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INTRAMOLECULAR DIELS-ALDER REACTIONS OF 2-(ALKYNYL)PYRIMIDINES AND 2-(ALKYNYL)PYRIDINES

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Pyrimidines **3**, **7** and **13** carrying an ω–alkynyl side-chain $-CR_2(CH_2)_nCH_2C{\equiv}CH$ (R = H, CN; n = 1, 2) at the 2-position undergo intramolecular inverse electron demand Diels-Alder reactions across the C-2 and C-5 positions. Loss of hydrogen cyanide, caused by a retro-Diels-Alder reaction, from the intermediate cycloadducts leads to annelated pyridines **5**, **9** and **15**, respectively. Similarly, from the nitropyridines **16** the 2,3-dihydronitro-1*H*-indenes **18** are obtained. The influence of electronic and steric effects on the rate of cycloaddition is discussed. *Gem*-disubstitution on the chain connecting the reaction centers leads to a considerable rate enhancement for compounds **3** vs **13**. Compounds **7**, having an extra methylene group in the tether between diene and dienophile, react much slower than compounds **3** due to decreased entropic assistance.

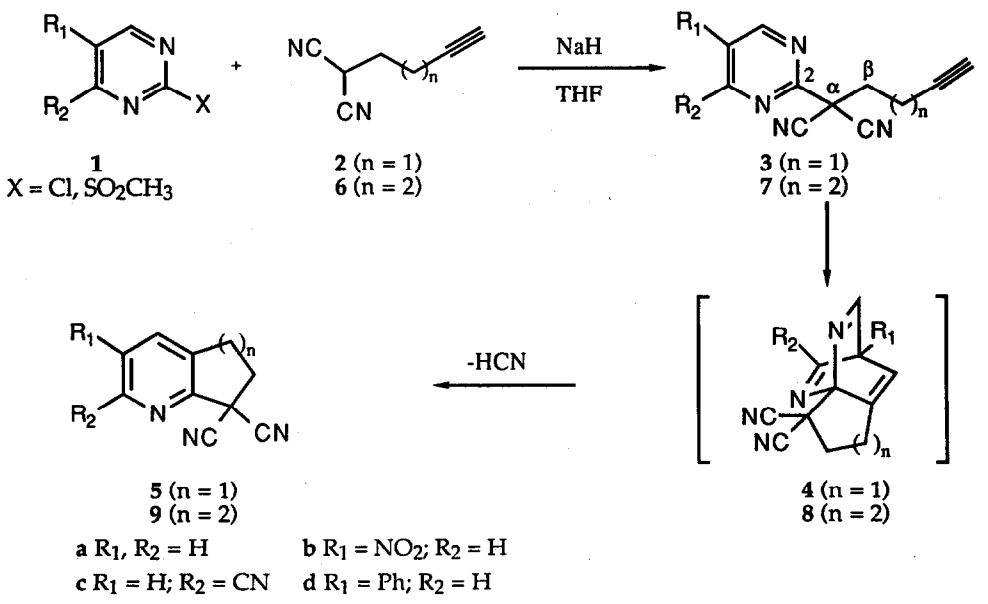
INTRODUCTION

Reports on inverse electron demand Diels-Alder reactions of diazines have until recently been limited to examples[1], which usually require strong electron withdrawing groups on the diazine and electron rich dienophiles[2,3]. However, with the use of the intramolecular version of this reaction the scope has been expanded considerably[4-6]. Recently, we have described some intramolecular Diels-Alder reactions of pyrimidines carrying a dienophilic side-chain attached to the 2 or the 5 position of the pyrimidine via a hetero atom (oxygen, sulfur or nitrogen)[7]. These reactions have led to new syntheses of dihydrofuro[2,3-b]-, dihydrothieno[2,3-b]-, dihydropyrrolo[2,3-b]- and dihydrothieno[2,3-c]pyridines. Due to the electron donating effect of the hetero atom in the dienophilic side-chain the reactivity is low, resulting in a rather high reaction temperature (180-210°C) required to achieve cycloaddition. In order to eliminate this rate-retarding effect of the hetero atom, we also studied intramolecular cyclizations of 2-(1,1-dicyanopent-4-yn-1-yl)pyrimidines having on position 2 a dienophilic side-chain linked to the heterocycle through an aliphatic $C(CN)_2$ group[8]. Due to the relatively low temperatures required to achieve reaction (130°C), we extended this study by investigating the cycloaddition reactions of some 2-(1,1-dicyanohex-5-yn-1-yl)pyrimidines which have an extra CH_2-group in the side-chain and the Diels-Alder reactions of some 2-(1,1-dicyanopent-4-yn-1-yl)pyridines. To asses the influence of the cyano groups we included in our study the cycloaddition of some 2-(pent-4-yn-1-yl)pyrimidines, which have no α–CN groups.

RESULTS AND DISCUSSION

The 2-(1,1-dicyanopent-4-yn-1-yl)pyrimidines **3** and the 2-(1,1-dicyanohex-5-yn-1-yl)pyrimidines **7** were prepared in good yields from the corresponding 2-chloro- or 2-methylsulfonylpyrimidines **1** and the sodium salt of 5,5-dicyanopent-1-yne (**2**) and 6,6-dicyanohex-1-yne (**6**), respectively. By heating of compounds **3** in nitrobenzene at 130°C (140°C for **3d**) under nitrogen an intramolecular cycloaddition took place yielding the corresponding 7,7-dicyano-6,7-dihydro-5*H*-1-pyrindines **5** in excellent yields (Scheme 1; Table). The dicyanohexynylpyrimidines **7** were also found to undergo a Diels-Alder reaction in nitrobenzene, but only at considerably higher temperatures (210°C). Despite the more strenuous conditions the resulting 5,6,7,8-tetrahydroquinolines **15** were obtained in excellent yields. Until now there was only one precedent of an intramolecular inverse electron demand Diels-Alder reaction of a pyrimidine leading to a six-ring annelated pyridine; the reaction occurs in low yield[6a]. Previously, at our laboratory the 3-nitro derivatives of 6,7-dihydro-5*H*-1-pyrindine and 5,6,7,8-tetrahydroquinoline have been prepared by intermolecular inverse electron demand Diels-Alder reactions of 5-nitropyrimidine with five- or six-membered cyclic enamines[3]. The formation of compounds **5** and **9** probably occurs through the intermediacy of cycloadducts **4** and **8**, respectively, which are formed by addition of the acetylene group across the C-2 and C-5 positions of the pyrimidine ring. These cycloaddition products could not be isolated or identified by NMR-spectroscopy due to their fast conversion into **5** and **9**, respectively, by expulsion of hydrogen cyanide.

