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Electrophilic cyclizations of 2,3-dialkynylquinoxalines and 1,2-dialkynylbenzenes: a comparative study

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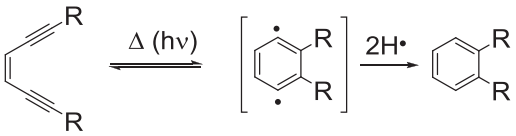
ABSTRACT

The reactivity of 2,3-dialkynylquinoxalines towards electrophiles (Br_2, I_2, ICl, NBS, HBr) has been studied. All tested reactions, except one with HBr, start with the addition of an electrophile to the carbon–carbon triple bond that promotes further 5-*exo*-*dig* carbocyclization ultimately yielding a mixture of stereoisomeric cyclopenta[*b*]quinoxaline derivatives. The nature of substituents on the C≡C bonds of the starting molecule influence the stereochemical result of the reaction. The ratio of isomeric cyclization products also depends on the electrophile used. *ortho*-Dialkynylbenzenes and *ortho*-dialkynylquinoxalines demonstrate rather similar reactivity towards halogen electrophiles, but differ in their reactions with hydrobromic acid, which is caused by the basic nature of the aza group of the quinoxaline substrate.

1. Introduction

Alkynes find ever-increasing use in synthetic organic and material chemistry.[1] One prominent group of alkynes is enediynes, because of the presence of the (*Z*)-hexa-3-en-1,5-diyne fragment in some naturally occurring antibiotics.[2] It is supposed that the antitumour and antibacterial activity of enediyne antibiotics is based on the Bergman cyclization,[3] which generates benzene-1,4-diradicals (Scheme 1), which are able to cleave DNA and rupture the protein structure via oxidative cleavage of the peptide bond.



Scheme 1.

The challenging chemical structures of enediyne antibiotics and their fascinating mode biochemical action have attracted considerable scientific attention.[2f] Most of the work on enediyne chemistry is focused on the synthesis of designed enediynes, their thermal reactivity modulation and anticancer activity evaluation. Meanwhile, besides thermal or photochemical Bergman reaction, cyclizations of enediynes can be induced by various reagents: radicals (Scheme 2, **A**),[4] nucleophiles (Scheme 2, **B**),[5] transition metal complexes (Scheme 2, **C**),[6] frustrated Lewis pair (Scheme 2, **D**)[7] and so on. In addition, substituents at the alkyne termini can also be involved in the cyclization process leading to polynuclear products (Scheme 2, **E** and **F**).[8,9]

Despite significant recent advances in this area, the synthetic potential of enediynes seems to be underestimated. To date, most of the research on the above cyclizations deals with acyclic and benzoannelated enediynes as substrates. Unfortunately, there are only a few reports on the reactivity of *ortho*-dialkynyl hetarenes. There is no doubt that the enediyne moiety incorporated into the heterocyclic skeleton may possess a reactivity that is more diverse than that of acyclic and benzofused counterparts. It may create a new opportunity for the synthesis of polynuclear heterocyclic compounds.

Recently, we reported several nucleophilic cyclizations of 2,3-dialkynylquinoxalines and some other condensed pyrazines.[10] It has been found that their reactivity towards nucleophiles differs from that of acyclic enediynes and *ortho*-dialkynylbenzenes. Due to the high π-deficiency of the azine ring, *ortho*-dialkynylpyrazines react readily even with neutral nucleophiles and undergo unprompted or base-induced cascade cyclizations with direct participation of the added nucleophile and the aza group.

The revealed specificity in the reactivity of *ortho*-dialkynylpyrazines encouraged us to turn our attention to electrophilic cyclizations of heterocyclic enediynes. Herein, we present reactions of 2,3-dialkynylquinoxalines with electrophiles (Br_2, I_2, ICl, NBS and HBr) and compare them with those of *ortho*-dialkynylbenzenes.

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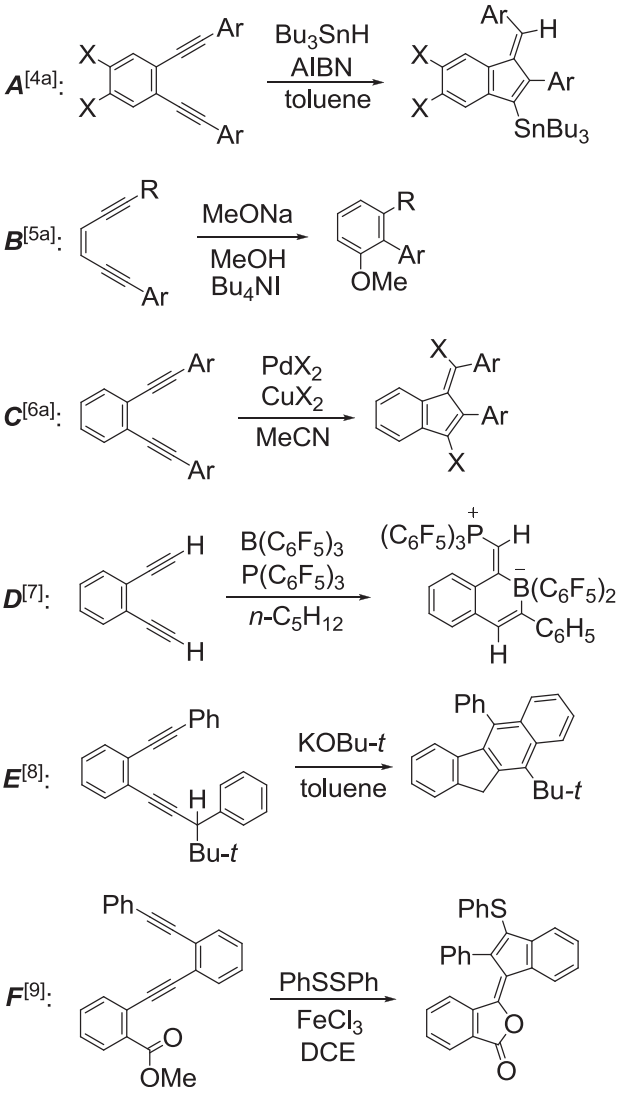
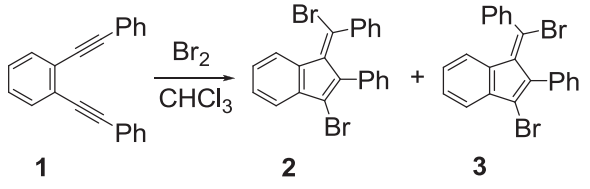


Scheme 2.

