Pergamon

Tetrahedron, Vol. 53, No. 43, pp. 14655-14670, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)01007-7

One-Step Synthesis of Dialkynyl-1,2-diones and their Conversion to Fused Pyrazines bearing Enediyne Units

Rüdiger Faust,* Christian Weber

Pharmazeutisch-Chemisches Institut der Ruprecht-Karls-Universität Heidelberg,
Im Neuenheimer Feld 364, D-69120 Heidelberg (Germany)

Vito Fiandanese, Giuseppe Marchese, Angela Punzi

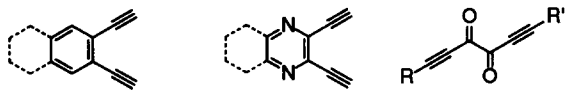
Centro CNR di Studio sulle Metodologie Innovative di Sintesi Organiche, Dipartimento di Chimica,
Università di Bari, via Amendola 173, I-70126 Bari (Italy)

Abstract: A convenient procedure for the preparation of symmetrically end-protected dialkynyl-1,2-diones **3** from lithium acetylides and oxalyl chloride in the presence of CuBr and LiBr is described. The condensation of **3** with various aromatic and heteroaromatic 1,2-diamines leads to pyrazine-based α-dialkynylated heterocycles. The enediyne substructure of diethynylquinoxaline can be thermally rearranged in a Bergman cyclization reaction.

Introduction

Polycyclic aromatic hydrocarbons (PAHs) with 1,2-diethynyl substructures of the general formula **1** play a fundamental role in structural organic chemistry,[1-5] in the design of polymers with high carbon content,[6-10] in the synthesis of theoretically interesting molecules,[11,12] and, furthermore, as readily assembled minimal model compounds[13-16] for potent DNA cleaving enediyne antibiotics like calicheamicin, esperamicin or the neocarzinostatin chromophor.[17-19] The active principle involved in these antibiotics is a (*Z*)-hex-3-ene-1,5-diyne substructure that is ingeniuosly triggered to cyclize to a highly reactive benzenoid 1,4-diradical (Bergman cyclization) that disrupts the DNA sugar phosphate backbone by H-abstraction. Aromatic model compounds for these DNA cleaving agents have the enediyne moiety embedded into a PAH skeleton, a synthetically convenient simplification that does not

significantly alter the thermal cyclization behavior of these aromatic enediynes[15,20] in comparison to their non-aromatic counterparts.



1 2 3

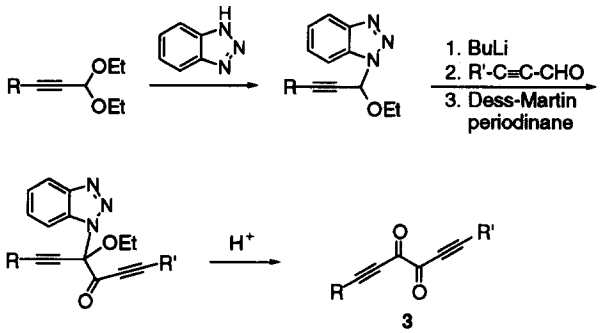
In view of the well-documented, often superior DNA intercalating properties of aromatic *N*-heterocycles,[21-24] an exploration of the aza-analogs of α-dialkynylated PAHs appeared to be worthwhile, since these heterocyclic compounds should be able to direct the enediyne unit via DNA intercalation close to the intended site of action. Surprisingly, α-dialkynylated heterocyclic PAHs of the pyrazine type (**2**) have not received much attention, a fact that may be attributed to the lack of general methods for their synthesis.

In a recent communication[25] we reported the first synthesis of dialkynyl-1,2-diones **3** that can be obtained in four steps starting from readily available propargyl aldehyde diethyl acetals. Since **3** appears to be ideally suited for the rapid assembly of dialkynyl *N*-heterocycles like **2**, we set out to explore the synthetic practicality of this approach in an effort to provide heterocyclic enediyne models. Reported below is a greatly improved procedure for the preparation of symmetrically end-protected derivatives of **3**, their condensation with selected 1,2-diamines, and a preliminary investigation of the thermal cyclization behavior of some of the thus prepared α-dialkynyl hetarenes.

Results and Discussion

The syntheses of dialkynyl-1,2-diones. In the course of a research project directed at the design of alkynylated NIR chromophores,[26] dialkynyl-1,2-diones **3** were identified as unique and versatile synthetic building blocks. However, satisfactory procedures for the preparation of **3** were not available at the time, and numerous attempts to obtain these compounds by a variety of standard routes for the construction of vicinal diones failed. After much experimentation we were able to adapt a protocol developed by Katritzky et al. who suggested 1*H*-benzotriazole as an efficient auxiliary for the synthesis of alkynyl diketones starting from the diethyl acetal of phenyl propargyl aldehyde.[27,28] Gratifyingly, slight modifications of the original procedure furnished the first derivatives of **3**, namely the 1-phenyl-hexa-1,5-diyne-3,4-diones **3a** - **3d**, in four steps (Scheme 1). The benzotriazole route could in the

meantime be extended to provide bis(triisopropylsilyl)-protected dialkynyl-1,2-dione **3e** from commercially available propynal diethyl acetal. Compound **3e** stands out not only as being the most readily available, but also as being the most stable and hence as being the most versatile derivative of **3** so far obtained.