Scheme 1



1
X = Cl, SO_2CH_3

2 (n = 1)
6 (n = 2)

3 (n = 1)
7 (n = 2)

4 (n = 1)
8 (n = 2)

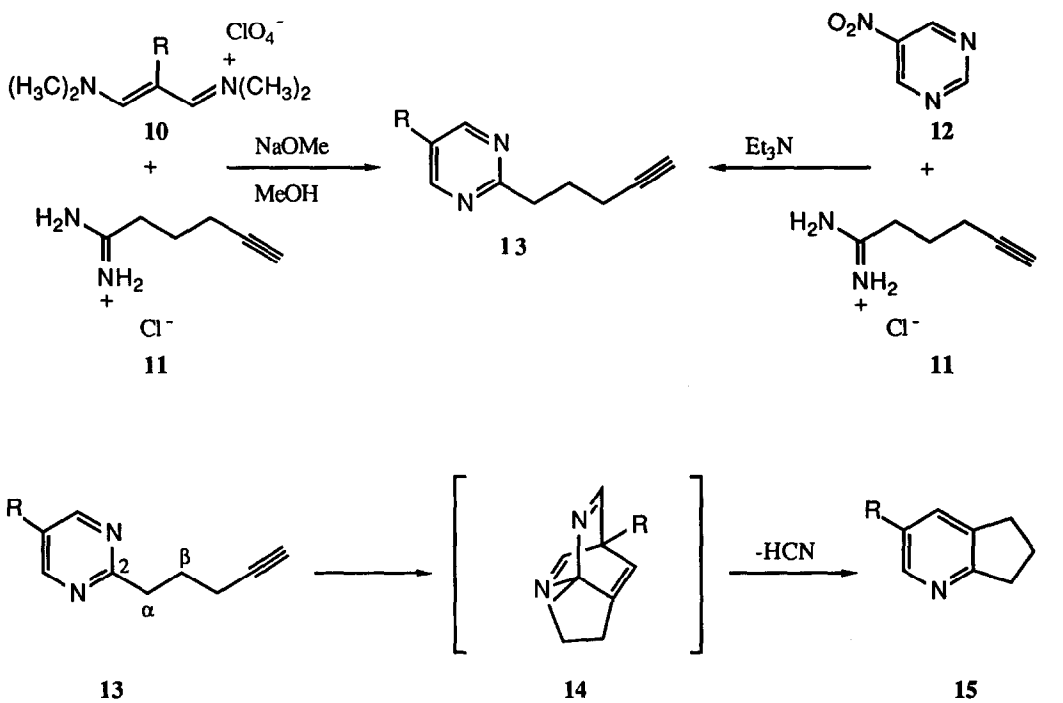
5 (n = 1)
9 (n = 2)

a R_1, R_2 = H **b** R_1 = NO_2; R_2 = H
c R_1 = H; R_2 = CN **d** R_1 = Ph; R_2 = H

As can be seen from the Table introduction of an electron-withdrawing cyano or nitro group in the pyrimidine results in an enhancement of the rate of cycloaddition. This result is in agreement with the inverse electron demand character of the cycloaddition reaction. The presence of the phenyl group at C-5 in **3** is found to lower slightly the reaction rate, probably due to steric hindrance which the dienophilic side-chain experiences in the approach of the pyrimidine ring. The higher temperature required for reaction of the hexynylpyrimidines **7** is due to a decreased entropic assistance caused by the additional methylene group. This phenomenon is general for intramolecular reactions and has for example also been found for cycloaddition reactions of triazines and tetrazines[9].

From all these results it can be concluded that in the compounds **3**, where the dienophile is linked to the pyrimidine via an aliphatic carbon atom ($C(CN)_2$), reactions occur at much lower temperature (about 130°C) than in compounds where the side-chain is linked to the azadiene via an oxygen, sulfur or nitrogen atom (about 210°C)[7].

Scheme 2



a R = H **b** R = Cl **c** R = Ph
d R = *p*-NO_2Ph **e** R = NO_2

In order to get insight in the contribution of the α–CN substituents to this increased reactivity we also examined the reactivity of pyrimidines **13** (Scheme 2) featuring the absence of CN

groups on the carbon atom α to the pyrimidine ring. Compounds **13a-d** were prepared from the appropriate 1-dimethylamino-3-dimethylimonioprop-1-ene salt **10** and hex-5-yn-1-ylamidine hydrochloride (**11**) in good yield. Compound **13e** was prepared from 5-nitropyrimidine (**12**) and the amidine **11** by a ring degenerate transformation reaction developped at our laboratory[10]. The intramolecular cycloaddition of compounds **13** could only be achieved when heated at 210°C in nitrobenzene under an atmosphere of nitrogen (Scheme 2). The resulting 6,7-dihydro-5*H*-1-pyrindines **15** were obtained in good yield (Table).

TABLE Intramolecular Diels-Alder reactions of pyrimidines **3**, **7**, **13** and pyridines **16**. Reaction products and yields.

