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NOVEL KINC TRANSFORMATIONS OF PYRAZINES BY INTRAMOLECULAR DIELS-ALDER REACTIONS

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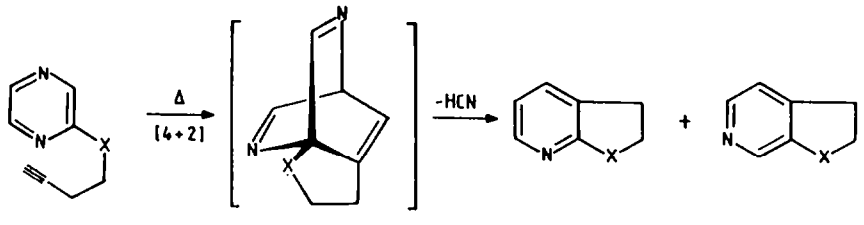
Abstract. Pyrazines carrying the ω-alkyne side-chain $-XCH_2CH_2C{\equiv}CH$, (X = O,N,S,SO,SO_2,$C(CN)_2$) undergo on heating an intramolecular Diels-Alder reaction. Pyrazines with the electron donating atom (O,N or S) in the side-chain afford [c]-fused pyridines as main products, whereas (3-butynylsulfinyl)pyrazine and (3-butynylsulfonyl)pyrazine are exclusively converted into [b]-fused pyridines. A [b]-fused pyridine is also the major product in the reaction of 2,5-bis(1,1-dicyano-4-pentynyl)pyrazine.

Inverse electron demand Diels-Alder reactions of heterocyclic azadienes with electron-rich dienophiles have received considerable attention.[1] Particularly, reactions of this type with 1,2,4,5-tetrazines and 1,2,4-triazines are well documented.[1,2] Also pyrimidines[3] and pyrazines[4] react, but less easily, with electron-rich dienophiles. To enhance reactivity, azadiene and dienophile are placed in the same molecule as shown by the intramolecular Diels-Alder reactions of appropriately substituted 1,2,4,5-tetrazines,[5] 1,2,4-triazines,[5,6] pyridazines[7] and pyrimidines.[8,9] Recently, also intramolecular cycloaddition reactions of nitropyridines carrying an appropriate side-chain were observed.[9]

In addition to our current studies on the intramolecular Diels-Alder reactions of pyrimidines and pyridines we extended our research to similar reactions of pyrazines carrying 5-membered ω-alkyne side-chains. An interesting feature of the reactions of these pyrazines is the possibility that from the intermediate cycloadduct resulting from cycloaddition across the C2 and C5 positions by elimination of hydrogen cyanide two different annelated pyridines can be obtained (see Scheme 1). Heterocyclic diazadienes hitherto investigated have never shown to yield two products.

Scheme 1



1 2 3 4

a. X = $NC(O)CH_3$
b. X = O
c. X = S
d. X = SO
e. X = SO_2

In this paper we present the initial results of our study directed on the influence of the electronic effect of the atom in the side-chain directly attached to the pyrazine ring on the course of the intramolecular cyclization reactions.

RESULTS AND DISCUSSION

We first examined pyrazines containing a side-chain dienophile linked to the heterocycle via a hetero atom. Heating of (3-butynylamino)pyrazine (**1**, X = NH) prepared from chloropyrazine and 4-aminobutyne in the solvent nitrobenzene gave no trace of the dihydropyrrolopyridines **3** and **4** (X = NH). Prolongued heating at 210°C also was not successful; only decomposition of the starting material took place. However, (N-acetyl-3-butynylamino)pyrazine (**1a**) gave on heating at 165°C a quantitative intramolecular cycloaddition reaction resulting in the formation of a mixture of 1-acetyl-2,3-dihydropyrrolo[2,3-b]pyridine (**3a**) and 1-acetyl-2,3-dihydropyrrolo[2,3-c]pyridine (**4a**) in a ratio 1:5. Apparently, due to the presence of the acetyl group on the amino nitrogen the electron donating character of the amino group is decreased making the pyrazine ring in **1a** more electron deficient than in **1** (X = NH) and, therefore, more susceptible to cycloaddition with the triple bond of the side-chain.

