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A NOVEL SYNTHESIS OF 14-ARYL-14*H*-NAPHTO [2,1-*b*]PYRANO[3,2-*e*][1,2,4]TRIAZOLO[1,5-*c*]PYRIMIDINES

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Abstract:

A new series of 14-aryl-14*H*-naphto[2,1-*b*]pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidines **5** were synthesised by reacting an excess of triethyl orthoformate with 11-aryl-1,12-dihydro-11*H*-naphtopyrano[2,3-*d*]pyrimidines **3**, as readily available starting materials, in moderate yields from imidates **2** and tosylhydrazine.

Keywords: Naphtopyrans, imidates, naphtopyranopyrimidines, triazolopyrimidines.

Introduction

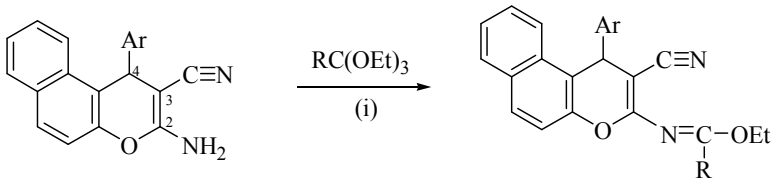
The triazole heterocyclic ring system has received considerable attention among synthetic chemists because molecules bearing this structural feature have been found to display a wide range of potent biological activities in medicinal chemistry, as antibacterial, antifungal, (1,2) antigenotoxic, (3) anti-inflammatory and analgesic agents, (4) and in the agrochemical field, showing herbicidal activity (5).

In our laboratory, the synthesis and reactivity of these substrates has been the subject of a number of publications (6-13). Now in this work we describe the synthesis of a series of new triazolopyrimidines from readily available 2-amino-4-aryl-3-cyano-4*H*-naphto[2,1-*b*]pyrans as precursors.

Results and Discussion

According to the previously reported method by Messaâd and al. (14), we have synthesized a new series of 2-amino-4-aryl-3-cyano-4*H*-naphto[2,1-*b*]pyrans **1**, and have submitted them to reaction with triethyl orthoformate using acetic anhydride as solvent to give imidates **2a-d** in good yields (Scheme 1).

Next, and based on our previous works, (3,14) we have tried to generalize the method for obtaining new compounds **2** with R groups as methyl, and ethyl by using other orthoesters. However, we noticed that the reaction in these cases was not selective, giving a mixture of compounds. For this reason, we have developed a new and facile synthetic procedure based on the reaction of pyrans **1** with triethyl orthoacetate or triethyl orthopropionate, in 1,4-dioxane, in presence of catalytic amount of acetic acid, under reflux, to give the corresponding **2e**-**i**, and **2j**-**n** derivatives, respectively, in good yields (Scheme 1).



1a: Ar= C_6H_5

1b: Ar= *p*-$CH_3C_6H_4$

1c: Ar= *o*-ClC_6H_4

1d: Ar= *m,p*-$Cl_2C_6H_3$

1e: Ar= *p*-ClC_6H_4

1f: Ar= *o*-$OCH_3C_6H_4$

1g: Ar= *o,p*-$(OCH_3)_2C_6H_3$

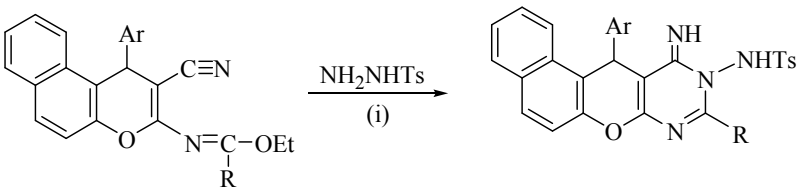
2a: Ar= C_6H_5, R: H
2b: Ar= *p*-$CH_3C_6H_4$, R: H
2c: Ar= o-ClC_6H_4, R: H
2d: Ar= *p*-ClC_6H_4, R: H

2e: Ar= C_6H_5, R: Me
2f: Ar= *p*-$CH_3C_6H_4$, R: Me
2g: Ar= *o*-$OCH_3C_6H_4$, R: Me
2h: Ar= *p*-ClC_6H_4, R: Me
2i: Ar= *o,p*-$(OCH_3)_2C_6H_3$, R: Me

2j: Ar= C_6H_5, R: Et
2k: Ar= *p*-$CH_3C_6H_4$, R: Et
2l: Ar= *o*-$OCH_3C_6H_4$, R: Et
2m: Ar= *p*-ClC_6H_4, R: Et
2n: Ar= *o,p*-$(OCH_3)_2C_6H_3$, R: Et

Scheme1. Synthesis of 2-[(ethoxyalkylidene)amino]-4-aryl-3-cyano-4*H*-naphto[2,1-*b*]pyrans **2**. Reaction conditions: (i) $RC(OEt)_3$, 1,4-dioxane, reflux 72 h and few drops of acetic acid.

Next, the reaction of these imidates **2,** with tosylhydrazine, in toluene, at reflux, afforded the desired key intermediates N^1-tosylamino-11-aryl-1,12-dihydro-11*H*-naphtopyrano[2,3-*d*]pyrimidines **3** (Scheme 2). All new compounds showed good analytical and spectroscopic data, in agreement with their structures.