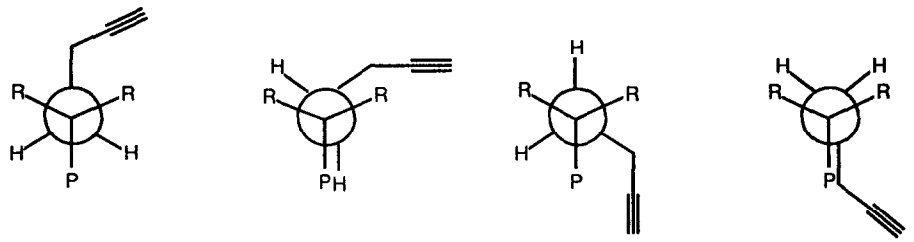
Pyrimidine/Pyridine Starting Compounds	Reaction Conditions Temp. (°C)	Time (h)	Reaction Product	Yield (%)
3a	130	24	**5a**	92
3b	130	6	**5b**	96
3c	130	4	**5c**	94
3d	140	15	**5d**	100
7a	210	96	**17a**	72
7b	210	21	**17b**	93
7c	210	21	**17c**	94
13a	210	2	**9a**	63
13b	210	1.5	**9b**	84
13c	210	3	**9c**	65
13d	210	3	**9d**	81
13e	210	0.5	**9e**	58
16a	180	10	**19a**	82
16b	210	3	**19b**	72
16c	210	12	**19c**	75

Only a slight influence on the reaction rate is observed for the substituents on C-5 of the pyrimidines. The electron withdrawing nitro and chloro substituents increase the reaction rate, whereas the phenyl and *p*-nitrophenyl substituents decrease the reaction rate due to steric hindrance.

The temperature required for reaction of compounds **13** is comparable to the temperature required for compounds where the dienophile is linked to the azadiene through an ether, thioether or amine bond[7]. Therefore, the conclusion seems justified that the much higher reactivity of the α,α–dicyanoalkynylpyrimidines **3** cannot solely be explained by an electronic effect. We ascribe the remarkable difference in cycloaddition rate between compounds **3** and **13**

to the so-called "*gem*-dimethyl" effect[11], in this case due to the two cyano substituents. This acceleration may be due to reduction of the internal C_2-C_α-C_β angle in **3** as compared to the same bond angle in compounds **13** (the so-called "Thorpe-Ingold" effect[12]). Thus, in compounds **3** the reacting centers are forced in closer proximity, resulting in added entropic assistence and, consequently, rate enhancement in the cycloaddition reaction. More recently, however, evidence has been presented that the rate increase on substitution can also be explained by a higher population of reactive *syn* rotamers due to substituents on the chain connecting the reaction centers[13]. This has recently been demonstrated for intramolecular Diels-Alder reactions of α,α-disubstituted furfuryl methyl fumarates[14]. Examination of the Newman projections about the carbon atoms α and β to the pyrimidine ring (Scheme 3) shows that the presence of the geminal substituents in **3** (R = CN) will affect the population distribution of the four presented rotational conformations when compared to **13** (R = H). Certainly, for both R = H and R = CN rotamer (A) is the most highly populated. However, due to the geminal CN substituents, rotamers (C) and especially (D) will have a much higher relative population in **3** than in **13**. The result is that on the average in time the dienophile is more in the vicinity of the azadiene in **3** than in **13** and hence a higher reactivity for the intramolecular Diels-Alder reaction of **3** versus **13** is observed.

Scheme 3



(A) (B) (C) (D)

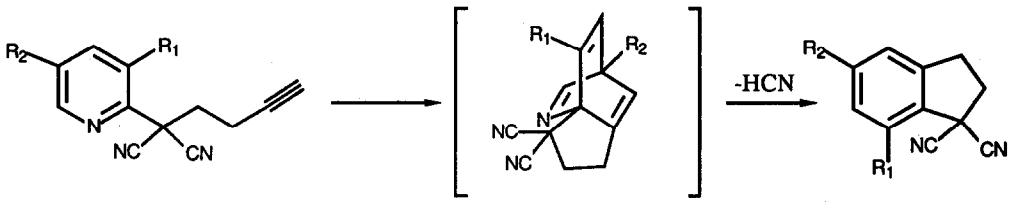
3 R = CN; **13** R = H.

P = pyrimidine.

The ease of inverse electron demand Diels-Alder reactions of pyrimidines **3** (and **7**) with a 1,1-dicyanoalkynyl side-chain induced us to study the cycloaddition reaction of the less electron deficient pyridines **16** (Scheme 4). These compounds were prepared in good yield from the corresponding 2-chloropyridines and the sodium salt of 5,5-dicyanopent-1-yne. We found that by heating of 2-(1,1-dicyanopent-4-yn-1-yl)-3,5-dinitropyridine (**16a**) for ten hours in nitrobenzene at 180°C under nitrogen 1,1-dicyano-2,3-dihydro-5,7-dinitro-1*H*-indene (**18a**) was obtained in good yield. The formation of this compound probably also occurs through the intermediacy of a cycloaddition product, i.e. **17a**, which can easily aromatize after expulsion of hydrogen cyanide.

The presence of two electron-withdrawing nitro groups in the pyridine ring is not a structural requirement for the occurrence of the cycloaddition. When the *mono* nitro compounds

Scheme 4



16 **17** **18**

a $R_1, R_2 = NO_2$ **b** $R_1 = NO_2, R_2 = H$
c $R_1 = H, R_2 = NO_2$

16b and **16c** were heated at 210°C in nitrobenzene, in good yields 1,1-dicyano-2,3-dihydro-7-nitro-1*H*-indene (**18b**) and 1,1-dicyano-2,3-dihydro-5-nitro-1*H*-indene (**18c**), respectively, are obtained (see Table).

The cycloaddition reactions of **16b** and **16c** require a higher temperature (210°C) than **16a** (180°C). This result is certainly due to the lower π-electron deficiency of the pyridine ring in **16b,c**. Furthermore, the fact that the reaction of **16b** to **18b** was complete in about 3 hours, whereas the reaction of **16c** to **18c** took about 12 hours, indicates that the formation of cycloadduct **17c** is hindered by the presence of the nitro group at the C-5 position of the pyridine. All these findings clearly indicate the inverse electron demand nature of the cycloaddition reaction. Recently, another example of an intramolecular Diels-Alder reaction of a pyridine derivative has been published[15].

