Synthesis and Transformation of Methyl 2-(6-Hydroxy-2-phenyl-pyrimidin-4-yl)acetate: Simple Preparation of Pyrimidines with Heterocyclic Substituents

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A simple and efficient synthesis of four new substituted pyrimidines, compounds **9a**–**d**, from the title compound **3** is described. Conversion of **3** to methyl (*E*)-3-(dimethylamino)-2-(6-methoxy-2-phenyl-pyrimidin-4-yl)prop-2-enoate (**4**), followed by condensation with various dinucleophiles according to the 'enaminone methodology', afforded the target compounds **9** in medium-to-good yields.

Introduction. – Pyrimidines with aromatic or non-aromatic heterocyclic groups are an important class of compounds, which have found application as ligands for metal-ion coordination [1], as components for molecular recognition [2], as therapeutic agents [3], and as fluorophores and electron transporters in light-emitting organic devices [4]. Recently, compounds based on a pyridinylpyrimidine core structure were identified as inhibitors of both human methionine aminopeptidases MetAP1 and MetAP2 [5].

There are many methods described in the literature for the preparation of pyrimidines [6]. The synthesis of many aryl- and heteroaryl-substituted pyrimidines has been accomplished by cyclization of acyclic precursors [7]. Palladium (Pd)-catalyzed reactions are a powerful tool for the synthesis of heterocycles, especially for the formation of C–C bonds in aryl- and heteroaryl-substituted heterocycles [8], and readily allow one to introduce diversity to heterocyclic ring systems [9][10]. Most Pd-catalyzed couplings used for carbocyclic systems employ organic bromides, iodides, and triflates as substrates; unfortunately, the corresponding chlorides are unreactive under typical coupling conditions [11]. In some instances, though, halopyrimidines [12] and 5-pyrimidinylboronic acid derivatives [13] have been used in Pd-catalyzed *Suzuki–Miyaura* cross-coupling reactions [14].

Recently, an expedient parallel synthesis of 2-amino-4-heteroarylpyrimidines *via* a 2-chloropyrimidine intermediate was developed, and a series of potentially biologically active congeners were synthesized in two steps [15].

In connection with our interest in enaminones as building blocks for the preparation of various functionalized heterocyclic systems such as heteroaryl-substituted α-amino- and α-hydroxy acids, fused pyridinones, pyrimidinones, pyranones, and related systems [16], including some naturally occurring alkaloids and their analogues [17], we recently reported the transformation of (*Z*)-3-(benzoylamino)-4-(dimethylamino)-2-oxobut-3-ene by treatment with amidines, guanidines, and guanidine-like compounds into pyrimidine derivatives [18]. We also described the preparation of 6-aminopyrimidine-

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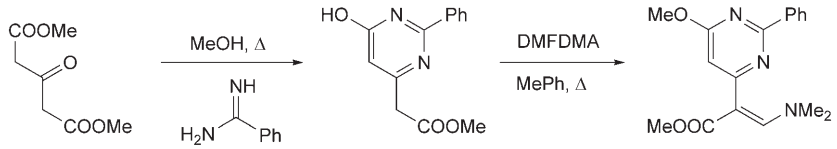
4-carboxylic acid derivatives by treatment of methyl 2-(acylamino)-3-cyanopropenoates with methyl- and benzylamine [19], as well as the formation of substituted, fused pyrimidinones from 2-substituted 3-(dimethylamino)propenoates and heterocyclic α-amino compounds in hot acetic acid. Under these conditions, the cyclization of intermediates, 2-substituted 3-heteroarylaminopropenoates, afforded some fused pyrimidines [20]. Finally, a simple and efficient synthesis of novel 2-heteroaryl-substituted 1*H*-indole-2-carboxylates and γ-carbolines from 2-(2-methoxy-2-oxoethyl)-1-methyl-1*H*-indole-3-carboxylate by the 'enaminone methodology' was reported recently [21].