2a: Ar= C_6H_5, R: H
2b: Ar= *p*-$CH_3C_6H_4$, R: H
2c: Ar= o-ClC_6H_4, R: H
2d: Ar= *p*-ClC_6H_4, R: H

2e: Ar= C_6H_5, R: Me
2f: Ar= *p*-$CH_3C_6H_4$, R: Me
2g: Ar= *o*-$OCH_3C_6H_4$, R: Me
2h: Ar= *p*-ClC_6H_4, R: Me
2i: Ar= *o*,*p*-$(OCH_3)_2C_6H_3$, R: Me

2j: Ar= *o*-OCH*3*C_6H_4, R: Et
2k: Ar= *p*-ClC_6H_4, R: Et
2l: Ar= *o*,*p*-$(OCH_3)_2C_6H_3$, R: Et
2m:Ar= C_6H_5, R: Et
2n: Ar= *p*-$CH_3C_6H_4$, R: Et

3a: Ar= C_6H_5, R: H
3b: Ar= *p*-$CH_3C_6H_4$, R: H
3c: Ar= *o*-ClC_6H_4, R: H
3d: Ar= *o*-$OCH_3C_6H_4$, R: H
3e: Ar= *p*-ClC_6H_4, R: H

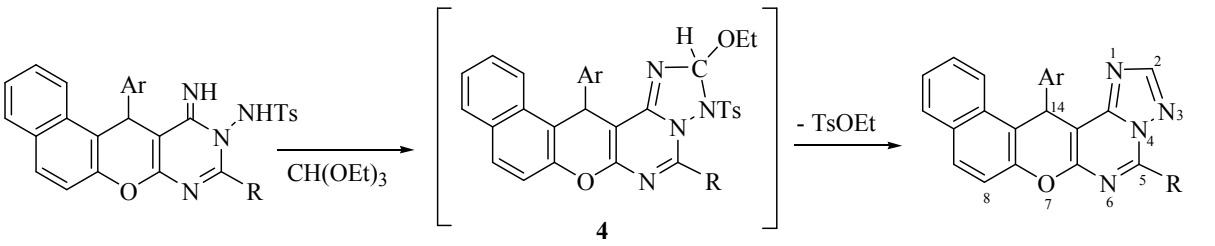
3f: Ar= *p*-$CH_3C_6H_4$, R: Me
3g: Ar= *o*-$OCH_3C_6H_4$, R: Me
3h:Ar= *p*-ClC_6H_4, R: Me

3i: Ar= *o*-$OCH_3C_6H_4$, R: Et
3j: Ar= *p*-ClC_6H_4, R: Et
3k: Ar= *o*,*p*-$(OCH_3)_2C_6H_3$, R: Et

Scheme2. Synthesis of *N*^{1}-tosylamino-11-aryl-1,12-dihydro-11*H*-naphtopyrano[2,3-*d*]pyrimidines **3**. Reaction conditions: (i) NH_2NHTs, toluene, reflux 48 h and few drops of acetic acid.

In the next step, we condensed the *N*^{1}-tosylaminonaphtopyrano[2,3-*d*]pyrimidines **3** with an excess of triethyl orthoformate to give 14-aryl-14*H*-naphto[2,1-*b*]pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidines **5**. To the best of our knowledge these compounds are new and have been described here for the first time (Scheme 3). In agreement with their structure, in the ^{1}H NMR spectral we did not observe the signals for the tosyl and the ethyl groups, but a singlet at 8.66-8.30 ppm range, corresponding to H_2 was observed. In addition, the microanalysis, and the mass spectra confirmed the final structure in all the examples.

The formation of compounds **5** can be explained by a sequence of events *via* intermediates of type **4**, formed in the reaction of *N*^{1}-tosylaminonaphtopyrano[2,3-*d*]pyrimidines **3** with triethyl orthoformate, followed by spontaneous ethyl 4-methylbenzenesulfonate elimination (Scheme 3).



3a: Ar= C_6H_5, R: H
3d: Ar= *o*-$OCH_3C_6H_4$, R: H
3e: Ar= *p*-ClC_6H_4, R: H

3f: Ar= *p*-$CH_3C_6H_4$, R: Me
3g: Ar= *o*-$OCH_3C_6H_4$, R: Me

3i: Ar= *o*-$OCH_3C_6H_4$, R: Et
3j: Ar= *p*-ClC_6H_4, R: Et

5a: Ar= C_6H_5, R: H
5b: Ar= *o*-$OCH_3C_6H_4$, R: H
5c: Ar= *p*-ClC_6H_4, R: H

5d: Ar= *p*-$CH_3C_6H_4$, R: Me
5e: Ar= *o*-$OCH_3C_6H_4$, R: Me

5f: Ar= *p*-ClC_6H_4, R: Et
5g: Ar= *o*-$OCH_3C_6H_4$, R: Et

Scheme3. Synthesis of 14-aryl-14*H*-naphto[2,1-*b*]pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidines **4**.

