Efficient Syntheses of Some New Pyridine Based Heterocycles

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Abstract: A facile and convenient synthesis of a series of 1,2,4-triazolo[5,1-c][1,2,4]triazine, 1,3,4-thiadiazole, thiazolidine, and pyrido[1,2-a]pyrimidine derivatives incorporating pyridine moiety via the versatile, readily accessible 2-cyano-N-(pyrid-2-yl)acetamide are described.

Keywords: pyridine; 1,2,4-triazolo[5,1-c][1,2,4]triazine; 1,3,4-thiadiazole; thiazolidine; pyrido[1,2-a]pyrimidine; synthesis.

1. Introduction

Pyridine derivatives are known to possess antitubercular [1], antiulcer [2], antimicrobial [3-5], antineoplastic [6], antitumor [7-9], antiviral [10], insecticidal [11] and cardiotonic [12] properties. Encouraged by these findings and in continuation of our recent interest in the synthesis of a variety of heterocyclic ring systems for biological evaluations [13-21], we found that 2-cyano-N-(pyridin-2-yl)acetamide (1) [22] is a highly versatile and useful building block for the synthesis of a variety of 1,2,4-triazolo[5,1-c][1,2,4]triazine, 1,3,4-thiadiazole, thiazolidine and pyrido[1,2-a]pyrimidine derivatives incorporating pyridine moiety of potential biological activity.
2. Materials and Methods

2.1. Instruments

All melting points were measured on a Gallenkamp melting point apparatus (Weiss-Gallenkamp, London, UK). The infrared spectra were recorded in potassium bromide disks on a pye Unicam SP 3300 and Shimadzu FT IR 8101 PC infrared spectrophotometers (Pye Unicam Ltd. Cambridge, England and Shimadzu, Tokyo, Japan, respectively). The NMR spectra were recorded on a Varian Mercury VX-300 NMR spectrometer. $^1$H spectra were run at 300 MHz and $^{13}$C spectra were run at 75.46 MHz in deuterated chloroform (CDCl$_3$) or dimethyl sulfoxide (DMSO-$d_6$). Chemical shifts were related to that of the solvent. Mass spectra were recorded on a Shimadzu GCMS-QP 1000 EX mass spectrometer (Shimadzu-Tokyo, Japan) at 70 eV. Elemental analyses were carried out at the Micro-analytical Center of Cairo University, Giza, Egypt. 2-Cyano-N-(pyrid-2-yl)acetamide (1) [22], 2-benzylidenemalononitrile (11)[23], 2-cyano-3-phenyl-2-propenoic acid ethyl ester (15) [23], hydrazonoyl halides 21a [24], 21b [25], 21c [26] and 26 [27] were prepared following the literature procedures.

2.2. Synthesis

Reactions of acetamide 1 with heterocyclic diazonium salts

To a cold solution of the acetamide 1 (0.32 g, 2 mmol) in pyridine (25 mL) was added the appropriate diazonium salt of heterocyclic amine (5-amino(1H)-1,2,4-triazole, 2-aminobenzimidazole and 5-amino-3-phenylpyrazole) (2 mmol) (prepared according to literature procedures) [28]. The addition was carried out portionwise with stirring at 0-5 °C over a period of 30 min. After complete addition, the reaction mixture was stirred for further 4 h then kept in an ice chest for 12 h and finally diluted with water. The precipitated solid product was collected by filtration, washed with water, dried and finally recrystallized from DMF/EtOH to afford the corresponding hydrazone products 3, 8 and 9, respectively.

2-Oxo-2-(pyridin-2-ylamino)-N'(1H-1,2,4-triazol-5-yl)acetohydrazonoyl cyanide (3):

Yield (70%). M.p. 252-4 °C (DMF/ethanol). FT-IR (KBr, cm$^{-1}$): 3320 (NH), 3285 (NH), 3117 (NH), 2216 (C$\equiv$N), 1647 (C=O). $^1$H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 7.23 (t, 1H, J = 7.2 Hz), 7.92 (t, 1H, J = 7.2 Hz), 8.20 (d, 1H, J = 7.2 Hz), 8.42 (d, 1H, 1H, J = 7.2 Hz), 8.81 (s, 1H, triazole), 9.20 (s, 1H, D$_2$O-exchangeable, NH), 9.79 (s, 1H, D$_2$O-exchangeable, NH), 10.42 (s, 1H, D$_2$O-exchangeable, NH). Anal. Calcd for C$_{10}$H$_8$N$_8$O: Calcd: C, 46.88; H, 3.15; N, 43.73. Found: C, 46.76; H, 3.08; N, 43.79%.
**N’-(1H-Benzimidazol-2-yl)-2-oxo-2-(pyridin-2-ylamino)acetohydrazonoyl cyanide (8):**

