# An Efficient One-Pot Synthesis of Some New 2,4-Diaryl Pyrido[3,2-c]coumarins as Potent Antimicrobial Agents



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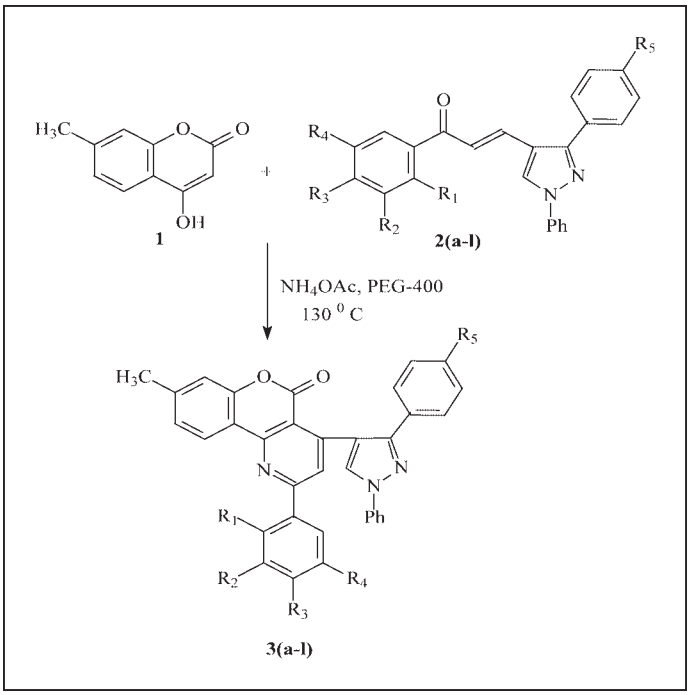


Poly(ethylene glycol) (PEG-400) has been used as sustainable, nonvolatile, and environmental friendly reaction solvent for the synthesis of title compounds. Various diaryl pyrido[3,2-c]coumarins have been synthesized in one step by reacting 4-hydroxy-7-methyl-coumarin with α,β-unsaturated ketones in the presence of ammonium acetate. Further, *in vitro* antimicrobial (antibacterial and antifungal) activities of the compounds were screened against different pathogens. The results revealed that most of them showed potent activity.

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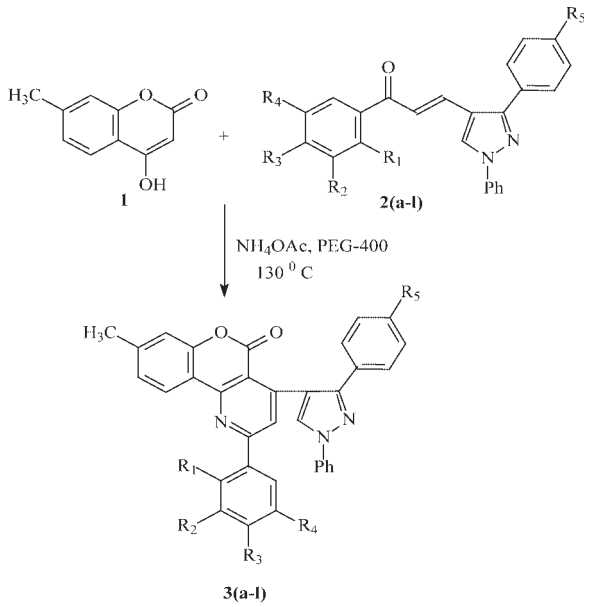
## INTRODUCTION

Coumarins are well-known natural products and may exhibit high level of biological activity [1]. Coumarins are also used as food additives, in cosmetics [2], as optical brightening agents [3], dispersed fluorescent and laser dyes [4]. For instance, coumarin nucleus is present in promising drug candidates as nonpeptidic HIV protease inhibitors [5], topoisomerase II [6], and tyrosine kinase [7] inhibitors. Coumarins fused with pyridines have also been reported to posses antiallergic [8], anticoagulant [9], antidiabetic [10], and analgesic [11] properties, being characterized by a phenanthrene like structure as found in tetrahydrocannabinol. Pyrido[3,2-c]coumarin, the back bone of naturally occurring alkaloid, santiagonamine [12] isolated from Berberis Dawinii (Barberidaca). This alkaloid has interesting wound healing properties [13]. Owing to such interesting properties, synthesis of pyrido-coumarins has remained an active subject of interest. However, a survey of these literatures quotes reveals that the most of the methods are multistep or difficult starting materials. Hence, it

**Scheme 1**




was thought worthwhile to envisage a synthesis of pyrido-fused coumarins.