2. Results and discussion

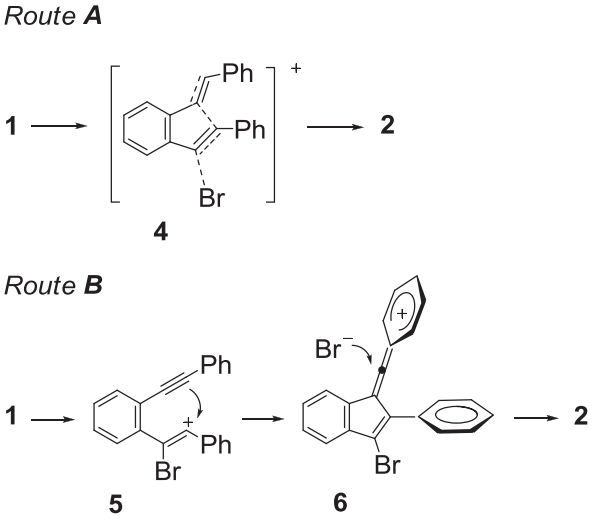
Only limited studies on the electrophilic cyclizations of enediynes have been reported. In the majority of studies, benzoannelated enediynes have been used as substrates.[5b,11] There are no data on the reactivity of acyclic and heterocyclic[12] enediynes.

The reaction of 1,2-bis(phenylethynyl)benzene with bromine was reported to produce isomeric benzofulvene derivatives **2** and **3** in a ~4:1 ratio (Scheme 3).[5b,11a,11d] Reactions of **1** with other electrophiles (I_2, HBr, H_2SO_4) proceeded in analogous manner.[5b]



Scheme 3.

In the original work,[11a,5b] a concerted mechanism of electrophilic addition—5-*exo*-*dig* cyclization for this transformation was proposed (Scheme 4, route **A**). The predominance of the (*E*)-isomer **2** in the reaction products was attributed to the sterically less hindered attack of the bromide ion on the cation **4**. Subsequently, another mechanism was proposed, based on DFT calculations.[11d] According to this, the electrophilic cyclization of **1** to give **2** can be rationalized by the formation of the stabilized cation **6** (Scheme 4, route **B**). The cyclization to give an aromatic six-membered ring (6-*endo*-*dig* cyclization) would yield a highly unfavourable naphthyl cation. The bromovinyl cation **5** is a true minimum (at B3LYP6-31G*) with a classic, nonbridging structure.

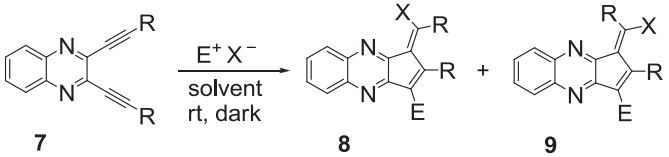


Scheme 4.

It should be noted that there are no data on the effect of the alkyne substituents on the cyclization process. Meanwhile, in both articles[5b,11d] the formation of a resonance-stabilized carbenium ion **6** as an intermediate is emphasized.

With this in mind, we synthesized 2,3-dialkynylquinoxalines **7a**–**d**, with various substituents (Ph, *p*-Tol, *n*-Bu, $SiMe_3$) on the C≡C bond, via a Sonogashira coupling in accordance with reported procedures.[10b]

The reaction of 2,3-bis(phenylethynyl)quinoxaline **7a** with bromine in dry chloroform at room temperature in the dark afforded a mixture of isomeric 3-bromo-1-(bromo(phenyl)methylene)-2-phenyl-1*H*-cyclopenta[*b*]quinoxalines **8a** and **9a** in nearly quantitative total yield and in a 2.6:1 ratio (^{1}H NMR spectroscopic data) (Scheme 5, Table 1, entry 1). Flash column chromatography and subsequent recrystallization gave pure product **8a**. Compound **7b** reacted with bromine in a completely analogous manner (Scheme 5, Table 1, entry 1).



7: R = Ph (**a**), *p*-Tol (**b**), *n*-Bu (**c**), $SiMe_3$ (**d**)
8,**9**: R, E, X = Ph, Br, Br (**a**); *p*-Tol, Br, Br (**b**); Ph, I, I (**c**); Ph, I, Cl (**d**); *n*-Bu, Br, Br (**e**); $SiMe_3$, Br, Br (**f**)

Scheme 5.

The reaction of **7a** with iodine in chloroform proceeded gave only traces of the desired product. The use of nitromethane as the solvent gave a better result (Scheme 5, Table 1, entry 3). The X-ray crystal structure of the major reaction product **8c** supported the

Table 1
Halogen-promoted electrophilic cyclizations of 2,3-dialkynylquinoxalines

Entry	R	$E^+ X^-$	Solvent, reaction time	**8**:**9** Ratio (NMR data)	Yield (%)
1	Ph	Br_2	$CHCl_3$ 2 h	2.6:1	64 (**8a**)
2	*p*-Tol	Br_2	$CHCl_3$ 2 h	2.6:1	63 (**8b**)
3	Ph	I_2	CH_3NO_2 24 h	2.8:1	59 (**8c**)
4	Ph	ICl	$CHCl_3$ 24 h	1.5:1	45 (**8d**) 31 (**9d**)
5	*n*-Bu	Br_2	$CHCl_3$ 20 h	—	73 (**9e**)
6	$SiMe_3$	Br_2	$CHCl_3$ 20 h	—	57 (**9f**)

structural assignment (Fig. 1). The peripheral phenyl groups are coplanar to each other with a separation between their centroids of about 3.54 Å and are perpendicular to the fully conjugated cyclopentaquinoxaline moiety.

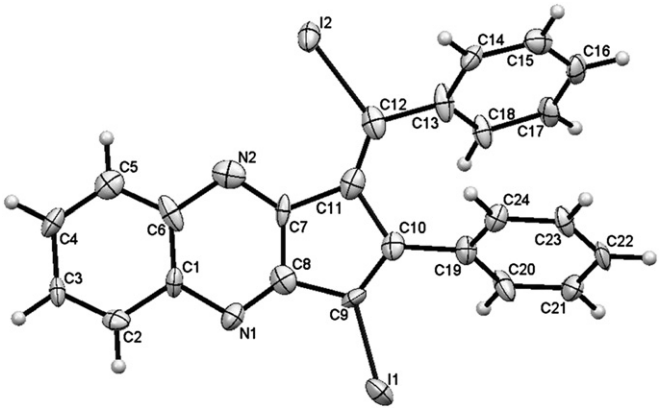


Fig. 1. ORTEP Plots for X-ray crystal structure of **8c**.

The use of iodine chloride as the electrophile changed the **8**:**9** ratio strongly, though isomer **8d** prevailed as before (Scheme 5, Table 1, entry 4). Both (*Z*)-isomer **8d** and (*E*)-isomer **9d** were isolated in pure form. The structure of the minor product **9d** was unambiguously secured by X-ray crystal structure analysis (Fig. 2).

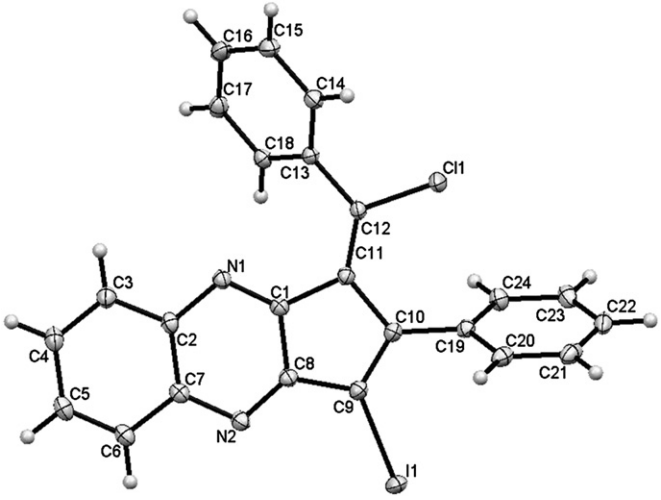


Fig. 2. ORTEP Plots for X-ray crystal structure of **9d**.