Experimental Section

General Procedures. All melting points were determined on a Kofler type microscope and are uncorrected. IR spectra were recorded on a Perkin Elmer FT-IR spectrophotometer (4000-400 cm^{-1}) using KBr pellets. ^1H NMR and ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$ or DMSO-d_6 at 300, 400 or 500 MHz and at 75, 100 or 125 MHz, respectively, using solvent peaks ($CDCl_3$: 7.27 (*D*), 77.2 (*C*) ppm and DMSO-d_6 2.50 (D) and 39.7 (C) ppm) as internal reference. Mass spectra were recorded on a GC/MS spectrometer with an API-ES ionization source. Elemental analyses were performed at the Instituto de Química Orgánica General de Madrid (Consejo Superior de Investigaciones Científicas, Spain). All solvents were dried by standard methods.

General procedure for the synthesis of 2-amino-4-aryl-3-cyano-4*H*-naphto[2,1-*b*]pyrans 1a-g. The required naphto[2,1-*b*]pyrans **1a-e** were obtained using known experimental procedures developed previously by Messaâd and al. (14). Following this typical experiment, a mixture of 2-naphtol (0.01 mmol, 1.5 g) and enaminonitrile (0.01 mmol, 1.7 g) in ethanol (30 mL) was refluxed for 10 hours with the presence of 0.2 equivalent of piperidine. The solvent was evaporated to dryness under reduced pressure. The solid was collected by filtration and purified by recrystallization from toluene. Based on this typical method, we were able to synthesize the new compounds **1f,g**.

2-Amino-3-cyano-4-(*o*-methoxyphenyl)-4*H*-naphto[2,1-*b*]pyran 1f. Yellow solid; yield 66%; 1.5g; mp 228 °C; IR (ν_{max}, cm^{-1}) 3342 and 3456 (NH_2), 2182 (C≡N). ^1H NMR (DMSO-d_6, 300 MHz) δ_H, ppm: 3.36 (s, 3H, OCH_3), 5.58 (s, 1H, H_4), 6.73-7.90 (m, 10H, Ar-H), 7.74 (br, s, 2H, NH_2); ^{13}C NMR (DMSO-d_6, 75 MHz) δ_C, ppm: 32.0 (C_4), 56.4 (OCH_3), 57.4 (C_3), 112.1 (CN), 116.3, 117.2, 120.9, 121.5, 123.4, 125.3, 127.6, 128.4, 128.9, 129.0, 129.6, 130.7, 131.1, 134.1, 147.6, 156.1, 160.6.

2-Amino-3-cyano-4-(*o*,*p*-dimethoxyphenyl)-4*H*-naphto[2,1-*b*]pyran 1g. Yellow solid; yield 30%; 0.7g; mp 188°C; IR (ν_{max}, cm^{-1}) 3335 and 3429 (NH_2), 2185(C≡N). ^1H NMR (DMSO-d_6, 300 MHz) δ_H, ppm: 3.62 (s, 3H, OCH_3), 3.65 (s, 3H, OCH_3), 5.24 (s, 1H, H_4), 6.56-8.88 (m, 9H, Ar-H), 7.40 (br, s, 2H, NH_2); ^{13}C NMR (DMSO-d_6, 75 MHz) δ_C, ppm: 38.1 (C_4), 55.8 (2x OCH_3, 2C), 58.5 (C_3), 111.4 (CN), 112.5, 116.3, 117.2, 119.4, 121.2, 124.2, 125.3, 127.5, 128.9, 129.8, 130.7, 131.2, 138.8, 147.2, 147.9, 149.0, 160.1.

General procedure for the synthesis of 2-[(ethoxyalkyliden)amino]-4-aryl-3-cyano-4*H*-naphto[2,1-*b*]pyrans 2a-n. A solution of naphtopyrans **1** (0.001 mol, 0.3 g) and triethyl orthoester (0.002 mmol, 0.4 g) was heated at reflux in 1,4-dioxane (15 mL) for 72 h in the presence of few drops of acetic acid. The solvent was evaporated and the solid was collected by filtration and purified by recrystallisation with suitable solvent to give compounds **2e-n** in good yields. The 2-[(ethoxymethyliden)amino]-3-cyano-4-aryl-4*H*-naphto[2,1-*b*]pyrans **2a-d** have already been prepared following a procedure reported by Messaâd and al. (14).

2-[(Ethoxyethyliden)amino]-3-cyano-4-phenyl-4*H*-naphto[2,1-*b*]pyran 2e. White powder; yield 65%; 0.24 g; mp 94-97 °C; IR (ν_{max}, cm^{-1}) 2199 (C≡N), 1644 (C=N). ^1H NMR ($CDCl_3$, 300 MHz) δ_H, ppm: 1.34 (t, ^3J= 7.5 Hz, 3H, $OCH_2\underline{CH_3}$), 2.07 (s, 3H, CH_3), 4.29 (q, ^3J= 7.5 Hz, 2H, $O\underline{CH_2}CH_3$), 5.35 (s, 1H, H_4), 7.19-7.83 (m, 11H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C, ppm: 13.8, 18.0, 40.5, 63.7, 76.6, 113.9, 117.0, 118.5, 123.6, 125.1, 127.2, 127.2, 127.4 (2C), 128.4, 129.0 (2C), 129.7, 130.6, 131.4, 143.6, 147.9, 159.8, 168.3.

