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# RING-TRANSFORMATIONS OF PYRIMIDINES BY INTRAMOLECULAR DIELS-ALDER REACTIONS. SYNTHESIS OF ANNELATED PYRIDINES

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Abstract: Pyrimidines carrying an ω-alkyne side-chain -$XCH_2CH_2C{\equiv}CH$ (X=O,N,S,SO,$SO_2$) at the 2 or 5 position undergo intramolecular inverse electron demand Diels-Alder reactions across the C-2 and C-5 positions; elimination of hydrogen (or alkyl) cyanide from the intermediate adducts leads to condensed pyridines. The influence of the hetero atom (X) in the dienophilic side-chain and that of substituents in the pyrimidine ring on the reactivity is discussed.

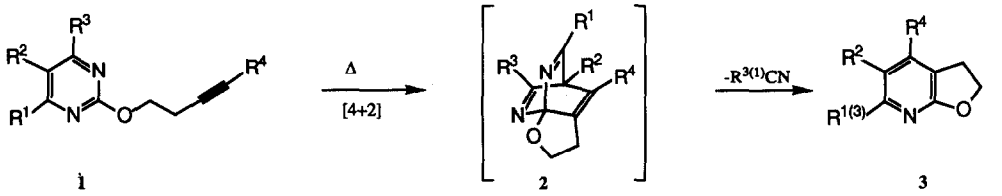
In the last two decades inverse electron demand Diels-Alder reactions of heterocyclic azadienes with electron-rich dienophiles have recieved considerable attention [1]. Both **inter**molecular reactions [2-4] and **intra**molecular reactions [5-10] have been studied. Recently, intramolecular inverse electron demand cycloaddition reactions of pyrimidines [11] and nitropyridines [11b] carrying an appropriate dienophilic side-chain at the 2 or 5-position were observed at our laboratory. In this paper we describe detailed results of our research on intramolecular Diels-Alder reactions of pyrimidines carrying an appropriate dienophilic side-chain, connected through a hetero atom (oxygen, sulfur or nitrogen) to the pyrimidine ring.

## RESULTS AND DISCUSSION

First, the cycloaddition reaction of 2-(3-butynyloxy)pyrimidines **1a-d** and 2-(3-pentynyloxy)pyrimidines **1e-f** was investigated. These compounds were prepared from the corresponding 2-chloropyrimidines and the sodium salt of 3-butyn-1-ol or 3-pentyn-1-ol, respectively, in good yields. Heating of compounds **1** in refluxing nitrobenzene under nitrogen led to the formation of 2,3-dihydrofuro[2,3-b]pyridines **3** in reasonable yields (Scheme 1). Their formation is supposed to occur via the intermediacy of tricyclic adducts **2** resulting from an intramolecular cycloaddition across the C2 and C5 position and subsequent elimination of hydrogen cyanide or acetonitrile. The supposed intermediate cycloaddition products **2** could not be isolated or identified by NMR spectroscopy.

The reaction conditions necessary for the complete disappearance of **1a** and **1b** (see Table) are comparable. This means that the activating effect of the strong electron withdrawing nitro group at the 5-position of the pyrimidine does not lead to an increased rate of cycloaddition. This may be due to steric effects.

Scheme 1



1 2 3

a $R^1$, $R^2$, $R^3$, $R^4$ = H
b $R^1$, $R^3$, $R^4$ = H; $R^2$ = $NO_2$
c $R^2$, $R^4$ = H; $R^1$, $R^3$ = $CH_3$
d $R^2$, $R^3$, $R^4$ = H; $R^1$ = $CH_3$
e $R^1$, $R^2$, $R^3$ = H; $R^4$ = $CH_3$
f $R^1$, $R^3$ = H; $R^2$ = $NO_2$; $R^4$ = $CH_3$

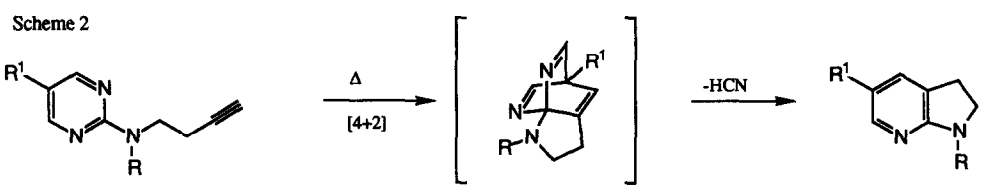
Introduction of one weak electron donating methylgroup at C-4 (C-6), i.e. compound **1d**, does not lead to a considerable decrease of cycloaddition rate. Interestingly, a mixture of 2,3-dihydrofuro[2,3-b]pyridine **3a** and 2,3-dihydro-6-methylfuro[2,3-b]pyridine **3c** is obtained in a ratio of approximately 1:1.8. These cyclization products arise from intermediate cycloadduct **2d** by loss of acetonitrile or hydrogen cyanide, respectively. In this case the loss of hydrogen cyanide is favoured more than the loss of acetonitrile [12]. It is interesting that introduction of methyl groups at both C-4 and C-6, i.e. **1c**, results in a considerable decreased rate of cycloaddition. Taking into account that introduction of one methyl group hardly influences the rate of cycloaddition it is reasonable to suggest that in the conversion of **1c** into **3c** not only the electron donating character of the methyl groups must be taken into account, but also that the combined steric effects of both methyl groups at C-4 and C-6 disfavour the cycloaddition.

Comparison of the reaction conditions for complete disappearance of **1a** and **1e** shows that introduction of a methyl group at the triple bond of the dienophilic side-chain decreases reactivity. We have to conclude that in this reaction the activating electronic effect of the methyl group is exceeded by steric hindrance of this group exerted by approach of the dienophile to C-5. The higher reactivity of 5-nitro-2-(3-pentynyloxy)pyrimidine **1f** towards cycloaddition as compared to that of 2-(3-pentynyloxy)pyrimidine **1e** reflects the activating effect of the nitro group on the pyrimidine towards cycloaddition.

In order to investigate the influence of different hetero atoms in α–position of the dienophilic side-chain we also studied the intramolecular Diels-Alder reactions of 2-(3-butynylamino)pyrimidines **4** and 2-(3-butynylthio)pyrimidines **7**. Heating of **4a** and **4b**, prepared in good yields from the corresponding 2-chloropyrimidines and 4-amino-1-butyne, in refluxing nitrobenzene under nitrogen for 36 hours only led to decomposition and no indication for the formation of 1H-2,3-dihydropyrrolo[2,3-b] pyridines **6a** and **6b** could be found. However, when the NH group was acetylated, the resulting 2-(N-acetyl-3-butynylamino) pyrimidines **4c** and **4d**, in which the pyrimidine rings are less electron rich than in case of **4a**, **4b**, smoothly underwent the intramolecular Diels-Alder reaction in high yield at 180°C, affording the 1-acetyl-2,3-dihydropyrrolo[2,3-b]pyridines **6c** and **6d**.

