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TETRAHEDRON

An Easy Strategy for the Synthesis of 5-Phosphorylated Pyrimidin-2,4-diones from β-Phosphine Oxide and Phosphonate Enamines

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Abstract: An easy and efficient synthesis of pyrimidin-2,4-diones substituted with a phosphine oxide or phosphonate group in the 5-position is described. The key step is the cyclization of functionalized amides, with ethyl chloroformate in the presence of base. In the same way, functionalized thioamides afforded substituted 5-phosphorylated 2-oxo-pyrimidin-4-thiones.

Pyrimidone ring systems represent an important class of compounds,[1] within which 2,4-dioxo-pyrimidines constitute a part of the backbone of the antibiotic Sparsomycin[2a] and have been used for molecular recognition and self-replication.[2b] Likewise, *uracil* **I** (Scheme 1) is an important naturally occurring pyrimidine base, which is a constituent of nucleic acids[3a] and can be used for the preparation of biologically active enzymatic inhibitors,[3b] oligonucleotides[3c] or nucleosides.[3d] *5-Fluoracil*[4a,b] **IIa** and its derivatives,[4c,d] mainly *tegafur* (1-(2-tetrahydrofuryl)-5-fluorouracil) **IIb** alone, or in combination with cisplatin,[4e] have been widely used for cancer therapy while *orotic acid* **III** has been recently applied to industrial enzymatic production of cytidine diphosphate (CDP) choline[5a] and pyrimidine nucleotides[5b] and used for the protection of post heart attacks against global ischemia[5c] and for the formation of palladium and platinum compounds with antitumour activity.[5d]

With this in mind and taking into account the importance of regioselective functionalization[6a] at the 5-position of uracil derivatives, as has been observed for 5-substituted fluoro compounds[4] **II**, we are interested in the design of new pyrimidone derivatives substituted with a phosphine oxide or a phosphonate in the 5-position of the heterocyclic system. These substituents could regulate important biological functions and could increase the biological activity of these types of compounds in a similar way to that reported for other pharmaceuticals.[6b,c]

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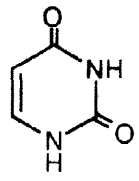
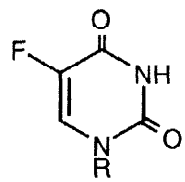
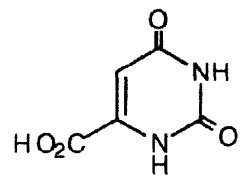


I Uracil



IIa R = H 5-Fluoracil

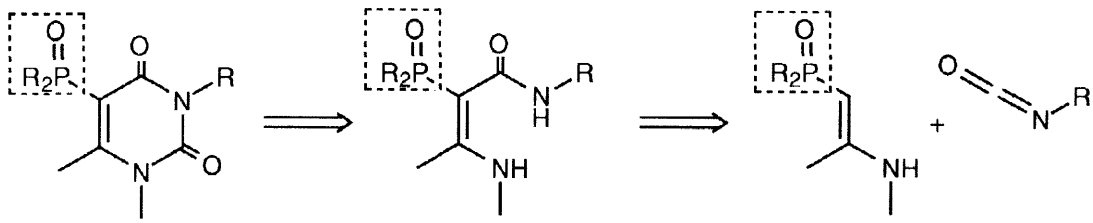
IIb R = thf Tegafur



III Orotic acid

Scheme 1

Classical approaches[1] to pyrimidin-2,4-diones have been reported and recently the preparation of phosphonoalkyl substituted uracils has been described.[7] However, to the best of our knowledge, the synthesis of phosphorus substituted pyrimidin-2,4-dione derivatives has not been reported. In this context and in connection with our interest in the synthesis of five[8] and six[9] membered phosphorylated nitrogen heterocycles we have used β-functionalized enamines derived from phosphazenes, phosphonium salts, phosphine oxides and phosphonates as synthetic intermediates in the synthesis of acyclic derivatives such as oximes,[10a] allylamines,[10b] hydrazones,[10c] azadienes,[10d] aminodienes[10e] and β-amino functionalized compounds[10f,g] as well as of phosphorus containing heterocycles.[11] Furthermore, in previous papers we have reported a preparation of primary β-enamines derived from phosphazenes[12] and from phosphonates[9d] and we have used them in the synthesis of cyclic[8a,9b,d,11a,13] and acyclic[10g,12] compounds. Continuing with our interest in the synthesis of new phosphorus heterocycles and with the reactivity of functionalized enamines, we report here an easy and high yielding synthesis of 5-phosphonyl pyrimidin-2,4-dione derivatives **IV**, from ethylchloroformate and amide-enamines or amide-enehydrazines containing a phosphoryl or a phosphonyl group **V**, prepared from functionalized enamines[11a,14] or ene hydrazines[15] **VI** (Scheme 2).

