ChemPubSoc Europe

DOI: 10.1002/ejoc.201600660

EurJOC European Journal of Organic Chemistry

Full Paper

Benzo[*a*]phenazines by Iodocyclization

Electrophile-Induced Cyclization of 3-Alkynyl-2-arylquinoxalines: A Method for Benzo- and Naphthophenazine Synthesis

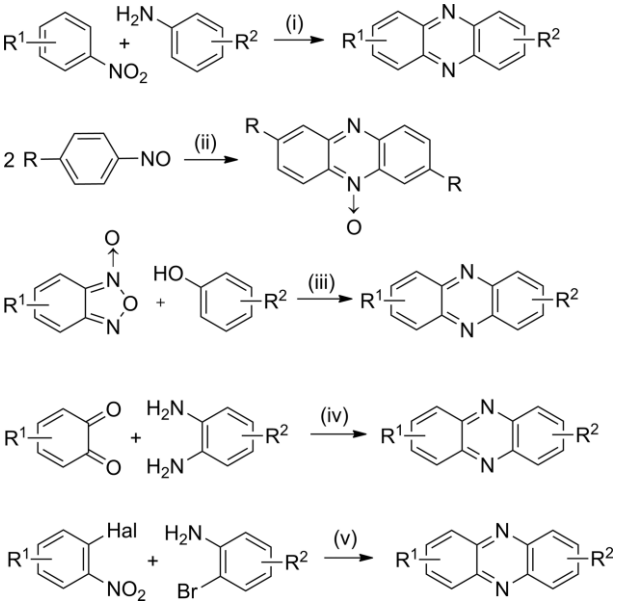
Anna V. Gulevskaya*[a]

Abstract: A facile synthesis of benzo[*a*]-, naphtho[1,2-*a*]- and naphtho[2,1-*a*]phenazines by ICl-promoted 6-*endo*-*dig* cyclization of 3-alkynyl-2-arylquinoxalines has been developed. The starting 3-alkynyl-2-arylquinoxalines were synthesized from 2,3-dichloroquinoxaline by two successive Sonogashira and Suzuki–Miyaura reactions. The method works well for 3-alkynyl-2-arylquinoxalines bearing various functional groups at the alkyne moiety. The arrangement and nature of the substituent in the 2-aryl fragment affect the regioselectivity of the cyclization. For the substrate of one particular type, namely 2-(4-methoxyphenyl)-3-(*p*-tolylethynyl)quinoxaline, the treatment with ICl leads to the alternative 5-*endo*-*dig* cyclization followed by demethylation of the methoxy group to give a spirocyclohexadienone derivative.

Introduction

The phenazine core is an integral part of many biologically active compounds, including more than 100 natural antibiotics, produced by *Pseudomonas*, *Streptomyces*, marine and other microorganisms.[1a] Antibiotic, antitumor, antimalarial and antiparasitic properties of phenazines are well documented.[1a–1i] The biological activity of phenazines is based on their ability for intercalation, inhibition of topoisomerases and radical oxidation processes, transfer of electrons in the process of methanogenesis and so on.

The most general approaches for the synthesis of phenazines, including condensed ones, consist of (Scheme 1):[1a] (i) base-catalyzed thermal condensation of anilines with nitrobenzenes (Wohl–Aue method),[1j] (ii) fusing of two molecules of 4-substituted nitrosobenzene under acidic conditions (Bamberger–Ham method),[1k] (iii) dehydrative condensation of benzofuroxanes with phenols (Beirut reaction),[1l] (iv) condensation of *ortho*-quinones (sometimes in situ generated) with benzene-1,2-diamines,[1m] and (v) condensation of 2-halonitrobenzenes with 2-bromoanilines by two sequential Pd-catalyzed Buchwald–Hartwig arylamination reactions.[1n] The majority of the known methods have some limitations due to the arrangement and the electronic nature of substituents in the starting reagents. The low output of products and rather harsh reaction conditions are other drawbacks in the existing protocols. Currently, catalytic methods for phenazine synthesis, based on the Buchwald–Hartwig reactions, seem to be the most effective. The development of new strategies to enable the preparation of phenazines therefore remains of major interest.



Scheme 1. Synthetic methods for the preparation of phenazines.

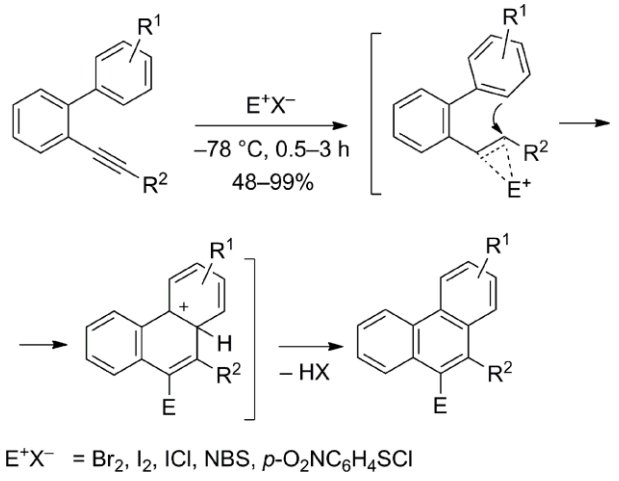
Some years ago, the electrophile-induced carbocyclization of 2-(1-alkynyl)biphenyls to phenanthrene derivatives had been reported (Scheme 2).[2] Despite tremendous synthetic potential of this type of cyclization its other applications are still limited.[3]

From this and following our interest in quinoxalines[4a–4d] and phenazines[4e] we reasoned that the analogous reaction of 3-alkynyl-2-arylquinoxalines **1** with electrophiles could result in the formation of benzo[*a*]phenazine derivatives **2** (Scheme 3).

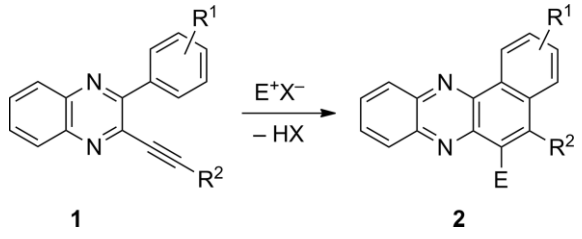
Herein, we wish to report on the results of this approach allowing to synthesize benzo[*a*]-, naphtho[1,2-*a*]- and naphtho[2,1-*a*]phenazines in a simple and convenient way.

[a] *Department of Chemistry, Southern Federal University, Zorge str., 7 Rostov-on-Don 344090, Russian Federation*
E-mail: agulevskaya@sfedu.ru
http://www.sfedu.ru

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201600660.



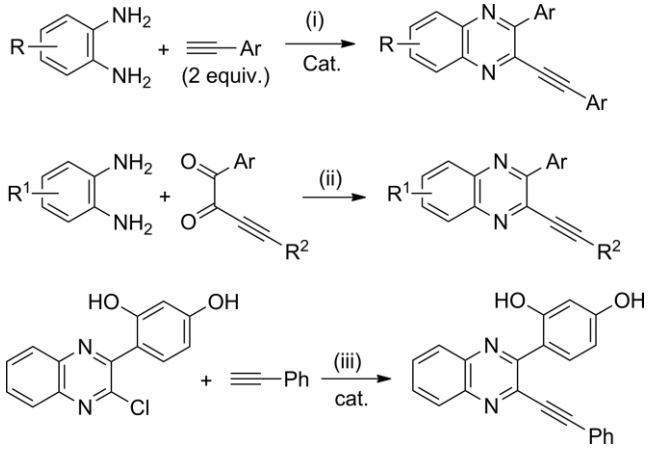
Scheme 2. Electrophile-induced cyclization of 2-(1-alkynyl)biphenyls to phenanthrenes.



Scheme 3. Strategy for the synthesis of benzo[*a*]phenazines.

Results and Discussion

We began our study by preparing 3-alkynyl-2-arylquinoxalines **1**. Three methods for their synthesis have been described previously (Scheme 4): (i) transition-metal-catalyzed cyclization of *ortho*-phenylenediamines with terminal alkynes,[5a–5c] (ii) cyclization of ynediones and *ortho*-phenylenediamines in the presence of acetic acid,[5d–5f] and (iii) Sonogashira coupling of 4-(3-chloroquinoxalin-2-yl)benzene-1,3-diol with phenylacetylene.[5g]

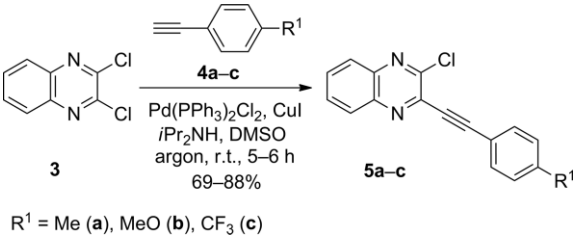


Scheme 4. Synthetic methods for the preparation of 3-alkynyl-2-arylquinoxalines.