## RESULTS AND DISCUSSION

In view of the current emphasis on green chemistry [14], our approach is to reduce the use of solvents that are volatile organic compounds (VOCs), which are potentially toxic and hazardous [15]. Recently, liquid polymers or low-melting polymers have emerged as alternative green reaction media with unique properties such as thermal stability, commercial availability, nonvolatility, immiscibility with a number of organic solvents, and recyclability. Poly(ethylene glycols) (PEGs) are preferred over other polymers because they are inexpensive, completely nonhalogenated, easily degradable, and of low toxicity [16]. Many organic reactions have been carried out using PEGs as solvent or cosolvent such as Heck reaction [17], asymmetric dihydroxylation [18], Suzuki crosscoupling reaction [19], oxydehydrogenation of alcohols and cyclic dienes, oxidation of sulfides and the Wacker reaction [20], and partial reduction reaction of alkynes [21]. The use of PEG as a recyclable solvent system for the metal mediated radical polymerization of methyl methacrylate and styrene has also been reported [22].

As quoted by Kroehnke [23], reaction of α,β-unsaturated ketones with the active methylene function of phenacyl bromide pyridinium salt of ammonium acetate and acetic acid yields pyridine. This methodology has been successfully utilized by us for the synthesis of variety of pyridyl substituted coumarins. In this article, here, we wish to report the expeditious synthesis of novel pyrido-fused coumarin derivatives (**3a–l**) under benign reaction solvent.

The starting 4-hydroxy-7-methyl-coumarin (**1**) was prepared by the literature procedure using an appropriately *m*-cresol and malonic acid, a Lewis acid ($ZnCl_2$) and as condensing agent phosphorous oxychloride ($POCl_3$), whereas the α,β-unsaturated carbonyl compounds (**2a–l**) were already reported [24]. Thus, various 2,4-diaryl pyrido[3,2-c]coumarins **3**(**a–l**) have been synthesized by reacting 4-hydroxy-7-methyl-coumarin **1** with α,β-unsaturated ketones **2**(**a–l**) in the presence of ammonium acetate in PEG-400 (Scheme 1).

**Mechanism of pyrido-coumarin formation.** The formation of products **3**(**a–l**) involves the Kroehnke's mechanism. Mannich bases provide the required α,β-unsaturated ketones *in situ* during the course of reaction, to which the Micheal addition of coumarioyl methyl pyridinium salts takes place resulting in a 1,5-dionyl pyridinium (not isolated) derivative, which subsequently cyclization in the presence of ammonium acetate afford the 2,4-diaryl pyrido[3,2-c]coumarins (Scheme 2). The

**Scheme 2**

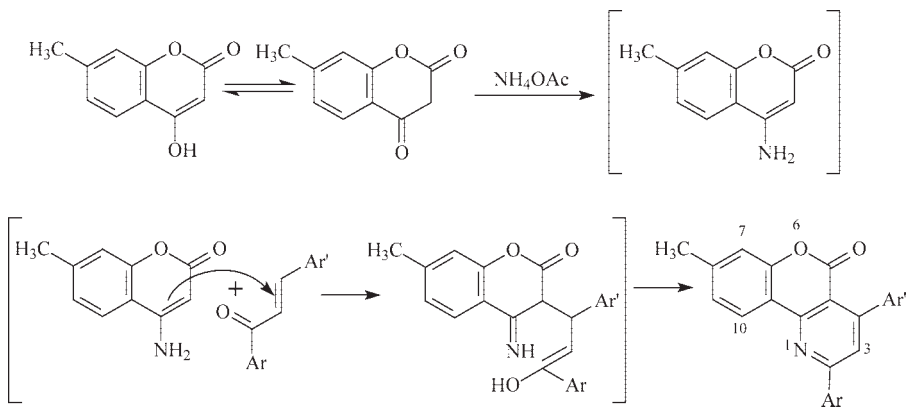


**Table 1**

Physical and analytical data of 2,4-diaryl-pyrido[3,2-c]coumarins.

