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Novel Approaches for the Synthesis of a Library of Fluorescent Chromenopyrimidine Derivatives

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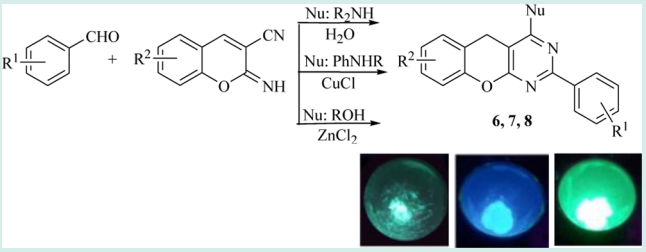
Supporting Information

ABSTRACT: A library of some new fluorescent chromenopyrimidine derivatives has been synthesized by new approaches. Water-promoted and one-pot reaction can produce new dialkylylamino)-5*H*-chromeno[2,3-*d*]pyrimidin-2-yl) phenols. These compounds can also be produced using domino reaction. Two parallel methods are compared. Novel *N*-alkyl-*N*-phenyl-5*H*-chromeno[2,3-*d*]-pyrimidin-4-amines and 4-alkoxy-5*H*-chromeno[2, 3-*d*]pyrimidines are synthesized by Lewis-acid catalyzed reactions. The fluorescence emission intensity of the four compounds from each of libraries after excitation in 290 nm is measured. Compound 2-(4,5-bis(*N*-methyl-*N*-phenylamino)-5*H*-chromeno[2,3-*d*]pyrimidin-2-yl)phenol was isolated as a byproduct. The details of an interesting exchangeable intramolecular H- bonding of two of the new compounds are reported by X-ray analysis data.



KEYWORDS: *green procedure, chromenopyrimidine, fluorescent, intramolecular H-bonding, one-pot reaction, Lewis acid*

INTRODUCTION

Development of efficient methods and strategies for the combinatorial synthesis of organic compounds is of interest, especially for the organic compounds with potential biological and medicinal activities.[1] On the one hand, multicomponent reactions (MCRs) are of increasing significance in organic and medicinal chemistry. MCRs allow organic compounds to be synthesized in a few steps or in a one-pot operation.[2] On the other hand, optoelectronic devices, such as fiber switchers, tunable lasers and amplifiers, and modulators with various applications need compounds emitting in the blue spectral region. There are many reports on using fluorescent compounds in biochemical and medical research.[3] Design of new multicomponent synthetic approaches for the synthesis of diverse fluorescent compounds can be interesting. Among various synthetic strategies in the literature for the synthesis of pyrimidine derivatives, some reports the synthesis of libraries of these compounds.[4] In 2010, we reported a multicomponent, one-pot solvent-free, microwave-assisted synthesis of chromeno[2,3-*d*]pyrimidines by a condensation reaction of 2-hydroxybenzldehyde derivatives (salicylaldehyde), malononitrile and secondary amines.[5a] Following our previous research on multicomponent reactions,[5] we now report novel approaches for the synthesis of a library of fluorescent chromenopyrimidine derivatives. We have used water without the aid of microwave irradiation or any catalysts to synthesize dialkylamino-5*H*-chromeno[2,3-*d*]pyrimidin-2-yl-phenols **6** using a one-pot reaction of salicylaldehyde derivatives, malononitrile, and some other secondary amines. We have found that imino-2*H*-chromen-3-carbonitrles (iminocoumarines) **2** are produced as intermediates in the above-mentioned reaction. When we started the reaction by iminocoumarines, salicylaldehydes and secondary amines in H_2O as the solvent, the products **6** were obtained again. We compared these two parallel procedures. The present research also focused on the reaction of iminocoumarines **2** with aromatic amines and alcohols as nucleophiles. When we used aromatic secondary amines instead of aliphatic amines in the above procedure, the yields were poor, probably because of their lower nucleophilicity. Between the different Lewis acids used, 15 mol % CuCl proved to be the best. Using this catalyst, a small library of compounds **7** was produced. Finally, we tested the reaction of iminocoumarines in alcohol as solvent. Although there are some reports on the synthesis of chromenopyrimidine derivatives in alcohols as solvent, to our surprise, alcohols acted as a reactant and produced the compounds **8**. In this procedure, inexpensive Lewis acid $ZnCl_2$ catalyzed the reaction. There is also an interesting, exchangeable, intramolecular H-bonding in these structures. The details of this H-bonding has been presented for two of the derivatives.

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RESULTS AND DISCUSSION

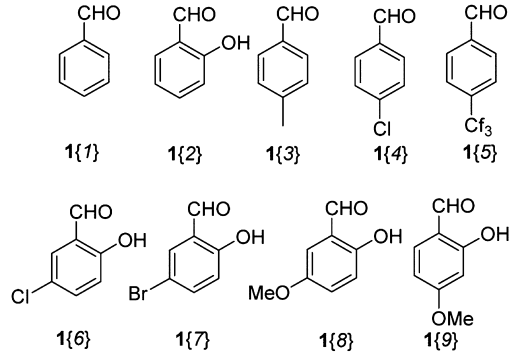
One of the key areas of green chemistry is the elimination of catalysts and solvents in chemical processes or the replacement of hazardous solvents with relatively benign solvents. H_2O is the best solvent for this purpose.[6] Considering this point and in continuation of our quest for developing a one-pot procedure for heterocylic frameworks,[5] we now report new environmentally benign approaches for the synthesis of a library of some new fluorescent chromenopyrimidine derivatives **6**, **7**, **8**, and **9**. Diverse reagents which have been used in the present approaches are listed in Chart 1.