Yield (73%). M.p. 231-2 °C (ethanol/DMF). FT-IR (KBr, cm⁻¹): 3352 (NH), 3128 (NH), 2233 (C≡N), 1686 (C=O). ¹H NMR (300 MHz, DMSO-d₆, δ, ppm): 7.72-8.41 (m, 8H, ArH), 8.10 (br., s, 1H, D₂O-exchangeable, amide NH), 10.50 (br., s, 1H, D₂O-exchangeable, hydrazide NH), 12.32 (br., s, 1H, D₂O-exchangeable, benzimidazole NH). Anal. Calcd for C₁₅H₁₃N₅O: C, 59.01; H, 3.69; N, 32.06. Found: C, 59.15; H, 3.69; N, 32.06%.

**2-Oxo-N’-(3-phenyl-1H-pyrrozol-5-yl)-2-(pyridin-2-ylamino)acetohydrazonoyl cyanide (9):**

Yield (75%). M.p. 293-295 °C (ethanol/DMF). FT-IR (KBr, cm⁻¹): 3335 (NH), 3121 (NH), 3142 (NH), 2218 (C≡N), 1686 (C=O). ¹H NMR (300 MHz, DMSO-d₆, δ, ppm): 7.24-9.24 (m, 10H, ArH), 9.80 (br., 1H, D₂O-exchangeable NH), 10.33 (s, 1H, D₂O-exchangeable NH) 12.33 (s, 1H, D₂O-exchangeable, pyrazole NH). MS (EI, m/z (%)): 337 (0.2), 336 (0.3), 333 (0.3), 332 (3.1), 331 (M⁺, 17.2), 121 (29.6), 78 (17.1). Anal. Calcd for C₁₇H₁₃N₅O: C, 61.62; H, 4.45; N, 16.86. Found: C, 61.69; H, 3.88; N, 29.50%.

It should be noted that the hydrazone 3 was easily cyclized into the corresponding fused ring system upon prolonged heating in pyridine to afford 4-amino-N-(pyridin-2-yl)-[1,2,4]triazolo[5,1-c][1,2,4]triazine-3-carboxamide (5). Yield (77%), M.p > 300 °C. FT-IR (KBr, cm⁻¹): 2903-3123 NH and NH₂, 1647 (C=O). ¹H NMR (300 MHz, DMSO-d₆, δ, ppm): 6.42 (s, br., 2H, D₂O-exchangeable NH₂), 6.80-8.85 (m, 5H, ArH), 10.40 (s, 1H, D₂O-exchangeable NH). Anal. Calcd for C₁₀H₆N₆O: C, 46.88; H, 3.15; N, 43.73. Found: C, 46.81; H, 3.12; N, 43.79%.

**2-Cyano-3-phenyl-N-(pyridin-2-yl)acrylamide (10):**

To an ethanolic solution of the acetamide 1 (0.32 g, 2 mmol) and benzaldehyde (0.21 g, 2 mmol) was added few drops of piperidine, and the reaction mixture was refluxed for 4 h. The excess solvent was evaporated under reduced pressure, and the solid product was filtered off, washed with EtOH and purified by recrystallization from EtOH to afford compound 10 in 85% yield, M.p. 143-4 °C. FT-IR (KBr, cm⁻¹): 3398 (NH), 2206 (C≡N), 1693 (C=O). ¹H NMR (300 MHz, CDCl₃, δ, ppm): 6.65-8.40 (m, 10H, ArH), 8.71 (br., 1H, D₂O-exchangeable, NH). MS (EI, m/z (%)): 251 (2.0), 250 (12.9), 249 (M⁺, 71.1), 121 (17.8), 78 (55.9). Anal. Calcd for C₁₃H₁₁N₃O·C, 72.28; H, 4.45; N, 16.86. Found: C, 72.34; H, 4.48; N, 16.81%.

