H, *J*=3.9 Hz, NH_2), 8.48 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ=20.8 (PhCH_3), 104.7 (C^5), 128.1 and 130.6 (4CH_{ar}), 131.9 and 138.8 (2C_{ar}), 158.0, 160.4 and 162.0 (C^2, C^4, and C^6), 165.1 ($CONH_2$) ppm. MS (EI, 70 eV): *m*/*z* (%)=245 (20), 244 (88) $[M]^+$, 228 (78), 227 (27), 133 (53), 91 (100), 77 (20), 65 (27), 44 (16). HRMS (ESI^+): calcd for $C_{12}H_{12}N_4NaO_2$ $[M+Na]^+$ 267.0853; found 267.0848.

*4.8.3. 2-Amino-3-p-tolyl-5-trifluoromethylpyrimidin-4(3H)-one (**7b**).* Yellow solid (275 mg, 100%). Mp 199–202 °C. IR (KBr): ν=3480 (s), 3325 (s), 2926 (w), 1709 (s), 1643 (s), 1601 (s), 1525 (s), 1489 (m), 1375 (w), 1331 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.43 (s, 3H, PhCH_3), 5.69 (br s, 2H, NH_2), 7.18 and 7.39 (AB system, 4H, *J*=8.0 Hz, H_{ar}), 7.99 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.4 (PhCH_3), 106.7 (C^5, q, *J*=20 Hz), 123.4 (CF_3, q, *J*=268 Hz), 127.8 (2CH_{ar}), 130.7 (C_{ar}), 131.6 (2CH_{ar}), 141.1 (C_{ar}), 154.2 (C^6), 157.7 (C^2), 158.3 (C^4) ppm. MS (EI, 70 eV): *m*/*z* (%)=270 (26), 269 (100) $[M]^+$, 268 (25), 248 (13), 133 (58), 118 (14), 91 (60), 65 (26). HRMS (MALDI): calcd for $C_{12}H_{11}F_3N_3O$ $[M+H]^+$ 270.0849; found 270.0850.

*4.8.4. 2-Amino-3-p-tolylpyrimidin-4(3H)-one (**7c**).* White solid (180 mg, 100%). Mp 184–185 °C. IR (KBr): ν=3447 (s), 3316 (s), 2921 (w), 1680 (s), 1636 (s), 1580 (m), 1521 (s), 1457 (m), 1373 (w), 1313 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.43 (s, 3H, PhCH_3), 5.60 (br s, 2H, NH_2), 6.00 (d, 1H, *J*=6.9 Hz, H^5), 7.18 and 7.38 (AB system, 4H, *J*=8.1 Hz, H_{ar}), 7.58 (d, 1H, *J*=6.9 Hz, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.4 (PhCH_3), 105.1 (C^5), 127.8 and 131.6 (4CH_{ar}), 131.7 and 140.7 (2C_{ar}), 152.6 (C^6), 155.6 (C^2), 162.1 (C^4) ppm. MS (EI, 70 eV): *m*/*z* (%)=201 (34) $[M]^+$, 173 (20), 133 (14), 91 (22), 77 (14), 43 (100). HRMS (ESI^+): calcd for $C_{11}H_{12}N_3O$ $[M+H]^+$ 202.0975; found 202.0973.

*4.8.5. 2-Amino-5-phenyl-3-p-tolylpyrimidin-4(3H)-one (**7d**).* White solid (273 mg, 100%). Mp 209–212 °C. IR (KBr): ν=3264 (s), 3122 (s), 1689 (s), 1630 (s), 1592 (s), 1515 (s), 1447 (m), 1401 (s), 1344 (m), 814 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.43 (s, 3H, PhCH_3), 5.53 (br e, 2H, NH_2), 7.22 and 7.37 (m, 5H, H_{ar}), 7.36 and 7.63 (AB system, 4H, *J*=7.2 Hz, H_{ar}), 7.85 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.4 (PhCH_3), 117.0 (C^5), 127.2–131.4 (9 CH_{ar}), 132.1 and 134.4 (2C_{ar}), 140.3 (C_{ar}), 151.7 (C^6), 154.9 (C^2), 161.4 (C^4) ppm. MS (EI, 70 eV): *m*/*z* (%)=278 (23), 277 (100) $[M]^+$, 276 (40), 133 (31), 116 (21), 91 (86), 65 (32). HRMS (MALDI): calcd for $C_{17}H_{16}N_3O$ $[M+H]^+$ 278.1288; found 278.1280.

*4.8.6. 2-Amino-3-methyl-5-methoxycarbonylpyrimidin-4(3H)-one (**7f**).* Yellow solid (200 mg, 78%). Mp 266–268 °C. IR (KBr): ν=3365 (m), 3122 (m), 3029 (m), 2957 (m), 2850 (w), 1740 (s), 1673 (s), 1580 (s), 1530 (m), 1508 (s), 1432 (m), 1365 (w), 1299 (s), 1059 (m), 817 (m) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ=3.24 (s, 3H, NCH_3), 3.66 (s, 3H, CO_2CH_3), 7.92 (br s, 2H, NH_2), 8.32 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ=27.8 (NCH_3), 50.8 (CO_2CH_3), 102.0 (C^5), 158.1 and 158.6 (C^2 and C^4), 160.5 (C^6), 164.8 (CO_2CH_3) ppm. MS (EI, 70 eV): *m*/*z* (%)=183 (42) $[M]^+$, 152 (100), 124 (16), 83 (23), 69 (15), 57 (77), 53 (28). HRMS (ESI^+): calcd for $C_7H_9N_3NaO_3$ $[M+Na]^+$ 206.0536; found 206.0533.

*4.8.7. 2-Amino-3-methyl-5-phenylpyrimidin-4(3H)-one (**7g**).* White solid (220 mg, 100%). Mp 165–166 °C. IR (KBr): ν=3361 (m), 3118 (m), 1684 (m), 1646 (s), 1589 (m), 1525 (s), 1487 (w), 1400 (m), 1327 (w), 1208 (s), 1193 (s) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.51 (s, 3H, NCH_3), 5.52 (br s, 2H, NH_2), 7.29–7.41 and 7.57–7.60 (m, 5H, H_{ar}), 7.77 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=28.3 (NCH_3), 116.8 (C^5), 127.4 and 128.2–128.4 (5 CH_{ar}), 134.5 (C_{ar}), 150.5 (C^6), 154.7 (C^2), 161.0 (C^4) ppm. MS (EI, 70 eV): *m*/*z* (%)=202 (16), 201 (100) $[M]^+$, 144 (22), 117 (30), 116 (25), 89 (58), 77 (15), 57 (74).

HRMS (ESI$^+$): calcd for $C_{11}H_{11}N_3O$ $[M+H]^+$ 202.0975; found 202.0979.

