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Synthesis of 1,3-Diynes in the Purine, Pyrimidine, 1,3,5-Triazine and Acridine Series

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Abstract—A range of conjugated 1,3-diynes, $R^1C{\equiv}CC{\equiv}CR^2$, has been prepared that incorporate the following heteroaromatic units as head groups of the substituents R^1 and/or R^2: pyrimidinyl, purinyl, 2,4-diamino-1,3,5-triazinyl and acridinyl. Compounds containing the first three groups as terminal heterocyclic substituents in both R^1 and R^2 are bonded through methylene linkers $\{(CH_2)_n, n{=}1, 4 \text{ or } 9\}$ to the 1,3-diyne; also reported are amphiphilic species with $R^2{=}n\text{-}C_{10}H_{21}$ and a single heteroaromatic head group in chain R^1. Compounds in the acridine series are also amphiphiles and contain quaternised 1′-(9-acridinylamino)- and 1′-(6-chloro-2-methoxyacridinylamino)- terminal substituents linked by PEG and methylene units to the diyne function. The new diynes have been synthesised by oxidative coupling of the corresponding ω-heteroaromatic functionalised 1-alkyne or by transformation of terminal groups on preformed diynes.

Introduction

Polydiacetylenes (PDAs) [**B**, Scheme 1] can be generated from conjugated 1,3-diynes (**A**) through a solid state (topochemical) polymerisation by thermal treatment or by UV- and γ-irradiation.[1] Highly conjugated polymers in this class are often very insoluble, but many, including those with urethane,[2] sulfonate[3] and ester[4] side chains, are soluble in common organic solvents. PDAs have generated interest in the area of advanced materials because of their unusually high third-order nonlinearity[5] and through aspects of their property of chromism.[6] Recent investigations harnessing the latter effect have been fruitful in the design and successful demonstration of a biosensor for influenza viruses. Thus, polymerised PDA liposomes incorporating a sialic acid head group undergo a quantifiable colorimetric response when exposed to influenza virus.[7] It is apparent that organised arrays of PDAs, as manifested in liposomes, can exhibit unusual properties resulting from conformational effects in side-chains.

In continuation of our studies of PDAs,[8] we required two classes of functionalised 1,3-diynes. The first type was needed for the synthesis of monomers and polymers, which might self-assemble through strong hydrogen bonding. In principle, this effect could be achieved through introduction of appropriate substituents (R^1, R^2) in the monomer so as to achieve strong intermolecular bonding in the polymer (see Scheme 1). Also, discrete PDAs can be envisaged which contain, separately, *only* R^1 and R^2 substituents such that self-assembly could be achieved through intermolecular hydrogen bonding. In the present work, the following base-pair combinations were selected for use in 1,3-diyne synthesis: adenin-9-yl/thymin-1-yl, guanin-9-yl/cytosin-1-yl, and 2,4-diamino-1,3,5-triazin-1-yl/uracil-1-yl.[9] Purine and pyrimidine derivatives are often relatively insoluble in common organic solvents; therefore the target 1,3-diynes also included aliphatic methylene chains to aid solubility, and were of general structure: $[R(CH_2)_nC{\equiv}C{-}]_2$ (R=adeninyl, thyminyl, guanyl, cytosinyl); and $R^1C{\equiv}C{-}C{\equiv}C(CH_2)_nR^2$, R^1=long hydrocarbon chain, R^2=guanyl, cytosinyl, 2,4-diamino-*s*-triazinyl and uracyl.

The second type of 1,3-diyne, containing the DNA-intercalating acridinyl substituent,[10] was designed with the intention of generating liposomes which might be expected to exhibit chromic effects through binding to nucleic acids. Therefore, in this work, the synthetic targets incorporated the following: a long alkyl chain at one terminus and a second chain at the other end comprising a polymethylene segment, a polar linker [viz polyethyleneglycol (PEG)] and an acridinyl head group.

Scheme 1.

Keywords: 1,3-diyne; purine; pyrimidine; 1,3,5-triazine; acridine.

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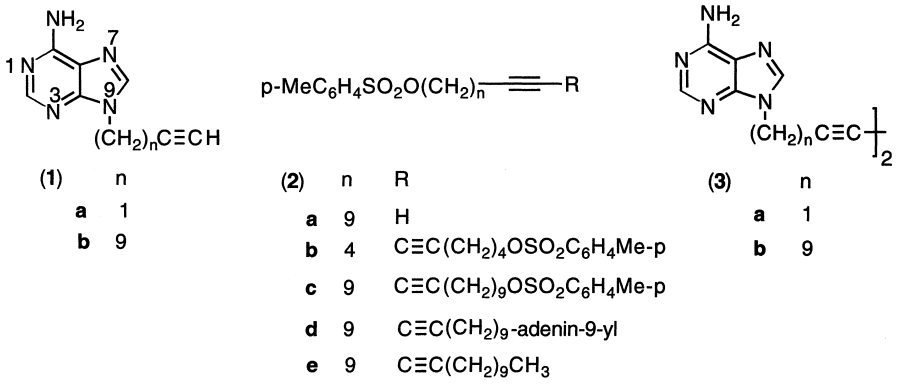


Scheme 2.

Results and Discussion

Adenine derivatives

At the outset of the work a brief preliminary report appeared on the synthesis of the hexa-2,4-diyne derivative (**3a**) and a related uracil.[11] In our work, the propargylic derivative (**1a**) was oxidatively coupled by a modification[12] of the Eglinton/Galbraith procedure [$Cu(OAc)_2.H_2O$/pyridine][13] in which the solvent is acetonitrile/pyridine; the poorly soluble coupled product (**3a**) was formed in slightly improved yield compared to the reported procedure.[11] No success was achieved in attempts to oxidatively couple longer chain analogues of (**1a**) (e.g. **1b** was not converted to **3b** through the Hay oxidative coupling but formed a black intractable product). Therefore, the diyne (**3b**) was prepared by treating the bis tosylate (**2c**) with adenine in the presence of potassium carbonate in anhydrous DMF; in this reaction the monoadenin-9-yl-substituted derivative (**2d**) was isolated as a minor product but was not purified to analytical standard. The preference for alkylation at the 9-position of adenine under basic conditions is in accord with related processes using dibromoalkanes[14] (Scheme 2).

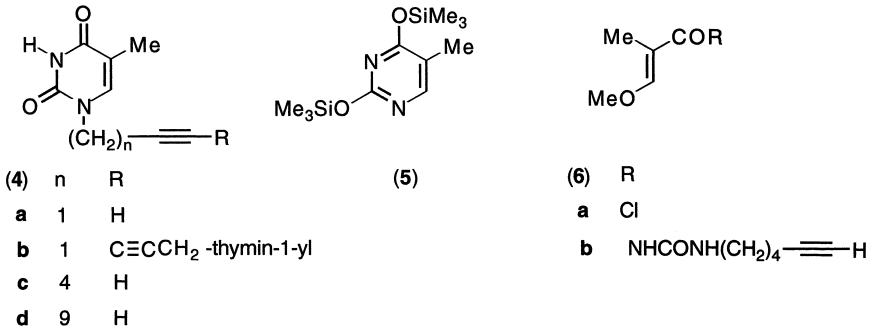
Thymine derivatives

Thymine was selectively alkylated[15] at N-1 with propargyl bromide through use of the bis silylated derivative (**5**). Analytical and NMR spectral data (^1H, ^{13}C) for the product (**4a**) were in accord with expected values[16] but the FAB mass spectrum indicated a peak corresponding to a 'dimer' $(2M+1)^{\cdot+}$ in addition to the molecular ion $(M+1)^{\cdot+}$. This acetylene derivative (**4a**) was oxidatively coupled[12] to afford the 1,3-diyne (**4b**) in 75% yield. Unfortunately, it proved impossible to obtain an analytically pure sample, although the ^1H NMR and mass spectral data were in accord with the proposed structure; the molecular ion (EI) or the M+1 ion (FAB) were too weak to allow high resolution mass measurements (Scheme 3).

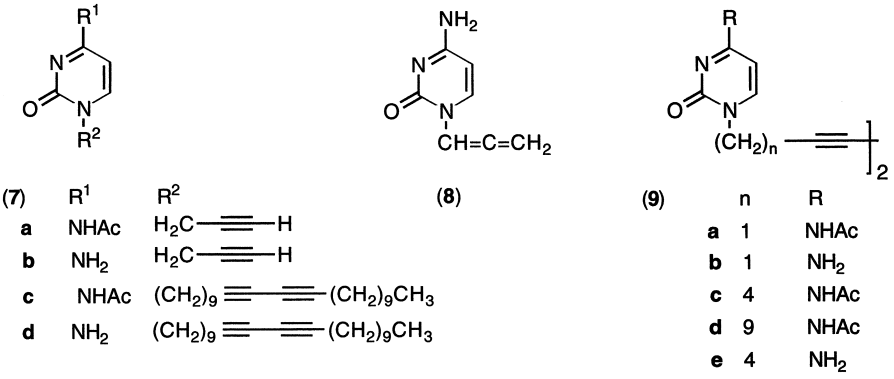
An attempt was then made to prepare analogues of (**4a**) (viz **4c**, **d**) but no success was achieved in attempts to alkylate the bis silyl derivative (**5**) by heating it in THF with a bis tosylate (e.g. **2c**) or dibromo analogue (e.g. **2c**, Br for OTos). Therefore, an alternative procedure was employed:[17] 3-methoxy-2-methacryloyl chloride (**6a**) was treated with silver cyanate followed by 5-hexyn-1-ylamine[18] to afford the urea derivative (**6b**) [39%]. The latter did not cyclise when heated with aqueous sodium hydroxide[17] but afforded only 5-hexyn-1-ylamine and 3-methoxy-2-methacrylic acid.[19] Successful conversion into the acetylene derivative (**4c**) [25%] was achieved by pyrolysis of the potassium salt of (**6b**) at 200°C in vacuo. Unfortunately, this compound (**4c**) proved to be unreactive towards oxidative coupling [e.g. CuCl/tetramethylethylenediamine (Hay) procedure[20]] and no further work was carried out on thymine derivatives.

Cytosine derivatives

N-1 Alkylation of cytosine is hampered by competing O-2 alkylation but this problem can be alleviated to some extent by employing N-4 acetylcytosine as an intermediate.[21] Thus, the product from base-promoted reaction of the latter with propargyl bromide afforded a 96:4 regioisomeric mixture of N-1 and O-2 alkylated products from which the desired (**7a**) [52%] could be purified by recrystallisation



Scheme 3.



Scheme 4.

from water. Since the oxidative coupling of acetylenes containing amino groups can be problematical (see e.g. earlier comment on (**1b**) and also Ref. 22), it was decided to compare substrate (**7a**) and the parent cytosine derivative (**7b**) in this type of process. Attempted hydrolysis of the former (**7a**) with aqueous sodium hydroxide gave the allene derivative (**8**) [75%] in good yield. The structure of (**8**) was assigned on the basis of spectral data, with particular regard to the similarity of the ^{1}H NMR spectrum to analogous structures in the imidazole series, prepared in related fashion.[23] In contrast, hydrolysis of (**7a**) with 5% ammoniacal methanol afforded the required de-acetylated product (**7b**) quantitatively. Oxidative coupling [$Cu(OAc)_2$/MeCN/pyridine[12]] of both acetylene derivatives (**7a**) and (**7b**) proceeded satisfactorily to give 1,3-diynes (**9a** [58%] and **9b** [80%], respectively) although only (**9a**) could be purified to analytical standard; the latter (**9b**) was also obtained quantitatively from hydrolysis of (**9a**) with 5% ammoniacal methanol (Schemes 4 and 5).

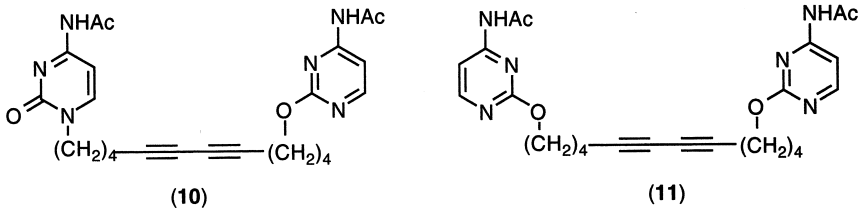
The higher homologue (**9c**) of (**9a**) was prepared in 47% yield through alkylation of N-4 acetylcytosine with the bis tosylate (**2b**) [K_2CO_3/18-crown-6], but two products of O-alkylation (**10**, **11**) were also formed in 33% combined yield. Using compounds (**9c**) and (**11**) as 'models', the ^{1}H NMR spectrum of (**10**) can be easily interpreted, with triplets at δ 3.78 and 4.23 assigned to CH_2N and CH_2O moieties, respectively; also, doublets at δ 7.12 and 8.06 are attributed to C_5-H and C_6-H of the *N*-alkylated ring, whilst those at δ 7.64 and 8.37 correspond to analogous protons of the *O*-alkylated ring.