2-[(Ethoxyethyliden)amino]-3-cyano-4-(*p*-methylphenyl)-4*H*-naphto[2,1-*b*]pyran 2f. White powder; yield 80%; 0.30 g; mp 100-103 °C; IR (ν_{max}, cm^{-1}) 2202 (C≡N), 1639 (C=N). ^1H NMR ($CDCl_3$, 300 MHz) δ_H, ppm: 1.36 (t, ^3J= 7.5 Hz, 3H, $OCH_2\underline{CH_3}$), 2.10 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 4.31 (q, ^3J= 7.5 Hz, 2H, $O\underline{CH_2}CH_3$), 5.31 (s, 1H, H_4), 7.08-7.82 (m, 10H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C, ppm: 14.0, 18.1, 21.1, 40.2, 63.8, 76.7, 114.2, 117.1, 118.8, 123.8, 125.1, 127.4 (2C), 128.5, 129.7 (4C), 130.8, 131.5, 136.9, 140.9, 147.9, 159.8, 168.4.

2-[(Ethoxyethyliden)amino]-3-cyano-4-(*o*-methoxyphenyl)-4*H*-naphto[2,1-*b*]pyran 2g. Yellow powder; yield 92%; 0.28 g; mp 124-125 °C; IR (ν_{max}, cm^{-1}) 2205 (C≡N), 1661 (C=N). ^1H NMR ($CDCl_3$, 300 MHz) δ_H, ppm: 1.34 (t, ^3J= 7.5 Hz, 3H, $OCH_2\underline{CH_3}$), 2.11 (s, 3H, CH_3), 3.90 (s, 3H, OCH_3), 4.32 (q, ^3J= 7.5 Hz, 2H, $O\underline{CH_2}CH_3$), 5.93 (s, 1H, H_4), 6.79-7.79 (m, 10H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C, ppm: 14.0, 18.1, 33.1, 56.0, 63.7, 76.5, 111.3, 114.9, 117.0, 118.7, 121.4, 123.6, 125.1, 127.3, 128.5 (2C), 129.4 (2C), 130.9, 131.4, 132.40, 148.3, 155.9, 160.5, 168.3.

2-[(Ethoxyethyliden)amino]-4-(*p*-chlorophenyl)-3-cyano-4*H*-naphto[2,1-*b*]pyran 2h. White powder; yield 60%; 0.22 g; mp 110-112 °C; IR (ν_{max}, cm^{-1}) 2200 (C≡N), 1658 (C=N). ^1H NMR ($CDCl_3$, 300 MHz) δ_H, ppm: 1.37 (t, ^3J= 7.5 Hz, 3H, $OCH_2\underline{CH_3}$), 2.11 (s, 3H, CH_3), 4.31 (q, ^3J= 7.5 Hz, 2H, $O\underline{CH_2}CH_3$), 5.32 (s, 1H, H_4), 7.19-7.85 (m, 10H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C, ppm: 14.3, 18.6, 40.4, 64.3, 77.0, 113.7, 117.4, 118.9, 123.9, 125.7, 127.8, 129.0 (2C), 129.2 (2C), 129.6, 130.5, 130.8, 131.9, 133.4, 142.6, 148.3, 160.3, 168.8.

2-[(Ethoxyethyliden)amino]-3-cyano-4-(*o*,*p*-dimethoxyphenyl)-4*H*-naphto[2,1-*b*]pyran **2i**. Yellow hite powder; yield 92%; 0.35 g; mp 114-116 °C; IR (ν_{max}, cm^{-1}) 2207 (C≡N), 1664 (C=N). ^{1}H NMR ($CDCl_3$; 300 MHz) δ_H, ppm: 1.33 (t, ^3J= 7.5 Hz, 3H, $OCH_2\underline{CH_3}$), 2.08 (s, 3H, CH_3), 3.78 (s, 6H, 2x OCH_3), 4.28 (q, ^3J= 7.5 Hz, 2H, $O\underline{CH_2}CH_3$), 5. 82 (s, 1H, H_4), 6.73-7.81 (m, 9H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C, ppm: 13.9, 18.1, 40.2, 55.8, 55.9, 63.8, 76.7, 110.5, 111.4, 114.0, 117.0, 118.8, 119.6, 123.8, 125.2, 127.3, 128.5, 129.8, 130.8, 131.5, 136.5, 147.9, 148.1, 149.3, 159.73, 168.4.