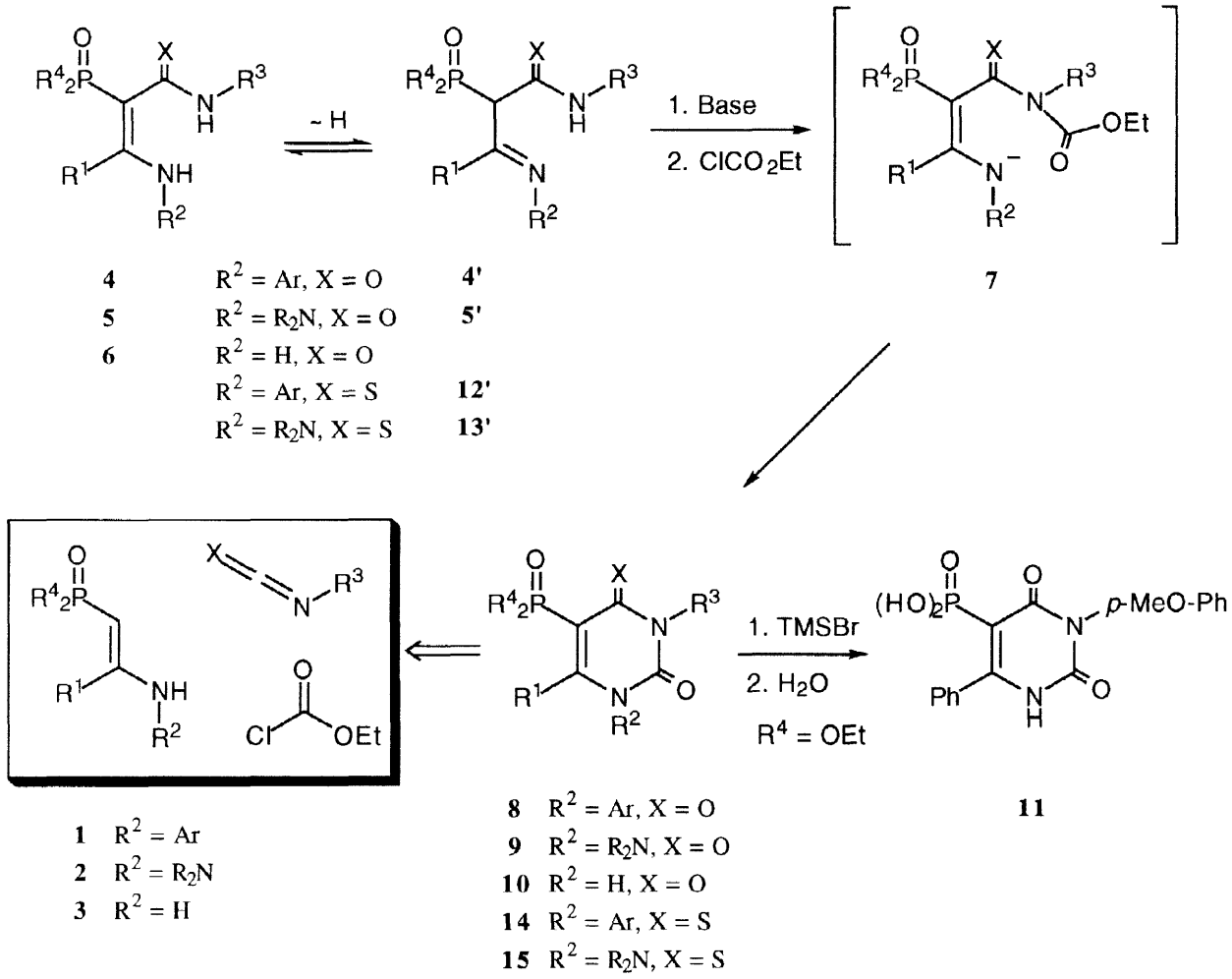


IV **V** **VI**

Scheme 2

Functionalized secondary β-enamino (R^2 = Ar) **4** and β-ene hydrazino amides ($R^2 = R_2N$) **5** were easily prepared by reaction of β-enamines[14] **1** and β-ene hydrazines[15] **2** derived from phosphine oxides and phosphonates with isocyanates (see Experimental Section). The reaction of enamino-amides, derived from phosphine oxides (**4**, R^4 = Ph), with ethylchloroformate in the presence of MeLi (1.6 M in Et_2O) and aqueous work-up gave high yields of 5-phosphoryl-2,4-dioxo-pyrimidines **8** (see Table 1, entries 1-3). The formation of these heterocycles **8** can be explained by cyclocondensation reaction of adducts **7** and insertion of the

carbonyl group between both nitrogen atoms to give 5-phosphoryl-2,4-dioxopyrimidines **8** (Scheme 3). Compounds **8** were characterized on the basis of their spectroscopic data. Thus, in the ^{31}P-NMR spectrum of compound **8a** the phosphoryl group resonates at δ_P = 29.0 ppm while the ^{13}C-NMR spectrum of this compound **8a** showed absorption at δ_C = 151.7 ppm for the urea carbonyl group, as well as doublets at δ_C = 161.7 ppm with a $^2J_{PC}$ = 11.3 Hz, at δ_C = 103.1 ppm with a $^1J_{PC}$ = 115.3 Hz and at δ_C = 164.1 ppm with a $^2J_{PC}$ = 12.2 Hz for the heterocyclic carbon atoms C-4, C-5 and C-6. In a similar way, the use of a mixture[14] of enamino and imino-amides **4/4'd** (66:34) led to the formation of 2,4-dioxo-pyrimidine **8d** (see Table 1, entry 4).



4 R^2 = Ar, X = O **4'**
5 R^2 = R_2N, X = O **5'**
6 R^2 = H, X = O
R^2 = Ar, X = S **12'**
R^2 = R_2N, X = S **13'**

7

1 R^2 = Ar
2 R^2 = R_2N
3 R^2 = H

8 R^2 = Ar, X = O
9 R^2 = R_2N, X = O
10 R^2 = H, X = O
14 R^2 = Ar, X = S
15 R^2 = R_2N, X = S

11

Scheme 3

This methodology, used for the preparation of pyrimidin-2,4-diones derived from phosphine oxides **8**, can also be applied to amino substituted (R^2 = R_2N) compounds **9** (Table 1, entries 5-9) when mixtures of amido-enehydrazines and -hydrazones[15] **5/5'a-e** are used. Likewise, pyrimidin-2,4-diones derived from phosphine oxides **8** and **9** were alternatively prepared in a "one pot" synthesis from isocyanates and β-enamine **1** or β-ene hydrazines **2**, when crude 1:1 adducts **4** and **5/5'** are directly treated, without their isolation, with base in THF (Table 1, entries 1, 5, 6). However, the reaction of substituted amido-enamines **4e,f** and amido-

enehydrazines **5f-i** derived from phosphonates (R^4 = OEt) does not allow us the preparation of the corresponding pyrimidin-2,4-diones **8** and **9** recovering the starting functionalized phosphonates **4** and **5**.

These results prompted us to extend this process and to explore whether primary enamino-amides derived from phosphonates **6** with ethyl chloroformate showed a similar reaction pattern leading to new pyrimidin-2,4-diones with phosphonic ester group **10**, in order to enhance the scope and the synthetic use of this reaction. Treatment of primary enamino-amides[11a] **6** with ethyl chloroformate in the presence of **BuLi** (1.6 **M** in hexanes) at 0 °C led to the formation of 5-phosphorylated pyrimidin-2,4-diones (**10**, R^4 = OEt) in excellent yields (Table 1, entries 10-12). Taking into account the interest in aminophosphonic acid derivatives,[6b,c,16,17] the ester cleavage of phosphonates was explored. Phosphorylated pyrimidin-2,4-dione (**10c**, R^4 = OEt) underwent ester cleavage with trimethylsilyl bromide[8e] in chloroform followed by hydrolysis with water to give heterocycle **11**.

Table 1. Pyrimidin-2,4-diones **8**, **9** and **10** and 2-oxopyrimidin-4-thiones **14** and **15** obtained.

Entry	Comp.	R^1	R^2	R^3	R^4	Yield (%)	m.p. (°C)
1	**8a**	Me	*p*-Me-Ph	Ph	Ph	81[a] 66[b]	> 275
2	**8b**	Me	*p*-Me-Ph	Et	Ph	76[a]	105-106
3	**8c**	Et	*p*-Me-Ph	Ph	Ph	71[a]	> 275
4	**8d**	*p*-Me-Bn	*p*-Me-Ph	Ph	Ph	66[c]	216-217
5	**9a**	Me	Me_2N	Ph	Ph	88[d] 73[e]	203-204
6	**9b**	Me	Me_2N	Et	Ph	80[d] 70[e]	215-216
7	**9c**	Me	Me_2N	*p*-Me-Ph	Ph	77[d]	231-232
8	**9d**	Et	Me_2N	Ph	Ph	81[d]	175-176
9	**9e**	Et	Me_2N	Et	Ph	85[d]	184-185
10	**10a**	*p*-Me-Ph	H	Ph	OEt	66[f]	211-212
11	**10b**	Ph	H	Ph	OEt	71[f]	224-225
12	**10c**	Ph	H	*p*-MeO-Ph	OEt	59[f]	221-222
13	**11**	Ph	H	*p*-MeO-Ph	OH	82[g]	265 (dec)
14	**14a**	Me	*p*-Me-Ph	Ph	Ph	74[h]	275-276
15	**14b**	Et	*p*-Me-Ph	Ph	Ph	77[h]	235-236
16	**15a**	Me	Me_2N	Ph	Ph	78[i]	236-237
17	**15b**	Me	Me_2N	Et	Ph	76[i]	215-216

[a] Yield of isolated products **8** based on **4**. [b] Yield of isolated products **8** in "one pot" reaction from **1**. [c] Yield of isolated product **8d** based on **4/4'd**. [d] Yield of isolated products **9** based on **5/5'**. [e] Yield of isolated products **9** in "one pot" reaction from **2**. [f] Yield of isolated products **10** based on **6**. [g] Yield of isolated product **11** based on **10c**. [h] Yield of isolated products **14** based on **12'**. [i] Yield of isolated products **15** based on **13'**.