The analogue (**9d**) of (**9c**) was prepared in very low yield [12%] from the reaction of N-4 acetylcytosine, the bis tosylate (**2c**), potassium carbonate and 18-crown-6 in anhydrous DMF. The site of alkylation was assumed to be exclusively at N-1 from the presence of a triplet resonance at δ 3.77 (cf. **9c**). The de-acetylated compound (**9e**) was prepared quantitatively from (**9c**) under the conditions described above for the conversion (**9a→9b**) (NH_3/MeOH). It was discovered that, in general in this work, compounds bearing heteroaromatic groups at both termini were very insoluble in common organic solvents. In contrast, the amphiphilic 1,3-diynes were more soluble in organic solvents. Preparation of the acetylamino derivative (**7c**) [30%] was accomplished by the method described above (cf. **2b→9c**) but the *O*-alkylated isomer was also formed as a minor product (3:1 ratio); the cytosine derivative (**7d**) was formed quantitatively from (**7c**) by treatment with 5% ammoniacal methanol.

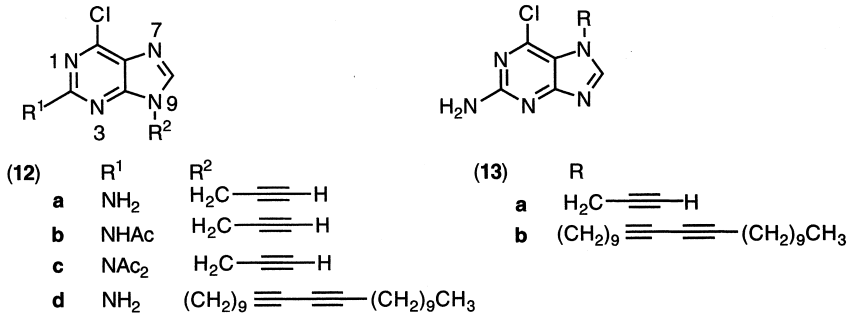
An interesting feature in the ^{1}H NMR spectra of two cytosine derivatives prepared in this work (**8**, **9b**) is the existence of two separate, broad NH resonances for the amino groups. Further investigations, for example, of solvent effects, are required to identify the cause, but the existence of other tautomers of (**8**) and (**9b**) is possible.

Guanine derivatives

The regioselectivity of N-9 (versus N-7) alkylation of guanine has been improved through use of intermediate 2-acetylamino-[24] and 6-chloro-[25] derivatives. In this work, the latter approach was employed, with subsequent hydrolysis of chloroguanines under alkaline[26] rather than acidic conditions.[25] 6-Chloroguanine was alkylated in reasonable yield (69%) with propargyl bromide (Na_2CO_3/DMF) to give a regioisomeric mixture (82:18) of N-9 (**12a**) and N-7 (**13a**) derivatives, respectively; structures were assigned from spectroscopic data with particular reference to comparison



Scheme 5.



Scheme 6.

of UV data with known[25] N-9- and N-7-alkylguanines (Scheme 6).

Unfortunately, attempted oxidative coupling [$Cu(OAc)_2$/pyridine/MeCN][13] of the acetylene derivative (**12a**) afforded a black tarry product that could not be purified. It was assumed that the free amino group in (**12a**) was undesirable and a protected compound (**12b**) was synthesised. However, treatment of the chloroguanine (**12a**) with acetic anhydride afforded a very low yield (15%) of the 2-acetylamino derivative (**12b**) together with the diacetylated compound (**12c**) [32%]. In view of the poor yields obtained in this step, the oxidative coupling was not attempted. The alternative approach of alkylation of 6-chloroguanine with the bis tosylate precursor [cf. synthesis of (**3b**)] afforded poorly soluble guanine-containing compounds (**14a**,**b**; **15a**,**b**)[27] that were characterised spectroscopically but were not isolated as analytically pure species. In contrast, pure lipophilic guanine derivatives, (**12d**) [72%] and (**13b**) [18%], were obtained through alkylation of chloroguanine and the former was successfully converted (NaOH, aqueous dioxan) into the guanine derivative (**16**) [47%]. The ^{1}H NMR purine resonances of (**16**) were in accord with values recorded for substituted guanines[28] (Scheme 7).

1,3,5-Triazine derivatives

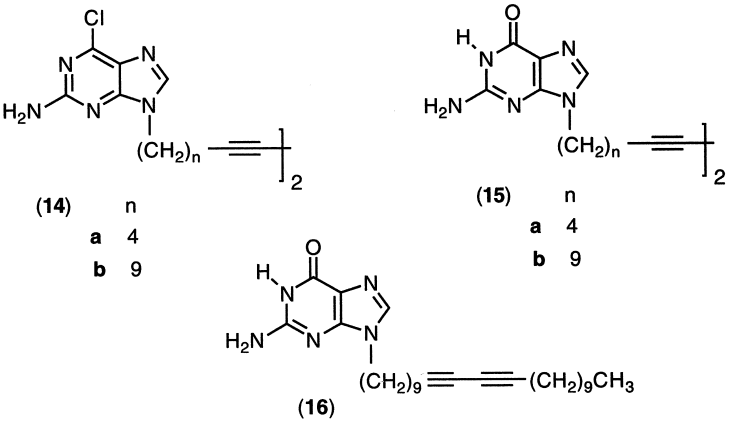
Synthetic methods leading to 2,4-diamino-1,3,5-triazines include the reaction of biguanide with esters[29] or acid chlorides,[30] and of alkyl nitriles with dicyandiamide.[31] In the present work the first procedure[29] was employed using the mono- and di-esters (**17a**) and (**18a**), respectively, as precursors to *s*-triazine derivatives (**17b**) and (**18b**). The latter (**18b**) was formed in low yield (21%) and was accompanied by a product (**17c**) [29%] formed through incomplete condensation with ensuing ester exchange. ^{13}C NMR resonances of *s*-triazine carbon atoms in compounds (**17b**) and (**18b**) were in accord with anticipated values;[32] (e.g. for **17b**, C-6=167.0 ppm: C-2 and C-4=179.6 ppm) (Scheme 8).

Uracil derivatives

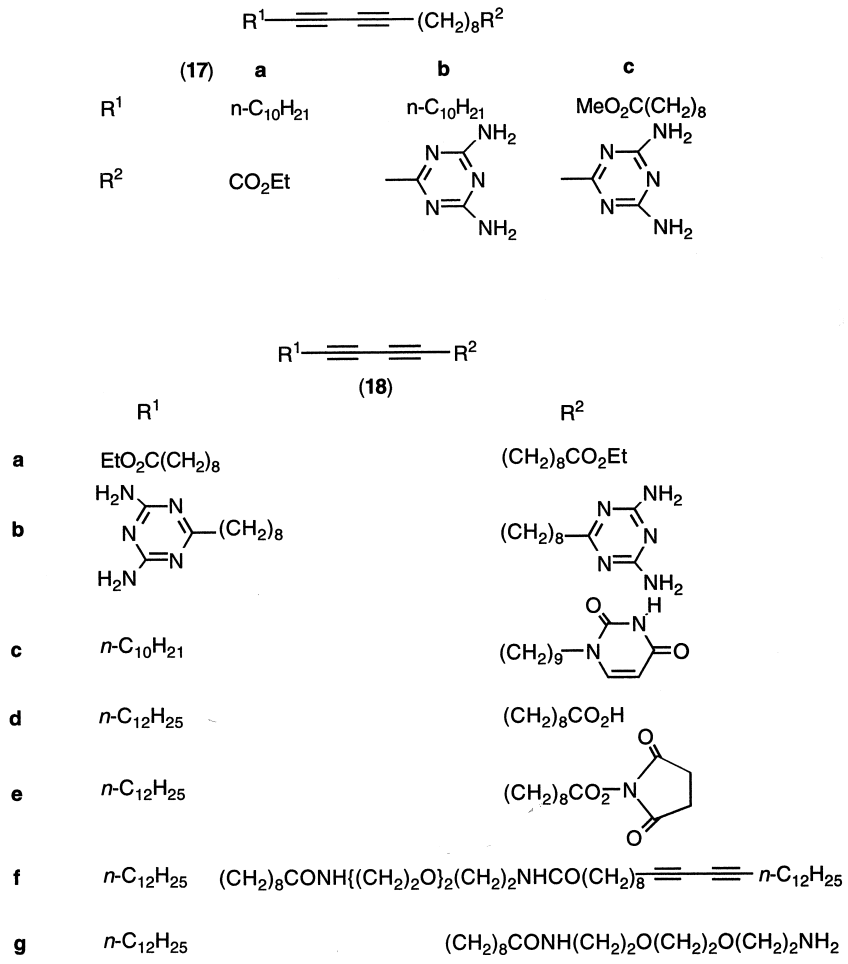
An attempt to prepare the bis uracil analogue of the thymine derivative (**9e**) by analogy with the previously described procedure (cf. **5**→**9e**) was unsuccessful because the product could not be purified chromatographically. In contrast, the amphiphilic uracil derivative (**18c**) [30%] was prepared by direct alkylation of uracil with the tosylate (**2e**) and anhydrous potassium carbonate in DMF. The site of alkylation was determined to be N-1 by comparison of ^{13}C NMR resonances of the uracil ring with those of the reported 1,3-diyne ($[UCH_2C{\equiv}C]_2$: U=uracil-1-yl).[11]

Acridine derivatives

Commercially available 10,12-pentacosadiynoic acid (**18d**) was converted into *N*-succinimidyl-10,12-pentacosadiynate (**18e**) [93%] by a reported method,[33] but transformation of the latter into the amine (**18g**) was initially unsuccessful. Thus, dropwise addition of a solution of (**18e**) to a solution of 1,8-diamino-3,6-dioxaoctane over 30 min afforded the tetrayne (**18f**) in 85% yield, despite a successful reported synthesis of an analogue of (**18g**) by this method.[34] The



Scheme 7.

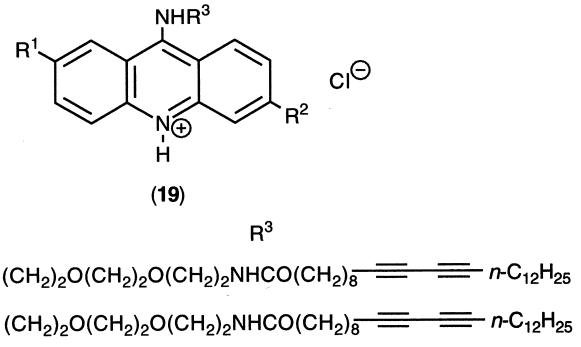


Scheme 8.

tetrayne (**18f**) is a colourless solid that rapidly turns blue in ambient light, indicating a diacetylene derivative prone to polymerisation. Synthesis of the desired amine (**18g**) was achieved, albeit in poor yield (38%) by dropwise addition of a solution of (**18e**) through a syringe pump to a solution of the co-reactant diamine over 16 h. It was hoped that the target acridine-containing 1,3-diyne (**19a**) could be prepared in standard fashion[35] from 9-chloroacridine and (**18g**) in the presence of a catalytic amount of methane sulfonic acid; unfortunately, no reaction occurred even after heating under reflux for 18 h. Therefore, the target acridines (**19a**, 74%) and (**19b**, 69%) were prepared by an alternative method[36] involving heating 9-chloroacridine and, separately, 6,9-dichloro-2-methoxyacridine[37] with the amine (**18g**) in a solution of phenol; both diacetylenes (**19a**,**b**) turned from bright yellow to blue-green in the solid state on exposure to ambient light, indicating partial topotactic polymerisation (Scheme 9).