Amino-5*H*-chromeno[2,3-*d*]pyrimidine-2-yl-phenols **6** have been produced in water by heating the reaction mixtures at about 80 °C for 8−10 h. Using H_2O afforded a simple and clean purification of the products (filtration followed by recrystallization).

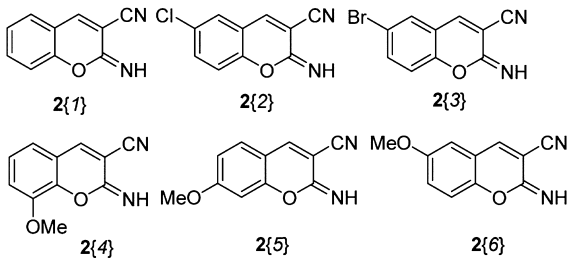
Reaction times and yields of the new compounds synthesized by this procedure are listed in Scheme 1.

Chart 1. Diverse of Reagents

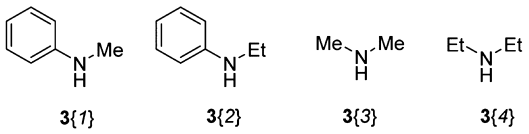
Diverse Reagents 1{*1-9*}:



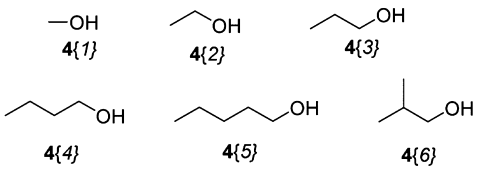
Diverse Reagents 2{*1-6*}:



Diverse Reagents 3{*1-4*}:

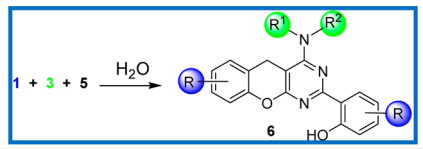


Diverse Reagents 4{*1-6*}:



Diverse Reagent 5

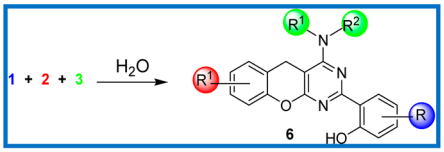
Scheme 1. Synthesis of Water-Promoted One-Pot Reaction of 6



Entry	Comp. 1	Comp. 3	Product 6	Time(h)	Yield(%)
1	1{2}	3{3}	6{2,3}	8	85
2	1{6}	3{3}	6{6,3}	8	77
3	1{7}	3{3}	6{7,3}	8	82
4	1{8}	3{3}	6{8,3}	8	78
5	1{9}	3{3}	6{9,3}	10	88
6	1{2}	3{4}	6{2,4}	10	82
7	1{6}	3{4}	6{6,4}	10	90
8	1{7}	3{4}	6{7,4}	10	83
9	1{8}	3{4}	6{8,4}	10	87
10	1{9}	3{4}	6{9,4}	10	80

Imino-2*H*-chromen-3-carbonitrles (iminocoumarines) are interesting, reactive compounds because of their potential to react with both electrophiles and nucleophiles. In continuation of our previous research and to better clarify the reaction mechanism, a different synthesis of the same products was designed as a parallel procedure. Using iminocoumarins as the reactants (they can be synthesized by the condensation of salicylaldehydes and malononitrile[7]), salicylaldehydes and secondary amines in H_2O as solvent produced the same products **6**. Times and yields of the reactions were similar across the tested conditions (8−10 h, 77−90% listed in Scheme 2)

Scheme 2. Synthesis of 6



Entry	Com.1	Comp. 2	Comp. 3	Product 6	Time(h)	Yield(%)
1	1{2}	2{1}	3{3}	6{2,1,3}	8	85
2	1{6}	2{2}	3{3}	6{6,2,3}	8	77
3	1{7}	2{3}	3{3}	6{7,3,3}	8	85
4	1{8}	2{6}	3{3}	6{8,6,3}	9	77
5	1{9}	2{5}	3{3}	6{9,5,3}	9	90
6	1{2}	2{1}	3{4}	6{2,1,4}	9	83
7	1{6}	2{2}	3{4}	6{6,2,4}	10	90
8	1{7}	2{3}	3{4}	6{7,3,4}	10	85
9	1{8}	2{6}	3{4}	6{8,6,4}	10	88
10	1{9}	2{5}	3{4}	6{9,5,4}	10	81

For the synthesis of amino-5*H*-chromeno[2,3-*d*]pyrimidine-2-yl-phenols, the water-promoted one-pot reaction is the better and simpler procedure among these parallel procedures. In 2010, Bazgir and co-workers have reported the synthesis of compound **6**{*2,1,3*} using a one-pot reaction of 2-iminocoumarin, salicylaldehyde and secondary amines in the presence of $LiClO_4$ (15 mol %) in EtOH, 15 h.[8] Although the presented domino reaction is similar to their report, using H_2O as solvent, without any hazardous catalyst, makes the present method

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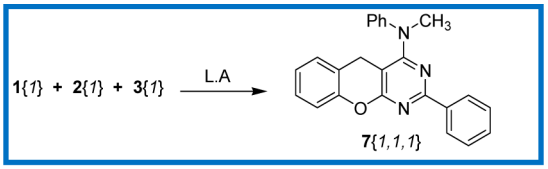
easier and safer. We report similar reactions with other reactants, in H_2O as the solvent and without using any hazardous catalyst.

