

**ACTION OF PRIMARY AMINES AND HYDROXYLAMINE  
ON ETHOXYMETHYLENEAMINONAPHTOPYRANES:  
SYNTHESIS OF NEW NAPHTOPYRANO [2, 3-d] PYRIMIDINES DERIVATIVES**

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**Abstract:** A variety of naphtopyrans 1 has been prepared by reaction of 2-naphtol with aryl (or alkyl) idenemalononitriles. The reaction of the naphtopyrans with triethylorthoformiate and then with primary amines and hydroxylamine, leads to new naphtopyrano [2, 3-d] pyrimidines 3 and 4, whose structures were confirmed by IR and NMR spectroscopy.

### Introduction

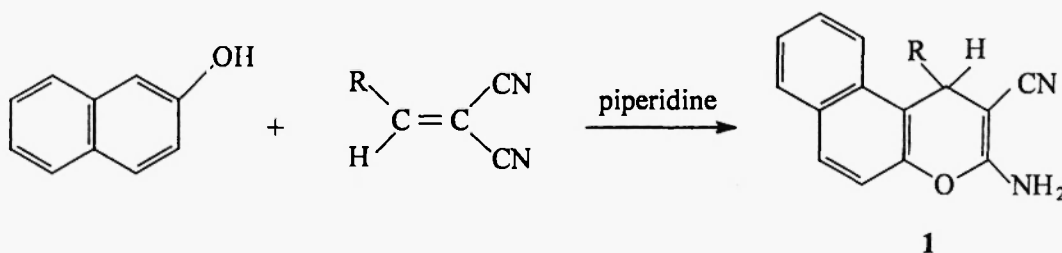
The analysis of the bibliographical data shows that pyrans are biologically interesting compounds (1-4). Infact, some pyran derivatives present antibacterial activities (5-6); antifungal activities (7); antitumor activity (8) and they can have a hypotensive effect (9). We report here the synthesis of a variety of new 2-amino-3-cyano-4H-naphto [2,1-b] pyrans 1, and we show their usefulness as building blocks for the preparation of new pyranopyrimidine 3 and 4 .

### Results and discussion

#### Synthesis of 2-amino-3-cyano-4H-naphto [2, 1-b] pyrans 1

Several recent work mentioned the synthesis of the 2-amino-3-cyano-4H-naphto [2,1-b] pyrans (10-14). These products were prepared via a standard addition of Michael of naphtol on arylidenemalononitriles with piperidine as a base.

To generalize the synthesis of compounds 1, we have prepared a new serie of 2-amino-4-aryl-3-cyano-4H-naphto[2,1-b] pyrans and for the first time a new variety of 2-amino-4-alkyl-3-cyano-4H-naphto[2,1-b]pyrans by condensation of 2-naphtol and alkylidenemalononitriles .(Scheme 1)



SCHEME 1

Table-I: Synthesis of naphto[2,1-b]pyrans 1a-h

compound	1a	1b	1c	1d	1e	1f	1g	1h
R	Ph	o-ClC <sub>6</sub> H <sub>4</sub>	p-ClC <sub>6</sub> H <sub>4</sub>	p-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	(3,4)Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	Furyl	Ipr	pentyle
Yields	82%	83%	84%	77%	79%	72%	74%	78%

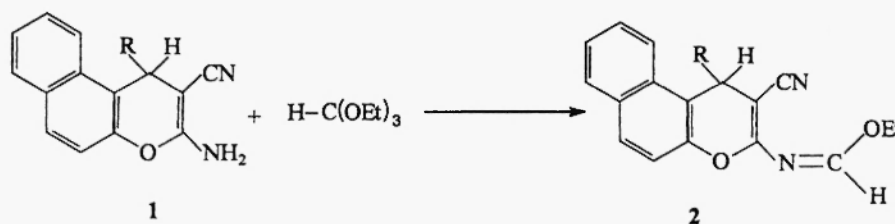
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The structure of compounds 1 was deduced from their IR,  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra. Indeed, IR spectra of these compounds showed two bands towards  $3330$  and  $3420\text{ cm}^{-1}$  due to the vibration of the amino group. Another intense peak at  $2180\text{ cm}^{-1}$  is revealed and which can be ascribed to the nitrile group.