Conclusions

Two distinct series of heterocyclic-containing 1,3-diynes have been synthesised: one contains heteroaromatic groups



Scheme 9.

which facilitate intermolecular hydrogen-bonding, and the second contains a head group (acridinyl) known to bind to nucleic acids. Preliminary investigations[27,38] indicate that the new 1,3-diynes reported herein will provide novel polydiacetylenes through topochemical polymerisation and in the form of liposomes.

Experimental

Melting points were determined using an Electrothermal instrument and are uncorrected. IR spectra were recorded on Perkin–Elmer FTIR 1600 or 1430 instruments and calibrated against polystyrene. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded on Bruker AC 200 or DPX 400 spectrometers; chemical shifts are reported with respect to $SiMe_4$ as reference (positive shifts to high frequency/low field) and *J* values are given in Hz. UV–Vis spectra were recorded on a Shimadzu UV-160 spectrophotometer. Mass spectra were measured on an upgraded VG MS9 instrument; high resolution mass spectra were also determined at the EPSRC National Mass Spectrometry Service Centre, University of Wales, Swansea. Elemental analyses were performed at Heriot-Watt University or Napier University, Edinburgh. Silica gel 60 (200–400 mesh) was used for column chromatography unless otherwise stated, and analytical TLC was carried out on aluminium plates precoated with silica gel 60 F_{254} (Merck). Drying agents for solvents were Na/benzophenone [for petroleum ether, diethyl ether and tetrahydrofuran (THF) and CaH_2 for dichloromethane. HPLC grade *N*,*N*-dimethylformamide (DMF) was used as supplied.

9-(Prop-1-ynyl)-9*H*-purin-6-amine (1a). Adenine (1.00 g; 7.40 mmol), potassium carbonate (1.53 g; 11.07 mmol) and propargyl bromide (1.32 g; 11.10 mmol) were stirred in anhydrous dimethylformamide (20 cm^3) at 20°C for 24 h. The solvent was evaporated under reduced pressure and the resulting solid was recrystallised from methanol to give colourless 9-(prop-1-ynyl)-9*H*-purin-6-amine (**1a**) (0.85 g; 66%), mp 213–214°C (lit.[11] 214°C). ν_{max} (KBr, cm^{-1}): 3369, 3272, 3249 (N–H str.), 3146 (alkyne C–H str.), 2928, 2878 (aliphatic C–H str.), 2111 (C≡C str.), 1693 (C=N str.), 1610 (N–H def.). δ_H (d_6-DMSO): 3.46 (t, 1H, *J*=2.5 Hz, C≡C–H), 5.02 (d, 2H, *J*=2.5 Hz, $CH_2C{\equiv}C$), 7.29 (br s, 2H, NH_2) 8.16 (s, 1H, H-2 or H-8), 8.19 (s, 1H, H-8 or H-2). δ_C (d_6-DMSO): 32.7, 76.3, (C≡*C*) 78.8 (C≡*C*) 118.9, 140.5, 149.5, 153.2, 156.4. *m*/*z* (EI) 173.0745; $C_8H_7N_5$ requires 173.0701($M^{\cdot+}$)

9-(Undec-10-ynyl)-9*H*-purin-6-amine (1b). Undec-10-ynyl toluene-*p*-sulfonate (5.2 g, 16.1 mmol), potassium carbonate (3.2 g, 23.2 mmol) and adenine (2.10 g, 15.5 mmol) were stirred for 18 h at 20°C in *N*,*N*-dimethylformamide (DMF, 50 cm^3). The solvent was evaporated under reduced pressure to leave a solid that was pre-adsorbed on to silica from methanol. Purification by column chromatography [CH_2Cl_2/CH_3OH (95:5) eluant] afforded the colourless title compound (**1b**) (2.8 g, 63%), mp 145–146°C. ν_{max} (KBr, cm^{-1}): 3170 (N–H str.), 2930, 2920, 2850 (aliphatic C–H str.), (C=N str.), 1612 (N–H def.). δ_H ($CDCl_3$) 1.20–1.58 (m, 12H), 1.81–1.99 (m, 2H, CH_2–CH_2N), 1.92 (t, 1H, *J*=2.6 Hz, C≡CH), 2.17 (td, 2H, *J*=2.6, 6.9 Hz, $CH_2C{\equiv}C$), 4.29 (t, 2H, *J*=7.2 Hz, CH_2N), 5.79 (s, 2H, NH_2), 7.80 (s, 1H, H-2 or H-8), 8.37 (s, 1H, H-8 or H-2). δ_C ($CDCl_3$): 18.2, 26.2, 28.3, 28.5, 28.8, 29.1, 30.0, 43.8, 68.0 (C≡*C*), 84.6, (*C*≡C), 119.6, 140.3, 150.0, 152.8, 155.4. *m*/*z* (EI): 285.194 (1%). $C_{16}H_{23}N_5$ requires 285.195. (Found: C, 67.4; H, 8.3; N, 24.7%. $C_{16}H_{23}N_5$ requires: C, 67.34; H, 8.12; N, 24.54%).

Undec-10-ynyl toluene-*p*-sulfonate (2a). To undec-10-yn-1-ol (4.20 g, 25.0 mmol) and toluene-*p*-sulfonyl chloride (6.79 g, 35.7 mmol) in chloroform at 0°C was added pyridine (2.92 g, 37.0 mmol) dropwise over 5 min with the temperature maintained at 0°C. After stirring for 3 h, conc. HCl (10 cm^3) in water (100 cm^3) was added and the lower chloroform layer was separated, washed with water (100 cm^3) and dried ($CaCl_2$). The solvent was evaporated under reduced pressure to afford the colourless title compound (**2a**) (5.38 g; 70%), mp 39–40°C. ν_{max} (KBr, cm^{-1}): 3293 (alkyne CH), 2918 (aliphatic CH). 2133 (C≡C). δ_H ($CDCl_3$): 1.18–1.72 (m, 14H), 1.85 (t, 1H, *J*=2.7 Hz, C≡CH), 2.19 (td, 2H, *J*=2.7, 6.9 Hz, $CH_2C{\equiv}C$), 2.46 (s, 3H, $ArCH_3$), 4.01 (t, 2H, *J*=6.5 Hz, CH_2OTos), 7.35 and 7.80 (A_2B_2 system of Ar). δ_C ($CDCl)_3$: 18.2, 21.5, 25.2, 28.3, 28.5, 28.7, 28.8, 29.1, 68.0 (C≡C), 70.5, (C≡C), 84.6, 127.8, 129.7, 133.2, 144.5. (Found: C, 66.4; H, 8.0%. $C_{18}H_{26}O_3S$ requires: C, 67.04; H, 8.13%).

9,9′-(Hexa-2,4-diyne-1,6-diyl)di-9*H*-purin-6-amine (3a). 9-(Prop-2-ynyl)-9*H*-purin-6-amine (**1a**) (0.50 g; 2.88 mmol) and copper (II) acetate monohydrate (2.88 g; 14.4 mmol) were stirred in acetonitrile/pyridine (10:1) (50 cm^3) at 60°C for 2 h. Water (100 cm^3) was then added and the precipitate collected by filtration was washed with water (25 cm^3), followed by methanol (25 cm^3), to give colourless 9,9′-(hexa-2,4-diyne-1,6-diyl)di-9*H*-purin-6-amine (**3a**) (0.34 g; 69%), mp 195–197°C (lit.[11] 196–198°C). ν_{max} (KBr, cm^{-1}): 3327, 3149 (N–H str.), 1657 (C=N str.), 1600 (N–H def.). δ_H (d_6-DMSO): 5.20 (s, 4H, $CH_2C{\equiv}C$–), 7.30 (bs, 4H, NH_2), 8.16 (s, 4H, H-2 and H-8).

Docosa-10,12-diyne-1,22-diyl bis(toluene-*p*-sulfonate) (2c). This compound was prepared as previously described.[5a]

Tricosa-10,12-diynyl toluene-*p*-sulfonate (2e). Tricosa-10,12-diyn-1-ol (2.44 g, 7.33 mmol) and toluene-*p*-sulfonyl chloride (1.54 g; 8.07 mmol) were dissolved in dry chloroform (50 cm^3). Pyridine (1.27 g; 16.14 mmol) was slowly added and the mixture was stirred at room temperature overnight. The solution was washed with a mixture of water (90 cm^3) and hydrochloric acid (10 cm^3). The organic layer was separated, washed with water (50 cm^3) and dried ($CaCl_2$). The chloroform was evaporated under reduced pressure and diethylether was added. The volume of diethylether was reduced by half by evaporation with cooling to cause precipitation of the title compound: this process was repeated to give a second crop, giving tricosa-10,12-diynyl toluene-*p*-sulfonate (**2e**) (1.50 g; 42%) as a colourless crystalline solid which rapidly turned blue on exposure to daylight, mp 47–48°C. ν_{max} (KBr, cm^{-1}): 2920, 2847 (aliphatic C–H str.), 1470 (C–H def.), 1356, 1174 (S=O str.). δ_H ($CDCl_3$): 0.87 (t, 3H, *J*=6.4 Hz, CH_3), 1.10–1.72 (m, 30H), 2.24 (t, 4H, *J*=6.6 Hz, $CH_2C{\equiv}C$), 2.46 (s, 3H, CH_3), 4.01 (t, 2H, *J*=6.5 Hz,

CH_2OTs), 7.35 (d, 2H, J=8.2 Hz, Ar–H), 7.80 (d, 2H, J=8.2 Hz, Ar–H). δ_C ($CDCl_3$): 14.1, 19.1, 21.6, 22.6, 25.2, 28.2, 28.7, 28.8, 29.0, 29.1, 29.2, 29.4, 29.5, 31.8, 65.2, 70.6, 77.3, 127.8, 129.7, 133.1, 144.6. m/z (FAB, NOBA matrix): 488 (3%, $[M+1]^+$). (Found: C, 74.1; H, 9.4%. $C_{30}H_{46}O_3S$ requires: C, 74.03; H 9.53%.)

9,9′-(Docosa-10,12-diyne-1,22-diyl)di-9*H*-purin-6-amine (3b) and 9-[22-(4-methylphenylsulfonyloxy)docosa-10,12-diynyl)-9*H*-purin-6-amine (2d). Adenine (0.63 g, 4.66 mmol), anhydrous potassium carbonate (0.65 g; 4.70 mmol) and 10,12-docosadiyn-1,22-bis(4-methylbenzenesulfonate) (0.99 g; 1.55 mmol) (**2c**) were stirred in DMF (25 cm^3) at 20°C for 72 h. The solvent was evaporated under reduced pressure and the residual solid was dissolved in methanol, pre-adsorbed on to silica and chromatographed with CH_2Cl_2/MeOH (95:5) as eluant. The following were isolated:

*9,9′-(docosa-10,12-diyne-1,22-diyl)di-9H-purin-6-amine (**3b**):* (0.20 g; 22%) as a colourless amorphous solid, mp 178–179°C. ν_{max} (KBr, cm^{-1}): 3300, 3100 (N–H str.), 2940, 2860 (aliphatic C–H str.), 1650 (C=N str.), 1600 (N–H def.). δ_H (d_6-DMSO): 1.18–1.49 (m, 24H), 1.78–1.87 (m, 4H), 2.23 (t, 4H, J=6.6 Hz, $CH_2C{\equiv}C$), 4.11 (t, 4H, J=7.0 Hz, CH_2N), 7.18 (s, 4H, NH_2), 8.12 (s, 4H, H-2 and H-8). m/z (FAB, NOBA matrix): 569 (9%, $[M+1]^+$). (Found: C, 65.6; H, 7.6; N, 24.6%. $C_{32}H_{44}N_{10}{\cdot}H_2O$ requires: C, 65.5; H, 7.9; N, 23.9%.)

