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PAPER

Silver-catalysed intramolecular cyclisation of 2-alkynylacetophenones and 3-acetyl-2-alkynylpyridines in the presence of ammonia

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Silver-catalysed/microwave-assisted domino reactions of 2-alkynyl-acetophenones and 3-acetyl-2-alkynylpyridines in the presence of ammonia are widely described. In most cases the reaction give a mixture of the imino- and carbo-cyclisation products, with a general preference for the former. A plausible mechanism is proposed and the dual activity of silver salts is supported by NMR experiments.

Introduction

From many years, we have been interested in the development of domino synthetic strategies[1] for the construction of nitrogen-containing heterocycles[2] starting from alkyne derivatives.[3] In particular, many efforts have been devoted to the synthesis of nitrogen-containing rings by sequential addition/annulation reactions of γ- or δ-ketoalkynes in the presence of ammonia.[4] For example, 5-*exo-dig* cyclisation of 4-pentynones[5] gave polysubstituted and fused pyrrole derivatives (Scheme 1, a), whereas the presence of a γ-ketoalkyne moiety in an aromatic framework is responsible for the 6-*endo-dig* cyclisation of 5-acetyl-4-alkynylthiazoles[6] and 2-acyl-3-alkynylindoles[7] to pyrido[3,4-*c*]thiazoles and pyrido[3,4-*b*]indoles, respectively (Scheme 1, b and c). More recently, we reported an in depth investigation on the synthesis of the pyrazino[1,2-*a*]indole nucleus through the sequential imination/annulation reaction of 2-carbonyl-1-propargylindoles in the presence of ammonia in methanol.[8] The reaction worked well with *N*-propargylindole-2-carbaldehydes, but yields and selectivities were unsatisfactory using 2-acetyl-*N*-propargylindoles.[8a]

Moreover, the reaction totally failed when using 2-benzoyl-*N*-propargylindoles. These drawbacks were overcome when we found that 3 equiv. of $TiCl_4$ and microwave heating were able to improve both yields and selectivities in the reactions of ketone derivatives, together with a widespread reduction of reaction times[8b] (Scheme 1, d). This sequential approach to hetero(poly)cyclic rings (with and without titanium catalysis) has been very recently applied to the synthesis of pyrrolo[1,2-*a*]pyrazines and isoquinolines starting from 2-acetyl-*N*-propargylpyrroles (Scheme 1, e) and 2-alkynyl-benzaldehydes (Scheme 1, f), respectively,[9] and the approach to isoquinolines was also successfully transformed into a multicomponent process[10] (Scheme 1, g). But, unexpectedly, when we tried to synthesize 1-methylisoquinolines by reacting 2-alkynylacetophenones with ammonia under our standard domino conditions, the reactions gave very poor results (see below). These outcomes prompted us to investigate the reactions of alkynyl ketones in more depth.

Whereas the use of 2-alkynylbenzaldehydes (and related compounds characterized by the presence of a γ-alkynylaldehyde framework on an (hetero)aromatic scaffold) as starting materials for the preparation of (hetero)cyclic compounds has been widely explored and is in continuous evolution, the reactivity of keto-homologous, 2-alkynylacetophenones, is less investigated.[11] In many articles, 2-alkynylacetophenones are only marginally treated as a digression in more comprehensive works on 2-alkynylbenzaldehydes.[12] In some cases, 2-alkynylacetophenones show a different behaviour with respect to the corresponding 2-alkynylbenzaldehydes, in terms of reaction yield[13] or product selectivity.[14] It is worth noting that reactions of 2-alkynylacetophenones or their *N*-heterocyclic analogues, 3-acetyl-2-alkynylpyridines, with secondary[15] or branched primary amines[15a] have only few precedents, whereas, to the best of our knowledge, no example of their reaction with ammonia has been reported yet. Thus, in this paper we report our recent findings on microwave-assisted, domino addition/annulation reactions of 2-alkynyl-acetophenones and 3-acetyl-2-alkynylpyridines in the presence of ammonia.[16]

Results and discussion

We started our study looking for the best conditions to trigger the domino reaction of *o*-(*p*-tolylethynyl)acetophenone **1a**, chosen as model compound, with ammonia (Table 1). As mentioned above, the uncatalysed[7,8a] reaction of **1a** with 2 M ammonia in methanol at 120 °C under microwave heating gave the corresponding isoquinoline **2a** in very low yield (Table 1, entry 1). A simple tentative approach to promote the formation of the imine intermediate by the use of molecular sieves did not result in any improvement (Table 1, entry 2). On the basis of our previous experiences,[8b,9] we planned to catalyse the reaction with 3 equiv. of titanium tetrachloride, but, under these conditions, only traces of the

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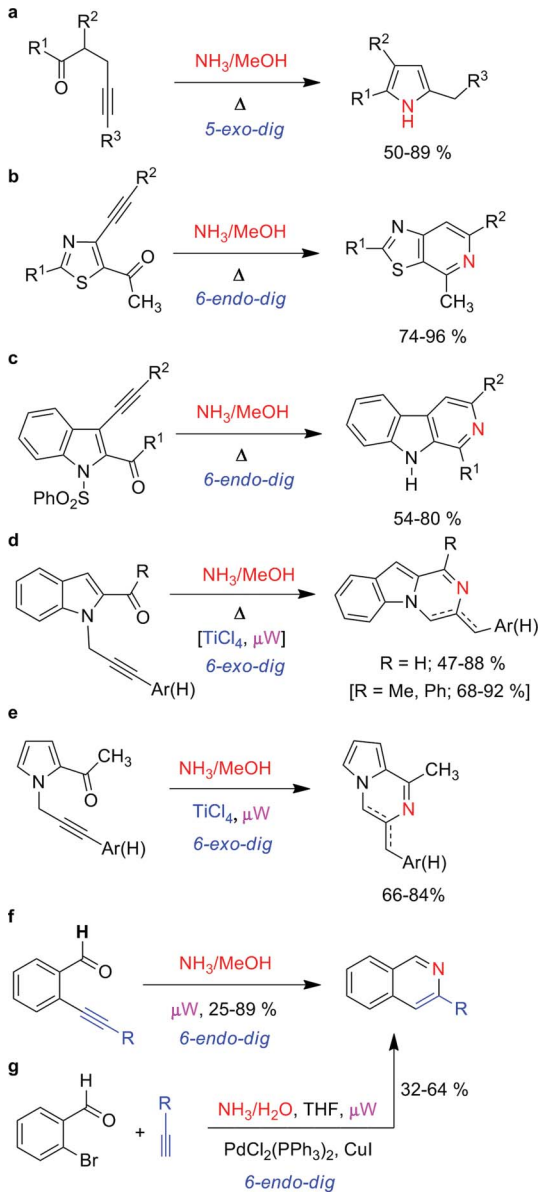
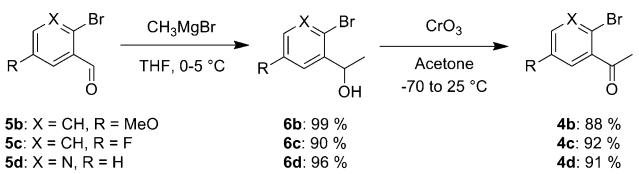


Scheme 1 Our previous works on cyclization of γ- or δ-ketoalkynes in the presence of ammonia.

isoquinoline **2a** were identified together with a complex mixture of tarry unidentified by-products (probably derived from a titanium-catalysed polymerisation process) (Table 1, entry 3). A similar behaviour was observed using a catalytic amount of titanium (Table 1, entry 4), whereas the less acidic complex $TiCl_4$·2THF also gave poor yield after a prolonged reaction time (Table 1, entry 5). Due to these disappointing outcomes, we tried some other metal catalysts potentially able to promote both the imine formation as a Lewis acid, and the intermolecular hydroamination step as an alkynophilic catalyst.[17] There are many examples in the literature of this double activity of palladium,[18] copper,[19] silver,[12c] gold[20] and indium[11b,21] salts and complexes in the intramolecular cyclizations involving alkynes bearing a neighboring nucleophile. We were delighted to find that in the presence of $Pd(OAc)_2$ the reaction gave the desired isoquinoline **2a** in a promising 46% yield, as well as a not negligible amount of the isomeric naphtalen-1-amine **3a** (Table 1, entry 6). $PdCl_2$ gave poorer results in terms of yield and regioselectivity (Table 1, entry 7), whereas $Cu(OTf)_2$ gave a similar ratio **2a** : **3a** but in lower overall yield (Table 1, entry 8). In the presence of CuI, yield and selectivity were comparable to those observed using $Pd(OAc)_2$ (Table 1, *cf.* entry 9 and 6). Among the five silver-based catalysts tested (Table 1, entries 10–14), AgF and Ag_2O gave modest results even after prolonged reaction times (Table 1, entries 10 and 11), whereas $AgSbF_6$ was more active and selective, and gave slightly better yield (Table 1, entry 12). $AgNO_3$ was a little more effective than palladium, despite the ratio of products being slightly shifted toward the naphtalen-1-amine **3a** (Table 1, entry 13). The best result was obtained with AgOTf, which gave an almost quantitative conversion with a quite good regioselectivity (with respect to the other catalysts tested) in a relatively short reaction time (Table 1, entry 14). $NaAuCl_4$ was ineffective (Table 1, entry 15), whereas PPh_3AuCl was as active as $AgNO_3$[22] (Table 1, entry 16). Surprisingly, in the presence of both PPh_3AuCl and AgOTf a reversed selectivity was observed (Table 1, entry 17). Finally, indium salts seemed to be completely unsuited for our purpose (Table 1, entries 18 and 19).

It is worth noting that our results with silver salts "fit-well" with all other emerging examples in which simple and cheap silver salts seem to be equally or more effective than more expensive gold catalysts.[12c,23]

Afterwards, we investigated the scope and limitations of the approach. Initially, we prepared a library of 2-alkynylacetophenones **1a–m** and 3-acetyl-2-alkynylpyridines **1n–t** by a standard Sonogashira procedure[24] from 2-bromoacetophenones **4a–c** and 2-bromo-3-acetylpyridine **4d** in the presence of a variety of terminal alkynes (Table 2). Whereas 2-bromoacetophenone **4a** is a cheap commercially available reagent, the more expensive 2-bromo-3-acetylpyridine **4d** was prepared in two steps in very good yields by a Grignard reaction of 2-bromonicotinaldehyde **5d** with CH_3MgBr,[15b] followed by Jones oxidation[25] (Scheme 2). The same procedure was followed to prepare 2-bromo-5-methoxyacetophenone **4b** and 2-bromo-5-fluoroacetophenone **4c** starting from the corresponding aldehydes **5b** and **5c**, respectively (Scheme 2).

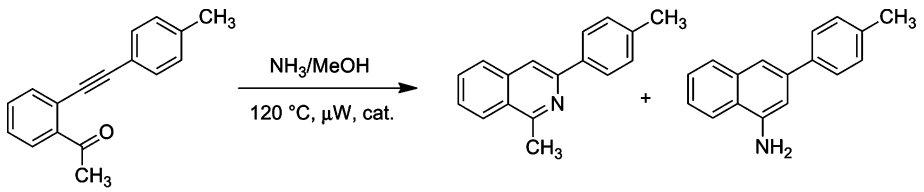


Scheme 2 Preparation of 2-bromo-5-methoxyacetophenone **4b**, 2-bromo-5-fluoroacetophenone **4c** and 2-bromo-3-acetylpyridine **4d**.

