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Indole as Neutral Leaving Group in Silver Nitrate Induced Cyclization Reactions of *N*-{2-[Alkynyl(hetero)aryl]methylene}indolin-1-amines for the Synthesis of Annulated Pyridine Derivatives

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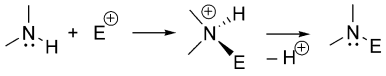
Dedicated to Professor Christian Reichardt at the occasion of his 75th birthday

Keywords: Lewis acids / Cyclization / Nitrogen heterocycles / Silver / Quantum chemical calculations

N-{2-[Alkynyl(hetero)aryl]methylene}indolin-1-amines **3** undergo, upon treatment with silver nitrate in chloroform at 60 °C, electrophilic cyclization reactions to afford annulated pyridine derivatives **4**. Mechanistically, the silver(I)-assisted 6-*endo*-*dig* ring-closure process of compounds **3** leads to the formation of an intermediate pyridinium cation, which releases – besides the products **4** – indole as unusual but efficient neutral leaving group after N–N bond cleavage. It is shown that among the hydrazones studied, only the 1-aminoindoline-derived substrates *N*-{2-[alkynyl(hetero)aryl]methylene}indolin-1-amines **3** are suitable to produce annulated pyridine derivatives **4** in high yield. The reaction can be performed in air and even in the presence of water in the reaction medium. Since during the course of the reaction indole is oxidized by the silver(I) ions, stoichiometric amounts of silver salt are required. Quantum chemical calculations have been applied in order to gain additional information on the reaction mechanism and the key reactive intermediates.

Introduction

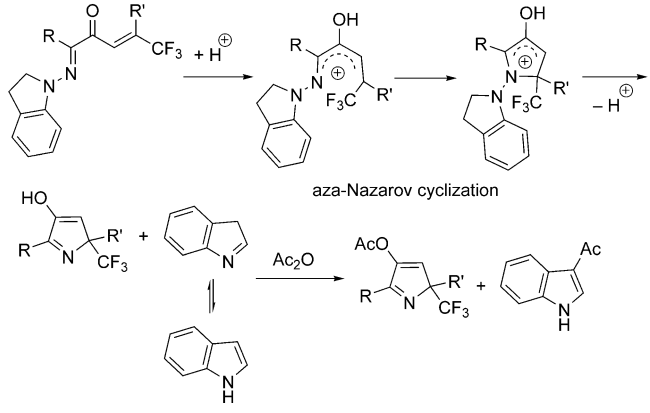
Electrophilic substitution reactions at a nitrogen atom usually involve a proton as leaving group (diazotization, *N*-nitrosation or *N*-nitroso-dehydrogenation, formation of azo compounds from amines, conversion of nitroso compounds to azoxy compounds, *N*-halogenation or *N*-halo-dehydrogenation, and reactions of amines with CO or CO_2) (Scheme 1).[1]



Scheme 1.

In the present study we introduce indole as an efficient neutral leaving group in electrophilic substitution reactions at a nitrogen atom. To the best of our knowledge there is only one other example of the use of a heterocyclic moiety as a neutral leaving group, given by Katritzky et al.; they utilized substituted pyridines as heterocyclic leaving groups.[2]

We have recently reported on a synthesis of 2*H*-pyrrole derivatives by the aza-Nazarov reaction[3] from 1-aminoindoline-derived azadienones, where 3*H*-indole acted as neutral leaving group (Scheme 2).[4]



Scheme 2. Aza-Nazarov synthesis of 2*H*-pyrroles.

We assumed that the driving force of this reaction is the formation of the stable aromatic 1*H*-indole molecule from the initial 3*H*-indole after cleavage of the N–N bond, along with the exothermic 1,5-cyclization reaction.

Based on this discovery, one might expect that the basic mechanism of this reaction sequence, namely the treatment of 1-aminoindoline-derived hydrazones by suitable electro-

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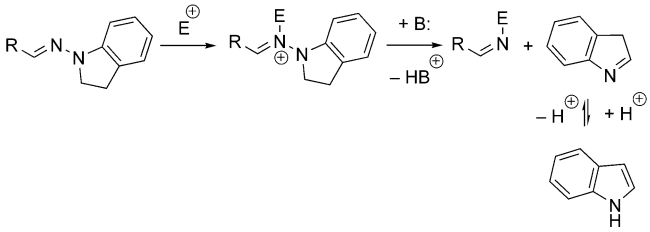
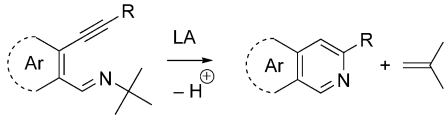
philes with subsequent N–N bond cleavage – liberating indole – may find many other applications in organic nitrogen chemistry (Scheme 3).



Scheme 3.

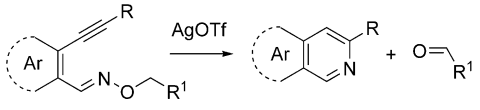
As part of our ongoing project establishing indole as an efficient leaving group in electrophilic substitution reactions at a nitrogen atom, we are pleased to report now the successful application of this protocol for cyclization reactions of *N*-{2-[alkynyl(hetero)aryl]methylene}indolin-1-amines leading to novel annulated pyridine derivatives.

In this context Larock et al. reported in a series of papers the Lewis acid (Pd^0, Pd^{II}, Ag^I, Cu^I) catalyzed synthesis of isoquinoline derivatives from *N*-*tert*-butyl-2-(1-alkynyl)arylaldimines, liberating isobutene as neutral leaving group (Scheme 4).[5]



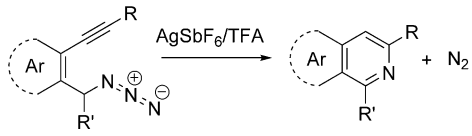
Scheme 4.

Recently, Zhang et al. reported a synthesis of isoqinolines from *ortho*-alkynylarenecarbaldehyde oxime derivatives catalyzed by catalytic amounts of AgOTf. They postulated that here an aldehyde acted as leaving group (Scheme 5).[6]



Scheme 5.

Liang et al. investigated the 2-alkynylbenzyl azide system,[7] where – similarly to Yamamoto's iodocyclization of 2-alkynylbenzyl azides – N_2 acts as the leaving group to give substituted isoquinolines (Scheme 6).[8a–8c]



Scheme 6.

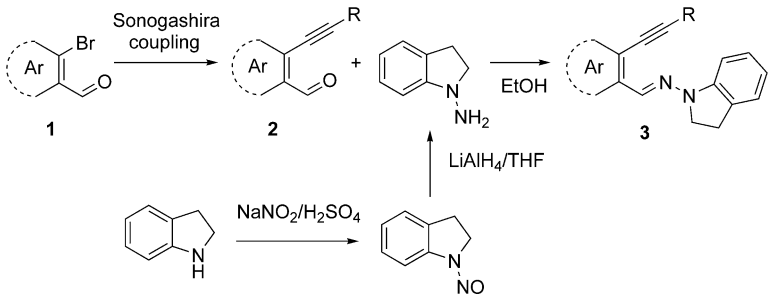
In contrast, cyclization reactions of phenylimines or oximes of 2-(alkynyl)benzaldehydes or *N*′-(2-alkynylbenzylidene)hydrazides are known to lead to *N*-phenyl-substituted structures, *N*-oxides and isoquinolinium-2-yl amides, respectively (however without cleavage of N–C, N–O or N–N bonds).[9]

Results and Discussion

Various examples of *N*-{2-[alkynyl(hetero)aryl]methylene}indolin-1-amines **3a**–**i** can easily be obtained from *o*-bromoarenecarbaldehydes **1** in a two-step procedure. The first step is a Sonogashira cross-coupling reaction to afford 2-(alkynyl)arenecarbaldehydes **2**. This step is followed by condensation of the carbonyl function of **2** with *N*-aminoindoline to give the hydrazones **3a**–**i** in 66–93% yield. The necessary *N*-aminoindoline was synthesized from indoline by a nitrosation/reduction reaction sequence (Scheme 7, Table 1).[10] We were able to obtain an X-ray diffraction structure of compound **3a** showing the conformation and in particular the (*E*) configuration of the C=N bond in the solid state (Figure 1).

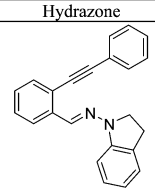
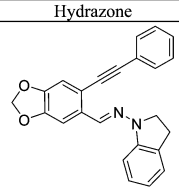
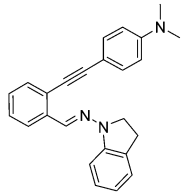
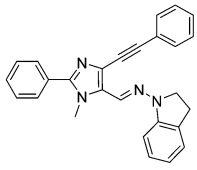
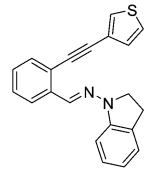
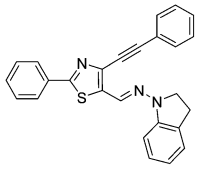
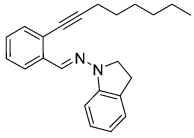
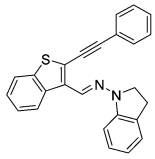
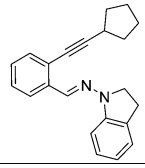
Upon treatment with 1.2 equiv. of $AgNO_3$, hydrazones **3a**–**i** underwent – in $CHCl_3$ as solvent at 60 °C – a cyclization reaction leading to several quite different types of compounds with an annulated pyridine moiety **4a**–**i** (Scheme 8, Table 2). The products were obtained in 44–98% yield after purification by column chromatography. Interestingly, in all experiments a silver mirror on the reaction flask was observed. A second product, stemming from the indoline moiety, was not detected (see below). Thus, we were able to introduce several different substituents and heterocycles (thiazole, imidazole, benzothiophene) into the hydrazone system. Substituents at the 3-position of the formed ring can be alkyl, cycloalkyl, aryl or heteroaryl.