| Product | $R_1$ | $R_2$ | $R_3$ | $R_4$ | $R_5$ | Time[a] | Yield (%)[b] | MP (°C) |
|---|---|---|---|---|---|---|---|---|
| **3a** | H | H | Cl | H | Cl | 2 | 85 | 240 |
| **3b** | OH | H | H | Cl | Cl | 3 | 89 | 266 |
| **3c** | OH | Br | H | Cl | Cl | 2 | 83 | 258 |
| **3d** | OH | I | H | Cl | Cl | 2 | 85 | 230 |
| **3e** | OH | H | OH | H | Cl | 3 | 82 | 172 |
| **3f** | OH | H | Me | Cl | Cl | 3 | 86 | 260 |
| **3g** | OH | Cl | OH | Cl | Cl | 2 | 81 | 243 |
| **3h** | OH | I | Me | Cl | Cl | 3 | 85 | 251 |
| **3i** | OH | H | H | Cl | OH | 2 | 86 | 265 |
| **3j** | OH | Br | H | Cl | OH | 2 | 85 | 170 |
| **3k** | OH | I | H | Cl | OH | 3 | 81 | 255 |
| **3l** | OH | I | H | Me | OH | 3 | 85 | 225 |

[a] Time in hours.
[b] Pure isolated yields of products.

presence of IR absorption bands in the region 1660–1690 $cm^{-1}$ clearly indicates that >C=O group of chalcone has been transformed into coumarin (lactone). $^1H$ NMR revealed that singlet of methyl proton at δ 2.30–2.50 ppm. The multiplet at δ 7.00–8.20 is due to aromatic protons. A singlet of phenolic proton appeared at δ 11.00–12.50 ppm ($D_2O$ exchangeable).

In summary, we have demonstrated an efficient, one-pot method toward the expeditious synthesis of 2,4-diaryl pyrido[3,2-c]coumarins using PEG-400 as an alternative reaction solvent. The advantages of the present protocol are the simplicity of operation, the high yields of products, the recyclability of PEG-400 and preclusion of the usage of volatile organic solvents. Antimicrobial and antifungal activities of the all synthesized compounds were summarized in Table 2. The compounds **3b**, **3d**, **3e**, **3f, 3h**, **3j**, and **3l** showed good antibacterial activity against one or more bacteria. Compounds **3a**, **3c**, **3d**, **3i**, and **3k** were found to be active against *Escherichia coli*. On the other hand, the compounds **3i**, **3k** was found to be active against *Salmonella typhi*. The compounds **3i**, **3j**, and **3k** were also found to be active against *Bacillus subtilis*. Most of the compounds showed inhibitory effect against fungi. The compounds **3a**, **3c**, **3d**, **3g**, **3j**, and **3l** showed most potent activity against all pathogens than other tested compounds. The substitution of hydroxyl group in position 2 and presence of halo groups in 3 and 5 positions of aryl nucleus, which may enhance the antimicrobial activity of the products against various pathogens.

## EXPERIMENTAL

Melting points were determined by open capillary method and were uncorrected. IR spectra were recorded (in KBr pallets) on Shimadzu spectrophotometer. $^1H$ NMR spectra were recorded (in DMSO-$d_6$) on Avance-300 MHz spectrometer using TMS as an internal standard. The mass were recorded on EI-Shimazdu-GC-MS spectrometer. Elemental analyses were performed on a Carlo Erba 106 Perkin-Elmer model 240 analyzer.

