# 167. Methyl and Phenylmethyl 2-Acetyl-3-{[2-(dimethylamino)-1-(methoxycarbonyl)ethenyl]amino}prop-2-enoate in the Synthesis of Heterocyclic Systems: Preparation of 3-Amino-4*H*-pyrido-[1,2-*a*]pyrimidin-4-ones

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Methyl 2-acetyl-3-{[2-(dimethylamino)-1-(methoxycarbonyl)ethenyl]amino}prop-2-enoate (**4**) and phenylmethyl 2-acetyl-3-{[2-(dimethylamino)-1-(methoxycarbonyl)ethenyl]amino}prop-2-enoate (**5**) were prepared in three steps from the corresponding acetoacetic esters, and used as reagents for the preparation of $N^3$-protected 3-amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones **10**–**12**, 5*H*-thiazolo[3,2-*a*]pyrimidin-5-one **13**, 4*H*-pyrido[1,2-*a*]-pyridin-4-one **19** and 2*H*-1-benzopyran-2-ones **20**–**23**. Free 3-amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones **24**–**26** were prepared from **10**–**12** by removal of the 2-(methoxycarbonyl)-3-oxobut-1-enyl or 3-oxo-2-[(phenylmethoxy)carbonyl]but-1-enyl as *N*-protecting group by various methods.

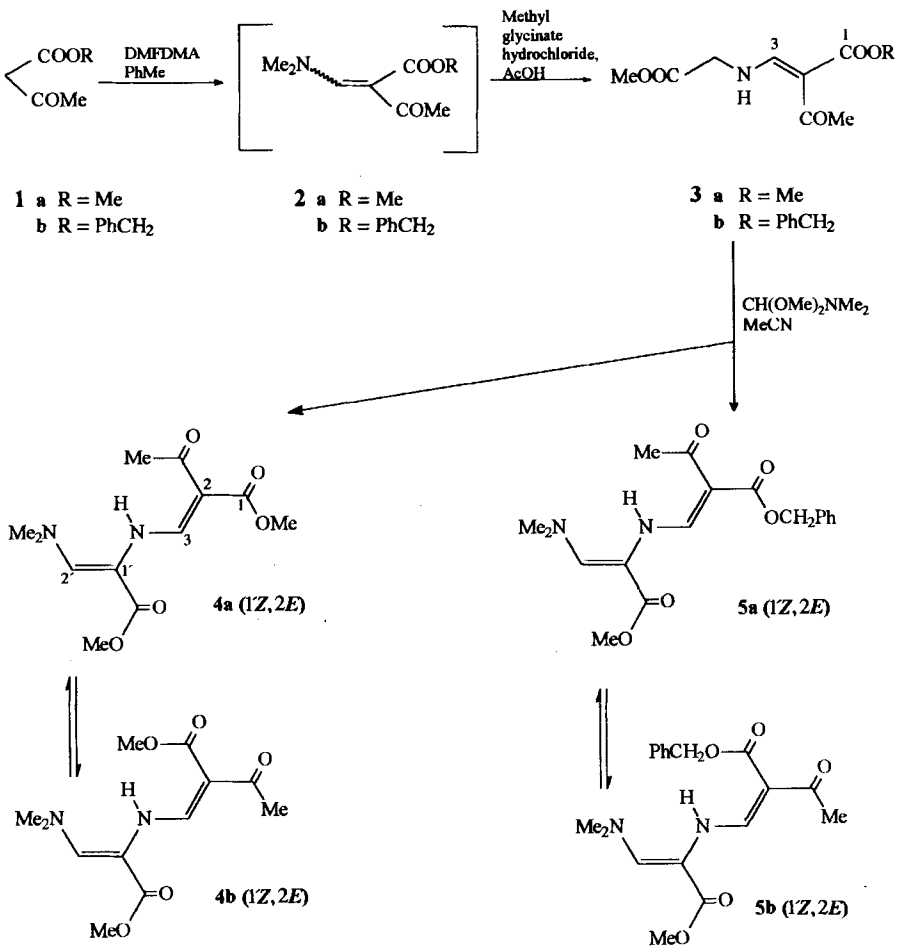
**Introduction.** – Substituted 3-amino-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones have been recently studied as candidate fluorescent probes for hypoxic cells in solid tumors [1]. They have been prepared by condensation of substituted pyridin-2-amines with ethyl 3-ethoxy-2-nitroprop-2-enoate followed by cyclization in polyphosphoric acid, to give substituted 3-nitro-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones. Reduction of the nitro group has been achieved using either titanium(III) chloride, Pd/C in the presence of $H_2$, or cyclohexene by transfer hydrogenation in 53–82% yield [2]. They have also been prepared by hydrolysis of the benzoylamino group of 3-(benzoylamino)-4*H*-pyrido[1,2-*a*]-pyrimidin-4-ones in concentrated hydrochloric acid in yields below 30% [3].

Recently, we have prepared a series of substituted alkyl 2-(acylamino)-3-(dimethylamino)propenoates and alkyl 2-[(2,2-disubstituted ethenyl)amino]-3-(dimethylamino)-propenoates as versatile reagents in the synthesis of many heterocyclic systems, such as indolizines, quinolizines, pyranones, benzo- and naphthopyranones, pyranopyrimidines, azolo- and azinopyrimidines [4], with a monosubstituted amino group at position 3 in the newly formed pyrimidinone [5–8] or pyridinone ring [6] [8]. On the other hand, we have recently observed that 2,2-disubstituted ethenyl groups, such as 2-benzoyl-2-(ethoxycarbonyl)ethenyl and 2-(benzoylamino)-2-(methoxycarbonyl)ethenyl groups, can be applied as *N*-protecting groups in the synthesis of didehydropeptides containing an N-terminal 3-(heteroarylamino)-2,3-didehydroalanine moiety, since they can be easily removed with hydrazine or hydroxylamine under mild conditions in high yields [9]. Similarly, 3-amino-8-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one has been prepared in 91% yield [7].