2-[(Ethoxypropyliden)amino]-3-cyano-4-phenyl-4*H*-naphto[2,1-*b*]pyran **2j**. White powder; yield 95%; 0.26 g; mp 166-168 °C; IR (ν_{max}, cm^{-1}) 2198 (C≡N), 1663 (C=N). ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H, ppm: 1.16 (t, ^3J= 7.5 Hz, 3H, $CH_2\underline{CH_3}$), 1.34 (t, ^3J= 7.5 Hz, 3H, $OCH_2\underline{CH_3}$), 2.38 (q, ^3J= 7.5 Hz, 2H, $\underline{CH_2}CH_3$), 4.28 (q, ^3J= 7.5 Hz, 2H, $O\underline{CH_2}CH_3$), 5.35 (s, 1H, H_4), 7.19-7.83 (m, 11H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C, ppm: 10.3, 13.8, 25.5, 40.5, 63.6, 76.6, 114.0, 117.0, 118.7, 123.7, 125.1, 127.2, 127.2, 127.4 (2C), 128.4, 128.9 (2C), 129.7, 130.7, 131.5, 143.6, 147.9, 159.6, 171.8.

2-[(Ethoxypropyliden)amino]-3-cyano-4-(*p*-methylphenyl)-4*H*-naphto[2,1-*b*]pyran **2k**. White powder; yield 90%; 0.35 g; mp 112-114 °C; IR (ν_{max}, cm^{-1}) 2199 (C≡N), 1633 (C=N). ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H, ppm: 1.20 (t, ^3J= 7.5 Hz, 3H, $CH_2\underline{CH_3}$), 1.37 (t, ^3J= 7.5 Hz, 3H, $OCH_2\underline{CH_3}$), 2.28 (s, 3H, CH_3), 2.44 (q, ^3J= 7.5 Hz, 2H, $\underline{CH_2}CH_3$), 4.33 (q, ^3J= 7.5 Hz, 2H, $O\underline{CH_2}CH_3$), 5.32 (s, 1H, H_4), 7.08-7.83 (m, 10H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C, ppm: 10.5, 13.9, 21.1, 25.6, 40.2, 63.7, 76.7, 114.2, 117.1, 118.9, 123.8, 125.1, 127.3, 127.4 (2C), 128.5, 129.7 (3C), 130.8, 131.5, 136.8, 140.9, 147.9, 159.6, 171.8.

2-[(Ethoxypropyliden)amino]-3-cyano-4-(*o*-methoxyphenyl)-4*H*-naphto[2,1-*b*]pyran **2l**. Yellow powder; yield 93%; 0.38 g; mp 126 °C; IR (ν_{max}, cm^{-1}) 2197 (C≡N),1643 (C=N). ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H, ppm: 1.20 (t, ^3J= 7.5 Hz, 3H, $CH_2\underline{CH_3}$), 1.36 (t, ^3J= 7.5 Hz, 3H, $OCH_2\underline{CH_3}$), 2.42 (q, ^3J= 7.5 Hz, 2H, $\underline{CH_2}CH_3$), 3.99 (s, 3H, OCH_3), 4.32 (q, ^3J= 7.5 Hz, 2H, $O\underline{CH_2}CH_3$), 5.93 (s, 1H, H_4), 6.76-7.79 (m, 10H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C, ppm: 10.5, 13.9, 25.5, 33.0, 56.0, 63.6, 76.2, 111.2, 115.0, 116.9, 118.8, 121.3, 123.6, 125.0, 127.2, 128.4 (2C),129.3 (2C), 130.9, 131.4, 132.4, 148.3, 155.9, 160.3, 171.7.

2-[(Ethoxypropyliden)amino]-3-cyano-4-(*p*-chlorophenyl)-4*H*-naphto[2,1-*b*]pyran **2m**. White powder; yield 95%; 0.36 g; mp 92 °C; IR (ν_{max}, cm^{-1}) 2203 (C≡N), 1652 (C=N). ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H, ppm: 1.20 (t, ^3J= 7.5 Hz, 3H, $CH_2\underline{CH_3}$), 1.36 (t, ^3J= 7.5 Hz, 3H, $OCH_2\underline{CH_3}$), 2.39 (q, ^3J= 7.5 Hz, 2H, $\underline{CH_2}CH_3$), 4.31 (q, ^3J= 7.5 Hz, 2H, $O\underline{CH_2}CH_3$), 5.32 (s, 1H, H_4), 7.17-7.84 (m, 11H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C, ppm: 10.5, 13.9, 25.6, 29.8, 40.0, 63.8, 76.3, 113.4, 117.1, 118.6, 123.6, 125.3, 127.4, 128.7 (2C), 128.8, 129.2, 130.1, 130.5, 131.5, 133.1, 142.3, 147.9, 159.8, 171.9.

2-[(Ethoxypropyliden)amino]-3-cyano-4-(*o*,*p*-dimethoxyphenyl)-4*H*-naphto[2,1-*b*]pyran **2n**. Yellow powder; yield 81%; 0.16 g; mp 52 °C; IR (ν_{max}, cm^{-1}) 2203 (C≡N), 1655 (C=N). ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H, ppm: 1.19 (t, ^3J= 7.5 Hz, 3H, $CH_2\underline{CH_3}$), 1.35 (t, ^3J= 7.5 Hz, 3H, $OCH_2\underline{CH_3}$), 2.42 (q, ^3J= 7.5 Hz, 2H, $\underline{CH_2}CH_3$), 3.79 (s, 6H, 2x OCH_3), 4.30 (q, ^3J= 7.5 Hz, 2H, $O\underline{CH_2}CH_3$), 5.29 (s, 1H, H_4), 6.75-7.82 (m, 9H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C, ppm:

10.8, 14.2, 25.9, 40.5, 56.1, 56.2, 64.1, 77.2, 110.8, 111.7, 114.8, 117.4, 119.2, 120.0, 124.1, 125.5, 127.6, 128.9, 130.1, 131.1, 131.8, 136.8, 148.2, 148.4, 149.6, 159.8, 172.2.

