THE REACTIONS OF 2,6-DICHLOROBENZONITRILE OXIDE WITH PYRIMIDINE DERIVATIVES

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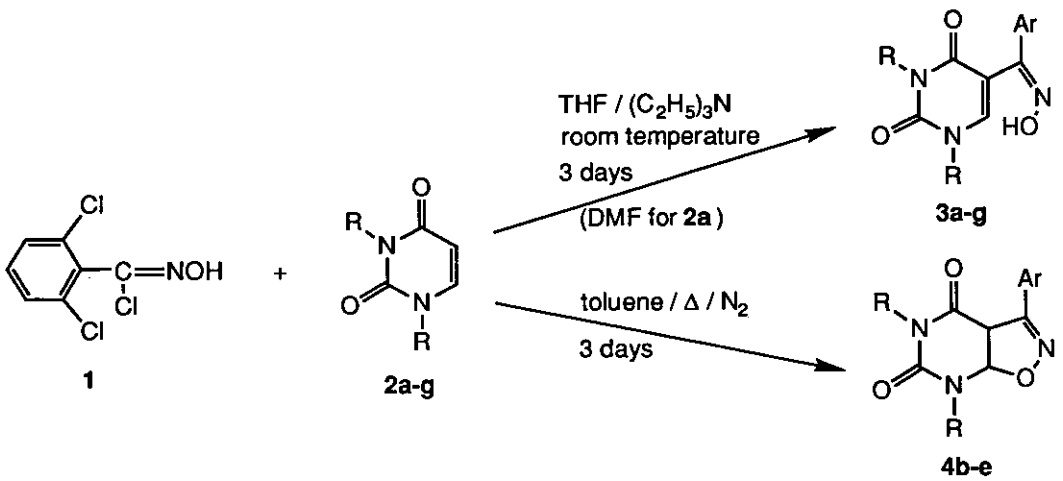
Abstract - The reactions of 2,6-dichlorobenzonitrile oxide with various kinds of pyrimidine derivatives (**2a-g, 5-14**) in different reaction conditions were studied.

Nitrile oxide is an important class of 1,3-dipoles, and used to form isoxazoline and isoxazole derivatives.[1] These heterocyclic compounds were further transformed in most cases to a variety of synthetically useful derivatives that have diverse functional groups.[2]

Recently, we have reported that the reactions of nitrile oxides with the 5,6-double bond of uracil nucleosides[3] and cytosine nucleosides. In the case of uracil nucleosides, we obtained the 1,3-addition products derived from the ring-opening reaction of the initially formed [3+2] cycloaddition products. The mechanism for the formation of these 1,3-addition products has been studied by using 1,3-dimethyluracil (**2b**) as a model substrate. Interestingly, in the case of cytosine nucleosides, the initially formed cycloaddition products were stable, thus we could isolate them. In this paper, we described the extention of our recent experiments with various kinds of pyrimidine derivatives. The reactions of 2,6-dichlorobenzonitrile oxide (generated *in situ* from **1**) with uracil (**2a**) and 1,3-dialkyluracil derivatives (**2b-g**) were conducted in two different reaction conditions (**Scheme 1**).

Thus, the reaction mixtures of 2,6-dichlorobenzohydroximoyl chloride (**1**) and **2a-g** in THF (DMF was used for **2a**) were treated with triethylamine, stirred for 3 days at room temperature, to afford the corresponding oxime derivatives (**3a-g**) in 20-77% yields. Whereas, refluxing the solution of



a. R = H
b. R = CH_3
c. R = CH_2CH_3
d. R = $CH_2CH_2CH_3$
e. R = CH_2Ph
f. R = CH_2Ph(*p*-OMe)
g. R = CH_2Ph(*p*-NO_2) Ar = 2,6-$Cl_2C_6H_3$

Scheme 1

1 and **2b-e** in dry toluene for 3 days with a gentle nitrogen stream to repel out the liberated HCl from 1 afforded the [3+2] cycloaddition products (**4b-e**) in 48-86% yields. The oxime derivatives (**3a-g**) were derived from the corresponding cycloaddition products (**4a-g**) *via* the ring-opening reaction as mentioned in our previous report.[3] The results and the meaningful peaks in the ^{1}H nmr spectra are summarized in **Table I** and **Table II**.