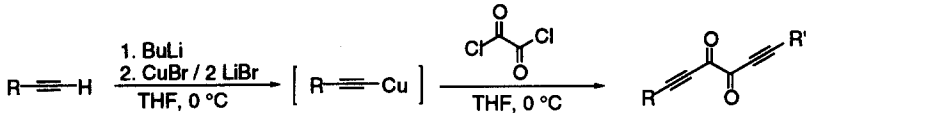
3

3	**a**	**b**	**c**	**d**	**e**
R	Ph	Ph	Ph	Ph	Si(*i*-Pr)$_3$
R'	Ph	*t*-Bu	SiMe$_3$	Si(*i*-Pr)$_3$	Si(*i*-Pr)$_3$
overall yield [%]	24	23	0.3	17	40

Scheme 1

Although the benzotriazole-mediated route provided the first synthetic entry to these functionalized molecules and allowed a first exploration of their promising chemistry, the fact that a multistep procedure in conjunction with a relatively low overall yield is required to obtain derivatives of **3** remained rather unsatisfactory. A more economic way to assemble the molecular framework of **3** would naturally employ oxalic acid derivatives, in which the central CC bond is already preformed. Reaction of oxalyl chloride with metal acetylides, for example, would lead to compounds of type **3** in only a single step, provided that overalkynylation to the corresponding tetraalkynyl diols could be prevented. And indeed, oxalyl chloride had previously been used by some of us[29] to prepare symmetrical diketones by treatment with organomagnesium halides in the presence of CuBr and 2 equiv. LiBr. Despite the failure of initial attempts[25] to apply this protocol to the synthesis of **3**, the prospect of developing an efficient one-step procedure to **3** motivated continuous efforts to use oxalyl chloride as a starting material.

Much to our delight, it was soon found that instead of generating copper acetylides *in situ* by metal exchange of the corresponding organomagnesium reagents with cuprous bromide, freshly prepared phenyl copper acetylide[30] in the presence of 2 equiv. of LiBr smoothly reacts with oxalyl chloride in THF at room temperature to furnish **3a** in a yield of 55%. This protocol could be further simplified by transmetallating lithium acetylides *in situ* with CuBr in THF (Scheme 2).



3a: R = R' = Ph, 60%
3e: R = R' = Si(*i*-Pr)$_3$, 85%
3f: R = R' = C(OMEM)Me$_2$, 37%

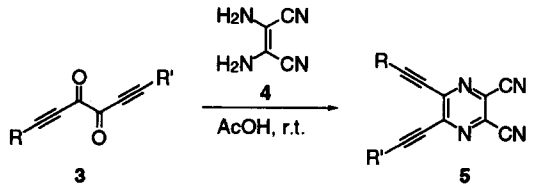
Scheme 2

Hence, adding a solution of lithium phenyl acetylide in THF to a suspension of CuBr/2 LiBr in THF and treatment of this mixture with oxalyl chloride in the same solvent at 0 °C furnished **3a** in a yield of 60%. The more robust silyl-protected dialkynyl-1,2-dione **3e** is generated by this procedure in a remarkable yield of 85%. It has been observed before[25] that the size of the terminal alkyne protecting group has to be large enough to endow derivatives of **3** with a degree of stabilization sufficient for their isolation. Hence, while the novel bis(MEM)-protected dihydroxydione **3f** (MEM = methoxyethoxymethyl) can be prepared in moderate 37%, the sterically less demanding bis(trimethylsilyl)-derivative of **3**, although formed in the course of the reaction, cannot be isolated in pure form. The feasibility of the modified oxalyl chloride route to diones like **3** suggests that lithium acetylides are more readily and/or more comprehensively transmetallated by CuBr than their organomagnesium counterparts, thereby allowing a smooth transfer of the organyl group from copper to oxalyl chloride. As pointed out previously,[29] the presence of LiBr is mandatory to suppress subsequent nucleophilic additions to the newly generated ynone-moiety.

The oxalyl chloride route presented here is not only an extremely efficient one-step procedure, but also nicely complements our initial benzotriazole methodology (Scheme 1), which continues to be the method of choice for the preparation of unsymmetrically end-protected dialkynyl-1,2-diones.

***ortho*-Dialkynylated *N*-heterocycles with a pyrazine core.** Only few compounds bearing an α-dialkynyl pyrazine core[31-33] have been described in the literature, and this despite the fact that some of

them have been reported to exhibit pharmacological activity in, for example, the treatment of ulcers.[34] All of the previously reported derivatives were prepared by palladium-mediated routes starting from the corresponding α-dichloro *N*-heterocycles. With the dialkynyl-1,2-diones **3** now available, we were able to explore alternative routes to compounds like **2** and hence investigated the behavior of **3** towards various 1,2-diamines (Schemes 3 and 4)



3 **5**

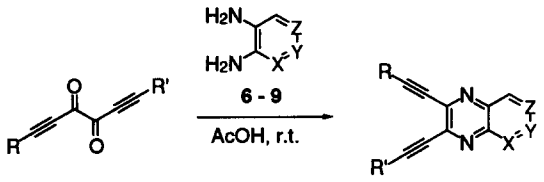
5	**a**	**d**	**e**
R	Ph	Ph	Si(*i*-Pr)$_3$
R'	Ph	Si(*i*-Pr)$_3$	Si(*i*-Pr)$_3$
yield [%]	0	72	81

