Synthesis and antimicrobial evaluation of some alkoxyphthalimide derivatives of naphthyridine

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Received 8 July 2008; accepted ( revised) 5 January 2009

5-(4-Substitutedphenyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8]naphthyridin-7H-one 1a-e have been converted to their N-substituted alkoxyphthalimide derivatives using two alternative pathways. In route one, 1a-e are treated with formalin (37%) to yield 5-(4-(substitutedphenyl)-10-(hydroxymethyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8]naphthyridin-6-7H-one 2a-e, which is further changed to corresponding chloro derivatives 3a-e by the treatment with thionyl chloride. Condensation of 3a-e with N-hydroxyphthalimide furnished the final compounds 2-{5-(4-substitutedphenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydrobenzo[b][1,8]naphthyridin-10-5H-yl}methoxy)phthalimide 4a-e. In another route, 1a-e is directly condensed with o-bromoalkoxyphthalimide to yield higher homologues of 4a-e i.e. 2-{5-(4-(substituted pheny)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydrobenzo[b][1,8]naphthyridin-10-5H-yl}ethoxy)phthalimide derivatives 5a-e. Structures of all the synthesized compounds have been established on the basis of elemental analysis and spectral studies. All the synthesized compounds have been screened for antibacterial and antifungal activities.

Keywords: Naphthyridine, o-bromoalkoxyphthalimide, multicomponent condensation, antimicrobial activity, N-hydroxyphthalimide

Naphthyridine derivatives have been reported to possess antibacterial1, antimicobacterial2, antitumoral3, anti-inflammatory4,5, antiplatelet6, gastric antisecretary7, antiallergic8, local anaesthetic9 and benzodiazepine receptor activities10. 1,8-Naphthyridine derivatives are also reportedly associated with positive ionotropic11, β-adrenergic blocking12 and antihypertensive13 activities. A series of naphthyridine carboxamide attached to triazole have been synthesized, found to possess anti-inflammatory activity14 and its analogues have been found to be very useful intermediate for the synthesis of molecular building blocks15,21. Antimalarial22, antihypertensive23, antimicrobial24 and HIV-I inhibitor25 activities are reported in the literature for 1,8-naphthyridine derivatives. 2-Fluronaphthyridine containing ketolides have been assayed26 for inhibition of protein synthesis. Effect on topoisomerase targeting activity and cytotoxicity has been studied27 by Singh et al. on nitro and amino substituted dibenzonaphthyridine-6-ones.

Alkoxyphthalimide derivatives are used as potent anticonvulsant28, diuretic29, fungicidal30 and trypanocidal31 agents. These have ability to inhibit growth of malarial parasite Plasmodium falciparum32. Earlier work on the synthesis of alkoxyphthalimide derivative of various heterocycles has been very useful to achieve enhanced biological activity33,34 of particular molecule. In the present investigation the derivatives of naphthyridines have been prepared and evaluated for their bioactivity.

Result and Discussion

The Synthetic route for obtaining the final products is presented in Scheme I. The cyclocondensation of 2-amino pyridine with dinedone and substituted aromatic aldehydes yielded 5-(4-substitutedphenyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8]naphthyridin-6-7H-one 1a-e. The structure of the compounds 1a-e was assigned on the basis of their spectral and analytical data. In addition, to the characteristic NH band in the region 3214 cm\(^{-1}\), the IR spectra of the compound 1a revealed C=O and C=N absorption band in the region of 1690 and 1634 cm\(^{-1}\) respectively. \(^1\)H NMR spectra of all compounds exhibited two characteristic singlet of NH and CH proton. Further 5-(4-substitutedphenyl)-10-(hydroxymethyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8]naphthyridin-6-7H-one 2a-e were obtained from tetrahydropyranyl derivative 1a-e and formalin via condensation reaction.
Disappearance of sharp absorption band NH and appearance of broad band at 3407 cm$^{-1}$ for OH group were obtained in IR spectra. The $^1$H NMR spectra of compound 2a revealed the absence of NH proton and the presence of two new singlets at $\delta$ 4.51 and 3.93 of CH$_2$ and OH group respectively. Hydroxynaphthyridine 2a-e were further converted into their chloride derivatives 5-(4-substitutedphenyl)-10-(chloromethyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8]naphthyridin-6-7H-one 3a-e by reaction with thionylchloride. Formation of the product was confirmed by the disappearance of characteristic OH signals in IR and $^1$H NMR spectra. Subsequently, the chlorine atom in N-CH$_2$-Cl was replaced by the phthalimidoxy group to give 2-[(5-(4-substitutedphenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydrobenzo-[b][1,8]naphthyridin-10-5H-ylmethoxy)phthalimide 4a-e. Stretching of CO-N-CO around 1725 cm$^{-1}$.
confirming the presence of imidoxy moiety in 4a, this was further supported by molecular ion peak in the mass spectrum.