4.9. General procedure for the preparation of 2-[(*N*,*N*-dimethylaminomethylen)amino]pyrimidinones 8

N,*N*-Dimethylformamide dimethyl acetal (1.2 equiv) was added to a solution of aminopyrimidinone **7** (1.0 equiv) in dichloromethane. The mixture was stirred at room temperature for 3–6 h (3 h for **8a**′,**b**–**d**,**f**; 6 h for **8a**,**e**,**g**). The solvent was removed and the residue purified by chromatography on silica gel (ethyl acetate for **8a**, **8c**, and **8f**; ethyl acetate/petroleum ether: (9:1) for **8e**; ethyl acetate/petroleum ether: (8:2) for **8a**′ and **8g**; ethyl acetate/petroleum ether: (6:4) for **8d**; ethyl acetate/petroleum ether: (2:8) for **8b**).

*4.9.1. 2-[(N,N-Dimethylaminomethylen)amino]-5-methoxycarbonyl-3-p-tolylpyrimidin-4(3H)-one (**8a**).* White solid (383 mg, 89%). Mp 241–242 °C. IR (KBr): ν=3064 (w), 3032 (w), 2972 (w), 2948 (w), 2925 (w), 1685 (s), 1635 (s), 1566 (m), 1481 (m), 1391 (m), 1343 (w), 1293 (s), 816 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.35 (s, 3H, PhCH_3), 2.74 and 3.09 (2s, 6H, N(CH_3)$_2$), 3.81 (s, 3H, CO_2CH_3), 6.97 and 7.18 (AB system, 4H, J=8.3 Hz, H_{ar}), 8.59 (br s, 2H, H^6 and N=CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.3 (PhCH_3), 35.2 and 41.4 (N(CH_3)$_2$), 51.8 (CO_2CH_3), 108.7 (C^5), 127.8 and 129.4 (4CH_{ar}), 134.6 and 137.6 (2C_{ar}), 158.6 and 160.7 (C^6 and N=CH), 162.5–165.1 (C^2, C^4, and CO_2CH_3) ppm. MS (EI, 70 eV): m/z (%)=315 (10), 314 (35) $[M]^+$, 283 (15), 188 (53), 133 (30), 132 (30), 99 (63), 91 (100), 65 (16). HRMS (MALDI): calcd for $C_{16}H_{18}N_4NaO_3$ $[M+Na]^+$ 337.1271; found 337.1265.

*4.9.2. 5-Carbamoyl-2-[(N,N-dimethylaminomethylen)amino]-3-p-tolylpyrimidin-4(3H)-one (**8a**′).* White solid (220 mg, 90%). Mp 245–246 °C. IR (KBr): ν=3390 (m), 3245 (w), 3060 (w), 3039 (w), 2923 (w), 2867 (w), 1691 (s), 1648 (s), 1624 (s), 1561 (m), 1490 (s), 1473 (s), 1425 (s), 1375 (s), 1326 (m), 814 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.40 (s, 3H, PhCH_3), 2.77 and 3.13 (2 s, 6H, N(CH_3)$_2$), 5.57 (br s, 1H, NH_2), 7.04 and 7.26 (AB system, 4H, J=6.9 Hz, H_{ar}), 8.65 (s, 1H, N=CH), 8.81 (br s, 1H, NH_2), 8.82 (s, 1H, H^6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.4 (PhCH_3), 35.3 and 41.5 (N(CH_3)$_2$), 109.6 (C^5), 127.6 and 129.6 (4CH_{ar}), 134.4 and 138.1 (2C_{ar}), 158.6 (N=CH), 159.8 (C^6), 161.8 and 163.8 (C^2 and C^4), 166.3 ($CONH_2$) ppm. MS (EI, 70 eV): m/z (%)=300 (15), 299 (100) $[M]^+$, 298 (30), 188 (28), 99 (33), 91 (33), 84 (17), 49 (16), 44 (23). HRMS (MALDI): calcd for $C_{15}H_{17}N_5NaO_2$ $[M+Na]^+$ 322.1274; found 322.1272.

*4.9.3. 2-[(N,N-Dimethylaminomethylen)amino]-3-p-tolyl-5-trifluoromethylpyrimidin-4(3H)-one (**8b**).* Yellow solid (338 mg, 92%). Mp 205–206 °C. IR (KBr): ν=3067 (w), 3039 (w), 2928 (w), 1691 (s), 1634 (s), 1599 (m), 1486 (m), 1450 (m), 1397 (m), 1332 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.38 (s, 3H, PhCH_3), 2.75 and 3.10 (2 s, 6H, N(CH_3)$_2$), 7.03 and 7.22 (AB system, 4H, J=7.8 Hz, H_{ar}), 8.07 (q, 1H, J=1.0 Hz, H^6), 8.55 (s, 1H, N=CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.3 (PhCH_3), 35.2 and 41.4 (N(CH_3)$_2$), 109.2 (C^5, q, J=31 Hz), 123.8 (CF_3, q, J=269 Hz), 127.9 and 129.5 (4CH_{ar}), 134.0 and 137.9 (2 C_{ar}), 153.2 (C^6), 158.4 (N=CH), 160.0 and 162.1 (C^2 and C^4) ppm. ^{19}F NMR (300 MHz, $CDCl_3$): δ=−63.6 (CF_3) ppm. MS (EI, 70 eV): m/z (%)=325 (21), 324 (100) $[M]^+$, 188 (33), 99 (44), 91 (91), 69 (23), 44 (39). HRMS (MALDI): calcd for $C_{15}H_{15}F_3N_4NaO$ $[M+Na]^+$ 347.1090; found 347.1103.

*4.9.4. 2-[(N,N-Dimethylaminomethylen)amino]-3-p-tolylpyrimidin-4(3H)-one (**8c**).* White solid (182 mg, 78%). Mp 157–158 °C. IR (KBr): ν=3088 (w), 3037 (w), 2918 (w), 2860 (w), 1670 (s), 1630 (s), 1568 (w), 1488 (s), 1423 (m), 1359 (m), 830 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.37 (s, 3H, PhCH_3), 2.71 and 3.05 (2 s, 6H, N(CH_3)$_2$), 6.15 (d, 1H, J=6.3 Hz, H^5), 7.05 and 7.22 (AB system, 4H, J=8.3 Hz, H_{ar}), 7.69 (d, 1H, J=6.3 Hz, H^6), 8.42 (s, 1H, N=CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.3 (PhCH_3), 34.8 and 41.0 (N(CH_3)$_2$), 108.2 (C^5), 127.9 and 129.4 (4CH_{ar}), 135.0 and 137.5 (2C_{ar}), 153.4 (C^6), 157.1 (N=CH), 160.1 (C^2), 164.2 (C^4) ppm. MS (EI, 70 eV): m/z (%)=257 (13), 256 (100) $[M]^+$, 188 (24), 185 (19), 128 (20), 99 (32), 91 (39), 44 (30). HRMS (ESI$^+$): calcd for $C_{14}H_{17}N_4O$ $[M+H]^+$ 257.1397; found 257.1394.

