Synthesis of some new pyridines, thienopyridines and pyridothienopyrimidines bearing 1,3-diphenyl-1H-pyrazole moiety

ARTICLE - FEBRUARY 2016

READS
4

4 AUTHORS, INCLUDING:

Elham Altaifi
Sana’a University
11 PUBLICATIONS 50 CITATIONS

Available from: Elham Altaifi
Retrieved on: 30 January 2016
Synthesis of some new pyridines, thienopyridines and pyridothonopyrimidines bearing 1,3-diphenyl-1H-pyrazole moiety

Elham A. Al-Taifi, 1 Eman A. Thabet, 2 Eify A. Bakhite 3* and Talaat I. El-Emary 3

1 Department of Chemistry, Faculty of Science, Sana’a University, Sana’a, Yemen
2 Department of Chemistry, Faculty of Science, Taiz University, Taiz, Yemen
3 Department of Chemistry, Faculty of Science, Assiut University, Assiut71516, Egypt

*Corresponding author. E-mail: betiya@yahoocom

Received November, 2015; Accepted December, 2015

Abstract: 1-phenyl/(2-thienyl)-3-(1,3-Diphenyl-1H-pyrazol-4-yl)-2-propen-1-ones (3a,b) were prepared. Reaction of 3b with hydroxyl amine, phenyl hydrazine or ethyl cyanoacetate gave the corresponding heterocyclic compounds 4, 5 and 6 respectively. Treatment compounds 3a,b with cyanothioacetamide furnished 3-cyano-4-(1,3-diphenyl-1H-pyrazol-4-yl)-6-phenyl/(2-thienyl)pyridine-2(1H)-thiones (7a,b). Reaction of 7a,b with chloroacetamide, p-methylphenacyl chloride, ethyl chloroacetate, chloro- N-(aryl)acetamides gave S-substituted methylthiopyridines 8a-g. Upon treatment of compounds 8a-g with sodium ethoxide in boiling ethanol, they underwent intramolecular Thorpe-Zeigler cyclization giving 2-functionalized 3-amino-4-(1,3-diphenyl-1H-pyrazol-4-yl)-6-phenyl/(2-thienyl)thieno[2,3-b]pyridines (9a-g). Compounds 9a-c were subjected to some sequence reactions to produce new pyrazolylpyridothienopyrimidines 10a-c, 11a,b and 13-16.

Key words: 1,3-diphenylpyrazole, 3-cyanopyridine-2(1H)-thiones, pyrazolylthienopyridines, pyrazolylpyridothonopyrimidines

INTRODUCTION

Pyrazole derivatives are the subject of many research studies due to their widespread potential biological activities such as antimicrobial (Pimerova and Voronina, 2001), antiviral (Janus et al., 1999), antitumor (Bouabdallah et al., 2006; Park et al., 2005), antihiostaminic (Yildirim, 2005), antidepressant (Bailey et al., 1985), insecticides and fungicides (Chu and Cutler, 1986). On the other hand, many pyridines (Ahmed et al., 2009; Amr et al., 2006; Galya et al., 2008; Onnis et al., 2009; Shi et al., 2009; Thapa et al., 2010) and thienopyridines (Bakhite, 2003; Bompart et al., 1988; El-Abadelah et al., 1998; Miki et al., 1999; Furuya et al., 1998; Vieweg et al., 1992; Litvinov et al., 2005) are reported to possess versatile applications as biologically active compounds. In view of the above facts and as a continuation of our previous work on pyridine-containing compounds (Abdel-Rahman et al., 2015; El-Emary and Bakhite, 1999; Mohamed et al., 2007), the present project was planned to synthesize other new heterocyclic compounds containing mainly 4-(1,3-diphenyl-1H-pyrazol-4-yl)-6-phenyl/(2-thienyl)pyridine skeleton hoping to get novel compounds with anticipated biological activities.

