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Facile Synthesis of Novel Pyrimido[1,2-*a*]pyrimidin-4-ones from Highly Reactive Malonates

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A very simple and efficient procedure for the synthesis of novel 2-hydroxy-4*H*-pyrimido[1,2-*a*]pyrimidin-4-ones is described. Title compounds were obtained from the room temperature reaction of 2-aminopyrimidine and its substituted derivatives with bis(2,4,6-trichlorophenyl) malonates. High product yields were observed under optimized conditions. Applicability and reactivity of a range of substituted and unsubstituted phenyl malonates were also investigated. Structural identification of all new compounds was accomplished by spectroscopic methods and elemental analysis.

Introduction

Novel bi- or tricyclic pyrimidine derivatives are important and such compounds have always been at the center of interest in the search for new pharmaceutical candidates. Many pyrimidine and pyrimidopyrimidine derivatives show interesting pharmaceutical properties, such as: antiviral, antibacterial, anti-HIV, antiallergic, and antitumoral activities. For instance, pyrimidine ring containing sulfonamides constitute one of the oldest groups of antibacterial agents. Aminopyrimidines and their derivatives, especially those having substituents on the pyrimidine ring, are also valuable drug intermediates in addition to possessing significant biological activities.[1]

Pyrimidopyrimidines are bicyclic pyrimidine derivatives containing two fused pyrimidine rings, and have four structural isomers. Pyrimido[4,5-*d*]pyrimidine and pyrimido[5,4-*d*]pyrimidine ring systems have been the main focus of drug investigations due to the ease of access to this type of compound by various simple synthetic methods.[2] For example, the reaction of 1,3-dimethyl-6-aminouracil with formaline and benzylamine in ethanol produced a pyrimido[4,5-*d*]pyrimidine derivative that was found to have antidepressant activity.[2] Sanghvi and coworkers reported that isopropylidene ribofuranosylamine derivatives of several pyrimido[5,4-*d*]pyrimidines have antitumoral and antiviral activities.[2]

On the other hand, pyrimido[1,2-*a*]pyrimidines are a less known group of bicyclic pyrimidine heterocycles, probably because of the lack of a widely applicable method for the synthesis of these compounds. Although many bicyclic pyrimidine derivatives have been successfully prepared from the corresponding starting materials by thermal cyclization, there are only a few methods for the synthesis of pyrimido[1,2-*a*]pyrimidines in the literature.[3]

Hurd and Hayao[3] were the first researchers to introduce examples of pyrimido[1,2-*a*]pyrimidines, which were made in the salt form by the reaction of 2-amino-4,6-dimethylpyrimidine with 3-bromopropionic acid. In another method, it was shown that cyclization of guanidine with some α,β-unsaturated nitriles or carbonyl compounds produced hindered derivatives of pyrimido[1,2-*a*]pyrimidines, although in low yields.[3] A pyrimido[1,2-*a*]pyrimidine synthesis was also described by Eynde et al.[3] that involved the reaction of 3-formylchromone or diethyl ethoxymalonate (EMME) with highly substituted 2-aminopyrimidines. Under microwave heating without a solvent, this procedure resulted in the formation of some highly substituted pyrimido[1,2-*a*]pyrimidines in good yields. In a few other synthetic procedures, pyrimido[1,2-*a*]pyrimidines were synthesized in low to moderate yields by the reaction of 2-aminopyrimidines with reagents such as 2-fluorobenzoyl chlorides and iminopropadienones[3] under thermal conditions by either classical or microwave heating. Other methods that are described in the literature are specific examples of the synthesis of some simple pyrimido[1,2-*a*]pyrimidines.[3]

Thomas Kappe[4] reported the synthesis of a pyrimido[1,2-*a*]pyrimidinium derivative by the reaction of bis(2,4,6-trichlorophenyl) ethylmalonate, one of the so-called “magic malonates” (or active malonates), with 2-(methylamino)-pyrimidine for the first time. This is the sole example of the use of an active malonate in the synthesis of pyrimido[1,2-*a*]-pyrimidines. No detailed study on the applicability of Kappe’s or any other method for the production of pyrimido[1,2-*a*]pyrimidine derivatives has yet been presented in the literature. Therefore, the development of a methodology for the synthesis of such compounds would be highly desirable for providing new bicyclic pyrimidine heterocycles that

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can be applied in different fields of chemistry such as chelating compounds, as bases, as well as in the search for new drug candidates.

In this study, as part of our ongoing research on the synthesis of fused pyrimidine ring systems, we have developed a method that is widely applicable, simple and uses easily accessible starting materials for the synthesis of pyrimido[1,2-*a*]pyrimidines. The synthesis of several 2-aminopyrimidines and their reaction with a range of malonates was investigated in detail.

Results and Discussion

Herein, we report the results of our attempts to prepare pyrimido[1,2-*a*]pyrimidines from malonates and 2-aminopyrimidines. Initially, we investigated the reaction of 2-aminopyrimidines with diethyl malonate and diethyl alkylmalonates by thermal condensation. However, our efforts did not produce even trace amounts of pyrimido[1,2-*a*]pyrimidine derivative under thermal conditions even after long reaction periods; e.g., temperature range 120–250 °C and reaction times of 1–50 h. In most cases, whereas starting materials were recovered at lower temperatures (below 170–180 °C), decomposition of reaction mixture and formation of tar-like masses at higher temperatures were observed. Although, thermal condensation of diethyl malonates with 2-aminoheterocycles is known to be very successful for the synthesis of several bicyclic compounds (including pyrido[1,2-*a*]pyrimidines[5]), unfortunately, similar results were not observed with 2-aminopyrimidines.

The application of controlled microwave heating (120–250 °C) with a single mod microwave oven (CEM Discovery S Model) to a mixture of diethyl malonate and 2-aminopyrimidine, either in the presence of a few drops of a suitable solvent (e.g. DMF, DMSO etc.) or without any solvent, also produced none of the desired pyrimido[1,2-*a*]pyrimidine type of compound. Again, either recovery of starting materials or formation of a tarry mass was observed in microwave-assisted reactions.