In conclusion, intramolecular inverse electron demand Diels-Alder reactions of appropriately substituted pyrimidines lead to 6,7-dihydro-5*H*-1-pyrindines and 5,6,7,8-tetrahydroquinolines. Similarly, appropriately substituted nitropyridines lead to 2,3-dihydronitro-1*H*-indenes. Our studies indicate that steric effects play a more important role in governing the rate of cycloaddition than electronic effects.

EXPERIMENTAL SECTION

Melting points are uncorrected. ^1H NMR spectra were recorded on a Varian EM 390 spectrometer. Chemical shifts are determined in ppm downfield from TMS. Mass spectral data were obtained from 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-(1,1-dicyanopent-4-yn-1-yl)pyrimidines (**3**) and 2-(1,1-dicyanohex-5-yn-1-yl)pyrimidines (**7**).

To a stirred suspension of sodium hydride (2.20 mmole [1.1 eq], 80% oil dispersion) in anhydrous tetrahydrofuran (10 ml) at room temperature was added 5,5-dicyanopent-1-yne[16] (**2**; 2.20 mmole; 1.1 eq; for compounds **3**) or 6,6-dicyanohex-1-yne[16] (**6**; 2.20 mmole; 1.1 eq; for compounds **7**). After the initial effervescence had subsided, the appropriate 2-chloro- or 2-

methylsulfonylpyrimidine **1** (2.00 mmole) was added as a solid in one portion at room temperature and the reaction mixture was stirred at room temperature or under reflux for the appropriate time. Water was then added and the aqueous layer was extracted twice with dichloromethane. The organic layers were washed with water, dried ($MgSO_4$) and the solvent evaporated under reduced pressure. Column chromatography (eluting with dichloromethane) of the residue afforded the desired products.

2-(1,1-Dicyanopent-4-yn-1-yl)pyrimidine (**3a**). From 2-chloropyrimidine and 5,5-dicyanopent-1-yne[16]. Reflux time: 4 hours. Obtained as a colourless oil (64%). ^1H NMR ($CDCl_3$) δ 8.89 (d, J = 5.3 Hz, 2H), 7.50 (t, J = 5.3 Hz, 1H), 2.6 (mc, 4H), 1.98 (t, J = 2.5 Hz, 1H).
HRMS Calcd. for $C_{11}H_8N_4$: 196.0749. Found: 196.0745.

2-(1,1-Dicyanopent-4-yn-1-yl)-5-nitropyrimidine (**3b**). From 2-chloro-5-nitropyrimidine[17] and 5,5-dicyanopent-1-yne. Reaction time: 0.5 hour at room temperature. Obtained as a pale yellow solid (88%): m.p. 99-100.5°C (hexanes/toluene); ^1H NMR ($CDCl_3$) δ 9.62 (s, 2H), 2.9-2.5 (mc, 4H), 1.93 (t, J = 2.4 Hz, 1H). MS: m/e 241 (M^+).
Anal. Calcd. for $C_{11}H_7N_5O_2$ (241.21): C, 54.77; H, 2.93; N, 29.04. Found: C, 54.64; H, 2.92; N, 29.34.

4-Cyano-2-(1,1-dicyanopent-4-yn-1-yl)pyrimidine (**3c**). From 2-chloro-4-cyanopyrimidine[18] and 5,5-dicyanopent-1-yne. Reaction time: 1 hour at room temperature. Obtained as a colourless solid (91%): m.p. 90-91°C (hexanes/chloroform); ^1H NMR ($CDCl_3$) δ 9.17 (d, J = 5.4 Hz, 1H), 7.86 (d, J = 5.4 Hz, 1H), 2.7 (mc, 4H), 1.93 (t, J = 2.4 Hz, 1H). MS: m/e 221 (M^+).
Anal. Calcd. for $C_{12}H_7N_5$ (221.22): C, 65.15; H, 3.19; N, 31.66. Found: C, 64.80; H, 3.04; N, 31.93.

2-(1,1-Dicyanopent-4-yn-1-yl)-5-phenylpyrimidine (**3d**). From 2-methylsulfonyl-5-phenylpyrimidine[19] and 5,5-dicyanopent-1-yne. Reflux time: 2 hours. Column chromatography (eluting with dichloromethane/petroleum ether 5:1) gave **3d** (91%) as a colourless solid: m.p. 97-98°C (hexanes/toluene); ^1H NMR ($CDCl_3$) δ 9.00 (s, 2H), 7.55 (mc, 5H), 2.7 (mc, 4H), 1.97 (t, J = 2.4 Hz, 1H). MS: m/e 272 (M^+).
Anal. Calcd. for $C_{17}H_{12}N_4$ (272.30): C, 74.97; H, 4.44; N, 20.57. Found: C, 74.93; H, 4.44; N, 20.64.

2-(1,1-Dicyanohex-5-yn-1-yl)pyrimidine (**7a**). From 2-chloropyrimidine and 6,6-dicyanohex-1-yne[16]. Reflux time: 5 hours. Obtained as a colourless solid (60%): m.p. 83.5-84.5°C (hexanes/chloroform); ^1H NMR ($CDCl_3$) δ 8.90 (d, J = 4.8 Hz, 2H), 7.47 (t, J = 5.1 Hz, 1H), 2.60 (mc, 2H), 2.34 (dt, J_1 = 6.9 Hz, J_2 = 2.4 Hz, 2H), 2.02 (t, J = 2.4 Hz, 1H), 1.95 (mc, 2H). MS: m/e 210 (M^+).
Anal. Calcd. for $C_{12}H_{10}N_4$ (210.23): C, 68.55; H, 4.79; N, 26.65. Found: C, 68.41; H, 4.77; N, 26.53.