In order to synthesize 2-{2-[5-(4-substitutedphenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydrobenzo[b][1,8]naphthyridin-10-5H-yl]ethoxy}phthalimide derivatives 5a-e, tetrahydronapthyridines 1a-e were treated with phthalimidoxyethyl bromide in the presence of DMF/TEA. Disappearance of sharp NH band in the IR spectrum and presence of two triplets at δ 4.45 and 3.52 for OCH3 and NCH3 respectively in 1H NMR spectrum confirmed the formation of final compound 5a. Physical and analytical data of synthesized compounds are summarized in Table I.

Antimicrobial Activity

Ten compounds have been tested for their biological activity against four bacteria and two fungi using 50 µg/mL concentration in DMF by cup and well method.35,36 The micro-organisms used as antibacterial are *Proteus mirabilis*, *Bacillus subtilis*, *Klebsiella pneumoniae*, *Escherichia coli* and *Candida albicans* as fungal strains. The activity is presented as zone of inhibition in mm and compared with activity of controls C1 and C2 (for antibacterial activity C1=ciprofloxacin, C2=roxithromycin and for antifungal activity C1= amphotericin and C2= flucanazole) to give activity index value.

From the data presented in Table II, it is clear that majority of the compounds show moderate to strong activity as compared to the standard drug. These compounds show better activity on *E. coli*, *B. subtilis* as antibacterial and on both the pathogenic fungal strains. Compound 4d, 5d and 5e show weak inhibition whereas 4b and 5b show strong activity in general. All the compounds except 5e show good activity against *C. albicans*. Antifungal activity against *A. fumigatus* is stronger then standard for all the compounds. Conclusively, these compounds show weak antibacterial but strong antifungal agents.

Experimental Section

Melting points of all synthesized compounds were determined in open capillaries and are uncorrected. IR spectra (KBr) were recorded on a Perkin-Elmer 1300 FT IR spectrometer and 1H NMR spectra were recorded on a Bruker WM-400 (400 MHz FT NMR) spectrometer using TMS as internal standard. Mass spectra were recorded on a JEOL SX 102/DA-6000 mass spectrometer. All compounds gave satisfactory micro analytical results. Homogeneity of the synthesized compounds was checked by TLC using silica gel-G plates, n-hexane-ethyl acetate as developing solvent and the spots were visualized using iodine vapor. N-Hydroxyphthalimide37, phthalimidoxy ethyl bromide38 were prepared by reported methods.

Synthesis of 5-(4-substitutedphenyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8]naphthyridin-6-7H-one, 1a

A solution of 2-aminopyridine (0.01 mole), dimedone (0.01 mole) and aromatic aldehydes (0.01 mole) in absolute ethanol (20 mL) was refluxed for 1 hr. The product was separated by cooling followed by filtration, washing with ethanol, drying and purified by recrystallization from absolute ethanol.

IR (KBr): 3214 (N-H str.), 3054 (C-H str., Ar-H), 2936 (C-H str., CH3), 1687 (C=O str.), 1645 (C=N str.).

5 - (4 - Florophenyl) - 8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8]naphthyridin-6-7H-one, 1b

IR (KBr): 3202 (N-H str.), 3062 (C-H str., Ar-H), 2958 (C-H str., CH3), 1684 (C=O str.), 1625 (C=N str.), 1172 cm−1 (C-F str.); 1H NMR (CDCl3): δ 9.52 (s, 1H, NH), 7.75-7.14 (m, 7H, ArH), 2.20 (s, 2H, =C-CH3), 1.03 (s, 6H, CH2CO).