*4.9.5. 2-[(N,N-Dimethylaminomethylen)amino]-5-phenyl-3-p-tolylpyrimidin-4(3H)-one (**8d**).* White solid (210 mg, 91%). Mp 230 °C. IR (KBr): ν=3039 (w), 3004 (w), 2927 (w), 2866 (w), 1668 (m), 1653 (s), 1624 (s), 1579 (w), 1495 (s), 1486 (s), 1420 (m), 1377 (s), 916 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.39 (s, 3H, PhCH_3), 2.76 and 3.09 (2 s, 6H, N(CH_3)$_2$), 7.09 and 7.72 (AB system, 4H, J=8.0 Hz, H_{ar}), 7.23–7.39 (m, 5H, H_{ar}), 7.99 (s, 1H, H^6), 8.50 (s, 1H, N=CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.4 (PhCH_3), 34.9 and 41.1 (N(CH_3)$_2$), 119.7 (C^5), 127.2–129.5 (9CH_{ar}), 134.9–137.5 (3C_{ar}), 151.4 (C^4), 156.9 (N=CH), 159.1 (C^2), 162.9 (C^6) ppm. MS (EI, 70 eV): m/z (%)=333 (21), 332 (100) $[M]^+$, 234 (58), 188 (80), 116 (63), 102 (86), 99 (87), 91 (83), 65 (38). HRMS (MALDI): calcd for $C_{20}H_{20}N_4NaO$ $[M+Na]^+$ 355.1529; found 355.1543.

*4.9.6. 2-[(N,N-Dimethylaminomethylen)amino]-5-methoxy-3-p-tolylpyrimidin-4(3H)-one (**8e**).* Yellow solid (31 mg, 45%). Mp 146–148 °C. IR (KBr): ν=3035 (w), 3002 (w), 2926 (w), 1683 (s), 1629 (s), 1590 (m), 1508 (s), 1446 (m), 1390 (m), 1355 (m), 1308 (w) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.38 (s, 3H, PhCH_3), 2.68 and 3.03 (2 s, 6H, N(CH_3)$_2$), 3.84 (s, 3H, OCH_3), 7.05 and 7.22 (AB system, 4H, J=8.1 Hz, H_{ar}), 7.34 (s, 1H, H^4), 8.31 (s, 1H, N=CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.4 (PhCH_3), 34.8 and 40.9 (N(CH_3)$_2$), 57.1 (OCH_3), 128.0 and 129.5 (4CH_{ar}), 131.0 (C^4), 134.8 and 137.7 (2C_{ar}), 142.4 (C^5), 154.0 (C^2), 156.1 (N=CH), 159.8 (C^6) ppm. MS (EI, 70 eV): m/z (%)=286 (17) $[M]^+$, 121 (18), 91 (26), 44 (24), 43 (100). HRMS (MALDI): calcd for $C_{15}H_{19}N_4O_2$ $[M+H]^+$ 287.1503; found 287.1509.

*4.9.7. 2-[(N,N-Dimethylaminomethylen)amino]-5-methoxycarbonyl-3-methylpyrimidin-4(3H)-one (**8f**).* White solid (160 mg, 99%). Mp 148–149 °C. IR (KBr): ν=2996 (w), 2953 (w), 2878 (w), 1690 (s), 1658 (m), 1559 (m), 1486 (s), 1431 (m), 1378 (m), 1301 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.16 and 3.21 (2s, 6H, N(CH_3)$_2$), 3.53 (s, 3H, NCH_3), 3.83 (s, 3H, CO_2CH_3), 8.49 (s, 1H, H^6), 8.69 (s, 1H, N=CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=29.5 (NCH_3), 35.6 and 41.8 (N(CH_3)$_2$), 51.8 (CO_2CH_3), 107.8 (C^5), 159.3 (N=CH), 159.6 (C^6), 160.7 and 162.0 (C^2 and C^4), 166.1 (CO_2CH_3) ppm. MS (EI, 70 eV): m/z (%)=239 (14), 238 (53) $[M]^+$, 207 (72), 194 (16), 167 (14), 136 (42), 112 (60), 98 (54), 83 (70), 69 (41), 59 (62), 53 (74), 42 (100). HRMS (ESI$^+$): calcd for $C_{10}H_{14}N_4NaO_3$ $[M+Na]^+$ 261.0958; found 261.0957.

*4.9.8. 2-[(N,N-Dimethylaminomethylen)amino]-5-phenyl-3-methylpyrimidin-4(3H)-one (**8g**).* Yellow solid (233 mg, 96%). Mp 175–177 °C. IR (KBr): ν=3042 (w), 3030 (w), 2999 (w), 2963 (w), 2928 (w), 1641 (s), 1600 (m), 1569 (m), 1487 (s), 1445 (s), 1373 (m), 1325 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.08 (s, 6H, N(CH_3)$_2$), 3.65 (s, 3H, NCH_3), 7.27–7.43 (m, 3H, H_{ar}), 7.70–7.73 (m, 2H, H_{ar}), 7.91 (s, 1H, H^6), 8.54 (s, 1H, N=CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=29.5 (NCH_3), 35.0 and 41.0 (N(CH_3)$_2$), 118.4 (C^5), 126.7 and 128.0 (5CH_{ar}), 135.1 (C_{ar}), 150.6 (C^6), 157.5 (N=CH), 158.6 (C^2), 162.5 (C^4) ppm. MS (EI, 70 eV): m/z (%)=257 (21), 256 (100) $[M]^+$, 212 (51), 158 (85), 116 (84), 98 (45), 89 (83), 44 (27), 42 (36). HRMS (ESI$^+$): calcd for $C_{14}H_{17}N_4O$ $[M+H]^+$ 257.1397; found 257.1400.

4.10. General procedure for the preparation of pyrimido[1,2-*a*]pyrimidine-2,6-diones 9

Acyl chloride (3.0 equiv) was added to a solution of **8** (1.0 equiv) in dichloromethane. Triethylamine (3.0 equiv) was

added dropwise to the reaction medium at 0 °C, and the reaction mixture was stirred at room temperature for 3–12 h (3 h for **9m**,**p**,**s**,**u**–**x**; 6 h for **9a**–**c**,**f**–**i**,**o**,**q**,**r**; 9 h for **9d**,**e**; 12 h for **9j**–**l**,**n**,**t**). The solvent was then removed and the residue was dissolved in dichloromethane, washed with water, brine, dried with magnesium sulfate, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (ethyl acetate/petroleum ether: (7:3) for **9a**–**d**,**f**,**l**,**m** and **s**–**u**; ethyl acetate/petroleum ether: (6:4) for **9e** and **9p**–**r**; ethyl acetate/petroleum ether: (5:5) for **9j**,**k**, and **9v**–**x**; ethyl acetate/petroleum ether: (3:7) for **9g**,**i**,**n**, and **o**; ethyl acetate/petroleum ether: (2:8) for **9h**).