Similar ring transformations were also obtained when studying the intramolecular cycloaddition reactions of (3-butynyloxy)pyrazine (**1b**) and (3-butynylthio)pyrazine (**1c**). On heating **1b**, prepared by reacting chloropyrazine with the sodium salt of 3-butyn-1-ol, in nitrobenzene we obtained in good yield a mixture of 2,3-dihydrofuro[2,3-b]pyridine (**3b**) and 2,3-dihydrofuro[2,3-c]pyridine (**4b**) (ratio 1:3.5). Similarly compound **1c**, prepared from thiopyrazine and 4-iodobutyne, also gave in excellent yield a mixture of 2,3-dihydrothieno[2,3-b]pyridine (**3c**) and 2,3-dihydrothieno[2,3-c]pyridine (**4c**) (ratio 1:3).

Table Intramolecular Diels-Alder reactions of pyrazines **1** and **5**. Reaction conditions, products and yields

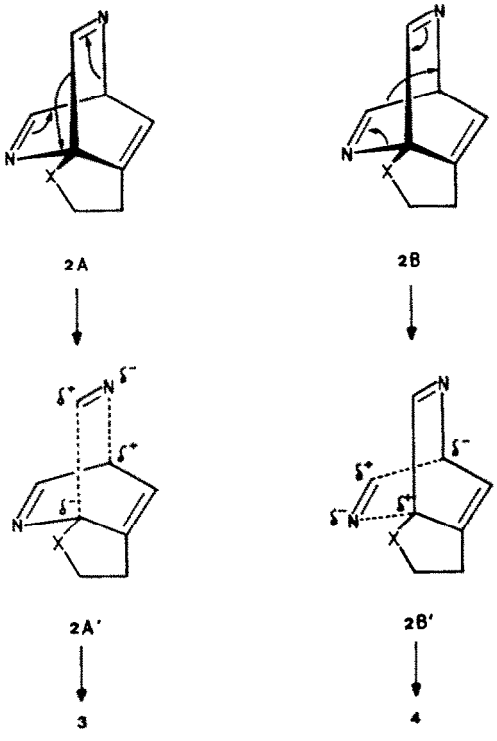
Pyrazines Starting compounds	Reaction conditions Temp. (°C)	Time (h)	Reaction products Compounds (% isolated yield)
1a	165	4	**3a** (17), **4a** (83)
1b	210	4	**3b** (12), **4b** (44)
1c	180	3	**3c** (24), **4c** (68)
1d	120	3	**3d** (57)
1e	150	4.5	**3e** (88)
5	120	2	**6** (53), **7** (35)
5	210	25	**8** (60)

Comparing temperature and reaction time for complete conversion (see Table) of **1a**, **1b** and **1c** we see that the reactivity increases in the order X = NH < X = O < X = S < X = N C(O)CH_3. This order reflects the decrease of the π-electron deficiency of the pyrazine ring on varying X and is similar to those found in the 1,2,4-triazine and pyrimidine series.[6b,8a]

We also studied the cyclization reaction of **1c** in solvents less polar than nitrobenzene. By determining the time that **1c** is converted for 50% at 180°C into the products **3c** and **4c**, it was found that **1c** cyclizes in nitrobenzene, p-bromotoluene and p-cymene with relative rates of 2.9, 1.7 and 1.0, respectively. The ratio of the products **3c** and **4c** (measured by glc) is independent of the solvent used. The effects of the solvent on the rates are small, but not negligible and may indicate that in the reaction course a transition state with some ionic character may be involved.

We suggest that in all these reactions cycloadduct 2 is intermediate, being formed by addition of the triple bond across the C2 and C5 positions in the pyrazine ring. Loss of hydrogen cyanide as indicated in 2A (see Scheme 2) leads to [b]-annelated product 3, while loss of hydrogen cyanide as indicated in 2B (Scheme 2) gives the [c]-annelated product 4. What may be the leading principle which determines that the formation of 4a, 4b and 4c is favored to that of 3a, 3b and 3c.