As an extension of our interest in studying water-promoted reactions, we tried to use aromatic secondary amines in similar manner. Phenylalkyl amines were submitted to a similar reaction in H_2O, but the yields were poor, probably as a result of the relatively lower nucleophilicity of phenylalkyl amines. We have found that the mentioned amines, iminocoumarines and benzaldehydes can condense in the presence of inexpensive Lewis acids. The selectivity of different Lewis acids for the synthesis of *N*-methyl-*N*-phenyl-5*H*-chromeno[2,3-*d*]-pyrimidin-4-amine derivatives **7** are shown in Scheme 3. Since CuCl was the best catalyst in this procedure, we report this new procedure using 15 mol % CuCl (Scheme 4).

Scheme 3. Synthesis of Compounds 7{*1,1,1*} in the Presence of Lewis Acids at 85−90 °C

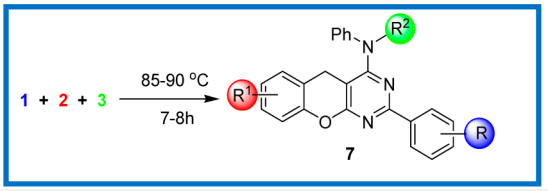


Entry	Lewis Acid	Time(h)	Yield(%)
1	-	12	15
2	SiO_2(10 mol%)	12	15
3	$Ti(NO_3)_2$ (10 mol%)	12	17
4	$ZnCl_2$(10 mol%)	12	41
5	$ZnAc_2$(10 mol%)	12	44
6	Al_2O_3(10 mol%)	12	51
7	CuO(10 mol%)	7	60
8	CuCl(10 mol%)	7	64
9	CuCl(15 mol%)	7	72
10	CuCl(20 mol%)	7	72

Literature shows some reports on the reaction of iminocoumarines in alcoholic solvents. In many of these reports, amines act as nucleophiles. In 2008, Costa and co-workers reported the condensation of salicylaldehyde and malononitrile in the CH_3OH and H_2O media.[9] They had reported the synthesis of dimeric chromene derivatives. During this dimerization process, CH_3OH, as well as malononitrile, could be added as nucleophile to the intermediate of the reaction. Until now there has been no other report on the use of reaction of alcohol as a reactant for the synthesis of pyrimidine derivatives. In the present work, the alcohol could not react as a nucleophile without a catalyst, probably because of the lower nucleophylicity of alcohols. When Lewis acids were used as catalysts, surprisingly primary alcohols, salicylaldehydes, and iminocoumarines condensed to produced 4-alkoxy-5*H*-chromen[2,3-*d*]pyrimidines **8** (Scheme 5). These one-pot and three-component reactions were run under reflux in the corresponding alcohols for 4−8 h. Secondary and tertiary alcohols reacted in lower yields (10−20%); therefore, we recommend this method only for primary alcohols, which afforded higher yields (63−85%).

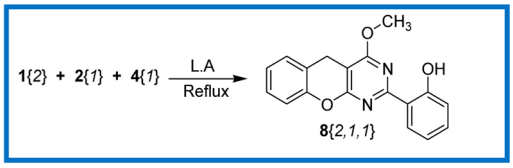
Various Lewis acids have been used as catalysts. Scheme 5 shows the catalysts and their optimal amounts, reaction times

Scheme 4. Synthesis of Compounds 7 Using CuCl (15 mol %)



Entry	Comp. 1	Comp. 2	Comp. 3	Product 7	Time(h)	Yield(%)
1	1{*1*}	2{*1*}	3{*1*}	7{*1,1,1*}	7	78
2	1{*2*}	2{*1*}	3{*1*}	7{*2,1,1*}	7	74
3	1{*3*}	2{*1*}	3{*1*}	7{*3,1,1*}	7	80
4	1{*4*}	2{*1*}	3{*1*}	7{*4,1,1*}	8	77
5	1{*5*}	2{*1*}	3{*1*}	7{*5,1,1*}	8	75
6	1{*1*}	2{*4*}	3{*1*}	7{*1,4,1*}	8	75
7	1{*3*}	2{*3*}	3{*1*}	7{*3,3,1*}	8	77
8	1{*1*}	2{*1*}	3{*2*}	7{*1,1,2*}	7	70
9	1{*2*}	2{*1*}	3{*2*}	7{*2,1,2*}	7	71
10	1{*3*}	2{*1*}	3{*2*}	7{*3,1,2*}	7	82
11	1{*4*}	2{*1*}	3{*2*}	7{*4,1,2*}	7	79
12	1{*1*}	2{*4*}	3{*2*}	7{*1,4,2*}	8	76
13	1{*2*}	2{*4*}	3{*2*}	7{*2,4,2*}	8	78
14	1{*2*}	2{*3*}	3{*2*}	7{*2,3,2*}	8	73
15	1{*7*}	2{*1*}	3{*2*}	7{*7,1,2*}	8	75