RESULTS AND DISCUSSION

The starting compounds, 1-phenyl or (2-thienyl)-3-(1,3-diphenyl-1H-pyrazol-4-yl)-2-propen-1-ones 3a,b were prepared by condensation of acetophenone (1a) or 2-acetylthiophene (1b) with 1,3-diphenyl-1H-pyrazole-4-carboxaldehyde (2) in an ethanolic sodium hydroxide solution (Figure 1).

Compound 3b underwent a cyclocondensation reaction upon treatment with hydroxyamine hydrochloride in the presence of sodium acetate to give the isooxazoline derivative 4. By the same manner, the reaction of 3b with phenyl hydrazine in ethanol produced the pyrazoline compound 5 (Figure 2).

Heating compound 3b with ethyl cyanoacetate in glacial acetic acid containing an excess amount of ammonium acetate led to the formation of 3-cyanopyridine-2(1H)-one 6 in a good yield. The thione analogues 7a,b were prepared by refluxing...
compounds 3a,b with cyanothioacetamide in ethanol containing catalytic amount of triethylamine (Figure 3).

Reaction of 3-cyanopyridine-2(1H)-thiones 7a,b with some halocompounds namely: chloroacetamide, chloro-N-
phenylacetamide, chloroacetonitrile, phenacyl bromide, ethyl chloroacetate or chloro-N-(p-tolyl)acatamide, in the presence of sodium acetate as a basic catalyst produced the corresponding substituted methylthio-pyridines 8a-g. On treatment of the latter compounds (8a-g) with sodium ethoxide in boiling ethanol, they underwent intramolecular Thorpe-Zeigler

Figure 1

Figure 2

Figure 3
cyclization giving 2-functionalized 3-amino-4-(1,3-diphenyl-1H-pyrazol-4-yl)-6-phenyl-(2-thienyl)thieno [2,3-b]pyridines (9a-g) in nearly quantitative yields (Figure 4).

Compound 9a was reacted with some aromatic aldehydes namely; benzaldehyde, p-methoxybenzaldehyde or p-chlorobenzaldehyde in ethanol containing few drops of conc. HCl at reflux temperature to give 2-aryl-9-(1,3-diphenyl-1H-pyrazol-4-yl)-4-oxo-7-phenyl-1,2,3,4-tetrahydropyrido[3',2':4,5]thieno[3,2-d]pyrimidines (10a-c). In the same manner, reaction of compound 9a with cyclopentanone or cyclohexanone furnished the corresponding spiro compounds 11a,b in excellent yields (Figure 5).

Condensation of o-aminocarbonitrile 9c with triethyl orthoformate, in the presence of acetic anhydride, led to the formation of ethyl N-(2-cyano-4-(1,3-diphenyl-1H-pyrazol-4-yl)-6-phenylthieno[2,3-b]pyridine-3-yl)methanimidate(12).

Treatment compound 12 with hydrazine hydrate in dioxane at room temperature furnished 3-amino-3,4-dihydro-9-(1,3-
diphenyl-1H-pyrazol-4-yl)-4-imino-7-phenylpyrido[3',2':4,5]thieno[3,2-d]pyrimidine(13). Heating compound 13 with an excess amount of triethyl orthoformate in the presence of few crystals of p-toluene sulphinic acid led to the formation of pyrazolyltriazolopyridothienopyrimidine derivative 14. Compound 15 was synthesized by reacting 13 with acetic anhydride at reflux temperature. Reaction of compound 13 with neat diethyl malonate gave the expected ethyl1-(1,3-diphenyl-1H-pyrazol-4-yl)-9-phenyl[1,2,4]triazolo[2',3'-c]pyrido [3',2:4,5]thieno[2,3-e]pyrimidine-2-acetate (16) (Figure 6).

The structures of all newly synthesized compounds were elucidated and confirmed by elemental analyses, IR and 1H NMR spectral data (cf. Experimental part).

