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The synthesis and spectral characteristics of novel 6-(2-substituted-1,3,4-oxadiazol-5-yl)-2-phenylthieno[2,3-*d*]pyrimidine fluorescent compounds derived from 5-cyano-1,6-dihydro-4-methyl-2-phenyl-6-thioxopyrimidine

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ABSTRACT

A series of novel 6-(2-substituted-1,3,4-oxadiazol-5-yl)-2-phenylthieno[2,3-*d*]-pyrimidine fluorescent compounds were obtained by the condensation of 6-(2-methylthio-1,3,4-oxadiazol-5-yl)-2-phenylthieno[2,3-*d*]pyrimidine with appropriate secondary amines. The structures were characterized by IR, ^{1}H NMR, mass, elemental analysis and UV–vis spectroscopy and the fluorescence characteristics were investigated in ethyl acetate and acetone by UV–vis absorption and emission spectra. The absorption spectra and fluorescence characteristics were correlated with substituents of the 6-(2-substituted-1,3,4-oxadiazol-5-yl)-2-phenylthieno[2,3-*d*]pyrimidine compounds and solvent polarity. The novel compounds also displayed intense blue to yellow-green fluorescence in ethyl acetate and acetone solutions.

1. Introduction

Among the derivatives of thieno[2,3-*d*]pyrimidines, substances that have antiviral, fungicidal, and insecticidal activity [1], antibacterial and antiplastic properties [2], antihypertensive [3], anticonvulsant activity [4], and antihistaminic [5] action have been observed. Likewise, 1,3,4-oxadiazole (OXD) derivatives are useful targets in the search for antivirals as they have been associated with many types of biological properties such as anti-inflammatory [6,7], antibacterial, antifungal activities [8,9] and inhibit HIV replication [10]. Moreover, the electron-withdrawing OXD containing materials have attracted much attention since they have the strong electron affinity and possess the electron-transporting characteristic [11–13]. In addition, the high efficiency and blue-purple light emissive characteristics of small OXD molecules make them more favorable. In this family, several organic molecules containing an OXD, such as 2-(4-biphenylyl)-5-(4-*tert*-butylphenyl)-1,3,4-oxadiazole (PBD) have been used successfully as electron-injection materials to improve the balance of charge injection and to increase the photo/electron quantum efficiency [14–16].

Some analogues of OXD derivatives, for example 1,3-bis[2-(4-*N*,*N*-dimethylaminophenyl)-1,3,4-oxadiazol-5-yl]benzene, 1,4-bis[2-(4-*tert*-butylphenyl)-1,3,4-oxadiazol-5-yl]benzene (PDPDP) and 2,5-bis[2-(4-*tert*-butylphenyl)-1,3,4-oxadiazol-5-yl]pyridine (PDPyDP) [17] were also prepared as the effective electron-transporting materials. The 2,5-bis(2-phenyl-1,3,4-oxadiazol-5-yl)-thiophene derivative [18] has also been used as fluorescent brightening agent for synthetic fibers. Although a number of papers have been published concerning the synthesis of OXD fluorescent compounds, those containing a new heterocyclic system of thieno[2,3-*d*]pyrimidine moiety have not yet been reported. Thus, combining 5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine moiety with substituted 1,3,4-oxadiazole is expected to give new fluorescent compounds. Herein, in this report, we describe the synthesis of a series of novel OXD fluorescent derivatives incorporating a 5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine moiety derived from 5-cyano-1,6-dihydro-4-methyl-2-phenyl-6-thioxopyrimidine **1**. The absorption and fluorescence characteristics of the compounds are also discussed.

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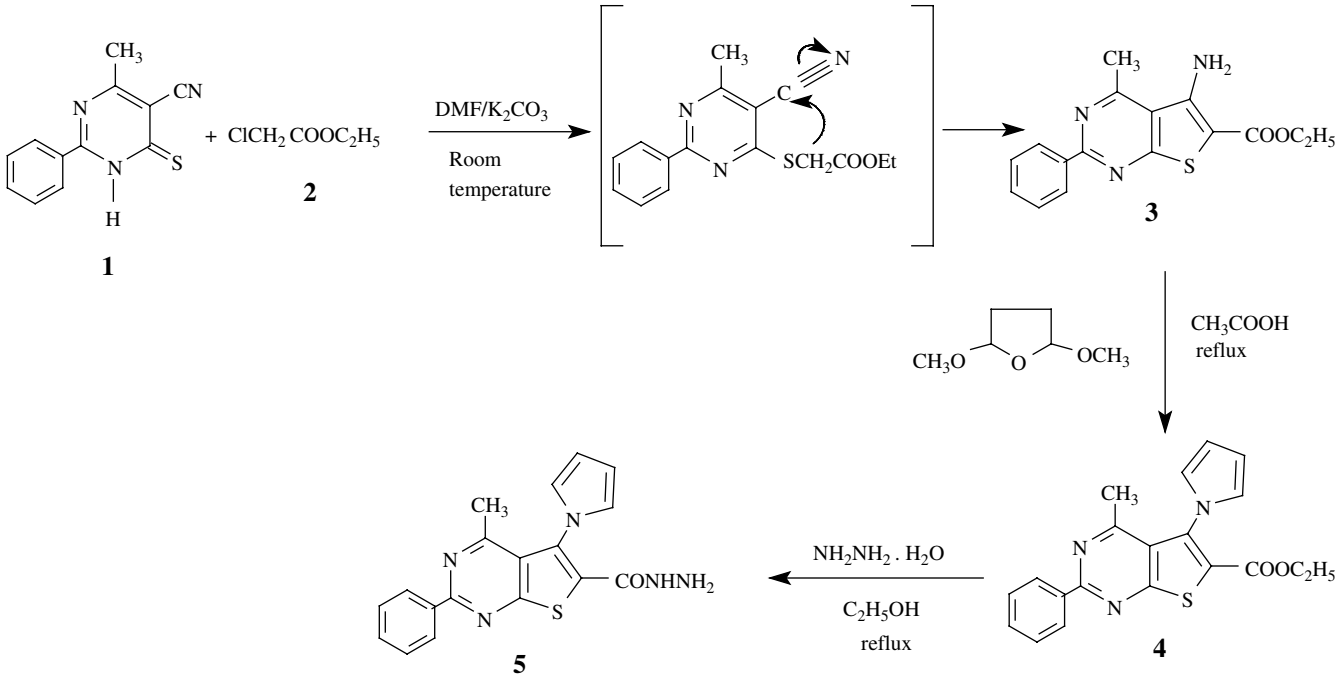