In this paper, we present, as an extension of our research in this area [10], the synthesis of methyl 2-acetyl-3-{[2-(dimethylamino)-1-(methoxycarbonyl)ethenyl]amino}-prop-2-enoate[1]) (**4**) and phenylmethyl 2-acetyl-3-{[2-(dimethylamino)-1-(methoxycarbonyl)ethenyl]amino}prop-2-enoate[1]) (**5**) and their application for the synthesis of fused pyrimidinones and pyranones with an amino group attached at position 3 in the newly formed systems.

**Results and Discussion.** – Compound **4** was prepared in the following way: methyl 3-oxobutanoate (= methyl acetoacetate; **1a**) was converted with *N*,*N*-dimethylformamide dimethyl acetal in toluene, followed by addition of methyl glycinate hydrochloride into methyl 2-acetyl-3-[(2-methoxy-2-oxoethyl)amino]prop-2-enoate (**3a**). This was heated with *N*,*N*-dimethylformamide dimethyl acetal in MeCN to give compound **4**.

*Scheme 1*




[1]) The esters **4** and **5** can also be considered as {[2-acetyl-2-(methoxycarbonyl)ethenyl]amino}- and {{2-acetyl-2-[(phenylmethoxy)carbonyl]ethenyl}amino}-substituted propenoates.

Analogously, phenylmethyl 3-oxobutanoate (= benzyl acetoacetate; **1b**) was converted into the corresponding phenylmethyl propenoate (*Scheme 1*). The structure of the propenoates **3**–**5** was determined by $^1$H-NMR spectroscopy. Chemical-shift differences of the two signal sets observed for **4** and **5** and NOESY experiments showed that there is an equilibrium between the major (1′*Z*,2*E*)-isomer and the minor (1′*Z*,2*Z*)-isomer of **4** and **5**, in ratio of 88:12 (**4a**/**4b**) and 87:13 (**5a**/**5b**), respectively (*Fig.*).

Compound **3a** shows three *s* at 2.28, 3.62, and 3.68 ppm for the acetyl and the two ester Me groups, a *d* (4.30 ppm, *J* (1′, NH) = 6.2 Hz) for the $CH_2$(1′) group, a *d* (8.03 ppm, *J* (3, NH) = 13.9 Hz) for the olefinic H–C(3) and a *td* (10.76 ppm) for NH. Compound **3b** shows two *s* (2.34 and 3.67 ppm) for the acetyl and ester methyl group, respectively, and two *s* (5.18 and 7.24 ppm) for the $PhCH_2$ group, besides signals similar to those of **3a**.

Two sets of peaks were observed in for **4** ($D_6$)DMSO. The major isomer **4a** with (1′*Z*,2*E*) configuration shows three *s* at 2.36, 3.59, and 3.62 ppm (each 3 H) for the acetyl group and the two ester Me groups, a *s* at 2.97 ppm (6 H) for the $Me_2N$ group, a *s* at 7.30 ppm for the olefinic H–C(2′) geminal to the $Me_2N$ group, a *s* at 7.81 ppm (*J* (3, NH) = 13.6 Hz) for the olefinic H–C(3) geminal to the NH group, and a *d* at (11.40 ppm) for NH. The signals of the acetyl and one ester Me group, of H–C(3), and of NH of the minor isomer **4b** are characteristically shifted as compared to those of **4a**; they are consistent with the (1′*Z*,2*Z*)-configuration.

Similarly, compound **5** exhibits two sets of $^1$H-NMR signals in ($D_6$)DMSO corresponding to the major (1′*Z*,2*E*)-isomer **5a** and the minor (1′*Z*,2*Z*)-isomer **5b**.

The $Me_2N$ group in compounds **4** and **5** can formally be substituted with N- and C-nucleophiles. The following N-nucleophiles were used: pyridin-2-amine (**6**), 4-methylpyridin-2-amine (**7**), 5-chloropyridin-2-amine (**8**), and thiazol-2-amine (**9**). They were treated with an equimolar amount of **4** or **5** in AcOH under reflux. After 1–3.5 h, derivatives of 4*H*-pyrido[1,2-*a*]pyrimidin-4-one (see **10**–**12**) and 5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (see **13**) were isolated (*Scheme 2*).

Two types of C-nucleophiles were selected: pyridine-2-acetonitrile (**14**) was transformed with compound **5** into 4*H*-pyrido[1,2-*a*]pyridin-4-one derivative **19**, while cyclic 1,3-diketones, such as cyclohexane-1,3-dione (**15**) and dimedone (**16**), and benzene-1,3,5-triol (**17**) and 2-methylbenzene-1,3-diol (**18**) gave 5,6,7,8-tetrahydro-2*H*-1-benzopyran-2-one derivatives **20** and **21**, and 2*H*-1-benzopyran-2-one derivatives **22** and **23**, respectively (*Scheme 3*).

Removal of the 2-(methoxycarbonyl)-3-oxobut-1-enyl group at the $N^3$-atom of **10a**–**12a** and of the 3-oxo-2-[(phenylmethoxy)carbonyl]but-1-enyl group at the $N^3$-atom of **10b**–**12b** was achieved by treatment with hydrazine hydrate in EtOH at reflux temperature to gave the free amino compounds **24**–**26** in 53–89% yield (*Scheme 4*). An alternative *N*-deprotection procedure would be the reduction with $NaBH_4$ in dimethylsulfoxide which gave, in the case of **12b**, in 20% yield.