Scheme 2

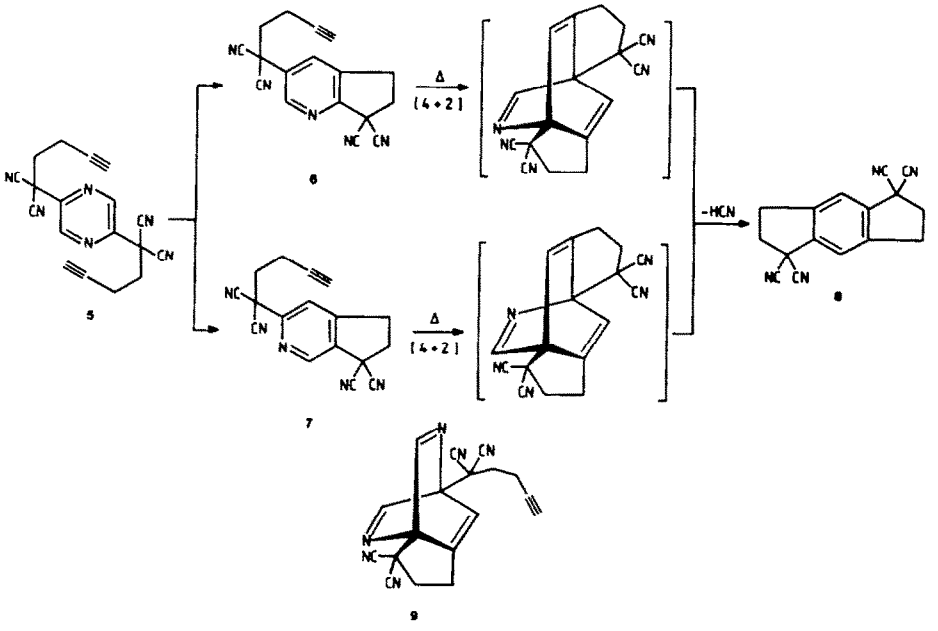


We suppose that in the transition state from 2A → 3, i.e. 2A' breaking of the C-C bond partly develops a negative charge on the bridgehead carbon atom adjacent to X, which is destabilized due to the electron donating character of N, O and S. On the contrary, in the transition state 2B' leading from 2B to 4 a positive charge is developed on the bridgehead carbon atom adjacent to X, which is of course favored due to the electron donating character of N, O and S. The formation of a transition state with some ionic character seems to be supported by the slight solvent dependency as has been observed (see above).

In order to test this hypothesis further we extended our study to the intramolecular Diels-Alder reactions of (3-butynylsulfinyl)pyrazine (1d) and (3-butynylsulfonyl)pyrazine (1e). Since a sulfinyl and a sulfonyl group are not able to stabilize an adjacent positive charge 1d and 1e can be expected to yield mainly products 3. This has been found indeed: 1-oxo-2,3-dihydrothieno[2,3-b]pyridine (3d), or 1,1-dioxo-2,3-dihydrothieno[2,3-b]pyridine (3e), respectively, are exclusively formed during thermolysis of 1d and 1e. These results seem to support our view that the electronic effect of atom X attached to the pyrazine ring clearly influences the product distribution in the intramolecular Diels-Alder reactions of pyrazines.

We also want to report on a "double" ringtransformation being observed when 2,5-bis(1,1-dicyano-4-pentynyl)pyrazine (5) is heated at 210°C in nitrobenzene. It was found that thermolysis of 5, that is obtained by reacting 2-bromo-5-nitropyrazine (the preparation of this compound from aminopyrazine following the route given by Taylor[10] is described in the Experimental Section) with 5,5-dicyanopentyne, yields 1,1,5,5-tetracyano-1,2,3,5,6,7-hexahydro-s-indacene (8) (see Scheme 3). Since both 3-(1,1-dicyano-4-pentynyl)-7,7-dicyano-6,7-dihydro-5H-pyrindine (6) and the isomeric 5H-2-pyrindine (7) could be expected to be intermediates in the formation of 8, we

Scheme 3



subjected 5 to heating in nitrobenzene at lower temperature and found that already at 120°C a mixture of both isomers 6 and 7 was indeed formed (ratio 1.5:1). Both compounds were isolated and each of them when heated at 210°C exclusively leads to the formation of 8. That the ratio of 6:7 is much closer to one than in case of 1a, 1b or 1c is in agreement with the transition state considerations (see above) for the loss of hydrogen cyanide from cycloadduct 9, being supposed the intermediate in the formation of 6 and 7 from 5. Attempts to isolate 9 or to identify it as intermediate stage by NMR techniques failed. That the formation of 6/7 occurs at a relative low temperature compared to the conversion of 1a-1c is in agreement with the higher electron deficiency of the pyrazine ring when carbon instead of a hetero atom is bound to the ring.