This methodology used for the preparation of pyrimidin-2,4-diones **8-10** can also be applied to the synthesis of 2-oxo-pyrimidin-4-thiones **14** and **15** when imino-thioamides[14] **12'** or hydrazono-thioamides[15] **13'** are used. The reaction of imino-thioamides[14] **12'** or hydrazono-thioamides[15] **13'** with ethyl chloroformate

in the presence of base (Scheme 3), gave substituted 2-oxo-pyrimidin-4-thiones **14** and **15** in excellent yields (Table 1, entries 14-17).

In conclusion, the synthesis described in this paper provides an efficient and easy access to pyrimidin-2,4-diones **8-10** and the corresponding 2-oxo-pyrimidin-4-thio derivatives **14**, **15** substituted with a phosphine oxide or a phosphonate group in the 5-position, making use of readily available starting materials.

ACKNOWLEDGEMENTS

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EXPERIMENTAL SECTION

General directions have been described previously.[11a]

General procedure for the reaction of enamine carbanions derived from phosphine oxides 1 (R^4=Ph) and phosphonates 1 (R^4=OEt) with isocyanates or isothiocyanates. For experimental details for preparation of compounds **4a**, **4c**, **4/4'd** (66:34), **4e** and **12'a** and NMR spectroscopic data, see reference 9c. Compounds **4b**, **4f** and **12'b** were prepared similarly.

1-Ethylcarboxamide-2-*p*-tolylaminoprop-1-enyldiphenylphosphine oxide (4b). 1360 mg (65 %) of **4b** as a white solid. Data for **4b**: mp 128-129 °C; *^{1}H-NMR* (300 MHz) 0.93 (t, 3H, $^3J_{HH}$ = 7.2 Hz, CH_3), 1.41 (s, 3H, CH_3), 2.23 (s, 3H, CH_3), 3.15 (t, 2H, $^3J_{HH}$ = 7.2 Hz, CH_2), 6.85-7.80 (m, 14H, arom), 8.70 (s, 1H, NH), 10.90 (s, 1H, NH) ppm; *^{13}C-NMR* (75 MHz) 13.0 (CH_3), 20.4 (CH_3), 21.2 (d, $^3J_{PC}$ = 6.2 Hz, CH_3), 84.3 (d, $^1J_{PC}$ =115.1 Hz, C-P), 115.2-148.6 (C-arom), 164.1, 164.3 ppm; *^{31}P-NMR* (150 MHz) 34.4 ppm; *IR (KBr)* 3323, 2919, 1659, 1514, 1129 cm^{-1}; *MS* (70 eV) 418 (M^+, 5). Anal. Calcd for $C_{25}H_{27}N_2O_2P$: C, 71.77; H, 6.46; N, 6.70. Found: C, 71.85; H, 6.61; N, 6.59.

Diethyl 2-allylamino-1-phenylcarboxamideprop-1-enylphosphonate (4f). 710 mg (67 %) of **4f** as an oil. Data for **4f**: *^{1}H-NMR* (300 MHz) 1.26 (t, 6H, $^3J_{HH}$ = 7.0 Hz, CH_3), 2.16 (s, 3H, CH_3), 3.87 (m, 2H, CH_2-N), 4.04 (m, 4H, CH_2), 5.16 (m, 2H, CH_2=), 5.81 (m, 1H, CH=), 6.92-7.49 (m, 5H, arom), 11.29 (s, 1H, NH), 12.35 (s, 1H, NH) ppm; *^{13}C-NMR* (75 MHz) 15.9 and 16.0 (CH_3), 17.4 (d, $^3J_{PC}$ = 3.0 Hz, CH_3), 45.4 (CH_2-N), 61.2 and 61.3 (CH_2-O), 79.6 (d, $^1J_{PC}$ =196.9 Hz, C-P), 116.6 (CH_2=), 120.2 (CH=), 122.3-139.1 (C-arom), 169.7 (d, $^2J_{PC}$ = 19.6 Hz), 170.4 (d, $^2J_{PC}$ = 16.1 Hz) ppm; *^{31}P-NMR* (150 MHz) 28.4 ppm; *IR (KBr)* 3207, 2985, 1649, 1555, 1266, 1031 cm^{-1}; *MS* (70 eV) 352 (M^+, 8). Anal. Calcd for $C_{17}H_{25}N_2O_4P$: C, 57.95; H, 7.10; N, 7.95. Found: C, 57.67; H, 7.21; N, 7.69.

1-Phenylthiocarboxamide-2-*p*-tolyliminebutyldiphenylphosphine oxide (12'b). 1860 mg (75 %) of **12'b** as a white solid. Data for **12'b**: mp 154-155 °C; *^{1}H-NMR* (300 MHz) 0.91 (t, 3H, $^3J_{HH}$ = 7.8 Hz, CH_3), 2.06 (q, 2H, $^3J_{HH}$ = 7.8 Hz, CH_2), 2.24 (s, 3H, CH_3), 5.36 (d, 1H, $^2J_{PH}$ = 9.9 Hz, CH-P), 6.72-7.96 (m, 19H, arom), 11.74 (s, 1H, NH) ppm; *^{13}C-NMR* (75 MHz) 11.0 (CH_3), 20.8 (CH_3), 29.0 (CH_2), 65.7 (d, $^1J_{PC}$ = 47.8 Hz, C-P), 119.1-139.0 (C-arom), 169.8 (C=N), 189.0 (C=S) ppm; *^{31}P-NMR* (150 MHz) 29.5 ppm; *IR (KBr)* 3174, 3013, 1582, 1520, 1367 cm^{-1}; *MS* (70 eV) 496 (M^+, 21). Anal. Calcd for $C_{30}H_{29}N_2OPS$: C, 72.59; H, 5.85; N, 5.65. Found: C, 72.70; H, 5.93; N, 5.52.

General procedure for reaction of hydrazone carbanions derived from phosphine oxides 2 (R^4=Ph) and phosphonates 2 (R^4=OEt) with isocyanates or isothiocyanates. For experimental

details for preparation of compounds **5/5'a-e** (R^4 = Ph) and **13'a-b** (R^4 = Ph) and NMR spectroscopic data, see reference 15. General procedure for the preparation of compounds **5f-i** (R^4 = OEt): to a - 78 °C 1.6 M solution of MeLi in Et_2O (5 mmol) in THF (45 mL) was added a solution of diethyl β-*N,N*-dimethylhydrazonopropylphophonate **2**[10c] (R^1 = Me, R^4 = OEt) (1.18 g, 5 mmol) in THF (40 mL). The mixture was allowed to stir at this temperature for 1 h and a solution of isocyanate (5 mmol) in THF (10 mL) was then added at the same temperature. After the mixture was allowed to warm to rt, the reaction mixture was stirred at rt until *TLC* indicated the disappearance of the compound **2** (~ 24 h). The mixture was diluted with water (40 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with water, dried over $MgSO_4$, and concentrated. The crude residue was purified by flash-chromatography eluting with 1:1 Et_2O/hexanes.

