Synthesis and biological study of some new naphtho[2,1-*b*]furan and related heterocyclic systems

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In the reaction of 1-cyano-2-naphthol (**4**) or its sodium salt with different alkylating agent, the *O*-alkylated derivatives (**5a–d**) were produced which underwent ring closure reactions using sodium ethoxide solution to give aminonaphtho [2,1-*b*]furan derivatives (**6a–d**). Ethyl 3-aminonaphtho[2,1-*b*]furan-2-carboxylate (**8**) was reacted with formamide to afford naphtho[1',2':4,5]furo[3,2-*d*]pyrimidine (**11**) derivatives. The produced pyrimidino compound underwent various reactions to synthesise other heterocyclic compounds.

Keywords: synthesis, reactions, naphthofuran, naphthofuropyrimidine, naphthofurotriazolopyrimidine

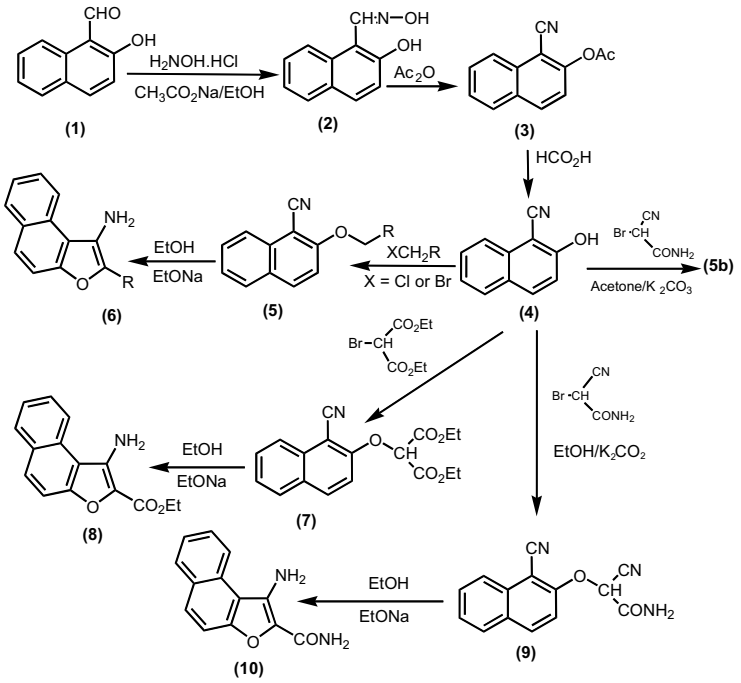
Benzofurans and naphthofurans have attracted widespread interest in view of their presence in natural products and their biological and pharmacological activities.[1–4]

Benzofurans have been the subject of the most extensive studies and numerous synthetic methods have been developed for them.[5-20] Compared to benzofurans, the reports on the synthesis of naphthofurans[21-24] are rather limited. Benzofuran derivatives have received considerable attention owing to their antifungal N-myristoyl transferase inhibitor activity[25] and their activity as potent non-steroidal reversible inhibitors of P-450 aromatase.[26] Benzofuran neolignans which are contained in most plants have attracted much attention in medical chemistry for their wide range of various bioligical activities, including insectcidal, fungicidal, antimicrobial and antioxidant properities.[27]

Results and discussion

2-Hydroxynaphthalene-1-carbaldehyde (**1**)[28,29] when allowed to react with hydroxylamine hydrochloride in the presence of fused sodium acetate yielded the corresponding oxime[30] (**2**) which was acetylated using acetic anhydride to give 2-acetyloxynaphthalene-1-carbonitrile (**3**).[30] Treatment of compound **3** with formic acid yielded 1-cyano-2-naphthol (**4**).[30]