EXPERIMENTAL SECTION

Melting points are uncorrected. ^{1}H NMR spectra were recorded on a Varian EM 390 spectrometer. Me_4Si was used as internal standard (δ = 0 ppm). Mass spectral data were obtained on a AEI MS 902 spectrometer equipped with VG ZAB console.
Column chromatography was carried out over Merck silica gel 60 (70-230 mesh ASTM). GLC measurements were performed on a Varian Vista 6000 gas chromatograph equipped with a column: 200 x 2 mm i.d. filled with 3% SP 2250 on chromosorb W/HP 100-120 mesh.

Starting Materials

(N-acetyl-3-butynylamino)pyrazine (1a). A mixture of chloropyrazine (4.60 g, 40 mmol), 4-aminobutyne (5.52 g, 80 mmol) and triethylamine (8 mL) was heated at 130°C for 24 h. After cooling the reaction mixture was purified by column chromatography (eluting first with dichloromethane and then with 9:1 dichloromethane/EtOH) to yield 1.26 g (21%) of (3-butynylamino)pyrazine: mp 73-74°C (water); ^{1}H NMR ($CDCl_3$) δ 7.95 (m, 2H), 7.80 (d, J = 2.8 Hz, 1H), 5.28 (br, 1H), 3.56 (q, $J_{CH_2-CH_2} = J_{CH_2-NH}$ = 6.2 Hz, 2H), 2.53 (dt, J_1 = 6.2 Hz, J_2 = 2.7 Hz, 2H), 2.05 (t, ^2J = 2.7 Hz, 1H).
Anal. Calcd. for $C_8H_9N_3$ (147.18): C, 65.28; H, 6.16; N, 28.55. Found: C, 65.03; H, 6.15; N, 28.90.
A mixture of the latter compound (1.0 g, 6.8 mmol), acetic anhydride (5 mL), acetic acid (2.5 mL) and sulfuric acid (3 drops) was heated at 90°C for 15 h. After cooling the excess of acetic anhydride and acetic acid were removed under reduced pressure. The residue was treated with water (20 mL), neutralized with sodium bicarbonate and extracted with dichloromethane. The organic layer was dried (anhydrous $MgSO_4$) and evaporated under reduced pressure. Column chromatography of the residue (ether as eluent) yielded 0.92 g (72%) of 1a as an oil: ^{1}H NMR ($CDCl_3$) δ 8.84 (s, 1H), 8.45 (s, 2H), 4.08 (t, J = 7.0 Hz, 2H), 2.55 (dt, J_1 = 7.0 Hz, J_2 = 2.7 Hz, 2H), 2.20 (s, 3H), 1.95 (t, J = 2.7 Hz, 1H).
MS Calcd. for $C_{10}H_{11}N_3$ (M^+): m/e 189.0902. Found: m/e 189.0902.

(3-Butynyloxy)pyrazine (1b). To a solution of sodium (0.31 g, 13.4 mmol) in 3-butyn-1-ol (7 mL) was added chloropyrazine (1.54 g, 13.4 mmol). The mixture was stirred at 80°C for 2 h and then washed with water (4 x 10 mL). The organic layer was taken up in ether (10 mL), dried (anhydrous $MgSO_4$) and evaporated under reduced pressure. The residual solid was purified by crystallization from petroleum ether 40-60 to yield 1.04 g (52%) of 1b: mp 34-36°C; ^1H NMR ($CDCl_3$) δ 8.30 (d, J = 1.2 Hz, 1H), 8.13 (m, 2H), 4.50 (t, J = 7.2 Hz, 2H), 2.73 (dt, J_1 = 7.2 Hz, J_2 = 2.7 Hz, 2H), 2.10 (t, J = 2.7 Hz, 1H).
Anal. Calcd. for $C_8H_8N_2O$ (148.16): C, 64.85; H, 5.44; N, 18.91. Found: C, 65.03; H, 5.52; N, 19.18.