*4.10.1. 3,7-Dimethoxycarbonyl-1-p-tolyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9a**).* White solid (49 mg, 84%). Mp 236–238 °C. IR (KBr): ν=3058 (w), 3041 (s), 2959 (s), 2923 (w), 2854 (w), 1754 (s), 1641 (w), 1564 (s), 1520 (s), 1505 (s), 1453 (m), 1380 (w), 1291 (m), 1204 (m), 1085 (m), 815 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.43 (s, 3H, PhCH_3), 3.86 and 3.92 (2 s, 6H, 2CO_2CH_3), 7.08 and 7.35 (AB system, 4H, J=8.3 Hz, H_{ar}), 8.58 (s, 1H, H^8), 9.44 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.2 (PhCH_3), 52.3 and 53.0 (2CO_2CH_3), 107.5 (C^7), 113.7 (C^3), 127.5 and 130.4 (4CH_{ar}), 131.3 (C_{ar}), 138.4 (C^4), 139.8 (C_{ar}), 151.8, 153.3 and 155.7 (C^2, C^6 and C^{9a}), 161.4 (C^8), 161.5 and 163.3 (2CO_2CH_3) ppm. MS (EI, 70 eV): m/z (%)=369 (26) [M]$^+$, 368 (81), 175 (35), 132 (52), 131 (41), 91 (64), 77 (17), 65 (27), 59 (100), 53 (58). HRMS (MALDI): calcd for $C_{18}H_{15}N_3NaO_6$ [M+Na]$^+$ 392.0859; found 392.0847.

*4.10.2. 3-Methoxycarbonyl-1-p-tolyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9b**).* White solid (44 mg, 89%). Mp 200–202 °C. IR (KBr): ν=3091 (w), 3077 (w), 3044 (w), 2957 (w), 2928 (w), 2849 (w), 1744 (s), 1714 (s), 1697 (s), 1576 (m), 1505 (s), 1436 (m), 1364 (w), 1315 (m), 1088 (m), 867 (m), 815 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.43 (s, 3H, PhCH_3), 3.93 (s, 3H, CO_2CH_3), 6.18 (d, 1H, J=6.9 Hz, H^7), 7.10 and 7.35 (AB system, 4H, J=8.3 Hz, H_{ar}), 7.78 (d, 1H, J=6.9 Hz, H^8), 9.44 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.4 (PhCH_3), 53.0 (CO_2CH_3), 106.1 (C^7), 113.2 (C^3), 127.2 and 130.5 (4CH_{ar}), 132.1 (C_{ar}), 138.6 (C^4), 139.7 (C_{ar}), 149.8 (C^{9a}), 155.4 (C^8), 156.3 and 156.8 (C^2 and C^6), 162.0 (CO_2CH_3) ppm. MS (EI, 70 eV): m/z (%)=312 (9), 311 (46) [M]$^+$, 310 (100), 185 (22), 132 (10), 91 (31), 77 (4), 65 (10). HRMS (MALDI): calcd for $C_{16}H_{13}N_3NaO_4$ [M+Na]$^+$ 334.0804; found 334.0808.

*4.10.3. 7-Methoxy-3-methoxycarbonyl-1-p-tolyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9c**).* Yellow solid (41 mg, 76%). Mp 215–216 °C. IR (KBr): ν=3087 (w), 3055 (w), 3035 (w), 2987 (w), 2928 (w), 2846 (w), 1716 (s), 1636 (w), 1594 (s), 1552 (s), 1514 (m), 1454 (w), 1434 (m), 1362 (m), 1308 (m), 1266 (m), 813 (w) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.43 (s, 3H, PhCH_3), 3.82 (s, 3H, OCH_3), 3.93 (s, 3H, CO_2CH_3), 7.09 and 7.35 (AB system, 4H, J=8.3 Hz, H_{ar}), 7.41 (s, 1H, H^8), 9.41 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5 (PhCH_3), 53.0 (CO_2CH_3), 57.3 (OCH_3), 113.2 (C^3), 128.1 and 130.6 (4 CH_{ar}), 132.1 (C^8), 138.4 (C^4), 139.6 and 140.3 (2 C_{ar}), 143.0 (C^7), 153.6–156.2 (C^2, C^6, and C^{9a}), 162.1 (CO_2CH_3) ppm. MS (EI, 70 eV): m/z (%)=341 (32) [M]$^+$, 340 (17), 243 (22), 175 (35), 132 (32), 131 (39), 117 (37), 116 (30), 91 (100), 65 (30), 59 (93), 53 (38), 49 (85). HRMS (MALDI): calcd for $C_{17}H_{15}N_3NaO_5$ [M+Na]$^+$ 364.0909; found 364.0909.

*4.10.4. 3-Carbamoyl-7-methoxycarbonyl-1-p-tolyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9d**).* White solid (69 mg, 72%). Mp 295 °C. IR (KBr): ν=3455 (s), 3396 (s), 3086 (w), 3045 (w), 2953 (w), 2925 (w), 2852 (w), 1765 (s), 1745 (s), 1716 (s), 1568 (m), 1501 (s), 1442 (s), 1373 (m), 1279 (w) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.47 (s, 3H, PhCH_3), 3.91 (s, 3H, CO_2CH_3), 5.86 (br s, 1H, NH_2), 7.12 and 7.41 (AB system, 4H, J=8.3 Hz, H_{ar}), 8.43 (s-e, 1H, NH_2), 8.63 (s, 1H, H^8), 9.83 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5 (PhCH_3), 52.6 (CO_2CH_3), 108.5 (C^7), 113.9 (C^3), 127.6 and 130.9 (4CH_{ar}), 131.4 (C_{ar}), 139.7 (C^4), 140.5 (C_{ar}), 159.8–160.2 (C^2, C^6, and C^{9a}), 161.3 (C^8), 163.6 and 163.8 (CO_2CH_3 and $CONH_2$) ppm. MS (EI, 70 eV): m/z (%)=355 (11), 354 (50) [M]$^+$, 353 (100), 158 (17), 133 (23), 132 (34), 91 (45), 65 (19), 53 (16). HRMS (MALDI): calcd for $C_{17}H_{14}N_4NaO_5$ [M+Na]$^+$ 377.0862; found 377.0855.

*4.10.5. 3-Carbamoyl-1-p-tolyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9e**).* White solid (28 mg, 71%). Mp 285 °C. IR (KBr): ν=3358 (m), 3167 (m), 3105 (w), 3030 (w), 2920 (w), 2851 (w), 1703 (s), 1679 (s), 1620 (w), 1578 (m), 1497 (s), 1425 (m), 1377 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.43 (s, 3H, PhCH_3), 5.87 (br s, 1H, NH_2), 6.22 (d, 1H, J=6.8 Hz, H^7), 7.11 and 7.38 (AB system, 4H, J=8.1 Hz, H_{ar}), 7.78 (d, 1H, J=6.8 Hz, H^8), 8.50 (br s, 1H, NH_2), 9.74 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5 (PhCH_3), 106.8 (C^7), 113.1 (C^3), 127.7 and 130.9 (4CH_{ar}), 132.0 (C_{ar}), 139.6 (C^4), 140.5 and 142.5 (C_{ar} and C^{9a}), 155.0 (C^8), 156.6 and 160.5 (C^2 and C^6), 161.9 ($CONH_2$) ppm. MS (EI, 70 eV): m/z (%)=297 (7), 296 (48) [M]$^+$, 295 (100), 270 (6), 252 (6), 185 (20), 130 (14), 117 (16), 91 (46), 65 (18), 53 (13). HRMS (MALDI): calcd for $C_{15}H_{12}N_4NaO_3$ [M+Na]$^+$ 319.0807; found 319.0816.