As an alternative, we used active malonates to synthesize the pyrimido[1,2-*a*]pyrimidines. These highly reactive malonates, namely bis(2,4,6-trichlorophenyl) or bis(pentachlorophenyl) esters of malonates, were introduced by Thomas Kappe around 1967 and used effectively for the synthesis of a range of fused heterocycles,[4,6] especially fused pyrimidine systems. This method involves the reaction of an aminoheterocycle with an active malonate in an inert solvent either with or without a tertiary amine (e.g. triethylamine) catalyst. As a fine example of this method, in our earlier work, high yields of 2-hydroxy-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones were obtained from the reaction of bis(2,4,6-trichlorophenyl) malonates with 2-aminopyridines.[5]

In a similar manner, the reaction of 2-aminopyrimidine with bis(2,4,6-trichlorophenyl) butylmalonate[5] was performed in acetone in the presence of triethylamine as a catalyst. Although low in yield, formation of 3-butyl-2-hydroxy-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (**3f**) was realized in sufficiently pure state. After the structure of this compound was confirmed from its spectroscopic data and elemental analysis, several reaction parameters (type of the solvent, presence and type of a catalyst, reaction period and temperature) were investigated to improve the product yield. The results of these optimization experiments showed that a high yield (82%) of the desired compound could be achieved by simply stirring the starting materials in diethyl ether for 12 h at room temperature without any catalyst (Table 1).

With these initial results in hand, similar cyclization reactions of other 2-aminopyrimidine derivatives with bis(2,4,6-trichlorophenyl) malonate and bis(2,4,6-trichlorophenyl) alkylmalonates were carried out both to obtain novel pyrimido[1,2-*a*]pyrimidine derivatives and to determine the applicability of this procedure in more detail (Scheme 1). The results obtained from the optimized reaction are summarized in Table 1.

As seen in Table 1, this method was very successful for the synthesis of the desired pyrimido[1,2-*a*]pyrimidine heterocycles. The reactions were carried out simply by stirring the starting materials in a suitable solvent at room temperature. In some cases, refluxing the solution increased the reaction rate but did not improve the yield due to rapid decomposition of the active malonates. Hence, long reaction periods at room temperature was preferred in order to avoid thermal decomposition of the esters. Reaction times needed to be extended in some cases, although in most cases the reactions were complete in 5–10 h.

Some aliphatic and aromatic amines, namely triethylamine, *N*,*N*-dimethylaniline and 4-(dimethylamino)pyridine (DMAP), were used as basic catalysts in these reactions. Only in the preparation of compounds **3a**, **3h**, and **3o** were higher yields obtained in the presence of catalyst than in the absence of catalyst. Triethylamine was observed to be a better catalyst than others and can be used in excess due to its low cost.

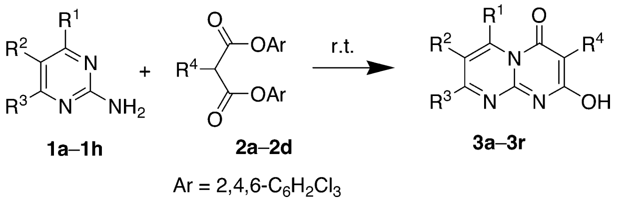
Acetone was the first choice of solvent because it had been effectively used in previous cyclization reactions.[4–5] However, except **3b** and **3h**, low product yields were observed in acetone for some pyrimido[1,2-*a*]pyrimidines. In order to find a solvent system that was more suitable for these types of product and starting material, several other common solvents were also investigated. From the solvents tested, tetrahydrofuran (THF) and diethyl ether were found to be very successful and even better than acetone in some cases. Chloroform was fairly good only in cases where the desired product was not soluble in chloroform because, otherwise, it was difficult to separate the pyrimido[1,2-*a*]pyrimidine derivatives from 2,4,6-trichlorophenol and 2-aminopyrimidines, which were the main by-product and minor impurity, respectively, in the reaction media.

As a result of these investigations, a common solvent with an average polarity was found to be optimal for the synthesis of pyrimido[1,2-*a*]pyrimidines. Ideally, both starting materials were soluble in the solvent and the product was less soluble, so that the target pyrimido[1,2-*a*]pyrimidine derivatives could be easily purified. One other important point to mention about the solvent is its hygroscopic

Table 1. Reaction of 2-aminopyrimidines with bis(2,4,6-trichlorophenyl) malonates.[a]

R^1	R^2	R^3	R^4	Solvent	Time [h]	Product (%)
H	H	CH_3	H	$CHCl_3$	6	**3a** (84)[b]
CH_3	H	CH_3	H	acetone	4	**3b** (87)
H	H	H	H	acetone	2	**3c** (75)
CH_3	H	OCH_3	H	$CHCl_3$	8	**3d** (78)
CH_3	H	OCH_3	butyl	Et_2O	24	**3e** (86)
H	H	H	butyl	Et_2O	12	**3f** (82)
CH_3	H	CH_3	butyl	THF	2	**3g** (62)
H	H	CH_3	butyl	acetone	2	**3h** (72)[b]
H	butyl	H	H	THF	12	**3i** (57)
CH_3	H	morpholin-4-yl	H	THF	6	**3j** (41)
H	H	morpholin-4-yl	H	THF	12	**3k** (46)
CH_3	H	morpholin-4-yl	butyl	THF	8	**3l** (46)
CH_3	H	morpholin-4-yl	allyl	THF	24	**3m** (51)
H	H	H	allyl	THF	16	**3n** (85)
H	H	CH_3	cyclohex-2-en-1-yl	$CHCl_3$	10	**3o** (79)[b]
H	H	H	cyclohex-2-en-1-yl	$CHCl_3$	5	**3p** (84)
Cl	H	CH_3	H	Et_2O	3	**3r** (75)
H	Cl	H	H	DMF	24	–[c]
CH_3	H	OH	H	DMSO	48	–[c]

[a] Bis(2,4,6-trichlorophenyl) malonates were used. All reactions were carried out at room temperature. [b] Triethylamine was used as a catalyst. [c] No product could be isolated.