Alkylation of naphthol **4** using different activated halogenated compounds, namely chloroacetonitrile, chloroacetone, phenacyl bromide and its derivatives in acetone and in the presence of potassium carbonate, *O*-alkylated products (**5a–d**) were produced, that under went ring closure by sodium ethoxide to afford the corresponding naphthofurans (**6a–d**). Attempts to apply the previous method in the case of using ethyl chloroacetate as an alkylating agent was failed. Ethyl 3-aminonaphtho[2,1-*b*]furan-2-carboxylate **8** was prepared with another route using diethyl bromomalonate as alkylating agent, which produced diethyl (1-cyanonaphthalene-2-yloxy)malonate (**7**), and which upon refluxing with sodium ethoxide was cyclised and spontaneously decarboxylated to give compound **8**. The structure of compound **7** was established using ^{13}C NMR ($CDCl_3$), whereas its spectrum revealed signals 82.15 for CH of diethyl malonate –CH– and at 167 two identical carbon of –C=O, at 63.1 for two identical carbon of $–CH_2–$ ester, and at 14.1 for two carbons of $–CH_3$ esters, and at 125–160 for 10 aromatic carbons.



5a,**6a**, R = CN; **5b**,**6b**, R = COMe; **5c**,**6c** = COph; **5d**,**6d**, R = $C_6H_4CH_3$-p; **5e**, R = Co_2Et

Scheme 1

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On the other hand, the structure of produced compound **8** was confirmed using ^{1}H NMR which revealed signals at 1.3–1.6 (t) and at 4.30–4.6 (q) for three and two protons corresponding (ethyl ester group) and at 5.25 (s) for two protons corresponding to NH_2, which disappeared when the sample treated with D_2O.

On other hand, when 1-hydroxynaphthalen-2-carbonitrile (**4**) refluxed with bromocyanoacetamide in acetone in the presence of K_2CO_3, instead of 3-aminonaphtho[2,1-*b*]furan-2-carboxamide **10**, compound **5b** was produced. To interpret this reaction we postulate that bromocyanoacetamide acted as a brominating agent to acetone to give bromoacetone which in turn acts as alkylating agent to give **5b.** The formation of **5b** through this reaction was confirmed using mass spectroscopy, which gave the molecular ion beak at 225 which corresponding to **5b** not for **9** or cyclised product **10**. Also the ^{1}H NMR and ^{13}C NMR of compound **5b** in $CDCl_3$ proton NMR gave signals at 2.5 (s, 3H, CH_3), 4.8 (s, 2H, CH_2) and its ^{13}C NMR revealed a signals at 77.1 for –CH_2– carbon, 25.9 for –CH_3 carbon, 202.1 for –C=O carbon, 118.2 for –CN carbon and at 96.2–139.3 10 signals for aromatic carbons**.** In addition to NMR and mass spectra its IR spectrum does not show any absorption band characteristic for NH_2 (Scheme 1).

Ethyl 3-aminonaphtho[2,1-*b*]furan-2-carboxylate **8** was reacted with formamide to afford naphtho[1',2' : 4,5]furo[3,2-*d*] pyrimidin-4(3*H*)-one (**11**). The later compound was obtained by an alternative route through the condensation of 3-aminonaphtho[2,1-*b*]furan-2-carboxamide (**10**) with triethyl orthoformate in the presence of catalytic amount of acetic acid. The pyrimidinone derivative (**11**) can be converted into 4-chloropyrimidine derivative (**12**) by refluxing with phosphorus oxychloride.

Naphtho[1',2' : 4,5]furo[3,2-*d*]pyrimidin-4(3*H*)-thione (**13**) was prepared by two methods, either by thionation of compound **11** using phosphorus pentasulfide in pyridine or by the reaction of chloropyrimidine derivative **12** with thiourea in ethanol. The produced naphthofuropyrimidinthione was *S*-alkylated using different halo compounds in ethanol in the presence of sodium acetate to afford *S*-alkylated derivatives **14**.

4-Hydrazinonaphtho[1',2': 4,5]furo[3,2-*d*]pyrimidine (**15)** was prepared by condensation of hydrazine hydrate with either chloropyrimidine derivative (**12**) or with pyrimidinthione derivative **13**.