All these approaches have some limitations. The Sonogashira coupling of 4-(3-chloroquinoxalin-2-yl)benzene-1,3-diol with phenylacetylene gave the target product in low yield.[5g] Ynediones with π-excessive hetaryl substituents were mostly used in method (ii), though being modified the method also enables the introduction of electroneutral aryl substituents (phenyl, mesityl) at position 2 of 3-alkynyl-2-arylquinoxalines.[5f] The best of these protocols, e.g. cyclization of *ortho*-phenylenediamines with terminal alkynes, strongly depends on the catalyst. For example, the use of the $Cu(OAc)_2/Cs_2CO_3$/DMAP/toluene system led to complicated product compositions and formation of isomeric 3-alkynyl-2-arylquinoxalines when using substituted *ortho*-phenylenediamines.[5a] CuCl[5b] and Fe_3O_4@Cu_2O-graphene oxide nanocomposite[5b] catalysts did not give isomers. However, this method does not allow the preparation of 3-alkynyl-2-arylquinoxalines with different substituents at the triple bond and in position 2 of the quinoxaline ring.

We suggested that the desired 3-alkynyl-2-arylquinoxalines could be obtained from available 2,3-dichloroquinoxaline[6] through a Sonogashira reaction/Suzuki–Miyaura coupling or reverse synthetic sequence. We chose the Sonogashira reaction/Suzuki–Miyaura coupling way, because it was reported that the Suzuki coupling of 2,3-dichloroquinoxaline with phenylboronic acid (1.2 equiv.) produced a hardly separable mixture of 2-chloro-3-phenylquinoxaline (50 %) and 2,3-diphenylquinoxaline (20 %).[7] Another known method for 3-aryl-2-chloroquinoxalines consists of the $AlCl_3$-induced arylation of 2,3-dichloroquinoxaline.[8] Unfortunately, it allows to introduce π-excessive hetaryl or aryl substituents only.

3-Alkynyl-2-chloroquinoxalines **5a**–**c** were readily prepared by the Sonogashira reaction of 2,3-dichloroquinoxaline **3** with arylacetylenes **4a**–**c** using the $Pd(PPh_3)_2Cl_2$/CuI/iPr_2NH/DMSO catalytic system (Scheme 5). The yields of this process range from 69 % to 88 % for arylacetylenes with both electron-withdrawing and electron-releasing groups.

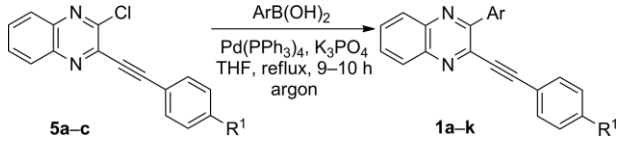


Scheme 5. Synthesis of 3-alkynyl-2-chloroquinoxalines.

Coupling of 3-alkynyl-2-chloroquinoxalines **5a**–**c** with arylboronic acids by using the $Pd(PPh_3)_4/K_3PO_4$/THF catalytic system under reflux for 9–10 h afforded the desired 3-alkynyl-2-arylquinoxalines **1a**–**k** in 66–88 % yields (Table 1). The reaction was tolerant to both electron-withdrawing and electron-donating groups in the starting compounds. The nature and arrangement of the substituent in the used arylboronic acid has a greater influence on the yield. Taking into account that the boronic acid is formally a nucleophilic component in the Suzuki reaction, the highest yield of the coupled product **1d** with 4-methoxyphenylboronic acid (Table 1, Entry 4) looks quite logical. Apparently, some decrease in the yields with *meta*-substituted arylboronic acids (Table 1, Entries 3, 5, 9, 11) and

naphthylboronic acids (Table 1, Entries 6 and 7) is due to steric reasons.

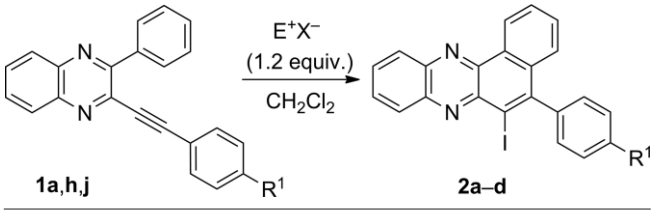
Table 1. Synthesis of 3-alkynyl-2-arylquinoxalines.



Entry	R^1	Ar	Product	Yield [%]
1	Me	Ph	**1a**	82
2	Me	*p*-Tol	**1b**	85
3	Me	*m*-Tol	**1c**	72
4	Me	4-$MeOC_6H_4$	**1d**	88
5	Me	3-$OHCC_6H_4$	**1e**	66
6	Me	naphthalen-1-yl	**1f**	71
7	Me	naphthalen-2-yl	**1g**	71
8	CF_3	Ph	**1h**	80
9	CF_3	*m*-Tol	**1i**	70
10	MeO	Ph	**1j**	75
11	MeO	*m*-Tol	**1k**	79

To explore the feasibility of the above electrophilic cyclization strategy, the reactions of 2-phenyl-3-(*p*-tolylethynyl)quinoxaline (**1a**) with various electrophiles (ICl, Br_2, NCS) in dry CH_2Cl_2 at room temperature for 24 h were been studied (Table 2). The expected 6-iodo-5-*p*-tolylbenzo[*a*]phenazine (**2a**) was obtained in 62 % yield when ICl (1.2 equiv.) was used as electrophile (Table 2, Entry 1). However, the reaction was not selective producing small amounts of side-products (presumably 1,2-adducts formed by ICl addition to the C≡C bond and oligomerization products). The use of bromine as electrophile led to a complicated reaction mixture. From this we were able to isolate the desired product **2b** in only 15 % yield (Table 2, Entry 4). NCS did not react noticeably with 2-phenyl-3-(*p*-tolylethynyl)quinoxaline (**1a**) even for 6 d (Table 2, Entry 5).

Table 2. Electrophile-induced cyclization of 3-alkynyl-2-phenylquinoxalines.

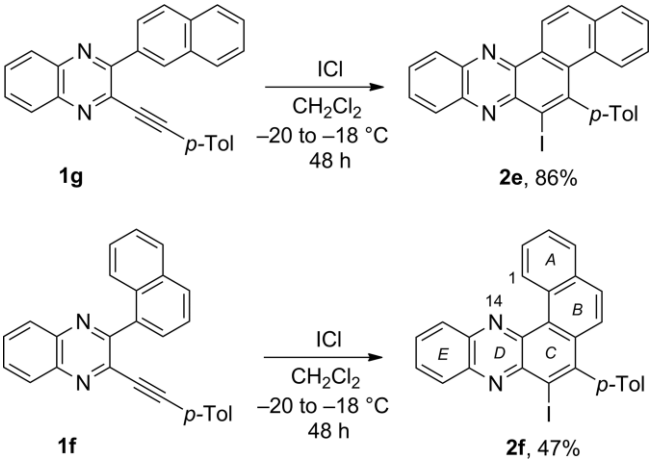


Entry	R^1	E^+X^-	Reaction conditions	Product	Yield [%]
1	Me	ICl	r.t., 24 h	**2a**	62
2	Me	ICl	–20 to –18 °C, 24 h	**2a**	63
3	Me	ICl	–20 to –18 °C, 72 h	**2a**	67
4	Me	Br_2	r.t., 24 h	**2b**	15
5	Me	NCS	r.t., 6 d	–	–
6	MeO	ICl	–20 to –18 °C, 48 h	**2c**	66
7	CF_3	ICl	–20 to –18 °C, 72 h	**2d**	38

Next, we carried out the reaction of **1a** with ICl in CH_2Cl_2 at –20 °C for 24 h in order to increase the selectivity. However, benzophenazine **2a** was obtained with the same yield (Table 2, Entry 2). Besides **2a**, the reaction mixture contained the starting material and again some other inseparable by-products. Prolongation of the reaction time resulted in only a slight increase of the yield of **2a** (Table 2, Entry 3). Thus, our optimized reaction conditions employ 0.2 mmol of **1** and 1.2 equiv. of ICl in dry CH_2Cl_2 at –20 °C.

With this protocol in hand, we examined the substrate scope of this transformation. 3-[(4-Methoxyphenyl)ethynyl]-2-phenylquinoxaline (**1j**) worked smoothly to afford benzophenazine **2c** in 66 % yields (Table 2, Entry 6). It should be noted that the direct electrophilic substitution to the electron-rich 4-methoxyphenyl fragment of **1j** does not appear to be competitive with iodocyclization. At the same time, alkyne **1h** with the electron-withdrawing trifluoromethyl group gave **2d** in 38 % yield, even after 72 h of reaction time (Table 2, Entry 7).

We were pleased to find that 2-(naphthalen-2-yl)-3-(*p*-tolylethynyl)quinoxaline (**1g**) afforded the cyclization product **2e** in 86 % yield (Scheme 6). Changing the naphthalen-2-yl group of **1g** to the naphthalen-1-yl group of **1f** dramatically decreased the yield to 47 % (Scheme 6). This agrees with the well-known fact that electrophilic attack on the position β of the naphthalene ring proceeds more difficult than on the C(α) atom.



Scheme 6. Synthesis of naphtho[2,1-*a*]- and naphtho[1,2-*a*]phenazines.