*4.10.6. 3-Carbamoyl-7-methoxy-1-p-tolyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9f**).* Yellow solid (41 mg, 94%). Mp 250 °C. IR (KBr): ν=3180 (w), 3098 (w), 3065 (w), 3009 (w), 2924 (w), 2852 (w), 1714 (s), 1597 (s), 1544 (s), 1510 (s), 1477 (m), 1427 (m), 1363 (m), 1267 (s), 884 (m), 813 (m) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.43 (s, 3H, PhCH_3), 3.81 (s, 3H, OCH_3), 5.89 (br s, 1H, NH), 7.10 and 7.37 (AB system, 4H, J=7.4 Hz, H_{ar}), 7.38 (s, 1H, H^8), 8.57 (br s, 1H, NH), 9.71 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5 (PhCH_3), 57.2 (OCH_3), 112.9 (C^3), 127.9 and 130.8 (4CH_{ar}), 131.4 (C^8), 132.0 (C_{ar}), 139.4 (C^4), 140.0 (C_{ar}), 140.7 and 142.5 (C^7 and C^{9a}), 153.5 (C^6), 160.2 (C^2), 162.0 ($CONH_2$) ppm. MS (EI, 70 eV): m/z (%)=327 (19), 326 (100) [M]$^+$, 325 (59), 283 (14), 238 (24), 143 (21), 130 (21), 117 (38), 91 (45), 65 (18). HRMS (MALDI): calcd for $C_{16}H_{14}N_4NaO_4$ [M+Na]$^+$ 349.0913; found 349.0921.

*4.10.7. 7-Methoxycarbonyl-1-p-tolyl-3-trifluoromethyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9g**).* White solid (58 mg, 94%). Mp 223–224 °C. IR (KBr): ν=3067 (w), 2953 (w), 2924 (w), 2853 (w), 1761 (s), 1740 (s), 1717 (s), 1580 (w), 1518 (s), 1445 (m), 1382 (m), 1260 (w) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.45 (s, 3H, PhCH_3), 3.87 (s, 3H, CO_2CH_3), 7.11 and 7.37 (AB system, 4H, J=7.8 Hz, H_{ar}), 8.60 (s, 1H, H^8), 9.19 (q, 1H, J=0.8 Hz, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.4 (PhCH_3), 52.5 (CO_2CH_3), 108.1 (C^7), 113.8 (q, J=33.8 Hz, C^3), 121.3 (q, J=196.0 Hz, CF_3), 127.6 and 130.6 (4 CH_{ar}), 130.9 (C_{ar}), 134.1 (C^4), 140.3 (C_{ar}), 151.9, 153.4, and 155.1 (C^2, C^6, and C^{9a}), 161.4 (C^8), 163.2 (CO_2CH_3) ppm. ^{19}F NMR (300 MHz, $CDCl_3$): δ=−65.0 (CF_3) ppm. MS (EI, 70 eV): m/z (%)=380 (8), 379 (100) [M]$^+$, 348 (11), 164 (11), 91 (15), 59 (52). HRMS (MALDI): calcd for $C_{17}H_{12}F_3N_3NaO_4$ [M+Na]$^+$ 402.0678; found 402.0662.

*4.10.8. 1-p-Tolyl-3-trifluoromethyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9h**).* White solid (51 mg, 93%). Mp 249–250 °C. IR (KBr): ν=3067 (w), 2955 (w), 2925 (w), 2854 (w), 1728 (s), 1713 (s), 1660 (m), 1585 (m), 1505 (s), 1436 (m), 1371 (w), 1326 (m), 1267 (w) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.45 (s, 3H, PhCH_3), 6.22 (d, 1H, J=6.9 Hz, H^7), 7.12 and 7.37 (AB system, 4H, J=8.1 Hz, H_{ar}), 7.81 (d, 1H, J=6.9 Hz, H^8), 9.17 (q, 1H, J=1.2 Hz, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5 (PhCH_3), 106.5 (C^7), 113.2 (q, J=33.5 Hz, C^3), 121.1 (q, J=195.6 Hz, CF_3), 127.8 and 130.7 (4CH_{ar}), 131.5 (C_{ar}), 134.0 (C^4), 140.0 (C_{ar}), 149.7 (C^{9a}), 155.1 (C^8), 155.5 and 156.7 (C^2 and C^6) ppm. ^{19}F NMR (300 MHz, $CDCl_3$): δ=−64.9 (CF_3) ppm. MS (EI, 70 eV): m/z (%)=321 (42) [M]$^+$, 320 (100), 185 (13), 116 (15), 91 (35), 53 (20).

HRMS (MALDI): calcd for $C_{15}H_{11}F_3N_3O_2$ $[M+H]^+$ 322.0803; found 322.0808.

*4.10.9. 7-Methoxy-1-p-tolyl-3-trifluoromethyl-1H-pyrimido[1,2-a] pyrimidine-2,6-dione (**9i**).* Yellow solid (53 mg, 95%). Mp 164–165 °C. IR (KBr): ν=3049 (w), 2959 (w), 2854 (w), 1721 (s), 1705 (s), 1660 (m), 1595 (s), 1513 (s), 1458 (w), 1384 (w), 1367 (m), 1268 (s), 1040 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.44 (s, 3H, PhCH_3), 3.83 (s, 3H, OCH_3), 7.12 and 7.36 (AB system, 4H, J=8.0 Hz, H_{ar}), 7.41 (s, 1H, H^8), 9.12 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.4 (PhCH$_3$), 57.2 (OCH$_3$), 112.9 (q, J=33.3 Hz, C^3), 121.1 (q, J=195.8 Hz, CF_3), 128.0 and 130.6 (4CH$_{ar}$), 131.5 (C_{ar}), 131.9 (C^8), 133.7 (C^4), 139.8 (C^7), 140.4 (C_{ar}), 142.5 (C^{9a}), 153.5 and 155.2 (C^2 and C^6) ppm. ^{19}F NMR (300 MHz, $CDCl_3$): δ=−64.8 (CF_3) ppm. MS (EI, 70 eV): m/z (%)=352 (19), 351 (100) $[M]^+$, 350 (73), 260 (35), 163 (38), 117 (33), 91 (74), 65 (26), 53 (26). HRMS (MALDI): calcd for $C_{16}H_{12}F_3N_3NaO_3$ $[M+Na]^+$ 374.0728; found 374.0725.

