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Polysubstituted 2,3-dihydrofuro[2,3-*b*]pyridines and 3,4-dihydro-2*H*-pyrano[2,3-*b*]pyridines via microwave-activated inverse electron demand Diels–Alder reactions

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Abstract—Polysubstituted 2,3-dihydrofuro[2,3-*b*]pyridines and 3,4-dihydro-2*H*-pyrano[2,3-*b*]pyridines have been synthesized from 1,2,4-triazines using the inverse electron Diels–Alder reaction. For this purpose, 3-methylsulfanyl-1,2,4-triazines were reacted with several nucleophiles allowing the formation of appropriately substituted alkynes to undergo the intramolecular inverse electron demand Diels–Alder reaction. Sealed-tube microwave activation of the cycloaddition reaction has proved to be very efficient and allowed shorter reaction times. This strategy enabled an efficient synthesis of 3-hydroxy-2,3-dihydrofuro[2,3-*b*]pyridines and 4-hydroxy-3,4-dihydro-2*H*-pyrano[2,3-*b*]-pyridines with several points of diversity on the bicyclic scaffold.
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1. Introduction

Inverse electron demand Diels–Alder reactions of heterocyclic azadienes with electron-rich dienophiles have received considerable attention.[1] Among all the electron-deficient heteroaromatic azadiene studied, we were interested in the use of 1,2,4-triazine as part of our on going research on this heterocycle.[2] Many electron-rich dienophiles such as olefins,[3] enamines,[4] indoles,[5] pyrroles,[6] imidazoles,[7] nitriles[8] or alkynes[9] proved to be very efficient. Inverse electron demand Diels–Alder reaction with 1,2,4-triazines, in fact, consist in a Diels–Alder/retro Diels–Alder (with nitrogen exclusion) sequence followed by an extra elimination/aromatization step in the case of 'alkenyl' dienophiles. When enamines were generated in situ as dienophiles, Taylor and Raw have recently reacted the dihydropyridine intermediate in a cascade reaction with an internal dienophile[4d] and described the one-pot synthesis of highly substituted pyridines, employing microwave irradiation or the tethered imine–enamine methodology.[4c,4g] This cycloaddition with 1,2,4-triazines proved to be valuable fundamental reactions for the construction of various heterocyclic compounds.[10]

In the course of our studies on the synthesis of serotoninergic ligands, we were interested in the synthesis of 2,3-dihydrofuro[2,3-*b*]pyridines and 3,4-dihydro-2*H*-pyrano[2,3-*b*]-pyridines. Those heterocycles, when substituted at positions 3 and 4, respectively, on the non-aromatic ring, were not much studied although they may have biological interest due to their structural similarity to quinolines, substituted pyridines, and chromanes.[11] Looking at the literature,[12] only few syntheses were reported. In the last decade, with regards to dihydro[2,3-*b*]pyranopyridine derivatives, 8-azachromanones[13] were used as precursor of 4-hydroxypyrano[2,3-*b*]pyridine.[14] Synthesis of pyranopyridines via a LiCl mediated palladium-catalyzed[15] or zirconium-mediated[16] cyclization as well as an approach using thermal[3,3]sigmatropic rearrangement were mentioned.[17] For dihydrofuropyridine derivatives, Shiotani et al. dealt with some examples in the course of their studies on the preparation and reactivity of furopyridines.[18] Few other syntheses were described[19] and surprisingly, as far as we know and despite the tremendous potential of the inverse electron demand Diels–Alder strategy, only basic 2,3-dihydrofuro[2,3-*b*]pyridines and 3,4-dihydro-2*H*-pyrano-[2,3-*b*]pyridines were reported using this cycloaddition strategy.[3a–c,8a,20]

At this stage, we thought that using judiciously functionalized 1,2,4-triazines with an alkyne moiety as dienophile, could be a very potent synthetic pathway to polysubstituted

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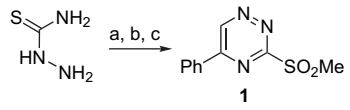
2,3-dihydrofuro[2,3-*b*]pyridines and 3,4-dihydro-2*H*-pyrano[2,3-*b*]pyridines allowing several points of diversity.

2. Results and discussion

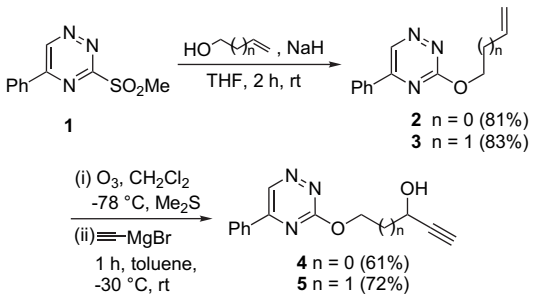
2.1. Synthesis of 3-hydroxy-2,3-dihydrofuro[2,3-*b*]-pyridines and 4-hydroxy-3,4-dihydro-2*H*-pyrano-[2,3-*b*]pyridines

Our strategy was first based on the functionalization of the 1,2,4-triazine ring at position C-3 by nucleophilic substitution with different acetylenic alkoxide. Thus, the 3-methylsulfonyl-1,2,4-triazine **1** was synthesized in agreement with reported procedure[10b] from phenylglyoxal and *S*-methylthiosemicarbazide followed by MCPBA oxidation (Scheme 1).



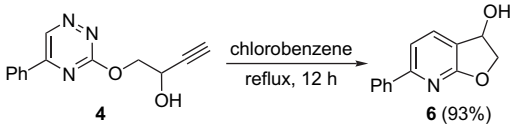
Scheme 1. (a) MeI, EtOH, reflux, 3 h (96%); (b) phenylglyoxal, Na_2CO_3, H_2O, 5 °C, 6 h (82%); (c) MCPBA, CH_2Cl_2, rt, 4 h (87%).

In Scheme 2, nucleophilic displacement of methylsulfinate from **1** with the sodium salt of allylic alcohol (n=0) and homoallylic alcohol (n=1) afforded the 3-(3-propenyloxy)-1,2,4-triazine **2** and 3-(4-butenyloxy)-1,2,4-triazine **3**, respectively. Double bond ozonolysis in dichloromethane at −78 °C gave the corresponding aldehyde, which reacts with 2 equiv of ethynylmagnesium bromide in anhydrous toluene. The resulting alkynols **4** and **5** were isolated in 61 and 72% yield over two steps.



Scheme 2. Synthesis of alkynols **4** and **5**.

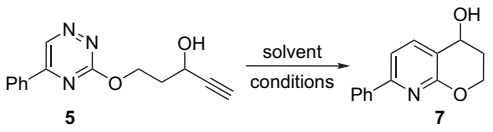
Following the experimental procedure described by Taylor and Macor,[20c] the triazine **4** was engaged in an intramolecular cycloaddition in chlorobenzene at reflux for 12 h to give the novel 3-hydroxy-6-phenyl-2,3-dihydrofuro[2,3-*b*]-pyridine **6** in excellent yield (Scheme 3).



Scheme 3. Synthesis of compound **6** via an intramolecular inverse electron demand Diels–Alder.

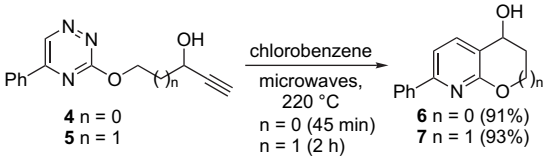
Unfortunately, when refluxing **5** in the same experimental conditions, i.e., in chlorobenzene (134 °C) for 48 h, only the starting material was recovered (Table 1, entry 1). This result is in accordance with Taylor comments about the necessity to use more drastic cyclization conditions, probably due to reduced 'entropic assistance'.[20c] However, to avoid degradation at higher temperature, we turned to microwave activation.[21] Indeed, this technology was applied to 1,2,4-triazines synthesis[22] and inverse electron demand Diels–Alder reaction with alkenyl.[4c,23] Thus, alkynol **5** was carefully heated in a sealed tube (see Section 3) at 220 °C for 2 h under microwave irradiation to afford the more challenging 4-hydroxy-7-phenyl-3,4-dihydro-2*H*-pyrano[2,3-*b*]pyridine **7** with an excellent yield of 93% (Table 1, entry 3). Those microwave benefits (i.e., higher reaction temperature and increased kinetic) are undeniable. Indeed, **5** did not react in refluxing chlorobenzene (vide infra), and at higher temperature in refluxing dichlorobenzene (Table 1, entry 2) or in a sealed tube in chlorobenzene at 220 °C (Table 1, entry 4), the cycloaddition did occur in 48 h with 72 and 90% yields, respectively. Expected that the limiting step might be the inverse electron demand Diels–Alder reaction compared to the nitrogen extrusion in the retro Diels–Alder step, we were curious to evaluate if the former cycloaddition could be activated at high pressure. Indeed, few cases of hyperbaric intramolecular Diels–Alder cycloadditions were described. The results show limited but consistent yield improvement.[24] Thus, **5** was reacted in dichloromethane at 11.3 kbar for 48 h at room temperature. The starting material was completely recovered indicating that pressure has no effect on this type of cycloaddition.

Table 1. Cycloaddition activation conditions



Entry	Experimental conditions	Solvent	T (°C)	Reaction time (h)	Yield (%)
1	Reflux	Chlorobenzene	134	48	0
2	Reflux	Dichlorobenzene	178	48	72
3	Microwaves (sealed tube)	Chlorobenzene	220	2	93
4	Classical heat (sealed tube)	Chlorobenzene	220	48	90

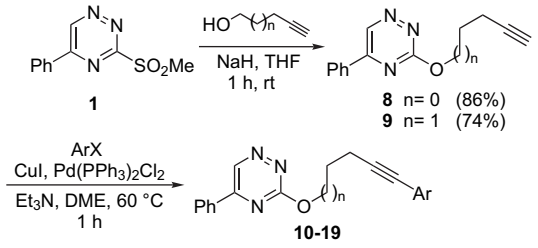
Improved experimental conditions were then applied to compound **4**. In this case, microwave heating at 220 °C for only 45 min (in contrast to 12 h in classical thermal conditions) was sufficient to isolate the cycloadduct **6** in 91% yield (Scheme 4).



Scheme 4. Intramolecular inverse electron demand Diels–Alder reaction under microwave irradiation.

