Synthesis and transformations of methyl (Z)-2-[(tert-butoxycarbonyl)amino]-3-(dimethylamino)propenoate

Janez Baš[a], Simon Rečnik[a], Jurij Svete[a]*, Simona Golič-Grdadolnik[b], and Branko Stanovnik[a]*

[a] *Faculty of Chemistry and Chemical Technology, University of Ljubljana, Ljubljana, Slovenia*
E-mail: branko.stanovnik@Uni-Lj.si
[b] *National Institute of Chemistry, Ljubljana, Slovenia*

Dedicated to Professor Emeritus Fritz Sauter, Vienna University of Technology, on the occasion of his 70th birthday

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Abstract

Methyl (*Z*)-2-[(*tert*-butoxycarbonyl)amino]-3-(dimethylamino)propenoate (**3**) was prepared in 2 steps from glycine methyl ester hydrochloride (**1**). Acid catalysed reactions of **3** with various alkyl-, aryl-, and heteroarylamines **4a–g**, performed at 20–80 °C, proceeded by substitution of the dimethylamino group giving the corresponding substitution products, 3-*N*-substituted methyl (*Z*)-2-[(*tert*-butoxycarbonyl)-amino]amino)propenoates **5a–g**. Treatment of **3** with ambident 1,3-nucleophiles, such as 2-pyridineacetonitrile (**6**), 2-aminothiazole (**4d**), 2-aminopyridine (**4f**), and 4-hydroxy-6-methyl-2*H*-pyran-3-one (**7**) in acetic acid at 85–120 °C afforded fused pyridones **8** and **12**, pyrimidones **9** and **10** and pyranones **11** and **13**.

Keywords: Heterocycles, amino acids, enamines, 3-(dimethylamino)propenoates, ambident nucleophiles

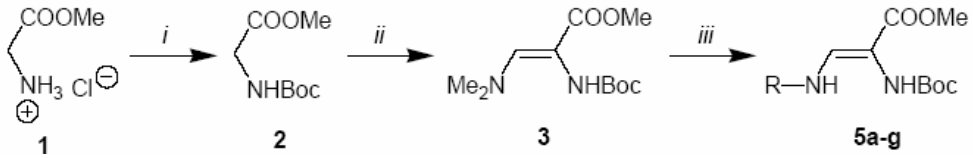
Introduction

Quinolizines, pyridinopyrimidines, and related systems with a bridgehead nitrogen atom are the constituents of many naturally occurring compounds and exhibit like their synthetic derivatives various biological activities.[1,2] 3-Aminopyridino[1,2–a]pyrimidines have been prepared in the past by reduction of the corresponding 3-nitro derivatives using either titanium(III) chloride or Pd–C in the presence of hydrogen[3] or by hydrolysis of 3-benzoyl-amino derivatives in concentrated hydrochloric acid in yields below 40%. In the last decade, alkyl 2-substituted 3-(dimethylamino)propenoates and their cyclic analogs proved to be easily available, efficient, and versatile reagents for the preparation of a variety of heterocyclic systems. Until now, several

reviews on this topic have been published. [5-9] Alkyl 2-acylamino-3-(dimethylamino)propenoates are an important subclass of 2-substituted alkyl 3-(dimethylamino)propenoates and were employed as reagents in one step syntheses of 3-*N*-substituted alkyl 2-acylamino-3-aminopropenoates and heterocycles with an incorporated α-amino acid structural element. Examples of such heterocyclic systems are acylamino-substituted azolo- and azino-fused pyridinones, pyrimidinones, pyranones, and their tetrahydro analogs.[5-10] In continuation of our work in this field, we report the preparation of methyl (*Z*)-2-[(tert-butoxycarbonyl)amino]-3-(dimethylamino)propenoate (**3**) and its transformations with amines and ambident 1,3-dinucleophiles with the intention to prepare acylamino derivatives, which can be deprotected under milder conditions.