### Chemistry

***General procedure for the synthesis of α,β-unsaturated carbonyl compounds (2a–l)[24].*** A mixture of substituted 2-hydroxy acetophenone (5 mmol), 1-phenyl-3-(4-sustituted phenyl) pyrazol-4-carboxaldehyde (5 mmol), KOH (1 mmol), and PEG-400 (20 mL) was stirred at 40°C for 1 h. After completion of the reaction (monitored by TLC), the crude mixture was worked up in ice cold water (100 mL). Separated product was filtered out. The PEG-400 was recovered from water and utilized to synthesize further chalcones.

***Typical procedure for the synthesis of 2,4-diaryl pyrido[3,2-c]coumarins (3a–l).*** To a well-stirred solution of 4-hydroxy-7-methyl-coumarin **1** (0.528 g; 6 mmol) in PEG-400 (20 mL) was added ammonium acetate (6.0 g) followed by chalcone **2a** (2.514 g; 6 mmol) in PEG-400 (10 mL). The reaction mixture was stirred at room temperature for 30 min and then refluxed gently on oil-bath at 130°C for the period as shown in Table 1. After completion of the reaction (checked by TLC), the reaction mixture was allowed to reach room temperature and was poured into ice cold water (100 mL). The resultant solid was filtered, washed with 2 × 5 mL ice cold water and recrystallized by chloroform to give pure product **3a**.

To check the reusability of the solvent, the filtrate was evaporated to remove water leaving PEG behind in the container and subjected for second run by charging the same substrates. The results of the first and second experiments were almost consistent in yield.

***3-(4-Chloro-phenyl)-1-[3-(4-chloro-phenyl)-1-phenyl-1H-pyrazol-4-yl]-7-methyl-9-oxa-4-aza-phenanthren-10-one (3a).*** IR (KBr $cm^{-1}/\upsilon_{max}$): 1668, 1598 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$): δ 2.35 (s, 3H, $CH_3$), 7.10–8.15 (m, 17H, Ar—H), 8.90 (s, 1H, -5H of pyrazole) ppm; MS (m/z): 574 [$M^+$], 576 [M + 2], 578 [M + 4]; *Anal.* Found for $C_{34}H_{21}O_2N_3Cl_2$: C, 71.02; H, 3.61; N, 7.34 requires: C, 71.19; H, 3.78; N, 7.21%.

***3-(5-Chloro-2-hydroxy-phenyl)-1-[3-(4-chloro-phenyl)-1-phenyl-1H-pyrazol-4-yl]-7-methyl-9-oxa-4-aza-phenanthren-10-one (3b).*** IR (KBr $cm^{-1}/\upsilon_{max}$): 3413, 1671, 1605 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$): δ 2.33 (s, 3H, $CH_3$), 7.16–8.24 (m, 16H, Ar—H),

**Table 2**

Antimicrobial activities of synthesized products (**3a–l**).

| | Bacteria[a] | | | | Fungi germination | | | |
|---|---|---|---|---|---|---|---|---|
| Product | *Ec* | *St* | *Sa* | *Bs* | *An* | *Af* | *Pc* | *Fm* |
| **3a** | 21 | 19 | 16 | 19 | RD | RD | −ve | −ve |
| **3b** | 12 | 10 | 08 | 10 | −ve | −ve | RD | RD |
| **3c** | 19 | 22 | 21 | 20 | −ve | −ve | −ve | −ve |
| **3d** | 18 | 14 | 16 | 08 | RD | RD | +ve | +ve |
| **3e** | 19 | 12 | 10 | 14 | RD | −ve | RD | RD |
| **3f** | 08 | 10 | 07 | 14 | +ve | +ve | +ve | +ve |
| **3g** | 22 | 20 | 18 | 22 | −ve | −ve | RD | −ve |
| **3h** | 09 | 12 | 15 | 12 | +ve | +ve | +ve | +ve |
| **3i** | 21 | 20 | 19 | 18 | −ve | −ve | −ve | −ve |
| **3j** | 19 | 12 | 18 | 16 | RD | RD | −ve | RD |
| **3k** | 20 | 16 | 19 | 22 | −ve | −ve | −ve | −ve |
| **3l** | 18 | 12 | 15 | 18 | RD | −ve | −ve | RD |
| Control | – | – | – | – | +ve | +ve | +ve | +ve |
| *Penicillin* | 22 | 22 | 24 | 24 | NA | NA | NA | NA |
| *Nystatin* | NA | NA | NA | NA | −ve | −ve | −ve | −ve |