For the compound **4i** an X-ray diffraction structure was obtained (Figure 2).



Scheme 7. Synthesis of *N*-(2-alkynylbenzylidene)indolin-1-amines **3**.

Table 1. Structures and yields of *N*-{2-[alkynyl(hetero)aryl]methylene}indolin-1-amines **3**.

No.	Hydrazone	Yield [%]	No.	Hydrazone	Yield [%]
3a		93	**3f**		81
3b		93	**3g**		84
3c		79	**3h**		71
3d		86	**3i**		66
3e		86			

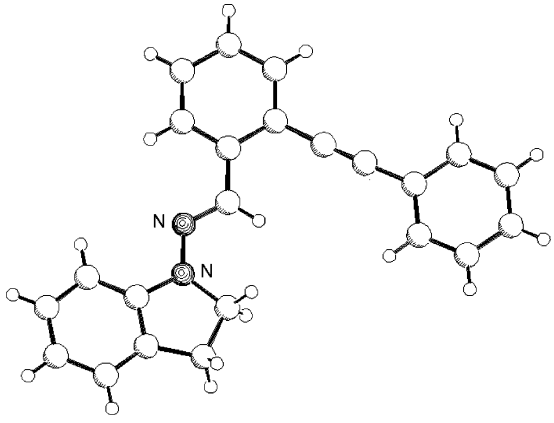
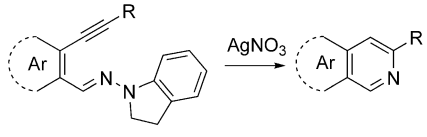


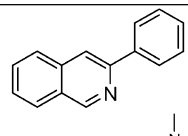
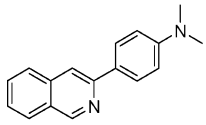
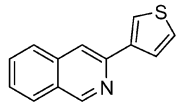
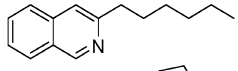
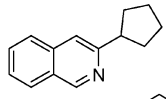
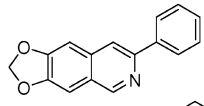
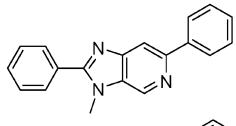
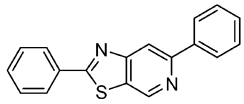
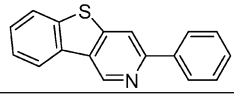
Figure 1. Molecular structure of compound **3a** in the solid state (X-ray diffraction).[11]



3 **4**

Scheme 8. Silver nitrate assisted cyclization of *N*-{2-[alkynyl(hetero)aryl]methylene}indolin-1-amines **3** to give the pyridine derivatives **4** (liberating indole as a leaving group).

Table 2. Structures and yields of the cyclization products **4**.

Hydrazone	Product	Product	Reaction time [h]	Yield [%]
3a		**4a**	3	98
3b		**4b**	1	65
3c		**4c**	4	83
3d		**4d**	8	52
3e		**4e**	5	46
3f		**4f**	3	50
3g		**4g**	4	76
3h		**4h**	4	44
3i		**4i**	4	48

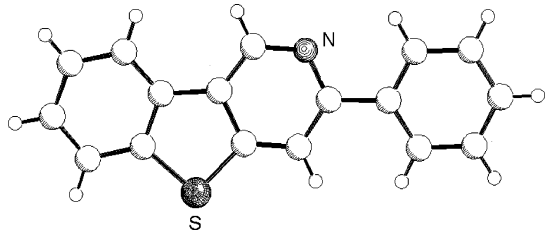
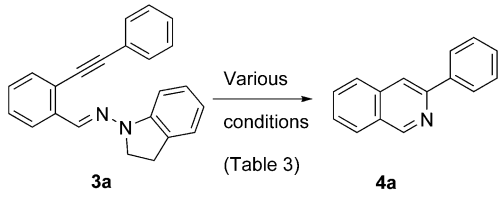


Figure 2. Molecular structure of compound **4i** in the solid state (X-ray diffraction).[11]

The coinage metal assisted activation of triple bonds is widely used in the synthesis of heterocyclic systems.[12] We tested also other coinage metal salts [copper(I), gold(I), gold(III)] and palladium(II) salts as catalysts for the cyclization of *o*-alkynylarenecarbaldehyde hydrazones **3** and some other silver salts besides $AgNO_3$. However, only silver nitrate gave good results. Acid treatment (catalytic amounts of concd. HNO_3) of **3** did not lead to cyclic products (Scheme 9, Table 3).

Table 3. Optimization of the reaction conditions for the cyclization reaction of compound **3a** leading to compound **4a**.

Metal salt	Base	Solvent	*T* [°C]	*t* [h]	Yield [%]
10 mol-% CuI	1 equiv. K_2CO_3	DMF	100	6	no reaction
10 mol-% $PdCl_2$·$(PhCN)_2$	1 equiv. K_2CO_3	DMF	100	4	no reaction
10 mol-% $PdCl_2$·$(PPh_3)_2$	1 equiv. K_2CO_3	DMF	50	5	no reaction
5 mol-% $AuCl_3$	1 equiv. Na_2CO_3	DCE	50	5	no reaction
10 mol-% CuBr	1 equiv. Na_2CO_3	DCE	50	5	no reaction
2 equiv. $AgNO_3$	–	$CHCl_3$	60	3	99
1.2 equiv. $AgNO_3$	–	$CHCl_3$	60	3	98
5 mol-% AuCl·PPh_3	–	$CHCl_3$	60	5	no reaction
AgOAc	–	$CHCl_3$	60	3	trace
AgOTf	–	$CHCl_3$	60	4	trace
$AgSbF_6$	–	$CHCl_3$	60	4	trace
–	1 equiv. K_2CO_3	EtOH	70	5	no reaction
–	cat. amount concd. HNO_3	$CHCl_3$	room temp.	3	decomp.

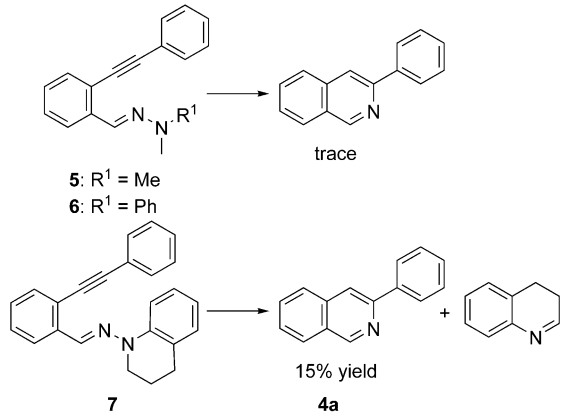


Scheme 9.

Thus, we found the optimal conditions for this reaction to be heating of the hydrazone **3** in $CHCl_3$ at 60 °C in the presence of 1.2 equiv. of silver nitrate. Catalytic amounts of silver salt give only partial conversion. The reason for this behaviour is discussed later in the text.

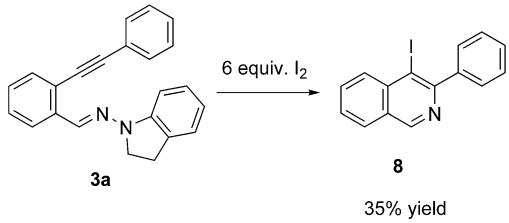
It has to be underlined that neither the hydrazone-forming step nor the cyclization reaction require absolute solvents and inert conditions. The reactions can be carried out in air, and the presence of water in the reaction medium does not have any effect on the outcome of these reactions.

In order to be sure that exclusively *N*-aminoindoline-derived hydrazones are suitable for the reaction, we also tested the hydrazones **5** and **6**, derived from 1,1-dimethylhydrazine and 1-methyl-1-phenylhydrazine under the conditions discussed above. They gave only traces of the isoquinoline product, the rest of the starting material was decomposed. The *N*-aminotetrahydroquinoline-derived hydrazone **7** led to the desired product **4a**, but the reaction was much less efficient, and the yield of **4a** was only 15% (compared to 98% for the *N*-aminoindoline-derived analogue). In this experiment the reaction mixture was heated in chloroform for 4 h in the presence of 1.2 equiv. of $AgNO_3$, the remaining substrate **7** was found to be decomposed (Scheme 10). We were able to detect a peak at *m*/*z* = 132.0814 in the ESI mass spectrum, which corresponds to the calculated mass of the protonated dihydroquinoline (*m*/*z* = 132.0813) formed in the reaction. However, we were not able to isolate it from the crude reaction mixture by column chromatography.