Results and Discussion

Methyl (*Z*)-2-[(*tert*-butoxycarbonyl)amino]-3-(dimethylamino)propenoate (**3**) was prepared in 2 steps from glycine methyl ester hydrochloride (**1**) which was first transformed with bis(*tert*-butyl) dicarbonate into *N*-(*tert*-butoxycarbonyl)glycine methyl ester (**2**).[11] Compound **2** was then treated with commercially available (Fluka) bis(dimethylamino)-*tert*-butoxymethane (Bredereck's reagent) in refluxing toluene to give **3** in 55% yield. Treatment of **3** with various alkyl- **4a**, aryl- **4b,c**, and heteroarylamines **4d–f** in ethanol at 20–80 °C in the presence of equimolar amounts of hydrochloric acid proceeded with substitution of the dimethylamino group giving the corresponding substitution products, 3-*N*-substituted methyl 2-[(*tert*-butoxycarbonyl)amino]-3-aminopropenoates **5a–f**. Similarly, methyl 2-[(*tert*-butoxycarbonyl)amino]-3-[(4-methylpyridin-2-yl)amino]propenoate (**5g**) was obtained from **3** and 2-amino-4-methylpyridine (**4g**) in acetic acid at 80 °C. Under these reaction conditions, the *tert*-butoxycarbonyl (*t*-Boc) group, remained more or less unaffected (Scheme 1).

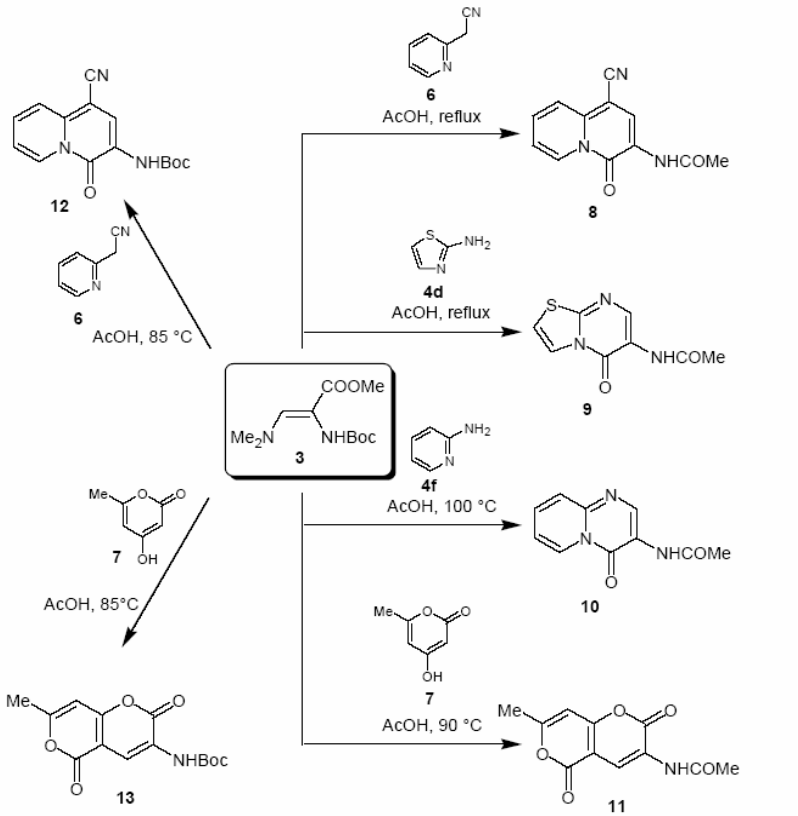


Scheme 1 Reagents and conditions: i) Boc_2O, Et_3N, CH_2Cl_2, 20 °C; ii) bis(dimethylamino)-*tert*-butoxymethane (Bredereck's reagent), toluene, reflux; iii) R–NH_2 (4a–f), EtOH, HCl (aq.), 20 °C (Method A) or R–NH_2 (4g), AcOH, 80 °C (Method B).