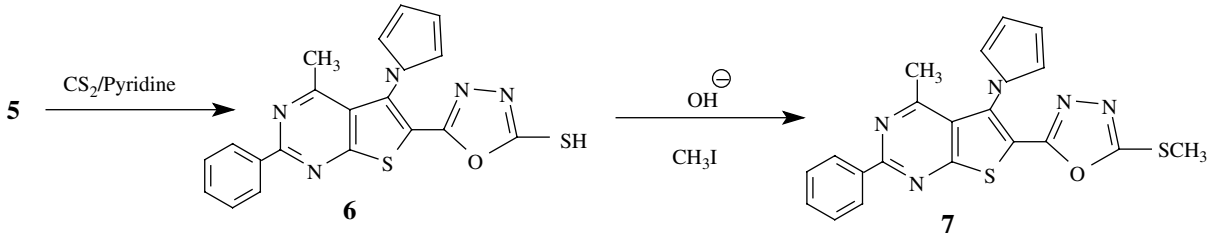
Scheme 1. Synthesis of pyrrolothieno[2,3-*d*]pyrimidine carbohydrazide **5**.

2. Results and discussion

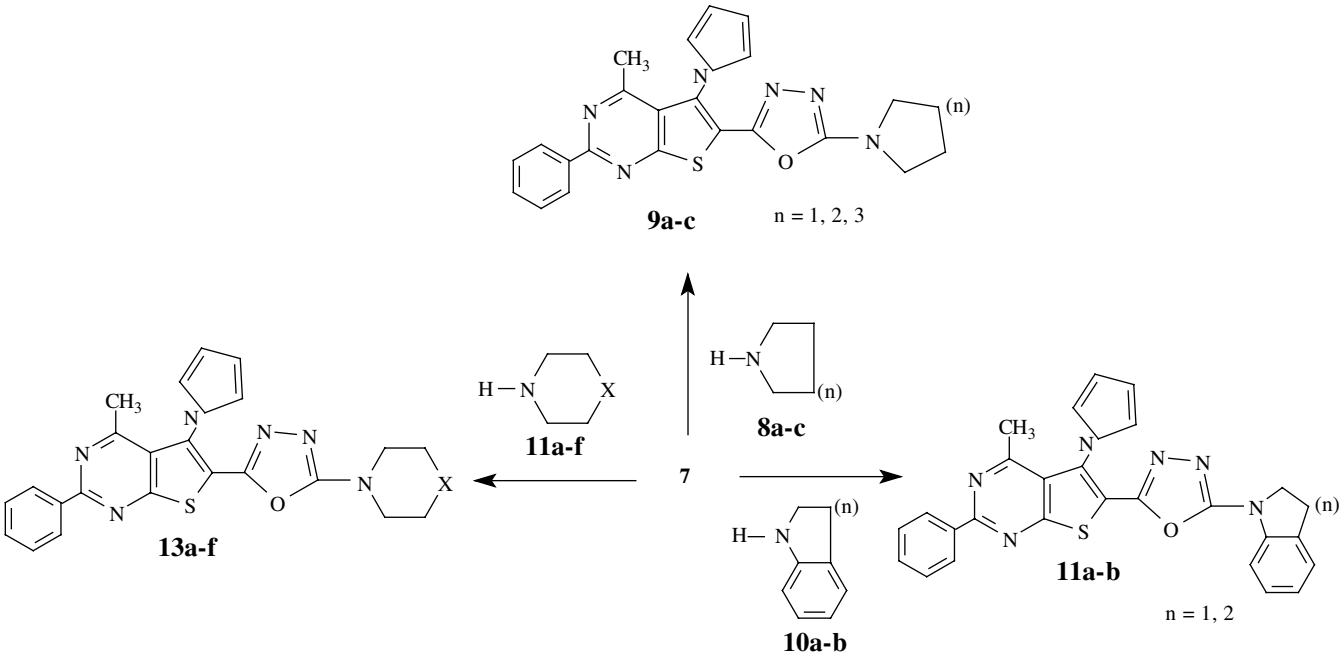
2.1. Synthesis of intermediates and fluorescent compounds