Scheme 3

The condensation of the terminally Si(*i*-Pr)$_3$-protected dialkynyl-1,2-diones **3d** and **3e** with 2,3-diaminomaleic dinitrile **4** (Scheme 3) occurs as anticipated and leads in good yield to the corresponding α-dialkynylated dicyanopyrazines **5d** and **5e** by simply stirring the reaction mixture in glacial acetic acid at room temperature. In case of the diphenyl-terminated diketone **3a**, however, the aromatic stabilization of the resulting pyrazine is evidently not sufficient to shift the equilibrium to the product side even under more vigorous reaction conditions (refluxing toluene, molecular sieves), and a mixture of starting diketone and easily hydrolyzable bis(phenylethynyl)dicyanopyrazine **5a** was isolated after workup.[35] No further attempts were made to obtain **5a** in pure form. The dicyanopyrazines **5d** and **5e** are either a pale yellow solid (**5d**) or a colorless oil (**5e**), and could subsequently be employed as intermediates en route to strongly absorbent NIR chromophores of the phthalocyanine type.[26] In addition, compounds like **5** show promise as components in conducting polymers,[36,37] and an in-depth evaluation of their electrochemistry is currently under way.

The condensation of **3** with various aromatic and heteroaromatic *ortho*-diamines **6** - **9** turned out to be similarly straightforward (Scheme 4). For example, heating **3a**, **3d** or **3e** in toluene with 1,2-diaminobenzene **6** furnished symmetrically and unsymmetrically terminated 2,3-diethynylquinoxalines

11a, **11d**, and **11e** in good to excellent yields. In contrast to the very moisture-sensitive pyrazine-derivative **5a**, the formation of the larger quinoxaline π-system of **11a** appears to be beneficial in stabilizing the product, and its isolation succeeded without any precautions to prevent hydrolysis.

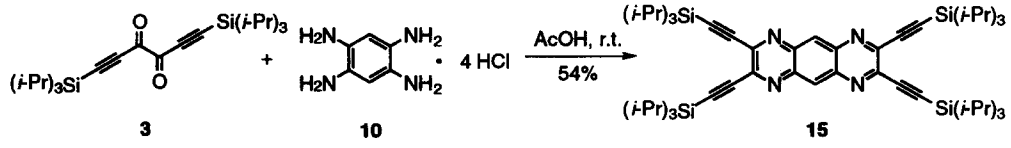


3 **11 - 14**

Dialkynyl-1,2-dione	1,2-Diamine	Product	Yield [%]
3a	X =Y =Z= CH (**6**)	**11a**: R = R' = Ph	80
3d	**6**	**11d**: R = Ph, R' = Si(*i*-Pr)$_3$	75
3e	**6**	**11e**: R = R' = Si(*i*-Pr)$_3$	95
3e	X = N, Y =Z = CH (**7**)	**12**: R = R' = Si(*i*-Pr)$_3$	85
3e	X =Z = CH, Y = N (**8**)	**13**: R = R' = Si(*i*-Pr)$_3$	83
3e	X =Z = N, Y = CH (**9**)	**14**: R = R' = Si(*i*-Pr)$_3$	66

Scheme 4

Indeed, **11a** had been reported previously,[33] although without analytical or spectroscopic data. Using Si(*i*-Pr)$_3$ as terminal alkyne protecting groups as in **3d** and **3e** leads to the highly soluble, stable, colorless oils of **11d** and **11e**. It was especially reassuring to see that also the heterocyclic aromatic diamines **7** - **9** react smoothly with **3e** to the corresponding dialkynylated pyridopyrazines **12** and **13**, and the pteridine-derivative **14**, respectively. The ring sytems of these compounds are integral parts of many pharmacologically active substances for which an *ortho*-dialkynyl substitution pattern was previously inaccessible or, in best cases, could be realized only with difficulty. In particular, the successful preparation of **14** stimulates the synthesis of ring-modified isoalloxazine analogues that could serve, *inter alia*, as inhibitors of flavine-dependent enzymes in the treatment of malaria.[38-40] The *ortho*-diethynylated heterocycles **12** - **14** are isolated as pale-yellow oils.

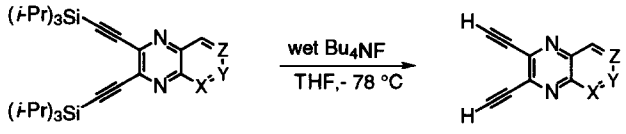


3 **10** **15**

Scheme 5

The fact that the construction of pyrazine cores is not limited to a single condensation is demonstrated by the reaction of the tetrahydrochloride of 1,2,4,5-tetraaminobenzene **10** with dialkynyl-1,2-dione **3e**, which produced the tetraalkynyl pyrazino[2,3-*g*]quinoxaline (1,4,5,8-tetraazaanthracene) derivative **15** in a yield of 54 %. (Scheme 5)

Bergman cycloaromatization of *ortho*-dialkynylquinoxalines. As alluded to in the introduction, the fused dialkynylpyrazines can be thought of as minimal model systems for the DNA cleaving enediyne antibiotics, and hence an investigation of their aptitude to partake in thermally induced Bergman cycloaromatization reactions was warranted. A first series of experiments revealed that, in contrast to the cyclization reactions of analogous diethynylbenzene-type derivatives,[14,20] free terminal alkyne groups appear to be a prerequisite for the cycloaromatization of dialkynylated *N*-heterocycles. Bis(phenylethynyl)quinoxaline **11a**, for example, resisted attempts to induce ring closure even if the material was heated in chlorobenzene in the presence of cyclohexa-1,4-diene to a maximum of 280 °C over a period of two days! Not surprisingly, the material fully deteriorated under these harsh reaction conditions.