$^1\text{H}$  NMR spectrum clearly showed the presence of a singlet characteristic of the 4-H pyran towards  $4.0$ - $5.0$  ppm for the compounds 1g et 1h ( $\text{R}=\text{alkyl}$ ) and towards  $5.0$ - $5.5$  ppm for the compounds 1a-1f ( $\text{R}=\text{aryl}$ ).  $^{13}\text{C}$  NMR of these compounds confirms without ambiguity the structure of the obtained product by comparison with the known chemical shifts of similar compounds (11).

## II-2: Action of ethyl orthoformate on compounds 2

Compounds such as 2-amino-8-bromo-2-cyano-1-(p-methoxyphenyl)-1H-naphto[2,1-b] pyrans and 3-amino-2-cyano-9-chloro-1-(4-halophenyl)-1H-benzo[h]chromene have an important synthetic use in the field of condensed heterocyclic compounds incorporating the pyrimidinic nucleus (5,14). The chemical behaviour of compounds 1 towards ethyl orthoformate was investigated. Thus treating compounds 1 with ethyl orthoformate under reflux of acetic anhydride was carried out at the purpose of production of the corresponding ethoxymethyleneamino derivatives 2. (Scheme 2)



Scheme-2

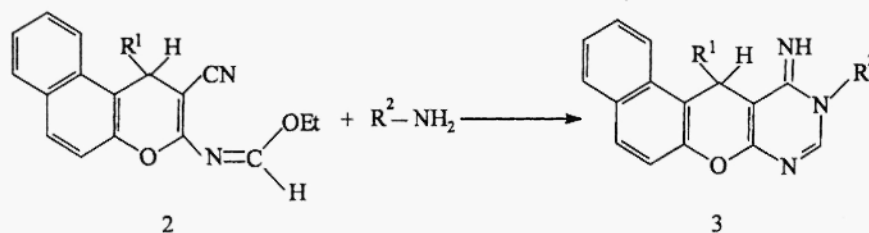
Table-II: Synthesis of iminoethers 2a-g

compound	2a	2b	2c	2d	2e	2f	2g
R	Ph	o- $\text{ClC}_6\text{H}_4$	p- $\text{ClC}_6\text{H}_4$	p- $\text{CH}_3\text{C}_6\text{H}_4$	(3,4) $\text{Cl}_2\text{C}_6\text{H}_3$	Furyle	Ipr
Yields	83%	81%	84%	80%	78%	79%	75%

The structure of compounds 2 was determined by IR,  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra. I.R. spectra revealed in particular the absence of the absorption bands corresponding to the amino group ( $3330$  - $3420\text{ cm}^{-1}$ ) while exhibiting a band corresponding to C=N group at  $1610\text{ cm}^{-1}$ .  $^1\text{H}$  NMR of compounds 2 gave us useful information about the nature of protons in this molecule, thus we observe the appearance of a triplet towards  $1.4$  ppm and a quadruplet towards  $4.5$  ppm corresponding to the protons of ethoxy group. We can also observe a singlet towards  $8.4$  ppm corresponding to the proton of the  $\text{N}=\text{C}(\text{OEt})\text{H}$  group.

## II-3: Action of primary amines on compounds 2

During the course of cyclization reaction between primary amines and iminoethers 2, the latter react with their two electrophilic sites 1, 5 to yielding the corresponding pyrimidinic derivatives 3. This condensation was carried out in boiling toluene with the presence of some drops of acetic acid for 24 hours. (Scheme 3)



Scheme-3

Table-II: Synthesis of naphtopyrano [2, 3-d] pyrimidine 3a-e

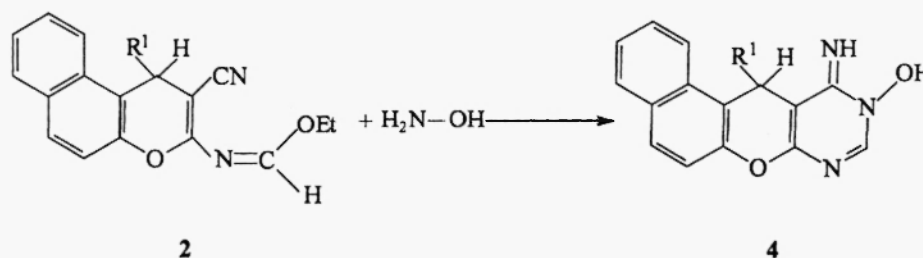
compound	R <sup>1</sup>	R <sup>2</sup>	Yields
3a	<i>o</i> -ClC <sub>6</sub> H <sub>4</sub>	CH <sub>2</sub> Ph	62%
3b	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	CH <sub>2</sub> Ph	54%
3c	3,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	82%
3d	Ipr	Ph	78%
3e	Ipr	CH <sub>2</sub> Ph	56%