*Ec*, Escherichia coli; *St*, Salminella typhi; *Sa*, Staphylococcus aureus; *Bs*, Bacillus subtilis; *An*, Aspergillus niger; *Af*, Aspergillus flavus; *Fm*, Fusarium moniliforme, *Pc*, Penicillium chrysogenum. +ve, Growth; −ve, No growth; RD, reduced growth, NA, not applicable.
[a] Zone of inhibition in millimeters.

8.89 (s, 1H, -5H of pyrazole), 11.26 (s, 1H, —OH, $D_2O$ exchangeable) ppm; MS (m/z): 590 [$M^+$], 592 [M + 2], 594 [M + 4]; *Anal*. Found for $C_{34}H_{21}O_3N_3Cl_2$: C, 69.16; H, 3.51; N, 7.08 requires: C, 69.21; H, 3.68; N, 7.22%.

***3-(3-Bromo-5-chloro-2-hydroxy-phenyl)-1-[3-(4-chloro-phenyl)-1-phenyl-1H-pyrazol-4-yl]-7-methyl-9-oxa-4-aza-phenanthren-10-one (3c).*** IR (KBr $cm^{-1}/\upsilon_{max}$): 3433, 1679, 1606 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$): δ 2.38 (s, 3H, $CH_3$), 7.18–8.25 (m, 15H, Ar—H), 8.90 (s, 1H, -5H of pyrazole), 11.64 (s, 1H, —OH, $D_2O$ exchangeable) ppm; MS (m/z): 669 [$M^+$], 671 [M + 2], 673 [M + 4], 675 [M + 6]; *Anal*. Found for $C_{34}H_{20}O_3N_3Cl_2Br$: C, 61.06; H, 3.05; N, 6.21 requires: C, 60.88; H, 3.19; N, 6.34%.

***3-(5-Chloro-2-hydroxy-3-iodo-phenyl)-1-[3-(4-chloro-phenyl)-1-phenyl-1H-pyrazol-4-yl]-7-methyl-9-oxa-4-aza-phenanthren-10-one (3d)*** IR (KBr $cm^{-1}/\upsilon_{max}$): 3421, 1681, 1604 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$): δ 2.43 (s, 3H, $CH_3$), 7.15–8.25 (m, 15H, Ar—H), 8.91 (s, 1H, -5H of pyrazole), 11.68 (s, 1H, —OH, $D_2O$ exchangeable) ppm; MS (m/z): 716 [$M^+$], 718 [M + 2], 720 [M + 4]; *Anal*. Found for $C_{34}H_{20}O_3N_3Cl_2I$: C, 57.04; H, 2.81; N, 5.85 requires: C, 57.18; H, 2.72; N, 5.97%.

***3-(2,4-Dihydroxy-phenyl)-1-[3-(4-chloro-phenyl)-1-phenyl-1H-pyrazol-4-yl]-7-methyl-9-oxa-4-aza-phenanthren-10-one (3e).*** IR (KBr $cm^{-1}/\upsilon_{max}$): 3398, 3152, 1676, 1602 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$): δ 2.38 (s, 3H, $CH_3$), 5.68 (s, 1H, OH), 7.16–8.22 (m, 16H, Ar—H), 8.90 (s, 1H, -5H of pyrazole), 12.22 (s, 1H, —OH, $D_2O$ exchangeable) ppm; MS (m/z): 572 [$M^+$], 574 [M + 2]; *Anal*. Found for $C_{34}H_{22}O_4N_3Cl$: C, 71.36; H, 3.81; N, 7.31 requires: C, 71.49; H, 3.95; N, 7.38%.