Scheme 5. Synthesis of Compound 8{*2,1,1*} in the Presence of Lewis Acids



Entry	Lewis Acid	Time(h)	Yield(%)
1	-	24	-
2	$ZnAc_2$ (10 mol%)	7	20
3	CuO (10 mol%)	7	30
4	$Ti(NO_3)_2$ (10 mol%)	7	35
5	CuCl (10 mol%)	7	55
6	Al_2O_3 (10 mol%)	7	61
7	$ZnCl_2$ (10 mol%)	7	79
8	$ZnCl_2$ (15 mol%)	4	80
9	$ZnCl_2$ (20 mol%)	4	80

and yields for the synthesis of 4-methoxy-5*H*-chromen[2,3-*d*]pyrimidine **8**{*2,1,1*}.

$ZnCl_2$ 10 mol % was optimal for the preparation of compound **8**{*2,1,1*}, but the same catalyst amount was not efficient for alcohols other than MeOH. Larger amounts of $ZnCl_2$ were tested and 15 mol % proved the best. Using this amount a small library of compounds **8** was prepared (Scheme 6).

When the aromatic secondary amine (*N*-methylaniline **3**{*1*}) was used in excess amounts the reaction proceeded as seen in Scheme 7, and compound **9** was produced in a 20% yield as a byproduct. Mixture of 2 mmol of salicylaldehyde **1**{*2*} and iminocoumarine **2**{*1*} in excess amounts of *N*-methylaniline **3**{*1*} (5−7 mL) was heated for 24 h (Scheme7). Unfortunately our attempts to synthesize other similar derivatives were not successful, probably due to steric hindrance.

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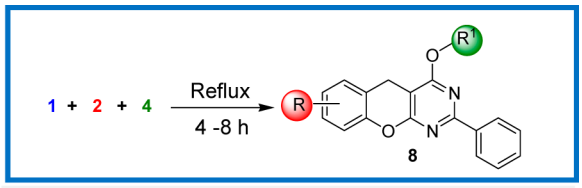
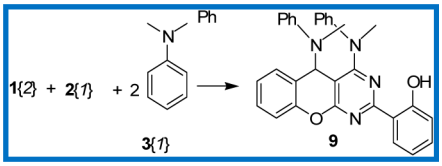
Scheme 6. Synthesis of 8 Using $ZnCl_2$(15 mol %)



Entry	Comp.1	Comp.2	Comp. 3	Product 8	Time(h}	Yield(%)
1	1{2}	2{1}	4{1}	8{2,1,1}	4	80
2	1{2}	2{1}	4{2}	8{2,1,2}	6	72
3	1{2}	2{1}	4{4}	8{2,1,4}	8	69
4	1{2}	2{4}	4{1}	8{2,4,1}	7	85
5	1{2}	2{3}	4{1}	8{2,3,1}	8	75
6	1{2}	2{4}	4{2}	8{2,4,2}	8	83
7	1{2}	2{3}	4{2}	8{2,3,2}	8	70
8	1{2}	2{4}	4{4}	8{2,4,4}	8	78
9	1{2}	2{3}	4{4}	8{2,3,4}	8	66
10	1{2}	2{1}	4{3}	8{2,1,3}	8	69
11	1{2}	2{1}	4{5}	8{2,1,5}	8	65
12	1{2}	2{1}	4{6}	8{2,1,6}	8	63

Scheme 7. Synthesis of 9



In chemical biology and medicinal chemistry, compounds containing H-bonding can provide access to new pharmacophores leading to opportunities for the discovery of new tools to probe biological systems.[10] Some of the compounds reported here have an exchangeable H-bond. The details of the H-bondings for the compounds **6**{2,1,3} and 7{2,1,3} are presented as follows:[11] Single crystals of **6**{2,1,3} were obtained from a mixture of methanol and acetone.[11] Its X-ray structure was obtained and showed an exchangeable intramolecular hydrogen bond arising from free rotation around the C_6-C_7 between O_1-H group of aryl ring and N_1 or N_2 atoms of pyrimidine ring. (Figure 1). Details of the $O_1-H\cdots N_1$bond are $d(O_1\cdots N_1$ = 2.49 Å, $d(O_1-H)$ = 0.84 Å, d $(H\cdots N_1)$ = 1.82 Å, $\angle O_1-H\cdots N_1$ = 135°, and details of the $O_1-H\cdots N_2$ bond are $d(O_1\cdots N_2)$ = 2.57 Å, $d(O_1-H)$ = 0.85 Å, $d(H\cdots N_2)$ = 1.77 Å, $\angle O_1-H\cdots N_2$ = 158°.