All of the newly obtained compounds were characterized using I.R. <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy. I.R. spectra of compounds 3 showed the absence of the absorption band corresponding to C=N group (2180 cm<sup>-1</sup>) and the appearance of another band at 1645 cm<sup>-1</sup> corresponding to C=NH group. <sup>1</sup>H NMR spectrum clearly showed that the ethoxy group disappeared and aromatic and aliphatic protons were integrated in the spectrum chart.

### II-3: Action of hydroxylamine on compounds 2

Reaction of hydroxylamine with iminoethers 2 gave a new variety of hydroxypyranopyrimidine 4. (Scheme 4).

The structure of compounds 4 was confirmed on the basis of their spectral analyses. It's clear that –like for the previous condensation- the reaction pathway proceed via a double nucleophilic attack of the amino group on nitrile group and on imidic carbon.



Scheme -4

Table-III: Synthesis of hydroxypyranopyrimidine 4a-e

compound	4a	4b	4c	4d	4e
R <sup>1</sup>	Ph	<i>o</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	(3,4)Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	Ipr
Yields	63%	71%	54%	53%	58%

The I.R spectra of these compounds showed the absence of the absorption band corresponding to CN group and the appearance of new bands corresponding to –OH and –NH groups (3460-3370 cm<sup>-1</sup>).

The <sup>1</sup>H NMR spectra of compounds 4 are in agreement with the proposed structure. Infact, we note the same observations that we have mentioned for compounds 3, like the disappearance of the signals of the ethoxy group.

In the <sup>13</sup>C NMR spectra we could unequivocally assign the signals on the basis of the observed chemical shifts. In particular we observe the disappearance of the signal of nitril's carbon.

## III- EXPERIMENTAL SECTION

### III-1-General information

- NMR: NMR spectra were recorded on a Bruker A C 200 (<sup>1</sup>H: 300 MHz, <sup>13</sup>C: 75 MHz) in CDCl<sub>3</sub> solution or in DMSO-d<sub>6</sub> solution. All chemical shifts are recorded in parts per million (ppm) downfield from tetramethylsilane. Coupling constants (<sup>3</sup>J) are given in hertz (Hz).

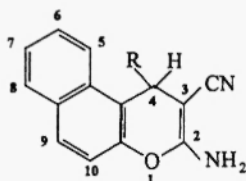
- IR: IR spectra were determined for KBr discs on a JASCO FT-IR-420 spectrometer with the incertitude as  $\pm 2 \text{ cm}^{-1}$  in the field of 4000-400  $\text{cm}^{-1}$ .

- Melting point: the melting points were determined in Electrothermal 9100 apparatus and are uncorrected.

The reactions were monitored by thin layer chromatography using aluminium sheets with silica gel 60 F<sub>254</sub> (Merck).

### III-2- Synthesis of naphto [2, 1-b] pyrans 1

A mixture of 2-naphthol (0,01mmol) and enamionitrile (0,01mmol) in ethanol (30 ml) was refluxed for 10 h, with the presence of 0,2 equivalent of piperidine. The solvent was evaporated to dryness under reduced pressure. The solid was collected by filtration. The crude product was purified by recrystallization from toluene to give compounds 1a-h .



#### Compound 1a:

Yield:82%; Mp: 277°C; IR:  $\nu_{\text{CN}}$ :2178  $\text{cm}^{-1}$ ;  $\nu_{\text{NH}_2}$ :3337-3428  $\text{cm}^{-1}$ ; RMN <sup>1</sup>H (DMSO d<sub>6</sub>):5.29(s,1H);7.11-7.91(m,13H)

RMN <sup>13</sup>C (DMSO d<sub>6</sub>): 38.39(C-4); 58.18(C-3); 116.01(CN); 120.89-146.06(C arom); 147.15(C ipso); 159.99(C-2).