2.2. Synthesis of 4-substituted-2,3-dihydrofuro[2,3-*b*]-pyridines and 5-substituted-3,4-dihydro-2*H*-pyrano[2,3-*b*]pyridines

In order to allow functionalization on the final pyridine ring, to extend diversity and to evaluate the reactivity of bis-substituted alkynes towards the inverse electron demand Diels–Alder reaction, we decided to prepare a series of aryl- and heteroarylalkynes (**10**–**19**) via the sequence described in Scheme 5.

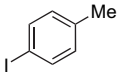
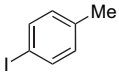
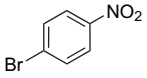
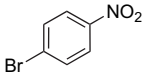
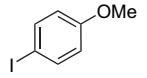
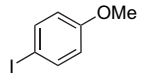


Scheme 5. Synthesis of arylalkynes **10**–**19**.

The methylsulfone **1** was substituted by propargylic alcohol (n=0) and homopropargylic alcohol (n=1) in the presence of NaH in THF. The resulting terminal alkynes **8** and **9** were then engaged in a Sonogashira cross-coupling reaction. Thus, treating 4-bromopyridine in DMF with $Pd(PPh_3)_2Cl_2$ (5 mol %), CuI, and Et_3N, allowed the formation of the corresponding arylalkynes **10** and **15** in, respectively, 46 and 42% yields. In order to improve these moderate yields, the same reaction was performed with DME as solvent. The coupled products **10** and **15** were isolated in 79 and 74% yields (Table 2, entries 1 and 2). With these optimized experimental conditions, 2-iodothiophene (Table 2, entries 3 and 4), 4-iodotoluene (Table 2, entries 5 and 6), *p*-bromonitrobenzene (Table 2, entries 7 and 8), and *p*-iodomethoxybenzene (Table 2, entries 9 and 10) were reacted in DME with $Pd(PPh_3)_2Cl_2$ (5 mol %), CuI, and Et_3N, to afford the corresponding arylalkynes (**10**–**19**) in good yields (62–97%). Inverse electron demand Diels–Alder reactions were then carried out under the experimental conditions described above. As illustrated in Table 3, 4-substituted-2,3-dihydrofuro[2,3-*b*]pyridines (**20**–**24**) were obtained in very good yields (82–99%) at 180 °C. In the case of 5-substituted-3,4-dihydro-2*H*-pyrano[2,3-*b*]pyridines (**25**–**29**) the presence of the aryl moiety generate longer reaction times and higher temperatures (240 °C vs 180 °C). Nevertheless, desired heterocycles were isolated in 72–84% yields. It is noteworthy that even with electron-deficient hetaryl (Table 3, entries 1 and 2) or electron-withdrawing group on the aryl moiety (Table 3, entries 7 and 8) linked to the alkyne, the reaction proceeds in good yields.

With this efficient approach in hand, we investigated what would be the cumulative effect of both alcohol and aryl moieties as a new way toward the synthesis of polysubstituted dihydrofuro- and dihydropyranopyridines. Starting from alkynol **4**, the Sonogashira cross-coupling reaction was performed using the optimized experimental conditions (vide supra). Surprisingly, the resulting compounds **30**–**33** were isolated in moderate yields (Table 4, entries 1, 3, 5, and 7) without any traces of starting material. However, the same reaction carried out with the alkynol **5** gave coupling compounds **34**–**37** in better yields (Table 4, entries 2, 4, 6, and 8).

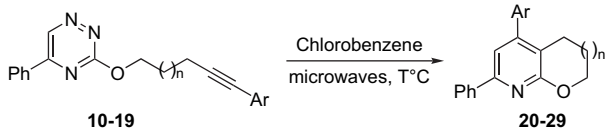
Table 2. Sonogashira cross-coupling reaction

Entry	ArX	Product	Yield[a] (%)
1		**10**, n=0	79
2		**15**, n=1	74
3		**11**, n=0	78
4		**16**, n=1	97
5		**12**, n=0	81
6		**17**, n=1	76
7		**13**, n=0	71
8		**18**, n=1	62
9		**14**, n=0	73
10		**19**, n=1	70

[a] Yield of pure isolated product.

The cycloaddition reaction was first undertaken with alkyne **30** under microwave irradiation in a sealed tube. Under our optimal experimental conditions (i.e., 180 °C for the five-membered ring formation) the trisubstituted heterocycle **38** was isolated in 40% yield (Table 5, entry 1). Only traces

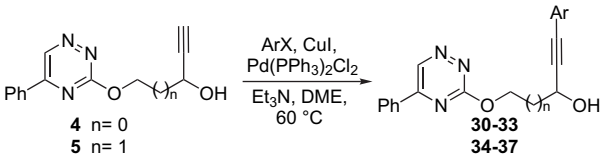
Table 3. Intramolecular inverse electron demand Diels–Alder reactions under microwave irradiation

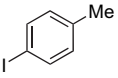
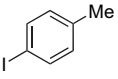
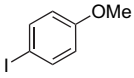
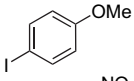
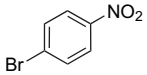
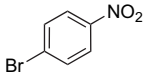


Entry	Aryl	Product	T (°C)/t (h)	Yield[a] (%)
1	Pyrid-4-yl	**20**, n=0	180/3.5	94
2	Pyrid-4-yl	**25**, n=1	240/8	72
3	Thien-2-yl	**21**, n=0	180/2.5	82
4	Thien-2-yl	**26**, n=1	240/8	72
5	*p*-Tolyl	**22**, n=0	180/2.5	99
6	*p*-Tolyl	**27**, n=1	240/6	84
7	*p*-Nitrophenyl	**23**, n=0	180/4	74
8	*p*-Nitrophenyl	**28**, n=1	240/8	67
9	*p*-Methoxyphenyl	**24**, n=0	180/3	83
10	*p*-Methoxyphenyl	**29**, n=1	240/6	79

[a] Yield of pure isolated product.

Table 4. Sonogashira cross-coupling reactions from alkynols **4** and **5**



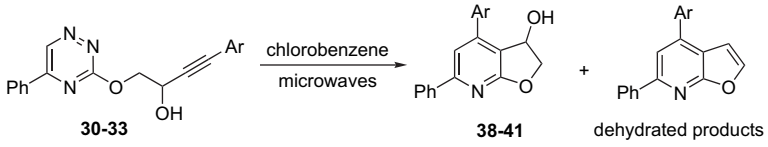
Entry	ArX	Product	*t* (h)	Yield[a] (%)
1		**30**, *n*=0	1	53
2		**34**, *n*=1	3	70
3		**31**, *n*=0	1	49
4		**35**, *n*=1	3	81
5		**32**, *n*=0	1	55
6		**36**, *n*=1	1	64
7		**33**, *n*=0	1	42
8		**37**, *n*=1	4	47

[a] Yield of pure isolated product.

of the corresponding dehydrated compound were observed. In order to minimize degradation products, the reaction was done at 160 °C for 1.5 h, **38** was isolated in only 31% yield with traces of dehydrated compound. From these results, it appears that reactions carried out at lower temperature need longer reaction times and consequently increase the amount of degradation products. Using the former conditions, this approach was then extended to other aryl substituents as reported in Table 5. In all cases, dihydrofuropyridine derivatives were isolated in moderate to good yields with traces of the dehydrated compounds.

We then turned our attention to alkynol **34**. We were pleased to obtain 40% yield of the dihydropyranopyridine **42** at 200 °C (optimal conditions for the six-membered ring formation). Unfortunately, we have noted the presence of 16% of the dehydrated compound **45**. To avoid this side reaction, the cycloaddition reaction was carried out at lower temperature. No improvement was observed as the formation of **45** (5%) occurred whereas the starting material was still present (26%) in the mixture (Table 6, entry 2). The same result was observed with alkyne **36** (Table 6, entries 6 and 7). At higher temperature, **34** and **35** only gave the dehydrated products **45** and **46**, respectively (Table 6, entry 5). It is noteworthy that for the nitro derivative **37**, only degradation products were observed (Table 6, entry 8). These two last examples show that the nature of the substituents on the aryl moiety have an impact on the efficiency of the cycloaddition. In all cases, the dehydration side reaction seems to occur after the inverse electron demand Diels–Alder reaction as we never observed formation of any enyne derivatives.

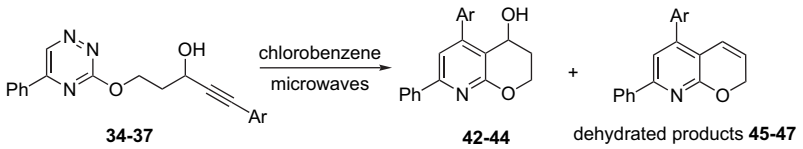
Table 5. Inverse electron demand Diels–Alder reactions from alkynols **30–33**



Entry	Starting alkynol (Ar)	*T* (°C)/*t* (min)	Alcohols (yield %)[a]	Dehydrated product
1	**30** (Thien-2-yl)	180/45	**38** (40)	Traces
2	**31** (*p*-Tolyl)	180/60	**39** (40)	Traces
3	**32** (*p*-Methoxyphenyl)	180/45	**40** (82)	Traces
4	**33** (*p*-Nitrophenyl)	180/90	**41** (34)	Traces

[a] Yield of pure isolated product.

Table 6. Inverse electron demand Diels–Alder reactions from alkynols **34–37**



Entry	Starting alkynol (Ar)	*T* (°C)/*t* (h)	Alcohol (yield %)[a]	Dehydrated product (yield %)[a]	Recovered starting material (yield %)[a]
1	**34** (Thien-2-yl)	200/1	**42** (40)	**45** (16)	—
2	**34** (Thien-2-yl)	180/4.5	**42** (21)	**45** (5)	**34** (26)
3	**34** (Thien-2-yl)	220/1	—	**45** (66)	—
4	**35** (*p*-Tolyl)	200/1.5	**43** (39)	**46** (14)	—
5	**35** (*p*-Tolyl)	220/1	—	**46** (51)	—
6	**36** (*p*-Methoxyphenyl)	180/4.5	**44** (43)	**47** (5)	**36** (50)
7	**36** (*p*-Methoxyphenyl)	200/1	**44** (64)	**47** (14)	—
8	**37** (*p*-Nitrophenyl)	200/2		Degradation	

[a] Yield of pure isolated product.