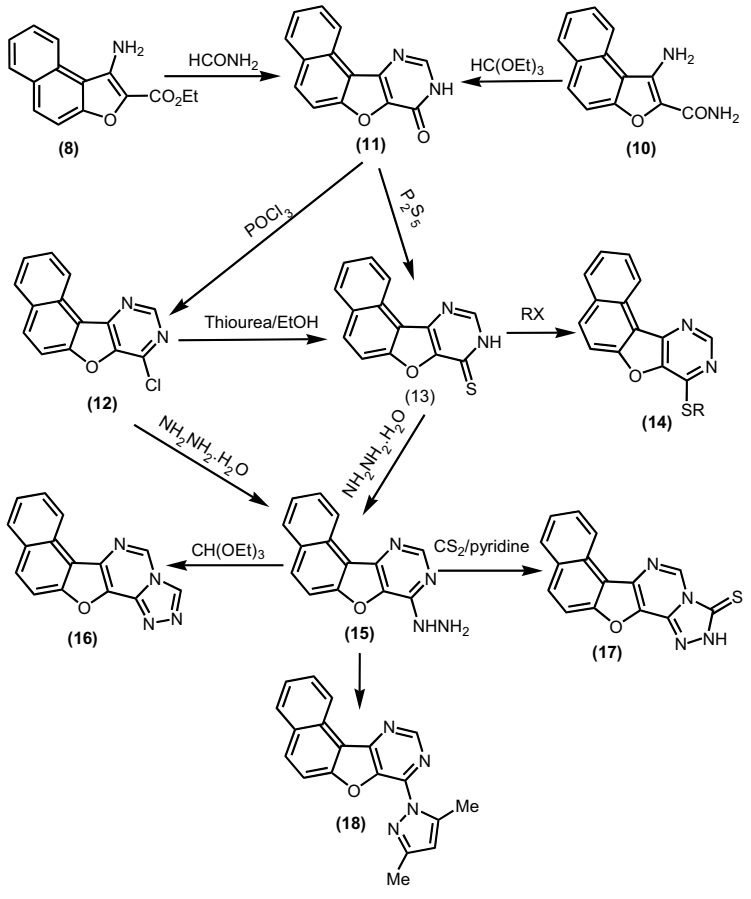
4-Hydrazinonaphthofuropyrimidine (**15**) was used as a versatile precursor to synthesise other heterocyclic compounds. It reacts with triethyl orthoformate in the presence of catalytic drops of acetic acid to afford naphthofurotriazolopyrimidine **16**. Another naphthofurotriazolopyrimidine **(17**) was prepared by refluxing compound **15** with carbon disulfide in pyridine.

On the other hand, when compound **15** was allowed to react with acetylacetone in ethanol, pyrazolylnapthofuropyrimidine **18** was produced (Scheme 2).

Biological activities

Some of the synthesised compounds in this work were chosen and screened *in vitro* for their antimicrobial activity against some strains of bacteria and fungi.

The antifungal activities of tested compounds were evaluated by the reported method[31] using 2% concentration of selected compounds in DMSO as a solvent. The inhibition zone (mm) compared with sertaconazole as a reference. In the case of antibacterial the concentration of tested compound is also 2% and the inhibition zone in mm were compared with chloramphenicol as a reference.



Scheme 2

Tested compounds show remarkable antibacterial activities while the activities towards fungi are not remarkable except in some cases like **6a** which reveals activity against *Aspergillus Niger* which approximately like activity of antifungal reference used.

Compound **5c** shows antibacterial activity against most strains tested. It gave inhibition zone four times that from the antibiotic chloramphenicol which was used as a reference sample in case of *Serratia marcescens*, while it gave three times the inhibition zone in cases using *Bacillus cereus* and *Micrococcus luteus* compared with the reference sample. When the compound was cyclised into a naphthofuran derivative **6c** the antibacterial activity of compound **5** was decreased.

In conclusion all the tested compounds revealed promising antibacterial activity which in some cases outdo known antibiotics.

Experimental

Melting points were uncorrected and determined using a Kofler melting point apparatus. IR spectra were recorded in a Pye Unicam SP 3-100 spectrometer using KBr Wafer technique. ^{1}H NMR spectra were recorded on a varian EM-390 90 MHZ spectrometer in a suitable deuterated solvent using TMS as internal standard. Mass spectra were recorded on a JO MS600 mass spectrometer. 1-Naphthalenle-2-carboxaldehyde (**1**),[28,29] 3-aminonaphthalenl-2-carboxaldehydeoxime (**2**),[30] 2-acetyloxynaphthalen-1-carbonitrile (**3**)[30] and 2-hydroxynapthalene-1-carbonitrile (**4**)[30] were prepared according literature procedures.