#### Compound 1b:

Yield: 83%; Mp: 265 °C; IR:  $\nu_{\text{CN}}$ :2176  $\text{cm}^{-1}$ ;  $\nu_{\text{NH}_2}$ :3335-3431  $\text{cm}^{-1}$ , RMN <sup>1</sup>H (CDCl<sub>3</sub>): 4.75(s, 2H), 5.43(s, 1H); 7.14-7.86(m, 10H); RMN <sup>13</sup>C (CDCl<sub>3</sub>): 38.13(C-4); 60.43(C-3); 115.22(CN); 120.65-142.33(C arom); 147.08(C ipso) ; 159.26(C-2).

#### Compound 1c:

Yield: 84% ; Mp: 218 °C; IR:  $\nu_{\text{CN}}$ :2189  $\text{cm}^{-1}$ ;  $\nu_{\text{NH}_2}$ :3319-3405  $\text{cm}^{-1}$ ; RMN <sup>1</sup>H (CDCl<sub>3</sub>): 4.66(s, 2H); 5.23(s, 1H); 7.11-7.83(m, 10H); RMN <sup>13</sup>C (CDCl<sub>3</sub>): 38.26(C-4); 61.80(C-3); 114.36(CN); 119.65-142.81(C arom); 147.07(C ipso) ; 158.63(C-2).

#### Compound 1d:

Yield: 77% ; Mp: 270°C; IR:  $\nu_{\text{CN}}$ :2178  $\text{cm}^{-1}$ ;  $\nu_{\text{NH}_2}$ :3331-3423  $\text{cm}^{-1}$ ; RMN <sup>1</sup>H (DMSO d<sub>6</sub>):2.17(s,3H); 5.23(s, 1H); 6.94-7.87(m, 12H); RMN <sup>13</sup>C (DMSO d<sub>6</sub>): 20.52(CH<sub>3</sub>); 37.74(C-4); 58.04(C-3); 115.77(CN); 120.53-142.79(C arom); 146.75(C ipso) ; 159.60(C-2).

#### Compound 1e:

Yield: 79% ; Mp: 230 °C; IR:  $\nu_{\text{CN}}$ : 2175 $\text{cm}^{-1}$ ;  $\nu_{\text{NH}_2}$ :3331-3421 $\text{cm}^{-1}$ ; RMN <sup>1</sup>H (DMSO d<sub>6</sub>): 5.43(s, 1H); 7.08-8.30(m,11H); RMN <sup>13</sup>C (DMSO d<sub>6</sub>):37.35(C-4); 57.28(C-3); 114.85(CN); 120.51-147.05(C arom);147.22(C ipso) ; 160.21(C-2).

#### Compound 1f:

Yield: 72%; Mp: 268 °C; IR:  $\nu_{\text{CN}}$ :2178 $\text{cm}^{-1}$ ;  $\nu_{\text{NH}_2}$ :3332-3415 $\text{cm}^{-1}$ ; RMN <sup>1</sup>H (DMSO d<sub>6</sub>):5.28(s, 1H); 6.20-7.92(m, 11H); RMN <sup>13</sup>C (DMSO d<sub>6</sub>):32.41(C-4); 67.46(C-3); 115.78(CN); 119.26-144.29(C arom);151.32(C ipso); 159.63(C-2).

#### Compound 1g :

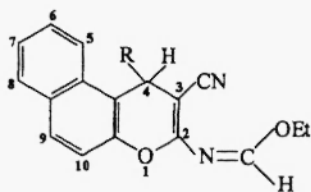
Yield: 74%; Mp: 196°C; IR:  $\nu_{\text{CN}}$ :2178 $\text{cm}^{-1}$ ;  $\nu_{\text{NH}_2}$ :3331-3434 $\text{cm}^{-1}$ ; RMN <sup>1</sup>H (CDCl<sub>3</sub>):0.68(d,<sup>3</sup>J=7;3H); 1.24(d,<sup>3</sup>J=7.2;3H); 2.20(m,1H); 4.16(d,<sup>3</sup>J=7.2 ;1H); 4.70(s,2H); 7.13-7.89(m, 6H); RMN <sup>13</sup>C (CDCl<sub>3</sub>): 16.17((CH<sub>3</sub>)<sub>2</sub>CH); 21.31((CH<sub>3</sub>)<sub>2</sub>CH); 35.43((CH<sub>3</sub>)<sub>2</sub>CH); 38.89(C-4) ; 55.45(C-3); 116.81(CN); 118.05-131.83(C arom); 148.02(C ipso) ; 162.42(C-2).