Diethyl 2-(*N,N*-dimethylhydrazino)-1-phenylcarboxamideprop-1-enylphosphonate (5f). 1330 mg (75 %) of **5f** as an oil. Data for **5f**: *^{1}H-NMR* (300 MHz) 1.33 (t, 6H, $^3J_{HH}$ = 7.1 Hz, CH_3), 2.39 (s, 3H, CH_3), 2.57 (s, 6H, CH_3N), 4.08 (q, 4H, $^3J_{HH}$ = 7.1 Hz, OCH_2), 6.97-7.53 (m, 5H, arom), 8.45 (s, 1H, NH), 9.72 (s, 1H, NH) ppm; *^{13}C-NMR* (75 MHz) 14.5 (CH_3), 16.5 (CH_3), 47.9 (CH_3N), 61.5 (OCH_2), 80.3 (d,$^1J_{PC}$ = 174.5 Hz, C-P), 118.7-139.2 (C-arom), 169.8, 170.3 ppm; *^{31}P-NMR* (150 MHz) 27.9 ppm; *IR (KBr)* 3560, 3279, 2785, 1784, 1737, 1637 cm^{-1}; *MS* (70 eV) 355 (M^+, 19). Anal. Calcd for $C_{16}H_{26}N_3O_4P$: C, 54.06; H, 7.38; N, 11.83. Found: C, 54.16; H, 7.36; N, 11.86.

Diethyl 2-(*N,N*-dimethylhydrazino)-1-ethylcarboxamideprop-1-enylphosphonate (5g). 1120 mg (73 %) of **5g** as an oil. Data for **5g**: *^{1}H-NMR* (300 MHz) 1.09 (t, 6H, $^3J_{HH}$ = 7.2 Hz, CH_3), 1.25 (t, 3H, $^3J_{HH}$ = 7.1 Hz, CH_3), 2.28 (s, 3H, CH_3), 2.49 (s, 6H, CH_3N), 3.18 (q, 2H, $^3J_{HH}$ = 7.1 Hz, CH_2), 3.97 (q, 4H, $^3J_{HH}$ = 7.2 Hz, OCH_2), 8.72 (s, 1H, NH), 9.08 (s, 1H, NH) ppm; *^{13}C-NMR* (75 MHz) 13.6 (CH_3), 14.9 (CH_3), 15.0 (CH_3), 32.5 (CH_2), 46.7 (CH_3N), 59.7 (OCH_2), 76.1 (d, $^1J_{PC}$ = 198.4 Hz, C-P), 167.8 (d, $^2J_{PC}$ = 16.0 Hz), 169.7 (d, $^2J_{PC}$ = 19.5 Hz) ppm; *^{31}P-NMR* (150 MHz) 28.3 ppm; *IR (KBr)* 3572, 3495, 3270, 1621, 1425, 1270, 1032 cm^{-1}; *MS* (70 eV) 307 (M^+, 3). Anal. Calcd for $C_{12}H_{26}N_3O_4P$: C, 46.90; H, 8.53; N, 13.67. Found: C, 47.02; H, 8.50; N, 13.64.

Diethyl 1-^{t}butylcarboxamide-2-(*N,N*-dimethylhydrazino)prop-1-enylphosphonate (5h). 921 mg (55 %) of **5h** as an oil. Data for **5h**: *^{1}H-NMR* (300 MHz) 1.28 (t, 6H, $^3J_{HH}$ = 7.0 Hz, CH_3), 1.32 (s, 9H, CH_3), 2.29 (s, 3H, CH_3), 2.53 (s, 6H, CH_3N), 3.92-4.15 (m, 4H, OCH_2), 8.94 (s, 1H, NH), 12.55 (s, 1H, NH) ppm; *^{13}C-NMR* (75 MHz) 15.9 (CH_3), 16.0 (CH_3), 28.9 (CH_3), 47.8 (CH_3N), 50.1 (C), 60.8 (OCH_2), 78.1 (d, $^1J_{PC}$ = 196.9 Hz, C-P), 168.9 (d, $^2J_{PC}$ = 16.1 Hz), 170.5 (d, $^2J_{PC}$ = 19.6 Hz) ppm; *^{31}P-NMR* (150 MHz) 28.2 ppm; *IR (KBr)* 3264, 3078, 2965, 1554, 1281, 1222, 1023 cm^{-1}; *MS* (70 eV) 335 (M^+, 23). Anal. Calcd for $C_{14}H_{30}N_3O_4P$: C, 50.14; H, 9.02; N, 12.53. Found: C, 51.16; H, 8.99; N, 12.47.

Diethyl 2-(*N,N*-dimethylhydrazino)-1-*p*-methoxyphenylcarboxamideprop-1-enylphosphonate (5i). 1270 mg (66 %) of **5i** as an oil. Data for **5i**: *^{1}H-NMR* (300 MHz) 1.31 (t, 6H, $^3J_{HH}$ = 6.9 Hz, CH_3), 2.36 (s, 3H, CH_3), 2.54 (s, 6H, CH_3N), 3.74 (s, 3H, OCH_3), 3.98-4.13 (m, 4H, OCH_2), 6.77-7.40 (m, 4H, AA'BB' system), 11.09 (s, 1H, NH), 12.66 (s, 1H, NH) ppm; *^{13}C-NMR* (75 MHz) 15.8 (CH_3), 16.1 (CH_3), 47.6 (CH_3N), 55.0 (OCH_3), 61.1 (OCH_2), 77.0 (d, $^1J_{PC}$ = 197.3 Hz, C-P), 113.5, 122.1, 132.0, 155.2 (C-arom), 169.2 (d, $^2J_{PC}$ = 20.1 Hz), 169.6 (d, $^2J_{PC}$ = 16.1 Hz) ppm; *^{31}P-NMR* (150 MHz) 27.7 ppm; *IR (KBr)* 3201, 3061, 2987, 1538, 1235, 1020 cm^{-1}; *MS* (70 eV) 385 (M^+, 19). Anal. Calcd for $C_{17}H_{28}N_3O_5P$: C, 52.98; H, 7.32; N, 10.90. Found: C, 53.20; H, 7.11; N, 10.67.

General procedure for reaction of enamine carbanions derived from phosphonates 3 (R^4=OEt) with isocyanates. To a 0 °C 1.6 M solution of BuLi in hexanes (5 mmol) in THF (25 mL) was added a solution of β-enaminophosphonate **3**[9d] (R^4 = OEt) (5 mmol) in THF (40 mL). The mixture was allowed to stir at this temperature for 1 h and a solution of isocyanate (5 mmol) in THF (10 mL) was then added at the same temperature. After the mixture was allowed to warm to rt, the reaction mixture was stirred at rt until *TLC* indicated the disappearance of the compound **3** (~ 15 h). The mixture was diluted with water (40 mL) and

extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with water, dried over $MgSO_4$, and concentrated. The crude residue was purified by flash-chromatography eluting with 1:1 AcOEt/hexanes.

Diethyl *E*-2-amino-1-phenylcarboxamide-2-*p*-tolylethenylphosphonate (6a). 890 mg (46 %) of **6a** as a white solid. Data for **6a**: mp 184-185 °C; *^{1}H-NMR* (300 MHz) 1.05 (t, 6H, $^3J_{HH}$ = 7.2 Hz, CH_3), 2.33 (s, 3H, CH_3), 3.77 (m, 4H, $^3J_{HH}$ = 7.2 Hz, OCH_2), 5.30 (s, 1H, NH), 7.13-7.54 (m, 9H, arom), 10.97 (s, 1H, NH), 11.24 (s, 1H, NH) ppm; *^{13}C-NMR* (75 MHz) 15.8 (CH_3), 21.4 (CH_3), 61.2 (OCH_2), 82.8 (d, $^1J_{PC}$ = 199.4 Hz, C-P), 120.5-139.4 (C-arom), 168.9 (d, $^2J_{PC}$ = 18.6 Hz, CN), 170.9 (d, $^2J_{PC}$ = 15.6 Hz, C=O) ppm; *^{31}P-NMR* (150 MHz) 24.8 ppm; *IR (KBr)* 3213, 3120, 3072, 1655, 1246 cm^{-1}; *MS* (70 eV) 388 (M^+, 16). Anal. Calcd for $C_{20}H_{25}N_2O_4P$: C, 61.85; H, 6.44; N, 7.22. Found: C, 61.62; H, 6.33; N, 7.48.