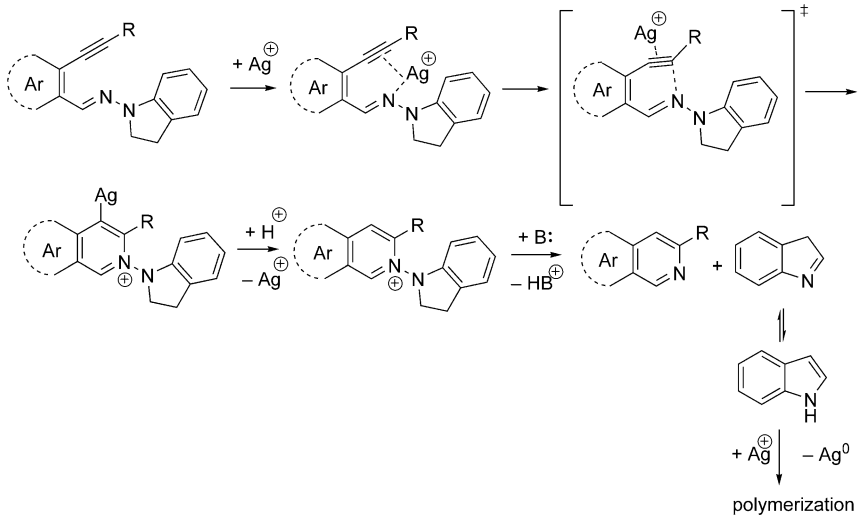
Scheme 10. Cyclization of 1,1-dimethyl-2-[2-(phenylethynyl)benzylidene]hydrazine (**5**), 1-methyl-1-phenyl-2-[2-(phenylethynyl)benzylidene]hydrazine (**6**), and *N*-[2-(phenylethynyl)benzylidene]-3,4-dihydroquinolin-1-amine (**7**).

Iodine may also be used as electrophile[8,13] in these cyclization reactions to afford the I-substituted product **8** in 35% yield (heating at 60 °C in chloroform for 8 h) (Scheme 11).



Scheme 11. Iodocyclization of *N*-[2-(phenylethynyl)benzylidene]-indolin-1-amine **3a**.

We propose the following mechanism for the observed silver(I)-induced reaction (Scheme 12). Silver(I) activation at the alkyne moiety of the substrate is expected to initiate a 6-*endo*-*dig* cyclization to afford a pyridinium cation, which in turn undergoes an N–N bond-fission reaction

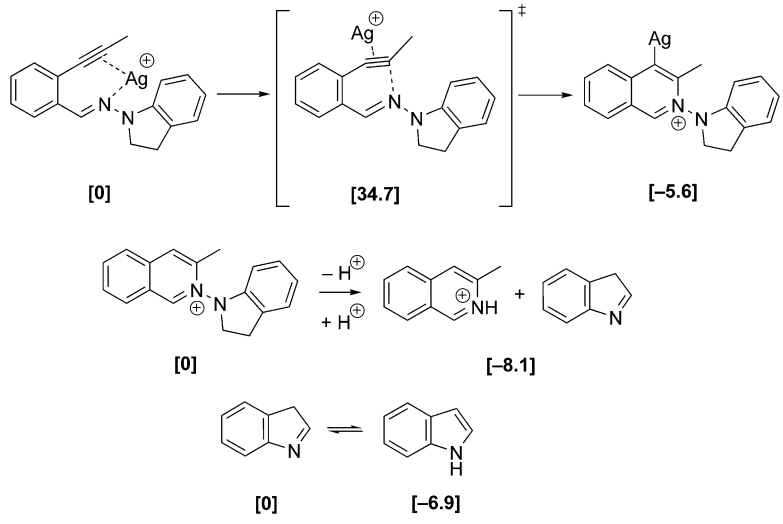


Scheme 12. Proposed mechanism of the silver-assisted cycliaztion reaction of *N*-{2-[alkynyl(hetero)aryl]methylene}indolin-1-amines **3**.

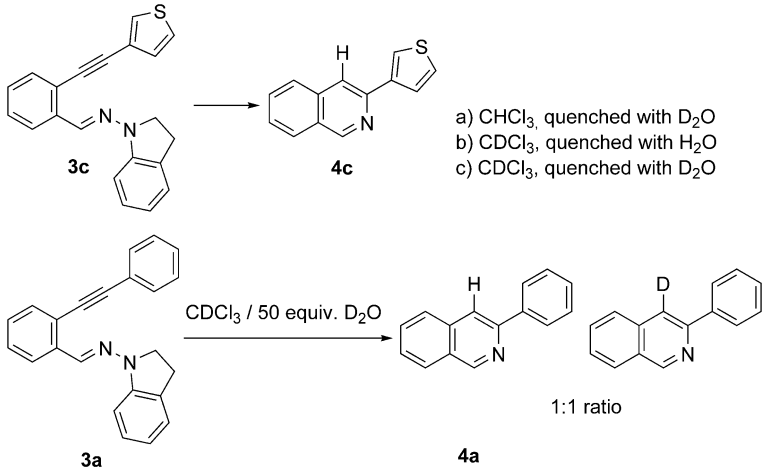
after removal of a proton from the indoline α-carbon atom, thereby releasing indole together with the annulated pyridine derivatives **4**.

We were also able to clarify the fate of indole as the second product and the origin of the observed silver mirror. In principle, catalytic amounts of the silver salt should be sufficient for the cyclization reaction, but under the reaction conditions Ag^I is reduced to Ag^0 by indole, which is formed after the N–N bond cleavage. The reduction process most probably proceeds by a single-electron transfer mechanism, and the intermediate indole radical undergoes uncontrolled polymerization. We performed a test reaction by treating 1*H*-indole in chloroform with $AgNO_3$ in the presence of nitrogen base (TEA, quinoline) at 60 °C. After 5 min, a silver mirror is formed, thus indicating the reduction of the silver cation by indole.

The proposed mechanism is supported by quantum chemical calculations[14] at the SCS-MP2/6-311G(d,p)//B3LYP/6-311G(d,p)-level[15] for the non-silver-containing species and at the SCS-MP2/6-311G(d,p)&SDD//B3LYP/6-311G(d,p)&SDD-level for silver-containing ones. The calculations of the silver(I) complex of *N*-[2-(prop-1-ynyl)-benzylidene]indolin-1-amine as model system (for simplicity we replaced larger groups by a methyl substituent at the triple bond) in the gas phase without any solvation, show that the cyclization step has an calculated activation barrier of 34.7 kcal/mol (for this less reactive alkyl-substituted example); the product formed is 5.6 kcal/mol lower in energy compared to the silver substrate complex (Scheme 13, upper line). The N–N bond-fission step is calculated to be exothermic as well. The sum of the energies of the protonated isoquinoline and 3*H*-indole is 8.1 kcal/mol lower in energy than that of the pyridinium cation (Scheme 13, middle line). By tautomerization of 3*H*-indole into 1*H*-indole an extra energy gain of 6.9 kcal/mol is achieved (Scheme 13, lower line).



Scheme 13. Calculated relative energies and activation barrier of the reactive species for the model system *N*-[2-(prop-1-ynyl)benzylidene]-indolin-1-amine [SCS-MP2/6-311G(d,p)&SDD//B3LYP/6-311G(d,p)&SDD+ ZPE].



Scheme 14. Results of the deuterium-labelling experiments.

According to the quantum chemical calculations, the silver cation as a Lewis acid shows a significant affinity towards the C–C triple bond (π-electrophilicity) and also to the lone pair of the hydrazone nitrogen atom (σ-electrophilicity).[16] Thus, the Ag^I ion in the pre-TS complex is coordinated to both, the triple bond and the N^1-hydrazone nitrogen atom (Figure 3).

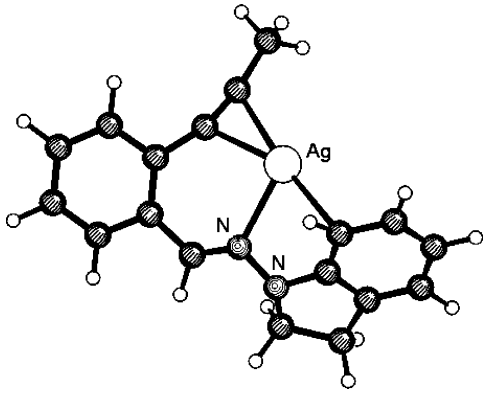


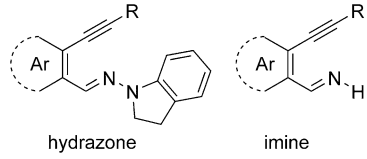
Figure 3. Calculated σ,π-chelate structure of the silver(I) complex based on the model system *N*-[2-(prop-1-ynyl)benzylidene]indolin-1-amine [B3LYP/6-311G(d,p)&SDD].

Similarly to Larock et al.[5f] we tried to determine the origin of the proton, which replaces the silver cation at the 4-position of the formed isoquinoline derivatives (Scheme 14).

When we performed the reaction in $CHCl_3$ and quenched the reaction mixture for the substrate **3c** with D_2O, the only observed product was non-deuterated **4c**. Similar results were obtained then we performed the reaction in $CDCl_3$ and quenched with H_2O or D_2O. These experiments indicate that the replacement of the Ag^I ion by the proton is finished before the workup. However, in the presence of 50 equiv. D_2O in $CDCl_3$ as solvent for the cyclization reaction of compound **3a** we obtained a 1:1 mixture of non-deuterated and deuterated product **4a**. In this case a certain amount of D^+ ions is assumed to be present in the reaction medium, which stems from dissociation of D_2O. Furthermore, during the reaction H^+ ions are also produced from the indoline part of the substrate as it is oxidized to indole.

Conclusions

We have disclosed a useful second example of the use of the indolyl substituent as leaving group from a nitrogen moiety, provided as hydrazones of type **3**. The silver nitrate promoted cyclization reaction of *N*-{2-[alkynyl(hetero)-aryl]methylene}indolin-1-amines **3** described here affords several different annulated pyridine compounds **4** in good to excellent yield. The hydrazones **3** might be considered as stable alternatives to [2-alkynyl(hetero)aryl]methanimines. Thus, in hydrazones **3** bearing an *N*-indolyl substituent instead of a hydrogen atom as in imines, the indolyl fragment may be considered to act as a "large hydrogen atom" under our reaction conditions (Scheme 15).



Scheme 15.