In this communication, we report a simple, Pd-free synthesis of pyrimidinylacetic acid derivatives and their transformation into heteroaryl-substituted pyrimidines.

Results and Discussion. – As shown in *Scheme 1*, dimethyl 3-oxopentanedioate (**1**) was reacted with benzamidine (**2**) to methyl 2-(6-hydroxy-2-phenylpyrimidin-4-yl)acetate (**3**). In the subsequent reaction with *N*,*N*-dimethylformamide dimethylacetal (DMFDMA) in toluene at reflux, the reactive methylene group of **3** was converted to the corresponding *N*,*N*-dimethylaminomethylidene derivative, under simultaneous methylation of the OH group, to afford the (*E*)-configured propenoate **4**.

Scheme 1



1 **2** **3** **4**

DMFDMA = *N*,*N*-Dimethylformamide dimethylacetal

Theoretically, the reaction of **3** with DMFDMA could afford three different congeners, depending on the site of methylation. It is known from the literature [22] that, in most cases, methylation of cyclic lactams with this reagent takes place at the ring N-atom. Accordingly, one would expected the formation of the N(1)- or N(3)-methylated compounds, or a mixture thereof. However, the ^{1}H-NMR chemical shift (δ(H) 3.61) of the newly introduced Me group strongly indicated that, as a matter of fact, *O*-methylation had taken place, giving rise to the formation of **4**.

The configuration of the C=C bond in **4** could not be determined on the basis of the $^3J(^{13}C,^1H)$ coupling between the ester C=O group and the olefinic H-atom, due to broadening of the methylidene signal. However, an X-ray crystal-structure analysis of **4** clearly confirmed the (*E*)-configuration, as shown in the *Figure*.

Some transformations of **4** with different nucleophiles were studied next (*Scheme 2*). In the reaction with aqueous MeOH in the presence of HCl, hydrolysis took place to give the corresponding enol **5**. In contrast, N-nucleophiles such as methyl glycinate (**6a**), aniline (**6b**), 4-methylaniline (**6c**), and 4-nitroaniline (**6d**), when reacted with **4** in MeOH in the presence of HCl at room temperature, afforded the corresponding substitution products **7a**–**d**, respectively, in different yields (*Table 1*).

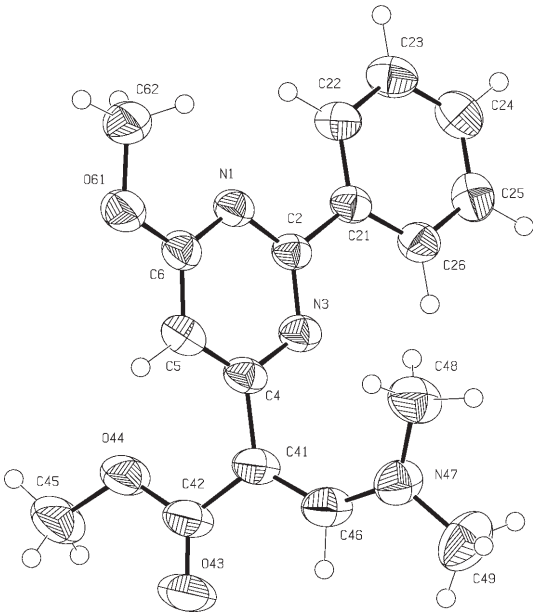


Figure. *X-Ray crystal structure of* **4**. ORTEP Plot at the 50%-probability level; H-atoms are drawn as ellipsoids of arbitrary radii.

In solution, compounds **7** exist as mixtures of (*E*)- and (*Z*)-isomers. In all cases, the (*E*)-isomer was found to predominate (*Table 1*). The configuration of (*E*)-**7a** was determined on the basis of the ^3J(C,H) coupling constant (4.5 Hz) between the methylidene H-atom and the ester C=O group. Further, the ^{1}H-NMR spectra of compounds **7** indicated antiperiplanar orientations of the H-atoms in the NH–CH structural elements of the (*E*)- and (*Z*)-isomers, with J(NH,CH) values of 12.6–13.4 Hz (*E*) and 13.0–14.5 Hz (*Z*).