5-(4-Methoxyphenyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8]naphthyridin-6-7H-one, 1c

IR (KBr): 3221 (N-H str.), 3059 (C-H str., Ar-H), 2949 (C-H str., CH3), 1687 (C=O str.), 1622 (C=N str.), 1092 cm−1 (C-O str.); 1H NMR (CDCl3): δ 9.49 (s, 1H, NH), 7.80-7.19 (m, 7H, ArH), 5.29 (d, 1H, CH, J = 6.4 Hz), 3.92 (s, 3H, OCH3), 2.53 (s, 2H, =C-CH3), 2.15 (s, 2H, CH2CO), 1.12 (s, 6H, CH3).

5-(4-Nitrophenyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8]naphthyridin-6-7H-one, 1d

IR (KBr): 3229 (N-H str.), 3050 (C-H str., Ar-H), 2951 (C-H str., CH3), 1679 (C=O str.), 1622 (C=N...
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<th>Mol. Wt.</th>
<th>Ar</th>
<th>Yield (%)</th>
<th>m.p. °C</th>
<th>Found (Calcd) %</th>
<th>N</th>
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<td>59</td>
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BHAMBI et al.: SYNTHESIS OF ALKOXYPTHALIMIDE DERIVATIVES OF NAPHTHYRIDINE

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IR (KBr): 3210 (N-H str.), 3060 (C-H str., Ar-H), 2948 (C-H str., CH₃), 1676 (C=O str.), 1621 cm⁻¹ (C=N str.);

1H NMR (CDCl₃): δ 9.59 (s, 1H, NH), 7.83-7.29 (m, 7H, ArH), 5.31 (d, 1H, CH, J = 6.6 Hz), 2.47 (s, 2H, =C-CH₂), 2.07 (s, 2H, CH₂-CO), 1.11 (s, 6H, CH₃).

5-(4-Phenyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8]naphthyridin-6-7H-one, 1e

IR (KBr): 3410 (b, O-H str.), 2952, 2819 (C-H str., Ar-H), 1682 (C=O str.), 1633 cm⁻¹ (C=N str.); 1H NMR (CDCl₃): δ 7.54-7.18 (m, 7H, ArH), 5.30 (s, 1H, CH), 4.51 (s, 2H, N-CH₂), 3.93 (s, 1H, -OH), 2.57 (s, 2H, =C-CH₂), 2.18 (s, 2H, CH₂-CO), 0.99 (s, 6H, CH₃).

Table II — Antimicrobial activity of the synthesized compounds 4a-e and 5a-e.

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<th>Compd. No.</th>
<th>Proteus mirabilis</th>
<th>Klebsiella pneumoniae</th>
<th>Escherichia coli</th>
<th>Bacillus subtilis</th>
<th>Candida albicans</th>
<th>Aspergillus fumigatus</th>
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Zone of inhibition (mm) (activity index) = Inhibition zone of compound/Inhibition zone of the standard drug.
For antibacterial activity: C₁ = ciprofloxacin, C₂ = roxithromycin
For antifungal activity: C₁ = amphotericin B, C₂ = flucanazole
NA = Nil activity

Synthesis of 5-(4-Chlorophenyl)-10-(hydroxymethyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8]-naphthyridin-6-7H-one, 1a

Compound 1a (0.01 mole) was suspended in ethanol (25 mL) then formalin (37%, 1 mL) and HCl in catalytic amount were added with vigorous stirring. The reaction-mixture was scratched, kept overnight and the separated solid was filtered, washed thoroughly with water, dried and purified by recrystallization from ethanol.

IR (KBr): 3410 (b, O-H str.), 2952, 2819 (C-H str., Ar-H), 1682 (C=O str.), 1633 cm⁻¹ (C=N str.); 1H NMR (CDCl₃): δ 7.54-7.18 (m, 7H, ArH), 5.30 (s, 1H, CH), 4.51 (s, 2H, N-CH₂), 3.93 (s, 1H, -OH), 2.57 (s, 2H, =C-CH₂), 2.18 (s, 2H, CH₂-CO), 0.99 (s, 6H, CH₃).