Then, we tested compounds **1b–t** in the AgOTf-catalysed domino reaction with ammonia. The obtained results are depicted in Table 3.

The reactions of acetophenone derivatives substituted on the triple bond with an aryl group always lead to a mixture of isoquinoline and naphtalenamine isomers in variable ratio (Table 3, entries 1–6). Better results were obtained with neutral and electron-donating groups on the aryl moiety (Table 3, entries 1–3), whereas electron-withdrawing groups gave lower yields and worse selectivity or inhibited the reaction (Table 3, entries 4–6). In the presence of alkyl substituents on the triple bond the

Table 1 Screening of reaction conditions for domino addition/annulation of **1a** with ammonia



1a **2a** **3a**

Entry	*t*/min[a]	Catalyst	**2a** yield %[b]	**3a** yield %[b]	**1a** (rec.) yield %[b]	Overall yield %[b]	Ratio **2a**/**3a**
1	120	—	11[c]	—	72	11	—
2	120	4 Å molecular sieve (100 mg mmol^{-1})	4	—	45	4	—
3	30	$TiCl_4$ (3 equiv.)	traces[d]	—	—	—	—
4	15	$TiCl_4$[e]	traces[d]	—	—	—	—
5	80	$TiCl_4$·2THF[e]	11	—	18	11	—
6	100	$Pd(OAc)_2$[e]	46	25	—	71	1.8
7	60	$PdCl_2$[e]	23	19	7	42	1.2
8	120	$Cu(OTf)_2$[e]	23	13	8	36	1.8
9	120	CuI[e]	38	20	—	58	1.9
10	120	AgF[e]	15	14	17	29	1.1
11	120	Ag_2O[e]	10	10	18	20	1.0
12	60	$AgSbF_6$[e]	26	17	4	43	1.5
13	60	$AgNO_3$[e]	46	36	9	82	1.3
14	**45**	**AgOTf**[e]	**58**	**40**	—	**98**	1.5
15	120	$NaAuCl_4$·$2H_2O$[e]	11	6	31	17	1.8
16	30	PPh_3AuCl[e]	41	34	10	75	1.2
17	60	PPh_3AuCl (7.5 mol%) AgOTf[e]	27	43	—	70	0.6
18	120	$InCl_3$[e]	5	—	18	5	—
19	120	$In(OTf)_3$[e]	traces[d]	—	—	—	—

[a] Not including 11 min "ramp time" (≅ 10 °C min^{-1}). [b] Yields refer to pure isolated compounds. [c] The reaction performed under conventional heating at 110 °C overnight gave only traces of isoquinoline **2a**. [d] The reaction gave a complex mixture of tarry unidentified by-products. [e] 10 mol%.

reactions run with good yields and a better selectivity toward the isoquinoline isomers (Table 3, entries 7–12). The approach also tolerates the presence of bulky substituents on the triple bond such as cyclohexanol, but in this case the yields were moderate (Table 3, entry 10). An electronic perturbation on the acetophenone ring does not seem to substantially affect the course of reaction (Table 3, entries 11–12), although the presence of an electron-withdrawing substituent leads to a slight reduction of yield (Table 3, entry 12). In the reactions of the aryl- and alkyl-substituted 3-acetyl-2-alkynylpyridines (Table 3, entries 13–19) we observed a general behavior comparable to that of 3-alkynylacetophenones, with an improved selectivity to the 1,6-naphthyridine isomer for the substrates substituted with an aryl moiety on the alkyne (Table 3, entries 13–14, *cf*. entry 2 with 14). Finally, the reaction of 3-acetyl-2-(trimethylsilylethynyl)pyridine **1t** gave the desilylated 5-methyl-1,6-naphthyridine in moderate yield (Table 3, entry 19). All the obtained products have been identified and fully characterized by NMR spectroscopy, IR and MS.

According to the literature,[12c,23a] the proposed mechanism for the AgOTf-catalysed nucleophilic addition/annulation sequence involves two key steps (Scheme 3): in the first step, the nucleophilic attack of ammonia on the carbonyl leads to the formation of imine intermediate **A**, in equilibrium with its enamine tautomer **B**. Although silver triflate is generally considered a Lewis acid with a strong π-philic character,[12c] we believe that it is also able to increase the electrophilic character of the carbonyl carbon atom[17,18] and therefore promote the nucleophilic attack of ammonia. In a similar way, it is probably able to also coordinate the imine,[17,26] and affect the tautomeric equilibrium imine/enamine, thus highlighting the bidentate character of the nucleophilic intermediate. The second step involves the intramolecular addition of the N- or C-nucleophile on the Ag-activated triple bond.[12c] The cycloisomerisation occurs with selective *6-endo-dig* geometry leading to the corresponding σ-silver complex of isoquinoline **C** and/or naphtalenamine **D**. The final products **2** and/or **3** are then achieved by a solvent-mediated protodemetalation that restores the catalyst.

To verify the hypothesis that silver can act as a σ-philic Lewis acid and thus is able to enhance the electrophilicity of the carbonyl and to affect the tautomeric processes, some NMR experiments were performed. First, we acquired two ^{13}C NMR spectra of acetophenone in deuterated methanol, in the absence (**A**) and in the presence (**B**) of 1 equiv. of AgOTf (Fig. 1). It is well-known that one of the most important parameters that determine the chemical shift in nuclear magnetic resonance is the shielding effect, determined by the electron density of the atomic nucleus observed. Therefore, the shift of a signal in response to an interaction with a catalyst can be related to the change of charge density of the

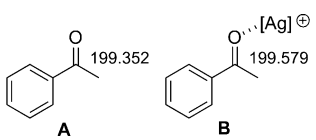
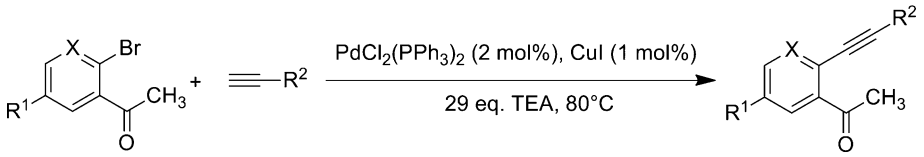
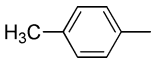
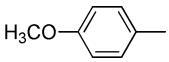
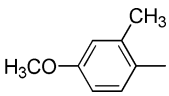
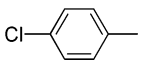
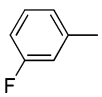
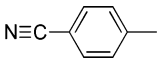
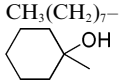
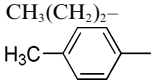
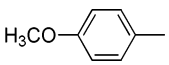
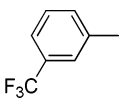
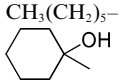


Fig. 1 Chemical shift of acetophenone carbonyl with and without the catalyst.

Table 2 Preparation of 2-alkynylacetophenones **1a–m** and 3-acetyl-2-alkynylpyridines **1n–t**

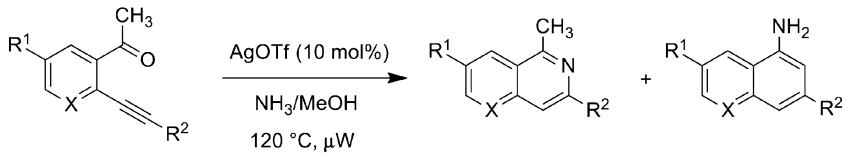


1 a-t

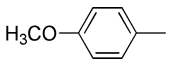
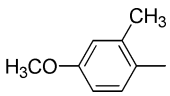
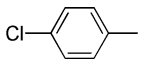
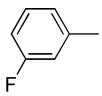
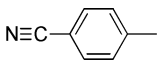
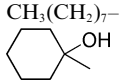
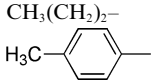
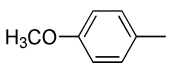
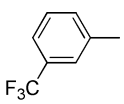
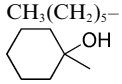
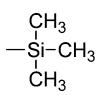
X	R^1	R^2	*t*/h	Product	Yield%[a]
CH	H		6	**1a**	98
CH	H		2.5	**1b**	66
CH	H		5	**1c**	62
CH	H		5	**1d**	87
CH	H		2	**1e**	38[b]
CH	H		6.5	**1f**	45
CH	H		6.5	**1g**	39
CH	H	$CH_3(CH_2)_4$–	12	**1h**	57
CH	H	$CH_3(CH_2)_5$–	12	**1i**	95
CH	H	$CH_3(CH_2)_7$–	12	**1j**	93
CH	H		2	**1k**	98
CH	MeO	$CH_3(CH_2)_2$–	12	**1l**	63
CH	F	$CH_3(CH_2)_2$–	1	**1m**	94
N	H		1	**1n**	84
N	H		1	**1o**	78
N	H		2	**1p**	84
N	H	$CH_3(CH_2)_4$–	1.5	**1q**	67
N	H	$CH_3(CH_2)_5$–	3	**1r**	76
N	H		1	**1s**	98
N	H		1	**1t**	98

[a] Yields refer to pure isolated compounds. [b] Prepared by reaction of 2-ethynylacetophenone with 4-iodoacetophenone under standard Sonogashira conditions.

Table 3 AgOTf-catalysed domino addition/cyclization reaction of derivatives **1b–t**



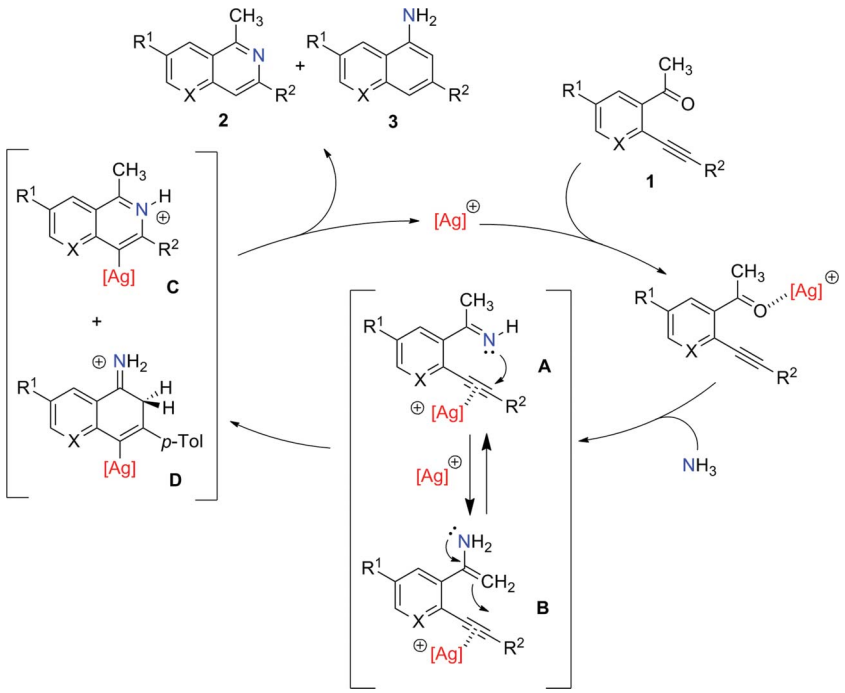
1 b-t **2 b-t** **3 b-t**

Entry	1,2,3	X	R^1	R^2	*t*/min[a]	**2** (yield %)[b]	**3** (yield %)[b]
1	**b**	CH	H		120	36	44
2	**c**	CH	H		90	32	41
3	**d**	CH	H		90	35	40
4	**e**	CH	H		120	23	39
5	**f**	CH	H		210	traces	traces
6	**g**	CH	H		90	traces	—
7	**h**	CH	H	$CH_3(CH_2)_4$–	90[c]	63	15
8	**i**	CH	H	$CH_3(CH_2)_5$–	90	61	20
9	**j**	CH	H	$CH_3(CH_2)_7$–	90[d]	44	14
10	**k**	CH	H		120	25	—
11	**l**	CH	MeO	$CH_3(CH_2)_2$–	150	71	17
12	**m**	CH	F	$CH_3(CH_2)_2$–	150	55	15
13	**n**	N	H		60	41	25
14	**o**	N	H		30	48	19
15	**p**	N	H		105	—	—
16	**q**	N	H	$CH_3(CH_2)_4$–	60	57	25
17	**r**	N	H	$CH_3(CH_2)_5$–	60	75	—
18	**s**	N	H		60	20	7
19	**t**	N	H		60	(R^2 = H) 37[e]	traces[e]