(3-Butynylthio)pyrazine (1c). To a solution of thiopyrazine[11] (1.12 g, 10 mmol) and 4-iodobutyne[12] (1.8 g, 10 mmol) in water (25 mL) was added triethylamine (4 mL). The mixture was heated at 70°C for 3 h, then cooled and extracted with ether. The organic layer was dried (anhydrous $MgSO_4$) and evaporated under reduced pressure to afford a solid material which was purified by column chromatography (ether as eluent) to yield 0.73 g (44%) of 1c: mp 43-44°C (petroleum ether 40-60); ^1H NMR ($CDCl_3$) δ 8.47 (d, J = 1.2 Hz, 1H), 8.36 (dd, J_1 = 2.8 Hz, J_2 = 1.2 Hz, 1H), 8.20 (d, J = 2.8 Hz, 1H), 3.34 (t, J = 7.2 Hz, 2H), 2.63 (dt, J_1 = 7.2 Hz, J_2 = 2.4 Hz, 2H), 2.09 (t, J = 2.4 Hz, 1H).
Anal. Calcd. for $C_8H_8N_2S$ (164.23): C, 58.50; H, 4.91; N, 17.06. Found: C, 58.50; H, 4.90; N, 17.31.

(3-Butynylsulfinyl)pyrazine (1d). To a suspension of (3-butynylthio)pyrazine (2.07 g, 12.6 mmol) in water (100 mL) was added sodium metaperiodate (2.70 g, 12.6 mmol). The mixture was stirred at room temperature for 24 h and subsequently extracted with ether. The organic layer was dried (anhydrous $MgSO_4$) and evaporated under reduced pressure. The residual solid material was purified by column chromatography (ether as eluent) to yield 1.41 g (62%) of 1d: mp 71-72°C; IR ($CHCl_3$) 3300, 1060 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.19 (s, 1H), 8.77 (d, J = 1.5 Hz, 1H), 8.65 (d, J = 1.5 Hz, 1H), 3.57-3.01 (m, 2H), 2.80-2.50 (m, 2H), 1.97 (t, J = 2.7 Hz, 1H).
Anal. Calcd. for $C_8H_8N_2OS$ (180.23): C, 53.30; H, 4.47; N, 15.54. Found: C, 53.30; H, 4.41; N, 15.47.

(3-Butynylsulfonyl)pyrazine (1e). To a stirred solution of (3-butynylthio)pyrazine (0.82 g, 5.0 mmol) in dry dichloromethane (15 mL) at -15°C was added a solution of m-chloroperbenzoic acid (85%, 2.1 g, 10.4 mmol) in dry dichloromethane (35 mL). This mixture was stirred at room temperature for 16 h, cooled to 0°C and filtered. The filtrate was washed with a saturated solution of sodium sulfite (2 x 15 mL) and subsequently with a saturated solution of sodium bicarbonate (2 x 25 mL). The organic layer was dried (anhydrous $MgSO_4$) and evaporated under reduced pressure. The residual oil was purified by column chromatography (ether as eluent) to yield 0.62 g (63%) of 1e as an oil: IR ($CHCl_3$) 3315, 1340, 1130 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.33 (s, 1H), 8.81 (d, J = 1.1 Hz, 1H), 8.73 (d, J = 1.0 Hz, 1H), 3.66 (t, J = 7.2 Hz, 2H), 2.75 (dt, J_1 = 7.3 Hz, J_2 = 2.7 Hz, 2H), 1.81 (t, J = 2.7 Hz, 1H).
MS Calcd. for $C_8H_8N_2O_2S$ (M^+): m/e 196.0307. Found: m/e 196.0312.