General procedure for the synthesis of 11-aryl-1,12-dihydro-11*H*-naphtopyrano[2,3-*d*]pyrimidines 3a-k. The method of preparation of these naphtopyranopyrimidines **3a-d** has already been presented previously by Messaâd and al. (15). Following this typical experiment, compounds **3a-d** were obtained by refluxing, for 24 h, a solution of imidates **2** (0.001 mol, 0.4 g) with one equivalent of tosylhydrazine (0.001 mol, 0.2 g) in toluene (30 mL) with the presence of few drops of acetic acid. The solid product which formed was filtered and washed several times with ether. Based on this protocol, we could easily obtain the new compounds **3e-k**.

11-(*p*-Chlorophenyl)-12-imino-N^1-tosylamino-1,12-dihydro-11*H*-naphtopyrano[2,3-*d*]pyrimidine 3e. White powder; yield 50%; 0.35 g; mp 290-292 ºC; IR (ν_{max}, cm^{-1}) 1586 and 1644 (C=N). MS (APCI+) m/z (%) = 529 ($M+H^+$, 100), 358 (M-NHTs, 4). Anal.Calcd for $C_{28}H_{21}ClN_4O_3S$ (528.5) : C, 63.57; H, 4.00; Cl, 6.70; N, 10.59; S, 6.06 %. Found: C, 63.52; H, 4.15; Cl, 6.53; N, 10.63; S, 5.79 %.

12-Imino-2-methyl-11-(*p*-methylphenyl)-N^1-tosylamino-1,12-dihydro-11*H*-naphtopyrano[2,3-*d*]pyrimidine 3f. White powder; yield 37%; 0.20 g; mp 281-283 ºC; IR (ν_{max}, cm^{-1}) 1623 and 1637 (C=N). MS (APCI+) m/z (%) = 523 ($M+H^+$, 100), 368 ($C_{23}H_{20}N_4O$, 2), 354 ($C_{22}H_{18}N_4O$, 5). Anal.Calcd for $C_{30}H_{26}N_4O_3S$ (522): C, 68.95; H, 5.01; N, 10.72; S, 6.14 %. Found: C, 68.69; H, 5.30; N, 10.46; S, 5.92 %.

12-Imino-2-methyl-11-(*o*-methoxyphenyl)-N^1-tosylamino-1,12-dihydro-11*H*-naphtopyrano[2,3-*d*]pyrimidine 3g. White powder; yield 31%; 0.16 g; mp 254-257 ºC; IR (ν_{max}, cm^{-1}) 1659 and 1679 (C=N). MS (APCI+) m/z (%) = 539 ($M+H^+$, 100), 385 ($C_{23}H_{21}N_4O_2$, 2), 216 (M-NHTs, OCH_3 and CH_3, 3). Anal.Calcd for $C_{30}H_{26}N_4O_4S$ (538): C, 66.90; H, 4.87; N, 10.40; S, 6.20 %. Found: C, 66.87; H, 5.02; N, 10.17; S, 6.31 %.

11-(*p*-Chlorophenyl)-2-methyl-N^1-tosylamino-1,12-dihydro-11*H*-naphtopyrano[2,3-*d*]pyrimidine 3h. White powder; yield 20%; 0.08 g; mp 290-292 ºC; IR (ν_{max}, cm^{-1}) 1632 and 1670 (C=N). MS (APCI+) m/z (%) = 543 ($M+H^+$, 100). Anal.Calcd for $C_{29}H_{23}ClN_4O_3S$ (542.5): C, 64.14; H, 4.27; Cl, 6.53; N, 10.32; S, 5.90 %. Found: C, 63.98; H, 4.12; Cl, 6.53; N, 10.24; S, 5.81 %.

2-Ethyl-12-imino-11-(*o*-methoxyphenyl)-N^1-tosylamino-1,12-dihydro-11*H*-naphtopyrano[2,3-*d*]pyrimidine 3i. White powder; yield 40%; 0.16 g; mp 234-236 ºC; IR (ν_{max}, cm^{-1}) 1643 and 1578 (C=N). MS (APCI+) m/z (%) = 553 ($M+H^+$, 100), 400 ($C_{21}H_{12}N_4O_3S$, 4), 382 (M-NHTs, 2). Anal.Calcd for $C_{31}H_{28}N_4O_4S$ (552): C, 67.37; H, 5.11; N, 10.14; S, 5.80 %. Found: C, 67.40; H, 5.22; N, 9.98; S, 6.11 %.