#### Compound 1h:

Yield: 78%; Mp: 192°C; IR:  $\nu_{\text{CN}}$ : 2187 $\text{cm}^{-1}$ ;  $\nu_{\text{NH}_2}$ : 3329-3401 $\text{cm}^{-1}$ ; RMN <sup>1</sup>H (CDCl<sub>3</sub>): 0.87(t, <sup>3</sup>J=7.2 , 3H); 1.2-1.5(m, 6H); 2.31(td, 2H); 4.42(t, <sup>3</sup>J=7.4 , 1H); 4.70(s,2H); 7.20-7.71(m, 6H); RMN <sup>13</sup>C (CDCl<sub>3</sub>): 14.04(CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>); 14.19(CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>); 24.46(CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>); 31.71(CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>); 32.41(CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>); 36.29(C-4);59.98(C-3); 117.75(CN);121.05-131.83(C arom);149.31(C ipso); (C-2)159.26

### III-3-Synthesis of iminoethers 2

A mixture of ethyl orthoformate (0.01mmol) and naphto[2,1-b] pyran (0.01mmol) in acetic anhydride (30 ml) was refluxed for 6 h. On cooling, the solid that separated out was collected by filtration. The crude product was purified by recrystallization from ethanol to give iminoethers 2.

**Compound 2a:**

Yield: 83% ; Mp: 215 °C; IR:  $\nu_{C=N}$ :1614 $\text{cm}^{-1}$ ;  $\nu_{CN}$ :2203 $\text{cm}^{-1}$ ; RMN  $^1\text{H}$  (DMSO  $d_6$ ): 1.17(t,  $^3J=7$ ; 3H); 4.20(q,  $^3J=7$ ; 2H); 5.42(s, 1H); 7.03-8.15(m, 11H); 8.57(s, 1H); RMN  $^{13}\text{C}$  (DMSO  $d_6$ ): 14.22(OCH $_2$ CH $_3$ ); 38.46(C-4); 64.30(OCH $_2$ CH $_3$ ); 79.51(C-3); 114.38(CN); 118.31-144.13(C arom); 157.19(N=CH-OEt); 162.28(C-2).

**Compound 2b:**

Yield: 81% ; Mp: 228 °C; IR:  $\nu_{C=N}$ :1615  $\text{cm}^{-1}$ ;  $\nu_{CN}$ :2207  $\text{cm}^{-1}$ ; RMN  $^1\text{H}$  (DMSO  $d_6$ ): 1.30(t,  $^3J=7$ ; 3H); 4.32(q,  $^3J=7$ ; 2H); 5.93(s, 1H); 7.20-8.29(m, 10H); 8.72(s, 1H); RMN  $^{13}\text{C}$  (DMSO $d_6$ ):14.36(OCH $_2$ CH $_3$ ); 39.15(C-4); 63.40(OCH $_2$ CH $_3$ ); 79.66(C-3); 114.85(CN); 120.51-147.05(Carom); 156.19(N=CH-OEt); 160.21(C-2).

**Compound 2c:**

Yield: 84% ; Mp: 191 °C; IR:  $\nu_{C=N}$ :1610  $\text{cm}^{-1}$ ;  $\nu_{CN}$ :2201  $\text{cm}^{-1}$ ; RMN  $^1\text{H}$  (CDCl $_3$ ): 1.39(t,  $^3J=7$ ; 3H); 4.43(q,  $^3J=7$ ; 2H); 5.34(s, 1H); 7.16-7.86(m, 10H); 8.45(s, 1H); RMN  $^{13}\text{C}$  (CDCl $_3$ ): 13.86(OCH $_2$ CH $_3$ ); 40.24(C-4); 64.22(OCH $_2$ CH $_3$ ); 81.60(C-3); 113.29(CN); 118.07-147.56(Carom); 156.78(N=CH-OEt); 159.58(C-2).