*9-(22-(4-methylphenylsulfonyloxy)docosa-10,12-diynyl)-9H-purin-6-amine (**2d**):* (0.01 g; 10%) as a colourless solid, mp 68–70°C. ν_{max} (KBr, cm^{-1}): 3304, 3146 (N–H str.), 2925, 2854 (aliphatic C–H str.), 1675 (C=N str.), 1602 (N–H def.) δ_H (d_6-DMSO): 1.14–1.78 (m, 28H), 2.26 (t, 4H, J=6.4 Hz, $CH_2C{\equiv}C$), 2.41 (s, 3H, CH_3), 3.98 (t, 2H, J=6.2 Hz, CH_2OTs), 4.10 (t, 2H, J=6.9 Hz, CH_2N), 7.20 (s, 2H, NH_2), 7.45 (d, 2H, J=8.1 Hz, Ar–H), 7.77 (d, 2H, J=8.1 Hz, Ar–H), 8.11 (s, 2H, H-2 and H-8). δ_C (d_6-DMSO): 18.7, 21.5, 25.1, 26.4, 28.1, 28.6, 28.7, 29.1, 29.8, 43.3, 65.8, 71.3, 78.4, 119.2, 128.0, 130.6, 133.0, 141.2, 145.2, 150.0, 152.7, 156.4. m/z (FAB, NOBA matrix): 606 (94%, $[M+1]^+$).

1-(Prop-2-ynyl)-5-methylpyrimidine-2,4(1H,3H)-dione (4a). Chlorotrimethylsilane (0.77 cm^3; 7.12 mmol) and thymine (3.84 g; 30.46 mmol) were heated under reflux in excess hexamethyldisilazane (5.89 g; 36.55 mmol) for 21 h. Excess hexamethyldisilazane was evaporated under reduced pressure to give crude 5-methyl-bis-2,4-trimethylsilyloxypyrimidine (**5**).[15] This was not purified further but was then stirred at room temperature with propargyl bromide (3.35 g; 28.4 mmol) for 9 days. Water (50 cm^3) was then added and the mixture was extracted with chloroform (5×50 cm^3). The chloroform solution was dried ($MgSO_4$) and evaporated to afford colourless 1-(prop-2-ynyl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (**4a**) (3.28 g; 70%), mp 157–158°C. ν_{max} (KBr, cm^{-1}): 3265 (alkyne C–H str.), 3170, 3120 (N–H str.), 3040 (alkene C–H str.), 2945, 2905, 2845 (aliphatic C–H *str*), 2135 (C≡C str.), 1710, 1665 (amide I, II). δ_H ($CDCl_3$): 1.96 (d, 3H, J=1.2 Hz, CH_3), 2.47 (t, 1H, J=2.6 Hz, C≡CH), 4.55 (d, 2H, J=2.6 Hz, $CH_2C{\equiv}C$), 7.26 (q, 1H, J=1.2 Hz, CH=C), 9.12 (s, 1H, NH). δ_C (d_6-DMSO): 12.3, 36.7, 76.1, 79.1, 109.6, 140.6, 150.8, 164.6. m/z (FAB, NOBA matrix) 165 (100%, $[M+1]^+$), 329 (6%, $[2M+1]^+$). (Found: C, 58.6; H, 4.7; N, 17.3%. $C_8H_8N_2O_2$ requires: C, 58.5; H, 4.9; N, 17.0%.)

5,5′-Dimethyl-1,1′-(hexa-2,4-diyne-1,6-diyl)dipyrimidine-2,4(1*H*,3*H*)-dione (4b). 1-(Prop-2-ynyl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (**4a**) (1.45 g; 8.85 mmol) and copper (II) acetate monohydrate (7.06 g; 35.34 mmol) were dissolved in acetonitrile/pyridine (60 cm^3, 85:15) under a nitrogen atmosphere and stirred at 60°C for 2 h. The resulting suspension was filtered and the solid portion was separated and washed with water (100 cm^3) then filtered to give yellow 5,5′-dimethyl-1,1′-(hexa-2,4-diyne-1,6-diyl)dipyrimidine-2,4(1*H*,3*H*)-dione (**4b**) (1.08 g, 75%), mp 204°C dec. (from methanol). ν_{max} (KBr, cm^{-1}): 3195, 3070 (N–H str.), 2980, 2940, 2820 (aliphatic C–H str.), 1707, 1680 (amide I, II). δ_H (d_6-DMSO): 1.73 (s, 6H, CH_3), 4.59 (s, 4H, $CH_2C{\equiv}C$), 7.55 (s, 2H, HC=), 11.41 (s, 2H, NH). δ_C (d_6-DMSO): 12.0, 37.1, 67.5, 74.9, 109.7, 140.2, 150.4, 164.2. m/z (FAB, NOBA matrix): 327 (4%, $[M+1]^+$).

1-(Hex-5-ynyl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (4c). *N*-(3-Methoxy-2-methacryloyl)-*N*′-(hex-5-ynyl)urea (**6b**) (100 mg; 0.41 mmol), potassium hydroxide (450 mg; 0.81 mmol) and 18-crown-6 (11 mg; 0.04 mmol) were stirred in toluene (25 cm^3) for 16 h at 20°C. The solvent was evaporated under reduced pressure and the residue was fused by heating at 200°C for 10 min. The product was cooled, water (2 cm^3) was added and the solution was neutralised with conc. hydrochloric acid. This product was extracted with dichloromethane (3×10 cm^3) and the organic extract was dried ($MgSO_4$) and evaporated under reduced pressure. The residue was chromatographed [40:60 petroleum ether/diethyl ether (1:1) eluant] to afford colourless 1-(hex-5-ynyl)-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (**4c**) (20 mg; 25%), mp 103–104°C. ν_{max} (KBr, cm^{-1}): 3158, 3065 (N–H str.), 3029 (alkene C–H str.), 2831 (aliphatic C–H str.), 1691, 1657 (amide I, II), 1475, 1423 (aliphatic C–H def.). δ_H ($CDCl_3$): 1.80 (t, 1H, J=2.5 Hz, C≡CH), 1.87 (t, 4H, J=2.5 Hz, CH_2CH_2), 1.93 (d, 3H, J=1.2 Hz, CH_3C=), 2.20 (td, 2H, J=2.5, 6.6 Hz, $CH_2C{\equiv}C$), 3.83 (t, 2H, J=6.9 Hz, NCH_2), 7.05 (q, 1H, J=1.2 Hz, HC=), 8.38 (s, 1H, NH). δ_C ($CDCl_3$): 3.8, 12.9, 28.8, 40.0, 77.3, 78.6, 110.6, 140.7, 152.1, 165.4. m/z (EI) 206.10354 ($M^{\cdot+}$), $C_{11}H_{14}N_2O_2$ requires 206.10553 ($M^{\cdot+}$). (Found: C, 64.4; H, 7.0; N, 13.7%. $C_{11}H_{14}N_2O_2$ requires: C, 64.1; H, 6.8; N, 13.6%.)

***N*-(3-Methoxy-2-methacryloyl)-*N*′-(hex-5-ynyl)urea (6b).** Silver cyanate (1.79 g; 12.00 mmol) and absolute chloroform (25 cm^3) were cooled to 0°C and 3-methoxy-2-methacryloyl chloride[17] (**6a**) (1.68 g; 12.5 mmol) was added. The mixture was allowed to warm to room temperature and stirred at 20°C for 12 h. The product was filtered through celite, 5-hexyn-1-ylamine[18] (1.15 g; 11.8 mmol) was added and the solution was stirred at 20°C for 3 h. The solvent was evaporated under reduced pressure to leave colourless *N*-(3-methoxy-2-methacryloyl)-*N*′-(hex-5-ynyl)urea (**6b**) (1.14 g; 39%), mp 75°C (from *n*-hexane). ν_{max} (KBr, cm^{-1}): 3248 (alkyne C–H str.), 2944, 2857 (aliphatic C–H str.), 1685, 1656 (amide I, II). δ_H ($CDCl_3$): 1.47–1.80 (m, 4H), 1.78 (d, 3H, J=1.1 Hz, CH_3C=), 1.98 (t, 1H, J=2.7 Hz, C≡CH),

2.25 (td, 2H, J=2.7, 6.7 Hz, $CH_2C{\equiv}C$), 3.35 (q, 2H, J=6.4 Hz, NCH_2), 3.88 (s, 3H, CH_3O), 7.36 (s, 1H, HC=), 7.99 (br s, 1H, NH), 9.70 (br s, 1H, N*H*CH_2). δ_C ($CDCl_3$): 6.7, 18.0, 25.6, 28.6, 39.1, 61.4, 68.6, 83.8, 107.0, 154.2, 158.4, 169.3. *m/z* (EI): 238 (1%, $M^{\cdot+}$). (Found: C, 60.0; H, 7.4; N, 11.9%. $C_{12}H_{18}N_2O_3$ requires: C, 60.5; H, 7.6; N, 11.8%.)

1-(Prop-2-ynyl)-4-acetylaminopyrimidin-2(1*H*)-one (7a). A suspension of ^{4}N-acetylcytosine (1.00 g; 6.53 mmol), anhydrous potassium carbonate (1.04 g; 7.50 mmol) and propargyl bromide (0.67 g; 5.64 mmol) DMF (50 cm^3) was stirred for 18 h at room temperature. The mixture was filtered and the solvent was evaporated under reduced pressure to leave a brown solid. This solid was then dissolved in hot water (20 cm^3) and the solution treated with decolourising charcoal (0.2 g). The mixture was filtered and the filtrate cooled to precipitate a colourless solid. This solid was separated and dried to afford colourless 1-(prop-2-ynyl)-4-acetylaminopyrimidin-2(1*H*)-one (**7a**) (0.56 g; 52%), mp 199°C. ν_{max} (KBr, cm^{-1}): 3450, 3195 (N–H str.), 2980 (aliphatic C–H str.), 2114 (C≡C str.), 1695 (C=O str.), 1657, 1619 (amide I, II). δ_H (d_6-DMSO): 2.12 (s, 3H, CH_3), 3.50 (t, 1H, J=2.5 Hz, C≡CH), 4.67 (d, 2H, J=2.5 Hz, NCH_2), 7.20 (d, 1H, J=7.3 Hz, H-5 or H-6), 8.20 (d, 1H, J=7.3 Hz, H-6 or H-5), 10.89 (br s, 1H, NH). δ_C (d_6-DMSO): 24.8, 38.8, 76.8, 78.7, 96.1, 149.7, 155.0, 163.1, 171.4. *m/z* (EI) 191.06984 ($M^{\cdot+}$), $C_9H_9N_3O_2$ requires 191.06948 ($M^{\cdot+}$). (Found: C, 56.2; H, 4.5; N, 21.9%. $C_9H_9N_3O_2$ requires: C, 56.5; H, 4.7; N, 22.0%.)

1-(Prop-2-ynyl)-4-aminopyrimidin-2(1*H*)-one (7b). 1-(Prop-2-ynyl)-4-acetylaminopyrimidin-2(1*H*)-one (**7a**) (0.10 g; 0.54 mmol) was stirred with 5% (v/v) methanolic ammonia (10 cm^3) at 20°C for 5 h. The solvent was evaporated under reduced pressure giving 1-(prop-2-ynyl)-4-aminopyrimidin-2(1*H*)-one (**7b**) (0.08 g; 100%) as colourless needles, mp 226–227°C dec. ν_{max} (KBr, cm^{-1}): 3380 (N–H str.), 2230 (alkyne C–H str.), 3100 (alkene C–H str.), 2120 (C≡C str.), 1730 (C=O str), 1625 (N–H def.). λ_{max} H_2O (nm): 232 (ϵ 6152), 271 (7954). δ_H (d_6-DMSO): 3.35 (t, 1H, J=2.5 Hz, C≡CH), 4.47 (d, 2H, J=2.5 Hz, CHC≡C), 5.73 (d, 1H, J=7.2 Hz, H-5), 7.29 (br s, 2H, NH_2), 7.65 (d, 1H, J=7.2 Hz, H-6). δ_C (d_6-DMSO): 37.8, 75.7, 79.9, 94.6, 145.3, 155.6, 166.5. *m/z* (EI): 149.05726 ($M^{\cdot+}$), $C_7H_7N_3O$ requires 149.05891. (Found: C, 56.6; H, 4.7; N, 28.1%. $C_7H_7N_3O$ requires: C, 56.37; H, 4.73; N, 28.17%.)

1-(Tricosa-10,12-diynyl)-4-acetylaminopyrimidin-2(1*H*)-one (7c). Tricosa-10,12-diynyl toluene-*p*-sulfonate) (**2e**) (0.75 g; 1.54 mmol), ^{4}N-acetylcytosine (0.24 g; 1.61 mmol), potassium carbonate (0.22 g; 1.61 mmol) and DMF (50 cm^3) were stirred under an atmosphere of nitrogen for 24 h. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography [CH_2Cl_2/MeOH (98:2), eluant] to give 1-(tricosa-10,12-diynyl)-4-acetylaminopyrimidin-2(1*H*)-one (**7c**) (213 mg; 30%) and 2-(tricosa-10,12-diynyloxy)-4-acetylaminopyrimidine (72 mg; 10%). Both of these compounds were isolated as colourless amorphous solids and both turned pink on exposure to daylight.