The ^{1}H NMR spectra of the aryl substituted products **8a**–**d** and **9a**–**d** provided a highly satisfactory method of defining their stereochemistry. In the ^{1}H NMR spectra of products **8a**–**d**, the protons corresponding to the two aryl groups were seen as multiplets at δ 6.7–7.2 ppm, while those of **9a**–**d** were seen as multiplets at δ 7.4–7.7 ppm (Fig. 3).

2,3-Dialkynylquinoxalines **7c**,**d** bearing non-aromatic substituents on the C≡C bonds are also able to react with bromine in chloroform, although extended reaction times are required (Scheme 5, Table 1, entries 5 and 6). In both cases, the isomer **9** was the only reaction product.

The structural assignment for compound **9e**, apart from elemental analysis, was based on the following evidence. The IR and ^{13}C NMR spectra reveal the absence of the C≡C bond in this molecule. For comparison, in the ^{13}C NMR spectrum of the starting compound **7c** the C≡C bond carbons manifest themselves as peaks at δ 79.0 and 98.2 ppm. In the ^{13}C NMR spectrum of **9e** eight upfield peaks at δ 14–40 ppm (sp^3 C) and twelve peaks at δ 112–152 ppm (sp^2 C) are observed. The ^{1}H NMR spectrum of **9e** displays signals of protons belonging to two different butyl groups (Fig. 4). The α-methylene protons of one of them resonate as a broad multiplet at δ 2.3–2.5 ppm, whereas those of the other butyl group show a broad doublet of multiplets at δ 2.6–3.2 ppm. The proposed structure **9e** was also confirmed by the ^{1}H–^{1}H NOESY experiment, which indicated the absence of the spatial interaction between protons of the above α-methylene groups.

The structure **9f** was proved by a combination of mass spectrometry, IR, ^{1}H and ^{13}C NMR spectroscopic measurements. The chemical shifts of the aromatic protons H(6) and H(7) (δ 7.79–7.87 ppm), H(5) and H(8) (δ 8.06–8.20 ppm) in the ^{1}H NMR spectrum of **9f** are similar to those of **9e** providing evidence to suggest a similarity in their stereo structures. The ^{13}C NMR spectra of both compounds (excluding the sp^3 carbons region) are also very similar.

Returning to the mechanism, previously proposed for electrophilic cyclization of 1,2-bis(phenylethynyl)benzene **1**, and taking into account the above experimental data, one can conclude that the resonance stabilization of the intermediate carbenium ion **6** (see, Scheme 4) is not a crucial factor for the cyclization. However, the nature of the substituents on the alkyne termini influences the stereochemical result of the reaction. In the case of an aryl substituent, the stabilized cation **10** serves as an intermediate (Scheme 6). It can be attacked by the halide ion from the less hindered left side (to provide the major product **8**) or from the right side (to yield the minor isomer **9**). The ratio of the cyclization products depends on the electrophile used (to be more precise, its counterion). The attack of a chloride ion on intermediate **10** (from the right side) affording compound **9d** is less sterically demanding than in the cases of bromide or iodide ions. As a consequence, the yield of the minor isomer **9d** increases. Reactions of 2,3-dialkynylquinoxaline **7c** or **7d**, with non-aromatic substituents on the C≡C bonds, with electrophiles, evidently, proceed via the vinyl cation **11** with an intrinsically more stable geometry affording the corresponding compound **9** as a single product.

In the next experiment, *N*-bromosuccinimide was used as an electrophile. Treatment of **7a** with NBS in glacial acetic acid gave dibromo ketone **13** in 57% yield (Scheme 7). The mass spectrum of **13** shows a combination of peaks *m*/*z* 508 $[M+2]^+$, 506 $[M]^+$, 504 $[M-2]^+$ with ~1:2:1 relative intensities, which are typical for dibromo compounds. Its IR and ^{13}C NMR spectra indicate the presence of a C=O bond ($\nu_{C=O}$ 1656 cm^{-1}, δ 192.4 ppm). The structure of **13** was also proved by X-ray crystal structure analysis (Fig. 5). Presumably, compound **13** is formed by a mechanism analogous to that shown in Scheme 6. However, during the course of the reaction acetic acid serves as the source of a nucleophile after the carbocyclization step (**10**→**12**). The acetoxy compound **12** undergoes further electrophilic addition of a bromonium ion

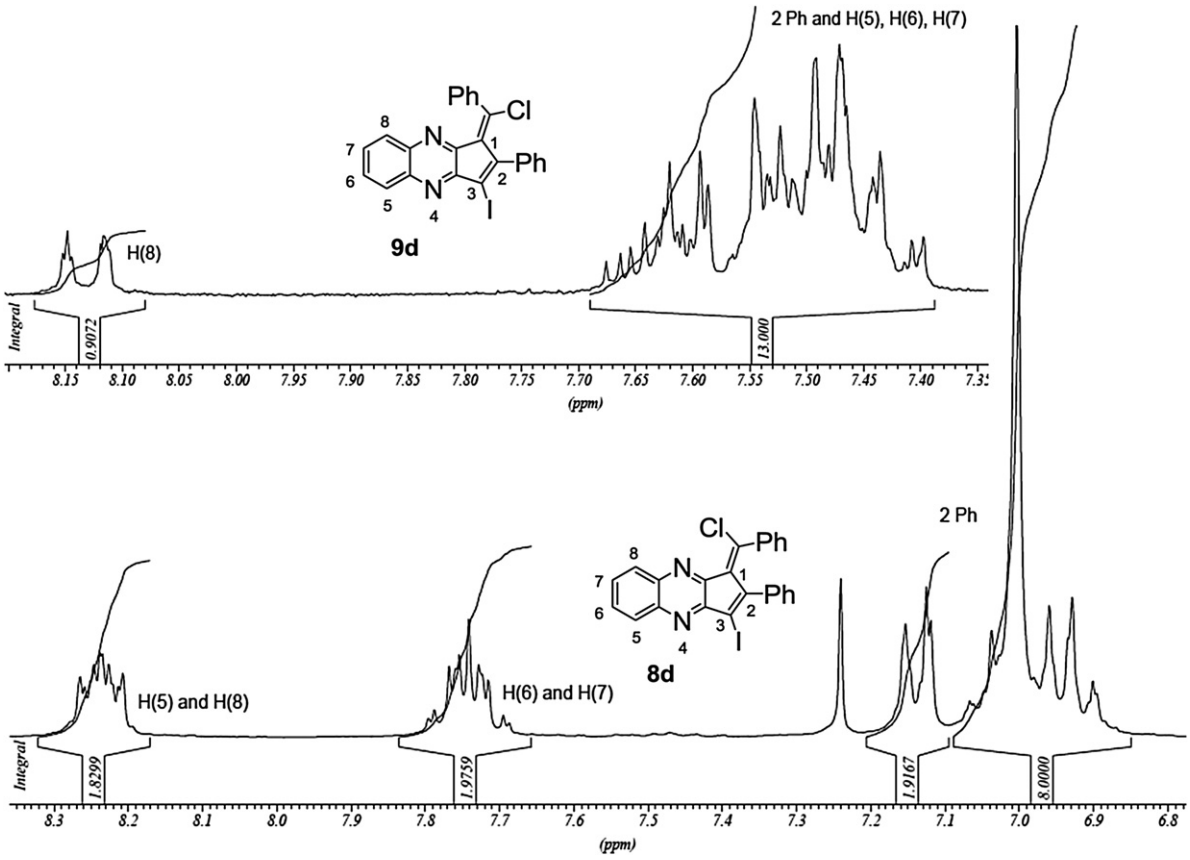


Fig. 3. The ^{1}H NMR spectra of compounds **8d** and **9d** ($CDCl_3$).