In the pyranone series, the 2-(methoxycarbonyl)-3-oxobut-1-enyl group of the $N^3$-atom could be removed with $Et_2NH$ in refluxing EtOH. In this manner, **21a** was transformed into the 3-amino-2*H*-1-benzopyran-2-one derivative **27** (*Scheme 5*).

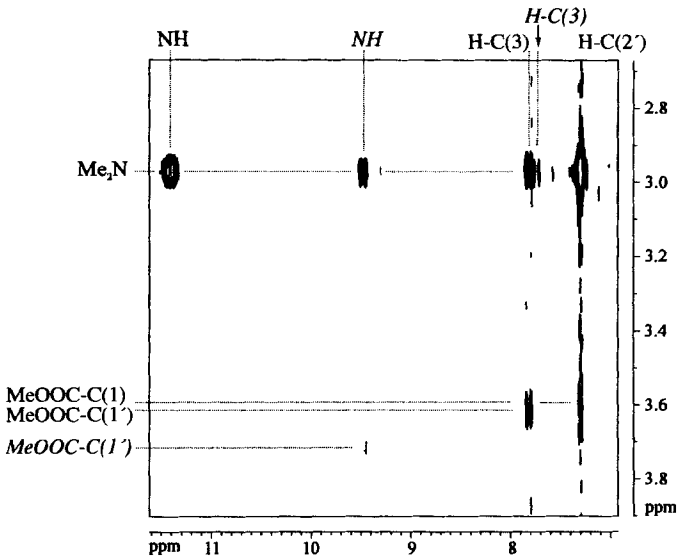
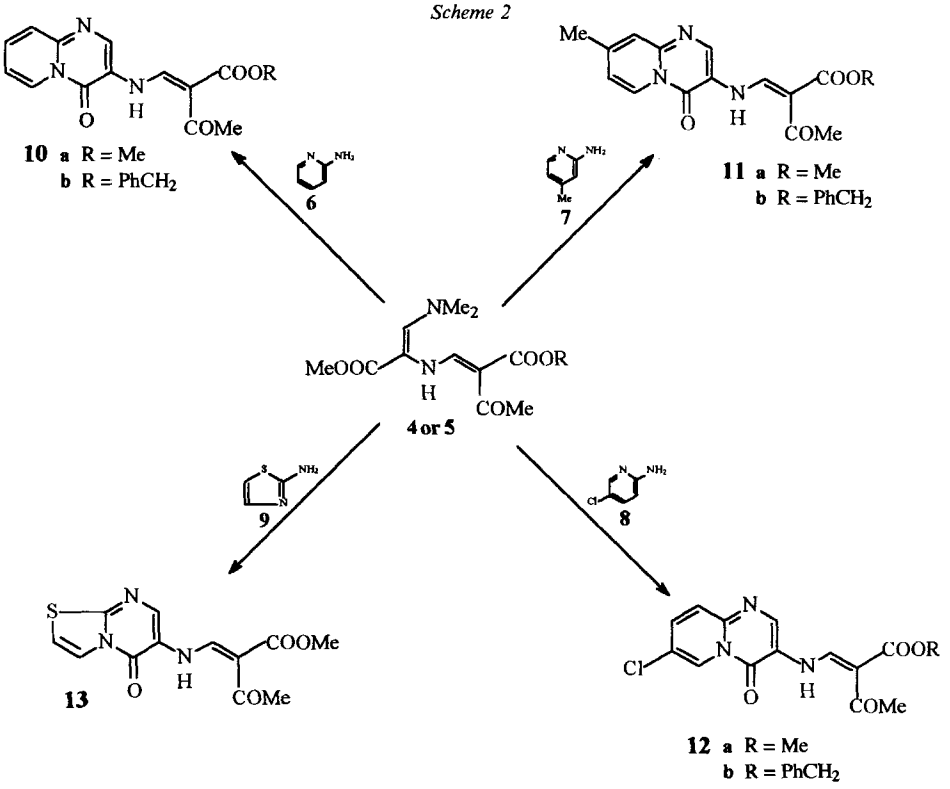
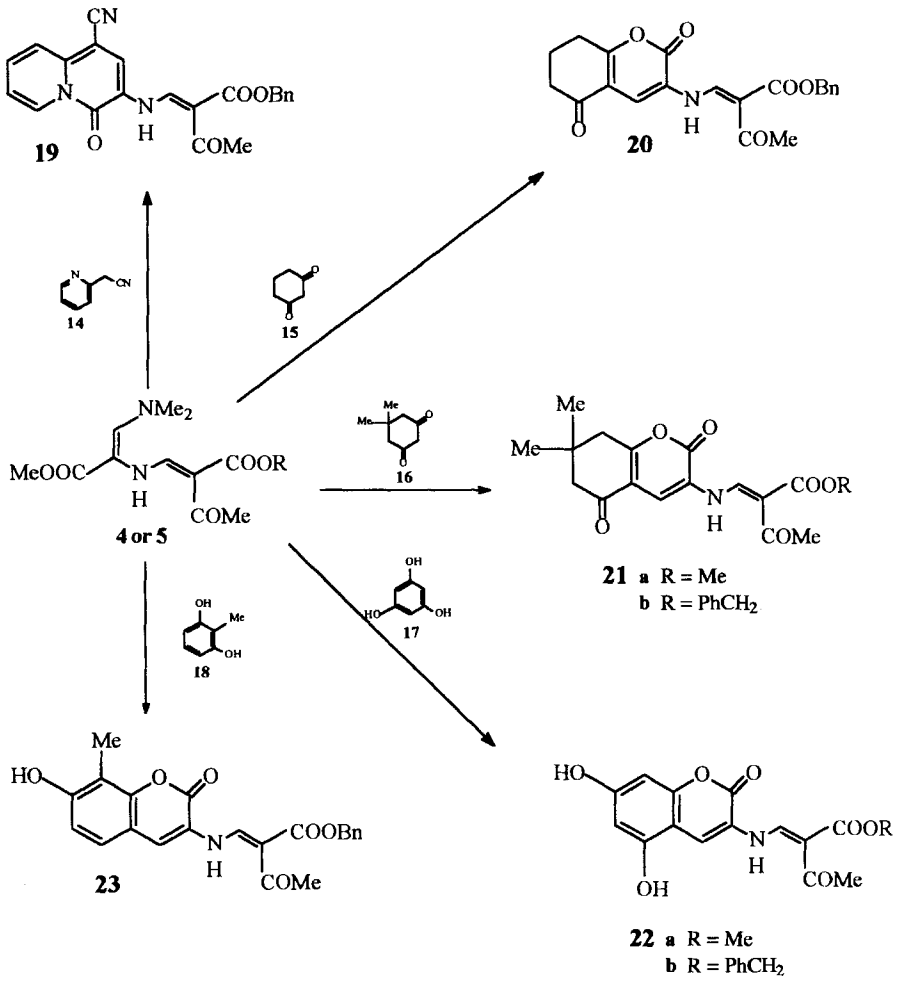