The transformations described here are very robust. They can be performed in air and even in the presence of water. This is a significant advantage compared to procedures employing imines as substrates in similar types of reactions. Some of the reaction substrates and products were characterized by X-ray diffraction.

Quantum chemical calculations were used in order to support the proposed reaction mechanism and to identify and characterize the key reactive intermediates at a high theoretical level.

Further investigations to establish indole as neutral leaving group in electrophilic substitution reactions at the nitrogen atom are underway in our laboratory.

Experimental Section

Melting points: Büchi Melting Point B-540, melting points are uncorrected. ^{1}H, ^{13}C NMR spectroscopy: AMX 400, Bruker WM 300 spectrometer. TMS (^{1}H: δ = 0.00 ppm) and $CDCl_3$ (^{13}C: δ = 77.0 ppm) were used as internal reference. IR: Varian 3100 FT-IR (Excalibur Series). MS: Mass spectra were recorded with a Finnigan MAT 4200S, a Bruker Daltonics micrOTOF, a Waters-Micromass Quatro LCZ (ESI). Elemental analysis: Elementar Vario EL III. Column chromatography: Silica gel Merck 60 (0.040–0.063 mm). TLC: Merck silica gel plates (silica gel 60 F254), detection with UV light.

General Procedure for the Preparation of *N*-{2-[Alkynyl(hetero)-aryl]methylene}indolin-1-amines 3: *N*-Indolin-1-amines **3a**–**i** were prepared from the corresponding *o*-alkynylarenecarbaldehydes **2**[17] and *N*-aminoindoline.[18] *o*-Alkynylarenecarbaldehyde **2** (1 mmol) was dissolved in of ethanol (4 mL), and *N*-aminoindoline (1.1 mmol) in ethanol (1 mL) was added slowly at 0 °C. Acetic acid (1 equiv.) and a small amount of sodium acetate were added to the reaction mixture in order to maintain a pH of 5–6. The reaction mixture was stirred at room temp. for 4 h. The resulting product was either separated by filtration and washed with water and cold ethanol or purified by column chromatography after standard aqueous workup.

***N*-[2-(Phenylethynyl)benzylidene]indolin-1-amine (3a):** From 2-(phenylethynyl)benzaldehyde (0.420 g, 2.00 mmol) and *N*-aminoindoline (0.295 g, 2.20 mmol) according to the general procedure. The subsequent recrystallization from ethanol gave 0.600 g (1.86 mmol, 93%) of **3a** as a yellow solid, m.p. 133–134 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 3.25 (t, J = 8.3 Hz, 2 H, CH_2), 3.92 (t, J = 8.3 Hz, 2 H, CH_2N), 6.83 (m, 1 H, *H*-arom.), 7.12–7.24 (m, 4 H, *H*-arom.), 7.31–7.39 (m, 4 H, *H*-arom.), 7.51–7.55 (m, 3 H, *H*-arom.), 7.89 (s, 1 H, C*H*-imine), 8.11 (d, J = 8.0 Hz, 1 H, *H*-arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 27.1 (*C*H$_2$), 47.9 (*C*H$_2$N), 87.4 (*C*-trip), 94.3 (*C*-trip), 109.0 (*C*H), 120.5 (*C*H), 121.0, 123.3, 124.0 (*C*H), 124.8 (*C*H), 127.1 (*C*H), 127.4, 127.8 (*C*H), 128.3 (*C*H), 128.4 (*C*H), 128.5 (*C*H), 131.3 (*C*H), 131.4 (*C*H), 132.3 (*C*H), 137.5, 147.8 ppm. IR (neat): $\tilde{\nu}$ = 3080 (w), 3057 (w), 3030 (w), 2991 (w), 2166 (w), 1609 (m), 1593 (w), 1566 (m), 1547 (m), 1485 (s), 1464 (m), 1440 (m), 1402 (s), 1325 (w), 1300 (m), 1269 (m), 1254 (m), 1192 (m), 1169 (m), 1150 (w), 1086 (w), 1069 (w), 1011 (w), 912 (w), 883 (m), 872 (w), 849 (w), 752 (s), 687 (s), 669 (w), 571 (w), 523 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{18}N_2Na$ 345.1362; found 345.1368. $C_{23}H_{18}N_2$ (322.41): calcd. C 85.68, H 5.63, N 8.69; found C 85.62, H 5.52, N 8.80.

X-ray Crystal Structure Analysis of 3a:[11] Empirical formula $C_{23}H_{18}N_2$, M = 322.39, yellow crystal 0.45 × 0.30 × 0.08 mm, a = 34.5200(2), b = 6.6330(1), c = 15.6070(10) Å, β = 102.501(4)°, V = 3448.8(2) Å^3, $\rho_{calcd.}$ = 1.228 g cm^{-3}, μ = 0.556 mm^{-1}, empirical absorption correction ($0.788 \leq T \leq 0.957$), Z = 8, monoclinic, space group $C2/c$ (No. 15), λ = 1.54178 Å, T = 223(2) K, ω and ϕ scans, 14013 reflections collected ($\pm h$, $\pm k$, $\pm l$), [(sinθ)/λ] = 0.60 Å^{-1}, 3076 independent (R_{int} = 0.054) and 2651 observed reflections [$I \geq 2\sigma(I)$], 226 refined parameters, R = 0.045, wR^2 = 0.134, max. (min.) residual electron density 0.12 (–0.16) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

***N*-{2-[4-(Dimethylamino)phenylethynyl]benzylidene}indolin-1-amine (3b):** From 2-[4-(dimethylamino)phenylethynyl]benzaldehyde (0.060 g, 0.24 mmol) and *N*-aminoindoline (0.035 g, 0.26 mmol) according to the general procedure. The subsequent recrystallization from ethanol gave 0.082 g (0.22 mmol, 93%) of **3b** as a yellow solid, m.p. 201–202 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 3.00 (s, 6 H, CH_3), 3.24 (t, J = 8.3 Hz, 2 H, CH_2), 3.92 (t, J = 8.3 Hz, 2 H, CH_2N), 6.69 (d, J = 8.5 Hz, 2 H, *H*-arom.), 6.82 (td, J = 7.3, 1.1 Hz, 1 H, *H*-arom.), 7.12–7.31 (m, 5 H, *H*-arom.), 7.40–7.49 (m, 3 H, *H*-arom.), 7.73 (s, 1 H, C*H*-imine), 8.08 (d, J = 7.9 Hz, 1 H, *H*-arom.) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 27.1 (*C*H$_2$), 40.3 (*C*H$_3$), 48.0 (*C*H$_2$N), 85.3 (*C*-trip), 95.6 (*C*-trip), 109.0 (*C*H), 112.0 (*C*H), 120.3 (*C*H), 122.1, 123.9 (*C*H), 124.8 (*C*H), 127.1 (*C*H), 127.5, 127.76 (*C*H), 127.82 (*C*H), 131.91 (*C*H), 131.98 (*C*H), 132.6 (*C*H), 136.9, 147.9, 150.0 ppm. IR (neat): $\tilde{\nu}$ = 3053 (w), 3021 (w), 2920 (w), 2899 (w), 2847 (w), 2801 (w), 2203 (m), 1607 (m), 1595 (m), 1568 (m), 1524 (m), 1483 (s), 1464 (m), 1404 (s), 1366 (s), 1300 (m), 1267 (s), 1190 (s), 1153 (m), 1086 (w), 1065 (w), 1036 (w), 1013 (w), 945 (m), 885 (w), 866 (w), 816 (s), 748 (s), 586 (w), 563 (w), 550 (m), 509 (s) cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{23}N_3Na$ 388.1784; found 388.1787. $C_{25}H_{23}N_3$ (365.48): calcd. C 82.16, H 6.34, N 11.50; found C 82.38, H 6.49, N 11.45.

***N*-[2-(Thiophen-3-ylethynyl)benzylidene]indolin-1-amine (3c):** From 2-(thiophen-3-ylethynyl)benzaldehyde (0.280 g, 1.32 mmol) and *N*-aminoindoline (0.195 g, 1.45 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:2) gave 0.340 g (1.04 mmol, 79%) of **3c** as orange solid, m.p.130–131 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 3.26 (t, J = 8.3 Hz, 2 H, CH_2), 3.93 (t, J = 8.3 Hz, 2 H, CH_2N), 6.84 (td, J = 7.3, 1.3 Hz, 1 H, *H*-arom.), 7.12–7.24 (m, 5 H, *H*-arom.), 7.31–7.37 (m, 2 H, *H*-arom.), 7.49 (dd, J = 7.7, 0.9 Hz, 1 H, *H*-arom.), 7.53 (dd, J = 3.0, 1.2 Hz, 1 H, *H*-arom.), 7.87 (s, 1 H, C*H*-imine), 8.09 (dd, J = 8.0, 1.2 Hz, 1 H, *H*-arom.) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 27.1 (*C*H$_2$), 47.9 (*C*H$_2$N), 86.9 (*C*-trip), 89.5 (*C*-trip), 109.0 (*C*H), 120.5 (*C*H), 121.0, 122.2, 124.1 (*C*H), 124.8 (*C*H), 125.6 (*C*H), 127.1 (*C*H), 127.5, 127.9 (*C*H), 128.47 (*C*H), 128.51 (*C*H), 129.8 (*C*H), 131.3 (*C*H), 132.3 (*C*H), 137.4, 147.8 ppm. IR (KBr): $\tilde{\nu}$ = 3117 (w), 3094 (w), 3055 (w), 3021 (w), 2212 (w), 1605 (m), 1566 (m), 1547 (m), 1479 (s), 1458 (m), 1447 (m), 1402 (s), 1354 (w), 1325 (w), 1300 (w), 1275 (w), 1258 (s), 1200 (m), 1188 (m), 1161 (m), 1126 (w), 1090 (w), 1076 (w), 1015 (w), 939 (w), 885 (w), 870 (m), 827 (m), 775 (s), 756 (s), 741 (s), 706 (w), 689 (m), 623 (s), 577 (m), 559 (w), 527 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{16}N_2SH$ 329.1107; found 329.1125.