2,5-Bis(1,1-dicyano-4-pentynyl)pyrazine (5). a. Preparation of 2-bromo-5-nitropyrazine. To a solution of aminopyrazine (5.0 g, 52.6 mmol) in dry dichloromethane (300 mL), cooled to 0°C, was added N-bromosuccinimide (9.4 g, 52.8 mmol). The mixture was stirred at 0°C for 24 h and then washed with four 50 mL portions of a saturated solution of sodium carbonate and water (50 mL). The organic layer was dried (anhydrous $MgSO_4$) and evaporated under reduced pressure to give 5.1 g (55%) of 2-amino-5-bromopyrazine: mp 112-114°C (EtOH/H_2O) (Lit.[15] 113°C).
To a stirred solution of dimethyl sulfoxide (1.2 g, 15.4 mmol) in dry dichloromethane (40 mL), cooled to -75°C, was added trifluoromethanesulfonic anhydride (3.1 g, 10.7 mmol) at -70°C under nitrogen. After 30 min, at -70°C a solution of 2-amino-5-bromopyrazine (1.5 g, 8.6 mmol) in a mixture of dichloromethane (30 mL) and dimethylsulfoxide (1 mL) was added. The reaction mixture was stirred at -75°C for 3 h, and then at -40°C for 1 h. A 5% sodium hydroxide solution (20 mL) and subsequently dichloromethane (30 mL) were added maintaining the temperature below -10°C. After stirring for 30 min the organic layer was separated. The aqueous layer was extracted with five 30 mL portions of dichloromethane. The combined dichloromethane extracts were washed with water (30 mL), dried over anhydrous $MgSO_4$ and evaporated under reduced pressure. The residue was purified by column chromatography (ethyl acetate as eluens) to yield 1.7 g (85%) of N-(2-bromo-5-pyrazinyl)-S,S-dimethylsulfilimine: mp 122-123°C; ^1H NMR ($CDCl_3$) δ 7.93 (d, J = 1.2 Hz, 1H), 7.80 (d, J = 1.2 Hz, 1H), 2.75 (s, 6H).
MS Calcd. for $C_6H_8N_3S^{79}Br$ (M^+): m/e 232.9623. Found: m/e 232.9630.
To a solution of m-chloroperbenzoic acid (85%, 2.95 g, 14.6 mmol) in dry dichloromethane (130 mL), was added a solution of N-(2-bromo-5-pyrazinyl)-S,S-dimethylsulfilimine (1.08 g, 4.6 mmol) at -8°C over a period of 3.5 h. The mixture was stirred at -8°C to -5°C for 30 min and subsequently filtered rapidly. Ozone was bubbled through the clear orange filtrate at -5°C until it turned pale yellow. The mixture was washed with two 20 mL portions of a saturated solution of sodium bicarbonate. The organic layer was dried (anhydrous $MgSO_4$) and evaporated under reduced pressure. Column chromatography (eluting with 1:1 dichloromethane/petroleum ether 40-60) yielded 0.78 g (82%) of 2-bromo-5-nitropyrazine: mp 114°C; ^1H NMR ($CDCl_3$) δ 9.30 (d, J = 1.2 Hz, 1H), 8.73 (d, J = 1.2 Hz, 1H).
MS Calcd. for $C_4H_2N_3O_2{}^{79}Br$ (M^+): m/e 202.9331. Found: m/e 202.9336.
Anal. Calcd. for $C_4H_2N_3O_2Br$ (203.99): C, 23.55; H, 0.98; N, 20.60. Found: C, 23.62; H, 0.95; N, 20.43.
b. Reaction of 2-bromo-5-nitropyrazine with 5,5-dicyanopentyne. To a stirred suspension of sodium hydride (80% dispersion, 0.063 g, 2.1 mmol) in anhydrous THF (15 mL) at room temperature under nitrogen was added a solution of 5,5-dicyanopentyne[13] (0.25 g, 2.1 mmol) in anhydrous THF (15 mL) and the mixture was then stirred for 20 min. A solution of 2-bromo-5-nitropyrazine

(0.426 g, 2.1 mmol) in anhydrous THF (5 mL) was added and the mixture was stirred for 2 h. After addition of water (100 mL) the mixture was extracted with ether (4 x 40 mL). The organic extracts were combined, dried (anhydrous $MgSO_4$) and evaporated under reduced pressure. The residue was purified by column chromatography (dichloromethane as eluent) to afford 0.156 g (48%) of 5: mp 123-124°C (EtOH); ^{1}H NMR ($CDCl_3$) δ 9.18 (s, 2H), 2.90-2.50 (m, 8H), 1.96 (t, J = 2.7 Hz, 2H).
MS Calcd. for $C_{18}H_{12}N_6$ (M^+): m/e 312.1123. Found: m/e 312.1130.
Anal. Calcd. for $C_{18}H_{12}N_6$ (312.32): C, 69.22; H, 3.87; N, 26.91. Found: C, 69.42; H, 3.78; N, 26.75.