Scheme 1.

nature. In our experience, a well dried, less hygroscopic solvent is much better than a polar, hygroscopic solvent because the presence of moisture in the system decreased the yield of product by provoking decomposition of the bis(2,4,6-trichlorophenyl) malonates.

Several 2-aminopyrimidines and malonates were used as starting materials to provide information on the applicability of this reaction. However, since only 2-aminopyrimidine and 2-amino-4-methylpyrimidine are commercially available, a number of other starting materials were prepared using known literature methods.[7] Cyclization of all the 2-aminopyrimidine derivatives with the active malonates were carried out under the optimized conditions described above. However, a number of starting materials did not produce the desired product in high yields under similar conditions. Therefore, reaction parameters (solvent, temperature, duration, and presence of a catalyst) were re-evaluated and optimized for each set.

Most of the 2-aminopyrimidines gave the corresponding target compounds in good yields. The presence of one or two substituents (CH_3, OCH_3, Cl, and/or morpholinyl) at the 4- and/or 6-positions, which are adjacent to the ring nitrogen atoms of the pyrimidine, did not much hinder the cyclization. In the reaction of 2-amino-4-methylpyrimidine with bis(2,4,6-trichlorophenyl) malonate, butylmalonate, or (cyclohex-2-en-1-yl)malonate, it was observed that only one regioisomeric product was formed in each case, respectively: 2-hydroxy-8-methyl-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (**3a**), 3-butyl-2-hydroxy-8-methyl-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (**3h**), and 3-(cyclohex-2-enyl)-2-hydroxy-8-methyl-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (**3o**) (Figure 1).

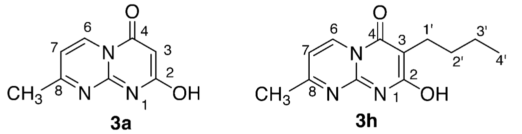


Figure 1. Regioselectively formed isomers **3a** and **3h**.

In a similar manner, 2-hydroxy-8-methoxy-6-methyl-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (**3d**), 3-butyl-2-hydroxy-8-methoxy-6-methyl-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (**3e**), 2-hydroxy-6-methyl-8-(morpholin-4-yl)-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (**3j**), 3-butyl-2-hydroxy-6-methyl-8-(morpholin-4-yl)-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (**3l**), and 3-allyl-2-hydroxy-6-methyl-8-(morpholin-4-yl)-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (**3m**) were obtained, respectively, from the reaction of 2-amino-4-methoxy-6-methylpyrimidine or 2-amino-4-methyl-6-(morpholin-4-yl)pyrimidine with bis(2,4,6-trichlorophenyl) malonates, even though two structural isomers are possible in all cases (Figure 2). It was understood that the steric effect of both methoxy and morpholinyl groups decreased the reactivity of the neighboring nitrogen towards the cyclization reaction in the second part of the two-step process of pyrimido[1,2-*a*]pyrimidin-4-one formation. However, a bulky butyl group at the 5-position of pyrimidine ring did not much influence the cyclization (**3i**).

These results showed that the presence of several different substituents on the 2-aminopyrimidine ring did not preclude the formation of desired pyrimido[1,2-*a*]pyrim-

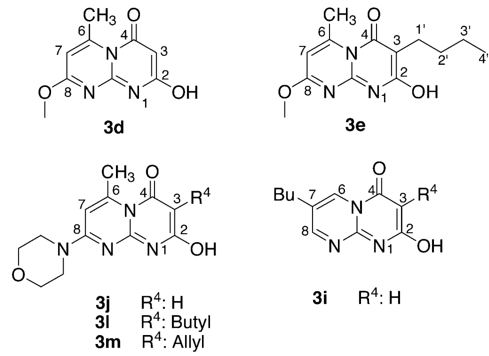


Figure 2. Examples of regioselectively formed pyrimido[1,2-*a*]pyrimidines.

idin-4-ones. The presence of a hydroxy group on the pyrimidine ring, on the other hand, gave rise to decomposition of active malonates due its acidic and nucleophilic nature. Therefore, the reaction of 2-amino-4-hydroxy-6-methylpyrimidine with active malonates did not result in formation of the corresponding pyrimido[1,2-*a*]pyrimidine derivatives. Another unsuccessful outcome was observed from the reactions of 2-amino-5-chloropyrimidine with malonates; in these cases, the electron-withdrawing effect of the chlorine substituent on the ring nitrogen of the pyrimidine moiety reduced the nucleophilicity and, hence, disfavored the ring-closure in the second step of the cyclization.

The effect of alkyl or alkenyl groups at the C-2 carbon of malonate was also investigated by studying the reaction of bis(2,4,6-trichlorophenyl) esters of butyl, allyl and cyclohexenyl malonate with a range of 2-aminopyrimidines. These esters were prepared by using a modification of Kappe's method,[4–5] and all successfully gave the corresponding pyrimido[1,2-*a*]pyrimidines (Table 1). The presence of an alkyl or alkenyl group at the 3-position of the target compounds improved the solubility of the pyrimido[1,2-*a*]pyrimidine in common solvents.

The use of bis(2,4,6-trichlorophenyl) malonates was found to be very successful for preparing the desired pyrimido[1,2-*a*]pyrimidines at room temperature in high yields. However, their unstable nature combined with problems associated with toxicity and the separation of 2,4,6-trichlorophenol from the products, led us to study the possibility of replacing it with an alternative phenol. To this end, malonates with phenol and 4-chlorophenol were also prepared in a similar manner and used in the synthesis of pyrimido[1,2-*a*]pyrimidines. Their reactions with 2-aminopyrimidines were investigated under a range of conditions and the results are given in Table 2.