11e, 12, 14 **16 - 18**

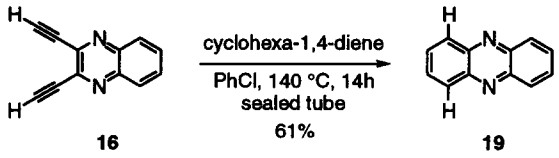
	16	17	18
X	CH	N	N
Y	CH	CH	CH
Z	CH	CH	N
yield [%]	95	95	25

Scheme 6

We therefore turned our attention to silylated derivatives and attempted to obtain the corresponding free terminal alkynes by protodesilylation with wet Bu_4NF in THF (Scheme 6). Of the compounds investigated, namely quinoxaline **11e**, pyridopyrazine **12**, and pteridine **14**, only the two former derivatives could be protodesilylated to the parent alkynes **16** and **17**, respectively, in acceptable yields. Treatment of **14** with fluoride solution on the other hand furnished the desired dialkyne **18** in only minor

amounts despite complete consumption of the starting material. Apparently, the major portion of **14** suffers from extensive decomposition presumably arising from the interaction of the nucleophilic fluoride with the electron-poor pteridine core.

Subjecting the dialkynylated *N*-heterocycles **16** and **17** individually to the conditions typical for thermal Bergman cycloaromatizations (PhCl as solvent, excess cyclohexa-1,4-diene as H-donor, sealed tube) led to results that differ substantially from one another. The less electron-rich aromatic system of the pyridopyrazine core of **17** did not withstand the cyclization conditions and decomposed in the temperature interval between 120 and 130 °C before a ring closure could be detected. This somewhat negative result suggests that further functionalization of the enediyne unit of **17** is necessary to lower its activation barrier for Bergman cyclizations.[41-43] The less *N*-substituted heteroaromatic compound **16** on the other hand is readily converted after 14 hours at 140 °C to the cyclization product phenazine **19** in 61% yield (Scheme 7).



16 **19**

Scheme 7

Extending the reaction times further did not increase the amount of **19**, since thermal decomposition of the starting material began to interfere with product formation. Without knowing the exact kinetics of this reaction, it can be stated that this cyclization temperature compares well with that of 1,2-diethynylbenzenes, whose Bergman rearrangements are usually conducted in a temperature range between 150 and 190 °C.[20] As shown by mass spectrometry, a recurring side-product of the cyclization reaction in yields of up to 15% was 1-(cyclohexa-2,5-dienyl)phenazine resulting from the combination of the benzenoid 1,4-diradical with cyclohexa-2,5-dienyl.

Conclusion

With the present work we have established two complementary procedures for the preparation of dialkynyl-1,2-diones with identical or different terminal protecting groups. Particularly the bis-silylated derivative **3e** is endowed with superior stability compared to the other members of this class of vicinal diketones and may now be obtained in a one-step procedure from the terminal alkyne and oxalyl chloride.

In general, dialkynyl-1,2-diones **3** smoothly condense with 1,2-diamines to furnish stable α-dialkynylated aromatic *N*-heterocycles bearing a pyrazine nucleus. Hetarenes with such a substitution pattern were previously accessible only with difficulty and are now being investigated as intermediates for acetylenic NIR chromophores and isoalloxazine-based enzyme inhibitors. We could also demonstrate that protodesilylation of the Si(*i*-Pr)$_3$-protected dialkynyl quinoxaline **11e** and pyridopyrazine **12** to **16** and **17**, respectively, is possible and that **16** can be thermally cycloaromatized. An investigation of the DNA intercalating behavior of the new dialkynylated heteroaromatic compounds is underway.

Experimental

General. All reactions were carried in an argon atmosphere. Solvents were purified and dried according to standard procedures.[44] Tetrahydrofuran was distilled from sodium benzophenone before use. Silica gel (60-200 mesh) for column chromatography was kindly provided by *Merck KGaA*, Darmstadt.
Melting points were determined on a Reichert hotstage and are uncorrected. UV-VIS spectra were recorded on a Hewlett Packard HP 8453 UV-Vis ChemStation spectral photometer. Infrared spectra were recorded as KBr pellets or films on a Perkin-Elmer PE 1600 FT-IR spectral photometer. ^{1}H NMR spectra were measured at 299.95 MHz on a Varian XL 300 spectrometer or at 500 MHZ on a Bruker AM-500; ^{13}C NMR spectra were obtained at 125.8 MHZ on a Bruker AM-500, at 90.56 MHz on a Bruker AM-360 spectrometer, at 62.89 MHz on a Bruker WM-250 spectrometer, or at 75.43 MHz on the Varian spectrometer described above. The degree of substitution was determined by *J*-modulated spin-echo experiments. δ-Values are reported in ppm downfield from internal Me_4Si. Mass spectra were obtained on a Varian MAT-311 A mass spectrometer at 70 eV. Elemental analyses were performed on a Foss-Heraeus Vario EL.