General procedure for the intramolecular Diels-Alder reactions of pyrazines 1 and 5.
A stirred solution of the pyrazine derivative in nitrobenzene (100 mg solute/1 mL solvent) under nitrogen was heated under conditions depending on the substrate (see Table). The resultant solution was chromatographed over silica gel; elution with the appropriate solvent system yielded the reaction products 3, 4, 6, 7 and 8.

Cyclization of (N-acetyl-3-butynylamino)pyrazine (1a). Column chromatography (eluting first with dichloromethane to remove nitrobenzene, followed by 2:1 dichloromethane/ether and finally 4:1 ether/methanol) of the reaction mixture obtained from 1a (4.0 mmol) yielded 1-acetyl-2,3-dihydropyrrolo[2,3-b]pyridine (**3a**, 17%), mp 122-123°C (lit.[8a] 123-124°C), ^{1}H NMR ($CDCl_3$) identical with that reported in the literature,[8a] and 1-acetyl-2,3-dihydropyrrolo[2,3-c]pyridine (**4a**, 83%), mp 115-116°C (toluene); ^{1}H NMR ($CDCl_3$) δ 9.36 (s, 1H), 8.23 (d, J = 5.1 Hz, 1H), 7.07 (d, J = 5.2 Hz, 1H), 4.01 (t, J = 8.6 Hz, 2H), 3.17 (t, J = 8.6 Hz, 2H), 2.20 (s, 3H).
Anal. Calcd. for $C_9H_{10}N_2O$ (162.19): C, 66.64; H, 6.21; N, 17.27. Found: C, 66.47; H, 6.18; N, 17.34.

Cyclization of (3-butynyloxy)pyrazine (1b). Purification of the reaction mixture originating from 1b (3.4 mmol) by column chromatography (eluting with dichloromethane) yielded 2,3-dihydrofuro[2,3-b]pyridine (**3b**, 12%) as an oil, ^{1}H NMR ($CDCl_3$) spectrum identical with that reported in the literature,[14] and 2,3-dihydrofuro[2,3-c]pyridine (**4b**, 44%) as an oil; ^{1}H NMR ($CDCl_3$) δ 8.13 (s, 1H), 8.10 (d, J = 4.9 Hz, 1H), 7.13 (d, J = 4.8 Hz, 1H), 4.56 (t, J = 8.7 Hz, 2H), 3.20 (t, J = 8.6 Hz, 2H).
MS Calcd. for C_7H_7NO (M^+): m/e 121.0528. Found: m/e 121.0534.

Cyclization of (3-butynylthio)pyrazine (1c). Column chromatography (eluting first with dichloromethane to remove nitrobenzene, followed by ether) of the reaction mixture obtained from 1c (0.18 mmol) yielded 2,3-dihydrothieno[2,3-b]pyridine (**3c**, 24%) as an oil, ^{1}H NMR ($CDCl_3$) spectrum identical with that reported in the literature,[9a] and 2,3-dihydrothieno[2,3-c]pyridine (**4c**, 68%) as an oil; ^{1}H NMR ($CDCl_3$) δ 8.40 (s, 1H), 8.21 (d, J = 4.8 Hz, 1H), 7.08 (d, J = 4.8 Hz, 1H), 3.34-3.24 (m, 4H).
MS Calcd. for C_7H_7NS (M^+): m/e 137.0299. Found: m/e 137.0291.