As shown in **Table I**, singlets due to the oxime protons and the H6 protons appeared in the range of 11.74-12.25 ppm and 7.71-8.90 ppm, respectively in DMSO-d_6. Dihydroisoxazolopyrimidine derivatives (**4b-e**) were unstable in polar solvents (*vide infra*), thus the ^{1}H nmr spectra were recorded in benzene-d_6. As shown in **Table II**, a doublet due to the H9 proton appeared in 3.95-4.28 ppm and a doublet due to the H8 proton appeared in 4.78-5.07 ppm. Both doublets had an identical coupling constant ranged J = 9.2-9.3 Hz. As mentioned in our previous paper,[3] the

Table I. Synthesis of 1,3-Addition Products (**3a-g**)

entry	starting material	product	yield (%)	^{1}H nmr (δ)[a]	
				H6	oxime proton
1	**2a**	**3a**	20	7.71	11.74
2	**2b**	**3b**[b]	74	8.63	12.10
3	**2c**	**3c**	64	8.65	12.14
4	**2d**	**3d**	49	8.60	12.13
5	**2e**	**3e**	77	8.79	12.17
6	**2f**	**3f**	62	8.74	12.13
7	**2g**	**3g**	37	8.90	12.25

[a]Determined in DMSO-d_6.

[b]Previously reported (see Reference 3).

Table II. Synthesis of Cycloaddition Products (**4b-e**)

entry	starting material	product	yield (%)	^{1}H nmr (δ)[a]		
				H8	H9	*J* (Hz)
1	**2b**	**4b**[b]	48	4.78	4.17	9.3
2	**2c**	**4c**	86	4.96	4.14	9.2
3	**2d**	**4d**	76	5.14	4.28	9.2
4	**2e**	**4e**	50	5.07	3.95	9.3

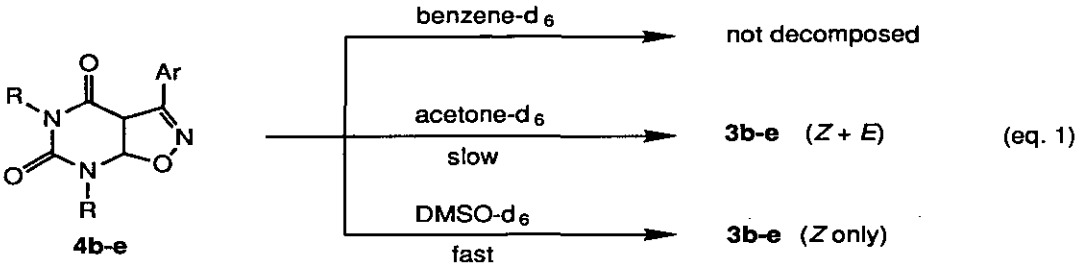
[a]Determined in benzene-d_6.

[b]Previously reported (see Reference 3).

use of dry toluene as solvent and a nitrogen stream to repel out the liberated HCl from the reaction mixtures as needed to obtain the cycloaddition products (**4b-e**).

As studied before in brief,[3] the dihydroisoxazolopyrimidine derivatives (**4b-e**) were unstable toward acid, base, and even to polar solvents. Thus, preparation, isolation, and structure determination procedures of these unstable compounds must be carried out carefully by using non-polar solvents such as toluene, benzene, or methylene chloride. The use of polar solvents such as acetone, *N,N*-dimethylformamide, or dimethyl sulfoxide caused contaminations with the decomposed side products. Such instability of these cycloaddition products (4) to solvents was studied,

and summarized in equation 1 and **Table III**.



(eq. 1)

Ar = 2,6-$Cl_2C_6H_3$

Table III. Decomposition of **4b-e** with Time in Polar Solvents at Room Temperature