On the other hand, treatment of methyl (*Z*)-2-[(*tert*-butoxycarbonyl)amino]-3-(dimethylamino)propenoate (**3**) in acetic acid at 90–120 °C with the following ambident nucleophiles: 2-pyridineacetonitrile (**6**), 2-aminothiazole (**4d**), 2-aminopyridine (**4f**), and 4-hydroxy-6-methyl-2*H*-pyran-2-one (**7**), gave the corresponding 3-acetylamino substituted fused pyridone (**8**), pyrimidones (**9**, **10**), and pyranone (**11**), respectively.

However, with 2-pyridineacetonitrile (**6**) and with 4-hydroxy-6-methyl-2*H*-pyran-2-one (**7**)

in acetic acid at 85 °C, 3-[(*tert*-butoxycarbonyl)amino]-1-cyano-4*H*-quinolizin-4-one (**12**) and 3-[(*tert*-butoxycarbonyl) amino]-7-methyl-2*H*,5*H*-pyrano[4,3–*b*]pyran-2,5-dione (**13**) were obtained, respectively. Therefore, the *t*-Boc group proved to be stable towards treatment with acetic acid up to 85°, while at higher temperatures removal of the *t*-Boc group followed by acetylation of the free amino group occurred (Scheme 2).The structures of compounds **3**, **5a–g**, **8–13** were confirmed by spectroscopic methods and by C, H, N analyses. Spectral data of the novel compounds **3**, **5a–g**, **9**, **11–13** are in agreement with the literature data for closely related compounds.[5-11] Spectral and analytical data of 3-acetylamino-1-cyano-4*H*-quinolizin-4-one (**8**) and 3-acetylamino-4*H*-pyridino[1,2–*a*]pyrimidin-4-one (**10**) are in agreement with the literature data for these two compounds, prepared previously from methyl (*Z*)-2-acetylamino-3-(dimethylamino)propenoate.[10,12] The configuration of the C(2),C(3) double bond in compounds **3** and **5c** was studied using the 2D HMBC NMR technique. The $^{3}J_{H,CO}$ values ($^{3}J_{H,CO}$ = 4.8 Hz for **3**; $^{3}J_{H,CO}$ = 3.0 Hz for **5c**) are in agreement with previously observed ^{3}J values for the *Z*-isomers of closely related propenoates (Figure 1).[8,13–18]



Scheme 2

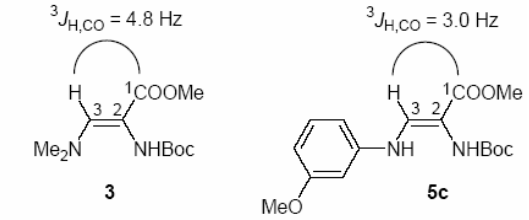


Figure 1

Experimental Section

General Procedures. All starting materials were commercially available (in most cases from Fluka) and purified following standard techniques. Melting points were taken with a Kofler micro hot stage. The ^{1}H NMR (300 MHz), ^{13}C NMR (75.5 MHz) and 2D HMBC (300 MHz, $CDCl_3$, 302 K) spectra were obtained with a Bruker Avance DPX 300 spectrometer with DMSO-*d*$_6$ and $CDCl_3$ as solvents and Me_4Si as internal standard. IR spectra were recorded with a Perkin-Elmer 1310 spectrophotometer (KBr discs). The mass spectra were recorded with an Autospeck Q (VG-Analytical) spectrometer in the Laboratory for Mass Spectroscopy (Josef Stefan Institute, Ljubljana). The C, H, N microanalyses were obtained with a Perkin-Elmer CHN Analyser 2400. Flash chromatography was performed on silica gel (Fluka, Kieselgel 60, 0.040−0.063 mm).