**6-Amino-2-oxo-4-phenyl-1-(pyridin-2-yl)-1,2-dihydropyridine-3,5-dicarbonitrile (14a):**

Method A: To a solution of the 2-benzylidenemalononitrile (11) (0.77 g, 5 mmol) in EtOH (20 mL) was added the acetamide 1 (0.805 g, 5 mmol), and few drops of piperidine and the reaction
mixture was heated under reflux for 2 h. The formed solid product was collected by filtration, washed with EtOH and then crystallized from DMF to afford 14a in 72% yield. Mp. 298-300 °C (DMF). FT-IR (KBr, cm⁻¹): 3211 and 3327 (NH₂), 2220 (C≡N), 2208 (C≡N), 1655 (C=O). ¹H NMR (300 MHz, DMSO-d₆, δ, ppm): 6.36 (s, 2H, D₂O-exchangeable NH₂), 7.25-8.52 (m, 9H, ArH).

Method B: To a solution of compound 10 (5 mmol) in ethanol (20 mL) was added malononitrile (0.33 g, 5 mmol) and few drops of piperidine and the reaction mixture was heated under reflux for 2 h. The obtained solid product was collected by filtration, washed with EtOH and then crystallized from DMF to give a product identical in all respects (M.p, mixed M.p. and IR spectra) with that obtained from method A above.

Reaction of the cyanoacetamide 1 with ethyl 2-cyano-3-phenyl-2-propenoate (15)

To a solution of compound 15 (5 mmol) in EtOH (20 mL) was added the acetamide 1 (0.81 g, 5 mmol), and few drops of piperidine and the reaction mixture was heated for 2 h. The formed solid product was collected by filtration, washed with EtOH and then recrystallized from DMF to afford 6-hydroxy-2-oxo-4-phenyl-1-(pyridin-2-yl)-1,2-dihydropyridine-3,5-dicarbonitrile (14b) in 66% yield. M.p > 300 °C. FT-IR (KBr, cm⁻¹): 2222 (2C≡N), 1715 (C=O). ¹H NMR (300 MHz, DMSO-d₆, δ, ppm): 7-24-7.56 (m, 7H), 8.02-8.08 (m, 1H), 8.71-8.74 (d, 1H, J = 7.2 Hz), 12.6 (br., 1H, OH). ¹³C NMR (75 MHz, DMSO-d₆, δ, ppm) 95.78, 102.47, 115.14, 115.73, 120.75, 124.46, 127.03, 127.84, 128.22, 128.52, 136.56, 141.02, 151.62, 154.39, 160.07, 161.53. Anal. Calcd for C₁₈H₁₁N₅O₂: C, 69.00; H, 3.54; N, 22.35. Found: C, 69.09; H, 3.48; N, 22.39%.

Reactions of the acetamide 1 with phenyl isothiocyanate, hydrazonoyl halides 21a-c, 26, ethyl chloroacetate and chlorocetonitrile

General procedure: To a stirred solution of potassium hydroxide (0.11 g, 2 mmol) in DMF (20 mL) was add the acetamide 1 (0.32 g, 2 mmol). After stirring for 30 min., phenyl isothiocyanate (0.27 g, 0.24 mL, 2 mmol) was added to the resulting mixture. Stirring was continued for 6 h, then the appropriate hydrazonoyl halide 21a-c, 26, ethyl chloroacetate or chlorocetonitrile (2 mmol) was added portionwise over a period of 30 min. After the addition was complete, the reaction mixture was stirred for additional 12 h, during which the reactants went into solution and a colored product was precipitated. The solid product was filtered off, washed with water and dried. Recrystallization from the suitable solvent afforded the corresponding products 25a-c, 29 and 31, respectively.
5-(1-Cyano-2-oxo-2-(pyridin-2-ylamino)ethylidene)-N-phenyl-4-p-tolyl-4,5-dihydro-1,3,4-thiadiazole-2-carboxamide (25a):

Yield (86%). M.p. 272-3 °C (DMF/H2O). FT-IR (KBr, cm⁻¹): 3397 (NH), 3340 (NH), 2193 (C≡N), 1670 (C=O), 1651 (C=O). ¹H NMR (300 MHz, DMSO-d₆, δ, ppm): 2.43 (s, 3H, CH₃), 7.39 (m, 2H), 8.22 (s, 1H, D₂O-exchangeable NH), 10.98 (s, 1H, D₂O-exchangeable NH). Anal. Calcd for C₂₄H₁₈N₆O₂S: C, 64.37; H, 4.15; N, 17.11%. Found: C, 64.42; H, 4.10; N, 17.16%.