All relevant reactions are depicted in Schemes 1–3, the novel OXD fluorescent derivatives are prepared in six steps starting from 5-cyano-1,6-dihydro-4-methyl-2-phenyl-6-thioxopyrimidine **1**. The required compound thioxopyrimidine **1** was prepared by treating benzoylisothiocyanate with 3-aminocrotononitrile in refluxing dioxane [19,20]. Cyclization of thioxopyrimidine **1** with ethyl chloroacetate **2** in DMF in the presence of excess anhydrous potassium carbonate at room temperature formed the nonisolable *S*-alkylated intermediate, which *via* nucleophilic substitution and intramolecular cyclocondensation gave the ethyl 5-amino-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine-6-carboxylate **3** (Scheme 1). The structure of compound **3** was established by examining spectral data and elemental analysis. The IR spectrum of compound **3** indicated the absence of the C≡N and C═S absorption bands, and showed the characteristic absorption bands at 3488 and 3359 cm^{-1} for the NH_2 group and at 1663 cm^{-1} for the C═O group. The ^1H NMR spectrum ($CDCl_3$) showed a triplet at δ 1.41 (3H, t) and a quartet at δ 4.37 (2H, q) assigned to the ethyl group (CH_2CH_3), a broad singlet at δ 6.23 (2H, br) assigned to the NH_2 protons, and a multiplet at δ 8.55–7.48 (5H, m) assigned to the phenyl protons. Treatment of compound **3** with 2,5-dimethoxytetrahydrofuran in glacial acetic acid produced ethyl 5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine-6-carboxylate **4**, which reacted with excess of 85% hydrazine hydrate in refluxing ethanol to give the corresponding 5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-*d*]pyrimidine carbohydrazide **5** (Scheme 1). The IR spectra of compound **4** indicated the absence of the NH_2 group and compound **5** showed the characteristic absorption bands at 3398 and 3335 cm^{-1} for the NH_2 group, at 3110 cm^{-1} for the NH group and 1638 cm^{-1} for the C═O group. The ^1H NMR spectra ($CDCl_3$) of compounds **4** and **5** revealed two multiplets at δ 6.49–6.35 (2H, m) and 6.81–6.72 (2H, m), which were readily assigned to the hydrogen attached at C_3, C_4 and C_2, C_5 of the pyrrolyl ring, respectively. Moreover, carbohydrazide **5** showed a broad singlet at δ 6.42 (2H, br) assigned to the NH_2 protons, a broad singlet at δ 9.72 (1H, br) assigned to the NH proton.

Next, cyclization of carbohydrazide **5** with CS_2 in the presence of pyridine afforded 6-(2,3-dihydro-2-mercapto-1,3,4-oxadiazol-5-yl)-4-methyl-5-(1-pyrrolyl)-2-phenylthieno[2,3-*d*]pyrimidine **6**, which reacted with methyl iodide in the presence of sodium methoxide to yield 6-(2-methylthio-1,3,4-oxadiazol-5-yl)-4-methyl-5-(1-pyrrolyl)-2-phenylthieno[2,3-*d*]pyrimidine **7** (84% yield) (Scheme 2). The structures of **6** and **7** were established on the basis of their elemental analysis and spectral data. On the other hand, a series of novel 6-(2-substituted-1,3,4-oxadiazol-5-yl)-4-methyl-5-(1-pyrrolyl)-2-phenylthieno[2,3-*d*]pyrimidine (OXD-THPM) fluorescent derivatives **9a–c**, **11a** and **b** and **13a–f** were also obtained by the condensation reaction of compound **7** with appropriate secondary amines **8a–c**, **10a** and **b**, and **12a–f** such as pyrrolidine, piperidine,



Scheme 2. Synthesis of (2-methylthio-1,3,4-oxadiazol-5-yl)-pyrrolothieno[2,3-*d*]pyrimidine carbohydrazide **7**.



Scheme 3. Synthesis of OXD-THPM fluorescent derivatives **9a–c**, **11a** and **b**, and **13a–f**.

hexamethyleneimine, indoline, 1,2,3,4-tetrahydroquinoline, morpholine, *N*-methylpiperazine, *N*-ethylpiperazine, ethyl 1-piperazinecarboxylate, 1-phenylpiperazine and 1-(2-pyrimidyl)piperazine (Scheme 3). Compounds **9a–c**, **11a** and **b** and **13a–f** were obtained generally in 56–95% yields. The structures of these compounds were verified by elemental analysis and by spectroscopic methods. Physical and spectral data of compounds **9a–c**, **11a** and **b** and **13a–f** are recorded in Tables 1 and 2. Typical assignments for **9b** and **13f** by ^{1}H NMR are shown in Fig. 1.

2.2. Absorption spectral characteristics

The absorption maxima (λ_{max}) of compounds **7**, **9a–c**, **11a** and **b** and **13a–f** were measured in ethyl acetate and acetone solutions and are shown in Table 3. For compounds **7**, **9a–c**, **11a** and **b** and **13a–f** in ethyl acetate, absorption maxima in the UV region were in the range 339–374 nm, while in acetone it was 340–376 nm. It was apparent that the λ_{max} values of these compounds showed only a slight bathochromic shift (1–2 nm) or were equal when the solvent changed from ethyl acetate to acetone. The substituent R acts as a strong donor and the (1,3,4-oxadiazol-5-yl)-thieno[2,3-*d*]pyrimidine (OXD-THPM) moiety acts as a strong acceptor, and the π-conjugations through the donor (R) to the OXD-THPM moiety produce strong donor–acceptor systems. Compound **7**, as a standard, absorbed at 340 nm (acetone) and substituent effects on the absorption maxima were evaluated compared with this value. As is apparent from Table 3, introduction of electron donating substituents into the OXD-THPM moiety produces bathochromic shifts of the absorption maxima. The differences of these values are shown by $\Delta\lambda^a_{max}$. As a result, all the compounds produced bathochromic shifts of 14–36 nm (with the exception of **11b**, $\Delta\lambda^a_{max}$ 1 nm). In addition, we assume that the bathochromic shift of the compounds is due to the electronic substituent effect and special type of bridging since these molecules are somewhat twisted around the C–C single bond at 5-position of the OXD moiety; according to molecular orbital (MO) theory, mode twisting around a single bond should give rise to a bathochromic shift [21,22].