accompanied by deacetylation as depicted in Scheme 7. As reported previously,[5b] 1,2-bis(phenylethynyl)benzene reacts with bromine in methanol to yield (1,1-dibromo-2-phenyl-1*H*-inden-3-yl)(phenyl)methanone as the major product. Thus, both substrates **1** and **7a** demonstrate rather similar reactivity towards halogen electrophiles.

The different behaviour of benzofused and heterocyclic enediynes towards electrophiles is illustrated by their reactions with hydrobromic acid. The interaction of 1,2-bis(phenylethynyl)benzene **1** with HBr proceeds in agreement with Scheme 4 to afford a mixture of isomeric 1-(bromo(phenyl)methylene)-2-phenyl-1*H*-indenes.[5b] While, 2,3-bis(phenylethynyl)quinoxaline **7a** under the

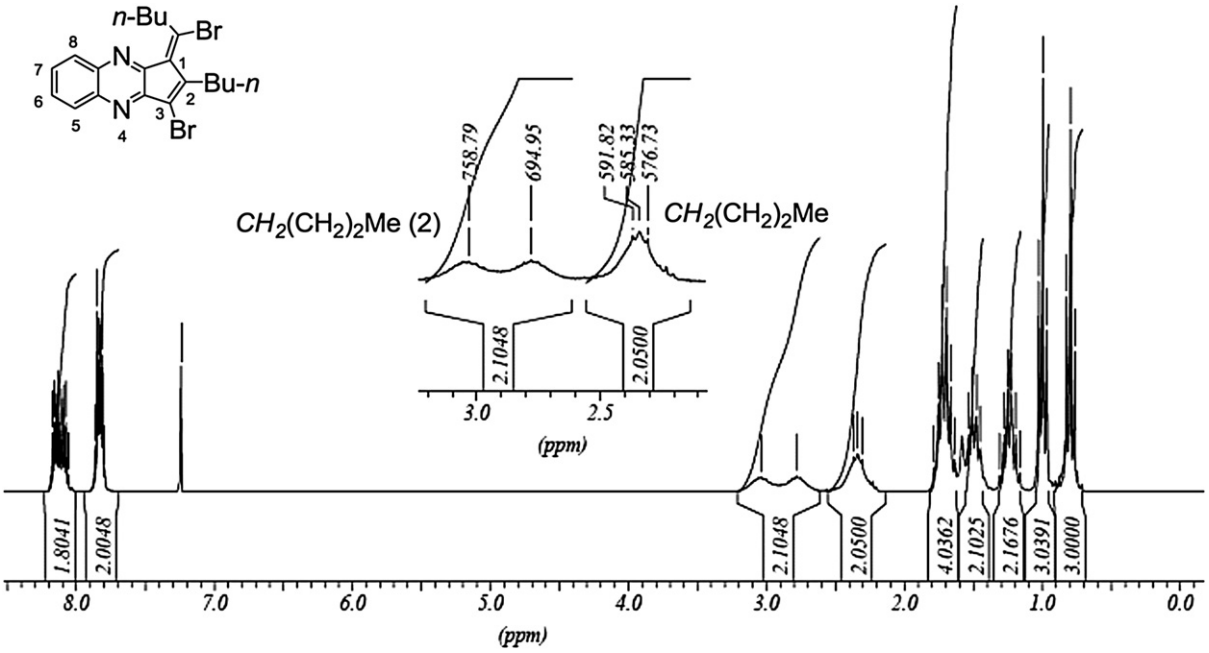
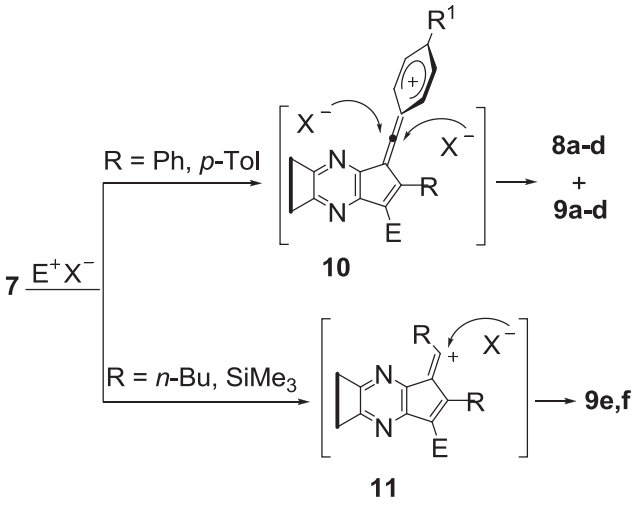
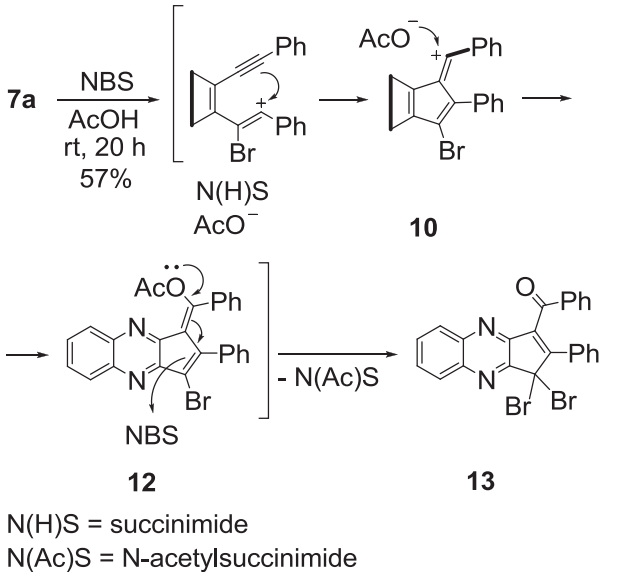


Fig. 4. The ^{1}H NMR spectrum of compound **9e** ($CDCl_3$).



Scheme 6.



Scheme 7.