5-(4-Florophenyl)-10-(hydroxymethyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8]-naphthyridin-6-7H-one, 2b

IR (KBr): 3396 (b, O-H str.), 2959, 2824 (C-H str., Ar-H), 1679 (C=O str.), 1629 (C=N str.), 1168 cm⁻¹ (C-F str.);

1H NMR (CDCl₃): δ 7.54-7.18 (m, 7H, ArH), 5.30 (s, 1H, CH), 4.51 (s, 2H, N-CH₂), 3.93 (s, 1H, -OH), 2.57 (s, 2H, =C-CH₂), 2.18 (s, 2H, CH₂-CO), 0.99 (s, 6H, CH₃).

Compounds 2b-e were also prepared by similar method with minor change in reaction conditions. Spectral data of these compounds are given below:

5-(4-Methoxyphenyl)-10-(hydroxymethyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8]-naphthyridin-6-7H-one, 2c

IR (KBr): 3402 (b, O-H str.), 2950, 2811 (C-H str., Ar-H), 1677 (C=O str.), 1628 (C=N str.), 1092 cm⁻¹ (C-O str.);

1H NMR (CDCl₃): δ 7.54-7.18 (m, 7H, ArH), 5.30 (s, 1H, CH), 4.51 (s, 2H, N-CH₂), 3.93 (s, 1H, -OH), 3.42 (s, 3H, OCH₃), 2.49 (s, 2H, =C-CH₂), 2.16 (s, 2H, CH₂-CO), 1.02 (s, 6H, CH₃).
5-(4-Nitrophenyl)-10-(hydroxymethyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8] naphthyridin-6-7H-one, 2d

IR (KBr): 3416 (b, O-H str.), 2947, 2817 (C-H str., CH), 4.40 (s, 2H, N-CH3), 2.52 (s, 2H, =C-CH2), 2.12 (s, 2H, CH2-CO), 0.96 (s, 6H, CH3).

5-(4-Phenyl)-10-(hydroxymethyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8] naphthyridin-6-7H-one, 2e

IR (KBr): 3386 (b, O-H str.), 2957, 2831 (C-H str., CH), 4.49 (s, 2H, N-CH3), 2.08 (s, 2H, CH2-CO), 1.11 (s, 6H, CH3).

Synthesis of 5-(4-Chlorophenyl)-10-(chloromethyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8] naphthyridin-6-7H-one, 3a

A mixture of 2a (0.01 mole) and thionyl chloride (0.02 mole) was refluxed in benzene (30 mL) in presence of pyridine (1 mL) for 2-3 hr. Excess of solvent and thionyl chloride was removed under reduce pressure. On cooling, the solid obtained was crystallized from absolute alcohol to afford chloromethyl naphthyridine.

IR (KBr): 3069 (b, CH str, ArH.), 2933 (C-H str., CH3), 1688 (C=O str.), 1635 (C=N str.), 760 cm\(^{-1}\) (C-Cl str.); \(^1\)H NMR (CDCl3): \(\delta\): 7.67-7.24 (m, 8H, ArH), 5.22 (s, 1H, CH), 4.38 (s, 2H, N-CH3), 3.84 (s, 1H, -OH), 2.52 (s, 2H, =C-CH2), 2.12 (s, 2H, CH2-CO), 0.96 (s, 6H, CH3).

Similarly, other compounds 3b-e were also synthesized. Their characterization spectral data are given below:

5-(4-Fluorophenyl)-10-(chloromethyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8] naphthyridin-6-7H-one, 3b

IR (KBr): 3063 (b, CH str, ArH.), 2924 (C-H str., CH3), 1672 (C=O str.), 1626 (C=N str.), 1186 cm\(^{-1}\) (C-F str.) 880 cm\(^{-1}\) (Ar-H bend, 1,4-disubs.); \(^1\)H NMR (CDCl3): \(\delta\): 7.73-7.12 (m, 7H, ArH), 5.38 (s, 1H, CH), 4.69 (s, 2H, N-CH2), 2.57 (s, 2H, =C-CH2), 2.16 (s, 2H, CH2-CO), 1.09 (s, 6H, CH3).

5-(4-Methoxyphenyl)-10-(chloromethyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8] naphthyridin-6-7H-one, 3c

IR (KBr): 3088 (CH str, ArH.), 2938 (C-H str., CH3), 1679 (C=O str.), 1621 (C=N str.), 1072 cm\(^{-1}\) (C-O str.) 887 cm\(^{-1}\) (Ar-H bend, 1,4-disubs.); \(^1\)H NMR (CDCl3): \(\delta\): 7.67-7.19 (m, 7H, ArH), 5.28 (s, 1H, CH), 4.58 (s, 2H, N-CH2), 3.86 (s, 3H, OCH3), 2.24 (s, 2H, CH2-CO), 1.10 (s, 6H, CH3).