Ethyl 5-(1-cyano-2-oxo-2-(pyridin-2-ylamino)ethylidene)-4-p-tolyl-4,5-dihydro-1,3,4-thiadiazole-2-carboxylate (25b):

Yield (76%). M.p. 258-60 °C (DMF/H2O). FT-IR (KBr, cm⁻¹): 3381 (NH), 2193 (C≡N), 1724 (C=O), 1678 (C=O). ¹H NMR (300 MHz, DMSO-d₆, δ, ppm): 1.42 (t, 3H, CH₃), 2.47 (s, 3H, CH₃), 4.48 (q, 2H, CH₂) 6.99-8.28 (m, 8H, ArH), 8.35 (s, 1H, D₂O-exchangeable NH). MS (EI, m/z (%)): 409 (7.6), 408 (24.0), 407 (M⁺, 100.0), 334 (0.9), 286 (57.7), 121 (29.7), 93 (2.3), 91 (81.8), 78 (84.1), 73 (1.9). Anal. Calcd for C₂₉H₂₈N₅O₂S: C, 58.96; H, 4.21; N, 17.19. Found: C, 58.89; H, 4.28; N, 17.11%.

2-Cyano-2-(3,5-diphenyl-1,3,4-thiadiazol-2(3H)-ylidene)-N-(pyridin-2-yl)acetamide (25c):

Yield (77%). M.p. 188 °C (EtOH). FT-IR (KBr, cm⁻¹): 3055 (NH), 2191 (C≡N), 1677 (C=O). ¹H NMR (300 MHz, DMSO-d₆, δ, ppm): 7.09-8.05 (m, 14H, ArH), 8.54 (s, 1H, D₂O-exchangeable NH). MS (EI, m/z (%)): 376 (0.4), 375 (0.4), 374 (2.7), 373 (8.1), 372 (0.1), 371 (M⁺, 0.1), 105 (100.0). Anal. Calcd for C₂₂H₁₉N₅O₂S: C, 71.14; H, 4.61; N, 11.31. Found: C, 71.21; H, 4.56; N, 11.27%.

Phenyl(5-(phenylimino)-4-p-tolyl-4,5-dihydro-1,3,4-thiadiazol-2-yl)methanone (29):

Yield (63%). M.p. 163 °C (EtOH). FT-IR (KBr, cm⁻¹): 1630 (C=O). ¹H NMR (300 MHz, DMSO-d₆, δ, ppm): 2.45 (s, 3H, CH₃), 7.01-8.56 (m, 14H, ArH). MS (EI, m/z (%)): 376 (0.4), 375 (0.4), 374 (2.7), 373 (8.1), 372 (0.1), 371 (M⁺, 0.1), 105 (100.0). Anal. Calcd for C₂₂H₁₉N₅O₂S: C, 71.14; H, 4.61; N, 11.31. Found: C, 71.21; H, 4.56; N, 11.27%.

2-Cyano-2-(4-oxo-3-phenylthiazolidin-2-ylidene)-N-(pyridin-2-yl)acetamide (31):

Yield (77%). M.p. 270-1 °C (DMF/H₂O). FT-IR (KBr, cm⁻¹): 3096 (NH), 2206 (C≡N), 1653 (C=O). ¹H NMR (300 MHz, DMSO-d₆, δ, ppm): 4.3 (s, 2H, CH₂), 6.84 (m, 2H), 6.92 (t, 1H, J = 7.5 Hz), 7.23 (m, 2H), 7.39 (m, 2H), 8.22 (t, 1H, J = 7.5 Hz), 9.48 (d, 1H, J = 7.5 Hz), 12.37 (s, 1H, D₂O-exchangeable NH). Anal. Calcd for C₁₇H₁₃N₃O₃S: C, 60.70; H, 3.60; N, 16.66. Found: C, 60.79; H, 3.67; N, 16.60%.
4-Amino-2-oxo-N-phenyl-2H-pyrido[1,2-a]pyrimidine-3-carbothioamide (36)