In this article, we have extended the efficiency of the inverse electron demand Diels–Alder reaction to the synthesis of highly substituted 2,3-dihydrofuro[2,3-*b*]pyridines and 3,4-dihydro-2*H*-pyrano[2,3-*b*]pyridines. The developed approach allows a high diversity of substituent on the bicyclic scaffold. Microwave activation has proven to be very efficient as it allows an easy access to higher temperature with shorter reaction time. Further studies to extend diversity and to limit dehydration side reaction on these heterocycles are underway.

3. Experimental

3.1. General

Microwave-assisted reactions were carried out in a Biotage Initiator microwave synthesis instrument. *Caution*, the microwave apparatus has to be equipped with a safety pressure shutoff. Experiments carried out on 0.3 mmol scale of triazine in a 2–5 mL vial can generate 3–6 bars of pressure. ^{1}H NMR and ^{13}C NMR were recorded on a Bruker Avance DPX250 spectrometer (250.19 MHz ^{1}H, 62.89 MHz ^{13}C) using tetramethylsilane as the internal standard, multiplicities were determined by the DEPT 135 sequence, chemical shifts were reported in parts par million (ppm, δ units). Coupling constants were reported in units of hertz (Hz) if applicable. Infrared (IR) spectra were obtained on Perkin–Elmer Paragon 1000 PC FTIR. Infrared spectra were recorded using NaCl films or KBr pellets. Low-resolution mass spectra (MS) were recorded on a Perkin–Elmer SCIEX API 3000 spectrometer. Melting points were determined in open capillary tubes and are uncorrected. Flash chromatography was performed on silica gel 60 (40–63 mesh). Thin layer chromatography (TLC) was carried out on Merck silica gel 60F_{254} precoated plates. Visualization was made with ultraviolet light. Reactions requiring anhydrous conditions were performed under argon. Ethylene glycol dimethyl ether, toluene and tetrahydrofuran were freshly distilled from sodium/benzophenone under argon prior to use. Dichloromethane was distilled from calcium hydride under argon prior to use. Chemicals products were obtained from the following sources: Aldrich and Acros.

3.2. General procedure for the preparation of alkenes 2 and 3

To a stirred suspension of NaH (0.22 g of 60% oil dispersion, 5.53 mmol) in dry THF (20 mL) under a nitrogen atmosphere, was added the required alcohol (5.53 mmol) at 0 °C. After 10 min, the triazine **1** (1 g, 4.25 mmol) was added. Then, the mixture was warmed to room temperature and monitored by TLC. After complete conversion of the starting material, the reaction was quenched with 40 mL of water and extracted with ethyl acetate (3×60 mL). The organic layer was dried over $MgSO_4$, evaporated, and purified by column chromatography (eluant: petroleum ether–ethyl acetate, 8:2) to give the corresponding ether **2** or **3**.

3.2.1. 3-Allyloxy-5-phenyl-1,2,4-triazine (2). Yield 81%, 0.73 g, as a yellow oil; IR (NaCl) cm^{-1}: 3062, 1914, 1648, 1550, 1188; ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.42 (s, 1H), 8.16 (dd, J=1.2 Hz, J'=7.1 Hz, 2H), 7.62–7.55 (m, 3H), 6.26–6.11 (m, 1H), 5.43 (dd, J=0.9 Hz, J'=17.2 Hz, 1H), 5.36 (dd, J=0.9 Hz, J'=10.4 Hz, 1H), 5.13 (d, J=5.6 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.2 (C), 157.9 (C), 141.6 (CH), 141.5 (C), 132.8 (CH), 132.0 (C), 129.4 (CH), 127.8 (CH), 119.1 (CH_2), 69.1 (CH_2). HRMS calculated for $C_{12}H_{11}N_3O$ 213.09021, found 213.0894.

3.2.2. 3-But-3-enyloxy-5-phenyl-1,2,4-triazine (3). Yield 83%, 0.80 g, as a yellow oil; IR (NaCl) cm^{-1}: 3018, 1640, 1518, 1446, 1218, 1078; ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.25 (s, 1H), 8.01 (dd, J=1.4 Hz, J'=7.5 Hz, 2H), 7.98–7.32 (m, 3H), 5.88–5.71 (m, 1H), 5.02 (dd, J=1.6 Hz, J'=17.2 Hz, 1H), 4.95 (dd, J=1.0 Hz, J'=10.1 Hz, 1H), 4.47 (t, J=6.9 Hz, 2H), 2.67 (q, J=6.9 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.6 (C), 158.0 (C), 141.7 (CH), 134.1 (CH), 133.4 (C), 132.9 (CH), 129.6 (CH), 128.1 (CH), 117.8 (CH_2), 68.0 (CH_2), 33.5 (CH_2). HRMS calculated for $C_{13}H_{13}N_3O$ 227.10586, found 227.1044.

3.3. General procedure for the preparation of alkynols 4 and 5

Ozone in oxygen was bubbled into a solution of alkene **2** or **3** (8.80 mmol) in 120 mL of CH_2Cl_2 and 10 mL of MeOH at −78 °C until the solution turned pale blue. Then, 40 mL of dimethyl sulfide was added dropwise. The mixture was allowed to warm to room temperature over 30 min. The solvents were evaporated in vacuo. The residual oil (10.90 mmol) was dissolved in anhydrous toluene (30 mL), cooled to −30 °C, and ethynylmagnesium bromide (17.60 mmol, 0.5 M in tetrahydrofuran) was added dropwise over a period of 15 min. After 1 h at −30 °C, the reaction mixture was quenched with a saturated aqueous solution of ammonium chloride (60 mL). The separated aqueous layer was extracted with CH_2Cl_2 (3×40 mL) and the combined organic extracts were dried over $MgSO_4$, evaporated, and purified by chromatography with petroleum ether–ethyl acetate (8:2), to give the corresponding alkynol **4** or **5**.

3.3.1. 1-(5-Phenyl-1,2,4-triazin-3-yloxy)-but-3-yn-2-ol (4). Yield 61%, 1.29 g, as a white solid; mp 130–132 °C; IR (KBr) cm^{-1}: 3450, 3260, 3019, 2881, 2121, 1598, 1470, 1215; ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.45 (s, 1H), 8.15 (dd, J=1.6 Hz, J'=8.1 Hz, 2H), 7.65–7.53 (m, 3H), 4.93 (br s, 1H), 4.77 (d, J=5.3 Hz, 2H), 3.16 (d, J=5.0 Hz, OH), 2.55 (d, J=2.2 Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.3 (C), 158.4 (C), 142.1 (CH), 133.1 (CH), 132.9 (C), 129.5 (CH), 128.0 (CH), 80.7 (C), 74.9 (CH_2), 71.5 (C), 61.1 (CH). HRMS calculated for $C_{13}H_{11}N_3O_2$ 241.08513, found 241.0859.

3.3.2. 5-(5-Phenyl-1,2,4-triazin-3-yloxy)-pent-1-yn-3-ol (5). Yield 72%, 1.62 g, as a yellow solid; mp 92–94 °C; IR (KBr) cm^{-1}: 3304, 3013, 2891, 2220, 1542, 1420; ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.42 (s, 1H), 8.15 (dd, J=1.8 Hz, J'=7.5 Hz, 2H), 7.61–7.52 (m, 3H), 4.92–4.75 (m, 3H), 2.79 (d, J=2.2 Hz, 1H, OH), 2.50 (d, J=2.0 Hz, 1H), 2.31 (q, J=6.9 Hz, 2H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 165.4 (C), 158.1 (C), 141.6 (CH), 133.0 (C), 132.9 (CH), 129.5 (CH), 127.9 (CH), 84.2 (C), 73.5 (C), 65.1 (CH_2), 59.3 (CH), 36.8 (CH_2); m/z (M+1)=256. HRMS calculated for $C_{14}H_{13}N_3O_2$ 255.10078, found 255.0999.

3.3.3. 6-Phenyl-2,3-dihydrofuro[2,3-*b*]pyridin-3-ol (6). Compound **4** (0.1 g, 0.41 mmol) was dissolved in chlorobenzene (2 mL), and was heated at 180 °C under microwave irradiation for 45 min. The solvent was removed in vacuo and the residue was purified by chromatography with petroleum ether–ethyl acetate (4:6) to afford **6** (0.079 g, 91% yield), as a yellow solid; mp 111–113 °C; IR (KBr) cm^{-1}: 3258, 3017, 1605, 1576, 1413, 1214; ^1H NMR (250 MHz, $CDCl_3$) δ 7.87 (dd, J=1.9 Hz, J'=7.8 Hz, 2H), 7.61 (d, J=7.9 Hz, 1H), 7.47–7.39 (m, 3H), 7.19 (d, J=7.9 Hz, 1H), 5.38–5.31 (m, 1H), 4.56 (dd, J=6.9 Hz, J'=10.7 Hz, 1H), 4.43 (dd, J=2.8 Hz, J'=10.7 Hz, 1H), 3.54 (d, J=8.1 Hz, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 168.1 (C), 157.8 (C), 138.4 (C), 135.8 (CH), 129.3 (CH), 128.7 (CH), 127.1 (CH), 119.5 (C), 114.0 (CH), 78.2 (CH_2), 70.1 (CH); *m/z* (M+1)=214. Anal. Calcd for $C_{13}H_{11}NO_2$+H_2O (33%): C, 71.71; H, 5.32; N, 6.43. Found: C, 71.72; H, 4.94; N, 6.46.

3.3.4. 7-Phenyl-3,4-dihydro-2*H*-pyrano[2,3-*b*]pyridin-4-ol (7). Compound **5** (0.1 g, 0.39 mmol) was dissolved in chlorobenzene (2 mL), and was heated at 220 °C under microwave irradiation for 2 h. The solvent was removed in vacuo and the residue was purified by chromatography with petroleum ether–ethyl acetate (6:4) to afford **7** (0.082 g, 93% yield) as a red dark oil; IR (KBr) cm^{-1}: 3405, 2960, 1734, 1599, 1473, 1060; ^1H NMR (250 MHz, $CDCl_3$) δ 7.98 (d, J=7.4 Hz, 2H), 7.63 (d, J=7.5 Hz, 1H), 7.45–7.36 (m, 3H), 7.27 (d, J=7.5 Hz, 1H), 5.43 (t, J=4.4 Hz, 1H), 4.48–4.28 (m, 2H), 3.40 (s, 1H), 2.14–1.91 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 160.4 (C), 156.4 (C), 139.7 (CH), 138.3 (C), 129.2 (CH), 128.6 (CH), 127.0 (CH), 118.1 (C), 114.1 (CH), 63.3 (CH), 63.0 (CH_2), 30.7 (CH_2); *m/z* (M+1)=228. Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.60; H, 5.59; N, 6.24.