Scheme 2

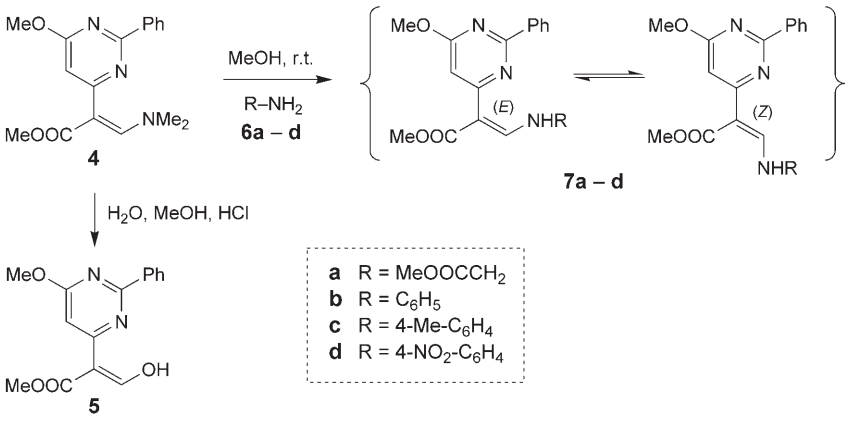
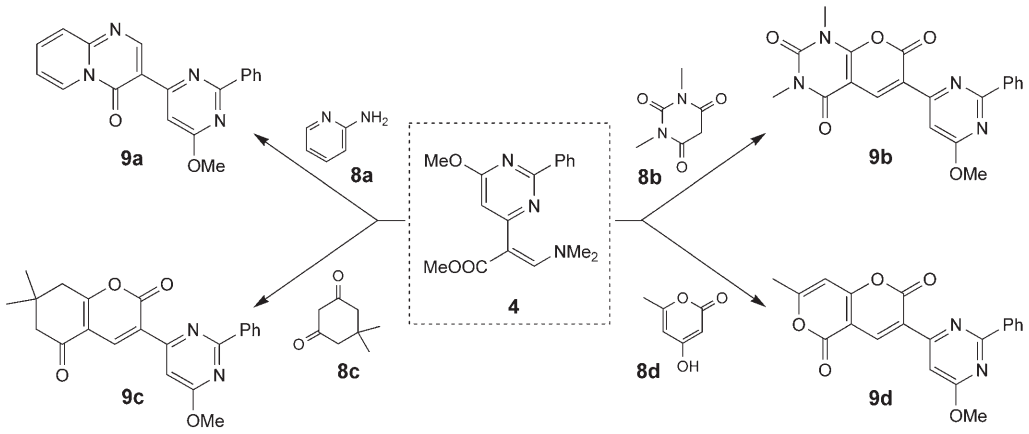


Table 1. *Selected Data of Compounds* **7**

No.	Yield [%]	(*E*/*Z*)	(*E*)-Isomer			(*Z*)-Isomer		
			δ(H) C=CH	δ(H) NH	^3J	δ(H) C=CH	δ(H) NH	^3J
7a	81	66 : 34	8.17	10.82	13.4	8.63	9.01	14.5
7b	48	78 : 22	8.62	12.89	12.9	9.02	10.56	14.0
7c	63	87 : 13	8.58	12.88	12.9	9.01	10.52	14.1
7d	22	72 : 28	8.61	12.70	12.6	8.92	10.66	13.0

Finally, reaction of **4** with the dinucleophiles 2-aminopyridine (**8a**), 1,3-dimethylbarbituric acid (**8b**), 5,5-dimethylcyclohexane-1,3-dione (**8c**), or 4-hydroxy-6-methyl-2*H*-pyran-2-one (**8d**) was carried out in AcOH at reflux, which readily afforded, through substitution and intramolecular cyclization, the target compounds **9a**–**d** in yields of 30, 67, 56, and 73%, respectively (*Scheme 3*). All compounds were fully characterized (see *Exper. Part*).