**Experimental**

Melting points were measured with Gallan-Kamp melting-point apparatus and are uncorrected. IR spectra were recorded on a Shimadzu 470 IR-spectrophotometer (KBr; $\nu_{max}$ in cm$^{-1}$). 1H-NMR spectra were taken on a Varian EM-390, 90 MHz spectrometer using TMS as internal standard. Chemical shifts are given in $\delta$, ppm. Elemental analyses (C, H, N and S) were performed on an Elemental Analyses system GmbH VARIO EL V_3.1998 CHNS Mode.

3-(1,3-Diphenyl-1H-pyrazol-4-yl)-1-phenyl-2-propen-1-one (3a)

This compound was prepared according to the reported method (El-Emary and Bakhite, 1999).

To a mixture of 1.3-Diphenyl-1H-pyrazole-4-carboxaldehyde (2) (2.48 g, 10 mmol) and 2-acetyltithiophene (2b) (1.1 ml, 10 mmol) in ethanol (20 mL), 0.5 mL of aqueous NaOH 10 % was added. The reaction mixture was stirred at room temperature for 3 h whereby a precipitate formed. It was collected and recrystallized from aqueous ethanol as pale yellow crystals of 3b. Yield: 87 %, m. p.: 182-184°C. IR: 1650 (C=O) cm$^{-1}$.

Elemental Anal. Calculated for C$_{32}$H$_{26}$N$_2$OS (536.44): C, 74.13; H, 4.52; N, 7.86; S, 8.99 %. Found: C, 74.44; H, 4.48; N, 7.61; S, 8.77 %.

5-(1,3-diphenyl-1H-pyrazol-4-yl)-3-(2-thienyl)-N$_2$-isooxazoline (4)

To a suspension of chalcone 3 (1.78 g, 5 mmol) and hydroxylamine hydrochloride (0.4 g) in ethanol (20 ml), anhydrous sodium acetate (1.0 g) was added. The resulting mixture heated under reflux for 4 h. The solid that formed after cooling and dilution with water (15 ml) was collected and recrystallized from methanol to give white needles of compound 4. Yield: 68 %; m.p. 150-152°C. IR: 1600 (C=N) cm$^{-1}$. 1H NMR (DMSO-$d_6$): $\delta$ 8.7 (s, 1H, CH pyrazole), 7.2-8.2 (m, 13H, aryl, pyridyl and thienyl protons), 4.5-4.7 (t, 1H, CH isooxazole), 3.1-3.3 (d, 2H, CH$_2$). Elemental Anal. Calculated for C$_{22}$H$_{16}$N$_2$OS (371.46): C, 71.14; H, 4.53; N, 11.31; S, 8.63 %. Found: C, 71.00; H, 4.53; N, 11.25; S, 8.49 %.

5-(1,3-diphenyl-1H-pyrazol-4-yl)-1-phenyl-3-(2-thienyl)-N$_2$-pyrazoline (5)

A mixture of chalcone 3b (1.78 g, 5 mmol) and phenyl hydrazine (0.5 ml, 5 mmol) in ethanol (20 ml) was heated under reflux for 4 h. The solid that formed after cooling and dilution with water (15 ml) was collected and recrystallized from methanol to give yellow needles of compound 5. Yield: 78 %; m.p. 220-222°C. IR: 1600 (C=N) cm$^{-1}$. 1H NMR (DMSO-$d_6$): $\delta$ 8.8 (s, 1H, CH pyrazole), 7.0-8.2 (m, 18H, aryl and thienyl protons), 4.3-4.6 (t, 1H, CH pyrazoline), 3.0-3.3 (d, 2H, CH$_2$). Elemental Anal. Calculated for C$_{32}$H$_{26}$N$_2$S (446.57): C, 75.31; H, 4.97; N, 12.55; S, 7.18 %. Found: C, 75.11; H, 4.80; N, 12.64; S, 7.00 %.