Single crystals of 7{2,1,3} were obtained from methanol. Its ORTEP diagram is shown in Figure 2. For this compound an

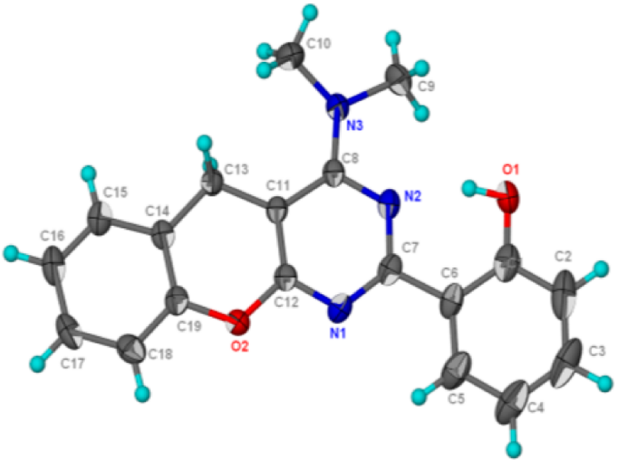


Figure 1. X-ray crystal structure of **6**{2,1,3}.

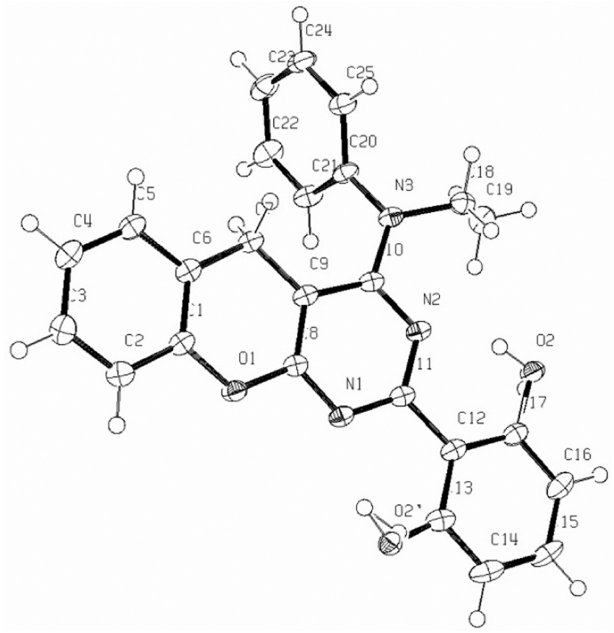


Figure 2. ORTEP diagram of 7{2,1,3}.

exchangeable intramolecular hydrogen bond arising from free rotation around the $C_{11}-C_{12}$ between O_2-H group of aryl ring and N_1 or N_2 atoms of pyrimidine ring was identified by X-ray analysis data. Details of the $O_2-H\cdots N_1$ bond are $d(O_2\cdots N_1$ = 2.60 Å, $d(O_2-H)$ = 0.84 Å, $d(H\cdots N_1)$ = 1.81 Å, $\angle O_2-H\cdots N_1$ = 158°, and details of the $O_2-H\cdots N_2$ bond are $d(O_2\cdots N_2)$ = 2.56 Å, $d(O_2-H)$ = 0.84 Å, $d(H\cdots N_2)$ = 1.78 Å, $\angle O_2-H\cdots N_2$ = 153°.

All of the new compounds reported here are insoluble in water and show blue to green fluorescence. For example the fluorescence of some of the new compounds are shown in Figure 3.

Fluorescence molecular spectroscopy of some of new compounds has been studied. Each sample (0.5 mL) in $CHCl_3$ (10^{-10} mol L^{-1}) was first coated on a glass sheet and dried at room temperature, then placed in a 1 cm length quartz cell. The excited and emission slits were adjusted on 5−7 nm. The fluorescence emission intensity of the four compounds from each of small libraries **6**, 7, and **8** after excitation in 290 nm was shown in Figure 4. We are hopeful that the library of the fluorescent compounds **6**, 7, **8**, and **9** can play a significant role in biochemical research and technology upgrading.

CONCLUSION

The novel approaches reported here provide concise routes for the synthesis of some new fluorescent chromenopyrimidine derivatives **6**, 7, **8**, and **9**. These procedures show some significant advantages compared to the previously reported ones. Synthesis of compounds **6** can be described as environmentally benign; the novel water-promoted, one-pot procedure of their synthesis is compared to the domino procedure. These parallel procedures have a clear advantage