1-(Tricosa-10,12-diynyl)-4-acetylaminopyrimidin-2(1H)-one (7c): mp 96–97°C. ν_{max} (KBr, cm^{-1}): 3326 (N–H str.), 2922, 2848 (aliphatic C–H str.), 1690, 1664 (C=O str.). δ_H ($CDCl_3$): 0.88 (t, 3H, J=6.4 Hz, CH_3), 1.16–1.85 (m, 30H), 2.25 (t, 4H, J=6.8 Hz, $CH_2C{\equiv}C$), 2.30 (s, 3H, CH_3), 3.87 (t, 2H, J=7.3 Hz, CH_2N), 7.41 (d, 1H, J=7.3 Hz, H-5), 7.58 (d, 1H, J=7.3 Hz, H-6), 10.18 (br s, 1H, NH). δ_C ($CDCl_3$): 14.1, 19.1, 22.6, 24.8, 26.4, 28.2, 28.2, 28.6, 28.8, 29.0, 29.2, 29.4, 29.5, 31.8, 51.0, 65.1, 77.4, 96.7, 148.6, 155.7, 162.8, 171.2. *m/z* (FAB, NOBA matrix): 468 (17%, $[M+1]^+$). (Found: C, 74.1; H, 9.7; N, 8.9%. $C_{29}H_{45}N_3O_2$ requires: C, 74.47; H, 9.70; N, 8.98%.)

2-(Tricosa-10,12-diynyloxy)-4-acetylaminopyrimidine: mp 63–64°C. ν_{max} (KBr, cm^{-1}): 3204 (N–H str.), 2923, 2850 (aliphatic C–H str.), 1713 (C=O str.). δ_H ($CDCl_3$) 0.88 (t, 3H, J=6.4 Hz, CH_3), 1.13–1.88 (m, 30H), 2.22 (t, 4H, J=6.7 Hz, $CH_2C{\equiv}C$), 4.28 (t, 2H, J=6.6 Hz, CH_2O), 7.76 (d, 1H, J=7.3 Hz, H-5), 8.09 (br s, 2H, N*H*), 8.40 (d, 1H, J=7.3 Hz, H-6). δ_C ($CDCl_3$): 14.0, 19.1, 22.6, 24.7, 25.8, 28.2, 28.7, 28.9, 29.0, 29.2, 29.4, 29.5, 31.8, 65.2, 67.6, 77.4, 103.7, 158.8, 160.4, 164.6, 169.3. *m/z* (FAB, NOBA matrix) 468 (100%, $[M+1]^+$). (Found: C, 74.0; H, 9.8; N 8.6%. $C_{29}H_{45}N_3O_2$ requires: C, 74.47; H, 9.70; N, 8.98%.)

1-(Tricosa-10,12-diynyl)-4-aminopyrimidin-2(1*H*)-one (7d). 1-(Tricosa-10,12-diynyl)-4-acetylaminopyrimidin-2(1*H*)-one (**7c**) (213 mg; 0.45 mmol) was stirred with 5% ammoniacal methanol (25 cm^3) for 18 h. The solvent was evaporated under reduced pressure to leave a pink solid which was dried in vacuo to afford 1-(tricosa-10,12-diynyl)-4-aminopyrimidin-2(1*H*)-one (**7d**) (192 mg; 100%), mp 188–190°C. ν_{max} (KBr, cm^{-1}): 3347, 3127 (N–H str.), 2915, 2850 (aliphatic C–H str.), 1663, 1618 (C=O str., N–H def.). δ_H ($CDCl_3$): 0.87 (t, 3H, J=6.4 Hz, CH_3), 1.13–1.79 (m, 30H), 2.25 (t, 4H, J=6.7 Hz, $CH_2C{\equiv}C$), 3.73 (t, 2H, J=7.3 Hz, CH_2N), 5.73 (d, 1H, J=6.8 Hz, H-5), 6.38 (br s, 2H, NH_2), 7.22 (d, 1H, J=6.8 Hz, H-6). δ_C ($CDCl_3$): 14.0, 19.1, 22.6, 26.5, 28.2, 28.7, 28.8, 28.9, 29.0, 29.1, 29.2, 29.4, 29.5, 31.8, 50.1, 65.2, 77.4, 93.8, 145.4, 156.5, 165.8. *m/z* (FAB, NOBA matrix): 426 (100%, $[M+1]^+$), 852 (3%, $[2M+1]^+$). (Found: C, 76.0; H, 10.3; N, 9.7%. $C_{27}H_{43}N_3O$ requires: C, 76.17; H, 10.19; N, 9.88%.)

1-(Propa-1,2-dienyl)-4-aminopyrimidin-2(1*H*)-one (8). 1-(Prop-2-ynyl)-4-acetylamino-pyrimidin-2(1*H*)-one (**7a**) (0.36 g; 1.87 mmol) and sodium hydroxide (0.14 g; 3.50 mmol) were heated in water (10 cm^3) at 80°C for 30 min. The mixture was cooled and filtered to afford cream 1-(propa-1,2-dienyl)-4-aminopyrimidin-2(1*H*)-one (**8**) (0.21 g; 75%), mp 207°C dec. ν_{max} (KBr, cm^{-1}): 3361 (N–H str.), 3086, 2923 (alkene C–H str.), 1669, (C=O str.), 1626 (N–H def.), 1488 (alkene C–H def.). λ_{max} H_2O (nm): 240 (ϵ 8250), 289 (10609). δ_H (d_6-DMSO): 5.70 (d, 2H, J=6.6 Hz, =CH_2), 5.84 (d, 1H, J=7.4 Hz, H-5), 7.33 (t, 1H, J=6.6 Hz, =CHN), 7.43 and 7.47 (br, 2H, NH_2), 7.50 (d, 1H, J=7.4 Hz, H-6). δ_C (d_6-DMSO): 89.9, 96.2, 98.3, 141.2, 154.0, 165.9, 201.2. *m/z* (EI) 149.05957 ($M^{\cdot+}$), $C_7H_7N_3O$ requires: 149.05891.

4,4′-Bis(acetylamino)-1,1′-(hexa-2,4-diyne-1,6-diyl)dipyrimidin-2(1*H*)-one (9a). 1-(Prop-2-ynyl)-4-acetylaminopyrimidin-2(1*H*)-one (**7a**) (1.22 g; 6.37 mmol), copper(II) acetate monohydrate (5.09 g; 25.48 mmol), acetonitrile (40 cm^3) and pyridine (10 cm^3) were stirred at 60°C for

2 h under an atmosphere of nitrogen. The solid product was separated and washed with water (100 cm^3). The resultant pale green solid was stirred with water (100 cm^3) and tetrasodium ethylenediaminetetraacetic acid (1.00 g; 2.63 mmol) for 24 h at room temperature. Filtration and further washing with water afforded 4,4′-bis(acetylamino)-1,1′-(hexa-2,4-diyne-1,6-diyl)dipyrimidin-2(1*H*)-one (**9a**) (0.71 g; 58%) as a lilac powder, mp >360°C. ν_{max} (KBr, cm^{-1}): 3420, 3290, 3130 (N–H str.), 2925, 2855 (C–H str.), 1695, 1670 (Amide I,II), 1625 (N–H def.). δ_H (d_6-DMSO): 2.10 (s, 6H, CH_3), 4.80 (s, 4H, NCH_2), 7.20 (d, 2H, *J*=7.3 Hz, H-5), 8.13 (d, 2H, *J*=7.3 Hz, H-6), 10.92 (s, 2H, NH). δ_C (d_6-DMSO): 24.8, 74.9, 96.2, 163.2, 171.4 (Signals for four other carbons were not observed due to the high insolubility of this compound.) *m/z* (FAB, NOBA matrix) 381 (23%, $[M+1]^+$). (Found: C, 55.1; H, 4.1; N, 21.6%. $C_{18}H_{16}N_6O_4 \cdot 0.5H_2O$ requires: C, 55.5; H, 4.4; N, 21.6%.)

4,4′-Diamino-1,1′-(hexa-2,4-diyne-1,6-diyl)dipyrimidin-2-(1*H*)-one (9b). 1-(Prop-2-ynyl)-4-aminopyrimidin-2(1*H*)-one (**7b**) (0.30 g; 2.01 mmol), copper(II) acetate monohydrate (0.80 g; 4.04 mmol), acetonitrile (40 cm^3) and pyridine (10 cm^3) were stirred at 60°C for 2 h under an atmosphere of nitrogen. Work-up as described above gave 4,4′-diamino-1,1′-(hexa-2,4-diyne-1,6-diyl)dipyrimidin-2-(1*H*)-one (**9b**) (0.24 g; 80%) as a brown powder, mp >360°C. ν_{max} (KBr, cm^{-1}): 3417, 3127 (N–H str.), 1677 (C=O str.), 1639, 1619 (N–H def.). δ_H (d_6-DMSO): 4.61 (s, 4H, NCH_2), 5.70 (d, 2H, *J*=7.3 Hz, H-5), 7.15 and 7.22 (br, 4H, NH_2), 7.62 (d, 2H, *J*=7.3 Hz, H-6). δ_C (d_6-DMSO): 38.0, 67.1, 75.2, 94.2, 144.7, 154.9, 166.0. *m/z* (FAB, NOBA matrix): 149 (100%, $[M+1]^+ - C_7H_6N_3O$).

4,4′-Bis(acetylamino)-1,1′-(dodeca-5,7-diyne-1,12-diyl)-dipyrimidin-2(1*H*)-one (9c), dodeca-5,7-diyne-1-yl-(1-(4-acetylaminopyrimidin-2(1*H*)-one))-12-yloxy-(2-(4-acetylaminopyrimidine)) (10) and 2,2′-(dodeca-5,7-diyne-1,12-diyldioxy)bis-(4-acetylamino-pyrimidine) (11). ^{4}N-Acetylcytosine (0.73 g; 4.74 mmol), anhydrous potassium carbonate (0.66 g; 4.74 mmol) and 18-crown-6 (0.04 g; 0.15 mmol) were suspended in dry DMF (50 cm^3) and stirred at 20°C for 1 h. Dodeca-5,7-diyne-1,12-diyl bis(toluene-*p*-sulfonate) (**2b**) (1.00 g; 2.15 mmol) was added and the mixture was stirred for 5 h at 60°C then a further 18 h at 20°C. Column chromatography [CH_2Cl_2/MeOH (95:5) eluant] afforded the following:

*4,4′-bis(acetylamino)-1,1′-(dodeca-5,7-diyne-1,12-diyl)dipyrimidin-2(1H)-one (**9c**):* (0.47 g; 47%) as a colourless powder, mp 220°C. ν_{max} (KBr, cm^{-1}): 3434, 3237 (N–H str.), 3028 (alkene C–H str.), 2953, 2929, 2863 (aliphatic C–H str.), 1710 (C=O str.), 1662 (N–H def.). δ_H (d_6-DMSO): 1.32–1.53 (m, 4H, CH_2CH_2–C≡C), 1.58–1.77 (m, 4H, CH_2CH_2N), 2.07 (s, 6H, CH_3), 2.32 (t, 4H, *J*=6.7 Hz, CH_2C≡C), 3.79 (t, 4H, *J*=6.9 Hz, CH_2N), 7.13 (d, 2H, *J*=7.2 Hz, *H*-5 or H-6) 8.06 (d, 2H, *J*=7.2 Hz, H-6 or H-5), 10.79 (br s, 2H, NH). δ_C (d_6-DMSO): 18.4, 24.7, 25.2, 28.0, 49.4, 66.0, 78.2, 95.4, 150.6, 155.7, 162.7, 171.3. *m/z* (FAB, NOBA matrix): 465.2237 (100%, $[M+1]^+$); $C_{24}H_{29}N_6O_4$ requires: 465.2250.