Methyl *N*-(*tert*-Butoxycarbonyl)glycinate (2). This compound was prepared by a modified procedure described in the literature. [11] A mixture of methyl glycinate hydrochloride (1.256 g, 10 mmol) and anhydrous dichloromethane (40 mL) was stirred at 0 °C (ice bath) for 10 min. Then triethylamine (1.4 mL, 10 mmol) was added and the mixture was stirred at 0 °C for 20 min. The ice bath was then removed, bis(*tert*-butyl) dicarbonate (2.227 g, 10 mmol) was added, and the mixture was stirred at r.t. for 24 h. The reaction mixture was then washed with water (40 mL), hydrochloric acid (1%, 40 mL), saturated aqueous sodium bicarbonate (40 mL), and finally with brine (40 mL). The organic phase was dried over anhydrous sodium sulfate for 2 h, filtered, and the filtrate evaporated *in vacuo* to give crude **2**, which was used for further transformation without purification. Yield: 95% (1.792 g). ^{1}H NMR ($CDCl_3$): δ 1.44 (9H, s, CMe_3); 3.74 (3H, s, OMe); 3.89 (2H, d, J = 5.6 Hz, CH_2); 5.52 (1H, br s, NH).

Methyl (*Z*)-2-[(*tert*-butoxycarbonyl)amino]-3-(dimethylamino)propenoate (3). A mixture of methyl *N*-(*tert*-butoxycarbonyl)glycinate (**2)** (1.792 g, 9.5 mmol), anhydrous toluene (8 mL), and bis(dimethylamino)-*tert*-butoxymethane (1.74 g, 10 mmol) was stirred under argon at the reflux temperature (oil bath) for 3 h. Volatile components were evaporated *in vacuo* and the oily residue was purified by flash chromatograpy (diethyl ether). Fractions containing the product were combined, volatile components were evaporated *in vacuo*, and the solid residue was crystallized from *n*-hexane to give **3**. Yield: 55% (1.278 g), m.p. 108–109 °C (*n*-hexane). IR (cm^{-1}): 3300 (NH), 1720-1680 (C=O). ^{1}H NMR ($CDCl_3$): δ 1.46 (9H, s, CMe_3); 3.04 (6H, s, NMe_2); 3.67 (3H, s, OMe); 5.33 (1H, br s, NH); 7.29 (1H, br s, 3–H). ^{13}C NMR ($CDCl_3$): δ 28.68, 42.32, 51.48, 79.96, 94.93, 146.79, 156.83, 168.85. Anal. calcd. for $C_{11}H_{20}N_2O_4$ (244.3): C, 54.08; H, 8.25; N, 11.47. Found: C, 54.31; H, 8.12; N, 11.59.

Preparation of methyl 3-*N*-substituted 2-[(*tert*-Butoxycarbonyl)amino]-3-amino-propenoates 5a–f. General procedure

Hydrochloric acid (37%, 3 drops, ~1 mmol) was added to a solution of methyl (*Z*)-2-[(*tert*-butoxycarbonyl)amino]-3-(dimethyl-amino) propenoate (**3)** (244 mg, 1 mmol) and amine **4a–f** (1 mmol) in anhydrous ethanol (3 mL). The reaction mixture was then stirred at 20–80 °C for 2–28 h. Volatile components were evaporated *in vacuo*, and the residue was triturated with diethyl

ether (4 mL). The precipitate was collected by filtration and crystallized from aqueous methanol to give **5a–f**. The following compounds were prepared in this manner:

Compound	R	Method
4a, **5a**	4-methoxybenzyl	A
4b, **5b**	phenyl	A
4c, **5c**	3-methoxyphenyl	A
4d, **5d**	1,3-thiazol-2-yl	A
4e, **5e**	6-chloropyridazin-3-yl	A
4f, **5f**	pyridin-2-yl	A
4g, **5g**	4-methylpyridin-2-yl	B