11-(*p*-Chlorophenyl)-2-ethyl-12-imino-N^1-tosylamino-1,12-dihydro-11*H*-naphtopyrano[2,3-*d*]pyrimidine 3j. White powder; yield 40%; 0.15 g; mp 258-260 ºC; IR (ν_{max}, cm^{-1}) 1641 and 1596 (C=N). MS (APCI+) m/z (%) = 557 ($M+H^+$, 100), 386 (M-NHTs, 2). Anal.Calcd for

$C_{30}H_{25}ClN_4O_3S$ (556.5): C, 64.68; H, 4.52; N, 10.06; S, 5.76 %. Found: C, 64.49; H, 4.65; N, 9.82; S, 5.71 %.

11-(*o*,*p*-Dimethoxyphenyl)-2-ethyl-N^1-tosylamino-1,12-dihydro-11*H*-naphtopyrano[2,3-*d*]pyrimidine 3k. White powder; yield 40%; 0.15 g; mp 274-276 ºC; IR (ν_{max}, cm^{-1}) 1637 and 1594 (C=N). MS (APCI+) m/z 583 ($M+H^+$, 100), 430 (M- $(OCH_3)_2C_6H_3$ and CH_3, 4), 414 (M-2xOCH_3, CH_3 and $CH_3C_6H_4$, 7). Anal.Calcd for $C_{32}H_{30}N_4O_5S$ (582): C, 65.96; H, 5.19; N, 9.62; S, 5.50 %. Found: C, 65.78; H, 4.95; N, 9.53; S, 5.36 %.

General procedure for the synthesis of 14-aryl-14*H*-naphto[2,1-*b*]pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidines 5a-g. A solution of compounds **3** (0.01 mmol, 0.5g) was treated with an excess of triethyl orthoformate (5 mL). The mixture was stirred under reflux for 48 h. After cooling, the white solid obtained, was filtered, washed and dried to obtain compounds **5a-g**.

14-Phenyl-14*H*-naphto[2,1-*b*]pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine 5a. Yield 30%; 0.15 g; mp 278-280 ºC; IR (ν_{max}, cm^{-1}) 1617 and 1633 (C=N). ^1H NMR ($CDCl_3$, 300 MHz) δ_H, ppm: 6.35 (s, 1H, H_{14}), 7.06-8.10 (m, 11H, Ar-H), 8.65 (s, 1H, H_2), 9.67 (s, 1H, H_5); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C, ppm: 37.1, 102.8, 114.9, 117.5, 123.5, 125.2, 127.0, 127.4, 128.3 (2C), 128.5 (2C), 128.7, 130.0, 130.3, 131.2, 140.5, 143.1, 148.0, 151.9, 153.0, 156.6; MS (APCI+) m/z (%) = 350 ($M^{+\cdot}$, 24), 273 (M-C_6H_5, 100).

14-(*o*-Methoxyphenyl)-14*H*-naphto[2,1-*b*]pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine 5b. Yield 45%; 0.21 g; mp 266-268 ºC; IR (ν_{max}, cm^{-1}) 1617 and 1632 (C=N). ^1H NMR ($CDCl_3$, 300 MHz) δ_H, ppm: 3.89 (s, 3H, OCH_3), 6.64 (s, 1H, H_{14}), 6.80-8.26 (m, 10H, Ar-H), 8.30 (s, 1H, H_2), 9.14 (s, 1H, H_5); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C, ppm: 33.3, 56.1, 103.5, 112.0, 115.5, 117.6, 121.1, 123.7, 125.1, 127.3, 128.7, 128.9, 129.6, 131.0, 131.2, 131.5, 131.6, 138.5, 148.7, 152.9, 154.8, 156.9, 156.9; MS (APCI+) m/z (%) = 380 ($M^{+\cdot}$, 65), 322 ($C_{21}H_{12}N_3O$, 34), 273 (M-$OCH_3C_6H_4$, 100). Anal. Calcd for $C_{23}H_{16}N_4O_2$ (380) : C, 72.62; H, 4.24; N, 14.73 %. Found: C, 72.49; H, 4.52; N, 14.55 %.

14-(*p*-Chlorophenyl)-14*H*-naphto[2,1-*b*]pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine 5c. Yield 37%; 0.18 g; mp 245-247ºC. ^1H NMR ($CDCl_3$, 500 MHz) δ_H, ppm: 6.38 (s, 1H, H_{14}), 7.26-8.07 (m, 10H, Ar-H), 8.66 (s, 1H, H_2), 9.68 (s, 1H, H_5); ^{13}C NMR ($CDCl_3$, 125 MHz) δ_C, ppm: 36.5, 102.2, 114.3, 117.6, 123.5, 125.3, 127.5, 128.5 (2C), 128.7, 130.2 (2C), 130.2 (2C), 131.2, 131.6, 140.6, 142.0, 148.0, 151.8, 153.0, 156.6; MS (APCI+) m/z (%) = 384 ($M^{+\cdot}$, 21), 273 (M-ClC_6H_5, 100).