3.4. General procedure for the preparation of alkynes 8 and 9

To a stirred suspension of NaH (0.22 g of 60% oil dispersion, 5.53 mmol) in dry THF (20 mL) under nitrogen atmosphere was added the appropriated alcohol (5.53 mmol) at 0 °C. After 10 min, the triazine **1** (4.25 mmol) was added. The mixture was then warmed to room temperature and monitored by TLC. After complete conversion of the starting material, the reaction was quenched with 40 mL of water and extracted with ethyl acetate (3×60 mL). The organic layer was dried over $MgSO_4$, evaporated, and purified by column chromatography (eluant: petroleum ether–ethyl acetate, 8:2) to give the corresponding alkene **8** or **9**.

3.4.1. 3-But-3-ynyloxy-5-phenyl-1,2,4-triazine (8).[20c] Yield 86%, 0.82 g, as a yellow solid; mp 103–105 °C (lit.[25] mp 105–106.5 °C); IR (KBr) cm^{-1}: 3227, 3096, 2980, 2241, 1597, 1413; ^1H NMR (250 MHz, $CDCl_3$) δ 9.43 (s, 1H), 8.19–8.16 (m, 2H), 7.61–7.53 (m, 3H), 4.74 (t, J=7.0 Hz, 2H), 2.83 (dt, J=2.9 Hz, J'=7.0 Hz, 2H), 2.50 (t, J=2.9 Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.2 (C), 158.1 (C), 141.8 (CH), 133.1 (C), 132.9 (CH), 129.5 (CH), 127.9 (CH), 79.9 (C), 70.4 (CH_2), 66.3 (CH), 19.5 (CH_2); *m/z* (M+1)=226.

3.4.2. 3-Pent-4-ynyloxy-5-phenyl-1,2,4-triazine (9).[20c] Yield 74%, 0.75 g, as a yellow solid; mp 85–87 °C (lit.[25] mp 85.5–88 °C); IR (KBr) cm^{-1}: 3065, 3055, 2911, 2115, 1600, 1447; ^1H NMR (250 MHz, $CDCl_3$) δ 9.41 (s, 1H), 8.19–8.15 (m, 2H), 7.63–7.52 (m, 3H), 4.72 (t, J=6.4 Hz, 2H), 2.51–2.45 (m, 2H), 2.20–2.09 (m, 2H), 2.01 (t, J=2.5 Hz, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.5 (C), 158.0 (C), 141.6 (CH), 133.9 (C), 132.9 (CH), 129.4 (CH), 127.9 (CH), 83.2 (C), 69.2 (CH), 67.2 (CH_2), 27.8 (CH_2), 15.3 (CH_2); *m/z* (M+1)=240.

3.5. General procedure for the Sonogashira cross-coupling reaction (10–19 and 30–37)

A solution of the appropriate aryl halide (1.11 mmol) in 2.0 mL of anhydrous ethylene glycol dimethyl ether was treated with alkynes **8** and **9** or alkynols **4** and **5** (1.11 mmol) and Et_3N (3 mL). After 5 min, copper iodide (0.021 g, 0.11 mmol) and bis(triphenylphosphine)-palladium(II) dichloride (0.04 mg, 0.055 mmol) were added. The mixture was then stirred vigorously at 60 °C and monitored by TLC. After complete conversion of the starting material, the mixture was diluted with ethyl acetate and filtered through Celite. The filtrate was washed with brine, dried over $MgSO_4$, evaporated, and purified by column chromatography to give the corresponding compounds **10–19** or **30–33**.

3.5.1. 5-Phenyl-3-(4-pyrid-4-ylbut-3-ynyloxy)-1,2,4-triazine (10). Yield 79%, as a white solid; mp 118–120 °C; IR (KBr) cm^{-1}: 3015, 2200, 1598, 1366, 1214; ^1H NMR (250 MHz, $CDCl_3$) δ 9.45 (s, 1H), 8.52 (d, J=5.8 Hz, 2H), 8.17 (dd, J=1.6 Hz, J'=7.5 Hz, 2H), 7.62–7.52 (m, 3H), 7.27 (d, J=5.8 Hz, 2H), 4.80 (t, J=6.9 Hz, 2H), 3.10 (t, J=6.9 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.0 (C), 158.0 (C), 149.6 (CH), 141.8 (CH), 132.8 (CH), 131.5 (C), 129.3 (CH), 127.8 (CH), 127.7 (C), 125.8 (CH), 90.8 (C), 80.0 (C), 65.93 (CH_2), 20.1 (CH_2); *m/z* (M+1)=303. HRMS calculated for $C_{18}H_{14}N_4O$ 302.11676, found 302.1176.

3.5.2. 5-Phenyl-3-(4-thien-2-ylbut-3-ynyloxy)-1,2,4-triazine (11). Yield 78%, as a red oil; IR (KBr) cm^{-1}: 3015, 2060, 1542, 1022; ^1H NMR (250 MHz, $CDCl_3$) δ 9.43 (s, 1H), 8.15 (d, J=7.5 Hz, 2H), 7.61–7.55 (m, 3H), 7.20–7.55 (m, 2H), 6.91 (dd, J=3.8 Hz, J'=5.1 Hz, 1H), 4.80 (t, J=7.0 Hz, 2H), 3.05 (t, J=7.0 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.2 (C), 158.0 (C), 141.7 (CH), 133.0 (C), 132.8 (CH), 131.7 (CH), 129.4 (CH), 127.9 (CH), 126.8 (CH), 126.5 (CH), 123.4 (C), 89.4 (C), 75.6 (C), 66.2 (CH_2), 20.4 (CH_2); *m/z* (M+1)=308. HRMS calculated for $C_{17}H_{13}N_3OS$ 307.07793, found 307.0764.

3.5.3. 5-Phenyl-3-(4-*p*-tolylbut-3-ynyloxy)-1,2,4-triazine (12). Yield 81%, as a red solid; mp 177–179 °C; IR (KBr) cm^{-1}: 3000, 2241, 1620, 1599, 1542, 1470; ^1H NMR (250 MHz, $CDCl_3$) δ 9.43 (s, 1H), 8.16 (dd, J=0.9 Hz, J'=7.5 Hz, 2H), 7.61–7.51 (m, 3H), 7.29 (d, J=7.8 Hz, 2H), 7.07 (d, J=7.8 Hz, 2H), 4.78 (t, J=7.2 Hz, 2H), 3.02 (t, J=7.2 Hz, 2H), 2.32 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.3 (C), 158.1 (C), 141.8 (CH), 138.1 (C), 133.1 (C), 132.9 (CH), 131.6 (CH), 129.5 (CH), 129.1 (CH), 128.0 (CH), 120.3 (C), 84.4 (C), 82.5 (C), 66.6 (CH_2), 21.5 (CH_3), 20.2 (CH_2); *m/z* (M+1)=316. HRMS calculated for $C_{20}H_{17}N_3O$ 315.13716, found 315.1343.

3.5.4. 3-(4-(4-Nitrophenyl)but-3-ynyloxy)-5-phenyl-1,2,4-triazine (13). Yield 71%, as a yellow solid; mp 154–156 °C; IR (KBr) cm^{-1}: 3165, 2256, 1537, 1463, 1339, 1201; ^1H NMR (250 MHz, $CDCl_3$) δ 9.45 (s, 1H), 8.17 (dd, J=1.5 Hz, J'=7.4 Hz, 2H), 8.13 (d, J=9.1 Hz, 2H), 7.62–7.55 (m, 3H), 7.53 (d, J=9.1 Hz, 2H), 4.82 (t, J=6.9 Hz, 2H), 3.09 (t, J=6.9 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.2 (C), 158.2 (C), 147.0 (C), 142.0 (CH), 133.0 (CH), 133.0 (C), 132.5 (CH), 130.4 (C), 129.5 (CH), 128.0 (CH), 123.6 (CH), 91.5 (C), 80.9 (C), 66.1 (CH_2), 20.4 (CH_2); m/z (M+1)=347. HRMS calculated for $C_{19}H_{14}N_4O_3$ 345.09877, found 345.0995.

3.5.5. 3-[4-(4-Methoxyphenyl)but-3-ynyloxy)-5-phenyl-1,2,4-triazine (14). Yield 73%, as a yellow orange solid; mp 114–116 °C; IR (KBr) cm^{-1}: 3020, 2248, 1325, 1214, 1012; ^1H NMR (250 MHz, $CDCl_3$) δ 9.43 (s, 1H), 8.16 (dd, J=1.2 Hz, J'=8.1 Hz, 2H), 7.61–7.52 (m, 3H), 7.26 (d, J=8.5 Hz, 2H), 6.78 (d, J=8.5 Hz, 2H), 4.78 (t, J=7.2 Hz, 2H), 3.79 (s, 3H), 3.02 (t, J=7.2 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.3 (C), 159.4 (C), 158.1 (C), 141.8 (CH), 133.1 (CH), 132.9 (CH), 132.3 (C), 129.5 (CH), 128.0 (CH), 115.6 (C), 113.9 (CH), 83.7 (C), 82.2 (C), 66.7 (CH_2), 55.3 (CH_3), 20.2 (CH_2); m/z (M+1)=332. HRMS calculated for $C_{20}H_{16}N_3O_2$ $(M-H)^+$ 330.12425, found 330.1210.

3.5.6. 5-Phenyl-3-(4-pyrid-4-ylpent-4-ynyloxy)-1,2,4-triazine (15). Yield 74%, as a yellow solid; mp 120–122 °C; IR (KBr) cm^{-1}: 3390, 3025, 2212, 1614, 1012; ^1H NMR (250 MHz, $CDCl_3$) δ 9.43 (s, 1H), 8.51 (d, J=4.8 Hz, 2H), 8.16 (d, J=6.9 Hz, 2H), 7.64–7.51 (m, 3H), 7.24 (d, J=4.8 Hz, 2H), 4.76 (t, J=6.0 Hz, 2H), 2.71 (t, J=7.0 Hz, 2H), 2.29–2.19 (dt, J=6.0, 7.0 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.4 (C), 158.0 (C), 149.5 (CH), 141.6 (CH), 133.1 (CH), 132.8 (C), 129.4 (CH), 128.6 (CH), 128.4 (C), 127.8 (CH), 94.8 (C), 79.2 (C), 67.1 (CH_2), 27.7 (CH_2), 16.4 (CH_2); m/z (M+1)=317. HRMS calculated for $C_{19}H_{17}N_4O$ $(M+H)^+$ 317.14024, found 317.1405.