With exception of **7b** the 2-(3-butynylthio)pyrimidines **7** were prepared in good yields from the corresponding 2-mercaptopyrimidines and 4-iodo-1-butyne in the presence of triethylamine. Compound **7b** was obtained from sodium nitromalonaldehyde and S-3-butynylthiourea hydroiodide in low yield. On

Scheme 2



4 5 6

a R, $R^1$ = H
b R = H; $R^1$ = $NO_2$
c $R^1$ = H; R = C(O)$CH_3$
d $R^1$ = $NO_2$; R = C(O)$CH_3$

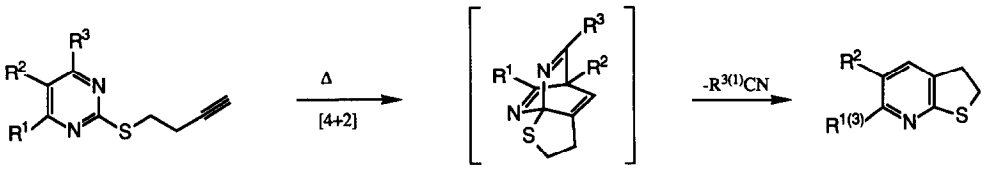
TABLE Intramolecular Diels-Alder reactions of pyrimidines **1, 4, 7, 10b** and **12**. Reaction conditions, products and yields.

| Pyrimidines Starting Compounds | Reaction Conditions Temp. (°C) | Time (h) | Reaction Compounds | % Yield |
|---|---|---|---|---|
| **1a** | 210 | 24 | **3a** | 52 |
| **1b** | 210 | 24 | **3b** | 55 |
| **1c** | 210 | 60 | **3c** | 68 |
| **1d** | 210 | 26 | **3a + 3c** | 60 |
| **1e** | 210 | 96 | **3e** | 40 |
| **1f** | 210 | 28 | **3f** | 83 |
| **4c** | 180 | 12 | **6c** | 85 |
| **4d** | 180 | 12 | **6d** | 87 |
| **7a** | 210 | 18 | **9a** | 57 |
| **7b** | 210 | 18 | **9b** | 75 |
| **7c** | 210 | 26 | **9c** | 51 |
| **7d** | 210 | 18 | **9a + 9c** | 69 |
| **7e** | 210 | 21 | **9e** | 75 |
| **10b** | 180 | 16 | **11b** | 63 |
| **12a** | 180 | 12 | **14a** | 85 |
| **12c** | 180 | 46 | **14c** | 64 |
| **12d** | 180 | 34 | **14c** | 60 |

heating in refluxing nitrobenzene the compounds **7** cyclized to the corresponding 2,3-dihydrothieno[2,3-b]pyridines **9**. In analogy with **1d**, 2-(3-butynylthio)-4-methylpyrimidine **7d** cyclized to a mixture of thieno[2,3-b]pyridines **9a** and **9c** in a ratio of approximately 1:2.2 by loss of either acetonitrile or hydrogen cyanide from intermediate cycloadduct **8d**.

Comparison of the temperature and the reaction time for complete conversion of the compounds **4c** and **4d** and also **7a** and **7b** confirm that the presence of the nitrogroup at C-5 does not considerably influence the rate of the reaction (see Table). We obtained the same result with the compounds **1a** and **1b**.

Scheme 3



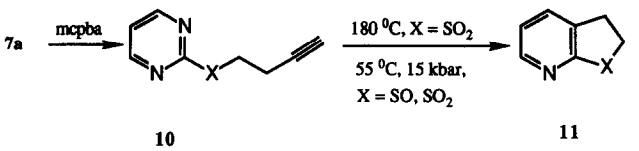

**7** **8** **9**

**a** $R^1, R^2, R^3 = H$ **b** $R^1, R^3 = H; R^2 = NO_2$
**c** $R^2 = H; R^1, R^3 = CH_3$ **d** $R^2, R^3 = H; R^1 = CH_3$
**e** $R^1, R^3 = H; R^2 = Ph$

However, it is clear that the nature of the hetero atom in the dienophilic side-chain influences the reactivity. The reactivity increases in the order NH<O<S<NC(O)$CH_3$ . This order of reactivity reflects the decrease of the electron donation into the π-system of the pyrimidine ring [13] and is similar to those found in the 1,2,4-triazine and pyrazine series [6b, 8].

From the observations described above it may be inferred that the reactivity towards intramolecular inverse electron demand Diels-Alder reactions may be enhanced by increasing the electron deficiency of the pyrimidine ring. Therefore, the highly electron deficient sulfoxide **10a** (X= SO) and sulfone **10b** (X= $SO_2$ ) were also studied. These compounds were easily prepared from the sulfide **7a** by oxidation with one or two equivalents of m-chloroperbenzoic acid, respectively. Indeed, 2-(3-butynylsulfonyl)pyrimidine **10b** (X= $SO_2$ ) already cyclized to 1,1-dioxo-2,3-dihydrothieno[2,3-b]pyridine **11b** when heated at 180°C for 16 hours, conditions being less strenuous than those for the sulfide **7a**. Unfortunately, 2-(3-butynyl-sulfinyl)pyrimidine **10a** (X= SO) decomposes when heated above 100°C. No product formation could be detected. However, **10a** underwent cycloaddition when heated at 55°C in $CDCl_3$ under a pressure of 15 kBar, yielding **11a**. In order to compare the reactivities of **7a**, **10a** and **10b** we also reacted **7a** and **10b**

Scheme 4



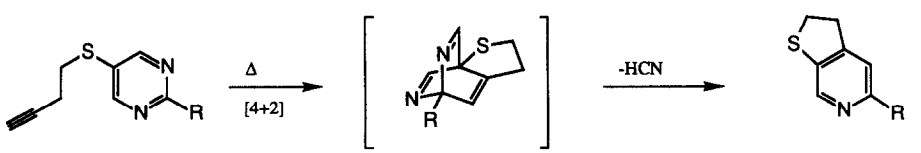

**10** **11**

a X = SO b X = $SO_2$

under the same high pressure conditions as **10a**. $^1H$ NMR spectroscopy showed that after one night **10a** was converted into **11a** for more than 90%, whereas **10b** was only converted into**11b** for approximately 25%. Under these conditions **7a** did not give the cycloadduct **9a** at all. This violation of the "normal" order of reactivity (sulfoxide > sulfone > sulfide) agrees with observations of Taylor and Macor in the 1,2,4-triazine series [6a]. It can be explained if one considers that in intramolecular cycloaddition reactions the reactivity is not only determined by electronic effects, but that also the possibility for a good overlap between the HOMOdienophile and LUMOazadiene is essential. This is influenced by the nature of the tether between diene and dienophile. The smaller the C-S-C bond angle in the dienophilic side-chain, the closer the dienophile can approach the heterocyclic diene. Thus, the sulfoxide **10a**, having the smallest C-S-C bond angle [6a] has the fastest rate of intramolecular cyclization. The higher degree of electron deficiency in the ring in sulfone **10b** is partly negated by its larger C-S-C bond angle.