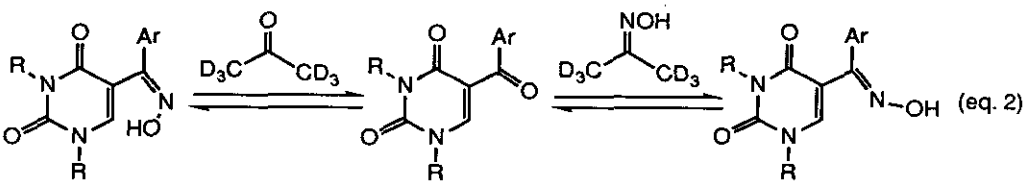
starting material[a]	time[b]	solvent	products (%)[c]		
			remaining SM	*Z*-oxime	*E*-oxime
4b	< 10 min	acetone-d_6	100	0	0
4b	10 h	acetone-d_6	100	0	0
4b	24 h	acetone-d_6	100	0	0
4b	24 h	DMSO-d_6	0	100	0
4c	< 10 min	acetone-d_6	84	16	0
4c	10 h	acetone-d_6	80	9	11
4c	24 h	acetone-d_6	80	7	13
4c	24 h	DMSO-d_6	11	89	0
4d	< 10 min	acetone-d_6	100	0	0
4d	10 h	acetone-d_6	88	8	4
4d	24 h	acetone-d_6	86	7	7
4d	24 h	DMSO-d_6	0	100	0
4e	< 10 min	acetone-d_6	78	21	0
4e	10 h	acetone-d_6	0	100	0
4e	24 h	acetone-d_6	0	96	4
4e	24 h	DMSO-d_6	0	100	0

[a]Purity of starting materials were garanteed (> 98%) by ^{1}H nmr in benzene-d_6.

[b]Error limits in time are < ± 10 min.

[c]Determined by the peak integration in ^{1}H nmr spectra (H8 or H9 proton for **4b-e** and H6 proton for **3b-e** were used).

As shown in **Table III**, **4b-e** were quite unstable in DMSO-d_6, thus these compounds decomposed quantitatively (except for **4c**) to the *Z*-oxime derivatives (**3b-e**) within 1 day. In DMSO-d_6 we could not observe any *E*-oxime derivatives of **3b-e**. In acetone-d_6, **4b-e** decomposed slowly than in DMSO-d_6. 1,3-Dimethyl derivative (**4b**) was stable up to 1 day. 1,3-Diethyl- and 1,3-dipropyl derivatives (**4c-d**) decomposed in about 14-20% after 1 day. Interestingly, the 1,3-dibenzyl derivative (**4e**) was quite unstable in acetone-d_6, thus after 10 h no starting material remained. It is interesting to note that *E*-oxime derivatives of **3b-e** were formed in acetone-d_6 to a considerable amount which increased according to time. The $Z \rightarrow E$ isomerization in acetone-d_6 could be explained as shown in equation (2), which was not observed in DMSO-d_6.



(eq. 2)

3b-e (*Z*) (*E*)

Ar = 2,6-$Cl_2C_6H_3$

Thus, the *Z*-oximes (**3b-e**) in acetone-d_6 (Aldrich, 99+ atom %D) isomerized slowly to the more stable *E*-oximes of **3b-e** with the aid of traces of moisture and the appropriate carbonyl compound, acetone-d_6.[4]

As a continuous work, the reactions of 2,6-dichlorobenzonitrile oxide with various kinds of pyrimidines that have substituents at C5 or C6 position were examined. The results are summarized in **Table IV**.

Table IV. The Reaction of **1** with Various Pyrimidine Derivatives (4-14)

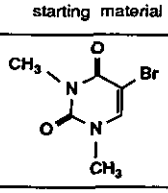
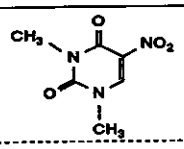
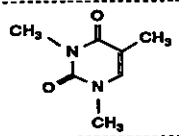
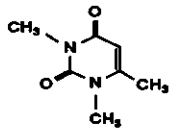
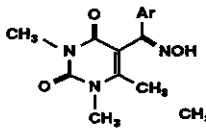
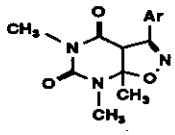
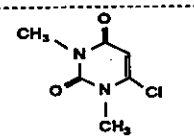
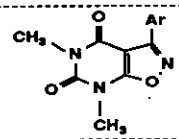
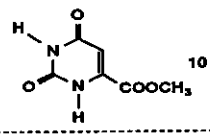
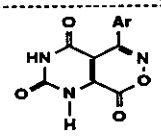
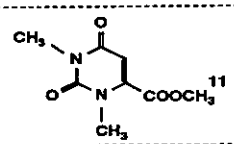
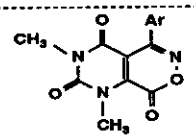
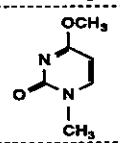
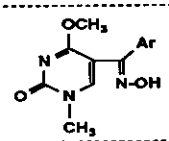
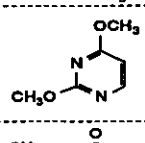
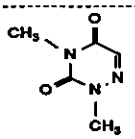
entry	starting material	method[a]	product (% yield)
1	 **5**	A	no reaction
2		B	no reaction