***N*-[2-(Oct-1-ynyl)benzylidene]indolin-1-amine (3d):** From 2-(oct-1-ynyl)benzaldehyde (0.400 g, 1.87 mmol) and *N*-aminoindoline (0.278 g, 2.06 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:5) gave 0.530 g (1.61 mmol, 86%) of **3d** as a brown viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.88–0.93 (m, 3 H, CH_3), 1.31–1.35 (m, 4 H, CH_2), 1.49–1.51 (m, 2 H, CH_2), 1.61–1.66 (m, 2 H, CH_2), 2.49 (t, J = 6.9 Hz, 2 H, CH_2), 3.24 (t, J = 8.3 Hz, 2 H, CH_2), 3.88 (t, J = 8.3 Hz, 2 H, CH_2N), 6.82 (td, J = 7.3, 1.3 Hz, 1 H, *H*-arom.), 7.12–7.29 (m, 5 H, *H*-arom.), 7.37 (dd, J = 7.7, 1.0 Hz, 1 H, *H*-arom.), 7.82 (s, 1 H, C*H*-imine), 8.06 (dd, J = 8.0, 1.0 Hz, 1 H, *H*-arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 14.1 (*C*H$_3$), 19.6 (*C*H$_2$), 22.6 (*C*H$_2$), 27.0 (*C*H$_2$), 28.7 (*C*H$_2$), 28.9 (*C*H$_2$), 31.5 (*C*H$_2$), 48.0 (*C*H$_2$N), 78.5 (*C*-trip), 95.5 (*C*-trip), 109.0 (*C*H), 120.3 (*C*H), 122.1, 123.8 (*C*H), 124.8 (*C*H), 127.1 (*C*H), 127.4 (*C*H), 127.7 (*C*H), 127.8 (*C*H), 132.0 (*C*H), 132.3 (*C*H), 137.2, 147.9 ppm. IR (neat): $\tilde{\nu}$ = 3055 (w), 3024 (w), 2953 (m), 2926 (m), 2852 (m), 2224 (w), 1609 (m), 1568 (m), 1547 (m), 1483 (s), 1468 (s), 1445 (m), 1406 (s), 1328 (m), 1300 (m), 1260 (m), 1246 (m), 1211 (w), 1188 (m), 1171 (m), 1152 (w), 1096 (w), 1013 (w), 978 (w), 949 (w), 883 (m), 827 (w), 802 (w), 756 (s), 743 (s), 704 (w), 667 (w), 588 (w) 561 (m), 527 (s) cm^{-1}. HRMS (ESI): calcd. for

$C_{23}H_{26}N_2H$ 331.2169; found 331.2177. $C_{23}H_{26}N_2$ (330.47): calcd. C 83.59, H 7.93, N 8.48; found C 83.19, H 7.96, N 8.30.

***N*-[2-(Cyclopentylethynyl)benzylidene]indolin-1-amine (3e):** From 2-(cyclopentylethynyl)benzaldehyde (0.265 g, 1.34 mmol) and *N*-aminoindoline (0.198 g, 1.47 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:5) gave 0.360 g (1.15 mmol, 86%) of **3e** as a yellow solid, m.p. 80–81 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.61–1.77 (m, 6 H, CH_2), 1.99–2.09 (m, 2 H, CH_2), 2.92 (m, 1 H, C*H*), 3.26 (t, J = 8.3 Hz, 2 H, CH_2), 3.88 (t, J = 8.3 Hz, 2 H, CH_2N), 6.82 (td, J = 7.2, 1.4 Hz, 1 H, *H*-arom.), 7.13–7.29 (m, 5 H, *H*-arom.), 7.36 (dd, J = 7.7, 1.1 Hz, 1 H, *H*-arom.), 7.81 (s, 1 H, C*H*-imine), 8.05 (dd, J = 8.0, 1.2 Hz, 1 H, *H*-arom.) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 25.0, 27.1, 31.0, 34.1, 47.9 (*C*H_2N), 78.0 (*C*-trip), 99.8 (*C*-trip), 109.0 (*C*H), 120.3 (*C*H), 122.1, 123.8 (*C*H), 124.8 (*C*H), 127.1 (*C*H), 127.4 (*C*H), 127.7 (*C*H), 127.8 (*C*H), 132.06 (*C*H), 132.1 (*C*H), 137.2, 147.9 ppm. IR (neat): $\tilde{\nu}$ = 3055 (w), 2959 (m), 2864 (w), 2224 (w), 1607 (m), 1570 (m), 1549 (m), 1481 (s), 1445 (m), 1398 (s), 1298 (m), 1269 (m), 1250 (m), 1186 (m), 1163 (m), 1097 (w), 1036 (w), 1015 (w), 980 (w), 891 (m), 881 (w), 835 (w), 802 (w), 745 (s), 706 (m), 577 (m), 525 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{22}N_2H$ 315.1856; found 315.1865.

***N*-[(6-(Phenylethynyl)benzo[*d*][1,3]dioxol-5-yl)methylene]indolin-1-amine (3f):** From 6-(phenylethynyl)benzo[*d*][1,3]dioxole-5-carbaldehyde (0.220 g, 0.88 mmol) and *N*-aminoindoline (0.130 g, 0.97 mmol) according to the general procedure. The subsequent recrystallization from ethanol gave 0.260 g (0.71 mmol, 81%) of **3f** as a yellow solid, m.p. 169–170 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 3.23 (t, J = 8.3 Hz, 2 H, CH_2), 3.88 (t, J = 8.3 Hz, 2 H, CH_2N), 5.98 (d, J = 0.9 Hz, 2 H, OCH_2O), 6.82 (m, 1 H, *H*-arom.), 6.92 (s, 1 H, *H*-arom.), 7.11–7.22 (m, 3 H, *H*-arom.), 7.34–7.40 (m, 3 H, *H*-arom.), 7.48–7.52 (m, 2 H, *H*-arom.), 7.56 (s, 1 H, *H*-arom.), 7.84 (s, 1 H, C*H*-imine) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 27.1 (*C*H_2), 48.0 (*C*H_2N), 87.4 (*C*-trip), 93.2 (*C*-trip), 101.4 (O*C*H_2O), 103.8 (*C*H), 108.9 (*C*H), 111.0 (*C*H), 114.8, 120.3 (*C*H), 123.4, 124.8 (*C*H), 127.4, 127.8 (*C*H), 128.2 (*C*H), 128.4 (*C*H), 131.3 (*C*H), 131.5 (*C*H), 133.5, 147.1, 147.9, 148.6 ppm. IR (neat): $\tilde{\nu}$ = 3055 (w), 3005 (w), 2901 (w), 1886 (w), 2207 (w), 1607 (m), 1601 (m), 1558 (m), 1491 (m), 1474 (s), 1441 (m), 1412 (m), 1377 (w), 1298 (w), 1267 (w), 1242 (s), 1209 (s), 1153 (m), 1138 (w), 1034 (s), 937 (m), 910 (w), 889 (s), 860 (m), 841 (w), 799 (w), 762 (s), 752 (s), 687 (s), 637 (w), 608 (w), 538 (w) cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{18}N_2O_2Na$ 389.1260; found 389.1265. $C_{24}H_{18}N_2O_2$ (366.42): calcd. C 78.67, H 4.95, N 7.65; found C 78.49, H 4.90, N 7.58.

***N*-[(1-Methyl-2-phenyl-4-(phenylethynyl)-1*H*-imidazol-5-yl)methylene]indolin-1-amine (3g):** From 1-methyl-2-phenyl-4-(phenylethynyl)-1*H*-imidazole-5-carbaldehyde (0.110 g, 0.38 mmol) and *N*-aminoindoline (0.060 g, 0.46 mmol) according to the general procedure. The subsequent recrystallization from ethanol gave 0.130 g (0.32 mmol, 84%) of **3g** as a yellow solid, m.p. 222–223 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 3.28 (t, J = 8.2 Hz, 2 H, CH_2), 3.92 (t, J = 8.2 Hz, 2 H, CH_2N), 4.05 (s, 3 H, CH_3), 6.85 (td, J = 7.3, 0.8 Hz, 1 H, *H*-arom.), 7.04 (m, 1 H, *H*-arom.), 7.16 (m, 2 H, *H*-arom.), 7.33–7.35 (m, 3 H, *H*-arom.), 7.46–7.49 (m, 3 H, *H*-arom.), 7.54–7.59 (m, 3 H, *H*-arom.), 7.68–7.71 (m, 2 H, *H*-arom.) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 27.0 (*C*H_2), 35.8 (*C*H_3), 47.5 (*C*H_2N), 82.5 (*C*-trip), 93.5 (*C*-trip), 108.6 (*C*H), 120.6 (*C*H), 123.2, 123.5 (*C*H), 125.0 (*C*H), 127.5, 127.8 (*C*H), 128.1 (*C*H), 128.3 (*C*H), 128.5 (*C*H), 129.2 (*C*H), 129.3 (*C*H), 131.4 (*C*H), 133.5, 147.6, 149.9 ppm. IR (neat): $\tilde{\nu}$ = 3059 (w), 3019 (w), 2967 (w), 2949 (w), 2920 (w), 2849 (w), 2212 (w), 1607 (m), 1587 (m), 1524 (m), 1481 (s), 1468 (s), 1439 (m), 1414 (m), 1383 (w), 1369 (w), 1294 (m), 1260 (m), 1204 (m), 1184 (s), 1159 (s), 1042 (w), 1024 (w), 974 (w), 912 (w), 897 (w), 880 (w), 860 (w), 772 (m), 750 (s), 714 (m), 702 (s), 689 (s), 629 (w), 559 (m), 528 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{22}N_4H$ 403.1917; found 403.1921. $C_{27}H_{22}N_4$ (402.50): calcd. C 80.57, H 5.51, N 13.92; found C 80.23, H 5.58, N 13.82.