[a] Not including 11 min "ramp time" (≅ 10 °C min^{-1}). [b] Yields refer to pure isolated compounds. [c] The reaction performed without catalyst under conventional heating at 110 °C overnight gave only the isoquinoline **2h** in 35% yield. [d] Catalysed with $AgNO_3$ (10 mol%). [e] Desilylated product.

corresponding nucleus. The results showed a slight shift of the C carbonyl signal at higher frequencies (+0.227 ppm), indicating a weak interaction between the metal and the carbonyl oxygen with consequent deshielding of the carbonyl carbon.[27]

A second dynamic experiment has been performed by recording the ^{1}H NMR spectrum of acetophenone in deuterated methanol at different times with and without the catalyst. The spectra of the sample containing AgOTf (50 mol%) displayed gradual reduction



Scheme 3 Proposed reaction mechanism.

and increasing complexity of the methyl signal of acetophenone due to progressive deuteration, and the simultaneous rise of the integral for the signal of the OH of solvent (Table 4 and Fig. 2). This behavior was not observed in the control experiment, supporting the hypothesis that the catalyst is able to speed up the tautomeric equilibria.

Conclusions

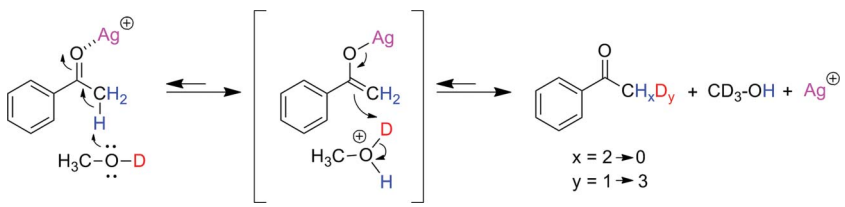
In summary, we found that silver triflate is the catalyst of choice for the microwave-promoted domino nucleophilic addition/annulation reaction of a wide variety of 2-alkynylacetophenones and 3-acetyl-2-alkynylpyridines in the presence of ammonia. In most cases the reactions gave mixtures of imino- and carbo-cyclisation products with a general preference for the former. A variety of substituted 1-methylisoquinolines and 5-methyl-1,6-naphthyridines can be synthesized by this approach. Simple NMR experiments strongly supported the hypothesis that silver triflate exerts the dual role of σ- and π-philic Lewis acid.

Experimental

General

All chemicals and solvents are commercially available. Silica gel F254 thin-layer plates were employed for thin layer chromatography (TLC). Silica gel 40–63 micron/60A was employed for flash column chromatography. Melting points are uncorrected.

Table 4 Dynamic ^{1}H NMR study



	Acetophenone in CD_3OD		Acetophenone + AgOTf (50 mol%) in CD_3OD	
	Integral (ref. to 2 CH arom.)		Integral (ref. to 2 CH arom.)	
Time/h	CH_3-CO-Ph	CD_3OH	CH_3-CO-Ph	CD_3OH
0	3.08	1.01	3.30	2.19
16	3.11	1.12	2.94	2.40
21	3.05	1.09	2.81	3.55
44	3.07	1.10	1.92	4.42
65	3.09	1.11	1.30	5.05

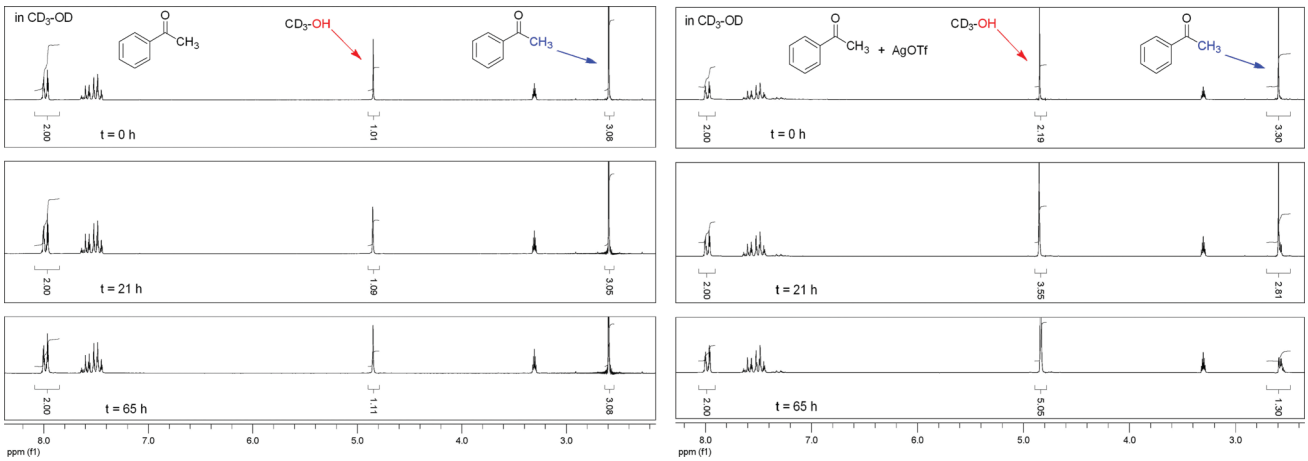


Fig. 2 Selected spectra of the dynamic ^{1}H NMR study.

Infrared spectra were recorded on a FT-IR spectrophotometer using KBr tablets for solids and NaCl disks for oils. Proton NMR spectra were recorded at room temperature in $CDCl_3$, at 200, 300 or 500 MHz, with residual chloroform as the internal reference (δ_H = 7.26 ppm). ^{13}C NMR spectra were recorded at room temperature in $CDCl_3$ at 50.3, 75.45 or 125.75 MHz, with the central peak of chloroform as the internal reference (δ_C = 77.3 ppm). The APT sequence was used to distinguish the methine and methyl carbon signals from those due to methylene and quaternary carbons. All ^{13}C NMR spectra were recorded with complete proton decoupling. Microwave-assisted reactions were performed with a MILESTONE microSYNT multimode labstation, using 12 mL sealed glass vessels. The internal temperature was detected with a fiber optic sensor.

Compounds **6b–d** are known compounds and were prepared following the method reported in ref. 15b.

1-(2-Bromo-5-methoxyphenyl)ethanol 6b. Yellow wax. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.47 (d, 3H, CH_3, J = 6.2 Hz), 1.98 (br, 1H, OH), 3.81 (s, 3H, CH_3), 5.19 (q, 1H, CH, J = 6.2 Hz), 6.69 (dd, 1H, arom. J = 8.8, 3.3), 7.16 (d, 1H, arom. J = 2.9), 7.40 (dd, 1H, arom. J = 8.7, 5.1) ppm. These data are in good agreement with literature values.[28]

1-(2-Bromo-5-fluorophenyl)ethanol 6c. Yellow oil. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.47 (d, 3H, CH_3, J = 6.2 Hz), 2.00 (br, 1H, OH), 5.18 (q, 1H, CH, J = 6.4 Hz), 6.85 (ddd, 1H, arom. J = 8.8, 7.7, 3.3), 7.34 (dd, 1H, arom. J = 9.5, 2.9), 7.46 (dd, 1H, arom. J = 8.7, 5.1) ppm. These data are in good agreement with literature values.[29]

1-(2-Bromopyridin-3-yl)ethanol 6d. Yellow oil. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.50 (d, 3H, CH_3, J = 6.2 Hz), 1.98 (br, 1H, OH), 5.18 (q, 1H, CH, J = 6.2 Hz), 7.30 (dd, 1H, arom. J = 7.7, 4.7), 7.92 (dd, 1H, arom. J = 7.7, 1.8), 8.26 (dd, 1H, arom. J = 4.7, 1.8) ppm. These data are in good agreement with literature values.[25,30]

Compounds **4b–d** are known compounds and were prepared following the methods reported in ref. 25

2-Bromo-5-methoxyacetophenone 4b. Colorless oil. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.63 (s, 3H, CH_3), 3.81 (s, 3H, CH_3), 6.85 (dd, 1H, arom. J = 8.8, 2.6), 6.97 (d, 1H, arom. J = 2.9), 7.48 (d, 1H, arom. J = 8.8) ppm. These data are in good agreement with literature values.[31]

2-Bromo-5-fluoroacetophenone 4c. Colorless oil. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.63 (s, 3H, CH_3), 7.03 (ddd, 1H, arom. J = 8.8, 7.7, 2.9), 7.18 (dd, 1H, arom. J = 8.4, 2.9), 7.58 (dd, 1H, arom. J = 8.8, 4.7) ppm. These data are in good agreement with literature values.[29]

2-Bromo-3-acetylpyridine 4d. Pale yellow oil. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.68 (s, 3H, CH_3), 7.36 (dd, 1H, arom. J = 7.7, 4.7), 7.76 (dd, 1H, arom. J = 7.7, 2.2), 8.45 (dd, 1H, arom. J = 4.7, 2.2) ppm. These data are in good agreement with literature values.[25,32]

General procedure for the synthesis of 2-alkynylacetophenones 1a–m and 3-acetyl-2-alkynylpyridines 1n–t. Under a nitrogen atmosphere, to a solution 2-bromoacetophenone or 2-bromo-3-acetylpyridine (5.00 mmol) in TEA (20 mL) the appropriate alkyne (6.00 mmol) and *trans*-dichlorobis(triphenylphosphine)-palladium(II) (0.10 mmol) were added. The reaction was stirred at rt for 15 min, then CuI (0.05 mmol) was added. The reaction mixture was stirred at 80 °C (see Table 2) until no more starting product was detectable by TLC analysis (eluent: hexane/EtOAc (95 : 5)). Then, the solvent was evaporated under reduced pressure and the crude purified by flash chromatography over a silica gel column (for times and yields see Table 2).