***3-(5-Chloro-2-hydroxy-4-methyl-phenyl)-1-[3-(4-chloro-phenyl)-1-phenyl-1H-pyrazol-4-yl]-7-methyl-9-oxa-4-aza-phenanthren-10-one (3f).*** IR (KBr $cm^{-1}/\upsilon_{max}$): 3410, 1670, 1602 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$): δ 2.24 (s, 3H, $CH_3$), 2.48 (s, 3H, $CH_3$), 7.14–8.21 (m, 15H, Ar—H), 8.91 (s, 1H, -5H of pyrazole), 11.31 (s, 1H, —OH, $D_2O$ exchangeable) ppm; MS (m/z): 604 [$M^+$], 606 [M + 2], 608 [M + 4]; *Anal*. Found for $C_{35}H_{23}O_3N_3Cl_2$: C, 69.51; H, 3.86; N, 6.91 requires: C, 69.64; H, 3.97; N, 6.85%.

***3-(3,5-Dichloro-2,4-dihydroxy-phenyl)-1-[3-(4-chloro-phenyl)-1-phenyl-1H-pyrazol-4-yl]-7-methyl-9-oxa-4-aza-phenanthren-10-one (3g).*** IR (KBr $cm^{-1}/\upsilon_{max}$): 3412, 3168, 1681, 1606 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$): δ 2.38 (s, 3H, $CH_3$), 6.26 (s, 1H, OH), 7.15–8.25 (m, 14H, Ar—H), 8.90 (s, 1H, -5H of pyrazole), 12.28 (s, 1H, —OH, $D_2O$ exchangeable) ppm; MS (m/z): 641 [$M^+$], 643 [M + 2], 645 [M + 4], 647 [M + 6]; *Anal*. Found for $C_{34}H_{20}O_4N_3Cl_3$: C, 63.76; H, 3.11; N, 6.58 requires: C, 63.62; H, 3.25; N, 6.65%.

***3-(5-Chloro-2-hydroxy-3-iodo-4-methyl-phenyl)-1-[3-(4-chloro-phenyl)-1-phenyl-1H-pyrazol-4-yl]-7-methyl-9-oxa-4-aza-phenanthren-10-one (3h).*** IR (KBr $cm^{-1}/\upsilon_{max}$): 3433, 1682, 1605 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$): δ 2.26 (s, 3H, $CH_3$), 2.52 (s, 3H, $CH_3$), 7.18–8.26 (m, 14H, Ar—H), 8.90 (s, 1H, -5H of pyrazole), 12.06 (s, 1H, —OH, $D_2O$ exchangeable) ppm; MS (m/z): 730 [$M^+$], 732 [M + 2], 734 [M + 4]; *Anal*. Found for $C_{35}H_{22}O_3N_3Cl_2I$: C, 57.61; H, 3.01; N, 5.78 requires: C, 57.56; H, 3.04; N, 5.75%.

***3-(5-Chloro-2-hydroxy-phenyl)-1-[3-(4-hydroxy-phenyl)-1-phenyl-1H-pyrazol-4-yl]-7-methyl-9-oxa-4-aza-phenanthren-10-one (3i).*** IR (KBr $cm^{-1}/\upsilon_{max}$): 3398, 3169, 1666, 1599 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$): δ 2.38 (s, 3H, $CH_3$), 7.14–8.18 (m, 16H, Ar—H), 8.86 (s, 1H, -5H of pyrazole), 10.48 (s, 1H, OH), 11.78 (s, 1H, —OH, $D_2O$ exchangeable) ppm; MS (m/z): 572 [$M^+$], 574 [M + 2]; *Anal*. Found for $C_{34}H_{22}O_4N_3Cl$: C, 71.36; H, 3.91; N, 7.31 requires: C, 71.51; H, 3.78; N, 7.39%.