***N*-[(2-Phenyl-4-(phenylethynyl)thiazol-5-yl)methylene]indolin-1-amine (3h):** From 2-phenyl-4-(phenylethynyl)thiazole-5-carbaldehyde (0.080 g, 0.28 mmol) and *N*-aminoindoline (0.045 g, 0.33 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:10) gave 0.080 g (0.20 mmol, 71%) of **3h** as an orange solid, m.p.196–197 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 3.29 (t, J = 8.2 Hz, 2 H, CH_2), 3.99 (t, J = 8.2 Hz, 2 H, CH_2N), 6.89 (m, 1 H, *H*-arom.), 7.15–7.22 (m, 3 H, *H*-arom.), 7.38 (m, 3 H, *H*-arom.), 7.46 (m, 3 H, *H*-arom.), 7.61 (m, 2 H, *H*-arom.), 7.64 (s, 1 H, C*H*-imine) 8.02–8.04 (m, 2 H, *H*-arom.) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 27.0 (*C*H_2), 48.1 (*C*H_2N), 82.6 (*C*-trip), 94.3 (*C*-trip), 109.3 (*C*H), 121.3 (*C*H), 122.5, 124.4 (*C*H), 125.0 (*C*H), 126.8 (*C*H), 127.7, 128.0 (*C*H), 128.4 (*C*H), 128.8 (*C*H), 129.0 (*C*H), 130.6 (*C*H), 131.8 (*C*H), 132.7, 133.6, 140.6, 146.7, 165.2 ppm. IR (neat): $\tilde{\nu}$ = 3053 (w), 3030 (w), 2992 (w), 2959 (w), 2924 (w), 2850 (w), 2208 (w), 1734 (w), 1665 (w), 1611 (w), 1599 (m), 1541 (m), 1503 (m), 1485 (s), 1462 (m), 1439 (m), 1402 (m), 1356 (w), 1298 (m), 1260 (m), 1227 (w), 1188 (w), 1175 (w), 1163 (w), 1094 (w), 1016 (m), 978 (w), 907 (w), 854 (w), 802 (w), 746 (s), 708 (w), 687 (s), 679 (s), 635 (w), 604 (m), 547 (w), 540 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{19}N_3SH$ 406.1372; found 406.1362.

***N*-[(2-(Phenylethynyl)benzo[*b*]thiophen-3-yl)methylene]indolin-1-amine (3i):** From 2-(phenylethynyl)benzo[*b*]thiophene-3-carbaldehyde (0.262 g, 1.00 mmol) and *N*-aminoindoline (0.148 g, 1.10 mmol) according to the general procedure. The subsequent recrystallization from ethanol gave 0.250 g (0.66 mmol, 66%) of **3i** as an orange solid, m.p. 184–185 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 3.29 (t, J = 8.3 Hz, 2 H, CH_2), 3.97 (t, J = 8.3 Hz, 2 H, CH_2N), 6.86 (td, J = 7.1, 1.6 Hz, 1 H, *H*-arom.), 7.16 (d, J = 7.2 Hz, 1 H, *H*-arom.), 7.22–7.29 (m, 2 H, *H*-arom.), 7.38–7.45 (m, 4 H, *H*-arom.), 7.50 (ddd, J = 8.2, 7.2, 1.2 Hz, 1 H, *H*-arom.), 7.56–7.58 (m, 2 H, *H*-arom.), 7.76 (d, J = 7.7 Hz, 1 H, *H*-arom.), 7.93 (s, 1 H, C*H*-imine), 8.98 (d, J = 7.8 Hz, 1 H, *H*-arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 27.1 (*C*H_2), 47.4 (*C*H_2N), 82.5 (*C*-trip), 99.9 (*C*-trip), 109.0 (*C*H), 120.5 (*C*H), 121.0, 121.9 (*C*H), 122.7, 124.9 (*C*H), 125.2 (*C*H), 125.9 (*C*H), 126.0 (*C*H), 127.6, 128.0 (*C*H), 128.5 (*C*H), 128.8 (*C*H), 129.7 (*C*H), 131.5 (*C*H), 135.77, 135.80, 139.5, 147.8 ppm. IR (neat): $\tilde{\nu}$ = 3053 (w), 3021 (w), 3001 (w), 2930 (w), 2866 (w), 2847 (w), 2197 (w), 1607 (m), 1562 (m), 1547 (m), 1483 (w), 1458 (m), 1412 (m), 1366 (m), 1298 (w), 1271 (m), 1252 (s), 1202 (m), 1076 (w), 1017 (w), 868 (m), 839 (w), 806 (w), 754 (s), 737 (s), 729 (s), 689 (s), 642 (w), 575 (m), 542 (s), 529 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{25}H_{18}N_2SNa$ 401.1083; found 401.1088.

1,1-Dimethyl-2-[2-(phenylethynyl)benzylidene]hydrazine (5): From 2-(phenylethynyl)benzaldehyde (0.155 g, 0.75 mmol) and 1,1-dimethylhydrazine (0.048 g, 0.80 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:5) gave 0.170 g (0.69 mmol, 91%) of **5** as a brown oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 3.02 (s, 6 H, CH_3), 7.17 (td, J = 7.7, 1.1 Hz, 1 H, *H*-arom.), 7.28 (m, 1 H, *H*-arom.), 7.31–7.37 (m, 3 H, *H*-arom.), 7.47–7.53 (m, 3 H, *H*-arom.), 7.80 (s, 1 H, C*H*-imine), 7.93 (dd, J = 8.0, 0.4 Hz, 1 H, *H*-arom.) ppm. ^{13}C

NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 42.7 (*C*H_3), 87.5 (*C*-trip), 94.1 (*C*-trip), 120.7, 123.4, 123.8 (*C*H), 126.7 (*C*H), 128.3 (*C*H), 128.4 (*C*H), 128.5 (*C*H), 131.4 (*C*H), 132.1 (*C*H), 137.9 ppm. IR (neat): $\tilde{\nu}$ = 3055 (w), 2995 (w), 2859 (w), 2789 (w), 2212 (w), 1599 (m), 1566 (m), 1545 (m), 1491 (m), 1462 (m), 1445 (m), 1423 (w), 1402 (w), 1273 (m), 1260 (m), 1159 (w), 1132 (w), 1096 (w), 1057 (s), 1042 (m), 978 (m), 922 (m), 856 (m), 816 (w), 752 (s), 692 (s), 629 (m), 577 (m), 554 (w), 522 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{16}N_2H$ 249.1386; found 249.1387.

1-Methyl-1-phenyl-2-[2-(phenylethynyl)benzylidene]hydrazine (6): From 2-(phenylethynyl)benzaldehyde (0.155 g, 0.75 mmol) and 1-methyl-1-phenylhydrazine (0.098 g, 0.80 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:5) gave 0.215 g (0.69 mmol, 92%) of **6** as a yellow solid. m.p. 119–120 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 3.44 (d, *J* = 0.6, 3 H, CH_3), 6.94 (td, *J* = 7.3, 0.7 Hz, 1 H, *H*-arom.), 7.21(td, *J* = 7.5, 1.0 Hz, 1 H, *H*-arom.), 7.29–7.41 (m, 8 H, *H*-arom.), 7.50–7.55 (m, 3 H, *H*-arom.), 8.06 (s, 1 H, C*H*-imine), 8.09 (d, *J* = 8.0 Hz, 1 H, *H*-arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 33.2 (*C*H_3), 87.5 (*C*-trip), 94.4 (*C*-trip), 115.5 (*C*H), 120.8 (*C*H), 121.3, 123.3, 124.3 (*C*H), 127.2 (*C*H), 128.35 (*C*H), 128.43 (*C*H), 128.6 (*C*H), 129.0 (*C*H), 130.4 (*C*H), 131.4 (*C*H), 132.3 (*C*H), 137.7, 147.7 ppm. IR (neat): $\tilde{\nu}$ = 3076 (w), 3057 (w), 3024 (w), 2216 (w), 1595 (m), 1568 (m), 1551 (m), 1493 (s), 1443 (m), 1379 (m), 1317 (m), 1275 (m), 1192 (m), 1179 (m), 1145 (m), 1090 (m), 1028 (m), 993 (m), 914 (w), 887 (m), 845 (w), 754 (s), 746 (s), 689 (s), 640 (w), 584 (m), 534 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{18}N_2Na$ 333.1362; found 333.