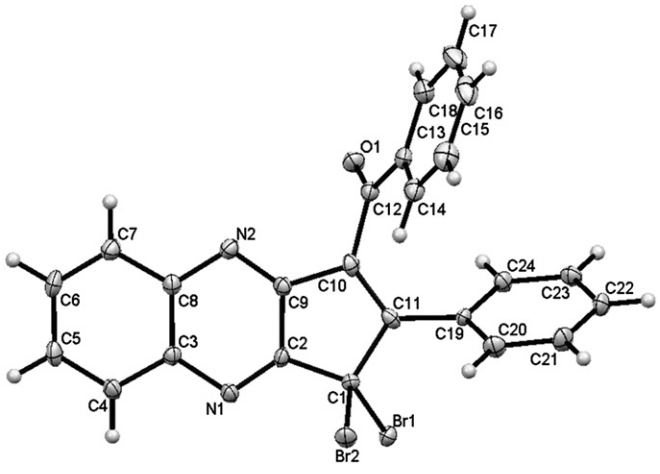
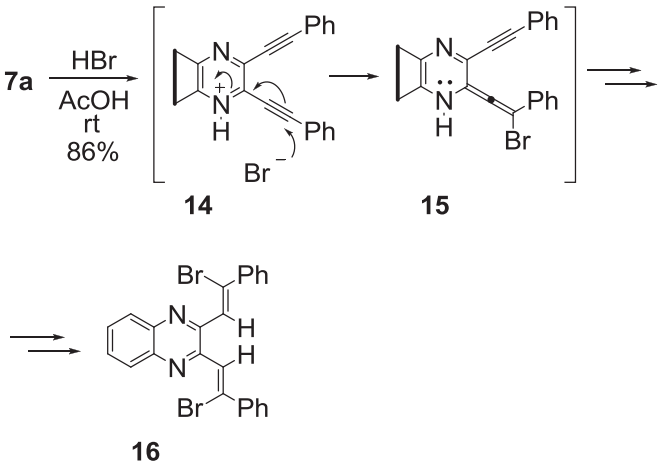


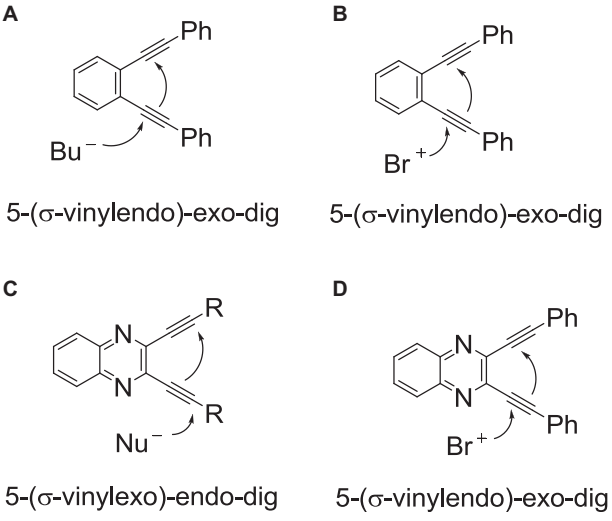
Fig. 5. ORTEP Plots for X-ray crystal structure of **13**.

same conditions forms only the addition product **16** (Scheme 8). The main reason for this difference is the basic nature of the aza group. Evidently, the reaction starts with its protonation to give a cation **14**. Subsequent nucleophilic attack of the bromide ion on the C≡C bond provides an allene intermediate **15**, that rearranges into adduct **16**. The IR spectrum indicates the absence of C≡C bonds in this molecule. The ^{1}H NMR spectrum of **16** also confirmed its symmetrical structure.



Scheme 8.

Comparing the reactivity of benzofused and heterocyclic enediynes, we should also mention another important point. In case of 1,2-bis(phenylethynyl)benzene **1** both nucleophilic[5b] and electrophilic[5b] attacks are directed on the same carbon atom of the C≡C bond resulting in 5-*exo-dig* cyclizations (Scheme 9, **A** and **B**).[13] The polarity of the triple bonds of dialkynylquinoxalines **7** causes differences in the reaction sites[10a] as well in the modes of subsequent cyclizations (Scheme 9, **C** and **D**).



Scheme 9.

3. Conclusion

In summary, we have found that *ortho*-dialkynylbenzenes and *ortho*-dialkynylquinoxalines demonstrate rather similar reactivity towards halogen electrophiles. All tested reactions of *ortho*-dialkynylquinoxalines with Br_2, I_2, ICl, NBS start with the addition of an electrophile to the carbon–carbon triple bond that promotes further 5-*exo-dig* carbocyclization ultimately yielding a mixture of

isomeric cyclopenta[*b*]quinoxaline derivatives. The presence of an aryl substituent on the alkyne termini of *ortho*-dialkynylquinoxaline is not crucial for this cyclization. At the same time, the nature of substituents on the C≡C bonds influence the stereochemical result of the reaction. The ratio of isomeric cyclization products depends also on the electrophile used.

ortho-Dialkynylbenzenes and *ortho*-dialkynylquinoxalines differ in their reactivity towards hydrobromic acid due to the basic nature of the aza group of the quinoxaline substrate.

4. Experimental

4.1. General

Proton (^{1}H) nuclear magnetic resonance (NMR) spectra were recorded on a Bruker DPX−250 (250 MHz) spectrometer. ^{13}C NMR spectra were recorded on Bruker DPX-250 (62.9 MHz) spectrometer. ^{1}H and ^{13}C NMR chemical shifts are in parts per million relative to Me_4Si. Coupling constants are in Hertz. The IR spectra were recorded on a Varian Excalibur 3100 FT-IR spectrometer using Nujol. Mass spectra were measured on a Finnigan MAT INCOS 50 spectrometer. CHN analysis was accomplished by combustion analysis (Dumas and Pregl method). Melting points were determined in glass capillaries using a Stuart SMP30 device and are uncorrected. Flash column chromatography was performed on silica gel. All commercial reagents (1-alkynes, palladium catalysts, NBS) were purchased from Acros and Aldrich.

4.2. X-ray structure determination

Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC) and allocated the deposition numbers CCDC 893084 (**8c**), CCDC 893085 (**9d**) and CCDC 893086 (**13**).

4.3. Synthesis of the starting compounds

Starting 2,3-dialkynylquinoxalines **7a**,**b**,[10b] were synthesized in accordance with known procedures.