Diethyl *E*-2-amino-2-phenyl-1-phenylcarboxamideethenylphosphonate (6b). 900 mg (48 %) of **6b** as a white solid. Data for **6b**: mp 170-171 °C; *^{1}H-NMR* (300 MHz) 1.04 (m, 6H, CH_3), 3.76 (m, 4H, OCH_2), 5.29 (s, 1H, NH), 7.19-7.34 (m, 10H, arom), 10.99 (s, 1H, NH), 11.24 (s, 1H, NH) ppm; *^{13}C-NMR* (75 MHz) 15.7 (CH_3), 61.3 (OCH_2), 83.8 (d, $^1J_{PC}$ = 191.5 Hz, C-P), 118.5-139.1 (C-arom), 168.3 (d, $^2J_{PC}$ = 18.2 Hz, CN), 170.6 (d, $^2J_{PC}$ = 15.1 Hz, C=O) ppm; *^{31}P-NMR* (150 MHz) 24.7 ppm; *IR (KBr)* 3210, 3121, 3088, 1667, 1203 cm^{-1}; *MS* (70 eV) 374 (M^+, 9). Anal. Calcd for $C_{19}H_{23}N_2O_4P$: C, 60.96; H, 6.15; N, 7.49. Found: C, 61.13; H, 5.89; N, 7.40.

Diethyl *E*-2-amino-2-phenyl-1-*p*-methoxyphenylcarboxamideethenylphosphonate (6c). 830 mg (41 %) of **6c** as a white solid. Data for **6c**: mp 180-181 °C; *^{1}H-NMR* (300 MHz) 1.05 (m, 6H, CH_3), 3.73 (m, 4H, OCH_2), 3.74 (s, 3H, OCH_3), 5.48 (s, 1H, NH), 6.79-7.46 (m, 9H, arom), 10.96 (s, 1H, NH), 11.07 (s, 1H, NH) ppm; *^{13}C-NMR* (75 MHz) 15.7 (CH_3), 55.4 (OCH_3), 61.1 (OCH_2), 83.6 (d, $^1J_{PC}$ = 198.7 Hz, C-P), 113.8-155.7 (C-arom), 168.5 (d, $^2J_{PC}$ = 18.5 Hz, CN), 170.4 (d, $^2J_{PC}$ = 15.6 Hz, C=O) ppm; *^{31}P-NMR* (150 MHz) 24.9 ppm; *IR (KBr)* 3235, 3113, 3078, 1696, 1234 cm^{-1}; *MS* (70 eV) 404 (M^+, 42). Anal. Calcd for $C_{20}H_{25}N_2O_5P$: C, 59.40; H, 6.19; N, 6.93. Found: C, 59.23; H, 6.39; N, 7.07.

General procedure for the preparation of 5-phosphorylated pyrimidin-2,4-diones 8 and 2-oxopyrimidin-4-thiones 14. To a 0 °C solution of enamino-amide **4/4'** or imino-thioamide **12'** (3 mmol) in THF (20 mL) was added a 1.6 M solution of MeLi in Et_2O (2.19 mL, 3.5 mmol) in THF (10 mL). The mixture was allowed to stir at this temperature for 1 h and a solution of ethyl chloroformate (0.29 mL, 3 mmol) in THF (10 mL) was then added at the same temperature. After the mixture was allowed to warm to rt, the reaction mixture was stirred and refluxed until *TLC* indicated the disappearance of the compound **4/4'** or **12'** (~ 2-3 days). The mixture was diluted with water (30 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with water, dried over $MgSO_4$, and concentrated. The crude residue was purified by flash-chromatography eluting with 1:1 AcOEt/hexanes. An analytical sample was obtained by recrystallization from CH_2Cl_2/hexanes. Pyrimidin-2,4-diones **8** can also be obtained in "one pot" reaction: to a 0 °C solution of a mixture of enaminophosphine oxide and iminophosphine oxide **1** (3 mmol) in THF (20 mL) was added a 1.6 M solution of MeLi in Et_2O (2.19 mL, 3.5 mmol) in THF (10 mL). The mixture was allowed to stir at this temperature for 1 h and a solution of isocyanate (3 mmol) in THF (10 mL) was then added at the same temperature. After the mixture was allowed to warm to rt, the reaction mixture was stirred for 15 h at rt and a solution of ethyl chloroformate (0.29 mL, 3 mmol) in THF (10 mL) was then added at rt. Pyrimidin-2,4-diones **8** obtained was purified as described above.

5-Diphenylphosphinoyl-6-methyl-3-phenyl-1-*p*-tolylpyrimidin-2,4-dione (8a). 1400 mg (81 %) of **8a** as a white solid. Data for **8a**: mp >275 °C; *^{1}H-NMR* (300 MHz) 2.42 (s, 3H, CH_3), 2.67 (s, 3H, CH_3), 7.11-7.95 (m, 19H, arom) ppm; *^{13}C-NMR* (75 MHz) 18.9 (CH_3), 21.3 (CH_3), 103.1 (d, $^1J_{PC}$=115.3 Hz, C-P), 128.2-139.9 (C-arom), 151.7 (C=O), 161.7 (d, $^2J_{PC}$= 11.3 Hz, C=O), 164.1 (d, $^2J_{PC}$= 12.2 Hz, =C-N) ppm; *^{31}P-NMR* (150 MHz) 29.0 ppm; *IR (KBr)* 3031, 1721, 1569, 1401, 1193 cm^{-1}; *MS* (70 eV) 492 (M^+, 80). Anal. Calcd for $C_{30}H_{25}N_2O_3P$: C, 73.17; H, 5.08; N, 5.69. Found: C, 73.36; H, 5.19; N, 5.72.

5-Diphenylphosphinoyl-3-ethyl-6-methyl-1-*p*-tolylpyrimidin-2,4-dione (8b). 1010 mg (76 %) of **8b** as a white solid. Data for **8b**: mp 105-106 °C; *^{1}H-NMR* (300 MHz) 1.12 (t, $^3J_{HH}$ = 7.2 Hz, 3H, CH_3), 2.45 (s, 3H, CH_3), 2.58 (s, 3H, CH_3), 3.88 (q, $^3J_{HH}$ = 7.2 Hz, 2H, CH_2), 7.12-7.37 (m, 4H, AA'BB'system), 7.48-7.93 (m, 10H, arom) ppm; *^{13}C-NMR* (75 MHz) 12.6 (CH_3), 18.6 (CH_3), 21.2 (CH_3), 36.7 (CH_2), 101.6 (d, $^1J_{PC}$ =116.3 Hz, C-P), 128.0-139.7 (C-arom), 151.1 (C=O), 161.4 (d, $^2J_{PC}$ = 11.1 Hz), 163.2 (d, $^2J_{PC}$ = 12.6 Hz) ppm; *^{31}P-NMR* (150 MHz) 29.5 ppm; *IR* (*KBr*) 3210, 2986, 1716, 1657, 1407, 1130 cm^{-1}; *MS* (70 eV) 444 (M^+, 80). Anal. Calcd for $C_{26}H_{25}N_2O_3P$: C, 70.27; H, 5.63; N, 6.31. Found: C, 70.56; H, 5.49; N, 6.12.