***N*-[2-(Phenylethynyl)benzylidene]-3,4-dihydroquinolin-1(2*H*)-amine (7):** From 2-(phenylethynyl)benzaldehyde (0.260 g, 1.26 mmol) and 1-amino-1,2,3,4-tetrahydroquinoline (0.205 g, 1.39 mmol) according to the general procedure. 0.215 g (0.69 mmol, 92%) of **7** as a yellow solid, m.p. 144–145 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 2.19 (m, 2 H, CH_2), 2.77 (m, 2 H, CH_2), 3.73 (t, *J* = 6.2 Hz, 2 H, CH_2N), 6.82 (td, *J* = 7.3, 1.1 Hz, 1 H, *H*-arom.), 7.03 (dd, *J* = 7.4, 1.0 Hz, 1 H, *H*-arom.), 7.17–7.22 (m, 2 H, *H*-arom.), 7.33–7.40 (m, 4 H, *H*-arom.), 7.51–7.56 (m, 3 H, *H*-arom.), 7.80 (d, *J* = 8.3 Hz, 1 H, *H*-arom.), 8.08 (s, 1 H, C*H*-imine), 8.12 (dd, *J* = 8.0, 0.7 Hz, 1 H, *H*-arom.) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.9 (*C*H_2), 27.0 (*C*H_2), 44.9 (*C*H_2), 87.5 (*C*-trip), 94.2 (*C*-trip), 114.7 (*C*H), 119.9 (*C*H), 121.2, 123.3, 123.9, 124.3 (*C*H), 127.1 (*C*H), 127.4 (*C*H), 128.2 (*C*H), 128.3 (*C*H), 128.4 (*C*H), 128.6 (*C*H), 129.2 (*C*H), 131.5 (*C*H), 132.4 (*C*H), 138.0, 142.8 ppm. IR (neat): $\tilde{\nu}$ = 3057 (w), 3028 (w), 2938 (w), 2926 (w), 2839 (w), 2141 (w), 1601 (w), 1566 (m), 1549 (w), 1485 (s), 1460 (w), 1445 (m), 1393 (s), 1277 (w), 1221 (m), 1194 (m), 1161 (s), 1074 (w), 1057 (m), 1034 (w), 1022 (w), 935 (w), 876 (w), 800 (w), 750 (s), 689 (s), 650 (w), 571 (w), 524 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{20}N_2Na$ 359.1519; found 359.1531. $C_{24}H_{20}N_2$ (336.44): calcd. C 85.68, H 5.99, N 8.33; found C 85.57, H 6.07, N 8.38.

General Procedure for the Silver Nitrate Assisted Cyclization of *N*-{2-[Alkynyl(hetero)aryl]methylene}indolin-1-amines 3 into Annulated Pyridine Derivatives 4: The respective *N*-{2-[alkynyl(hetero)aryl]-methylene}indolin-1-amine **3** (1 mmol) was dissolved in $CHCl_3$ (5 mL); silver nitrate (1.2 mmol; 1.2 equiv.) was added to the solution in one portion. The reaction mixture was heated at 60 °C for the time indicated in Table 2. After cooling to room temperature, the reaction mixture was diluted with chloroform and washed with water. The organic phase was separated, dried with magnesium sulfate and purified by column chromatography.

3-Phenylisoquinoline (4a):[19] From compound **3a** (0.081 g, 0.25 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:3) gave 0.050 g (0.24 mmol, 98%) of **4a** as a brown solid, m.p. 91–92 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.42 (td, *J* = 9.2, 4.3 Hz, 1 H, *H*-arom.), 7.51 (t, *J* = 7.5 Hz, 2 H, *H*-arom.), 7.58 (dd, *J* = 11.1, 4.0 Hz, 1 H, *H*-arom.), 7.69 (m, 1 H, *H*-arom.), 7.87 (d, *J* = 8.3 Hz, 1 H, *H*-arom.), 7.99 (d, *J* = 8.2 Hz, 1 H, *H*-arom.), 8.07 (s, 1 H, *H*-arom.), 8.13 (d, *J* = 8.5 Hz, 2 H, *H*-arom.), 9.34 (s, 1 H, C*H*N) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 116.5 (*C*H), 126.9 (*C*H), 127.0 (*C*H), 127.1 (*C*H), 127.6 (*C*H), 127.7, 128.5 (*C*H), 128.8 (*C*H), 130.5 (*C*H), 136.6, 139.6, 151.3, 152.4 (*C*HN) ppm. HRMS (ESI): calcd. for $C_{15}H_{11}NH$ 206.0964; found 206.0962.

4-(Isoquinolin-3-yl)-*N*,*N*-dimethylaniline (4b): From compound **3b** (0.050 g, 0.14 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:1) gave 0.022 g (0.09 mmol, 65%) of **4b** as a yellow solid, m.p. 139–140 °C. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 3.03 [s, 6 H, N(CH_3)$_2$], 6.84 (dd, *J* = 9.5, 2.4 Hz, 2 H, *H*-arom.), 7.50 (m, 1 H, *H*-arom.), 7.64 (m, 1 H, *H*-arom.), 7.81 (d, *J* = 8.3 Hz, 1 H, *H*-arom.), 7.94 (d, *J* = 9.3 Hz, 1 H, *H*-arom.), 7.95 (s, 1 H, *H*-arom.), 8.05 (d, *J* = 9.0 Hz, 2 H, *H*-arom.), 9.28 (s, 1 H, C*H*N) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 40.4 [N(*C*H_3)$_2$], 112.4 (*C*H), 114.2 (*C*H), 126.1 (*C*H), 126.6 (*C*H), 127.1, 127.4, 127.6 (*C*H), 127.8 (*C*H), 130.3 (*C*H), 136.9, 150.8, 151.6, 152.1 (*C*HN) ppm. IR (neat): $\tilde{\nu}$ = 2922 (w), 2853 (w), 2804 (w), 1605 (s), 1580 (s), 1524 (s), 1481 (w), 1441 (s), 1354 (s), 1321 (w), 1261 (w), 1225 (m), 1194 (s), 1167 (m), 1123 (m), 1063 (w), 1013 (w), 941 (m), 883 (s), 862 (m), 818 (s), 764 (s), 729 (m), 683 (m), 667 (m), 611 (w), 551 (m), 532 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{16}N_2H$ 249.1386; found 249.1380.

3-(Thiophen-3-yl)isoquinoline (4c): From compound **3c** (0.131 g, 0.40 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:3) gave 0.070 g (0.33 mmol, 83%) of **4c** as a red solid, m.p. 90–91 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.43 (dd, *J* = 5.0, 3.1 Hz, 1 H, *H*-arom.), 7.56 (d, *J* = 7.1 Hz, 1 H, *H*-arom.), 7.66 (t, *J* = 7.5 Hz, 1 H, *H*-arom.), 7.73 (dd, *J* = 5.1, 1.2 Hz, 1 H, *H*-arom.), 7.82 (d, *J* = 8.2 Hz, 1 H, *H*-arom.), 7.92 (s, 1 H, *H*-arom.), 7.94 (d, *J* = 8.3 Hz, 1 H, *H*-arom.), 8.03 (dd, *J* = 3.0, 1.2 Hz, 1 H, *H*-arom.), 9.26 (s, 1 H, C*H*N) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 115.8 (*C*H), 123.1 (*C*H), 126.0 (*C*H), 126.3 (*C*H), 126.7 (*C*H), 126.8 (*C*H), 127.59, 127.61 (*C*H), 130.6 (*C*H), 136.6, 142.2, 147.5, 152.5 (*C*HN) ppm. IR (neat): $\tilde{\nu}$ = 3103 (w), 3053 (w), 2922 (w), 2855 (w), 1622 (m), 1582 (m), 1530 (w), 1485 (w), 1437 (m), 1379 (m), 1339 (w), 1300 (m), 1277 (m), 1229 (m), 1196 (m), 1167 (w), 1140 (w), 1013 (w), 962 (m), 945 (m), 908 (w), 881 (m), 837 (m), 804 (s), 746 (s), 691 (s), 654 (m), 617 (m), 514 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{13}H_9NSH$ 212.0528; found 212.0526. $C_{13}H_9NS$ (211.28): calcd. C 73.90, H 4.29, N 6.63; found C 73.46, H 4.44, N 7.04.

3-Hexylisoquinoline (4d): From compound **3d** (0.066 g, 0.20 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:3) gave 0.022 g (0.10 mmol, 52%) of **4d** as an orange oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.88 (t, *J* = 7.0 Hz, 3 H, CH_3.),1.31–1.41 (m, 6 H, CH_2), 1.77–1.85 (m, 2 H, CH_2), 2.93 (m, 2 H, CH_2), 7.47 (s, 1 H, *H*-arom.), 7.51–7.55 (m, 1 H, *H*-arom.), 7.62–7.67 (m, 1 H, *H*-arom.), 7.75 (d, *J* = 8.2 Hz, 1 H, *H*-arom.), 7.93 (d, *J* = 8.2 Hz, 1 H, *H*-arom.), 9.20 (s, 1 H, C*H*N) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 14.1 (*C*H_3), 22.6 (*C*H_3), 29.1 (*C*H_3), 30.0 (*C*H_3), 31.8 (*C*H_3), 38.2 (*C*H_3), 117.9 (*C*H), 126.1 (*C*H), 126.2 (*C*H), 127.0, 127.5 (*C*H), 130.2 (*C*H), 152.0 (*C*HN), 155.9 ppm. IR (neat): $\tilde{\nu}$ = 3055 (w), 2926 (m), 2855 (m), 1630 (m), 1591 (m), 1582 (m), 1491

(w), 1456 (m), 1377 (w), 1275 (w), 1167 (w), 1140 (w), 1015 (w), 949 (m), 878 (m), 851 (w), 746 (m), 630 (s), 534 (s) cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{19}NH$ 214.1590; found 214.1598.