Table IV. Continued

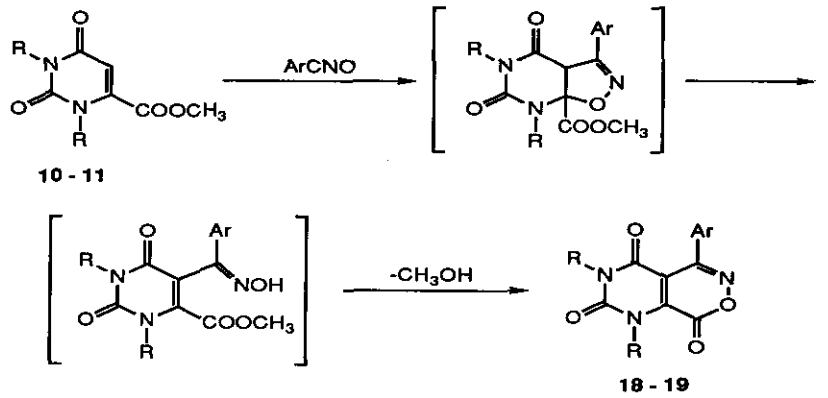
3		6	A	no reaction
4			B	no reaction
5		7	A	no reaction
6			B	no reaction
7		8	A	 15 (27%)
8			B	 16 (63%)
9		9	A	17 (trace)  17 (50%)
10			B	
11		10	A[b]	 18 (26%)
12		11	A	 19 (72%)
13		12	A	 20 (21%)
14		13	A	no reaction
15		14	A	no reaction

[a]Method A: THF / Et_3N, room temperature, 3 days; Method B: toluene / reflux, 3 days.

[b]DMF was used as solvent.

Ar = 2,6-$Cl_2C_6H_3$.

As shown in **Table IV**, the reactions of **1** with 5-substituted pyrimidine derivatives (**5-7**) have failed irrespective of the used reaction conditions (entries 1-6). 1,3,6-Trimethyluracil (**8**) afforded the desired products (**15**) and (**16**) according to the reaction conditions, which was the same results as observed in the case of **4b-e**. 1,3-Dimethyl-6-chlorouracil (**9**) afforded **17**, the dehydrochlorinated product of the initially formed cycloaddition product. Methyl orotate (**10**) and its 1,3-dimethyl derivative (**11**) afforded the corresponding oxazinone derivatives (**18**) and (**19**), respectively. These compounds could be obtained as shown in equation (3).



(eq. 3)

Ar = 2,6-$Cl_2C_6H_3$

In the case of 4-methoxy-1-methyl-2-pyrimidinol (**12**), we could obtain the desired oxime derivative (**20**) in low yield. However, with 2,4-dimethoxypyrimidine (**13**) and 1,3-dimethyl-6-azauracil (**14**) where the dipolarophilic reactivity of the double bond was decreased due to the increased aromaticity of the ring, we could not obtain any of the desired products.

In summary, we examined the reactions of 2,6-dichlorobenzonitrile oxide with various kinds of pyrimidine derivatives. 1,3-Disubstituted uracil derivatives afforded the corresponding oxime derivatives or dihydroisoxazolopyrimidine derivatives depending on the reaction conditions. The oxime derivatives were derived from the ring-opening reaction of the initially formed [3+2] dipolar cycloaddition products (dihydroisoxazolopyrimidine derivatives) by base (Et_3N) or polar solvents such as DMF or THF. In acetone solution, *Z* oxime derivatives were isomerized to the more stable *E* oxime derivatives. The reactivity of other pyrimidine derivatives that have 5- or 6-substituent toward nitrile oxide was also examined. 5-Substituted pyrimidine derivatives did not reacted with 2,6-dichlorobenzonitrile oxide, whereas 6-substituted derivatives afforded the

corresponding products. It is interesting to note that the oxazinone derivatives could be obtained from the orotic acid derivatives.