Methyl 2-[(*tert*-butoxycarbonyl)amino]-3-[(4-methoxybenzyl)amino]propenoate (5a). From **3** and 4-methoxybenzylamine (**4a**) (137 mg, 1 mmol); 20 °C, 28 h. Yield: 59% (199 mg), m.p. 138 °C (methanol/water). IR (cm^{-1}): 3380 (NH), 1700 (C=O). ^{1}H NMR (DMSO-d_6): δ 1.39 (9H, s, CMe_3); 3.50 (3H, s, OMe); 3.73 (3H, s, OMe); 4.23 (2H, d, J = 6.0 Hz, CH_2); 6.75–6.95 (1H, broad signal, 3–H); 6.88 (2H, d, J = 8.7 Hz, *m*–C_6H_4); 7.15 (1H, br s, 2–NH); 7.21 (2H, d, J = 8.7 Hz, *o*–C_6H_4); 7.31 (1H, br d, J = 13.8 Hz, 3–NH). Anal. calcd. for $C_{17}H_{24}N_2O_5$ (336.4): C, 60.70; H, 7.19; N, 8.33. Found: C, 60.66; H, 7.30; N, 8.34.

Methyl 2-[(*tert*-Butoxycarbonyl)amino]-3-anilinopropenoate (5b). From **3** and aniline (**4b**) (93 mg, 1 mmol); 20 °C, 2 h. Yield: 75% (219 mg), m.p. 117–119 °C (methanol/water). IR (cm^{-1}): 3360–3320 (NH), 1740–1660 (C=O). ^{1}H NMR ($CDCl_3$): δ 1.51 (9H, s, CMe_3); 3.78 (3H, s, OMe); 6.32 (1H, br s, 2–NH); 6.95–6.99 (3H, m, *o,p*–C_6H_5); 7.26–7.28 (2H, m, *m*–C_6H_5); 7.66 (1H, d, J = 12.1 Hz, 3–H); 8.10 (1H, br s, 3–NH). ^{13}C NMR ($CDCl_3$): δ 28.65, 52.52, 81.35, 102.95, 115.87, 122.51, 129.95, 141.45, 146.52, 155.06, 166.69. Anal. calcd. for $C_{15}H_{20}N_2O_4$ (292.3): C, 61.63; H, 6.90; N, 9.58. Found: C, 61.27; H, 6.90; N, 9.52.

Methyl 2-[(*tert*-butoxycarbonyl)amino]-3-[(3-methoxyphenyl)amino]propenoate (5c). From **3** and 3-methoxyaniline (**4c)** (123 mg, 1 mmol); 20 °C, 3 h. Yield: 47% (151 mg), m.p. 119–120 °C (methanol/water). IR (cm^{-1}): 3360–3320 (NH), 1740–1660 (C=O). ^{1}H NMR ($CDCl_3$): δ 1.51 (9H, s, CMe_3); 3.78 (3H, s, OMe); 3.81 (3H, s, OMe); 6.32 (1H, br s, 2–NH); 6.48–6.57 (3H, m, 3H–Ar); 7.19 (1H, t, J = 8.1 Hz, 1H–Ar); 7.63 (1H, d, J = 12.1 Hz, 3–H); 8.12 (1H, br s, 3–NH). ^{13}C NMR ($CDCl_3$): δ 28.65, 52.25, 55.73, 81.38, 102.07, 103.07, 107.66, 108.61, 130.76, 142.77, 155.05, 161.23, 166.65. Anal. calcd. for $C_{16}H_{22}N_2O_5$ (322.4): C, 59.61; H, 6.88; N, 8.69. Found: C, 59.48; H, 7.00; N, 8.91.

Methyl 2-[(*tert*-butoxycarbonyl)amino]-3-[(thiazol-2-yl)amino]propenoate (5d). From **3** and 2-aminothiazole (**4d**) (100 mg, 1 mmol); 20 °C, 2 h. Yield: 41% (123 mg), m.p. 145–146 °C (methanol/water). IR (cm^{-1}): 3000 (NH), 1720 (C=O). ^{1}H NMR ($CDCl_3$): δ 1.50 (9H, s, CMe_3); 3.80 (3H, s, OMe); 6.60 (1H, br s, 2–NH); 6.73 (1H, d, J = 2.3 Hz, 5'–H); 7.29 (1H, d, J = 2.3 Hz, 4'–H); 7.70 (1H, d, J = 10.2 Hz, 3–H); 9.71 (1H, br s, 3–NH). Anal. calcd. for $C_{12}H_{17}N_3O_4S$ (299.4): C, 48.15; H, 5.72; N, 14.04. Found: C, 48.14; H, 5.69; N, 13.88.