Figure. *Partial NOESY spectrum* ((D$_6$)DMSO, 302 K) *of compound* **4** (88% of (1′*Z*,2*E*)- and 12% of (1′*Z*,2*Z*)-isomer). The separated signals of the (1′*Z*,2*Z*)-isomer **4b** are marked in italics.

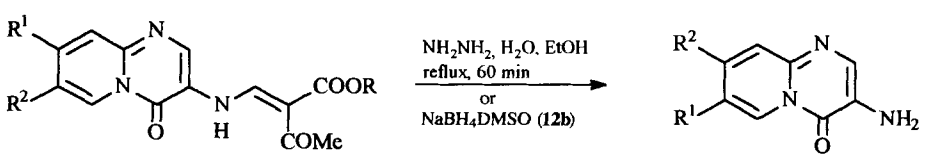
*Scheme 2*



*Scheme 3*



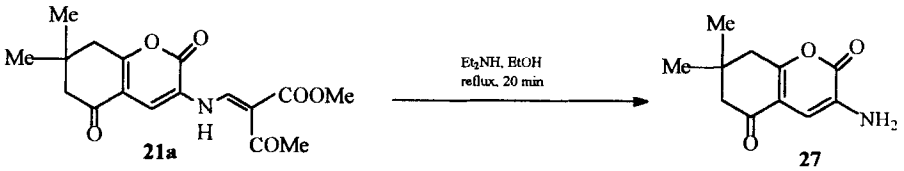

*Scheme 4*




**10-12** **a** R = Me
**b** R = $PhCH_2$

| | $R^1$ | $R^2$ | Yield | Yield |
|---|---|---|---|---|
| **24** | H | H | 65% from **10a** | 55% from **10b** |
| **25** | H | Me | 77% from **11a** | 89% from **11b** |
| **26** | Cl | H | 64% from **12a** | 53% from **12b** |

*Scheme 5*




## Experimental Part

*General.* Melting points: *Kofler* micro hot stage. $^1$H-NMR Spectra: *Bruker-Avance-DPX-300* spectrometer; $\delta$ in ppm rel. to internal $SiMe_4$, $J$ in Hz. Elemental analyses for C, H, and N on a *Perkin-Elmer-CHN-240-C*-analyser.

*Methyl 2-Acetyl-3-[(2-methoxy-2-oxoethyl)amino]prop-2-enoate* (**3a**). To a soln. of methyl 3-oxobutanoate (**1a**; 11 ml, 100 mmol) in toluene (20 ml), *N,N*-dimethylformamide dimethyl acetal (130 mmol, 19.5 ml) was added, and the mixture was heated under reflux for 2 h. After evaporation methyl glycinate hydrochloride (100 mmol, 12.57 g) and AcOH (50 ml) were added to the oily residue. The mixture was heated under reflux for 1.5 h and then evaporated. EtOH was added for crystallization and the isolated precipitate recrystallized from EtOH: **3a** (42%, 90% (*E*)). M.p. 78–80°. $^1$H-NMR (300 MHz, $(D_6)$DMSO): 2.28 (*s*, COMe); 3.62, 3.68 (2*s*, COOMe); 4.30 (*d*, $J$ = 6.2, $CH_2$NH); 8.03 (*d*, $J$ = 13.9, H–C(3)); 10.76 (*td*, NH). Anal. calc. for $C_9H_{13}NO_5$ (215.21): C 50.23, H 6.09, N 6.51; found: C 50.18, H 6.01, N 6.54.

*Phenylmethyl 2-Acetyl-3-[(2-methoxy-2-oxoethyl)amino]prop-2-enoate* (**3b**). As described for **3a**, with phenylmethyl 3-oxobutanoate (**1b**; 120 mmol, 20.4 ml), toluene (20 ml), $CH(OMe)_2NMe_2$ (180 mmol, 27 ml; 2 h), methyl glycinate hydrochloride (100 mmol), and AcOH (830 ml; 1 h). The oily residue was crystallized in EtOH: **3b** (70%, 88% (*E*)). M.p. 97–98°. $^1$H-NMR (60 MHz, $(D_6)$DMSO): 2.34 (*s*, COMe); 3.67 (*s*, COOMe); 4.32 (*d*, $J$ = 6, $CH_2$NH); 5.18 (*s*, PhC$H_2$); 7.42 (*s*, Ph); 8.11 (*d*, $J$ = 15, H–C(3)); 10.83 (*m*, NH). Anal. calc. for $C_{15}H_{15}NO_5 \cdot {}^1/_2$ EtOH (312.32): C 61.53, H 5.80, N 4.49; found: C 61.64, H 5.81, N 4.81.