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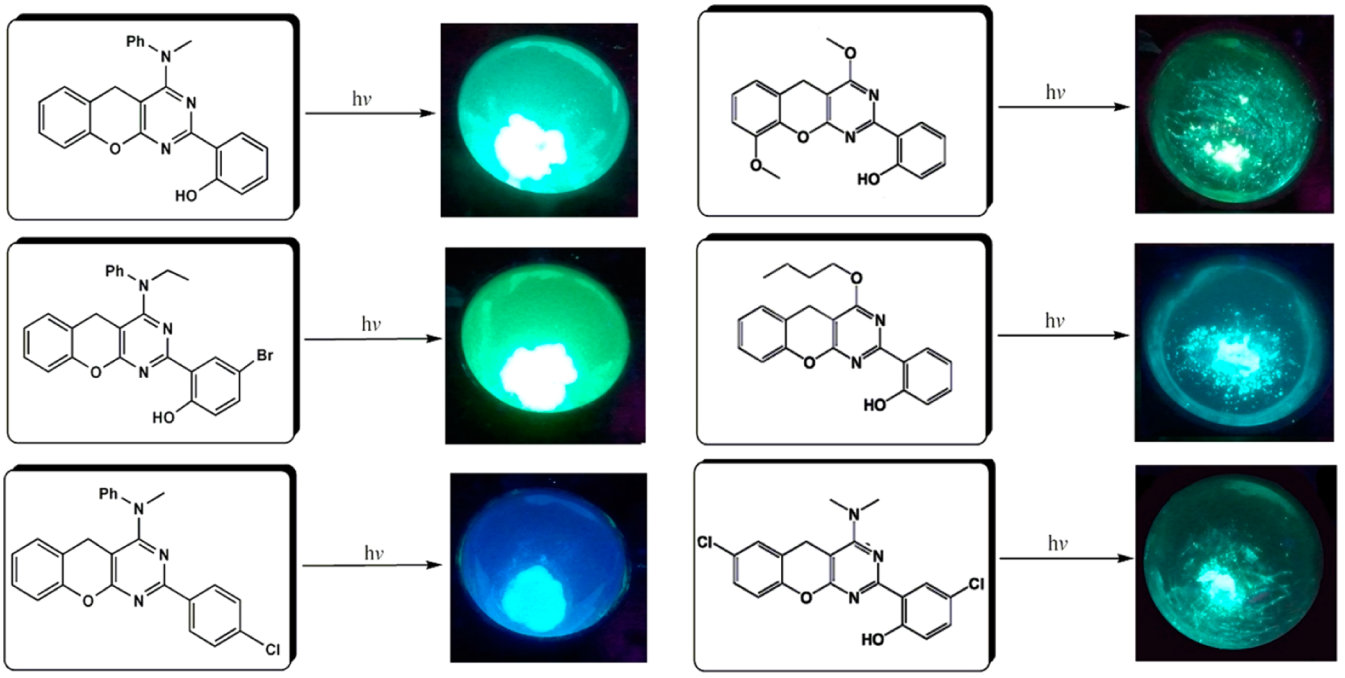

Figure 3. Photo of some new compounds under lamp λ = 366 nm TL8W/08F8T5/BLC Philips made in Holland.[12]

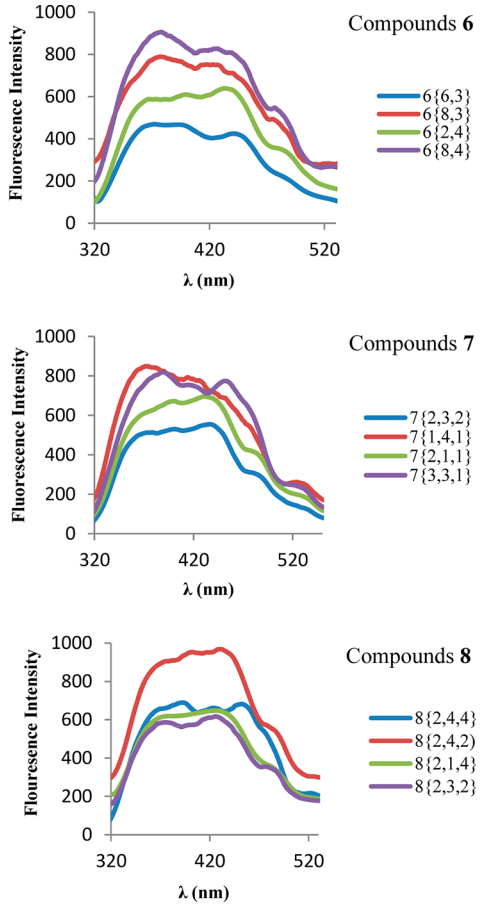

Figure 4. Fluorescence emission spectra of compounds **6**, **7**, and **8** after excitation in 290 nm.

over the previous ones, which used hazardous catalyst or solvents. Moreover, inexpensive Lewis acids were used to help nucleophilic addition of aromatic secondary amines and alcohols in the solvent-free synthesis of compounds **7** and **8**, respectively. High atom economy, easy procedures, and fairly high yields of these one-pot reactions provide obvious advantages. Further investigation of this method is currently in progress to establish its scope and utility. All of the new compounds are insoluble in water and show blue to green fluorescence. The fluorescence emission intensity of the four compounds from each of libraries **6**, **7**, and **8** after excitation in 290 nm are measured. Also, we here report an interesting exchangeable intramolecular H-bonding for the compounds **6**{*2,1,3*} and **7**{*2,1,3*}.

EXPERIMENTAL PROCEDURES

Chemicals and solvents were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. Column chromatography purifications were performed using silica gel (0.015−0.04 mm, mesh-size) and TLC analyses were performed on precoated plastic sheets (25 $DC_{UV\text{-}254}$). Melting points were measured on Barnstead Electrothermal melting point apparatus and were not corrected. Elemental analysis for C, H, and N were performed using a Thermo Finnigan Flash EA1112 instrument. IR spectra were measured on a Bruker EQUINOX 55 spectrophotometer as ATR method. ^{1}H NMR and ^{13}C NMR spectra were determined in $CDCl_3$ on a Bruker 500 spectrophotometer and chemical shifts were expressed in parts per million downfield from tetramethylsilane. Mass spectra were recorded on a Finnigan-MAT 8430 spectrometer at an ionization potential of 70 eV. The fluorescence emissions were obtained by a luminescence PERKIN ELMER LS 50B spectrometer.