Alkylation of 2-hydroxynaphthalene-1-carbonitrile **(l)***: synthesis of 2-alkyloxy-1-naphthonitrile* **(5a–e)**

General procedure

A mixture of 2-hydroxynaphthalene-1-carbonitrile (**l**) (1.7 g, 0.01 mol), alkylating agent (0.01 mol) and anhydrous potassium carbonate (2.0 g) in acetone (20 ml) was refluxed for 3 h then allowed to cool and poured into cold water (100 ml). The solid precipitate was filtered off, washed with water and dried. The physical properties and spectral data of compounds **5a–e** were listed in Table 1 and 2.

Cyclisation of 2-alkoxynaphthalene-1-carbonitrile **(5a–d)***: synthesis of 3-amino-2-substituted naphtho[3,2-b]furan* **(6a–d)**

To a solution of the appropriate 2-alkyloxynaphthalene-1-carbonitrile (0.01 mol) in ethanol was added, a few drops of sodium ethoxide solution (prepared from 0.5 g of clean sodium in 20 ml ethanol). The mixture was refluxed for 15 min and left to cool. The solid product was filtered off, dried and recrystallised from ethanol to give compounds **6a–d**. The physical constants and spectral data of compounds **6a–d** are listed in Tables 1 and 2.

Diethyl (1-cyanonaphthalen-2-yloxy)malonate **(7)**: A mixture of 2-hydroxynaphthalene-1-carbonitrile (1.7 g, 0.01 mol), diethyl bromomalonate (2.39 g, 0.01 mol) and anhydrous potassium carbonate (2.0 g) in acetone (20 ml) was refluxed for 3 h, then allowed to cool, and poured into cold water. The produced solution was extracted with ethyl acetate, dried and evaporated under reduced pressure. The solid residue was recrystallised from ethanol in 42% yield, m.p. 78°C.

Anal.calcd. for $C_{18}H_{17}NO_5$ (327.34): C, 66.05; H, 5.23; N, 4.28%. Found: C, 65.82; H, 4.98; N, 4.46%. IR: ν 2220 (CN), 1730–1700 (2C=O). ^{1}H NMR($CDCl_3$): δ = 1.25–1.55 (t, 6H, $2CH_3$), 4.30–4.55 (q, 4H, $2CH_2$), 5.05 (s, 1H, CH), and at 7.5–8.2 (m, 6H, ArH),

Ethyl 3-aminonaphtho[2,1-b]furan-2-carboxylate **(8)**:

Method a: To a solution of the produced compound (**7**) in ethanol (20 ml), ethanolic solution of sodium ethoxide was added and the mixture was refluxed for 1 h then allowed to cool and poured into water (100 ml). The solid precipitate was filtered washed with water and recrystallised from ethanol in 67% yield, m.p. 94°C.

Method b: A mixture of sodium salt of 2-hydroxynaphthalene-1-carbonitrile (1.91 g, 0.01 mol) and diethyl bromomalonate (2.39 g, 0.01 mol) was refluxed in absolute ethanol (20 ml) for 4 hrs. After sodium bromide is formed, ethanolic solution of sodium ethoxide was added. The reflux was continued for additional 4 h., then pour into water. The solid product was recrystallised from ethanol as white needles in 77% yield, m.p. 94°C. Anal.calcd. for $C_{15}H_{13}NO_3$ (255): C, 70.58; H, 5.13; N, 5.49%. Found: C, 70.72; H, 4.93; N, 5.66%. IR: ν 3420, 3320 (NH_2),1655 (C=O). ^{1}H NMR($CDCl_3$): 1.3–1.6 (t, 3H,CH_3), 4.35–4.6 (q, 2H, CH_2), 5.25 (s, 2H, NH_2), 7.4–8.2 (m, 6H, ArH), MS *m/z* 255.03.