We also included in our investigations some pyrimidine derivatives with a dienophilic side-chain in the 5-position, i.e. the 5-(3-butynylthio)pyrimidines **12a-d**. The compounds **12a** and **12b** were prepared in good yield by treatment of the appropriate substituted bis-(pyrimidyl-5)disulfide with triethylamine and sodium dithionite followed by reaction with 4-iodo-1-butyne. On heating at 180°C **12a** cyclized to 2,3-dihydro-5-phenylthieno[2,3-c]pyridine **14a** in high yield. Under the same conditions **12c** and **12d** both reacted to 5-(acetylamino)-2,3-dihydrothieno[2,3-c]pyridine **14c**. The amino compound **12b** was found not to cyclise into **14b**.

Scheme 5




**12** **13** **14**

a R = Ph b R = $NH_2$ c R = $NHC(O)CH_3$ d R = $N(C(O)CH_3)_2$

In order to compare the reactivities of pyrimidines with a dienophilic side-chain attached to the 2 and 5 position, respectively, we heated 2-(3-butynylthio)-5-phenylpyrimidine **7e** and 5-(3-butynylthio)-2-phenylpyrimidine **12a** at 190°C in nitrobenzene in a NMR tube. The rate of product formation and the rate of decrease of starting material was monitored by means of NMR spectroscopy. It was found that **12a** cyclizes 18.4 times faster than **7e**. This difference in reactivity is probably caused by a different resonance donation of the 3-butynylthio group to the pyrimidine ring being larger in 2-(3-butynylthio)-5-phenylpyrimidine **7e** than in 5-(3-butynylthio)-2-phenylpyrimidine **12a**. This greater resonance contribution in **7e** hampers rotation about the S-pyrimidine bond and consequently the dienophilic side-

chain can more easily approach the azadiene in compound **12a** than in compound **7e**, resulting in a larger rate of cycloaddition of compound **12a**.

## EXPERIMENTAL SECTION

Melting points are uncorrected. $^1$H NMR spectra were recorded on a Varian EM 390 spectrometer. Chemical shifts are determined in ppm downfield from TMS. Mass spectral data were obtained on a AEI MS 902 spectrometer equipped with a VG ZAB console. Column chromatography was performed on Merck silica gel 60 (70-230 mesh ASTM).

General procedure for the synthesis of 2-(3-alkynyloxy)pyrimidines (1).
The appropriate chloropyrimidine (4.4 mmol, 1 eq) was added, with the exception of 2-chloro-5-nitropyrimidine, at room temperature to a solution of sodium (0.1 g, 4.4 mmol) in 3-butyn-1-ol (3 ml) or 3-pentyn-1-ol (3 ml, entries **1e** and **1f**). 2-Chloro-5-nitropyrimidine (entries **1b** and **1f**) was added at 0°C and the resulting mixture stirred first at room temperature for one hour. The mixture was then stirred at 80°C for the time given and after cooling ether (10 ml) was added. Sodium chloride was filtered off and the solvent evaporated under reduced pressure to afford the crude 2-(3-alkynyloxy)pyrimidine (**1**) which was purified by bulb-to-bulb destillation to remove any remaining alkynol, followed by column chromatography eluting with the given solvent.

2-(3-Butynyloxy)pyrimidine (**1a**). From 2-chloropyrimidine. Reaction time 2h. Eluent ether. Obtained as a pale yellow oil (75%) which slowly solidifies upon standing: mp 39-41°C (hexane); $^1$H NMR ($CDCl_3$) δ 8.50 (d, J = 5.0 Hz, 2H), 6.93 (t, J = 5.0 Hz, 1H), 4.45 (t, J = 7.2 Hz, 2H), 2.71 (dt, $J_1$ = 7.3 Hz, $J_2$ = 2.9 Hz, 2H), 2.03 (t, J = 2.8 Hz, 1H).
HRMS Calcd. for $C_8H_8N_2O$ ($M^+$): 148.0637. Found: 148.0640.
Anal. Calcd. for $C_8H_8N_2O$ (148.16): C, 64.84; H, 5.44; N, 18.90. Found: C, 64.58; H, 5.46; N, 19.21.

2-(3-Butynyloxy)-5-nitropyrimidine (**1b**). From 2-chloro-5-nitropyrimidine [14]. Reaction time 1h. Eluent ether. Obtained as a yellow solid (70%): mp 61-63°C (hexane/toluene); $^1$H NMR ($CDCl_3$) δ 9.32 (s, 2H), 4.62 (t, J = 6.9 Hz, 2H), 2.75 (dt, $J_1$ = 7.1 Hz, $J_2$ = 2.7 Hz, 2H), 2.10 (t, J = 2.7 Hz, 1H).
$^{13}$C NMR ($CDCl_3$) δ 166.7, 156.0, 138.5, 79.2, 70.5, 67.2, 19.0.
HRMS Calcd. for $C_8H_7N_3O_3$($M^+$): 193.0487. Found: 193.0486.
Anal. Calcd. for $C_8H_7N_3O_3$(193.16): C, 49.75; H, 3.65; N, 21.75. Found: C, 49.53; H, 3.73; N, 22.06.

2-(3-Butynyloxy)-4,6-dimethylpyrimidine (**1c**). From 2-chloro-4,6-dimethylpyrimidine [15]. Reaction time 3h. Eluent: ether/petroleum ether 40-60 (1:1). Obtained as a pale yellow solid (72%): mp 39-41°C (hexane); $^1$H NMR ($CDCl_3$) δ 6.75 (s, 1H), 4.51 (t, J = 7.2 Hz, 2H), 2.73 (dt, $J_1$ = 7.5 Hz, $J_2$ = 2.7 Hz, 2H), 2.44 (s, 6H), 2.05 (t, J = 2.7 Hz, 1H).
Anal. Calcd. for $C_{10}H_{12}N_2O$ (176.21): C, 68.16; H, 6.86; N, 15.90. Found: C, 67.94; H, 7.01; N, 15.99.

2-(3-Butynyloxy)-4-methylpyrimidine (**1d**). From 2-chloro-4-methylpyrimidine [16]. Reaction time 2.5h. Eluent dichloromethane/ether (3:1). Obtained as a pale yellow oil (73%); $^1$H NMR ($CDCl_3$) δ 8.34 (d, J = 4.8 Hz, 1H), 6.82 (d, J = 5.1 Hz, 1H), 4.47 (t, J = 7.2 Hz, 2H), 2.70 (dt, $J_1$ = 7.4 Hz, $J_2$ = 2.7 Hz), 2.45 (s, 3H), 2.03 (t, J = 2.7 Hz, 1H).
HRMS Calcd. for $C_9H_{10}N_2O$ ($M^+$): 162.0793. Found: 162.0787.