4.3.1. Synthesis of 2,3-di(hex-1-ynyl)quinoxaline ***7c***. CuI (10.0 mg, 0.05 mmol), $PdCl_2(PPh_3)_2$ (20.0 mg, 0.03 mmol) and Et_3N (4 mL) were added to 2,3-dichloroquinoxaline[14] (199 mg, 1.0 mmol) in dry DMF (4 mL) under a slow stream of argon. After 20 min stirring under argon, 1-hexyne (179 mg, 250 μL, 2.18 mmol) was added drop wise. Stirring was continued for 24 h at room temperature. The reaction mixture was then treated with a saturated aqueous solution of NH_4Cl (10 mL) and extracted with CH_2Cl_2 (3×30 mL). The solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (3×20 cm) with CH_2Cl_2 as the eluent. The yellowish fraction R_f 0.5 (CH_2Cl_2) gave **7c** (197 mg, 68%) as yellowish oil; ^{1}H NMR ($CDCl_3$, 250 MHz) δ ppm: 0.91 (t, J=7.3 Hz, 6H, 2(CH_2)$_3$*Me*), 1.42−1.70 (m, 8H, 2CH_2(*CH*$_2$)$_2$Me), 2.52 (t, J=7.0 Hz, 4H, 2*CH*$_2$$CH_2CH_2Me$), 7.59−7.67 (m, 2H, H(6) and H(7)), 7.89−7.97 (m, 2H, H(5) and H(8)); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ ppm: 14.0, 19.8, 22.5, 30.6, 79.0, 98.2, 129.0, 130.7, 140.6, 141.5; IR, cm^{-1}: 1530, 1556, 2230 (C≡C). MS m/z: 290 ([M]$^+$, 43), 262 (5), 261 (20), 248 (34), 247 (52), 234 (14), 233 (65), 219 (78), 205 (53), 182 (11), 167 (7), 154 (34), 140 (17), 127 (17), 113 (27), 102 (18), 89 (14), 77 (100). Anal. Calcd for $C_{20}H_{22}N_2$: C, 82.72; H, 7.64; N, 9.65. Found: C, 82.88; H, 7.51; N, 9.49.

4.3.2. Synthesis of 2,3-bis((trimethylsilyl)ethynyl)quinoxaline ***7d***. A mixture of CuI (10.0 mg, 0.05 mmol), $PdCl_2(PPh_3)_2$ (20.0 mg, 0.03 mmol), 2,3-dichloroquinoxaline[14] (199 mg, 1.0 mmol), trimethylsilylacetylene (206 mg, 300 μL, 2.10 mmol) and Et_3N (4 mL) was stirred for 24 h at 70 °C under argon. The reaction mixture was then evaporated to dryness under reduced pressure. The residue was purified by flash column chromatography on silica gel (3×15 cm) with CH_2Cl_2 as the eluent. The colourless fraction R_f 0.6 (CH_2Cl_2) gave **7d** (138 mg, 43%) as colourless crystals, mp 118−121 °C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ ppm: 0.33 (s, 18H, 2$SiMe_3$), 7.69−7.79 (m, 2H, H(6) and H(7)), 7.99−8.07 (m, 2H, H(5) and H(8)); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ ppm: 0.1, 101.2, 102.8, 129.3, 131.5, 140.6, 140.8; IR, cm^{-1}: 1556, 2182 (C≡C). MS m/z: 322 ([M]$^+$, 16), 308 (11), 307 (39), 146 (15), 73 (100). Anal. Calcd for $C_{18}H_{22}N_2Si_2$: C, 67.03; H, 6.87; N, 8.68; Si, 17.41. Found: C, 66.89; H, 6.97; N, 8.51.

4.4. Synthesis of (*Z*)-3-bromo-1-(bromo(phenyl)methylene)-2-phenyl-1*H*-cyclopenta[*b*]quinoxaline 8a

To a stirred solution of 2,3-bis(phenylethynyl)quinoxaline **7a** (165 mg, 0.499 mmol) in $CHCl_3$ (5 mL) under argon, solution of bromine (1 mL, 0.5 M in $CHCl_3$, 0.5 mmol) was added drop wise. The reaction was allowed to stir at room temperature for 2 h in the dark. The reaction mixture was diluted with CH_2Cl_2 (30 mL), washed with a saturated aqueous solution of Na_2SO_3 and then with water. The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel (3.5×20 cm) using CH_2Cl_2 as the eluent. The yellow fraction with R_f 0.6 (CH_2Cl_2) was separated. The crude product was crystallized from heptane/$CHCl_3$ (5:1, v/v) yielding **8a** (156 mg, 64%) as yellow needles, mp 192−194 °C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ ppm: 6.87−7.06 (m, 8H, 2Ph), 7.09−7.17 (m, 2H, 2Ph), 7.69−7.83 (m, 2H, H(6) and H(7)), 8.18−8.29 (m, 2H, H(5) and H(8)); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ ppm: 124.9, 127.8, 127.9, 128.2, 129.5, 129.8, 129.9, 130.0, 130.5, 130.7, 130.8, 133.5, 133.7, 133.9, 140.6, 141.4, 142.1, 150.3, 151.1, 152.9; IR, cm^{-1}: 1554, 1577; MS m/z: 492 ([M+2]$^+$, 2.4), 490 ([M]$^+$, 5.1), 488 ([M−2]$^+$, 2.6), 409 (4), 330 ([M−Br_2]$^+$, 100), 301 (4), 227 (5), 200 (5), 164 (13). Anal. Calcd for $C_{24}H_{14}Br_2N_2$: C, 58.81; H, 2.88; Br, 32.60; N, 5.71. Found: C, 58.63; H, 3.00; Br, 32.68; N, 5.58.

4.5. Synthesis of (*Z*)-3-bromo-1-(bromo(*p*-tolyl)methylene)-2-*p*-tolyl-1*H*-cyclopenta[*b*]quinoxaline 8b

The reaction of 2,3-bis(*p*-tolylethynyl)quinoxaline **7b** (179 mg, 0.499 mmol) with bromine was carried out in accordance with the procedure described in Section 4.4. Compound **8b** (164 mg, 63%) was obtained as yellow needles, mp 206−207 °C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ ppm: 2.18 (s, 3H, Me), 2.21 (s, 3H, Me), 6.71 (d, J=7.9 Hz, 2H, *p*-Tol), 6.79 (d, J=7.9 Hz, 2H, *p*-Tol), 6.88 (d, J=8.2 Hz, 2H, *p*-Tol), 6.99 (d, J=8.2 Hz, 2H, *p*-Tol), 7.68−7.79 (m, 2H, H(6) and H(7)), 8.19−8.26 (m, 2H, H(5) and H(8)); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ ppm: 21.5 (7), 21.5 (9), 123.9, 128.3, 128.5, 129.4, 129.9, 130.0, 130.3, 130.7, 130.8 (5), 130.8 (7), 131.0, 133.3, 134.1, 137.9, 140.2, 141.4, 142.1, 150.6, 151.2, 152.9; IR, cm^{-1}: 1557, 1580, 1607; MS m/z: 520 ([M+2]$^+$, 6), 518 ([M]$^+$, 13), 516 ([M−2]$^+$, 6), 437 (8), 358 ([M−Br_2]$^+$, 100), 343 (78), 259 (6), 240 (6), 211 (5), 179 (9), 171 (32), 164 (5), 140 (12), 114 (5). Anal. Calcd for $C_{26}H_{18}Br_2N_2$: C, 60.26; H, 3.50; Br, 30.84; N, 5.41. Found: C, 60.09; H, 3.61; Br, 31.03; N, 5.55.