Scheme 3



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Experimental Part

General. All chemicals and reagents were purchased from *Fluka* or *Aldrich*, and used as received. Melting points (m.p.) were determined on a *Kofler* hot-stage micro-melting-point apparatus. IR Spectra were recorded on a *Perkin-Elmer-BX* FT-IR spectrometer; in cm^{-1}. ^1H- and ^{13}C-NMR Spectra were recorded on a *Bruker Avance DPX-300* apparatus at 300 (^1H) and 75.5 MHz (^{13}C); δ in ppm rel. to Me_4Si, *J* in Hz. Elemental analyses were performed on a *Perkin-Elmer CHN Analyzer 2400-II.*

Methyl 2-(6-Hydroxy-2-phenylpyrimidin-4-yl)acetate (**3**). To a soln. of MeONa (500 mg Na dissolved in 20 ml MeOH), benzamidine hydrochloride (**2**) (3.132 g, 20 mmol) was added, and the mixture was stirred at r.t. for 10 min. Then, dimethyl 3-oxopentanedioate (**1**; 3 ml, 20 mmol) was added, and the mixture was heated at reflux for 7 h. After cooling, the product precipitated, and was filtered off. Yield: 3.661 g (75%). M.p. 172–173°. IR: 3070, 2960, 1740, 1660, 1540, 1440, 1330, 1170, 990, 700, 600, 530. ^{1}H-NMR ((D$_6$)DMSO): 3.66 (*s*, MeO); 3.69 (*s*, CH$_2$); 6.34 (*s*, H–C(5)); 7.49–7.60 (*m*, 3 arom. H); 8.08–8.10 (*m*, 2 arom. H); 12.59 (br. *s*, OH). Anal. calc. for $C_{13}H_{12}N_2O_3$ (244.25): C 63.93, H 4.95, N 11.47; found: C 64.08, H 4.89, N 11.75.

*Methyl (2*E*)-3-(Dimethylamino)-2-(6-methoxy-2-phenylpyrimidin-4-yl)prop-2-enoate* (**4**). To a soln. of **3** (488 mg, 2 mmol) in toluene (5 ml) was added Me$_2$NCH(OMe)$_2$ (DMFDMA; 0.86 ml, 6 mmol), and the mixture was heated at reflux for 7 h. After cooling, the solvent was removed *in vacuo*. The residue was taken up in MeOH (*ca.* 10 ml), and the mixture was cooled to −30°. The resulting precipitate was removed by filtration, and recrystallized from MeOH/H$_2$O. Yield: 372 mg (60%). M.p. 105–107°. IR: 2950, 2920, 1680, 1590, 1570, 1330, 1220, 1100, 860, 760, 700, 670. ^{1}H-NMR ((D$_6$)DMSO): 2.89 (br *s*, Me$_2$N); 3.61 (*s*, MeO); 4.02 (*s*, MeO); 6.72 (*s*, H–C(5)); 7.50–7.52 (*m*, 3 arom. H); 7.82 (br. *s*, =CH); 8.36–8.40 (*m*, 2 arom. H). Anal. calc. for $C_{17}H_{19}N_3O_3$ (313.35): C 65.16, H 6.11, N 13.41; found: C 65.37, H 6.21, N 13.42.