Thus, it can also be seen that compounds **9a–c** produced bathochromic shifts of 20–24 nm caused by introduction of the stronger electron donating substituents (*N*-cycloalkyl) into OXD-THPM moiety at the R position at which an electron density decrease should produce a bathochromic shift of λ_{max} [23]. Similar results are

Table 1
Physical and analytical data of 6-(2-substituted-1,3,4-oxadiazol-5-yl)-thieno[2,3-*d*]pyrimidine fluorescent derivatives (**9a–c**, **11a** and **b** and **13a–f**)

Compd.	Mp[a] (°C)	Yield (%)	Molecular formula	Elemental analysis (%) calcd./found		
				C	H	N
9a	286	95	$C_{23}H_{20}N_6OS$	64.48/64.41	4.67/4.41	19.62/19.55
9b	293	87	$C_{24}H_{22}N_6OS$	65.15/65.14	4.97/4.89	19.00/19.33
9c	307	71	$C_{25}H_{24}N_6OS$	65.78/65.59	5.26/5.12	18.42/18.69
11a	279	74	$C_{27}H_{20}N_6OS$	68.06/68.15	4.20/4.14	17.64/17.55
11b	185	56	$C_{28}H_{22}N_6OS$	68.57/68.88	4.48/4.59	17.14/17.38
13a	281	90	$C_{23}H_{20}N_6O_2S$	62.16/62.29	4.50/4.41	18.91/19.01
13b	252	68	$C_{24}H_{23}N_7OS$	63.01/63.28	5.03/5.33	21.44/21.58
13c	273	87	$C_{25}H_{25}N_7OS$	63.69/63.79	5.30/5.14	20.80/20.69
13d	274	86	$C_{26}H_{25}N_7O_3S$	60.58/60.79	4.85/4.99	19.02/19.25
13e	290	70	$C_{29}H_{25}N_7OS$	67.05/67.25	4.81/4.65	18.88/18.67
13f	307	58	$C_{27}H_{23}N_9OS$	62.18/62.36	4.41/4.59	24.18/24.33

[a] Recrystallization from $CHCl_3$/THF.

Table 2
Spectral data of 6-(2-substituted-1,3,4-oxadiazol-5-yl)-thieno[2,3-*d*]pyrimidine fluorescent derivatives (**9a–c**, **11a** and **b** and **13a–f**)