4.6. Synthesis of (*Z*)-3-iodo-1-(iodo(phenyl)methylene)-2-phenyl-1*H*-cyclopenta[*b*]quinoxaline 8c

To a stirred solution of 2,3-bis(phenylethynyl)quinoxaline **7a** (66.0 mg, 0.199 mmol) in CH_3NO_2 (3 mL) under argon, a solution of iodine (254 mg, 1.0 mmol) in CH_3NO_2 (6 mL) was added drop wise. The reaction was allowed to stir at room temperature for 24 h in the dark. The reaction mixture was diluted with CH_2Cl_2 (30 mL), washed with a saturated aqueous solution of Na_2SO_3 and then with water. The solvent was evaporated under reduced pressure and the

residue was purified by flash column chromatography on silica gel (3.5×20 cm) using CH_2Cl_2 as the eluent. The yellow fraction with R_f 0.6 (CH_2Cl_2) was separated. The crude product was crystallized from heptane/$CHCl_3$ (5:1, v/v) yielding **8c** (69.0 mg, 59%) as orange crystals, mp 214–216 °C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ ppm: 6.81–7.10 (m, 10H, 2Ph), 7.69–7.81 (m, 2H, H(6) and H(7)), 8.19–8.31 (m, 2H, H(5) and H(8)); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ ppm: 104.4, 109.8, 127.6, 127.9, 128.1, 129.2, 129.4, 130.0, 130.2 (8), 130.3 (3), 130.5, 130.9, 136.5, 138.4, 140.8, 142.7, 145.4, 150.6, 155.5, 156.3; IR, cm^{-1}: 1554, 1573; MS *m*/*z*: 584 ([M]$^+$, 4), 457 (5), 330 ([M−I_2]$^+$, 100), 301 (12), 292 (14), 252 (11), 227 (20), 201 (20), 176 (12), 165 (89), 151 (21), 137 (10), 127 (51), 100 (20). Anal. Calcd for $C_{24}H_{14}I_2N_2$: C, 49.34; H, 2.42; I, 43.45; N, 4.80. Found: C, 49.48; H, 2.32; I, 43.62; N, 4.77.

4.7. Synthesis of (*Z*)-1-(chloro(phenyl)methylene)-3-iodo-2-phenyl-1*H*-cyclopenta[*b*]quinoxaline 8d and (*E*)-1-(chloro-(phenyl)methylene)-3-iodo-2-phenyl-1*H*-cyclopenta[*b*]quinoxaline 9d

To a stirred solution of 2,3-bis(phenylethynyl)quinoxaline **7a** (132 mg, 0.399 mmol) in $CHCl_3$ (5 mL) under argon, solution of iodine chloride (1 mL, 0.4 M in $CHCl_3$, 0.4 mmol) was added drop wise. The reaction was allowed to stir at room temperature for 24 h in the dark. The reaction mixture was diluted with CH_2Cl_2 (30 mL), washed with a saturated aqueous solution of Na_2SO_3 and then with water. The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel (3.5×30 cm) using CH_2Cl_2 as the eluent. The yellow fraction with R_f 0.6 (CH_2Cl_2) gave (*Z*)-1-(*chloro*(*phenyl*)*methylene*)-3-*iodo*-2-*phenyl*-1*H*-*cyclopenta*[*b*]*quinoxaline* **8d**. The yellow fraction with R_f 0.5 (CH_2Cl_2) gave (*E*)-1-(*chloro*(*phenyl*)*methylene*)-3-*iodo*-2-*phenyl*-1*H*-*cyclopenta*[*b*]*quinoxaline* **9d**. Both crude products were crystallized from heptane/$CHCl_3$ (5:1, v/v).

Compound **8d** was obtained (88.0 mg, 45%) as yellow needles, mp 182–184 °C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ ppm: 6.87–7.09 (m, 8H, 2Ph), 7.10–7.19 (m, 2H, 2Ph), 7.67–7.82 (m, 2H, H(6) and H(7)), 8.18–8.31 (m, 2H, H(5) and H(8)); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ ppm: 105.5, 128.0, 128.8, 128.9 (8), 129.0 (3), 129.5, 129.7, 129.9, 130.2, 130.7, 130.8, 132.2, 138.0, 138.7, 141.3, 142.2, 142.4, 149.2, 153.5, 156.5; IR, cm^{-1}: 1563, 1586; MS *m*/*z*: 494 ([M+2]$^+$, 7), 492 ([M]$^+$, 20), 365 (13), 363 (13), 330 ([M−ICl]$^+$, 99), 329 (100), 301 (12), 292 (14), 252 (11), 246 (14), 227 (16), 202 (22), 182 (21), 175 (9), 164 (69), 151 (20), 137 (10), 127 (32), 102 (21). Anal. Calcd for $C_{24}H_{14}ClIN_2$: C, 58.50; H, 2.86; Cl, 7.20; I, 25.75; N, 5.69. Found: C, 58.32; H, 3.03; I+Cl, 33.07; N, 5.83.

Compound **9d** was obtained (61.0 mg, 31%) as orange crystals, mp 183–186 °C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ ppm: 7.39–7.68 (m, 13H, 2Ph, H(6), H(7) and H(8)), 8.14 (dm, *J*=7.9 Hz, 1H, H(5)); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ ppm: 103.9, 127.9, 128.0, 128.2, 129.4, 129.9, 130.0, 130.1, 130.3, 130.5 (5), 130.5 (7), 132.9, 136.1, 138.5, 141.9, 142.3, 142.8, 151.0, 154.7, 155.2; IR, cm^{-1}: 1549, 1581; MS *m*/*z*: 494 ([M+2]$^+$, 24), 492 ([M]$^+$, 72), 365 (11), 363 (11), 330 ([M−ICl]$^+$, 100), 329 (99), 301 (12), 252 (11), 246 (15), 227 (21), 202 (19), 182 (15), 164 (53), 151 (16), 137 (7), 127 (20), 102 (10). Anal. Calcd for $C_{24}H_{14}ClIN_2$: C, 58.50; H, 2.86; Cl, 7.20; I, 25.75; N, 5.69. Found: C, 58.65; H, 2.70; I+Cl, 32.75; N, 5.61.

4.8. Synthesis of (*E*)-3-bromo-1-(1-bromopentylidene)-2-butyl-1*H*-cyclopenta[*b*]quinoxaline 9e

To a stirred solution of 2,3-di(hex-1-ynyl)quinoxaline **7c** (145 mg, 0.499 mmol) in $CHCl_3$ (3 mL) under argon, solution of bromine (1 mL, 0.5 M in $CHCl_3$, 0.5 mmol) was added drop wise. The reaction was allowed to stir at room temperature for 20 h in the dark. The reaction mixture was diluted with CH_2Cl_2 (30 mL), washed with a saturated aqueous solution of Na_2SO_3 and then with water. The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel (3.5×20 cm) using $CHCl_3$ as the eluent. The yellowish fraction with R_f 0.6 (CH_2Cl_2) gave **9e** (165 mg, 73%) as yellowish oil; ^{1}H NMR ($CDCl_3$, 250 MHz) δ ppm: 0.79 (t, *J*=7.3 Hz, 3H, $(CH_2)_3$*Me*), 1.00 (t, *J*=7.3 Hz, 3H, $(CH_2)_3$*Me*), 1.17–1.32 (m, 2H, $(CH_2)_2$*CH*$_2$Me), 1.43–1.62 (m, 2H, $(CH_2)_2$*CH*$_2$Me), 1.64–1.78 (m, 4H, 2CH_2*CH*$_2$$CH_2$Me), 2.31–2.45 (m, 2H, *CH*$_2$$CH_2$$CH_2$Me), 2.90 (br dm, *J*=63.8 Hz, 2H, *CH*$_2$$CH_2$$CH_2$Me), 7.79–7.89 (m, 2H, H(6) and H(7)), 8.05–8.19 (m, 2H, H(5) and H(8)); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ ppm: 14.2, 14.4, 22.3, 22.5, 29.7, 31.4, 40.2, 40.7, 111.8, 117.1, 128.7, 129.8, 129.9, 131.7, 131.8, 138.0, 141.2, 141.5, 150.5, 152.9; IR, cm^{-1}: 1562, 1614. Anal. Calcd for $C_{20}H_{22}Br_2N_2$: C, 53.36; H, 4.93; Br, 35.50; N, 6.22. Found: C, 53.45; H, 5.07; Br, 35.29; N, 6.33.