5-Diphenylphosphinoyl-6-ethyl-3-phenyl-1-*p*-tolylpyrimidin-2,4-dione (8c). 1080 mg (71 %) of **8c** as a white solid. Data for **8c**: mp >275 °C; *^{1}H-NMR* (300 MHz) 1.07 (t, $^3J_{HH}$ = 7.3 Hz, 3H, CH_3), 2.35 (s, 3H, CH_3), 3.25 (q, $^3J_{HH}$ = 7.3 Hz, 2H, CH_2), 7.03-7.87 (m, 19H, arom) ppm; *^{13}C-NMR* (75 MHz) 14.8 (CH_3), 21.2 (CH_2), 22.9 (CH_3), 101.2 (d, $^1J_{PC}$ = 113.8 Hz, C-P), 128.0-139.7 (C-arom), 151.5 (C=O), 161.9 (d, $^2J_{PC}$ = 11.1 Hz, C=O), 169.4 (d, $^2J_{PC}$ = 12.1 Hz, =C-N) ppm; *^{31}P-NMR* (150 MHz) 28.5 ppm; *IR* (*KBr*) 2950, 1706, 1613, 1390, 1097 cm^{-1}; *MS* (70 eV) 506 (M^+, 32). Anal. Calcd for $C_{31}H_{27}N_2O_3P$: C, 73.51; H, 5.37; N, 5.53. Found: C, 73.76; H, 5.16; N, 5.42.

5-Diphenylphosphinoyl-3-phenyl-1-*p*-tolyl-6-*p*-tolylmethylenpyrimidin-2,4-dione (8d). 1920 mg (66 %) of **8d** as a white solid. Data for **8d**: mp 216-217 °C; *^{1}H-NMR* (300 MHz) 1.59 (s, 2H, CH_2), 2.20 (s, 3H, CH_3), 2.29 (s, 3H, CH_3), 7.03-7.87 (m, 23H, arom) ppm; *^{13}C-NMR* (75 MHz) 20.9 (CH_3), 21.1 (CH_3), 34.4 (CH_2), 104.2 (d, $^1J_{PC}$ =113.3 Hz, C-P), 127.9-139.2 (C-arom), 151.4 (C=O), 161.9 (d, $^2J_{PC}$ = 11.6 Hz, C=O), 165.1 (d, $^2J_{PC}$ = 12.1 Hz, =C-N) ppm; *^{31}P-NMR* (150 MHz) 28.8 ppm; *IR* (*KBr*) 3120, 2897, 1698, 1643, 1175 cm^{-1}; *MS* (70 eV) 582 (M^+, 20). Anal. Calcd for $C_{37}H_{31}N_2O_3P$: C, 76.27; H, 5.36; N, 4.81. Found: C, 76.66; H, 5.16; N, 4.42.

5-Diphenylphosphinoyl-6-methyl-2-oxo-3-phenyl-1-*p*-tolylpyrimidin-4-thione (14a). 1130 mg (74 %) of **14a** as a white solid. Data for **14a**: mp 275-276 °C; *^{1}H-NMR* (300 MHz) 2.35 (s, 3H, CH_3), 2.50 (s, 3H, CH_3), 7.00-7.86 (m, 19H, arom) ppm; *^{13}C-NMR* (75 MHz) 20.6 (CH_3), 20.7 (CH_3), 115.0 (d, $^1J_{PC}$ =121.8 Hz, C-P), 127.9-139.9 (C-arom), 149.4 (C=O), 160.3 (d, $^2J_{PC}$ = 15.1 Hz, =C-N), 160.3 (d, $^2J_{PC}$ = 15.1 Hz, C=S) ppm; *^{31}P-NMR* (150 MHz) 33.9 ppm; *IR* (*KBr*) 3021, 1721, 1569, 1401, 1176 cm^{-1}; *MS* (70 eV) 508 (M^+, 62). Anal. Calcd for $C_{30}H_{25}N_2O_2PS$: C, 70.87; H, 4.92; N, 5.51. Found: C, 70.66; H, 4.79; N, 5.70.

5-Diphenylphosphinoyl-6-ethyl-2-oxo-3-phenyl-1-*p*-tolylpyrimidin-4-thione (14b). 2010 mg (77 %) of **14b** as a white solid. Data for **14b**: mp 235-236 °C; *^{1}H-NMR* (300 MHz) 1.00 (t, $^3J_{HH}$ = 7.5 Hz, 3H, CH_3), 2.30 (s, 3H, CH_3), 3.29 (q, $^3J_{HH}$ = 7.5 Hz, 2H, CH_2), 6.98-7.84 (m, 19H, arom) ppm; *^{13}C-NMR* (75 MHz) 14.5 (CH_3), 21.2 (CH_3), 23.4 (CH_2), 113.1 (d, $^1J_{PC}$ = 121.4 Hz, C-P), 127.8-139.9 (C-arom), 149.4 (C=O), 165.7 (d, $^2J_{PC}$ = 16.1 Hz, =C-N), 190.0 (d, $^2J_{PC}$ = 5.6 Hz, C=S) ppm; *^{31}P-NMR* (150 MHz) 33.9 ppm; *IR* (*KBr*) 3402, 3086, 1703, 1542 cm^{-1}; *MS* (70 eV) 522 (M^+, 34). Anal. Calcd for $C_{31}H_{27}N_2O_2PS$: C, 71.26; H, 5.17; N, 5.36. Found: C, 71.66; H, 5.46; N, 5.49.

General procedure for the preparation of 5-phosphorylated pyrimidin-2,4-diones 9 and 2-oxopyrimidin-4-thiones 15. To a - 78 °C solution of LDA (5 mmol) in THF (45 mL) was added a solution of one hydrazino-amide **5/5'** or hydrazono-thioamide **13'** (5 mmol) in THF (40 mL). The mixture was allowed to stir at this temperature for 1 h and a solution of ethyl chloroformate (0.48 mL, 5 mmol) in THF (10 mL) was then added at the same temperature. After the mixture was allowed to warm to rt, the reaction mixture was stirred and refluxed until *TLC* indicated the disappearance of the compound **5/5'** or **13'** (~ 2-3 days). The mixture was diluted with water (40 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with water, dried over $MgSO_4$, and concentrated. The crude residue was purified by flash-chromatography eluting with EtO_2. Pyrimidin-2,4-diones **9** can also be obtained in a "one pot" reaction: to a - 78 °C solution of LDA (5 mmol) was added a solution β-N,N-dimethylhydrazonopropyldiphenylphophine oxide **2**[10c] (R^1 = Me, R^4 = Ph) (1.50 g, 5 mmol) in THF (40 mL). The mixture was allowed to stir at this temperature for 1 h and a solution of isocyanate (5 mmol) in THF (10 mL) was then added at the same

temperature. After the mixture was allowed to warm to rt, the reaction mixture was stirred for 3 h at rt and a solution of ethyl chloroformate (0.48 mL, 5 mmol) in THF (10 mL) was then added at rt. Pyrimidin-2,4-diones **9** obtained was purified as described above.

1-Dimethylamino-5-diphenylphosphinoyl-6-methyl-3-phenylpyrimidin-2,4-dione (9a). 1960 mg (88 %) of **9a** as a white solid. Data for **9a**: mp 203-204 °C; *^{1}H-NMR* (300 MHz) 2.96 (s, 6H, CH_3N), 3.03 (s, 3H, CH_3), 7.06-7.89 (m, 15H, arom) ppm; *^{13}C-NMR* (75 MHz) 16.0 (CH_3), 43.2 (CH_3N), 101.7 (d, $^1J_{PC}$ = 117.1 Hz, C-P), 119.7-134.4 (C-arom), 149.7, 161.1, 167.2 (d, $^2J_{PC}$ = 11.7 Hz, C=O) ppm; *^{31}P-NMR* (150 MHz) 29.3 ppm; *IR (KBr)* 1716, 1664, 1585, 1403, 1182 cm^{-1}; *MS* (70 eV) 445 (M^+, 25). Anal. Calcd for $C_{25}H_{24}N_3O_3P$: C, 67.39; H, 5.43; N, 9.44. Found: C, 67.25; H, 5.44; N, 9.41.