Cyclization of (3-butynylsulfinyl)pyrazine (1d). Column chromatography (eluting with 5:1 chloroform/acetone) of the reaction mixture resulting from 1d (7.2 mmol) yielded 1-oxo-2,3-dihydrothieno[2,3-b]pyridine (**3d**, 53%), mp 97-99°C (lit.[6b] 96-97.5°C). IR and ^{1}H NMR spectra identical with the reported spectra.[6b]

Cyclization of (3-butynylsulfonyl)pyrazine (1e). Column chromatography (eluting first with dichloromethane to remove nitrobenzene, followed by 5% methanol in dichloromethane) of the reaction mixture obtained from 1e (2.1 mmol) yielded, 1,1-dioxo-2,3-dihydrothieno[2,3-b]pyridine (**3e**, 88%), mp 109-111°C (dichloromethane/petroleum ether 40-60); IR ($CHCl_3$) 1330, 1160, 1130 cm^{-1} (one of the absorptions at 1160 and 1130 cm^{-1} belongs to the SO_2-group); ^{1}H NMR ($CDCl_3$) δ 8.65 (d, J = 4.7 Hz, 1H), 7.85 (d, J = 7.8 Hz, 1H), 7.51 (dd, J_1 = 7.9 Hz, J_2 = 4.6 Hz, 1H), 3.65-3.28 (m, 4H).
Anal. Calcd. for $C_7H_7NO_2S$ (169.20): C, 49.68; H, 4.17; N, 8.27. Found: C, 49.52; H, 4.10; N, 8.17.

Cyclization of 2,5-bis(1,1-dicyano-4-pentynyl)pyrazine (5) at 120°C. Column chromatography (eluting with dichloromethane) of the solution obtained from 5 (0.64 mmol) afforded a mixture of 3-(1,1-dicyano-4-pentynyl)-7,7-dicyano-6,7-dihydro-5H-1-pyrindine (**6**) and 3-(1,1-dicyano-4-pentynyl)-7,7-dicyano-6,7-dihydro-5H-2-pyrindine (**7**). Column chromatography (eluting with ether) of the latter mixture yielded 6 (53%) and 7 (35%).
Analytical and spectroscopic data of 6 and 7:
6: mp 153-155°C (ethanol); IR ($CHCl_3$) 3300, 2250 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.85 (d, J = 1.6 Hz, 1H), 7.98 (d, J = 1.6 Hz, 1H), 3.33 (m, 2H), 3.05 (m, 2H), 2.56 (br s, 4H), 2.05 (t, J = 2.6 Hz, 1H).
MS Calcd. for $C_{17}H_{11}N_5$ (M^+): m/e 285.1014. Found: m/e 285.1014.
Anal. Calcd. for $C_{17}H_{11}N_5$ (285.30): C, 71.56; H, 3.89; N, 24.55. Found: C, 70.97; H, 3.76; N, 24.46.
7: mp 122-124°C (ether): IR ($CHCl_3$) 3300, 2250 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.90 (s, 1H), 7.80 (s, 1H), 3.31 (t, J = 6.4 Hz, 2H), 3.05 (t, J = 6.4 Hz, 2H), 2.63 (br s, 4H), 2.05 (t, J = 2.7 Hz, 1H).
MS Calcd. for $C_{17}H_{11}N_5$ (M^+): m/e 285.1014. Found: m/e 285.1015.

Cyclization of 5 at 210°C. Column chromatography (eluting with dichloromethane) of the reaction mixture obtained from 5 (0.40 mmol) yielded 1,1,5,5-tetracyano-1,2,3,5,6,7-hexahydro-s-indacene (**8**, 60%), mp 245-247°C (ethanol). IR ($CHCl_3$) 2280 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.63 (s, 2H), 3.31 (t, J = 6.7 Hz, 4H), 3.00 (t, J = 6.8 Hz, 4H).
MS Calcd. for $C_{16}H_{10}N_4$ (M^+) m/e 258.0905. Found: m/e 258.0913.
Anal. Calcd. for $C_{16}H_{10}N_4$ (258.27): C, 74.40; H, 3.90; N, 21.69. Found: C, 74.65; H, 3.97; N, 21.97.

Cyclization of 6 and 7. Solutions of 6 (0.22 mmol) and 7 (0.15 mmol) in nitrobenzene (1 mL) were heated at 210°C for 25 h. Column chromatography (ether as eluent) of each of the reaction mixtures gave 8 (65%).

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