The structure of 8-iodo-7-*p*-tolylnaphtho[1,2-*a*]phenazine (**2f**) was proved by X-ray single crystal study (Figure 1). Compound **2f** has a helicene-like structure with an interplanar angle between the rings A and D of ca. 14°. For comparison, the interplanar angle between the two terminal rings of [4]helicene (benzo[*c*]phenanthrene) is equal to 26.7°.[9] To date, only one structure containing the 1-aza-[4]helicene fragment was registered in the CCDC database, namely, 14-aza-9-methyldibenzo[*f*,*pqr*]picene. The interplanar angle between the two terminal rings of this fragment in the last molecule is 20.4°.[10] Thus, 1-aza-[4]helicenes are not so twisted as [4]helicene. One can suggest that this originates from the existence of C–H···N hydrogen bonding in 1-aza-[4]helicenes. The short intramolecular contact H(1)···N(14) (2.195 Å) in the crystal of **2f** strongly supports this opinion. Apparently, such kind of interaction is also realized in solution since the signal of the H(1) proton of **2f** in the ^1H NMR spectrum appeared at an extremely low field of δ = 11.1 ppm. This observation is consistent with the remarkable deshielding of the H(12) proton of a helicene-like naphtho[2,1-*h*]quinoline (δ = 11.25 ppm).[11] For comparison, the chemical shifts of the

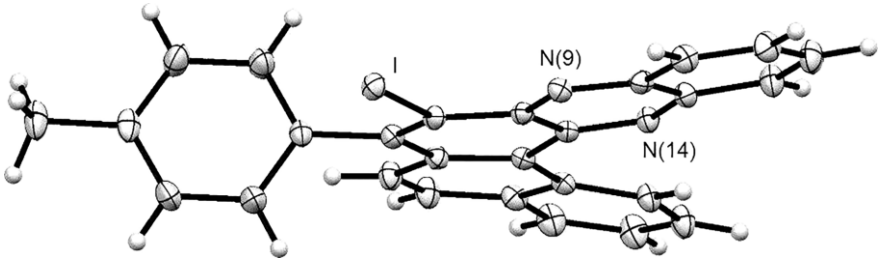
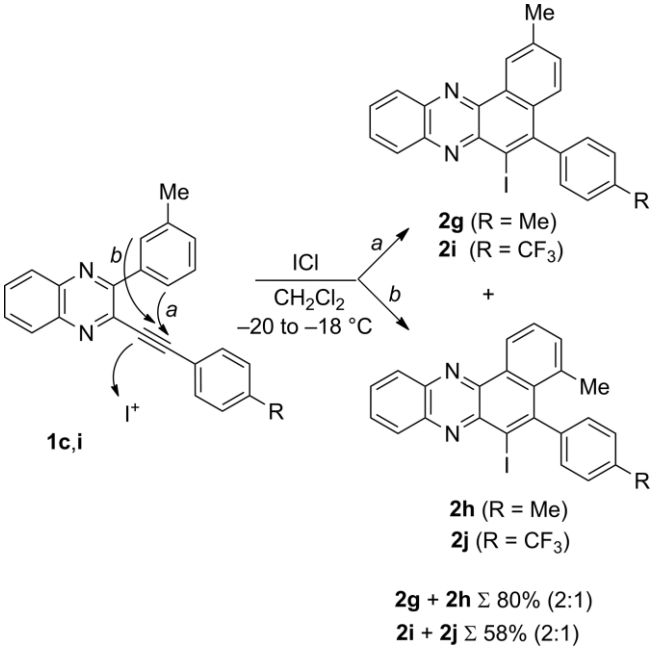


Figure 1. ORTEP plot of the X-ray crystal structure of **2f**.

H(1) protons of other compounds **2** range between δ = 9.5 ppm and δ = 9.7 ppm.

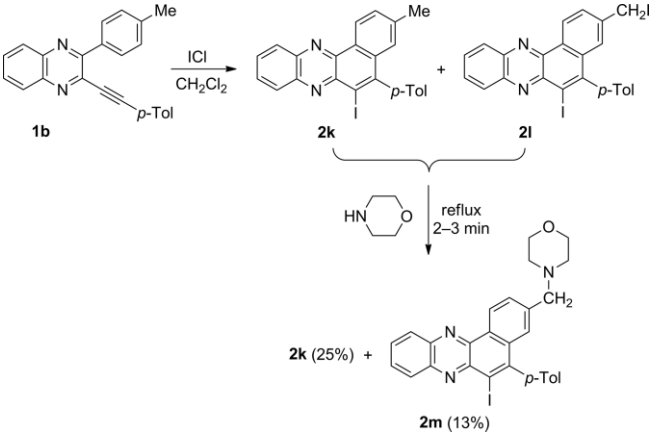
To the best of our knowledge, only two derivatives of naphtho[1,2-*a*]phenazine have been described in literature: 8-isopropyl-4-methylnaphtho[1,2-*a*]phenazine[12a] and 2-methoxynaphtho[1,2-*a*]phenazin-7-ol[12b] prepared by condensation of *ortho*-phenylenediamine with 2-isopropyl-8-methylphenanthrene-3,4-dione and 3,6-dimethoxyphenanthrene-1,4-dione, respectively. Data on the synthesis of naphtho[2,1-*a*]phenazines are also very limited.[13]

Encouraged by the success with the aforementioned substrates we also investigated the cyclizations of acetylenes **1b**–**c**,**i** in which various substituents were placed in the 2-phenyl fragment. Treatment of 3-(*p*-tolylethynyl)-2-*m*-tolylquinoxaline (**1c**) with ICl at –20 °C for 48 h afforded a mixture of isomeric cyclization products **2g** and **2h** (Scheme 7) in 80 % total yield and in a 2:1 ratio (^{1}H NMR spectroscopic data). The predominant isomer **2g** evidently arose from cyclization onto the less hindered position 4 of the *m*-tolyl moiety. A similar result was obtained using **1i** as a substrate, though the total yield of regioisomers **2i** and **2j** was lower (58 %).



Scheme 7. ICl-induced cyclizations of 3-alkynyl-2-*m*-tolylquinoxalines **1c**,**i**.

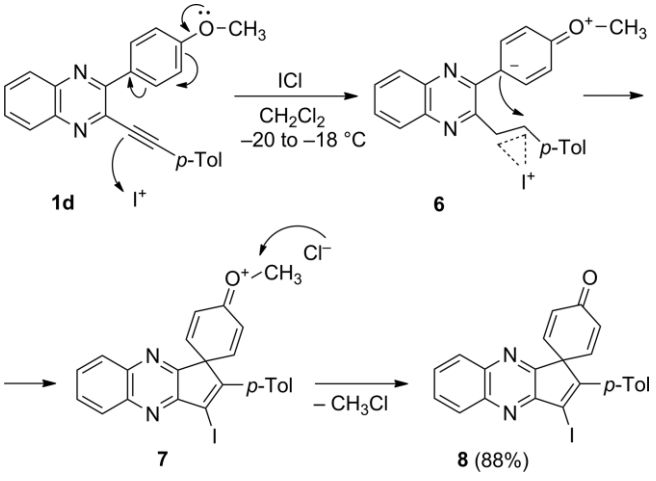
Substrate **1b**, containing the 2-*p*-tolyl group, underwent iodocyclization to afford a mixture of the desired benzophenazine **2k** and iodomethyl derivative **2l** in 43 % total yield (Scheme 8). The ratio of these products strongly depended on the reaction temperature. When the cyclization was carried out at –20 °C for 48 h, a ca. 4.3:1 mixture of **2k**/**2l** was obtained (^{1}H NMR spectroscopic data). The room-temperature protocol provided compounds **2k** and **2l** in a ca. 2:1 ratio. We were unable to separate these compounds because of the similarity of their retention factors. However, short-term heating of their mixture with an excess of morpholine allowed to convert compound **2l** into the aminomethyl derivative **2m**. Fortunately, retention factors of compounds **2k** and **2m** were significantly different allowing to separate them. Evidently, the formation of compound **2l** is the result of iodination of 3-methylbenzo[*a*]phenazine (**2k**). The exact mechanism (radical or ionic) of this transformation is not clear. However, there are some published examples of iodination of alkylbenzenes in the alkyl chain by *tert*-butyl hypoiodate.[14]



Scheme 8. ICl-induced cyclizations of 3-(*p*-tolylethynyl)-2-*p*-tolylquinoxaline **1b**.

When substrate **1d** containing a *p*-methoxyphenyl fragment was treated with iodochloride at –20 °C for 48 h, spirocyclic compound **8** was obtained as the only product in 88 % yield (Scheme 9). The distinct behavior of compound **1d** may be attributed to the directing effect of the *p*-methoxy group to favor 5-*endo*-*dig* cyclization of intermediate **6** instead of the usual 6-*endo*-*dig* process. Thus formed spirocycle **7** underwent the S_N2 demethylation producing compound **8**. The structure of 3′-iodo-2′-*p*-tolylspiro[cyclohexa-2,5-diene-1,1′-cyclopenta[*b*]quinoxalin]-4-one (**8**) was proved by X-ray single crystal study (Figure S1). Previously, ICl-induced *ipso*-cyclization was reported for 4′-methoxy-2-alkynylbiphenyls,[3d] 4-(*p*-methoxyaryl)-1-alk-

ynes,[15a] 1-[4′-methoxy-1,1′-biphenyl-2-yl]alkynones,[15b] bis(4-methoxybenzylthio)acetylenes,[15c] *N*-arylpropiolamides, and phenyl 3-phenylpropiolates.[15d]



Scheme 9. Electrophile-induced cyclization of 2-(4-methoxyphenyl)-3-(*p*-tolylethynyl)quinoxaline (**1d**).