3-Cyano-4-(1,3-diphenyl-1H-pyrazol-4-yl)-6-(2-thienyl)pyridine-2(1H)-one (6)

A mixture of chalcone 3b (1.78 g, 10 mmol), ethyl cyanoacetate (2.26 g, 20 mmol) and ammonium acetate (7.7 g, 100 mmol) was heated at 150°C in an oil bath for 3 h. The solid that formed after cooling was collected and recrystallized from acetic acid to give pale yellow crystals of compound 6. Yield: 62 %; m.p. 260-261°C. IR: 3428 (NH), 2209 (C=O), 1639 (C=O) cm$^{-1}$. 1H NMR (DMSO-$d_6$): $\delta$ 9.8 (s, 1H, NH), 9.2 (s, 1H, CH pyrazole), 7.0-8.2 (m, 14H, aryl, pyridyl and thienyl protons). Elemental Anal. Calculated for C$_{23}$H$_{16}$NO$_2$ (420.49): C, 71.41; H, 3.84; N, 13.32; S, 7.62 %. Found: C, 71.47; H, 3.83; N, 13.12; S, 7.55 %.

3-Cyano-4-(1,3-diphenyl-1H-pyrazol-4-yl)-6-phenylpyridine-2(1H)-thione (7a)

This compound was prepared by reacting chalcone 3a with cyanothioacetamide according to the reported method (El-Emary and Bakhite, 1999).

3-Cyano-4-(1,3-diphenyl-1H-pyrazol-4-yl)-6-(2-thienyl)pyridine-2(1H)-thione (7b)
To a solution of chalcone 3b (3.56 g, 10 mmol) and cyanothioacetamide (1.0 g, 10 mmol) in ethanol (25 ml), few drops of triethylamine were added. The resulting mixture was heated under reflux for 3 h. The precipitate that formed while hot was collected and recrystallized from acetic acid to give compound 7b in the form of orange crystals. Yield: 88 %; m.p.
290-292°C. C: 3432 (NH), 2214 (CN) cm⁻¹. ¹H NMR (DMSO-d₆): δ 12.4 (s, 1H, NH), 9.1 (s, 1H, CH pyrazole), 6.7-8.1 (m, 14H, aryl, pyridyl and thienyl protons). Elemental Anal. Calculated for C₂₅H₂₅N₂S (436.55): C, 68.78; H, 3.69; N, 12.83; S, 14.69 %. Found: C, 68.51; H, 3.68; N, 12.63; S, 14.54 %.

3-Cyano-4-(1,3-diphenyl-1H-pyrazol-4-yl)-6-phenylpyridin-2-ylthioacetamide (8a)

It was prepared according to the reported method (El-Emary and Bakhte, 1999).

3-Cyano-4-(1,3-diphenyl-1H-pyrazol-4-yl)-6-phenyl-2-(N-phenyl)carbamoylmethylthiopyridine (8b)

It was prepared by reaction of 7a with chloro-N-phenylacetamide. Yield: 82 %; m.p.: 255-256°C. IR: 3130 (NH), 2200 (C≡N), 1660 (C=O) cm⁻¹. ¹H NMR (DMSO-d₆): δ 10.5 (s, 1H, NH), 9.3 (s, 1H, CH pyrazole), 7.0-8.1 (m, 21H, aryl and pyridyl protons), 4.3 (s, 2H, SCH₂). Elemental analysis calculated for C₅₅H₅₁N₂S (554.68): C, 71.46; H, 4.00; N, 10.10; S, 11.56 %.

3-Cyano-2-cyanoethylthio-4-(1,3-diphenyl-1H-pyrazol-4-yl)-6-phenyl pyridine (8c)

It was prepared by reaction of 7a with chloroacetonitrile. Yield: 80 %; m.p.: 210-211°C. IR: 2230 (C≡N, non conjugated), 2200 (C≡N, conjugated) cm⁻¹. ¹H NMR (DMSO-d₆): 9.2 (s, 1H, CH pyrazole), 7.0-8.2 (m, 16H, aryl and pyridyl protons), 4.4 (s, 2H, SCH₂). Elemental Anal. Calculated for C₃₂H₂₇N₂S (563.68): C, 74.58; H, 4.47; N, 12.42; S, 6.49 %. Found: C, 73.83; H, 3.94; N, 14.98; S, 6.49 %.