3.5.7. 5-Phenyl-3-(5-thien-2-ylpent-4-ynyloxy)-1,2,4-triazine (16). Yield 97%, as a yellow oil; IR (KBr) cm^{-1}: 3430, 3022, 2211, 1646, 1542; ^1H NMR (250 MHz, $CDCl_3$) δ 9.41 (s, 1H), 8.15 (dd, J=1.5 Hz, J'=6.6 Hz, 2H), 7.63–7.50 (m, 3H), 7.11 (dd, J=1.0 Hz, J'=5.1 Hz, 1H), 7.11 (dd, J=1.0 Hz, J'=3.8 Hz, 1H), 6.90 (dd, J=3.8 Hz, J'=5.1 Hz, 1H), 4.75 (t, J=6.4 Hz, 2H), 2.69 (t, J=7.0 Hz, 2H), 2.17 (tt, J=6.4 Hz, J'=7.0 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.5 (C), 158.0 (C), 141.6 (CH), 133.2 (C), 132.8 (CH), 131.3 (CH), 129.4 (CH), 127.9 (CH), 126.8 (CH), 126.2 (CH), 123.8 (C), 92.8 (C), 74.6 (C), 67.3 (CH_2), 28.2 (CH_2), 16.8 (CH_2); m/z (M+1)=322. HRMS calculated for $C_{18}H_{15}N_3OS$ 321.09358, found 321.0928.

3.5.8. 5-Phenyl-3-(5-*p*-tolylpent-4-ynyloxy)-1,2,4-triazine (17). Yield 76%, as a yellow solid; mp 97–99 °C; IR (KBr) cm^{-1}: 3425, 3018, 2194, 1620, 1541, 1241; ^1H NMR (250 MHz, $CDCl_3$) δ 9.40 (s, 1H), 8.18–8.14 (dd, J=1.5 Hz, J'=8.1 Hz, 2H), 7.59–7.48 (m, 3H), 7.26 (d, J=8.3 Hz, 2H), 7.04 (d, J=8.3 Hz, 2H), 4.76 (t, J=6.4 Hz, 2H), 2.66 (t, J=7.0 Hz, 2H), 2.31 (s, 3H), 2.16 (tt, J=6.4, 7.0 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.5 (C), 157.9 (C), 141.5 (CH), 137.7 (C), 133.2 (C), 132.7 (CH), 131.5 (CH), 129.4 (CH), 129.0 (CH), 127.9 (CH), 120.6 (C), 87.9 (C), 81.5 (C), 67.4 (CH_2), 28.1 (CH_2), 21.4 (CH_3), 16.3 (CH_2); m/z (M+1)=330. HRMS calculated for $C_{21}H_{19}N_3O$ 329.15281, found 329.1524.

3.5.9. 3-(5-(4-Nitrophenyl)pent-4-ynyloxy)-5-phenyl-1,2,4-triazine (18). Yield 62%, as a green solid; mp 112–114 °C; IR (KBr) cm^{-1}: 3429, 3009, 2229, 1788, 1596, 1541, 1215; ^1H NMR (250 MHz, $CDCl_3$) δ 9.42 (s, 1H, H_6), 8.18 (dd, J=1.5, 7.8 Hz, 2H), 8.14 (d, J=8.4 Hz, 2H), 7.58–7.51 (m, 3H), 7.49 (d, J=8.4 Hz, 2H), 4.77 (t, J=5.9 Hz, 2H), 2.73 (t, J=6.9 Hz, 2H), 2.31–2.20 (tt, J=5.9 Hz, J'=6.9 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.4 (C), 158.1 (C), 146.8 (C), 141.7 (CH), 133.1 (C), 132.9 (C), 132.4 (CH), 130.8 (CH), 129.4 (CH), 127.9 (CH), 123.5 (CH), 95.0 (C), 80.1 (C), 67.1 (CH_2), 27.8 (CH_2), 16.5 (CH_2); m/z (M+1)=361. HRMS calculated for $C_{20}H_{16}N_4O_3$ 360.12224, found 360.1214.

3.5.10. 3-[5-(4-Methoxyphenyl)-pent-4-ynyloxy]-5-phenyl-1,2,4-triazine (19). Yield 70%, as a maroon oil; IR (KBr) cm^{-1}: 3444, 3068, 2214, 1425, 1213; ^1H NMR (250 MHz, $CDCl_3$) δ 9.41 (s, 1H), 8.15 (dd, J=1.8 Hz, J'=8.4 Hz, 2H), 7.60–7.53 (m, 3H), 7.26 (d, J=8.6 Hz, 2H), 6.77 (d, J=8.6 Hz, 2H), 4.76 (t, J=6.2 Hz, 2H), 3.78 (s, 3H), 2.65 (t, J=6.9 Hz, 2H), 2.26 (tt, J=6.2 Hz, J'=6.9 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.5 (C), 159.2 (C), 157.9 (C), 141.5 (CH), 133.2 (C), 133.0 (CH), 132.8 (CH), 129.4 (CH), 127.9 (CH), 115.9 (C), 113.9 (CH), 87.1 (C), 81.2 (C), 67.5 (CH_2), 55.3 (CH_3), 28.2 (CH_2), 16.3 (CH_2); m/z (M+1)=346. HRMS calculated for $C_{21}H_{19}N_3O_2$ 345.14773, found 345.1494.

3.5.11. 1-(5-Phenyl-1,2,4-triazin-3-yloxy)-4-thien-2-yl-but-3-yn-2-ol (30). Yield 53%, as a yellow solid; mp 122–124 °C; IR (KBr) cm^{-1}: 3417, 3017, 1681, 1518, 1215; ^1H NMR (250 MHz, $CDCl_3$) δ 9.42 (s, 1H), 8.18–8.14 (dd, J=1.7 Hz, J'=8.2 Hz, 2H), 7.61–7.48 (m, 3H), 7.24–7.19 (m, 2H), 6.91 (dd, J=3.5 Hz, J'=5.0 Hz, 1H), 5.13 (t, J=5.2 Hz, 1H), 4.82 (d, J=5.2 Hz, 2H), 3.51 (s, 1H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.0 (C), 158.0 (C), 141.6 (CH), 132.7 (CH), 132.6 (CH), 129.2 (CH), 127.7 (CH), 127.5 (CH), 126.7 (CH), 121.7 (C), 89.5 (C), 79.6 (C), 71.1 (CH_2), 61.5 (CH_2); m/z (M+1)=324. HRMS calculated for $C_{17}H_{14}N_3O_2S$ $(M+H)^+$ 324.08067, found 324.0808.

3.5.12. 1-(5-Phenyl-1,2,4-triazin-3-yloxy)-4-*p*-tolylbut-3-yn-2-ol (31). Yield 49%, as a yellow solid; mp 132–134 °C; IR (KBr) cm^{-1}: 3460, 1670, 1524, 1411, 1278; ^1H NMR (250 MHz, $CDCl_3$) δ 9.44 (s, 1H), 8.16 (dd, J=1.2 Hz, J'=7.8 Hz, 2H), 7.65–7.53 (m, 3H), 7.33 (d, J=8.1 Hz, 2H), 7.10 (d, J=8.1 Hz, 2H), 5.11 (t, J=5.6 Hz, 1H), 4.84 (t, J=5.6 Hz, 2H), 2.84 (s, 1H, OH), 2.34 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.3 (C), 158.2 (C), 141.9 (CH), 138.9 (C), 133.0 (CH), 132.9 (C), 131.8 (CH), 129.4 (CH), 129.1 (CH), 128.0 (CH), 119.0 (C), 86.6 (C), 85.2 (C), 71.7 (CH_2), 61.7 (CH), 21.5 (CH_3); m/z (M+1)=332. HRMS calculated for $C_{20}H_{18}N_3O_2$ $(M+H)^+$ 332.13990, found 332.1399.

3.5.13. 4-(4-Methoxyphenyl)-1-(5-phenyl-1,2,4-triazin-3-yloxy)-but-3-yn-2-ol (32). Yield 55%, as a yellow solid; mp 120–122 °C; IR (KBr) cm^{-1}: 3244, 3004, 1671, 1509, 1471, 1217; ^1H NMR (250 MHz, $CDCl_3$) δ 9.45 (s, 1H),

8.16 (dd, J=1.2 Hz, J'=7.8 Hz, 2H), 7.62–7.52 (m, 3H), 7.37 (d, J=6.9 Hz, 2H), 6.81 (d, J=6.9 Hz, 2H), 5.10 (t, J=5.6 Hz, 1H), 4.84 (d, J=5.6 Hz, 2H), 3.81 (s, 3H), 2.86 (s, 1H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.3 (C), 159.9 (C), 158.2 (C), 141.9 (CH), 133.4 (CH), 133.0 (CH), 133.0 (C), 129.5 (CH), 128.0 (CH), 114.2 (C), 114.0 (CH), 86.5 (C), 84.3 (C), 71.7 (CH_2), 61.7 (CH), 55.4 (CH_3); m/z (M+1)=348. HRMS calculated for $C_{20}H_{17}N_3O_3$ 347.12699, found 347.1272.

3.5.14. 4-(4-Nitrophenyl)-1-(5-phenyl-1,2,4-triazin-3-yloxy)-but-3-yn-2-ol (33). Yield 42%, as a yellow solid; mp 152–154 °C; IR (KBr) cm^{-1}: 3330, 2270, 1822, 1579, 1518, 1365, 1318, 1087; ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.47 (s, 1H), 8.17 (m, 4H), 7.63–7.54 (m, 5H), 5.18 (t, J=5.3 Hz, 1H), 4.88 (d, J=5.3 Hz, 2H,), 3.28 (s, 1H, OH); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.3 (C), 158.5 (C), 147.5 (C), 142.2 (CH), 133.2 (CH), 132.8 (CH), 132.7 (C), 129.6 (CH), 129.0 (C), 128.0 (C), 123.7 (CH), 91.1 (C), 84.6 (C), 71.3 (CH_2), 61.8 (CH); m/z (M+1)=363. HRMS calculated for $C_{19}H_{14}N_4O_4$ 362.10151, found 362.0998.