EXPERIMENTAL

General Remarks. Melting points were measured with a Thomas-Hoover melting point apparatus and are uncorrected. ^{1}H Nmr spectra were recorded on a Bruker AM-300 Nmr Spectrometer with TMS as an internal standard. Mass spectra were recorded on a Shimadzu QP 1000 Spectrometer. Elemental analyses for C, H, and N were performed with Perkin-Elmer 240 C Elemental Analyzer. Thin layer chromatography (tlc) was carried out with precoated silica gel plates (Kieselgel 60 F-254, Merck). Flash chromatography was performed using 230-400 mesh Kieselgel 60 (E. Merck).

Materials. 1,3-Dialkyluracil derivatives (**2b-d**), 1,3-dibenzyluracil derivatives (**2e-g**), and 1,3-dimethyluracil derivatives (**5-8**) that have substituent at C-5 or C-6 position were prepared from the corresponding uracil derivatives by the general procedures.[5] 1,3-Dimethyl-6-chlorouracil (**9**) was prepared from 1,3-dimethylbarbituric acid with phosphorous oxychloride according to the literature method.[6] 1,3-Dimethyl methylorotate (**11**) was prepared by esterification of the 1,3-dimethylorotic acid.[7] 4-Methoxy-1-methyl-2-pyrimidinol (**12**) was prepared from 2,4-dimethoxypyrimidine with methyl iodide according to the reported procedure.[8] 1,3-Dimethyl-6-azauracil (**14**) was prepared from 6-azauracil with *N,N*-dimethylformamide dimethylacetal according to the literature method.[9] All the starting materials thus prepared were identified by their mp, mass spectra, and ^{1}H nmr spectra.

Synthesis of 5-(2,6-Dichlorobenzoyl)uracil Oxime (3a). To a stirred solution of uracil (**2a**, 1.12 g, 10 mmol) and 2,6-dichlorobenzohydroximoyl chloride (**1**, 2.25 g, 10 mmol) in DMF (120 ml) was added dropwise triethylamine (1.11 g, 11 mmol) in DMF (5 ml) at room temperature. The reaction mixture was stirred for 3 days, and then poured into cold 1 N HCl solution (250 ml). Ether (200 ml) was added, and the mixture was stirred for 10 min. White solids formed near the interface of two layers were filtered, washed with water and ether. This solid was further purified by column chromatography (CH_2Cl_2 / MeOH, 9 : 1) to afford the desired product as a white solid (610 mg, 20%): mp 201-203 °C (decomp.); ^{1}H nmr (DMSO-d_6) δ 7.38-7.60 (m, 3H), 7.71 (s, 1H, H6), 11.74 (s, 1H), 11.87 (s, 1H); ms (70 eV) m/z (rel intensity) 44 (57), 75 (52), 124 (68), 173 (97), 175 (51), 187 (92), 189 (62), 221 (100), 264 (78), 299 (M^+, 5). Anal. Calcd for $C_{11}H_7N_3O_3Cl_2$: C, 44.03;

H, 2.35; N, 14.00. Found: C, 44.23; H, 2.47; N, 13.89.

Synthesis of 1,3-Diethyl-5-(2,6-dichlorobenzoyl)uracil Oxime (3c); General Procedure: To a stirred solution of 1,3-diethyluracil (**2c**, 1.68 g, 10 mmol) and **1** (2.25 g, 10 mmol) in dry THF (50 ml) was added, drop-by-drop, Et_3N (1.10 g, 11 mmol) in THF (10 ml) over 1 h. The mixture was stirred at room temperature for 3 days. After removal of the precipitate by filtration, the filtrate was evaporated. The residual solid materials were purified by column chromatography (CH_2Cl_2, then Et_2O) to give pure product **3c** as a white solid (2.28 g, 64 %): mp 188-190 °C; ^{1}H nmr (DMSO-d_6) δ 1.01 (t, J = 6.7 Hz, 3H), 1.22 (t, J = 6.7 Hz, 3H), 3.75 (q, J = 6.7 Hz, 2H), 3.90 (q, J = 6.7 Hz, 2H), 7.32-7.46 (m, 3H, Ar), 8.65 (s, 1H, H6), 12.14 (s, 1H, oxime proton); ms (70 eV) m/z (rel intensity) 56 (13), 291 (12), 292 (15), 319 (93), 320 (100), 322 (36), 355 (M^+, 8). Anal. Calcd for $C_{15}H_{15}N_3O_3Cl_2$: C, 50.58; H, 4.24; N, 11.80. Found: C, 50.31; H, 4.29; N, 11.71.