3-Cyano-4-(1,3-diphenyl-1H-pyrazol-4-yl)-2-(p-methylphenacylthio)-6-(2-thienyl)pyridine (8d)

It was prepared by reaction of 7b with p-methylphenacyl chloride. Yield: 79 %; m.p.: 228-230°C. IR: 2210 (C≡N), 1680 (C=O) cm⁻¹. ¹H NMR (DMSO-d₆): 9.2 (s, 1H, CH pyrazole), 7.0-8.2 (m, 20H, aryl and pydidy protons), 5.1 (s, 2H, SCH₂), 2.0 (s, 3H, CH₃). Elemental analysis calculated for C₃₂H₂₅N₂S (553.64): C, 71.46; H, 4.00; N, 10.10; S, 11.56 %. Found: C, 71.66; H, 4.12; N, 10.00; S, 11.39 %.

Ethyl (3-cyano-4-(1,3-diphenyl-1H-pyrazol-4-yl)-6-(2-thienyl)pyridin-2-ylthio)acetate (8e)

It was prepared by reaction of 7b with ethyl chloroacetate. Yield: 80 %; m.p.: 175-176°C. IR: 2210 (C≡N), 1731 (C=O) cm⁻¹. ¹H NMR (DMSO-d₆): 9.0 (s, 1H, CH pyrazole), 7.1-8.0 (m, 14H, aryl, pyridyl and thienyl protons), 4.0-4.3 (m, 4H).

3-Cyano-4-(1,3-diphenyl-1H-pyrazol-4-yl)-2-(N-(phenyl)carbamoylmethyl-thio)-6-(2-thienyl)pyridine (8f)

It was prepared by reaction of 7b with chloro-N-(phenyl)acetamide. Yield: 79 %; m.p. 241-243°C. IR: 3300 (NH), 2220 (C≡N), 1670 (C=O) cm⁻¹. ¹H NMR (DMSO-d₆): δ 10.6 (s, 1H, NH), 9.0 (s, 1H, CH pyrazole), 6.9-8.0 (m, 19H, aryl, pyridyl and thienyl protons), 4.2 (s, 2H, CH₂). Elemental Anal. Calculated for C₃₄H₃₂N₂OS (583.73): C, 69.96; H, 4.32; N, 12.00; S, 10.98 %. Found: C, 69.89; H, 4.19; N, 12.10; S, 10.82 %.

Cyclization of compounds 8a-g; Formation of pyrazolylthienopyridines 9a-f; General procedure.

Compound 8a-g (10 mmol) was suspended in sodium ethoxide solution (0.12 g of sodium in 30 ml of abs. ethanol) and heated under reflux for 5 mins. The yellow precipitate that formed on cooling was collected and recrystallized from ethanol-acetone mixture to give 9a-g.
3-Amino-4-(1,3-diphenyl-1H-pyrazol-4-yl)-6-phenylthieno[2,3-b]pyridine-2-carboxamide (9a)

It was prepared by cyclization of compound 8a according to the reported method (El-Emary and Bakhite, 1999).

3-Amino-4-(1,3-diphenyl-1H-pyrazol-4-yl)-6-phenyl-2-(N-phenyl)carbamoyl thieno[2,3-b]pyridine (9b)

It was prepared by cyclization of compound 8b. Yield: 92 %; m.p.: 278-290° C. IR: 3490, 3300, 3150 (NH₂, NH), 1640 (C=O) cm⁻¹. 1H NMR (DMSO-d₆): δ 9.9 (s, 1H, NH), 9.2 (s, 1H, CH pyrazole), 7.0-8.1 (m, 2H, aryl and pyridyl protons), 6.1 (s, 2H, NH₂). Elemental analysis calculated for C₃₂H₂₃N₅O₅S (563.68): C, 74.58; H, 4.47; N, 12.42; S, 5.69 %. Found: C, 74.46; H, 4.46; N, 12.27; S, 5.82 %.