Conclusions

We have achieved a facile synthesis of benzo[*a*]-, naphtho[1,2-*a*]- and naphtho[2,1-*a*]phenazines by ICl-promoted cyclization of 3-alkynyl-2-arylquinoxalines under very mild conditions. The starting 3-alkynyl-2-arylquinoxalines were synthesized from 2,3-dichloroquinoxaline in two steps by the Sonogashira reaction/Suzuki–Miyaura coupling. The methodology accommodates various functional groups and affords little-known benzo- and naphthophenazines in good yields. For the substrate of one particular type, namely 2-(4-methoxyphenyl)-3-(*p*-tolylethynyl)-quinoxaline, it was found that the ICl treatment leads to *ipso*-cyclization to give a spirocyclohexadienone derivative. It is also obvious that the presence of the iodo and alkynyl groups in the synthesized phenazines allows further modification of these molecules.

Experimental Section

General Procedure for the Synthesis of 3-Alkynyl-2-chloroquinoxalines 5: A mixture of 2,3-dichloroquinoxaline **3** (199 mg, 1.0 mmol), $Pd(PPh_3)_2Cl_2$ (10 mg, 0.014 mmol), CuI (2 mg, 0.01 mmol), iPr_2NH (1 mL), and DMSO (2 mL) was stirred under argon at room temperature for 20 min. Then, a solution of the corresponding alkyne (1.1 mmol) in iPr_2NH (1.5 mL) was added dropwise. The reaction mixture was stirred at room temperature for 5–6 h, then concentrated without heating to remove iPr_2NH, treated with H_2O (100 mL) and extracted with $CHCl_3$ (2 × 20 mL). The extract was dried with Na_2SO_4, and the solvents were evaporated to dryness. The residue was purified by flash column chromatography on silica gel (3.5 × 40 cm) with CH_2Cl_2 as the eluent. The colorless fraction with R_f = 0.7–0.8 and blue violet fluorescence gave **5**.

2-Chloro-3-(*p*-tolylethynyl)quinoxaline (5a): Yield 223 mg (80 %), colorless needles with m.p. 172–174 °C (EtOH) (ref.[16] light brown semi solid). ^1H NMR (250 MHz, $CDCl_3$): δ = 2.39 (s, 3 H), 7.12 (d, *J* = 8.0 Hz, 2 H), 7.60 (d, *J* = 8.0 Hz, 2 H), 7.73–7.80 (m, 2 H), 7.96–8.02 (m, 1 H), 8.05–8.12 (m, 1 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.7, 85.2, 97.7, 118.2, 128.2, 128.8, 129.4, 130.6, 131.2, 132.4, 138.8, 140.2, 140.6, 140.7, 148.0 ppm. IR (KBr): $\tilde{\nu}$ = 2212 (C≡C) cm^{-1}. MS: *m/z* (%) = 280 (33) $[M(^{37}Cl)]^+$, 278 (100) $[M(^{35}Cl)]^+$, 243 (68). $C_{17}H_{11}ClN_2$ (278.74): calcd. C 73.25, H 3.98, N 10.05; found C 73.41, H 4.05, N 9.83.

2-Chloro-3-[(4-methoxyphenyl)ethynyl]quinoxaline (5b): Yield 204 mg (69 %), yellow needles with m.p. 147–149 °C (*i*PrOH). ^1H NMR (250 MHz, $CDCl_3$): δ = 3.84 (s, 3 H), 6.92 (d, *J* = 8.9 Hz, 2 H), 7.65 (d, *J* = 8.9 Hz, 2 H), 7.72–7.79 (m, 2 H), 7.95–8.01 (m, 1 H), 8.04–8.11 (m, 1 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.4, 84.9, 98.0, 113.2, 114.3, 128.2, 128.8, 130.6, 131.1, 134.2, 138.9, 140.1, 140.8, 147.9, 161.1 ppm. IR (KBr): $\tilde{\nu}$ = 2212 (C≡C) cm^{-1}. MS: *m/z* (%) = 296 (23) $[M(^{37}Cl)]^+$, 294 (100) $[M(^{35}Cl)]^+$, 259 (44), 244 (12), 216 (24), 114 (11), 102 (12), 76 (15). $C_{17}H_{11}ClN_2O$ (294.74): calcd. C 69.28, H 3.76, N 9.50; found C 69.06, H 3.90, N 9.33.

2-Chloro-3-{[4-(trifluoromethyl)phenyl]ethynyl}quinoxaline (5c): Yield 292 mg (88 %), off-white needles with m.p. 138–140 °C (*i*PrOH). ^1H NMR (250 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 8.3 Hz, 2 H), 7.78–7.82 (m, 4 H), 7.98–8.05 (m, 1 H), 8.07–8.12 (m, 1 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 87.2, 94.8, 123.7 (q, *J* = 272.5 Hz), 125.0, 125.5 (q, *J* = 3.8 Hz), 128.3, 128.9, 130.8, 131.3, 131.8, 132.7, 137.9, 140.5, 140.7, 147.9 ppm. IR (KBr): $\tilde{\nu}$ = 2215 (C≡C) cm^{-1}. MS: *m/z* (%) = 334 (32) $[M(^{37}Cl)]^+$, 332 (98) $[M(^{35}Cl)]^+$, 297 (100). $C_{17}H_8ClF_3N_2$ (332.71): calcd. C 61.37, H 2.42, N 8.42; found C 61.15, H 2.49, N 8.23.

General Procedure for the Synthesis of 3-Alkynyl-2-arylquinoxalines 1: 3-Alkynyl-2-chloroquinoxaline **5** (0.5 mmol), arylboronic acid (0.6 mmol), $Pd(PPh_3)_4$ (15 mg, 0.013 mmol), K_3PO_4 (212 mg, 1.0 mmol) and dry THF (5 mL) were stirred and refluxed under argon for 9 h. The reaction mixture was then concentrated to dryness. The residue was treated with water (30 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The extract was dried with Na_2SO_4 and purified by flash column chromatography on silica gel (3.5 × 40 cm) with CH_2Cl_2 as the eluent. The fraction with R_f = 0.7–0.8 was recovered starting compound **5**. The next yellowish fraction with R_f = 0.3–0.5 gave 3-alkynyl-2-arylquinoxaline **1** (see Table 1 for yields). The product was crystallized from *i*PrOH.

2-Phenyl-3-(*p*-tolylethynyl)quinoxaline (1a): Colorless needles with m.p. 139–141 °C. ^1H NMR (250 MHz, $CDCl_3$): δ = 2.33 (s, 3 H, Me), 7.12 (d, *J* = 8.0 Hz, 2 H, *p*-Tol), 7.36 (d, *J* = 8.0 Hz, 2 H, *p*-Tol), 7.52–7.59 (m, 3 H), 7.72–7.76 (m, 2 H), 8.07–8.14 (m, 4 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.7, 88.0, 95.7, 118.7, 128.2, 128.7, 129.2(8), 129.3(2), 129.7, 129.8, 130.3, 130.6, 132.1, 137.7, 138.3, 140.1, 140.7, 141.0, 155.1 ppm. IR (KBr): $\tilde{\nu}$ = 2212 (C≡C) cm^{-1}. MS: *m/z* (%) = 320 (100) $[M^+]$, 305 (26), 178 (13), 140 (15), 76 (11). $C_{23}H_{16}N_2$ (320.39): calcd. C 86.22, H 5.03, N 8.74; found C 86.45, H 5.19, N 8.90.

2-*p*-Tolyl-3-(*p*-tolylethynyl)quinoxaline (1b): Colorless solid with m.p. 159–161 °C (ref.[5a] light yellow solid with m.p. 112–114 °C). ^1H NMR (250 MHz, $CDCl_3$): δ = 2.36 (s, 3 H, Me), 2.46 (s, 3 H, Me), 7.15 (dd, *J* = 8.5, 0.6 Hz, 2 H, *p*-Tol), 7.35 (dd, *J* = 8.5, 0.6 Hz, 2 H, *p*-Tol), 7.41 (m, 2 H, *p*-Tol), 7.70–7.77 (m, 2 H), 8.03 (m, 2 H, *p*-Tol), 8.07–8.13 (m, 2 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.5, 21.7, 88.2, 95.3, 118.8, 128.7, 128.9, 129.2(6), 129.2(7), 129.7, 130.0, 130.5, 132.1, 134.9, 138.2, 139.8, 140.0, 140.8, 140.9, 154.9 ppm. IR (KBr): $\tilde{\nu}$ = 2214 (C≡C) cm^{-1}. MS: *m/z* (%) = 334 (100) $[M^+]$, 319 (71), 216 (16), 192 (40), 165 (37), 159 (40), 140 (61), 116 (29), 89 (26), 76 (43). $C_{24}H_{18}N_2$ (334.42): calcd. C 86.20, H 5.43, N 8.38; found C 86.17, H 5.25, N 8.21.