2-Cyano-2-(1-cyano(2-naphthyloxy)acetamide **(9)**: A mixture of 2-hydroxynaphthalene-1-carbonitrile (**4**) (0.5 g, 0.003 mol), bromocyanoacetamide (0.5 g, 0.003 mol) and anhydrous potassium carbonate (0.7 g, 0.005 mol) in 20 ml of ethanol was refluxed for 3 h,

Table 1 Physical constants of compounds **5a–d**, **6a–d** and **14a–d**

Compd	R	M.p./°C	Yield/%	Molecular formula (MW)	Analytical analysis Calcd/Found		
					C	H	N
5a	CN	136	93	$C_{13}H_8N_2O$	74.99	3.87	13.45
				(208.22)	75.18	4.09	13.21
5b	COMe	132	61	$C_{14}H_{11}NO_2$	74.65	4.92	6.22
	(ethanol)			(225.25)	74.82	5.11	6.43
5c	COPh	120	65	$C_{19}H_{13}NO_2$	79.43	4.56	4.87
	(ethanol)			(287.32)	79.66	4.71	5.03
5d	$COC_6H_4CH_3$-p	117	70	$C_{20}H_{15}NO_2$	79.72	5.02	4.65
	(ethanol)			(301.35)	79.56	4.88	4.78
5e	CH_2CO_2Et	85	38	$C_{15}H_{13}NO_3$	70.58	5.13	5.49
				(255)	70.72	4.92	5.67
6a	CN	210	50	$C_{13}H_8N_2O$	74.99	3.87	13.45
	(ethanol)			(208.22)	74.77	4.09	13.68
6b	COMe	184	80	$C_{14}H_{11}NO_2$	74.65	4.92	6.22
	(ethanol)			(225.25)	74.32	5.16	6.00
6c	COPh	160	85	$C_{19}H_{13}NO_2$	79.43	4.56	4.87
	(ethanol)			(287.32)	79.19	4.37	5.09
6d	$COC_6H_4CH_3$-p	185	87	$C_{20}H_{15}NO_2$	79.72	5.02	4.65
	(ethanol)			(301.35)	79.95	4.88	4.82
14a[a]	CH_2CO_2Et	136-38	80	$C_{18}H_{14}N_2O_3S$	63.89	4.17	8.28
				(338)	64.13	3.97	8.06
14b[b]	CH_2COCH_3	168-70	90	$C_{17}H_{12}N_2O_2S$	66.22	3.92	9.08
				(208)	65.98	4.14	9.00
14c[c]	Me	156-58	86	$C_{15}H_{10}N_2OS$	67.65	3.76	10.52
				(266)	67.90	4.00	10.70
14d[d]	CH_2COPh	198-200	76	$C_{22}H_{14}N_2O_2S$	71.35	3.78	7.57
				(370)	71.22	4.01	7.72

[a]Calc. S = 9.48; Found S = 9.72%. [b]Calc. S = 10.40; Found S = 10.63%.
[c]Calc S = 12.04; Found S = 11.88%. [d]Calc S = 8.65; found S = 8.89%.