1,3-Dipropyl-5-(2,6-dichlorobenzoyl)uracil Oxime (3d): yield, 1.88 g (49%); mp 190-192 °C; ^{1}H nmr (DMSO-d_6) δ 0.77 (t, J = 7.4 Hz, 3H), 0.88 (t, J = 7.4 Hz, 3H), 1.43 (app. sextet, J = 7.0 Hz, 2H), 1.63 (app. sextet, J = 7.3 Hz, 2H), 3.68 (t, J = 7.3 Hz, 2H), 3.84 (t, J = 6.9 Hz, 2H), 7.32-7.46 (m, 3H), 8.60 (s, 1H, H6), 12.13 (s, 1H, oxime proton); ms (70 eV) m/z (rel intensity) 41 (22), 43 (31), 348 (100), 350 (35), 384 (M^++1, 17). Anal. Calcd for $C_{17}H_{19}N_3O_3Cl_2$: C, 53.14; H, 4.98; N, 10.94. Found: C, 52.89; H, 4.81; N, 11.02.

1,3-Dibenzyl-5-(2,6-dichlorobenzoyl)uracil Oxime (3e): yield, 3.69 g (77%); mp broad (127~132 °C); ^{1}H nmr (DMSO-d_6) δ 4.91 (s, 2H), 5.11 (s, 2H), 7.10-7.46 (m, 13H), 8.79 (s, 1H, H6), 12.17 (s, 1H, oxime proton); ms (70 eV) m/z (rel intensity) 91 (100), 444 (31), 479 (M^+, 7). Anal. Calcd for $C_{25}H_{19}N_3O_3Cl_2$: C, 62.51; H, 3.99; N, 8.75. Found: C, 62.47; H, 3.73; N, 8.70.

1,3-Di-(p-methoxybenzyl)-5-(2,6-dichlorobenzoyl)uracil Oxime (3f): yield, 3.35 g (62%); mp 172-174 °C; ^{1}H nmr (DMSO-d_6) δ 3.70 (s, 3H), 3.74 (s, 3H), 4.84 (s, 2H), 5.02 (s, 2H), 6.80-7.47 (m, 11H), 8.74 (s, 1H, H6), 12.13 (s, 1H, oxime proton); ms (70 eV) m/z (rel intensity) 91 (25), 121 (100), 539 (M^+, 3), 541 (2).

1,3-Di-(p-nitrobenzyl)-5-(2,6-dichlorobenzoyl)uracil Oxime (3g): yield, 2.11 g (37%); ^{1}H nmr (DMSO-d_6) δ 5.04 (s, 2H), 5.30 (s, 2H), 7.33-8.28 (m, 11H), 8.90 (s, 1H, H6), 12.25 (s, 1H, oxime proton); ms (70 eV) m/z (rel intensity) 89 (58), 136 (38), 356 (100), 534 (M^+-Cl, 26).

Synthesis of 3-(2,6-Dichlorophenyl)-5,7-diethyl-8,9-dihydroisoxazolo[5,4-*d*]pyrimidine-4, 6(5H, 7H)-dione (4c); General Procedure: A stirred solution of **1** (1.13 g, 5 mmol) and **2c** (0.84 g, 5 mmol) in dry toluene (30 ml) was heated to reflux for 3 days under a gentle stream of