2-*m*-Tolyl-3-(*p*-tolylethynyl)quinoxaline (1c): Colorless prisms with m.p. 116–117 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.31 (s, 3 H, Me), 2.46 (s, 3 H, Me), 7.10 (d, J = 7.9 Hz, 2 H), 7.31–7.46 (m, 4 H), 7.67–7.74 (m, 2 H), 7.91 (dm, J = 8.6 Hz, 2 H), 8.06–8.13 (m, 2 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.6, 21.7, 88.2, 95.6, 118.7, 126.9, 128.0, 128.7, 129.2, 129.3, 130.2, 130.3, 130.4, 130.5, 132.1 (2 C), 137.6, 137.8, 138.3, 140.0, 140.7, 141.0, 155.2 ppm. IR (KBr): $\tilde{\nu}$ = 2210 (C≡C) cm^{-1}. MS: *m/z* (%) = 334 (86) [M$^+$], 333 (100), 319 (89), 192 (10), 165 (11), 159 (12), 140 (15). $C_{24}H_{18}N_2$ (334.42): calcd. C 86.20, H 5.43, N 8.38; found C 86.39, H 5.28, N 8.43.

2-(4-Methoxyphenyl)-3-(*p*-tolylethynyl)quinoxaline (1d): Light yellow needles with m.p. 122–124 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.36 (s, 3 H, Me), 3.89 (s, 3 H, OMe), 7.06 (dm, J = 8.9 Hz, 2 H), 7.15 (d, J = 8.0 Hz, 2 H), 7.42 (d, J = 8.0 Hz, 2 H), 7.69–7.76 (m, 2 H), 8.05–8.15 (m, 4 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.7, 55.5, 88.2, 95.3, 113.6, 118.7, 128.7, 129.1, 129.3 (2 C), 129.9, 130.1, 130.5, 131.3, 132.1, 138.1, 140.1, 140.8, 154.4, 161.0 ppm. IR (KBr): $\tilde{\nu}$ = 2212 (C≡C) cm^{-1}. MS: *m/z* (%) = 350 (100) [M$^+$], 335 (13), 319 (18), 307 (11), 166 (10), 140 (10). $C_{24}H_{18}N_2O$ (350.42): calcd. C 82.26, H 5.18, N 7.99; found C 82.15, H 5.43, N 7.83.

3-[3-(*p*-Tolylethynyl)quinoxalin-2-yl]benzaldehyde (1e): Colorless needles with m.p. 158–160 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.35 (s, 3 H, Me), 7.14 (d, J = 7.9 Hz, 2 H), 7.36 (d, J = 8.1 Hz, 2 H), 7.72 (t, J = 7.7 Hz, 1 H), 7.76–7.83 (m, 2 H), 8.06 (dm, J = 7.7 Hz, 1 H), 8.10–8.18 (m, 2 H), 8.41 (dm, J = 7.7 Hz, 1 H), 8.68 (t, J = 1.5 Hz, 1 H), 10.14 (s, 1 H, CH=O) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.7, 87.6, 96.1, 118.3, 128.8, 128.9, 129.3, 129.4, 130.4, 130.7, 130.8, 131.3, 132.0, 135.6, 136.4, 137.8, 138.6, 140.3, 140.6, 141.2, 153.2, 191.8 ppm. IR (KBr): $\tilde{\nu}$ = 1703 (C=O), 2208 (C≡C) cm^{-1}. MS: *m/z* (%) = 348 (79) [M$^+$], 347 (100), 319 (30), 305 (11), 216 (11), 178 (16), 159 (11), 152 (14), 140 (35), 114 (12), 76 (37). $C_{24}H_{16}N_2O$ (348.40): calcd. C 82.74, H 4.63, N 8.04; found C 82.55, H 4.72, N 8.19.

2-(Naphthalen-1-yl)-3-(*p*-tolylethynyl)quinoxaline (1f): Colorless needles with m.p. 146–147 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.25 (s, 3 H, Me), 6.76 (dm, J = 8.1 Hz, 2 H), 6.96 (dm, J = 7.0 Hz, 2 H), 7.42 (ddd, J = 8.2, 6.8, 1.4 Hz, 1 H), 7.51 (ddd, J = 8.2, 6.8, 1.4 Hz, 1 H), 7.63 (dd, J = 8.2, 7.1 Hz, 1 H), 7.71–7.87 (m, 4 H), 7.96 (dd, J = 8.4, 1.0 Hz, 1 H), 8.03 (d, J = 8.2 Hz, 1 H), 8.13–8.24 (m, 2 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.6, 87.6, 96.6, 118.3, 125.2, 125.7, 126.2, 126.7, 128.2, 128.4, 128.9, 129.0, 129.4, 129.8, 130.6, 130.7, 131.6, 132.0, 133.7, 135.7, 139.9, 140.3, 140.5, 141.4, 156.2 ppm. IR (KBr): $\tilde{\nu}$ = 2210 (C≡C) cm^{-1}. MS: *m/z* (%) = 370 (51) [M$^+$], 369 (100), 355 (34), 228 (27), 202 (10), 184 (27), 153 (38), 140 (29), 126 (22), 114 (11), 77 (11). $C_{27}H_{18}N_2$ (370.45): calcd. C 87.54, H 4.90, N 7.56; found C 87.32, H 4.67, N 7.39.

2-(Naphthalen-2-yl)-3-(*p*-tolylethynyl)quinoxaline (1g): Colorless needles with m.p. 157–158 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.33 (s, 3 H, Me), 7.10 (d, J = 8.0 Hz, 2 H, *p*-Tol), 7.35 (d, J = 8.0 Hz, 2 H, *p*-Tol), 7.54–7.60 (m, 2 H), 7.75–7.80 (m, 2 H), 7.91–7.98 (m, 2 H), 8.01 (d, J = 8.7 Hz, 1 H), 8.13–8.18 (m, 2 H), 8.22 (dd, J = 8.5, 1.8 Hz, 1 H), 8.69 (d, J = 1.0 Hz, 1 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.7, 88.3, 95.8, 118.6, 126.5, 127.0, 127.1, 127.8, 128.7, 128.8, 129.2, 129.3, 129.4, 129.9, 130.3, 130.6, 132.1, 133.0, 133.9, 135.0, 138.4, 140.1, 140.8, 141.0, 154.7 ppm. IR (KBr): $\tilde{\nu}$ = 2209 (C≡C) cm^{-1}. MS: *m/z* (%) = 370 (77) [M$^+$], 369 (100), 355 (33), 228 (14), 177 (14), 153 (21), 140 (12). $C_{27}H_{18}N_2$ (370.45): calcd. C 87.54, H 4.90, N 7.56; found C 87.40, H 5.09, N 7.41.

2-Phenyl-3-{[4-(trifluoromethyl)phenyl]ethynyl}quinoxaline (1h): Colorless needles with m.p. 173–175 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.54–7.62 (m, 7 H), 7.74–7.82 (m, 2 H), 8.03–8.17 (m, 4 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 90.2, 93.0, 123.7 (q, J = 272.4 Hz), 125.4 (q, J = 3.8 Hz), 128.2, 128.9, 129.4, 129.7, 129.9, 130.5, 130.9, 131.1, 131.4, 132.3, 137.5, 137.6, 140.9, 141.0, 155.2 ppm. IR (KBr): $\tilde{\nu}$ = 2220 (C≡C) cm^{-1}. MS: *m/z* (%) = 374 (100) [M$^+$], 305 (11), 179 (10). $C_{23}H_{13}F_3N_2$ (374.36): calcd. C 73.79, H 3.50, N 7.48; found C 73.92, H 3.73, N 7.23.

2-*m*-Tolyl-3-{[4-(trifluoromethyl)phenyl]ethynyl}quinoxaline (1i): Colorless needles with m.p. 158–159 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.47 (s, 3 H, Me), 7.35 (d, J = 7.8 Hz, 1 H), 7.44 (t, J = 7.6 Hz, 1 H), 7.54–7.63 (m, 4 H), 7.75–7.82 (m, 2 H), 7.86–7.89 (m, 2 H), 8.10–8.18 (m, 2 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.6, 90.3, 92.9, 123.7 (q, J = 272.4 Hz, CF_3), 125.4 (q, J = 3.8 Hz, *C*-CF_3), 126.8, 128.0, 128.8, 129.4, 130.3, 130.4, 130.6, 130.8, 131.0, 131.4, 132.3, 137.4, 137.5, 138.0, 140.9, 141.0, 155.3 ppm. IR (KBr): $\tilde{\nu}$ = 2219 (C≡C) cm^{-1}. MS: *m/z* (%) = 388 (89) [M$^+$], 387 (100), 373 (37), 319 (33), 192 (40), 176 (13), 165 (41), 116 (31), 102 (19), 90 (29), 76 (83). $C_{24}H_{15}F_3N_2$ (388.39): calcd. C 74.22, H 3.89, N 7.21; found C 74.02, H 4.02, N 7.44.

2-[(4-Methoxyphenyl)ethynyl]-3-phenylquinoxaline (1j): Colorless needles with m.p. 142–143 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.79 (s, 3 H, OMe), 6.84 (d, J = 8.8 Hz, 2 H), 7.40 (d, J = 8.8 Hz, 2 H), 7.53–7.59 (m, 3 H), 7.69–7.77 (m, 2 H), 8.06–8.12 (m, 4 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.3, 87.7, 95.8, 113.7, 114.2, 128.1, 128.6, 128.7, 129.3, 129.7, 130.2, 130.4, 133.8, 137.8, 138.5, 140.6, 141.1, 155.0, 160.7 ppm. IR (KBr): $\tilde{\nu}$ = 2202 (C≡C) cm^{-1}. MS: *m/z* (%) = 336 (100) [M$^+$], 321 (26), 305 (10), 292 (28), 190 (15), 178 (24), 157 (13), 152 (12), 146 (11), 114 (23), 76 (21). $C_{23}H_{16}N_2O$ (336.39): calcd. C 82.12, H 4.79, N 8.33; found C 81.95, H 4.93, N 8.45.