3.5.15. 5-(5-Phenyl-1,2,4-triazin-3-yloxy)-1-(thien-2-yl)-pent-1-yn-3-ol (34). Yield 70%, as a maroon solid; mp 94–96 °C; IR (KBr) cm^{-1}: 3356, 2968, 2230, 1672, 1541, 1475, 1256; ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.41 (s, 1H), 8.14 (d, J=6.9 Hz, 2H), 7.60–7.51 (m, 3H), 7.17 (dd, J=0.9 Hz, J'=5.0 Hz, 1H), 7.17 (dd, J=0.9 Hz, J'=3.7 Hz, 1H), 6.91 (dd, J=3.7 Hz, J'=5.0 Hz, 1H), 4.99 (t, J=6.2 Hz, 1H), 4.89 (m, 2H), 2.79 (s, 1H, OH), 2.38 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.4 (C), 158.1 (C), 141.5 (CH), 133.0 (C), 132.9 (CH), 132.4 (CH), 129.4 (CH), 127.9 (CH), 127.4 (CH), 127.0 (CH), 122.3 (C), 93.3 (C), 78.6 (C), 65.1 (CH_2), 60.0 (CH), 36.8 (CH_2); m/z (M+1)=338. HRMS calculated for $C_{18}H_{16}N_3O_2S$ (M+H) 338.09632, found 338.0972.

3.5.16. 5-(5-Phenyl-1,2,4-triazin-3-yloxy)-1-*p*-tolylpent-1-yn-3-ol (35). Yield 81%, as a yellow solid; mp 74–76 °C; IR (KBr) cm^{-1}: 3400, 3018, 1644, 1542, 1398, 1214; ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.41 (s, 1H), 8.14 (d, J=6.5 Hz, 2H), 7.60–7.51 (m, 3H), 7.28 (d, J=8.3 Hz, 2H), 7.06 (d, J=8.3 Hz, 2H), 4.98 (t, J=6.4 Hz, 1H), 4.89 (t, J=6.2 Hz, 2H), 2.43 (m, 3H), 2.32 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.4 (C), 158.1 (C), 141.5 (CH), 138.6 (C), 133.0 (C), 132.8 (CH), 131.6 (CH), 129.4 (CH), 129.0 (CH), 127.9 (CH), 119.4 (C), 88.7 (C), 85.5 (C), 65.2 (CH_2), 60.0 (CH), 37.0 (CH_2), 21.5 (CH_3); m/z (M+1)=346. HRMS calculated for $C_{21}H_{19}N_3O_2$ 345.1477, found 345.1460.

3.5.17. 1-(4-Methoxyphenyl)-5-(5-phenyl-1,2,4-triazin-3-yloxy)-pent-1-yn-3-ol (36). Yield 64%, as a yellow-chestnut oil; IR (KBr) cm^{-1}: 3387, 2947, 2220, 1738, 1609, 1412, 1241; ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.38 (s, 1H), 8.10 (dd, J=1.2 Hz, J'=6.9 Hz, 2H), 7.61–7.47 (m, 3H), 7.31 (d, J=8.4 Hz, 2H), 6.74 (d, J=8.4 Hz, 2H), 4.94 (t, J=5.6 Hz, 1H), 4.85 (t, J=5.4 Hz, 2H), 3.76 (s, 3H), 3.20 (s, 1H, OH), 2.42 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.4 (C), 159.7 (C), 158.0 (C), 141.4 (CH), 133.2 (CH), 133.0 (C), 132.8 (CH), 129.3 (CH), 127.8 (CH), 114.5 (C), 113.9 (CH), 88.1 (C), 85.2 (C), 65.2 (CH_2), 59.9 (CH), 55.2 (CH_3), 37.0 (CH_2); m/z (M+1)=362. HRMS calculated for $C_{21}H_{19}N_3O_3Na$ $(M+Na)^+$ 384.13241, found 383.1322.

3.5.18. 1-(4-Nitrophenyl)-5-(5-phenyl-1,2,4-triazin-3-yloxy)-pent-1-yn-3-ol (37). Yield 64%, as a white solid; mp 144–146 °C; IR (KBr) cm^{-1}: 3440, 3230, 2235, 1810, 1530, 1120; ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.41 (s, 1H), 8.16–8.10 (m, 4H), 7.61–7.52 (m, 5H), 5.04–4.86 (m, 3H), 2.86 (d, J=5.3 Hz, 1H, OH), 2.49–2.41 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 165.4 (C), 158.3 (C), 147.3 (C), 141.8 (CH), 133.1 (C), 132.9 (C), 132.6 (CH), 129.5 (CH), 129.3 (CH), 127.9 (CH), 123.6 (CH), 94.6 (C), 83.5 (C), 64.9 (CH_2), 60.0 (CH), 36.8 (CH_2); m/z (M+1)=377. HRMS calculated for $C_{20}H_{16}N_4O_4$ 376.11716, found 376.1166.

3.6. General procedure for the intramolecular inverse electron demand Diels–Alder reaction

Triazines **10**–**19** or **30**–**37** (0.33 mmol) were dissolved in chlorobenzene (2 mL) and heated at 180–240 °C under microwave irradiation (3–6 bars of pressure can be involved). The reaction was monitored by TLC (reaction time–temperature; see Tables 3, 5 and 6). After complete conversion of the starting material, the reaction was purified by chromatography using petroleum ether–ethyl acetate as eluant to give the desired products **20**–**29** or **38**–**44**.

3.6.1. 6-Phenyl-4-pyrid-4-yl-2,3-dihydrofuro[2,3-*b*]pyridine (20). Compound **20** was obtained as a white solid (94% yield), mp 180–182 °C, after purification by column chromatography (petroleum ether–ethyl acetate, 4:1); IR (KBr) cm^{-1}: 3017, 1612, 1595, 1498, 1210; ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.72 (d, J=5.6 Hz, 2H), 7.99 (dd, J=1.8, 8.1 Hz, 2H), 7.45–7.40 (m, 5H), 7.33 (s, 1H), 4.65 (t, J=8.4 Hz, 2H), 3.34 (t, J=8.4 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 169.5 (C), 156.2 (C), 150.5 (CH), 145.8 (C), 144.6 (C), 138.5 (C), 129.1 (CH), 128.7 (CH), 126.8 (CH), 122.3 (CH), 115.8 (C), 112.5 (CH), 69.2 (CH_2), 28.1 (CH_2); m/z (M+1)=275. Calcd for $C_{18}H_{14}N_2O$: C, 78.81; H, 5.14; N, 10.21. Found: C, 77.95; H, 5.07; N, 10.02.

3.6.2. 6-Phenyl-4-thien-2-yl-2,3-dihydrofuro[2,3-*b*]pyridine (21). Compound **21** was obtained as a dark red oil (82% yield), after purification by column chromatography (petroleum ether–ethyl acetate, 4:1); IR (KBr) cm^{-1}: 3090, 1718, 1592, 1413, 1214; ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.00 (dd, J=2.8 Hz, J'=6.9 Hz, 2H), 7.52–7.38 (m, 6H), 7.16 (dd, J=3.8 Hz, J'=5.3 Hz, 1H), 4.69 (t, J=8.5 Hz, 2H), 3.46 (t, J=8.5 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 169.7 (C), 155.5 (C), 140.5 (C), 139.7 (C), 138.8 (C), 128.8 (CH), 128.6 (CH), 128.1 (CH), 127.3 (CH), 126.8 (CH), 126.8 (CH), 113.5 (C), 110.9 (CH), 68.9 (CH_2), 29.3 (CH_2); m/z (M+1)=280. Anal. Calcd for $C_{17}H_{13}NOS$: C, 73.09; H, 4.69; N, 5.01; S, 11.48. Found: C, 73.56; H, 5.13; N, 4.83; S, 10.66.

3.6.3. 6-Phenyl-4-*p*-tolyl-2,3-dihydrofuro[2,3-*b*]pyridine (22). Compound **22** was obtained as a yellow solid (99% yield), mp 118–120 °C, after purification by column chromatography (petroleum ether–ethyl acetate, 4:1); IR (KBr) cm^{-1}: 3017, 1612, 1599, 1514, 1414, 1213; ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.03 (dd, J=1.2 Hz, J'=8.2 Hz, 2H), 7.46–7.37 (m, 3H), 7.34 (d, J=8.3 Hz, 2H), 7.29 (s, 1H), 7.24 (d, J=8.3 Hz, 2H), 4.61 (t, J=8.5 Hz, 2H), 3.33 (t, J=8.5 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 169.4 (C), 155.5 (C), 147.4 (C), 139.1 (C), 138.8

(C), 135.3 (C), 129.6 (CH), 128.7 (CH), 128.6 (CH), 127.7 (CH), 126.9 (CH), 115.3 (C), 113.2 (CH), 69.1 (CH_2), 28.4 (CH_2), 21.3 (CH_3); *m/z* (M+1)=288. Anal. Calcd for $C_{20}H_{17}NO$: C, 83.60; H, 5.96; N, 4.87. Found: C, 83.70; H, 5.77; N, 4.93.

3.6.4. 4-(4-Nitrophenyl)-6-phenyl-2,3-dihydrofuro[2,3-*b*]pyridine (23). Compound **23** was obtained as a yellow solid (74% yield), mp 160–162 °C, after purification by column chromatography (petroleum ether–ethyl acetate, 4:1); IR (KBr) cm^{-1}: 3018, 1596, 1511, 1344, 1220; ^1H NMR (250 MHz, $CDCl_3$) δ 8.33 (d, J=6.9 Hz, 2H), 8.00 (dd, J=1.9 Hz, J'=8.2 Hz, 2H), 7.70 (d, J=6.9 Hz, 2H), 7.49–7.39 (m, 3H), 7.34 (s, 1H), 4.68 (t, J=8.5 Hz, 2H), 3.34 (t, J=8.5 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 169.5 (C), 156.4 (C), 147.9 (C), 145.2 (C), 144.8 (C), 138.5 (C), 129.3 (CH), 128.8 (CH), 128.8 (CH), 126.9 (CH), 124.2 (CH), 115.8 (C), 112.8 (CH), 69.2 (CH_2), 28.2 (CH_2); *m/z* (M+1)=319. HRMS calculated for $C_{19}H_{14}N_2O_3$ 318.10044, found 318.0994.