2-(3-Pentynyloxy)pyrimidine (**1e**). From 2-chloropyrimidine. Reaction time 2h. Eluent ether. Obtained as a pale yellow oil (65%); $^1$H NMR ($CDCl_3$) δ 8.53 (d, J = 4.5 Hz, 2H), 6.95 (t, J = 4.9 Hz, 1H), 4.44 (t, J = 7.2 Hz, 2H), 2.65 (qt, $J_1$ = 7.2 Hz, $J_2$ = 2.7 Hz, 2H), 1.75 (t, J = 2.6 Hz, 3H).
HRMS Calcd. for $C_9H_{10}N_2O$ ($M^+$): 162.0793. Found: 162.0787.

2-(3-Pentynyloxy)-5-nitropyrimidine (**1f**). From 2-chloro-5-nitropyrimidine. Reaction time 2h. Eluent dichloromethane. Obtained as a yellow solid (52%): mp 74-75°C (hexane/toluene); $^1$H NMR ($CDCl_3$) δ 9.30 (s, 2H), 4.57 (t, J = 7.2 Hz, 2H), 2.68 (dt, $J_1$ = 7.3 Hz, $J_2$ = 2.5 Hz), 1.77 (t, J = 2.4 Hz, 3H).
Anal. Calcd. for $C_9H_9N_3O_3$ (207.19): C, 52.16; H, 4.37; N, 20.28. Found: C, 52.16; H, 4.39; N, 20.36.

General procedure for the synthesis of the 2-(3-butynylamino)pyrimidines **4a** and **4b** and 2-(N-acetyl-3-butynylamino)pyrimidines **4c** and **4d**.
A mixture of the appropriate chloropyrimidine (4.4 mmol) and 4-amino-1-butyne [17] (0.61 g; 8.8 mmol) in ethanol was refluxed for the time given. After cooling the solvent was evaporated from the reaction mixture and the residue purified by column chromatography (eluting with ether) to yield the corresponding 2-(3-butynylamino)pyrimidine (**4a** or **4b**). The latter compound (**4a** or **4b**; 2 mmol) was heated for 4 hours at 90°C in acetic anhydride (3 ml) containing two drops of concentrated sulfuric acid. After cooling the excess of acetic anhydride was removed under reduced pressure. The residue was treated with water (10 ml), neutralized with sodium bicarbonate and extracted with dichloromethane. The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by column chromatography (ether as eluent) to give the corresponding 2-(N-acetyl-3-butynyl-amino)pyrimidine (**4c** or **4d**).

2-(3-Butynylamino)pyrimidine (**4a**). From 2-chloropyrimidine. Reflux time 24h. Obtained as a colourless solid (76%): mp 60-61°C (hexane/toluene): $^1$H NMR ($CDCl_3$) δ 8.29 (d, J = 4.9 Hz, 2H), 6.6 (br, 1H), 6.51 (t, J = 4.8 Hz, 1H), 3.58 (q, $JCH_2$-$CH_2$ = $JCH_2$-NH = 6.6 Hz, 2H), 2.51 (dt, $J_1$ = 6.6 Hz, $J_2$ = 2.7 Hz, 2H), 2.02 (t, J = 2.5 Hz, 1H).

MS: m/e 147 ($M^+$).
Anal. Calcd. for $C_8H_9N_3$ (147.18): C, 65.28; H, 6.16; N, 28.55. Found: C, 65.21; H, 6.18; N, 28.13.

2-(N-acetyl-3-butynylamino)pyrimidine (4c). Obtained as a yellow oil (65%) which slowly crystalizes: mp 68-69°C (hexane/toluene); $^1H$ NMR ($CDCl_3$) δ 8.68 (d, J = 5.0 Hz, 2H), 7.09 (t, J = 5.0 Hz, 1H), 4.28 (t, J = 7.5 Hz, 2H), 2.56 (dt, $J_1$ = 7.6 Hz, $J_2$ = 2.5 Hz, 2H), 2.45 (s, 3H), 1.88 (t, J = 2.7 Hz, 1H).
MS: m/e 189 ($M^+$).
Anal. Calcd. for $C_{10}H_{11}N_3O$ (189.21): C, 63.47; H, 5,86; N, 22.21. Found: C, 63.62; H, 5.91; N, 22.55.

2-(3-Butynylamino)-5-nitropyrimidine (4b). From 2-chloro-5-nitropyrimidine. Reflux time 3h. Obtained as a pale yellow solid (65%): mp 124-126°C (hexane/toluene); $^1H$ NMR ($CDCl_3$) δ 9.09 (s, 2H), 6.5 (br, 1H), 3.72 (q, $JCH_2$-$CH_2$ = $JCH_2$-NH = 6.4 Hz, 2H), 2.52 (dt, J = 6.5 Hz, $J_2$ = 2.7 Hz, 2H), 2.03 (t, J = 2.7 Hz, 1H).
Anal. Calcd. for $C_8H_7N_4O_2$ (192.18): C, 49.99; H, 4.19; N, 29.15. Found: C, 49.72; H, 4.16; N, 29.45.

2-(N-acetyl-3-butynylamino)-5-nitropyrimidine (4d). Obtained as a yellow oil (60%) which slowly solidifies upon standing in a refrigarator: mp 66-68°C (hexane/toluene); $^1H$ NMR ($CDCl_3$) δ 9.33 (s, 2H), 4.46 (t, J = 7.2 Hz, 2H), 2.60 (dt, $J_1$ = 7.2 Hz, $J_2$ = 2.7 Hz, 2H), 2.60 (s, 3H), 1.87 (t, J = 2,4 Hz, 1H).
Anal. Calcd. for $C_{10}H_{10}N_4O_3$ (234.21): C, 51.27; H, 4.30; N, 23.92. Found: C, 51.16; H, 4.31; N, 24.07.