1-(2-(*p*-Tolylethynyl)phenyl)ethanone 1a. Eluent for chromatography: hexane/EtOAc (97 : 3). Yellow solid. Mp: 45–46 °C. IR (KBr): ν = 2214, 1687 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.38 (s, 3H, CH_3), 2.80 (s, 3H, CH_3), 7.18 (d, 2H, arom., J = 8.1 Hz), 7.34–7.51 (m, 4H, arom.), 7.62 (d, 1H, arom., J = 7.2 Hz), 7.75 (d, 1H, arom., J = 7.2 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 21.8, 30.3, 88.2, 95.6, 120.0, 122.2, 128.3, 128.9, 129.5, 131.5, 131.7, 134.0, 139.3, 140.9, 200.7 ppm. ESI-MS m/z: 235 ((M + 1)$^+$, (100)), 102 (13). Calcd for $C_{17}H_{14}O$ (234.29): C, 87.15; H, 6.02. Found: C, 87.11; H, 6.01. These data are in good agreement with literature values.[11a]

1-(2-(Phenylethynyl)phenyl)ethanone 1b. Eluent for chromatography: hexane/EtOAc (98 : 2). Orange oil. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.79 (s, 3H, CH_3), 7.33–7.48 (m, 5H,

arom.), 7.51–7.57 (m, 2H, arom.), 7.61 (dd, 1H, arom. J = 7.6, 1.1), 7.74 (dd, 1H, arom. J = 7.8, 1.2) ppm. These data are in good agreement with literature values.[11a]

1-(2-((4-Methoxyphenyl)ethynyl)phenyl)ethanone 1c. Eluent for chromatography: hexane/EtOAc (98 : 2). Orange oil. IR (neat): ν = 2213, 1683 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.79 (s, 3H, CH_3), 3.83 (s, 3H, CH_3), 6.89 (d, 2H, arom. J = 9.2 Hz), 7.32–7.52 (m, 4H, arom.), 7.60 (d, 1H, arom., J = 7.9 Hz), 7.74 (d, 1H, arom., J = 7.0 Hz) ppm. These data are in good agreement with literature values.[11a,33]

1-(2-((4-Methoxy-2-methylphenyl)ethynyl)phenyl)ethanone 1d. Eluent for chromatography: hexane/EtOAc (97 : 3). Orange oil. IR (neat): ν = 2205, 1688 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.52 (s, 3H, CH_3), 2.78 (s, 3H, CH_3), 3.81 (s, 3H, O-CH_3), 6.71 (s, 1H, arom.), 6.76 (d, 1H, arom., J = 7.2 Hz), 7.32–7.50 (m, 3H, arom.), 7.60 (d, 1H, arom., J = 7.2 Hz), 7.75 (d, 1H, arom., J = 8.1 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 21.3, 30.2, 55.5, 91.1, 94.6, 111.6, 115.2, 115.4, 122.6, 128.0, 128.8, 131.4, 133.6, 134.1, 140.5, 142.5, 160.2, 200.7 ppm. ESI-MS m/z: 265 ((M + 1)$^+$, (100)). Calcd for $C_{18}H_{16}O_2$ (264.32): C, 81.79; H, 6.10. Found: C, 81.71; H, 6.06.

1-(2-((4-Chlorophenyl)ethynyl)phenyl)ethanone 1e. Eluent for chromatography: hexane/EtOAc (98 : 2). Orange solid. Mp: 61–62 °C. IR (KBr): ν = 2211, 1672 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.76 (s, 3H, CH_3), 7.31–7.37 (m, 2H, arom.), 7.40–7.52 (m, 4H, arom.), 7.60 (dd, 1H, arom., J = 7.3, 1.5 Hz), 7.74 (dd, 1H, arom., J = 7.3, 1.8 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 30.0, 89.6, 93.8, 121.6, 121.7, 128.7, 129.0, 129.1, 131.6, 133.0, 134.1, 135.0, 140.8, 200.3 ppm. ESI-MS m/z: 255 ((M + 1)$^+$, (100)). Calcd for $C_{16}H_{11}ClO$ (254.17): C, 75.45; H, 4.35. Found: C, 75.38; H, 4.39

1-(2-((3-Fluorophenyl)ethynyl)phenyl)ethanone 1f. Eluent for chromatography: hexane/EtOAc (97 : 3). Yellow oil. IR (neat): ν = 1689 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.76 (s, 3H, CH_3), 7.06, (m, 1H, arom.), 7.21–7.53 (m, 5H, arom.), 7.62 (dd, 1H, arom. J = 7.3, 1.5), 7.76 (dd, 1H, arom. J = 7.2, 2.0) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 30.0, 89.5, 93.6 (d, $^4J_{C\text{-}F}$ = 3.4), 116.3 (d, $^2J_{C\text{-}F}$ = 21), 118.2 (d, $^2J_{C\text{-}F}$ = 23), 121.4, 125.0 (d, $^3J_{C\text{-}F}$ = 9.5), 127.7 (d, $^4J_{C\text{-}F}$ = 3.1), 128.8, 129.0, 130.3 (d, $^3J_{C\text{-}F}$ = 8.4), 131.6, 134.2, 141,0, 162.7 (d, $^1J_{C\text{-}F}$ = 247), 200.1 ppm. ESI-MS m/z: 239 ((M + 1)$^+$, (100)). Calcd for $C_{16}H_{11}FO$ (238.26): C, 80.66; H, 4.65. Found: C, 80.56; H, 4.62.

4-((2-Acetylphenyl)ethynyl)benzonitrile 1g. Eluent for chromatography: hexane/EtOAc (92 : 8). Orange solid. Mp: 85–86 °C. IR (KBr): ν = 2226, 1672 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.72 (s, 3H, CH_3), 7.41–7.61 (m, 2H, arom.), 7.63–7.77 (m, 5H, arom.), 7.80 (dd, 1H, arom., J = 6.7, 1.8 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 29.7, 92.7, 92.9, 112.1, 118.6, 120.8, 128.1, 129.2, 129.3, 131.7, 132.3, 132.4, 134.4, 140.8, 199.5 ppm. ESI-MS m/z: 246 ((M + 1)$^+$, (100)). Calcd for $C_{17}H_{11}NO$ (245.28): C, 83.25; H, 4.52; N, 5.71. Found: C, 83.42; H, 4.50; N, 5.67.

1-(2-(Hept-1-ynyl)phenyl)ethanone 1h. Eluent for chromatography: hexane/EtOAc (98 : 2). Yellow oil. IR (neat): ν = 2232, 1685 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.92 (t, 3H, CH_3, J = 6.9 Hz), 1.25–1.47 (m, 4H, 2 CH_2), 1.58–1.67 (m, 2H, CH_2), 2.45 (t, 2H, CH_2, J = 7.7), 2.72 (s, 3H, CH_3), 7.31–7.50 (m, 3H, arom.), 7.64 (dd, 1H, arom., J = 6.9, 1.8 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 14.2, 19.9, 22.4, 28.3, 30.3, 31.4, 79.8, 97.1, 122.7, 127.7, 128.5, 131.3, 134.2, 141.2, 201.3 ppm. ESI-MS m/z: 215 ((M + 1)$^+$, (100)). Calcd for $C_{15}H_{18}O$ (214.30): C, 84.07; H, 8.47. Found: C, 83.95; H, 8.41.

1-(2-(Oct-1-ynyl)phenyl)ethanone 1i. Eluent for chromatography: hexane/EtOAc (98 : 2). Pale yellow oil. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.90 (t, 3H, CH_3, J = 6.5), 1.25–1.69 (m, 8H, CH_2), 2.45 (t, 2H, CH_2, J = 7.0), 2.72 (s, 3H, CH_3), 7.27–7.50 (m, 3H, arom.), 7.66 (dd, 1H, arom. J = 7.7, 1.5) ppm. These data are in good agreement with literature values.[34]

1-(2-(Dec-1-ynyl)phenyl)ethanone 1j. Eluent for chromatography: hexane/EtOAc (99 : 1). Yellow oil. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.87 (t, 3H, CH_3, J = 7.0), 1.20–1.35 (m, 8H, CH_2), 1.44–1.64 (m, 6H, CH_2), 2.43 (t, 2H, CH_2, J = 7.0), 2.71 (s, 3H, CH_3), 7.31 (t, 1H, arom., J = 7.6), 7.37 (t, 1H, arom., J = 7.6), 7.47 (t, 1H, arom., J = 7.6), 7.65 (t, 1H, arom., J = 7.8) ppm. These data are in good agreement with literature values.[34b]

1-(2-((1-Hydroxycyclohexyl)ethynyl)phenyl)ethanone 1k. Eluent for chromatography: hexane/EtOAc (85 : 15). Orange oil. IR (neat): ν = 2935, 2219, 1685 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.24–1.28 (m, 2H, CH_2), 1.40–2.05 (m, 8H, CH_2), 2.43 (br, 1H, OH), 2.70 (s, 3H, CH_3), 7.31–7.54 (m, 3H, arom.), 7.69 (dd, 1H, arom. J = 6.9, 2.2) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 23.3, 23.4, 25.2, 25.4, 30.1, 39.8, 39.9, 69.3, 83.3, 99.0, 121.6, 128.4, 128.7, 131.4, 134.4, 140.9, 200.6 ppm. ESI-MS m/z: 225 ((M + 1 -OH)$^+$, (100)). Calcd for $C_{16}H_{18}O_2$ (242.33): C, 79.31; H, 7.49. Found: C, 79.24; H, 7.48.

1-(5-Methoxy-2-(pent-1-ynyl)phenyl)ethanone 1l. Eluent for chromatography: hexane/EtOAc (98 : 2). Brown oil. IR (neat): ν = 3306, 2963, 2230, 1682 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.05 (t, 3H, CH_3, J = 7.0), 1.54–1.69 (m, 2H, CH_2), 2.42 (t, 2H, CH_2, J = 7.0), 2.74 (s, 3H, CH_3), 3.83 (s, 3H, CH_3), 6.95 (dd, 1H, arom. J = 8.4, 2.9), 7.18 (d, 1H, arom., J = 2.9), 7.34 (dd, 1H, arom., J = 8.4) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 13.7, 21.8, 22.2, 30.2, 55.6, 79.8, 95.2, 112.8, 115.1, 118.0, 135.5, 142.7, 159.1, 200.9 ppm. ESI-MS m/z: 217 ((M + 1)$^+$, (100)). Calcd for $C_{14}H_{13}O_2$ (216.15): C, 77.75; H, 7.46. Found: C, 77.82; H, 7.47

1-(5-Fluoro-2-(pent-1-ynyl)phenyl)ethanone 1m. Eluent for chromatography: hexane/EtOAc (98 : 2). Brown oil. IR (neat): ν = 2965, 2234, 1686 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.05 (t, 3H, CH_3, J = 7.0), 1.55–1.69 (m, 2H, CH_2), 2.42 (t, 2H, CH_2, J = 7.0), 2.77 (s, 3H, CH_3), 7.05–7.14 (m, 1H, arom.), 7.33–7.50 (m, 2H, arom.) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 13.7, 21.8, 22.1, 30.2, 79.0, 96.7, 115.3 (d, $^2J_{C\text{-}F}$ = 23.2), 118.5 (d, $^2J_{C\text{-}F}$ = 22.1), 118.9, 136.1 (d, $^3J_{C\text{-}F}$ = 7.6), 143.2 (d, $^3J_{C\text{-}F}$ = 6.5), 161.9 (d, $^1J_{C\text{-}F}$ = 247), 199.6 ppm. ESI-MS m/z: 205 ((M + 1)$^+$, (50)), 176 (100). Calcd for $C_{13}H_{13}FO$ (204.24): C, 76.45; H, 6.42. Found: C, 76.38; H, 6.39