5-(4-Nitrophenyl)-10-(chloromethyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8] naphthyridin-6-7H-one, 3d

IR (KBr): 3073 (CH str, ArH.), 2929 (C-H str., CH3), 1680 (C=O str.), 1631 (C=N str.), 1560, 1348 cm\(^{-1}\) (NO2 asym. & sym. Str.), 887 cm\(^{-1}\) (Ar-H bend, 1,4-disubs.); \(^1\)H NMR (CDCl3): \(\delta\): 7.80-7.29 (m, 7H, ArH), 5.41 (s, 1H, CH), 4.60 (s, 2H, N-CH2), 2.50 (s, 2H, =C-CH2), 2.13 (s, 2H, CH2-CO), 1.02 (s, 6H, CH3).

5-(Phenyl)-10-(chloromethyl)-8,8-dimethyl-5,8,9,10-tetrahydrobenzo[b][1,8] naphthyridin-6-7H-one, 3e

IR (KBr): 3070 (CH str, ArH.), 2948 (C-H str., CH3), 1688 (C=O str.), 1614 cm\(^{-1}\) (C=N str.); \(^1\)H NMR (CDCl3): \(\delta\): 7.84-7.31 (m, 7H, ArH), 5.21 (s, 1H, CH), 4.52 (s, 2H, N-CH2), 2.59 (s, 2H, =C-CH2), 2.17 (s, 2H, CH2-CO), 0.96 (s, 6H, CH3).

2-[[5-(4-Chlorophenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydrobenzo[b][1,8]naphthyridin-10-5H-yl]methoxy]phthalimide, 4a

N-Hydroxyphtalimide (0.01 mole) was added to a well stirred solution of chloromethyl naphthyridine 3a (0.01mole) in ethanol (30 mL) containing pyridine (0.01 mole) as a base. The reaction-mixture was refluxed for 6-7 hr., filtered and the filtrate was poured into crushed ice. The precipitated solid was collected and recrystallized from absolute ethanol.

IR (KBr): 3001 (CH str, ArH.), 2954, 2839 (C-H str., CH3), 1725 (C=O str., CO-N-CO), 1690 (C=O str.), 1634 (C=N str.), 957 (N-O str.), 829 (Ar-H bend, 1,4-disubs.), 751 cm\(^{-1}\) (C-Cl str.); \(^1\)H NMR (CDCl3): \(\delta\): 7.87-7.16 (m, 11H, ArH), 5.47 (s, 1H, CH), 4.50 (s, 2H, N-CH2), 2.57 (s, 2H, =C-CH2), 2.10 (s, 2H, CH2-CO), 1.10 (s, 6H, CH3); MS: \(m/z\): 515 [M]+, 513, 497, 493, 415, 356, 342, 162, 132, 111, 104, 76.
Compounds 4b-e were also prepared by similar method with minor change in reaction conditions. Spectral data of these compounds are given below:

**2-[[5-(4-Fluorophenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydrobenzo[b][1,8]naphthyridin-10-5H-yl]methoxy]phthalimide, 4b**

IR (KBr): 3006 (CH str, ArH.), 2950, 2831 (C-H str., CH3), 1722 (C=O str., CO-N-CO), 1683 (C=O str.), 1627 (C=N str.), 1666 (C-F str.), 950 (N-O str.), 822 cm\(^{-1}\) (Ar-H bend, 1,4-disubs.); \(^1^H\) NMR (CDCl\(_3\)): \(\delta\) 7.82-7.10 (m, 11H, ArH), 5.42 (s, 1H, CH), 4.51 (s, 2H, N-CH\(_2\)), 2.53 (s, 2H, =C-CH\(_2\)), 2.13 (s, 2H, CH\(_2\)-CO), 1.04 (s, 6H, CH\(_3\)); MS: \(m/z\) 497 [M\(^{+}\)], 481, 467, 399, 340, 326, 162, 132, 104, 76.