Compd.	MS (*m*/*e* M^+)	IR (KBr) ν (cm^{-1})	^1H NMR ($CDCl_3$) δ (ppm)
9a	428 (100), 357 (34), 332 (9), 316 (8), 301 (65), 287 (4), 214 (10), 151 (4), 96 (18), 68 (1), 53 (12).	1602 (C=N)	1.65 (4H, m, 3,4-H of pyrrolidinyl), 2.21 (3H, s, CH_3), 3.33–3.32 (4H, m, 2,5-H of pyrrolidinyl), 6.39 (2H, m, 3,4-H of pyrrolyl), 6.83 (2H, m, 2,5-H of pyrrolyl), 8.53–8.52, 7.48 (5H, m, phenyl-H).
9b	442 (100), 357 (38), 332 (10), 316 (14), 301 (62), 288 (5), 221 (10), 197 (5), 110 (20), 68 (18), 53 (2).	1603 (C=N)	1.69–1.57, 3.32–3.30 (10H, m, piperidinyl-H), 2.24 (3H, s, CH_3), 6.39 (2H, m, 3,4-H of pyrrolyl), 6.82 (2H, m, 2,5-H of pyrrolyl), 8.55–8.53, 7.50–7.49 (5H, m, phenyl-H).
9c	456 (100), 400 (2), 372 (8), 357 (38), 332 (23), 316 (38), 301 (70), 288 (8), 276 (4), 228 (9), 198 (10), 144 (4), 126 (18), 55 (5).	1603 (C=N)	1.56–1.54, 1.68–1.67, 3.40–3.37 (12H, m, hexamethyleneiminyl-H), 2.23 (3H, s, CH_3), 6.39 (2H, m, 3,4-H of pyrrolyl), 6.82 (2H, m, 2,5-H of pyrrolyl), 8.56–8.53, 7.51–7.49 (5H, m, phenyl-H).
11a	476 (100), 434 (5), 357 (18), 331 (10), 315 (42), 302 (49), 288 (9), 276 (2), 261 (11), 238 (12), 198 (20), 146 (9), 128 (20), 118 (70), 91 (10), 78 (7).	1600 (C=N)	2.13 (3H, s, CH_3), 3.43 (2H, t, $J = 1.67$ Hz, 3-H of indolinyl), 2.92 (2H, t, $J = 1.67$ Hz, 2-H of indolinyl), 6.48 (2H, m, 3,4-H of pyrrolyl), 7.04 (2H, m, 2,5-H of pyrrolyl), 7.07–6.94 (2H, m, 5,6-H of indolinyl), 7.13 (1H, d, $J = 1.0$ Hz, 4-H of indolinyl), 7.20 (1H, d, $J = 1.0$ Hz, 7-H of indolinyl), 8.49–7.49 (5H, m, phenyl-H).
11b	490 (100), 438 (5), 405 (44), 358 (18), 331 (41), 315 (52), 302 (60), 288 (28), 278 (10), 261 (11), 245 (39), 198 (22), 160 (29), 128 (20), 133 (78), 117 (7), 77 (4).	1602 (C=N)	2.01–1.98 (2H, m, 3-H of quinolizinyl), 2.24 (3H, s, CH_3), 2.81 (2H, t, $J = 1.28$ Hz, 4-H of quinolizinyl), 3.72 (2H, t, $J = 1.25$ Hz, 2-H of quinolizinyl), 6.45 (2H, m, 3,4-H of pyrrolyl), 6.84 (2H, m, 2,5-H of pyrrolyl), 7.01–6.98 (1H, m, 6-H of quinolizinyl), 7.08 (1H, d, $J = 1.0$ Hz, 5-H of quinolizinyl), 7.19–7.16 (1H, m, 7-H of quinolizinyl), 7.64 (1H, d, $J = 1.0$ Hz, 8-H of quinolizinyl), 8.55–8.53, 7.50–7.48 (5H, m, phenyl-H).
13a	444 (100), 387 (1), 357 (35), 331 (10), 315 (11), 301 (81), 288 (8), 275 (1), 262 (1), 222 (12), 196 (8), 164 (2), 151 (4), 112 (12), 68 (16).	1611 (C=N)	2.52 (3H, s, CH_3), 3.86 (4H, d, $J = 1.0$ Hz, 2,6-H of morpholinyl), 4.17 (4H, d, $J = 1.0$ Hz, 3,5-H of morpholinyl), 6.78 (2H, m, 3,4-H of pyrrolyl), 7.10 (2H, m, 2,5-H of pyrrolyl), 8.49–8.47, 7.90–7.86 (5H, m, phenyl-H).
13b	457 (100), 442 (5), 400 (91), 387 (21), 372 (6), 357 (30), 331 (34), 315 (98), 302 (58), 288 (38), 275 (9), 262 (12), 222 (4), 212 (13), 198 (29), 184 (11), 99 (15), 83 (51), 70 (48), 56 (8).	1606 (C=N)	2.22 (3H, s, CH_3), 2.33 (3H, s, N–CH_3), 2.44 (4H, d, $J = 1.0$ Hz, 2,6-H of piperazinyl), 3.39 (4H, d, $J = 1.0$ Hz, 3,5-H of piperazinyl), 6.39 (2H, t, 3,4-H of pyrrolyl), 6.83 (2H, t, 2,5-H of pyrrolyl), 8.53–8.51, 7.49–7.48 (5H, m, phenyl-H).
13c	471 (81), 456 (8), 442 (2), 400 (100), 387 (15), 374 (7), 357 (16), 331 (19), 315 (45), 302 (18), 288 (10), 275 (2), 262 (3), 228 (5), 199 (20), 184 (8), 153 (6), 138 (15), 97 (48), 84 (70), 72 (72), 56 (4).	1603 (C=N)	1.10 (3H, t, $J = 1.0$ Hz, N–$CH_2\underline{CH_3}$), 2.24 (3H, s, CH_3), 2.46–2.42 (6H, m, N–$\underline{CH_2}CH_3$and 2,6-H of piperazinyl), 3.39 (4H, d, $J = 1.0$ Hz, 3,5-H of piperazinyl), 6.40 (2H, m, 3,4-H of pyrrolyl), 6.82 (2H, m, 2,5-H of pyrrolyl), 8.55–8.53, 7.50–7.49 (5H, m, phenyl-H).
13d	515 (100), 470 (1), 442 (1), 400 (10), 387 (25), 374 (2), 357 (65), 331 (23), 315 (60), 301 (98), 288 (14), 275 (5), 262 (8), 243 (15), 228 (2), 199 (19), 184 (10), 171 (4), 113 (7), 70 (7), 56 (4).	1705 (C=O), 1604 (C=N)	1.28 (3H, t, $J = 2.5$ Hz, CH_3), 2.24 (3H, s, CH_3), 3.34 (4H, t, $J = 1.0$ Hz, 2,6-H of piperazinyl), 3.51 (4H, d, $J = 1.0$ Hz, 3,5-H of piperazinyl), 4.18 (2H, q, $J = 2.1$ Hz, $COCH_2$), 6.41 (2H, m, 3,4-H of pyrrolyl), 6.83 (2H, m, 2,5-H of pyrrolyl), 8.54–8.52, 7.50–7.49 (5H, m, phenyl-H).
13e	519 (39), 400 (58), 387 (10), 358 (17), 331 (16), 315 (41), 302 (23), 288 (19), 275 (3), 260 (18), 243 (1), 228 (1), 212 (5), 199 (22), 184 (9), 171 (4), 161 (21), 145 (88), 104 (100), 91 (16), 56 (7).	1604 (C=N)	2.26 (3H, s, CH_3), 3.20 (4H, d, $J = 1.0$ Hz, 2,6-H of piperazinyl), 3.52 (4H, d, $J = 1.0$ Hz, 3,5-H of piperazinyl), 6.44 (2H, t, 3,4-H of pyrrolyl), 6.85 (2H, t, 2,5-H of pyrrolyl), 8.56–8.54, 7.51–6.94 (10H, m, phenyl-H).
13f	521 (50), 506 (1), 426 (3), 400 (21), 387 (10), 358 (11), 331 (18), 315 (72), 302 (45), 288 (21), 275 (5), 261 (20), 243 (6), 228 (2), 212 (8), 199 (23), 188 (26), 163 (52), 134 (100), 120 (41), 108 (31), 80 (15).	1606 (C=N)	2.26 (3H, s, CH_3), 3.43 (4H, d, $J = 1.05$ Hz, 2,6-H of piperazinyl), 3.89 (4H, d, $J = 1.02$ Hz, 3,5-H of piperazinyl), 6.43 (2H, t, 3,4-H of pyrrolyl), 6.57 (1H, m, 5-H of pyrimidinyl), 6.84 (2H, t, 2,5-H of pyrrolyl), 9.35 (2H, d, $J = 1.0$ Hz, 4,6-H of pyrimidinyl), 8.56–8.54, 7.51–7.49 (5H, m, phenyl-H).

Abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet.

observed in the case of compounds **13a–f** which resulted in bathochromic shifts of 14–17 nm. Next, comparison of the λ_{max} of compounds **9a–c** as the ring size increases from $n = 1$ to $n = 3$ resulted in the following order: **9c** > **9a** > **9b**. Furthermore, the spectroscopic data also demonstrate that compound **11a** (λ_{max} 376 nm, acetone) containing the indolinyl group showed a largest bathochromic shift of 36 nm. Nevertheless, the substitution of SCH_3 group of compound **7** by a 1,2,3,4-tetrahydroquinolinly group (**11b**) does not significantly change the absorption maxima ($\Delta\lambda^a_{max}$ 1 nm). In general, with respect to the substituents R of compounds **7**, **9a–c**, **11a** and **b** and **13a–f**, the compounds were bathochromically shifted in the order: **11a** > **9a–c** > **13a–f** > **11b** ≒ **7**.

On the other hand, it is well known that ε values reflect the molecular planarity and enlargement of π-conjugation. Compounds **7** and **11b** have higher ε values than those of other compounds which indicates that compounds **7** and **11b** have much more planar and rigid π-conjugation system than that of other compounds [24].