*Dodeca-5,7-diyne-1-yl-(1-(4-acetylaminopyrimidin-2(1H)-one))-12-yloxy-(2-(4-acetylaminopyrimidine)) (**10**):* (0.26 g; 26%), softens and polymerises at ca.>100°C. ν_{max} (KBr, cm^{-1}): 3418, 3245 (N–H str.), 2933, 2863 (aliphatic C–H str.), 1706 (C=O str.), 1662, 1583, 1492, 1435 (amide I,II, alkene and aliphatic C–H *def*). δ_H (d_6-DMSO): 1.33–1.85 (m, 8H), 2.08 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 2.21 (t, 2H, *J*=6.4 Hz, CH_2C≡C), 2.26 (t, 2H, *J*=6.5 Hz, CH_2C≡C), 3.78 (t, 2H, *J*=6.9 Hz, CH_2N), 4.23 (t, 2H, *J*=6.2 Hz, CH_2), 7.12 (d, 1H, *J*=7.2 Hz, H-5), 7.64 (d, 1H, *J*=5.6 Hz, H-5 or H-6), 8.06 (d, 1H, *J*=7.2 Hz, H-6), 8.37 (d, 1H, *J*=5.6 Hz, H-5 or H-6), 10.80 (br s, 2H, NH). δ_C (d_6-DMSO): 18.4, 18.5, 24.6, 24.7, 24.8, 25.2, 28.0, 28.0, 49.4, 65.9, 66.4, 78.1, 78.3, 95.4, 103.8, 150.6, 155.7, 160.0, 160.6, 162.7, 164.7, 170.9, 171.3. *m/z* (FAB, NOBA matrix) 465 (100%, $[M+1]^+$). (Found: C, 61.8; H, 6.1; N, 17.8%. $C_{24}H_{28}N_6O_4$ requires: C, 62.1; H, 6.1; N, 18.1%.)

*2,2′-(Dodeca-5,7-diyne-1,12-diyldioxy)bis-(4-acetylamino-pyrimidine) (**11**):* (0.09 g; 9%), mp 142–143°C. ν_{max} (KBr, cm^{-1}): 3418, 3241 (N–H str.), 2963, 2926 (aliphatic C–H str.), 1709 (C=O str.), 1604, 1587 (amide I,II). δ_H (d_6-DMSO): 1.41–1.84 (m, 8H), 2.09 (s, 6H, CH_3), 2.37 (t, 4H, *J*=6.9 Hz, CH_2C≡C), 4.25 (t, 4H, *J*=6.3 Hz, CH_2O), 7.66 (d, 2H, *J*=5.7 Hz, H-5), 8.39 (d, 2H, *J*=5.7 Hz, H-6), 10.82 (s, 2H, NH). δ_C (d_6-DMSO): 18.4, 24.6, 24.8, 28.0, 65.9, 66.4, 78.3, 103.9, 160.1, 160.7, 164.8, 170.9. *m/z* (FAB, NOBA matrix) 465 (15%, $[M+1]^+$). (Found: C, 62.4; H, 5.8; N, 17.8%. $C_{24}H_{28}N_6O_4$ requires: C, 62.1; H, 6.1; N, 18.1%.)

4,4′-Bis(acetylamino)-1,1′-(docosa-10,12-diyne-1,22-diyl)-dipyrimidin-2(1*H*)-one) (9d).- ^{4}N-Acetylcytosine (0.84 g; 5.48 mmol), potassium carbonate (0.78 g; 5.64 mmol) and 18-crown-6 (0.03 g; 0.01 mmol) and DMF (50 cm^3) were stirred at room temperature for 2 h. Docosa-10,12-diyne-1,22-diyl bis(toluene-*p*-sulfonate) (1.50 g; 2.33 mmol) was added and the mixture was stirred for a further 5 days at room temperature. The solvent was evaporated under reduced pressure and the resulting yellow solid was pre-adsorbed on to silica gel and purified by column chromatography [CH_2Cl_2/MeOH (95:5) eluant] to afford 4,4′-bis-(acetylamino)-1,1′-(docosa-10,12-diyne-1,22-diyl)dipyrimidin-2(1*H*)-one) (**9d**) (0.17 g; 12%), mp 139°C. ν_{max} (KBr, cm^{-1}): 3235 (N–H str.), 2925, 2850 (aliphatic C–H str.), 1662, 1636 (amide I, II), 1497 (aliphatic C–H str.). δ_H (d_6-DMSO) 1.15–1.69 (m, 28H), 2.08 (s, 6H, CH_3), 2.26 (t, 4H, *J*=6.2 Hz, CH_2C≡C), 3.77 (t, 4H, *J*=7.2 Hz, CH_2N), 7.11 (d, 2H, *J*=7.1 Hz, H-5), 8.05 (d, 2H, *J*=7.1 Hz, H-6), 10.78 (s, 2H, NH). *m/z* (FAB, NOBA matrix) 605 (25%, $[M+1]^+$). (Found: C, 67.5; H, 8.3; N, 13.9%. $C_{34}H_{48}N_6O_4$ requires: C, 67.5; H, 8.0; N, 13.9%.)

4,4′-Diamino-1,1′-(dodeca-5,7-diyne-1,12-diyl)dipyrimidin-2(1*H*)-one (9e). Compound (**9c**) was stirred in 5% ammoniacal methanol (50 cm^3/100 mg) at room temperature for 18 h. The solvent was evaporated under reduced pressure to afford the title compound (**9e**) (ca. 100%) as a white powder. mp >360°C. ν_{max} (KBr, cm^{-1}): 3351 (N–H str.), 3110 (alkene C–H str.), 2928, 2862 (aliphatic C–H str.), 1659 (C=O str.), 1621 (N–H def.), 1489 (aliphatic C–H def.). δ_H (d_6-DMSO): 1.29–1.79 (m, 8H), 2.30 (t, 4H, *J*=6.6 Hz, CH_2C≡C), 3.62 (t, 4H, *J*=6.7 Hz, CH_2N), 5.63 (br d, 2H, *J*=7.0 Hz, H-5), 6.98 (bs, 4H, NH_2), 7.55 (d, 2H, *J*=7.0 Hz, H-6). δ_C (d_6-DMSO): 18.4, 25.2, 28.4, 48.4,

65.9, 78.3, 93.5, 146.4, 156.2, 166.3. *m/z* (FAB, NOBA matrix) 381.2045 (47%, $[M+1]^+$); $C_{20}H_{25}N_6O_2$ requires: 381.2039.

9-(Prop-2-ynyl)-6-chloro-9H-purin-2-amine (12a) and 7-(prop-2-ynyl)-6-chloro-7*H*-purin-2-amine (13a). To a suspension of 2-amino-6-chloropurine (2.00 g; 11.79 mmol) in DMF (50 cm^3) was added anhydrous potassium carbonate (1.64 g; 11.85 mmol). The suspension was stirred at room temperature for 20 min, during which time a clear solution was formed. Propargyl bromide (1.40 g; 11.79 mmol) was added and the resulting solution was stirred for a further 44 h at room temperature. The solvent was evaporated under reduced pressure to afford a brown powder that was purified by column chromatography [CH_2Cl_2/MeOH (98:2) eluant]. The products were 9-(prop-2-ynyl)-6-chloro-9*H*-purin-2-amine (**12a**) (1.40 g; 57%) and 7-(prop-2-ynyl)-6-chloro-7*H*-purin-2-amine (**13a**) (0.31 g; 12%).

*Compound (**12a**):* mp 237°C. λ_{max} MeOH (nm): 226 (ϵ 6094), 246 (6812), 310 (8116). δ_H (d_6-DMSO): 3.52 (t, 1H, *J*=2.3 Hz, C≡CH), 4.98 (d, 2H, *J*=2.3 Hz, CH_2C≡C), 7.08 (s, 2H, NH_2), 8.22 (s, 1H, H-8). δ_C (d_6-DMSO): 32.9, 76.6, 78.4, 123.5, 142.9, 150.0, 154.0, 160.4. *m/z* (EI) 207.02927 and 209.02813 ($M^{\cdot+}$); $C_8H_6N_5Cl$ requires: 207.03117 and 209.02822. (Found: C, 46.2; H, 2.8; N, 33.4%. $C_8H_6N_5Cl$ requires: C, 46.28; H, 2.91; N 33.73%.)

*Compound (**13a**):* mp 221°C. λ_{max} MeOH (nm): 233 (ϵ 8805), 322 (6472). δ_H (d_6-DMSO) 3.61 (t, 1H, *J*=2.4 Hz, C≡CH), 5.22 (d, 2H, *J*=2.4 Hz, CH_2C≡C), 6.73 (s, 2H, NH_2), 8.48 (s, 1H, H-8). δ_C (d_6-DMSO): 36.5, 77.6, 78.8, 115.0, 143.0, 149.4, 160.6, 164.6. *m/z* (EI) 207.03146 ($M^{\cdot+}$); $C_8H_6N_5{}^{35}Cl$ requires: 207.03117. (Found: C, 46.0; H, 2.8; N, 33.4%. $C_8H_6N_5Cl$ requires: C, 46.28; H, 2.91; N, 33.73%.)

9-(Prop-2-ynyl)-6-chloro-2-acetylamino-9*H*-purine (12b) and 9-(prop-2-ynyl)-6-chloro-2-(diacetylamino)-9*H*-purine (12c). 9-(Prop-2-ynyl)-6-chloro-9*H*-purin-2-amine (110 mg; 0.53 mmol) was heated under reflux with acetic anhydride (10 cm^3) for 3 h. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography [CH_2Cl_2/MeOH (96:4) eluant] to afford 9-(prop-2-ynyl)-6-chloro-2-acetylamino-9*H*-purine (**12b**) (20 mg; 15%) and 9-(prop-2-ynyl)-6-chloro-2-(diacetylamino)-9*H*-purine (**12c**) (50 mg; 32%).

*Compound (**12b**):* mp 239–240°C. δ_H(d_6-DMSO): 2.21 (s, 3H, CH_3), 3.58 (t, 1H, *J*=2.5 Hz, C≡CH), 5.07 (d, 2H, *J*=2.5 Hz, CH_2C≡C), 8.59 (s, 1H, H-8), 11.85 (br s, 1H, NH). *m/z* (EI): 249.042 and 251.037 ($M^{\cdot+}$); $C_{10}H_8N_5OCl$ requires: 249.042 and 251.039. *Compound (**12c**):* mp 157°C. δ_H (d_6-DMSO): 2.24 (s, 6H, CH_3), 3.60 (t, 1H, *J*=2.5 Hz, C≡CH) 5.22 (d, 2H, *J*=2.5 Hz, CH_2C≡C), 8.89 (s, 1H, H-8). *m/z* (EI) 291.0521 ($M^{\cdot+}$); $C_{12}H_{10}N_5O_2{}^{35}Cl$ requires: 291.0523.

9-(Tricosa-10,12-diynyl)-6-chloro-9*H*-purin-2-amine (12d) and 7-(tricosa-10,12-diynyl)-6-chloro-7*H*-purin-2-amine (13b). 2-Amino-6-chloropurine (0.34 g; 2.00 mmol), tricosa-10,12-diynyl toluene-*p*-sulfonate (**2e**) (0.75 g; 1.54 mmol) potassium carbonate (0.28 g; 2.00 mmol) and DMF (25 cm^3) were stirred under an atmosphere of nitrogen at room temperature for 72 h. The solution was filtered and the solvent was evaporated under reduced pressure to give a yellow solid. This was pre-adsorbed on to silica gel and purified by column chromatography [CH_2Cl_2/MeOH (100:0–95:5) eluant] to afford 9-(tricosa-10,12-diynyl)-6-chloro-9*H*-purin-2-amine (**12d**) (0.54 g; 72%) and 7-(tricosa-10,12-diynyl)-6-chloro-7*H*-purin-2-amine (**13b**) (0.13 g; 18%).