***3-(3-Bromo-5-chloro-2-hydroxy-phenyl)-1-[3-(4-hydroxy-phenyl)-1-phenyl-1H-pyrazol-4-yl]-7-methyl-9-oxa-4-aza-phenanthren-10-one (3j).*** IR (KBr $cm^{-1}/\upsilon_{max}$): 3405, 3188, 1672, 1602 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$): δ 2.36 (s, 3H, $CH_3$), 7.16–8.22 (m, 15H, Ar—H), 8.71 (s, 1H, -5H of pyrazole), 10.61 (s, 1H, OH), 12.23 (s, 1H, —OH, $D_2O$ exchangeable) ppm; MS (m/z): 650 [$M^+$], 652 [M + 2], 654 [M + 4]; *Anal*. Found for $C_{34}H_{21}O_4N_3ClBr$: C, 62.72; H, 3.21; N, 6.51 requires: C, 62.84; H, 3.35; N, 6.46%.

***3-(5-Chloro-2-hydroxy-3-iodo-phenyl)-1-[3-(4-hydroxy-phenyl)-1-phenyl-1H-pyrazol-4-yl]-7-methyl-9-oxa-4-aza-phenanthren-10-one (3k).*** IR (KBr $cm^{-1}/\upsilon_{max}$): 3416, 3196, 1675, 1608 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$): δ 2.38 (s, 3H, $CH_3$), 7.15–8.26 (m, 15H, Ar—H), 8.84 (s, 1H, -5H of pyrazole), 10.68 (s, 1H, OH), 12.32 (s, 1H, —OH, $D_2O$ exchangeable) ppm; MS (m/z): 698 [$M^+$], 700 [M + 2]; *Anal*. Found for $C_{34}H_{21}O_4N_3ClI$: C, 58.54; H, 3.05; N, 6.01 requires: C, 58.62; H, 3.23; N, 6.14%.

***3-(2-Hydroxy-3-iodo-4-methyl-phenyl)-1-[3-(4-hydroxy-phenyl)-1-phenyl-1H-pyrazol-4-yl]-7-methyl-9-oxa-4-aza-phenanthren-10-one (3l).*** IR (KBr $cm^{-1}/\upsilon_{max}$): 3396, 3159, 1678, 1604 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$): δ 2.24 (s, 3H, $CH_3$), 2.42 (s, 3H, $CH_3$), 7.16–8.25 (m, 15H, Ar—H), 8.88 (s, 1H, -5H of pyrazole), 10.51 (s, 1H, OH), 12.36 (s, 1H, —OH, $D_2O$ exchangeable) ppm; MS (m/z): 677 [$M^+$]; *Anal*. Found for $C_{35}H_{24}O_4N_3I$: C, 62.01; H, 3.59; N, 6.18 requires: C, 62.18; H, 3.68; N, 6.11%.

**Biology.** All the synthesized compounds **3(a-l)** were screened for their *in vitro* antimicrobial activity by agar well diffusion method [25]. Antibacterial activity was checked against bacteria *Escherichia coli*, *Salmonella typhi*, *Staphylococcus aureus*, and *Bacillus subtilis*. The culture strains of bacteria maintained on nutrient agar slant at 37 ± 2°C temperature for 24–48 h. Antifungal activity was studied against *Aspergillus niger*, *Aspergillus flavus*, *Penicillium chrysogenum*, and *Fusarium moniliforme*. The results were compared with *Penicillin* and *Nystatin*, respectively. All the culture strains of fungi maintained on potato dextrose agar (PDA) slant at 27 ± 2°C temperature for 24–28 h, till sporulation. Spore of strains were transferred in 5 mL of sterile water containing 1% Tween-80 (to suspend the spore properly). The spores were counted by Hemocytometer ($10^6$ CFU/mL). Sterile plate PDA was prepared containing 2% agar 0.1 mL of each fungal spore suspension was spread on each plate and incubated at 27 ± 2°C temperature for 12 h. After incubation well prepared using sterile cork borer and each agar well was filled with 0.1 mL pyrido coumarin solution of concentration 50, 100, and 250 μg/mL for screening minimum inhibitory concentration (MIC). Dimethyl sulfoxide (DMSO) was used as control without compound.