*Methyl 2-Acetyl-3-{[2-(dimethylamino)-1-(methoxycarbonyl)ethenyl]amino}prop-2-enoate* (**4**). To a soln. of **3a** (50 mmol, 10.76 g) in MeCN (30 ml), $CH(OMe)_2NMe_2$ (65 mmol, 9.8 ml) was added, and the mixture was heated for 4 h under reflux. After evaporation, the solid residue was recrystallized from EtOH: **4** (92%; 88% (*E*)). M.p. 113–114°. $^1$H-NMR (300 MHz, $(D_6)$DMSO): **4a** (1′*Z*,2*E*): (*s*, COMe); 2.97 (*s*, $Me_2$N); 3.59, 3.62 (2*s*, COOMe); 7.30 (*s*, H–C(2′)); 7.81 (*d*, $J$ = 13.6, H–C(3)); 11.40 (*d*, $J$ = 13.6, NH); **4b** (1′*Z*,2*Z*): 2.29 (*s*, COMe); 2.97 (*s*, $Me_2$N); 3.58, 3.71 (2*s*, COOMe); 7.31 (*s*, H–C(2′)); 7.74 (*d*, $J$ = 1.51, H–C(3)); 9.47 (*d*, $J$ = 15.1, NH). Anal. calc. for $C_{12}H_{18}N_2O_5$ (270.29): C 53.33, H 6.71, N 10.36; found: C 53.75, H 6.82, N 10.24.

*Phenylmethyl 2-Acetyl-3-{[2-(dimethylamino)-1-(methoxycarbonyl)ethenyl]amino}prop-2-enoate* (**5**). As described for **4**, with **3b** (100 mmol, 28.93 g), MeCN, and $CH(OMe)_2NMe_2$ (150 mmol, 22.5 ml; 3 h). Recrystallization from i-PrOH gave **5** (98%, 88% (*E*)). M.p. 109–111°. $^1$H-NMR (300 MHz, $(D_6)$DMSO); **5a** (1′*Z*,2*E*): 2.37 (*s*, COMe); 2.96 (*s*, $Me_2$N); 3.62 (*s*, COOMe); 5.15 (*s*, PhC$H_2$); 7.29 (*s*, H–C(2′)); 7.42 (*s*, Ph); 7.89 (*d*, $J$ = 13.5, H–C(3)); 11.49 (*d*, $J$ = 13.5, NH); **5b** (1′*Z*,2*Z*): 2.28 (*s*, COMe); 2.96 (*s*, $Me_2$N); 3.62 (*s*, COOMe); 5.25 (*s*, PhC$H_2$); 7.29 (*s*, H–C(2′)); 7.42 (*s*, Ph); 7.78 (*d*, $J$ = 14.8, H–C(3)); 9.61 (*d*, $J$ = 14.8, NH). Anal. calc. for $C_{18}H_{22}N_2O_5$ (346.38): C 62.42, H 6.40, N 8.09; found: C 62.48, H 6.25, N 8.09.

*Reactions of* **4** *and* **5** *with Heteroarenamines and C-Nucleophiles*: *General Procedure.* To a soln. of the heteroarenamine or C-nucleophile in AcOH, an equimolar amount of **4** or **5** was added, and the mixture was heated under reflux for several h (TLC monitoring ('DC-Alufolien Kieselgel *60 F 254*', 0.2 mm, *E. Merck*; $CHCl_3$/MeOH 10:1)). Evaporation and the recrystallization of the solid residue yielded the products **10**–**13** and **19**–**23**.

*Methyl 2-Acetyl-3-[(4-oxo-4*H*-pyrido[1,2-a]pyrimidin-3-yl)amino]prop-2-enoate* (**10a**): from pyridin-2-amine (**6**) and **4** (3 h) in 44% yield (90% (*E*)). M.p. 180–182° (from toluene). $^1$H-NMR (300 MHz, $(D_6)$DMSO): 2.44 (*s*, COMe); 3.71 (*s*, COOMe); 7.41 (*ddd*, $J$(6, 7) = 6.8, $J$(7, 8) = 7.0, $J$(7, 9) = 1.5, H–C(7)); 7.76 (*dd*, $J$(8, 9) = 9.0, $J$(7, 9) = 1.5, H–C(9)); 7.91 (*ddd*, $J$(6, 8) = 1.5, $J$(8, 9) = 9.0, $J$(7, 8) = 7.0, H–C(8)); 8.77 (*d*, $J$ = 13.2, C=C*H*NH); 8.80 (*s*, H–C(2)); 8.98 (*dd*, $J$(6, 8) = 1.5, $J$(6, 7) = 6.8, H–C(6)); 12.68 (*d*, $J$ = 13.2, NH). Anal. calc. for $C_{14}H_{13}N_3O_4$ (287.27): C 58.53, H 4.56, N 14.63; found: C 58.22, H 4.79, N 14.33.

*Phenylmethyl 2-Acetyl-3-[(4-oxo-4*H*-pyrido[1,2-a]pyrimidin-3-yl)amino]prop-2-enoate* (**10b**); from **6** and **5** (2.5 h), in 48% yield (100% (*E*)). M.p. 161–163° (from toluene). $^1$H-NMR (300 MHz, $(D_6)$DMSO): 2.44 (*s*, COMe); 5.24 (*s*, PhC$H_2$); 7.33 (*dd*, $J$(6, 7) = 7.1, $J$(7, 9) = 1.5, H–C(7)); 7.35–7.48 (*m*, Ph); 7.76 (*dd*, $J$(7, 9) = 1.5, $J$(8, 9) = 8.8, H–C(9)); 7.91 (*dd*, $J$(6, 8) = 1.5, $J$(8, 9) = 8.8, H–C(8)); 8.77 (*s*, H–C(2)); 8.85

(*d*, *J* = 13.3, C=C*H*NH); 8.98 (*dd*, *J*(6, 7) = 7.1, *J*(6, 8) = 1.5, H–C(6)); 12.70 (*d*, *J* = 13.3, NH). Anal. calc. for $C_{20}H_{17}N_3O_4$ (363.37): C 66.11, H 4.72, N 11.56; found: C 65.77, H 4.70, N 11.30.