nitrogen to remove the liberated HCl. After evaporation of the solvent *in vacuo*, column chromatographic purification on silica gel (CH_2Cl_2) afforded pure product **4c** as a white solid (1.53 g, 86%): mp 167-168 °C; ^{1}H nmr (benzene-d_6) δ 1.09 (t, J = 7.0 Hz, 3H), 1.14 (t, J = 7.0 Hz, 3H), 3.14 (app. sextet, J = 7.0 Hz, 1H), 3.56 (app. sextet, J = 7.0 Hz, 1H), 3.81 (qd, J = 7.1 and 1.7 Hz, 2H), 4.14 (d, J = 9.2 Hz, 1H), 4.96 (d, J = 9.2 Hz, 1H), 6.35 (t, J = 8.1 Hz, 1H, Ar), 6.74 (d, J = 8.1 Hz, 2H, Ar); ms (70 eV) m/z (rel intensity) 56 (18), 194 (10), 292 (15), 320 (100), 322 (36), 355 (M^+, 7). Anal. Calcd for $C_{15}H_{15}N_3O_3Cl_2$: C, 50.58; H, 4.24; N, 11.80. Found: C, 50.29; H, 4.29; N, 11.77.

3-(2,6-Dichlorophenyl)-5,7-dipropyl-8,9-dihydroisoxazolo[5,4-*d*]pyrimidine-4,6(5H,7H)-dione (4d): yield, 1.47 g (76%); mp 122-124 °C; ^{1}H nmr (benzene-d_6) δ 0.84 (t, J = 7.5 Hz, 3H), 0.90 (t, J = 7.5 Hz, 3H), 1.64-1.85 (m, 4H), 3.22 (dt, J = 13.8 and 7.7 Hz, 1H), 3.66 (dt, J = 13.8 and 7.7 Hz, 1H), 3.89 (td, 2H), 4.28 (d, J = 9.2 Hz, 1H), 5.14 (d, J = 9.2 Hz, 1H), 6.48 (t, J = 8.2 Hz, 1H, Ar), 6.87 (d, J = 8.2 Hz, 2H, Ar); ms (70 eV) m/z (rel intensity) 42 (64), 43 (73), 82 (55), 113 (42), 153 (100), 154 (97), 155 (68), 196 (84), 383 (M^++1, 20). Anal. Calcd for $C_{17}H_{19}N_3O_3Cl_2$: C, 53.14; H, 4.98; N, 10.94. Found: C, 52.95; H, 4.94; N, 10.83.

3-(2,6-Dichlorophenyl)-5,7-dibenzyl-8,9-dihydroisoxazolo[5,4-*d*]pyrimidine-4,6(5H,7H)-dione (4e): yield, 1.20 g (50%); mp 127-132 °C; ^{1}H nmr (benzene-d_6) δ 3.95 (d, J = 9.3 Hz, 1H, H9), 4.30 (d, J = 14.7 Hz, 1H, benzyl), 4.96 (dd, J = 38.7 and 13.7 Hz, 2H, benzyl), 5.07 (d, J = 9.3 Hz, 1H, H8), 5.14 (d, J = 14.7 Hz, 1H, benzyl), 6.34 (t, J = 8.2 Hz, 1H, Ar), 6.86 (d, J = 8.2 Hz, 2H, Ar), 7.00-7.60 (m, 10H, Ar); ms (70 eV) m/z (rel intensity) 91 (100), 444 (31), 445 (10), 446 (11), 479 (M^+, 7), 480 (3), 481 (5). Anal. Calcd for $C_{25}H_{19}N_3O_3Cl_2$: C, 62.51; H, 3.99; N, 8.75. Found: C, 62.31; H, 4.02; N, 8.77.

Synthesis of 1,3-Dimethyl-5-(2,6-dichlorobenzoyl)-6-methyluracil Oxime (15): **15** was prepared from **8** (770 mg, 5 mmol) and **1** (1.13 g, 5 mmol) in the manner described above for the preparation of **3c**: yield, 460 mg (27%); mp 244-245 °C (decomp.); ^{1}H nmr (DMSO-d_6) δ 2.28 (s, 3H), 3.08 (s, 3H), 3.45 (s, 3H), 7.31-7.47 (m, 3H, Ar), 12.12 (s, 1H, oxime proton); ms (70 eV) m/z (rel intensity) 56 (100), 306 (57), 308 (20), 341 (M^+, 4), 343 (3). Anal. Calcd for $C_{14}H_{13}N_3O_3Cl_2$: C, 49.14; H, 3.83; N, 12.28. Found: C, 48.93; H, 3.87; N, 12.27.