2-[(4-Methoxyphenyl)ethynyl]-3-*m*-tolylquinoxaline (1k): Yellowish needles with m.p. 93–95 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.54 (s, 3 H, Me), 3.88 (s, 3 H, OMe), 6.92 (d, J = 8.9 Hz, 2 H), 7.31–7.53 (m, 4 H), 7.77–7.85 (m, 2 H), 7.94–7.98 (m, 2 H), 8.16–8.20 (m, 2 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.6, 55.3, 87.8, 95.8, 113.8, 114.2, 126.9, 128.0, 128.7, 129.3, 130.2, 130.3, 130.4, 130.5, 133.8, 137.7, 137.8, 138.5, 140.6, 141.0, 155.2, 160.7 ppm. IR (KBr): $\tilde{\nu}$ = 2206 (C≡C) cm^{-1}. MS: *m/z* (%) = 350 (32) [M$^+$], 335 (18), 111 (14), 97 (24), 85 (49), 57 (100). $C_{24}H_{18}N_2O$ (350.42): calcd. C 82.26, H 5.18, N 7.99; found C 82.06, H 5.31, N 8.23.

General Procedure for the Synthesis of Benzo- and Naphthophenazines 2: To a cooled (–20 °C) solution of 2-alkynyl-3-arylquinoxaline **1** (0.2 mmol) in dry CH_2Cl_2 (3 mL) was added a cooled (–20 °C) solution of ICl (39 mg, 0.24 mmol) in dry CH_2Cl_2 (2 mL). The reaction mixture was kept at –20 to –18 °C for 48 h. Then the reaction mixture was treated with saturated aqueous $Na_2S_2O_3$ (5 mL) and extracted with CH_2Cl_2 (2 × 5 mL). The extract was dried with Na_2SO_4 and purified by flash column chromatography on silica gel (2.5 × 40 cm) with $CHCl_3$ as the eluent. The first yellow or bright yellow fraction with R_f = 0.9 gave compound **2** (see Table 2 for yields). Product **2** was crystallized from *i*PrOH.

For the synthesis of **2b**, bromine (38 mg, 0.24 mmol) was used instead of ICl. The reaction was carried out at room temperature.

6-Iodo-5-*p*-tolylbenzo[*a*]phenazine (2a): Yellow solid with m.p. 256–258 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.51 (s, 3 H, Me), 7.25 (d, J = 7.8 Hz, 2 H, *p*-Tol), 7.47 (d, J = 7.8 Hz, 2 H, *p*-Tol), 7.45 (d, J = 8.4 Hz, 1 H), 7.58 (t, J = 7.5 Hz, 1 H), 7.79 (t, J = 7.5 Hz, 1 H), 7.88–7.92 (m, 2 H), 8.38–8.43 (m, 2 H), 9.47 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.5, 108.1, 125.6, 128.2, 128.5, 129.1, 129.3, 129.4, 129.6, 130.0, 130.3, 130.5, 131.1, 134.2, 138.0, 140.8, 141.6, 142.0, 142.4, 143.4, 151.1 ppm. UV/Vis: λ_{max} (lg ε) = 277 sh (4.56), 287 (4.62), 300 (4.64), 367 sh (3.98), 391 (4.10), 410 (4.08) nm . MS: *m/z* (%) = 446 (100) [M$^+$], 319 (56), 304 (19), 159 (27). $C_{23}H_{15}IN_2$

(446.29): calcd. C 61.90, H 3.39, N 6.28; found C 62.09, H 3.54, N 6.03.

6-Bromo-5-*p*-tolylbenzo[*a*]phenazine (2b): Yellow solid with m.p. 259–261 °C (decomp.). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.52 (s, 3 H, Me), 7.30 (d, J = 7.9 Hz, 2 H, *p*-Tol), 7.40 (d, J = 7.9 Hz, 2 H, *p*-Tol), 7.46 (d, J = 8.1 Hz, 1 H), 7.60 (ddd, J = 8.1, 7.0, 1.3 Hz, 1 H), 7.78 (ddd, J = 8.1, 7.0, 1.2 Hz, 1 H), 7.86–7.94 (m, 2 H), 8.37–8.44 (m, 2 H), 9.46 (d, J = 8.1 Hz, 1 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.5, 123.7, 125.6, 127.9, 128.0, 129.3(3), 129.3(6), 129.4, 129.8, 130.0, 130.4, 130.5, 130.6, 134.2, 136.7, 138.0, 140.8, 142.1, 142.2, 143.0, 145.6 ppm. UV/Vis: λ_{max} (lg ε) = 285 (4.52), 297 (4.49), 368 sh (3.84), 390 (3.97), 411 (3.97) nm. MS: *m/z* (%) = 400 (100) [M(^{81}Br)]$^+$, 398 (99) [M(^{79}Br)]$^+$, 319 (53), 317 (35), 304 (45), 159 (39). $C_{23}H_{15}BrN_2$ (399.29): calcd. C 69.19, H 3.79, N 7.02; found C 69.13, H 3.93, N 6.87.

6-Iodo-5-(4-methoxyphenyl)benzo[*a*]phenazine (2c): Yellow solid with m.p. 230–232 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.93 (s, 3 H, OMe), 7.12 (d, J = 8.7 Hz, 2 H), 7.28 (d, J = 8.7 Hz, 2 H), 7.48 (d, J = 8.1 Hz, 1 H), 7.58 (ddd, J = 8.0, 7.0, 1.3 Hz, 1 H), 7.79 (ddd, J = 8.0, 7.0, 1.2 Hz, 1 H), 7.86–7.93 (m, 2 H), 8.38–8.43 (m, 2 H), 9.47 (dd, J = 8.0, 0.9 Hz, 1 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 55.4, 108.7, 114.0, 125.6, 128.1, 128.5, 129.1, 129.6, 130.0, 130.3, 130.5, 130.7, 131.1, 134.4, 136.0, 141.6, 142.0, 142.4, 143.4, 150.9, 159.5 ppm. UV/Vis: λ_{max} (lg ε) = 286 (4.57), 300 (4.57), 371 sh (3.96), 393 (4.05), 410 (4.03) nm. MS: *m/z* (%) = 462 (100) [M$^+$], 292 (31). $C_{23}H_{15}IN_2O$ (462.29): calcd. C 59.76, H 3.27, N 6.06; found C 60.02, H 3.41, N 6.22.

6-Iodo-5-[4-(trifluoromethyl)phenyl]benzo[*a*]phenazine (2d): Yellow solid with m.p. 267–269 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.30 (d, J = 8.1 Hz, 1 H), 7.50 (d, J = 8.1 Hz, 2 H), 7.58 (ddd, J = 8.2, 7.0, 1.2 Hz, 1 H), 7.77–7.95 (m, 5 H), 8.36–8.42 (m, 2 H), 9.48 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 107.9, 124.2 (q, J = 272.2 Hz), 125.7(8) (q, J = 4.1 Hz), 125.8(2), 127.9, 128.4, 129.2, 129.6, 130.2, 130.3, 130.5, 130.8, 131.1, 133.5, 141.4, 141.6, 142.6, 143.5, 147.0(9), 147.1(1), 149.4 ppm. UV/Vis: λ_{max} (lg ε) = 287 (4.48), 300 (4.47), 368 sh (3.85), 388 (3.97), 408 nm (3.94). MS: *m/z* (%) = 500 (100) [M$^+$], 374 (11), 304 (11), 77 (10), 75 (13), 69 (16). $C_{23}H_{12}F_3IN_2$ (500.26): calcd. C 55.22, H 2.42, N 5.60; found C 55.04, H 2.65, N 5.37.

8-Iodo-7-*p*-tolylnaphtho[2,1-*a*]phenazine (2e): Bright yellow solid with m.p. 247–249 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.57 (s, 3 H, Me), 7.13 (ddd, J = 8.7, 6.9, 1.6 Hz, 1 H), 7.28 (d, J = 8.0 Hz, 2 H, *p*-Tol), 7.40 (d, J = 8.0 Hz, 2 H, *p*-Tol), 7.47 (ddd, J = 8.0, 6.9, 1.0 Hz, 1 H), 7.53 (d, J = 8.7 Hz, 1 H), 7.88–7.97 (m, 3 H), 8.18 (d, J = 8.8 Hz, 1 H), 8.40–8.49 (m, 2 H), 9.66 (d, J = 8.8 Hz, 1 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.6, 112.7, 122.6, 125.5, 126.6, 128.5, 128.8, 129.3, 129.6, 129.8, 129.9, 130.0, 130.1, 130.5, 130.6, 130.8, 131.1, 135.3, 138.1, 140.6, 141.5, 142.8, 143.8, 145.3, 149.7 ppm. UV/Vis: λ_{max} (lg ε) = 270 (4.76), 302 (4.64), 325 (4.60), 379 sh (4.01), 402 (4.16), 443 sh (3.79), end absorption up to 492 nm. MS: *m/z* (%) = 496 (100) [M$^+$], 369 (39), 354 (28), 183 (18). $C_{27}H_{17}IN_2$ (496.35): calcd. C 65.34, H 3.45, N 5.64; found C 65.25, H 3.19, N 5.80.