*Methyl 2-Acetyl-3-[(8-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)amino]prop-2-enoate* (**11a**): from 4-methyl-pyridin-2-amine (**7**) and **4** (3 h) in 32% yield (90% (*E*)). M.p. 195–198° (from toluene). $^1$H-NMR (300 MHz, (D$_6$)DMSO): 2.44 (*s*, COMe); 2.47 (*s*, Me–C(8)); 3.71 (*s*, COOMe); 7.28 (*dd*, *J*(6, 7) = 7.5, *J*(7, 9) = 1.9, H–C(7)); 7.58 (*d*, *J* = 1.9, H–C(9)); 8.73 (*s*, H–C(2)); 8.75 (*d*, *J* = 13.2, C=C*H*NH); 8.88 (*d*, *J* = 7.5, H–C(6)); 12.66 (*d*, *J* = 13.2, NH). Anal. calc. for $C_{15}H_{15}N_3O_4$ (301.30): C 59.80, H 5.02, N 13.95; found: C 59.53, H 5.13, N 13.81.

*Phenylmethyl 2-Acetyl-3-[(8-methyl-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)amino]prop-2-enoate* (**11b**): from 4-methylpyridin-2-amine (**7**) and **5** (3 h) in 38% yield (100% (*E*)). M.p. 196–198° (from toluene). $^1$H-NMR (300 MHz, (D$_6$)DMSO): 2.44 (*s*, COMe); 2.47 (*s*, Me–C(8)); 5.24 (*s*, PhC$H_2$); 7.29 (*dd*, *J*(6, 7) = 7.3, *J*(7, 9) = 1.9, H–C(7)); 7.31–7.42, 7.45–7.47 (2*m*, Ph); 7.58 (*d*, *J* = 1.9, H–C(9)); 8.70 (*s*, H–C(2)); 8.83 (*d*, *J* = 12.2, C=C*H*NH); 8.89 (*d*, *J* = 7.3, H–C(6)); 12.69 (*d*, *J* = 12.2, NH). Anal. calc. for $C_{21}H_{19}N_3O_4$ (377.40): C 66.83, H 5.07, N 11.13; found: C 66.48, H 4.96, N 11.11.

*Methyl 2-Acetyl-3-[(7-chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)amine]prop-2-enoate* (**12a**): from 5-chloropyridin-2-amine (**8**) and **4** (2.5 h) in 70% yield (90% (*E*)). M.p. 179–181° (from DMF/EtOH). $^1$H-NMR (300 MHz, (D$_6$)DMSO): 2.44 (*s*, COMe); 3.72 (*s*, COOMe); 7.78 (*d*, *J* = 9.5, H–C(9)); 7.94 (*dd*, *J*(8, 9) = 9.5, *J*(6, 8) = 2.3, H–C(8)); 8.76 (*d*, *J* = 13.6, C=C*H*NH); 8.81 (*s*, H–C(2)); 8.96 (*d*, *J* = 2.3, H–C(6)); 12.66 (*d*, *J* = 13.6, NH). Anal. calc. for $C_{14}H_{12}ClN_3O_4$ (321.72): C 52.27, H 3.76, N 13.06; found: C 51.82, H 3.89, N 12.75.

*Phenylmethyl 2-Acetyl-3-[(7-chloro-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)amino]prop-2-enoate* (**12b**): from **8** and **5** (2.5 h) in 60% yield (100% (*E*)). M.p. 178–180° (from toluene). $^1$H-NMR (300 MHz, (D$_6$)DMSO): 2.44 (*s*, COMe); 5.24 (*s*, PhC$H_2$); 7.30–7.47 (*m*, Ph); 7.77 (*d*, *J* = 9.5, H–C(9)); 7.93 (*dd*, *J*(6, 8) = 1.8, *J*(8, 9) = 9.5, H–C(8)); 8.78 (*s*, H–C(2)); 8.80 (*d*, *J* = 13.5, C=C*H*NH); 8.96 (*d*, *J* = 1.8, H–C(6)); 12.68 (*d*, *J* = 13.5, NH). Anal. calc. for $C_{20}H_{16}ClN_3O_4$ (397.82): C 60.38, H 4.05, N 10.56; found: C 60.07, H 3.96, N 10.61.

*Methyl 2-Acetyl-3-[(5-oxo-5*H*-thiazolo[3,2-*a*]pyrimidin-3-yl)amino]prop-2-enoate* (**13**): from thiazol-2-amine (**9**) and **4** (1 h) in 27% yield (91% (*E*)). M.p. 167–171° (from toluene). $^1$H-NMR (300 MHz, (D$_6$)DMSO): 2.38 (*s*, COMe); 3.70 (*s*, COOMe); 7.66 (*d*, *J* = 4.9, H–C(2)); 8.15 (*d*, *J* = 4.9, H–C(3)); 8.50 (*s*, H–C(7)); 8.67 (*d*, *J* = 13.2, C=C*H*NH); 12.51 (*d*, *J* = 13.2, NH). Anal. calc. for $C_{12}H_{11}N_3O_4S$ (293.30): C 49.14, H 3.78, N 14.33; found: C 49.13, H 3.86, N 14.19.