As seen in Table 2, reactions of the new malonates with 2-amino-4-methylpyrimidine and 2-amino-4,6-dimethylpyrimidine gave the expected pyrimido[1,2-*a*]pyrimidines **3a** and **3b**, respectively, but in lower yields than those obtained with bis(2,4,6-trichlorophenyl) malonate. These reactions could not be realized at room temperature in common solvents, but were successful at higher temperatures in solvents such as DMF or THF. On the other hand, 2-amino-5-chloropyrimidine and 2-amino-4-hydroxy-6-methylpyrimidine did not give any corresponding bicyclic pyrimidine derivative from the reaction with either diphenyl malonate or bis(4-chlorophenyl) malonates, even at elevated temperatures (150 °C) in polar solvents such as DMF. These results showed that neither of the malonates were as reactive as bis(2,4,6-trichlorophenyl) malonate and that both produced the target compounds in lower yields even under more vigorous conditions. Although 2,4,6-trichlorophenol is not a desired by-product of any reaction due to its toxic and unpleasant nature, its malonate ester, in contrast to ethyl, phenyl or 4-chlorophenyl esters of malonate, has the unique property of producing the bicyclic pyrimido[1,2-*a*]pyrimidine derivatives described above.

Structural identification of these novel pyrimido[1,2-*a*]pyrimidines were satisfactorily completed by studying the FTIR, NMR and mass spectroscopic data and the elemental analysis results. In the IR spectra, a medium strength, broad, hydrogen-bonded enolic O–H band between 3400 and 2600 cm^{-1} and two bands at around 1680 and 1630 cm^{-1}, together with the absence of any N–H stretching band around 3300–3100 cm^{-1}, were accepted as characteristic bands that could be used for monitoring 2-hydroxy-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one formation.

The ambiguous position of the methyl group in the products **3a**, **3h**, and **3o** (Figure 1), i.e., whether it was at the 6- or 8-position, was revealed by proton NMR spectroscopic data. The chemical shifts of the methyl hydrogen atoms in the products were consistent with the methyl group occupying the 8-position in all cases. The chemical shifts of the methyl hydrogen atoms for 6,8-dimethyl-2-hydroxy-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (**3b**) and 3-butyl-6,8-dimethyl-2-hydroxy-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (**3g**) were observed to be distinct; the 6-methyl hydrogen atoms

Table 2. Reactions of diphenyl malonate (**2e**) and bis(4-chlorophenyl) malonate (**2f**) with 2-aminopyrimidines.

Ar	2-Aminopyrimidine	Temperature [°C]	Solvent	Product (%)
Phenyl	4-methyl	110	DMF	**3a** (56)
Phenyl	4,6-dimethyl	120	DMF	**3b** (62)
Phenyl	5-chloro	150	DMF	–[a]
4-Cl-phenyl	4-methyl	60	THF	**3a** (68)
4-Cl-phenyl	4,6-dimethyl	60	THF	**3b** (65)
4-Cl-phenyl	5-chloro	150	DMF	–[a]
4-Cl-phenyl	4-hydroxy-6-methyl	150	DMF	–[a]

[a] No product formation was observed.

showed higher chemical shifts than those of the 8-methyl hydrogen atoms, owing to the deshielding effect of the neighboring carbonyl group (Figure 3).

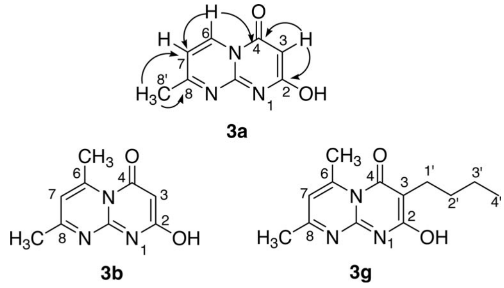


Figure 3. Structures of **3a**, **3b** and **3g**.

An ^{1}H-^{13}C HMBC experiment was carried out with **3a** (Figure 3) to confirm the position of the methyl group (Table 3). In the ^{1}H-^{13}C HMBC spectrum, the H-3 hydrogen at δ = 4.82 ppm coupled with both the C-2 (δ = 168.40 ppm) and C-4 (δ = 150.24 ppm) carbon atoms. A long-range ^{1}H-^{13}C coupling was also observed between the C-4 carbon atom and a hydrogen atom other than H-3. This result indicates that a proton must be attached to the C-6 carbon. It follows that, because two different hydrogen atoms (H-3 and H-6) couple with the C-4 carbon, the methyl group should be attached to the C-8 carbon (δ = 176.38 ppm). Additionally, the ^{1}H-^{13}C coupling between the methyl hydrogen atoms (δ = 2.63 ppm) with the C-8 (δ = 176.38 ppm) and C-7 (δ = 114.28 ppm) carbon atoms is also clearly indicative of the position of methyl group.

Table 3. ^{13}C and ^{1}H assignments for **3a** and ^{1}H-^{13}C HMBC correlations.

Position	^{13}C δ [ppm]	^{1}H δ [ppm]	^{1}H-^{13}C HMBC correlation
2	168.40	–	–
3	81.30	4.82	C3, C4, C2
4	150.24	–	–
6	138.25	9.08	C6, C7, C8, C4
7	114.28	7.36	C7, C6, C8, C8′
8	176.38	–	–
10	155.92	–	–
8′	25.55	2.63	C8, C7, C8′

In a similar manner, **3d** and **3e** (Figure 2) formed as cyclization products from the reaction of 2-amino-4-methoxy-6-methylpyrimidine with bis(2,4,6-trichlorophenyl) malonate and bis(2,4,6-trichlorophenyl) butylmalonate, respectively. The position of the methyl and methoxy groups were established from the proton NMR spectra by comparison of chemical shifts of the methyl group protons, which were found at δ = 2.87 and 2.82 ppm, proving that the methyl group occupied the 6-position and the methoxy group the 8-position of the target compounds. Both the spectroscopic data and the elemental analysis supported the structures of the isolated products of the condensation–cyclization reactions.