*Methyl (2*E*)-3-Hydroxy-2-(6-methoxy-2-phenylpyrimidin-4-yl)prop-2-enoate* (**5**). To a soln. of **4** (157 mg, 0.5 mmol) in MeOH (2 ml) was added conc. HCl (3 drops), the mixture was left at r.t. for 12 h. The resulting precipitate was removed by filtration and recrystallized from MeOH. Yield: 103 mg (57%). M.p. 134–135°. IR: 3130, 2950, 1690, 1620, 1530, 1480, 1390, 1330, 1270, 1180, 1070, 850, 690, 630. ^{1}H-NMR ((D$_6$)DMSO): 3.71 (*s*, MeO); 4.10 (*s*, MeO); 7.49 (*s*, H–C(5)); 7.66–7.76 (*m*, 3 arom. H); 8.17–8.20 (*m*, 2 arom. H); 9.44 (*s*, =CH). Anal. calc. for $C_{15}H_{14}N_2O_4$ (286.28): C 62.93, H 4.93, N 9.79; found: C 63.11, H 5.04, N 9.65.

General Procedure (*GP 1*) *for the Synthesis of Compounds* **7**. A soln. of **4** (157 mg, 0.5 mmol) and the appropriate amine **6** (0.5 mmol) in MeOH (2 ml) was left at r.t. for 12 h. The resulting product **7**, which precipitated from the mixture, was filtered off and recrystallized as indicated below.

*Methyl (*E*/*Z*)3-[(2-Methoxy-2-oxoethyl)amino]-2-(6-methoxy-2-phenylpyrimidin-4-yl)prop-2-enoate* (**7a**). According to *GP 1*, with methyl glycinate hydrochloride (**6a**; 63 mg, 0.5 mmol). Yield: 145 mg (81%). (*E*/*Z*)-Ratio: 66:34. M.p. 128–130° (MeOH). IR: 3490, 3150, 3000, 2950, 1760, 1690, 1640, 1570, 1430, 1330, 1220, 1130, 1043, 850, 780, 690, 570. ^{1}H-NMR ((D$_6$)DMSO; (*E*)-isomer): 3.69 (*s*, MeO); 3.73 (*s*, MeO); 4.02 (*s*, MeO); 4.50 (*d*, *J* = 5.9, CH$_2$); 7.49–7.54 (*m*, 3 arom. H); 7.57 (*s*, H–C(5)); 8.17 (*d*, *J* = 13.5, =CH); 8.32–8.35 (*m*, 2 arom. H); 10.82 (*td*, *J* = 13.4, 5.8, NH). ^{1}H-NMR ((D$_6$)DMSO; (*Z*)-isomer): 3.71 (*s*, MeO); 3.77 (*s*, MeO); 4.00 (*s*, MeO); 4.41 (*d*, *J* = 6.1, CH$_2$); 7.14 (*s*, H–C(5)); 7.49–7.54 (*m*, 3 arom. H); 8.44–8.48 (*m*, 2 arom. H); 8.63 (*d*, *J* = 14.6, =CH); 9.01 (*td*, *J* = 14.5, 6.1, NH). Anal. calc. for $C_{18}H_{19}N_3O_5$ (357.36): C 60.50, H 5.36, N 11.76; found: C 60.51, H 5.54, N 11.96.

*Methyl (*E*/*Z*)-2-(6-Methoxy-2-phenylpyrimidin-4-yl)-3-(phenylamino)prop-2-enoate* (**7b**). According to *GP 1*, with aniline hydrochloride (**6b**; 65 mg, 0.5 mmol). Yield: 87 mg (48%). (*E*/*Z*)-Ratio: 78:22. M.p. 132–134° (MeOH/DMF). IR: 3110, 1690, 1630, 1560, 1500, 1330, 1260, 1130, 1040, 960, 860, 750, 690, 570, 510. ^{1}H-NMR ((D$_6$)DMSO; (*E*)-isomer): 3.76 (*s*, MeO); 4.05 (*s*, MeO); 7.14–7.20 (*m*, 1 arom. H); 7.28–7.31 (*m*, 2 arom. H); 7.42–7.48 (*m*, 3 arom. H); 7.59 (*s*, H–C(5)); 8.28–8.32 (*m*, 2 arom. H); 8.62 (*d*, *J* = 12.9, =CH); 8.32–8.35 (*m*, 2 arom. H); 12.89 (*d*, *J* = 13.0, NH). ^{1}H-NMR ((D$_6$)DMSO; (*Z*)-isomer): 3.85 (*s*, MeO); 4.03 (*s*, MeO); 7.14–7.20 (*m*, 1 arom. H); 7.17 (*s*, H–C(5)); 7.52–7.54 (*m*, 3 arom. H); 7.60–7.66 (*m*, 2 arom. H); 8.41–8.44 (*m*, 2 arom. H); 9.02 (*d*, *J* = 14.0, =CH); 10.56 (*d*, *J* = 14.0, NH). Anal. calc. for $C_{21}H_{19}N_3O_3$ (361.39): C 69.79, H 5.30, N 11.63; found: C 69.96, H 5.41, N 11.66.