1-(2-(*p*-Tolylethynyl)pyridin-3-yl)ethanone 1n. Eluent for chromatography: hexane/EtOAc (9 : 1). Brown solid. Mp: 50–51 °C. IR (KBr): ν = 2924, 2215, 1675, 1552 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.38 (s, 3H, CH_3), 2.85 (s, 3H, CH_3), 7.19 (d, 2H, arom., J = 8.1 Hz), 7.34 (dd, 1H, arom. J = 7.7, 4.7), 7.51 (d, 2H, arom., J = 8.1 Hz), 8.06 (dd, 1H, arom. J = 8.0, 1.8), 8.73 (dd, 1H, arom. J = 4.7, 1.5) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 21.8, 30.3, 87.8, 95.7, 118.9, 122.75, 129.6, 132.7, 136.7, 136.8, 140.2, 141.4,

152.5, 199.4 ppm. ESI-MS *m/z*: 236 ((M + 1)$^+$, (50)), 221 (100). Calcd for $C_{16}H_{13}NO$ (235.28): C, 81.68; H, 5.57; N, 5.95. Found: C, 81.60; H, 5.59; N, 5.92. These data are in good agreement with literature values.[11a]

1-(2-((4-Methoxyphenyl)ethynyl)pyridin-3-yl)ethanone 1o. Eluent for chromatography: hexane/EtOAc (98 : 2). Brown oil. IR (neat): ν = 3369, 2964, 2936, 2217, 1682, 1553 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.85 (s, 3H, CH_3), 3.84 (s, 3H, CH_3), 6.91 (d, 2H, arom., J = 8.7 Hz), 7.32 (dd, 1H, arom. J = 8.0, 4.7), 7.56 (d, 2H, arom., J = 8.7 Hz), 8.05 (dd, 1H, arom. J = 8.0, 1.5), 8.71 (dd, 1H, arom. J = 4.7, 1.8) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 30.2, 55.5, 87.5, 95.7, 114.1, 114.5, 122.4, 133.8, 136.5, 136.8, 141.6, 152.3, 160.9, 199.2 ppm. ESI-MS *m/z*: 252 ((M + 1)$^+$, (100)). Calcd for $C_{16}H_{13}NO_2$ (251.14): C, 76.48; H, 5.21; N, 5.57. Found: C, 76.53; H, 5.19; N, 5.54.

1-(2-((3-(Trifluoromethyl)phenyl)ethynyl)pyridin-3-yl)ethanone 1p. Eluent for chromatography: hexane/EtOAc (8 : 2). Brown oil. IR (neat): ν = 3369, 2929, 2220, 1683, 1556 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.82 (s, 3H, CH_3), 7.39 (dd, 1H, arom. J = 8.0, 4.7), 7.47–7.55 (m, 1H, arom.), 7.65 (d, 1H, arom., J = 8.1 Hz), 7.79 (d, 1H, arom., J = 7.7 Hz), 7.87 (s, 1H, arom.), 8.07 (dd, 1H, arom. J = 8.0, 1.8), 8.74 (dd, 1H, arom. J = 4.7, 1.8) ppm.^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 29.9, 89.5, 92.8, 123.1, 123.2, 123.8 (q, $^1J_{C\text{-}F}$ = 272 Hz), 126.2 (q, $^3J_{C\text{-}F}$ = 3.81 Hz), 128.9 (q, $^3J_{C\text{-}F}$ = 3.81 Hz), 129.3, 131.5 (q, $^2J_{C\text{-}F}$ = 32.8 Hz), 135.2, 136.6, 137.1, 140.6, 152.5, 198.5 ppm. ESI-MS *m/z*: 290 ((M + 1)$^+$, (100)). Calcd for $C_{16}H_{10}F_3NO$ (289.25): C, 66.44; H, 3.48; N, 4.84. Found: C, 66.38; H, 3.48; N, 4.84.

1-(2-(Hept-1-ynyl)pyridin-3-yl)ethanone 1q. Eluent for chromatography: hexane/EtOAc (8 : 2). Yellow oil. IR (neat): ν = 3369, 2932, 2227, 1684, 1423 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.90 (t, 3H, CH_3, J = 7.0), 1.25–1.59 (m, 4H, 2 CH_2), 1.63–1.73 (m, 2H, CH_2), 2.50 (t, 2H, CH_2, J = 7.0), 2.77 (s, 3H, CH_3), 7.28 (dd, 1H, arom. J = 8.0, 4.7), 7.97 (dd, 1H, arom. J = 8.0, 1.8), 8.64 (dd, 1H, arom. J = 4.7, 1.8) ppm.^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 13.9, 19.8, 22.3, 27.9, 30.1, 31.4, 80.1, 97.9, 122.3, 136.3, 137.1, 141.6, 152.1, 199.7 ppm. ESI-MS *m/z*: 216 ((M + 1)$^+$, (100)). Calcd for $C_{14}H_{17}NO$ (215.29): C, 78.10; H, 7.96; N, 6.51. Found: C, 78.18; H, 7.99; N, 6.48.

1-(2-(Oct-1-ynyl)pyridin-3-yl)ethanone 1r. Eluent for chromatography: hexane/EtOAc (8 : 2). Brown oil. IR (neat): ν = 3369, 2931, 2229, 1686, 1423 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.90 (t, 3H, CH_3, J = 7.0), 1.25–1.49 (m, 6H, 3 CH_2), 1.61–1.70 (m, 2H, CH_2), 2.50 (t, 2H, CH_2, J = 7.0), 2.77 (s, 3H, CH_3), 7.29 (dd, 1H, arom. J = 8.0, 4.7), 7.97 (dd, 1H, arom. J = 8.0, 1.8), 8.65 (dd, 1H, arom. J = 4.7, 1.8) ppm.^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 14.2, 19.9, 22.7, 28.2, 28.9, 30.3, 31.5, 80.1, 97.9, 122.4, 136.4, 136.9, 141.5, 152.2, 199.8 ppm. ESI-MS *m/z*: 230 ((M + 1)$^+$, (100)). Calcd for $C_{15}H_{19}NO$ (229.32): C, 78.56; H, 8.35; N, 6.11. Found: C, 78.44; H, 8.39; N, 6.15.

1-(2-((1-Hydroxycyclohexyl)ethynyl)pyridin-3-yl)ethanone 1s. Eluent for chromatography: hexane/EtOAc (1 : 1). Brown oil. IR (neat): ν = 3368, 2935, 2222, 1694, 1424 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.24–2.12 (m, 10H, 5 CH_2), 2.76 (s, 3H, CH_3), 2.81 (s, 1H, OH), 7.32 (dd, 1H, arom. J = 8.0, 4.7), 7.99 (dd, 1H, arom. J = 8.0, 1.8), 8.68 (dd, 1H, arom. J = 4.7, 1.8) ppm.^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 23.2, 25.3, 30.1, 39.7, 69.0, 82.8, 99.6, 122.9, 136.4, 137.1, 140.7, 152.1, 199.2 ppm. ESI-MS *m/z*: 244 ((M + 1)$^+$, (100)). Calcd for $C_{15}H_{17}NO_2$ (243.30): C, 74.05; H, 7.04; N, 5.76. Found: C, 73.98; H, 7.02; N, 5.71.

1-(2-((Trimethylsilyl)ethynyl)pyridin-3-yl)ethanone 1t. Eluent for chromatography: hexane/EtOAc (8.5 : 1.5). Yellow oil. IR (neat): ν = 3369, 2961, 2168, 1689, 1417 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.29 (s, 9H, 3 CH_3), 2.81 (s, 3H, CH_3), 7.34 (dd, 1H, arom. J = 8.0, 4.7), 8.01 (dd, 1H, arom. J = 8.0, 1.8), 8.69 (dd, 1H, arom. J = 4.7, 1.8) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = –0.4, 30.2, 102.1, 103.0, 123.2, 136.5, 137.7, 140.7, 152.2, 199.4 ppm. ESI-MS *m/z*: 218 ((M + 1)$^+$, (100)). Calcd for $C_{12}H_{15}SiNO$ (217.09): C, 66.31; H, 6.96; N, 6.44. Found: C, 66.24; H, 6.97; N, 6.41. These data are in good agreement with literature values.[15b]

General procedure for microwave-assisted/AgOTf-catalyzed cyclization reaction of 2-alkynylacetophenones 1a–m and 3-acetyl-2-alkynylpyridines 1n–t. In a sealed tube, a well stirred solution of the appropriate 2-alkynylacetophenone (**1 a–m**) (0.359 mmol) or 3-acetyl-2-alkynylpyridines (**1 n–t**) and AgOTf (0.009 mg, 0.036 mmol) in dry ammonia in methanol (NH_3/MeOH 2 M solution, 3.59 mL, 7.18 mmol), was heated at 120 °C in a multimode microwave oven, until no more starting product was detectable by TLC. The reaction mixture was evaporated to dryness and the crude purified by flash chromatography over a silica gel column yielding progressively the 3-substituted-1-methylisoquinoline (**2a–m**) and the 3-substituted-1-naphthalenamine (**3a–m**), or the 1,6-naphthyridine (**2n–t**) and the quinolin-5-amine (**3n–s**), respectively (for times and yields see Table 3).

1-Methyl-3-*p*-tolylisoquinoline[4] 2a. Eluent for chromatography: hexane/EtOAc (95 : 5). Brown wax. IR (KBr): ν = 3056, 2920, 1621 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.43 (s, 3H, CH_3), 3.04 (s, 3H, CH_3), 7.30 (d, 2H, arom. J = 8.1 Hz), 7.05–7.69 (m, 2H, arom.), 7.86 (t, 2H, arom. J = 7.0 Hz), 8.07 (t, 2H, arom. J = 8.4 Hz), 8.14 (s, 1H, arom.) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 21.5, 22.9, 114.9, 125,9, 126.7, 126.8, 127.0, 127.8, 129.7, 130.2, 137.0, 137.3, 138.4, 150.3, 158.7 ppm. ESI-MS *m/z*: 234 ((M + 1)$^+$, (100)). Calcd for $C_{17}H_{15}N$ (233.31): C, 87.52; H, 6.48; N, 6.00. Found: C, 87.45; H, 6.42; N, 6.03.

1-Methyl-3-phenylisoquinoline 2b. Eluent for chromatography: hexane/EtOAc (97 : 3). Brown oil. IR (neat): ν = 3058, 2920, 1622, 1569, 1441, 1029 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 3.05 (s, 3H, CH_3), 7.39–7.64 (m, 5H, arom.), 7.86 (d, 1H, arom. J = 7.7), 7.92 (s, 1H, arom.), 8.14 (dd, 3H, arom. J = 8.1, 1.1 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 22.9, 115.5, 125.9, 126.8, 127.0, 127.2, 127.8, 128.5, 128.9, 130.3, 137.0, 140.0, 150.2, 158.8 ppm. ESI-MS *m/z*: 220 ((M + 1)$^+$, (100)). Calcd for $C_{16}H_{13}N$ (219.28): C, 87.64; H, 5.98; N, 6.39. Found: C, 87.76; H, 5.94; N, 6.34.