2-(1,1-Dicyanohex-5-yn-1-yl)-5-nitropyrimidine (**7b**). From 2-chloro-5-nitropyrimidine[17] and 6,6-dicyanohex-1-yne. Reaction time: 0.5 hour at room temperature. Obtained as a pale yellow solid (87%): m.p. 102-103°C (hexanes/chloroform); ^1H NMR ($CDCl_3$) δ 9.62 (s, 2H), 2.60 (mc, 2H), 2.33 (dt, J_1 = 6.3 Hz, J_2 = 2.4 Hz, 2H), 2.03 (t, J = 2.4 Hz, 1H), 1.85 (mc, 2H). MS: m/e 255 (M^+).
Anal. Calcd. for $C_{12}H_9N_5O_2$ (255.23): C, 56.47; H, 3.55; N, 27.44. Found: C, 56.47; H, 3.55; N, 27.71.

4-Cyano-2-(1,1-dicyanohex-5-yn-1-yl)pyrimidine (**7c**). From 2-chloro-4-cyanopyrimidine[18] and 6,6-dicyanohex-1-yne. Reaction time: 0.5 hour at room temperature. Obtained as a colourless solid (90%): m.p. 94-95°C (hexanes/chloroform); ^1H NMR ($CDCl_3$) δ 9.18 (d, J = 5.1 Hz, 1H), 7.85 (d, J = 5.1 Hz, 1H), 2.62 (mc, 2H), 2.37 (dt, J_1 = 6.3 Hz, J_2 = 2.7 Hz, 2H), 2.03 (t, J = 2.4 Hz, 1H), 1.9 (mc, 2H). MS: m/e 235 (M^+).
Anal. Calcd. for $C_{13}H_9N_5$ (235.24): C, 66.37; H, 3.86; N, 29.77. Found: C, 66.07; H, 3.79; N, 29.93.

2-(Pent-4-yn-1-yl)pyrimidine (**13a**). To a stirred suspension of 1-dimethylamino-3-dimethylimonioprop-1-ene perchlorate[20] (**10a**; 521 mg, 2.3 mmole) and hex-5-yn-1-ylamidine

hydrochloride[21] (**11**; 505 mg, 1.5 eq) in methanol (10 ml) 2M methanolic sodium methoxide (1.8 ml, 1.5 eq) was added dropwise at room temperature. After 0.5 hour another 1.2 ml (1 eq) of sodium methoxide solution was added and the reaction mixture refluxed for two hours. After cooling methanol was evaporated and the residue treated with water (20 ml) and extracted with dichloromethane (2 x 20 ml). The combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure to afford crude **13a** which was purified by column chromatography (eluting with ether). It was obtained as a clear colourless oil (233 mg, 69%); ^1H NMR ($CDCl_3$) δ 8.64 (d, J = 4.8 Hz, 2H), 7.10 (t, J = 4.9 Hz, 1H), 3.08 (t, J = 7.1 Hz, 2H), 2.5-2.0 (mc, 4H), 1.95 (t, J = 2.7 Hz, 1H).
HRMS Calcd. for $C_9H_{10}N_2$ (M^+): 146.0844. Found: 146.0830.

5-Chloro-2-(pent-4-yn-1-yl)pyrimidine (**13b**). This compound was prepared from 2-chloro-1-dimethylamino-3-dimethylimonioprop-1-ene perchlorate[20] (**10b**; 600 mg, 2.3 mmole) and hex-5-yn-1-ylamidine hydrochloride (**11**; 505 mg, 1.5 eq) in the same way as described for **13a**. It was obtained as a clear colourless oil (259 mg, 67%) after column chromatography (ether as eluent); ^1H NMR ($CDCl_3$) δ 8.60 (s, 2H), 3.07 (t, J = 7.2 Hz, 2H), 2.5-2.0 (mc, 4H), 1.96 (t, J = 2.6 Hz, 1H).
HRMS Calcd. for $C_9H_9ClN_2$ (M^+): 180.0454. Found: 180.0449.

2-(Pent-4-yn-1-yl)-5-phenylpyrimidine (**13c**). This compound was prepared from 1-dimethylamino-3-dimethylimonio-2-phenylprop-1-ene perchlorate[20] (**10c**; 696 mg, 2.3 mmole) and hex-5-yn-1-ylamidine hydrochloride (**11**, 505 mg, 1.5 eq) as described for **13a**. It was obtained as a colourless solid (485 mg, 95%) after column chromatography (eluting with ether): m.p. 41-43°C; ^1H NMR ($CDCl_3$) δ 8.86 (s, 2H), 7.49 (mc, 5H), 3.13 (t, J = 7.2 Hz, 2H), 2.5-2.0 (mc, 4H), 1.97 (t, J = 2.4 Hz, 1H). MS: m/e 222 (M^+).
Anal. Calcd. for $C_{15}H_{14}N_2$ (222.28): C, 81.04; H, 6.34; N, 12.60. Found: C, 81.26; H, 6.57; N, 12.70.

5-*p*-Nitrophenyl-2-(pent-4-yn-1-yl)pyrimidine (**13d**). This compound was prepared from 1-dimethylamino-3-dimethylimonio-2-*p*-nitrophenylprop-1-ene perchlorate[20] (**10d**; 799 mg; 2.3 mmole) and hex-5-yn-1-ylamidine hydrochloride (**11**; 505 mg; 1.5 eq) as described for **13a**. It was obtained as a pale yellow solid (510 mg; 83%) after column chromatography (eluting with dichloromethane/ether 9:1): m.p. 129-130°C (hexanes/toluene); ^1H NMR ($CDCl_3$) δ 8.92 (s, 2H), 8.36 (d, J = 8.7 Hz, 2H), 7.75 (d, J = 8.9 Hz, 2H), 3.19 (t, J = 7.1 Hz, 2H), 2.5-2.0 (mc, 4H), 1.99 (t, J = 2.4 Hz, 1H). MS: m/e 267 (M^+).
Anal. Calcd. for $C_{15}H_{13}N_3O_2$ (267.29): C, 67.41; H, 4.90; N, 15.72. Found: C, 67.57 ; H, 4.99 ; N, 16.04.