*4.10.10. 7-Methoxycarbonyl-1-p-tolyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9j**).* White solid (35 mg, 72%). Mp 246–248 °C. IR (KBr): ν=3092 (w), 3066 (w), 3040 (w), 2956 (w), 2924 (w), 2850 (w), 1754 (s), 1722 (s), 1687 (m), 1646 (m), 1567 (m), 1519 (s), 1500 (s), 1455 (s), 1387 (m), 1352 (w), 865 (w), 814 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.46 (s, 3H, PhCH_3), 3.90 (s, 3H, CO_2CH_3), 6.56 (d, 1H, J=8.3 Hz, H^3), 7.12 and 7.39 (AB system, 4H, J=7.5 Hz, H_{ar}), 8.65 (s, 1H, H^8), 8.86 (d, 1H, J=8.3 Hz, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.6 (PhCH$_3$), 52.5 (CO_2CH_3), 107.7 (C^7), 111.5 (C^3), 127.7 and 130.8 (4CH$_{ar}$), 131.7 (C_{ar}), 133.4 (C^4), 140.1 (C_{ar}), 152.2 (C^8), 154.2 (C^{9a}), 159.4 (C^6), 161.3 (C^2), 164.0 (CO_2CH_3) ppm. MS (EI, 70 eV): m/z (%)=312 (7), 311 (30) $[M]^+$, 310 (65), 185 (19), 179 (28), 151 (23), 132 (16), 107 (22), 105 (30), 91 (49), 78 (17), 57 (100), 53 (18). HRMS (MALDI): calcd for $C_{16}H_{13}N_3NaO_4$ $[M+Na]^+$ 334.0804; found 334.0804.

*4.10.11. 1-p-Tolyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9k**).* White solid (30 mg, 77%). Mp 226–227 °C. IR (KBr): ν=3078 (w), 3042 (w), 2951 (w), 2920 (w), 1690 (s), 1646 (m), 1576 (m), 1492 (s), 1423 (m), 1378 (m), 820 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.44 (s, 3H, PhCH_3), 6.19 (d, 1H, J=6.6 Hz, H^7), 6.47 (d, 1H, J=8.3 Hz, H^3), 7.13 and 7.37 (AB system, 4H, J=8.4 Hz, H_{ar}), 7.80 (d, 1H, J=6.6 Hz, H^8), 8.76 (d, 1H, J=8.3 Hz, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5 (PhCH$_3$), 106.2 (C^7), 110.8 (C^3), 127.9 and 130.7 (4 CH$_{ar}$), 132.4 (C_{ar}), 133.1 (C^4), 139.7 (C_{ar}), 150.1 (C^{9a}), 155.0 (C^8), 157.4 (C^2), 159.9 (C^6) ppm. MS (EI, 70 eV): m/z (%)=254 (8), 253 (38) $[M]^+$, 252 (100), 185 (12), 117 (12), 91 (20), 84 (12). HRMS (MALDI): calcd for $C_{14}H_{12}N_3O_2$ $[M+H]^+$ 254.0930; found 254.0927.

*4.10.12. 7-Methoxy-1-p-tolyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9l**).* White solid (37 mg, 84%). Mp 278–279 °C. IR (KBr): ν=3092 (w), 3066 (w), 3040 (w), 2956 (w), 2924 (w), 2850 (w), 1754 (s), 1722 (s), 1687 (m), 1646 (m), 1567 (m), 1519 (s), 1500 (s), 1455 (s), 1387 (m), 1352 (w), 865 (w), 814 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.44 (s, 3H, PhCH_3), 3.82 (s, 3H, OCH_3), 6.43 (d, 1H, J=8.3 Hz, H^3), 7.12 and 7.37 (AB system, 4H, J=8.3 Hz, H_{ar}), 7.43 (s, 1H, H^8), 8.72 (d, 1H, J=8.3 Hz, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5 (PhCH$_3$), 57.2 (OCH$_3$), 110.7 (C^3), 128.1 and 130.7 (4 CH$_{ar}$), 131.9 (C^8), 132.4 and 139.6 (2C_{ar}), 132.8 (C^4), 140.3 (C^7), 143.3 (C^{9a}), 153.9 (C^6), 159.7 (C^2) ppm. MS (EI, 70 eV): m/z (%)=284 (24), 283 (100) $[M]^+$, 282 (93), 240 (31), 212 (95), 185 (79), 117 (77), 91 (99), 77 (43), 65 (21). HRMS (MALDI): calcd for $C_{15}H_{14}N_3O_3$ $[M+H]^+$ 284.1035; found 284.1031.

*4.10.13. 7-Methoxycarbonyl-3-phenyl-1-p-tolyl-1H-pyrimido[1,2-a] pyrimidine-2,6-dione (**9m**).* White solid (40 mg, 86%). Mp 264–265 °C. IR (KBr): ν=3095 (w), 3064 (w), 2957 (w), 1726 (s), 1692 (s), 1640 (m), 1571 (s), 1505 (s), 1452 (m), 1372 (m), 1348 (w) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.46 (s, 3H, PhCH_3), 3.91 (s, 3H, CO_2CH_3), 7.17 and 7.40 (AB system, 4H, J=8.4 Hz, H_{ar}), 7.47 and 7.69 (m, 5H, H_{ar}), 8.67 (s, 1H, H^4), 9.00 (s, 1H, H^8) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5 (PhCH$_3$), 52.5 (CO_2CH_3), 107.4 (C^7), 123.8 (C^3), 127.8–130.7 (9CH$_{ar}$), 129.7 (C^4), 131.0, 132.2, and 140.0 (3C_{ar}), 151.6 (C^{9a}), 154.3 (C^8), 159.4 (C^6), 161.0 (C^2), 164.2 (CO_2CH_3) ppm. MS (EI, 70 eV): m/z (%)=388 (10), 387 (45) $[M]^+$, 386 (68), 175 (15), 132 (19), 116 (100), 102 (30), 91 (35), 89 (55), 77 (17), 65 (25). HRMS (MALDI): calcd for $C_{22}H_{18}N_3O_4$ $[M+H]^+$ 388.1292; found 388.1284.

*4.10.14. 3-Phenyl-1-p-tolyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9n**).* White solid (38 mg, 86%). Mp 239–240 °C. IR (KBr): ν=3099 (w), 3069 (w), 3035 (w), 2950 (w), 2923 (w), 1710 (s), 1701 (s), 1635 (w), 1571 (m), 1504 (s), 1488 (s), 1444 (m), 1351 (m), 815 (m), 786 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.45 (s, 3H, PhCH_3), 6.22 (d, 1H, J=6.6 Hz, H^7), 7.19 and 7.39 (AB system, 4H, J=8.1 Hz, H_{ar}), 7.45 and 7.70 (m, 5H, H_{ar}), 7.83 (d, 1H, J=6.6 Hz, H^8), 8.93 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5 (PhCH$_3$), 105.8 (C^7), 123.0 (C^3), 128.0–130.7 (9CH$_{ar}$), 129.6 (C^4), 131.4, 132.8, and 139.6 (3 C_{ar}), 149.6 (C^{9a}), 154.8 (C^8), 157.6 (C^6), 159.7 (C^2) ppm. MS (EI, 70 eV): m/z (%)= 330 (10), 329 (69) $[M]^+$, 328 (100), 300 (10), 185 (13), 117 (17), 116 (46), 91 (13), 77 (5). HRMS (MALDI): calcd for $C_{20}H_{16}N_3O_2$ $[M+H]^+$ 330.1237; found 330.1234.