*Phenylmethyl 2-Acetyl-3-[(1-cyano-4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-3-yl)amino]prop-2-enoate* (**19**): from pyridine-2-acetonitrile (**14**) and **5** (3.5 h) in 41% yield (91% (*E*)). M.p. 188° (dec; from toluene). $^1$H-NMR (300 MHz, (D$_6$)DMSO): 2.43 (*s*, COMe); 5.26 (*s*, PhC$H_2$); 7.30–7.49 (*m*, Ph, H–C(7)); 7.87 (*dd*, *J*(8, 9) = 8.7, H–C(8)); 7.95 (*d*, *J* = 8.7, H–C(9)); 8.62 (*s*, H–C(2)); 8.76 (*d*, *J* = 12.1, C=C*H*NH); 9.11 (*d*, *J* = 7.2, H–C(6)); 12.85 (*d*, *J* = 12.1, NH). Anal. calc. for $C_{22}H_{17}N_3O_4$ (387.39): C 68.21, H 4.42, N 10.85; found: C 68.09, H 4.59, N 10.67.

*Phenylmethyl 2-Acetyl-3-[(5,6,7,8-tetrahydro-2,5-dioxo-2*H*-1-benzopyran-3-yl)amino]prop-2-enoate* (**20**): from cyclohexane-1,3-dione (**15**) and **5** (2 h) in 36% yield (87% (*E*)). M.p. 127–129° (from EtOH). $^1$H-NMR (300 MHz, (D$_6$)DMSO): 2.07 (*t*, *J* = 6.1, CH$_2$); 2.42 (*s*, COMe); 2.50–2.54 (*m*, CH$_2$); 2.88 (*t*, *J* = 6.4, CH$_2$); 5.24 (*s*, PhC$H_2$); 7.32–7.49 (*m*, Ph); 7.78 (*s*, H–C(4)); 8.55 (*d*, *J* = 13.1, C=C*H*NH); 12.36 (*d*, *J* = 13.1, NH). Anal. calc. for $C_{21}H_{19}NO_6$ (381.38): C 66.14, H 5.02, N 3.67; found: C 65.86, H 4.96, N 3.73.

*Methyl 2-Acetyl-3-[(5,6,7,8-tetrahydro-7,7-dimethyl-2,5-dioxo-2*H*-1-benzopyran-3-yl)amino]prop-2-enoate* (**21a**): from 5,5-dimethylcyclohexane-1,3-dione (**16**) and **4** (2.5 h) in 39% yield (89% (*E*)). M.p. 141–144° (from EtOH). $^1$H-NMR (300 MHz, (D$_6$)DMSO): 1.07 (*s*, 2 Me–C(7)); 2.42 (*s*, COMe); 2.45 (*s*, CH$_2$); 2.81 (*s*, CH$_2$); 3.72 (*s*, COOMe); 7.80 (*s*, H–C(4)); 8.50 (*d*, *J* = 13.2, C=C*H*NH); 12.34 (*d*, *J* = 13.2, NH). Anal. calc. for $C_{17}H_{19}NO_6$ (333.34): C 61.25, H 5.75, N 4.20; found: C 60.87, H 6.02, N 4.20.

*Phenylmethyl 2-Acetyl-3-[(5,6,7,8-tetrahydro-7,7-dimethyl-2,5-dioxo-2*H*-1-benzopyran-3-yl)amino]prop-2-enoate* (**21b**): from **16** and **5** (2 h) in 73% yield (88% (*E*)). M.p. 182–184° (from i-PrOH/toluene). $^1$H-NMR (300 MHz, (D$_6$)DMSO): 1.07 (*s*, 2 Me–C(7)); 2.42 (*s*, COMe); 2.44, 2.81 (*s*, CH$_2$); 5.24 (*s*, PhC$H_2$); 7.32–7.47 (*m*, Ph); 7.77 (*s*, H–C(4)); 8.57 (*d*, *J* = 13.1, C=C*H*NH); 12.36 (*d*, *J* = 13.1, NH). Anal. calc. for $C_{23}H_{23}NO_6$ (409.44): C 67.47, H 5.66, N 3.42; found: C 67.52, H 5.44, N 3.42.

*Methyl 2-Acetyl-3[(5,7-dihydroxy-2-oxo-2*H*-1-benzopyran-3-yl)amino]prop-2-enoate* (**22a**): from benzene-1,3,5-triol (**17**) and **4** (2 h) in 56% yield (90% (*E*)). M.p. > 260° (dec.; from EtOH/AcOH). $^1$H-NMR (300 MHz, (D$_6$)DMSO): 2.42 (*s*, COMe); 3.72 (*s*, COOMe); 6.25, 6.33 (2*d*, *J* = 1.9, H–C(6), H–C(8)); 7.97 (*s*, H–C(4)); 8.48 (*d*, *J* = 13.2, C=C*H*NH); 10.34, 10.70 (br. *s*, OH–C(5), HO–(C7)); 10.73 (*d*, *J* = 13.2, NH). Anal. calc. for $C_{15}H_{13}NO_7 \cdot {}^1/_2 H_2O$ (328.28): C 54.88, H 4.30, N 4.27; found: C 55.13, H 4.44, N 4.14.

*Phenylmethyl 2-Acetyl-3-[(5,7-dihydroxy-2-oxo-2H-1-benzopyran-3-yl)amino]prop-2-enoate* (**22b**): from **17** and **5** (0.5 h) in 56% yield (88%) (*E*)). M.p. 270–272° (dec.; from DMF/toluene). $^1$H-NMR (300 MHz, $(D_6)$DMSO): 2.42 (*s*, COMe); 5.24 (*s*, PhC$H_2$); 6.25, 6.32 (*d*, $J$ = 1.9, H–C(6), H–C(8)); 7.30–7.40, 7.40–7.47 (2*m*, Ph); 7.92 (*s*, H–C(4)); 8.54 (*d*, $J$ = 13.4, C=C*H*NH); 10.36, 10.81 (br. *s*, OH–C(5), OH–C(7)); 12.47 (*d*, $J$ = 13.4, NH). Anal. calc. for $C_{21}H_{17}NO_7$ (395.37): C 63.80, H 4.33, N 3.54; found: C 63.58, H 4.13, N 3.58.