5-Nitro-2-(pent-4-yn-1-yl)pyrimidine (**13e**). To a stirred mixture of 5-nitropyrimidine[22] (**12**; 500 mg, 4.0 mmole) and hex-5-yn-1-ylamidine hydrochloride (**11**; 590 mg, 4.0 mmole) in absolute ethanol (5 ml) was added triethylamine (1.2 ml). The resulting solution was heated under reflux for 2.5 hour. After this time the solvent was removed under reduced pressure. The residue was treated with water (20 ml) and extracted with dichloromethane (2 x 20 ml). The combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure to afford crude **13e** which was purified by column chromatography (eluting with dichloromethane). It was obtained as a yellow oil (480 mg; 63%); ^1H NMR ($CDCl_3$) δ 9.40 (s, 2H), 3.24 (t, J = 7.1 Hz, 2H), 2.5 - 2.0 (mc, 4H), 1.98 (t, J = 2.6 Hz, 1H)
HRMS Calcd. for $C_9H_9N_3O_2$: 191.0695. Found: 191.0694.

General procedure for the synthesis of 2-(1,1-dicyanopent-4-yn-1-yl)nitropyridines **16**.
To a stirred suspension of sodium hydride (5.5 mmole, 80% oil dispersion) in anhydrous tetrahydrofuran (10 ml) at room temperature was added 5,5-dicyanopent-1-yne[16] (**2**, 5.5 mmole). After the initial effervescence had subsided, a solution of the appropriate 2-chloronitropyridine (5.0 mmole) in anhydrous tetrahydrofuran (10 ml) was added in one portion at room temperature and the reaction mixture stirred for the time given. Water was then added and the aqueous layer extracted twice with dichloromethane. The organic layers were washed with

water, dried ($MgSO_4$) and the solvent evaporated under reduced pressure. Column chromatography (eluting with the appropriate solvent system) of the residue afforded the desired products **16**.

2-(1,1-Dicyanopent-4-yn-1-yl)-3,5-dinitropyridine (**16a**). From 2-chloro-3,5-dinitropyridine[23]. Reaction time: 0.5 hour. After column chromatography (eluting with petroleum ether 40-60 / ether 2:1) **16a** was obtained as a yellow solid (58%): m.p. 109-110°C (chloroform/hexane); ^1H NMR ($CDCl_3$) δ 9.72 (d, J = 2.4 Hz, 1H), 9.23 (d, J = 2.4 Hz, 1H), 3.1-2.5 (mc, 4H), 2.02 (t, J = 2.5 Hz, 1H). MS: m/e 285 (M^+).
Anal. Calcd. for $C_{12}H_7N_5O_4$ (285.22): C, 50.53; H, 2.47; N, 24.56. Found: C, 50.25; H, 2.41; N, 24.61.

2-(1,1-Dicyanopent-4-yn-1-yl)-3-nitropyridine (**16b**). From 2-chloro-3-nitropyridine[23,24]. Reaction time: 2 hours. After column chromatography (eluting with petroleum ether 40-60 / ether 1:1) **16b** was obtained as a yellow oil (48%); ^1H NMR ($CDCl_3$) δ 8.96 (dd, J_1 = 4.5 Hz, J_2 = 1.5 Hz, 1H), 8.53 (dd, J_1 = 8.4 Hz, J_2 = 1.5 Hz, 1H), 7.79 (dd, J_1 = 4.5 Hz, J_2 = 8.4 Hz, 1H), 3.1-2.8 (mc, 2H), 2.8-2.5 (mc, 2H), 2.03 (t, J = 2.4 Hz, 1H).
HRMS Calcd. for $C_{12}H_8N_4O_2$: 240.0656. Found: 240.0647.

2-(1,1-Dicyanopent-4-yn-1-yl)-5-nitropyridine (**16c**). From 2-chloro-5-nitropyridine[23,24]. Reaction time: 2 hours. After column chromatography (eluting with petroleum ether 40-60 /ether 2:1) **16c** was obtained as a yellow solid (69%): m.p. 71-72°C (chloroform/hexane); ^1H NMR ($CDCl_3$) δ 9.52 (d, J = 2.4 Hz, 1H), 8.70 (dd, J_1 = 8.7 Hz, J_2 = 2.4 Hz, 1H), 7.99 (d, J = 8.7 Hz, 1H), 2.9-2.4 (mc, 4H), 2.03 (t, J = 2.4 Hz, 1H). MS: m/e 240 (M^+).
Anal. Calcd. for $C_{12}H_8N_4O_2$ (240.22): C, 60.00; H, 3.36; N, 23.33. Found: C, 59.72; H, 3.31; N, 23.67.

General procedure for the intramolecular Diels-Alder reaction of compounds **3**, **7**, **13** and **16**.
A stirred solution of the appropriate pyrimidine (or pyridine) derivative in nitrobenzene (100 mg solute/1 ml solvent) under nitrogen was heated under conditions mentioned in the Table. The temperature was kept constant within 1°C. The disappearance of starting material was followed by thin layer chromatography and/or ^1H NMR spectroscopy. The resultant solution was chromatographed over silica gel; elution with the appropriate solvent system yielded the reaction products **5**, **9**, **15** and **18**.

7,7-Dicyano-6,7-dihydro-5*H*-1-pyrindine (**5a**). Column chromatography (eluting first with dichloromethane, then dichloromethane/ether 5:1) of the reaction mixture obtained from **3a** (0.6 mmole) afforded **5a** (92%) as a colourless solid: m.p. 108-110°C (hexanes/toluene); ^1H NMR ($CDCl_3$) δ 8.60 (d, J = 4.8 Hz, 1H), 7.75 (d, J = 7.8 Hz, 1H), 7.38 (dd, J_1 = 7.8 Hz, J_2 = 4.8 Hz, 1H), 3.24 (mc, 2H), 2.96 (mc, 2H). MS: m/e 169 (M^+).
Anal. Calcd. for $C_{10}H_7N_3$ (169.18): C, 70.99; H, 4.17; N, 24.84. Found: C, 70.67; H, 4.09; N, 25.10.