The plates were kept in refrigerator for 20 min for diffusion and then incubated at 27 ± 2°C temperature for 24–28 h in incubator. After incubation, zone of inhibition of compounds was measured in millimeters, along with control and standard. MIC value of pyrido coumarins was obtained 100 μg/mL for both antibacterial and antifungal activity. Results of the study are shown in Table 2.

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## REFERENCES AND NOTES

[1] Murray, R. D. H.; Mendey, J.; Brown, S. A. The Natural Coumarins; Wiley: New York, 1982, p 147.

[2] Kennedy, R. O.; Tharnes, R. D. Coumarins: Biology, Application and Mode of Action; Wiley: Chichester, 1997, p 1.

[3] Zahradink, M. The Production and Application of Fluorescent Brightening Agents; Wiley: New York, 1992, p 284.

[4] Maeda, M. Laser Dyes; Academic Press: New York, 1984, p 19.

[5] Thaisrivongs, S.; Janakiraman, M. N.; Chong, K. T.; Tomich, P. K.; Dolack, L. A.; Turner, S. R.; Strohbach, J. W.; Lynn, J. C.; Horng, M. M.; Hinshaw, R. R.; Watenpugh, K. D. J Med Chem 1996, 39, 2400.

[6] Rappa, G.; Shyam, K.; Lorico, A.; Fodstad, O.; Sartorelli, A. C. Oncol Res 2000, 12, 113.

[7] Yang, E. D.; Zhao, Y. N.; Zhang, K.; Mack, P. Biochem Biophys Res Commun 1999, 260, 682.

[8] Ukawa, K.; Ishiguro, T.; Wada, Y.; Nohara, A. Heterocycles 1986, 24, 1931.

[9] Brauninger, H.; Plagemann, R.; Schalicke, H. D.; Peseke, K. Naturwiseenschaftliche Reihe 1986, 35, 34.

[10] Heber, D. Arch Pharm 1987, 320, 402.

[11] Heber, D.; Berghaus, T. J Heterocycl Chem 1994, 31, 1353.

[12] Valencia, E.; Patra, A.; Freyer, A. J.; Shamma, M.; Fajardo, V. Tetrahedron Lett 1984, 25, 31.

[13] Lewis, W. H.; Stonard, R. J.; Porras-Reyes, B.; Mustoe, T. A.; Thomas, A. U.S. Pat. 5,156,847 (1992).

[14] Tanaka, K.; Toda, F. Chem Res 2000, 100, 1025; references cited therein.

[15] Anstas, P. T.; Varner, J. C. Green Chemistry: Theory and Practice; Oxford University Press, 1998, p 160.

[16] Heldebrant, D.; Jessop, P. G. J Am Chem Soc 2003, 125, 5600.

[17] Chandrasekhar, S.; Narsihmulu, Ch.; Sultana, S. S.; Reddy, N. R. K. Org Lett 2002, 4, 4399.

[18] (a) Chandrasekhar, S.; Narsihmulu, Ch.; Sultana, S. S.; Reddy, N. R. K. Chem Commun 2003, 1716; (b) Jiang, R.; Kuang, Y.-Q.; Sun, X.-L.; Zhang, S. Y. Tetrahedron: Asymmetry 2004, 15, 743.

[19] Namboodiri, V. V.; Varma, R. S. Green Chem 2001, 3, 146.

[20] Haimov, A.; Neumann, R. Chem Commun 2002, 876.

[21] Chandrasekhar, S.; Narsihmulu, Ch.; Chandrashekar, G.; Shyamsunder, T. Tetrahedron Lett 2004, 45, 2421.

[22] Perrier, S.; Gemici, H.; Li, S. Chem Commun 2004, 604.

[23] Kroehnke, F. Synthesis 1976, 1, 1

[24] Dawane, B. S.; Bhosale, R. B.; Pekamwar, S. S. J Pharm Res 2007, 6, 119.

[25] Shrinivasan, D.; Sangeetha, N.; Suresh, T.; Lakshmanaperumalsamy, P. J. Ethnopharmacol 2001, 74, 217.