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

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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-2H-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. 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 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](image)

**Scheme 1** Reagents and conditions: i) Boc₂O, Et₃N, CH₂Cl₂, 20 °C; ii) bis(dimethylamino)-tert-butoxymethane (Bredereck's reagent), toluene, reflux; iii) R–NH₂ (4a–f), EtOH, HCl (aq.), 20 °C (Method A) or R–NH₂ (4g), AcOH, 80 °C (Method B).

On the other hand, treatment of 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-2H-pyran-2-one (7), gave the corresponding 3-acylamino substituted fused pyridone (8), pyrimidones (9, 10), and pyranone (11), respectively.

However, with 2-pyridineacetonitrile (6) and with 4-hydroxy-6-methyl-2H-pyran-2-one (7)
in acetic acid at 85 °C, 3-[(tert-butoxycarbonyl)amino]-1-cyano-4H-quinolizin-4-one (12) and 3-[(tert-butoxycarbonyl) amino]-7-methyl-2H,5H-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-4H-quinolizin-4-one (8) and 3-acetylamino-4H-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 $J_{H,CO}$ values ($J_{H,CO} = 4.8$ Hz for 3; $J_{H,CO} = 3.0$ Hz for 5c) are in agreement with previously observed $J$ 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$_4$Si as internal standard. IR spectra were recorded with a Perkin-Elmer 1310 spectrophotometer (KBr discs). The mass spectra were recorded with an Autospec 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 chromatography (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$_2$O$_4$ (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:

<table>
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<th>Compound</th>
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<th>Method</th>
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</tr>
<tr>
<td>4g, 5g</td>
<td>4-methylpyridin-2-yl</td>
<td>B</td>
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**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). ¹H NMR (DMSO-d₆): δ 1.39 (9H, s, CMe₃); 3.50 (3H, s, OMe); 3.73 (3H, s, OMe); 4.23 (2H, d, J = 6.0 Hz, CH₂); 6.75–6.95 (1H, broad signal, 3–H); 6.88 (2H, d, J = 8.7 Hz, m-C₆H₄); 7.15 (1H, br s, 2–NH); 7.21 (2H, d, J = 8.7 Hz, o-C₆H₄); 7.31 (1H, br d, J = 13.8 Hz, 3–NH). Anal. calcd. for C₁₇H₂₄N₂O₅ (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). ¹H NMR (CDCl₃): δ 1.51 (9H, s, CMe₃); 3.78 (3H, s, OMe); 6.32 (1H, br s, 2–NH); 6.95–6.99 (3H, m, o,p-C₆H₅); 7.26–7.28 (2H, m, m-C₆H₅); 7.66 (1H, d, J = 12.1 Hz, 3–H); 8.10 (1H, br s, 3–NH). ¹³C NMR (CDCl₃): 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 C₁₅H₂₀N₂O₄ (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). ¹H NMR (CDCl₃): δ 1.51 (9H, s, CMe₃); 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). ¹³C NMR (CDCl₃): δ 28.65, 52.55, 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 C₁₆H₂₂N₂O₅ (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). ¹H NMR (CDCl₃): δ 1.50 (9H, s, CMe₃); 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 C₁₂H₁₇N₅O₄S (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]-propenoate (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 (M+). IR (cm⁻¹): 3000 (NH), 1720 (C=O). ¹H NMR (CDCl₃): δ 1.51 (9H, s, CMe₃); 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 C₁₃H₁₇ClN₄O₄: 328.094950. Found: 328.093833. Anal. calcd. for C₁₃H₁₇ClN₄O₄ (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). ¹H NMR (CDCl₃): δ 1.53 (9H, s, CMe₃); 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). ¹³C NMR (CDCl₃): 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 C₁₄H₁₉N₃O₄ (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, volatile components were evaporated in vacuo and the residue crystallized from ethanol to give 5g. Yield: 48% (146 mg), m.p. 151–152 °C. IR (cm⁻¹): 3240 (NH), 1700–1660 (C=O). ¹H NMR (CDCl₃): δ 1.53 (9H, s, CMe₃); 2.29 (3H, s, 4’-Me); 3.79 (3H, s, OMe); 6.49 (1H, br s, 2–NH); 6.54 (1H, br 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 C₁₄H₂₁N₃O₄ (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-4H-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 (diethyl ether). 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-5H-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 (CDCl₃): 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 C₈H₇N₃O₂S (209.2): C, 45.92; H, 3.37; N, 20.08. Found: C, 46.24; H, 3.34; N, 19.81.

3-Acetylamino-4H-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-2H,5H-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-2H-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 (CDCl₃): 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 C₁₁H₉NO₅ (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-4H-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 (CDCl₃): δ 1.55 (9H, s, CMe₃); 7.13 (1H, d, J = 1.3, 6.8, 7.9 Hz, 7–H); 7.48 (1H, d, J = 1.1, 6.8, 9.1 Hz, 8–H); 7.60 (1H, br s, NH); 8.75 (1H, d, J = 2–H); 9.04 (1H, deg. dt, J = 1.1, 7.9 Hz, 6–H). Anal. calcd. for C₁₅H₁₅N₃O₃ (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-2H,5H-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-2H-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 (CDCl₃): δ 1.52 (9H, s, CMe₃); 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 C₁₄H₁₅NO₆ (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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References