3-(4-Methoxyphenyl)-1-methylisoquinoline 2c. Eluent for chromatography: hexane/EtOAc (96 : 4). Brown solid. Mp: 125–129 °C (dec.). IR (KBr): ν = 3022, 2924, 1605, 1567, 1513, 1439, 1248, 1175, 1030, 835 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 3.03 (s, 3H, CH_3), 3.88 (s, 3H, CH_3), 7.03 (d, 2H, arom. J = 8.9 Hz), 7.53 (ddd, 1H, arom. J = 8.1, 6.9, 1.3 Hz), 7.65 (ddd, 1H, arom. J = 8.2, 6.9, 1.3 Hz), 7.82 (d, 1H, arom. J = 7.6), 7.84 (s, 1H, arom.), 8.07–8.13 (m, 3H, arom.) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 22.9, 55.6, 114.3, 114.4, 125.9, 126.4, 126.6, 127.7,

128.4, 130.2, 132.8, 137.1, 150.0, 158.6, 160.2 ppm. ESI-MS *m/z*: 250 ((M + 1)$^+$, (100)), 235 (8). Calcd for $C_{17}H_{15}NO$ (249.31): C, 81.90; H, 6.06; N, 5.62. Found: C, 81.84; H, 6.03; N, 5.62.

3-(4-Methoxy-2-methylphenyl)-1-methylisoquinoline 2d. Eluent for chromatography: hexane/EtOAc (96 : 4). Light brown solid. Mp: 107–110 °C. IR (KBr): ν = 2953, 2921, 1707, 1608, 1567, 1505, 1442, 1241, 1162, 1045, 751 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 3.41 (s, 3H, CH_3), 3.01 (s, 3H, CH_3), 3.85 (s, 3H, CH_3), 6.82–6.86 (m, 2H, arom.), 7.45 (d, 1H, arom. J = 9.2 Hz), 7.55–7.71 (m, 3H, arom.), 7.82 (d, 1H, arom. J = 7.8 Hz), 8.15 (d, 1H, arom. J = 7.7) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 21.1, 22.7, 55.5, 111.5, 116.4, 118.8, 125.8, 126.1, 126.9, 127.6, 130.2, 131.5, 133.9, 136.7, 138.0, 152.5, 158.1, 159.6 ppm. ESI-MS *m/z*: 264 ((M + 1)$^+$, (100)), 249 (5). Calcd for $C_{18}H_{17}NO$ (263.33): C, 82.10; H, 6.51; N, 5.32. Found: C, 81.97; H, 6.48; N, 5.35.

3-(4-Chlorophenyl)-1-methylisoquinoline 2e. Eluent for chromatography: hexane/EtOAc (98 : 2). Brown oil. IR (neat): ν = 3369, 2924, 1622 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 3.03 (s, 3H, CH_3), 7.47 (d, 2H, arom. J = 8.8 Hz), 7.51–7.71 (m, 2H, arom.), 7.85 (d, 1H, arom. J = 7.3 Hz), 7.89 (s, 1H, arom.), 8.05–8.15 (m, 3H, arom.) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 22.8, 115.3, 125.9, 126.9, 127.2, 127.8, 128.4, 129.1, 130.4, 134.6, 136.9, 138.5, 148.9, 158.9 ppm. ESI-MS *m/z*: 254 ((M + 1)$^+$, (100)). Calcd for $C_{16}H_{12}NCl$ (253.73): C, 75.74; H, 4.77; N, 5.52. Found: C, 75.65; H, 4.75; N, 5.54.

1-Methyl-3-pentylisoquinoline 2h. Eluent for chromatography: hexane/EtOAc (98 : 2). Yellow oil. IR (neat): ν = 3067, 2954, 2927, 2857, 1625, 1591, 1569, 1445, 1390, 747 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.90 (t, 3H, CH_3, J = 6.9), 1.28–1.46 (m, 4H, 2 CH_2), 1.79 (qt, 2H, CH_2, J = 7.7), 2.92 (t, 2H, CH_2, J = 7.7), 2.94 (s, 3H, CH_3), 7.31 (s, 1H, arom.), 7.40–7.63 (m, 2H, arom.), 7.72 (d, 1H, arom. J = 8.0 Hz), 8.00 (d, 1H, arom. J = 8.4 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 14.3, 22.6, 22.8, 29.9, 31.9, 38.4, 116.7, 125.7, 126.0, 126.2, 127.0, 129.9, 136.9, 154.8, 158.2 ppm. ESI-MS *m/z*: 214 ((M + 1)$^+$, (100)). Calcd for $C_{15}H_{19}N$ (213.54): C, 84.46; H, 8.98; N, 6.57. Found:C, 84.42; H, 8.97; N, 6.59.

3-Hexyl-1-methylisoquinoline[4] 2i. Eluent for chromatography: hexane/EtOAc (96 : 4). Yellow–green oil. IR (neat): ν = 2953, 2925, 2855, 1692, 1625, 1590, 1568, 1444, 1390, 747 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.88 (t, 3H, CH_3, J = 7.0), 1.31–1.37 (m, 6H, 3 CH_2), 1.79 (qt, 2H, CH_2, J = 7.6), 2.88 (t, 2H, CH_2, J = 7.6), 2.95 (s, 3H, CH_3), 7.32 (s, 1H, arom.), 7.50 (ddd, 1H, arom. J = 8.2, 6.8, 1.5 Hz), 7.61 (ddd, 1H, arom. J = 8.2, 6.8, 1.3 Hz), 7.72 (d, 1H, arom. J = 7.5), 8.07 (d, 1H, arom. J = 7.8 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 14.3, 22.6, 22.9, 29.4, 30.2, 32.0, 38.5, 116.7, 125.8, 126.1, 126.2, 127.0, 129.9, 136.9, 154.9, 158.2 ppm. ESI-MS *m/z*: 228 ((M + 1)$^+$, (100)). Calcd for $C_{16}H_{21}N$ (227.343): C, 84.53; H, 9.31; N, 6.16. Found: C, 84.41; H, 9.22; N, 6.19.

1-Methyl-3-octylisoquinoline 2j. Eluent for chromatography: hexane/EtOAc (98 : 2). Yellow oil. IR (neat): ν = 3067, 2953, 2925, 2855, 1626, 1591, 1569, 1446, 1391, 747 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.90 (t, 3H, CH_3, J = 6.9), 1.28–1.46 (m, 10H, 5 CH_2), 1.79 (qt, 2H, CH_2, J = 7.7), 2.88 (t, 2H, CH_2, J = 7.7), 2.94 (s, 3H, CH_3), 7.31 (s, 1H, arom.), 7.45–7.65 (m, 2H, arom.), 7.72 (d, 1H, arom. J = 8.0 Hz), 8.06 (d, 1H, arom. J = 8.1 Hz) ppm. ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ = 14.5, 22.6, 23.1, 29.7, 29.8, 29.9, 30.4, 32.3, 38.5, 116.9, 125.9, 126.2, 126.4, 127.2, 130.2, 137.1, 154.9, 158.4 ppm. ESI-MS *m/z*: 256 ((M + 1)$^+$, (100)). Calcd for $C_{18}H_{25}N$ (255.40): C, 84.65; H, 9.87; N, 5.48. Found: C, 84.72; H, 9.84; N, 5.50.

1-(1-Methylisoquinolin-3-yl)cyclohexanol 2k. Eluent for chromatography: hexane/EtOAc (9 : 1). Violet solid. Mp: 89–92 °C. IR (KBr): ν = 3398, 2920, 2853, 1627, 1591, 1569, 1446, 1415, 1386, 742 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.22–1.41 (m, 2H, CH_2), 1.56–1.99 (m, 8H, 4 CH_2), 2.96 (s, 3H, CH_3), 5.12 (bs, 1H, OH), 7.50–7.65 (m, 3H, arom.), 7.78 (d, 1H, arom. J = 7.7 Hz), 8.01 (dd, 1H, arom. J = 7.7, 1.1 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 22.6, 22.7, 26.2, 39.2, 72.7, 113.6, 126.0, 126.7, 126.9, 127.8, 130.4, 137.2, 157.4, 158.8 ppm. ESI-MS *m/z*: 242 ((M + 1)$^+$, (100)). Calcd for $C_{16}H_{19}NO$ (241.33): C, 79.63; H, 7.94; N, 5.80. Found: C, 79.54; H, 7.97; N, 5.76.

7-Methoxy-1-methyl-3-propylisoquinoline 2l. Eluent for chromatography: hexane/EtOAc (9 : 1). Brown solid. Mp: 99–100 °C. IR (KBr): ν = 3369, 2958, 2929, 2871, 1597, 1572, 1411, 1227 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.00 (t, 3H, CH_3, J = 6.9), 1.75–1.86 (m, 2H, CH_2), 2.84 (t, 2H, CH_2, J = 7.7), 2.91 (s, 3H, CH_3), 3.95 (s, 3H, CH_3), 7.26–7.32 (m, 3H, arom.), 7.62 (dd, 1H, arom. J = 9.1, 1.1 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 14.0, 22.6, 23.4, 40.2, 55.6, 103.9, 116.5, 122.6, 126.9, 128.5, 132.4, 152.7,156.5, 157.8 ppm. ESI-MS *m/z*: 216 ((M + 1)$^+$, (100)). Calcd for $C_{14}H_{17}N$ (215.29): C, 78.10; H, 7.96; N, 6.51. Found: C, 78.00; H, 7.98; N, 6.48.

7-Fluoro-1-methyl-3-propylisoquinoline 2m. Eluent for chromatography: hexane/EtOAc (95 : 5). Violet wax. IR (KBr): ν = 3027, 2954, 2927, 2868, 1593, 1505, 1393, 1184, 878 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.00 (t, 3H, CH_3, J = 7.3), 1.76–1.87 (m, 2H, CH_2), 2.85 (t, 2H, CH_2, J = 7.7), 2.89 (s, 3H, CH_3), 7.31 (s, 1H, arom.), 7.35–7.45 (m, 1H, arom.), 7.62–7.76 (m, 2H, arom.) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 14.0, 22.5, 23.3, 40.3, 109.2 (d, $^2J_{C\text{-}F}$ = 20.9 Hz), 116.4 (d, $^5J_{C\text{-}F}$ = 1.5 Hz), 120.3 (d, $^2J_{C\text{-}F}$ = 25.1 Hz), 126.6 (d, $^3J_{C\text{-}F}$ = 7.6 Hz), 129.4 (d, $^3J_{C\text{-}F}$ = 8.4 Hz), 133.9, 154.2 (d, $^4J_{C\text{-}F}$ = 2.7 Hz), 157.5 (d, $^4J_{C\text{-}F}$ = 5.7 Hz), 160.4 (d, $^1J_{C\text{-}F}$ = 247 Hz) ppm. ESI-MS *m/z*: 204 ((M + 1)$^+$, (100)). Calcd for $C_{13}H_{14}FN$ (203.26): C, 76.82; H, 6.94; N, 6.89. Found: C, 76.89; H, 6.97; N, 6.83.