Methyl (E/Z)-2-(6-Methoxy-2-phenylpyrimidin-4-yl)-3-[(4-methylphenyl)amino]prop-2-enoate (**7c**). According to *GP 1*, with 4-methylaniline hydrochloride (**6c**; 72 mg, 0.5 mmol): 119 mg (63%). (*E*/*Z*)-Ratio: 87:13. M.p. 144–147° (MeOH/DMF). IR: 2950, 1690, 1630, 1570, 1520, 1330, 1260, 1200, 1130, 1050, 860, 810, 700, 510. ^{1}H-NMR ((D$_6$)DMSO; (*E*)-isomer): 2.30 (*s*, Me); 3.75 (*s*, MeO); 4.04 (*s*, MeO); 7.16–7.19 (*m*, 2 arom. H); 7.24–7.27 (*m*, 2 arom. H); 7.59–7.63 (*m*, 3 arom. H); 7.59 (*s*, H–C(5)); 8.26–8.29 (*m*, 2 arom. H); 8.58 (*d*, *J* = 12.9, =CH); 8.32–8.35 (*m*, 2 arom. H); 12.88 (*d*, *J* = 12.9, NH). ^{1}H-NMR ((D$_6$)DMSO; (*Z*)-isomer): 2.30 (*s*, Me); 3.84 (*s*, MeO); 4.02 (*s*, MeO); 7.26 (*s*, H–C(5)); 7.28–7.31 (*m*, 2 arom. H); 7.51–7.53 (*m*, 2 arom. H); 7.59–7.63 (*m*, 3 arom. H); 8.40–8.43 (*m*, 2 arom. H); 9.01

(*d*, *J* = 14.1, =CH); 10.52 (*d*, *J* = 14.1, NH). Anal. calc. for $C_{22}H_{19}N_3O_3$ (375.42): C 70.38, H 5.64, N 11.19; found: C 70.67, H 5.77, N 11.06.

Methyl (E/Z)-2-(6-Methoxy-2-phenylpyrimidin-4-yl)-3-[(4-nitrophenyl)amino]prop-2-enoate (**7d**). According to *GP 1*, with 4-nitroaniline hydrochloride (**6d**; 87 mg, 0.5 mmol). Yield: 45 mg (22%). (*E*/*Z*)-Ratio: 72:28. M.p. 227–230° (MeOH/DMF). IR: 3100, 2940, 1700, 1630, 1590, 1560, 1500, 1330, 1300, 1110, 1040, 870, 840, 750, 700. ^{1}H-NMR ((D$_6$)DMSO; (*E*)-isomer): 3.80 (*s*, MeO); 4.08 (*s*, MeO); 7.46–7.64 (*m*, 2 arom. H); 7.62–7.67 (*m*, 3 arom. H); 7.63 (*s*, H–C(5)); 8.27–8.34 (*m*, 4 arom. H); 8.61 (*d*, *J* = 12.5, =CH); 12.70 (*d*, *J* = 12.6, NH). ^{1}H-NMR ((D$_6$)DMSO; (*Z*)-isomer): 3.88 (*s*, MeO); 4.05 (*s*, MeO); 7.17 (*s*, H–C(5)); 7.46–7.64 (*m*, 2 arom. H); 7.54–7.56 (*m*, 2 arom. H); 7.62–7.67 (*m*, 3 arom. H); 8.44–8.48 (*m*, 2 arom. H); 8.92 (*d*, *J* = 13.0, =CH); 10.66 (br. *s*, NH). Anal. calc. for $C_{21}H_{18}N_4O_5$ (406.39): C 62.06, H 4.46, N 13.79; found: C 62.22, H 4.56, N 13.75.