5-Methyl-14-(*p*-methylphenyl)-14*H*-naphto[2,1-*b*]pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine 5d. Yield 37%; 0.19 g; mp 220-223 ºC; IR (ν_{max}, cm^{-1}) 1620 and 1633 (C=N). ^1H NMR ($CDCl_3$, 300 MHz) δ_H, ppm: 2.19 (s, 3H, CH_3), 2.96 (s, 3H, CH_3), 6.33 (s, 1H, H_{14}), 7.00-8.01 (m, 10H, Ar-H), 8.34 (s, 1H, H_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C, ppm: 19.5, 20.9, 37.3, 101.7, 115.2, 117.6, 123.4, 125.0, 127.3, 128.1 (2C), 128.5, 129.3 (2C), 129.7, 130.9, 131.5, 136.8, 140.0, 148.6, 149.1, 152.7, 153.3, 155.5; MS (APCI+) m/z (%) = 379 ($M^{+\cdot}$, 100), 288

(M-$CH_3C_6H_4$, 23), 246 ($C_{15}H_8N_3O$, 90). Anal. Calcd for $C_{24}H_{18}N_4O$ (378) : C, 76.17; H, 4.79; N, 14.81 %. Found: C, 76.28; H, 4.80; N, 14.59 %.

14-(*o*-Methoxyphenyl)-5-methyl-14*H*-naphto[2,1-*b*]pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine 5e. Yield 60%; 0.31 g; mp 249-251 ºC; IR (ν_{max}, cm^{-1}) 1619 and 1635 (C=N). ^1H NMR ($CDCl_3$, 300 MHz) δ_H, ppm: 2.86 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 6.47 (s, 1H, H_{14}), 6.77-8.23 (m, 10H, Ar-H), 8.51 (s, 1H, H_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C, ppm: 19.2, 32.3, 55.9, 99.8, 112.1, 115.2, 117.4, 120.6, 123.2, 124.8, 127.1, 128.4, 128.5, 129.3, 130.5, 130.7, 130.8, 131.4, 148.1, 149.3, 152.0, 153.1, 155.7, 156.3; MS (APCI+) m/z (%) = 394 ($M^{+\cdot}$, 75), 336 (M-OCH_3 and NCH, 35), 287(M-$OCH_3C_6H_4$, 100).

5-Ethyl-14-(*p*-chlorophenyl)-14*H*-naphto[2,1-*b*]pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine 5f. Yield 40%; 0.19 g; mp 204-206 ºC; IR (ν_{max}, cm^{-1}) 1616 and 1633 (C=N). ^1H NMR ($CDCl_3$, 300 MHz) δ_H, ppm: 1.51 (t, ^3J= 7.0 Hz, 3H, $CH_2\underline{CH_3}$), 3.33 (q, ^3J= 7.0Hz, 2H, $\underline{CH_2}CH_3$), 6.34 (s, 1H, H_{14}), 7.16-7.92 (m, 10H, Ar-H), 8.33 (s, 1H, H_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C, ppm: 9.8, 25.9, 37.1, 100.8, 114.5, 117.6, 123.3, 125.2, 127.4, 128.7, 128.7 (2C), 129.7 (2C), 130.0, 130.7, 131.5, 132.9, 141.3, 148.7, 152.6, 153.4, 153.5, 155.3; MS (APCI+) m/z (%) = 412 ($M^{+\cdot}$, 15), 301(M-ClC_6H_4, 100), 286 (M-ClC_6H_4 and CH_3, 7). Anal. Calcd for $C_{24}H_{17}ClN_4O$ (412.5) : C, 69.82; H, 4.15; N, 13.57 %. Found: C, 69.58; H, 4.45; N, 13.28 %.

5-Ethyl-14-(*o*-methoxyphenyl)-14*H*-naphto[2,1-*b*]pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine 5g. Yield 50%; 0.24 g; mp 252-254 ºC. ^1H NMR ($CDCl_3$, 300 MHz) δ_H, ppm: 1.38 (t, ^3J= 7.2 Hz, 3H, $CH_2\underline{CH_3}$), 3.30 (q, ^3J= 7.2 Hz, 2H, $\underline{CH_2}CH_3$), 3.82 (s, 3H, OCH_3), 6.56 (s, 1H, H_{14}), 6.79-8.22 (m, 10H, Ar-H), 8.54 (s, 1H, H_2); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C, ppm: 9.3, 25.1, 32.2, 56.0, 99.8, 112.2, 115.3, 117.5, 120.7, 123.2, 124.8, 127.1, 128.4, 128.6, 129.4, 130.5, 130.7, 130.9, 131.5, 148.2, 152.1, 152.9, 153.4, 155.7, 156.3; MS (APCI+) m/z (%) = 408 ($M^{+\cdot}$, 71), 350 (M-OCH_3 and NCH, 35), 301 (M-$OCH_3C_6H_4$, 100), 286 (M-$OCH_3C_6H_4$ and CH_3, 11).

Conclusion

To sum up, in this work we have reported the synthesis of a number of new 14-aryl-14*H*-naphto[2,1-*b*] pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidines **5** by reacting an excess of triethyl orthoformate with N^1-tosylamino-11-aryl-1,12-dihydro-11*H*-naphtopyrano[2,3-*d*]pyrimidines **3**, readily available in moderate yields from imidates **2** and tosylhydrazine.

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