2-(3-Butynylthio)pyrimidine (7a). To a stirred suspension of 2-mercaptopyrimidine (1.12 g; 10 mmol) in water (20 ml) was added 3 g of triethylamine (30 mmol). When all 2-mercaptopyrimidine was dissolved 4-iodo-1-butyne [18] (1.8 g; 10 mmol) was added. The mixture was heated at 70°C for two hours, then cooled and extracted with ether. The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure to afford an oil which was purified by column chromatography (ether as eluent) to yield 0.93 g (57%) of **7a** as a pale brown oil; $^1H$ NMR ($CDCl_3$) δ 8.52 (d, J = 4.8 Hz, 2H), 6.98 (t, J = 4.9 Hz, 1H), 3.41 (t, J = 7.5 Hz, 2H), 2.65 (dt, $J_1$ = 7.5 Hz, $J_2$ = 2.7 Hz, 2H), 2.06 (t, J = 2.6 Hz, 1H).
MS: m/e 164 ($M^+$).
Anal. Calcd. for $C_{14}H_{11}N_5O_7S$ (393.33; picrate: mp 87-89°C): C, 42.75; H, 2.82; N, 17.81. Found: C, 43.08; H, 2.90; N, 18.16.

S-3-butynylthiourea hydroiodide. This compound was prepared quantitatively from 4-iodo-1-butyne and thiourea according to a known literature method [19]. It was obtained as a white solid; mp 92-94°C; $^1H$ NMR (acetone-$d_6$) δ 8.98 (br s, 4H), 3.60 (t, J = 6.8 Hz, 2H), 2.75 (dt, $J_1$ = 6.8 Hz, $J_2$ = 2.4 Hz, 2H), 2.60 (t, J = 2.5 Hz, 1H).
Anal. Calcd. for $C_5H_9IN_2S$ (256.10): C, 23.44; H, 3.54; N, 10.93. Found: C, 23.43; H, 3.57; N, 11.23.

2-(3-Butynylthio)-5-nitropyrimidine (7b). A mixture of sodium nitromalonaldehyde [20] (2.56g; 18.4 mmol), S-3-butynylthiourea hydroiodide (4.21 g; 16.4 mmol) and ethylpiperidine (1.90 g; 16.8 mmol) in 40 ml of water was kept at 60°C for 15 minutes and then for 2 days at room temperature. The mixture was then extracted with dichloromethane. The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure to afford the crude product which was purified by column chromatography (dichloromethane as eluent) to give **7b** as a yellow solid (0.45 g; 13%): mp 74-75°C (hexane); $^1H$ NMR ($CDCl_3$) δ 9.24 (s, 2H), 3.36 (t, J = 7.2 Hz, 2H), 2.67 (dt, $J_1$ = 7.2 Hz, $J_2$ = 2.7 Hz, 2H), 2.06 (t, J = 2.7 Hz, 1H).
MS: m/e 209 ($M^+$).
Anal. Calcd. for $C_8H_7N_3O_2S$ (209.23): C, 45.92; H, 3.37; N, 20.09. Found: C, 45.87; H, 3.27; N,19.89.

2-(3-Butynylthio)-4,6-dimethylpyrimidine (7c). 4,6-Dimethyl-2-mercaptopyrimidine hydrochloride [21] (0.53 g; 3 mmol) in 10 ml of water was neutralized with sodium hydroxide (0.12 g; 3 mmol). Then 0.90 g (9 mmol) of triethylamine and 0.54 g (3 mmol) of 4-iodo-1-butyne were added and the mixture heated at 70°C for two hours. After cooling the mixture was extracted with ether. The organic layer was dried ($MgSO_4$) and evaporated. The residue was purified by column chromatography (ether as eluent) to afford **7c** (0.38 g; 66%) as a pale yellow oil; $^1H$ NMR ($CDCl_3$) δ 6.72 (s, 1H), 3.31 (t, J = 7.2 Hz, 2H), 2.66 (dt, $J_1$ = 7.5 Hz, $J_2$ = 2.7 Hz, 2H), 2.39 (s, 1H), 2.03 (t, J = 2.6 Hz, 1H).
HRMS Calcd. for $C_{10}H_{12}N_2S$ ($M^+$): 192.0721. Found: 192.0713.

2-(3-Butynylthio)-4-methylpyrimidine (7d). This compound was prepared according to the same procedure as described above for **7c** using 2-mercapto-4-methylpyrimidine hydrochloride [22] (0.49 g; 3 mmol). It was obtained as a yellow oil (0.34 g; 64%) after purification by column chromatography (ether as eluent); $^1H$ NMR ($CDCl_3$) δ 8.39 (d, J = 5.4 Hz, 1H), 6.85 (d, J = 5.2 Hz, 1H), 3.30 (t, J = 7.5 Hz, 2H), 2.64 (dt, $J_1$ = 7.7 Hz, $J_2$ = 2.6 Hz, 2H), 2.43 (s, 3H), 2.05 (t, J = 2.7 Hz, 1H).
HRMS Calcd. for $C_9H_{10}N_2S$ ($M^+$): 178.0565. Found: 178.0560.

2-(3-Butynylthio)-5-phenylpyrimidine (7e). 2-Mercapto-5-phenylpyrimidine [23] (1.00 g; 5.3 mmol) and triethylamine (1.6 g; 15.9 mmol) in 20 ml of water were stirred untill all of the pyrimidine was dissolved. Then 4-iodo-1-butyne (0.96 g; 5.3 mmol) was added and the reaction mixture heated at 70°C for one hour. After cooling the mixture was extracted with dichloromethane. The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure to afford **7e** as a pale yellow solid (1.07 g; 84%) : mp 75.5-77.5°C (hexane); $^1H$ NMR ($CDCl_3$) δ 8.74 (s, 2H), 7.63-7.37 (m, 5H), 3.35 (t, J = 7.2 Hz, 2H), 2.70 (dt, $J_1$ = 7.2 Hz, $J_2$ = 2.7 Hz, 2H), 2.06 (t, J = 2.5 Hz, 1H).
$^{13}C$ NMR ($CDCl_3$) δ 170.4, 155.4, 134.4, 129.8, 129.4, 128.6, 126.6, 82.5, 69.6, 30.0, 19.5.
Anal. Calcd. for $C_{14}H_{12}N_2S$ (240.32): C, 70.17; H, 5.08; N, 11.69. Found: C, 69.96; H, 5.03; N, 11.65.

2-(3-Butynylsulfinyl)pyrimidine (10a). To a stirred solution of 2-(3-butynylthio)pyrimidine (**7a**; 0.16 g; 1 mmol) in anhydrous chloroform (3 ml) at 0°C, m-chloroperbenzoic acid (85% techn. solid, 0.20 g; 1 mmol) was added. The mixture was stirred at room temperature for 20 hours and then washed with a 2N solution of sodium carbonate. The organic layer was dried ($MgSO_4$) and evaporated to afford a clear,

colourless oil which was purified by column chromatography (dichloromethane/methanol 9:1 as eluent) to yield **10a** (0.15 g; 86%) as a clear, colourless oil; $^1$H NMR ($CDCl_3$) δ 8.93 (d, J = 4.9 Hz, 2H), 7.48 (t, J = 4.9 Hz, 1H), 3.65-3.05 (mc, 2H), 3.05-2.35 (mc, 2H), 1.94 (t, J = 2.7 Hz, 1H).
HRMS Calcd. for $C_8H_8N_2OS$ ($M^+$): 180.0358. Found: 180.0359.