Conclusions

In summary, a highly efficient and simple synthetic procedure has been developed for the synthesis of 2-hydroxy-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one derivatives in high yields by the reaction of different 2-aminopyrimidines with bis(2,4,6-trichlorophenyl) malonates at room temperature. This method was found to be applicable to a wide selection of starting materials, even sterically hindered 2-aminopyrimidines. 2,4,6-Trichlorophenol was found to be a better leaving group than ethanol, phenol and 4-chlorophenol in comparable experiments with a range of malonates that were conducted to determine the optimal leaving group in terms of the reactivity, stability, ease of removal, and toxicity. Although 2,4,6-trichlorophenol can be difficult to work with due to its toxicity and pungent odor, its malonate ester was preferred in these reactions because of its high reactivity and stability. Such “magic malonates” were found to be the only malonates capable of reacting to produce bicyclic pyrimidine derivatives, 2-hydroxy-4*H*-pyrimido[1,2-*a*]pyrimidin-4-ones, in high yields under mild conditions.

Experimental Section

General: Melting points were determined with an Electrothermal melting point apparatus. Infrared spectra were recorded on a Perkin–Elmer Spectrum 100 FTIR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded with a Varian Mercury 400–400 MHz High Performance Digital FT-NMR spectrometer. Chemical shifts (δ) are expressed relative to tetramethylsilane (TMS). Mass spectra were recorded with a Shimadzu GC–MS QP2010 mass spectrometer operating at an ionization potential (EI) of 70 eV. Samples were injected into the MS using a DI-2010 direct inlet probe. Elemental analyses for C, H and N were performed with a EuroVector CHNS-O Elemental Analyser.

General Procedure for the Synthesis of Active Malonates: To malonic acid (0.1 mol) and 2,4,6-trichlorophenol (0.21 mol) in a round-bottomed flask, was added freshly distilled $POCl_3$ (20 mL) and the solution was heated to reflux until HCl evolution stopped. Then, excess $POCl_3$ was removed by vacuum distillation. Residual crude product was neutralized by controlled addition of saturated Na_2CO_3 to the cooled flask and then extracted with chloroform. After drying the solution with $MgSO_4$, it was filtered and the solvents evaporated to dryness under reduced pressure. The crude product was recrystallized from a suitable solvent. Bis(2,4,6-trichlorophenyl) malonate (**2a**) and bis(2,4,6-trichlorophenyl) butylmalonate (**2b**), diphenyl malonate (**2e**) and bis(4-chlorophenyl) malonate (**2f**) were identified by comparing their melting points and spectroscopic data (FTIR and ^{1}H NMR) with those reported in the literature.[4,5,8]

Bis(2,4,6-trichlorophenyl) Allylmalonate (2c): The product was recrystallized from acetone/water. White solid (47.69 g, 95%); m.p. 80–85 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3082, 3010 (C=C–H), 2984, 2822, 1770 (C=O), 1631 (C=C), 1569, 1515, 1450, 1384, 1336, 1320 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.0 (t, *J* = 7.2 Hz, 2 H, CH_2), 4.15 (t, *J* = 7.2 Hz, 1 H, CH), 5.23 (dd, *J* = 10.4, 1.2 Hz, 1 H, CH=), 5.32 (dd, *J* = 14.8, 1.2 Hz, 1 H, CH=), 5.95 (m, 1 H, CH=), 7.48 (s, 4 H, ArH) ppm.

Bis(2,4,6-trichlorophenyl) (Cyclohex-2-en-1-yl)malonate (2d): The product was recrystallized from acetone/water. White solid (42.5 g, 78%); m.p. 115 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3080 (C=C–H), 2938, 2835, 1789 (C=O), 1654 (C=C), 1565, 1448, 1384, 1328, 1228 cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 1.45–2.00 (m, 6 H, cyclo-CH$_2$), 3.2 (m, 1 H, cyclo-CH), 4.1 (d, J = 6 Hz, 1 H, CH), 5.89 (m, 1 H, cyclo CH=), 5.84 (dd, J = 11.2 Hz, 1 H, CH=), 7.2 (s, 4 H, ArH) ppm.

General Procedure for the Synthesis of 2-Hydroxy-4*H*-pyrimido[1,2-*a*]pyrimidin-4-ones: 2-Aminopyrimidine derivative (5 mmol) and bis(2,4,6-trichlorophenyl) butylmalonate (5 mmol) were dissolved in an appropriate anhydrous solvent (see Table 1, 20 mL), under nitrogen, in a dried reaction flask fitted with a reflux condenser. The homogeneous solution was stirred at room temperature and the progress of the reaction was monitored with TLC. If the reaction did not start, triethylamine (1 mL) was added slowly into the solution. After completion of the reaction, precipitated solids were filtered by suction, washed with solvent (2 × 20 mL) and dried at room temperature. The crude product was purified either by recrystallization from ethanol, acetone, ethanol/water or by column chromatography.

2-Hydroxy-8-methyl-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (3a): The reaction was carried out in CHCl$_3$ and the product was recrystallized from ethanol. Yellow solid (0.74 g, 84%); m.p. 256–268 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3400–2600 (O–H), 3074, 2901 and 2864 (aliphatic C–H), 1675 (C=O), 1627, 1540, 1465, 1236 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.43 (s, 3 H, 8-CH$_3$), 4.62 (s, 1 H, 3-H), 7.17 (d, J = 7 Hz, 1 H, 7-H), 8.4 (d, J = 7 Hz, 1 H, 6-H), 12.3 (s, 1 H, OH) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 25.55 (C8-CH$_3$), 81.30 (C3), 114.28 (C7), 138.25 (C6), 150.24 (C4), 155.92 (C10), 168.40 (C2), 176.38 (C8) ppm. MS: m/z (%) = 178 (100) [M + H]$^+$. C$_8$H$_7$N$_3$O$_2$ (177): calcd. C 53.73, H 4.14, N 23.15; found C 54.18, H 4.70, N 21.96.

6,8-Dimethyl-2-hydroxy-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (3b): The reaction was carried out in acetone and the product was recrystallized from ethanol/water. Yellow solid (0.83 g, 87%); m.p. 167–169 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3300–2600 (O–H), 2935 and 2853 (aliphatic C–H), 1708 (C=O), 1625, 1432, 1365, 1240, 1163, 1032, 945, 783 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.25 (s, 3 H, 8-CH$_3$), 2.7 (s, 3 H, 6-CH$_3$), 4.4 (s, 1 H, 3-H), 6.9 (s, 1 H, 7-H), 11.95 (1 H, enolic OH) ppm. MS: m/z (%) = 192 (100) [M + H]$^+$. C$_9$H$_9$N$_3$O$_2$ (191): calcd. C 56.54, H 4.74, N 21.98; found C 56.39, H 5.62, N 21.67.