General Procedure (*GP 2*) *for the Synthesis of Compounds* **9**. A mixture of **4** (157 mg, 0.5 mmol) and the appropriate dinucleophile **8** (0.5 mmol) in AcOH (2 ml) was heated at reflux for 1.0–4.5 h. After cooling, the product precipitated, and was filtered off and recrystallized as indicated below.

*3-(6-Methoxy-2-phenylpyrimidin-4-yl)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one* (**9a**). According to *GP 2*, with 2-aminopyridine (**8a**; 47 mg, 0.5 mmol) for 4.5 h. Yield: 50 mg (30%). M.p. 225–227° (toluene). IR: 3110, 1690, 1630, 1590, 1570, 1480, 1370, 1320, 1290, 1030, 870, 780, 700, 660, 590. ^{1}H-NMR ((D$_6$)DMSO): 4.09 (*s*, MeO); 7.54–7.60 (*m*, H–C(6), 3 arom. H); 7.88–7.91 (*m*, H–C(8)); 8.00 (*s*, H–C(5′)); 8.16 (*ddd*, *J* = 8.6, 6.8, 1,6, H–C(7)); 8.52–8.55 (*m*, 2 arom. H); 9.24–9.27 (*m*, H–C(5)); 9.68 (*s*, H–C(2)). Anal. calc. for $C_{19}H_{14}N_4O_2$ (330.34): C 69.08, H 4.27, N 16.96; found: C 69.03, H 4.25, N 17.00.

*6-(6-Methoxy-2-phenylpyrimidin-4-yl)-1,3-dimethyl-2*H*-pyrano[2,3-*d*]pyrimidine-2,4,7(1*H*,3*H*)-trione* (**9b**). According to *GP 2*, with 1,3-dimethylbarbituric acid (**8b**; 78 mg, 0.5 mmol) for 2 h. Yield: 132 mg (67%). M.p. 277–279° (toluene). IR: 3450, 3130, 1760, 1720, 1680, 1560, 1540, 1440, 1330, 1290, 1160, 1070, 950, 860, 770, 750, 700, 480. ^{1}H-NMR ((D$_6$)DMSO): 2.50 (*s*, MeN; masked by solvent signal); 3.46 (*s*, MeN); 4.10 (*s*, MeO); 7.56 (*s*, H–C(5′)); 7.58–7.61 (*m*, 3 arom. H); 8.44–8.47 (*m*, 2 arom. H); 9.20 (*s*, H–C(4)). Anal. calc. for $C_{20}H_{16}N_4O_5$ (392.36): C 61.22, H 4.11, N 14.28; found: C 61.50, H 4.19, N 14.16.

*7,8-Dihydro-3-(6-methoxy-2-phenylpyrimidin-4-yl)-7,7-dimethyl-2*H*-1-benzopyran-2,5(6*H*)-dione* (**9c**). According to *GP 2*, with 5,5-dimethylcyclohexane-1,3-dione (**8c**; 70 mg, 0.5 mmol) for 2 h. Yield: 106 mg (56%). M.p. 339–343° (toluene). IR: 2960, 1740, 1690, 1650, 1560, 1380, 1200, 970, 870, 700, 590, 520. ^{1}H-NMR ((D$_6$)DMSO): 1.10 (*s*, 2 Me); 1.24 (*s*, CH$_2$(8)); 3.28 (*s*, MeO); 7.30 (br. *s*, 1 arom. H); 7.55–7.63 (*m*, H–C(5′), 3 arom. H); 8.16–8.18 (*m*, 2 arom. H); 8.91 (*s*, H–C(4)). Anal. calc. for $C_{22}H_{20}N_2O_4$ (376.41): C 70.20, H 5.36, N 7.44; found: 69.92, H 5.02, N 7.74.