Synthesis of 3-(2,6-Dichlorophenyl)-5,7,8-trimethyl-8,9-dihydroisoxazolo[5,4-*d*]pyrimidine-4,6(5H,7H)-dione (16): **16** was prepared from **8** (770 mg, 5 mmol) and **1** (1.13 g, 5 mmol) in the manner described above for the preparation of **4c**: yield, 1.08 g (63%); mp 172-174 °C;

^{1}H nmr (DMSO-d_6) δ 1.89 (s, 3H), 3.00 (s, 3H), 3.02 (s, 3H), 4.94 (s, 1H), 7.53-7.68 (m, 3H); ms (70 eV) m/z (rel intensity) 56 (45), 97 (26), 154 (100), 341 (M^+, 4). Anal. Calcd for $C_{14}H_{13}N_3O_3Cl_2$: C, 49.14; H, 3.83; N, 12.28. Found: C, 49.09; H, 3.83; N, 12.32.

Synthesis of 3-(2,6-Dichlorophenyl)-5,7-dimethylisoxazolo[5,4-*d*]pyrimidine-4,6-dione (17): **17** was prepared from **9** (875 mg, 5 mmol) and **1** (1.13 g, 5 mmol) in the manner described above for the preparation of **4c**: yield, 814 mg (50%); mp 199-201 °C (decomp.); ^{1}H nmr ($CDCl_3$) δ 3.36 (s, 3H), 3.68 (s, 3H), 7.35-7.60 (m, 3H); ms (70 eV) m/z (rel intensity) 57 (37), 148 (39), 211 (52), 213 (38), 290 (100), 325 (M^+, 8). Anal. Calcd for $C_{13}H_9N_3O_3Cl_2$: C, 47.88; H, 2.78; N, 12.88. Found: C, 47.39; H, 2.77; N, 12.83.

Synthesis of Oxazinone Derivative 18: **18** was prepared from **10** (850 mg, 5 mmol) and **1** (1.13 g, 5 mmol) in the manner described above for the preparation of **3a**: yield, 424 mg (26%); mp 227-229 °C (decomp.); ^{1}H nmr (DMSO-d_6) δ 7.50-7.70 (m, 3H), 12.00 (s, 1H), 12.70 (br s, 1H); ms (20 eV) m/z (rel intensity) 155 (7), 290 (M^+-Cl, 79), 291 (100), 292 (84), 293 (36), 325 (M^+, 3), 326 (4), 327 (3), 328 (3). Anal. Calcd for $C_{12}H_5N_3O_4Cl_2$: C, 44.17; H, 1.53; N, 12.88. Found: C, 44.08; H, 1.59; N, 12.87.

Synthesis of Oxazinone Derivative 19: **19** was prepared from **11** (990 mg, 5 mmol) and **1** (1.13 g, 5 mmol) in the manner described above for the preparation of **3c**: yield, 1.28 g (72%); mp 264-265 °C (decomp.); ^{1}H nmr (DMSO-d_6) δ 3.17 (s, 3H), 3.82 (s, 3H), 7.50-7.65 (m, 3H); ms (20 eV) m/z (rel intensity) 211 (5), 318 (M^+-Cl, 82), 319 (100), 320 (48), 321 (36). Anal. Calcd for $C_{14}H_9N_3O_4Cl_2$: C, 47.46; H, 2.54; N, 11.86. Found: C, 47.42; H, 2.57; N, 11.83.

Synthesis of 1-Methyl-4-methoxy-5-(2,6-dichlorobenzoyl)uracil Oxime (20): **20** was prepared from **12** (560 mg, 5 mmol) and **1** (1.13 g, 5 mmol) in the manner described above for the preparation of **3c**: yield, 345 mg (21%); mp 194-196 °C; ^{1}H nmr (DMSO-d_6) δ 3.44 (s, 3H), 3.63 (s, 3H), 7.39-7.54 (m, 3H), 8.51 (s, 1H, H6), 12.12 (s, 1H, oxime proton); ms (70 eV) m/z (rel intensity) 42 (59), 176 (28), 252 (25), 253 (27), 254 (25), 260 (25), 285 (100), 292 (49), 327 (M^+, 6), 329 (4). Anal. Calcd for $C_{13}H_{10}N_3O_3Cl_2$: C, 47.71; H, 3.06; N, 12.84. Found: C, 47.75; H, 3.11; N, 12.80.

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