2.3. Fluorescence spectral characteristics

As shown in Table 3, the fluorescence maxima (F_{max}) of compounds **7**, **9a–c**, **11a** and **b** and **13a–f** in ethyl acetate and acetone were at around 412–494 nm and 438–511 nm, respectively. It can be seen from Table 3 that their F_{max} values show a significant increase and are clearly bathochromic shifted with an increase in solvent polarity; the differences of these values are shown by $\Delta\lambda_F$. For example, F_{max} values exhibited a bathochromic shift of 17 nm for **7**, 15 nm for **9a**, 28 nm for **11a**, 23 nm for **11b**, 19 nm for **13c** and 26 nm for **13e** when the solvent changed from ethyl acetate to acetone. The bathochromic shifts of F_{max} of these compounds with increase of solvent polarity can be due to dipole–dipole interaction of the excited state [13,25]. From these results, the fluorescence wavelength is found to be more sensitive to changes in solvent polarity.

On the other hand, fluorescent measurements of compounds **9a–c**, **11a** and **b** and **13a–f** indicate that replacement of the SCH_3 group of compound **7** for appropriate electron donating substituent, such as *N*-cycloalkyl (**9a–c**), *N*-cycloalkylaryl (**11a** and **b**), morpholinyl (**13a**) and piperazinyl (**13b–f**) groups, leads to a significant hypsochromic shift, the differences of these values are shown by ΔF^a_{max}. For instance, compound **7** emits at 511 nm (acetone), with increasing donor ability from the SCH_3 (**7**) to the piperidinyl (**9b**), morpholinyl (**13a**) and piperazinyl (**13e**) groups, their F^a_{max} values show large hypsochromic shifts to 448 nm ($\Delta F^a_{max} = -63$ nm), 444 nm ($\Delta F^a_{max} = -67$ nm) and 438 nm ($\Delta F^a_{max} = -73$ nm), respectively. In addition, Stoke's shift (SS) values

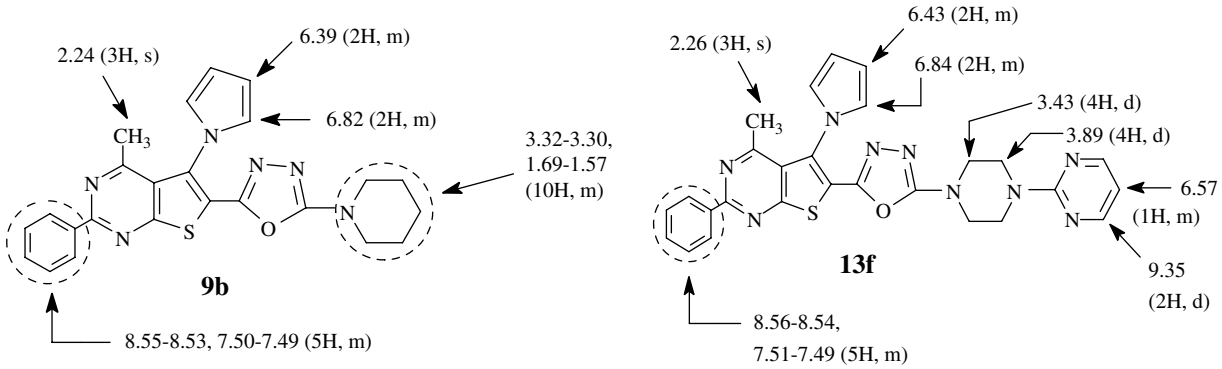


Fig. 1. Structural assignments of typical protons in **9b** and **13f** by ^{1}H NMR.

are quite different from each other and ranged from 74 to 171 nm (acetone), with compound **7** showing the highest Stoke's shift (171 nm) and **9c** the lowest (74 nm). The large Stoke's shift indicates an increase in the dipole moment on excitation. This behaviour has been attributed to a charge redistribution in the excited state with respect to the ground state [22,26,27]. Thus, the big difference in their Stoke's shift values indicates that compounds **7** (171 nm), **11a** (123 nm), **11b** (141 nm) and **13f** (100 nm) lose more energy in the excited state (bigger SS value) [24] than compounds **9a–c** and **13a–e**. On the other hand, compounds **7** and **11a** and **b** have an intense yellow-green fluorescence, with maximum between 459 and 494 nm (ethyl acetate) and 482 and 511 nm (acetone). Also, compounds **9a–c** and **13a–f** have an intense blue fluorescence, with maximum between 412 and 439 nm (ethyl acetate) and 438 and 457 nm (acetone) and they can be used as fluorescent brighteners [28,29].

3. Experimental

3.1. General

All melting points are uncorrected and expressed in °C. IR spectra were recorded on a JASCO FTIR-3 spectrometer (KBr); ^{1}H NMR spectra were obtained on a Bruker AM-300 WB FI-NMR spectrometer, and chemical shifts are expressed in δ ppm using TMS as an internal standard. Electron impact mass spectra were obtained at 70 eV using a Finingan Mat TSQ-46C spectrometer. Microanalyses for C, H, and N were performed on a Perkin–Elmer 240 Elemental Analyzer. Electronic spectra were recorded on a Shimadzu UV 240 from compound solutions in acetone and ethyl acetate at a concentration of 1.25×10^{-5} mol l^{-1}. Fluorescent measurements were recorded on a Perkin–Elmer LS 50 luminescence spectrophotometer.