2-Hydroxy-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (3c): The reaction was carried out in acetone and the product was recrystallized from water. Red solid (0.61 g, 75%); m.p. >300 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3300–2600 (O–H), 3092, 1697 (C=O), 1617, 1531, 1357, 1350, 1317 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 4.9 (s, 1 H, 3-H), 7.4 (q, J = 3 Hz, 1 H, 7-H), 9.15 (q, J = 3 Hz, 1 H, 8-H), 9.35 (q, J = 3 Hz, 1 H, 6-H), 12.3 (s, 1 H, OH) ppm. MS: m/z (%) = 164.45 (100) [M + H]$^+$. C$_7$H$_5$N$_3$O$_2$ (163.134): calcd. C 51.54, H 3.09, N 25.76; found C 51.28, H 3.40, N 25.63.

2-Hydroxy-8-methoxy-6-methyl-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (3d): The reaction was carried out in CHCl$_3$ and the product was recrystallized from ethanol. Yellow solid (0.81 g, 72%); m.p. 190–192 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3400–2500 (O–H), 2965 and 2823 (aliphatic C–H), 1693 (C=O), 1643, 1457, 1365, 1210, 1163 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.87 (s, 3 H, 6-CH$_3$), 4.02 (s, 3 H, 8-OCH$_3$), 5.35 (s, 1 H, 3-H), 6.64 (s, 1 H, 7-H) ppm. MS: m/z (%) = 207 (100) [M]$^+$, 190 (15), 179 (40), 166 (95), 123 (30), 83 (60), 109 (45). C$_9$H$_9$N$_3$O$_3$ (207): calcd. C 52.17, H 4.38, N 20.28; found C 52.48, H 4.50, N 19.76.

3-Butyl-2-hydroxy-8-methoxy-6-methyl-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (3e): The reaction was carried out in diethyl ether and the product was purified by column chromatography (SiO$_2$; EtOAc/hexane, 1:1). Yellow solid (1.13 g, 86%); m.p. 265–267 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3365–2650 (O-H), 3086, 2945, 2853, 1671 (C=O), 1612 (C=C), 1537 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 0.80 (t, J = 7 Hz, 3 H, 4′-CH$_3$), 1.27 (m, J = 7 Hz, 2 H, 3′-CH$_2$), 1.35 (m, J = 7 Hz, 2 H, 2′-CH$_2$), 2.23 (m, J = 7 Hz, 2 H, 1′-CH$_2$), 2.82 (s, 3 H, 6-CH$_3$), 3.9 (s, 3 H, 8-OCH$_3$), 6.25 (s, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 14.69 (C4′), 22.92 (C3′), 24.02 (C1′), 24.25 (C6-CH$_3$), 30.68 (C2′), 55.22 (C8-OCH$_3$), 94.25 (C3), 105.1 (C7), 151.35 (C6), 156.80 (C4), 160.97 (C2), 164.21 (C10), 168.15 (C8) ppm. MS: m/z (%) = 264 (100) [M + H]$^+$. C$_{13}$H$_{17}$N$_3$O$_3$ (263): calcd. C 59.30, H 6.51, N 15.96; found C 59.48, H 6.19, N 15.65.

3-Butyl-2-hydroxy-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (3f): The reaction was carried out in diethyl ether and the pure product was obtained by column chromatography (SiO$_2$; EtOAc). Yellow solid (0.89 g, 82%); m.p. 178–181 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3400–2500 (O–H), 3055, 2949 and 2868 (aliphatic C–H), 1687 (C=O), 1635, 1577, 1477, 1365, 775 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 0.89 (t, J = 7.6 Hz, 3 H, 4′-CH$_3$), 1.28 (m, J = 7.6 Hz, 2 H, 3′-CH$_2$), 1.4 (m, J = 7.6 Hz, 2 H, 2′-CH$_2$), 2.4 (m, J = 7.6 Hz, 2 H, 1′-CH$_2$), 7.39 (q, J = 2 Hz, 1 H, 7-H), 9.02 (q, J = 2 Hz, 1 H, 8-H), 9.2 (q, J = 2 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 14.67 (C4′), 22.83 (C3′), 24.09 (C2′), 30.74 (C1′), 95.26 (C3), 113.07 (C6), 138.72 (C7 and C9), 149.41 (C4), 156.17 (C10), 164.16 (C2) ppm. MS: m/z (%) = 220 (100) [M + H]$^+$. C$_{11}$H$_{13}$N$_3$O$_2$ (219): calcd. C 60.26, H 5.98, N 19.17; found C 60.79, H 6.02, N 18.73.

3-Butyl-6,8-dimethyl-2-hydroxy-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (3g): The reaction was carried out in THF and the product was recrystallized from ethanol/water. Yellow solid (0.83 g, 62%); m.p. 136–138 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3400–2500 (O–H), 3078, 2961 and 2859 (aliphatic C–H), 1673 (C=O), 1650, 1560, 1535, 1488, 1469 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 0.95 (t, J = 7.2 Hz, 3 H, 4′-CH$_3$), 1.44 (m, J = 7.2 Hz, 2 H, 3′-CH$_2$), 1.55 (m, J = 7.2 Hz, 2 H, 2′-CH$_2$), 2.55 (t, J = 7.2 Hz, 2 H, 1′-CH$_2$), 2.58 (s, 3 H, 8-CH$_3$), 3.14 (s, 3 H, 6-CH$_3$), 6.7 (s, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 14.12 (C4′), 22.92 (C3′), 24.02 (C2′), 24.40 (C1′), 24.67 (C8-CH$_3$), 30.36 (C6-CH$_3$), 96.79 (C3), 116.69 (C7), 128.38 (C6), 156.08 (C4), 159.93 (C5), 162.47 (C10), 172.64 (C2) ppm. MS: m/z (%) = 248 (100) [M + H]$^+$. C$_{13}$H$_{17}$N$_3$O$_2$ (247): calcd. C 63.14, H 6.93, N 16.99; found C 62.80, H 6.98, N 16.90.