**2-[[5-(4-Methoxyphenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydrobenzo[b][1,8]naphthyridin-10-5H-yl]methoxy]phthalimide, 4c**

IR (KBr): 2996 (CH str, ArH.), 2942, 2836 (C-H str., CH\(_3\)), 1715 (C=O str., CO-N-CO), 1678 (C=O str.), 1631 (C=N str.), 941 (N-O str.), 816 cm\(^{-1}\) (Ar-H bend, 1,4-disubs.); \(^1^H\) NMR (CDCl\(_3\)): \(\delta\) 7.85-7.17 (m, 11H, ArH), 5.43 (s, 1H, CH), 4.47 (s, 2H, N-CH\(_2\)), 3.82 (s, 3H, OCH\(_3\)), 2.52 (s, 2H, =C-CH\(_2\)), 2.17 (s, 2H, CH\(_2\)-CO), 1.13 (s, 6H, CH\(_3\)); MS: \(m/z\) 509 [M\(^{+}\)], 493, 479, 411, 352, 338, 162, 132, 104, 76.

**2-[[5-(4-Nitrophenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydrobenzo[b][1,8]naphthyridin-10-5H-yl]methoxy]phthalimide, 4d**

IR (KBr): 3012 (CH str, ArH.), 2959, 2834 (C-H str., CH\(_3\)), 1720 (C=O str., CO-N-CO), 1680 (C=O str.), 1621 (C=N str.), 1550, 1338 (NO\(_2\) asymm. and symm. Str.), 947 (N-O str.), 817 cm\(^{-1}\) (Ar-H bend, 1,4-disubs.); \(^1^H\) NMR (CDCl\(_3\)): \(\delta\) 7.91-7.16 (m, 11H, ArH), 5.41 (s, 1H, CH), 4.48 (s, 2H, N-CH\(_2\)), 2.56 (s, 2H, =C-CH\(_2\)), 2.10 (s, 2H, CH\(_2\)-CO), 1.07 (s, 6H, CH\(_3\)); MS: \(m/z\) 524 [M\(^{+}\)], 508, 494, 426, 367, 353, 162, 132, 122, 104, 76.

**2-[[5-(Phenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydrobenzo[b][1,8]naphthyridin-10-5H-yl]methoxy]phthalimide, 4e**

IR (KBr): 3095 (CH str, ArH.), 2945, 2830 (C-H str., CH\(_3\)), 1728 (C=O str., CO-N-CO), 1688 (C=O str.), 1630 cm\(^{-1}\) (C=N str.); \(^1^H\) NMR (CDCl\(_3\)): \(\delta\) 7.72-7.16 (m, 11H, ArH), 5.41 (s, 1H, CH), 4.50 (s, 2H, N-CH\(_2\)), 2.49 (s, 2H, =C-CH\(_2\)), 2.09 (s, 2H, CH\(_2\)-CO), 0.98 (s, 6H, CH\(_3\)); MS: \(m/z\) 479 [M\(^{+}\)], 463, 449, 381, 322, 308, 162, 132, 104.

**Synthesis of 2-[2-[5-(4-Chlorophenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydrobenzo[b][1,8]naphthyridin-10-5H-yl]ethoxy]phthalimide, 5a**

To a stirred solution of 1a (0.01 mole) and triethylamine (0.01 mole) in DMF, pthalimidoxyethyl bromide (0.01 mole) was added portion wise. The reaction-mixture was refluxed for 12 hr. It was cooled and precipitate of triethylamine hydrobromide was filtered off. The filtrate was poured into crushed ice with constant stirring. The solid obtained was recrystallized from absolute ethanol.

IR (KBr): 3066 (CH str, ArH.), 2983, 2814 (C-H str., CH\(_3\)), 1722 (C=O str., CO-N-CO), 1692 (C=O str.), 1642 (C=N str.), 940 (N-O str.), 805 (Ar-H bend, 1,4-disubs.), 773 cm\(^{-1}\) (C-Cl str.); \(^1^H\) NMR (CDCl\(_3\)): \(\delta\) 8.45-7.26 (m, 11H, ArH), 5.40 (s, 1H, CH), 4.45 (t, 2H, O-CH\(_2\)), 3.52 (t, 2H, -NCH\(_3\)), 2.52 (s, 2H, =C-CH\(_2\)), 2.16 (s, 2H, CH\(_2\)-CO), 1.16 (s, 6H, CH\(_3\)); MS: \(m/z\) 527 [M\(^{+}\)], 527, 511, 497, 485, 429, 336, 190, 162, 132, 111, 104, 76.