3-Amino-4-(1,3-diphenyl-1H-pyrazol-4-yl)-6-phenylthieno[2,3-b]pyridine-2-carbonitrile (9c)

It was prepared by cyclization of compound 8c. Yield: 94 %; m.p.: 247-248° C. IR: 3460, 3350 (NH₂), 2200 (C==N) cm⁻¹. 1H NMR (DMSO-d₆): δ 9.3 (s, 1H, CH pyrazole), 7.1-8.2 (m, 16H, aryl and pyridyl protons), 5.8 (s, 2H, NH₂). Elemental Anal.

Ethyl 3-amino-4-(1,3-diphenyl-1H-pyrazol-4-yl)-6-(2-thienyl)thieno[2,3-b]pyridine-2-carboxylate (9e)

It was prepared by cyclization of compound 8e. Yield: 91 %; m.p.: 204-205° C. IR: 3500, 3300 (NH₂), 1660 (C=O) cm⁻¹. 1H NMR (DMSO-d₆): δ 8.9 (s, 1H, CH pyrazole), 7.0-8.0 (m, 14H, aryl, pyridyl and thienyl protons), 5.7 (s, 2H, NH₂), 4.0-4.3 (q, 2H, OCH₃). Elemental Anal. Calculated for C₃₃H₂₃N₅O₄S (554.68): C, 71.46; H, 4.00; N, 10.10; S, 11.56 %. Found: C, 71.15; H, 4.22; N, 10.04; S, 11.40 %.

3-Amino-4-(1,3-diphenyl-1H-pyrazol-4-yl)-2-(N-(phenyl)carbamoyl thieno[2,3-b]pyridine (9f)

It was prepared by cyclization of compound 8f. Yield: 98 %; m.p. 259-260° C. IR: 3500, 3300, 3180 (NH₂, NH), 1630 (C=O) cm⁻¹. 1H NMR (DMSO-d₆): δ 10.0 (s, 1H, NH), 8.9 (s, 1H, CH pyrazole), 7.1-8.2 (m, 18H, aryl, pyridyl and thienyl protons), 5.9 (s, 2H, NH₂), 2.0 (s, 3H, CH₃). Elemental Anal. Calculated for C₃₄H₂₃N₅O₅S (583.73): C, 69.96; H, 4.32; N, 12.00; S, 10.98 %. Found: C, 69.88; H, 4.48; N, 12.26; S, 11.06 %.

3-Amino-4-(1,3-diphenyl-1H-pyrazol-4-yl)-2-(N-(p-tolyl)) carbamoyl-6-(2-thienyl)thieno[2,3-b]pyridine (9g)

It was prepared by cyclization of compound 8g. Yield: 95 %; m.p. 281-282° C. IR: 3480, 3310, 3160 (NH₂, NH), 1630 (C=O) cm⁻¹. 1H NMR (DMSO-d₆): δ 10.0 (s, 1H, NH), 8.9 (s, 1H, CH pyrazole), 7.1-8.2 (m, 18H, aryl, pyridyl and thienyl protons), 5.9 (s, 2H, NH₂), 2.0 (s, 3H, CH₃). Elemental Anal. Calculated for C₃₄H₂₃N₅O₅S (583.73): C, 69.96; H, 4.32; N, 12.00; S, 10.98 %. Found: C, 69.88; H, 4.48; N, 12.26; S, 11.06 %.

Reaction of compound 9a with aromatic aldehydes or cycloalkanones; Formation of compounds 10a-c and 11a,b; General procedure.