To a stirred solution of potassium hydroxide (0.11 g, 2 mmol) in DMF (20 mL) was added the acetamide 1 (0.32 g, 2 mmol). After stirring for 30 min, phenyl isothiocyanate (0.27 g, 0.24 mL, 2 mmol) was added to the resulting mixture and stirring was continued for 6 h, then poured onto crushed ice containing hydrochloric acid. The formed solid product was filtered off, washed with water, dried and finally recrystallized from dioxane/EtOH mixture to afford compound 36 in 0.49 g (85%) yield. M.p. 218-220 °C. FT-IR (KBr, cm⁻¹): 3075, 3200 (2 NH overlapped), 1628 (C=O). ¹H NMR (300 MHz, DMSO-d₆, δ, ppm): 6.83-8.49 (m, 10H, ArH + NH), 12.50 (s, 1H, D₂O-exchangeable NH), 13.89 (s, 1H, D₂O-exchangeable SH). MS (EI, m/z (%)): 299 (1.6 ), 298 (4.0), 297 (18.8 ), 296 (M⁺, 22.2), 295 (23.1), 121 (92.9), 92 (8.7), 77 (77.1). Anal. Calcd for C₁₅H₁₂N₄OS: C, 60.79; H, 4.08; N, 18.91. Found: C, 60.85; H, 4.01; N, 18.85%.

3. Results and Discussion

The acetamide 1 couples smoothly with 1,2,4-triazol-5-diazonium sulphate (2) in pyridine, at room temperature to afford 2-oxo-2-(pyridin-2-ylamino)-N′-(1H-1,2,4-triazol-5-yl)acetohydrazonoyl cyanide (3). The IR spectrum of the isolated product 3 showed bands in the region 3320-3117 cm⁻¹ due to three NH groups, a strong absorption band at 2216 cm⁻¹ due to nitrile function and a strong absorption band at 1647 cm⁻¹ due to carbonyl group. Compound 3 underwent intramolecular cyclization upon heating in pyridine to afford the corresponding 4-amino-N-(pyridin-2-yl)-[1,2,4]triazolo-[5,1-c][1,2,4]triazine-3-carboxamide (5) (Scheme 1). The IR spectrum of 5 revealed the absence of a band corresponding to nitrile function. Its ¹H NMR spectrum showed the absence of signal characteristic for hydrazone NH proton and revealed the appearance of D₂O-exchangeable signals at δ 6.42 and 10.40 due to amino and amido-NH protons, respectively in addition to aromatic protons in the region δ 6.80-8.85.

Also, the reaction of the acetamide 1 with the diazonium salt of 2-aminobenzimidazole 6 or 5-amino-3-phenylpyrazole 7 in pyridine, afforded the corresponding acyclic hydrazone products 8 and 9, respectively (Scheme 2).

Treatment of the acetamide 1 with benzaldehyde in refluxing EtOH, in the presence of a catalytic amount of piperidine afforded the acrylamide 10 (Scheme 3). The structure of compound 10 was elucidated from its spectroscopic as well as elemental analytical data. Thus, it showed absorption bands at 2206 cm⁻¹ due to nitrile function whereas its ¹H NMR spectra revealed the lack of signal characteristic for methylene protons.
Scheme 1. Synthesis of 4-amino-N-(pyridin-2-yl)-[1,2,4]triazolo-[5,1-c][1,2,4]triazine-3-carboxamide (5)

Scheme 2. Synthesis of acyclic hydrazone products 8 and 9

Refluxing of an equimolar amounts of the acetamide 1 and 2-benzylidenemalononitrile (11) [23], in the presence of a catalytic amount of piperidine afforded 1:1 cycloadduct (Scheme 3). The structure of the isolated cycloadduct was identified as 6-amino-2-oxo-4-phenyl-1-(pyridin-2-yl)-1,2-dihydropyridine-3,5-dicarbonitrile (14a) on the basis of its elemental analyses and spectrum data. Structure 14a is assumed to be formed via an initial Michael type-adduct 12 followed by an
intramolecular cyclization and subsequent oxidation to the final product 14a (Scheme 3). Moreover, the product 14a was further confirmed by an independent synthesis from the reaction of 2-phenylmethylen-2-(pyrid-2-ylcarboxamido)acetonitrile (10) with malononitrile under the same reaction condition. The product obtained was found to be identical in all respects (mp, mixed mp. and IR spectrum) with that obtained from the reaction of the acetamide 1 with phenylmethylenepropanedinitrile 11. When the acetamide 1 was treated with ethyl 2-cyano-3-phenyl-2-propenoate (15) [23] in EtOH and in the presence of catalytic amount of piperidine, it gave the pyridine-3,5-dicarbonitrile 14b (Scheme 3). Compound 14b was formed initially via Michael-type addition followed by elimination of EtOH molecule and dehydrogenation. The distinction between compound 14b and the other possible structure 20 was made on the basis of the elemental analysis and spectral data of the isolated product. The IR spectrum of 14b revealed the absence of amino absorption bands and the presence of absorption bands at 1715 and 2222 cm\(^{-1}\) due to carbonyl and two nitrile groups, respectively. Moreover, its \(^1\)H NMR spectrum showed D\(_2\)O-exchangeable signal at \(\delta\) 12.6 due to OH proton in addition to aromatic multiplet in the region \(\delta\) 7.24-8.74. Treatment of the acetamide 1 with phenyl isothiocyanate in DMF, in the presence of potassium hydroxide, followed by the addition of an equimolar amount of the hydrazonoyl chlorides 21a-c [24-26] furnished, in each case, one isolable product (as tested by TLC analysis). The reaction products were identified as the corresponding 1,3,4-thiadiazole derivatives 25a-c as confirmed by the NMR spectrum of 25a, for example, displayed a singlet signal at \(\delta\) 2.43, a multiplet in the region \(\delta\) 7.10-8.28, two singlet at \(\delta\) 8.60 and 10.98 (D\(_2\)O-exchangeable) due to methyl, aromatic and two NH protons, respectively.