3.2. Synthesis of intermediates **3–6**

3.2.1. Ethyl 5-amino-4-methyl-2-phenylthieno[2,3-d]pyrimidine-6-carboxylate (**3**)

A mixture of 5-cyano-1,6-dihydro-4-methyl-2-phenyl-6-thioxopyrimidine **1** (2.27 g, 0.01 mol), potassium carbonate anhydrous (2.76 g, 0.02 mol) and ethyl chloroacetate **2** (1.23 g, 0.01 mol) in DMF (50 ml) was stirred at room temperature for 4 h and then diluted with cold water (50 ml). The resulting solid product was collected by filtration, washed with water and recrystallized from ethyl acetate/ethanol to give 2.88 g of pale yellow needles (92% yield), mp 177 °C; IR: ν 3488, 3359 (NH_2), 1663 (CO) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.41 (3H, t, $J = 4.80$ Hz, CH_3), 2.98 (3H, s, CH_3), 4.37 (2H, q, $J = 3.0$ Hz, OCH_2), 6.23 (2H, br, NH_2), 8.55–8.53, 7.53–7.48 (5H, m, phenyl-H); MS: 313 (M^+, 100).

Anal. Calcd. for $C_{16}H_{15}N_3O_2S$: C, 61.34; H, 4.79; N, 13.41. Found: C, 61.23; H, 4.70; N, 13.41%.

3.2.2. Ethyl 5-(1-pyrrolyl)-4-methyl-2-phenylthieno[2,3-d]pyrimidine-6-carboxylate (**4**)

A mixture of ethyl 5-amino-4-methyl-2-phenylthieno[2,3-*d*] pyrimidine-6-carboxylate **3** (3.13 g, 0.01 mol) and 2,5-dimethoxytetrahydrofuran (editors' note: harmful irritant; avoid contact with water) (1.26 g, 0.01 mol) in glacial acetic acid (20 ml) was refluxed for 12 h. After cooling, the resulting solid product was collected by filtration and washed with water, and the crude product recrystallized from ethanol/glacial acetic acid to give 3.16 g of gray white needles (87% yield), mp 165 °C; IR: ν 1697 (CO) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.15 (3H, t, $J = 2.0$ Hz, CH_3), 2.18 (3H, s, CH_3), 4.18 (2H, q, $J = 2.0$ Hz, OCH_2), 6.35 (2H, m, 3,4-H of pyrrolyl), 6.72 (2H, m, 2,5-H of pyrrolyl), 8.48–8.46, 7.43–7.42 (5H, m, phenyl-H); MS: 363 (M^+, 83), 334 (82), 316 (100), 288 (58), 278 (38), 214 (2), 185 (14), 160 (10), 116 (9), 77 (9), 51 (5).

Anal. Calcd. for $C_{20}H_{17}N_3O_2S$: C, 66.11; H, 4.68; N, 11.57. Found: C, 66.13; H, 4.72; N, 11.45%.

3.2.3. 4-Methyl-5-(1-pyrrolyl)-2-phenylthieno[2,3-d]pyrimidine carbohydrazide (**5**)

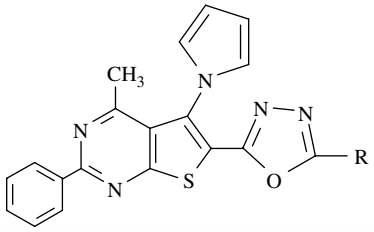
A mixture of compound **4** (3.63 g, 0.01 mol) and hydrazine hydrate (editors' note: incompatible with many materials, including oxidizing agents, heavy metal oxides, dehydrating agents, alkali metals, iron, silver salts; combustible; contact with many materials may cause fire or explosive decomposition; may react explosively with a variety of materials; vapour may explode in fire) (10 ml, 85% solution) was refluxed in absolute ethanol (20 ml) for 24 h. After cooling, the resulting solid product was collected by filtration and washed with water, and the crude product recrystallized from ethanol to give 3.42 g of gray white needles (98% yield), mp 230 °C; IR: ν 3398, 3335 (NH_2), 3110 (NH), 1638 (CO) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.10 (3H, s, CH_3), 6.46 (2H, br, NH_2), 6.49 (2H, m, 3,4-H of pyrrolyl), 6.81 (2H, m, 2,5-H of pyrrolyl), 8.46–8.44, 7.43–7.41 (5H, m, phenyl-H), 9.72 (1H, br, NH); MS: 349 (M^+, 39), 318 (100), 289 (9), 277 (26), 244 (8), 212 (2), 187 (6), 160 (8), 116 (9), 104 (5), 77 (7), 69 (2).

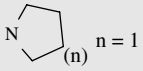
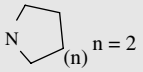
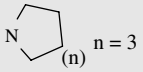
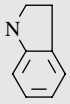
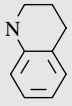
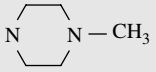
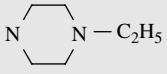
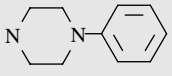
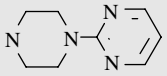
Anal. Calcd. for $C_{18}H_{15}N_5OS$: C, 61.89; H, 4.29; N, 20.05. Found: C, 61.84; H, 4.22; N, 20.15%.

3.2.4. 6-(2,3-Dihydro-2-mercapto-1,3,4-oxadiazol-5-yl)-4-methyl-5-(1-pyrrolyl)-2-phenylthieno[2,3-d]pyrimidine (**6**)

A mixture of compound **5** (0.35 g, 1 mmol) and carbon disulphide (editors' note: highly flammable and volatile; low flash point; poisonous; incompatible with strong oxidizing agents, azides, most common metals, halogens, hypochlorites) (5 ml) in pyridine (10 ml) was refluxed on a steam bath for 6 h. After cooling, the resulting solid product was collected by filtration, washed with water and recrystallized from ethanol to give 3.67 g of greenish yellow crystals (94% yield), mp 276 °C; IR: ν 1625 (C═N), 1182 (C═S) cm^{-1}; MS: 391 (M^+, 100).