5-Methyl-7-*p*-tolyl-1,6-naphthyridine 2n. Eluent for chromatography: hexane/EtOAc (8 : 2). Brown wax. IR (KBr): ν = 3369, 2920, 1605, 1423 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.43 (s, 3H, CH_3), 3.03 (s, 3H, CH_3), 7.30 (d, 2H, arom. J = 8.1), 7.41 (dd, 1H, arom. J = 8.4, 4.4), 8.08 (d, 2H, arom. J = 8.1), 8.14 (s, 1H, arom.), 8.37 (dd, 1H, arom. J = 8.4, 1.5 Hz), 9.08 (dd, 1H, arom. J = 4.4, 1.5 Hz) ppm.^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 21.4, 22.2, 115.9, 121.6, 121.7, 127.3, 129.7, 133.9, 136.6, 139.1, 152.0, 154.1, 154.5, 159.4 ppm. ESI-MS *m/z*: 235 ((M + 1)$^+$, (100)). Calcd for $C_{16}H_{14}N_2$ (234.30): C, 82.02; H, 6.02; N, 11.96. Found: C, 81.90; H, 5.96; N, 11.99.

7-(4-Methoxyphenyl)-5-methyl-1,6-naphthyridine 2o. Eluent for chromatography: hexane/EtOAc (8 : 2). Yellow oil. IR (neat): ν = 3391, 2957, 2935, 1601, 1575, 1515, 1441 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 3.02 (s, 3H, CH_3), 3.89 (s, 3H, CH_3), 7.04 (d, 2H, arom. J = 8.1 Hz), 7.45 (dd, 1H, arom. J = 8.4, 4.4 Hz), 8.11 (s, 1H, arom.), 8.15 (d, 2H, arom. J = 8.1 Hz), 8.42 (dd, 1H,

arom. J = 8.4, 1.5 Hz), 9.04 (dd, 1H, arom. J = 4.4, 1.8 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 22.2, 55.5, 114.5, 115.2, 121.4, 127.0, 131.9, 133.8, 133.9, 152.1, 153.7, 154.5, 159.3, 160.8 ppm. ESI-MS m/z: 251 ((M + 1)$^+$, (100)). Calcd for $C_{16}H_{14}N_2O$ (250.29): C, 76.78; H, 5.64; N, 11.19. Found: C, 76.63; H, 5.69; N, 11.22.

5-Methyl-7-pentyl-1,6-naphthyridine 2q. Eluent for chromatography: hexane/EtOAc (8 : 2). Yellow oil. IR (neat): ν = 3401, 2954, 2927, 1609, 1568 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.87 (t, 3H, CH_3, J = 6.9), 1.32–1.42 (m, 4H, 2 CH_2), 1.75–1.83 (m, 2H, CH_2), 2.91 (t, 2H, CH_2, J = 7.0), 2.91 (s, 3H, CH_3), 7.40 (dd, 1H, arom. J = 8.4, 4.0 Hz), 7.56 (s, 1H, arom.), 8.35 (dd, 1H, arom. J = 8.4, 1.5 Hz), 8.98 (dd, 1H, arom. J = 4.0, 1.5 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 14.1, 21.9, 22.7, 29.5, 31.8, 38.5, 118.1, 120.9, 121.2, 133.9, 151.7, 154.3, 158.9, 159.3 ppm. ESI-MS m/z: 215 ((M + 1)$^+$, (100)). Calcd for $C_{14}H_{18}N_2$ (214.30): C, 78.46; H, 8.47; N, 13.07. Found: C, 78.38; H, 8.44; N, 13.11.

7-Hexyl-5-methyl-1,6-naphthyridine 2r. Eluent for chromatography: hexane/EtOAc (8 : 2). Red oil. IR (neat): ν = 3206, 2956, 2926,2856, 1610, 1569, 1379 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.87 (t, 3H, CH_3, J = 6.9), 1.21–1.87 (m, 8H, 4 CH_2), 2.93 (t, 2H, CH_2, J = 8.0), 2.93 (s, 3H, CH_3), 7.42 (dd, 1H, arom. J = 8.4, 4.2 Hz), 7.58 (s, 1H, arom.), 8.38 (dd, 1H, arom. J = 8.4, 1.5 Hz), 9.00 (dd, 1H, arom. J = 4.2, 1.5 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 14.3, 21.9, 22.8, 29.3, 29.9, 31.9, 38.5, 118.1, 120.9, 121.3, 134.1, 151.6, 154.1, 159.1, 159.3 ppm. ESI-MS m/z: 229 ((M + 1)$^+$, (100)). Calcd for $C_{15}H_{20}N_2$ (228.33): C, 78.90; H, 8.83; N, 12.27. Found: C, 78.99; H, 8.80; N, 12.23.

1-(5-Methyl-1,6-naphthyridin-7-yl)cyclohexanol 2s. Eluent for chromatography: hexane/EtOAc (6 : 4). Brown wax. IR (KBr): ν = 3399, 3253, 2952, 2927, 2913, 2854, 1609, 1584, 1568, 1448, 1418, 1382 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.67–1.91 (m, 10H, 5 CH_2), 2.96 (s, 3H, CH_3), 4.87 (bs, 1H, OH), 7.46 (dd, 1H, arom. J = 8.4, 4.0), 7.81 (s, 1H, arom.), 8.40 (dd, 1H, arom. J = 8.4, 1.5 Hz), 9.03 (dd, 1H, arom. J = 4.0, 1.5 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 21.9, 22.4, 25.9, 38.8, 72.8, 115.1, 121.5, 121.9, 134.1, 151.8, 154.7, 158.3, 162.9 ppm. ESI-MS m/z: 243 ((M + 1)$^+$, (100)). Calcd for $C_{15}H_{18}N_2O$ (242.32): Found: C, 74.24; H, 7.54; N, 11.59.

5-Methyl-1,6-naphthyridine 2t. Eluent for chromatography: hexane/EtOAc (8 : 2). Red oil. IR (neat): ν = 3212, 2959, 1605 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.96 (s, 3H, CH_3), 7.51 (dd, 1H, arom. J = 8.4, 4.0 Hz), 7.77 (d, 1H, arom. J = 5.9 Hz), 8.43 (dd, 1H, arom. J = 8.4, 1.5 Hz), 8.61 (d, 1H, arom. J = 6.2 Hz), 9.06 (dd, 1H, arom. J = 4.4, 1.8 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 21.9, 120.9, 122.2, 122.8, 133.9, 145.8, 151.0, 154.4, 159.7 ppm. ESI-MS m/z: 145 ((M + 1)$^+$, (100)). Calcd for $C_9H_8N_2$ (144.17): C, 74.98; H, 5.59; N, 19.43. Found: C, 75.12; H, 5.59; N, 19.43.

3-*p*-Tolylnaphthalen-1-amine[4] 3a. Eluent for chromatography: hexane/EtOAc (95 : 5). Brown wax. IR (KBr): ν = 3425, 3024, 2915, 2855 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.43 (s, 3H, CH_3), 4.22 (bs, 2H, NH_2), 7.05 (d, 1H, arom, J = 1.1 Hz), 7.28 (d, 2H, arom, J = 8.4 Hz), 7.44–7.50 (m, 2H, arom), 7.52 (s, 1H, arom), 7.61 (d, 2H, arom, J = 8.1 Hz), 7.79–7.89 (m, 2H, arom) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 21.4, 109.5, 117.1, 120.9, 123.1, 125.0, 126.5, 127.4, 129.1, 129.7, 134.9, 137.3, 138.7, 139.3, 142.6 ppm. ESI-MS m/z: 234 ((M + 1)$^+$, (100)). Calcd for $C_{17}H_{15}N$ (233.31): C, 87.52; H, 6.48; N, 6.00. Found: C, 87.44; H, 6.43; N, 6.08.

3-Phenylnaphthalen-1-amine 3b. Eluent for chromatography: hexane/EtOAc (97.5 : 2.5). Brown solid. Mp: 79–81 °C. IR (KBr): ν = 3435, 2925, 2854, 1626, 1454, 1403, 1075, 763 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.26 (bs, 2H, NH_2), 7.07 (d, 1H, arom, J = 1.6 Hz), 7.36–7.42 (m, 1H, arom), 7.47–7.54 (m, 4H, arom), 7.56 (s, 1H, arom), 7.71–7.76 (m, 2H, arom.), 7.84–7.89 (m, 2H, arom) ppm. ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ = 109.7, 117.6, 121.1, 123.4, 125.3, 126.7, 127.6, 127.7, 129.1, 129.3, 135.1, 139.6, 141.8, 142.9. ESI-MS m/z: 220 ((M + 1)$^+$, (100)). Calcd for $C_{16}H_{13}N$ (219.28): C, 87.64; H, 5.98; N, 6.39. Found: C, 87.65; H, 5.99; N, 6.40.

3-(4-Methoxyphenyl)naphthalen-1-amine 3c. Eluent for chromatography: hexane/EtOAc (96 : 4). Dark purple solid. Mp: 125–129 °C (dec.). IR (KBr): ν = 3435, 2918, 1625, 1510, 1457, 1402, 1239, 1172, 1110, 1022, 822 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 3.87 (s, 3H, CH_3), 4.37 (bs, 2H, NH_2, exchange with D_2O), 7.00 (m, 3H, arom.), 7.45 (m, 3H, arom.), 7.63 (d, 2H, arom. J = 8.8 Hz), 7.83 (m, 2H, arom.) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 55.6, 109.4, 114.4, 116.7, 120.9, 122.9, 124.9, 126.5, 128.6, 129.0, 134.2, 135.0, 139.0, 142.6, 159.4 ppm. ESI-MS m/z: 250 ((M + 1)$^+$, (100)), 235 (6). Calcd for $C_{17}H_{15}N$ (249.31): C, 91.90; H, 6.06; N, 5.62. Found: C, 91.84; H, 6.01; N, 5.68.

3-(4-Methoxy-2-methylphenyl)naphthalen-1-amine 3d. Eluent for chromatography: hexane/EtOAc (96 : 4). Brown oil. IR (neat): ν = 3436, 2916, 1626, 1499, 1454, 1288, 1229, 1160, 1115, 1041, 822 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 3.31 (s, 3H, CH_3), 3.85 (s, 3H, CH_3), 4.18 (bs, 2H, NH_2, exchange with D_2O), 6.79 (m, 3H, arom.), 7.22 (s, 1H, arom.), 7.47 (m, 3H, arom.), 7.82 (m, 2H, arom.) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 21.1, 55.5, 111.2, 112.2, 115.9, 119.6, 120.9, 122.7, 124.9, 126.4, 128.8, 131.1, 134.6, 135.1, 137.2, 140.1, 141.8, 159.0 ppm. ESI-MS m/z: 264 ((M + 1)$^+$, (100)), 249 (7). Calcd for $C_{18}H_{17}NO$ (263.33): C, 82.10; H, 6.51; N, 5.32. Found: C, 82.01; H, 6.49; N, 5.34.

3-(4-Chlorophenyl)naphthalen-1-amine 3e. Eluent for chromatography: hexane/EtOAc (98 : 2 – 9 : 1). Brown oil. IR (neat): ν = 3435, 2923, 1625, 1492, 1090, 820 cm^{-1}. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 4.29 (bs, 2H, NH_2), 6.99 (s, 1H, arom.), 7.40–7.48 (m, 4H, arom.), 7.62 (d, 2H, arom, J = 8.4 Hz), 7.80–7.87 (m, 3H, arom.) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 109.0, 117.3, 120.9, 123.2, 125.4, 126.7, 128.8, 129.0, 129.1, 133.5, 134.9, 138.1, 140.1, 142.9 ppm. ESI-MS m/z: 254 ((M + 1)$^+$, (100)). Calcd for $C_{16}H_{12}NCl$ (253.73): C, 75.74; H, 4.77; N, 5.52. Found: C, 75.61; H, 4.72; N, 5.56.