3-Butyl-2-hydroxy-8-methyl-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (3h): The reaction was carried out in acetone and the crude product was purified by column chromatography (SiO$_2$; CHCl$_3$). Yellow solid (0.83 g, 72%); m.p. >300 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3400–2500 (O–H), 3082, 2953 and 2855 (aliphatic C–H), 1673 (C=O), 1648, 1558, 1535, 1488, 1465 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 0.88 (t, J = 7 Hz, 3 H, 4′-CH$_3$), 1.29 (m, J = 7 Hz, 2 H, 3′-CH$_2$), 1.42 (m, J = 7 Hz, 2 H, 2′-CH$_2$), 2.15 (t, J = 7.2 Hz, 2 H, 1′-CH$_2$), 2.5 (s, 3 H, 8-CH$_3$), 7.33 (d, J = 7 Hz, 1 H, 7-H), 9.09 (d, J = 7 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 14.71 (C4′), 24.11 (C3′), 25.50 (C2′), 30.87 (C1′), 22.87 (C8-CH$_3$), 94.04 (C3), 114.02 (C7), 138.01 (C6), 148.70 (C4), 155.55 (C5), 168.43 (C10), 175.24 (C2) ppm. MS: m/z (%) = 234 (100) [M + H]$^+$. C$_{12}$H$_{15}$N$_3$O$_2$ (233): calcd. C 61.79, H 6.48, N 18.01; found C 61.50, H 6.78, N 17.85.

7-Butyl-2-hydroxy-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (3i): The reaction was carried out in THF and the product was recrystallized from ethanol. Yellow solid (0.54 g, 57%); m.p. 226–228 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3400–2400 (O–H), 2974, 2920 and 2863 (aliphatic C–H), 1683 (C=O), 1589, 1547, 1513, 1444, 1372, 1310, 1242, 1117, 1013, 976, 796 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 0.92 (t, *J* = 7 Hz, 3 H, 4′-CH$_3$), 1.25 (m, *J* = 7.2 Hz, 2 H, 3′-CH$_2$), 1.43 (m, *J* = 7 Hz, 2 H, 2′-CH$_2$), 2.39 (t, *J* = 7.2 Hz, 2 H, 1′-CH$_2$), 4.96 (s, 1 H, 3-H), 9.01 (d, *J* = 7 Hz, 1 H, 8-H), 9.21 (d, *J* = 7 Hz, 1 H, 6-H) ppm. MS: *m*/*z* (%) = 219.1 (30) [M]$^+$, 207 (30), 190(10), 176 (100), 162 (5), 122 (80), 79 (75). $C_{11}H_{13}N_3O_2$ (219): calcd. C 60.26, H 5.98, N 19.17; found C 60.39, H 5.91, N 18.97.

2-Hydroxy-6-methyl-8-morpholin-4-yl-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (3j): The reaction was carried out in THF and the crude product was purified by column chromatography (SiO$_2$; EtOAc). Orange solid (0.62 g, 41%); m.p. 230–233 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3300–2500 (O–H), 3098, 2963, 2873, 1691 (C=O), 1502 (C=C), 1445, 1425 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 2.79 (s, 3 H, 6-CH$_3$), 3.67–3.69 (m, 6 H, 5′,6′-CH$_2$), 3.84 (2 H, 6-H), 4.25 (t, 1 H, H$_2$), 4.25 (s, 1 H, 3-H), 6.75 (s, 1 H, 7-H), 11.3 (s, 1 H, OH) ppm. MS: *m*/*z* (%) = 262 (70) [M]$^+$, 245 (5), 234 (20), 221 (100), 194 (30), 163 (65), 109 (45). $C_{12}H_{14}N_4O_2$ (262): calcd. C 54.96, H 5.38, N 21.36; found C 54.43, H 5.24, N 21.66.

2-Hydroxy-8-morpholin-4-yl-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (3k): The reaction was carried out in THF and the product was recrystallized from ethanol/water. Yellow solid (0.57 g, 46%); m.p. 252–256 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3500–2300 (O–H), 2979, 2955 and 2855 (aliphatic C–H), 1677 (C=O), 1627, 1587.1552, 1452, 1378, 1115 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 3.7–3.9 (m, 8 H, 5′,6′-H), 4.15 (s, 1 H, 3-H), 6.9 (d, *J* = 8 Hz, 1 H, 7-H), 8.6 (d, *J* = 7.6 Hz, 1 H, 6-H) ppm. MS: *m*/*z* (%) = 248 (45) [M]$^+$, 220 (30), 207 (40), 196 (100), 180 (75), 160 (25), 149 (80), 123 (35), 95 (60). $C_{11}H_{12}N_4O_3$ (248): calcd. C 53.22, H 4.87, N 22.57; found C 53.39, H 4.52, N 22.23.

3-Butyl-2-hydroxy-6-methyl-8-morpholin-4-yl-4*H*-pyrimido[1,2-*a*]-pyrimidin-4-one (3l): The reaction was carried out in THF and the product was recrystallized from acetone. Yellow solid (0.76 g, 46%); m.p. 231–233 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3200–2337 (O–H), 2984, 2959, 2855, 1677 (C=O), 1552 (C=C), 1452 cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.90 (t, *J* = 5.6 Hz, 3 H, 4′-CH$_3$), 1.38 (m, *J* = 7 Hz, 2 H, 3′-CH$_2$), 1.53 (m, *J* = 7 Hz, 2 H, 2′-CH$_2$), 2.4 (m, *J* = 7.6 Hz, 2 H, 1′-CH$_2$), 3.0 (s, 3 H, 6-CH$_3$), 3.6–4.05 (m, 8 H, 5′,6′-H), 6.1 (s, 1 H, 7-H) ppm. $C_{16}H_{22}N_4O_3$ (318): calcd. C 60.36, H 6.97, N 17.60; found C 60.76, H 6.14, N 17.44.