*3-(6-Methoxy-2-phenylpyrimidin-4-yl)-7-methyl-2*H*,5*H*-pyrano[4,3-*b*]pyran-2,5-dione* (**9d**). According to *GP 2*, with 4-hydroxy-6-methyl-2*H*-pyran-2-one (**8d**; 63 mg, 0.5 mmol) for 1 h. Yield: 132 mg (73%). M.p. 236–237° (toluene). IR: 3460, 3100, 1740, 1590, 1560, 1540, 1400, 1350, 1210, 1040, 990, 870, 780, 700, 660, 560, 490. ^{1}H-NMR ((D$_6$)DMSO): 2.41 (*s*, Me); 4.10 (*s*, MeO); 6.80 (*s*, H–C(5′)); 7.58–7.60 (*m*, 3 arom. H); 7.64 (*s*, H–C(8)); 8.45–8.48 (*m*, 2 arom. H); 9.05 (*s*, H–C(4)). Anal. calc. for $C_{20}H_{14}N_2O_5$ (362.34): C 66.30, H 3.89, N 7.77; found: C 66.54, H 3.95, N 7.62.

*X-Ray Crystal Structure of Methyl (2*E*)-3-(Dimethylamino)-2-(6-methoxy-2-phenylpyrimidin-4-yl)prop-2-enoate* (**4**)[1]. Single-crystal X-ray diffraction data of **4** were collected at r.t. on a *Nonius Kappa CCD* diffractometer, using the Nonius Collect software [23]. DENZO and SCALEPACK [24] were used for indexing and scaling of the data, and the structure was solved by means of SIR97 [25]. Refinement was done with the Xtal3.4 [26] program package. The crystal structure was refined on *F* values using the full-matrix least-squares procedure. The non-H-atoms were refined anisotropically in all cases, and the positions of the H-atoms were geometrically calculated, their positional and isotropic atomic displacement parameters not being refined. Absorption correction was not necessary. The *Regina* [27] weighting scheme was used. Difference *Fourier* maps did not show any significant features. The resulting crystal

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[1]) The crystallographic data of **4** have been deposited with the *Cambridge Crystallographic Data Centre* as supplementary publication number CCDC-643147. Copies of the data can be obtained, free of charge, at http://www.ccdc.cam.ac.uk/data_request/cif.

Table 2. *Crystallographic and Refinement Data of* **4**

Formula	$C_{17}H_{19}N_3O_3$
M_r [Da]	313.36
Crystal system	monoclinic
Space group	$P\,2_1/n$
a, b, c [Å]	8.52710(10), 19.3629(4), 10.4132(2)
β [°]	107.4884(9)
V [Å^3]	1639.85(5)
Z	4
ϱ [Mg m^{-3}]	1.269
μ [mm^{-1}]	0.089
Crystal color and dimension [mm]	colorless, 0.3 × 0.3 × 0.2
Temperature [K]	293(1)
Wavelength [Å]	0.71073
θ_{max} [°]	27.42
Integr. and indep. refl.	19203, 3845
Obs. refl.	2400
R_{int}	0.042
Threshold criterion	$I > 2.0\sigma(I)$
Refl. parameters	208
Final R and R_w	0.057, 0.045
$(\Delta/\sigma)_{max}$	0.0002
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	−0.26, 0.32

data and details concerning data collection and refinement are given in *Table 2*. An ORTEP-III [28] plot of the asymmetric unit of **4** is presented in the *Figure*.

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