1-Dimethylamino-5-diphenylphosphinoyl-3-ethyl-6-methylpyrimidin-2,4-dione (9b). 1590 mg (80 %) of **9b** as a white solid Data for **9b**: mp 215-216 °C; *^{1}H-NMR* (300 MHz) 1.07 (t, $^3J_{HH}$ = 7.0 Hz, 3H, CH_3), 2.89 (s, 3H, CH_3), 2.90 (s, 6H, CH_3N), 3.79 (q, $^3J_{HH}$ = 7.0 Hz, 2H, CH_2), 7.26-7.83 (m, 10H, arom) ppm; *^{13}C-NMR* (75 MHz) 12.6 (CH_3), 15.8 (CH_3), 36.0 (CH_2), 43.0 (CH_3N), 100.7 (d, $^1J_{PC}$ = 118.1 Hz, C-P), 127.9-134.2 (C-arom), 149.4, 160.7 (d, J_{PC} = 11.9 Hz), 166.4 (d, $^2J_{PC}$ = 12.0 Hz, C=O) ppm; *^{31}P-NMR* (150 MHz) 29.5 ppm; *IR (KBr)* 1720, 1662, 1576, 1440, 1117 cm^{-1}; *MS* (70 eV) 397 (M^+, 37). Anal. Calcd for $C_{21}H_{24}N_3O_3P$: C, 63.45; H, 6.09; N, 10.58. Found: C, 63.30; H, 6.10; N, 10.56.

1-Dimethylamino-5-diphenylphosphinoyl-6-methyl-3-*p*-totylpyrimidin-2,4-dione (9c). 1770 mg (77 %) of **9c** as a white solid. Data for **9c**: mp 231-232 °C; *^{1}H-NMR* (300 MHz) 2.32 (s, 3H, CH_3), 2.95 (s, 6H, CH_3N), 3.03 (s, 3H, CH_3), 6.94-7.22 (m, 4H, AA'BB' system), 7.41-7.89 (m, 10H, arom) ppm; *^{13}C-NMR* (75 MHz) 16.1 (CH_3), 21.2 (CH_3), 43.4 (CH_3N), 101.3 (d, $^1J_{PC}$ = 120.3 Hz, C-P), 127.8-138.9 (C-arom), 149.9, 161.8, 167.4 (d, $^2J_{PC}$ = 11.3 Hz, C=O) ppm; *^{31}P-NMR* (150 MHz) 28.6 ppm; *IR (KBr)* 1724, 1678, 1569, 1403, 1182, 1115 cm^{-1}; *MS* (70 eV) 459 (M^+, 9). Anal. Calcd for $C_{26}H_{26}N_3O_3P$: C, 67.95; H, 5.71; N, 9.15. Found: C, 67.76; H, 5.73; N, 9.12.

1-Dimethylamino-5-diphenylphosphinoyl-6-ethyl-3-phenylpyrimidin-2,4-dione (9d). 1860 mg (81 %) of **9d** as a white solid. Data for **9d**: mp 175-176 °C; *^{1}H-NMR* (300 MHz) 1.35 (t, $^3J_{HH}$ = 7.2 Hz, 3H, CH_3), 2.99 (s, 6H, CH_3N), 3.70 (q, $^3J_{HH}$ = 7.2 Hz, 2H, CH_2), 7.06-7.90 (m, 15H, arom) ppm; *^{13}C-NMR* (75 MHz) 14.7 (CH_3), 22.0 (CH_2), 44.1 (CH_3N), 101.2 (d, $^1J_{PC}$ = 114.9 Hz, C-P), 127.6-134.2 (C-arom), 150.0, 161.4 (d, J_{PC} = 11.5 Hz), 172.2 (d, $^2J_{PC}$ = 12.6 Hz, C=O) ppm; *^{31}P-NMR* (150 MHz) 28.9 ppm; *IR (KBr)* 1725, 1664, 1557, 1406, 1180 cm^{-1}; *MS* (70 eV) 460 (M^++1, 21). Anal. Calcd for $C_{26}H_{26}N_3O_3P$: C, 67.95; H, 5.71; N, 9.15. Found: C, 68.09; H, 5.69; N, 9.17.

3,6-Diethyl-1-dimethylamino-5-diphenylphosphinoylpyrimidin-2,4-dione (9e). 1750 mg (85 %) of **9e** as a white solid. Data for **9e**: mp 184-185 °C; *^{1}H-NMR* (300 MHz) 1.02 (t, $^3J_{HH}$ = 7.0 Hz, 3H, CH_3), 1.20 (t, $^3J_{HH}$ = 7.3 Hz, 3H, CH_3), 2.89 (s, 6H, CH_3N), 3.48 (q, $^3J_{HH}$ = 7.3 Hz, 2H, CH_2), 3.74 (q, $^3J_{HH}$ = 7.0 Hz, 2H, CH_2), 7.33-7.80 (m, 10H, arom) ppm; *^{13}C-NMR* (75 MHz) 12.7 (CH_3), 14.5 (CH_3), 21.7 (CH_2), 36.2 (CH_2), 43.9 (CH_3N), 100.0 (d, $^1J_{PC}$ = 117 Hz, C-P), 127.9-134.6 (C-arom), 149.8, 161.2 (d, J_{PC} = 10.9 Hz), 171.3 (d, $^2J_{PC}$ = 12.2 Hz, C=O) ppm; *^{31}P-NMR* (150 MHz) 29.3 ppm; *IR (KBr)* 1712, 1655, 1568, 1439, 1116 cm^{-1}; *MS* (70 eV) 411 (M^+, 2). Anal. Calcd for $C_{22}H_{26}N_3O_3P$: C, 64.21; H, 6.37; N, 10.22. Found: C, 64.41; H, 6.35; N, 10.25.

1-Dimethylamino-5-diphenylphosphinoyl-6-methyl-2-oxo-3-phenylpyrimidin-4-thione (15a). 1800 mg (78 %) of **15a** as a white solid. Data for **15a**: mp 236-237 °C; *^{1}H-NMR* (300 MHz) 2.92 (s, 3H, CH_3), 2.98 (s, 6H, CH_3N), 6.88-7.92 (m, 15H, arom) ppm; *^{13}C-NMR* (75 MHz) 17.4 (CH_3), 43.1 (CH_3N), 114.0 (d, $^1J_{PC}$ = 123.9 Hz, C-P), 118.3-140.5 (C-arom), 147.7, 163.4 (d, J_{PC} = 15.1 Hz), 189.0 (d, $^2J_{PC}$ = 15.6 Hz, C=S) ppm; *^{31}P-NMR* (150 MHz) 33.3 ppm; *IR (KBr)* 2895, 1714, 1552, 1182 cm^{-1}; *MS* (70 eV) 461 (M^+, 0.5). Anal. Calcd for $C_{25}H_{24}N_3O_2PS$: C, 65.06; H, 5.24; N, 9.10. Found: C, 64.86; H, 5.25; N, 9.07.