Table 2 Spectral data of compounds **5a–d**, **6a–d** and **14a–d**

Compd	IR (ν) cm^{-1}	^1H NMR (δ)
5a	2220 (CN), 1280,1020 (C–O acyclic ether)	($CDCl_3$) 5.1(s, 2H,CH_2),7.3–8.25 (m, 6H, ArH)
5b	1715 (C=O), 2220 (CN), 1240, 1020 (C–O ether)	($CDCl_3$): 2.5 (s, 3H, CH_3), 4.8 (s, 2H, CH_2), 7–8 (m, 6H, ArH)
5c	2220 (CN),1685 (C=O), 1220,1100 (C–O ether)	($CDCl_3$): 5.5 (s, 2H, CH_2), 7.2–8.2 (m, 11H, ArH).
5d	3450, 3300(NH_2), 1620 (C=O), 1050 (C–O) furan	($CDCl_3$) δ 2.3 (s, 3H, CH_3), 5.5 (s, 2H, CH_2), 7.2–8.3 (m, 10H, ArH).
5e	2220(CN), 1735 (C=O ester), 1020. 1240 (C–O)ether	($CDCl_3$) 1.2–1.45 (t, 3H, CH_3), 4.2–4.4 (q, 2H, CH_2), 4.8 (s, 2H, CH_2), 7.2–8.2 (m, 6H, ArH)
6a	3495, 3350 (NH_2), 2220 (CN), 1050 (C–O furan)	($CDCl_3$) 5.5 (s, 2H, NH_2), 7.4–8.3 (m, 6H, ArH).
6b	3495, 3350 (NH_2), 1640 (C=O), 1050 (C–O)furan	($CDCl_3$) 2.4 (s, 3H, CH_3), 6.7 (s, 2H, NH_2), 7.4–8.4 (m, 6H, ArH); MS *m/z* 224
6c	3450, 3300 (NH_2), 1620 (C=O), 1050 (C–O) furan	($CDCl_3$) 6.4 (s, 2H, NH_2), 7.5–8.3 (m, 11H, ArH); MS *m/z* 286
6d	3450, 3300 (NH_2), 1620 (C=O), 1050 (C–O) furan	($CDCl_3$) 2.3 (s, 3H, CH_3),6.3 (s, 2H, NH_2) disappeared by D_2O, 7.2–8.3 (m, 10H, ArH)
14a	1710 (C=O),1650 (C=N),1020 (C–O)furan	($CDCl_3$) 2.2–2.4 (t, 3H, CH_3), 4.15–4.4 (q, 2H, CH_2), 7.5–8 (m, 6H,ArH), 8.9 (s, 1H, CH)
14b	1720 (C=O),1630 (C=N),1020 (C–O)furan	($CDCl_3$) 2.4 (s, 3H, CH_3), 4.2 (s, 2H, CH_2), 7.5–8.1(m, 6H, ArH), 8.9 (s, 1H, CH); MS *m/z* 306
14c	1630 (C=N),1020 (C–O)furan	($CDCl_3$): 2.8 (s, 3H, CH_3), 7.2–8 (m, 6H, ArH), 8.95 (s, 1H, CH pyrimidine)
14d	1685 (C=O),1630 (C=N),1020 (C–O)furan	(DMSO): 4.9 (s, 2H, CH_2), 7.5–8 (m, 11H, ArH), 8.8 (m, 1H, CH pyrimidine)

the cooled mixture was diluted with water. The solid product wad filtered off, dried and recrystallised from ethanol in 50% yield, m.p. 140°C. Anal.calcd. for $C_{14}H_9N_3O_2$ (251); C, 66.93; H, 3.59; N, 16.73%. Found: C, 67.17; H, 3.78; N, 16.52%. IR: ν 2220 (CN), 3350, 3180 (NH_2 of $CONH_2$),1680 (C=O amide),1020, 1240 (C–O) ether. ^1H NMR($CDCl_3$): δ = 4.5 (s, 2H, NH_2) disappeared by D_2O, 7.5–8.4 (m, 6H, ArH)

3-Aminonaphtho[2,1-b]furan-2-carboxamide **(10)**: To a solution of compound (**9**) in ethanol a few drops of sodium ethoxide solution was added. The mixture was refluxed for 15 minutes then allowed to cool and diluted with water. The solid product was collected and crystallised from ethanol to give pale buff crystals m.p. 217°C yield 73%. Anal. calcd. for $C_{13}H_{10}N_2O_2$ (225): C, 69.02; H, 4.46; N, 12.38%. Found: C, 68.78; H, 4.70; N, 12.15%. IR: ν 3480, 3350 (NH_2),1680 (C=O amide),1050 (C–O)furan. ^1H NMR (DMSO-d_6): δ = 5.9 (s, 2H, $CONH_2$) disappeared by D_2O, 6.8 (s, 2H, NH_2) disappeared by D_2O,7.6-8.6 (m, 6H, ArH)

Naphtho[2',1': 4,5]furo[3,2-d]pyrimidin-4(3H)-one **(11)**: A sample of compound **8** (2.55 g, 0.01 mol) in formamide (20 ml) was refluxed for 6 h, then allowed to cool The solid product was collected and recrystallised from dioxin as orange crystals in 91% yield. m.p. >300°C. Anal.calcd. for $C_{14}H_8N_2O_2$(236.23): C, 71.18; H, 3.41; N, 11.86%. Found: C, 70.99; H, 3.62; N, 11.73%. IR: ν 3420 (NH),1675 (C=O),1650 (C=N) and 1050 (C–O) furan. ^1H NMR (DMSO-d_6): δ = 6–8.5 (m, 6H, ArH), 8.9 (s, 1H,CH pyrimidine); MS *m/z* 236.