3-Allyl-2-hydroxy-6-methyl-8-morpholin-4-yl-4*H*-pyrimido[1,2-*a*]-pyrimidin-4-one (3m): The reaction was carried out in THF and the pure product was obtained by column chromatography [SiO$_2$; EtOAc/hexane, 1:1]. Yellow solid (0.77 g, 51%); m.p. 233–235 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3500–2300 (O–H), 3077, 2971, 2922, 1681 (C=O), 1561 (C=C), 1418, 1366, 1115 cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 3.0 (s, 3 H, 6-CH$_3$), 3.6, 3.8 (6 H, 5′,6′-CH$_2$), 3.2 (d, *J* = 6 Hz, 2 H, 1′-CH$_2$), 4.98 (d, *J* = 11 Hz, 1 H, 3′a-CH-*cis*), 5.15 (d, *J* = 18 Hz, 1 H, 3′b-CH-*trans*), 5.96 (m, 1 H, 2′-CH), 6.15 (s, 1 H, 7-H) ppm. MS: *m*/*z* (%) = 302 (100) [M]$^+$, 274 (30), 259 (38), 245 (10), 221 (65), 163 (8), 109 (5). $C_{15}H_{18}N_4O_3$ (302): calcd. C 59.59, H 6.00, N 18.53; found C 59.50, H 5.94, N 18.82.

3-Allyl-2-hydroxy-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (3n): The reaction was carried out in THF and the product was recrystallized from THF. Yellow solid (0.86 g, 85%); m.p. 134–136 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3400–2400 (O–H), 3080, 2995 and 2897 (aliphatic C–H), 1691 (C=O), 1643, 1537, 1450, 1313 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 3.12 (d, *J* = 6 Hz, 2 H, 1′-CH$_2$), 4.87 (d, *J* = 11 Hz, 1 H, 3′a-CH-*cis*), 5.0 (d, *J* = 18 Hz, 1 H, 3′b-CH-*trans*), 5.85 (m, 1 H, 2′-CH), 7.33 (q, *J* = 8 Hz, 1 H, 7-H), 8.98 (q, *J* = 8 Hz, 1 H, 8-H), 9.17 (q, *J* = 8 Hz, 1 H, 6-H) ppm. MS: *m*/*z* (%) = 203 (10) [M]$^+$, 188 (5), 160 (25), 134 (40), 120 (15), 95 (45), 44 (100). $C_{10}H_9N_3O_2$ (203): calcd. C 59.11, H 4.46, N 20.68; found C 59.40, H 4.30, N 20.60.

3-(Cyclohex-2-en-1-yl)-2-hydroxy-8-methyl-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (3o): The reaction was carried out in chloroform and the crude product was purified by column chromatography (SiO$_2$; EtOAc). Yellow solid (0.85 g, 79%); m.p. 232–234 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3400–2200 (O–H), 3084, 2971 and 2878 (aliphatic C–H), 1667 (C=O), 1613, 1566, 1433 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 1.6–2.2 (m, 6 H, 2′-H, 3′-H, 4′-H), 2.75 (s, 3 H, 8-CH$_3$), 3.9 (m, 1 H, 1′-H), 5.6 (d, *J* = 10 Hz, 1 H, 6′-H), 5.85 (m, *J* = 10 Hz, 1 H, 5′-H), 6.5 (d, *J* = 7 Hz, 1 H, 7-H), 7.12 (d, *J* = 7 Hz, 1 H, 6-H) ppm. MS: *m*/*z* (%) = 257 (50) [M]$^+$, 229 (20), 203 (100), 175 (15), 136 (75), 109 (50), 93 (95). $C_{14}H_{15}N_3O_2$ (257): calcd. C 65.35, H 5.88, N 16.33; found C 65.12, H 5.50, N 15.98.

3-(Cyclohex-2-en-1-yl)-2-hydroxy-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (3p): The reaction was carried out in CHCl$_3$ and the product was recrystallized from acetone/water. Yellow solid (1.02 g, 84%); m.p. 212–214 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3400–2500 (O–H), 3020, 2928 and 2858 (aliphatic C–H), 1650 (C=O), 1614, 1565, 1439 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.3–2.04 (m, 6 H, 2′-H, 3′-H, 4′-H), 2.75–3.65 (m, 1 H, 1′-H), 6.55 (d, *J* = 13 Hz, 1 H, 6′-H), 7.4 (m, *J* = 10 Hz, 1 H, 5′-H), 8.2 (q, *J* = 5 Hz, 1 H, 8-H), 9.02 (q, *J* = 5 Hz, 1 H, 7-H), 9.19 (q, *J* = 7 Hz, 1 H, 6-H) ppm. MS: *m*/*z* (%) = 243 (60) [M]$^+$, 228 (10), 215 (40), 200 (15), 161 (35), 122 (100), 73 (55). $C_{13}H_{13}N_3O_2$ (243): calcd. C 64.19, H 5.39, N 17.27; found C 64.43, H 5.14, N 16.95.

6-Chloro-2-hydroxy-8-methyl-4*H*-pyrimido[1,2-*a*]pyrimidin-4-one (3r): The reaction was carried out in diethyl ether and the product was recrystallized from ethanol/water. Yellow solid (0.79 g, 75%); m.p. 190–1192 °C. FTIR (KBr): $\tilde{\nu}_{max}$ = 3400–2500 (O–H), 3074, 2915 and 2888 (aliphatic C–H), 1693 (C=O), 1598, 1412, 1355, 1240, 783 cm^{-1}. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 1.97 (s, 3 H, 8-CH$_3$), 5.59 (s, 1 H, 3-H), 8.05 (s, 1 H, 7-H), 12.03 (s, 1 H, enolic OH) ppm. MS: *m*/*z* (%) = 211 (100) [M + H]$^+$. $C_8H_6ClN_3O_2$ (211): calcd. C 54.41, H 2.86, N 19.86; found C 54.83, H 3.01, N 20.16.

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