1-Dimethylamino-5-diphenylphosphinoyl-3-ethyl-6-methyl-2-oxopyrimidin-4-thione (15b). 1570 mg (76 %) of **15b** as a white solid. Data for **15b**: mp 215-216 °C; *^{1}H-NMR* (300 MHz) 1.16 (t, $^3J_{HH}$ = 7.0 Hz, 3H, CH_3), 2.84 (s, 3H, CH_3), 2.96 (s, 6H, CH_3N), 4.34 (q, $^3J_{HH}$= 7.0 Hz, 2H, CH_2), 7.26-7.86

(m, 10H, arom) ppm; *^{13}C-NMR* (75 MHz) 11.4 (CH_3), 17.3 (CH_3), 42.2 (CH_2), 43.1 (CH_3N), 112.0 (d, $^1J_{PC}$ = 131.8 Hz, C-P), 127.9-134.9 (C-arom), 147.4, 162.6 (d, J_{PC} = 14.7 Hz), 187.4 (d, $^2J_{PC}$ = 15.8 Hz, C=S) ppm; *^{31}P-NMR* (150 MHz) 33.9 ppm; *IR (KBr)* 1703, 1552, 1403, 1176 cm^{-1}; *MS* (70 eV) 414 (M^++1, 100). Anal. Calcd for $C_{21}H_{24}N_3O_2PS$: C, 61.03; H, 5.85; N, 10.17. Found: C, 60.83; H, 5.83; N, 10.14.

General procedure for the preparation of 5-phosphorylated pyrimidin-2,4-diones 10. To a 0 °C 1.6 M solution of BuLi in hexanes (5 mmol) in THF (25 mL) was added a solution of primary enamino-amide **6** (5 mmol) in THF (40 mL). The mixture was allowed to stir at this temperature for 1 h and a solution of ethyl chloroformate (0.48 mL, 5 mmol) in THF (10 mL) was then added at the same temperature. After the mixture was allowed to warm to rt, the reaction mixture was stirred and refluxed until *TLC* indicated the disappearance of the compound **6** (~ 2-3 days). The mixture was diluted with water (40 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with water, dried over $MgSO_4$, and concentrated. The crude residue was purified by flash-chromatography eluting with 1:1 AcOEt/hexanes.

5-Diethoxyphosphoryl-3-phenyl-6-*p*-tolyl-1(*H*)pyrimidin-2,4-dione (10a). 1370 mg (66 %) of **10a** as a white solid. Data for **10a**: mp 211-212 °C; *^{1}H-NMR* (300 MHz) 1.03 (m, 6H, CH_3), 2.38 (s, 3H, CH_3), 3.99 (m, 4H, OCH_2), 7.17-7.49 (m, 9H, arom), 9.28 (s, 1H, NH) ppm; *^{13}C-NMR* (75 MHz) 15.8 (CH_3), 21.4 (CH_3), 62.5 (OCH_2), 101.3 (d, $^1J_{PC}$ = 215.0 Hz, C-P), 128.1-141.3 (C-arom), 150.7 (C=O), 159.0 (d, $^2J_{PC}$ = 16.1 Hz, CN), 162.1 (d, $^2J_{PC}$ = 11.1 Hz, C=O) ppm; *^{31}P-NMR* (150 MHz) 12.4 ppm; *IR (KBr)* 3230, 1733, 1671, 1235 cm^{-1}; *MS* (70 eV) 414 (M^+, 87). Anal. Calcd for $C_{21}H_{23}N_2O_5P$: C, 60.87; H, 5.55; N, 6.76. Found: C, 60.54; H, 5.71; N, 6.89.

5-Diethoxyphosphoryl-3,6-diphenyl-1(*H*)pyrimidin-2,4-dione (10b). 1420 mg (71 %) of **10b** as a white solid. Data for **10b**: mp 224-225 °C; *^{1}H-NMR* (300 MHz) 0.91 (m, 6H, CH_3), 3.75 (m, 2H, OCH_2), 3.78 (m, 2H, OCH_2), 7.11-7.44 (m, 10H, arom), 9.78 (s, 1H, NH) ppm; *^{13}C-NMR* (75 MHz) 15.9 (CH_3), 62.5 (OCH_2), 101.6 (d, $^1J_{PC}$ = 215.5 Hz, C-P), 128.0-133.6 (C-arom), 150.6 (C=O), 158.7 (d, $^2J_{PC}$ = 15.6 Hz, CN), 162.0 (d, $^2J_{PC}$ = 11.1 Hz, C=O) ppm; *^{31}P-NMR* (150 MHz) 12.0 ppm; *IR (KBr)* 3226, 1728, 1692, 1224 cm^{-1}; *MS* (70 eV) 400 (M^+, 100). Anal. Calcd for $C_{20}H_{21}N_2O_5P$: C, 60.00; H, 5.25; N, 7.00. Found: C, 58.75; H, 5.31; N, 6.96.

5-Diethoxyphosphoryl-3-*p*-methoxyphenyl-6-phenyl-1(*H*)pyrimidin-2,4-dione (10c). 1270 mg (59 %) of **10c** as a white solid. Data for **10c**: mp 221-222 °C; *^{1}H-NMR* (300 MHz) 0.95 (m, 6H, CH_3), 3.77 (s, 3H, OCH_3), 3.83 (m, 2H, OCH_2), 3.92 (m, 2H, OCH_2), 6.91-7.48 (m, 9H, arom), 9.06 (s, 1H, NH) ppm; *^{13}C-NMR* (75 MHz) 15.9 (CH_3), 55.4 (OCH_3), 62.6 (OCH_2), 102.3 (d, $^1J_{PC}$ = 218.1 Hz, C-P), 114.7-150.5 (C-arom), 158.4 (d, $^2J_{PC}$ = 15.6 Hz, CN), 159.7 (C=O), 162.6 (d, $^2J_{PC}$ = 7.9 Hz, C=O) ppm; *^{31}P-NMR* (150 MHz) 12.2 ppm; *IR (KBr)* 3228, 1726, 1654, 1211 cm^{-1}; *MS* (70 eV) 430 (M^+, 56). Anal. Calcd for $C_{21}H_{23}N_2O_6P$: C, 58.60; H, 5.35; N, 6.51. Found: C, 58.97; H, 5.23; N, 6.39.

General procedure for the synthesis of 2,4-Dioxo-3-*p*-methoxyphenyl-6-phenyl-1(*H*)pyrimidin (bis)phosphonic acid (11). To a solution of 5-diethoxyphosphoryl-3-*p*-methoxyphenyl-6-phenyl-1(*H*)pyrimidin-2,4-dione **10c** (5 mmol) in chloroform (25 mL) was added trimethylsilyl bromide (4.60 g, 30 mmol) at rt. The mixture was allowed to stir at 45 °C for 5 hours. The solvent was evaporated and the crude was diluted with AcOEt/H_2O. The mixture was stirred for 30 minutes, and the aqueous layer was filtered through celite. The solvent was evaporated and 1530 mg (82 %) of phosphonic acid **11** was obtained as a white solid. Data for **11**: mp 265 °C (dec); *^{1}H-NMR* (300 MHz) 3.80 (s, 3H, OCH_3), 7.07-7.45 (m, 9H, arom) ppm; *^{13}C-NMR* (75 MHz) 51.1 (OCH_3), 100.9 (d, $^1J_{PC}$ = 215.9 Hz, C-P), 110.7-173.4 (C-arom, CN and C=O) ppm; *^{31}P-NMR* (150 MHz) 4.8 ppm; *IR (KBr)* 3426, 1713, 1647, 1172 cm^{-1}; *MS* (70 eV) 374 (M^+, 2). Anal. Calcd for $C_{17}H_{15}N_2O_6P$: C, 54.54; H, 4.01; N, 7.49. Found: C, 54.71; H, 4.26; N, 7.38.

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