**Compound 2d:**

Yield: 80% ; Mp: 186 °C; IR:  $\nu_{C=N}$ :1610  $\text{cm}^{-1}$ ;  $\nu_{CN}$ :2207  $\text{cm}^{-1}$ ; RMN  $^1\text{H}$  (DMSO  $d_6$ ): 1.23(t,  $^3J=7$ ; 3H); 2.01(s, 3H); 4.31(q,  $^3J=7$ ; 2H); 5.54(s, 1H); 6.96-8.11(m, 10H); 8.39(s, 1H); RMN  $^{13}\text{C}$  (DMSO  $d_6$ ): 14.03(OCH $_2$ CH $_3$ ); 20.32(CH $_3$ ); 39.76(C-4); 64.13(OCH $_2$ CH $_3$ ); 66.52(C-3); 114.62(CN); 119.83-147.71(C arom); 157.19(N=CH-OEt); 160.17(C-2).

**Compound 2e:**

Yield: 78% ; Mp: 168 °C; IR:  $\nu_{C=N}$ :1611 $\text{cm}^{-1}$ ;  $\nu_{CN}$ :2204  $\text{cm}^{-1}$ ; RMN  $^1\text{H}$  (DMSO  $d_6$ ): 1.29(t,  $^3J=7$ ; 3H); 4.32(q,  $^3J=7$ ; 2H); 5.70(s, 1H); 7.19-8.29(m, 9H); 8.71(s, 1H); RMN  $^{13}\text{C}$  (DMSO  $d_6$ ): 14.35(OCH $_2$ CH $_3$ ); 38.74(C-4); 64.56(OCH $_2$ CH $_3$ ); 80.48(C-3); 113.38(CN); 118.20-145.21(C arom); 157.84(N=CH-OEt); 162.81(C-2).

**Compound 2f:**

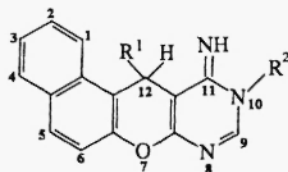
Yield: 79% ; Mp: 179 °C; IR:  $\nu_{C=N}$ :1610 $\text{cm}^{-1}$ ;  $\nu_{CN}$ :2201  $\text{cm}^{-1}$ ; RMN  $^1\text{H}$  (CDCl $_3$ ): 1.37(t,  $^3J=7$ ; 3H); 4.45(q,  $^3J=7$ ; 2H); 5.52(s, 1H); 6.13-7.88(m, 9H); 8.44(s, 1H); RMN  $^{13}\text{C}$  (CDCl $_3$ ): 13.97(OCH $_2$ CH $_3$ ); 34.43(C-4); 64.33(OCH $_2$ CH $_3$ ); 107.06(C-3); 111.05(CN); 118.22-142.46(Carom); 154.34(N=CH-OEt); 159.75(C-2).

**Compound 2g:**

Yield: 75% ; Mp: 137 °C; IR:  $\nu_{C=N}$ :1612  $\text{cm}^{-1}$ ;  $\nu_{CN}$ :2205  $\text{cm}^{-1}$ ; RMN  $^1\text{H}$  (CDCl $_3$ ): 0.73(d,  $^3J=7$ ; 3H); 1.29(d,  $^3J=7$ ; 3H); 1.41(t,  $^3J=7$ ; 3H); 2.26(m, 1H); 4.29(d,  $^3J=7$ ; 1H); 4.47(q,  $^3J=7$ ; 2H); 7.17-7.89(m, 6H); 8.41(s, 1H); RMN  $^{13}\text{C}$  (CDCl $_3$ ): 14.01(OCH $_2$ CH $_3$ ); 16.71((CH $_3$ ) $_2$ CH); 21.25((CH $_3$ ) $_3$ CH); 35.18((CH $_3$ ) $_2$ CH); 40.48(C-4); 64.20 (OCH $_2$ CH $_3$ ); 116.40(CN); 119.88-148.30(C arom); 159.12(N=CH-OEt); 160.35(C-2).

**III-4- Synthesis of naphthopyrano [2, 3-d] pyrimidine 3**

A mixture of iminoethers **2** (0.01mmol), primary amine (0.01mmol), toluene (30 ml) and few drops of acetic acid was refluxed for 24 h. On cooling, the separated solid was collected by filtration and dried. The crude product was purified by recrystallization from dioxan to give the pyrimidine derivative **3**.

**Compound 3a:**

Yield: 62% ; Mp: 200 °C; IR:  $\nu_{C=N}$ :1648  $\text{cm}^{-1}$ ;  $\nu_{NH}$ :3434  $\text{cm}^{-1}$ ; RMN  $^1\text{H}$  (CDCl $_3$ ): 4.89(d,  $^2J=15$ ; 1H); 5.27(d,  $^2J=15$ ; 1H); 5.53(s, 1H); 7.19-7.48(m, 16H); 7.98(s, 1H); RMN  $^{13}\text{C}$  (CDCl $_3$ ): 37.31(C-12); 51.12(CH $_2$ Ph); 99.94(C-11a); 115.47-156.22 (C arom); 156.97(C=NH).