8-Iodo-7-*p*-tolylnaphtho[1,2-*a*]phenazine (2f): Bright yellow solid with m.p. 275–277 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.54 (s, 3 H, Me), 7.27 (d, J = 8.1 Hz, 2 H, *p*-Tol), 7.43 (d, J = 8.1 Hz, 2 H, *p*-Tol), 7.55 (d, J = 8.9 Hz, 1 H), 7.70 (t, J = 7.3 Hz, 1 H), 7.85–7.99 (m, 5 H), 8.41–8.46 (m, 1 H), 8.53–8.59 (m, 1 H), 11.14 (d, J = 9.0 Hz, 1 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.6, 109.3, 125.8, 126.4, 127.0, 128.3, 128.7, 129.2, 129.4(1), 129.4(4), 129.4(5), 130.5(0), 130.5(3), 130.5(9), 131.2, 131.4, 133.8, 134.3, 138.0, 141.7(3), 141.7(4), 141.8, 142.0, 143.6, 151.3 ppm. UV/Vis: λ_{max} (lg ε) = 271 (4.45), 309 sh (4.25), 321 (4.32), 379 sh (3.61), 404 (3.91), 425 (3.94), end absorption up to 470 nm. MS: *m/z* (%) = 496 (100) [M$^+$], 369 (51), 354 (18), 184 (23). $C_{27}H_{17}IN_2$ (496.35): calcd. C 65.34, H 3.45, N 5.64; found C 65.49, H 3.61, N 5.36.

Synthesis of 6-Iodo-3-methyl-5-*p*-tolylbenzo[*a*]phenazine (2k) and 4-[(6-Iodo-5-*p*-tolylbenzo[*a*]phenazin-3-yl)methyl]morpholine (2m): A solution of 2-*p*-tolyl-3-(*p*-tolylethynyl)quinoxaline (**1b**) (80 mg, 0.24 mmol) and ICl (47 mg, 0.29 mmol) in dry CH_2Cl_2 (6 mL) was kept at room temperature for 48 h. Then the reaction mixture was treated with saturated aqueous $Na_2S_2O_3$ (5 mL) and extracted with CH_2Cl_2 (2 × 5 mL). The extract was dried with Na_2SO_4 and purified by flash column chromatography on silica gel (2.5 × 40 cm) with $CHCl_3$ as the eluent. The first yellow fraction with R_f = 0.9 gave 50 mg of 6-iodo-3-methyl-5-*p*-tolylbenzo[*a*]phenazine (**2k**) and 6-iodo-3-(iodomethyl)-5-*p*-tolylbenzo[*a*]phenazine (**2l**) as a 2:1 mixture (^{1}H NMR spectroscopic data). This mixture was heated with morpholine (0.5 mL) for 2–3 min, and the solvents were evaporated to dryness. The residue was purified by flash column chromatography on silica gel (2.5 × 40 cm) with $CHCl_3$ as the eluent. The first yellow fraction with R_f = 0.9 gave 6-iodo-3-methyl-5-*p*-tolylbenzo[*a*]phenazine (**2k**) (28 mg, 25 %). The yellow fraction with R_f = 0.1 was "cut" from the column, eluted with *i*PrOH and additionally purified by flash column chromatography on silica gel (2.5 × 15 cm) with CH_2Cl_2/acetone (50:1) as the eluent. The yield of 4-[(6-iodo-5-*p*-tolylbenzo[*a*]phenazin-3-yl)methyl]morpholine (**2m**) was 18 mg (13 %).

6-Iodo-3-methyl-5-*p*-tolylbenzo[*a*]phenazine (2k): Yellow solid with m.p. 281–283 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.43 (s, 3 H, Me), 2.52 (s, 3 H, Me), 7.22–7.25 (m, 3 H), 7.40 (d, J = 7.8 Hz, 2 H), 7.60 (dd, J = 8.2, 1.2 Hz, 1 H), 7.83–7.91 (m, 2 H), 8.36–8.41 (m, 2 H), 9.33 (d, J = 8.2 Hz, 1 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.6, 21.9, 108.2, 125.5, 128.3, 128.8, 129.0, 129.2(9), 129.3(1), 129.6, 129.7, 130.0, 130.4, 134.3, 137.9, 140.4, 140.9, 141.7, 141.8, 142.4, 143.2, 151.1 ppm. UV/Vis: λ_{max} (lg ε) = 291 (4.59), 301 (4.62), 371 sh (3.77), 391 (4.11), 411 nm (4.10). MS: *m/z* (%) = 460 (100) [M$^+$], 333 (19), 318 (14), 158 (13). $C_{24}H_{17}IN_2$ (460.32): calcd. C 62.62, H 3.72, N 6.09; found C 62.51, H 3.84, N 5.83.

4-[(6-Iodo-5-*p*-tolylbenzo[*a*]phenazin-3-yl)methyl]morpholine (2m): Yellow solid with m.p. 187–189 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.40–2.43 (m, 4 H), 2.52 (s, 3 H, Me), 3.59 (s, 2 H, CH_2), 3.64–3.68 (m, 4 H), 7.23 (d, J = 7.8 Hz, 2 H), 7.33 (d, J = 1.0 Hz, 1 H), 7.40 (d, J = 7.8 Hz, 2 H), 7.81 (dd, J = 8.4, 1.5 Hz, 1 H), 7.85–7.92 (m, 2 H), 8.36–8.42 (m, 2 H), 9.40 (d, J = 8.4 Hz, 1 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.6, 53.5, 62.9, 67.0, 108.3, 125.7, 128.5, 128.9, 129.1, 129.2(9), 129.3(1), 129.6, 130.2, 130.5, 134.2, 138.0, 140.2, 140.7, 141.5, 141.9, 142.4, 143.4, 151.0 ppm. MS: *m/z* (%) = 545 (42) [M$^+$], 460 (100), 331 (11), 56 (22). $C_{28}H_{24}IN_3O$ (545.42): calcd. C 61.66, H 4.44, N 7.70; found C 61.52, H 4.40, N 7.59.

Synthesis of 3′-Iodo-2′-*p*-tolylspiro[cyclohexa-2,5-diene-1,1′-cyclopenta[*b*]quinoxalin]-4-one (8): To a cooled (–20 °C) solution of 2-(4-methoxyphenyl)-3-(*p*-tolylethynyl)quinoxaline (**1d**) (105 mg, 0.3 mmol) in dry CH_2Cl_2 (4 mL) was added a cooled (–20 °C) solution of ICl (59 mg, 0.36 mmol) in dry CH_2Cl_2 (4 mL). The reaction mixture was kept at –20 to –18 °C for 48 h. The reaction mixture was filtered giving rise to orange needles of the crude product **8** (122 mg, 88 %). After recrystallization from *i*PrOH, compound **8** was obtained as off-white solid with m.p. 249–251 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.37 (s, 3 H, Me), 6.60 (pseudo s, 4 H), 7.20 (d, J = 8.1 Hz, 2 H), 7.38 (d, J = 8.1 Hz, 2 H), 7.68–7.83 (m, 2 H), 8.08 (dd, J = 8.1, 1.6 Hz, 1 H), 8.23 (dd, J = 8.2, 1.3 Hz, 1 H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 21.5, 61.7, 101.1, 128.0, 129.2, 129.3, 129.4, 129.8, 130.5, 131.2, 133.2, 140.3, 141.7, 142.9, 144.0, 155.2, 156.2, 159.1, 185.2 ppm. UV/

Vis: λ_{max} (lg ε) = 363 nm (4.34). MS: *m/z* (%) = 462 (100) [M^+], 447 (14), 335 (41), 320 (15), 307 (44), 292 (27). $C_{23}H_{15}IN_2O$ (462.29): calcd. C 59.76, H 3.27, N 6.06; found C 59.91, H 3.17, N 6.13.

Supporting Information: Copies of the ^1H and ^{13}C NMR spectra of all compounds, ORTEP plot of X-ray crystal structure of **8**.

Acknowledgments

The author gratefully acknowledges the Russian Foundation for Basic Research (grant no. 14-03-00032-a) for financial support of this research. The author also thanks Drs. Anna V. Tkachuk and Oleg N. Burov (Scientific and Educational Laboratory of Resonance Spectroscopy, Department of Natural and High Molecular Compound Chemistry, Southern Federal University) for NMR measurements and Dr. Kyrill Y. Suponitsky (A. N. Nesmeyanov Institute of Organoelement Compounds, Moscow) for X-ray studies.