The aforementioned results indicate that the reaction of the non-isolable intermediate potassium salt 22 with the hydrazonoyl chlorides 21a-c proceeds, in each case, via loss of potassium chloride and aniline molecules, respectively. Treatment of the potassium salt 22 with the hydrazonoyl bromide 26 [27] gave a product which has analytical and spectral data in accordance with phenyl-[5-(phenylimino)-4-(p-tolyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl]methanone structure (29) (Scheme 4). The IR spectrum of the latter product revealed the absence of bands in the region 3500-2000 cm\(^{-1}\) corresponding NH and nitrile functions and showed bands at 1630 cm\(^{-1}\) due to a conjugated carbonyl group. Also, the \(^1\)H NMR spectrum of 29 showed signal at \(\delta\) 2.45 due to CH\(_3\) in addition to aromatic protons in the region \(\delta\) 7.01-8.56. In addition, its mass spectrum revealed molecular ion peaks at \(m/z\) 371. The formation of the latter product is assumed to proceed via elimination of potassium bromide to afford the acyclic hydrazone 27 which underwent intramolecular cyclization to afford the non-isolable intermediate 28. The latter then loses the acetamide 1 via an S\(_N\)2 displacement to give the thiadiazole 29 (Scheme 4).
Scheme 3. Synthesis of pyridine-3,5-dicarbonitrile derivatives 14a and 14b

Ethyl chloroacetate reacted with the intermediate 22 to afford a product identified as 2-cyano-2-(4-oxo-3-phenylthiazolidin-2-ylidene)-N-(pyridin-2-yl)acetamide (31). The IR spectrum of the product 31 exhibits bands at 3096, 2206 and 1653 cm\(^{-1}\) due to NH, nitrile and carbonyl group, respectively. Its \(^1\)H NMR spectrum revealed a singlet signal at \(\delta 4.3\) due to thiazolidinone CH\(_2\) protons in addition to aromatic protons in the region \(\delta 6.84-9.48\) and D\(_2\)O-exchangeable signal at \(\delta 12.37\) due to NH proton. Treatment of the intermediate 22 with chloroacetonitrile affords a product identical in all respects with compound 31. This product is assumed be formed via the intermediate of the 4-iminothiazoline derivative 33 (Scheme 5).
Scheme 4. Synthesis of 1,3,4-thiadiazole derivatives 25a-c and 29.

When the intermediate potassium salt 22 was treated with dilute HCl, it gave the corresponding 4-amino-2-oxo-N-phenyl-2H-pyrido[1,2-a]pyrimidine-3-carbothioamide (36) (Scheme 6). The IR spectrum of compound 36 revealed the absence of nitrile band. Its 1H NMR spectrum showed two D$_2$O-exchangeable signals at $\delta$ 12.50 and at $\delta$ 13.89 corresponding to NH, and SH proton, respectively, in addition to aromatic protons as a multiplet in the region $\delta$ 7.08-8.73. Moreover, the mass spectrum of the product 36 exhibited a molecular ion peak at $m/z$ 296.
Scheme 5. Synthesis of 2-cyano-2-(4-oxo-3-phenylthiazolidin-2-ylidene)-N-(pyridin-2-yl)acetamide (31)

Scheme 6. Synthesis of pyrido[1,2-a]pyrimidine 36

4. Conclusions

In conclusion, the reactivity of 2-cyano-N-(pyridin-2-yl)acetamide (1) was investigated as a versatile and readily accessible building block for the synthesis of new heterocycles which could be of biological and pharmaceutical importance.
References