1,6-Bis(triisopropylsilyl)-hexa-1,5-diyne-3,4-dione (**3e**): To a stirred solution of CuBr (2.39 g, 16.64 mmol) and LiBr (2.89 g, 33.28 mmol) in THF (100 ml) was added at 0 °C a solution of lithium triisopropylsilyl acetylide (16.64 mmol) in THF (20 ml) previously prepared from ethynyltriisopropylsilane (3.13 g, 16.64 mmol) and *n*-BuLi (10.4 ml of a 1.6 M solution in hexane). The reaction mixture was stirred for 15 min until a solution of oxalyl chloride (960 mg, 7.56 mmol) in THF (20 ml) was added dropwise at the same temperature. After 1 h the reaction mixture was hydrolyzed with saturated aqueous ammonium chloride solution (100 ml), extracted three times with diethyl ether

(3 x 100 ml). The combined organic layers were dried over $MgSO_4$, the solvents were removed in vacuo and the residue chromatographed on silica gel (hexane/ethyl acetate, 10:1) to furnish **3e** as a yellow oil: Yield 85%, – IR (film): ν = 2946 cm^{-1} (s, CH), 2868 (s), 2146 (m, C≡C), 1678 (s, CO). – UV (CH_2Cl_2): λ_{max} (ε) = 254 nm (sh, 6300), 272 nm (7000). – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.2 - 1.0 (m, 42H, CH, CH_3). – ^{13}C NMR (90.56 MHz, $CDCl_3$): δ = 171.96 (CO), 107.09 (C≡C), 100.84 (C≡C), 18.39 (CH_3), 10.98 (CH). – MS (70 eV), *m/z* (%): 418 (0.3) [M^+], 376 (35) [$M^+ - CH(CH_3)_2$], 334 (35) [$M^+ - 2CH(CH_3)_2$], 209 (100) [(*i*-Pr)$_3$SiC≡CCO]. – $C_{24}H_{42}O_2Si_2$ (418.2723): calcd. C 68.85, H 10.12; found C 68.60, H 9.97.

Compound **3a** was prepared analogously on a 5 mmolar scale in 60% yield and was shown to possess spectroscopic and analytical data identical to those previously reported.[25]

Compound **3f** was prepared analogously from MEM-protected 2-methyl-but-3-yn-2-ol as a yellow oil in a yield of 37%. IR (film): ν = 2213 (s, C≡C), 1683 (s, C=O). – ^1H NMR (500 MHz, $CDCl_3$): δ =4.92 (s, 4H, CH_2), 3.72 - 3.66 (m, 4H, CH_2), 3.51 - 3.45 (m, 4H, CH_2), 3.30 (s, 6H, CH_3), 1.54 (s, 12H, CH_3).– ^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 171.68 (C=O), 102.91(C≡C), 92.13 (CH_2), 80.22 (C≡C), 71.54 (CH_2), 70.27 (C), 67.29 (CH_2), 58.80 (CH_3), 28.71 (CH_3).

2,3-Dicyano-5-triisopropylsilylethynyl-6-phenylethynylpyrazine (**5d**): A solution of **3d** (340 mg, 1 mmol) and **4** (110 mg, 1 mmol) in glacial acetic acid (20 ml) was stirred for 5 min at room temperature. The solvent was removed in vacuo and the residue subjected to column chromatography (SiO_2, hexane/ethyl acetate, 5:1) to afford crude **5d** as a viscous oil, from which pure material could be obtained by crystallization with dichloromethane: Yield 72 %, pale yellow solid; m.p. 151-152°C. – IR (KBr): ν = 2949 cm^{-1} (m, CH), 2864 (m, CH), 2208 (s, C≡C). – UV (CH_2Cl_2): λ_{max} (ε) = 254 nm (sh, 26600), 276 nm (29100), 350 nm (sh, 21600), 364 nm (22700). – ^1H NMR (300 MHz, $CDCl_3$): δ = 7.8 - 7.3 (m, 5H, CH), 1.3 - 1.1 (m, 21H, CH, CH_3). – ^{13}C NMR (75.43 MHz, $CDCl_3$): δ = 143.49 (C), 142.52 (C), 132.46 (CH), 130.92 (CH), 129.88 (C), 129.59 (C), 128.49 (CH), 119.96 (C), 112.29 (C), 109.71 (C), 103.02 (C≡C), 101.03 (C≡C), 100.49 (C≡C), 84.76 (C≡C), 18.57 (CH_3), 11.18 (CH). – MS (70 eV), *m/z* (%): 410 (18) [M^+], 367 (100) [$M^+ - CH(CH_3)_2$]. – $C_{25}H_{26}N_4Si$ (410.1927): calcd. C 73.14, H 6.39, N 13.66; found C 73.09, H 6.48, N 13.26.