*4.10.15. 7-Methoxy-3-phenyl-1-p-tolyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9o**).* Yellow solid (36 mg, 89%). Mp 215–216 °C. IR (KBr): ν=3056 (w), 3033 (w), 2965 (w), 2932 (w), 2852 (w), 1711 (s), 1701 (s), 1633 (w), 1584 (s), 1543 (s), 1494 (m), 1446 (m), 1385 (m), 1071 (m), 808 (w), 786 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.45 (s, 3H, PhCH_3), 3.84 (s, 3H, OCH_3), 7.16 and 7.37 (AB system, 4H, J=8.3 Hz, H_{ar}), 7.44 and 7.70 (m, 5H, H_{ar}), 7.48 (s, 1H, H^8), 8.86 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5 (PhCH$_3$), 57.2 (OCH$_3$), 122.8 (C^3), 128.1–130.6 (9CH$_{ar}$), 129.5 (C^4), 131.4 (C_{ar}), 132.1 (C^8), 132.8 and 139.4 (2C_{ar}), 140.2 (C^7), 143.4 (C^{9a}), 154.0 (C^6), 159.6 (C^2) ppm. MS (EI, 70 eV): m/z (%)=360 (24), 359 (100) $[M]^+$, 358 (42), 316 (15), 288 (19), 117 (20), 116 (90), 91 (9). HRMS (MALDI): calcd for $C_{21}H_{18}N_3O_3$ $[M+H]^+$ 360.1343; found 360.1353.

*4.10.16. 3-Methoxy-7-methoxycarbonyl-1-p-tolyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9p**).* White solid (22 mg, 99%). Mp 241–243 °C. IR (KBr): ν=3030 (w), 2956 (w), 2925 (w), 2853 (w), 1751 (s), 1732 (s), 1651 (m), 1565 (w), 1518 (s), 1503 (s), 1443 (m), 1384 (m), 1286 (s), 818 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.46 (s, 3H, PhCH_3), 3.90 (s, 3H, CO_2CH_3), 3.99 (s, 3H, OCH_3), 7.11 and 7.38 (AB system, 4H, J=8.3 Hz, H_{ar}), 8.38 (s, 1H, H^4), 8.63 (s, 1H, H^8) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5 (PhCH$_3$), 52.4 (CO_2CH_3), 57.1 (OCH$_3$), 106.9 (C^7), 109.4 (C^3), 127.8 and 130.8 (4 CH$_{ar}$), 131.8 and 140.1 (2C_{ar}), 142.9 (C^4), 149.6 (C^{9a}), 154.2 and 156.4 (C^2 and C^6), 159.8 (C^8), 164.3 (CO_2CH_3) ppm. MS (EI, 70 eV): m/z (%)=342 (9), 341 (55) $[M]^+$, 340 (100), 310 (15), 175 (10), 132 (22), 117 (15), 91 (23), 59 (16), 53 (14). HRMS (MALDI): calcd for $C_{17}H_{16}N_3O_5$ $[M+H]^+$ 342.1084; found 342.1075.

*4.10.17. 3-Methoxy-1-p-tolyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9q**).* White solid (45 mg, 99%). Mp 253–254 °C. IR (KBr): ν=3076 (w), 3034 (w), 2973 (w), 1716 (s), 1691 (s), 1649 (m), 1575 (m), 1516 (s), 1497 (s), 1456 (w), 1360 (w), 1169 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.44 (s, 3H, PhCH_3), 3.95 (s, 3H, OCH_3), 6.21 (d, 1H, J=6.3 Hz, H^7), 7.12 and 7.37 (AB system, 4H, J=8.3 Hz, H_{ar}), 7.80 (d, 1H, J=6.3 Hz, H^8), 8.28 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5 (PhCH$_3$), 57.1 (OCH$_3$), 105.3 (C^7), 109.2 (C^4), 127.9 and 130.6 (4 CH$_{ar}$), 132.3 and 139.7 (2C_{ar}), 142.2 (C^3), 147.7 (C^{9a}), 153.7 (C^8), 156.7 and 157.4 (C^2 and C^6) ppm. MS (EI, 70 eV): m/z (%)=283 (62) $[M]^+$, 282 (100), 185 (35), 117 (15), 91 (28), 65 (14). HRMS

(MALDI): calcd for $C_{15}H_{13}N_3NaO_3$ $[M+Na]^+$ 306.0849; found 306.0850.

*4.10.18. 3,7-Dimethoxy-1-p-tolyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9r**).* White solid (29 mg, 89%). Mp 248–250 °C. IR (KBr): ν=3091 (w), 3017 (w), 2945 (w), 1704 (s), 1656 (m), 1594 (s), 1543 (s), 1465 (s), 1426 (w), 1368 (m), 1327 (m), 1019 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=2.43 (s, 3H, PhCH_3), 3.82 and 3.95 (2 s, 6H, 2 °CH_3), 7.11 and 7.36 (AB system, 4H, J=8.4 Hz, H_{ar}), 7.46 (s, 1H, H^8), 8.22 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=21.5 (PhCH_3), 57.2 (2OCH_3), 109.0 (C^4), 128.0 and 130.7 (4CH_{ar}), 131.5 (C^8), 132.4 and 139.6 (2 C_{ar}), 140.0 (C^{9a}), 141.4 (C^7), 141.9 (C^3), 153.6 and 156.5 (C^2 and C^6) ppm. MS (EI, 70 eV): m/z (%)=314 (14), 313 (100) $[M]^+$, 312 (56), 270 (18), 242 (35), 227 (28), 117 (33), 91 (14), 70 (11). HRMS (MALDI): calcd for $C_{16}H_{15}N_3NaO_4$ $[M+Na]^+$ 336.0955; found 336.0955.

*4.10.19. 3,7-Dimethoxycarbonyl-1-methyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9s**).* Yellow solid (45 mg, 92%). Mp 146–147 °C. IR (KBr): ν=3050 (w), 2992 (w), 2953 (w), 2849 (w), 1754 (s), 1735 (s), 1695 (s), 1643 (m), 1576 (m), 1507 (s), 1458 (s), 1445 (s), 1384 (m), 1130 (m), 821 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=3.69 (s, 3H, NCH_3), 3.91 and 3.95 (2 s, 6H, 2CO_2CH_3), 8.77 (s, 1H, H^8), 9.41 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=30.4 (NCH_3), 52.6 and 53.3 (2CO_2CH_3), 107.6 (C^7), 113.3 (C^3), 138.0 (C^4), 151.0 (C^{9a}), 153.7 and 155.9 (C^2 and C^6), 161.6 (C^8), 161.7 and 163.8 (2CO_2CH_3) ppm. MS (EI, 70 eV): m/z (%)=294 (7), 293 (49) $[M]^+$, 263 (15), 262 (100), 235 (10), 167 (14), 99 (26), 91 (49), 83 (23), 71 (27), 69 (31), 59 (27), 57 (29), 53 (28), 43 (20). HRMS (MALDI): calcd for $C_{12}H_{11}N_3NaO_6$ $[M+Na]^+$ 316.0540; found 316.0538.