4-Bromo-2-(7-bromo-4-(diethylamino)-5*H*-chromeno-[2,3-*d*]pyrimidin-2-yl)phenol (6{*7,4*}). *Water-Promoted One-Pot Reaction.* To a magnetically stirred mixture of 5-bromo-2-hydroxy benzaldehyde **1**{*7*} (2 mmol) and malononitrile **5** (1 mmol) in a 50 mL three-necked flask with a thermometer, diethylamine (1−2 drops) were added at 5 °C and the reaction mixture was stirred for 20 min. Diethylamine

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(4.5 mmol) was added dropwise to the above mixture and stirred for 10 min at room temperature. Then 3−4 mL of H_2O was added to the reaction mixture and heated at about 80 °C for 8−10 h. When the iminocoumarine spot ($R_f \approx 0.4$, silica gel, ethyl acetate/*n*-hexane 1:4) disappeared, the product was filtered, washed with cold water, and recrystallized from EtOH. The colorless crystals of product were collected in 83% yield.

Water-Promoted Domino Reaction. **4-Bromo-2-(7-bromo-4-(diethylamino)-5*H*-chromeno[2,3-*d*]pyrimidin-2-yl)phenol (6{*7,3,4*}).** To a magnetically stirred mixture of iminocoumarine **2**{*3*} (2 mmol) and salicylaldehyde **1**{*7*} (2 mmol) in a 50 mL three-necked flask fitted with a thermometer dimethylamine **3**{*4*} 40% (3.5 mmol) was added at 5 °C before; the reaction mixture was left to stir for 20 min at room temperature. Addition of 5−6 mL of H_2O and heating at about 80 °C for 8−10 h produced a solid product which was collected as colorless crystals and recrystallized from chloroform and ethyl acetate as cosolvents in 85% yields.

Colorless crystals; mp 178−179 °C. IR (KBr): 3034, 1631, 1617, 1255, 1182, 1063, 813, 748 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ_H 1.29−1.37 (6H, t, $2CH_3$of Et), 3.59−3.63 (4H, q, J = 7.08 Hz, $2CH_2$ of Et), 4.06 (2H, s, CH_2), 6.89−6.91, 7.08−7.10, 7.38−7.40, 7.34−7.46, 8.51−8.52 (6H, 5m, H−Ar), 13.31(br s, OH) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 14.09 (CH_3 of Et), 26.10 (CH_2), 45.33 (CH_2 of Et), 98.96, 111.26, 117.17, 119.11, 119.96, 120.59, 121.82, 131.72, 131.78, 131.81, 135.89, 149.77, 159.88, 160.85, 164.71 (Ar, imine carbons). MS: m/z 507, 505 (M^+, M^+ + 2), 478,476 (M^+, M^+ + 2 − C_2H_5), 435, 433 (M^+, M^+ + 2 − $N(C_2H_5)_2$), 425(M^+ − HBr), 353 (M^+ − N (C_2H_5)$_2$, HBr), 72 (N^+ (C_2H_5)$_2$), 57 (N^+ C_3H_7). Anal. Calcd for $C_{21}H_{19}Br_2$ N_3O_2: C, 49.93; H, 3.77; N, 8.32. Found: C, 49.96; H, 3.81; N, 8.35.

Lewis Acid-Catalyzed Synthesis of *N*-Methyl-*N*-phenyl-2-*p*-tolyl-5*H*-chromeno[2,3-*d*]pyrimidin-4-amine (7{*3,1,1*}). To a magnetically stirred mixture of iminocoumarine **2**{*1*} (2 mmol) and benzaldehyde derivatives **1**{3} (2 mmol) in CH_2Cl_2 (2 mL), CuCl (15 mol %) was added gently. Then *N*-methyl aniline **3**{*1*} (3 mmol) was added to the above mixture. The reaction mixture was stirred for 20 min at room temperature and refluxed for 7−8 h. The progress of the reaction was monitored by TLC. When the product's spot (R_f ≈ 0.8 in silica gel, ethyl acetate/*n*-hexane (1:5)) was visible and the spot for iminocoumarine at $R_f \approx 0.4$ disappeared, the reaction was completed. The final product was purified by column chromatography using ethyl acetate/*n*-hexane 1:6 as eluent and recrystallized in ethanol 80% yield.

Colorless crystals; mp 169−170 °C. IR (KBr): ν_{max} 2920, 1597, 1570, 1158, 1110, 1088 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ_H 2.47 (3H, s, CH_3 of CH_3−Ar), 3.14 (2H, s, CH_2), 3.67 (3H, s, CH_3 of CH_3N), 6.81−6.83, 6.96−6.99, 7.17−7.18, 7.22−7.27, 7.31−7.33, 7.40−7.43, 8.43−8.45 (13H, 7m, aromatic protons) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 21.99 (CH_3 of CH_3−Ar), 25.90(CH_2), 42.56 (CH_3 of CH_3N), 97.39, 117.30, 120.36, 124.24, 125.59, 125.90, 128.18, 128.55, 129.11, 129.50, 130.05, 135.16, 141.15, 147.54, 150.89, 162.23, 164.03, 165.50 (Ar, imine carbons). MS: m/z 379 (M^+), 364 (M^+ − CH_3), 349 (M^+ − $2CH_3$), 302 (M^+ − Ar), 273 (M^+ − CH_3, Ar), 91, 77. Anal. Calcd for $C_{25}H_{21}N_3O$: C, 79.13; H, 5.58; N, 11.07. Found: C, 79.12; H, 5.57; N, 11.10.