4-Chloronaphtho[2',1': 4,5]furo[3,2-d]pyrimidine **(12)**: A sample of naphthofuropyrimidine (**11**) (2.36 g, 0.01 mol), was refluxed with phosphorusoxychloride (20 ml) for 3 h. Then allowed to cool and poured with stirring to an ice cooled water. The solid product was filtered off and recrystallised from ethanol as blue needles in 65% yield, m.p. 158°C. Anal. calcd. for $C_{14}H_7ClN_2O$ (254): C, 66.03; H, 2.77; Cl, 13.92; N 11.00%. Found: C, 65.87; H, 3.01; Cl, 14.09; N 10.82%. IR: ν = 1650 (C=N),1050 (C-O furan). ^1H NMR($CDCl_3$): δ = 7.3–8.3 (m, 6H, ArH) and 9.15 (s, 1H,CH pyrimidine).

Naphtho[3',2',4,5]furo[3,2-d]pyrimidino-4(3H)thione **(13)**

Method a: A mixture of chloronaphthofuropyrimidine (**12**) (2.5 g, 0.01 mol) and thio urea (1.52 g, 0.02 mol) in ethanol (30 ml) was refluxed for 5 h.The solid precipitate which formed on hot was collected, washed well with water and recrystallised from dioxan as green crystals in 81% yield. m.p. >300°C.

Method b: A mixture of compound (**11**) (2.36 g, 0.o1 mol) and phosphorus pentasulfide (2.22 g, 0.01 mol) in pyridine (20 ml) was refluxed for 5 h, then allowed to cool and poured into cold water (100 ml). The solid product was collected and recrystallised from dioxan as green crystals in 85% yield. m.p. >300°C. Anal.calcd. for $C_{14}H_8N_2OS$ (252): C, 66.03; H, 3.20; N, 11.10; S, 12.71%. Found: C, 65.79; H, 3.43; N, 10.91; S, 12.94%. IR: ν = 1650 (C=N), 1050 (C–O)furan. ^1H NMR (DMSO-d_6): δ = 4.15 (s, 1H, SH), 7.6-8.6 (m, 6H, ArH), 8.9 (s, 1H, CH pyrimidine).

Alkylation of naphtho[3',2': 4,5]furo[3,2-d]pyrimidino-4(3H)-thione: A mixture of compound (**13**) (2.52 g, 0.01 mol), appropriate halogenated compound (0.01 mol) and fused sodium acetate (3 g, 0.037 mol) was refluxed for 3 h, then allowed to cool and poured into cold water (100 ml). The solid product was filtered off and recrystallised from ethanol. The physical constants and spectral data of compounds **14a–d** were summarised in Table 1,2.

4-Hydrazinonaphtho[2',1': 4,5]furo[3,2-d]pyrimidine **(15)**: A mixture of compound **12** (2.54 g, 0.01 mol) and hydrazine hydrate (2.5 ml, 0.05 mol) in ethanol (30 ml) was refluxed for 1 h. The solid product was collected and recrystallised from dioxan as white crystals in 87.5% yield, m.p.282–284°C. Anal.calcd. for $C_{14}H_{10}N_4O$ (250.26): C 67.19; H, 4.03; N, 22.39%. Found: C, 66.98; H, 4.25; N, 22.16%. IR: ν = 3300, 3280(NH_2), 3180(NH), 1640(C=N),1060 (C–O) furan. ^1H NMR(DMSO): δ = 4.8-5.2 (broad, 2H, NH_2), 7.6–8.4 (m, 6H, ArH), 8.8(s, 1H, CH pyrimidine) and 10.4 (s, 1H, NH).