To a mixture of 9a (0.97 g, 2 mmol) and the respective aldehyde or cycloalkanone (2 mmol) in absolute ethanol (15 ml), few drops of conc. HCl were added. The reaction mixture was heated under reflux for 3 h. The product that formed on cooling was collected and recrystallized from dioxane as yellow needles of 10a-c or 11a,b.

2,7-Diphenyl-9-(1,3-diphenyl-1H-pyrazol-4-yl)-4-oxo-1,2,3,4-tetrahydro-pyrido[3',2':4,5]thieno[3,2-d]pyrimidine (10a)

Elemental Anal. Calculated for C₃₈H₂₃N₅O₅S (575.69): C 75.11; H, 4.38; N, 12.17; S, 5.57 %. Found: C, 75.01; H, 4.33; N, 12.00; S, 5.77 %.

9-(1,3-Diphenyl-1H-pyrazol-4-yl)-2-(4-methoxyphenyl)-4-oxo-7-phenyl-1,2,3,4-tetrahydropyrido[3',2':4,5]thieno[3,2-d]pyrimidine (10b)

It was prepared by using benzaldehyde. Yield: 97 %; m.p.: 304-306° C. IR: 3410 (NH), 3171 (NH), 1645 (C=O) cm⁻¹. 1H NMR (CDCl₃-D): δ 9.3 (s, 1H, CH pyrazole), 7.4-8.4 (m, 21H, aryl and pyridyl protons), 6.1 (s, 1H, CH at C-2).
It was prepared by using 4-methoxybenzaldehyde. Yield: 98%; m. p.: 308-309°C. IR: 3406 (NH), 3188 (NH), 1643 (C=O) cm⁻¹.

1H NMR (CDCl₃-D₂O): δ 9.2 (s, 1H, CH pyrazole), 7.2-8.3 (m, 20H, aryl and pyridyl protons), 6.0 (s, 1H, C-2), 4.1 (s, 3H, OCH₃). Elemental Anal. Calculated for C₂₇H₃₄N₄O₂S (605.71); 2-(4-Chlorophenyl)-9-(1,3-diphenyl-1H-pyrazol-4-yl)-4-oxo-7-phenyl-1,2,3,4-tetrahydropyrido[3',2':4,5]thieno[3,2-d]pyrimidine (10c).

It was prepared by using 4-chlorobenzaldehyde. Yield: 95%; m. p.: 309-310°C. IR: 3413 (NH), 3169 (NH), 1645 (C=O) cm⁻¹.

1H NMR (DMSO-d₆): δ 9.1 (s, 1H, CH pyrazole), 7.0-8.1 (m, 16H, aryl and pyridyl protons), 6.7 (s, 1H, CONH), 3.7 (s, 1H, NH), 1.6-2.0 (m, 6H, (CH₃)₃ of cyclopentylidene ring), 1.3-1.4 (m, 2H, CH₃ of cyclopentylidene ring). Elemental Anal. Calculated for C₃₈H₃₅ClN₄OS (610.13); C, 78.67; H, 5.47; N, 12.66%. Found: C, 78.76; H, 5.55; N, 12.69%.

9-(1,3-Diphenyl-1H-pyrazol-4-yl)-4-oxo-7-phenyl-2,2-tetramethylene-1,2,3,4-tetrahydropyrido[3',2':4,5]thieno[3,2-d]pyrimidine (11a).

It was prepared by using cyclopentanone. Yield: 98%; m. p.: 302-304°C. IR: 3411 (NH), 3160 (NH), 1640 (C=O) cm⁻¹.

1H NMR (DMSO-d₆): δ 9.1 (s, 1H, CH pyrazole), 7.2-8.3 (m, 16H, aryl and pyridyl protons), 6.7 (s, 1H, CONH), 3.7 (s, 1H, NH), 1.6-2.0 (m, 6H, (CH₃)₃ of cyclopentylidene ring), 1.3-1.7 (m, 4H, (CH₃)₂ of cyclopentylidene ring).