4.9. Synthesis of (*Z*)-3-bromo-1-(bromo(trimethylsilyl)methylene)-2-(trimethylsilyl)-1*H*-cyclopenta[*b*]quinoxaline 9f

To a stirred solution of 2,3-bis((trimethylsilyl)ethynyl)quinoxaline **7d** (80.0 mg, 0.248 mmol) in $CHCl_3$ (3 mL) under argon, solution of bromine (1 mL, 0.75 M in $CHCl_3$, 0.75 mmol) was added drop wise. The reaction was allowed to stir at room temperature for 20 h in the dark. The reaction mixture was diluted with CH_2Cl_2 (30 mL), washed with a saturated aqueous solution of Na_2SO_3 and then with water. The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel (3.5×20 cm) using CH_2Cl_2 as the eluent. The colourless fraction with R_f 0.6 (CH_2Cl_2) gave **9f** (69 mg, 57%) as yellowish oil; ^{1}H NMR ($CDCl_3$, 250 MHz) δ ppm: −0.08 (s, 9H, $SiMe_3$), 0.47 (s, 9H, $SiMe_3$), 7.79–7.87 (m, 2H, H(6) and H(7)), 8.06–8.20 (m, 2H, H(5) and H(8)); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ ppm: 0.4, 0.5, 118.2, 122.0, 127.2, 129.8, 129.9, 131.8, 131.9, 140.3, 140.8, 141.3, 150.1, 152.3; IR, cm^{-1}: 1558, 1611; MS *m*/*z*: 411 ([M+2−$SiMe_3$]$^+$, 9), 409 ([M−$SiMe_3$]$^+$, 19), 407 ([M−2−$SiMe_3$]$^+$, 9), 329 ([M−$BrSiMe_3$]$^+$, 3), 139 (22), 73 (100). Anal. Calcd for $C_{18}H_{22}Br_2N_2Si_2$: C, 44.82; H, 4.60; Br, 33.13; N, 5.81; Si, 11.65. Found: C, 44.66; H, 4.45; Br, 32.96; N, 6.00.

4.10. Synthesis of (1,1-dibromo-2-phenyl-1*H*-cyclopenta[*b*]quinoxalin-3-yl)(phenyl)methanone 13

To a stirred solution of 2,3-bis(phenylethynyl)quinoxaline **7a** (165 mg, 0.499 mmol) in glacial acetic acid (3 mL), a solution of NBS (178 mg, 1.0 mmol) in glacial acetic acid (5 mL) was added drop wise. The reaction was allowed to stir at room temperature for 20 h in the dark. The reaction mixture was filtered. The crude product was crystallized from heptane/$CHCl_3$ (5:1, v/v) yielding **13** (143 mg, 57%) as yellowish crystals, mp 168–170 °C (decomp.); ^{1}H NMR ($CDCl_3$, 250 MHz) δ ppm: 7.32–7.43 (m, 5H), 7.48–7.57 (m, 1H), 7.69–7.82 (m, 2H), 7.86–7.97 (m, 4H), 8.02–8.10 (m, 1H), 8.22–8.29 (m, 1H); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ ppm: 53.7, 128.9 (6), 129.0 (4), 129.2, 129.3, 130.0, 130.1, 130.2, 130.7, 131.1, 131.4, 133.9, 134.9, 136.0, 141.3, 143.2, 149.9, 153.9, 159.0, 192.4; IR, cm^{-1}: 1656 (C=O); MS *m*/*z*: 508 ([M+2]$^+$, 2), 506 ([M]$^+$, 4), 504 ([M−2]$^+$, 2), 427 (16), 426 ([M−Br]$^+$, 12), 425 (14), 399 (14), 397 (13), 347 (8), 318 (71), 270 (5), 241 (24), 214 (24), 189 (13), 173 (16), 159 (11), 139 (9), 113 (18), 105 (100). Anal. Calcd for $C_{24}H_{14}Br_2N_2O$: C, 56.95; H, 2.79; Br, 31.57; N, 5.53; O, 3.16. Found: C, 57.13; H, 2.95; Br, 31.44; N, 5.72.

4.11. Synthesis of 2,3-bis((*Z*)-2-bromo-2-phenylvinyl)quinoxaline 16

HBr gas prepared from KBr (500 mg, 4.20 mmol) and concd H_2SO_4 (4 mL) was passed through a stirred solution of 2,3-bis(phenylethynyl)quinoxaline **7a** (165 mg, 0.499 mmol) in glacial acetic acid (5 mL). The reaction was allowed to stir at room

temperature for 1 h in the dark. The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel (3.5×20 cm) using CH_2Cl_2 as the eluent. The yellowish fraction with R_f 0.6 (CH_2Cl_2) gave **16** (211 mg, 86%) as yellowish crystals, mp 108–109 °C; ^{1}H NMR ($CDCl_3$, 250 MHz) δ ppm: 7.43–7.42 (m, 6H, 2Ph), 7.60 (s, 2H), 7.66–7.74 (m, 4H, 2Ph), 7.76–7.83 (m, 2H, H(6) and H(7)), 8.12–8.19 (m, 2H, H(5) and H(8)); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ ppm: 126.7, 128.3, 128.9, 129.5, 130.1, 130.8, 131.9, 139.8, 141.2, 151.0; IR, cm^{-1}: 1616; MS *m*/*z*: 492 ([M]$^+$, 0.1), 413 (10), 411 (11), 332 (31), 331 (67), 330 (7), 255 (21), 229 (8), 204 (28), 176 (9), 165 (30), 128 (16), 102 (100), 77 (42). Anal. Calcd for $C_{24}H_{16}Br_2N_2$: C, 58.56; H, 3.28; Br, 32.47; N, 5.69. Found: C, 58.40; H, 3.35; Br, 32.63; N, 5.48.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2012.10.098. These data include MOL files and InChiKeys of the most important compounds described in this article.

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12. There is one exception, e.g., interaction of 2,3-bis((2-methoxyphenyl)ethynyl) benzo[*b*]thiophene with iodine producing 2,2′-(benzo[*b*]thiophene-2,3-diyl) bis(3-iodobenzofuran) [Mehta, S.; Larock, R. C. *J. Org. Chem.* **2010**, *75*, 1652–1658]. However, in this transformation the alkynyl groups react with an electrophile independently to each other.
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