Lewis Acid-Catalyzed Synthesis of 2-(4-methoxy-5*H*-chromeno[2,3-*d*]pyrimidin-2-yl)phenol (8{*2,1,1*}). To a magnetically stirred mixture of iminocoumarine **2**{*1*} (2 mmol) and salicylaldehyde **1**{*2*} (2 mmol) in CH_3OH **4**{*1*} (2 mL), $ZnCl_2$ (15 mol %) was added gently. The reaction mixture was stirred for 20 min at room temperature and refluxed for 4 h. The progress of the reaction was monitored by TLC. When the spot for the product (R_f ≈ 0.8 in silica gel, ethyl acetate/*n*-hexane (1:5)) was visible, the final product was purified by column chromatography using ethyl acetate/*n*-hexane 1:6 as eluent and recrystallized in ethanol with an 80% yield.

Colorless crystals; mp 200−201 °C. IR (KBr): ν_{max} 2989, 1600, 1541, 1187, 1155, 1074, 1028. ^1H NMR ($CDCl_3$, 500 MHz): δ_H 3.03 (2H, s, CH_2) 4.15(3H, s, CH_3O), 6.94−7.00, 7.11−7.14, 7.16−7.20, 7.25−7.37, 8.41−8.43 (8H, 5m, Ar), 12.78(1H, br s) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 21.29 (CH_2), 54.26 (CH_3 of CH_3O), 94.41, 116.84, 117.31, 117.88, 118.43, 124.16, 127.76, 128.70, 128.75, 132.62, 136.82, 149.81, 159.78, 161.70, 167.13, (Ar, imine carbons). MS: m/z 306 (M^+), 291 (M^+ − CH_3), 277 (M^+ − CH_3O). Anal. Calcd for $C_{18}H_{14}N_2O_3$: C, 70.58; H, 4.61; N, 9.15. Found: C, 70.64; H, 4.69; N, 9.20.

Synthesis of 2-(4,5-Bis(*N*-methyl-*N*-phenylamino)-5*H*-chromeno[2,3-*d*]pyrimidin-2-yl)phenol (9). To a magnetically stirred mixture of salicylaldehyde **1**{*2*} (2 mmol) and iminocoumarine **2**{*1*} (2 mmol) in a 50 mL three-necked flask with a thermometer, *N*-methyl aniline **3**{*1*} (5 mL) was added at 5 °C. The reaction mixture was heated for 24 h at 50 °C. The progress of the reaction was monitored by TLC. The spot for the product 7{*2,1,1*} is appeared at $R_f \approx 0.6$, and the spot for compound **9** appeared at $R_f \approx 0.74$ (ethyl acetate/*n*-hexane 1:4). The residue was purified by column chromatography using ethyl acetate/*n*-hexane 1:5 as byproduct. The colorless crystals of **9** were obtained in 20% yield.

Colorless crystals; mp 132−133 °C. IR (KBr): ν_{max} 2926, 1609, 1585, 1171, 1099 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ_H 2.78, 3.51 (6H, 2s, CH_3N), 4.12 (1H, s, CH), 6.43−6.45, 6.67−6.68, 6.76−6.77, 6.97−7.00, 7.04−7.07, 7.18−7.21, 7.24−7.33, 7.43−7.48, 8.54−8.56 (18H, 10m, H−Ar), 13.36(1H, br s) ppm. ^{13}C NMR($CDCl_3$, 125 MHz): δ_C 31.10 (CH), 39.97, 42.38($2CH_3$ of CH_3N), 101.50, 112.89, 117.38, 118.11, 119.07, 119.37, 124.77, 125.03, 125.49, 126.35, 128.17, 128.20, 128.95, 129.71, 130.31, 133.41, 133.73, 146.70, 148.55, 149.67, 159.15, 160.96, 162.76 (Ar, imine carbons). MS: m/z 486 (M^+), 469 (M^+ − CH_3), 380 (M^+ − NCH_3Ph), 376 (M^+ − PhOH, CH_3), 376 (M^+ − $C_{13}H_{14}NO$), 105, 91, 77. Anal. Calcd for $C_{31}H_{26}N_4O_2$: C, 76.52; H, 5.39; N, 11.51. Found: C, 76.54; H, 5.41; N, 11.57.

■ ASSOCIATED CONTENT

Supporting Information

General information, general procedure, spectral and analytical characterization, NMR spectra of the products, and the photo of 22 new compounds under lamp λ = 366 nm. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(11) Crystallographic data for the structure of compound **6**{*2,1,3*} and **7**{*2,1,3*} reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publications CCDC 737003 and 891212 respectively. These data can be obtained free of charge via www.ccdc.com.ac.uk/data_request/cif.

(12) The photo is taken under lamp λ = 366 nm TL8W/08F8T5/BLC Philips made in Holland.