2-(3-Butynylsulfonyl)pyrimidine (**10b**). To a stirred solution of 2-(3-butynylthio)pyrimidine (**7a**; 0.82 g; 5 mmol) in anhydrous chloroform (10 ml) at 0°C, m-chloroperbenzoic acid (85% techn. solid, 2.50 g; 12.3 mmol) in chloroform (25 ml) was added in small portions over the course of a few minutes. The mixture was stirred at room temperature for 20 hours and then washed with a saturated solution of sodium hydrogen sulfite (2x15 ml) and subsequently with a 2N solution of sodium carbonate (2x25 ml). The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure to give **10b** as a colourless solid (0.95 g; 97%): mp 68-69°C (hexane/chloroform); $^1$H NMR ($CDCl_3$) δ 9.00 (d, J = 4.8 Hz, 2H), 7.70 (t, J = 4.9 Hz, 1H), 3.77 (t, J =7.5 HZ, 2H), 2.79 (dt, $J_1$ = 7.5 HZ, $J_2$ = 2.7 Hz, 2H), 2.00 (t, J = 2.7 Hz, 1H).
$^{13}$C NMR ($CDCl_3$) δ 165.5, 158.7, 123.9, 79.3, 70.6, 49.9, 13.1.
Anal. Calcd. for $C_8H_8N_2O_2S$ (196.23): C, 48.96; H, 4.10; N, 14.27. Found: C, 48.84; H, 4.10; N, 14.12.

5-(3-Butynylthio)-2-phenylpyrimidine (**12a**). Bis-[2-phenylpyrimidyl-(5)]-disulfide [24] (0.75 g; 2 mmol), triethylamine (0.61 g; 6 mmol) and sodium dithionite (0.82 g; 4.7 mmol) in water (5 ml) were stirred at 60°C untill complete dissolution. After a further 3 hours at 60°C 4-iodo-1-butyne (0.72 g; 4 mmol) was added and the reaction mixture stirred for one hour at 60°C. After cooling the product was collected by filtration and washed with cold methanol to afford **12** (0.92 g; 95%) as a colourless solid: mp 72-73°C (methanol); $^1$H NMR ($CDCl_3$) δ 8.79 (s, 1H), 8.55-8.27 (m,2H), 7.59-7.37 (m, 3H), 3.07 (t, J = 7.5 Hz, 2H), 2.50 (dt, $J_1$ = 7.5 Hz, $J_2$ = 2,7 Hz, 2H), 2.03 (t, J = 2.7 Hz, 1H).
$^{13}$C NMR ($CDCl_3$) δ 163.0, 158.9, 136.9, 130.9, 128.6, 128.2, 81,3, 70.5, 33.5, 19.6.
HRMS Calcd. for $C_{14}H_{12}N_2S$ ($M^+$): 240.0721. Found: 240.0721.
Anal. Calcd. for $C_{14}H_{12}N_2S$ (240.32): C, 69.97; H, 5.03; N, 11.66. Found: C, 69.61; H, 5.06; N, 11.54.

2-Amino-5-(3-butynylthio)pyrimidine (**12b**)
This compound was prepared in the same way as described above for **12a** using bis-[2-aminopyrimidyl-(5)-]disulfide [24] (300 mg; 1.2 mmol). It was obtained as a colourless solid (290 mg; 68%): m.p. 137-139°C (ethanol); $^1$H NMR ($CDCl_3$) δ 8.36 (s, 2H), 5.55 (br s, 2H), 2.82 (t, J = 7.1 Hz, 2H), 2.40 (dt, $J_1$ = 7.2 Hz, $J_2$ = 2.5 Hz, 2H), 2.01 (t, J = 2.6 Hz, 1H).
Anal. Calcd. for $C_8H_9N_3S$ (179.24); C, 53.61; H, 5.06; N, 23.44. Found: C, 53.41; H, 4.99; N, 23.61.

2-(acetylamino)-5-(3-butynylthio)pyrimidine (**12c**) and 5-(3-butynylthio)-2-(diacetylamino)pyrimidine (**12d**)
Compound **12a** (110 mg; 0.62 mmol) was heated for 4 hours at 90°C in acetic anhydride (2 ml) containing one drop of concentrated sulfuric acid. After cooling the excess of acetic anhydride was removed under reduced pressure. The residue was treated with water (10 ml), neutralized with sodium bicarbonate and extracted with dichloromethane. The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure to afford a mixture of **12a** and **12d**. Column chromatography (eluting with dichloromethane/methanol 9:1) of the latter mixture yielded **12c** (68 mg; 50%) as a yellow solid and **12d** (65 mg; 40%) as a pale yellow oil. Analytical and spectroscopic data of **12c** and **12d**:
**12c**: m.p. 136-138°C (hexane/chloroform); $^1$H NMR ($CDCl_3$) δ 9.57 (brs, 1H), 8.63 (s, 2H), 2.94 (t, J = 7.2 Hz, 2H), 2.47 (s, 3H), 2.60-2.30 (m, 2H), 2.01 (t, J = 2.6 Hz).
Anal. Calcd. for $C_{10}H_{11}N_3OS$ (221.28); C, 54.28; H, 5.01; N, 18.99. Found: C, 53.99; H, 5.01; N, 19.06.
**12d**: $^1$H NMR ($CDCl_3$) δ 8.76 (s, 2H), 3.17 (t, J = 7.1 Hz, 2H), 2.58 (dt, $J_1$ = 7.1 Hz, $J_2$ = 2.7 Hz, 2H), 2.28 (s, 6H), 2.07 (t, J = 2.6 Hz, 2H).
HRMS Calcd. for $C_{12}H_{13}N_3O_2S$ ($M^+$): 263. 0727. Found: 263.0728.

General procedure for the intramolecular Diels-Alder reactions of pyrimidines **1**, **4**, **7**, **10b** and **12**.
A stirred solution of the appropriate pyrimidine derivative in nitrobenzene (100 mg solute/1 ml solvent) under nitrogen was heated under conditions mentioned in the Table. The resultant solution was chromatographed over silica gel; elution with the appropriate solvent system yielded the reaction products **3**, **6**, **9** , **11b** and **14**.

Cyclization of 2-(3-butynyloxy)pyrimidine (**1a**) to 2,3-dihydrofuro[2,3-b]pyridine (**3a**). Column chromatography (eluting first with dichloromethane to remove nitrobenzene, followed by ether) of the reaction mixture obtained from **1a** (1.4 mmol) yielded 2,3-dihydrofuro[2,3-b]pyridine (**3a**, 52%) as an oil; $^1$H NMR ($CDCl_3$) spectrum was identical with that reported in literature [25].