2,3-Dicyano-5,6-bis(triisopropylsilylethynyl)pyrazine (**5e**) was obtained analogous to **5a** as a colorless oil: Yield 81 %. – IR (film): ν = 2945 cm^{-1} (s, CH), 2867 (s, CH), 2155 (m, C≡C). – UV (CH_2Cl_2): λ_{max} (ε) = 248 nm (13500), 274 nm (12700), 280 nm (sh, 12500), 316 nm (14500), 338 nm (sh, 10900), 348 nm (11000). – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.3 - 1.1 (m, 42H, CH, CH_3). – ^{13}C NMR (75.43 MHz, $CDCl_3$): δ = 142.37 (C), 130.60 (C), 112.51 (C), 109.81 (C), 100.85 (C), 18.85 (CH_3), 11.45 (CH). – MS (70 eV), *m/z* (%): 490 (9) [M^+], 447 (31) [$M^+ - CH(CH_3)_2$], 405 (100) [$M^+ - C_6H_{13}$]. – $C_{28}H_{42}N_4Si_2$ (490.2948): calcd. C 68.53, H 8.63, N 11.42; found C 68.65, H 8.75, N 11.10.

General procedure for the preparation of the ortho-dialkynyl N-heterocycles **11 - 15**

A mixture of **3** (1 mmol) with the appropriate diamine **6 - 9** or the tetrahydrochloride of tetraamine **10** (1 mmol) was heated together with activated molecular sieves in toluene (10 ml) at 80 °C for 20 min. After cooling, the mixture was filtered and the solvents were evaporated in vacuo. The residue was subjected to column chromatography (SiO_2, hexane/ethyl acetate, 10:1) and furnished compounds **11**, **12**, **13**, and **14** as pale-yellow oils. Crystallization of crude **11a** with diethyl ether produced a colorless solid; **15** was recrystallized from hexane as an orange solid.

2,3-Bis(phenylethynyl)quinoxaline (**11a**)[33]: Yield 80 %, colorless solid, m.p. 118-119°C. – IR (KBr): ν = 3061 cm^{-1} (w, CH), 2203 (m, C≡C). – UV (CH_2Cl_2): λ_{max} (ε) = 270 nm (36100), 290 nm (sh, 45200), 296 nm (47900), 374 nm (18500), 386 nm (19100). – ^1H NMR (300 MHz, $CDCl_3$): δ = 8.0 - 7.9 (m, 2H, CH), 7.7 - 7.5 (m, 6H, CH), 7.4 - 7.2 (m, 6H, CH). – ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 140.89 (C), 140.46 (C), 132.84 (CH), 130.88 (CH), 129.78 (CH), 128.13 (CH), 127.52 (CH), 121.63 (C), 95.87 (C≡C), 86.81 (C≡C). – MS (70 eV), *m/z* (%): 330 (100) [M^+]. – $C_{24}H_{14}N_2$ (330.1157): calcd. C 87.25, H 4.27, N 8.48; found C 87.11, H 4.65, N 8.53.

2-Phenylethynyl-3-triisopropylsilylethynylquinoxaline (**11d**): Yield 75 %, colorless oil. – IR (film): ν = 3062 cm^{-1} (w, CH), 2943 (s, CH), 2865 (s, CH), 2224 (m, C≡C), 2204 (m, C≡C). – UV (CH_2Cl_2): λ_{max} (ε) = 272 nm (52000), 300 nm (sh, 23000), 366 nm (sh, 15200), 374 nm (15600), 382 nm (13800), 360 nm (sh, 13900). – ^1H NMR (300 MHz, $CDCl_3$): δ = 8.2 - 8.0 (m, 2H, CH), 7.8 - 7.7 (m, 2H, CH), 7.7 - 7.6 (m, 2H, CH), 7.5 - 7.3 (m, 3H, CH), 1.3 - 1.0 (m, 21H, CH, CH_3). – ^{13}C NMR (90.56 MHz, $CDCl_3$): δ = 140.85 (C), 140.53 (C), 140.51 (C), 140.36 (C), 132.30 (CH), 130.91 (CH), 130.80 (CH), 129.54 (CH), 129.00 (CH), 128.86 (CH), 128.29 (CH), 121.77 (C), 103.17 (C≡C), 99.66 (C≡C), 95.15 (C≡C),

86.65 (C≡C), 18.69 (CH), 11.33 (CH_3). – MS (70 eV), *m/z* (%): 410 (44) [M^+], 367 (100) [M^+ – $CH(CH_3)_2$]. – $C_{27}H_{30}N_2Si$ (410.2178): calcd. C 78.98, H 7.37, N 6.83; found C 78.76, H 7.36, N 6.93.

2,3-Bis(triisopropylsilylethynyl)quinoxaline (**11e**): Yield 95 %, colorless oil. – IR (film): ν = 3068 cm^{-1} (w, CH), 2944 (s, CH), 2866 (s, CH), 2162 (w, C≡C). – UV (CH_2Cl_2): λ_{max} (ε) = 246 nm (sh, 16800), 274 nm (55200), 342 nm (7900), 358 nm (13000), 350 nm (8900), 366 nm (sh, 9700), 376 (15700). – ^1H NMR (300 MHz, $CDCl_3$): δ = 8.2 - 8.0 (m, 2H, CH), 7.7 - 7.6 (m, 2H, CH), 1.4 - 1.0 (m, 42H, CH, CH_3). – ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 140.65 (C), 139.94 (C), 130.64 (CH), 128.91 (CH), 103.60 (C≡C), 98.82 (C≡C), 18.53 (CH), 11.48 (CH_3). – MS (70 eV), *m/z* (%): 490 (7) [M^+], 447 (26) [M^+ – $CH(CH_3)_2$], 405 (100) [M^+ – C_6H_{13}]. – $C_{30}H_{46}N_2Si_2$ (490.3200): calcd. C 73.42, H 9.46, N 5.71; found C 73.60, H 9.73, N 5.37.