Table 3
Absorption and fluorescence spectral data of 6-(2-substituted-1,3,4-oxadiazol-5-yl)-thieno[2,3-*d*]pyrimidine fluorescent derivatives (**9a–c**, **11a** and **b** and **13a–f**)



Compd.	R	λ^{ea}_{max} (nm)	λ^{a}_{max} (nm)	$\Delta\lambda^{a}_{max}$	ε^{a}_{max} (mol^{-1} cm^{-1})	F^{ea}_{max} (nm)	F^{a}_{max} (nm)	ΔF^{a}_{max}	$\Delta\lambda_F$	SS^a (nm)
7	SCH_3	339	340	–	32 384	494	511	–	17	171
9a	 n = 1	362	362	22	24 872	434	449	−62	15	87
9b	 n = 2	360	360	20	25 064	437	448	−63	11	88
9c	 n = 3	364	364	24	26 792	435	438	−73	3	74
11a		374	376	36	24 504	471	499	−12	28	123
11b		340	341	1	32 392	459	482	−29	23	141
13a		354	354	14	20 816	432	444	−67	12	90
13b		356	357	17	28 096	431	443	−68	2	86
13c		356	357	17	30 224	426	445	−66	19	88
13d		356	354	14	14 768	430	443	−68	3	86
13e		357	356	16	22 440	412	438	−73	26	82
13f		356	357	17	13 408	439	457	−54	18	100

'a' given in superscript denotes values measured in acetone and 'ea' measured in ethyl acetate. $\Delta\lambda_{max}$, ΔF_{max}: substituent effects in λ_{max} and F_{max}, respectively. F_{max}: fluorescence maximum excited at λ_{max} value. $\Delta\lambda_F$: $F^{a}_{max} - F^{ea}_{max}$. SS^a: Stoke's shift, $F_{max} - \lambda_{max}$ in acetone solution.

Anal. Calcd. for $C_{19}H_{13}N_5OS_2$: C, 58.31; H, 3.32; N, 17.90. Found: C, 58.33; H, 3.23; N, 17.77%.

3.3. Synthesis of 6-(2-substituted-1,3,4-oxadiazol-5-yl)-4-methyl-5-(1-pyrrolyl)-2-phenylthieno[2,3-d]pyrimidine fluorescent compounds **7**, **9a–c**, **11a** and **b** and **13a–f**

3.3.1. 6-(2-Methylthio-1,3,4-oxadiazol-5-yl)-4-methyl-5-(1-pyrrolyl)-2-phenylthieno[2,3-d]pyrimidine (**7**)

A mixture of compound **6** (0.39 g, 1 mmol) in methanol (10 ml) and sodium methoxide (editors' note: highly flammable; reacts violently with water; incompatible with water, acids, chlorinated solvents) (0.08 g, 1.5 mmol), iodomethane (0.17 g, 1.2 mmol) was added. After stirring at room temperature for 24 h, the resulting solid product was collected by filtration, washed with water and recrystallized from THF to give 0.34 g of pale yellow crystals (84% yield), mp 215 °C; IR: ν 1625 (C═N) cm^{-1}; ^1H NMR (CF_3COOD): δ 2.53 (3H, s, CH_3), 2.93 (3H, s, SCH_3), 6.23 (2H, m, 3,4-H of pyrrolyl), 7.08 (2H, m, 2,5-H of pyrrolyl), 8.44, 7.76–7.73 (5H, m, phenyl-H); MS: 405 (M^+, 100), 358 (12), 331 (38), 315 (20), 304 (53), 289 (18), 261 (8), 244 (2), 198 (10), 151 (4), 103 (3), 75 (4).

Anal. Calcd. for $C_{20}H_{15}N_5OS_2$: C, 59.25; H, 3.70; N, 17.28. Found: C, 59.13; H, 3.55; N, 17.33%.

3.3.2. 6-(2-Substituted-1,3,4-oxadiazol-5-yl)-4-methyl-5-(1-pyrrolyl)-2-phenylthieno[2,3-d]pyrimidine fluorescent compounds (**9a–c**, **11a** and **b** and **13a–f**): general procedure

A mixture of compound **7** (0.405 g, 1 mmol) and excess secondary amines **8a–c**, **10a** and **b** and **12a–f** (pyrrolidine, piperidine, hexamethyleneimine, indoline, 1,2,3,4-tetrahydroquinoline, morpholine, *N*-methylpiperazine, *N*-ethylpiperazine, ethyl 1-piperazinecarboxylate, 1-phenylpiperazine, 1-(2-pyrimidyl)piperazine) (5 mmol) was refluxed for 10 h and poured into ice-water, and the precipitated product was collected by filtration, washed with water, and the crude product recrystallized from chloroform/THF. The physical constants and spectral data of compounds **9a–c**, **11a** and **b** and **13a–f** are recorded in Tables 1 and 2.

4. Conclusions

A series of novel 6-(2-substituted-1,3,4-oxadiazol-5-yl)-2-phenylthieno[2,3-*d*]pyrimidine (OXD-THPM) fluorescent derivatives were synthesized from 5-cyano-1,6-dihydro-4-methyl-2-phenyl-6-thioxopyrimidine. The solvatochromic behaviours and substituent effects in ethyl acetate and acetone solutions were evaluated. The results indicated that the neutral donor–acceptor OXD-THPM fluorescent compounds show a significant increase and are clearly bathochromic shifted when the solvent polarity is increased from ethyl acetate to acetone, i.e. a positive solvatochromism, which shows that the compound molecules are more polar in the excited state than in the ground state. Moreover, with the introduction of electron donating substituents into the OXD moiety λ_{max} shifts bathochromically in all solvents used. On the other hand, the fluorescence maxima F_{max} of the OXD-THPM compounds were strongly dependent on solvents and show generally bathochromic shifts as the polarity of solvents was increased. Nevertheless, with the introduction of electron donating substituents into the OXD moiety F_{max} shifts hypsochromically in all solvents used. Also, the novel OXD-THPM compounds displayed intense blue to yellow-green fluorescence in all solvents used and they can be used as fluorescent dyes and fluorescent brightening agent, and for application to synthetic fibers. Investigations on their properties like photostability and quantum yields and relative photonic efficiencies of substituted OXD-THPM fluorescent dyes will be the subject in our next study.

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