Cyclization of 2-(3-butynyloxy)-5-nitropyrimidine (**1b**) to 2,3-dihydro-5-nitrofuro[2,3-b]pyridine (**3b**). Purification of the reaction mixture obtained from **1b** (1.2 mmol) by column chromatography (eluting first with dichloromethane, then ether) afforded **3b** (55%): mp 161-163°C (hexane/toluene); $^1$H NMR ($CDCl_3$) δ 8.97 (d, J = 2.4 Hz, 1H), 8.25 (d, J = 2.4 Hz, 1H), 4.82 (t, J = 8.3 Hz, 2H), 3.36 (t, J = 8.6 Hz,2H).
$^{13}$C NMR ($CDCl_3$) δ 172.4, 145.6, 140.0, 128.9, 121.2, 71.1, 27.4.
HRMS Calcd. for $C_7H_6N_2O_3$ ($M^+$): 166.0378. Found: 166.0378.
Anal. Calcd. for $C_7H_6N_2O_3$ (166.13): C, 50.60; H, 3.64; N, 16.86. Found: C, 50.68; H, 3.67; N, 17.31.

Cyclization of 2-(3-butynyloxy)-4,6-dimethylpyrimidine (**1c**) to 2,3-dihydro-6-methylfuro[2,3-b]pyridine (**3c**). Column chromatography (eluting first with dichloromethane, then dichloromethane/ether 1:1) of the reaction mixture resulting from **1c** (2.0 mmol) gave **3c** (68%): mp 39-41°C (hexane); $^1$H NMR ($CDCl_3$) δ 7.36 (d, J = 5.0 Hz, 1H), 6.64 (d, J = 5.0 Hz, 1H), 4.60 (t, J = 8.7 Hz, 2H), 3.20 (t, J = 8.4 Hz, 2H), 2.38 (s, 3H).
HRMS Calcd. for $C_8H_9NO$ ($M^+$): 135.0684. Found: 135.0672.
Anal. Calcd. for $C_8H_9NO$ (135.16): C, 71.08; H, 6.71; N, 10.36. Found: C, 70.71; H, 6.84; N, 10.50.

Cyclization of 2-(3-butynyloxy)-4-methylpyrimidine (**1d**) to **3a** and **3c**. Column chromatography (dichloromethane as eluent, subsequently ether) of the reaction mixture obtained from **1d** (1.3 mmol) gave a mixture of **3a** and **3c** (60%) in the ratio of approximately 1:1.8 as judged by $^1$H NMR.

Cyclization of 2-(3-pentynyloxy)pyrimidine (**1e**) to 2,3-dihydro-4-methylfuro[2,3-b]pyridine (**3e**). Column chromatography (first eluting with dichloromethane, then dichloromethane/ether 4:1) of the reaction mixture obtained from **1e** (0.7 mmol) gave crude **3e**. Further purification by column chromatography on Merck silica gel 60 (230-400 mesh ASTM) eluting with dichloromethane/ether 3:1 afforded pure **3e** (35%): mp 52-53°C (hexane); $^1$H NMR ($CDCl_3$) δ 7.83 (d, J = 5.1 Hz, 1H), 6.57 (d, J = 5.4 Hz, 1H), 4.57 (t, J = 8.6 Hz, 2H), 3.14 (t, 8.7 Hz, 2H), 2.23 (s, 3H).
Anal. Calcd. for $C_8H_9NO$ (135.16): C, 71.08; H, 6.71; N, 10.36. Found: C, 71.31; H, 6.63; N, 10.22.

Cyclization of 5-nitro-2-(3-pentynyloxy)pyrimidine (**1f**) to 2,3-dihydro-4-methyl-5-nitrofuro[2,3-b]pyridine (**3f**). Column chromatography (dichloromethane as eluent, then ether) of the crude reaction mixture obtained from **1f** (0.4 mmol) gave **3f** (83%): mp 101-102°C (hexane/toluene); $^1$H NMR ($CDCl_3$) δ 8.80 (s, 1H), 4.80 (t, J = 8.7 Hz, 2H), 3.30 (qt, $J_1$ = 8.7 Hz, $J_2$ = 0.7 Hz, 2H), 2.53 (t, J = 0.7 Hz, 3H).
Anal. Calcd. for $C_8H_8N_2O_3$ (180.16): C, 53.41; H, 4.50; N, 15.59. Found: C, 53.33; H, 4.47; N, 15.55.

Cyclization of 2-(N-acetyl-3-butynylamino)pyrimidine (**4c**) to 1-acetyl-2,3-dihydropyrrolo[2,3-b]pyridine (**6c**). Column chromatography (eluting first with dichloromethane, then ether) of the reaction mixture obtained from **4c** (0.6 mmol) yielded **6c** (85%): mp 123-124°C (hexane/toluene); $^1$H NMR ($CDCl_3$) δ 8.12 (d, J = 4.5 Hz, 1H), 7.45 (d, J = 7.5 Hz, 1H), 6.86 (dd, $J_1$ = 7.2 Hz, $J_2$ = 4.8 Hz, 1H), 4.10 (t, J = 8.7 Hz, 2H), 3.04 (t, J = 8.4 Hz, 2H), 2.67 (s, 3H).
MS: m/e 162 ($M^+$).
Anal. Calcd. for $C_9H_{10}N_2O$ (162.19): C, 66.65; H, 6.22; N, 17.27. Found: C, 66.79; H, 6.41; N, 17.41.

Cyclization of 2-(N-acetyl-3-butynylamino)-5-nitropyrimidine (**4d**) to 1-acetyl-2,3-dihydro-5-nitropyrrolo[2,3-b]pyridine (**6d**). Column chromatography (eluting first with dichloromethane, then dichloromethane/ether 9:1) of the reaction mixture obtained from **4d** (0.4 mmol) yielded **6d** (87%): mp 186°C (hexane/toluene); $^1$H NMR ($CDCl_3$) δ 9.03 (d, J = 2.4 Hz, 1H), 8.20 (dt, $J_1$ = 2.4 Hz, $J_2$ = 1.5 Hz, 1H), 4.22 (t, J = 8.6 Hz, 2H), 3.17 (t, J = 8.7 Hz, 2H), 2.69 (s, 3H).
MS: m/e 207 ($M^+$).
Anal. Calcd. for $C_9H_9N_3O_3$ (207.19): C, 52.17; H, 4.38; N, 20.28. Found: C, 52.20; H, 4.35; N, 20.49.

Cyclization of 2-(3-butynylthio)pyrimidine (**7a**) to 2,3-dihydrothieno[2,3-b]pyridine (**9a**). Column chromatography (eluting first with dichloromethane, then dichloromethane/ether 9:1) of the reaction mixture obtained from **7a** (1.2 mmol) yielded **9a** (57%) as a pale brown oil, $^1$H NMR ($CDCl_3$) spectrum identical with that reported in the literature [5a].
MS: m/e 137 ($M^+$).
Anal. Calcd. for $C_{13}H_{10}N_4O_7S$ (366.31; picrate: mp 103-105°C): C, 42.62; H, 2.75; N, 15.30. Found: C, 42.66; H, 2.73; N, 15.39.