7,7-Dicyano-6,7-dihydro-3-nitro-5*H*-1-pyrindine (**5b**). Column chromatography (eluting with dichloromethane) of the reaction mixture obtained from **3b** (0.7 mmole) afforded **5b** (96%) as a pale yellow solid: m.p. 106.5-107.5°C (hexanes/toluene); ^1H NMR ($CDCl_3$) δ 9.42 (d, J = 2.4 Hz, 1H), 8.53 (td, J_1 = 2.4 Hz, J_2 = 1.1 Hz, 1H), 3.35 (t, J = 6.4 Hz, 2H), 3.10 (mc, 2H). MS: m/e 214 (M^+).
Anal. Calcd. for $C_{10}H_6N_4O_2$ (214.18): C, 56.07; H, 2.82; N, 26.16. Found: C, 55.84; H, 2.75; N, 26.33.

2,7,7-Tricyano-6,7-dihydro-5*H*-1-pyrindine (**5c**). Column chromatography (first eluting with dichloromethane to remove nitrobenzene, then dichloromethane/ether 1:1) of the reaction mixture obtained from **3c** (0.7 mmole) gave **5c** (94%) as a slightly brownish solid: m.p. 152-153°C (hexanes/chloroform); ^1H NMR ($CDCl_3$) δ 7.97 (td, J_1 = 7.8 Hz, J_2 = 0.9 Hz, 1H), 7.81 (d, J = 7.8 Hz, 1H), 3.34 (mc, 2H), 3.04 (mc, 2H). MS: m/e 194 (M^+).
Anal. Calcd. for $C_{11}H_6N_4$ (194.19): C, 68.03; H, 3.11; N, 28.85. Found: C, 68.23; H, 3.04; N, 29.05.

7,7-Dicyano-6,7-dihydro-3-phenyl-5*H*-1-pyrindine (**5d**). Column chromatography (eluting with dichloromethane/ether 9:1) of the reaction mixture obtained from **3d** (1.0 mmole) gave **5d** (100%) as a colourless solid: m.p. 134-135°C (hexanes/toluene); ^{1}H NMR ($CDCl_3$) δ 8.74 (br s, 1H), 7.84 (t, J = 1.0 Hz, 1H), 7.50 (mc, 5H), 3.27 (br t, J = 6.1 Hz, 2H), 3.00 (mc, 2H). MS: m/e 245 (M^+).
Anal. Calcd. for $C_{16}H_{11}N_3$ (245.27): C, 78.34; H, 4.52; N, 17.13. Found: C, 78.10; H, 4.43; N, 17.01.

8,8-Dicyano-5,6,7,8-tetrahydroquinoline (**9a**). Column chromatography (eluting with dichloromethane/ether 19:1) of the reaction mixture obtained from **7a** (0.7 mmole) gave **9a** (72%) as a colourless solid: m.p. 98-99°C (hexanes/toluene); ^{1}H NMR ($CDCl_3$) δ 8.59 (dd, J_1 = 4.5 Hz, J_2 = 1.5 Hz, 1H), 7.61 (dd, J_1 = 7.8 Hz, J_2 = 1.5 Hz, 1H), 7.33 (dd, J_1 = 7.8 Hz, J_2 = 4.5 Hz, 1H), 2.93 (br t, J = 6.2 Hz, 2H), 2.64 (mc, 2H), 2.15 (mc, 2H). MS: m/e 183 (M^+).
Anal. Calcd. for $C_{11}H_9N_3$ (183.21): C, 72.11; H, 4.95; N, 22.94. Found: C, 72.28; H, 4.93; N, 23.01.

8,8-Dicyano-5,6,7,8-tetrahydro-3-nitroquinoline (**9b**). Column chromatography (eluting with dichloromethane) of the reaction mixture obtained from **7b** (0.6 mmole) afforded **9b** (93%) as a pale yellow solid: m.p. 120-121°C (hexanes/chloroform); ^{1}H NMR ($CDCl_3$) δ 9.35 (d, J = 2.4 Hz, 1H), 8.42 (d, J = 2.4 Hz, 1H), 3.10 (t, J = 6.8 Hz, 2H), 2.72 (mc, 2H), 2.22 (mc, 2H). MS: m/e 228 (M^+).
Anal. Calcd. for $C_{11}H_8N_4O_2$ (228.21): C, 57.89; H, 3.53; N, 24.55. Found: C, 57.96; H, 3.45; N, 24.66.

2,8,8-Tricyano-5,6,7,8-tetrahydroquinoline (**9c**). Column chromatography (eluting first with dichloromethane, then dichloromethane/ether 5:1) of the reaction mixture obtained from **7c** (0.6 mmole) afforded **9c** (94%) as a colourless solid: m.p. 153-155°C (hexanes/chloroform); ^{1}H NMR ($CDCl_3$) δ 7.76 (mc, 2H), 3.04 (t, J = 6.3 Hz, 2H), 2.69 (mc, 2H), 2.20 (mc, 2H). MS: m/e 208 (M^+).
Anal. Calcd. for $C_{12}H_8N_4$ (208.22): C, 69.22; H, 3.87; N, 26.91. Found: C, 68.97; H, 3.79; N, 27.03.

6,7-Dihydro-5*H*-1-pyrindine (**15a**). Column chromatography (eluting first with dichloromethane, then ether) of the reaction mixture obtained from **13a** (1.5 mmole) gave **15a** (63%) as a pale brown oil; ^{1}H NMR ($CDCl_3$) identical with that reported in literature[25]: δ 8.30 (d, J = 4.8 Hz, 1H), 7.43 (d, J = 7.5 Hz, 1H), 6.95 (dd, J_1 = 4.8 Hz, J_2 = 7.5 Hz, 1H), 2.95 (2 overlapping t, J = 7.6 Hz, 2H), 2.11 (m, 2H).