*Compound (**12d**):* mp 82–86°C. ν_{max} (KBr, cm^{-1}): 3431, 3330, 3212 (N–H str.), 3072 (aromatic C–H str.), 2925, 2854 (aliphatic C–H str.), 1645 (N–H def.), 1607 (C=N str.), 1560, 1523 (C–H def.). δ_H ($CDCl_3$): 0.88 (t, 3H, *J*=6.4 Hz, CH_3), 1.15–1.96 (m, 30H), 2.23 (t, 4H, *J*=6.7 Hz, CH_2C≡C), 4.08 (t, 2H, *J*=7.2 Hz, CH_2N), 5.37 (br s, 2H, NH_2), 7.78 (s, 1H, H-8). δ_C ($CDCl_3$): 14.0, 19.1, 22.6, 26.4, 28.1, 28.3, 28.6, 28.8, 29.0, 29.1, 29.2, 29.4, 29.4, 29.5, 31.8, 43.7, 65.1, 65.2, 77.3, 125.2, 142.3, 151.1, 153.7, 159.0. *m/z (*FAB, NOBA matrix): 485 (62%, $[M+1]^+$), 968 (1%, $[2M+1]^+$, for M=$C_{28}H_{42}N_5{}^{35}Cl$). (Found: C, 69.3; H, 8.8; N, 14.4%. $C_{28}H_{42}N_5Cl$ requires: C, 69.47; H, 8.74; N, 14.47%.)

*Compound (**13b**):* mp 164–167°C. ν_{max}: (KBr, cm^{-1}): 3396, 3314, 3177 (N–H str.), 3078 (aromatic C–H str.), 2925, 2852 (aliphatic C–H str.), 1638 (N–H def.), 1616 (C=N str.), 1542, 1505 (C–H def.). λ_{max} MeOH (nm): 229 (ϵ 10869), 321 (5981). δ_H ($CDCl_3$): 0.88 (t, 3H, *J*=6.4 Hz, CH_3), 1.14–2.00 (m, 30H), 2.25 (t, 4H, *J*=6.7 Hz, CH_2C≡C), 4.09 (t, 2H, *J*=7.2 Hz, CH_2N), 5.48 (br s, 2H, NH_2), 7.97 (s, 1H, H-8). δ_C ($CDCl_3$): 14.0, 19.1, 22.6, 26.2, 28.1, 28.2, 28.6, 28.8, 29.0, 29.1, 29.2, 29.4, 31.3, 31.8, 47.2, 65.1, 65.2, 77.2, 77.5, 116.1, 143.3, 148.3, 159.4, 164.2. *m/z* (FAB, NOBA matrix): 485 (98%, $[M+1]^+$), 968 (2%, $[2M+1]^+$, for M=$C_{28}H_{42}N_5{}^{35}Cl$). Found: C, 69.3 H, 8.8, N, 14.4%. $C_{28}H_{42}N_5Cl$ requires: C, 69.46; H, 8.74; N, 14.47%.)

9-(Tricosa-10,12-diynyl)-2-amino-1,9-dihydro-6*H*-purin-6-one (16). This was prepared by method described above for (**15b**) from 9-(tricosa-10,12-diynyl)-6-chloro-9*H*-purin-2-amine (**12d**) (0.50 g; 1.03 mmol), dioxane (15 cm^3) and 5% aqueous sodium hydroxide solution (20 cm^3). 9-(Tricosa-10,12-diynyl)-2-amino-1,9-dihydro-6*H*-purin-6-one (**16**) (0.23 g; 47%) was isolated as a white amorphous solid which turned pink slowly on exposure to daylight, mp 191–199°C. ν_{max} (KBr, cm^{-1}): 3484, 3325, 3195 (N–H str.), 2924, 2852, 2728 (C–H str.), 1724, 1689 (amide I, II), 1627 (N–H def.). δ_H (d_6-DMSO): 0.83 (t, 3H, *J*=6.7 Hz, CH_3), 1.10–1.84 (m, 30H), 2.25 (t, 4H, *J*=6.5 Hz, CH_2C≡C), 3.89 (t, 2H, *J*=7.0 Hz, CH_2N), 6.42 (br s, 2H, NH_2), 7.66 (s, 1H, H-8), 10.52 (br s, 1H, NHCO). δ_C (d_6-DMSO): 13.9, 18.3, 22.1, 25.9, 27.7, 28.2, 28.3, 28.4, 28.4, 28.7, 28.7, 28.9, 28.9, 31.3, 42.6, 48.6, 65.3, 77.9, 77.9, 116.6, 137.4, 151.1, 153.4, 156.8. *m/z* (FAB, NOBA matrix): 466.3538 $[M+1]^+$; $[C_{28}H_{43}N_5O+H^+]$ requires: 466.3545.

Ethyl tricosa-10,12-diynoate (17a). Tricosa-10,12-dynoic acid (1.00 g; 2.88 mmol), ethanol (50 cm^3) and 10 drops of conc. sulphuric acid were heated under reflux for 5 h. On cooling, saturated sodium bicarbonate solution was added until the solution became neutral. The mixture was

evaporated under reduced pressure and the resulting solid was digested in CH_2Cl_2 (50 cm^3) and dried ($MgCl_2$). The mixture was filtered and the filtrate was evaporated to give ethyl tricosa-10,12-diynoate (**17a**) (0.88 g; 81%) as a clear viscous liquid, bp 207°C. ν_{max} (KBr, cm^{-1}): 2927, 2854 (aliphatic C–H str.), 1737 (C=O str.), 1464, 1372 (aliphatic C–H def.), 1181 (C–O str.). δ_H ($CDCl_3$): 0.88 (t, 3H, J=6.7 Hz, CH_3), 1.12–1.73 (m, 31H), 2.24 (t, 2H, J=6.9 Hz, CH_2CO_2 or $CH_2C{\equiv}C$), 2.27 (t, 4H, J=6.8 Hz, $CH_2C{\equiv}C$ or CH_2CO_2), 4.13 (q, 2H, J=7.1 Hz, CH_2O). δ_C ($CDCl_3$): 14.0, 14.2, 19.1, 22.6, 24.8, 28.2, 28.6, 28.8, 29.0, 29.2, 29.4, 29.5, 31.8, 34.2, 60.1, 65.2, 77.3, 173.8. *m/z* (EI) 374.3159 ($M^{\cdot+}$), $C_{25}H_{42}O_2$ requires: 374.3185.

6-(Docosa-9,11-diynyl)-2,4-diamino-1,3,5-triazine (17b). Biguanide (0.24 g; 2.40 mmol) and dry methanol (50 cm^3) were heated to 40°C, with stirring. Ethyl tricosa-10,12-diynoate (**17a**) (0.60 g; 1.60 mmol) in dry methanol (20 cm^3) was added over 10 min and the resulting solution was stirred at 40°C under an atmosphere of nitrogen for 20 h. The solvent was then evaporated under reduced pressure and the resulting solid was purified by column chromatography [CH_2Cl_2/MeOH (98:2) eluant] to afford 6-(docosa-9,11-diynyl)-2,4-diamino-1,3,5-triazine (**17b**) (0.39 g; 59%) as an amorphous white solid, mp 99°C. λ_{max} $CHCl_3$ (nm): 257 (ϵ 1054). ν_{max} (KBr, cm^{-1}): 3486, 3321, 3178 (N–H str), 2923, 2851 (aliphatic C–H str.), 1669 (C=N str.), 1636 (N–H def.), 1545 (C–H def.). δ_H ($CDCl_3$): 0.88 (t, 3H, J=6.4 Hz, CH_3), 1.18–1.79 (m, 28H), 2.23 (t, 4H, J=6.7 Hz, $CH_2C{\equiv}C$), 2.46 (t, 2H, J=7.7 Hz, CH_2-triazine), 5.68 (br s, 4H, NH_2). δ_C ($CDCl_3$): 14.0, 19.1, 22.5, 27.7, 28.2, 28.7, 28.8, 28.9, 29.0, 29.1, 29.2, 29.3, 29.5, 31.8, 38.7, 65.2, 77.4, 167.0, 179.6. *m/z* (EI) 411 ($M^{\cdot+}$). (Found: C, 72.9; H, 10.2; N 17.0%. $C_{25}H_{41}N_5$ requires: C, 72.95; H, 10.04; N, 17.01%.)

Diethyl docosa-10,12-diyne dioate (18a). Docosa-10,12-diyne dioic acid (4.73 g; 13.05 mmol), ethanol (150 cm^3) and conc. sulfuric acid (0.5 cm^3) were heated under reflux for 4 h. On cooling, saturated aqueous sodium bicarbonate solution was added until no more carbon dioxide evolved. The mixture was evaporated under reduced pressure and the residue was partitioned between dichloromethane and water (100 cm^3/100 cm^3). The organic layer was separated and dried ($CaCl_2$). Diethyl docosa-10,12-diyne dioate (**18a**) (5.35 g; 98%) was isolated as a colourless solid after purification by column chromatography [CH_2Cl_2 eluant], mp 24°C. ν_{max} liq. film (cm^{-1}): 2979, 2931, 2856 (aliphatic C–H str.), 1736 (C=O str.). δ_H ($CDCl_3$): 1.18–1.83 (m, 24H), 1.26 (t, 6H, J=7.2 Hz, CH_3), 2.24 (t, 4H, J=6.9 Hz, CH_2), 2.29 (t, 4H, J=7.3 Hz, CH_2), 4.12 (q, 4H, J=7.2 Hz, CH_2O). δ_C ($CDCl_3$): 14.2, 19.1, 24.8, 28.2, 28.7, 28.8, 29.0, 34.3, 60.1, 65.1, 77.4, 173.8. *m/z* (EI): 373.2747 ($M^{\cdot+}-C_2H_5O$); $C_{24}H_{37}O_3$ requires: 373.2743.

6,6′-(Icosa-9,11-diyne-1,20-diyl)di-1,3,5-triazine-2,4-diamino (18b) and methyl 21-(4,6-diamino-1,3,5-triazin-2-yl)henicosa-10,12-diynoate (17c). Biguanide (2.41 g; 23.85 mmol) was heated in dry methanol (50 cm^3) to 40°C under an atmosphere of nitrogen with stirring. Diethyl docosa-10,12-diyne dioate (**18a**) (4.19 g; 10.00 mmol) in dry methanol (20 cm^3) was slowly added over 10 min with stirring. The solvent was evaporated under reduced pressure and the resulting solid was pre-adsorbed on silica gel and purified by flash chromatography [CH_2Cl_2/MeOH (98:2) eluant] to give 6,6′-(icosa-9,11-diyne-1,20-diyl)di-1,3,5-triazine-2,4-diamino (**18b**) (1.02 g; 21%) and methyl 21-(4,6-diamino-1,3,5-triazin-2-yl)henicosa-10,12-diynoate (**17c**) (1.27 g; 29%).

*Compound (**18b**):* mp 154°C. ν_{max} (KBr, cm^{-1}): 3334, 3185 (N–H str.), 2929, 2854 (aliphatic C–H str.), 1635, 1543 (N–H def.). δ_H (d_6-DMSO): 1.08–1.69 (m, 24H), 2.17–2.37 (m, 8H, $CH_2C{\equiv}C$ and CH_2-triazine), 6.55 (br s, 8H, NH_2). δ_C (d_6-DMSO): 18.7, 27.5, 28.2, 28.7, 28.8, 29.4, 38.4, 65.8, 78.5, 167.5, 178.2. *m/z* (FAB, NOBA matrix): 493 (100%, $[M+1]^+$). (Found: C, 63.0; H, 8.3; N, 28.5%. $C_{26}H_{40}N_{10}$ requires: C, 63.39; H, 8.18; N, 28.43%.)

*Compound (**17c**):* mp 124–125°C. ν_{max} (KBr, cm^{-1}): 3378, 3334, 3138 (N–H str.), 2930, 2854 (aliphatic C–H str.), 1722 (C=O str.) 1649, 1543 (N–H def.). δ_H (d_6-DMSO): 1.12–1.68 (m, 24H), 2.17–2.36 (m, 8H), 3.56 (s, 3H, CH_3O–), 6.53 (br s, 4H, NH_2). δ_C (d_6-DMSO): 18.7, 24.8, 27.5, 28.2, 28.6, 28.7, 28.8, 29.0, 29.3, 33.7, 38.4, 51.6, 65.8, 78.4, 167.5, 173.8, 178.2. *m/z* (FAB, NOBA matrix): 443 (100%, $[M+1]^+$). (Found: C, 68.5; H, 9.0; N, 15.9%. $C_{25}H_{39}N_5O_2$ requires: C, 67.99; H, 8.90; N, 15.86%.