Cyclization of 2-(3-butynylthio)-5-nitropyrimidine (**7b**) to 2,3-dihydro-5-nitrothieno[2,3-b]pyridine (**9b**). Column chromatography (eluting first with dichloromethane, then ether) of the reaction mixture obtained from **7b** (1.2 mmol) yielded **9b** (75%): mp 131-132°C (hexane/toluene); $^1$H NMR ($CDCl_3$) δ 9.02 (d, J = 2.4 Hz, 1H), 8.07 (d, J = 2.1 Hz, 1H), 3.69-3.25 (mc, 4H).
MS: m/e 182 ($M^+$).
Anal. Calcd. for $C_7H_6N_2O_2S$ (182.20): C, 46.14; H, 3.32; N, 15.38. Found: C, 46.29; H, 3.28: N, 15.27.

Cyclization of 2-(3-butynylthio)-4,6-dimethylpyrimidine (**7c**) to 2,3-dihydro-6-methylthieno[2,3-b]pyridine (**9c**). Column chromatography (eluens dichloromethane, then ether) of the reaction mixture obtained from **7c** (0.7 mmol) yielded **9c** (51%) as a pale brown oil; $^1$H NMR ($CDCl_3$) δ 7.27 (d, J = 7.5 Hz, 1H), 6.76 (d, J = 7.5 Hz, 1H), 3.40-3.07 (mc, 4H), 2.42 (s, 3H).
HRMS Calcd. for $C_8H_9NS$ ($M^+$): 151.0456. Found 151.0450.

Cyclization of 2-(3-butynylthio)-4-methylpyrimidine (**7d**) to **9a** and **9c**. Column chromatography (dichloromethane as eluent, then ether) of the reaction mixture obtained from **7d** (0.8 mmol) gave a mixture of **9a** and **9b** (69%) in the ratio of approximately 1:2.2 as established by $^1$H NMR.

Cyclization of 2-(3-butynylthio)-5-phenylpyrimidine (**7e**) to 2,3-dihydro-5-phenylthieno[2,3-b]pyridine (**9e**). The reaction mixture obtained from **7e** (0.8 mmol) was chromatographed twice using silica gel (first time eluting with dichloromethane, followed by dichloromethane/ether 2:1, second time eluting with dichloromethane/ether 9:1) to give **9e** (75%): mp 101-102°C (hexane); $^1$H NMR ($CDCl_3$) δ 8.41 (d, J = 2.1 Hz, 1H), 7.67-7.29 (m, 6H), 3.62-3.29 (mc, 4H).
$^{13}$C NMR ($CDCl_3$) δ 165.2, 146.8, 137.9, 134.0, 132.4, 129.8, 129.0, 127.7, 126.8, 33.6, 31.3.
Anal. Calcd. for $C_{13}H_{11}NS$ (213.29): C, 73.31; H, 5.30; N, 6.52. Found: C, 73.20; H, 5.19; N, 6.56.

Cyclization of 2-(3-butynylsulfonyl)pyrimidine (**10b**) to 1,1-dioxo-2,3-dihydrothieno[2,3-b]pyridine (**11b**). Column chromatography (eluting first with dichloromethane, then dichloromethane/methanol 9:1) of the reaction mixture obtained from **10b** (1.1 mmol) yielded **11b** (63%): mp 109 °C (hexane/chloroform) (lit. [8]: 109-111 °C); $^1$H NMR spectrum identical with the reported spectrum [8].
$^{13}$C NMR ($CDCl_3$) δ 156.3, 150.8, 136.3, 131.3, 127.1, 48.5, 22.3.

Cyclization of 5-(3-butynylthio)-2-phenylpyrimidine (**12a**) to 2,3-dihydro-5-phenylthieno[2,3-c]pyridine (**14a**). Column chromatography (dichloromethane as eluent) of the reaction mixture obtained from **12** (0.6 mmol) gave **14** (85%): mp 82-83 °C (hexane/toluene); $^1$H NMR ($CDCl_3$) δ 8.51 (s, 1H), 8.03-7.80 (m, 2H), 7.50 (s, 1H), 7.48-7.29 (m, 3H), 3.50-3.12 (mc, 4H).
$^{13}$C NMR ($CDCl_3$) δ 153.7, 150.2, 142.5, 139.3, 137.8, 128.7, 128.5, 126.6, 116.4, 35.9, 33.2.
MS: m/e 213 ($M^+$).
Anal. Calcd. for $C_{13}H_{11}NS$ (213.29): C, 73.20; H, 5.20; N, 6.57. Found: C, 73.36; H, 5.32; N, 6.59.

Cyclization of 2-(acetylamino)-5-(3-butynylthio)pyrimidine (**12c**) to 5-(acetylamino)-2,3-dihydrothieno [2,3-c]pyridine (**14c**). Column chromatography (eluting first with dichloromethane, then dichloromethane/ether 1:1) of the reaction mixture obtained from **12c** (0.2 mmol) gave **14c** (64%) as a pale yellow solid: mp 155-157°C (hexane/toluene); $^1$H NMR ($CDCl_3$) δ 8.90 (br s, 1H), 8.08 (s, 1H), 8.01 (s, 1H), 3.33 (mc, 4H), 2.16 (s, 3H).
Anal. Calcd. for $C_9H_{10}N_2OS$ (194.26): C, 55.65; H, 5.19; N, 14.42. Found: C, 55.61; H, 5.05; N, 14.51.

Cyclization of 5-(3-butynylthio)-2-(diacetylamino)pyrimidine (**12d**) to 5-(acetylamino)-2,3-dihydrothieno [2,3-c]pyridine (**14c**) Work up of the reaction mixture obtained from **12d** (0.2 mmol) as described above gave **14c** (60%), mp and $^1$H NMR ($CDCl_3$) identical with those reported above.

High pressure promoted cyclization of compounds **7a**, **10a** and **10b** into the 2,3-dihydrothieno[2,3-b]pyridines **9a**, **11a** and **11b**, respectively. These experiments were run in a high pressure apparatus equipped with a one wall piston-cylinder for pressures up to 15 kbar [26]. The reactions were performed on a 1 mmole scale in sealed teflon tubes of 0.8 ml. After one night at 55°C and 15 kbar pressure the degree of conversion of **7a**, **10a** and **10b** was determined by $^1$H NMR (see results and discussion). Detailed $^1$H NMR spectra of the cyclization products **9a** [5a], **11a** [6a] and **11b** [8] have been published before.

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