*Phenylmethyl 2-Acetyl-3-[(7-hydroxy-8-methyl-2-oxo-2H-1-benzopyran-3-yl)amino]prop-2-enoate* (**23**): from 2-methylbenzol-1,3-diol (**18**) and **5** (2.5 h in 15% yield (100% (*E*)). M.p. 226–227° (from EtOH/toluene). $^1$H-NMR (300 MHz, $(D_6)$DMSO): 2.16 (*s*, Me–C(8)); 2.43 (*s*, COMe); 5.26 (*s*, PhC$H_2$); 6.85 (*d*, $J$ = 8.4, H–C(5)); 7.34–7.44 (*m*, Ph, H–C(6)); 8.10 (*s*, H–C(4)); 8.57 (*d*, $J$ = 13.0, C=C*H*NH); 12.55 (*d*, $J$ = 13.0, NH). Anal. calc. for $C_{22}H_{19}NO_6 \cdot {}^1/_2\,H_2O$ (402.41): C 64.23, H 5.14, N 3.40; found: C 64.60, H 4.91, N 3.44.

N-*Deprotection with Hydrazine Hydrate: General Procedure.* To a starting compound (1 mmol), 0.5M hydrazine hydrate in EtOH (4 ml) was added. The mixture was heated under reflux for 1 h. Then the mixture was cooled until a precipitate was formed which was collected by filtration. Compounds **24**–**26** were recovered in anal. pure form without further purification.

*3-Amino-4H-pyrido[1,2-a]pyrimidin-4-one* (**24**): from **10a** (0.287 g, 1 mmol) in 65% and from **10b** (0.363 g, 1 mmol) in 55% yield. M.p. 176–178° (from EtOH; [3]: 180–182°). $^1$H-NMR (300 MHz, $(D_6)$DMSO): 5.18 (*s*, $NH_2$); 7.10 (*ddd*, $J$(6, 7) = 7.3, $J$(7, 8) = 5.6, $J$(7, 9) = 2.2, H–C(7)); 7.40–7.52 (*m*, H–C(8), H–C(9)); 7.91 (*s*, H–C(2)); 8.73 (*ddd*, $J$(6, 7) = 7.3, $J$(6, 8) = 1.1, $J$(6, 9) = 0.6, H–C(6)).

*3-Amino-7-methyl-4H-pyrido[1,2-a]pyrimidin-4-one* (**25**): from **11a** (0.301 g, 1 mmol) in 77% and from **11b** (0.377 g, 1 mmol) in 89% yield. M.p. 225–226° (from EtOH; [11]: 215–225°). $^1$H-NMR (300 MHz, $(D_6)$DMSO): 2.34 (*s*, Me–C(8)); 5.01 (*s*, $NH_2$); 6.97 (*dd*, $J$(6, 7) = 7.2, $J$(7, 9) = 1.9, H–C(7)); 7.26 (*d*, $J$ = 1.9, H–C(9)); 7.86 (*s*, H–C(2)); 8.66 (*d*, $J$ = 7.2, H–C(6)).

*3-Amino-7-chloro-4H-pyrido[1,2-a]pyrimidin-4-one* (**26**): from **12a** (0.321 g, 1 mmol) in 64% and from **12b** (0.397 g, 1 mmol) in 53% yield. M.p. 192–193° (from MeOH; [2]: 189–190°). $^1$H-NMR (300 MHz, $(D_6)$DMSO): 5.42 (*s*, $NH_2$); 7.43 (*dd*, $J$(8, 9) = 9.6, $J$(6, 8) = 2.2, H–C(8)); 7.49 (*dd*, $J$ = 9.6, H–C(9)); 7.89 (*s*, H–C(2)); 8.72 (*dd*, $J$(6, 8) = 2.2, $J$(6, 9) = 0.5, H–C(6)).

N-*Deprotection with Hydride*: **26**. To **12b** (0.397 g, 1 mmol), $NaBH_4$ (1.2 mmol, 45 mg) in DMSO (4 ml) was added. The mixture was heated at 80–100° for 0.5 h. Then i-PrOH was added and the mixture cooled to −20°. The addition of DMSO produced a precipitate which was quickly collected by filtration. The filtrate was evaporated, the residue extracted with $CHCl_3$ and $H_2O$, the org. phase dried ($Na_2SO_4$) and evaporated, and the residue treated with EtOH. The precipitate was purified by recrystallization from EtOH: **26** in 20% yield. M.p. 190–191°.

N-*Deprotection with Diethylamine: 3-Amino-7,8-dihydro-7,7-dimethyl-2H-1-benzopyran-2,5(6H)-dione* (**27**). To **21a** (0.333 g, 1 mmol), 0.5M $Et_2NH$ in EtOH (4 ml) was added. The mixture was heated under reflux for 20 min. Then the mixture was cooled until a precipitate was formed which was filtered off: **27** in 10% yield. M.p. 186–189° (from EtOH; [12]: 195.5–196.5°). $^1$H-NMR (300 MHz, $(D_6)$DMSO): 1.04 (*s*, 2 Me–C(7)); 2.34 (*s*, $CH_2$); 2.67 (*s*, $CH_2$); 5.43 (*s*, $NH_2$); 6.59 (*s*, H–C(4)).

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