Methyl 2-[(*tert*-butoxycarbonyl)amino]-3-[(6-chloropyridazin-3-yl)amino]-propeno-ate (5e). From **3** and 3-amino-6-chloropyridazine (**4e**) (130 mg, 1 mmol); reflux for 4.5 h. Yield: 91% (298 mg), m.p. 153–155 °C (methanol/water). MS (EI): m/z = 328 (M^+); (FAB): m/z = 329 (MH^+). IR (cm^{-1}): 3000 (NH), 1720 (C=O). ^{1}H NMR ($CDCl_3$): δ 1.51 (9H, s, CMe_3); 3.81 (3H, s, OMe); 6.79 (1H, br s, 2–NH); 6.92 (1H, d, *J* = 9.4 Hz, 4'–H); 7.29 (1H, d, *J* = 9.4 Hz, 5'–H); 8.20 (1H, dd, *J* = 0.8, 10.2 Hz, 3–H); 9.62 (1H, br s, 3–NH). HRMS Calcd for $C_{13}H_{17}ClN_4O_4$: 328.094950. Found: 328.093833. Anal. calcd. for $C_{13}H_{17}ClN_4O_4$ (328.8): C, 47.49; H, 5.21; N, 17.04. Found: C, 46.82; H, 5.11; N, 16.97.

Methyl 2-[(*tert*-butoxycarbonyl)amino]-3-[(pyridin-2-yl)amino] propenoate (5f). From **3** and 2-aminopyridine (**4f**) (94 mg, 1 mmol); 20 °C, 2 h. Yield: 32% (94 mg), m.p. 144–145 °C (methanol/water). IR (cm^{-1}): 3240 (NH), 1700–1660 (C=O). ^{1}H NMR ($CDCl_3$): δ 1.53 (9H, s, CMe_3); 3.82 (3H, s, OMe); 6.51 (1H, br s, 2–NH); 6.75 (1H, d, *J* = 7.9 Hz, 3'–H); 6.86 (1H, ddd, *J* = 0.8, 4.9, 6.4, Hz, 5'–H); 7.57 (1H, ddd, *J* = 1.9, 6.4, 8.3 Hz, 4'–H); 8.21 (1H, dd, *J* = 1.1, 11.3 Hz, 3–H); 8.27 (1H, d, *J* = 4.9 Hz, 6'–H); 8.83 (1H, br s, 3–NH). ^{13}C NMR ($CDCl_3$): δ 28.64, 52.41, 81.47, 104.50, 110.73, 117.43, 138.36, 148.75, 152.78, 155.04, 166.82. Anal. calcd. for $C_{14}H_{19}N_3O_4$ (293.3): C, 57.33; H, 6.53; N, 14.33. Found: C, 56.99; H, 6.79; N, 14.04.

Methyl 2-[(*tert*-butoxycarbonyl)amino]-3-[(4-methylpyridin-2-yl)amino] propenoate (5g). A solution of methyl (*Z*)-2-[(*tert*-butoxycarbonyl)amino]-3-(dimethylamino)propenoate (**3**) (244 mg, 1 mmol) and 2-amino-4-methylpyridine (**4g)** (108 mg, 1 mmol) in acetic acid (100%, 5 mL) was heated at 80 °C for 2 h. Volatile components were evaporated *in vacuo* and the oily residue was purified by flash chromatography (diethyl ether). Fractions containing the product were combined and volatile components evaporated *in vacuo* to give **5g**. Yield: 48% (146 mg), m.p. 151–152 °C. IR (cm^{-1}): 3240 (NH), 1700–1680 (C=O). ^{1}H NMR ($CDCl_3$): δ 1.53 (9H, s, CMe_3); 2.29 (3H, s, 4'-Me); 3.79 (3H, s, OMe); 6.49 (1H, br s, 2–NH); 6.54 (1H, s, 3'–H); 6.67 (1H, d, *J* = 4.9 Hz, 5'–H); 8.10 (1H, d, *J* = 5.3 Hz, 6'–H); 8.19 (1H, br d, *J* = 12.0 Hz, 3–H); 8.70 (1H, br s, 3–NH). Anal. calcd. for $C_{14}H_{21}N_3O_4$ (307.3): C, 58.62; H, 6.89; N, 13.67. Found: C, 58.76; H, 7.09; N, 13.68.