3-Chloro-6,7-dihydro-5*H*-1-pyrindine (**15b**). Column chromatography (first eluting with dichloromethane, then ether) of the reaction mixture obtained from **13b** (1.2 mmole) gave **15b** (84%) as an off-white solid: m.p. 58-59°C (hexanes); ^{1}H NMR ($CDCl_3$) δ 8.25 (d, J = 2.1 Hz, 1H), 7.41 (d, J = 2.1 Hz, 1H), 2.95 (t, J = 7.5 Hz, 2H), 2.90 (t, J = 7.4 Hz, 2H), 2.12 (m, 2H). MS: m/e 153/155 (M^+).
Anal. Calcd. for C_8H_8ClN (153.61): C, 62.55; H, 5.25; N, 9.12. Found: C, 62.21; H, 5.37; N, 9.01.

6,7-Dihydro-3-phenyl-5*H*-1-pyrindine (**15c**). Column chromatography (eluting with dichloromethane, then dichloromethane/ether 1:1) of the reaction mixture obtained from **13c** (0.7 mmole) afforded crude **15c**, which was dissolved in dichloromethane and treated with active charcoal. After filtration of the charcoal the organic layer was evaporated to yield **15c** (65%) as a white solid: m.p. 92-93°C (hexanes; lit.[26]: 94-95°C). ^{1}H NMR ($CDCl_3$) identical with that reported in literature[26]: δ 8.55 (d, J = 1.8 Hz, 1H), 7.66 (d, J = 1.8 Hz, 1H), 7.6-7.2 (m, 5H), 3.02 (2 overlapping t, J = 7.2 Hz, 4H), 2.16 (m, 2H).
Anal. Calcd. for $C_{14}H_{13}N$ (195.25): C, 86.11; H, 6.71; N, 7.17. Found: C, 86.22; H, 6.79; N, 7.08.

6,7-Dihydro-3-*p*-nitrophenyl-5*H*-1-pyrindine (**15d**). Column chromatography (eluting with dichloromethane/ether 9:1) of the reaction mixture obtained from **13d** (0.8 mmole) gave crude **15d**, which was dissolved in dichloromethane and treated with active charcoal. After filtration of the charcoal the filtrate was evaporated to afford **15d** (81%) as a pale yellow solid: m.p. 171-173°C (hexanes/toluene); ^{1}H NMR ($CDCl_3$) δ 8.59 (br s, 1H), 8.28 (d, J = 9.0 Hz, 2H), 7.70 (mc,

1H), 7.68 (d, J = 9.0 Hz, 2H), 3.07 (t, J = 7.5 Hz, 2H), 3.02 (t, J = 7.5 Hz, 2H), 2.19 (m, 2H). MS: m/e 240 (M^+).
Anal. Calcd. for $C_{14}H_{12}N_2O_2$ (240.26): C, 69.99; H, 5.03; N, 11.66. Found: C, 69.92; H, 5.01; N, 11.54.

6,7-Dihydro-3-nitro-5*H*-1-pyrindine (15e). Column chromatography (eluting first with dichloromethane, then ether) of the reaction mixture obtained from **13e** (1.5 mmole) afforded **15e** (58%) as a pale yellow solid: m.p. 94-95°C (hexanes; lit.[3]: 94-95°C). ^1H NMR ($CDCl_3$) identical with that reported in literature[3]: δ 9.17 (br s, 1H), 8.21 (br s, 1H), 3.10 (m, 4H), 2.30 (m, 2H).

1,1-Dicyano-2,3-dihydro-5,7-dinitro-1*H*-indene (18a). Column chromatography (eluting with dichloromethane) of the reaction mixture obtained from **16a** (1.4 mmole) afforded **18a** (82%) as a colourless solid: m.p. 148-149°C (hexanes/chloroform); ^1H NMR ($CDCl_3$) δ 9.03 (d, J = 2.1 Hz, 1H), 8.55 (td, J_1 = 2.1 Hz, J_2 = 1.1 Hz, 1H), 3.50 (t, J = 6.6 Hz, 2H), 3.10 (mc, 2H). MS: m/e 258 (M^+).
Anal. Calcd. for $C_{11}H_6N_4O_4$ (258.19): C, 51.17; H, 2.34; N, 21.70. Found: C, 50.90; H, 2.26; N, 21.92.

1,1-Dicyano-2,3-dihydro-7-nitro-1*H*-indene (18b). Column chromatography (eluting with dichloromethane) of the reaction mixture obtained from **16b** (0.6 mmole) gave **18b** (72%) as a colourless solid: m.p. 118-119°C (hexanes/chloroform); ^1H NMR ($CDCl_3$) δ 8.24 (dd, J_1 = 6.3 Hz, J_2 = 3.0 Hz, 1H), 7.76 (mc, 2H), 3.37 (mc, 2H), 3.12 (mc, 2H). MS: m/e 213 (M^+).
Anal. Calcd. for $C_{11}H_7N_3O_2$ (213.19): C, 61.97; H, 3.31, N, 19.71. Found: C, 61.82; H, 3.25; N, 19.88.

1,1-Dicyano-2,3-dihydro-5-nitro-1*H*-indene (18c). Column chromatography (eluting with dichloromethane) of the reaction mixture obtained from **16c** (1.0 mmole) gave **18c** (75%) as a colourless solid: m.p. 92-93°C (hexanes/chloroform); ^1H NMR ($CDCl_3$) δ 8.29 (mc, 2H), 7.83 (dd, J_1 = 7.8 Hz, J_2 = 0.7 Hz, 1H), 3.36 (br t, J = 6.8 Hz, 2H), 3.03 (mc, 2H). MS: m/e 213 (M^+).
Anal. Calcd. for $C_{11}H_7N_3O_2$ (213.19): C, 61.97; H, 3.31; N, 19.71. Found: C, 61.88; H, 3.29; N, 19.86.

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