Ethyl N-(2-cyano-(1,3-diphenyl-1H-pyrazol-4-yl)-6-phenylthieno[2,3-b]pyridin-3-yl)methanimidate (12).

A mixture of compound 9c (2.35 g, 5 mmol), triethyl orthoformate (7 ml) and acetic anhydride (20 ml) was refluxed for 4 h. The precipitate that formed after cooling was collected and recrystallized from ethanol as pale yellow plates of 12. Yield: 81%; m. p.: 216-218°C. IR: 2225 (C≡N). Elemental Anal. Calculated for C₃₈H₃₅ClN₄OS (610.13); C, 79.31; H, 5.65%.

3-Amino-3,4-dihydro-9-(1,3-diphenyl-1H-pyrazol-4-yl)-4-imino-7-phenyl-pyrido[3',2':4,5]thieno[3,2-d]pyrimidine (13).

To a suspension of compound 12 (2.10 g, 4 mmol) in dioxane (15 ml), hydrazine hydrate 99% (2 ml) was added. The resulting mixture was stirred at room temperature for 4 h. The product that formed was collected and recrystallized from ethanol to give fine white needles of 13. Yield: 81%; m. p.: 249-251°C. IR: 1731 (C≡O). Elemental Anal. Calculated for C₃₈H₃₅ClN₅S (611.60); C, 78.54; H, 5.67%; N, 19.16%; S, 6.07%. Found: C, 78.52; H, 5.60; N, 19.20; S, 6.07%.

7-(1,3-Diphenyl-1H-pyrazol-4-yl)-9 phenyl[1,2,4]triazolo[2',3'-c]pyrido[3',2':4,5]thieno[2,3-e]pyrimidine (14).

To a solution of compound 13 (1.02 g, 2 mmol) in triethyl orthoformate (10 ml), few crystals of p-toluenesulphonic acid were added. The reaction mixture was heated under reflux for 4 h. The precipitate that formed while hot was collected and recrystallized from ethanol to give white needles of 14. Yield: 76%; m. p.: 204-206°C. IR: 1731 (C≡O). Elemental Anal. Calculated for C₃₈H₃₅ClN₅S (621.60); C, 77.38; H, 3.67; N, 18.80; S, 6.15%. Found: C, 77.18; H, 3.62; N, 18.80; S, 6.12%.


Compound 13 (1.02 g, 2 mmol) in acetic anhydride (10 ml) was heated under reflux for 3 h. The crystalline precipitate that formed on cooling was collected by filtration and recrystallized from ethanol as white crystals of 15. Yield: 80%; m. p.: 267-270°C. IR: 3402 (NH), 3189 (NH), 1641 (C=O). Elemental Anal. Calculated for C₃₈H₃₅ClN₄OS (631.73); C, 78.56; H, 5.47; N, 12.70%. Found: C, 78.55; H, 5.51; N, 12.69%.
A suspension of compound 13 (1.02 g, 2 mmol) in diethyl malonate (12 ml) was gently heated under reflux for 2 h. The reaction mixture was triturated with ethanol (15 ml) and then allowed to cool. The formed precipitate was collected and recrystallized from an ethanol-chloroform mixture as pale yellow needles of 16. Yield: 73%; m.p. 228-229 °C. IR: 1713 (C=O), 1732 (C=O), 607.69; C, H NMR (CDCl3): δ 9.2 (s, 1H, CH pyrazole), 8.6 (s, 1H, CH pyrimidine), 7.2-8.2 (m, 16H, aryl and pyridyl protons), 4.2-4.5 (q, 2H, OCH3), 4.0 (s, 2H, CH2), 1.2-1.5 (t, 3H, CH3). Elemental Anal. Calculated for C35H35N4O6S (607.69); C, 69.18; H, 4.15; N, 16.13; S, 5.28 %. Found: C, 69.46; H, 4.31; N, 16.00; S, 5.32 %.

Conflict of interest

Authors have none to declare

REFERENCES