Compounds 5b-e were prepared by the similar method with minor change in reaction conditions. Their spectral data are given below:

**2-[[5-(4-Fluorophenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydrobenzo[b][1,8]naphthyridin-10-5H-yl]ethoxy]phthalimide, 5b**

IR (KBr): 3060 (CH str, ArH.), 2978, 2811 (C-H str., CH\(_3\)), 1727 (C=O str., CO-N-CO), 1687 (C=O str.), 1636 (C=N str.), 946 (N-O str.), 802 (Ar-H bend, 1,4-disubs.), 1172 cm\(^{-1}\) (C-F str.); \(^1^H\) NMR (CDCl\(_3\)): \(\delta\) 8.51-7.22 (m, 11H, ArH), 5.43 (s, 1H, CH), 4.39 (t, 2H, O-CH\(_2\)), 3.50 (t, 2H, -NCH\(_2\)), 2.48 (s, 2H, =C-CH\(_2\)), 2.13 (s, 2H, CH\(_2\)-CO), 1.14 (s, 6H, CH\(_3\)); MS: \(m/z\) 511 [M\(^{+}\)], 495, 481, 469, 413, 320, 190, 162, 132, 104, 76.

**2-[[5-(4-Methoxyphenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydrobenzo[b][1,8]naphthyridin-10-5H-yl]ethoxy]phthalimide, 5c**

IR (KBr): 3056 (CH str, ArH.), 2986, 2807 (C-H str., CH\(_3\)), 1725 (C=O str., CO-N-CO), 1684 (C=O str.), 1639 (C=N str.), 1068 (C-O str.), 945 (N-O str.), 801 cm\(^{-1}\) (Ar-H bend, 1,4-disubs.); \(^1^H\) NMR (CDCl\(_3\)): \(\delta\) 8.41-7.14 (m, 11H, ArH), 5.45 (s, 1H, CH), 4.40 (t, 2H, O-CH\(_2\)), 3.38 (s, 3H, OCH\(_3\)), 3.48 (t, 2H, -NCH\(_2\)), 2.46 (s, 2H, =C-CH\(_2\)), 2.06 (s, 2H, CH\(_2\)-CO), 1.11 (s, 6H, CH\(_3\)).
6H, CH₃); MS: m/z 523 [M⁺], 507, 495, 481, 425, 332, 190, 162, 132, 104, 76.

2-[2-[[5-(4-Nitrophenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydrobenzo[b][1,8]naphthyridin-10-5H-yl]ethoxy]phthalimide, 5d

IR (KBr): 3059 (CH str, ArH.), 2981, 2804 (C-H str), 1631 (C=N str.), 1550, 1342 (NO₂-{2-[5-(4-Nitrophenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydrobenzo[b][1,8]naphthyridin-10-5H-yl]ethoxy}phthalimide, 5d

IR (KBr): 3059 (CH str, ArH.), 2981, 2804 (C-H str), 1631 (C=N str.), 1550, 1342 (NO₂-{2-[5-(4-Nitrophenyl)-8,8-dimethyl-6-oxo-6,7,8,9-tetrahydrobenzo[b][1,8]naphthyridin-10-5H-yl]ethoxy}phthalimide, 5e

IR (KBr): 3062 (C=O str, CO-N-CO), 1682 (C=O str., CO-N-CO), 1.04 (s, 6H, CH₃), 2.42 (s, 2H, =C-CH₂) -NCH₃); MS: m/z 493 [M⁺], 477, 463, 351, 395, 451, 395, 302, 190, 162, 132, 104.

Acknowledgements

Authors are thankful to the Head, Department of Chemistry, M.L. Sukhadia University, Udaipur for providing laboratory facilities and to the Director, RSIC, CDRI, Lucknow, India for providing spectral and analytical data. Authors are grateful to Antimicrobial Research Laboratory, particularly to Dr. Kanika Sharma, Department of Botany, M. L. Sukhadia University for evaluating antimicrobial activity. Three of the authors (D B, V K S and A B) are thankful to UGC and CSIR, New Delhi respectively for providing necessary financial assistance.

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