**Compound 3b:**

Yield: 54% ; Mp: 217 °C; IR:  $\nu_{C=N}$ :1647  $\text{cm}^{-1}$ ;  $\nu_{NH}$ :3348  $\text{cm}^{-1}$ ; RMN  $^1\text{H}$  (CDCl $_3$ ): 4.87(d,  $^2J=15$ ; 1H); 5.30(s, 1H); 5.49(d,  $^2J=15$ ; 1H); 7.06-7.87(m, 16H); 8.25(s, 1H); RMN  $^{13}\text{C}$  (CDCl $_3$ ): 34.45(C-12); 51.31(CH $_2$ Ph); 101.03(C-11a); 116.88-157.02(C arom); 157.55(C=NH).

**Compound 3c:**

Yield: 82%; Mp: 250°C; IR:  $\nu_{C=N}$ :1643  $\text{cm}^{-1}$ ;  $\nu_{NH}$ :3411 $\text{cm}^{-1}$ ; RMN  $^1\text{H}$  (DMSO  $d_6$ ): 2.34(s, 3H); 5.80(s, 1H); 6.58-7.88(m, 14H); 8.05(s, 1H); RMN  $^{13}\text{C}$  (DMSO  $d_6$ ): 21.62(C $_6$ H $_4$ CH $_3$ ); 33.42(C-12); 98.69(C-11a); 116.53-159.08(C arom); 162.48(C=NH).

**Compound 3d:**

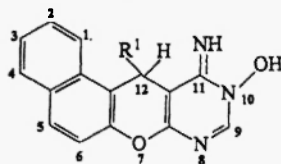
Yield: 78%; Mp: 225 °C; IR:  $\nu_{\text{C=N}}$ : 1631  $\text{cm}^{-1}$ ;  $\nu_{\text{NH}}$ : 3407  $\text{cm}^{-1}$ ;  $\text{RMN}^1\text{H}$  (DMSO  $d_6$ ): 0.64(d,  $^3J=7$ ; 3H); 0.90(d,  $^3J=7$ ; 3H); 2.06(m, 1H); 5.37(d,  $^3J=7$ ; 1H); 7.06-8.31(m, 12H); 9.06(s, 1H);  $\text{RMN}^{13}\text{C}$  (DMSO  $d_6$ ): 18.38(( $\text{CH}_3$ ) $_2\text{CH}$ ); 20.20(( $\text{CH}_3$ ) $_2\text{CH}$ ); 33.69(( $\text{CH}_3$ ) $_2\text{CH}$ ); 36.12(C-12); 96.95(C-11a); 117.58-160.35(C arom); 165.33(C=NH).

**Compound 3e:**

Yield: 56%; Mp: 153 °C; IR:  $\nu_{\text{C=N}}$ : 1643  $\text{cm}^{-1}$ ;  $\nu_{\text{NH}}$ : 3362  $\text{cm}^{-1}$ ;  $\text{RMN}^1\text{H}$ ( $\text{CDCl}_3$ ): 0.80(d,  $^3J=7$ ; 3H); 0.98(d,  $^3J=7$ ; 3H); 2.20(m, 1H); 4.59(d,  $^3J=7$ ; 1H); 5.13(d,  $^2J=15$ ; 1H); 5.37(d,  $^2J=15$ ; 1H); 7.16-8.06(m, 12H); 8.41(s, 1H);  $\text{RMN}^{13}\text{C}$  ( $\text{CDCl}_3$ ): 18.84(( $\text{CH}_3$ ) $_2\text{CH}$ ); 21.21(( $\text{CH}_3$ ) $_2\text{CH}$ ); 35.89(( $\text{CH}_3$ ) $_2\text{CH}$ ); 36.05(C-12); 51.27( $\text{CH}_2\text{Ph}$ ); 98.05(C-11a); 116.86-156.05(C arom); 158.81(C=NH).