3.6.5. 4-(4-Methoxyphenyl)-6-phenyl-2,3-dihydrofuro[2,3-*b*]pyridine (24). Compound **24** was obtained as a white solid (83% yield), mp 136–138 °C, after purification by column chromatography (petroleum ether–ethyl acetate, 4:1); IR (KBr) cm^{-1}: 3032, 1595, 1414, 1228; ^1H NMR (250 MHz, $CDCl_3$) δ 8.03 (dd, J=1.8, 7.8 Hz, 2H), 7.52–7.36 (m, 3H), 7.30 (d, J=6.6 Hz, 2H), 6.96 (d, J=6.6 Hz, 2H), 4.63 (t, J=8.4 Hz, 2H), 3.40 (t, J=8.4 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 169.4 (C), 160.0 (C), 155.4 (C), 147.0 (C), 139.0 (C), 130.5 (C), 129.1 (CH), 128.7 (CH), 128.6 (CH), 126.8 (CH), 115.0 (C), 114.3 (CH), 112.9 (CH), 69.0 (CH_2), 55.4 (CH_3), 28.4 (CH_2); *m/z* (M+1)=304. Anal. Calcd for $C_{20}H_{17}NO_2$: C, 79.19; H, 5.65; N, 4.62. Found: C, 78.88; H, 5.57; N, 4.61.

3.6.6. 7-Phenyl-5-pyrid-4-yl-3,4-dihydro-2*H*-pyrano[2,3-*b*]pyridine (25). Compound **25** was obtained as a yellow solid (72% yield), mp 170–172 °C, after purification by column chromatography (petroleum ether–ethyl acetate, 3:2); IR (KBr) cm^{-1}: 3056, 2942, 1968, 1678, 1592; ^1H NMR (250 MHz, $CDCl_3$) δ 8.72 (d, J=5.6 Hz, 2H), 8.00 (dd, J=1.2 Hz, J'=7.3 Hz, 2H), 7.46–7.34 (m, 4H), 7.30 (d, J=5.6 Hz, 2H), 4.41 (t, J=5.0 Hz, 2H), 2.66 (t, J=6.3 Hz, 2H), 1.95 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 161.3 (C), 154.4 (C), 150.2 (CH), 149.7 (C), 146.9 (C), 138.3 (C), 129.2 (CH), 128.7 (CH), 126.8 (CH), 123.4 (CH), 114.2 (CH), 113.0 (C), 67.3 (CH_2), 23.7 (CH_2), 21.9 (CH_2); *m/z* (M+1)=289. Anal. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59; N, 9.71. Found: C, 78.60; H, 5.43; N, 9.71.

3.6.7. 7-Phenyl-5-thien-2-yl-3,4-dihydro-2*H*-pyrano[2,3-*b*]pyridine (26). Compound **26** was obtained as a yellow oil (72% yield), after purification by column chromatography (petroleum ether–ethyl acetate, 3:2); IR (KBr) cm^{-1}: 2955, 2886, 1592, 1550, 1371; ^1H NMR (250 MHz, $CDCl_3$) δ 8.04 (dd, J=1.9 Hz, J'=8.1 Hz, 2H), 7.47–7.37 (m, 6H), 7.14 (dd, J=1.6, 5.3 Hz, 1H), 4.40 (t, J=5.3 Hz, 2H), 2.91 (t, J=6.6 Hz, 2H), 2.07–1.98 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 161.6 (C), 154.0 (C), 144.7 (C), 139.9 (C), 138.5 (C), 129.0 (CH), 128.6 (CH), 127.9 (CH), 127.6 (CH), 126.9 (CH), 126.8 (CH), 115.1 (CH), 113.3 (C), 67.1 (CH_2), 24.5 (CH_2), 22.1 (CH_2); *m/z* (M+1)=294. Anal. Calcd for $C_{18}H_{15}NOS$: C, 73.69; H, 5.15; N, 4.77; S, 10.93. Found: C, 73.19; H, 4.74; N, 5.33; S, 10.91.

3.6.8. 7-Phenyl-5-*p*-tolyl-3,4-dihydro-2*H*-pyrano[2,3-*b*]pyridine (27). Compound **27** was obtained as a yellow oil (84% yield), after purification by column chromatography (petroleum ether–ethyl acetate, 4:1); IR (KBr) cm^{-1}: 2936, 1602, 1514, 1311; ^1H NMR (250 MHz, $CDCl_3$) δ 8.00 (dd, J=1.6 Hz, J'=8.1 Hz, 2H), 7.45–7.32 (m, 3H), 7.30 (s, 1H), 7.28 (d, J=8.2 Hz, 2H), 7.24 (d, J=8.2 Hz, 2H), 4.39 (t, J=5.0 Hz, 2H), 2.69 (t, J=6.6 Hz, 2H), 2.42 (s, 3H), 1.91 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 161.2 (C), 153.7 (C), 152.6 (C), 138.8 (C), 138.0 (C), 136.1 (C), 129.2 (CH), 128.8 (CH), 128.6 (CH), 128.5 (CH), 126.8 (CH), 115.2 (CH), 113.5 (C), 67.2 (CH_2), 24.0 (CH_2), 22.2 (CH_2), 21.3 (CH_3); *m/z* (M+1)=302. Anal. Calcd for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65. Found: C, 83.76; H, 6.96; N, 4.64.

3.6.9. 5-(4-Nitrophenyl)-7-phenyl-3,4-dihydro-2*H*-pyrano[2,3-*b*]pyridine (28). Compound **28** was obtained as a yellow solid (67% yield), mp 121–123 °C, after purification by column chromatography (petroleum ether–ethyl acetate, 4:1); IR (KBr) cm^{-1}: 3018, 1596, 1344, 1220; ^1H NMR (250 MHz, $CDCl_3$) δ 8.32 (d, J=8.5 Hz, 2H), 8.00 (d, J=6.9 Hz, 2H), 7.55 (d, J=6.9 Hz, 2H), 7.58–7.38 (m, 3H), 7.26 (s, 1H), 4.42 (t, J=5.3 Hz, 2H), 2.64 (t, J=6.3 Hz, 2H), 2.05–1.96 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 161.4 (C), 154.4 (C), 150.2 (C), 147.8 (C), 145.7 (C), 138.2 (C), 129.7 (CH), 129.3 (CH), 128.7 (CH), 126.8 (CH), 123.9 (CH), 114.4 (CH), 113.1 (C), 67.3 (CH_2), 23.8 (CH_2), 21.9 (CH_2); *m/z* (M+1)=333. HRMS calculated for $C_{20}H_{17}N_2O_3$ $(M+H)^+$ 333.12392, found 333.1244.

3.6.10. 5-(4-Methoxyphenyl)-7-phenyl-3,4-dihydro-2*H*-pyrano[2,3-*b*]pyridine (29). Compound **29** was obtained as an orange solid (79% yield), mp 126–128 °C, after purification by column chromatography (petroleum ether–ethyl acetate, 4:1); IR (KBr) cm^{-1}: 3004, 2401, 1600, 1447, 1315; ^1H NMR (250 MHz, $CDCl_3$) δ 8.00 (dd, J=1.3 Hz, J'=7.1 Hz, 2H), 7.45–7.25 (m, 6H), 6.97 (d, J=8.6 Hz, 2H), 4.39 (t, J=5.0 Hz, 2H), 3.85 (s, 3H), 2.70 (t, J=6.3 Hz, 2H), 1.91 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 161.2 (C), 159.6 (C), 153.7 (C), 152.2 (C), 138.8 (C), 131.3 (C), 129.9 (CH), 128.8 (CH), 128.6 (CH), 126.8 (CH), 115.2 (CH), 113.9 (CH), 113.5 (C), 67.2 (CH_2), 55.4 (CH_3), 24.1 (CH_2), 22.2 (CH_2); *m/z* (M+1)=318. Anal. Calcd for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03; N, 4.41. Found: C, 79.54; H, 5.85; N, 4.44.

3.6.11. 6-Phenyl-4-thien-2-yl-2,3-dihydrofuro[2,3-*b*]pyridin-3-ol (38). Compound **38** was obtained as a dark red foam (40% yield), after purification by column chromatography (petroleum ether–ethyl acetate, 4:1); IR (KBr) cm^{-1}: 3416, 3033, 1585, 1457, 1317; ^1H NMR (250 MHz, $CDCl_3$) δ 7.82 (d, J=5.6 Hz, 2H), 7.71 (dd, J=0.9 Hz, J'=3.7 Hz, 1H), 7.34 (dd, J=0.9 Hz, J'=5.0 Hz, 1H), 7.44–7.32 (m, 4H), 7.07 (dd, J=3.7 Hz, J'=5.0 Hz, 1H), 5.45 (dd, J=2.2 Hz, J'=5.6 Hz, 1H), 4.64 (d, J=5.6 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 169.1 (C), 158.2 (C), 142.1 (C), 139.0 (C), 138.1 (C), 129.4 (CH), 129.2 (CH), 128.7 (CH), 128.6 (CH), 128.0 (CH), 127.1 (CH), 114.4 (C), 112.2 (CH), 77.9 (CH_2), 70.1 (CH_2); *m/z* (M+1)=296.

Anal. Calcd for $C_{17}H_{13}NO_2S$: C, 69.13; H, 4.44; N, 4.74; S, 10.86. Found: C, 69.18; H, 4.46; N, 4.69; S, 10.36.

3.6.12. 6-Phenyl-4-*p*-tolyl-2,3-dihydrofuro[2,3-*b*]pyridin-3-ol (39). Compound **39** was obtained as a brown foam (40% yield), after purification by column chromatography (petroleum ether–ethyl acetate, 3:2); IR (KBr) cm^{-1}: 3444, 3034, 1598, 1435, 1278; ^1H NMR (250 MHz, $CDCl_3$) δ 7.95 (d, J=7.8 Hz, 2H), 7.61 (d, J=8.1 Hz, 2H), 7.43–7.34 (m, 4H), 7.25 (d, J=8.1 Hz, 2H), 5.41 (dd, J=3.1 Hz, J'=4.7 Hz, 1H), 4.58 (d, J=4.7 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 168.9 (C), 158.2 (C), 149.9 (C), 139.3 (C), 138.6 (C), 134.3 (C), 129.8 (CH), 129.3 (CH), 128.7 (CH), 128.3 (CH), 127.2 (CH), 116.5 (C), 114.0 (CH), 77.7 (CH_2), 69.9 (CH), 21.4 (CH_3); m/z (M+1)=304. Anal. Calcd for $C_{20}H_{17}NO_2$: C, 79.19; H, 5.65; N, 4.62. Found: C, 79.52; H, 5.47; N, 4.69.