2,3-Bis(triisopropylsilylethynyl)pyrido[2,3-b]pyrazine (**12**): Yield 85 %, pale yellow oil. – IR (film): ν = 2944 (s, CH), 2866 (s, CH), 2155 (w, C≡C). – UV (CH_2Cl_2): λ_{max} (ε) = 256 nm (33300), 268 nm (sh, 29000), 282 nm (sh, 19700), 352 nm (sh, 13200), 360 nm (sh, 14900), 366 nm (14700), 372 (sh, 13900). – ^1H NMR (300 MHz, $CDCl_3$): δ = 9.2 - 9.1 (m, 1H, CH), 8.5 - 8.3 (m, 1H, CH), 7.8 - 7.6 (m, 1H, CH), 1.4 - 1.0 (m, 42H, CH, CH_3). – ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 154.77 (CH), 148.77 (C), 142.77 (C), 140.93 (C), 137.56 (CH), 136.29 (C), 125.62 (CH), 102.94 (C≡C), 102.86 (C≡C), 101.66 (C≡C), 100.51 (C≡C), 18.68 (CH_3), 11.32 (CH). – MS (70 eV), *m/z* (%): 491 (9) [M^+], 448 (64) [M^+ – $CH(CH_3)_2$], 406 (100) [M^+ – C_6H_{13}]. – $C_{29}H_{45}N_3Si_2$ (491.3152): calcd. C 70.83, H 9.23, N 8.55; found C 70.60, H 9.39, N 8.30.

2,3-Bis(triisopropylsilylethynyl)pyrido[3,4-b]pyrazine (**13**): Yield 83 %, pale yellow oil. – IR (film): ν = 2944 (s, CH), 2866 (s, CH), 2150 (w, C≡C). – UV (CH_2Cl_2): λ_{max} (ε) = 270 nm (46700), 348 nm (sh, 11100), 358 nm (13700), 376 nm (12000). – ^1H NMR (250 MHz, $CDCl_3$): δ = 9.46 (d, 1H, *J* = 0.6 Hz, CH), 8.77 (d, 1H, *J* = 5.8 Hz, CH), 7.85 (d, 1H, *J* = 5.8 Hz, CH), 1.5 - 1.0 (m, 42H, CH, CH_3). – ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 153.97 (CH), 147.89 (CH), 144.03 (C), 142.76 (C), 141.46 (C), 135.35 (C), 120.76 (CH), 103.05 (C≡C), 102.91 (C≡C), 102.57 (C≡C), 100.98 (C≡C), 18.75 (CH_3), 11.67 (CH). – MS (70 eV), *m/z* (%): 491 (5) [M^+], 448 (28) [M^+ – $CH(CH_3)_2$], 406 (100) [M^+ – C_6H_{13}]. – $C_{29}H_{45}N_3Si_2$ (491.3152): calcd. C 70.83, H 9.23, N 8.55; found C 70.62, H 9.29, N 8.08.

6,7-Bis(triisopropylsilylethynyl)pteridine (**14**): Yield 66 %, pale-yellow oil. – IR (film): ν = 2981 (s, CH), 2866 (s, CH), 2156 (w, C≡C). – UV (CH_2Cl_2): λ_{max} (ε) = 252 nm (21500), 270 nm (sh, 16100), 284 nm (sh, 11800), 342 nm (sh, 9300), 356 nm (13400), 372 nm (13800). – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.55 (s, 1H, CH), 9.44 (s, 1H, CH), 1.3 - 1.0 (m, 42H, CH, CH_3). – ^{13}C NMR (75.43 MHz, $CDCl_3$): δ = 161.96 (CH), 159.02 (CH), 151.07 (C), 146.91 (C), 142.31 (C), 132.27 (C), 106.00 (C≡C), 102.85 (C≡C), 102.55 (C≡C), 102.19 (C≡C), 18.75 (CH_3), 11.34 (CH). – MS (70 eV), *m/z* (%): 492 (7) [M^+], 449 (44) [$M^+ - CH(CH_3)_2$], 407 (100) [$M^+ - C_6H_{13}$]. – $C_{28}H_{44}N_4Si_2$ (492.3105): calcd. C 68.24, H 9.00, N 11.37; found C 68.43, H 8.86, N 11.25.