1-(Tricosa-10,12-diynyl)pyrimidine-2,4-(1*H*,3*H*)-dione (18c). Tricosa-10,12-diynyl toluene-*p*-sulfonate (**2e**) (0.83 g; 1.70 mmol), uracil (0.23 g; 2.04 mmol), anhydrous potassium carbonate (0.34 g; 2.45 mmol) and DMF (10 cm^3) were stirred under an atmosphere of nitrogen at room temperature for 20 h. The solvent was evaporated under reduced pressure and the residual solid was dissolved in CH_2Cl_2/MeOH (90:10) and pre-adsorbed on to silica gel. Purification by column chromatography using CH_2Cl_2, then CH_2Cl_2/MeOH (98:2), as eluants afforded 1-(tricosa-10,12-diynyl)pyrimidine-2,4-(1*H*,3H)-dione (**18c**) (220 mg; 30%) as a white solid which turned purple on exposure to daylight, mp 70–72°C. ν_{max} (KBr, cm^{-1}): 3162, 3053 (N–H str.), 2920, 2850 (aliphatic C–H str.), 1717, 1680 (amide I, II), 1463, 1392 (aliphatic C–H def.). δ_H ($CDCl_3$): 0.89 (t, 3H, J=6.4 Hz, CH_3), 1.16–1.81 (m, 30H), 2.26 (t, 4H, J=7.0 Hz, $CH_2C{\equiv}C$), 3.73 (t, 2H, J=7.3 Hz, CH_2N), 5.72 (dd, 1H, J=7.9 Hz, 2.1, H-5), 7.16 (d, 1H, J=7.9 Hz, H-6), 9.36 (br s, 1H, NH). δ_C ($CDCl_3$): 14.0, 19.1, 22.6, 26.3, 28.2, 28.3, 28.6, 29.0, 29.2, 29.4, 29.5, 31.8, 48.8, 65.2, 77.3, 102.0, 144.4, 150.8, 163.8. *m/z* (EI): 426.3231 ($M^{\cdot+}$); $C_{27}H_{42}N_2O_2$ requires: 426.3246.

***N*-Succinimidyl-10,12-pentacosadiynate (18e).** A solution of *N*-hydroxysuccinimide (0.70 g, 6.03 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.19 g, 6.20 mmol) and 10,12-pentacosadiynoic acid (2.10 g, 5.63 mmol) in dichloromethane (25 cm^3) was stirred at room temperature for 2 h. The solvent was evaporated under reduced pressure and the residue was triturated with diethyl ether (3×30 cm^3). The ether extract was washed with water (30 cm^3), dried ($MgSO_4$), then filtered and the solvent was evaporated under reduced pressure to give the title compound as a colourless solid (2.46 g, 93%), mp 66°C. ν_{max} (KBr, cm^{-1}) 1743 (C=O str). δ_H ($CDC1_3$) 0.90 (t, 3H, J=6.7 Hz, CH_3), 1.35–1.80 (m, 32H, CH_2), 2.25 (t, 4H, J=6.8 Hz, $CH_2C{\equiv}C$), 2.60 (t, 2H, J=7.7 Hz, CH_2CONR),

2.85 (s, 4H, CH_2CH_2). δ_C ($CDC1_3$) 14.0, 19.1, 22.6, 24.4, 25.5, 28.2, 28.3, 28.6, 28.8, 29.0, 29.2, 29.4, 29.5, 30.8, 31.8, 65.1 (C≡C), 168.6 (C=O), 169.1 (C=O). *m/z* (EI) 357.3155 $(M-NOCOCH_2CH_2CO)^{+\cdot}$, $C_{25}H_{41}O$ requires 357.3157.

1′,8′-Bis-(10,12-pentacosadiynamido)-3′,6′-dioxaoctane (18f). A solution of 1,8-diamino-3,6-dioxaoctane (0.93 cm^3, 6.36 mmol) in dichloromethane (25 cm^3) was added dropwise over 30 min to a solution of *N*-succinimidyl-10,12-pentacosadiynate (**18e**) (1.00 g, 2.12 mmol) in dichloromethane (20 cm^3). The reaction mixture was stirred for an additional 30 min, then the solvent was evaporated under reduced pressure. The residue was dissolved in ethyl acetate (30 cm^3) and the extract was washed with water (2×30 cm^3). The organic layer was dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The residue was chromatographed (silica gel, dichloromethane/methanol [95:5] eluant) to afford the *title compound* (R_f=0.36) as a colourless solid (1.56 g, 85%) which turned blue rapidly in ambient light, mp 100–102°C. ν_{max} (KBr, cm^{-1}) 1641 (C=O str.). Found: C, 78.2; H, 11.2; N, 3.2%; $C_{56}H_{96}N_2O_4$ requires C, 78.1; H, 11.2; N, 3.3%. δ_H ($CDC1_3$) 0.85 (t, 6H, *J*=6.9 Hz, CH_3), 1.30–1.43 (br.s, 48H, CH_2), 1.43–1.70 (br. m, 16H, CH_2), 2.18 (t, 4H, *J*=7.5 Hz, C*H*$_2$CONHR), 2.25(t, 8H, J6.7, CH_2C≡C), 3.48 (t, 4H, *J*=4.9 Hz, CH_2O), 3.56 (m, 4H, C*H*$_2$NHCOR), 3.61 (s, 4H, OCH_2CH_2O), 5.98 (br. s, 2H, NH). δ_C ($CDC1_3$) 14.0, 19.1, 22.6, 25.6, 28.2, 28.8, 29.0, 29.1, 29.2, 29.4, 29.5, 30.8, 31.8, 36.6, 39.0, 65.1, 69.9, 70.1, 77.5, 173.0 (C=O).

***N*-(8′-Amino-3′,6′-dioxaoctyl)-10,12-pentacosadiynamide (18g).** A solution of *N*-succinimidyl-10,12-pentacosadiynate (**18e**) (1.5 g, 3.18 mmol) in dichloromethane (25 cm^3) was added over 16 h by syringe pump to a stirred solution of 1,8-diamino-3,6-dioxaoctane (1.88 g, 12.7 mmol) in dichloromethane (25 cm^3) at room temperature. The solution was stirred for an additional 1 h and then evaporated to a low volume under reduced pressure. The residual slurry was chromatographed (silica gel, using a gradient of chloroform/methanol [25:1–8:1] as eluant) to yield the *title compound* (0.61 g, 38%). ν_{max} (KBr, cm^{-1}) 3297, 3085 (NH str.), 2952 (CH str.), 1642 (C=O str.). δ_H ($CDC1_3$/CD_3OD [1:1]) 0.89(t, 3H, *J*=6.3 Hz, CH_3), 1.20–1.70 (m, 32H, CH_2), 2.20 (t, 2H, *J*=7.9 Hz, CH_2), 2.25 (t, 4H, *J*=6.5 Hz, C≡CCH_2), 2.85 (t, 2H, *J*=4.9 Hz, CH_2), 3.40 (t, 4H, *J*=5.1 Hz, CH_2), 3.56 (t, 4H, *J*=5.3 Hz, CH_2O), 3.65 (s, 4H, OCH_2CH_2O) [NH not observed]. δ_C ($CDC1_3$)/CD_3OD [1:1]) 15.3, 20.4, 24.0, 27.2, 29.7, 30.1, 30.3, 30.4, 30.6, 30.7, 30.8, 31.0, 33.3, 37.7, 40.5, 42.2, 66.6, 71.1, 71.5, 71.6, 73.5, 78.6, 176.3. *m/z* (FAB, NOBA matrix) 505.4373 $(M+H)^{+\cdot}$, $C_{31}H_{57}N_2O_3$ requires *m/z* 505.4369.

1′-(9-Acridinylamino)-8′-(10″,12″-pentacosadiynamido)-3′,6′-dioxaoctyne hydrochloride (19a). A mixture of *N*-(8′-amino-3′,6′-dioxaoctyl)-10,12-pentacosadiyne-1-amide (**18g**) (1.50 g, 2.97 mmol), 9-chloroacridine (0.64 g, 3.00 mmol) and phenol (20 g) was heated to 80°C for 16 h. The mixture was cooled and phenol and unreacted 9-chloroacridine were removed from the reaction chromatographically (silica gel, diethyl ether eluant). The eluant was then changed to CH_2Cl_2/methanol [9:1] to afford the *title compound* as a bright yellow solid (1.57 g, 74%), mp 99–101°C. Found: C, 73.9; H, 9.1; N, 5.9%; $C_{44}H_{64}N_3O_3Cl$ requires C, 73.6; H, 9.0; N, 5.9%. ν_{max} (KBr, cm^{-1}) 1643 (C=O str.). δ_H ($CDC1_3$) 0.83 (t, 3H, *J*=6.0 Hz, CH_3) 1.20–1.65 (br. s, 32H, CH_2), 2.21 (m, 6H, C*H*$_2$C≡C, C*H*$_2$CONHR), 3.41 (m, 2H, CH_2), 3.53 (t, 2H, *J*=5.2 Hz, CH_2), 3.62 (dd, 2H, *J*=5.7, 2.7 Hz, CH_2), 3.73 (dd, 2H, *J*=5.8, 2.6 Hz, CH_2), 4.03 (t, 2H, *J*=5.1 Hz, CH_2), 4.23 (t, 2H, *J*=5.1 Hz, CH_2), 6.45 (br. s, 1H, NH), 7.20 (t, 2H, *J*=7.6 Hz, ArH), 7.45 (t, 2H, *J*=7.5 Hz, ArH), 7.90 (d, 2H, *J*=8.6 Hz, ArH), 8.27 (d, 2H, *J*=8.6 Hz, ArH), 9.5 (br. s, 1H, N^+HCl^-). δ_C ($CDC1_3$) 14.0, 19.1, 22.6, 25.6, 28.2, 28.7, 28.7, 28.8, 29.0, 29.1, 29.2, 29.4, 29.5, 31.8, 36.5, 39.1, 48.7, 65.1, 69.0, 70.0, 70.2, 70.5, 77.4, 112.8, 119.4, 123.2, 124.6, 133.6, 140.7, 156.4, 173.9. m/z (FAB, NOBA matrix) 682.3 (100%) (M^+-HCl).

1′-(6-Chloro-2-methoxy-9-acridinylamino)-8′-(10′,12′-pentacosadiynyl-amido)-3′,6′-dioxaoctane (19b). This compound was prepared as described above for (**19a**) from 6,9-dichloro-2-methoxyacridine (0.50 g, 1.90 mmol), *N*-(8′-amino-3′,6′-dioxaoctyl)-10,12-pentacosadiyne-1-amide (**18g**) (0.94 g, 1.87 mmol) and phenol (20 g). The *title compound* was a yellow solid (1.05 g, 72%), mp 144–146°C. Found: C, 67.5; H, 8.6; N, 5.3%; $C_{45}H_{65}N_3O_4Cl_2\cdot H_2O$ requires C, 67.5; H, 8.4; N, 5.3%. ν_{max} (KBr, cm^{-1}) 3300, 3080, 2918, 2848, 1647, 1560, 1467. δ_H ($CDC1_3$) 0.88 (t, 3H, *J*=6.2 Hz, CH_3), 1.20–1.65 (br. s, 32H, CH_2), 2.21 (m, 6H, C*H*$_2$C≡C, C*H*$_2$CONHR), 3.45 (t, 2H, *J*=5.1 Hz, CH_2), 3.52 (t, 2H, *J*=4.9 Hz, CH_2), 3.65 (dd, 2H, *J*=5.9, 3.6 Hz, CH_2), 3.78 (dd, 2H, *J*=5.3, 3.0 Hz, CH_2), 3.95 (s, 3H, CH_3O), 4.10 (m, 2H, CH_2), 4.31 (m, 2H, CH_2), 6.40 (br. t, 1H, NH), 7.13 (d, 2H, *J*=9.1 Hz, ArH), 7.55 (s, 1H, ArH), 7.80 (d, 1H, *J*=9.3 Hz, ArH), 7.90 (s, 1H, ArH), 8.23 (d, 1H, *J*=9.3 Hz, ArH). δ_C ($CDC1_3$) 14.0, 19.1, 22.6, 25.9, 28.2, 28.8, 29.0, 29.1, 29.2, 29.4, 29.5, 31.8, 35.9, 39.6, 48.8, 56.4, 65.1, 69.6, 70.4, 77.3, 109.8, 113.7, 117.7, 120.4, 123.8, 126.8, 134.3, 139.4, 140.1, 156.0, 174.8. *m/z* (FAB, NOBA matrix, for free base) 746.6 (68%, $M^{+\cdot}$), $C_{45}H_{64}{}^{35}ClN_3O_4$ requires: 746.5.

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