3-Acetylamino-1-cyano-4*H*-quinolizin-4-one (8). A solution of methyl (*Z*)-2-[(*tert*-butoxycarbonyl)amino]-3-(dimethylamino)propenoate (**3**) (244 mg, 1 mmol) and 2-pyridineacetonitrile (**6**) (118 mg, 1 mmol) in acetic acid (100%, 5 mL) was heated at reflux temperature for 2 h. Volatile components were evaporated *in vacuo*, and the oily residue was purified by flash chromatography (ethyl acetate). Fractions containing the product were combined, volatile components were evaporated *in vacuo* and the residue crystallized from ethanol to give **8**. Yield: 86% (195 mg), m.p. 243–245 °C (ethanol); lit.[10] m.p. 243–245 °C (ethanol).

6-Acetylamino-5*H*-thiazolo[3,2–*a*]pyrimidin-4-one (9). A solution of methyl (*Z*)-2-[(*tert*-butoxycarbonyl)amino]-3-(dimethylamino)propenoate (**3**) (244 mg, 1 mmol) and 2-aminothiazole (**4d**) (100 mg, 1 mmol) in acetic acid (100%, 5 mL) was heated at the reflux temperature for 2 h. Volatile components were evaporated *in vacuo* and the oily residue was purified by flash chromatography (ethyl acetate). Fractions containing the product were combined, volatile components were evaporated *in vacuo* and the residue crystallized from

ethanol to give **9**. Yield: 57% (120 mg), m.p. 189–192 °C (ethanol). IR (cm^{-1}): 3290 (NH), 1620 (C=O). ^1H NMR ($CDCl_3$): δ 2.24 (3H, s, MeCO); 7.06 (1H, d, *J* = 4.9 Hz, 2–H); 7.83 (1H, br s, NH); 7.95 (1H, d, *J* = 5.3, Hz, 3–H); 9.23 (1H, s, 7–H). Anal. calcd. for $C_8H_7N_3O_2S$ (209.2): C, 45.92; H, 3.37; N, 20.08. Found: C, 46.24; H, 3.34; N, 19.81.

3-Acetylamino-4*H*-pyridino[1,2–*a*]pyrimidin-4-one (10). A solution of methyl (*Z*)-2-[(*tert*-butoxycarbonyl)amino]-3-(dimethylamino)propenoate (**3**) (244 mg, 1 mmol) and 2-aminopyridine (**4f**) (94 mg, 1 mmol) in acetic acid (100%, 5 mL) was heated at 100 °C for 6 h. Volatile components were evaporated *in vacuo*, water (3 mL) was added to the residue, neutralized with aqueous sodium bicarbonate to pH 9, and the product was extracted with chloroform (5 x 20 mL). Organic phases were combined, dried over anhydrous sodium sulfate, filtered, and the filtrate evaporated *in vacuo*. The oily residue was purified by flash chromatography (ethyl acetate). Fractions containing the product were combined, volatile components were evaporated *in vacuo*, and the residue was crystallized from ethanol to give **10**. Yield: 56% (113 mg), m.p. 204–206 °C (ethanol); lit.[12] m.p. 207–208 °C (acetic acid).