3.6.13. 4-(4-Methoxyphenyl)-6-phenyl-2,3-dihydrofuro[2,3-*b*]pyridin-3-ol (40). Compound **40** was obtained as a yellow-orange solid (82% yield), mp 170–172 °C, after purification by column chromatography (petroleum ether–ethyl acetate, 4:1); IR (KBr) cm^{-1}: 3444, 3014, 1604, 1514, 1441; ^1H NMR (250 MHz, $CDCl_3$) δ 7.92 (d, J=7.8 Hz, 2H), 7.68 (d, J=8.9 Hz, 2H), 7.43–7.35 (m, 4H), 6.97 (d, J=8.9 Hz, 2H), 5.39 (dd, J=3.1 Hz, J'=4.8 Hz, 1H), 4.60 (d, J=4.8 Hz, 2H), 3.86 (s, 3H), 3.08 (s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 169.0 (C), 160.5 (C), 158.1 (C), 149.5 (C), 138.6 (C), 129.8 (CH), 129.6 (C), 129.5 (C), 129.3 (CH), 128.7 (CH), 127.2 (CH), 114.5 (CH), 113.8 (CH), 77.8 (CH_2), 70.0 (CH), 55.5 (CH_3); m/z (M+1)=320. Anal. Calcd for $C_{20}H_{17}NO_2$+H_2O (33%): C, 73.83; H, 5.47; N, 4.30. Found: C, 73.95; H, 5.19; N, 4.41.

3.6.14. 4-(4-Nitrophenyl)-6-phenyl-2,3-dihydrofuro[2,3-*b*]pyridin-3-ol (41). Compound **41** was obtained as a brown oil (34% yield), after purification by column chromatography (petroleum ether–ethyl acetate, 4:1); IR (KBr) cm^{-1}: 3444, 3230, 2170, 1820, 1590, 1335; ^1H NMR (250 MHz, $CDCl_3$) δ 8.33 (dd, J=1.6 Hz, J'=8.5 Hz, 2H), 7.98–7.88 (m, 4H), 7.44–7.41 (m, 3H), 7.36 (s, 1H), 5.35 (dd, J=3.1 Hz, J'=4.7 Hz, 1H), 4.67 (d, J=4.7 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 166.9 (C), 156.9 (C), 145.5 (C), 141.4 (C), 135.8 (C), 135.8 (C), 127.7 (CH), 127.4 (CH), 126.7 (CH), 125.1 (CH), 122.0 (CH), 114.7 (C), 111.7 (CH), 75.2 (CH_2), 67.6 (CH); m/z (M+1)=335. HRMS calculated for $C_{19}H_{14}N_2O_4$ 334.09536, found 334.0937.

3.6.15. 7-Phenyl-5-thien-2-yl-3,4-dihydro-2*H*-pyrano[2,3-*b*]pyridin-4-ol (42). Compound **42** was obtained as a white solid (40% yield), mp 187–189 °C, after purification by column chromatography (petroleum ether–ethyl acetate, 3:2); IR (KBr) cm^{-1}: 3390, 3034, 1684, 1471, 1241; ^1H NMR (250 MHz, $CDCl_3$) δ 8.04 (m, 2H), 7.60 (dd, J=1.2 Hz, J'=3.7 Hz, 1H), 7.58–7.41 (m, 5H), 7.15 (dd, J=3.7 Hz, J'=5.3 Hz, 1H), 4.97–4.92 (m, 1H), 4.68–4.49 (m, 2H), 2.31 (s, 1H, OH), 2.10–2.03 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 161.1 (C), 156.4 (C), 146.2 (C), 138.7 (C), 138.1 (C), 129.5 (CH), 128.9 (CH), 128.7 (CH), 128.1 (CH), 127.5 (CH), 127.1 (CH), 115.7 (CH), 114.0 (C), 62.0 (CH_2), 60.7 (CH), 30.2 (CH_2); m/z (M+1)=310. HRMS calculated for $C_{18}H_{15}NO_2S$ 309.08235, found 309.0808.

3.6.16. 7-Phenyl-5-*p*-tolyl-3,4-dihydro-2*H*-pyrano[2,3-*b*]pyridin-4-ol (43). Compound **43** was obtained as a white solid (39% yield), mp 175–177 °C, after purification by column chromatography (petroleum ether–ethyl acetate, 3:2); IR (KBr) cm^{-1}: 3438, 2939, 1592, 1515, 1397; ^1H NMR (250 MHz, $CDCl_3$) δ 8.02 (d, J=7.5 Hz, 2H), 7.43–7.38 (m, 5H), 7.27 (m, 3H), 4.83 (t, J=2.5 Hz, 1H), 4.64–4.45 (m, 2H), 2.43 (s, 3H), 2.06–1.99 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 160.8 (C), 155.9 (C), 154.1 (C), 138.5 (C), 138.4 (C), 135.3 (C), 129.4 (CH), 129.3 (CH), 128.7 (CH), 128.5 (CH), 127.1 (CH), 115.8 (CH_2), 115.0 (C), 62.1 (CH_2), 60.5 (CH), 30.1 (CH_2), 21.3 (CH_3); m/z (M+1)=318. HRMS calculated for $C_{21}H_{19}NO_2$ 317.14158, found 317.1423.

3.6.17. 5-(4-Methoxyphenyl)-7-phenyl-3,4-dihydro-2*H*-pyrano[2,3-*b*]pyridin-4-ol (44). Compound **44** was obtained as a yellow oil (64% yield), after purification by column chromatography (petroleum ether–ethyl acetate, 4:1); IR (KBr) cm^{-1}: 3368, 3014, 1604, 1519, 1414; ^1H NMR (250 MHz, $CDCl_3$) δ 8.02 (d, J=8.1 Hz, 2H), 7.49–7.40 (m, 5H), 7.30 (s, 1H), 6.99 (d, J=6.5 Hz, 2H), 4.85 (t, J=3.1 Hz, 1H), 4.65–3.87 (m, 2H), 3.87 (s, 3H), 2.04–2.01 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 160.8 (C), 159.9 (C), 156.0 (C), 153.8 (C), 138.4 (C), 130.5 (C), 130.0 (CH), 129.4 (CH), 128.7 (CH), 127.1 (CH), 115.9 (CH), 115.0 (C), 114.1 (CH), 62.1 (CH_2), 60.6 (CH), 55.5 (CH_3), 30.2 (CH_2); m/z (M+1)=334. HRMS calculated for $C_{21}H_{19}NO_3$ 333.13649, found 333.1351.

3.6.18. 7-Phenyl-5-thien-2-yl-2*H*-pyrano[2,3-*b*]pyridine (45). Compound **45** was obtained as a pale yellow oil (66% yield), after purification by column chromatography (petroleum ether–ethyl acetate, 4:1); IR (KBr) cm^{-1}: 1684, 1591, 1441, 1371, 1254; ^1H NMR (250 MHz, $CDCl_3$) δ 8.04 (m, 2H), 7.51–7.40 (m, 5H), 7.24 (dd, J=0.9 Hz, J'=4.0 Hz, 1H), 7.17 (dd, J=0.9 Hz, J'=5.0 Hz, 1H), 6.80 (dt, J=1.5 Hz, J'=3.4 Hz, 1H), 5.90 (dt, J=3.4 Hz, J'=7.2 Hz, 1H), 5.15 (dd, J=1.5 Hz, J'=7.2 Hz, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 161.6 (C), 154.8 (C), 140.6 (C), 139.1 (C), 138.3 (C), 129.2 (CH), 128.7 (CH), 128.5 (CH), 127.9 (CH), 127.4 (CH), 126.8 (CH), 122.8 (CH), 122.2 (CH), 115.6 (CH), 112.8 (C), 66.6 (CH_2); m/z (M+1)=292.

3.6.19. 7-Phenyl-5-*p*-tolyl-2*H*-pyrano[2,3-*b*]pyridine (46). Compound **46** was obtained as a maroon oil (51% yield), after purification by column chromatography (petroleum ether–ethyl acetate, 4:1); IR (KBr) cm^{-1}: 1577, 1431, 1100, 908, 733; ^1H NMR (250 MHz, $CDCl_3$) δ 7.95 (d, J=8.1 Hz, 2H), 7.39–7.32 (m, 3H), 7.31–7.18 (m, 5H), 6.45–6.40 (dt, J=1.8 Hz, J'=9.6 Hz, 1H), 5.74–5.67 (dt, J=3.4 Hz, J'=9.6 Hz, 1H), 5.03 (dd, J=1.8 Hz, J'=3.4 Hz, 2H), 2.36 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 161.3 (C), 154.5 (C), 148.4 (C), 138.5 (C), 138.5 (C), 134.8 (C), 129.4 (CH), 129.1 (CH), 129.1 (CH), 128.7 (CH), 126.3 (CH), 126.0 (CH), 122.2 (CH), 115.7 (CH), 112.9 (C), 66.8 (CH_2), 21.4 (CH_3); m/z (M+1)=300.

3.6.20. 5-(4-Methoxyphenyl)-7-phenyl-2*H*-pyrano[2,3-*b*]pyridine (47). Compound **47** was obtained as a yellow oil (14% yield), after purification by column chromatography (petroleum ether–ethyl acetate, 4:1); IR (KBr)

cm^{-1}: 3014, 1628, 1500, 1452, 1280, 1247, 1038, 757; ^1H NMR (250 MHz, $CDCl_3$) δ 8.04 (dd, J=1.6 Hz, J'=8.2 Hz, 2H), 7.46–7.25 (m, 6H), 6.99 (d, J=6.9 Hz, 2H), 6.50 (dt, J=1.9 Hz, J'=9.8 Hz, 1H), 5.79 (dt, J=3.4 Hz, J'=9.8 Hz, 1H), 5.11 (dd, J=1.9 Hz, J'=3.4 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 161.4 (C), 160.0 (C), 154.5 (C), 148.1 (C), 138.6 (C), 130.5 (CH), 130.0 (C), 129.1 (CH), 128.7 (CH), 126.8 (CH), 122.3 (CH), 122.1 (CH), 115.6 (CH), 114.1 (CH), 112.9 (C), 66.7 (CH_2), 55.5 (CH_3); m/z (M+1)=316.

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