2,3,7,8-Tetrakis(triisopropylsilylethynyl)pyrazino[5,6-g]quinoxaline (**15**): For the preparation of **15** it was necessary to reflux the reaction mixture over a period of 16 h. Yield 54 %, orange solid, m.p. 282-285 °C (dec.). – IR (film): ν = 2943 (s, CH), 2864 (s, CH), 2166 (w, C≡C), 2149 (w, C≡C). – UV (CH_2Cl_2): λ_{max} (ε) = 236 nm (32700), 314 nm (sh, 76900), 324 nm (92700), 386 nm (sh, 7700), 394 nm (sh, 9300), 406 nm (18800), 416 (15600), 428 nm (41100), 438 nm (sh, 17300), 454 (56600). – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.73 (s, 2H, CH), 1.4 - 1.0 (m, 84H, CH, CH_3). – ^{13}C NMR (62.89 MHz, $CDCl_3$): δ = 141.33 (C), 139.65 (C), 128.13 (CH), 103.67 (C≡C), 101.49 (C≡C), 18.78 (CH_3), 11.48 (CH). – MS (70 eV), *m/z* (%): 902 (7) [M^+], 860 (44) [$M^+ - C_3H_6$], 818 (100) [$M^+ - C_6H_{12}$]. – $C_{54}H_{86}N_4Si_4$ (902.5930): calcd. C 71.79, H 9.60, N 6.21; found C 71.50, H 9.66, N 6.09.

General procedure for the protodesilylation of **11e**, **12**, *and* **14**

A solution of the Si(*i*-Pr)$_3$-protected derivative **11e**, **12** or **14** (1 mmol each) in moist THF (20 ml) was treated at -78°C with 1.0 M tetrabutylammonium fluoride in THF (2ml, 2 mmol). After 5 min the mixture was quenched with water (20 ml), extracted three times with diethyl ether (3 x 50 ml). The combined organic layers were dried over $MgSO_4$ and the residue chromatographed (SiO_2, hexane/ethyl acetate, 2:1). The products were isolated as colorless oils. **16** could be crystallized from diethyl ether as a colorless solid.

2,3-Diethynylquinoxaline (**16**): Yield 95 %, colorless solid, m.p. 152 °C (dec.). – IR (KBr): ν = 3227 cm^{-1} (s, C≡C<u>H</u>), 2925 (w, CH), 2104 (s, C≡C). – UV (CH_2Cl_2): λ_{max} (ε) = 262 nm (49400), 326 nm (sh, 2400), 334 nm (sh, 3700), 340 nm (sh, 4600), 348 nm (6900), 352 nm (sh, 5600), 364 nm (8100). – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.0 - 7.9 (m, 2H, CH), 7.8 - 7.6 (m, 2H, CH), 3.52 (s, 2H, CH). – ^{13}C

NMR (62.89 MHz, $CDCl_3$): δ = 139.49 (C), 138.56 (C), 130.41 (CH), 127.94 (CH), 82.54 (C≡CH), 78.97 (C). – MS (70 eV), *m/z* (%): 178 (100) [M^+], 127 (57) [$M^+ - C_4H_3$]. – $C_{12}H_6N_2$ (178.0531): calcd. C 80.87, H 3.40, N 15.73; found C 80.71, H 3.59, N 15.68.

2,3-Diethynylpyrido[2,3-b]pyrazine (**17**): Yield 95 %, colorless oil. – ^1H NMR (250 MHz, $CDCl_3$): δ = 9.3 - 9.1 (m, 1H, CH), 8.5 - 8.3 (m, 1H, CH), 7.8 - 7.7 (m, 1H, CH), 3.67 (s, 1H, CH), 3.64 (s, 1H, CH). – MS (70 eV), *m/z* (%): 179 (100) [M^+], 128 (34) [$M^+ - C_4H_3$]. – $C_{11}H_5N_3$ (HR-MS): calcd. 179.0484; found: 179.0485.

6,7-Diethynylpteridine (**18**): Yield 25 %, colorless oil. – ^1H NMR (250 MHz, $CDCl_3$): δ = 9.68 (s, 1H, CH), 9.60 (s, 1H, CH), 3.85 (s, 1H, CH), 3.74 (s, 1H, CH). – MS (70 eV), *m/z* (%): 180 (100) [M^+], 129 (18) [$M^+ - C_4H_3$]. – $C_{11}H_5N_4$ (HR-MS): calcd. 180.0435; found: 180.0434.

*Thermal cycloaromatization of 2,3-diethynylquinoxaline (**16**):*

A glass tube was charged with **16** (200 mg, 1.12 mmol), cyclohexa-1,4-diene (4.0 g, 50 mmol) and chlorobenzene (30 ml), and the contents was deareated by three freeze-pump-thaw cycles and venting with argon. The tube was slowly heated to 140 °C and kept at this temperature for 14h. After cooling to room temperature, the volatiles were evaporated in vacuo and the residual material chromatographed (SiO_2, hexane/ethyl acetate, 5:1) to elute first phenazine **19**[45] (120 mg, 0.68 mmol, 61%; ^1H NMR (250 MHz, $CDCl_3$): δ = 8.4 -8.2 (m, 4H, CH), 7.9 - 7.8 (m, 4H, CH). – MS (70 eV), *m/z* (%): 180 (100) [M^+]) and second 1-(cyclohexa-2,5-dienyl)phenazine (15%). The identity of the latter compound was ascertained by mass spectrometry: MS (70 eV), *m/z* (%): 257 (100) [M^+ - H], 255 (34) [M^+ - 3H].

Acknowledgment. This work was financially supported in part by the Fonds der Chemischen Industrie, Germany, and by the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (MURST, 40 and 60%), Italy. We are grateful to Isabell Hamm for experimental assistance and to Prof. Dr. R. Neidlein for his continuing interest in our work.

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(*Received in Germany* 4 *July* 1997; *accepted* 18 *August* 1997)