3-Acetylamino-7-methyl-2*H*,5*H*-pyrano[4,3–*b*]pyran-2,5-dione (11). A solution of methyl (*Z*)-2-[(*tert*-butoxycarbonyl)amino]-3-(dimethylamino)propenoate (**3**) (244 mg, 1 mmol) and 4-hydroxy-6-methyl-2*H*-pyran-2-one (**7**) (126 mg, 1 mmol) in acetic acid (100%, 5 mL) was heated at 90 °C for 2.5 h. Volatile components were evaporated *in vacuo* and the oily residue was purified by flash chromatography (ethyl acetate). Fractions containing the product were combined, volatile components were evaporated *in vacuo* and the residue crystallized from ethanol to give **11**. Yield: 41% (97 mg), m.p. 227–229 °C (ethanol). IR (cm^{-1}): 3400 (NH), 1700 (C=O). ^1H NMR ($CDCl_3$): δ 2.22 (3H, s, MeCO); 2.35 (3H, s, 5–Me); 6.15 (1H, s, 8–H); 7.85 (1H, br s, NH); 8.71 (1H, s, 4–H). Anal. calcd. for $C_{11}H_9NO_5$ (235.2): C, 56.17; H, 3.86. N, 5.96. Found: C, 56.01; H, 3.84; N, 6.07.

3-[(*tert*-Butoxycarbonyl)amino]-1-cyano-4*H*-quinolizin-4-one (12). A solution of methyl (*Z*)-2-[(*tert*-butoxycarbonyl)amino]-3-(dimethylamino)propenoate (**3**) (244 mg, 1 mmol) and 2-pyridineacetonitrile (**6**) (118 mg, 1 mmol) in acetic acid (100%, 5 mL) was heated at 85 °C for 2 h. Volatile components were evaporated *in vacuo* and the semi-solid residue was crystallized from ethanol to give **12**. Yield: 73% (208 mg), m.p. 198–201 °C (ethanol). IR (cm^{-1}): 3360, 3260 (NH), 2100 (CN), 1700, 1640 (C=O). ^1H NMR ($CDCl_3$): δ 1.55 (9H, s, CMe_3); 7.13 (1H, ddd, *J* = 1.3, 6.8, 7.9 Hz, 7–H); 7.48 (1H, ddd, *J* = 1.1, 6.8, 9.1 Hz, 8–H); 7.60 (1H, br s, NH); 7.93 (1H, dd, *J* = 1.4, 9.1 Hz, 9–H); 8.75 (1H, s, 2–H); 9.04 (1H, deg. dt, *J* = 1.1, 7.9 Hz, 6–H). Anal. calcd. for $C_{15}H_{15}N_3O_3$ (285.3): C, 63.15; H, 5.30; N, 14.73. Found: C, 63.42; H, 5.29; N, 14.71.

3-[(*tert*-Butoxycarbonyl)amino]-7-methyl-2*H*,5*H*-pyrano[4,3–*b*]pyran-2,5-dione (13). A solution of methyl (*Z*)-2-[(*tert*-butoxycarbonyl)amino]-3-(dimethylamino) propenoate (**3**) (244 mg, 1 mmol) and 4-hydroxy-6-methyl-2*H*-pyran-2-one (**7**) (126 mg, 1 mmol) in acetic acid (100%, 5 mL) was heated at 85 °C for 3 h. Volatile components were evaporated *in vacuo* and the residue was crystallized from ethanol to give **13**. Yield: 61% (179 mg), m.p. 289–291 °C (ethanol). IR (cm^{-1}): 3440, 3340 (NH), 1700 (C=O). ^1H NMR ($CDCl_3$): δ 1.52 (9H, s, CMe_3); 2.34 (3H, s, 5–Me); 6.16 (1H, s, 8–H); 7.20 (1H, br s, NH); 8.35 (1H, s, 4–H). Anal. calcd. for $C_{14}H_{15}NO_6$ (293.3): C, 57.34; H, 5.16; N, 4.78. Found: C, 57.21; H, 5.02; N, 5.05.

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