Keywords: Synthetic methods · Electrophilic addition · Nitrogen heterocycles · Alkynes · Spiro compounds · Benzo[*a*]phenazines · Naphthophenazines

[1] a) J. B. Laursen, J. Nielsen, *Chem. Rev.* **2004**, *104*, 1663; b) D. V. Mavrodi, W. Blankenfeldt, L. S. Thomashow, *Annu. Rev. Phytopathol.* **2006**, *44*, 417; c) L. S. Pierson, E. A. Pierson, *Appl. Microbiol. Biotechnol.* **2010**, *86*, 1659; d) D. V. Mavrodi, J. A. Pareiko, O. V. Mavrodi, Y.-S. Kwak, D. M. Weller, W. Blankenfeldt, L. S. Thomashow, *Environ. Microbiol.* **2013**, *15*, 675; e) C. E. J. Van Rensburg, G. K. Jooné, F. A. Sirgel, N. M. Matlola, J. F. O'Sullivan, *Chemotherapy* **2000**, *46*, 43; f) A. Cimmino, A. Evidente, V. Mathieu, A. Andolfi, F. Lefranc, A. Kornienko, R. Kiss, *Nat. Prod. Rep.* **2012**, *29*, 487; g) D. F. Gloster, L. Cincotta, J. W. Foley, *J. Heterocycl. Chem.* **1999**, *36*, 25; h) M. Conda-Sheridan, L. Marler, E.-J. Park, T. P. Kondratyuk, K. Jermihov, A. D. Mesecar, J. M. Pezzuto, R. N. Asolkar, W. Fenical, M. Cushman, *J. Med. Chem.* **2010**, *53*, 8688; i) N. V. Borrero, F. Bai, C. Perez, B. Q. Duong, J. R. Rocca, S. Jin, R. W. Huigens, *Org. Biomol. Chem.* **2014**, *12*, 881; j) A. Wohl, *Ber. Dtsch. Chem. Ges.* **1901**, *34*, 2442; k) E. Bamberger, W. Ham, *Justus Liebigs Ann. Chem.* **1911**, *382*, 382; l) M. J. Haddadin, C. H. Issodorides, *Tetrahedron Lett.* **1965**, *6*, 3253; m) R. Merz, *Ber. Dtsch. Chem. Ges.* **1886**, *19*, 2206; n) T. Emoto, N. Kubosaki, Y. Yamagiwa, T. Kamikawa, *Tetrahedron Lett.* **2000**, *41*, 355.

[2] T. Yao, M. A. Campo, R. C. Larock, *J. Org. Chem.* **2005**, *70*, 3511.

[3] a) J. Barluenga, J. M. González, P. J. Campos, G. Asensio, *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1546; *Angew. Chem.* **1988**, *100*, 1604; b) M. B. Goldfinger, T. M. Swager, *J. Am. Chem. Soc.* **1994**, *116*, 7895; c) M. B. Goldfinger, K. B. Crawford, T. M. Swager, *J. Am. Chem. Soc.* **1997**, *119*, 4578; d) C.-W. Li, C.-I. Wang, H.-Y. Liao, R. Chaudhuri, R.-S. Liu, *J. Org. Chem.* **2007**, *72*, 9203.

[4] a) A. V. Gulevskaya, H. T. L. Nguyen, A. S. Tyaglivy, A. F. Pozharskii, *Tetrahedron* **2012**, *68*, 488; b) A. V. Gulevskaya, R. Yu. Lazarevich, A. F. Pozharskii, *Tetrahedron* **2013**, *69*, 910; c) A. S. Tyaglivy, A. V. Gulevskaya, A. F. Pozharskii, O. I. Askalepova, *Tetrahedron* **2013**, *69*, 9804; d) A. V. Gulevskaya, A. S. Tyaglivy, A. F. Pozharskii, J. I. Nelina-Nemtseva, D. V. Steglenko, *Org. Lett.* **2014**, *16*, 1582; e) J. I. Nelina-Nemtseva, A. V. Gulevskaya, A. F. Pozharskii, H. T. L. Nguyen, E. A. Filatova, *Tetrahedron* **2016**, *72*, 2327.

[5] a) W. Wang, Y. Shen, X. Meng, M. Zhao, Y. Chen, B. Chen, *Org. Lett.* **2011**, *13*, 4514; b) Y. Liang, P.-Z. Liu, C.-C. Wu, Q. Zhang, *Asian J. Chem.* **2015**, *27*, 3921; c) Z. Wang, G. Hu, J. Liu, W. Liu, H. Zhang, B. Wang, *Chem. Commun.* **2015**, *51*, 5069; d) E. Merkul, J. Dohe, C. Gers, F. Rominger, T. J. J. Müller, *Angew. Chem. Int. Ed.* **2011**, *50*, 2966; *Angew. Chem.* **2011**, *123*, 3023; e) Z. Zhang, X. Jiang, *Org. Lett.* **2014**, *16*, 4400; f) C. F. Gers, J. Nordmann, C. Kumru, W. Frank, T. J. J. Müller, *J. Org. Chem.* **2014**, *79*, 3296; g) K. Shiva Kumar, D. Rambabu, B. Prasad, M. Mujahid, G. R. Krishna, M. V. B. Rao, C. M. Reddy, G. R. Vanaja, A. M. Kalle, M. Pal, *Org. Biomol. Chem.* **2012**, *10*, 4774.

[6] J. R. Stevens, K. Pfister, F. G. Wolf, *J. Am. Chem. Soc.* **1946**, *68*, 1035.

[7] D. Villemin, A. Jullien, N. Bar, *Tetrahedron Lett.* **2007**, *48*, 4191.

[8] K. S. Kumar, D. Rambabu, S. Sandra, R. Kapavarapu, G. R. Krishna, M. V. B. Rao, K. Chatti, C. M. Reddy, P. Misra, M. Pal, *Bioorg. Med. Chem.* **2012**, *20*, 1711.

[9] Y. Shen, C.-F. Chen, *Chem. Rev.* **2012**, *112*, 1463.

[10] Y.-Q. He, Y.-W. Zhong, *Chem. Commun.* **2015**, *51*, 3411.

[11] R. H. Martin, N. Defay, F. Geerts-Evrard, D. Bogaert-Verhoogen, *Tetrahedron* **1966**, *22, Suppl, 8*, 181.

[12] a) M. Onitsuka, M. Fujiu, N. Shinma, H. B. Maruyama, *Chem. Pharm. Bull.* **1983**, *31*, 1670; b) K. W. Bentley, R. Robinson, *J. Chem. Soc.* **1952**, 947.

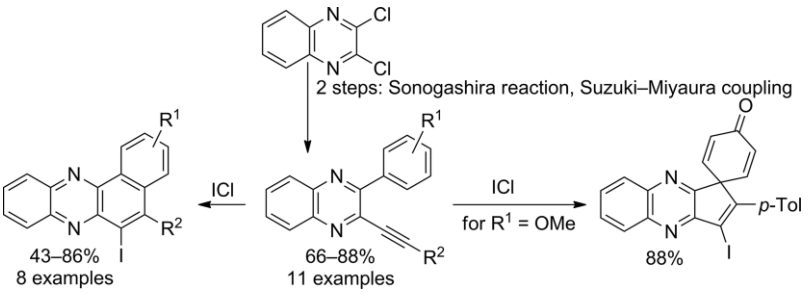
[13] a) F. R. Hewgill, R. Slamet, J. M. Stewart, *J. Chem. Soc. Perkin Trans. 1* **1991**, 3033; b) B. C. Raju, K. V. Prasad, G. Saidachary, B. Sridhar, *Org. Lett.* **2014**, *16*, 420; c) H. Hopf, J. Hucker, L. Ernst, *Eur. J. Org. Chem.* **2007**, 1891.

[14] a) R. Montoro, T. Wirth, *Org. Lett.* **2003**, *5*, 4729; b) R. Montoro, T. Wirth, *Synthesis* **2005**, 1473; c) O. Kh. Poleshchuk, A. G. Yureva, V. D. Filimonov, G. Frenking, *J. Mol. Struct.: THEOCHEM* **2009**, *912*, 67 (and references cited therein).

[15] a) X. Zhang, R. C. Larock, *J. Am. Chem. Soc.* **2005**, *127*, 12230; b) Y. Chen, X. Liu, M. Lee, C. Huang, I. Inoyatov, Z. Chen, A. C. Perl, W. H. Hersh, *Chem. Eur. J.* **2013**, *19*, 9795; c) T. R. Appel, N. A. M. Yehia, U. Baumeister, H. Hartung, R. Kluge, D. Ströhl, E. Fanghänel, *Eur. J. Org. Chem.* **2003**, 47; d) B.-X. Tang, D.-J. Tang, S. Tang, Q.-F. Yu, Y.-H. Zhang, Y. Liang, P. Zhong, J.-H. Li, *Org. Lett.* **2008**, *10*, 1063.

[16] A. Nakhi, M. S. Rahman, G. P. K. Seerapu, R. K. Banote, K. L. Kumar, P. Kulkarni, D. Haldar, M. Pal, *Org. Biomol. Chem.* **2013**, *11*, 4930.

Received: May 28, 2016
Published Online: ■



A facile synthesis of benzo[*a*]-, naphtho[1,2-*a*]- and naphtho[2,1-*a*]-phenazines by ICl-promoted 6-*endo*-*dig* cyclization of 3-alkynyl-2-arylquinoxalines is reported. For 2-(4-methoxyphenyl)-3-(*p*-tolylethynyl)quinoxaline, the treatment with ICl leads to the alternative 5-*endo*-*dig* cyclization followed by demethylation of the methoxy group to give a spirocyclohexadienone derivative.

DOI: 10.1002/ejoc.201600660