3-Pentylnaphthalen-1-amine 3h. Eluent for chromatography: hexane/EtOAc (98 : 2 – 97 : 3). Brown oil. IR (neat): ν = 3369, 2955, 2924, 2851, 1627, 1598, 1576, 1514, 1463, 1409, 742 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.93 (t, 3H, CH_3, J = 6.9), 1.29–1.39 (m, 4H, 2 CH_2), 1.69–1.74 (m, 2H, CH_2), 2.70 (t, 2H, CH_2, J = 7.6), 4.12 (bs, 2H, NH_2), 6.69 (s, 1H, arom), 7.14 (s, 1H, arom), 7.39–7.46 (m, 2H, arom), 7.75–7.80 (m, 2H, arom.) ppm. ^{13}C NMR ($CDCl_3$, 125.75 MHz): δ = 13.3, 21.9, 29.0, 30.2, 35.5, 110.5, 117.1, 119.9, 121.6, 123.3, 125.1, 127.3, 133.9, 140.5, 141.1 ppm. ESI-MS m/z: 214 ((M + 1)$^+$, (100)). Calcd for $C_{15}H_{19}N$ (213.54): C, 84.46; H, 8.98; N, 6.57. Found: C, 84.56; H, 9.02; N, 6.53.

3-Hexylnaphthalen-1-amine[4] 3i. Eluent for chromatography: hexane/EtOAc (98 : 2). Yellow-orange oil. IR (neat): ν = 3369, 2954, 2926, 2854, 1626, 1597, 1576, 1512, 1460, 1408, 741 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.90 (t, 3H, CH_3, J = 6.8), 1.27–1.41 (m, 6H, 3 CH_2), 1.61–1.76 (m, 2H, CH_2), 2.68 (t, 2H, CH_2, J = 7.6), 3.82 (bs, 2H, NH_2), 6.66 (s, 1H, arom), 7.12 (s, 1H, arom), 7.35–7.46 (m, 2H, arom), 7.70–7.79 (m, 2H, arom) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 14.4, 22.9, 29.3, 31.5, 32.0, 36.5, 111.5, 118.0, 120.9, 122.6, 124.2, 126.1, 128.3, 134.9, 141.4, 142.0 ppm. ESI-MS m/z: 228 ((M + 1)$^+$, (100)), 144 (40). Calcd for $C_{16}H_{21}N$ (227.343): C, 84.53; H, 9.31; N, 6.16. Found: C, 84.36; H, 9.28; N, 6.12.

3-Octylnaphthalen-1-amine 3j. Eluent for chromatography: hexane/EtOAc (98 : 2). Brown oil. IR (neat): ν = 3369, 2953, 2925, 2855, 1626, 1591, 1569, 1446, 747 cm^{-1}.^1H NMR ($CDCl_3$, 200 MHz): δ = 0.88 (t, 3H, CH_3, J = 6.8), 1.27–1.40 (m, 10H, 5 CH_2), 1.63–1.71 (m, 2H, CH_2), 2.67 (t, 2H, CH_2, J = 7.6), 3.40 (bs, 2H, NH_2), 6.68 (s, 1H, arom), 7.12 (s, 1H, arom), 7.37–7.43 (m, 2H, arom), 7.71–7.80 (m, 2H, arom) ppm. ESI-MS m/z: 256 ((M + 1)$^+$, (100)). Calcd for $C_{18}H_{25}N$ (255.40): C, 84.65; H, 9.87; N, 5.48. Found: C, 84.74; H, 9.89; N, 5.45.

7-Methoxy-3-propylisoquinolin-1-amine 3l. Eluent for chromatography: hexane/EtOAc (9 : 1). Brown solid. Mp: 51–54 °C. IR (KBr): ν = 3359, 2960, 2928, 2868, 1626, 1604, 1511, 1260, 1024 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.96 (t, 3H, CH_3, J = 7.3), 1.64–1.75 (m, 2H, CH_2), 2.64 (t, 2H, CH_2, J = 7.3), 3.92 (s, 3H, CH_3), 6.71 (s, 1H, arom.), 7.06–7.15 (m, 3H, arom.), 7.63 (d, 1H, arom. J = 8.8 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 14.0, 24.5, 38.3, 55.6, 100.3, 112.9, 118.4, 118.6, 123.6, 129.8, 130.3, 138.5, 140.3, 157.1 ppm. ESI-MS m/z: 216 ((M + 1)$^+$, (100)). Calcd for $C_{14}H_{17}N$ (215.29): C, 72.19; H, 7.46; N, 12.95. Found: C, 72.11; H, 7.49; N, 12.99.

7-Fluoro-3-propylisoquinolin-1-amine 3m. Eluent for chromatography: hexane/EtOAc (95 : 5). Brown oil. IR (neat): ν = 3369, 3232, 2958, 2929, 2870, 1624, 1517, 1473, 1193, 852 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.96 (t, 3H, CH_3, J = 7.3), 1.64–1.79 (m, 2H, CH_2), 2.65 (t, 2H, CH_2, J = 7.3), 3.99 (bs, 2H, NH_2), 6.68 (s, 1H, arom.), 7.11 (s, 1H, arom.), 7.15–7.25 (m, 1H, arom.), 7.37 (dd, 1H, arom. J = 11, 2.2), 7.71 (dd, 1H, arom. J = 8.8, 5.8) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 14.0, 24.4, 38.4, 104.8 (d, $^2J_{C\text{-}F}$ = 21.7 Hz), 112.4, 116.1 (d, $^2J_{C\text{-}F}$ = 24.8 Hz), 118.1, 123.08 (d, $^3J_{C\text{-}F}$ = 7.6 Hz), 130.5 (d, $^3J_{C\text{-}F}$ = 8.8 Hz), 131.8, 140.2 (d, $^4J_{C\text{-}F}$ = 2.7 Hz), 141.6 (d, $^4J_{C\text{-}F}$ = 5.3 Hz), 160.1 (d, $^1J_{C\text{-}F}$ = 247 Hz) ppm. ESI-MS m/z: 204 ((M + 1)$^+$, (100)). Calcd for $C_{13}H_{14}FN$ (203.26): C, 70.57; H, 6.42; N, 13.72. Found: C, 70.64; H, 6.44; N, 13.71.

7-*p*-Tolylquinolin-5-amine 3n. Eluent for chromatography: hexane/EtOAc (8 : 2). Brown oil. IR (neat): ν = 3351, 3214, 2917, 2850, 1612, 1588, 1560, 1503, 1397, 807 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ = 2.42 (s, 3H, CH_3), 4.25 (bs, 2H, NH_2), 7.09 (s, 1H, arom.), 7.29 (d, 2H, arom. J = 8.1), 7.32 (dd, 1H, arom. J = 8.4, 4.4), 7.63 (d, 2H, arom. J = 8.1), 7.79 (s, 1H, arom.), 8.17 (dd, 1H, arom. J = 8.4, 1.5 Hz), 8.90 (dd, 1H, arom. J = 4.4, 1.5 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 21.3, 109.8, 118.0, 118.1, 119.5, 127.4, 129.6, 129.8, 137.9, 138.0, 142.7, 143.0, 149.7, 150.7 ppm. ESI-MS m/z: 235 ((M + 1)$^+$, (100)). Calcd for $C_{16}H_{14}N_2$ (234.30): C, 82.02; H, 6.02; N, 11.96. Found: C, 81.95; H, 6.00; N, 11.97.

7-(4-Methoxyphenyl)quinolin-5-amine 3o. Eluent for chromatography: hexane/EtOAc (8 : 2). Yellow oil. IR (neat): ν = 3349, 3214, 2960, 2836, 1608, 1589, 1564, 1505, 1248, 830 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ = 3.87 (s, 3H, CH_3), 4.22 (bs, 2H, NH_2), 7.01 (d, 2H, arom. J = 8.1), 7.06 (s, 1H, arom.), 7.32 (dd, 1H, arom. J = 8.4, 4.4), 7.67 (d, 2H, arom. J = 8.1), 7.75 (s, 1H, arom.), 8.16 (dd, 1H, arom. J = 8.4, 1.5 Hz), 8.89 (dd, 1H, arom. J = 4.4, 1.5 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 55.6, 109.6, 114.6, 117.8, 117.9, 119.4, 128.6, 129.5, 133.4, 142.6, 142.7, 149.8, 150.8, 159.9 ppm. ESI-MS m/z: 251 ((M + 1)$^+$, (100)). Calcd for $C_{16}H_{14}N_2O$ (250.29): C, 76.78; H, 5.64; N, 11.19. Found: C, 76.65; H, 5.69; N, 11.14.

7-Pentylquinolin-5-amine 3q. Eluent for chromatography: hexane/EtOAc (8 : 2). Green oil. IR (neat): ν = 3342, 3215, 2929, 1621, 1570 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.88 (t, 3H, CH_3, J = 6.9), 1.33–1.39 (m, 4H, 2 CH_2), 1.65–1.76 (m, 2H, CH_2), 2.70 (t, 2H, CH_2, J = 7.7), 4.14 (bs, 2H, NH_2), 6.68 (s, 1H, arom.), 7.26 (dd, 1H, arom. J = 8.4, 4.4), 7.37 (s, 1H, arom.), 8.11 (dd, 1H, arom. J = 8.4, 1.5 Hz), 8.83 (dd, 1H, arom. J = 4.0, 1.5 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 14.1, 22.7, 30.7, 31.7, 36.5, 111.7, 117.5, 118.9, 119 3, 129.4, 142.0, 145.6, 149.6, 150.3 ppm. ESI-MS m/z: 215 ((M + 1)$^+$, (100)). Calcd for $C_{14}H_{18}N_2$ (214.30): C, 78.46; H, 8.47; N, 13.07. Found: C, 78.32; H, 8.51; N, 13.11.

1-(5-Aminoquinolin-7-yl)cyclohexanol 3s. Eluent for chromatography: hexane/EtOAc (6 : 4). Brown oil. IR (neat): ν = 3369, 3235, 2927, 2853, 1617, 1590, 1571, 1446, 1407 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.71–1.88 (m, 10H, 5 CH_2), 4.18 (bs, 2H, NH_2), 4.70 (bs, 1H, OH), 7.07 (s, 1H, arom.), 7.31 (dd, 1H, arom. J = 8.4, 4.4), 7.64 (s, 1H, arom.), 8.13 (dd, 1H, arom. J = 8.4, 1.5 Hz), 8.85 (dd, 1H, arom. J = 4.0, 1.5 Hz) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 22.4, 25.8, 38.8, 73.5, 108.2, 115.8, 117.9, 119.6, 129.5, 142.3, 149.3, 150.5, 151.9 ppm. ESI-MS m/z: 243 ((M + 1)$^+$, (100)). Calcd for $C_{15}H_{18}N_2O$ (242.32): C, 74.35; H, 7.49; N, 11.56. Found: C, 74.24; H, 7.52; N, 11.51.

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