**III-4- Synthesis of hydroxypyranopyrimidine 4**

To a solution of hydroxylamine (0.01mmol) in toluene (20ml) containing triethylamine (0.2 ml), the iminoethers 2 (0.01mmol) was added and the mixture was heated under reflux for 2 h. the reaction mixture was left to cool and poured onto crushed ice-cold water (20 ml). The precipitate so obtained was filtered off and crystallized from DMF to give the pyrimidine derivative 4.

**Compound 4a:**

Yield: 63%; Mp: 292 °C; IR:  $\nu_{\text{C=N}}$ : 1644  $\text{cm}^{-1}$ ;  $\nu_{\text{NH}}$ : 3372  $\text{cm}^{-1}$ ;  $\nu_{\text{OH}}$ : 3453  $\text{cm}^{-1}$ ;  $\text{RMN}^1\text{H}$ (DMSO): 6.01(s, 1H); 6.83-8.07(m, 13H); 8.35(s, 1H);  $\text{RMN}^{13}\text{C}$  (DMSO): 31.70(C-12); 98.28(C-11a); 116.72-153.38 (C arom); 153.44 (C=NH)

**Compound 4b:**

Yield: 71%; Mp: 290 °C; IR:  $\nu_{\text{C=N}}$ : 1648  $\text{cm}^{-1}$ ;  $\nu_{\text{NH}}$ : 3386  $\text{cm}^{-1}$ ;  $\nu_{\text{OH}}$ : 3460  $\text{cm}^{-1}$ ;  $\text{RMN}^1\text{H}$ (DMSO): 3.80(s, 3H); 6.13(s, 1H); 6.83-8.15(m, 12H); 8.57(s, 1H);  $\text{RMN}^{13}\text{C}$  (DMSO): 35.28(C-12); 56.21( $\text{OCH}_3$ ); 96.97(C-11a); 112.37-153.51 (C arom); 156.21(C=NH).

**Compound 4c:**

Yield: 54%; Mp: 290 °C; IR:  $\nu_{\text{C=N}}$ : 1644  $\text{cm}^{-1}$ ;  $\nu_{\text{NH}}$ : 3386  $\text{cm}^{-1}$ ;  $\nu_{\text{OH}}$ : 3409  $\text{cm}^{-1}$ ;  $\text{RMN}^1\text{H}$ (DMSO): 2.25(s, 3H); 6.12(s, 1H); 7.00-8.14(m, 12H); 8.57(s, 1H);  $\text{RMN}^{13}\text{C}$  (DMSO): 20.98( $\text{CH}_3$ ); 35.07(C-12); 98.54(C-11a); 116.96-148.11 (C arom); 153.38(C=NH).

**Compound 4d:**

Yield: 53%; Mp: 285 °C; IR:  $\nu_{\text{C=N}}$ : 1644  $\text{cm}^{-1}$ ;  $\nu_{\text{NH}}$ : 3381  $\text{cm}^{-1}$ ;  $\nu_{\text{OH}}$ : 3470  $\text{cm}^{-1}$ ;  $\text{RMN}^1\text{H}$ (DMSO): 6.27(s, 1H); 7.33-8.31(m, 11H); 8.60(s, 1H);  $\text{RMN}^{13}\text{C}$  (DMSO): 34.56(C-12); 98.63(C-11a); 117.96-118.15 (C arom); 152.11(C=NH).

**Compound 4e:**

Yield: 58%; Mp: 289 °C; IR:  $\nu_{\text{C=N}}$ : 1644  $\text{cm}^{-1}$ ;  $\nu_{\text{NH}}$ : 3362  $\text{cm}^{-1}$ ;  $\nu_{\text{OH}}$ : 3409  $\text{cm}^{-1}$ ;  $\text{RMN}^1\text{H}$ (DMSO): 0.48(d,  $^3J=7$ ; 3H); 0.50(d,  $^3J=7$ ; 3H); 1.85(m, 1H); 5.00(d,  $^3J=7$ ; 1H); 7.23-8.12(m, 8H); 8.39(s, 1H);  $\text{RMN}^{13}\text{C}$  (DMSO): 18.68(( $\text{CH}_3$ ) $_2\text{CH}$ ); 19.81(( $\text{CH}_3$ ) $_2\text{CH}$ ); 34.83(( $\text{CH}_3$ ) $_2\text{CH}$ ); 36.15(C-12); 95.94(C-11a); 116.96-154.45(C arom); 155.84(C=NH).

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