*4.10.20. 3-Methoxycarbonyl-1-methyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9t**).* White solid (26 mg, 66%). Mp 190–191 °C. IR (KBr): ν=3094 (w), 3070 (w), 3011 (w), 2955 (w), 1742 (s), 1717 (s), 1679 (m), 1655 (m), 1576 (s), 1512 (s), 1442 (s), 1425 (s), 1370 (m), 800 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=3.62 (s, 3H, NCH_3), 3.92 (s, 3H, CO_2CH_3), 6.20 (d, 1H, J=6.6 Hz, H^7), 7.92 (d, 1H, J=6.6 Hz, H^8), 9.33 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=29.9 (NCH_3), 53.0 (CO_2CH_3), 105.9 (C^7), 112.5 (C^3), 137.9 (C^4), 148.8 (C^{9a}), 155.3 (C^8), 156.3 and 156.9 (C^2 and C^6), 162.1 (CO_2CH_3) ppm. MS (EI, 70 eV): m/z (%)=236 (10), 235 (57) $[M]^+$, 204 (36), 176 (20), 148 (32), 136 (42), 109 (48), 92 (54), 91 (100), 81 (37), 79 (28), 68 (25), 55 (40), 53 (38). HRMS (MALDI): calcd for $C_{10}H_9N_3NaO_4$ $[M+Na]^+$ 258.0485; found 258.0480.

*4.10.21. 7-Methoxy-3-methoxycarbonyl-1-methyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9u**).* Yellow solid (32 mg, 72%). Mp 159–161 °C. IR (KBr): ν=3089 (w), 3010 (w), 2973 (w), 2918 (w), 2839 (w), 1721 (s), 1703 (s), 1641 (m), 1598 (s), 1547 (s), 1474 (m), 1429 (m), 1393 (m), 1325 (s), 1089 (m), 802 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=3.59 (s, 3H, NCH_3), 3.87 (s, 3H, OCH_3), 3.92 (s, 3H, CO_2CH_3), 7.54 (s, 1H, H^8), 9.29 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=29.6 (NCH_3), 53.0 (CO_2CH_3), 57.4 (OCH_3), 112.6 (C^3), 132.1 (C^8), 137.6 (C^4), 140.2 (C^7), 141.9 (C^{9a}), 153.7 and 156.1 (C^2 and C^6), 162.1 (CO_2CH_3) ppm. MS (EI, 70 eV): m/z (%)=266 (15), 265 (81) $[M]^+$, 222 (26), 167 (100), 140 (59), 99 (73), 84 (28), 59 (37), 43 (33), 35 (69). HRMS (MALDI): calcd for $C_{11}H_{11}N_3NaO_5$ $[M+Na]^+$ 288.0591; found 288.0584.

*4.10.22. 7-Methoxycarbonyl-1-methyl-3-phenyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9v**).* White solid (54 mg, 98%). Mp 169–170 °C. IR (KBr): ν=3098 (w), 3052 (w), 3026 (w), 2955 (w), 2924 (w), 1732 (s), 1706 (s), 1688 (s), 1637 (m), 1579 (m), 1509 (s), 1429 (s), 1378 (m), 1311 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=3.74 (s, 3H, NCH_3), 3.89 (s, 3H, CO_2CH_3), 7.42–7.44 (m, 3H, H_{ar}), 7.59–7.63 (m, 2H, H_{ar}), 8.77 (s, 1H, H^4), 8.83 (s, 1H, H^8) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=30.3 (NCH_3), 52.3 (CO_2CH_3), 106.9 (C^3), 123.1 (C^7), 128.8 and 129.1 (5 CH_{ar}), 129.6 (C^4), 131.1 (C_{ar}), 150.5 (C^8), 154.2 (C^{9a}), 159.1 (C^6), 160.7 (C^2), 164.2 (CO_2CH_3) ppm. MS (EI, 70 eV): m/z (%)=312 (14), 311 (82) $[M]^+$, 281 (14), 280 (100), 116 (47), 102 (14). HRMS (MALDI): calcd for $C_{16}H_{13}N_3NaO_4$ $[M+Na]^+$ 334.0798; found 334.0812.

*4.10.23. 1-Methyl-3-phenyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9w**).* Yellow solid (47 mg, 95%). Mp 148–149 °C. IR (KBr): ν=3097 (w), 3062 (w), 3002 (w), 2966 (w), 2925 (w), 1695 (s), 1652 (m), 1595 (s), 1550 (s), 1492 (m), 1446 (m), 1368 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=3.70 (s, 3H, NCH_3), 6.21 (d, 1H, J=6.6 Hz, H^7), 7.42–7.44 (m, 3H, H_{ar}), 7.61–7.64 (m, 2H, H_{ar}), 7.95 (d, 1H, J=6.6 Hz, H^8), 8.78 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=30.0 (NCH_3), 105.5 (C^7), 122.4 (C^3), 128.6–129.0 (5CH_{ar}), 129.3 (C^4), 131.6 (C_{ar}), 148.5 (C^{9a}), 154.5 (C^8), 157.5 (C^6), 159.4 (C^2) ppm. MS (EI, 70 eV): m/z (%)=254 (20), 253 (100) $[M]^+$, 225 (26), 224 (66), 197 (16), 196 (40), 116 (13), 109 (12). HRMS (ESI^+): calcd for $C_{14}H_{11}N_3NaO_2$ $[M+Na]^+$ 276.0744; found 276.0735.

*4.10.24. 7-Methoxy-1-methyl-3-phenyl-1H-pyrimido[1,2-a]pyrimidine-2,6-dione (**9x**).* White solid (55 mg, 99%). Mp 183–184 °C. IR (KBr): ν=3097 (w), 3062 (w), 3002 (w), 2966 (w), 2925 (w), 2854 (w), 1695 (s), 1595 (s), 1539 (m), 1491 (s), 1446 (s), 1390 (w), 1368 (w), 1245 (m), 1154 (w) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ=3.66 (s, 3H, NCH_3), 3.88 (s, 3H, OCH_3), 7.41–7.43 (m, 3H, H_{ar}), 7.59 (s, 1H, H^8), 7.60–7.63 (m, 2H, H_{ar}), 8.73 (s, 1H, H^4) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=29.7 (NCH_3), 57.3 (OCH_3), 122.3 (C^3), 128.6–129.0 (5CH_{ar}), 129.3 (C^4), 131.7 (C_{ar}), 132.1 (C^8), 140.0 (C^7), 142.0 (C^{9a}), 154.0 (C^6), 159.2 (C^2) ppm. MS (EI, 70 eV): m/z (%)=284 (24), 283 (92) $[M]^+$, 268 (14), 254 (11), 240 (18), 185 (100), 116 (22), 44 (14), 40 (36). HRMS (MALDI): calcd for $C_{15}H_{14}N_3O_3$ $[M+H]^+$ 284.1030; found 284.1019.

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