Nonaphtho[2',1': 4,5]furo[2,3-e][1,3,4]triazolo[5,1-c]pyrimidine **(16)**: To a mixture of hydrizno compound (**15**) (0.25 g, 0.001 mol) and triethyl orthoformate (3 ml) were added a few drops of acetic acid. The mixture was refluxed for 3 h, then allowed to cool. The solid product was collected and recrystallised from acetic acid as white crystals in 80% yield, m.p.330°C. Anal.calcd. for $C_{15}H_8N_4O$ (260.26): C, 69.23; H, 3.10; N, 21.53%. Found: C, 69.00; H, 3.34; N, 21.72%. IR: ν = 1620 (C=N), 1025(C–O) furan. ^1H NMRδ (DMSO-d_6): δ = 7.5-8.2 (m, 8H, ArH, CH-pyrimidine and CH-triazole).

Nonaphtho[2',1': 4,5]furo[2,3-e][1,3,4]triazolo[5,1-c]pyrimidin-5(4H)-thione **(17)**: A mixture of hydrizno compound (**16**) (0. 5 g, 0.002 mol) and carbon disulfide (1 ml) in pyridine (5 ml) was refluxed on water bath for 8 h. The solid precipitate which was formed on hot was collected and recrystallised from ethanol in 64% yield, m.p. >300°C. Anal.calcd. for $C_{15}H_8N_4OS$ (292.32): C, 61.63; H, 2.76; N, 19.17; S 10.97%. Found: C, 61.81; H, 2.93; N, 18.99; S 11.20%.

Table 3 Antifungal activities

Compd	*Aspergillus flavus*	*Aspergillus niger*	*Candida albicans*	*Geotrichum candidum*	*Scopulairopsis brevicaulis*	*Fusaium oxysporum*	*Trichophyton rubrum*
5a	0	0	9	0	0	0	0
5b	6	0	10	0	0	0	0
5c	0	0	6	0	0	0	10
5d	0	0	11	0	0	0	0
5e	0	0	7	7	0	0	0
6a	6	17	10	0	7	0	10
6b	0	0	9	0	7	0	0
6c	0	0	6	0	0	0	7
6d	0	0	8	0	0	0	0
8	6	7	9	0	0	7	0
Sertaconazol	23	18	12	6	23	10	15

Table 4 Antibacterial activity

Compd	*Bacillus cereus*	*Escherichia coli*	*Pseudomonas aeruginosa*	*Staphylococcus aureus*	*Micrococcus luteus*	*Serratia marcescens*
5a	12	8	6	9	10	10
5b	0	8	6	6	6	12
5c	36	0	20	25	36	45
5d	12	12	10	12	10	10
5e	10	10	8	12	10	10
6a	15	10	8	10	14	8
6b	6	10	6	8	0	10
6c	10	10	12	10	10	10
6d	10	10	12	12	6	6
8	10	8	12	10	10	12
Chloramphenicol	12	15	12	12	12	10

IR: ν = 3390 (NH),1650 (C=N) ^{1}H NMR this compound is insoluble in the common ^{1}H NMR solvents.

4-(3,5-dimethylpyrazol-1-yl)naphtho[2',1': 4,5]furo[3,2-d]pyrimidine **(18)**: A mixture of 4-hydrazinonaphthofuropyrimidine (**15**) (0.5 g, 0.002 mol) and acetylacetone (0.2 ml, 0.002 mol) was refluxed in ethanol (20 ml) for 3 h, then allowed to cool and diluted with water the solid precipitate formed was collected and recrystallised from ethanol as white needles in 96% yield, m.p.190–192°C. Anal. calcd. for $C_{19}H_{14}N_4O$ (314.35): C, 72.60; H, 4.49; N, 17.82%. Found: C, 72.36; H, 4.72; N, 18.03%. IR: ν 1620 (C=N),1025 (C–O)furan. ^{1}H NMRδ ($CDCl_3$): δ = 2.6 (s, 3H,CH_3), 2.9 (s, 3H,CH_3), 6.25 (s, 1H, CH pyrazole), 7.7–8.3 (m, 6H, ArH), 9.3(s, 1H, CH pyrimidine); MS *m/z* 312.

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