3-Cyclopentylisoquinoline (4e): From compound **3e** (0.126 g, 0.40 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 2:5) gave 0.036 g (0.18 mmol, 46%) of **4e** as a brown solid, m.p. 145–146 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.77–1.92 (m, 6 H, CH_2), 2.21–2.29 (m, 2 H, CH_2), 3.48 (m, 1 H, C*H*), 7.61–7.66 (m, 2 H, *H*-arom.), 7.76–7.86 (m, 2 H, *H*-arom.), 8.04 (d, J = 8.2 Hz, 1 H, *H*-arom.), 9.34 (s, 1 H, C*H*N) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 25.6 (*C*H_2), 33.6 (*C*H_2), 46.1 (*C*H), 118.2 (*C*H), 126.4 (*C*H), 126.7, 127.5 (*C*H), 128.3 (*C*H), 132.3 (*C*H), 137.5, 149.9 (*C*HN), 156.0 ppm. IR (neat): $\tilde{\nu}$ = 2949 (m), 2862 (m), 2488 (m), 1645 (m), 1626 (m), 1614 (m), 1580 (m), 1562 (w), 1489 (m), 1450 (m), 1389 (w), 1254 (w), 1207 (w), 1155 (m), 962 (m), 914 (m), 885 (s), 777 (s), 750 (s), 696 (w), 563 (m), 532 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{14}H_{15}NH$ 198.1277; found 198.1277.

7-Phenyl-[1,3]dioxolo[4,5-*g*]isoquinoline (4f):[5f] From compound **3f** (0.104 g, 0.28 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 2:3) gave 0.035 g (0.14 mmol, 50%) of **4f** as a red solid. m.p. 117–118 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 6.09 (s, 2 H, CH_2), 7.11 (s, 1 H, *H*-arom.), 7.20 (s, 1 H, *H*-arom.), 7.40 (m, 1 H, *H*-arom.), 7.49 (m, 2 H, *H*-arom.), 7.89 (s, 1 H, *H*-arom.), 8.07 (m, 2 H, *H*-arom.), 9.06 (s, 1 H, C*H*N) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 101.6 (*C*H_2), 102.8 (*C*H), 103.1 (*C*H), 116.4 (*C*H), 125.0, 126.8 (*C*H), 128.3 (*C*H), 128.7 (*C*H), 135.0, 139.6, 148.3, 150.1 (*C*HN), 150.5, 151.1 ppm. HRMS (ESI): calcd. for $C_{16}H_{11}NO_2H$ 250.0863; found 250.0862.

3-Methyl-2,6-diphenyl-3*H*-imidazo[4,5-*c*]pyridine (4g): From compound **3g** (0.028 g, 0.07 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O) gave 0.015 g (0.05 mmol, 76%) of **4g** as a yellow solid, m.p. 169–170 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 4.02 (s, 3 H, CH_3), 6.98 (s, 1 H, *H*-arom.), 7.38–7.44 (m, 1 H, *H*-arom.), 7.49–7.54 (m, 2 H, *H*-arom.), 7.58–7.60 (m, 2 H, *H*-arom.), 7.81–7.84 (m, 2 H, *H*-arom.), 8.05–8.08 (m, 2 H, *H*-arom.), 8.14 (d, J = 1.0 Hz, 1 H, *H*-arom.), 8.93 (d, J = 1.0 Hz, 1 H, *H*-arom.) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 32.3(*C*H_3), 111.2 (*C*H), 127.1 (*C*H), 128.2 (*C*H), 128.8 (*C*H), 129.0 (*C*H), 129.1, 129.6 (*C*H), 130.7 (*C*H), 132.4 (*C*H), 133.7, 140.1, 149.3, 151.1, 157.3 ppm. IR (neat): $\tilde{\nu}$ = 3055 (w), 3030 (w), 2955 (w), 2924 (m), 2853 (m), 1734 (w), 1670 (w), 1607 (m), 1570 (w), 1520 (w), 1476 (s), 1466 (s), 1441 (s), 1381 (m), 1344 (m), 1287 (w), 1261 (m), 1213 (w), 1190 (w), 1117 (m), 1074 (w), 1016 (m), 972 (w), 916 (m), 899 (w), 866 (m), 858 (w), 843 (w), 779 (s), 760 (s), 721 (m), 696 (s), 675 (s), 610 (w), 602 (m), 522 (w) cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{15}N_3H$ 286.1339; found 286.1340.

2,6-Diphenylthiazolo[5,4-*c*]pyridine (4h): From compound **3h** (0.080 g, 0.20 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 1:3) gave 0.025 g (0.09 mmol, 44%) of **4h** as an orange solid, m.p. 147–148 °C. ^1H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.47–7.59 (m, 6 H, *H*-arom.), 8.10–8.13 (m, 2 H, *H*-arom.), 8.16–8.19 (m, 2 H, *H*-arom.), 8.39 (d, J = 0.7 Hz, 1 H, *H*-arom.), 9.31(s, 1 H, C*H*N) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 114.6 (*C*H), 120.6, 127.3 (*C*H), 128.3 (*C*H), 129.2 (*C*H), 129.4 (*C*H), 129.8 (*C*H), 130.9, 132.5, 132.7 (*C*H), 142.3 (*C*H), 147.6, 148.5, 161.3 ppm. IR (neat): $\tilde{\nu}$ = 3057 (w), 3028 (w), 2963 (w), 2851 (w), 1587 (m), 1523 (w), 1506 (m), 1476 (m), 1437 (s), 1420 (m), 1260 (m), 1240 (m), 1198 (w), 1096 (w), 1072 (w), 1018 (m), 962 (s), 905 (m), 864 (m), 802 (m), 756 (s), 745 (m), 681 (s), 667 (s), 610 (s), 540 (m), 513 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{12}N_2SH$ 289.0794; found 289.0786.

3-Phenylbenzo[4,5]thieno[3,2-*c*]pyridine (4i): From compound **3i** (0.150 g, 0.40 mmol) according to the general procedure. The subsequent chromatographic purification (Et_2O/pentane, 2:5) gave 0.050 g (0.19 mmol, 48%) of **4i** as a yellow solid, m.p. 167–168 °C. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.44 (m, 1 H, *H*-arom.), 7.49–7.52 (m, 4 H, *H*-arom.), 7.88 (m, 1 H, *H*-arom.), 8.10 (m, 2 H, *H*-arom.), 8.20 (d, J = 0.8 Hz, 1 H, *H*-arom.), 8.27 (m, 1 H, *H*-arom.), 9.47 (s, 1 H, C*H*N) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 114.4 (*CH*), 121.7 (*CH*), 122.9 (*CH*), 125.4 (*CH*), 127.2 (*CH*), 127.7 (*CH*), 128.9 (*CH*), 129.1 (*CH*), 130.5, 133.4, 139.1, 142.7 (*C*HN), 149.5, 153.5 ppm. IR (neat): $\tilde{\nu}$ = 3053 (w), 3022 (w), 2963 (w), 1595 (w), 1574 (m), 1528 (w), 1470 (w), 1454 (w), 1441 (m), 1435 (m), 1368 (m), 1321 (w), 1300 (m), 1246 (m), 1225 (m), 1086 (m), 1070 (m), 1018 (m), 989 (w), 932 (w), 918 (w), 860 (m), 822 (m), 781 (m), 752 (s), 721 (s), 687 (s), 629 (s), 557 (w), 534 (w) cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{11}NSH$ 262.0685; found 262.0672.

X-ray Crystal Structure Analysis of 4i:[11] Empirical formula $C_{17}H_{11}NS$, M = 261.33, light yellow crystal 0.25 × 0.15 × 0.03 mm, a = 8.7552(1), b = 5.8014(1), c = 24.4634(1) Å, β = 97.434(1)°, V = 1232.11(3) $Å^3$, $\rho_{calcd.}$ = 1.409 $g\,cm^{-3}$, μ = 2.168 mm^{-1}, empirical absorption correction ($0.613 \le T \le 0.938$), Z = 4, monoclinic, space group $P2_1/c$ (No. 14), λ = 1.54178 Å, T = 223(2) K, ω and ϕ scans, 8954 reflections collected ($\pm h$, $\pm k$, $\pm l$), [(sinθ)/λ] = 0.60 $Å^{-1}$, 2161 independent (R_{int} = 0.058) and 1779 observed reflections [$I \ge 2\sigma(I)$], 176 refined parameters, R = 0.054, wR^2 = 0.138, max. (min.) residual electron density 0.20 (–0.19) $e\,Å^{-3}$, disorder refined with a ratio of 88:12, hydrogen atoms calculated and refined as riding atoms.

4-Iodo-3-phenylisoquinoline (8):[5c] From compound **3a** (0.100 g, 0.30 mmol) by addition of I_2 (6 equiv., 0.450 g, 1.80 mmol) in of $CHCl_3$ (5 mL). The reaction mixture was stirred at 60 °C for 8 h. After aqueous workup and extraction with $CHCl_3$, chromatographic purification (Et_2O/pentane, 2:3) gave 0.035 g (0.11 mmol, 35%) of **8** as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.44–7.53 (m, 3 H, *H*-arom.), 7.61–7.65 (m, 2 H, *H*-arom.), 7.69 (ddd, J = 8.0, 7.0, 1.0 Hz, 1 H, *H*-arom.), 7.84 (ddd, J = 8.5, 7.0, 1.3 Hz, 1 H, *H*-arom.), 7.97 (d, J = 8.1 Hz, 1 H, *H*-arom.), 8.24 (dd, J = 8.5, 0.8 Hz, 1 H, *H*-arom.), 9.17 (s, 1 H, C*H*N) ppm. HRMS (ESI): calcd. for $C_{15}H_{10}INH$ 331.9931; found 331.9939.

Supporting Information (see footnote on the first page of this article): ^1H and ^{13}C NMR spectra for the new compounds, deuterium-labelling NMR spectra. Quantum chemical calculations: Cartesian coordinates, SCS-MP2/6-311G(d,p)//B3LYP/6-311G(d,p)& SDD+ZPE energies (au). Thermal ellipsoid plots for the crystal structures (ellipsoid probability contours 50%).

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